Effective Health Care Program

Comparative Effectiveness Review
Number 37

Chronic Kidney Disease Stages 1–3: Screening, Monitoring, and Treatment

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Chronic Kidney Disease Stages 1–3: Screening, Monitoring, and Treatment

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Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children's Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting Comparative Effectiveness Reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

We welcome comments on this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

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Chronic Kidney Disease Stages 1–3: Screening, Monitoring, and Treatment

Structured Abstract

Objective. The objective was to systematically review and synthesize evidence regarding benefits and harms of screening for and monitoring and treatment of chronic kidney disease (CKD) stages 1–3.

Data Sources. The data sources were MEDLINE® and Cochrane Database of Systematic Reviews electronic databases, hand searches of references from relevant systematic reviews and eligible trials, and references from expert consultants.

Review Methods. We screened abstracts and full text articles of identified references for eligibility and reviewed randomized controlled trials (RCTs) for evidence on benefits and harms of CKD treatments. We reviewed RCTs and observational studies for evidence regarding possible benefits and harms of CKD screening or monitoring. For all included RCTs, data were extracted, quality was rated, and strength of evidence was graded. Evidence on the benefits and harms of CKD treatments was quantitatively synthesized when possible. Additional evidence on CKD screening and monitoring was qualitatively described.

Results. We found no RCTs of CKD screening or monitoring. In treatment RCTs, several interventions significantly reduced clinical events. In patients with proteinuria, nearly all with diabetes and hypertension, angiotensin converting enzyme inhibitors (ACEIs) (relative risk [RR], 0.60, 95 percent confidence interval [CI], 0.43 to 0.83) and angiotensin receptor blockers (ARBs) (RR 0.77, 95 percent CI, 0.66 to 0.90) significantly reduced risk of end-stage renal disease (ESRD) versus placebo. In patients with microalbuminuria who had cardiovascular disease or diabetes with other cardiovascular risk factors, ACEI treatment reduced mortality risk (RR 0.79, 95 percent CI, 0.66 to 0.96) versus placebo. In individuals with hyperlipidemia and impaired estimated glomerular filtration rate (eGFR) or creatinine clearance, HMG CoA-reductase inhibitors (statins) reduced risk of mortality (RR 0.80, 95 percent CI, 0.68 to 0.95), myocardial infarction (MI), and stroke compared with placebo. However, limited data addressed whether these effects differed between patients with and without CKD or as a function of CKD severity. In RCTs that directly compared different treatments, including high dose versus low dose, combination versus monotherapy, and strict versus standard control, it was unclear whether intensification of treatment improves clinical outcomes. Reporting of study withdrawals and adverse events was limited. Based on treatment RCT findings and additional indirect data, including high CKD prevalence, low CKD recognition and limited CKD monitoring in usual care, uncertain sensitivity of screening and monitoring measures for CKD, and insufficient evidence on CKD screening and monitoring harms, the overall benefits of CKD screening and monitoring are unclear. The likelihood of benefit, if present, appears to be greater in specific subgroups. For example, individuals not being treated with ACEIs or ARBs who have cardiovascular disease or diabetes combined with other cardiovascular risk factors may benefit from screening for albuminuria. Individuals not being treated with a statin who have hyperlipidemia and no cardiovascular disease may benefit from screening for impaired eGFR. Younger patients, and those without diabetes, hypertension, cardiovascular disease, or obesity,

are the least likely to benefit from CKD screening. Individuals with impaired eGFR and at high risk for cardiovascular complications who are not being treated with ACEIs or ARBs may benefit from monitoring for incident albuminuria.

Conclusions. No trials directly show a benefit for CKD screening or monitoring. The likelihood of benefit, if present, appears to be greater in specific subgroups. Screening and monitoring harms are poorly described. In selected CKD patients, ACEI or ARB treatment reduces ESRD risk, ACEI treatment reduces mortality risk, and statin treatment reduces risk of mortality, MI, and stroke. Many of these patients may already warrant treatment with these therapies regardless of CKD status. Many knowledge gaps remain, and additional research should increase understanding regarding optimal approaches to CKD screening, monitoring, and treatment.

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Executive Summary

Objectives

This systematic review evaluates the evidence regarding the potential benefits and harms of: (1) screening adults for early-stage chronic kidney disease (CKD stages 1–3); (2) monitoring adults with CKD stages 1–3 for progression of kidney dysfunction and/or kidney damage; and (3) treating adults with CKD stages 1–3.

This report's scope is limited to CKD stages 1–3 to inform patient care decisions of primary care physicians. Management of patients with CKD stages 4–5, generally performed by nephrologists, is outside the scope of the report. An additional aim of the report is to provide a synthesis of evidence to assist groups developing clinical practice recommendations regarding CKD screening and management.

Background

Definition of CKD

In CKD, the kidneys are damaged and/or cannot filter blood normally.[1] CKD increases the risk for many adverse health outcomes, including cardiovascular disease, end-stage renal disease (ESRD), and mortality. However, CKD is usually asymptomatic until its most advanced state.

CKD has been defined as decreased kidney function and/or kidney damage persistent for at least 3 months. Kidney dysfunction is indicated by a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2, while kidney damage most frequently is manifested as increased urinary albumin excretion.[2] Within this framework, CKD has been categorized into five stages:

- Stage 1: Kidney damage with GFR ≥90 mL/min/1.73 m^2.
- Stage 2: Kidney damage with GFR 60–89 mL/min/1.73 m^2.
- Stage 3: GFR 30–59 mL/min/1.73 m^2 regardless of kidney damage.
- Stage 4: GFR 15–29 mL/min/1.73 m^2 regardless of kidney damage.
- Stage 5: GFR <15 mL/min/1.73 m^2 regardless of kidney damage, or kidney failure treated by dialysis or transplantation.

A recent series of meta-analyses of large prospective cohort studies demonstrated the independent associations of each level of estimated GFR (eGFR) and albuminuria or dipstick proteinuria with total and cardiovascular mortality, ESRD, and acute kidney injury (AKI).[3,4] These associations were independent of cardiovascular risk factors. Informed by these results, a CKD consensus conference concluded that CKD staging should be modified:[5]

- Divide Stage 3 into 3a (GFR 45–59 mL/min/1.73m^2) and 3b (GFR 30–44 mL/min/1.73m^2).
- Add albuminuria strata within each GFR stage (urine albumin-creatinine ratio <30 mg/g [normoalbuminuria], 30–299 mg/g [microalbuminuria], or >300 mg/g [macroalbuminuria]).
- Identify the cause of CKD when possible.

Epidemiology of CKD

Approximately 11 percent of U.S. adults age 20 or older (23.5 million persons) have CKD.[6] Of these, nearly half are stage 1 or 2, nearly another half are stage 3, fewer than 4 percent are stage 4, and fewer than 2 percent are stage 5 and receive dialysis. Also, about half have albuminuria without impaired GFR, one-third have decreased GFR without albuminuria, and one-sixth have albuminuria plus impaired GFR. Of individuals with albuminuria, nearly 85 percent have microalbuminuria and the remainder have macroalbuminuria. Data from the National Health and Nutrition Examination Survey (NHANES) suggest that the prevalence of CKD is rising, particularly for stage 3.[7]

Etiology of CKD

Infrequently, CKD is caused by primary kidney disease (e.g., glomerular diseases, tubulointerstitial diseases, obstruction, and polycystic kidney disease). But in the vast majority of cases, it is associated with other medical conditions, such as diabetes and hypertension. For example, excluding those with ESRD, in 2008, 48 percent of Medicare patients with CKD had diabetes, 91 percent had hypertension, and 46 percent had atherosclerotic heart disease.[1] Other risk factors for CKD include older age, obesity, family history, and African American, Native American, or Hispanic ethnicity.

Screening for Early-Stage CKD

The rationale for considering screening for early-stage CKD includes the high and rising prevalence of CKD, its known risk factors, its numerous adverse health consequences, its long asymptomatic phase, the availability of potential screening tests for CKD, and the availability of treatments that may alter the course of early-stage CKD and reduce complications of early-stage CKD or its associated health conditions.

Some organizations already recommend CKD screening in selected populations. Kidney Disease: Improving Global Outcomes (KDIGO) recommends screening of all patients with hypertension, diabetes, or cardiovascular disease.[8] The American Diabetes Association recommends annual screening of all adults with diabetes, based on "expert consensus or clinical experience."[9] The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) recommends annual screening of all patients with combined hypertension and diabetes.[10] Also advocating selected screening, the National Kidney Foundation sponsors free CKD screening for all adults with hypertension, diabetes, or a primary relative with a history of kidney disease, hypertension, or diabetes.[11]

Nevertheless, the benefit of screening for early-stage CKD is uncertain. For screening to be beneficial, it should improve important clinical outcomes (while limiting harms) for screened individuals identified with CKD compared with individuals with CKD whose treatment started at a later time or stage. However, potential CKD treatments may be indicated for conditions associated with CKD. So demonstration of benefit from CKD screening requires that the treatment benefits CKD populations who would have had no indication for such treatment in the absence of CKD or that, among patients with an indication for the treatment, those with CKD have a relatively greater treatment benefit or benefit from the treatment at doses or treatment targets different from those of non-CKD patients.

Monitoring Early-Stage CKD for Progression

In most patients with CKD stages 1–3, GFR declines slowly.[12] However, the rate of decline varies among individuals, and many factors appear to impact progression.[13] Because CKD stages 1–3 usually progress asymptomatically, detection of early-stage CKD requires laboratory testing.

Some organizations recommend monitoring for changes in kidney function or damage in patients with CKD. For example, the Kidney Disease Outcomes Quality Initiative (KDOQI) recommends at least annual eGFR measurement in adults with CKD in order to predict onset of ESRD and evaluate the effect of CKD treatments.[13] JNC7 recommends annual quantitative measurement of albuminuria in all patients with "kidney disease."[14] KDOQI also recommends more frequent monitoring of CKD patients with worsening kidney function.[15]

Confirming the benefits of monitoring patients with CKD stages 1–3 for changes in kidney function and/or damage requires evidence similar to that for CKD screening. Treatment modified because of monitoring results would need to improve important clinical outcomes more than treatment modified at a later time or stage does, while limiting harms.

Treatment of CKD Stages 1–3

In most patients with nonprimary CKD stages 1–3, treatment is not directed at the CKD but at associated conditions or cardiovascular risk factors, such as diabetes and hypertension.[16] In efforts to reduce the risk of complications from these conditions, therapeutic goals are sometimes set more strictly for CKD patients than non-CKD patients. For example, JNC7 recommends a blood pressure goal of <130/80 mm Hg for patients with CKD or diabetes.[14] It has been suggested that medications such as angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) may specifically treat CKD. However, whether their impact on CKD outcomes (e.g., incident ESRD) or markers (e.g., albuminuria)[17] is independent of their effect to lower blood pressure is not clear.[18]

Analytic Framework and Key Questions

During this project's topic refinement, we received feedback regarding the scope and relevance of draft Key Questions and feedback regarding the details of a draft protocol. The feedback came from the topic nominators, public reviewers, and a Technical Expert Panel (TEP) composed of researchers, clinicians, and representatives from numerous interested professional organizations and Federal and State agencies. These parties agreed that an independent comprehensive review of the issues introduced above would provide helpful guidance to clinicians and policymakers regarding diagnosis and management of early-stage CKD. There was consensus that the analytic framework, shown in Figure A, and Key Questions addressed the most important issues regarding CKD stages 1–3.

Key Question 1. In asymptomatic adults with or without recognized risk factors for CKD incidence, progression, or complications, what direct evidence is there that systematic CKD screening improves clinical outcomes?

Key Question 2. What harms result from systematic CKD screening in asymptomatic adults with or without recognized risk factors for CKD incidence, progression, or complications?

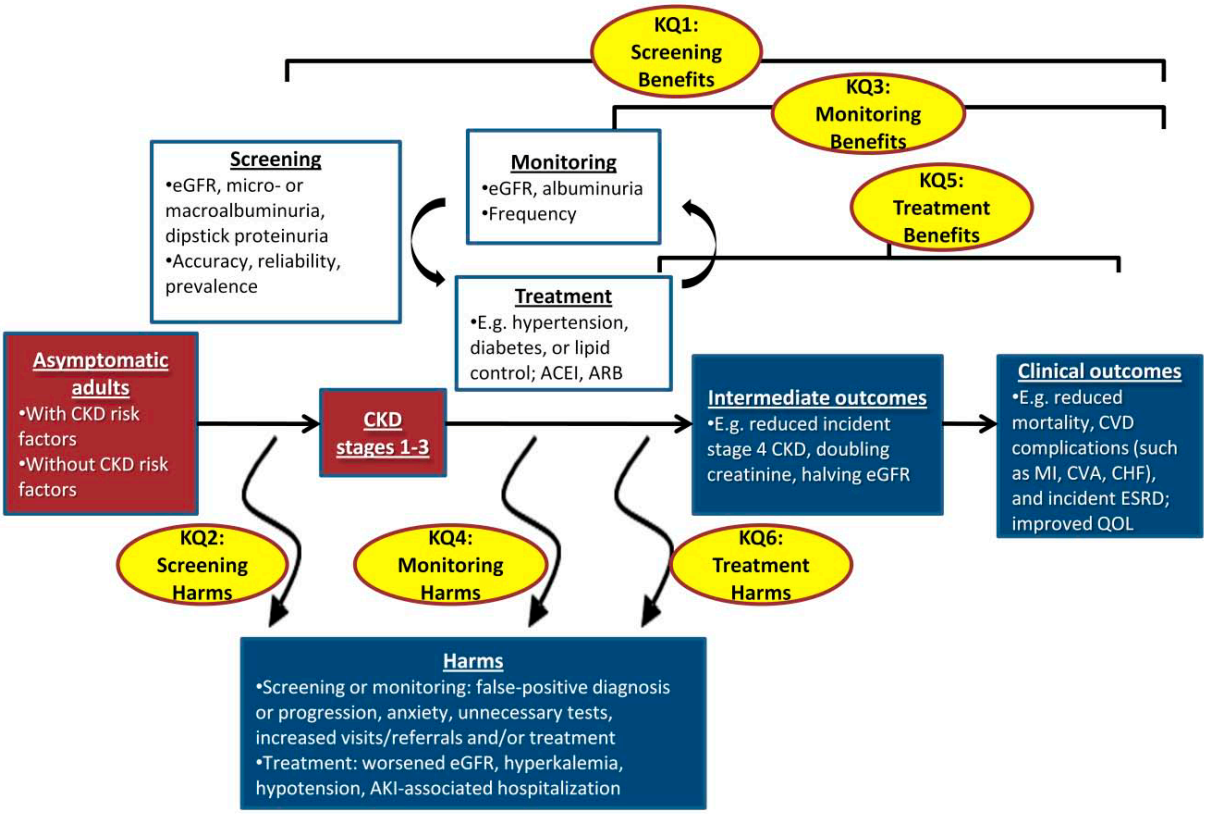
Key Question 3. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what direct evidence is there that monitoring for worsening kidney function and/or kidney damage improves clinical outcomes?

Key Question 4. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what harms result from monitoring for worsening kidney function and/or kidney damage?

Key Question 5. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what direct evidence is there that treatment improves clinical outcomes?

Key Question 6. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what harms result from treatment?

Figure A. Analytic framework for screening, monitoring, and treatment of chronic kidney disease stages 1–3



ACEI = angiotensin converting enzyme inhibitor; AKI = acute kidney injury; ARB = angiotensin receptor blocker; CHF = congestive heart failure; CKD = chronic kidney disease; CVA = cerebrovascular accident; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; MI = myocardial infarction; QOL = quality of life.

Methods

We searched MEDLINE® and the Cochrane Database of Systematic Reviews (January 1985 to January 2011) to identify randomized controlled trials (RCTs) and controlled clinical trials (CCTs) of screening for and monitoring and treatment of patients with CKD. When no RCTs were identified that evaluated a CKD screening or monitoring intervention and reported outcomes, indirect evidence was reviewed regarding possible benefits and harms. This indirect evidence included observational studies on CKD prevalence, progression, and clinical recognition as well as accuracy and reliability of CKD screening and monitoring tests, and RCTs of CKD treatments. Although these observational studies were not identified through a comprehensive literature search, whenever possible we evaluated data from large representative U.S. cohorts. Assessment of CKD treatment benefits and harms was based strictly on direct evidence from RCTs. All titles and abstracts were assessed for eligibility based on Key Question–specific inclusion/exclusion criteria. For treatment intervention studies, data were extracted pertaining to study quality, trial characteristics, population characteristics, efficacy outcomes, and withdrawals and adverse events. Study quality for each trial was rated to formally assess risk of bias.[19] For each treatment comparison and major outcome, overall strength of evidence for the RCTs was evaluated using methods developed by the Agency for Healthcare Research and Quality and the Effective Health Care Program.[20] Briefly, strength of the evidence was evaluated based on four required domains: risk of bias, consistency, directness, and precision. Based on these four domains, the overall evidence was rated as: (1) high, indicating high confidence that further research is very unlikely to change the confidence in the estimate of effect; (2) moderate, indicating moderate confidence that further research may change our confidence in the estimate of effect and may change the estimate; (3) low, indicating low confidence that further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate; and (4) insufficient, indicating that evidence either is unavailable or does not permit a conclusion. If heterogeneity of patient populations, interventions, and outcomes was minimal, we pooled results using Review Manager 5.0.[21] Random effects models were used to generate pooled estimates of relative risks and 95 percent confidence intervals. Statistical heterogeneity was summarized using the I^2 statistic.[22] Additional evidence on CKD screening and monitoring was qualitatively described.

Results

We found no direct RCT evidence that addressed whether systematic CKD screening or monitoring improves clinical outcomes or increases harms. Indirect evidence that these interventions improve outcomes would need to include evidence that CKD treatment improves outcomes. Therefore, the ordering of the Results section has been changed from that of the Key Questions to be consistent with this logical flow.

CKD Treatment Benefits and Harms

- In RCTs of patients with CKD stages 1–3, several treatments reduced the risk of clinical outcomes, but the benefits appeared to be limited to specific CKD subgroups, some of which already had a clinical indication for the treatment studied (Table A).
- Only limited data addressed whether the relative effectiveness of treatment differed between patients with and without CKD or between patients with different severities of CKD.

- Trials used heterogeneous entrance criteria for renal function and damage, which often did not match KDOQI definitions for CKD stages 1–3 precisely, so we considered reasonable overlap sufficient for inclusion in this evidence synthesis. Because trials also rarely reported outcomes stratified by CKD stage or other CKD markers, it often was difficult to determine if trial clinical benefits applied to patients within individual CKD stages or eGFR or albuminuria categories.
  - ACEI and/or ARB treatment significantly reduced ESRD risk in patients with proteinuria (macroalbuminuria), most of whom had diabetes and hypertension. ESRD was not significantly reduced in patients with CKD stages 1–3 who did not have proteinuria. Patients with proteinuria, diabetes, and hypertension may benefit from ACEI or ARB treatment.
  - ACEI treatment significantly reduced mortality risk in patients known to have microalbuminuria who had either cardiovascular disease or the combination of diabetes and other cardiovascular risk factors. Relative risk reduction was not significantly different than in similar patients who did not have microalbuminuria. Patients who had microalbuminuria and were at high risk for cardiovascular complications may benefit from ACEI treatment at adequate doses.
  - Statins significantly reduced the risk of mortality, myocardial infarction (MI), and stroke in patients with hyperlipidemia and impaired eGFR or creatinine clearance, including those without coronary artery disease. Patients with hyperlipidemia and no coronary artery disease may not otherwise have an indication for statins, but the subset with CKD may benefit from treatment. No statin trials reported clinical outcomes data for patients with albuminuria.
  - Beta blockers significantly reduced the risk of mortality, MI, and congestive heart failure (CHF) events in patients with CHF and impaired eGFR, most of whom already were treated with an ACEI or ARB. Patients with systolic CHF already have an indication for beta blockers, regardless of whether they have CKD.
  - In RCTs that compared different active treatments head to head (e.g., ACEI versus ARB, ACEI versus beta blocker), there was no consistent significant difference in clinical outcomes between treatments, with strength of evidence ranging between low and insufficient for different comparisons.
  - In RCTs that compared high- versus low-dose treatment (ARB, statin), strict versus standard control (blood pressure, glycemia), combination versus monotherapy, and intensive multidisciplinary interventions (simultaneous targeting of blood pressure, diabetes, cholesterol, and/or reducing nephrotoxic drug exposure) versus usual care, there was no consistent significant difference in clinical outcomes between treatments, with strength of evidence ranging between low and insufficient for different comparisons.
  - Low-protein diets did not significantly reduce risk of mortality, ESRD, or any clinical vascular outcome compared with usual protein diets; risk for a composite renal outcome was significantly reduced in one trial, but this study also included participants with CKD stages 4–5.
- Few RCTs reported information on study withdrawals. When reported, withdrawals were often high and infrequently were separated by treatment group.

- Few trials reported adverse events. When reported, adverse events often did not appear to be predefined, were not systematically collected or reported, and often were not reported separately by treatment group.
- Although limitations in reporting impeded the quantitative synthesis of withdrawal and adverse events data from different studies, adverse events reported generally were consistent with known potential adverse effects of these treatments (e.g., hypotension with antihypertensives; cough with ACEIs; edema with calcium channel blockers; hyperkalemia with ACEIs, ARBs, and aldosterone).

CKD Screening Benefits and Harms

- We found no direct RCT evidence that addressed whether systematic screening of adults for CKD improves clinical outcomes or increases harms.
- Results from studies not directly linking systematic CKD screening to clinical outcomes contributed indirect evidence regarding whether CKD screening improves clinical outcomes.
  - Microalbuminuria and eGFR are sensitive screening tests for detecting one-time kidney abnormalities that may reflect CKD, but false positive rates are substantial, particularly for microalbuminuria; their sensitivity and specificity for CKD as defined by kidney dysfunction or damage lasting 3 months or longer is unknown.
  - Most patients with CKD stages 1–3 are clinically unrecognized. Because even populations with a high CKD prevalence (e.g., diabetes, hypertension, cardiovascular disease, older age) are not routinely tested for CKD, especially for albuminuria, systematic screening likely would lead to a large increase in CKD diagnoses.
  - Because of the above-noted treatment benefits in patients who have cardiovascular disease or diabetes combined with other cardiovascular risk factors (e.g., hypertension) and are known to have albuminuria, screening such patients for microalbuminuria or macroalbuminuria could lead to early initiation of ACEI or ARB treatment and reduced risk of mortality or ESRD.
  - Because of the above-noted treatment benefits in patients who have hyperlipidemia without cardiovascular disease and are known to have impaired eGFR or creatinine clearance, screening such patients for impaired eGFR could lead to early initiation of statin treatment and reduced risk of mortality, MI, or stroke.
  - Virtually no RCTs of CKD treatments identified participants through screening, so the generalizability of treatment RCT results to patients with CKD stages 1–3 identified through screening is unknown.
- We found insufficient strength of evidence addressing potential harms associated with systematic CKD screening.

CKD Monitoring Benefits and Harms

- We found no direct RCT evidence regarding whether systematic monitoring of adults with CKD stages 1–3 for worsening kidney function or damage improves clinical outcomes.
- Results from studies not directly linking systematic CKD monitoring to clinical outcomes contributed indirect evidence regarding whether CKD monitoring improves clinical outcomes.

- Because of the above-noted treatment benefits in patients with albuminuria who have cardiovascular disease or have diabetes combined with other cardiovascular risk factors (e.g., hypertension), monitoring patients with impaired eGFR for development of albuminuria could lead to early initiation of ACEI or ARB treatment and reduced mortality or ESRD risk.
- Because of the above-noted treatment benefits in patients with hyperlipidemia who have impaired eGFR or creatinine clearance, monitoring such patients for development of impaired eGFR could lead to early initiation of statin treatment and reduced risk of mortality, MI, or stroke.
- In patients with CKD stages 1–3, kidney function usually slowly worsens over years, but may worsen faster in selected subgroups (e.g., those with diabetes, proteinuria, hypertension, older age, obesity, or dyslipidemia).
- The sensitivity and specificity of eGFR and albuminuria for identifying CKD progression in patients with CKD stages 1–3 are unknown.
- The vast majority of patients with recognized CKD stages 1–3 have serum creatinine measured regularly, so implementation of systematic eGFR monitoring may have only a limited impact on current practice. Because only a minority of patients with CKD stages 1–3 are annually tested for albuminuria, systematic albuminuria monitoring likely would lead to an increase in patients identified with clinical worsening of CKD.

- We found insufficient strength of evidence addressing potential harms associated with systematic CKD monitoring.

Table A summarizes the evidence for specific comparative effectiveness studies addressed in Key Question 5.

Table A. Summary of evidence for Key Question 5: Benefits of treatment for patients with CKD stages 1–3

Treatment, Trials, Number of Patients	Level of Evidence	Summary, Conclusion, Comments
ACEI vs. placebo 17 trials; 11,661 patients	Mortality: moderate ESRD: moderate	• There was no significant difference in risk of all-cause or cardiovascular mortality, MI, or stroke overall, but significantly reduced risk of mortality in patients at high risk for cardiovascular complications who had microalbuminuria. • ACEI did not significantly reduce risk of all-cause or cardiovascular mortality, MI, or stroke. • ACEI significantly reduced ESRD risk in patients with overt proteinuria. • ACEI significantly reduced risk of all examined composite renal outcomes, but of few examined composite vascular outcomes. • Limits: Few studies were designed to assess clinical outcomes; there was considerable variability in the definitions of clinical outcomes.
ACEI vs. ARB 6 trials; 4,799 patients	Mortality: low ESRD: insufficient	• There was no significant difference in risk of all-cause or cardiovascular mortality, MI, or CHF; no data for stroke, ESRD, or composite vascular outcomes. • Results from the CKD subset of the ONTARGET study, whether defined by GFR <60 ml/min/1.73m^2 or albuminuria, showed no difference in risk of composite renal outcome. • Limits: There were small sample sizes in all but one trial; few trials reported most outcomes; there were few events in trials reporting.

Table A. Summary of evidence for Key Question 5: Benefits of treatment for patients with CKD stages 1–3 (continued)

Treatment, Trials, Number of Patients	Level of Evidence	Summary, Conclusion, Comments
ACEI vs. CCB 6 trials; 4,357 patients	Mortality: low ESRD: low	• There was no significant difference in risk of all-cause or cardiovascular mortality, stroke, CHF, any composite vascular endpoint, or ESRD. • ACEI significantly reduced risk of composite renal outcome in one of three trials. • Limits: Several studies were not designed for/reported no clinical outcomes; most outcomes were reported in few trials; there were few events in trials reporting.
ACEI vs. BB 3 trials; 1,080 patients	Mortality: low ESRD: low	• There was no significant difference in risk of all-cause or cardiovascular mortality, stroke, CHF, composite vascular endpoints, or ESRD. • In one trial, ACEI significantly reduced risk of composite renal outcome. • Limits: Only one trial was designed to evaluate clinical vascular outcomes.
ACEI vs. diuretic 2 trials; 4,716 patients	Mortality: insufficient ESRD: low	• There was no significant difference in risk of all-cause mortality, stroke, ESRD, or composite vascular or renal outcomes. • Limits: One trial was not designed for clinical events; one trial was post hoc subgroup analysis with no mortality data by CKD status.
ARB vs. placebo 5 trials; 5,769 patients	Mortality: high ESRD: high	• There was no significant difference in risk of all-cause mortality, cardiovascular mortality, MI, or composite vascular outcomes. • ARB significantly reduced risk of CHF hospitalization and ESRD; results were mixed regarding risk of composite renal outcomes. • Limits: Several outcomes came from only one trial or were not reported.
ARB vs. CCB 3 trials; 3,924 patients	Mortality: low ESRD: low	• There was no significant difference in risk of all-cause mortality, stroke, composite vascular outcomes, or ESRD. • Limits: Most outcomes were uncommon or reported in only one trial.
ACEI+ARB vs. ACEI 6 trials; 7,357 patients	Mortality: moderate ESRD: insufficient	• There was no significant difference in risk of all-cause mortality. • Few vascular outcomes were reported, although combination significantly reduced risk of composite vascular outcome in one trial. • Limits: There were few clinical events and little data on renal outcomes.
ACEI+ARB vs. ARB 3 trials; approximately 4,300 patients	Mortality: insufficient ESRD: insufficient	• Only one trial reported all-cause mortality (no deaths in any treatment group); no trials reported information on vascular outcomes or ESRD. • Limits: There were few clinical events.
ACEI+ARB vs. ACEI or ARB 1 trial; 8,933 patients	Mortality: moderate ESRD: low	• There was no significant difference in risk of all-cause mortality, cardiovascular mortality, ESRD, or single composite vascular outcome reported. • Limits: This was a single post hoc analysis.
ACEI+CCB vs. ACEI 1 trial; 481 patients	Mortality: insufficient ESRD: insufficient	• No data were reported for mortality or individual vascular or renal outcomes. • There was no significant difference in risk of composite vascular outcome of serious cardiovascular events. • Limits: Few events were reported.
ACEI+CCB vs. ACEI+diuretic 2 trials; 1,425 patients	Mortality: insufficient ESRD: insufficient	• There was no significant difference in risk of mortality, “cardiac disorders,” “vascular disorders,” or a single composite renal outcome. • Limits: There were few deaths or renal events; no other clinical outcomes were reported.
ACEI+diuretic vs. placebo 1 trial; 4,526 patients	Mortality: low ESRD: insufficient	• There was no significant difference in risk of all-cause or cardiovascular mortality, MI, stroke, composite vascular outcome, or composite renal outcome. • Limits: This was a single post hoc analysis.

Table A. Summary of evidence for Key Question 5: Benefits of treatment for patients with CKD stages 1–3 (continued)

Treatment, Trials, Number of Patients	Level of Evidence	Summary, Conclusion, Comments
ARB vs. different ARB 2 trials; 1,745 patients	Mortality: Telmisartan vs. losartan low; telmisartan vs. valsartan low ESRD: Telmisartan vs. losartan insufficient; telmisartan vs. valsartan low	• Compared with losartan, telmisartan significantly reduced risk of mortality and one composite vascular outcome but not a composite renal outcome. • There was no significant difference between telmisartan and valsartan in risk of all-cause or cardiovascular mortality, MI, stroke, CHF hospitalization, ESRD, or composite vascular or renal outcomes. • Limits: There were few clinical events; no studies compared losartan and valsartan.
ARB vs. ARB (high vs. low dose) 3 trials; 998 patients	Mortality: insufficient ESRD: insufficient	• One trial reported three total deaths; a second trial reported that there were no deaths in any treatment groups. • No other cardiovascular or renal outcomes were reported. • Limits: There were few clinical events.
BB vs. placebo 2 trials; 2,173 patients	Mortality: low ESRD: insufficient	• BB significantly reduced risk of all-cause mortality, CHF hospitalizations, and CHF death; reduced composite vascular outcomes risk in one of two trials. • There was no significant difference in risk of cardiovascular mortality. • Inconsistent data suggested greater relative risk reduction for several clinical vascular outcomes in lower eGFR category. • Limits: This was a post hoc analysis from two CHF treatment trials in which CKD was defined only by impaired eGFR; no renal outcomes were reported.
CCB vs. placebo 2 trials; 1,226 patients	Mortality: low ESRD: low	• There was no significant difference in risk of all-cause or cardiovascular mortality, stroke, CHF, ESRD, or composite vascular or renal outcomes. • CCB significantly reduced risk of MI. • Limits: Outcomes were mainly derived from one trial.
CCB vs. BB 3 trials; 12,766 patients	Mortality: low ESRD: low	• There was no significant difference in risk of all-cause mortality, ESRD, or composite renal outcome. • Limits: Most outcomes were not reported by treatment group in more than one study; 95% of subjects were derived from one post hoc analysis, in which it is uncertain if “renal dysfunction” meets CKD criteria.
CCB vs. diuretic 1 trial; 4,129 patients	Mortality: insufficient ESRD: low	• There was no significant difference in risk of stroke, ESRD, or any composite clinical vascular or renal outcomes. • Limits: This was a post hoc subgroup analysis; no results were reported for risk of mortality or MI between treatment groups.
Diuretic vs. placebo 1 trial; 393 patients	Mortality: low ESRD: insufficient	• There was no significant difference in risk of all-cause mortality. • Diuretic significantly reduced risk of stroke and one of two composite vascular outcomes. • Limits: There were few patients; this was a single post hoc subgroup analysis; no renal outcomes were reported.
ACEI vs. non-ACEI (other BP control) 1 trial; 131 patients	Mortality: insufficient ESRD: low	• There was no significant difference in risk for ESRD or a composite renal outcome. • Limits: Sample size was small; there were few clinical events; no data were reported for mortality or other clinical vascular or renal outcomes.
Strict BP control vs. usual BP control 6 trials; 2,520 patients	Mortality: low ESRD: low	• There was no significant difference in risk of all-cause or cardiovascular mortality, MI, stroke, ESRD, or several composite renal outcomes. • Limits: Generalizability is limited for some of the older included studies; there was heterogeneity in patient populations and antihypertensive regimens; there were few vascular events.

Table A. Summary of evidence for Key Question 5: Benefits of treatment for patients with CKD stages 1–3 (continued)

Treatment, Trials, Number of Patients	Level of Evidence	Summary, Conclusion, Comments
Statins vs. placebo or usual care 12 trials; 17,460 patients	Mortality: high ESRD: low	• Statins significantly reduced risk of all-cause mortality, MI, stroke, and most composite vascular outcomes reported. • There was no significant difference in risk of CHF hospitalization, ESRD, or composite renal outcome. • Limits: All but one study were post hoc analyses in which CKD was defined by impaired eGFR or creatinine clearance; most trials excluded patients with moderate or severe renal impairment.
Statin vs. statin (high vs. low dose) 2 trials; 4,793 patients	Mortality: low ESRD: insufficient	• There was no significant difference in risk of all-cause mortality. • High-dose statin significantly reduced risk of CHF hospitalization and reduced risk of all composite vascular endpoints in one of two trials. • Limits: These were post hoc analyses; no outcomes were reported for MI, stroke, or renal outcomes.
Gemfibrozil vs. placebo 1 trial; 470 patients	Mortality: low ESRD: insufficient	• There was no significant difference in risk of mortality. • Gemfibrozil significantly reduced risk of one of two composite vascular outcomes. • Limits: This was a post hoc analysis; no ESRD events were reported; no data were reported for other renal outcomes.
Gemfibrozil vs. low-triglyceride diet 1 trial; 57 patients	Mortality: insufficient ESRD: insufficient	• There was no significant difference in risk of ESRD. • Limits: There were few patients and only three ESRD events; no data were reported for mortality or clinical vascular outcomes.
Low-protein diet vs. usual protein diet 6 trials; 1,480 patients	Mortality: low ESRD: low	• Low-protein diet did not significantly reduce risk of all-cause or cardiovascular mortality, or of ESRD. • Low-protein diet was associated with significant reduction in risk of composite renal outcome of dialysis. • Limits: Few vascular outcomes were reported; at least four trials also included participants with CKD stages 4 and/or 5.
Low-protein diet vs. low-carb, low-iron-available, polyphenol-enriched diet 1 trial; 191 patients	Mortality: low ESRD: low	• There was no significant difference in risk of all-cause mortality or ESRD. • Treatment with low-protein diet significantly increased risk of composite outcome of mortality and ESRD. • Limits: This was a small trial; there were few outcomes.
Low-protein, low-phosphate diet vs. low-phosphate diet vs. usual diet 1 trial; 98 patients	Mortality: insufficient ESRD: low	• There was no significant difference in risk of all-cause mortality or ESRD. • Limits: This was a small trial with few deaths; no data were reported for clinical vascular outcomes; trial was restricted to participants with deteriorating renal function and appears to have included many with eGFR <30 mg/ml/1.73m^2.
Intensive vs. standard glycemic control studies 2 trials; 1,861 patients	Mortality: insufficient ESRD: insufficient	• Limits: No data were reported for mortality, ESRD, or other clinical vascular or renal outcomes.

Table A. Summary of evidence for Key Question 5: Benefits of treatment for patients with CKD stages 1–3 (continued)

Treatment, Trials, Number of Patients	Level of Evidence	Summary, Conclusion, Comments
Intensive multicomponent intervention vs. control studies 4 trials; 892 patients	Mortality: low ESRD: low	• There was no significant difference in risk of all-cause mortality, MI, fatal stroke, or ESRD. • Multicomponent intervention significantly reduced risk of nonfatal stroke, a composite vascular endpoint, in single trials reporting that endpoint. • Limits: There was heterogeneity between interventions.

Note: For all-cause mortality and end-stage renal disease, the strength of the evidence was evaluated based on: (1) risk of bias, (2) consistency, (3) directness, and (4) precision. Based on these four domains, the overall evidence was rated as: (1) high, meaning high confidence that the evidence reflects the true effect; (2) moderate, indicating moderate confidence that further research may change our confidence in the estimate of effect and may change the estimate; (3) low, meaning there is low confidence that the evidence reflects the true effect; and (4) insufficient, indicating that evidence either is unavailable or does not permit a conclusion.
ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; BB = beta blocker; BP = blood pressure; CCB = calcium channel blocker; CHF = congestive heart failure; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; GFR = glomerular filtration rate; MI = myocardial infarction; ONTARGET = Ongoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial.

Discussion

For CKD screening or monitoring to be of benefit, each would need to improve clinically important outcomes, presumably by leading to specific changes in treatment. However, we identified no RCTs that randomized individuals without known CKD to CKD screening, or randomized those with CKD stages 1–3 to CKD monitoring, and collected and reported associated clinical outcomes.

With no direct link between screening or monitoring and clinical outcomes, concluding that there is a likely benefit to screening or monitoring requires, at minimum, the availability of accurate screening tests and sufficient evidence that treatment for CKD stages 1–3 improves clinically important outcomes while limiting harms. For treatment benefits in CKD patients to be relevant to screening or monitoring, treatments also would need to improve outcomes in individuals who would not otherwise receive them; i.e., patients without specific treatment indications in the absence of a CKD diagnosis. In patients with other treatment indications, diagnosis of CKD or of CKD progression might be beneficial if outcomes in these patients are significantly improved with a higher treatment dose or by treatment to a stricter target than indicated in individuals with no or less severe CKD. Finally, any treatment benefit would need to outstrip treatment harms and potential screening and monitoring harms, and the applicability of treatment RCT results to screening or monitoring would be increased if subjects were identified for participation in these treatment trials through screening.

In this synthesis of RCT evidence, several treatments reduced the risk of clinical events in patients with CKD stages 1–3. Compared with placebo, ACEI and ARB treatment significantly reduced the risk of ESRD in patients with proteinuria, nearly all of whom had concomitant diabetes and hypertension. While there was no significant reduction in the risk of ESRD with ACEIs or ARBs in patients without proteinuria, the present analysis had limited statistical power to detect such a difference because of the low rate of progression to ESRD in these patients. While it does not constitute direct evidence that testing patients with diabetes and hypertension for proteinuria will reduce ESRD risk, it suggests that knowledge of these results might inform the treatment decision in patients not currently being treated with ACEIs or ARBs. Also, compared with placebo, ACEIs significantly reduced the risk of mortality in patients with

microalbuminuria who had cardiovascular disease or had diabetes and other cardiovascular risk factors. Although the relative reduction in mortality risk appeared to be slightly greater in patients with microalbuminuria than in those without microalbuminuria, the difference was not statistically significant, suggesting that such patients may have an indication for ACEI treatment regardless of CKD status.

In individuals with hyperlipidemia and impaired eGFR or creatinine clearance, we found that statins significantly reduced the risk of mortality, MI, and stroke compared with placebo, including the risk in patients without coronary artery disease. This does not constitute direct evidence that testing patients with hyperlipidemia for eGFR will reduce the risk of these outcomes, in part because some of these patients already have a clinical indication for statin treatment. Determining CKD status in these patients would not alter their management. Specifically, as previously documented, patients with hyperlipidemia and coronary artery disease randomized to statins have a significantly reduced risk of mortality compared with placebo;[23] they have an indication for statin treatment regardless of their CKD status. In contrast, as also previously documented, hyperlipidemic patients without coronary artery disease, taken as a whole, did not have a significant mortality benefit from statins.[24] The current results suggest that knowledge of impaired eGFR might inform the treatment decision in patients with hyperlipidemia and no coronary artery disease who are not being treated with a statin.

In individuals with CHF and impaired eGFR, beta blockers significantly reduced the risk of mortality, MI, and CHF events compared with placebo. Patients in all eGFR strata had a significant reduction in the risk of these clinical outcomes. Inconsistent results suggested possibly a greater relative risk reduction with beta blockers in patients with lower eGFR than in those with higher eGFR. However, as patients with systolic CHF already have an indication for beta blocker treatment, testing for eGFR is not likely to inform this treatment decision.

With regard to patients with CKD stages 1–3 already receiving treatments for conditions associated with CKD (e.g., ACEIs for treatment of hypertension), no clear RCT evidence showed whether intensification of treatment improves clinical outcomes. We identified no eligible RCTs that compared clinical outcomes in CKD patients randomized to different fixed ACEI doses, although separate trials suggested that ramipril at 1.25 mg per day in patients with albuminuria lacks the mortality benefit of ramipril at 10 mg per day in patients with microalbuminuria. For other treatments in CKD patients, we did not find evidence of significant or consistent benefit in clinical outcomes in high-dose versus low-dose ARBs, strict versus standard blood pressure control, high-dose versus low-dose statins, tight versus standard glycemic control, intensive multidisciplinary interventions versus standard care, or combination treatment versus monotherapy. While data limited to these latter trials suggest an absence of evidence for benefit from intensification of therapy as a justification for either CKD screening or monitoring, most had low statistical power to detect a significant difference in clinical outcomes.

In RCTs included in this evidence synthesis, many treatments reduced the risk of doubling of serum creatinine and progression from microalbuminuria to macroalbuminuria. However, these renal endpoints are not clinical outcomes. Although impaired GFR and albuminuria are unquestionably adverse prognostic markers, treatments that target and even improve these measures will not necessarily reduce the risk of mortality, ESRD, or important clinical vascular outcomes. Findings reported from the large Randomized Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) study[25]—in which patients with diabetes and at least one additional CKD risk factor were randomized to ARB versus non-ARB blood pressure control—illustrated the potential danger of utilizing albuminuria as a surrogate marker for

clinical outcomes in kidney disease. Although blood pressure control was significantly better and time to onset of microalbuminuria was significantly delayed in the ARB treatment group, these patients also experienced a significant increase in fatal cardiovascular events.

As we have noted, establishing the benefit of CKD screening and/or monitoring requires evidence of treatment benefit. Yet treatment benefit does not by itself prove screening or monitoring benefit. First, the accuracy of available screening and monitoring measures for persistent CKD and progressive CKD is uncertain. Second, only two of the dozens of RCTs included in this evidence synthesis reported that study participants were identified through screening.[26,27] Consequently, patients with CKD stages 1–3 enrolled in all these trials may not be representative of those who would be identified through systematic screening. For example, patients identified through screening may be earlier in their course of CKD, less likely to progress during treatment followup, and thus less likely to benefit from treatment intervention than those not identified through screening. In addition, formal diagnosis of CKD requires that impairment in kidney function or kidney damage persist for at least 3 months. The vast majority of trials included in this evidence synthesis categorized patients as having CKD based on one-time abnormalities. Other trials that required repeated or sustained kidney abnormalities for entry did not mandate persistence for 3 months. Study participants thus may have had transient impairments, been more likely to improve regardless of treatment, and been less likely to develop progressive CKD than patients with CKD confirmed over 3 months duration. Finally, we identified no evidence to quantify harms that may be associated with CKD screening and monitoring. Potential harms of systematic CKD screening could include adverse effects from screening and followup tests, including followup of false positive tests, psychological effects from labeling asymptomatic individuals as diseased, medication adverse effects, increased medical visits, and increased difficulty keeping health insurance coverage. Analogously, potential harms of systematic monitoring of patients with CKD stages 1–3 for worsening kidney function or damage could include adverse effects from monitoring and followup tests, including potentially unnecessary testing, medication adverse effects, and increased medical visits. Accurate information on screening and monitoring harms is needed to evaluate their overall impact in CKD.

Considering these issues, if there is a benefit from CKD screening, evidence suggests that the likelihood of benefit is greatest in individuals with diabetes, cardiovascular disease, and possibly hyperlipidemia. For other populations with a high prevalence of CKD, such as patients with hypertension, obesity, and older age, evidence for benefit from screening appears to be weaker. Individuals under 50 years old and without diabetes, hypertension, cardiovascular disease, or obesity infrequently have CKD and seem least likely to benefit from CKD screening, although this also is based only on indirect data.

Finally, because of the imprecision and high intraindividual variability of eGFR and albuminuria, providers who monitor patients with CKD stages 1–3 for worsening kidney function and/or damage will identify both declines and improvements in these measures, including many that are transient and/or clinically insignificant. We identified no RCTs that assigned patients with CKD stages 1–3 to systematic monitoring versus control, or that modified treatment based on followup levels of eGFR or albuminuria and evaluated clinical outcomes. Rather, trials either assigned participants to a fixed dose to be maintained throughout the trial or titrated upward from an initial dose to achieve a specific target dose or clinical target (e.g., systolic blood pressure less than 140 mm Hg). Although treatment RCT results suggest that monitoring could inform decisions regarding whether to start ACEI or ARB treatment in patients

with diabetes and hypertension who develop albuminuria, or statin treatment in patients with hyperlipidemia who develop impaired eGFR, considering the uncertainty in the accuracy of monitoring tests for identifying CKD progression and the uncertainty regarding possible monitoring harms, the relative benefits and harms of CKD monitoring are unclear.

Future Research Recommendations

Key Question 1. CKD Screening Benefits

Knowledge Gaps

- No RCT evidence directly addresses whether systematic CKD screening improves clinical outcomes.
- The sensitivity and specificity of one-time measures of microalbuminuria, macroalbuminuria, and eGFR for persistent (at least 3 months' duration) CKD is unknown; the impact of patient factors on persistence also is unknown.
- Only two trials were performed in patients with CKD identified through screening.

Research Recommendations

- Long-term RCTs of systematic CKD screening versus usual care that are adequately powered to evaluate impact on clinical outcomes.
  - Target populations with high CKD prevalence and high risk for complications.
  - May test different screening measures (e.g., microalbuminuria, macroalbuminuria, eGFR, combination).
- Modeling studies evaluating efficacy and harms of different CKD screening strategies versus usual care. In addition to parameters in published models, consider impact of:
  - Variations in target populations.
  - Variations in screening measures and frequency.
  - Prevalence in the target population of indications for and use of specific CKD treatments.
  - Yield of one-time screening tests based on actual association with persistent CKD.
  - Take into account potential screening harms.
- Determine eGFR and albuminuria from baseline and followup blood and urine available from large prospective cohorts or RCT/CCT control groups (or collect new samples).
  - Estimate the proportion of individuals with abnormal one-time abnormalities who meet the criteria for CKD for at least 3 months.
  - Evaluate the impact of patient factors (e.g., eGFR severity, albuminuria, age) on persistence.

Key Question 2. CKD Screening Harms

Knowledge Gaps

- No RCT evidence directly addresses whether systematic CKD screening increases harms.

Research Recommendations

- Long-term RCTs comparing systematic CKD screening versus usual care to assess potential screening harms.
  - Predefine potential harms, and collect and report them in all study participants.
  - May include as potential harms adverse effects from screening/followup tests, including from false positive tests; psychological effects of labeling asymptomatic individuals as diseased; medication adverse effects; increased medical visits; increased costs; difficulty keeping health insurance.
- Prospectively collect predefined harms data from all participants in large observational CKD screening cohort studies.
- Conduct modeling studies evaluating the effectiveness and harms of different CKD screening strategies versus usual care.

Key Question 3. CKD Monitoring Benefits

Knowledge Gaps

- No RCT evidence directly addresses whether systematic CKD monitoring for worsened kidney function or damage improves clinical outcomes.
- The sensitivity and specificity of changes in eGFR and albuminuria for CKD progression are unknown.
- Only limited RCT data address whether treatment relative risk reduction for clinical outcomes differs based on CKD severity. Such information could inform decisions regarding whether to change treatment in patients identified by monitoring with worsened CKD severity.
- No RCT data address whether treatments have different relative risk reduction in clinical outcomes for patients with recently worsened kidney function or damage, as detectable by monitoring, compared with those with stable CKD.

Research Recommendations

- Long-term RCTs of systematic CKD monitoring versus usual care that are adequately powered to evaluate impact on clinical outcomes.
  - Target populations with high risk for CKD complications.
  - Consider testing different monitoring measures, alone and in combination (e.g., quantitative microalbuminuria, macroalbuminuria, eGFR).
- Modeling studies evaluating the efficacy and harms of different CKD monitoring strategies compared with usual care. Parameters of these models may include:
  - Variations in monitoring measures and frequency (quantitative albuminuria, eGFR, or a combination).
  - Variations in baseline CKD severity (i.e., stage, eGFR, quantitative albuminuria).
  - Variations in CKD patient characteristics (e.g., diabetes, hypertension, age, cardiovascular disease, hyperlipidemia, race/ethnicity), including possible indications for specific CKD treatments and prevalence of use of these treatments.
  - Take into account potential monitoring harms.

Key Question 4. CKD Monitoring Harms

Knowledge Gaps

- No RCT evidence directly addresses whether systematic CKD monitoring for worsening kidney function or damage increases harms.

Research Recommendations

- Long-term RCTs comparing systematic CKD monitoring versus usual care to assess potential monitoring harms.
  - Predefine potential harms associated with monitoring, and collect and report them in all study participants.
  - May include as potential harms adverse effects from monitoring/followup tests, including from false positive tests (for progression); medication adverse effects; increased medical visits; increased costs.
- Prospectively collect predefined harms data from all participants in large observational CKD monitoring cohort studies.
- Conduct modeling studies evaluating the effectiveness and harms of different CKD monitoring strategies versus usual care.

Key Question 5. CKD Treatment Benefits

Knowledge Gaps

- Only limited RCT data address whether the relative efficacy of treatments differs between patients with and without CKD.
- Only limited RCT data address whether treatment risk reduction differs based on CKD severity.
- Only limited RCT data address whether treatments improved outcomes in CKD subgroups in which treatments were not already indicated.
- In RCTs of high versus low dose, combination versus monotherapy, and strict versus standard control, it was unclear whether intensification of treatment improves clinical outcomes.
- The effect of diet interventions on clinical outcomes in patients with CKD stages 1–3 is unclear because diet intervention RCTs were small, included patients with both stage 1–3 and stage 4–5 CKD, and did not separate results by CKD stage or severity.
- In head-to-head RCTs, there was little evidence of a significant difference in mortality or any clinical vascular outcome between different active treatment groups.
- Trials used heterogeneous eligibility criteria for kidney function and damage, and rarely reported outcomes stratified by CKD stage or albuminuria category, impeding evidence synthesis.

Research Recommendations

- Post hoc analyses of ongoing or completed RCTs that already have collected or are collecting clinical outcomes.

    - Determine baseline eGFR and quantitative albuminuria, categorize participants by CKD stage and albuminuria category, and perform analyses to evaluate the relative effectiveness of treatment versus control on clinical outcomes within these strata.
- Merge data from large-scale treatment RCTs with Medicare data to identify incident ESRD cases occurring in the post-trial followup period.
- Long-term RCTs of CKD treatment adequately powered to evaluate impact on clinical outcomes.
    - In addition to mortality, ESRD, and clinical vascular outcomes, consider additional clinical outcomes for evaluation, including quality of life, acute kidney injury complications (e.g., hospitalization), health care utilization, physical function, and cognitive function.
    - If composite outcomes are reported, also report complete data for individual composite components.
    - To increase trial relevance to a screened population, consider recruitment using population-based sampling.
    - Stratify results by CKD stage, albuminuria category, and other characteristics associated with CKD complications, including diabetes, hypertension, cardiovascular disease, older age, race/ethnicity, obesity, and hyperlipidemia.
    - Consider future RCTs of statins in patients with albuminuria, ACEI or ARB treatment in patients with macroalbuminuria, ACEI or ARB treatment in combination with other therapy, and treatments other than ACEIs or ARBs.
    - Consider trials of dietary interventions restricted to patients with CKD stages 1–3.
    - Consider trials comparing system-level interventions to aid providers in avoidance of nephrotoxic agents, medication renal dose adjustment, and other measures targeted to reduce CKD-associated complications compared with complications in usual care.
- Patient-level meta-analyses of treatment RCTs to evaluate the effect of treatments relative to control in relevant CKD subgroups.
- Analysis of administrative data to evaluate the effect of nephrology referral on clinical outcomes, performing propensity analysis to account for factors associated with early referral.

Key Question 6. CKD Treatment Harms

Knowledge Gaps

- Withdrawals and adverse events were reported in few RCTs.
- Withdrawals often were not reported separately by treatment group; adverse events often did not appear to be predefined, systematically collected and reported, or separated by treatment group.

Research Recommendations

- In future RCTs, predefine withdrawals and adverse effects, and collect and report them in all patients with CKD stages 1–3.
- May report withdrawal and adverse effects stratified by CKD stage, albuminuria category, and other patient characteristics.

Glossary

ACEI Angiotensin converting enzyme inhibitor
AKI Acute kidney injury
ARB Angiotensin receptor blocker
CCT Controlled clinical trial
CHF Congestive heart failure
CKD Chronic kidney disease
eGFR Estimated glomerular filtration rate
ESRD End-stage renal disease
GFR Glomerular filtration rate
JNC7 Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
KDIGO Kidney Disease: Improving Global Outcomes
KDOQI Kidney Disease Outcomes Quality Initiative
MI Myocardial infarction
RCT Randomized controlled trial

References

1. United States Renal Data System. United States Renal Data System 2010 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2010. www.usrds.org/adr.htm.
2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002 Feb;39(2 Suppl 1):S1-266. PMID 11904577.
3. Matsushita K, van der Velde M, Astor BC, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet 2010 Jun 12; 375(9731):2073-81. PMID 20483451.
4. Astor BC, Matsushita K, Gansevoort RT, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. A collaborative meta-analysis of kidney disease population cohorts. Kidney Int 2011 Jun;79(12):1331-40. Epub 2011 Feb 2.
5. Levey AS, de Jong PE, Coresh J, et al. The definition, classification and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. Kidney Int 2010 Jul;80(1):17-28. Epub 2010 Dec 8. PMID 21150873.
6. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009 May 5;150(9):604-12. PMID 19414839.
7. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. JAMA 2007 Nov 7;298(17):2038-47. PMID 17986697.
8. Levey AS, Atkins R, Coresh J, et al. Chronic kidney disease as a global public health problem: approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. Kidney Int 2007 Aug;72(3):247-59. PMID 17568785.
9. American Diabetes Association. Standards of medical care in diabetes--2011. Diabetes Care 2011 Jan; 34(Suppl 1):S11-61. PMID 21193625.
10. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003 Dec;42(6):1206-52. PMID 14656957.

11. McCullough PA, Vassalotti JA, Collins AJ, et al. National Kidney Foundation‘s Kidney Early Evaluation Program (KEEP) annual data report 2009: executive summary. Am J Kidney Dis 2010 Mar; 55(3 Suppl 2):S1-3. PMID 20172443.

12. Hunsicker LG, Adler S, Caggiula A, et al. Predictors of the progression of renal disease in the Modification of Diet in Renal Disease Study. Kidney Int 1997 Jun; 51(6):1908-19. PMID 9186882.

13. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002 Feb;39(2 Suppl 1):S1-266. PMID 11904577.

14. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003 May 21;289(19):2560-72. PMID 12748199.

15. Renal Association. Chronic Kidney Disease in Adults: UK Guidelines for Identification, Management and Referral of Adults. 2005. www.renal.org/CKDguide/full/SupportingEvidence1.htm.

16. American Diabetes Association. Standards of medical care in diabetes--2009. Diabetes Care 2009 Jan; 32(Suppl 1):S13-61. PMID 19118286.

17. Levey AS, Cattran D, Friedman A, et al. Proteinuria as a surrogate outcome in CKD: report of a scientific workshop sponsored by the National Kidney Foundation and the US Food and Drug Administration. Am J Kidney Dis 2009 Aug;54(2):205-26. PMID 19577347.

18. Nelson RG, Tuttle KR. Prevention of diabetic kidney disease: negative clinical trials with renin-angiotensin system inhibitors. Am J Kidney Dis 2010 Mar; 55(3):426-30. PMID 20005029.

19. Higgins JPT, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.0.2 [updated September 2009]. The Cochrane Collaboration; 2009.

20. Owens DK, Lohr KN, Atkins D, et al. AHRQ series paper 5: grading the strength of a body of evidence when comparing medical interventions--Agency for Healthcare Research and Quality and the Effective Health-Care Program. J Clin Epidemiol 2010 May;63(5):513-23. PMID 19595577.

21. Review Manager [computer program]. Version 5.0. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration; 2008.

22. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003 Sep 6;327(7414):557-60. PMID 12958120.

23. Wilt TJ, Bloomfield HE, MacDonald R, et al. Effectiveness of statin therapy in adults with coronary heart disease. Arch Intern Med 2004 Jul 12;164(13):1427-36. PMID 15249352.

24. Ray KK, Seshasai SR, Erqou S, et al. Statins and all-cause mortality in high-risk primary prevention: a meta-analysis of 11 randomized controlled trials involving 65,229 participants. Arch Intern Med 2010 Jun 28;170(12):1024-31. PMID 20585067.

25. Haller H, Ito S, Izzo JL, et al. Olmesartan for the delay or prevention of microalbuminuria in type 2 diabetes. N Engl J Med 2011 Mar 10; 364(10):907-17. PMID 21388309.

26. Asselbergs FW, Diercks GFH, Hillege HL, et al. Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. Circulation 2004 Nov 2;110(18):2809-16. PMID 15492322.

27. Pahor M, Shorr RI, Somes GW, et al. Diuretic-based treatment and cardiovascular events in patients with mild renal dysfunction enrolled in the Systolic Hypertension in the Elderly Program. Arch Intern Med 1998 Jun 22;158(12):1340-5. PMID 9645829.

Introduction

Scope and Purpose

The objective of this systematic review is to evaluate the evidence for the potential benefits and harms of: (1) screening adults for chronic kidney disease (CKD) stages 1–3, (2) monitoring adults with CKD stages 1–3 for progression of kidney dysfunction and/or damage, and (3) treatment of adults with CKD stages 1–3.

This report's scope is limited to early stage CKD because it is intended to inform patient care decisions of primary care physicians. This report also is intended as background material to assist groups developing clinical practice recommendations.

Definition of CKD

CKD is a condition in which the kidneys are damaged and/or cannot filter blood normally.[1] CKD usually is asymptomatic, except in its most advanced state. Consequently, blood and/or urine tests generally are required to make a diagnosis.

There has been substantial debate regarding how to define early stages of CKD. The definition of CKD developed by Kidney Disease Outcomes Quality Initiative (KDOQI)[2] was:

1. Kidney damage present at least 3 months, as defined by structural or functional abnormalities (most often based on increased albuminuria, e.g., urinary albumin-creatinine ratio [UACR] ≥30 mg/g); and/or
2. Glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 present at least 3 months.

Within this framework, KDOQI then classified CKD into five stages, as follows:

- Stage 1: Kidney damage with GFR ≥90 mL/min/1.73 m2.
- Stage 2: Kidney damage with GFR 60-89 mL/min/1.73 m2.
- Stage 3: GFR 30-59 mL/min/1.73 m2.
- Stage 4: GFR 15-29 mL/min/1.73 m2.
- Stage 5: GFR <15 mL/min/1.73 m2 or kidney failure treated by dialysis or transplantation.

A limitation of the KDOQI definition and staging was that they were based on cross sectional data, and that there were limited data associating adverse clinical outcomes with specific levels of GFR, albuminuria, or proteinuria. However, results of a recent series of meta-analyses of multiple large prospective cohort studies clearly demonstrated the independent associations of each level of GFR and albuminuria (or alternatively of dipstick proteinuria), with total and cardiovascular mortality, ESRD and acute kidney injury (AKI).[3-6] These associations were independent of cardiovascular risk factors. Based in part on these data, a consensus conference led by Kidney Disease: Improving Global Outcomes (KDIGO), on Chronic Kidney Disease: Definition, Classification and Prognosis, concluded that the current CKD definition should be preserved. However, the conference recommended that staging be altered to subdivide stage 3 into 3a (GFR 45-59 mL/min/1.73 m^2) and 3b (GFR 30-44 mL/min/1.73 m^2), to add albuminuria strata within each GFR stage (UACR <30 mg/g, 30-299 mg/g, or ≥300 mg/g), and to assign a cause of CKD when possible.[7]

Prevalence of CKD

In the United States, based on data from the 1999-2006 National Health and Nutrition Examination Survey (NHANES) study, an estimated 11.1 percent (22.4 million) of adults aged 20 or older have CKD stages 1–3.[8] Because this estimate was based on one-time measurements of urinary albumin-creatinine ratio (UACR) and serum creatinine, and the definition of CKD requires persistent kidney abnormalities, statistical adjustments were made to estimate persistence. An additional 0.8 million U.S. adults aged 20 or older have CKD stage 4, and more than 0.3 million have stage 5 CKD and receive hemodialysis.[9]

Among adults with CKD stages 1–3, approximately half have either stage 1 or 2 CKD (increased albuminuria with normal GFR), and half have stage 3 CKD (low GFR, with approximately one third of these having increased albuminuria and two thirds having normal albuminuria).[8] Of individuals with albuminuria, nearly 85 percent have microalbuminuria (UACR 30-299 mg/g).

Analyses of NHANES data between 1988-1994 and 1999-2004 suggest that the prevalence of CKD is rising for every CKD stage, but with a particular increase in the prevalence of individuals classified with CKD stage 3.[10] The number of patients with stage 5 CKD requiring dialysis also has increased.[9] It has been estimated that more than 700,000 individuals will have end-stage renal disease (ESRD) by 2015.[11]

Factors Associated With CKD

Prevalence of CKD stages 1–3 in U.S. adults rises from 3.1 percent among those aged 20-39 years, to 6.7 percent in those aged 40-59, 17.6 percent in those aged 60-69, and 44.4 percent among adults aged 70 years or older.[8] CKD prevalence is somewhat higher in women (12.6 percent) than in men (9.7 percent) and is similar in whites (11.6 percent) and blacks (11.2 percent).

Although CKD can be caused by primary kidney disease (predominantly glomerular diseases, tubulointerstitial diseases, obstruction, and polycystic kidney disease), in the vast majority of patients with CKD, the kidney damage is associated with other medical conditions such as diabetes and hypertension. Other risk factors for CKD include older age, cardiovascular disease, obesity, family history, and African American, Native American, or Hispanic ethnicity. With respect to diabetes as a CKD risk factor, based on NHANES 1999-2006 data, prevalence of diabetes was approximately 5 percent in individuals without CKD and 20 percent in individuals with CKD stages 1–3.[12] Prevalence of hypertension was 24 percent among individuals without CKD, but rose from 36 percent in those with CKD stage 1 to 64 percent in those with CKD stage 3. Similarly, prevalence of cardiovascular disease was 6 percent among individuals without CKD, and rose from 7 percent in those with CKD stage 1 to 36 percent in those with CKD stage 3. Compared with the NHANES population, the prevalence of comorbidities was higher in the older Medicare population. Excluding those with ESRD, in 2008, 48 percent of Medicare patients with CKD had diabetes, 91 percent had hypertension, and 46 percent had atherosclerotic heart disease.[12]

Association of CKD With Adverse Outcomes

CKD has been associated with numerous adverse health outcomes. Many studies have reported that a GFR of 30-59 mL/min/1.73 m^2 is associated with an increased risk of mortality,[3,13] cardiovascular disease,[14] fractures,[15] bone loss,[16] infections,[17] cognitive

impairment,[18] and frailty.[19] Similarly, there appears to be a graded relationship between the severity of proteinuria or albuminuria and adverse health outcomes, including mortality,[3,20] ESRD,[21] and cardiovascular disease.[22] Further, the risk for adverse outcomes conferred by reduced GFR and increased albuminuria (or proteinuria) appears to be independent and multiplicative.[3,21]

A number of possible explanations exist for the observed association of CKD with adverse health outcomes. First, CKD shares many of the same risk factors as other vascular diseases, such as older age, hypertension, and diabetes, so CKD may be a marker for undiagnosed vascular disease or for a worsened prognosis among individuals with known vascular disease. Second, CKD may be associated with a number of nontraditional risk factors for vascular disease and mortality, such as increased inflammation or bone mineral disorders. Third, CKD may be a marker for individuals less likely to receive proven medical therapies. For example, among individuals with myocardial infarction, those with CKD are less likely to receive proven effective therapies such as coronary artery bypass grafting, angiotensin converting enzyme inhibitors (ACEI), beta-blockers, or HMG CoA-reductase inhibitors (i.e., statins).[23] Therefore, systematic undertreatment may in part underlie the association between CKD and adverse health outcomes. Finally, the associations of CKD with adverse health outcomes and increased healthcare costs may be related to a combination of the above mechanisms.

Rationale for CKD Screening

Factors that impact the potential benefit of screening adults for CKD stages 1–3 include: (1) whether undiagnosed CKD is sufficiently prevalent in the population, overall or in certain high risk groups; (2) whether CKD is associated with significant adverse health consequences and/or healthcare costs; (3) whether CKD is accurately diagnosable while asymptomatic; (4) whether there are valid and reliable screening tests for CKD that are acceptable to patients and available in primary care settings; and (5) whether there are treatments for patients with CKD that improve clinically important health outcomes.

Going further, determination that CKD screening is beneficial would require evidence that treatment of screen-detected CKD is associated with an improvement in health outcomes compared with treatment initiated once an individual is symptomatic or has CKD detected through usual care, while limiting harms. In addition, since potential CKD treatments often are indicated for conditions associated with CKD, such as diabetes, hypertension, or cardiovascular disease, demonstration that CKD screening is beneficial may require evidence that treatment benefits CKD populations who don’t have another indication for treatment or, that among patients with another indication for treatment, those with CKD experience a greater relative treatment benefit than those without CKD. Alternatively, because patients with diabetes, hypertension, and/or cardiovascular disease who also have CKD are at significantly higher risk for adverse health outcomes than patients with these comorbid conditions who don’t have CKD, diagnosis of CKD resulting from screening patients with these conditions would identify a group, if currently untreated, who could derive a greater absolute benefit in health outcomes even if the relative benefit of treatment versus no treatment was similar in CKD and non-CKD patients.

Several organizations have made recommendations regarding screening for CKD. KDIGO recommends screening for CKD in patients with hypertension, diabetes, or cardiovascular disease using both a urine test for proteinuria and a blood test for creatinine to estimate GFR.[24] KDIGO further recommends that CKD screening be considered in patients who are older, have a family history of kidney disease, have other cardiovascular disease risk factors, have certain

chronic infections or cancers, or are treated with potentially nephrotoxic drugs, and that screening need not be performed more often than annually. The American Diabetes Association (ADA) recommends that all adults with diabetes undergo annual measurement of serum creatinine to estimate GFR, and that all type 2 diabetics and all type 1 diabetics with a diabetes duration of at least 5 years undergo annual measurement of urinary albumin excretion.[25] Ongoing CKD screening programs include the National Kidney Foundation's Kidney Early Evaluation Program (KEEP®), which offers free screening for all adults with hypertension, diabetes, or a first degree relative with a history of kidney disease, hypertension, or diabetes.[26]

Rationale for Monitoring for Progression of CKD

Because CKD in stages 1–3 is usually asymptomatic, monitoring these patients for worsening kidney function or damage requires laboratory testing (i.e., measures to estimate GFR, albuminuria).

Factors that impact the potential benefit of monitoring adults with CKD stages 1–3 for worsening kidney function or damage include: (1) whether undiagnosed progression of patients with CKD stages 1–3 to worse kidney function or damage is sufficiently frequent in the population, overall or in certain high risk groups; (2) whether CKD that has progressed from stages 1–3 is associated with significant adverse health consequences and/or healthcare costs; (3) whether CKD that has progressed from stages 1–3 is diagnosable while asymptomatic; (4) whether there are valid and reliable monitoring tests for CKD stages 1–3 that are acceptable to patients and available in primary care settings; and (5) whether there are treatments for patients whose CKD has progressed from stages 1–3 that improve clinically important health outcomes.

Strictly considered, determination that monitoring patients with CKD stages 1–3 for worsened kidney function or damage is beneficial would require evidence that modified treatment of worsened CKD detected by monitoring is associated with an improvement in health outcomes compared with treatment modified once an individual becomes symptomatic or has CKD worsening detected through usual care, while limiting harms.

Several organizations have made recommendations regarding monitoring kidney function and/or damage in patients with CKD. KDOQI recommends that adults with CKD receive monitoring of urinary albumin or protein to creatinine ratio, though no frequency of monitoring was recommended.[27] The U.K. National Health Service (NHS) National Institute for Health and Clinical Excellence (NICE) guidelines suggest "more frequent monitoring" in CKD patients with worsening kidney function and a "relaxed frequency" of estimated GFR measurements in patients with stable kidney function.[28]

Rationale for Treatment of CKD

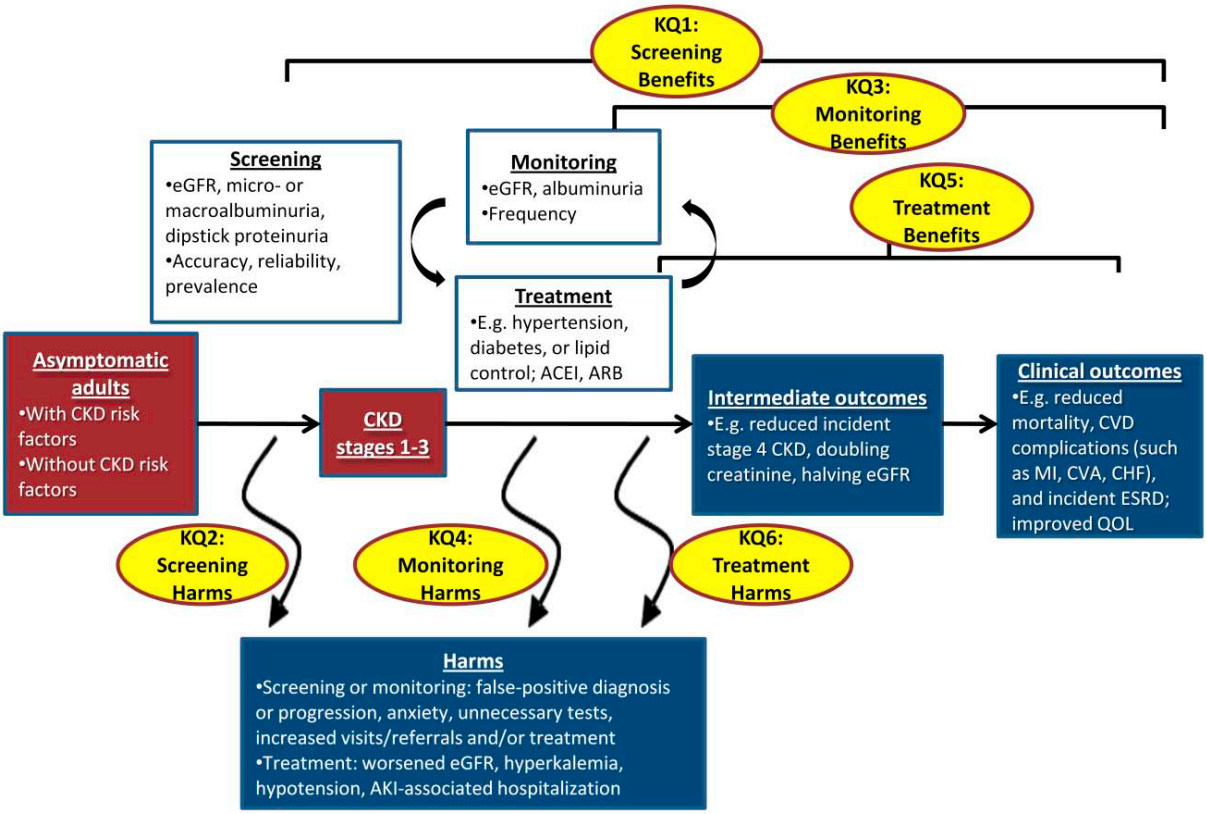
In patients treated for nonprimary CKD, treatment most often is not directed specifically at the CKD but rather at the associated underlying conditions or cardiovascular risk factors, such as hypertension or diabetes,[29] with therapeutic goals for these conditions sometimes set more strictly for CKD patients than for non-CKD patients.[30] An aim of this systematic review is to evaluate the evidence regarding whether the benefits and harms of treatment differ between patients with and without CKD, both in patients with and without other indications for treatments. Medications such as ACEI and angiotensin receptor blockers (ARB) potentially could be directed specifically towards treatment of CKD. However, whether their impact on CKD outcomes or markers (e.g., incident ESRD, albuminuria severity[31]) is independent of their blood pressure lowering effect is not clear.[32] Additional nonspecific therapies may include other

medications and nonpharmacological interventions targeted, for example, at blood pressure control, glycemic control, cholesterol control, and obesity treatment.

Analytic Framework and Key Questions

During this project's topic development, the topic nominators and other interested parties agreed that an independent, comprehensive review of the issues introduced above would provide helpful guidance to clinicians and policymakers regarding diagnosis and management of early stage CKD. There was consensus that the following analytic framework (Figure 1) and Key Questions addressed the most important issues regarding CKD stages 1–3:

Figure 1. Analytic framework for screening, monitoring, and treatment of chronic kidney disease stages 1–3



Key Question 1. In asymptomatic adults with or without recognized risk factors for chronic kidney disease (CKD) incidence, progression or complications, what direct evidence is there that systematic CKD screening improves clinical outcomes?

- In asymptomatic adults with or without risk factors for CKD incidence, progression, or complications, what is the accuracy and reliability of CKD screening and the prevalence of CKD identifiable by screening?
- Does initiating treatment for CKD as a result of systematic screening improve clinical outcomes compared with treatment initiated after incidental CKD diagnosis during routine clinical practice?
- How do patient factors and CKD screening thresholds modify the yield of CKD screening and its association with clinical benefits?

Key Question 2. What harms result from systematic CKD screening in asymptomatic adults with or without recognized risk factors for CKD incidence, progression or complications?

- How do patient factors and CKD screening thresholds modify the association of CKD screening with harms?

Key Question 3. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what direct evidence is there that monitoring for worsening kidney function and/or kidney damage improves clinical outcomes?

- How do patient factors, CKD severity/stage, and CKD monitoring intervals modify the association of CKD monitoring with clinical benefits?

Key Question 4. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what harms result from monitoring for worsening kidney function/kidney damage?

- How do patient factors, CKD severity/stage, and CKD monitoring intervals modify the association of CKD monitoring with harms?

Key Question 5. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what direct evidence is there that treatment improves clinical outcomes?

- Does the presence of CKD modify the likelihood of improvement in clinical outcomes associated with treatment of vascular disease or vascular risk factors?
- Among adults with CKD, what patient factors modify the association of specific treatments with improved clinical outcomes?

Key Question 6. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what harms result from treatment?

- Does the presence of CKD modify the likelihood of harms associated with treatment of vascular disease or of vascular risk factors?
- How do patient factors and CKD severity/stage modify the association of CKD treatment with harms?

Methods

Topic Refinement

The initial nominator of this topic, first titled "Management of Mild Renal Impairment," proposed questions related to clinical typology, frequency of monitoring, calculation of creatinine clearance, management, and secondary prevention of mild renal impairment. Subsequently, a second nominator proposed questions related to screening for and treatment of screen-detected CKD. It was determined to be feasible to combine the two sets of questions. The scope of the combined questions explicitly excluded management of patients with more advanced kidney disease.

Key Questions were drafted with input from representatives of the nominating organizations. These Key Questions and project scope were submitted for AHRQ approval and then posted on the Effective Health Care web site for public comment.

Comparative Effectiveness Review

Public comments were reviewed with AHRQ and the nominators, and incorporated as appropriate in a draft protocol. The draft protocol was circulated to a Technical Expert Panel (TEP) composed of researchers, clinicians, and representatives from professional organizations and federal and state agencies including the American College of Physicians, United States Preventive Services Task Force, National Kidney Foundation, American Association for Clinical Chemistry, Centers for Disease Control and Prevention, American Academy of Family Practice, and KDIGO. Based on TEP feedback, including on the relevance and scope of the review, the protocol was revised and a final protocol, including the revised Key Questions and proposed project methods, was approved by the Agency for Healthcare Research and Quality (AHRQ) and posted on the Effective Health Care website.

Based on feedback received during protocol development, the terminology used in this project was changed to be consistent with the currently accepted terminology for referring to impairments in kidney function and kidney damage as established by the National Kidney Foundation's KDOQI[2] and later modified by the KDIGO.[33] In addition, its title was changed for the protocol to "Screening for and Management of Chronic Kidney Disease Stages 1–3." Finally, based on public and peer reviewer feedback to the draft report, the final report title was changed to more accurately and transparently reflect its content and organization: "Chronic Kidney Disease Stages 1–3: Screening, Monitoring, and Treatment."

Systematic Review

Search Strategy

We developed separate search strategies for the screening, monitoring, and treatment Key Questions. Search strings were developed and tested to identify randomized controlled trials (RCTs) or controlled clinical trials (CCTs). We included studies that enrolled an adult population (18 years of age and older), were published since 1985, and were written in the English language. Evidence suggests that for systematic reviews of conventional medicine, as were evaluated in the present review, restriction to include only English language trials should not bias estimates of the effectiveness of the interventions.[34] Only full articles were included. We

searched MEDLINE® and the Cochrane Database of Systematic Reviews. Details of the major search strategies are provided in Appendix A.

To identify systematic reviews related to the three topic areas, we completed a search of MEDLINE® and the Cochrane Database of Systematic Reviews using the same search strategies as above with the addition of publication type terms to identify systematic reviews. We manually searched the reference lists of the identified systematic reviews to identify any RCTs or CCTs not detected in our electronic literature search. We also manually searched reference lists of the primary reports that were eligible for inclusion in the review. Per project protocol, because we did not find evidence from RCTs or CCTs to directly address whether screening or monitoring impact clinical outcomes or harms, we conducted a nonsystematic search for observational studies to identify indirect evidence regarding the benefits and harms of screening for and monitoring of CKD. All citations then were imported into EndNote X and Excel for abstract review and database management.

A broad search of the grey literature was completed by the AHRQ Scientific Resource Center librarian. Grey literature, which by definition is literature that is not systematically stored or indexed,[35] included abstracts presented at conferences, unpublished trial data, government documents, and pharmaceutical company scientific information packets on medications evaluated in this topic.

We conducted the initial searches in March and April of 2010. All searches were updated in January 2011.

Inclusion/Exclusion Criteria

We developed criteria for inclusion and exclusion of studies based on patient populations, interventions, outcome measures, and types of evidence relevant to the Key Questions. Within the sections for each pair of Key Questions immediately below, inclusion criteria are detailed in the 'Patients' sections and exclusion criteria are detailed in the 'Study Selection' sections. We retrieved full-text articles of potentially relevant abstracts and conducted a second review for inclusion by reapplying the inclusion criteria. If no abstract was available electronically, the full text of the article was obtained for review.

Key Questions 1 and 2

Patients

We restricted the review to studies that enrolled adults who were without known CKD, were with or without recognized risk factors for CKD, and who were systematically screened for CKD. Because much of our search period preceded the development and wide implementation of the current CKD staging system, studies whose definitions of CKD at least closely approximated the current KDOQI and KDIGO definitions for CKD stages 1–3 were considered eligible.

Study Selection

We sought RCTs or CCTs that assessed the direct impact of systematic screening for CKD stages 1–3 on clinical outcomes and harms. Examples of tests to screen for CKD that were considered eligible were direct measurements of GFR or creatinine clearance, estimation of GFR or creatinine clearance with creatinine-based formulae, serum creatinine, albuminuria, proteinuria, albumin/creatinine ratio, and cystatin C. The screening method must have been feasible within a primary care setting. Our exclusion criteria were as follows: nonadult

population, study participants already diagnosed with CKD, not an RCT that assigned participants to systematic screening for CKD versus usual care or a comparator intervention, study followup duration less than 1 year, and sample size less than 1,000 randomized participants.

When no RCTs were identified that evaluated a CKD screening intervention and reported clinical outcomes and harms, indirect evidence was reviewed regarding its possible benefits and harms. This indirect evidence included observational studies on CKD prevalence, clinical recognition, accuracy and reliability of CKD screening tests, and RCTs of CKD treatments. Although these observational studies were not identified through a comprehensive literature search, whenever possible we evaluated data from large representative U.S. cohorts. Assessment of CKD treatment benefits and harms was based strictly on direct evidence from RCTs.

Comparators

Studies were to compare systematic screening for CKD stages 1–3 with no CKD screening, usual care, or an alternative CKD screening regimen. Any monitoring or treatment interventions that followed screening were allowed.

Outcomes

We restricted the review to studies that reported clinical outcomes or harms. Clinical outcomes included: all-cause mortality, cardiovascular mortality, MI (any, fatal, nonfatal), stroke (any, fatal, nonfatal), CHF (hospitalization, death), composite vascular outcomes, composite renal outcomes, ESRD (progression to kidney transplant or dialysis), quality of life, physical function, and activities of daily living. Intermediate outcomes included: progression to stage 4 or stage 5 kidney disease, composite renal outcomes, doubling of serum creatinine or halving of GFR, and conversion from microalbuminuria to macroalbuminuria. Harms included: any adverse events, serious adverse events, specific adverse events, and any renal adverse events.

Study Designs

We initially included only RCTs. As described above, when no relevant RCTs were identified, we expanded our search to include observational studies that could provide indirect evidence regarding these questions.

Key Questions 3 and 4

Patients

We restricted the review to studies that enrolled adults with CKD stages 1–3 who were systematically monitored for worsening of kidney function and/or damage. As above, studies whose definitions of CKD stages 1–3 at least closely approximated the current KDOQI and KDIGO definitions were considered eligible.

Study Selection

We sought RCTs or CCTs that assessed the direct impact of monitoring on clinical outcomes and harms. Examples of tests to monitor for worsening kidney function and/or damage that were considered eligible were direct measurements of GFR or creatinine clearance, estimation of GFR or creatinine clearance with creatinine-based formulae, serum creatinine, albuminuria, proteinuria, albumin/creatinine ratio, and cystatin C. The monitoring method must have been

feasible within a primary care setting. Our exclusion criteria were as follows: nonadult population, population entirely or predominately not CKD stages 1–3, not an RCT that assigned participants to systematic monitoring for worsening of kidney function and/or damage versus usual care or a comparator intervention, and sample size of less than 50 randomized participants.

When no RCTs were identified that evaluated a CKD monitoring intervention and reported clinical outcomes or harms, indirect evidence was reviewed regarding its possible benefits and harms. This indirect evidence included observational studies on CKD progression, clinical recognition, accuracy and reliability of CKD monitoring tests, and RCTs of CKD treatments. Although these observational studies were not identified through a comprehensive literature search, whenever possible we evaluated data from large representative U.S. cohorts. Assessment of CKD treatment benefits and harms was based strictly on direct evidence from RCTs.

Comparators

Studies were to compare systematic monitoring of patients with CKD stages 1–3 for changes in kidney function and/or damage with usual care or an alternative CKD monitoring regimen. Any interventions that followed CKD monitoring were allowed.

Outcomes

We restricted the review to studies that reported clinical outcomes or harms. Clinical outcomes included: all-cause mortality, cardiovascular mortality, MI (any, fatal, nonfatal), stroke (any, fatal, nonfatal), CHF (hospitalization, death), composite vascular outcomes, composite renal outcomes, ESRD (progression to kidney transplant or dialysis), quality of life, physical function, and activities of daily living. Intermediate outcomes included: progression to stage 4 or stage 5 kidney disease, composite renal outcomes, doubling of serum creatinine or halving of GFR, and conversion from microalbuminuria to macroalbuminuria. Harms included: any adverse events, serious adverse events, specific adverse events, and any renal adverse events.

Study Designs

We initially included only RCTs. As described above, when no relevant RCTs were identified, we expanded our search to include observational studies that could provide indirect evidence regarding these questions.

Key Questions 5 and 6

Patients

We restricted the review to studies that enrolled adults with CKD stages 1–3. Again, studies whose definitions of CKD stages 1–3 at least closely approximated the current KDOQI and KDIGO definitions were considered eligible.

Interventions

We included studies of both CKD specific and nonspecific treatments. Specifically, we attempted to identify studies of ACEI, ARB, calcium channel blockers (CCB), aldosterone antagonists, alpha blockers, beta blockers (BB), loop diuretics, thiazide and related diuretics, combination antihypertensive regimens, targeting thresholds of blood pressure control independent of specific antihypertensive agent(s), insulin, sulfonylureas, thiazolidinediones, biguanides (e.g., Metformin), targeting thresholds for glycemic control, HMG CoA-reductase

inhibitors (i.e., statins), bile acid sequestrants, cholesterol absorption inhibitors (e.g., Ezetimibe), anorexiants, lipase inhibitors, low protein diets, and other diets.

Comparators

These studies compared active treatment of patients with CKD stages 1–3 with placebo, usual care/no treatment, or with other active treatments, including combination treatment and comparisons with the same active treatments using different dose levels or targeting different treatment thresholds.

Outcomes

We restricted the review to studies that reported clinical outcomes or harms. Clinical outcomes included: all-cause mortality, cardiovascular mortality, MI (any, fatal, nonfatal), stroke (any, fatal, nonfatal), CHF (hospitalization, death), composite vascular outcomes, composite renal outcomes, ESRD (progression to kidney transplant or dialysis), quality of life, physical function, and activities of daily living. Intermediate outcomes included: progression to stage 4 or stage 5 kidney disease, composite renal outcomes, doubling of serum creatinine or halving of GFR, and conversion from microalbuminuria to macroalbuminuria. Harms included: any adverse events, serious adverse events, specific adverse events, and any renal adverse events.

Study Designs

We only included RCTs.

Study Selection

Separate literature searches were completed for the three main topic areas: screening, monitoring, and treatment. Results of each literature search were imported to a spreadsheet for screening. Trained reviewers examined all titles and abstracts for eligibility based on the inclusion/exclusion criteria for the topic area of the search. Titles and abstracts with insufficient information to determine eligibility were pulled for full article text review. If the initial reviewer was uncertain about eligibility, one of the physician project leads reviewed the abstract (or article) and made a final decision about inclusion or exclusion. We selected a 10 percent sample (representing the work of all abstract reviewers) for repeat review. Based on discrepancies between the results of one initial reviewer and the second reviewer, all abstracts reviewed by that initial reviewers were reviewed a second time. Overall, we asked abstract reviewers to err on the side of inclusion rather than exclusion. Reasons for exclusion were tallied in the spreadsheet and entered in an EndNote file for reference list management. We also applied the inclusion/ exclusion criteria to studies identified in the hand search of reference lists and in the review of studies cited in relevant systematic reviews. Additional references suggested by members of our TEP and by the public during the comment period also were reviewed for eligibility. A list of excluded studies is included in Appendix B.

Data Extraction

For the treatment interventions, trained clinicians or research assistants extracted data onto a spreadsheet. After verifying study eligibility, we extracted the following data from each trial:

- Study quality: Allocation concealment, intention-to-treat analysis, blinding, withdrawals, and dropouts adequately described;

- Study characteristics: Location, number of sites, subject inclusion and exclusion criteria, source of study subjects, total number randomized, details of treatment and control group interventions;
- Baseline participant data: age, weight, body mass index, gender, race/ethnicity, CKD stage, estimated or directly measured GFR, serum creatinine, urinary albumin or protein excretion rate, creatinine clearance, urine albumin or protein creatinine ratio, glycosylated hemoglobin or hemoglobin A_{1c} (HbA_{1c}), blood pressure, cholesterol, smoking status, and history of diabetes, hypertension, dyslipidemia, coronary artery disease, congestive heart failure (CHF), peripheral arterial disease, myocardial infarction (MI), stroke, and history of acute kidney injury;
- Efficacy outcomes: Duration of followup, all-cause mortality, cardiovascular mortality, MI (any, fatal, nonfatal), stroke (any, fatal, nonfatal), CHF (hospitalization, death), composite vascular outcomes, ESRD (progression to kidney transplant or dialysis), progression to stage 4 or stage 5 kidney disease, composite renal outcomes, doubling of serum creatinine or halving of GFR, conversion from microalbuminuria to macroalbuminuria, whether continuous renal outcomes were reported, and whether quality of life, physical function or activities of daily living were reported; and
- Withdrawals and adverse events: any withdrawals, withdrawals due to adverse events, any adverse events, serious adverse events, specific adverse events, and any renal adverse events.

Articles identified as not meeting eligibility criteria during the extraction phase were tallied and documented on the study flow diagram. In preparing the tables and text, a second clinician or research assistant confirmed the accuracy of the extracted information by comparing the extracted information with the original article. A physician project lead verified all entries in tables included in the review and appendices.

Quality Assessment

Study quality for the individual RCTs was rated by using the following criteria based on the domains the Cochrane Collaboration recommends to assess the risk of bias of studies included in a systematic review:[36] (1) adequate allocation concealment, based on the approach by Schulz and Grimes;[37] (2) blinding methods (participant, investigator, and/or outcome assessor); (3) how incomplete data are addressed (did the study analyze the data based on the intention-to-treat principle, i.e., were all participants who were randomized included in the outcomes analyses); and (4) whether reasons for dropouts/attrition were reported. Studies were rated as good, fair, or poor quality. A rating of good generally indicated that the trial reported adequate allocation concealment, blinding, analysis by intent-to-treat, and reasons for dropouts/attrition were reported. Studies were generally rated poor if the method of allocation concealment was inadequate or not defined, blinding was not defined, analysis by intent-to-treat was not utilized, and reasons for dropouts/attrition were not reported and/or there was a high rate of attrition.

Rating the Body of Evidence

The overall strength of evidence for the randomized trials was evaluated using methods developed by AHRQ and the Effective Health Care Program.[38] For each of several important clinical outcomes within each comparison evaluated, the strength of the evidence was evaluated

based on four required domains: (1) risk of bias (do the studies for a given outcome or comparison have good internal validity); (2) consistency (the degree of similarity in the effect sizes, i.e., same direction of effect, of the included studies); (3) directness (reflecting a single, direct link between the intervention of interest and the outcome); and (4) precision (degree of certainty surrounding an effect estimate of a given outcome). The risk of bias, based on study design and conduct, is rated low, medium, or high. Consistency is rated consistent, inconsistent, or unknown/not applicable (e.g., a single study was evaluated). Directness can either be direct or indirect and precision is either precise or imprecise. A precise estimate is one that would yield a clinically meaningful conclusion. Based on these four domains, the overall evidence was rated as: (1) high, indicating high confidence that further research is very unlikely to change the confidence in the estimate of effect, meaning that the evidence reflects the true effect; (2) moderate, indicating moderate confidence that further research may change our confidence in the estimate of effect and may change the estimate; (3) low, indicating low confidence that further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate, meaning there is low confidence that the evidence reflects the true effect; and (4) insufficient, indicating that evidence either is unavailable or does not permit a conclusion. An overall rating of high strength of evidence would imply that the included studies were RCTs with a low risk of bias, with consistent, direct, and precise domains.

Applicability

Applicability of the results reported in this review is affected by the representativeness of the patient samples in the included studies to general populations and specific subpopulations of nonstudy patients with CKD stages 1–3, both those identified through screening and through other means. All treatment trials included patients with CKD stages 1–3, but because of the variability in CKD definitions used in identified studies, some trials also included some patients outside the bounds defined by CKD stages 1–3. This may limit the applicability of results reported here to patients who meet the currently accepted definition for CKD stages 1–3. Incomplete reporting of patient characteristics in many included trials also limits our ability to judge applicability of study results to specific CKD patient populations. The evidence tables in Appendix C identify reported details on the patient inclusion and exclusion criteria, as well as baseline patient characteristics.

Data Synthesis

Text; evidence, outcomes, and summary tables; and figures were organized by intervention. If clinical heterogeneity of patient populations, interventions, and outcomes was minimal, we pooled results. For many interventions, there were only one or two trials and reported outcomes did not overlap. Narratives provide details on study populations, interventions, clinical outcomes, and harms. Data were analyzed in Review Manager 5.0.[39] Random effects models were used to generate pooled estimates of relative risks (RR) and 95 percent confidence intervals (CI). Statistical heterogeneity was summarized using the I^2 statistic (50 percent indicates moderate heterogeneity and 75 percent or greater indicates high heterogeneity).[40]

Publication Bias

Grey literature was searched for relevant trials and other material to estimate the likelihood of publication bias. Sources of regulatory documents included Federal Drug Administration –

Medical Reviews and Statistical Reviews, Health Canada – Drug Monographs, and Authorized Medicines for the European Union. Clinical trial registries accessed were ClinicalTrials.gov, Current Controlled Trials, Clinical Study Results, and World Health Organization's Clinical Trials. Conference papers and abstracts were identified from the CSA Conference Papers Index and Scopus.

Results

Our literature search was designed to identify RCTs and CCTs of screening to identify patients with CKD stages 1–3, and monitoring and treatment of patients with CKD stages 1–3. For the screening questions, our search yielded 324 references (Key Questions 1 and 2; Figure 2). We excluded 315 references in the initial review of titles and abstracts and we excluded the remaining nine references based on a full text review. The results were similar for the monitoring questions (Key Questions 3 and 4; Figure 3). Of 816 references identified in the search, we excluded 803 in title and abstract review and excluded the remaining 13 after obtaining the full text. For the treatment questions, 4,706 references were identified by the literature search (Key Questions 5 and 6; Figure 4). We excluded 3,676 references during title and abstract review and excluded an additional 939 when we reviewed the full text. In addition to the 91 eligible references identified from the literature search, an additional eight eligible references were identified by hand searching reference lists of related articles or systematic reviews or were suggested by members of our TEP or reviewers of our protocol.

The grey literature search yielded 1,899 documents or citations; 1,065 from regulatory sources, 416 from clinical trials, and 418 conference papers and abstracts. Of the treatments analyzed for this report, our literature review yielded the most references for ACEIs. We therefore looked at the grey literature for ACEI studies not identified in our literature search. In the conference abstract and papers grey literature, there were 74 references pertaining to ACEIs. Ten of the references were identified in our literature search. The remainder did not meet inclusion criteria. In the clinical trials grey literature, there were 13 citations pertaining to ACEIs. Nine did not meet inclusion criteria. The four remaining studies are in progress with no results reported, to date. We concluded that our literature search adequately identified the relevant studies.

Figure 2. Reference flow chart for CKD literature search—screening

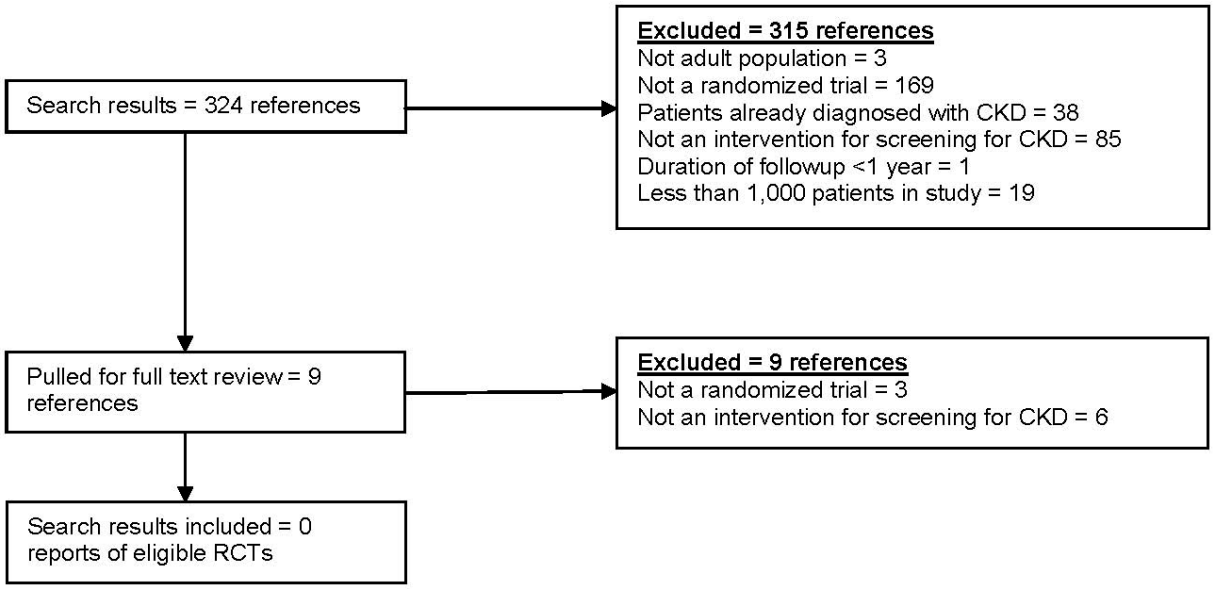


Figure 3. Reference flow chart for CKD literature search—monitoring

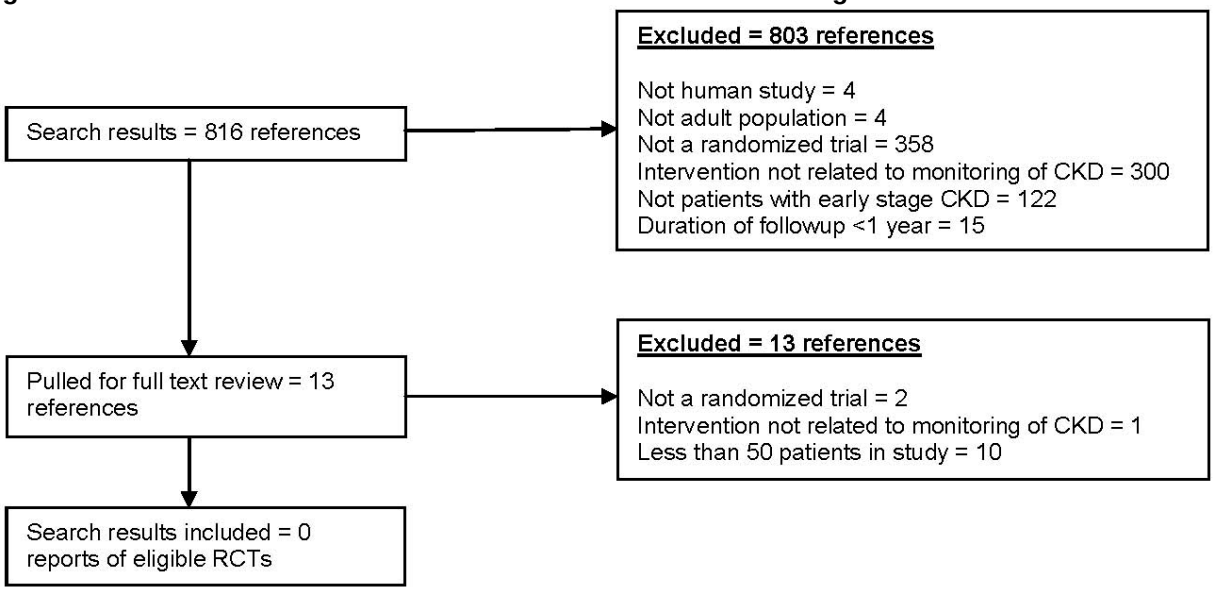
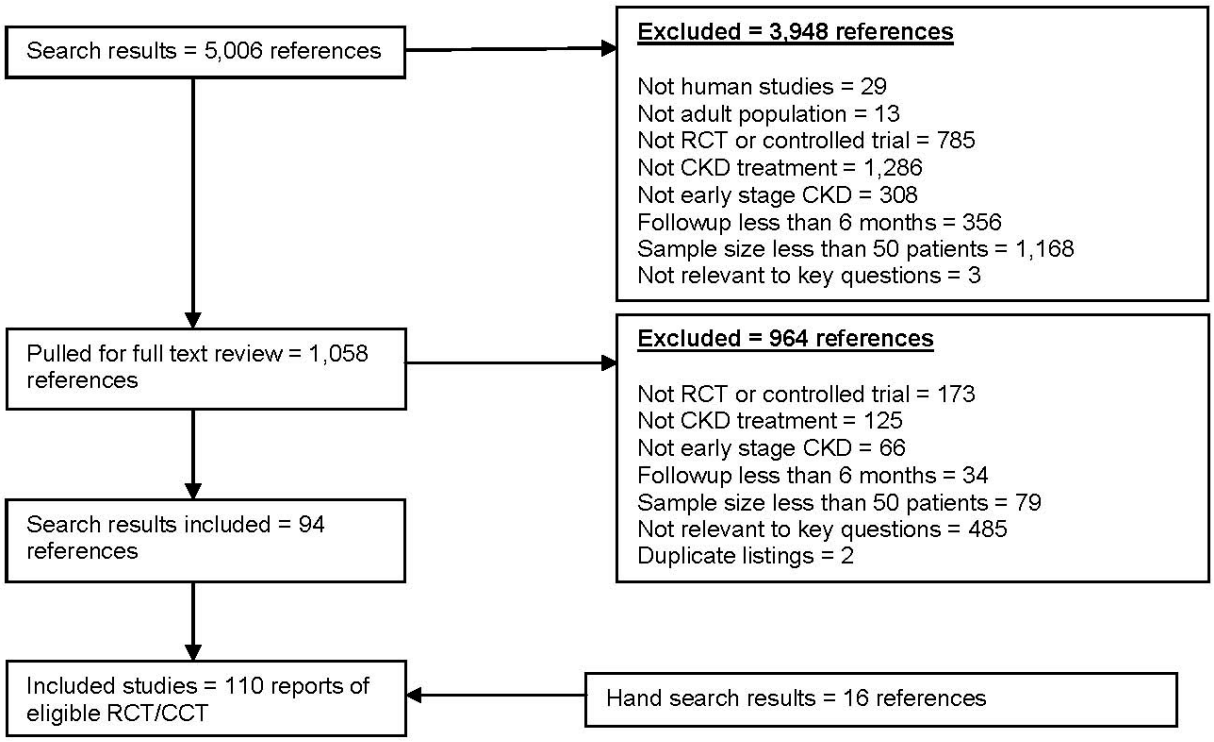


Figure 4. Reference flow chart for CKD literature search—treatment



Key Question 1. In asymptomatic adults with or without recognized risk factors for chronic kidney disease (CKD) incidence, progression or complications, what direct evidence is there that systematic CKD screening improves clinical outcomes?

We found insufficient evidence regarding whether systematic screening for CKD improves clinical outcomes.

Direct Evidence

We identified no RCTs that compared systematic CKD screening versus no CKD screening, versus usual care, or versus an alternative CKD screening regimen and evaluated clinical outcomes.

Indirect Evidence

Not finding direct evidence regarding whether systematic CKD screening improved clinical outcomes, we nevertheless identified data to address at least some parameters that would be needed to indirectly assess the potential clinical benefits of systematic CKD screening.

Is Undiagnosed CKD Stages 1–3 Sufficiently Prevalent?

Determination of how many individuals need to be screened to identify each new case of CKD in the population overall and within high risk groups will be a function both of the prevalence of undiagnosed CKD in these groups and the frequency with which such patients already are tested for CKD in usual practice.

As described earlier, approximately 11.1 percent (22.4 million) of U.S. adults age 20 or older have CKD stages 1–3.[8] This estimate is derived from the NHANES population by using the CKD-EPI formula to estimate GFR and the urine albumin-creatinine ratio to estimate kidney damage. Of individuals with CKD stages 1–3, half have increased albuminuria only (nearly all with microalbuminuria), one-third have decreased GFR only, and the remainder have both abnormalities. Of individuals with albuminuria, nearly 85 percent have microalbuminuria, with the remainder (approximately 1 percent of NHANES participants) having macroalbuminuria. In another population-based sample, prevalence of macroalbuminuria among adults aged 28 to 75 years was 0.6 percent.[41] Compared with the overall population, prevalence of CKD stages 1–3 is higher among older adults, including 17.6 percent in those aged 60-69, and 44.4 percent among adults aged 70 years or older[8] Also based on NHANES data, prevalence of CKD stages 1–3 is 39.0 percent in patients with diabetes, 27.8 percent in patients with hypertension, and 37.9 percent in those with cardiovascular disease[42] (Table 1) Combining these risk factors, NHANES data have been used to stratify individuals into different groups with respect to their likelihood of having CKD[9] (Tables 2 and 3). For example, only 5 percent of individuals less than 52 years old and without diabetes, hypertension, or obesity were estimated to have CKD compared with 68 percent of those aged 81 years or older.

Other data suggest that most individuals with CKD stages 1–3 are not clinically recognized to have this diagnosis. In one study, among patients with GFR <60 ml/min/1.73m^2, just 26.5 percent were documented to have a clinical diagnosis of CKD.[43] In 2008 data from the VA system, even in patients with CKD stages 3-5, only 33 percent had a provider-coded ICD-9 diagnosis for CKD.[44] Awareness of CKD appears even lower in patients. According to the CDC

CKD Surveillance Project 2009 Report, among NHANES participants in 1999-2006, fewer than 5 percent with proteinuria and an estimated GFR ≥60 ml/min/1.73m^2 (based on a single measurement) reported being aware of having CKD, and only 7.5 percent of participants with a GFR between 30-59 ml/min/1.73m^2 were aware of having CKD.[44]

Most patients without CKD, even those in high risk groups, do not appear to be undergoing CKD testing in usual clinical care. Based on 2007-2008 Medicare data, among patients without CKD who had diabetes, the annual probability of urine microalbumin testing was just over 30 percent.[12] In those without CKD who had hypertension, the annual probability of urine microalbumin testing was 4 percent. Based on 2004 Medicare data, among patients without CKD who had either diabetes or hypertension, the annual probability of serum creatinine measurement was less than 20 percent.[45]

Is CKD Stages 1–3 Associated With Sufficient Adverse Health Consequences?

As described earlier, early stage CKD is usually asymptomatic. However, data from many studies indicate that a GFR 30-59 mL/min/1.73 m^2 (stage 3 CKD) is associated with an increased risk of mortality,[3,13] cardiovascular disease,[14] fractures,[15] bone loss,[16] infections,[17] cognitive impairment,[18] and frailty. Similarly, albuminuria and proteinuria (stage 1–4 CKD) are associated with an increased risk of mortality,[3,20] ESRD,[21] and cardiovascular disease,[22] with risk increasing according to the severity of albuminuria or proteinuria. Further, the risk for adverse outcomes conferred by reduced GFR and increased albuminuria or proteinuria appear independent and multiplicative.[3,21]

Are There Valid, Reliable, and Clinically Available CKD Screening Tests?

Serum creatinine is measured from a simple blood test. Formulas to estimate GFR are now automatically reported in many clinical labs from serum creatinine and are highly correlated (i.e., >0.9)[46] with direct GFR measurement based on urinary clearance of ^{125}I-iothalamate. At present, the Modification of Diet in Renal Disease (MDRD) formula is the one most commonly used in clinical practice. A large external validation study indicated that compared with measured GFR the CKD-EPI formula had a small median bias (measured GFR minus estimated GFR) of +/-4 ml/min/1.73m^2 or less at all levels of measured GFR.[47] This represents a significant improvement in accuracy compared with the MDRD formula for measured GFR ≥30 ml/min/1.73m^2, which is known to underestimate measured GFR above this level, particularly in individuals with GFR ≥60 ml/min/1.73m^2. However, the precision of both formulas are limited in that the percentage of their estimates that diverge by more than 30 percent from measured GFR exceeds 15 percent.[8] Framed differently, the sensitivity and specificity of a one-time estimate of GFR <60 mL/min/1.73m^2 for detection of a one-time direct measurement of GFR <60 mL/min/1.73m^2 were 91 percent and 87 percent according to the CKD-EPI equation and 95 percent and 82 percent according to the MDRD Study equation.[8] These data correspond to a false-positive rate of 13 percent and 18 percent for GFR estimation with CKD-EPI and MDRD, respectively. We did not identify studies that compared estimated GFR with directly measured GFR based on two or more measurements three or more months apart as would be consistent with the definition of CKD. It would be expected that when compared with persistently abnormal measured GFR, the false-positive rate of one-time estimated GFR would be higher.

There are many sources of variability in measurement of urinary albumin excretion. Intra-individual variability is high, with many published coefficients of variance estimates clustering around 30 to 50 percent.[48] Factors that can impact urinary albumin excretion include body position, exercise, and fever.[48] While most groups recommend use of spot tests and calculation of the urine albumin-creatinine ratio, methodology for its collection and for measurement of both urinary albumin and creatinine has yet to be standardized. Although these are additional sources of variation, they appear considerably smaller in magnitude than the intra-individual variability.[48-50] Impacted by these issues, among individuals with one-time microalbuminuria and GFR ≥60 ml/min/1.73m^2 in the NHANES study, only 63 percent had either microalbuminuria or macroalbuminuria on repeat testing two months later.[51] Further, even in a diabetic population with persistent microalbuminuria, as defined by repeated UACR measurements during a 2-year period, regression of the microalbuminuria to normal occurred in 59 percent patients over a subsequent 6-year evaluation period.[52]

Unfortunately, we did not identify any population-based studies that tested the sensitivity or specificity of one-time screening using both estimated GFR and albuminuria for diagnosis of CKD as defined by persistence of impaired GFR and/or albuminuria for at least 3 months (the current "gold standard"). We also did not identify any data on the validity and reliability of repeated screening for CKD.

Do Treatments for Screen-Detected CKD Patients Improve Important Clinical Outcomes?

We did not identify RCTs involving treatment of CKD patients identified through systematic screening, but did systematically review the RCT evidence on the effectiveness of treatments of CKD patients identified more generally in the Results section for Key Question 5.

Table 1. Percentage of U.S. adult population age 20 years or older with each stage of CKD, overall and within subgroups defined by age, gender, race, and comorbidities using the creatinine based CKD-Epi formula for estimating GFR

Population Characteristic	% of Population With Stage 1 CKD	% of Population With Stage 2 CKD	% of Population With Stage 3 CKD	% of Population With Stages 4–5 CKD
Overall	4.3	3.2	6.3	0.6
Age 20-39	4.7	0.7	0.2*	0.1*
Age 40-59	4.9	2.5	2.0	0.2
Age 60+	2.4	8.6	24.3	2.1
Male	3.5	3.4	5.2	0.6
Female	5.0	3.0	7.4	0.6
Non-Hispanic white	3.2	3.3	7.4	0.6
Non-Hispanic African American	6.3	3.4	4.9	1.2
Diabetes (SR)	11.8	10.2	17.0	3.1
Hypertension (SR)	5.4	5.9	14.6	1.7
CVD (SR)	3.3	8.7	25.9	4.3
Current smoker	5.9	2.3	2.4	0.5
Obese (BMI ≥30)	5.5	4.2	6.6	0.6

*Not Reliably Estimated. SR= Self-Reported
CKD Stages defined as:
Stage 1: eGFR ≥90 mL/min/1.73 m^2, UACR ≥30 mg/g
Stage 2: eGFR 60–89 mL/min/1.73 m^2, UACR ≥30 mg/g
Stage 3: eGFR 30–59 mL/min/1.73 m^2
Stage 4: eGFR 15–29 mL/min/1.73 m^2
Stage 5: eGFR <15 with dialysis patients excluded from this analysis
Note: Adapted from USRDS Annual Report 2010.[12]

Table 2. Sensitivity and specificity of different population characteristics for identifying individuals who would have one-time eGFR <60 ml/min/1.73 m^2: using creatinine and CKD-Epi formula

Screened Population	Sensitivity of Demographic Characteristics	Specificity of Demographic Characteristics
Age 20+	100.0	0
Age 50+	94.6	65.7
Age 50+ or <50 with DM or HTN	98.0	55.4
Age 50+ or <50 with DM, HTN, or CVD	98.6	54.7
Age 60+	85.3	82.3
Age 60+ or <60 with DM or HTN	94.6	65.5
Age 60+ or <60 with DM, HTN, or CVD	95.4	64.2

CKD-Epi Formula: estimated GFR = 141 * min(Scr /κ, 1)**α* max(Scr/κ, 1)**(-1.209) * 0.993**age * 1.018 [if female] * 1.159 [if African American], where Scr is standardized serum creatinine in mg/dl, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/ κ or 1, and max indicates the maximum of Scr/κ or 1.
DM=Diabetes Mellitus, HTN=Hypertension, CVD=Cardiovascular Disease.
Note: Adapted from USRDS Annual Report 2010.[12]

Table 3. Sensitivity and specificity of different population characteristics for identifying individuals who would have one-time UACR ≥30 mg/g

Screened Population	Sensitivity	Specificity
Age 20+	100.0	0
Age 50+	60.5	64.3
Age 50+ or <50 with DM or HTN	73.3	54.9
Age 50+ or <50 with DM, HTN, or CVD	73.9	54.1
Age 60+	44.9	80.5
Age 60+ or <60 with DM or HTN	67.6	65.1
Age 60+ or <60 with DM, HTN, or CVD	68.6	63.7

ACR: urinary Albumin (mg/l) to urinary Creatinine (mg/dl) Ratio.
DM=Diabetes Mellitus, HTN=Hypertension, CVD=Cardiovascular Disease.
Note: Adapted from USRDS Annual Report 2010.[12]

Key Question 2. What harms result from systematic CKD screening in asymptomatic adults with or without recognized risk factors for CKD incidence, progression, or complications?

We found insufficient evidence to address the question regarding whether systematic CKD screening causes adverse effects for patients.

Direct Evidence

We identified no RCTs that compared systematic CKD screening versus no CKD screening, versus usual care, or versus an alternative CKD screening regimen and evaluated adverse effects for patients.

Indirect Evidence

We considered numerous potential adverse effects of systematic CKD screening (Table 4), but found only very limited literature addressing this issue.[53] Based on expert opinion only, the primary harms from CKD screening are likely to be misclassification of patients with CKD, unnecessary tests and their associated adverse effects (e.g., from phlebotomy or renal biopsies), psychological effects of being labeled with CKD, adverse events associated with

pharmacological treatments initiated or changed following a CKD diagnosis, and possible financial and insurance ramifications of a new CKD diagnosis.

Table 4. Potential harms associated with screening for CKD

A)	Psychological effects of screening tests
B)	Adverse physical effects of screening tests (e.g., phlebotomy-associated bruising)
C)	Misclassification/false positive diagnosis
D)	Unnecessary tests to further evaluate patients with positive screening test and their associated effects, e.g., phlebotomy-associated bruising; pain, bleeding with need for transfusion, and infection associated with renal biopsy
E)	Psychological effects associated with CKD diagnostic label and of further evaluations following diagnosis
F)	Increased visits to primary provider, increased referrals to specialists
G)	Adverse effects associated with increased treatment, possibly including worsened estimated GFR, hyperkalemia, hypotension, cough, hospitalization for AKI, cardiovascular morbidity, other
H)	Increased difficulty obtaining/keeping health insurance coverage

Psychological Effects of Screening

We did not identify any studies that reported on the psychological effects of screening tests for CKD.

Adverse Physical Effects of Screening Tests and of Followup Tests To Evaluate Abnormal Screening Test

Phlebotomy required to measure serum creatinine may be associated with a small degree of bruising or discomfort. In a small number of patients, postscreening evaluation will include a renal biopsy, which has an associated risk of pain, bleeding, and infection.

Misclassification/False Positive Test for CKD

We did not identify any studies that reported on the effects of a false positive result from tests used to screen for CKD. False positive results may be common with tests for microalbuminuria. As described above, intra-individual variability in albuminuria is high. In one study, more than one-third of individuals with microalbuminuria and normal GFR on first testing regressed to normoalbuminuria on repeat testing two months later.[51] Raising questions about the sufficiency of the requirement that albuminuria be persistent for at least 3 months to diagnose CKD, in a second study, 59 percent of individuals with persistent microalbuminuria over a 2 year period regressed to normal during a subsequent 6 year evaluation period.[52] We did not identify any studies that reported the specificity of a single measurement of GFR estimated from serum creatinine for a diagnosis of CKD defined by abnormalities in kidney function or damage that persist for at least 3 months.

Labeling of an Individual With CKD

We did not identify any studies that reported on the effects of labeling an individual with CKD.

Increased Clinic Visits to Primary and/or Specialist Providers

We did not identify any studies that reported on the effect of CKD screening tests on subsequent patient visits to primary or specialist providers. However, to the extent that their provider is aware of it, individuals who have an abnormal result on CKD screening, seem likely to be seen more frequently in primary and specialty clinics. These visits may be for further evaluation to confirm the abnormal screening test, or providers may follow and treat these

patients under the assumption that they have diagnosed CKD. According to recent U.S. Renal Data System (USRDS) data, in the year following a claim-documented CKD diagnosis, approximately 90 percent of individuals have at least one physician visit and 30 percent have a visit with a nephrologist.[12]

Adverse Effects Associated With Treatment

We systematically reviewed the RCT evidence on adverse effects of treatments of CKD patients in the Results section for Key Question 6.

Impact on Insurance Coverage

We did not identify any studies that reported the effects of being diagnosed with CKD on obtaining or keeping health insurance coverage.

Key Question 3. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what direct evidence is there that monitoring for worsening kidney function and/or kidney damage improves clinical outcomes?

We found insufficient evidence regarding whether systematic monitoring of individuals with CKD stages 1–3 for worsening kidney function and/or kidney damage improves clinical outcomes.

Direct Evidence

We identified no RCTs that compared systematic monitoring of individuals with CKD stages 1–3 for changes in kidney function and/or damage versus no CKD monitoring, versus usual care, or versus an alternative CKD monitoring regimen and evaluated clinical outcomes.

Indirect Evidence

Though we did not find direct evidence regarding whether systematic monitoring of individuals with CKD stages 1–3 for changes in kidney function and/or damage improved clinical outcomes, we identified data to address at least some parameters that would be needed to indirectly assess the potential clinical benefits of such systematic monitoring in these patients.

Is Undiagnosed Worsening of Kidney Function and/or Damage Sufficiently Frequent in Patients With CKD Stages 1–3?

Determination of whether and how frequently individuals with CKD stages 1–3 need to be monitored to identify patients with CKD progression, overall and within high risk groups, will be a function both of the incidence of undiagnosed CKD progression in these groups, the incidence of CKD regression (e.g., to normoalbuminuria), and the frequency with which these patients already have their level of kidney function and/or damage tested in usual practice.

In patients with CKD, reported rates of CKD progression vary widely. Mean annual GFR decline may range from approximately 1 to >10 ml/min/1.73m^2.[27] Factors shown in at least some studies to predict faster decline include diabetes, proteinuria, increased blood pressure, older age, obesity, dyslipidemia, smoking, male gender, and etiology of primary kidney disease. The high intra-individual variation in albuminuria makes it harder to estimate rates at which albuminuria increases in CKD. However, in several RCTs that randomized individuals with diabetes and

microalbuminuria to either ACEI or ARB versus placebo,[54-59] the average annual progression rate to macroalbuminuria was approximately 5 to 9 percent (Table 5). A lower annual conversion rate of 2.8 percent was reported in the United Kingdom Prospective Diabetes Study.[60] However, these estimates of progression in albuminuria from RCTs are limited both in that being derived from RCTs they may not be representative of all patients with microalbuminuria, and in that a substantial portion of individuals with microalbuminuria also will regress (i.e., to normoalbuminuria) over time.

Contrasted to the lower frequency of testing among individuals who do not carry a CKD diagnosis, most patients with CKD stages 1–3 appear to be undergoing at least some CKD testing in usual clinical care. Based on 2008 data, the annual probability that patients with CKD stages 1–3 receive serum creatinine testing is about 95 percent in the Medicare population and about 80 percent in a younger privately insured population.[12] By comparison, the annual probability that patients with CKD stages 1–3 get albuminuria measured is between 30 and 40 percent.

Table 5. Rate of progression from microalbuminuria to macroalbuminuria

Trial	Baseline CKD Level	Followup Duration	Incidence of Macroalbuminuria
O'Hare, 2000[58] (ATLANTIS)	N=46 100% had microalbuminuria; 100% Insulin Dependent Diabetics GFR (ioexol) mean±SD= 100 ± 23ml/min	2 years	10.9% (5/46) ~5% per year
Strippoli, 2006[54] MICRO HOPE 2000[56]	N=587 100% had microalbuminuria 100% Diabetics	Median 4.5 years	21.6% (127/587) ~5% per year
Crepaldi, 1998[55]	N=34 100% had microalbuminuria 100% Insulin Dependent Diabetics	3 years	20.6% (7/34) ~7% per year
Laffel, 1995[57]	N=70 100% had microalbuminuria; 100% Insulin Dependent Diabetics CrCl (mean±SD)= 80 ± 22 mL/min per $1.73m^2$ at baseline	2 years	18.6% (13/70) ~9% per year
Ravid, 1993[59]	N=45 100% had microalbuminuria 100% Type 2 Diabetics Proteinuria mean±SD= 123 ± 58 mg/24 h	5 years	42.2% (19/45) ~8% per year

In Patients With CKD Stages 1–3, Is CKD Progression Associated With Sufficient Adverse Health Consequences?

As described earlier, data from many studies indicate that a GFR 30-59 mL/min/1.73 m^2 (stage 3 CKD) is associated with an increased risk of mortality,[3,13] cardiovascular disease,[14] fractures,[15] bone loss,[16] infections,[17] cognitive impairment,[18] and frailty. Similarly, albuminuria and proteinuria are associated with an increased risk of mortality,[3,20] ESRD,[21] and cardiovascular disease,[22] with risk increasing according to the severity of albuminuria or proteinuria. Further, the risk for adverse outcomes conferred by reduced GFR and increased albuminuria or proteinuria is independent and multiplicative.[3,21]

We did not identify studies that longitudinally recalibrated risk of adverse health consequences among individuals with CKD stages 1–3 as their CKD progressed. However, a large, recent meta-analysis of prospective cohort studies reported risk of all-cause and

cardiovascular mortality for different strata defined by baseline eGFR and albuminuria as follows:[3]

- Within individuals who had albuminuria and GFR >60 ml/min/1.73m^2 (CKD stages 1–2):
  - Mortality risk was higher in those with macroalbuminuria than in those with microalbuminuria.
  - A lower GFR within this range was not associated with a higher mortality risk.
  - Mortality is increased for each lower level of eGFR below 60 ml/min/1.73m^2, higher for 45–59 (CKD stage 3), still higher for 30–44, and higher for GFR <30 ml/min/1.73m^2 (CKD stage 4).
- Within individuals with GFR <60 ml/min/1.73m2 (CKD stage 3):
  - Mortality risk is increased for each lower level of eGFR, lowest for 45–59, higher for 30–44, and higher for GFR <30 ml/min/1.73m2 (CKD stage 4).
  - Mortality risk is lowest in those without albuminuria, higher in those with microalbuminuria, and highest in those with macroalbuminuria.

Are There Valid, Reliable, and Clinically Available Tests To Monitor CKD Progression in Patients With CKD Stages 1–3?

Tests used to monitor CKD progression in patients with CKD stages 1–3, most typically quantitative measures of albuminuria and estimates of GFR calculated from serum creatinine, are derived from simple blood and urine tests that are widely available in primary care settings.

As described earlier in the section on screening, formulas to estimate GFR are automatically reported in many clinical labs from serum creatinine and are highly correlated with direct GFR measurement.[46] Compared with measured GFR, the CKD-EPI formula to estimate GFR has only a small bias at all levels of measured GFR,[47] which represents an improvement in accuracy compared with the MDRD formula, particularly in individuals with GFR ≥60 ml/min/1.73m^2. Both formulas suffer from some imprecision, however, as more than 15 percent of their estimates diverge from measured GFR by at least 30 percent.[8] Still, they appear to perform well for one-time classification of individuals as either having CKD or not. The sensitivity and specificity of estimated GFR <60 mL/min/1.73m^2 for detection of directly measured GFR <60 mL/min/1.73m^2 were 91 percent and 87 percent according to the CKD-EPI equation and 95 percent and 82 percent according to the MDRD Study equation.[8] Unfortunately, we did not identify data regarding the accuracy and precision of these formulas for assessing change in GFR within individuals over time, or their sensitivity and specificity for detecting change in GFR category over time (e.g., a decline from a GFR of 30 to 59 ml/min/1.73m2 to one of <30 ml/min/1.73m^2).

Also as described in the section on screening, inter-assay and intra-assay coefficient of variance for urinary albumin is less than 5 percent.[49,50] However, as is the case for individuals without CKD, intra-individual variation of urinary albumin excretion is high in individuals with CKD. The impact of hydration can be addressed by accounting for urine output (e.g., using urine albumin-to-creatinine ratio), but nonhydration factors that may impact estimates of urinary albumin excretion include body position, exercise, certain medications, fever, and urinary tract infections.[27] As an illustration of this variability, based on NHANES data, among individuals with one-time microalbuminuria and GFR ≥60 ml/min/1.73m^2, only 63 percent had either microalbuminuria or macroalbuminuria on repeat testing two months later.[51] Further, even in a diabetic population with persistent microalbuminuria over a 2-year period, regression of the microalbuminuria to normal occurred in 59 percent patients during a subsequent 6-year

evaluation period.[52] This variability makes it more difficult to determine whether longitudinal changes in measured albuminuria represent progression of CKD.

In Patients With CKD Stages 1–3 Whose CKD Has Progressed, Do Treatments Improve Important Clinical Outcomes?

For monitoring to improve clinical outcomes, changes in CKD status (such as the patient reaching a specific threshold or rate of change in kidney function or damage) would need to impact patient behavior or provider treatment in ways that improve these outcomes. RCT evidence that certain treatments had differential effects on clinical outcomes between patients with CKD stages 1–3 and those with CKD stage 4, or differential effects between different categories of patients within CKD stages 1–3 might suggest that treatment should be modified when change in CKD status is identified. While RCT data on CKD treatments are reviewed in greater detail elsewhere in this report, there is limited evidence to suggest that some treatments may have such differential effects based on CKD stage. For example, in RCTs comparing ACEI versus placebo treatment, a significant 40 percent reduction in relative risk of ESRD with ACEI is evident in trials comprised of patients with macroalbuminuria. By comparison, in ACEI versus placebo trials comprised of patients with microalbuminuria only, with very low power to detect changes in ESRD events, the pooled effect size suggests no difference between treatments. In a post hoc analysis in CHF patients with CKD, tests for interaction between study participants with GFR of >60, 45 to 60, and 30 to 44 ml/min/1.73m^2 suggest that benefit of beta blocker treatment versus placebo may be greater in the lower GFR group for reducing risk of hospitalizations due to CHF (p=.038), of two composite outcomes including all-cause mortality and hospitalization (both p <.05), and may be borderline significant with regard to all-cause mortality (p=.095).

Key Question 4. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what harms result from monitoring for worsening kidney function/kidney damage?

We found insufficient evidence to address the question regarding whether systematic monitoring of patients with CKD stages 1–3 for worsening kidney function or kidney damage causes adverse effects for patients.

Direct Evidence

We identified no RCTs that compared systematic monitoring of patients with CKD stages 1–3 for worsening kidney function or kidney damage versus no CKD monitoring, versus usual care, or versus an alternative CKD monitoring regimen and evaluated adverse effects for patients.

Indirect Evidence

We considered numerous potential adverse effects of systematic monitoring of patients with CKD stages 1–3 for worsening kidney function or kidney damage (Table 6), but found no literature directly addressing this issue. The primary harms from such monitoring are likely to be incorrect reclassification of patients as having improved or worsened CKD, unnecessary tests and their associated adverse effects (e.g., from phlebotomy or renal biopsies), psychological effects of being labeled with progressive or regressed CKD, adverse events associated with pharmacological treatments initiated or changed following testing that indicates that CKD has

worsened or improved, and possible financial and insurance ramifications of a more advanced CKD diagnosis.

Table 6. Potential harms associated with monitoring patients with CKD stages 1–3 for worsening kidney function

A)	Psychological effects of monitoring tests
B)	Adverse physical effects of screening tests (e.g., phlebotomy-associated bruising)
C)	Incorrect reclassification of CKD severity
D)	Unnecessary tests and associated effects, e.g., phlebotomy-associated bruising; pain, bleeding with need for transfusion, and infection associated with renal biopsy
E)	Psychological effects associated with label of worse CKD stage and of further evaluations following diagnosis
F)	Increased visits to primary provider, increased referrals to specialists
G)	Adverse effects associated with increased treatment, possibly including worsened estimated GFR, hyperkalemia, hypotension, cough, hospitalization for AKI, cardiovascular morbidity, other
H)	increased difficulty obtaining/keeping health insurance coverage

Psychological Effects of Monitoring

We did not identify any studies that reported on the psychological effects of monitoring tests for CKD.

Adverse Physical Effects of Monitoring Tests and of Followup Tests To Further Evaluate Monitoring Tests

Phlebotomy required to measure serum creatinine may be associated with a small degree of bruising or discomfort. In a small number of patients, postscreening evaluation will include a renal biopsy, which has an associated risk of pain, bleeding, and infection.

Incorrect Reclassification of CKD Severity

We did not identify any studies that reported on the effects of testing that incorrectly reclassifies patients with CKD stage 1–3 as having worse or improved CKD, or even no CKD. Limitations in the precision of formulas that estimate GFR means there is a reasonable likelihood that any one test will suggest that a patient's CKD has changed or remained stable when this isn't the case. However, the small bias, in particular of the CKD-EPI formula, suggests that multiple GFR estimates will cluster accurately around true measured GFR. The high intra-individual variability of albuminuria in the absence of changes in underlying disease means there is at least a modest likelihood that findings of any one quantitative test will be inaccurate, whether it indicates that a patient's albuminuria is improving, stable, or worsening. As an example, in one study cited above, more than half of individuals with persistent microalbuminuria during a 2-year period regressed to normal over a subsequent 6-year evaluation period.[52]

Labeling of an Individual With More Advanced CKD Stage

We did not identify any studies that reported on the effects of labeling an individual with a more advanced CKD stage.

Increased Clinic Visits to Primary and/or Specialist Providers

We did not identify any studies that reported on the effect of CKD monitoring tests on subsequent patient visits to primary or specialist providers. However, individuals whose monitoring tests indicate progression of their CKD seem likely to be seen more frequently in primary and specialty clinics. These visits may be for further evaluation to confirm the abnormal

monitoring test, or providers may follow and treat these patients under the assumption that they have more severe CKD.

Adverse Effects Associated With Treatment

We systematically reviewed the RCT evidence on adverse effects of treatments of CKD patients in the Results section for Key Question 6.

Impact on Insurance Coverage

We did not identify any studies that reported the effects of being diagnosed with worsening CKD on obtaining or keeping health insurance coverage.

Key Question 5. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what direct evidence is there that treatment improves clinical outcomes?

and

Key Question 6. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what harms result from treatment?

ACE Inhibitor Monotherapy Versus Placebo/No Treatment Trials (n=17)

Overview

In patients with CKD, compared with placebo, we found moderate strength of evidence that ACEI treatment does not reduce risk of all-cause mortality more than placebo, and low strength of evidence that ACEI treatment does reduce risk of ESRD. Compared with placebo, ACEI treatment did not appear to reduce risk of MI or stroke, but significantly reduced risk of doubling serum creatinine and risk of progression from microalbuminuria to macroalbuminuria.

Description of Studies

Seventeen trials met all eligibility criteria and randomized participants with CKD (n=11,661, range 52 to 4,912) to an ACEI versus placebo (n=16 trials).[55,57-59,61-72] or no treatment (n=1 trial).[73] Two of the included reports were post hoc analyses performed within subsets of participants with CKD from larger trial populations that were not originally limited to subjects with CKD.[61,66] Detailed baseline characteristics are presented in Appendix Tables C1 and C2.

Among eligible trials, 7,537 participants were randomized to ramipril versus placebo (n=7 trials),[58,63,65,66,68,69,71] 1,757 to perindopril versus placebo (n=1 trial),[61] 864 to fosinopril versus placebo (n=1 trial),[62] 665 to captopril versus placebo (n=4 trials)[57,64,67,72] 583 to benazepril versus placebo (n=1 trial),[70] 108 to enalapril versus placebo (n=1 trial),[59] 97 to lisinopril versus placebo (n=1 trial),[55] and 52 to enalapril versus no treatment (n=1 trial).[73] The mean age of subjects was 60 years (range 33 to 70; n=16 trials), and men constituted 66 percent (range 35 to 82; n=15 trials) of all patients randomized. Among the five trials reporting ethnicity, the patients were mostly of white race (77 percent).[57,61,62,67,72] Most trials were conducted in Europe (including North Africa and Israel), three were conducted primarily or partially in the United

States, and two were conducted in Japan. Mean or median study duration ranged from 6 months to 5 years. Seven trials had a followup of 3 years or longer and 12 trials had a followup of at least 2 years. Only one trial had a study duration of less than 1 year.[71] One trial was conducted in a subset of individuals who previously had responded to an effort to screen all city residents aged 28 to 75 years for albuminuria.[62]

Renal Function

One of the two post hoc analyses restricted inclusion to participants with GFR <60 ml/min/1.73m^2, by definition CKD stage 3 or worse.[61] Otherwise, no trial based study eligibility on CKD stage or reported baseline distribution of participants by CKD stage. In 15 of 17 trials, participants were required to have albuminuria or proteinuria. In 10 of these trials, participants must have been microalbuminuric,[55,57-59,62,65-67,71,73] most commonly with a urinary albumin excretion rate of 20 to 200 µg/minute. In three of the 15 trials, they were required to have overt proteinuria, with minimum thresholds ranging from ≥500 mg/day,[72] to ≥1 but ≤3 g/day,[68] and to >3 g/day.[69] In the last two of the 15 trials, both microalbuminuric and macroalbuminuric participants were allowed,[63,64] with approximately three-quarters of the participants in one of these trials being microalbuminuric,[63] but no similar data reported for the other trial. Among the 15 trials requiring participants to have albuminuria or proteinuria, seven required that participants also have normal creatinine, creatinine clearance or GFR,[55,57,58,62,67,71,73] three allowed some participants with abnormal levels for these renal function measures but mandated a maximally abnormal limit,[63,66,72] and the remaining five trials did not specify an eligibility requirement with respect to these measures.[59,64,65,68,69] Finally, inclusion in two of 17 studies was based strictly on elevated serum creatinine, or reduced creatinine clearance or GFR.[61,70]

Among the 10 trials restricted to microalbuminuric patients, mean baseline urinary albumin excretion rate was reported as 61.0 µg/min (range 53 to 71.5) in five trials[55,57,58,67,71] and as 25.6 mg/24 hour (range 23 to 72) in two trials,[62,73] and mean urinary protein excretion rate was 133 mg/24 hours in one trial.[59] Among the three trials restricted to patients with overt proteinuria, mean urinary protein excretion was 3.0 g/day (range 1.7 to 5.3).[68,69,72] In the two trials that permitted inclusion of both microalbuminuric and macroalbuminuric patients, one reported mean baseline urinary albumin excretion rate of 711 mg/24 hours.[64] One of two trials that did not require albuminuria for inclusion nevertheless had an elevated mean baseline urinary protein excretion rate of 1.8 g/day,[70] while the other did not report baseline albuminuria or proteinuria.[61] In trials reporting, mean baseline serum creatinine was 1.0 mg/dL (range 0.8 to 2.4; n=10 trials),[55,57,59,62-64,68-70,72] mean creatinine clearance was 64.1 ml/min/1.73m^2 (range 43 to 114; n=8 trials),[55,57,64,68-70,72,73] and mean GFR was 68.5 ml/min/1.73m^2 (range 39 to 114; n=5 trials).[55,58,67-69]

Baseline Comorbidities

Twelve of 17 studies were restricted to patients with diabetes, including seven limited to those with type 1 diabetes,[55,57-59,64,65,72] four limited to those with type 2 diabetes,[63,67,71,73] and one analysis that was open to both types of diabetics.[66] Among the five trials that did not report restricting enrollment solely to diabetics,[61,62,68-70] two nevertheless excluded participants with type 1 diabetes,[69,70] and three reported no data on baseline prevalence of diabetes[68-70] Mean glycosylated hemoglobin was 8.2 percent (range 7.1 to 11.7, n=10 trials).[55,57-59,63-65,71-73]

Seven trials excluded participants with hypertension,[55,57-59,62,65,73] including five that mandated that blood pressure be controlled without antihypertensive medications.[57,58,62,73] Four

additional trials excluded participants only for severe hypertension.[68-71] In addition, though information on hypertension was not available for all participants from two studies, prevalence was at least 35 percent[71] and 53 percent[61] in these two trials. Prevalence of hypertension across all trials excluding these two with incomplete information was 49.8 percent (n=14 trials). Mean systolic and diastolic blood pressures at baseline were 144 mm Hg (range 126 to 149) and 83 mm Hg (range 74 to 92), respectively.

One trial reported data on prevalence of "cardiovascular disease," at 24 percent.[63] Another trial was comprised entirely of participants with a history of cerebrovascular disease, including 71 percent with ischemic stroke, 10 percent with hemorrhagic stroke, and 7 percent with a stroke of unknown type.[61] Prevalence of specific cardiovascular conditions was reported in few trials, including coronary artery disease (18.5 percent, range 0 to 20, n=2 trials),[57,61] myocardial infarction (5.1 percent, range 0 to 6, n=3 trials),[57,62,63] and stroke (3.5 percent, range 0.8 to 4; n=2 trials).[62,63] Participants with CHF were excluded from four trials,[57,62,63,66] and prevalence of CHF was not reported in other trials.

Study Quality (Appendix Table C140)

Among the 17 studies, five were rated good quality and 12 were rated fair quality. Allocation concealment was adequate in seven trials and unclear in the remaining studies. All 16 placebo-controlled trials were double blinded. Nine trials reported outcomes assessment by blinded adjudication committees. Analysis by intention-to-treat principle was reported in nine trials. All trials adequately described reasons for study withdrawal except for the two reports that were post hoc subgroup analyses from larger trials. Percentages of study withdrawals ranged from 7 to 32 percent, including nine trials with withdrawal rates greater than 20 percent.[55,57,58,62,64,68-70,72] No data were reported on withdrawals in the two studies that were post hoc analyses of CKD subsets from larger trial populations not limited to CKD.[61,66]

Results

Mortality (Table 7, Appendix Table C3, and Appendix Figure C1)

All-Cause Mortality

Patients with CKD randomized to ACEIs did not have a significantly reduced risk of all-cause mortality compared with those assigned placebo (RR 0.94, 95% CI, 0.80 to 1.12; n=16 trials, 11,536 patients). In two trials reporting, effect of ACEI versus placebo on mortality risk appeared similar in patients with and without CKD. In the HOPE trial,[66,74] relative risk of mortality was 0.77 [95% CI, 0.64 to 0.93] in patients with microalbuminuria and 0.90 [95% CI, 0.78 to 1.04] in patients without microalbuminuria (p=0.20 for interaction). In a second trial,[61] relative risk of mortality was 1.04 [95% CI, 0.83 to 1.31] in patients with creatinine clearance <60 ml/min and 0.84 [95% CI, 0.68 to 1.04] in patients with creatinine clearance ≥60 ml/min (p=0.1 for interaction).

Cardiovascular Mortality

Compared with placebo treatment, trial participants assigned to ACEIs also were not at lower risk for cardiovascular mortality (RR 1.03, 95% CI, 0.86 to 1.23).[61-63] Effect of treatment appeared similar in patients with and without CKD.[61]

Vascular Outcomes (Table 7, Appendix Tables C3-5, and Appendix Figure C1)

Myocardial Infarction

Compared with CKD patients randomized to placebo, risk for myocardial infarction was not significantly reduced in those assigned ACEI (2.4 versus 3.1 percent; RR=0.79, 95% CI 0.57 to 1.09; n=3 trials, 5,100 patients).[55,63,71]

Stroke

Compared with CKD patients randomized to placebo, those assigned to ACEI did not have a significant reduction in risk for stroke (6.0 versus 7.2 percent; RR=0.80, 95% CI, 0.52 to 1.23; n=4 trials, 7,719 patients).[61-63,68] However, there was evidence of substantial heterogeneity between the trials (I^2=68 percent). Two trials reported significant reductions in risk of stroke in ACEI patients compared with those assigned placebo (0.2 versus 2.3 percent; RR 0.10, 95% CI, 0.01 to 0.78; n=864 patients)[62] and (12.5 versus 17.6 percent; RR 0.71, 95% CI, 0.57 to 0.89; n=1,757 patients).[61] This latter trial, a post hoc analysis in patients with cerebrovascular disease, reported a similar relative reduction in stroke risk in patients with or without CKD.[61] A third trial reported no difference in risk of stroke between ACEI and placebo groups (4.8 versus 4.7 percent; RR 1.03, 95% CI, 0.80 to 1.32; n=4,912 patients),[63] while there was only one stroke in both treatment groups in the fourth trial.[68]

Other Vascular Outcomes

Seven trials reported a composite vascular endpoint (Appendix Table C5). Due to variability in these composite outcome definitions, results were not pooled between trials. Two of seven trials reported significant reductions in risk of their defined composite vascular outcome with ACEI treatment compared with placebo (Appendix Figure C1),[61,66] both of which further reported that this ACEI benefit was similar regardless of whether or not patients had microalbuminuria[56] or whether or not they had impaired creatinine clearance.[61] No trials reported a significant increase in risk of the composite vascular outcome in the ACEI group.

Renal Outcomes (Table 7, Appendix Tables C6 and C7, and Appendix Figure C1)

End-Stage Renal Disease

In CKD patients overall, ACEIs significantly reduced the risk of ESRD versus placebo (1.7 versus 2.6 percent; RR 0.65, 95% CI, 0.49 to 0.88; n=7 trials, 7,490 patients).[59,63,66,68-70,72]

Other Renal Outcomes

CKD patients assigned ACEI treatment had a significantly reduced risk compared with placebo for doubling of baseline serum creatinine (RR 0.60, 95% CI, 0.40 to 0.89; n=7 trials), and in progression from microalbuminuria to macroalbuminuria (RR 0.38, 95% CI, 0.18 to 0.84; n=7 trials). Three trials defined composite renal outcomes (Appendix Table C7), as doubling of serum creatinine or ESRD in one trial,[69] doubling of serum creatinine or need for dialysis in a second trial,[70] and as death, dialysis or renal transplantation in the third trial.[72] In each of these studies, participants randomized to ACEI were about half as likely to reach the composite outcome as participants assigned to placebo, a statistically significant finding in all three trials. In

the two trials in which doubling of serum creatinine was part of the composite renal outcome definition, it accounted for 21 percent[69] and 98 percent of the composite events,[70] respectively.

Study Withdrawals and Adverse Events (Appendix Table C8)

Overall study withdrawal rates were comparable in the ACEI and placebo groups, 17.3 percent versus 16.3 percent (RR 1.06, 95% CI, 0.96 to 1.17; 12 trials; n=7,336). Patients allocated to an ACEI were more likely to withdraw from treatment due to any or a serious adverse event than patients assigned placebo (20.7 percent versus 18.7 percent; RR 1.12, 95% CI, 1.02 to 1.23; 14 trials; n=7,055). Worsening renal insufficiency leading to study withdrawal was reported in three trials, with four events (0.8 percent) in the ACEI group compared with eight (1.7 percent) in the placebo group.[68-70] Specific adverse events were not often reported. Cough was the most commonly reported adverse event and was significantly more likely in the ACEI group compared with placebo (4.7 percent versus 1.8 percent; RR 2.33, 95% CI, 1.49 to 3.63; 10 trials; n=7,361). Hyperkalemia was not significantly increased with use of an ACEI (1.3 percent versus 0.9 percent; RR 1.08, 95% CI, 0.53 to 2.23; 8 trials; n=2,758).

Subgroup Results

Albuminuria or Impaired eGFR (Figures 5 and 6)

In trials restricted to patients with overt proteinuria at baseline, there was no significant difference in risk between those assigned ACEI versus placebo for all-cause mortality (RR 0.71, 95% CI, 0.33 to 1.54; n=3 trials, 761 patients). However, there was a significant 40 percent relative reduction in risk of ESRD (12.0 versus 20.7 percent; RR 0.60, 95% CI, 0.43 to 0.83; n=861 patients).[68,69,72] In trials restricted to patients with microalbuminuria, mortality risk was significantly reduced in the ACEI group versus placebo (9.3 versus 12.1 percent; RR 0.79, 95% CI, 0.66 to 0.96; n=3,440 patients), with similar results in the diabetic (RR 0.78, 95% CI, 0.61 to 1.00; n=1,140 patients) and nondiabetic (RR 0.75, 95% CI, 0.55 to 1.02; n=816 patients) microalbuminuria subgroups. However, there was no significant reduction in risk of ESRD between ACEI and placebo groups (0.8 versus 0.9 percent; RR 0.88, 95% CI, 0.27 to 2.88; n=1,234 patients).[59,66] In trials restricted to patients with microalbuminuria or worse, there was no significant difference between treatment groups in risk of ESRD (0.4 versus 0.5 percent; RR 0.93, 95% CI, 0.42 to 2.03; n=5,495 patients)[63,70] or mortality (RR 0.92, 95% CI, 0.74 to 1.15; n=9,192 patients). However, the two trials that together contributed more than 95 percent of the deaths for the ACEI versus placebo albuminuria subgroup analyses presented contrasting results, with a significant reduction in mortality risk in the HOPE trial[66,74] (15.7 versus 20.3 percent; RR 0.77, 95% CI, 0.64 to 0.93) but not the DIABHYCAR trial[63] (13.7 versus 13.1 percent; RR 1.04, 95% CI, 0.90 to 1.20). In the overall HOPE study population, 80 percent of participants had a history of coronary artery disease, including 52 percent with a history of MI, and 38 percent had diabetes, though comorbidity data were not reported for the subset with CKD. HOPE study participants were randomized to ramipril 10 mg per day versus placebo, and those with CKD were defined as having microalbuminuria. In the DIABHYCAR trial, prevalence of cardiovascular disease was lower at 24 percent, with only 6 percent having a history of MI, and 100 percent had diabetes. Participants were randomized to ramipril 1.25 mg per day versus placebo. Those with CKD were defined as having either microalbuminuria or macroalbuminuria. In results from two trials restricted to patients with impaired eGFR, there was no significant difference between treatments in risk of mortality (RR 2.14, 95% CI, 0.34 to 13.39).

Diabetes

In 12 trials restricted to patients with diabetes, there was no significantly reduced risk with ACEI versus placebo for mortality (RR 0.91, 95% CI, 0.70 to 1.18, n=11 trials), ESRD (RR 0.73, 95% CI 0.48 to 1.10, n=4 trials), MI, stroke, or doubling of serum creatinine (RR 0.69, 95% CI, 0.44 to 1.09, n=5 trials). With respect to mortality risk, results appeared clinically heterogeneous between diabetic participants from the HOPE trial[66,74] (16.3 versus 20.8 percent; RR 0.78, 95% CI, 0.61 to 1.00) and those from the DIABHYCAR trial[63] (13.7 versus 13.1 percent; RR 1.04, 95% CI, 0.90 to 1.20). In contrast, diabetic participants randomized to ACEI had a significant reduction in risk of conversion from microalbuminuria to macroalbuminuria (RR 0.38, 95% CI, 0.18 to 0.84, n=7 trials). In four trials reporting a composite vascular outcome, risk was significantly reduced in the ACEI group in one trial.[66,74]

Hypertension

No trials were restricted to patients with hypertension, but in seven trials that excluded patients with hypertension, there was a significantly reduced risk of stroke (RR 0.10, 95% CI, 0.01 to 0.78, n=1 trial), doubling of serum creatinine (RR 0.15, 95% CI, 0.04 to 0.65), and conversion from microalbuminuria to macroalbuminuria (RR 0.29, 95% CI, 0.13 to 0.64), but no significant treatment group difference in mortality (RR 1.87, 95% CI, 0.65 to 5.37; n=7 trials, 1,454 patients) or other clinical vascular outcomes.

Congestive Heart Failure

No trials were restricted to patients with CHF, but in four trials that excluded patients with CHF, there was no significant difference between ACEI and placebo treatment groups in risk of mortality (RR 1.07, 95% CI, 0.52 to 2.18; n=4 trials, 1,192 patients), ESRD, or any other vascular or renal outcome.

Cerebrovascular Disease

In one trial restricted to patients with a history of cerebrovascular disease, risk of stroke was significantly reduced with ACEI versus placebo (RR 0.71, 95% CI, 0.57 to 0.89).However, there was no significant difference in risk of mortality (RR 1.07, 95% CI, 0.87 to 1.32), and no other vascular or renal outcomes were reported. Otherwise, no trials were limited to or excluded participants with cardiovascular disease.

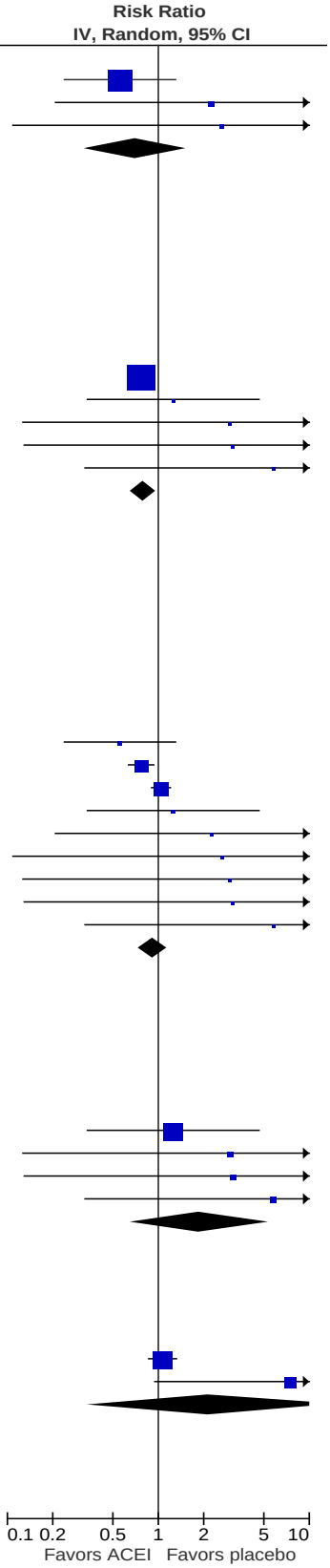
Summary

In patients with CKD stages 1–3, compared with placebo, ACEI monotherapy did not significantly reduce risk of all-cause mortality in results overall. However, results appeared discordant between the two trials that together reported nearly all the deaths. In a study comprised of patients with microalbuminuria, and a high prevalence of cardiovascular disease who were treated with ramipril 10 mg per day versus placebo, mortality risk was significantly reduced. Results were similar in study subsets with and without diabetes. In a study comprised of patients with diabetes, microalbuminuria or macroalbuminuria, and a low prevalence of cardiovascular disease who were treated with ramipril 1.25 mg per day versus placebo, mortality was not significantly reduced. Because the latter trial appeared to be comprised of participants at only slightly lower absolute mortality risk and had a large total number of deaths, the difference between ramipril treatment doses seems the most likely explanation for the difference in outcomes. There was no significant difference between ACEI and placebo in risk of cardiovascular mortality, or MI. Overall, there was no significant reduction in risk of stroke,

though results appeared heterogeneous between trials, with two moderate-sized trials reporting a significant reduction in stroke risk and another one finding no difference. Two of seven trials reporting found a significantly reduced risk in a composite vascular outcome in participants randomized to ACEI. Overall, subjects assigned to ACEIs had a significant 35 percent reduction in risk of ESRD compared with patients assigned to placebo. This risk reduction appeared restricted to studies that enrolled only patients with overt proteinuria. CKD patients assigned to ACEIs had a significant 40 percent reduction in risk of doubling serum creatinine, 62 percent reduction in risk of converting from microalbuminuria to macroalbuminuria, and approximately 50 percent reductions in all composite renal outcomes reported. Overall study withdrawals were not significantly different between ACEI and placebo groups. ACEIs increased risk of cough, but there was little apparent difference from placebo subjects in hyperkalemia. Results were limited in that few trials were of sufficient size to assess mortality or clinical vascular outcomes.

Figure 5. ACEI versus placebo: All-cause mortality by albuminuria subgroups

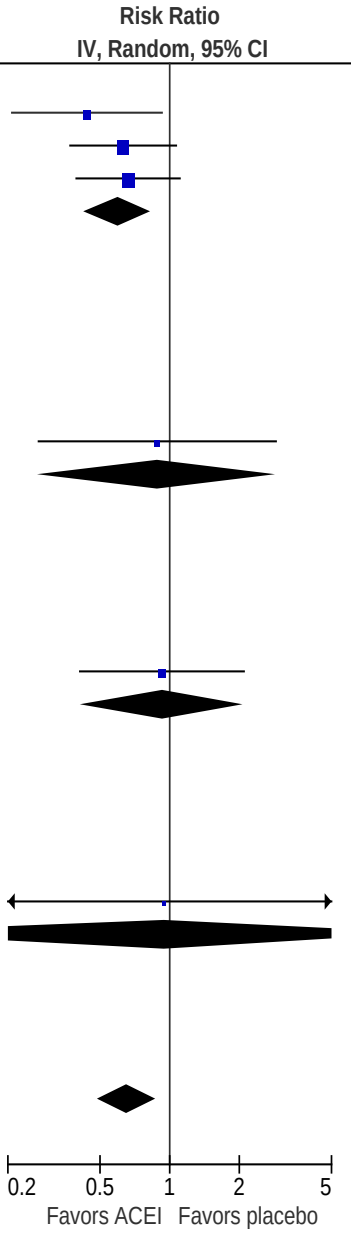
Study or Subgroup	ACE Inhibitor Events	ACE Inhibitor Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
17.1.1 Limited inclusion to macroalbuminuria						
Lewis 1993	8	207	14	202	83.5%	0.56 [0.24, 1.30]
REIN Stratum-2 1997	2	78	1	88	10.6%	2.26 [0.21, 24.41]
REIN Stratum-1 1999	1	99	0	87	5.9%	2.64 [0.11, 63.98]
Subtotal (95% CI)		**384**		**377**	**100.0%**	**0.71 [0.33, 1.54]**
Total events	11		15			
Heterogeneity: Tau² = 0.00; Chi² = 1.87, df = 2 (P = 0.39); I² = 0%						
Test for overall effect: Z = 0.87 (P = 0.38)						
17.1.2 Limited inclusion to microalbuminuria						
Bojestig 2001	0	37	0	18		Not estimable
Crepaldi 1998	0	32	0	34		Not estimable
Ravid 1993	0	49	0	45		Not estimable
Muirhead 1999	0	29	0	31		Not estimable
Gerstein (HOPE) 2001	149	952	204	1004	96.8%	0.77 [0.64, 0.93]
Asselbergs (PREVEND) 2004	5	431	4	433	2.1%	1.26 [0.34, 4.64]
Sano 1994	1	31	0	31	0.4%	3.00 [0.13, 70.92]
Laffel 1995	1	70	0	73	0.4%	3.13 [0.13, 75.49]
O'Hare (ATLANTIS) 2000	5	92	0	48	0.4%	5.80 [0.33, 102.66]
Subtotal (95% CI)		**1723**		**1717**	**100.0%**	**0.79 [0.66, 0.96]**
Total events	161		208			
Heterogeneity: Tau² = 0.00; Chi² = 3.80, df = 4 (P = 0.43); I² = 0%						
Test for overall effect: Z = 2.42 (P = 0.02)						
17.1.3 Limited inclusion to albuminuria						
Crepaldi 1998	0	32	0	34		Not estimable
Katayama 2002	0	52	0	27		Not estimable
Bojestig 2001	0	37	0	18		Not estimable
Muirhead 1999	0	29	0	31		Not estimable
Ravid 1993	0	49	0	45		Not estimable
Lewis 1993	8	207	14	202	6.2%	0.56 [0.24, 1.30]
Gerstein (HOPE) 2001	149	952	204	1004	40.8%	0.77 [0.64, 0.93]
Marre (DIABHYCAR) 2004	334	2443	324	2469	47.2%	1.04 [0.90, 1.20]
Asselbergs (PREVEND) 2004	5	431	4	433	2.8%	1.26 [0.34, 4.64]
REIN Stratum-2 1997	2	78	1	88	0.9%	2.26 [0.21, 24.41]
REIN Stratum-1 1999	1	99	0	87	0.5%	2.64 [0.11, 63.98]
Sano 1994	1	31	0	31	0.5%	3.00 [0.13, 70.92]
Laffel 1995	1	70	0	73	0.5%	3.13 [0.13, 75.49]
O'Hare (ATLANTIS) 2000	5	92	0	48	0.6%	5.80 [0.33, 102.66]
Subtotal (95% CI)		**4602**		**4590**	**100.0%**	**0.92 [0.74, 1.15]**
Total events	506		547			
Heterogeneity: Tau² = 0.02; Chi² = 11.33, df = 8 (P = 0.18); I² = 29%						
Test for overall effect: Z = 0.74 (P = 0.46)						
17.1.4 Limited inclusion to albuminuria and normal GFR/creatinine clearance [CKD stages 1-2]						
Muirhead 1999	0	29	0	31		Not estimable
Crepaldi 1998	0	32	0	34		Not estimable
Asselbergs (PREVEND) 2004	5	431	4	433	64.6%	1.26 [0.34, 4.64]
Sano 1994	1	31	0	31	11.1%	3.00 [0.13, 70.92]
Laffel 1995	1	70	0	73	10.9%	3.13 [0.13, 75.49]
O'Hare (ATLANTIS) 2000	5	92	0	48	13.4%	5.80 [0.33, 102.66]
Subtotal (95% CI)		**685**		**650**	**100.0%**	**1.87 [0.65, 5.37]**
Total events	12		4			
Heterogeneity: Tau² = 0.00; Chi² = 1.14, df = 3 (P = 0.77); I² = 0%						
Test for overall effect: Z = 1.17 (P = 0.24)						
17.1.5 Limited inclusion to impaired GFR/creatinine clearance						
Perkovic (PROGRESS) 2007	153	895	138	862	64.5%	1.07 [0.87, 1.32]
Maschio 1996	8	300	1	283	35.5%	7.55 [0.95, 59.96]
Subtotal (95% CI)		**1195**		**1145**	**100.0%**	**2.14 [0.34, 13.39]**
Total events	161		139			
Heterogeneity: Tau² = 1.35; Chi² = 3.39, df = 1 (P = 0.07); I² = 70%						
Test for overall effect: Z = 0.81 (P = 0.42)						



Test for subgroup differences: Chi² = 4.35, df = 4 (P = 0.36), I² = 8.1%

Figure 6. ACEI versus placebo: End-stage renal disease by albuminuria subgroups

Study or Subgroup	ACE Inhibitor Events	ACE Inhibitor Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
17.18.1 Macroalbuminuria at baseline						
REIN Stratum-1 1999	9	99	18	87	15.6%	0.44 [0.21, 0.93]
Lewis 1993	20	207	31	202	31.2%	0.63 [0.37, 1.07]
REIN Stratum-2 1997	17	78	29	88	32.7%	0.66 [0.40, 1.11]
Subtotal (95% CI)		**384**		**377**	**79.6%**	**0.60 [0.43, 0.83]**
Total events	46		78			
Heterogeneity: Tau² = 0.00; Chi² = 0.84, df = 2 (P = 0.66); I² = 0%						
Test for overall effect: Z = 3.04 (P = 0.002)						
17.18.2 Microalbuminuria at baseline						
Ravid 1993	0	49	0	45		Not estimable
Micro-HOPE 2001	5	553	6	587	6.2%	0.88 [0.27, 2.88]
Subtotal (95% CI)		**602**		**632**	**6.2%**	**0.88 [0.27, 2.88]**
Total events	5		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.20 (P = 0.84)						
17.18.3 Mixed micro- and macroalbuminuria at baseline						
Marre (DIABHYCAR) 2004	11	2443	12	2469	13.1%	0.93 [0.41, 2.10]
Subtotal (95% CI)		**2443**		**2469**	**13.1%**	**0.93 [0.41, 2.10]**
Total events	11		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.18 (P = 0.85)						
17.18.4 Impaired GFR and no albuminuria at baseline						
Maschio 1996	1	300	1	283	1.1%	0.94 [0.06, 15.01]
Subtotal (95% CI)		**300**		**283**	**1.1%**	**0.94 [0.06, 15.01]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.04 (P = 0.97)						
Total (95% CI)		**3729**		**3761**	**100.0%**	**0.65 [0.49, 0.88]**
Total events	63		97			
Heterogeneity: Tau² = 0.00; Chi² = 2.13, df = 5 (P = 0.83); I² = 0%						
Test for overall effect: Z = 2.83 (P = 0.005)						
Test for subgroup differences: Chi² = 1.29, df = 3 (P = 0.73), I² = 0%						



ACE Inhibitor Monotherapy Versus ARB Monotherapy Trials (n=6)

Overview

In patients with CKD, we found low strength of evidence suggesting that there is no difference between ACEI and ARB treatment for the outcome of all-cause mortality. We found insufficient evidence regarding whether there is a difference between these treatments for ESRD.

Description of Studies

Six trials met all eligibility criteria and randomized participants (n=4,799, range 90 to 4,046) to ACEI monotherapy versus ARB monotherapy.[67,75-79] Detailed baseline characteristics are presented in Appendix Tables C1 and C2.

Among eligible trials, 4,046 participants were randomized to ramipril versus ARB (n=1 trial), 353 were randomized to enalapril versus ARB (n=2 trials), 309 were randomized to lisinopril versus ARB (n=2 trials), 91 were randomized to captopril versus ARB (n=1 trial), 4,515 were randomized to telmisartan versus ACEI (n=3 trials), 181 were randomized to valsartan versus ACEI (n=2 trials), and 103 were randomized to losartan versus ACEI (n=1 trial). While five of the six trials maintained the ACEI versus ARB comparison throughout the entire treatment period, in a single partial crossover trial, after 24 weeks patients initially assigned to ACEI were randomized to ACEI plus ARB versus continued ACEI monotherapy, and patients initially assigned to ARB monotherapy were randomized to ARB plus ACEI versus continued ARB monotherapy.[77] By far the largest study, comparing ramipril versus telmisartan, was a post hoc analysis performed within the subset of ONTARGET trial participants with CKD (n=4,046 out of 25,620).[75] The mean age of subjects was 59 years (range 56 to 61; n=5 trials) and men constituted 62 percent (range 37 to 81; n=5 trials) of all patients evaluated. The ethnicity of patients in the three trials reporting was nearly all white race (96 percent).[67,78,79] Two trials were conducted exclusively in Canada, two exclusively in Europe, one in Turkey, and one trial included sites in the United States, Canada, and Europe, as well as Asia, Africa, and Australia. Mean or median study duration was 1 year in three trials, 2.5 years in one trial, and about 5 years in two trials.

Renal Function

The single post hoc analysis restricted inclusion to participants with GFR <60 ml/min/1.73m^2, by definition CKD stage 3 or worse,[75] and a second trial required participants to have microalbuminuria and a GFR $\geq$60 ml/min/1.73m^2, by definition CKD stages 1–2.[67] Otherwise, no trial based study eligibility on CKD stage and no trial reported baseline distribution of participants by CKD stage. Among the six trials, five required participants to be albuminuric, including four restricted to patients with microalbuminuria,[67,76,77,79] and one that allowed subjects to have either microalbuminuria or macroalbuminuria.[78] Among the five trials requiring participants to have albuminuria, two required that they also have normal creatinine or GFR,[67,78] and three allowed some participants with abnormal levels for these renal function measures but mandated a maximally abnormal limit.[76,77,79] One trial determined eligibility based only on impaired GFR.[75] Within trials, measures of baseline renal function were inconsistently reported. The ONTARGET post hoc analysis reported no data on baseline renal function in its CKD population.[75] In other trials, the most commonly reported measure was urinary albumin excretion rate (UAER), with mean UAER 62 μg/min in two trials[67,79] and 260 mg/24 hours in one trial,[77] and median UAER 46 μg/min (ACEI treatment arm) to 60 μg/min (ARB treatment arm) in one trial.[78] The mean GFR was 92 ml/min/1.73 m^2 (range 91 to 96, n=3 trials).[67,78,79] In two trials, mean baseline serum creatinine was 1.0 mg/dL in both trials.[77,78] Mean creatinine clearance was 101 ml/min/1.73 m^2 (range 97 to 112, n=2 trials).[76,77]

Baseline Comorbidities

The study within the subset of ONTARGET participants with impaired GFR did not report any data on their baseline characteristics,[75] though the main study required subjects to have established atherosclerotic vascular disease or diabetes associated with end-organ damage. In the main study, prevalence of comorbidities included diabetes 37.3 percent, hypertension 68.3 percent, and MI 48.7 percent.[80] Within the five other trials, prevalence of diabetes was 97 percent, including four trials comprised entirely of subjects with type 2 diabetes[67,77-79] and another that excluded type 1 diabetics and had a prevalence of type 2 diabetes of 74 percent.[76] Nearly all study participants were hypertensive at baseline (94 percent; range 33 to 100), including four trials that enrolled only patients with hypertension.[76-79] Five trials excluded patients with severe hypertension,[75-79] and mean baseline systolic and diastolic blood pressure measurements were 151 and 87 mm Hg, respectively. Nearly half the enrollees from one trial had cardiovascular disease,[78] a history of non-MI cardiac disorder was reported in 19 percent of subjects in another trial,[76] and two trials excluded participants with CHF.[76,79] Otherwise, studies reported no data on baseline cardiovascular disease.

Study Quality (Appendix Table C140)

Among the six trials, two were rated good quality and four were rated fair quality. Allocation concealment was adequate in three trials[75,76,78] and unclear in the remaining trials. All trials were double blinded except one open-label study.[77] Analysis by the intention-to-treat principle was reported in two trials.[75,78] All trials adequately described reasons for study withdrawals. No data on study withdrawals were reported in one trial.[75] Otherwise, withdrawals were 33 percent in one trial,[78] and ranged between 11 and 14 percent in the other trials.

Results

Mortality (Table 7, Appendix Table C3, and Appendix Figure C1)

All-Cause Mortality

There were few deaths in trials reporting this outcome. Between CKD patients assigned to ACEI versus those assigned to ARB, there was no significant difference in risk of all-cause mortality (2.7 versus 2.2 percent; RR 1.04, 95% CI, 0.37 to 2.95; n=4 trials, 534 patients). Due to wide confidence intervals around this estimate, results are unable to exclude a meaningful advantage for either ACEI or ARB for this outcome.

Cardiovascular Mortality

There were few deaths in trials reporting this outcome. Between CKD patients assigned to ACEI versus those assigned to ARB, there was no significant difference in risk of cardiovascular mortality (1.2 versus 1.0 percent; RR 0.88, 95% CI, 0.19 to 4.13; n=4 trials, 534 patients). Due to wide confidence intervals around this estimate, results are unable to exclude a meaningful advantage for either ACEI or ARB for this outcome.

Vascular Outcomes (Table 7, Appendix Tables C3 and C4, and Appendix Figure C1)

Only two trials reported data for cardiovascular outcomes, one of which reported no events.[79] In the other small trial, there were relatively few events.[78]

Myocardial Infarction

There was a nonsignificant 38 percent lower risk of MI in the group of CKD patients receiving ACEI compared with the group receiving ARB (3 versus 5.2 percent for MI; RR 0.62, 95% CI, 0.23 to 1.68; n=353 patients).

Stroke

No studies of ACEI versus ARB in CKD patients reported results for stroke.

Other Vascular Outcomes

For patients with CKD, there was a 28 percent lower risk of CHF with ACEI compared with ARB but the result was not significant (3.9 versus 5.2 percent for CHF; RR 0.72, 95% CI, 0.28 to 1.87; n=353 patients). No studies of ACEI versus ARB in CKD patients reported results for composite cardiovascular events.

Renal Outcomes (Appendix Table C6)

End-Stage Renal Disease

None of the trials reported data for ESRD.

Other Renal Outcomes

None of the trials reported data for doubling of serum creatinine as an individual endpoint. With regard to progression from microalbuminuria to macroalbuminuria, though this outcome was reported in the ONTARGET trial, results for the number of participants with baseline microalbuminuria were inconsistent throughout the paper, could not be verified, and could not be incorporated in a pooled analysis. In the only other trial that reported this outcome, it occurred in only two participants.[67] The ONTARGET trial reported results for a composite renal outcome, defined as first occurrence of either dialysis, renal transplantation, doubling of baseline serum creatinine, or death.[75] Based on graphical display of the data (risk ratios and number of events in each treatment arm were not reported), there appeared to be no significant difference between ACEI and ARB for reaching this endpoint in either the ONTARGET subgroup with GFR <60 ml/min/1.73m^2 or the subgroup with baseline microalbuminuria.[75] Further, that the relative reduction in risk of the composite renal outcome between treatment groups in ONTARGET was not significantly different in the CKD subgroup than in ONTARGET participants without CKD (p for interaction 0.84).

Study Withdrawals and Adverse Events (Appendix Table C8)

Overall study withdrawal rates were comparable in the ACEI and ARB groups, 20.2 percent versus 18.1 percent (RR 1.07, 95% CI, 0.80 to 1.42; 5 trials; n=753). Though patients assigned ACEI treatment appeared possibly more likely to withdraw from a study due to an adverse event compared with ARB treatment, 14.4 percent versus 9.7 percent (4 trials, n=534), respectively, this difference was not statistically significant. Renal adverse events were rarely reported. Laboratory abnormalities led to four study discontinuations in the DETAIL trial, two cases of raised serum creatinine levels (both < 2.3mg/dL) in both the ACEI and ARB arms.[78] One subject receiving an ARB in the Muirhead study was withdrawn from treatment due to a decreased GFR and creatinine clearance.[67] Cough was the most commonly reported specific adverse event, and was significantly more likely in participants assigned to ACEI treatment compared with those

allocated to ARB treatment (4.7 percent versus 1.8 percent; RR 4.10, 95% CI, 1.47 to 11.48; 3 trials; n=284).

Summary

In trials comparing ACEI and ARB treatments individuals with CKD, there were very few vascular events reported, based on which there was no significant difference between treatments for the outcomes of all-cause mortality, cardiovascular mortality, MI, or CHF. No data were reported for stroke, ESRD, or any composite vascular outcome. Results from the CKD subset of the ONTARGET study population, whether defined by GFR <60 ml/min/1.73m^2 or by albuminuria, appeared to show no difference in the risk of the composite renal outcome of doubling creatinine, dialysis, renal transplant, or death. Results were limited by small sample sizes in all but one trial, and by the small number of events among trials reporting them. Because no trial provided followup beyond 5 years, longer term effects of ACEI monotherapy versus ARB monotherapy in CKD patients could not be determined from these trials. Overall study withdrawals were not significantly different between ACEI and ARB treatment groups, though cough was significantly more likely in participants assigned to ACEI.

ACE Inhibitor Monotherapy Versus CCB Monotherapy Trials (n=6)

Overview

In comparing ACEI versus CCB for treatment of patients with CKD, we found low strength of evidence, suggesting that there was no difference in risk of all-cause mortality or ESRD. We found no significant difference between treatment groups in risk of cardiovascular mortality, stroke, or halving of GFR.

Description of Studies

Six trials met all eligibility criteria and randomized participants (n=4,357, range 88 to 3,049) to ACEI monotherapy versus CCB monotherapy.[55,81-88] Baseline characteristics are presented in Appendix Tables C1 and C2.

Among eligible trials, 3,137 participants were randomized to lisinopril versus CCB (n=2 trials), 653 were randomized to ramipril versus CCB (n=1 trial), 446 were randomized to fosinopril versus CCB (n=2 trials), 121 were randomized to captopril versus CCB (n=1 trial), 3,907 were randomized to amlodipine versus ACEI (n=3 trials), and 450 were randomized to nifedipine versus ACEI (n=3 trials). By far the largest eligible study was a post hoc analysis performed in the subset of 3,049 individuals with GFR <60 ml/min/ 1.73m^2 from the larger Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) (N= 42,418).[81-83] In the AASK trial, designed as a 3x2 factorial study, besides randomizing 653 participants to ACEI versus CCB, an additional 441 were randomized to beta blocker, and all participants also were randomized to one of two blood pressure target groups.[89,90] The CCB treatment arm was stopped early by recommendation of the data and safety monitoring board, with patients switched to open label medication. The mean age of study participants was 66 years (range 37 to 71; n=6 trials) and men constituted 51 percent (range 48 to 69) of all subjects studied. In the two trials that reported race/ethnicity,[81-83,85] 48 percent of participants were white and 38 percent were African American, including one trial comprised entirely of African American participants.[85] Two trials were conducted primarily in the United States,[81-83,85] three

trials were conducted in Italy, and one was performed in Spain. Mean or median study duration ranged from 3 to approximately 5 years.

Renal Function

The single post hoc analysis restricted inclusion to participants with GFR <60 ml/min/1.73m^2, by definition CKD stage 3 or worse,[81] and a second trial required participants to have microalbuminuria and a GFR ≥80 ml/min/1.73m^2, by definition CKD stages 1-2.[55] Otherwise, no trial based study eligibility on CKD stage and no trial reported baseline distribution of participants by CKD stage. Among the six trials, two required that participants have microalbuminuria to be included,[55,84] while four determined eligibility based only on impaired creatinine or GFR.[81-83,85-88] Within included participants, there was no single measure of renal function or damage that was reported in every trial. The most commonly reported measure of baseline renal function was serum creatinine, with a mean of 2 mg/dL (range 0.96 to 2.8, n=5 trials)[55,84-88] The mean baseline GFR, reported in three trials, was 50 ml/min/1.73m2 (range 46 to 120),[55,81-83,85] and the mean baseline creatinine clearance concentration was 66 ml/min/1.73m^2 (range 36 to 109, n=3 trials).[55,84,86] Mean proteinuria was 0.94 gm/24 hours (range 1.7 to 1.8, n=3 trials),[85-88] and mean urinary albumin excretion rate was 89 μg/min (range 61 to 97, n=2 trials).[55,84]

Baseline Comorbidities

Thirty percent of study participants had diabetes, which included two trials that restricted enrollment to participants with diabetes[55,84] and three trials that excluded patients with diabetes.[85-88] In two trials reporting data, mean baseline hemoglobin A_{1c} was 7.2.[55,84] Ninety-nine percent of study participants had hypertension, which included five trials that restricted enrollment to participants with hypertension and one small trial that excluded patients with hypertension.[55] Mean baseline systolic and diastolic blood pressure measurements were 149 and 87 mm Hg, respectively. One trial excluded any participants with a history of coronary artery disease,[84] three excluded participants with either recent[55,86] or severe[87,88] cardiovascular events but provided no data on past history of coronary artery disease, while the remaining two trials reported that 29 percent[81-83] and 52 percent[85] of randomized participants, respectively, had a history of coronary artery disease.

Study Quality (Appendix Table C140)

Among the six trials, two were rated good quality and four were rated fair quality. Allocation concealment was adequate in three of six trials and three trials were double blinded. Analysis by the intention-to-treat principle was reported in four trials[81-83,85-88] All trials, except the single post hoc analysis, adequately described reasons for study withdrawal. Withdrawals across studies ranged from 0 to 37 percent.

Results

Mortality (Table 7, Appendix Table C3, and Appendix Figure C1)

All-Cause Mortality

Risk of all-cause mortality, reported in five studies, was not significantly different in individuals with CKD randomized to ACEI treatment compared with those allocated to CCB

therapy (5.4 versus 6.2 percent; RR 0.75, 95% CI, 0.48 to 1.16; n=1,307). The estimate of effect was driven primarily by data from the AASK trial, which accounted for 75 percent of the weight and deaths.[85,91] All-cause mortality data for the largest study, ALLHAT, was not available.

Cardiovascular Mortality

Cardiovascular mortality was reported in three trials totaling 1,014 patients,[85-88,91] including one small 3-year trial not designed to evaluate the effect of therapy on clinical outcomes. As with all-cause mortality, risk of cardiovascular mortality was not significantly different in individuals with CKD randomized to ACEI treatment compared with those allocated to CCB therapy (RR 0.75, 95% CI, 0.36 to 1.57), and the estimate of effect again was driven primarily by data from the AASK trial.

Vascular Outcomes (Table 7, Appendix Tables C3–C5, and Appendix Figure C1)

Myocardial Infarction

Myocardial infarction was reported in only one small trial (n=64 participants).[55] In this trial, there were no myocardial infarctions in either treatment group; therefore, the relative risk for this outcome between CKD patients randomized to ACEI versus CCB treatment could not be determined.

Stroke

Risk of stroke, reported in three trials,[82,83,86,91] was not significantly different between CKD patients assigned an ACEI versus CCB treatment (RR 1.00, 95% CI, 0.78 to 1.28; n=3,943 participants). This estimate was driven mainly by the ALLHAT study, which comprised 88 percent of the weight. There was a 27 percent increased relative risk for stroke in the ACEI group in the AASK trial but this was not statistically significant.[91]

Other Vascular Outcomes

Based on pooled data from two studies, there was no apparent difference in risk for CHF between CKD patients allocated to ACEI versus CCB treatment (RR 1.09, 95% CI, 0.91 to 1.32).[82,91] Two trials reported data on one or more composite cardiovascular outcomes (Appendix Table C5), which, because of their different components, were not pooled.[82,91] There was no statistically significant difference between ACEI and CCB treatment in CKD patients for any composite cardiovascular outcome in any trial. The ALLHAT trial performed additional analyses of clinical outcomes among CKD patients with diabetes.[82] In this subgroup, there was no statistically significant difference between treatment groups in risk of stroke, CHF, or either of two composite vascular endpoints.

Renal Outcomes (Table 7, Appendix Tables C6 and C7, and Appendix Figure C1)

End-Stage Renal Disease

Overall risk of ESRD, reported in three trials, was not significantly different between CKD patients randomized to ACEI versus CCB treatment (RR 0.89, 95% CI, 0.66 to 1.21; n=3,823 patients).[81,85,87,88,90] However, there was evidence of low heterogeneity (I^2=29 percent), with results suggesting benefit in those assigned to ACEI treatment versus CCB treatment in the

AASK (RR 0.86, 95% CI, 0.59 to 1.25) and Zucchelli (RR 0.51, 95% CI, 0.22 to 1.17) studies, respectively, but not in the ALLHAT study (RR 1.06, 95% CI, 0.77 to 1.48), with none of the results from the individual trials achieving statistical significance. Of note, the definitions of ESRD varied slightly between these studies, defined as death due to kidney disease, kidney transplantation, or start of long-term renal dialysis in the ALLHAT study; as need for renal replacement therapy in the AASK study; and as need for dialysis (creatinine clearance below 4 ml/minute) in the Zucchelli study.

Other Renal Outcomes

Overall risk of 50 percent or greater decline in GFR, reported in two trials, was not significantly different between CKD patients randomized to ACEI treatment versus CCB treatment (RR 1.02, 95% CI, 0.55 to 1.91, n=3,702).[81,85] However, there was evidence of substantial heterogeneity (I^2=71 percent), and though differences were not statistically significant in either trial, results from the AASK trial appeared to favor ACEI treatment (10.1 percent versus 13.4 percent), while results from the ALLHAT trial appeared worse in the ACEI group (2.3 percent versus 1.6 percent).

Three trials reported data on composite renal outcomes, which, because of their different components, detailed in Appendix Table C7, were not pooled.[81,86,91] In the AASK trial, in which the composite renal outcome included ESRD (i.e., need for renal replacement therapy), death, or reduction from baseline GFR by 50 percent or by 25 mL/min/1.73m^2, CKD patients randomized to ACEI treatment had a nonsignificantly lower risk of this composite outcome than those assigned to CCB treatment (20 versus 26 percent, RR 0.77, 95% CI, 0.58 to 1.04).[85] Approximately half of these incident renal events were attributed to halving of GFR (73 of 143 composite events). In the ALLHAT trial, in which the composite renal outcome included ESRD (death due to kidney disease, dialysis, or renal transplantation), reduction in GFR by 50 percent or by 25 mL/min/1.73 m^2, but did not include all-cause death, the risk of a composite renal event was similar in both treatment groups (7 versus 6 percent, RR 1.16, 95% CI, 0.89 to 1.53).[81] Approximately one-third of these incident renal events appeared to be attributed to halving of GFR. In the ESPIRAL trial, in which the composite renal outcome included need for dialysis or doubling of serum creatinine, the risk of a composite renal event was significantly lower in CKD patients allocated to ACEI versus CCB treatment (RR 0.59, 95% CI, 0.39 to 0.89).[86] In this trial, it was not reported what proportion of incident cases were due to doubling of serum creatinine.

The ALLHAT trial performed additional analyses of renal outcomes among CKD patients with diabetes and reported that there were no statistically significant differences in risk of ESRD or the above described composite renal outcome between treatment groups[82]

Study Withdrawals and Adverse Events (Appendix Table C8)

CKD patients randomized to treatment with an ACEI were no more likely to withdraw from treatment (13.3 versus 18.4 percent, p=0.81) or withdraw from treatment due to an adverse event (3.2 versus 4.7 percent, p=0.77) compared with patients assigned to treatment with a CCB. No patient in the AASK trial was reported to have withdrawn from treatment or was lost to followup.[89,90] No study withdrawal or adverse event data were reported for the ALLHAT CKD subgroup.[81-83]

In the AASK trial, adverse events were reported as percentage per patient year. Compared with study participants randomized to CCB, those assigned to ACEI had a significantly higher rate of cough (55 versus 46 percent), angioedema (6 versus 2 percent), and syncope (7 versus 2 percent).[89,90] In contrast, edema was significantly more frequent in the CCB group compared

with the ACEI group, 60 versus 46 percent. Hyperkalemia was reported for three ACEI group patients and none in the CCB group. In the ESPIRAL trial, withdrawals due to adverse events occurred in small numbers of CKD patients in both groups, for cough (n=3 in the ACEI group versus n=0 in the CCB group), hyperkalemia (n=6 versus n=0), edema (n=1 versus n=10), and impaired renal function (n=4 versus n=1).[86] In the study by Zucchelli, cough led to study withdrawal in two ACEI patients and severe edema led to study withdrawal in three CCB patients.[87] In the trial by Fogari, two subjects each in the ACEI and CCB groups were withdrawn from treatment due to worsening kidney function.[84]

Summary

In patients with CKD, there was no apparent difference between treatment with ACEI monotherapy and CCB monotherapy for the outcomes of all-cause mortality, cardiovascular mortality, stroke, CHF, any composite vascular endpoint, or ESRD. Relative risk of MI could not be determined. While results for the composite renal outcome indicated significant benefit for ACEI treatment compared with CCB in one trial,[86] there was no between-treatment group difference in the composite renal endpoints reported in two other trials.[81-83,85] Results were limited in that several studies were not designed for and reported no clinical outcomes data, and the modest number of clinical events overall may have limited power to detect differences between treatment groups. Further, no trial provided followup beyond 5 years; therefore, longer term effects of ACE-inhibitor monotherapy versus CCB monotherapy cannot be determined from these data. Withdrawals appeared similar between treatment groups, with cough appearing more common in patients assigned ACEI and edema more common in patients assigned CCB.

ACE Inhibitor Monotherapy Versus Beta Blocker Trials (n=3)

Overview

In comparing ACEI versus beta blocker treatment in patients with CKD, there was low strength of evidence that there is no difference in risk of all-cause mortality and ESRD. We found no significant difference between treatments for risk of cardiovascular mortality, stroke, or heart failure.

Description of Studies

Three trials met all eligibility criteria and randomized participants (n=1,080, range 100 to 877) to ACEI versus beta blocker monotherapy.[90,92,93] Baseline characteristics are presented in Appendix Tables C1 and C2.

Among eligible trials, 877 participants were randomized to ramipril versus metoprolol (n=1 trial),[90] 103 were randomized to enalapril versus atenolol (n=1 trial),[92] and 100 were randomized to enalapril versus either atenolol or acebutelol (n=1 trial).[93] The mean age of study participants was 54 years, and men constituted 61 percent of patients studied. In the single trial that reported race/ethnicity, 100 percent of participants self-identified as African American.[90] One trial was conducted in the United States,[90] while two trials were performed in Europe.[92,93] Mean or median study durations were three years or greater in all trials.

Renal Function

No trial based study eligibility on CKD stage and no trial reported baseline distribution of participants by CKD stage. All three trials based eligibility on impairment in GFR (20 to 65

ml/min/1.73m^2),[90] creatinine clearance (30 to 90 ml/min),[92] or creatinine (2.3 to 5.2 mg/dL).[93] None based inclusion on the presence of albuminuria, though one excluded patients with urinary protein-creatinine ratio >2.5,[90] and another excluded participants with nephrotic syndrome.[93] Mean serum creatinine, reported in all three trials, was 2.0 mg/dL (range 1.8 to 3.0). Mean baseline GFR was 47 ml/min/1.73m^2 (range 46 to 53, n=2 trials).[90,92] Urinary protein excretion ranged from 0.5 g/24 hour[90] to 2.2 g/24 hour[93] in two trials. In the third trial, median urinary protein excretion was 3.3 g/24 hour.[92]

Baseline Comorbidities

All three trials excluded individuals with diabetes. Approximately 51 percent of participants had a history of heart disease in one trial,[90,91] patients with coronary artery disease were excluded from one trial,[93] and no data were reported regarding cardiovascular disease in the third trial.[92] While two trials were limited to patients with hypertension,[90,93] more than half of the participants in the third trial were reported to have diastolic blood pressure less than 90 mm Hg off antihypertensive medications.[92] Overall, 96 percent of participants in the three trials had hypertension. Mean baseline systolic and diastolic blood pressure measurements were 152 and 95 mm Hg, respectively.

Study Quality (Appendix Table C140)

Among the three trials, one was rated good quality and two were rated fair quality. Allocation concealment was adequate in two trials,[90,93] two trials were double blinded,[90,92] and analysis was performed by intention-to-treat in two trials.[90,93] All trials adequately described reasons for study withdrawal. Percentages of study withdrawals ranged from 0 to 23 percent. The AASK trial reported that no participants withdrew from treatment or were lost to followup.[90]

Results

Mortality (Table 7, Appendix Table C3, and Appendix Figure C1)

All-Cause Mortality

For patients with CKD, risk of all-cause mortality between those randomized to ACEI and those assigned beta blocker monotherapy was not significantly different (6.9 versus 9.6 percent; RR 0.71, 95% CI, 0.48 to 1.07; n=3 trials, 1,080 patients). The estimate of effect was driven primarily by data from the AASK trial, which accounted for 94 percent of the weight and 93 percent of deaths.[91]

Cardiovascular Mortality

In two trials reporting, there were relatively few cardiovascular deaths, and, though confidence intervals were wide, no difference in risk of cardiovascular mortality between CKD patients assigned to ACEI and those assigned to beta blocker (2.9 versus 2.6 percent; RR 1.08, 95% CI, 0.51 to 2.28).[91,92] As with all-cause mortality, the estimate of effect was again driven primarily by data from the AASK trial.

Vascular Outcomes (Table 7, Appendix Tables C3-C5, and Appendix Figure C1)

Myocardial Infarction

Two trials reported no data on myocardial infarctions,[90,93] and the third reported that two participants in the ACEI group (4.7 percent) and one in the beta blocker group (2.2 percent) experienced a fatal myocardial infarction.[92]

Stroke

In data derived entirely from the AASK trial, there was no difference for CKD patients allocated to ACEI versus beta blocker treatment groups for the outcomes of stroke (RR 1.01, 95% CI, 0.58 to 1.78).[91]

Other Vascular Outcomes

There were no differences between treatment groups for heart failure (RR 0.92, 95% CI, 0.51 to 1.66), or for the composite outcome of coronary artery disease hospitalization or coronary artery disease-related death (4.4 versus 4.1 percent; RR 1.07, 95% CI 0.57 to 2.01) or the composite outcome of first cardiovascular hospitalization or cardiovascular death (14.0 versus 14.7 percent; RR 0.95, 95% CI, 0.69 to 1.31).[91]

Renal Outcomes (Table 7, Appendix Tables C6 and C7, and Appendix Figure C1)

End-Stage Renal Disease

In pooled results, among these CKD patients there was no significant reduction in risk of end-stage renal disease with ACEI compared with beta blocker treatment (RR 0.81,95% CI, 0.50 to 1.33; n=3 trials, 1,080 patients). However, the estimate of effect varied substantially between trials, ranging from RR 0.54 (95% CI, 0.28 to 1.07)[93] to RR 2.45 (95% CI, 0.50 to 12.07)[92] in two small trials, with an intermediate result in the largest trial (RR 0.86, 95% CI, 0.63 to 1.17).[90]

Other Renal Outcomes

The AASK trial reported that CKD patients assigned ACEI versus beta blocker treatment had a statistically significantly reduced risk of the composite renal outcome of >50 percent reduction in GFR, need for dialysis or transplant, or death (28.9 versus 35.1 percent; RR 0.82,95% CI, 0.68 to 1.00; p=0.048).[90] Results for halving of GFR as an isolated endpoint, doubling of baseline creatinine, or conversion from microalbuminuria to macroalbuminuria were not reported.

Study Withdrawals and Adverse Events (Appendix Table C8)

In results pooled from all three trials, patients assigned to an ACEI were not more likely to withdraw from treatment (3.7 versus 3.1 percent, p=0.76) or withdraw from treatment due to an adverse event (2.2 versus 1.5 percent, p=0.39) compared with patients receiving a beta blocker. No patient in the AASK was reported to have withdrawn from treatment.[90] Hyperkalemia, though uncommon, appeared slightly more frequent in subjects randomized to the ACEI group in all three trials at 2.9 versus 0 percent of patients in two trials,[92,93] and as 0.7 versus 0.2 percent per patient year in the AASK trial.[90] The AASK trial reported significant differences between ACEI and beta blocker subjects in angioedema (6.4 versus 2.7 percent per patient year) and cough (54.9 versus 41.5 percent per patient year).[90]

Summary

In patients with CKD, there was no significant difference between ACEI and beta blocker treatment for risk of all-cause mortality, cardiovascular mortality, stroke, heart failure, or either of two composite vascular endpoints. Overall, there was no difference between ACEI and beta blocker treatment for risk of ESRD, but results were heterogeneous between trials. However, ACEI treatment was associated with a significantly lower risk of the composite renal outcome of >50 percent reduction in GFR, need for dialysis or transplant, or death. With respect to adverse effects, ACEI treatment was associated with a significantly higher rate of cough and angioedema. Results were limited in that only one study, the AASK trial, was designed to evaluate the effect of ACEI and beta blocker treatment on clinical cardiovascular outcomes. The two smaller trials reported few or no events for most vascular endpoints and had very limited power to detect differences in these outcomes between treatment groups. No trial provided mean or median followup beyond 5 years; therefore, longer term effects of ACEI monotherapy versus beta blocker monotherapy cannot be determined from these study results.

ACE Inhibitor Monotherapy Versus Diuretic Trials (n=2)

Overview

In patients with CKD there was insufficient strength of evidence that there was no difference in risk of all-cause mortality risk between those assigned to ACEI and those allocated to diuretic treatment. There was low strength of evidence that there was no difference between ACEI and diuretic in risk of ESRD. There was no significant difference between treatment groups in risk of stroke or multiple composite cardiovascular outcomes, but there was a significantly increased risk of CHF in the group assigned to ACEI. Our confidence in these estimates is limited because they are based almost entirely on results reported from a post hoc analysis in a single large trial.

Description of Studies

Two trials met all eligibility criteria and randomized participants (n=4,716, range 570 to 4,146) to ACEI monotherapy versus diuretic monotherapy.[81-83,94] Detailed baseline characteristics are presented in Appendix Tables C1 and C2). One of the included reports was a post hoc analysis performed within a subset of participants with CKD from the ALLHAT trial, a population that was not originally limited to subjects with CKD.

In one study, from the ALLHAT trial, 4,146 participants were randomized to lisinopril versus chlorthalidone,[81-83] while in the second study, the NESTOR trial, 570 participants were randomized to enalapril versus indapamide.[94] The mean age in these two trials was 70 years (range 60 to 71), and men comprised slightly over half of all patients studied (51 percent; range 49 to 65). The most common race/ethnicity of patients in the two trials was white (61 percent), followed by black (23 percent).[81-83,94] Hispanics comprised 11 percent of participants in the ALLHAT study.[81-83] The NESTOR trial was conducted in Europe,[94] while the ALLHAT study was performed primarily in the United States.[81-83] Study durations were 1 year[94] and 4.9 years, respectively.[81-83]

Renal Function

The single post hoc analysis restricted inclusion to participants with GFR <60 ml/min/1.73m^2, by definition CKD stage 3 or worse, and reported a mean baseline GFR of 50 ml/min/1.73m^2.[81] The second study, the NESTOR trial, did not base eligibility on CKD stage

and neither trial reported baseline distribution of participants by CKD stage. In the NESTOR trial, participants were required to have microalbuminuria for inclusion, and the mean baseline urinary albumin excretion rate was 58 μg/min, the urinary albumin/creatinine ratio was 6.2 mg/g, and the creatinine clearance was 92 ml/min/1.73m^2.[94] The two studies excluded subjects with baseline creatinine levels exceeding 1.7 mg/dL[94] and 2 mg/dL,[81-83] respectively.

Baseline Comorbidities

Both studies were limited to patients with hypertension, with mean blood pressures at baseline being 147/83 mm Hg in the ALLHAT study[81-83] and 161/94 mm Hg in the NESTOR trial.[94] In the ALLHAT study, 61 percent of participants reported cardiovascular disease, 31 percent reported coronary artery disease, and 31 percent were diabetic. In the NESTOR trial, however, prevalence of type 2 diabetes was 100 percent (mean hemoglobin A_{1c} 7.6 percent), but no information was reported regarding history of any cardiovascular disease.

Study Quality (Appendix Table C140)

Of the two eligible trials, one was rated good quality and one was rated fair quality. Allocation concealment was adequate in the ALLHAT study and unclear in the NESTOR trial. Both trials were double blinded. Analysis by the intention-to-treat principle was reported in ALLHAT. However, the NESTOR trial excluded one randomized participant from analyses who was reported to not have been exposed to study drug.[94] The NESTOR trial reported an 11 percent withdrawal rate and adequately described reasons for study withdrawal. By contrast, the ALLHAT study reported no data regarding withdrawals.

Results

Mortality (Table 7, Appendix Table C3, and Appendix Figure C1)

Data for all-cause mortality was reported only in the NESTOR trial, in which there were only three total deaths, all of which were cardiovascular. There was one death within subjects assigned to ACEI treatment (0.3 percent) and two deaths in participants within the diuretic group (0.7 percent).

Vascular Outcomes (Table 7, Appendix Tables C3-C5, and Appendix Figure C1)

Myocardial Infarction

The NESTOR trial reported that within the diuretic group one patient had a fatal MI and two others discontinued treatment after an MI.[94] It was not clear whether this was a complete accounting of all MIs.

Stroke

In the ALLHAT study, among the CKD subgroup evaluated in this post hoc analysis, there was no significant difference between ACEI and diuretic treatment assignment in risk of stroke (6.5 versus 6.0 percent; RR 1.07, 95% CI, 0.84 to 1.37).[81-83]

Other Vascular Outcomes

In the ALLHAT study, there was a significantly increased risk of heart failure (included fatal, hospitalized, or treated nonhospitalized) in the ACEI treatment group (12.5 versus 9.9 percent;

RR 1.26, 95% CI, 1.05 to 1.50).[81-83] In data available only from the ALLHAT study, there was no significant between-treatment difference for the composite vascular outcome of nonfatal MI or coronary heart disease death (RR 0.99, 95% CI, 0.83 to 1.17), or for the composite outcome that included death from coronary heart disease, nonfatal MI, stroke, coronary revascularization procedures, hospitalized or treated angina, treated or hospitalized heart failure, or peripheral arterial disease requiring hospitalization or outpatient revascularization (RR1.07, 95% CI, 0.98 to 1.17).[81-83] The ALLHAT trial reported additional results within CKD patients with diabetes.[82] In this subgroup, there was no statistically significant difference between treatment groups in risk of stroke or the two composite cardiovascular endpoints described in detail above. However, risk of heart failure was significantly greater in CKD patients with diabetes randomized to ACEI treatment compared with diuretic treatment (RR 1.37, 95% CI, 1.05 to 1.79; n=1,382).

Renal Outcomes (Table 7, Appendix Tables C6 and C7, and Appendix Figure C1)

End-Stage Renal Disease

The ALLHAT study reported that ACEI and diuretic treatment were comparable in CKD patients regarding the risk of ESRD, defined as death due to kidney disease, kidney transplantation, or start of long-term renal dialysis (RR 0.9, 95% CI, 0.72 to 1.28).[81]

Other Renal Outcomes

The ALLHAT trial reported no difference between treatment groups in risk of the incident composite renal outcome defined by ESRD or >50 percent decline in GFR (7 versus 7 percent, RR 1.00, 95% CI, 0.80 to 1.27).[81] The ALLHAT trial also performed additional analyses of renal outcomes among CKD patients with diabetes and reported that there were no statistically significant differences in reduction in risk of ESRD or the above described composite renal outcome between treatment groups.[82] The NESTOR trial reported that CKD subjects with microalbuminuria who were assigned to ACEI were less likely than diuretic subjects to convert to macroalbuminuria (6 versus 9 percent; RR 0.69, 95% CI, 0.38 to 1.22),[94] though this result was not statistically significant.

Study Withdrawals and Adverse Events (Appendix Table C8)

No study withdrawal or adverse event data were reported for the ALLHAT CKD subgroup.[81-83] In the NESTOR trial, CKD patients randomized to ACEI treatment were not more likely to withdraw from treatment, withdraw from treatment due to an adverse event, or withdraw from treatment due to a “medical reason” compared with patients assigned a diuretic.[94]

Summary

Within the two eligible trials of patients with CKD, there was no apparent difference between the ACEI and diuretic monotherapy treatment groups in risk of all-cause or cardiovascular mortality, MI, stroke, ESRD, or other composite clinical vascular or renal outcomes. There was a statistically significantly greater risk of heart failure among CKD patients allocated to ACEI therapy versus diuretic treatment. Results were limited in that one trial was a 1 year bioequivalence study not designed to evaluate the effect of these treatments on clinical events[94] and that the second study was a post hoc subgroup analysis. The large ALLHAT study also did not provide mortality data based on CKD status. Also, since mean followup did not extend

beyond 5 years, longer term effects of ACE-inhibitor monotherapy versus diuretic monotherapy cannot be determined from these data. Withdrawals were not significantly different between treatment groups in the one trial reporting, and no adverse events data were available.

Table 7. Pooled clinical and renal outcomes, ACEI monotherapy versus control treatment trials

Outcome	Number of Trials Reporting	Quality of the Studies	ACEI Events/N (%)	Control Events/N (%)	Relative Risk (95% CI)	I^2 Test for Heterogeneity
ACEI vs. placebo trials (n=17)						
All-cause mortality	16	Good	667/5786 (11.5)	686/5750 (11.9)	0.94 [0.80-1.12]	33%
Cardiovascular mortality	3	Good	231/3769 (6.1)	222/3764 (5.9)	1.03 [0.86-1.23]	0%
Myocardial infarction, any	3	Fair	62/2535 (2.4)	80/2565 (3.1)	0.79 [0.57-1.09]	0%
Myocardial infarction, fatal	2	Fair	4/378 (1.1)	0/371	4.84 [0.55-2.34]	0%
Myocardial infarction, nonfatal	7	Fair	71/3436 (2.1)	76/3417 (2.2)	0.93 [0.67-1.28]	0%
Stroke	4	Good	232/3868 (6.0)	278/3851 (7.2)	0.80 [0.52-1.23]	68%
Stroke, nonfatal	2	Fair	91/2743 (3.3)	87/2752 (3.2)	0.62 [0.12-3.18]	0%
PREVEND trial composite vascular outcome[a]*	1	Fair	17/431 (3.9)	28/433 (6.5)	0.61 [0.34-1.10]	NA
DIABHYCAR trial composite vascular outcome[b]	1	Good	362/2443 (14.8)	377/2469 (15.3)	0.97 [0.85-1.11]	NA
HOPE trial composite vascular outcome[c]	1	Good	186/952 (19.5)	265/1004 (26.4)	0.74 [0.63-0.87]	NA
ATLANTIS trial composite vascular outcome[d]	1	Fair	16/92 (17.4)	8/46 (17.4)	1.00 [0.46-2.16]	NA
PROGRESS trial composite vascular outcome[e]	1	Good	178/895 (19.9)	222/862 (25.8)	0.77 [0.65-0.92]	NA
REIN, Stratum 1 trial composite vascular outcome[f]	1	Good	2/99 (2.0)	3/87 (3.4)	0.59 [0.10-3.43]	NA
REIN, Stratum 2 trial composite vascular outcome[g]	1	Fair	4/78 (5.1)	3/88 (3.4)	1.50 [0.35-6.51]	NA
End-stage renal disease	7	Good	63/3729 (1.7)	97/3761 (2.6)	0.65 [0.49-0.88]	0%
Doubling of serum creatinine concentration	7	Fair	129/3682 (3.5)	202/3710 (5.5)	0.60 [0.40-0.89]	58%
ACEI versus angiotensin II receptor blocker trials (n=6)						
All-cause mortality	4	Fair	7/257 (2.7)	6/277 (2.2)	1.04 [0.37-2.95]	0%
Cardiovascular mortality	4	Fair	3/257 (1.2)	3/277 (1.0)	0.88 [0.19-4.13]	0%
Myocardial infarction, nonfatal	2	Fair	6/181 (3.3)	9/172 (5.2)	0.62 [0.23-1.68]	NA**
Congestive heart failure	2	Fair	7/181 (3.9)	9/172 (5.2)	0.72 [0.28-1.87]	NA**
ACEI versus calcium channel blocker trials (n=6)						
All-cause mortality	5	Fair	42/774 (5.4)	33/533 (6.2)	0.75 [0.48-1.16]	0%
Cardiovascular mortality	3	Fair	16/625 (2.6)	13/389 (3.3)	0.75 [0.36-1.57]	0%
Congestive heart failure	2	Good	211/1969 (10.7)	182/1733 (10.5)	1.09 [0.91-1.32]	0%
Stroke, any	3	Good	123/2098 (5.9)	111/1845 (6.0)	1.00 [0.78-1.28]	0%
AASK trial composite vascular outcome #1†	1	Good	61/436 (14.0)	23/217 (10.6)	1.32 [0.84-2.07]	NA
AASK trial composite vascular outcome #2†	1	Good	19/436 (4.4)	5/217 (2.3)	1.89 [0.72-5.00]	NA
ALLHAT trial composite vascular outcome #1‡	1	Good	547/1533 (35.7)	537/1516 (35.4)	1.01 [0.92-1.11]	NA
ALLHAT trial composite vascular outcome #2‡	1	Good	184/1533 (12.0)	194/1516 (12.8)	0.94 [0.78-1.13]	NA
End-stage renal disease	3	Good	139/2029 (6.9)	115/1794 (6.4)	0.89 [0.66-1.21]	29%
Halving of GFR	2	Good	80/1969 (4.1)	54/1733 (3.1)	1.02 [0.55-1.91]	71%
AASK trial composite renal outcome¥	1	Good	87/436 (20.0)	56/217 (25.8)	0.77 [0.58-1.04]	NA
ALLHAT trial composite renal outcome§	1	Good	106/1533 (6.9)	90/1516 (5.9)	1.16 [0.89-1.53]	NA

Table 7. Pooled clinical and renal outcomes, ACEI monotherapy versus control treatment trials (continued)

Outcome	Number of Trials Reporting	Quality of the Studies	ACEI Events/N (%)	Control Events/N (%)	Relative Risk (95% CI)	I^2 Test for Heterogeneity
ACEI versus beta blocker trials (n=3)						
All-cause mortality	3	Fair	37/540 (6.9)	52/540 (9.6)	0.71 [0.48-1.07]	0%
Cardiovascular mortality	2	Fair	14/488 (2.9)	13/492 (2.6)	1.08 [0.51-2.28]	0%
AASK trial composite vascular outcome #2†	1	Good	19/436 (4.4)	18/441 (4.1)	1.07 [0.57-2.01]	NA
Stroke	1	Good	23/436 (5.3)	23/441 (5.2)	1.01 [0.58-1.78]	NA
Congestive heart failure	1	Good	20/436 (4.6)	22/441 (5)	0.92 [0.51-1.66]	NA
AASK trial composite vascular outcome #1†	1	Good	61/436 (14)	65/441 (14.7)	0.95 [0.69-1.31]	NA
End-stage renal disease	3	Fair	77/540 (14.3)	92/540 (17.0)	0.81 [0.50-1.33]	40%
AASK trial composite renal outcome¥	1	Good	126/436 (28.9)	155/441 (35.1)	0.82 [0.68-1.00]	NA
ACEI versus diuretics trials (n=2)						
All-cause mortality	1	Fair	1/286 (0.3)	2/284 (0.7)	0.50 [0.05-5.44]	NA
Cardiovascular mortality	1	Fair	1/286 (0.3)	2/284 (0.7)	0.50 [0.05-5.44]	NA
Stroke	1	Good	99/1533 (6.5)	157/2613 (6.0)	1.07 [0.84-1.37]	NA
Congestive heart failure	1	Good	191/1533 (12.5)	259/2613 (9.9)	1.26 [1.05-1.50]	NA
ALLHAT trial composite vascular outcome #1‡	1	Good	547/1533 (35.7)	870/2613 (33.3)	1.07 [0.98-1.17]	NA
ALLHAT trial composite vascular outcome #2‡	1	Good	184/1533 (12.0)	318/2613 (12.2)	0.99 [0.83-1.17]	NA
End-stage renal disease	1	Good	70/1533 (4.6)	124/2613 (4.7)	0.96 [0.72-1.28]	NA
ALLHAT trial composite renal outcome§	1	Good	106/1533 (6.9)	180/2613 (6.9)	1.00 [0.80-1.27]	NA

NA = not applicable; RR = relative risk reduction; ACEI = angiotensin converting enzyme inhibitor

[a]PREVEND = Cardiovascular death and hospitalization for cardiovascular morbidity, defined as hospitalization for documented (1) nonfatal MI or myocardial ischemia, (2) heart failure, (3) PVD, and/or (4) CVA.

[b]DIABHYCAR = Cardiovascular death (including sudden death), nonfatal acute MI, stroke, heart failure requiring admission to hospital, and end stage renal failure (defined as dialysis or kidney transplant)

[c]Micro-HOPE = Cardiovascular death, MI, stroke

[d]ATLANTIS = Not clearly defined, noted as "cardiovascular adverse events." Incidences of death, MI and angina/chest pain provided.

[e]PROGRESS = Major cardiovascular events, defined as the composite of nonfatal stroke, nonfatal MI, and cardiovascular death.

[f]REIN, Stratum 1 = Incidence of "non-fatal cardiovascular events" reported but not defined.

[g]REIN, Stratum 2 = Non-fatal cardiovascular events include MI, aortic aneurysm, and uncontrolled HTN.

**Pooling data was not possible for this outcome because only one trial reported events.

† In AASK study, two composite vascular endpoints were defined, as follows: (1) Cardiovascular mortality or first cardiovascular hospitalization; and (2) "Coronary heart disease event" defined as CAD hospitalization (probable MI) and/or fatal coronary heart disease death

‡ In ALLHAT study, two composite vascular endpoints were defined, as follows: (1) Death from coronary heart disease, nonfatal MI, stroke, coronary revascularization procedures, hospitalized or treated angina, treated or hospitalized heart failure, and peripheral arterial disease requiring hospitalization or outpatient revascularization; and (2) "Coronary heart disease event" defined as nonfatal MI or fatal coronary heart disease death

¥End stage renal disease (need for renal replacement therapy), reduction in GFR by 50% or by 25 mL/min/1.73 m^2 from the mean of the two baseline GFRs, or death.

§End stage renal disease (death due to kidney disease, dialysis, or renal transplantation) or reduction in GFR by 50% or by 25 mL/min/1.73 m^2 from the mean of the two baseline GFRs.

ARB Monotherapy Versus Placebo Trials (n=5)

Overview

In patients with CKD, we found high strength of evidence that ARB treatment reduces risk of ESRD compared with placebo. These results are based entirely on data from trials enrolling CKD patients with overt albuminuria. We found high strength of evidence that ARB treatment does not reduce risk of all-cause mortality compared with placebo. While patients with CKD randomized to ARB versus placebo had a significantly lower risk of progression from microalbuminuria to macroalbuminuria, we found no statistically significant difference between treatment groups for risk of MI, and mixed results regarding risk for CHF hospitalization. Our confidence in these estimates is limited by the small number of trials reporting different outcomes, the small number of clinical events in some trials, and the heterogeneity of the study populations.

Description of Studies

Five trials met all eligibility criteria and randomized participants with CKD (n=5,769, range 527 to 1,991) to an ARB versus placebo.[95-99] Detailed baseline characteristics are presented in Appendix Tables C9 and C10. One of the included reports was a post hoc analysis[99] performed within a subset of participants with CKD from the TRANSCEND trial, a population that was not originally limited to subjects with CKD.

Among eligible trials, 1,738 participants were randomized to irbesartan versus placebo (n=2 trials), 1,513 participants (n=1 trial) to losartan versus placebo, and 2,518 participants (n=2 trials) to telmisartan versus placebo. The mean age of subjects was 62.7 years (range 58 to 68.7; n=5 trials), and men constituted 60.0 percent (range 51 to 69; n=4 trials) of all patients randomized. Four trials reported race/ethnicity, within which 64 percent of subjects were white. One trial was conducted in the United States,[97] one in Japan,[95] and three were multinational.[96,98,99]

Renal Function

In four trials, patients were required to have albuminuria or proteinuria. In two of these trials, patients must have been microalbuminuric, with a urinary albumin excretion rate between 20-200 µg/min in one study[96] and a urinary albumin-creatinine ratio between 100-300 mg/g in the second study.[95] Both of these trials also were restricted to participants with a normal serum creatinine, defining them as CKD stages 1-2. In the other two trials that required albuminuria or proteinuria for entry, patients must have been overtly albuminuric or proteinuric, with either an albumin-creatinine ratio ≥300 mg/g or urinary protein excretion rate ≥0.5 g/day,[98] or a 24 hour urine protein excretion ≥900 mg.[97] These two trials required participants to be within a range that included both normal and moderately elevated serum creatinine values (e.g., between 1.0 and 3.0 mg/dL), so that it was not possible to determine CKD stage.[97,98] The fifth trial, a post hoc analysis of TRANSCEND study participants who had either impaired eGFR or albuminuria, excluded participants with serum creatinine >3.0 mg/dL. This study categorized participants with eGFR <60 ml/min/1.73m^2 versus ≥60 ml/min/1.73m^2, and with normoalbuminuria versus microalbuminuria versus macroalbuminuria, and all possible combinations so that they further could be categorized as either CKD stages 1-2 or CKD stages 3-4. At baseline, serum creatinine was the measure of renal function most frequently reported, with a mean of 1.5 mg/dL (range 1.2

to 1.9; n=4 trials). Two trials reported urinary albumin excretion rate, with results of 55.5 µg/min (0.08 g/day)[96] and 1.9 g/day,[97] respectively. Median urinary albumin-creatinine ratio reported in one trial was 1,250 mg/g.[98] One trial reported no baseline data on renal function/damage for its participants.[95]

Baseline Comorbidities

Four studies were restricted to subjects with type 2 diabetes, and three further specified exclusion of patients with any nondiabetic kidney disease.[95,96,98] Two trials also were limited to subjects with hypertension,[96,97] while in two trials 81 and 93.5 percent of participants had a diagnosis of hypertension.[98,99] In the fifth trial, the prevalence of hypertension was not reported, though patients with severe hypertension (>180/100 mm Hg) were excluded and mean baseline blood pressure was 137/77 mm Hg.[95] Across all five trials, mean baseline blood pressures were 149/83 mm Hg (range 137/77 to 159/90 mm Hg). In one trial 28 percent of participants reported a history of cardiovascular disease.[97] In a second trial, cardiovascular disease was more common, including 73 percent of participants with coronary artery disease and 22 percent with stroke.[99] However, in the two other trials reporting data,[96,98] cardiovascular disease was uncommon, including myocardial infarction (8.9 percent, range 3 to 11.2, n=2 trials), coronary artery disease (4.5 percent, n=1 trial), stroke (0.9 percent, range 0.1 to 3.1, n=2 trials). Two trials explicitly excluded patients with CHF,[96,99] and another excluded patients with an indication for ACEIs or ARBs, likely indicating an exclusion of patients with CHF.[96] Finally, in one trial no entrance criteria related to cardiovascular disease were listed and no baseline data on cardiovascular disease were reported.[95]

Study Quality (Appendix Table C140)

Of the five eligible trials, three were rated good quality and two were rated fair quality. Allocation concealment was adequate in three trials[97-99] and unclear in two trials.[95,96] All trials were double blinded. All but one trial[95] performed analyses using the intention-to-treat principle. All trials adequately described study withdrawal and reasons for withdrawals, with withdrawals ranging from 0.8 to 13.1 percent of randomized participants.

Results

Mortality (Table 8, Appendix Table C11, and Appendix Figure C2)

All-Cause Mortality

Among these CKD patients studied, overall incidence of death in trials reporting this outcome ranged from less than 1 percent of study participants in one trial,[96] to between 16 and 20 percent in the other three trials.[97-99] Nevertheless, no individual trial results suggested a difference in risk of death among CKD patients randomized to ARB versus those allocated to placebo. In pooled results, there was no between-treatment difference in mortality risk (RR 1.04, 95% CI, 0.92 to 1.18, n=4 trials, 5,242 patients). Only one trial reported results stratified by baseline category of albuminuria in patients with and without an eGFR <60 mL/min/1.73m^2. There was no difference in mortality stratified by baseline category of albuminuria in patients with and without an eGFR <60 mL/min/1.73m^2.[99]

Cardiovascular Mortality

In a single trial that reported data on cardiovascular mortality, there was no significant difference in risk between study participants randomized to ARB versus placebo (RR 1.03, 95% CI, 0.80 to 1.31).[99]

Vascular Outcomes (Table 8, Appendix Tables C11–C13, and Appendix Figure C2)

Myocardial Infarction

In the one trial reporting data, among CKD patients there was a 25 percent reduction in risk of MI between ARB and placebo that was not statistically significant (6.7 versus 8.9 percent; RR 0.75, 95% CI, 0.53 to 1.06).[98]

Stroke

No trials reported data on risk of stroke.

Other Vascular Outcomes

One trial reported a significant reduction in risk of hospitalization for CHF (11.9 versus 16.7 percent; RR 0.71, 95% CI, 0.55 to 0.91; n=1,513 patients.[98] A second trial reported that CKD patients assigned to ARB had a rate of hospitalization for CHF that was 23 percent lower than placebo, a difference that was not stated to be statistically significant.[97] This study did not report the proportion of patients with one or more CHF hospitalizations, overall or by treatment group. On the other hand, ARB treatment did not significantly reduce risk of composite vascular events (Appendix Table C13) compared with placebo in any of three trials reporting, (RR 0.94, 95% CI, 0.81 to 1.08;[98] RR 0.95, 95% CI, 0.80 to 1.12;[99] and RR 0.94, 95% CI, 0.77 to 1.15),[97] respectively.

Renal Outcomes (Table 8, Appendix Tables C14 and C15, and Appendix Figure C2)

End-Stage Renal Disease

In three trials reporting incident ESRD, subjects with CKD assigned to ARB treatment were 22 percent less likely to progress to ESRD than those allocated to placebo treatment, a statistically significant result (10.0 versus 12.9 percent; RR 0.78, 95% CI, 0.67 to 0.90; n=4,652 patients)[97-99] (Figure 7). Two of these trials were comprised entirely of participants with proteinuria, whereas the third trial reported results for risk of ESRD stratified by albuminuria groups.[99] It reported no interaction between category of albuminuria (normal, microalbuminuria, or macroalbuminuria) and the relative reduction in risk of ESRD with ARB treatment versus placebo.

Other Renal Outcomes

In three trials reporting, CKD patients randomized to ARB treatment were significantly less likely to develop a doubling of their baseline serum creatinine (11.8 versus 15.2 percent; RR 0.78, 95% CI, 0.68 to 0.90; n=4,652 patients).[97-99] Risk of conversion from microalbuminuria to macroalbuminuria was 58 percent lower in CKD patients assigned to ARB compared with those allocated to placebo (13.2 versus 31.2 percent; RR 0.42, 95% CI, 0.33 to 0.52; n=2 trials, 1,104 patients).[95,96] One or more composite renal outcomes were reported in three trials (Appendix

Table C15),[97,98] with all suggesting that assignment to ARB reduces risk of the composite outcome compared with placebo, though not all differences were statistically significant.

Study Withdrawals and Adverse Events (Appendix Table C16)

Among CKD patients allocated to either ARB or placebo treatment, 12.2 percent withdrew from studies (range 0.8 to 24.4; n=5 trials). One trial reported that patients assigned to ARB treatment had a significantly lower rate of adverse events per 1,000 treatment days than those assigned to placebo.[97] Another trial reported that more than 90 percent of participants had at least one adverse event,[95] but no trials reported data on the proportion of patients with any adverse event by treatment group. This study further reported that 61 percent of all subjects had a serious adverse event and that there was no between-group difference for this outcome. Again no results were reported by treatment group. A second trial also reported that fewer ARB patients than those assigned placebo had a serious adverse event (15.4 versus 22.9 percent, n=590 participants), and further that ARB patients were not more likely than those assigned to placebo to withdraw from the study due to an adverse event (6.7 versus 8.5 percent).[96] Hyperkalemia necessitating discontinuation of study medication occurred in a significantly higher proportion of patients randomized to ARB treatment than placebo (3.2 versus 1.3 percent; RR 2.38, 95% CI, 1.57 to 3.61; n=3 trials, 4,652 patients). In one study reporting, relative risk of hyperkalemia with ARB versus placebo did not differ by baseline category of albuminuria.[99] In one study reporting, serum creatinine elevation necessitating discontinuation of study medication appeared similar between treatment groups (ARB 1.5 percent versus placebo 1.2 percent). Another study reported one episode of an early increase in serum creatinine concentration suggestive of renal artery stenosis that necessitated stopping the study medication but did not indicate in which treatment group this adverse event occurred.

Subgroup Results

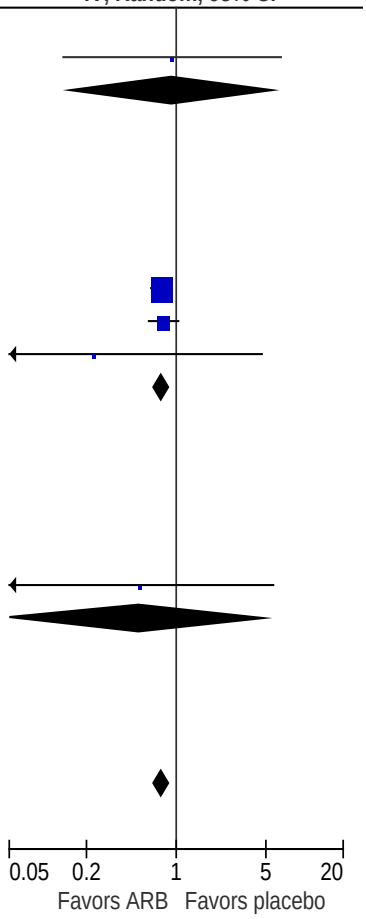
No trials reported outcomes stratified by any participant characteristic. In four trials restricted to patients with diabetes, all of which also required that participants have albuminuria, there was no significantly reduced risk with ARB versus placebo for mortality (RR 0.99, 95% CI 0.85 to 1.17; n=3 trials), MI, or composite vascular outcome. In the two trials restricted to diabetic participants with macroalbuminuria, those randomized to ARB had a significant reduction in risk of ESRD (RR 0.78, 95% CI 0.67 to 0.91; n=3 trials), CHF hospitalization (RR 0.71, 95% CI 0.55 to 0.91; n=1 trial), and doubling of serum creatinine (RR 0.78, 95% CI 0.68 to 0.91; n=2 trials). In the two trials restricted to diabetic participants with microalbuminuria, both of which also required normal eGFR for entry, participants randomized to ARB had a significant reduction in risk of conversion from microalbuminuria to macroalbuminuria (RR 0.42, 95% CI 0.33 to 0.52; n=2 trials). In two trials restricted to patients with hypertension, there was no significant difference between treatment groups in risk of mortality, ESRD or one composite vascular outcome reported, but there were statistically significant reductions in risk of doubling baseline creatinine, conversion from microalbuminuria to macroalbuminuria, and a single composite renal outcome reported. In three trials in which patients with CHF were excluded, there was a significant reduction in risk of CHF hospitalization (RR 0.71, 95% CI, 0.55 to 0.91), ESRD (RR 0.76, 95 percent CI, 0.63 to 0.92), and in doubling of baseline creatinine and conversion from microalbuminuria to macroalbuminuria. No trials were restricted to or excluded patients with cardiovascular disease.

Summary

In individuals with CKD, compared with placebo, assignment to ARB treatment was associated with significant reductions in risk of ESRD (reported only in patients with macroalbuminuria), and of doubling of serum creatinine and conversion from microalbuminuria to macroalbuminuria (both reported only in patients with microalbuminuria at baseline). Assignment to ARB treatment also was associated with reduction in risk in one of two composite renal outcomes, and in risk of CHF hospitalization. There was no significant difference between treatment groups for the outcomes of all-cause mortality, MI, or any reported composite vascular outcomes. No trials reported results for stroke. Results were limited in that several outcomes were reported in only one trial or not at all, in particular with neither of the studies that limited enrollment to microalbuminuric patients reporting results for MI, stroke, CHF, ESRD, or a composite vascular or renal endpoint. Though withdrawal and adverse event reporting were limited, individuals with CKD allocated to ARB were significantly more likely to experience hyperkalemia requiring discontinuation of study medication. In one trial that reported results stratified by baseline albuminuria category, there was no significant difference between these groups in the relative risk between ARB and placebo for any outcome or adverse event.

Figure 7. ARB versus placebo: End-stage renal disease by albuminuria subgroups

Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Weight	Risk Ratio IV, Random, 95% CI
18.13.1 Microalbuminuria at baseline						
Tobe (TRANSCEND) 2011	2	360	2	335	0.6%	0.93 [0.13, 6.57]
Subtotal (95% CI)		**360**		**335**	**0.6%**	**0.93 [0.13, 6.57]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.07 (P = 0.94)						
18.13.2 Macroalbuminuria at baseline						
Brenner (RENAAL) 2001	147	751	194	762	65.8%	0.77 [0.64, 0.93]
Lewis (IDNT) 2001	82	579	101	569	32.9%	0.80 [0.61, 1.04]
Tobe (TRANSCEND) 2011	0	63	2	72	0.3%	0.23 [0.01, 4.66]
Subtotal (95% CI)		**1393**		**1403**	**99.0%**	**0.78 [0.67, 0.91]**
Total events	229		297			
Heterogeneity: Tau² = 0.00; Chi² = 0.68, df = 2 (P = 0.71); I² = 0%						
Test for overall effect: Z = 3.22 (P = 0.001)						
18.13.3 Impaired eGFR and no albuminuria at baseline						
Tobe (TRANSCEND) 2011	1	569	2	592	0.4%	0.52 [0.05, 5.72]
Subtotal (95% CI)		**569**		**592**	**0.4%**	**0.52 [0.05, 5.72]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.53 (P = 0.59)						
Total (95% CI)		**2322**		**2330**	**100.0%**	**0.78 [0.67, 0.90]**
Total events	232		301			
Heterogeneity: Tau² = 0.00; Chi² = 0.82, df = 4 (P = 0.94); I² = 0%						
Test for overall effect: Z = 3.25 (P = 0.001)						
Test for subgroup differences: Chi² = 0.14, df = 2 (P = 0.93), I² = 0%						



ARB Versus CCB Trials (n=4)

Overview

In patients with CKD, we found low strength of evidence that ARB treatment does not reduce risk of all-cause mortality or ESRD relative to CCB. We found that patients assigned ARB treatment were significantly less likely to experience doubling of baseline creatinine, but that there was no significant difference between treatment groups for risk of stroke, or conversion from microalbuminuria to macroalbuminuria. Our confidence in these estimates is limited by the small number of trials reporting different outcomes, the small number of clinical events in some trials, and the heterogeneity of the study populations.

Description of Studies

Three trials met all eligibility criteria and randomized participants with CKD (n=3,924 patients, range 58 to 2,720) to an ARB versus CCB.[97,100,101] Detailed baseline characteristics are presented in Appendix Tables C9 and C10.

Among eligible trials, one compared candesartan to amlodipine (n=2,720 patients),[100] one compared irbesartan to amlodipine (n=1,146 patients),[97] and one compared candesartan to nifedipine (n=58 patients).[101] In total, there were 2,778 participants randomized to candesartan versus a CCB and 3,866 participants randomized to amlodipine versus an ARB. The mean age of subjects was 63.2 years (range 59 to 65; n=3 trials), and men constituted 55.4 percent (range 46.6 to 64.3; n=3 trials) of all patients randomized. Just one trial reported race/ethnicity, in which 72.1 percent of subjects were white.[97] Two other trials were conducted in Japan.[100,101] Median study durations ranged from 1.8 to 3.2 years.

Renal Function

In two trials, the initial study design specified restriction to patients with albuminuria (repeated urinary albumin-creatinine ratio 100-300 mg/g)[101] or proteinuria (urinary protein excretion ≥900 mg/24 hours).[97] In the third study, the current report[100] was a secondary analysis conducted in patients with either GFR <60ml/min/1.73m^2 or a positive dipstick test for proteinuria from among a larger trial population with either serum creatinine >1.3 mg/dL or undefined proteinuria.[101,102] Among the 2,720 participants enrolled in this study, 330 were reported in combined CKD stages 1 or 2, 2,265 were CKD stage 3, and 125 were CKD stage 4. No other study based inclusion on or reported distribution of participants by CKD stage. The only measure of renal function reported in more than one trial was serum creatinine, which ranged from 0.74 to 1.66 mg/dL in two trials reporting,[97,101] and was by definition >1.3 mg/dL in all participants in the third trial.[100] The baseline level of albuminuria differed considerably in two trials reporting, from an albumin-creatinine ratio of 237 mg/g[101] to a 24 hour urinary albumin excretion of 1.9 g.[97] Neither baseline GFR nor creatinine clearance was reported in any trials.

Baseline Comorbidities

All three studies included only subjects with hypertension and type 2 diabetes. Mean baseline systolic and diastolic blood pressures was 162/90 mmHg. Two trials excluded subjects with severe hypertension (systolic >200mmHg and/or diastolic >110 or 120 mmHg).[100,101] Trials provided little information on participant history of cardiovascular disease. In one trial, 28.7 percent of subjects had a history of cardiovascular disease,[97] while in a second trial 4.8 percent of participants had a history of MI.[100] One trial excluded subjects with “severe cerebral or

cardiovascular diseases,"[101] while a second trial excluded participants with MI or stroke ≤6 months before screening, coronary angioplasty or bypass ≤6 months before screening or currently scheduled, current treatment for class II-IV CHF or ejection fraction <40 percent, or coronary artery disease requiring BB or CCB.[100]

Study Quality (Appendix Table C140)

Among the three eligible trials, one was rated good quality and two were rated fair quality. Allocation concealment was adequate in two trials[97] and unclear in two trials.[100,101] One trial was double blinded.[97] Two trials were single blinded, one to the assessors only[100] and one to the patients only.[101] Analysis by the intention-to-treat principle was performed in two trials[97,100] and was unclear in one trial.[101] Two trials adequately described reasons for study withdrawals, with withdrawals ranging from 0.6 to 3.4 percent of randomized participants.[97,101] The third trial did not report any data on withdrawals.[100]

Results

Mortality (Table 8, Appendix Table C11, and Appendix Figure C2)

All-Cause Mortality

Results were heterogeneous between these two trials in that one reported no deaths among its 58 participants (and thus, no cardiovascular deaths),[101] while among the 1,146 participants in the other trial, 15.0 percent died in the ARB group versus 14.6 percent in the CCB group.[97] In pooled results, compared with CCB treatment, assignment to ARB therapy did not reduce risk of all-cause mortality among individuals with CKD (14.1 percent for ARB versus 14.2 percent for CCB; RR 1.03, 95% CI, 0.78 to 1.35; n=2 trials, 1,206 patients).

Vascular Outcomes (Table 8, Appendix Tables C11-C13, and Appendix Figure C2)

Myocardial Infarction

No trial reported results for MI.

Stroke

One trial reported stroke events, finding no difference in risk of stroke between CKD subjects randomized to ARB compared with those assigned to CCB (RR 1.07, 95% CI, 0.70 to 1.64).[100]

Other Vascular Outcomes

Two trials reporting a composite vascular outcome as a study endpoint found no significant difference between treatment groups (0.95, 95% CI, 0.73 to 1.24[100] and 1.06, 95% CI, 0.86 to 1.31),[97] respectively. In one trial that reported results for three composite vascular outcomes stratified by baseline CKD stage, cardiovascular events, cerebrovascular events, and cardiac events, respectively, there was no significant difference in risk of any of these composite outcomes between treatment groups for participants in CKD stages 1 or 2, or for participants in CKD stage 3.[100]

Renal Outcomes (Table 8, Appendix Tables C14 and C15, and Appendix Figure C2)

End-Stage Renal Disease

In the only trial that reported ESRD events, subjects with CKD assigned to ARB treatment were 23 percent less likely to progress to ESRD than those allocated to CCB treatment, though these results were not statistically significant (14.2 percent versus 18.3 percent; RR 0.77, 95% CI, 0.59 to 1.01; n=1,146 patients).[97]

Other Renal Outcomes

In one trial reporting, CKD patients randomized to ARB treatment were significantly less likely to develop a doubling of their baseline serum creatinine (16.9 versus 25.4 percent, RR 0.67, 95% CI, 0.53 to 0.84; n=1,146 patients).[97] In data based on one small trial, risk of conversion from microalbuminuria to macroalbuminuria was not statistically significantly lower in CKD subjects assigned to ARB treatment (10.0 versus 27.8 percent; RR 0.36, 95% CI, 0.11 to 1.18; n=58 patients).[101] A composite renal outcome was reported in two trials. In one trial, there was a significant reduction in risk among CKD patients assigned to ARB versus CCB (32.6 versus 42.1 percent; RR 0.80, 95% CI, 0.68 to 0.93).[97] In the second trial, there were few renal events and there was no significant difference in risk of this outcome between treatment groups, including 1.2 versus 1.9 percent (p=0.58) for participants with CKD stages 1 or 2, and 1.2 versus 0.8 percent (p=0.31) for participants with CKD stage 3.[100] It appeared that incidence of events included in the composite renal outcome definition in both trials (doubling of creatinine, ESRD) was far higher in the first trial,[97] suggesting that its CKD population had a substantially higher baseline risk for these events, possibly in part associated with a higher baseline level of proteinuria.

Study Withdrawals and Adverse Events (Appendix Table C16)

Few CKD patients allocated to either ARB or CCB treatment withdrew from studies (0.8 versus 0.7 percent, respectively, n=2 trials reporting). One trial reported that ARB subjects had a significantly lower rate of adverse events per 1,000 days than did CCB subjects but did not report the proportion of study participants with adverse events in each treatment group.[97] This study further reported that 61 percent of all subjects had a serious adverse event and that there was no between-group difference for this outcome. However, again no results were reported by treatment group. Hyperkalemia was significantly more frequent among CKD patients allocated to ARB than to CCB (1.9 versus 0.5 percent, p<0.05), though this outcome also was reported in only one trial.[97]

Summary

In individuals with CKD, compared with CCB, assignment to ARB treatment was associated with a significant 33 percent reduction in risk of doubling serum creatinine, but no significant difference in risk of all-cause mortality, MI, stroke, ESRD, or at least two defined composite vascular outcomes. Risk for a composite renal outcome including doubling creatinine, ESRD, or death was significantly lower with ARB in one trial that enrolled CKD patients with substantial baseline proteinuria. In another study of CKD patients at lower risk for these renal outcomes, there was no significant reduction in risk. Results were limited in that most outcomes were reported in only one trial or were uncommon. Evaluated CKD study populations appeared

heterogeneous with respect to risk of clinical events. However, small sample sizes and few clinical events in some studies, and the limited reported data on baseline vascular disease and renal function/damage, limited evaluation as to whether there are differences in the relative effect of ARB and CCB treatment according to these patient characteristics.

Table 8. Pooled clinical and renal outcomes, ARB monotherapy versus control treatment trials

Outcome	Number of Trials Reporting	Quality of the Studies	ARB Events/N (%)	Control Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
ARB versus placebo trials (n=5)						
All-cause mortality	4	Good	432/2711 (15.9)	415/2531 (16.4)	1.04 [0.92-1.18]	0%
Cardiovascular mortality	1	Good	114/992 (11.5)	112/999 (11.2)	1.03 [0.80-1.31]	NA
Myocardial infarction, any	1	Good	50/751 (6.7)	68/762 (8.9)	0.75 [0.53-1.06]	NA
CHF hospitalization	1	Good	89/751 (11.9)	127/762 (16.7)	0.71 [0.55-0.91]	NA
Composite vascular outcome, TRANSCEND study[a]	1	Good	205/992 (20.7)	218/999 (21.8)	0.95 [0.80-1.12]	NA
Composite vascular outcome, RENAAL study[b]	1	Good	247/751 (32.9)	268/762 (35.2)	0.94 [0.81-1.08]	NA
Composite vascular outcome, IDNT study[c]	1	Good	138/579 (23.8)	144/569 (25.3)	0.94 [0.77-1.15]	NA
End-stage renal disease	3	Good	232/2322 (10.0)	301/2330 (12.9)	0.77 [0.66-0.90]	0%
Doubling of serum creatinine concentration	3	Good	275/2322 (11.8)	354/2330 (15.2)	0.78 [0.68-0.90]	1%
Progression from micro to macroalbuminuria	2	Good	96/729 (13.2)	117/375 (31.2)	0.42 [0.33-0.52]	0%
Composite renal outcome, TRANSCEND study[d]	1	Good	16/992 (1.6)	27/999 (2.7)	0.60 [0.32-1.10]	NA
Composite renal outcome, RENAAL study[e]	1	Good	327/751 (43.5)	359762 (47.1)	0.92 [0.83-1.03]	NA
Composite renal outcome, IDNT study[f]	1	Good	189/579 (32.6)	144/569 (39.0)	0.84 [0.72-0.98]	NA
ARB versus CCB trials (n=4)						
All-cause mortality	2	Fair	87/619 (14.1)	93/587 (15.8)	0.92 [0.70-1.20]	NA
Stroke	1	Fair	44/1376 (3.1)	40/1344 (3.0)	1.07 [0.70-1.64]	NA
Composite vascular outcome, CASE-J study†	1	Fair	99/1376 (7.2)	102/1344 (7.6)	0.95 [0.73-1.24]	NA
Composite vascular outcome, IDNT study[c]	1	Good	138/579 (23.8)	128/567 (22.6)	1.06 [0.86-1.31]	NA
End-stage renal disease	1	Good	82/579 (14.2)	104/567 (18.3)	0.77 [0.59-1.01]	NA
Doubling of serum creatinine concentration	1	Good	98/579 (16.9)	144/567 (25.4)	0.67 [0.53-0.84]	NA
Progression from micro to macroalbuminuria	1	Fair	4/40 (10.0)	5/18 (27.8)	0.36 [0.11-1.18]	NA
Composite renal outcome, CASE-J study††	1	Fair	19/1376 (1.4)	26/1344 (1.9)	0.71 [0.40-1.28]	NA
Composite renal outcome, IDNT study[f]	1	Good	189/579 (32.6)	233/567 (41.1)	0.80 [0.68- 0.93]	NA

ARB = angiotensin receptor blocker; RR = relative risk; NA = not applicable; CHF = congestive heart failure; CCB = calcium channel blocker

[a]TRANSCEND = Cardiovascular death, MI, fatal or nonfatal stroke, or hospitalization for heart failure.

[b]RENAAL = MI, stroke, first hospitalization from heart failure or unstable angina, coronary or peripheral revascularization, or death from cardiovascular causes.

[c]IDNT = Death from cardiovascular causes, nonfatal MI, heart failure resulting in hospitalization, stroke resulting in permanent neurological defect, lower limb AKA.

[d]TRANSCEND = Doubling of baseline serum creatinine or chronic dialysis.

[e]RENAAL = Time to doubling serum creatinine, incident ESRD (hemodialysis or renal transplant), or death.

[f]IDNT = Doubling of baseline serum creatinine, incident ESRD (hemodialysis, renal transplant, serum creatinine concentration at least 6.0mg/dl), or death from any cause.

†First cardiovascular event defined as any of the following: sudden death (unexpected death within 24 h without external cause); cerebrovascular event (stroke or transient ischemic attack); cardiac event (heart failure, angina pectoris, or acute myocardial infarction); renal event (included serum creatinine concentration of 4.0 mg/dl or higher, doubling of serum creatinine concentration, or end-stage renal disease); and/or vascular event (dissecting aortic aneurysm or arteriosclerotic occlusion of a peripheral artery).

††Serum creatinine concentration of 4.0 mg/dl or higher, doubling of the serum creatinine concentration or end-stage renal disease.

ACE Inhibitor Plus ARB Therapy Versus ACE Inhibitor Alone Trials (n=6)

Overview

In patients with CKD, we found moderate strength of evidence that there is no difference between ACEI plus ARB combination therapy versus ACEI monotherapy for the outcome of all-cause mortality. We found insufficient strength of evidence that there is no difference between these treatments for ESRD. We found no significant difference between treatment groups in risk of stroke, CHF, doubling of serum creatinine, or progression from microalbuminuria to macroalbuminuria. Our confidence in these estimates is limited by the small number of trials reporting different outcomes, the small number of clinical events in some trials, and the heterogeneity of the study populations.

Description of Studies

Six trials met eligibility criteria and randomized participants with CKD (N=7,233, range of 54 to 3,988) to combination therapy with an ACEI plus an ARB versus ACEI therapy alone.[75-77,103-105] One of the included reports was a post-hoc analysis performed within a subset of participants with CKD from a larger trial population that was not originally limited to subjects with CKD,[105] while a second report was a post hoc analysis from a larger trial that evaluated outcomes in multiple participant subgroups, including impaired GFR and albuminuria.[75] Detailed baseline characteristics are presented in Appendix Tables C17 and C18.

The mean age of study subjects was 65 years (range of study means 51–66; n=5 trials), and men constituted 83 percent (range 37 to 88; n=5 trials) of all participants randomized. Among the three trials that reported race/ethnicity, one was entirely comprised of Japanese participants,[104] one reported only that 91 percent of participants were white,[105] and, in third trial, 45 percent of participants were Hispanic, 34 percent were black, and 19 percent were white.[103] Two studies were conducted solely in the United States,[103,105] one study was conducted in Japan[104] one study was conducted in Turkey,[77] and two studies were multinational.[75,76] The mean or median study duration ranged from 30 weeks to 3.1 years. All studies but two[76,103] had followup durations of at least 1 year.

Renal Function

One post hoc analysis restricted inclusion to participants with GFR <60 ml/min/1.73m^2, by definition CKD stage 3 or worse,[105] while a second post hoc analysis reported results for a subgroup defined by GFR <60 ml/min/1.73m^2 as well as for a subgroup defined by albuminuria, the latter by definition could have included CKD stages 1–4.[75] Otherwise, no trial based study eligibility on CKD stage or reported baseline distribution of participants by CKD stage. Of the six trials, two required that participants have microalbuminuria,[76,77] two required that participants have macroalbuminuria or overt proteinuria,[103,104] and one reported a post hoc analysis of participants with either microalbuminuria or macroalbuminuria.[75] Among these trials that required participants to have albuminuria or proteinuria, one required that participants also have a normal creatinine,[77] three allowed participants to have abnormal levels for creatinine or creatinine clearance but mandated a maximally abnormal limit,[76,103,105] while one required that participants also had an elevated creatinine between 1.2 and 5 mg/dL.[104]

Overall, four studies reported on some measure of proteinuria at baseline.[75-77,103,104] One reported a mean 24 hour proteinuria of 1.7 g/d,[104] one reported a mean urinary albumin: creatinine ratio of 9.4 mg/mmol,[76] one reported a mean 24 hour albumin excretion rate of 260 mg,[77] and one study reported a mean urinary albumin:creatinine ratio of 907 mg/g.[103] The study by Anand reported only on dipstick proteinuria.[105] Several measures of renal function were reported by the studies, including a mean serum creatinine 1.5 mg/dL (range 1 to 3, n=3 trials),[77,103,104] a mean creatinine clearance of 96 ml/min/1.73m2 (range 65 to 112, n=3 trials),[76,77,103] and a mean eGFR of 50 (range 48 to 51, n=2 trials).[75,105]

Baseline Comorbidities

Two of six trials were restricted to patients with diabetes,[77,103] including one limited to participants with type 2 diabetes.[77] Among the remaining trials, only two report data on diabetes prevalence, with 29 percent[105] and 74 percent[76] of study participants, respectively.

Three trials were restricted to participants with hypertension,[76,77,104] two trials excluded participants with hypertension,[75,103] while prevalence of hypertension in the remaining study was 15 percent.[105] Mean baseline blood pressures was 127/76 mmHg.

Three trials excluded participants with heart failure,[76,103,104] while one included only participants with heart failure.[105] Four trials excluded participants with a recent stroke or ischemic cardiac event. Prevalence of other cardiovascular disease was reported only in that heart failure was attributed to ischemic disease in 36 percent of participants in one trial,[105] and a history of MI or coronary artery procedure was reported in fewer than 10 percent of participants in a second study.[103,104]

Study Quality (Appendix Table C140)

Among six eligible trials, two were rated as good quality and four were rated as fair quality. Allocation concealment was adequate in three trials and unclear in the remaining studies. Four trials were double blinded.[75,76,103,105] Two studies were not blinded.[77,104] For the outcomes presented here, only two studies analyzed results according to the intention-to-treat principle.[75,105] All studies adequately described reasons for study withdrawals. Withdrawals ranged from 5 to 24 percent (n=4 trials).

Results

Mortality (Table 9, Appendix Table C19, and Appendix Figure C3)

All-Cause Mortality

Overall, there was no significant difference in risk of all-cause mortality between CKD patients randomized to ACEI+ARB versus those allocated to ACEI alone (RR 1.03, 95% CI, 0.91 to 1.18). More than 99 percent of events occurred in only one trial.[105]

Cardiovascular Mortality

No study reported data for cardiovascular mortality.

Vascular Outcomes (Table 9, Appendix Tables C19–C21, and Appendix Figure C3)

Myocardial Infarction

No study reported on MI (fatal or nonfatal).

Stroke

Only one study reported on nonfatal stroke,[103] with only two stroke events occurring during the study, one in each study arm.

Other Vascular Outcomes

Congestive heart failure events were reported only by one study[103] in which two CHF events occurred in participants randomized to ACEI+ARB versus no events in the ACE monotherapy group. A composite cardiovascular outcome was also only reported in one study.[105] This study had a broad outcome definition for their cardiovascular composite outcome (Appendix Table C21). Combination ACEI+ARB therapy was associated with a modest but statistically significant 11 percent relative risk decrease in CVD events (95% CI, 0.80 to 0.98).

Renal Outcomes (Table 9, Appendix Tables C22 and C23, and Appendix Figure C3)

End-Stage Renal Disease

Only one study reported results for ESRD.[104] The risk of ESRD was equivalent in those on combination ACEI+ARB therapy compared with ACEI therapy alone (HR 1.0, 95% CI, 0.2 to 6.8). This trial reported only four ESRD events, with two occurring in each arm.

Other Renal Outcomes

One study reported on the outcome of doubling of serum creatinine.[104] In this study, combination ACEI+ARB therapy was associated with a nonsignificant reduction in the risk for doubling of creatinine compared with solitary ACEI therapy (HR 0.07, 95% CI, 0.0 to 1.13). This outcome occurred in only seven study participants, though all had been assigned to the ACEI monotherapy group. Three trials reported on progression from microalbuminuria to macroalbuminuria.[75-77] Although by far the most events for this outcome were reported in the ONTARGET trial, results reported by this trial for the number of participants with baseline microalbuminuria were inconsistent throughout the paper and could not be incorporated in a pooled analysis. The ONTARGET trial reported results for a composite renal outcome, defined as first occurrence of either dialysis, renal transplantation, doubling of baseline serum creatinine, or death.[75] Based on graphical display of the data (risk ratios and number of events in each treatment arm were not reported), there appeared to be no significant difference between ACEI and ACEI+ARB for reaching this endpoint in either the ONTARGET subgroup with GFR <60 ml/min/1.73m^2 or the subgroup with baseline microalbuminuria.[75] Further, that the relative reduction in risk of the composite renal outcome between treatment groups in ONTARGET was not significantly different in the CKD subgroup than in ONTARGET participants without CKD (p for interaction 0.80).

Study Withdrawals and Adverse Events (Appendix Table C24)

Overall study withdrawals, reported in all four studies, ranged from 6 to 24 percent. Only one study reported on adverse events leading to withdrawal,[76] which was similar in both study arms. Two studies reported on any adverse events[76,103] that appeared to be similar between groups. The most common adverse events reported were hypotension and hyperkalemia. Hyperkalemia was more common in the combination therapy group in one study[105] but not in another.[76]

Summary

In patients with CKD, compared with ACEI monotherapy, assignment to combination ACEI+ARB therapy did not significantly reduce risk of all-cause mortality but was associated with significant reductions in risk of the one composite vascular outcome reported and in risk of progression from microalbuminuria to macroalbuminuria. Results suggested that combination treatment might reduce risk of doubling creatinine, but they did not achieve statistical significance. Too few events were reported for all other outcomes for the results to be clinically meaningful, including for stroke, MI, and ESRD. Reporting on study withdrawals and adverse effects was limited. No trial provided followup beyond 4 years.

Table 9. Pooled clinical and renal outcomes, ACE inhibitor plus ARB versus ACE inhibitor trials

Outcome	Number of Trials Reporting	Quality of the Studies	ACEI+ARB Events/N (%)	ACEI Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
All-cause mortality	3	Fair	363/1546 (23.5)	342/1513 (22.6)	1.03 [0.91-1.18]	0%
Stroke, nonfatal	1	Fair	1/26 (3.8)	1/27 (3.7)	1.04 [0.07- 15.75]	NA
CHF	1	Fair	2/26 (7.6)	0/27 (0)	5.19 [0.26- 103.11]	NA
Composite vascular outcome**	1	Good	499/1477 (33.8)	549/1439 (38.2)	0.89 [0.80- 0.98]	NA
End stage renal disease	1	Fair	2/45 (4.4)	2/45 (4.4)	1.00 [0.15- 6.79]	NA
Doubling of serum creatinine	1	Fair	0/45 (0)	7/45 (15.6)	0.07 [0.00-1.13]	NA
Progression to macroalbuminuria	2	Fair	1/139 (0.7)	3/95(3.2)	0.36 [0.04-3.37]	NA

ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker; RR = relative risk reduction; NA = not applicable

**Death, sudden death with resuscitation, hospitalization for heart failure, or administration of intravenous inotropic or vasodilator drugs for 4 hours or more without hospitalization

ACE Inhibitor Plus ARB Therapy Versus ARB Alone Trials (n=3)

Overview

In patients with CKD, we found insufficient evidence regarding whether there is a difference between ACEI+ARB combination therapy versus ARB monotherapy for all-cause mortality (no events) or ESRD (no data reported). Our confidence in these estimates is limited by the small number of trials reporting different outcomes, the small number of clinical events, and the heterogeneity of the study populations.

Description of Studies

Three trials met eligibility criteria and randomized participants with CKD (n=approximately 4,300) to combination therapy with an ACEI+ARB versus ARB therapy alone.[75-77] Baseline characteristics are presented in Appendix Tables C17, C18, and C25.

Among eligible trials, the mean age of study subjects was 57 years (range of study means 57 to 58; n=2 trials reporting), and men constituted 46 percent (range 37 to 69; n=2 trials reporting) of all participants. Ethnicity was not reported by any study. Two studies were multinational[75,76] and one was conducted in Turkey.[77] The mean or median study duration ranged from 30 weeks to 4.7 years. Two studies had a duration of followup of 1 year or greater.[75,77]

Renal Function

One post hoc analysis reported results for a subgroup defined by GFR <60 ml/min/1.73m^2 as well as for a subgroup defined by albuminuria, the latter by definition could have included CKD stages 1–4 but did not state the total number of participants with CKD.[75] Otherwise, no trial based study eligibility on CKD stage or reported baseline distribution of participants by CKD stage. Of the three trials, two required that participants have microalbuminuria,[76,77] and one reported a post hoc analysis of participants with either microalbuminuria or macroalbuminuria.[75] Of the two trials that required participants to have albuminuria or proteinuria, one required that participants also have a normal creatinine,[77] and one allowed participants to have abnormal levels for creatinine or creatinine clearance but mandated a maximally abnormal limit.[76]

Two studies reported on some measure of proteinuria at baseline.[76,77] One reported a mean urinary albumin:creatinine ratio of 9.4 mg/mmol,[76] and the other reported a mean 24-hour albumin excretion rate of 260 mg.[77] Two studies reported a mean creatinine clearance of 101 ml/min/1.73m2 (range 97 to 112, n=2 trials),[76,77] one reported a mean serum creatinine of 1.0 mg/dL,[77] and one reported a mean eGFR of 50 mL/min/1.73m2.[75]

Baseline Comorbidities

One trial was restricted to patients with type 2 diabetes.[77] In the only other study that reported data, diabetes prevalence was 74 percent.[76] Two trials were restricted to participants with hypertension,[76,77] and one trial excluded participants with hypertension.[75] Mean baseline blood pressures was 152/90 mmHg. One trial excluded participants with heart failure,[76] but otherwise the presence of cardiovascular disease at baseline was not reported in any study.

Study Quality (Appendix Table C140)

Among the three trials, one was rated good quality and two were rated fair quality. Allocation concealment was adequate in two studies and unclear the third study. Two studies

were double blinded.[75,76] The other study was not blinded.[77] For the outcomes presented here, only one study analyzed results according to the intention-to-treat principle.[75] All studies adequately described reasons for study withdrawals. Withdrawals ranged from 12 to 14 percent (n=2 trials).

Results

Mortality (Table 10, Appendix Table C19, and Appendix Figure C4)

Of the three studies, only one reported on mortality during the trial.[76] In this study of 86 patients with CKD there were no deaths.

Vascular Outcomes (Table 10, Appendix Tables C19–C20)

Myocardial Infarction

No study reported on MI events (fatal or nonfatal).

Stroke

No study reported on stroke events.

Other Vascular Outcomes

No studies reported on CHF events or any composite cardiovascular outcomes.

Renal Outcomes (Table 10, Appendix Table C22, and Appendix Figure C4)

End-Stage Renal Disease

No study reported on ESRD.

Other Renal Outcomes

No study reported on the outcome of doubling of serum creatinine. With regard to the outcome of progression from microalbuminuria to macroalbuminuria, it was reported that no events occurred in one trial,[77] and only four events in a second trial.[76] Although by far the most events for this outcome were reported in the ONTARGET trial, results reported by this trial for the number of participants with baseline microalbuminuria were impossibly inconsistent throughout the paper and could not be incorporated in a pooled analysis. No study reported on any renal composite outcomes.

Study Withdrawals and Adverse Events (Appendix Table C24)

Overall study withdrawals were reported in only one study at 14 percent. One study reported on adverse events leading to withdrawal,[76] which was similar in both study arms. One study reported on any serious adverse events,[76] which were more common in the combination therapy group (9.3 percent) versus the ARB alone group (2.3 percent). The most common adverse events reported were hypotension, hyperkalemia, and cough. In one study cough was more common in the combination therapy group that in the ARB alone group (4.3 percent versus 0 percent).

Summary

In individuals with CKD, trials comparing ACEI+ARB combination therapy versus ARB alone reported few or no clinical outcomes, including no deaths in one trial reporting this

outcome. No trials reported data on MI, stroke, CHF, ESRD, doubling of serum creatinine, or any composite vascular or renal outcome. Though trials reported data for progression from microalbuminuria to macroalbuminuria, all had either few events or errors in reporting that impeded interpretation. Reporting on study withdrawals and adverse effects was limited. No trial provided followup beyond 5 years.

Table 10. Pooled clinical and renal outcomes, ACE inhibitor plus ARB versus ARB trials

Outcome	Number of Trials Reporting	Quality of the Studies	ACEI+ARB Events/N (%)	ARB Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
All-cause mortality	1	Fair	0/43 (0)	0/43 (0)	-	NA
Progression to macroalbuminuria	2	Fair	1/139 (0.7)	3/91 (3.3)	0.33 [0.04-3.08]	NA

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; RR = relative risk reduction; NA = not applicable

ACE Inhibitor Plus ARB Therapy Versus ACE Inhibitor or ARB (Monotherapy) Trial (n=1)

Overview

In patients with CKD, we found moderate strength of evidence that combination ACEI and ARB treatment did not reduce risk of all-cause mortality compared with ACEI or ARB monotherapy. We found low strength of evidence that that there was no difference in risk of ESRD between treatment groups. There was no significant difference between treatment groups for risk of cardiovascular mortality, a composite vascular outcome, doubling of serum creatinine, or a composite renal outcome defined as doubling of serum creatinine or ESRD. Our confidence in these estimates is limited as data were drawn from only one trial.

Description of Studies

One trial met all eligibility criteria and randomized participants with CKD to either ACEI monotherapy, ARB monotherapy, or combined ACEI plus ARB treatment. Detailed baseline characteristics are presented in Appendix Tables C17 and C18. From the larger ONTARGET trial (n=23,422), this post hoc analysis was limited to 8,933 participants with either eGFR ≤60 ml/min/1.73m^2 or albuminuria and reported results only for combination therapy versus the pooled monotherapy arms.

In this post hoc analysis,[99] 2,943 participants were randomized to ramipril 10 mg/d plus telmisartan 80 mg/d versus either ramipril or telmisartan monotherapy (n=5,990). The mean age of subjects was 68.2 years, and men constituted 68.0 percent of patients randomized. Race was reported as 70 percent European and 16 percent Asian. This trial was multinational.[99]

Renal Function

Participants were excluded if they had a serum creatinine >3 mg/dL with no restriction on albuminuria. At baseline, mean serum creatinine was 1.1 mg/dL, mean eGFR was 73.6 ml/min/1.73m^2, and mean urinary albumin:creatinine ratio was 129.1 mg/g. In this post hoc analysis, 5,623 participants (62.9 percent) had eGFR <60 ml/min/1.73m^2, 2,631 (29.5 percent) had isolated microalbuminuria, and 679 (7.6 percent) had isolated macroalbuminuria.

Baseline Comorbidities

Participants were included if they were >55 years with established cardiovascular disease or with diabetes associated with end organ damage. Seventy-seven percent of participants had hypertension with a mean blood pressure of 144/82 mm Hg. Diabetes was present in 49 percent of participants. The prevalence of cardiovascular disease was 70 percent, including 45 percent with a previous myocardial infarction, 20 percent with a prior stroke and 17 percent with prior peripheral vascular disease.

Study Quality (Appendix Table C140)

The study was rated good quality. It was double blinded, performed analyses using the intention-to-treat principle, and adequately described study withdrawals and reasons for withdrawals. Study withdrawals occurred in 29 percent of participants.

Results

Mortality (Table 8, Appendix Table C19, and Appendix Figure C5)

All-Cause Mortality

Overall, incidence of all-cause mortality was 17.4 percent, with no difference between patients randomized to combination therapy versus monotherapy (RR 1.02, 95% CI, 0.93 to 1.13). However, there was a significant interaction between baseline albuminuria category and the association between treatment group and mortality (p=0.03). Relative risk of mortality with combination therapy versus monotherapy was 1.15 (95% CI, 1.02 to 1.24) in patients with normoalbuminuria, 1.09 (95% CI, 0.93 to 1.29) in patients with microalbuminuria, and 0.80 (95% CI, 0.64 to 1.01) in patients with macroalbuminuria. This association was independent of baseline eGFR.

Cardiovascular Mortality

Risk of cardiovascular death was not significantly different between combination therapy and monotherapy (RR 1.01, 95% CI, 0.86 to 1.19). This result did not differ by albuminuria status.

Vascular Outcomes (Table 8, Appendix Tables C19-C21, and Appendix Figure C5)

Myocardial Infarction

Risk of myocardial infarction was not reported.

Stroke

Risk of stroke was not reported.

Other Vascular Outcomes

There was no difference between treatment groups in risk of a single composite outcome defined as death from cardiovascular causes, myocardial infarction, stroke or hospitalization for heart failure (RR 0.97, 95% CI, 0.89 to 1.05).

Renal Outcomes (Table 8, Appendix Tables C22 and C23, and Appendix Figure C5)

End-Stage Renal Disease

ESRD occurred in a similar percentage of participants randomized to combination therapy as assigned monotherapy (RR 1.19, 95% CI, 0.77 to 1.85).

Other Renal Outcomes

There was no significant difference between treatment groups in risk of doubling of serum creatinine (RR 1.25, 95% CI, 0.96 to 1.63) or for the composite outcome of doubling of serum creatinine or ESRD (RR 1.22, 95% CI, 0.96 to 1.55).

Study Withdrawals and Adverse Events (Appendix Table C24)

Overall, 24.7 percent of individuals in this post hoc analysis withdrew from therapy. Risk of withdrawal was significantly greater in the group assigned combination treatment (RR 1.17, 95%

CI, 1.10 to 1.25). Risk for most specific adverse effects was greater in participants randomized to combination therapy, including need for acute dialysis (RR 1.95, 95% CI, 1.09 to 3.49), hyperkalemia (potassium > 5.5 meq/dL) (RR 1.65, 95% CI, 1.4 to 1.95), hypotension (RR 1.66, 95% CI, 1.29 to 2.12), cough (RR 1.72, 95% CI, 1.34 to 2.20), and syncope (RR 2.44, 95% CI, 0.75 to 8.00).

Summary

In individuals with CKD, compared with ACEI or ARB monotherapy, assignment to ACEI plus ARB combination treatment was associated with a similar risk of all-cause mortality, cardiovascular mortality, a composite vascular outcome, ESRD, and doubling of serum creatinine. However, there was a significant interaction between baseline category of albuminuria and the association of treatment assignment on risk of all cause mortality. While those with normoalbuminuria had an increased risk of death with combination therapy, those with macroalbuminuria demonstrated a trend towards a decreased risk of mortality. Results were limited in that they are derived from only one trial. Adverse effects were more likely in patients randomized to combination ACEI and ARB therapy compared with monotherapy with either an ACEI or ARB.

ACE Inhibitor Plus ARB Versus ACE Inhibitor Plus Aldosterone Antagonist Trial

Overview

In comparing ACEI plus ARB versus ACEI plus aldosterone antagonist, we found insufficient evidence regarding whether there is a difference between treatments in risk of mortality or ESRD. Our confidence in these estimates is limited because data are drawn from only one trial and because of the small number of clinical events.

Description of Study

One trial met all eligibility criteria and randomized 54 participants with CKD and taking an ACEI (lisinopril 80 mg/day) to the addition of either an ARB (losartan) or of an aldosterone antagonist (spironolactone).[103] A third arm of the trial, discussed elsewhere, involved addition of placebo to lisinopril. Detailed baseline characteristics are presented in Appendix Table C26.

The mean age of trial participants was 52 years, and males constituted 49 percent of study subjects. Most patients (55 percent) were Hispanic, with an additional 28 percent black, 15 percent white, and 2 percent Native American. The study duration was 48 weeks.

Renal Function

Patients were included if they had macroalbuminuria, defined as a urinary albumin to creatinine ratio of 300 mg/g or higher despite treatment with an ACEI or ARB for at least 3 months prior to study entry. Females with a serum creatinine greater than 3.0 mg/dl and males with a serum creatinine greater than 4.0 mg/dl were excluded. Baseline renal function for trial participants included mean urine albumin to creatinine ratio of 997.4 mg/g, mean baseline serum creatinine of 1.8 mg/dl, and mean creatinine clearance of 58.0 ml/min.

Baseline Comorbidities

All study participants were required to have hypertension, with a systolic blood pressure on antihypertensive treatment of greater than 130 mm Hg. Mean baseline blood pressure was 134.0/72.5 mm Hg. Trial participants also were required to have diabetes, but with an HbA_{1c} at or below 11 percent. The mean HbA_{1c} at baseline was 7.5 percent. Patients with any history of heart failure, or with a stroke or MI in the past 12 months were excluded. A history of either MI, coronary artery bypass grafting, or percutaneous transluminal coronary angioplasty was reported by 7.5 percent of the patients.

Study Quality (Appendix Table C140)

The trial was rated fair quality. The method used for treatment allocation was not clearly described. The study was double blinded; however, the analysis was not completed using intention-to-treat principles. From the 54 randomized participants, 35.2 percent withdrew, with reasons for withdrawals adequately explained.

Results

Mortality (Appendix Table C27 and Appendix Figure C6)

The trial reported one death in the ACEI plus ARB treatment group and no deaths in the ACEI plus aldosterone antagonist group.

Vascular Outcomes (Appendix Table C27 and Appendix Figure C6)

Myocardial Infarction

The trial reported no MIs in the ACEI plus ARB treatment group and one MI in the ACEI plus aldosterone antagonist group.

Stroke

No stroke events were reported.

Other Vascular Outcomes

The trial reported two hospitalizations attributed to heart failure in the ACEI plus ARB treatment group. This compared with two hospitalizations attributed to heart failure in the ACEI plus aldosterone antagonist group. No composite vascular outcomes were reported.

Renal Outcomes (Appendix Table C28 and Appendix Figure C6)

End-Stage Renal Disease

The trial did not report results for end-stage renal disease.

Other Renal Outcomes

There was no significant difference between treatment groups in risk of doubling of baseline serum creatinine (RR=1.04, 95% CI, 0.60 to 1.80).

Study Withdrawals and Adverse Events (Appendix Table C29)

Withdrawals occurred in 33.3 percent of study participants randomized to the ACEI plus ARB treatment arm versus 37.0 percent of the ACEI plus aldosterone antagonist arm. There were

more withdrawals due to adverse events in the ACEI plus aldosterone antagonist group (25.9 percent versus 7.7 percent). Two patients (7.4 percent) in the ACEI plus aldosterone antagonist group and none in the ACEI plus ARB group experienced recurrent hyperkalemia. Similarly, one patient (3.7 percent) in the ACEI plus aldosterone antagonist group and none in the ACEI plus ARB group withdrew from the study because of an increase in serum creatinine.

Summary (Appendix Table C140)

In this trial of diabetic, hypertensive CKD patients already on ACEI, there appeared to be no difference between subjects randomized to additional ARB versus additional aldosterone antagonist for the outcome of doubling of baseline creatinine. Few or no results were reported with respect to risk of all-cause mortality, MI, stroke, CHF, or ESRD. Withdrawals due to adverse events appeared possibly were more likely with ACEI combined with aldosterone antagonist. Results were limited in that they are based on only one small trial that reported few clinical endpoints. Further, the withdrawal rate was high and followup duration was less than 1 year.

ACE Inhibitor Plus CCB Versus ACE Inhibitor Monotherapy or CCB Monotherapy Trial

Overview

In patients with CKD, we found insufficient evidence regarding whether there is a difference between ACEI monotherapy, CCB monotherapy, and ACE+CCB combination therapy for reducing risk of mortality or any clinical vascular or renal outcome.

Description of Study

We identified one trial that met all eligibility criteria. Patients with CKD were randomized to receive ACEI and CCB combined, ACEI alone, or CCB alone.[84] Detailed baseline characteristics are presented in Appendix Table C30.

After randomization to CCB (amlodipine at 5 to 15 mg/day), ACEI (fosinopril at 10 to 30 mg/day), or the combination, participants began a three month dose titration phase to a goal diastolic blood pressure less than 90 mm Hg for the monotherapy groups and less than 85 mm Hg for the combination therapy group. Patients judged nonresponders or who complained of side effects during the titration phase were withdrawn (n=144 overall, with no data reported by treatment group) and were not entered into the subsequent treatment phase. Study followup during the treatment phase was 4 years.

Renal Function

Study participants were required to have microalbuminuria, defined by UAER 30 to 300 mg/24 hours. For the patients entered in the treatment phase into either the ACEI plus CCB group or the ACEI alone group, the mean baseline serum creatinine was 1.0 mmol/L, mean creatinine clearance was 89.9 mg/min, and mean UAER was 97.9 µg/min. For the patients entered into either the ACEI plus CCB group or the CCB alone group, baseline characteristics were similar. Mean serum creatinine was 1.0 mg/dL, creatinine clearance was 89.3 mg/min, and UAER was 96.6 µg/min.

Baseline Comorbidities

Study participants were required to have hypertension (diastolic blood pressure 90 to 110 mm Hg) and type 2 diabetes (well controlled without insulin). Patients with a history of coronary heart disease, CHF, MI, or stroke were excluded. For patients entered in the treatment phase into either the ACEI plus CCB group or the ACEI alone group, mean baseline blood pressure was 160/99 mm Hg and baseline HbA_{1c} was 7.1 percent. For the patients entered into either the ACEI plus CCB group or the CCB alone group, mean baseline blood pressure was 161/99 mm Hg and HbA_{1c} was 7.0 percent.

Study Quality (Appendix Table C140)

The trial was rated fair quality. Concealment of treatment allocation was adequate. This open-label study did not perform analysis according to the intention-to-treat principle. In addition to participants excluded during the dose titration phase, additional participants withdrew during treatment, resulting in 47 percent total withdrawals.

Results

Mortality (Appendix Table C31 and Appendix Figures C6 and C7)

All-Cause Mortality

The trial reported deaths in few participants, with 2.9 percent, 3.9 percent, and 1.9 percent in ACEI monotherapy, CCB monotherapy, and ACEI+CCB combination groups respectively. There were no significant differences in risk of all-cause mortality between any of these treatment groups.

Cardiovascular Mortality

The trial reported cardiovascular deaths in few participants, with 1.9 percent, 1.9 percent, and 1.0 percent in ACEI monotherapy, CCB monotherapy, and ACEI+CCB combination groups respectively. There were no significant differences in risk of all-cause mortality between any of these treatment groups.

Vascular Outcomes (Appendix Tables C31 and C32 and Appendix Figures C6 and C7)

Myocardial Infarction

There were few events and no difference between the ACEI plus CCB combination compared with either ACEI alone or CCB alone for all-cause MI.

Stroke

There were few events and no difference between the ACEI plus CCB combination compared with either ACEI alone or CCB alone for stroke.

Other Vascular Outcomes

No other vascular or composite vascular outcomes were reported.

Renal Outcomes

End-Stage Renal Disease

No outcomes were reported for end-stage renal disease.

Other Renal Outcomes

No other renal or composite renal outcomes were reported.

Study Withdrawals and Adverse Events (Appendix Table C33)

The overall withdrawal rate for the study was 45 percent. Thirty two percent withdrew during the titration period (treatment group not stated). Excluding deaths, an additional 20 percent withdrew during the study period (22 percent CCB, 23 percent ACE, 15 percent ACEI plus CCB). Between 1 and 2 percent of the patients in each group discontinued study medication due to worsening kidney function. Other reported adverse events (also reported for less than 2 percent of the patients in any treatment group) were cough and edema.

Summary

In one study of patients with CKD, hypertension, and diabetes without a history of cardiovascular disease, few participants died or experienced clinical vascular or renal events. There was no significant difference for any of these outcomes between ACEI plus CCB versus either ACEI monotherapy or CCB monotherapy groups, but wide confidence intervals around all estimates could not exclude large between-group differences. Adverse events were infrequent and risk did not appear significantly different between treatment groups. There were no data on clinical renal outcomes. The study was limited by its exclusion of one-third of randomized participants from the analyses, the large number of additional withdrawals during treatment, the small number of clinical vascular events, and the absence of any reported clinical renal outcomes.

ACE Inhibitor Plus Diuretic Versus ACE Inhibitor Plus CCB Trials (n=2)

Overview

In patients with CKD we found insufficient evidence regarding whether there is any difference between combination therapy with an ACEI and a diuretic and combination therapy with an ACEI and CCB for risk of mortality or ESRD. Our confidence in these estimates is limited by the small number of trials reporting different outcomes, the small number of clinical events, and the heterogeneity of the study populations.

Description of Study

Two trials met all eligibility criteria. One trial randomized 332 patients with CKD to ACEI plus diuretic versus ACEI plus CCB.[106] The second trial reported results from 1,093 patients with CKD enrolled in a trial of 11,506 patients with hypertension and randomized to ACEI plus diuretic or ACEI plus CCB.[107,108] Detailed baseline characteristics are presented in Appendix Table C34.

In the first trial, patients randomized to the ACEI plus CCB group received benazepril and amlodipine. Those randomized to the ACEI plus diuretic group received benazepril and

hydrochlorothiazide (HCTZ). Doses were titrated to reach a blood pressure target below 130/80 mm Hg, and additional antihypertensives were added as needed with the exception of ACEI, ARB, or aldosterone receptor antagonists. The mean age of study participants was 58 years, and men constituted 65 percent of subjects. Patients were mostly white race (60 percent), with blacks comprising another 26 percent of participants. Study followup duration was 12 months.[106]

The protocol was similar in the second trial. The mean age of the subgroup with CKD was 70.9 years and 67 percent were men. Approximately 77 percent of the patients were white; 20 percent were black. The followup period was 2.9 years.[107]

Renal Function

In the first study, participants were required to have either microalbuminuria or macroalbuminuria (UACR 20 to 500 mg/g), and to have serum creatinine ≤1.3 mg/dl for women and ≤1.5 mg/dl for men. In data available only for the 304 patients who completed followup, the median UACR was 60.6 mg/g, and the median estimated GFR was 90.6 ml/min/1.73m^2.[106]

Patients eligible for the second trial had hypertension and were at high risk for cardiovascular events based on evidence of cardiovascular or renal disease or target organ damage. Criteria for renal disease included serum creatinine >1.5 mg/dL for women or >1.7 mg/dL for men or macroalbuminuria (UACR > 300 mg/g or > 200 mg/g if receiving an ACEI or aldosterone receptor blocker).[107]

Baseline Comorbidities

Trial participants in the first study were required to have hypertension (mean systolic blood pressure 130 to 179 mm Hg and diastolic blood pressure 80 to 109 mm Hg). Mean baseline blood pressure was 151/88 mm Hg. Individuals with CHF, type 1 diabetes or uncontrolled type 2 diabetes were excluded, as were those with a cardiovascular disease event in the past 6 months (MI, stroke, transient ischemic attack, coronary artery bypass grafting, or percutaneous transluminal coronary angioplasty).[106]

The second study enrolled patients age 60 and older with systolic blood pressure of 160 mm Hg or higher (or currently on antihypertensive therapy). Within the participants with CKD, mean systolic blood pressure was 145 mm Hg and 59 percent had diabetes. Vascular and hypertension-related reasons for study exclusion included: current evidence for angina pectoris, history of symptomatic heart failure or evidence of left ventricular ejection fraction <40 percent, acute MI or revascularization in the prior month, stroke or other ischemic cerebrovascular events in the prior 3 months, or hypertension that is severe, refractory to treatment, or known to have a secondary cause.[107]

Study Quality (Appendix Table C140)

The first study was rated fair quality. Treatment allocation concealment was adequate. The study was double blinded. Analysis was not according to the intention-to-treat principle. Withdrawals were 19 percent.[106] The second study was rated good quality. Treatment allocation was adequate, the study was double-blinded, analysis was by intention to treat, and withdrawals were adequately reported.[107]

Results

Mortality (Appendix Table C35 and Appendix Figure C8)

In the first study, among 166 patients allocated to ACEI plus diuretic, there were two deaths. Among 166 patients allocated to ACEI plus CCB, there was one death.[106] The second study did not report mortality.

Vascular Outcomes (Appendix Tables C35 and C36 and Appendix Figure C9)

Myocardial Infarction

There were no reports of MI in either study.

Stroke

There were no reports of stroke in either study.

Other Vascular Outcomes

Three patients in the ACEI plus diuretic group were reported to have undefined "cardiac disorders," and two were reported to have undefined "vascular disorders." In the ACEI plus CCB group, two patients were reported to have "cardiac disorders," and none had a "vascular disorder." There was no significant difference between treatment groups for any of these outcomes.[106] The second study did not report any other vascular outcomes.[107]

Renal Outcomes (Appendix Tables C37 and C38 and Appendix Figure C9)

End-Stage Renal Disease

No data were reported for end-stage renal disease in either study.

Other Renal Outcomes

In the first study, the risk of progression from microalbuminuria to macroalbuminuria was not significantly different between the ACEI plus diuretic group and the ACEI plus CCB group (4.0 versus 4.6 percent, RR0.84, 95% C 0.29 to 2.44).[106] The second study reported composite renal outcomes only for patients with CKD and diabetic nephropathy. In 644 patients, the risk of doubling of serum creatinine, ESRD, or need for chronic dialysis was not significantly different between the ACEI plus diuretic group and the ACEI plus CCB group (5.5 versus 5.8 percent, RR 1.15, 95% CI, 0.59 to 2.24). Similar results were observed when cardiovascular mortality was added to the renal outcome defined above (9.7 versus 8.4 percent, RR 1.16, 95% CI, 0.71 to 1.90).[107]

Study Withdrawals and Adverse Events (Appendix Table C39)

For the first study, 47 percent of participants withdrew after randomization, most of whom withdrew during the dose titration period for nonresponse or adverse effects, during which these results were not reported by treatment group. The overall withdrawal rate during the study period was 18.7 percent (21.7 percent in the ACEI plus diuretic group and 15.7 percent in the ACEI plus CCB group). During the study period, adverse events resulted in study withdrawal for 10.8 percent of the ACEI plus diuretic group and 5.4 percent of the ACEI plus CCB group, but details were not provided regarding specific adverse events that led to withdrawal. Reported adverse events in the ACEI plus CCB group and ACEI plus diuretic group, respectively, included edema

in 17.5 percent and 7.2 percent, cough in 13.9 percent and 10.3 percent, and dizziness in 9.0 percent and 6.6 percent.[106] The second study was a subgroup analysis and did not report study withdrawals for the CKD patients. Adverse events included edema (33.7 percent of the ACEI plus CCB group, 16.0 percent of the ACEI plus diuretic group), dizziness (25.1 and 24.2 percent, respectively), cough 21.4 and 17.5 percent, respectively), hypotension (4.3 and 5.5 percent, respectively), and hyperkalemia (0.0 and 0.2 percent, respectively).[107]

Summary

In one study of patients with CKD defined by albuminuria, hypertension with no recent cardiovascular events, and no heart failure, there was no significant difference between patients allocated to ACEI plus diuretic versus ACEI plus CCB in risk of mortality, or of unspecified "cardiac disorders" or "vascular disorders." However, there were very few events for any of these outcomes, and confidence intervals around risk estimates were wide. No data were reported for MI, stroke, CHF, ESRD, or any transparently defined composite vascular or renal outcome. The risk of progression from microalbuminuria to macroalbuminuria appeared similar between treatment groups, but again confidence intervals were wide. A second study reported no difference between treatment groups for two composite renal outcomes assessed in patients with CKD and diabetic nephropathy. Risk of edema appeared somewhat higher in the ACEI plus CCB group in the first study and was significantly higher in the second study. Cough and dizziness appeared somewhat higher in the ACEI plus CCB groups in both studies.

ACE Inhibitor Plus Diuretic Versus ACE Inhibitor Monotherapy Trial

Overview

In patients with CKD, we found insufficient evidence regarding whether treatments differ for risk of mortality or ESRD. There was a significantly reduced risk of achieving the composite vascular outcome in the ACEI plus diuretic group. Our confidence in these estimates is limited because data are drawn from only one trial and there were few reported clinical events.

Description of Study

One trial met all eligibility criteria and randomized 481 patients with CKD to receive either an ACEI and diuretic or a different ACEI alone.[109] Detailed baseline characteristics are presented in Appendix Table C40 for the 457 patients who took at least one dose of study medication and who had albuminuria measured at least once during treatment.

The ACEI plus diuretic group received perindopril and indapamide, while the ACEI monotherapy group received enalapril. Both groups were titrated to achieve a blood pressure goal of less than 140/90 mm Hg. The mean age of subjects was 59 years and 61 percent of study participants were male. Ninety-one percent of the study participants were white. Mean followup duration was 10.7 months.

Renal Function

Study participants were required to have albuminuria (UAER of 20 to 499 µg/min) and to have a serum creatinine less than approximately 1.6 mg/dl. Mean UAER was 92.1µg/min and the mean urine albumin/creatinine ratio was 8.5 mg/mmol.

Baseline Comorbidities

Study participants were required to have type 2 diabetes with HbA_{1c} less than 9 percent in the 3 months prior to the study. Mean baseline HbA_{1c} was 7.2 percent. Participants also were required to have hypertension (systolic blood pressure 140 to 179 mm Hg and diastolic blood pressure less than 110 mm Hg). Mean baseline blood pressure was 158/93 mm Hg.

Study Quality (Appendix Table C140)

Study quality was rated fair. Though the study was double blind, allocation concealment was unclear and analysis was not intention-to-treat. Withdrawals were 23 percent and were not adequately described.

Results

Mortality

The number of deaths during the study could not be determined.

Vascular Outcomes (Appendix Tables C41 and C42 and Appendix Figure C10)

Myocardial Infarction

The number of MIs during the study could not be determined.

Stroke

The number of strokes during the study could not be determined.

Other Vascular Outcomes

The only clinical outcome reported was serious (fatal or requiring prolonged hospitalization) cardiovascular events (defined by ICD9-1975 revision codes for sudden death and many other cardiovascular conditions). There was a significantly reduced risk of achieving the composite vascular outcome in the ACEI plus diuretic group (RR 0.39, 95% CI, 0.15 to 0.98).

Renal Outcomes

End-Stage Renal Disease

There were no reports of end-stage renal disease.

Other Renal Outcomes

There were no other renal outcomes reported.

Study Withdrawals and Adverse Events (Appendix Table C43)

The overall withdrawal rate for the study was 23 percent, including 21 percent in the ACEI plus diuretic group and 25 percent in the ACEI group. Adverse events related to drug treatment were similar for the two groups (14 percent and 15 percent for the ACEI plus diuretic and ACEI groups, respectively) as were withdrawals due to adverse events (8 percent and 9 percent, respectively). Specific adverse events included hyperkalemia in 3.3 percent of the ACEI

plus diuretic group and 5.5 percent of the ACEI group and cough in 3.7 percent of the ACEI plus diuretic group and 2.1 percent of the ACEI group.

Summary

In patients with CKD, hypertension, and type 2 diabetes, a combination of ACEI and diuretics was associated with a significant reduction in risk of serious cardiovascular events compared with treatment with ACEI monotherapy. The risk of adverse events was similar in the two groups. Results were limited because there were no data on mortality or specific cardiovascular or renal outcomes. Further, analysis was not based on intention-to-treat principles and the study withdrawals or dropouts were not adequately described. Mean followup for this study was 10.7 months.

ACE Inhibitor Plus Diuretic Versus Placebo Trial

Overview

In patients with CKD, we found a low strength of evidence that combination therapy with an ACEI and a diuretic did not significantly reduce mortality compared with placebo. We found insufficient evidence that there was no difference between treatments in risk of ESRD.[110] We found no significant difference between treatment groups for risk of cardiovascular mortality; risk of major cardiovascular events, major coronary events, or major cerebrovascular events; or risk of a composite renal outcome. Our confidence in these estimates is limited because data are drawn from only one trial and there were few reported clinical events for several outcomes.

Description of Study

A subgroup analysis of a larger trial of patients with type 2 diabetes met all eligibility criteria. The analysis included 2,482 patients with stage 1 or 2 CKD and 2,044 patients with stage 3 CKD who had been randomized to receive either an ACEI and diuretic or placebo[109] Detailed baseline characteristics are presented in Appendix Table C44).

The ACEI plus diuretic group received perindopril and indapamide. The mean age of subjects in the subgroup analysis was 67 years and 53 percent of study participants were male. Race/ethnicity data were not reported. Mean followup duration was 4.3 years.

Renal Function

For inclusion in this post hoc analysis, study participants were required to have CKD. As noted above, 2,482 participants had CKD stages 1–2, and 2,044 had CKD stage 3 or worse. Mean urine albumin-creatinine ratio was 48.1 µg/mg, and mean eGFR was 70.7 ml/min/1.73m^2.

Baseline Comorbidities

Study participants were required to be age 55 or older, diagnosed with type 2 diabetes at age 30 or older. Mean baseline HbA_{1c} was 7.7 percent. A history of macrovascular disease was reported in 34.7 percent of participants, and 12.8 percent reported a history of MI, and 10.8 percent reported a history of stroke. Mean baseline blood pressure was 148/81 mm Hg.

Study Quality (Appendix Table C140)

Study quality was rated as good. Treatment allocation concealment was adequate, the study was double-blind, the study was analyzed as intention to treat, and withdrawals were adequately reported.

Results

Mortality (Appendix Table C45 and Appendix Figure C11)

All-Cause Mortality

There was no significant difference in risk of all-cause mortality between treatment groups for the subgroups of patients with CKD stages 1–2 (RR 0.91, 95% CI, 0.72 to 1.16), or CKD stages 3 or worse (RR 0.88, 95% CI, 0.70 to 1.11)). In patients without CKD, there also was no significant difference in risk for all-cause mortality between treatment groups (RR 0.91, 95% CI, 0.73 to 1.13). In pooled analyses including all CKD and non-CKD study participants, risk of all-cause mortality was significantly reduced in the group randomized to ACEI plus diuretic as compared with the placebo group (RR 0.86, 95% CI, 0.75 to 0.98). The p-value for trend was 0.74 between the three subgroups.

Cardiovascular Mortality

There was no significant difference in risk of cardiovascular mortality between treatment groups for the subgroups of patients with CKD stages 1–2 (RR 0.77, 95% CI, 0.55 to 1.06), or CKD stages 3 or worse (RR 0.81, 95% CI, 0.59 to 1.11). In patients without CKD, there also was no significant difference in risk for cardiovascular mortality between treatment groups (RR 1.00, 95% CI, 0.72 to 1.39). In pooled analyses including all CKD and non-CKD study participants, risk of cardiovascular mortality was significantly reduced in the group randomized to ACEI plus diuretic as compared with the placebo group (RR 0.82, 95% CI, 0.68 to 0.98). The p-value for trend was 0.36 between the three subgroups.

Vascular Outcomes (Appendix Tables C45-C47 and Appendix Figure C11)

Myocardial Infarction

No study data were reported for myocardial infarctions.

Stroke

No study data were reported for stroke.

Other Vascular Outcomes

Among study participants with CKD, there was no significant difference between treatment groups in risk of major cardiovascular events, major coronary events, or major cerebrovascular events. For major cardiovascular events, there was no reduced risk either for participants with CKD stages 1-2 (RR 0.89, 95% CI, 0.70 to 1.13), or for patients with CKD stages 3 or worse (RR 0.87, 95% CI, 0.68 to 1.10). For major coronary events, there was no reduced risk either for participants with CKD stages 1-2 (RR 0.89, 95% CI, 0.64 to 1.23), or for patients with CKD stages 3 or worse (RR 0.85, 95% CI, 0.62 to 1.1). For major cerebrovascular events, there was no reduced risk either for participants with CKD stages 1-2 (RR 0.88, 95% CI, 0.61 to 1.26), or for patients with CKD stages 3 or worse (RR 0.84, 95% CI, 0.58 to 1.22). For all these outcomes,

there also was no significant difference in risk between treatments for patients without CKD, or for patients considered overall. For all outcomes, the p-value for trend between subgroups was not statistically significant. Results were similar in analyses in which patients were stratified by eGFR or by urine albumin-creatinine ratio.

Renal Outcomes (Appendix Tables C48 and C49 and Appendix Figure C11)

End-Stage Renal Disease

No study data were reported for end-stage renal disease.

Other Renal Outcomes

Among study participants with CKD, there was no significant difference between treatment groups in risk of a composite renal outcome defined as occurrence of either incident macroalbuminuria, doubling of serum creatinine to a level of at least 2.26 mg/dL, need for renal replacement therapy, or death due to renal illness. Stratified by baseline CKD, there was a statistically significant reduction in risk in participants with CKD stages 1–2 (RR 0.69, 95% CI, 0.51 to 0.93), but not for patients with CKD stages 3 or worse (RR 0.93, 95% CI, 0.66 to 1.31), However, the p-value for trend between subgroups was 0.79. In results stratified by eGFR or by urine albumin-creatinine ratio, there was no significant difference between treatment groups for risk of the composite renal outcome within any stratum.

Study Withdrawals and Adverse Events (Appendix Table C50)

Adverse events leading to discontinuation of the treatment (including serious adverse events, dough, and hypotension/dizziness), regardless of whether they were considered to be drug related, are presented in Table C50. The incidence was higher in the active treatment group but no differences were observed for the subgroups based on CKD stage.

Summary

In a subgroup of patients with CKD, type 2 diabetes, and at high risk for vascular events, a combination of ACEI and diuretic was not associated with a significant reduction in risk of mortality or clinical cardiovascular or renal events compared with treatment with placebo. Risk for the composite renal outcome were significantly reduced with ACEI plus diuretic in patients with CKD stages 1-2, but given that this finding was not observed in analyses stratified by eGFR or albuminuria, and tests for interaction by CKD strata were not significant, the probability of this being a chance finding is substantial.

ARB (Higher Dose) Versus ARB (Lower Dose) Trial

Overview

We found insufficient strength of evidence regarding whether there is any difference between higher and lower dose ARB in risk of mortality or ESRD. We found that higher dose ARB significantly reduces risk of conversion from microalbuminuria to macroalbuminuria. Our confidence in these estimates is limited because data are drawn from only one trial and there were few reported clinical events.

Description of Studies

Three trials met eligibility criteria and randomized participants with CKD to at least two different fixed doses of ARB treatment. One trial randomized 269 participants to three different doses of candesartan (16 mg/day, 64 mg/day, and 128 mg/day.[111] A second trial randomized participants to telmisartan 40 mg/day versus 80 mg/day).[95] A third trial randomized participants to irbesartan 150 mg/day versus 300 mg/day.[96] Detailed baseline characteristics are presented in Appendix Tables C51 and C52.

Mean age of study participants was 58.5 years. Men constituted 73 percent of all study participants (2 trials reporting). In two studies reporting race/ethnicity, 91 percent of participants were white. The studies were conducted in Canada, Japan, and multinational. Median followup durations ranged from 7 months to 2 years.

Renal Function

Two trials required participants to have microalbuminuria, defined in one study by urinary albumin:creatinine ratio of 100-300 mg/g and in the other study by repeated urinary albumin excretion rate of 20-200 micrograms/minute. Both of these studies excluded participants with serum creatinine greater than 1.5 mg/dl in men and either greater than 1.1 or 1.3 mg/dl in women. The third study required repeated urinary protein excretion of at least 1 g/day and excluded participants with serum creatinine >3.4 mg/dl. One trial reported a mean serum creatinine of 1.44 mg/dl, eGFR of 52.0 ml/min/1.73m^2 and proteinuria of 2.83 g/day. A second trial reported a mean serum creatinine of 1.05 mg/dl, creatinine clearance of 109 ml/min/1.73m^2 and albuminuria of 55.9 micrograms/day. The third trial provided no data on baseline renal function. Mean serum creatinine in two trials reporting was 1.21 mg/dl.

Baseline Comorbidities

All participants in two trials were required to have hypertension, and all participants in two trials were required to have diabetes. One trial each provided no information on prevalence of diabetes or hypertension. Mean baseline blood pressure was 142/82 mm Hg. In one trial reporting, prevalence of cardiovascular disease was rare.

Study Quality (Appendix Table C140)

Two trials were rated as fair quality and one was rated as good quality. All trials were double blinded but only one reported using adequate concealment methods for treatment allocation. Results were analyzed according to the intention-to-treat principle in two studies and withdrawal and dropouts were adequately described in all trials. Withdrawals ranged from 12 to 14 percent in two trials reporting.[96,111]

Results

Mortality (Appendix Tables C53)

One trial reported deaths in 1.5 percent of participants randomized to high dose irbesartan versus in none of those assigned to low dose irbesartan. A second trial reported that there were no deaths in any of the three candesartan dose groups.

Vascular Outcomes (Appendix Tables C53–C55)

Myocardial Infarction

There were no reports of myocardial infarction.

Stroke

There were no reports of stroke.

Other Vascular Outcomes

No other vascular outcomes were reported.

Renal Outcomes (Appendix Tables C56 and C57)

End-Stage Renal Disease

There were no reports of end-stage renal disease.

Other Renal Outcomes

Risk of conversion from microalbuminuria to macroalbuminuria with high dose telmisartan was not significantly different than for low dose telmisartan (RR 0.74, 95% CI, 0.48 to 1.14) and also was not significantly different for high dose irbesartan than for low dose irbesartan (RR 0.53, 95% CI, 0.25 to 1.11). In pooled results, reduction in risk was significantly lower with higher dose ARB than lower dose ARB (RR 0.68, 95% CI, 0.46 to 0.98). No other renal outcomes were reported.

Study Withdrawals and Adverse Events (Appendix Table C58)

Study withdrawals ranged from 2.4 to 14 percent between trials. In the candesartan trial, withdrawals were 20 percent in the 16 mg/day candesartan group, 6.7 percent in the 64 mg/day group, and 15.7 percent in the 128 mg/day group. In the irbesartan trial, 13.8 percent of participants withdrew from the low dose group compared with 10.3 percent from the high dose group. Withdrawals were not reported by treatment group for the telmisartan trial. Study withdrawals due to serious adverse effects were 12.2 percent in the 16 mg/day candesartan group, 5.5 percent in the 64 mg/day group, and 9.0 percent in the 128 mg/day group. Withdrawals due to serious adverse effects were reported in 9.2 percent of individuals assigned to low dose irbesartan compared with 4.1 percent of those assigned high dose irbesartan. The incidence of hyperkalemia was reported in only one trial and was between 3.3 and 4.4 percent for each of the three candesartan dose groups.

Summary

In these three small trials of CKD patients with albuminuria, high dose ARB treatment was associated with a significant reduction in risk of conversion from microalbuminuria to macroalbuminuria. Trials reported very few deaths and no other vascular or renal outcomes. Withdrawals and adverse events did not appear higher in the higher dose ARB groups compared with the low dose group in either trial reporting these data.

ARB Versus Different ARB Trials (n=2)

Overview

In patients with CKD, we found a low level of evidence that telmisartan significantly reduces risk of all-cause mortality compared with losartan and a low level of evidence that there is no difference in risk of all-cause mortality between telmisartan and valsartan. In addition, we found a low level of evidence that there is no difference in risk of ESRD between telmisartan and losartan and insufficient (no) evidence regarding whether risk for ESRD differs between telmisartan and valsartan. Our confidence in these estimates is limited by the small number of trials reporting different outcomes and the small number of clinical events.

Description of Studies

Two trials met all eligibility criteria and randomized 1,745 participants with CKD to treatment comparing two different ARBs.[112,113] Detailed baseline characteristics are presented in Appendix Tables C51 and C52.

One trial randomized 860 participants to telmisartan versus losartan.[112] The second trial randomized 885 participants to telmisartan versus valsartan.[113] The mean age of study participants was 61 years (range 60 to 61) and men constituted 63 percent (range 62 to 64) of all participants studied. Both trials reported race/ethnicity, and 63 percent of participants were white, 30 percent were Asian, and 7 percent were black. Both were multinational studies and followup duration ranged from 10.7 to 12 months.

Renal Function

Both trials required that participants have overt proteinuria, and allowed subjects with either normal or elevated serum creatinine levels, setting an upper abnormal limit. In one trial, participants had to have proteinuria of 900 mg/24 hours or greater and a serum creatinine of 3.0 mg/dl or less.[113] This study reported a mean baseline proteinuria of 2.78 g/day. In the second trial, patients had to have a urine protein-creatinine ratio at least 700 mg/g and a serum creatinine <3.0 mg/dl in women and <3.2 mg/dl in men.[112] At baseline, this study reported a mean urine protein-creatinine ratio of 1,991 mg/g, mean urine albumin-creatinine ratio of 1,394 mg/g, and a mean serum creatinine of 1.55 mg/dl. For both trials considered together, the mean baseline GFR was 53.2 ml/min/1.73m^2 (range 49.6 to 56.6).

Baseline Comorbidities

Both trials were restricted to patients with type 2 diabetes and hypertension. At baseline, mean HbA_{1c} was 7.85 percent and mean blood pressure was 146/81 mm Hg. One trial excluded patients with a history of "clinically significant" heart disease or stroke, which was presumed to exclude patients with a history of coronary artery disease, MI, or congestive heart failure.[112] The second study excluded patients with any history of congestive heart failure and those with a "recent acute cardiovascular event."[113] It did not report data on prevalence of coronary artery disease, MI, or stroke.

Study Quality (Appendix Table C140)

Both trials were rated as fair quality. Allocation concealment was unclear in both studies. Both were double blinded. One study analyzed results according to the intention-to-treat principal and adequately described the 19.1 percent of subjects who withdrew from the study.[113]

The second study did not include an intention-to-treat analysis and did not adequately describe the 18.4 percent of participants who withdrew.[112]

Results

Mortality (Table 11, Appendix Table C53, and Figure C12)

All-Cause Mortality

Among these patients with CKD, those randomized to telmisartan had a significant 84 percent reduction in risk of all-cause mortality compared with those randomized to losartan (0.5 versus 2.9 percent; RR 0.16, 95% CI, 0.04 to 0.71).[112] However, the risk of all-cause mortality was higher, although not significantly so, for patients assigned telmisartan versus valsartan (3.5 versus 1.9 percent; RR 1.88, 95% CI, 0.81 to 4.39).[113] Results from these trials were not pooled as the results suggested large differences in the direction of the effect of losartan and valsartan compared with telmisartan. This was reflected in the I^2 of 75 percent.

Cardiovascular Mortality

One study reported no significant difference between the telmisartan or valsartan treatment groups for cardiovascular mortality (RR 1.34, 95% CI, 0.47 to 3.82).[113]

Vascular Outcomes (Table 11, Appendix Tables C53-C55 and Appendix Figure C12)

Myocardial Infarction

In one trial reporting, there was no significant difference between telmisartan and valsartan in risk of myocardial infarction (RR 0.36, 95% CI, 0.12 to 1.14).[113]

Stroke

In the same trial, there was no significant difference between telmisartan and valsartan in the risk of stroke (RR 2.21, 95% CI, 0.77 to 6.29).[113]

Other Vascular Outcomes

Again in one trial reporting, there was no significant difference between telmisartan and valsartan in the risk of hospitalization for congestive heart failure (RR 1.17, 95% CI, 0.39 to 3.52).[113] Both trials defined and reported results for composite vascular endpoints. One reported a borderline statistically significant 40 percent reduction in risk of cardiovascular mortality or cardiovascular morbidity (not defined) in its CKD population assigned to telmisartan versus those assigned to losartan (RR 0.60, 95% CI, 0.36 to 1.00).[112] The second trial reported no difference between its participants with CKD allocated to telmisartan versus valsartan for the composite outcome of MI, stroke, hospitalization for CHF or unstable angina, or coronary or peripheral revascularization (RR 0.94, 95% CI, 0.59 to 1.51).[113]

Renal Outcomes (Table 11, Appendix Tables C56 and C57, and Appendix Figure C10)

End-Stage Renal Disease

In the one trial reporting this outcome, there was no apparent difference in risk for ESRD between CKD patients randomized to telmisartan versus valsartan (RR 0.88, 95% CI, 0.32 to 2.40).[113]

Other Renal Outcomes

One trial reported that there was no difference between subjects randomized to telmisartan versus valsartan for doubling of serum creatinine (RR 1.0, 95% CI, 0.20 to 4.94).[113] Both trials reported no significant difference between assigned ARBs in risk of a composite renal outcome defined as doubling of serum creatinine, ESRD, or death. One trial reported a nonsignificant 41 percent reduced risk with telmisartan compared with losartan (RR 0.59, 95% CI 0.31 to 1.12),[112] but the other trial reported a nonsignificant 23 percent increased risk with telmisartan compared with valsartan (RR 1.23, 95% CI, 0.42 to 1.75).[113] Neither study reported results for halving of GFR or progression from microalbuminuria to macroalbuminuria.

Study Withdrawals and Adverse Events (Appendix Table C58)

Overall study withdrawals were comparable in the two studies at 18.4 percent[112] and 19.1 percent.[113] There were fewer serious adverse events in the telmisartan group (15.5 percent) than in the losartan group (22.4 percent)[112] but more serious adverse events in the telmisartan group (26.2 percent) than in the valsartan group (23.5 percent).[113] Overall withdrawals for serious adverse events were low (3.2 percent or less in all groups). Similarly, the incidence of hyperkalemia was low in all groups (<2.9 percent).

Summary

In individuals with CKD, type 2 diabetes mellitus, and hypertension, compared with losartan, telmisartan was associated with a significant 84 percent reduction in all-cause mortality and a borderline significant 40 percent reduction in cardiovascular morbidity or cardiovascular mortality. In addition, telmisartan was associated with a nonsignificant 41 percent reduction in risk of the composite endpoint of doubling of serum creatinine, ESRD, or death, and with fewer serious adverse events. However, compared with valsartan, CKD patients randomized to telmisartan appeared to have a nonsignificantly higher risk of all-cause and cardiovascular mortality, stroke, and CHF, but a lower risk of MI. There was little difference in the composite vascular outcome or in any of the adverse event measures recorded. Results were limited by relatively small sample size and number of clinical events, with most outcomes reported only in one trial, and heterogeneity in comparison groups and outcomes that prevented statistical pooling. This resulted in there being low statistical power to determine if even large differences in outcomes between treatment groups were statistically significant. Results also were limited in that there were no studies that directly compared losartan and valsartan. Because no trial was longer than 1 year, it was not possible from these studies to determine the longer term effects of telmisartan versus losartan or valsartan.

Table 11. Pooled clinical and renal outcomes, ARB versus ARB trials

Outcome	Number of Trials Reporting	Quality of the Studies	Intervention Events/N (%)	Control Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
Telmisartan vs. Different ARB						
All-cause mortality	2	Fair	17/847 (2.0)	21/870 (2.4)	0.59 [0.05-6.88]	88%
Bakris, 2008[112]	1	Fair	2/419 (0.5)	13/441 (2.9)	0.16 [0.04-0.71]	NA
Galle, 2008[113]	1	Fair	15/428 (3.5)	8/429 (1.9)	1.88 [0.81-4.39]	NA
Cardiovascular mortality	1	Fair	8/428 (1.9)	6/429 (1.4)	1.34 [0.47-3.82]	NA
Myocardial infarction	1	Fair	4/428 (0.9)	11/429 (2.6)	0.36 [0.12-1.14]	NA
Stroke	1	Fair	11/428 (2.6)	5/429 (1.2)	2.21 [0.77-6.29]	NA
CHF hospitalization	1	Fair	7/428 (1.6)	6/429 (1.4)	1.17 [0.40-3.45]	NA
Composite vascular† Bakris, 2008[112]	1	Fair	21/419 (5.0)	37/441 (8.4)	0.60 [0.36-1.00]	NA
Composite vascular* Galle, 2008[113]	1	Fair	31/428 (7.2)	33/429 (7.7)	0.94 [0.59-1.51]	NA
End-stage renal disease	1	Fair	7/428 (1.6)	8/429 (1.9)	0.88 [0.32-2.40]	NA
Doubling of serum creatinine	1	Fair	3/428 (0.7)	3/429 (0.7)	1.00 [0.20-4.94]	NA
Composite renal outcome**						
Bakris, 2008[112]	1	Fair	14/419 (3.3)	25/441 (5.7)	0.59 [0.31-1.12]	NA
Galle, 2008[113]	1	Fair	22/428 (5.1)	18/429 (4.1)	1.23 [0.67- 2.25]	NA

MI = myocardial infarction; NA = not applicable; RR = relative risk reduction

†Bakris = Cardiovascular morbidity (not defined) or mortality.

*Galle = Myocardial infarction, stroke, or hospitalization for heart failure or unstable angina, coronary or peripheral revascularization.

**Doubling of serum creatinine concentration, end-stage renal disease (need for long-term dialysis, renal transplantation, or serum creatinine ≥ 6 mg/dl), or death.

ACE Inhibitor Plus Aldosterone Antagonist Versus ACE Inhibitor Plus Placebo Trial

Overview

In patients with CKD, we found insufficient evidence regarding whether there is a difference between ACEI plus aldosterone antagonist versus ACEI alone for risk of all-cause mortality or ESRD. Our confidence in these estimates is limited because data are drawn from only one trial and there were few reported clinical events.

Description of Study

We identified one trial that met all eligibility criteria and randomized 54 patients with CKD being treated with ACEI to either additional aldosterone antagonist or placebo.[103] Detailed baseline characteristics for this comparison are presented in Appendix Table C59. Data regarding a third treatment arm, the addition of ARB to ACEI are discussed separately.

Mean age of randomized participants was 51 years, and men constituted 46 percent of the subjects. Fifty-four percent of patients were Hispanic, 32 percent were black, 11 percent were non-Hispanic white, and 3 percent were Native American. Mean study followup duration was 11.1 months.

Renal Function

For inclusion, participants were required to have macroalbuminuria (UACR at least 300 mg/g) despite run-in treatment. Women with serum creatinine above 3.0 mg/dL and men with creatinine above 4.0 mg/dL were excluded from the study. Among randomized participants, mean baseline UACR was 1,006 mg/g, mean serum creatinine was 1.6 mg/dL, and mean creatinine clearance was 62 ml/min.

Baseline Comorbidities

All study participants were required to be hypertensive prior to screening but were treated with diet and ACEI during a pre-randomization 3 month run-in period to a target systolic blood pressure of less than 130 mm Hg. Mean blood pressure at randomization was 132/74 mm Hg study participants also were required to have diabetes, and mean HbA_{1c} was 7.8 percent. Patients with a history of heart failure, and those with a stroke or MI within 12 months were excluded from the trial. A history of either MI, CABG, or PTCA was reported by 9.3 percent.

Study Quality (Appendix Table C140)

Study quality was rated fair. The trial was double blinded, but allocation concealment was unclear. While the overall study analysis was not by intention-to-treat, this pertained to exclusion from analyses of a single participant randomized into the ACEI plus ARB treatment group that is not the focus of this section of the report. Withdrawals were 30 percent.

Results

Mortality (Appendix Table C60)

There were no deaths during the followup period.

Vascular Outcomes (Appendix Tables C60 and C61 and Appendix Figure C13)

Myocardial Infarction

Among participants in the ACEI plus aldosterone antagonist group, there was one subject with MI, while in the ACEI plus placebo group, no subjects had an MI.

Stroke

Among participants in the ACEI plus aldosterone antagonist group, there were two subjects with stroke. In the ACEI plus placebo group, one subject had a stroke.

Other Vascular Outcomes

Among participants in the ACEI plus aldosterone antagonist group, two subjects were hospitalized for heart failure. In the ACEI plus placebo group, no subjects were hospitalized for heart failure. The study did not report results for any composite vascular outcomes.

Renal Outcomes

End-Stage Renal Disease

The study did not report results for ESRD.

Other Renal Outcomes

The study did not report results for doubling baseline creatinine, halving GFR, or for any composite renal outcome.

Study Withdrawals and Adverse Events (Appendix Table C62)

In the ACEI plus aldosterone antagonist group, withdrawals and withdrawals due to adverse effects occurred in 37 percent and 26 percent of participants respectively, as compared with 22 percent and 7 percent, respectively, in the ACEI plus placebo group. Adverse effects attributing to withdrawal were hyperkalemia (n=2), stroke (n=2), symptomatic hypotension (n=1), gynecomastia (n=1), and increased serum creatinine (n=1) in the ACEI plus aldosterone antagonist group, and stroke (n=1) and increased serum creatinine (n=1) in the ACEI plus placebo group.

Summary

In this small, short duration study of CKD patients with macroalbuminuria, hypertension, and diabetes, but with no history of heart failure and with a low prevalence of other cardiovascular disease, there were no deaths and very few cardiovascular outcomes. Differences in individual cardiovascular outcomes were not statistically significant. Participants in the ACEI plus aldosterone group appeared to be at higher risk for adverse events leading to discontinuation of treatment and study withdrawal. Results were limited by the short study duration, and small number of individual clinical vascular events. Also, no clinical renal outcomes data were reported.

ACE Inhibitor/ARB Plus Aldosterone Antagonist Versus ACE Inhibitor/ARB Plus Placebo Trial

Overview

In patients with CKD, there was insufficient evidence regarding whether, in comparison to treatment with ACEI or ARB plus placebo, treatment with ACEI or ARB plus aldosterone antagonist reduces mortality or ESRD. Our confidence in these estimates is limited because data are drawn from only one trial and there were few reported clinical events.

Description of Study

One trial met all eligibility criteria and randomized 59 participants with CKD and taking ACEI or ARB at baseline to the addition of an aldosterone antagonist versus addition of placebo.[114] Detailed baseline characteristics are presented in Appendix Table C63.

Participants using an ACEI or ARB in recommended dosages for at least 1 year were randomized to addition of the aldosterone antagonist, spironolactone, 50 mg daily versus placebo. Mean age in study participants was 52 years and 66 percent of subjects were men. Study followup duration was 1 year.

Renal Function

Eligible participants were required to have albuminuria, defined as either 24 hour urinary albumin excretion greater than 300 mg or UACR greater than 20 mg/mmol. Mean serum creatinine was 98.2 μmol/l, mean UACR was 81 mg/mmol, and mean protein-to-creatinine ratio was 128.5 mg/mmol. The mean estimated GFR was 70.5 ml/min/1.73m^2.

Baseline Comorbidities

All participants had type 2 diabetes. Patients with MI or stroke within the past 3 months or with unstable angina pectoris were excluded. Mean blood pressure was 146/81 mm Hg and mean HbA_{1c} was 8.1 percent.

Study Quality (Appendix Table C140)

Study quality was rated fair. Treatment allocation concealment was adequate. The study was double blinded. Analysis was not performed according to the intention to treat principle. Withdrawals were 11.9 percent and were adequately described.

Results

Mortality (Appendix Table C64 and Appendix Figure C14)

There were two deaths in the placebo group due to complications following an MI (RR 0.21, 95% CI, 0.01 to 4.13).

Vascular Outcomes (Appendix Table C64)

Myocardial Infarction

As noted above, there were two fatal MIs in the placebo group.

Stroke

There were no reports of stroke.

Other Vascular Outcomes

No other vascular outcomes were reported.

Renal Outcomes

End-Stage Renal Disease

There were no reports of end-stage renal disease.

Other Renal Outcomes

No other renal outcomes were reported.

Study Withdrawals and Adverse Events (Appendix Table C65)

Of 59 patients randomized, six (17.2 percent) in the aldosterone antagonist group and one (3.3 percent) in the placebo group discontinued treatment as a result of hyperkalemia developed during the first 2 to 12 weeks of treatment. During the rest of the study, two additional patients in the aldosterone antagonist group and one in the placebo group discontinued treatment.

Summary

In one trial in patients with CKD and diabetes, already on ACEI or ARB, there was no significant difference in risk of all-cause or cardiovascular mortality between those randomized to addition of aldosterone antagonist versus placebo. No data were reported for other vascular or clinical renal outcomes. Results were limited in that they were based on only one small study with low statistical power for clinical events, which do not appear to have been a priori study outcomes.

Beta Blocker (BB) Versus Placebo Trials (n=2)

Overview

We found low strength of evidence that in patients with heart failure and CKD who are on optimal medical therapy for their heart failure, treatment with BB significantly reduced risk of all-cause mortality. We found insufficient evidence in this population regarding whether there is a difference between BB and placebo regarding risk of ESRD as neither trial reported ESRD outcomes. Participants with CKD assigned to BB had a significantly lower risk of CHF complications, MI, or cardiac death. Our confidence in these estimates is limited by the small number of trials reporting different outcomes and the small number of clinical events.

Description of Study

We identified two trials that met all eligibility criteria and randomized participants with CKD to BB versus placebo.[115,116] One study was a post hoc subgroup analysis of 1,469 subjects with eGFR ≤60 ml/min/1.73m^2 from the larger MERIT-HF heart failure trial (n=3,991)[115] The second study was a post hoc subgroup analysis of 704 patients with eGFR <55.5 ml/min/1.73m^2 from the larger SENIORS heart failure trial (n=2,135). Detailed baseline characteristics are presented in Appendix Table C66.

All participants in MERIT-HF were required to have been on optimum heart failure therapy consisting of any combination or diuretics and an ACEI, with hydralazine, long acting nitrate, or ARB if an ACEI was not tolerated. Patients then were randomized to the BB, metoprolol XL/CR versus placebo. At baseline, 88 percent of the patients were taking an ACEI and 94 percent were taking diuretics. The mean age of study participants was 68 years and 68 percent of subjects were male. No data were reported on race/ethnicity in this multinational study. Study followup duration was 1 year.

Participants in the SENIORS trial had a documented clinical history of heart failure and were receiving optimal standard therapy. Patients were randomized to receive either BB (nebivolol) or placebo. Baseline use of other medications was not reported according to eGFR levels but it was noted that among participants with poorer renal function, more were taking diuretics and ARB and fewer were taking ACEI. The mean age of the CKD subgroup was 77 years and 59 percent were male. The study was conducted in 11 European countries, but no race/ethnicity data were reported. Mean followup was 21 months.

Renal Function

For inclusion in the post hoc analysis of the MERIT-HF trial, participants were required to have eGFR ≤60 ml/min/1.73m^2. There were 976 participants with eGFR 45 to 60 ml/min/1.73m^2, and 493 with eGFR <45 ml/min/1.73m^2. In these two strata combined, mean GFR was 48 ml/min/1.73m^2 and mean serum creatinine was 1.5 mg/dL. For the post hoc analysis of the SENIORS trial, tertiles of eGFR were created. In the tertile with eGFR <55.5 ml/min/1.73m^2, the mean eGFR was 43 ml/min/1.73m^2 and mean serum creatinine was 1.6 mg/dL.

Baseline Comorbidities

All participants in the MERIT-HF and SENIORS trials were required to have symptomatic or documented heart failure. Among participants in the MERIT-HF post hoc analysis, diabetes was reported for 29 percent, a history of hypertension for 49 percent, and a history of myocardial infarction for 55 percent. Mean baseline blood pressure was 130/77 mm Hg. Among participants in the SENIORS post hoc analysis, diabetes was reported for 29 percent, and 46 percent had a history of myocardial infarction. Mean baseline blood pressure was 134/78 mm Hg.

Study Quality (Appendix Table C140)

Study quality was rated as good for one trial and fair for one trial. Concealment of treatment allocation in both double-blind trials was adequate. Analyses were performed according to the intention-to-treat principle in the MERIT-HF trial; however, 23 randomized patients were excluded from the SENIORS trial post hoc analysis. No data on withdrawals were reported for the CKD subgroups.

Results

Mortality (Appendix Table C67 and Appendix Figure C15)

All-Cause Mortality

In the patients with CKD and heart failure, there was a significant reduction in the risk of all-cause mortality in those treated with BB versus placebo (12.4 versus 18.1 percent, RR 0.69, 95%

CI, 0.53 to 0.91). In both studies, results were stratified by baseline eGFR. The MERIT-HF study reported an adjusted HR 0.41, 95% CI, 0.25 to 0.68 for patients with eGFR <45 ml/min/1.73m^2, HR 0.68, 95% CI, 0.45 to 1.02 for patients with eGFR 45 to 60 ml/min/1.73m^2, and HR 0.71, 95% CI, 0.54 to 0.95 for those with eGFR greater than 60 ml/min/1.73m^2, with a test for interaction of p=.095. Similarly, in the SENIORS trial, the adjusted HR values were 0.76, 95% CI, 0.56 to 1.03 for patients with eGFR <55.5 ml/min/1.73m^2, 1.14, 95% CI, 0.78 to 1.66 for patients with eGFR of 55.6 to 72.8 ml/min/1.73m^2, and 0.82, 95% CI, 0.53 to 1.25 for patients with eGFR >72.8 ml/min/1.73m^2. The test for interaction was not significant (p=.521). No mortality data were reported for other patient subgroups.

Cardiovascular Mortality

In the SENIORS trial, in the subgroup with CHF and CKD there was no significant reduction in risk of cardiovascular mortality with BB versus placebo (HR 0.72, 95% CI, 0.50 to 1.04). There also was no significant reduction in risk in the non-CKD subgroups, with HR 1.11, 95% CI, 0.74 to 1.69 for patients with eGFR of 55.6 to 72.8 ml/min/1.73m^2, and HR 0.81, 95% CI, 0.49 to 1.35 for patients with eGFR >72.8 ml/min/1.73m^2. The test for interaction was not significant (p=.494).

Vascular Outcomes (Appendix Tables C67–C69 and Appendix Figure C15)

Myocardial Infarction

Neither study reported results for myocardial infarction as an isolated outcome.

Stroke

Neither study reported results for stroke.

Other Vascular Outcomes

In MERIT-HF study results in which all participants with eGFR ≤60 ml/min/1.73m^2 were pooled, assignment to BB treatment was associated with significant reductions in risks for hospitalization for CHF (12.2 versus 20.0 percent; RR 0.61, 95% CI, 0.48 to 0.78) and CHF death (2.0 versus 4.9 percent; RR 0.42, 95% CI, 0.23 to 0.75). Similarly, compared with placebo, CKD study participants randomized to BB had significant reductions in risk of the composite vascular outcomes of all cause mortality and hospitalization for CHF (18.5 versus 29.2 percent; RR 0.63, 95% CI, 0.53 to 0.77) and cardiac death or nonfatal MI (8.7 versus 14.6 percent; RR 0.60, 95% CI 0.45 to 0.80). In results stratified by baseline eGFR (<45, 45-60, and >60 ml/min/1.73m^2), the study consistently reported the numerically lowest HR for each of these outcomes in the patients with eGFR <45 ml/min/1.73m^2. The p-value for interaction between baseline eGFR stratum and treatment assignment was 0.038 for CHF hospitalization, 0.16 for CHF death, 0.011 for the composite outcome of all cause mortality and CHF hospitalization, and >0.2 for the composite outcome of cardiac death or nonfatal MI. In the SENIORS trial, treatment with BB was associated with a nonsignificant reduction in risk of a composite vascular outcome of all-cause mortality or cardiovascular hospitalization in the subgroup with eGFR <55.5 ml/min/1.73m^2 (37.1 versus 43.9 percent; RR 0.86, 95% CI, 0.72 to 1.03). The p value for the interaction across tertiles of eGFR was p=.442. No vascular outcomes data were reported for other patient subgroups.

Renal Outcomes

End-Stage Renal Disease

Neither study reported results for ESRD.

Other Renal Outcomes

Neither study reported results for other individual or composite clinical renal outcomes.

Study Withdrawals and Adverse Events (Appendix Table C70)

Neither study reported data on withdrawals within the CKD subgroups. In the MERIT-HF study, rate of study treatment discontinuation due to adverse events appeared higher in participants with worse eGFR, but not worse in those assigned to BB versus placebo. In patients with eGFR 45 to 60 ml/min/1.73m^2, the rate of discontinuations due to adverse events was 13.6 and 13.5 per 100 person years for those assigned BB versus placebo, respectively. In patients with eGFR <45 ml/min/1.73m^2, the rate was 16.9 and 20.8 per 100 person years for those assigned BB versus placebo, respectively. The most commonly reported adverse event resulting in discontinuation was heart failure. Fatigue, bradycardia, dizziness, and hypotension were also reported. In the SENIORS study, adverse event data were reported for patients with baseline eGFR <60 ml/min/1.73m^2 or ≥60 ml/min/1.73m^2. In the BB group, there was a higher incidence of bradycardia and any adverse event in patients with lower eGFR. In the placebo group, no significant differences were reported. In the total study group, patients treated with BB had significantly higher rates of hypotension and any adverse event.

Subgroup Results

No trials reported outcomes stratified by any participant characteristic. However, both trials were restricted to patients with CHF and impaired eGFR, so all results reported above apply to these subgroups. No other subgroup results are available since no trials were restricted to patients with albuminuria, or with a history of diabetes, hypertension, or cardiovascular disease, and no trials excluded patients with these conditions.

Summary

In two post hoc analyses, patients with well controlled heart failure and CKD who were randomized to BB versus placebo had a significantly lower risk of all-cause mortality. One trial also reported significantly lower risks of hospitalizations for CHF, CHF deaths, and of the composite vascular outcomes of all cause mortality or CHF hospitalization and of cardiac death or nonfatal MI. Analyses stratified by eGFR subgroup suggested that the relative benefit of BB versus placebo may be greatest in patients with eGFR <45 ml/min/1.73m^2 (MERIT-HF) or eGFR < 55.5 ml/min/1.73m^2 (SENIORS), though the statistical tests for interaction by eGFR strata did not approach statistical significance. Results were limited in that both studies were post hoc subgroup analyses, there were no measures of albuminuria available, and no clinical renal outcomes and little adverse events data were reported. Because trial followup was a mean of 21 months or less, longer term effects of BB monotherapy versus placebo in this population cannot be determined from these data.

CCB Versus Placebo Trials (n=2)

Overview

In patients with CKD, we found low strength of evidence that there is no difference in risk of all-cause mortalityor ESRD between participants randomized to CCB versus placebo. In participants randomized to CCB versus placebo, there was a statistically significant reduction in risk of MI and conversion from microalbuminuria to macroalbuminuria, but there was no significant difference between treatment groups for the outcomes of cardiovascular mortality, stroke, doubling of baseline creatinine, or any composite vascular or renal outcomes. Our confidence in these estimates is limited by the small number of trials reporting different outcomes and the small number of clinical events.

Description of Studies

Two trials met all eligibility criteria and randomized 1,226 participants (range 90 to 1,136) with CKD to CCB versus placebo.[55,97,117] Detailed baseline characteristics are presented in Appendix Tables C71 and C72.

The larger trial, IDNT, randomized 1,136 hypertensive, type 2 diabetic individuals to amlodipine versus placebo.[97,117] This trial also included an ARB treatment arm discussed elsewhere in this report. Mean age of study participants was 59 years, 67 percent of all subjects were male and 71 percent of participants were white. The study was multinational and followup duration was 2.6 years.

A second trial randomized 90 normotensive, type 1 diabetic subjects to nifedipine versus placebo,[55] and also included an ACEI treatment arm discussed elsewhere in this report. After randomization, 22 participants were excluded for having UAER outside the 20 to 200 µg/min range and an additional seven for adverse clinical events. Baseline data were only reported on these 61 participants. Within these participants, mean age was 37 years and 70 percent of all subjects were male. No information was reported on race/ethnicity, though the study was conducted in Italy. Followup duration was 3 years.

Renal Function

For inclusion in the IDNT trial, participants were required to have both elevated serum creatinine (1.0 to 3.0 mg/dL for women and 1.2 to 3.0 mg/dL for men) and proteinuria >900 mg/day. At baseline, mean serum creatinine was 1.7 mg/dL, mean proteinuria was 2.9 g/day, and mean albuminuria was 1.9 g/day.

For inclusion in the smaller trial, participants were required to have microalbuminuria, with a UAER of 20 to 200 µg/min, a GFR of 80 ml/min/1.73m^2 or greater, and a serum creatinine <10 percent higher than the upper limit of normal. After randomization, 22 participants were excluded for having UAER outside the 20 to 200 µg/min range. Within participants not withdrawn after baseline, baseline median UAER was 80.2 µg/min, mean serum creatinine was 0.97 mg/dL, mean creatinine clearance was 107.8 mL/min, and mean GFR was 111.8 ml/min/1.73m^2.

Baseline Comorbidities

In the IDNT trial, all participants were required to have hypertension, Mean baseline blood pressure was 159/87 mm Hg. All participants also were required to have diabetes, and mean

baseline HbA_{1c} was 8.2 percent. Thirty percent of study subjects had a history of cardiovascular disease.

In the smaller trial, participants with hypertension were excluded and no information on baseline blood pressure was reported. All participants were required to have type 1 diabetes. Baseline HbA_{1c} was not reported, though those with HbA_{1c} 11 percent or greater were excluded. The study did not report any information on the prevalence of cardiovascular disease, though patients with an MI in the prior 3 months were excluded.

Study Quality (Appendix Table C140)

Of the two studies, one was rated good quality and one was rated fair quality. The IDNT reported adequate concealment of treatment allocation, while concealment was unclear for the other study. Both trials were double blinded. The IDNT trial performed analyses according to the intention-to-treat principle, but the other study excluded 24 percent of participants after randomization from analyses. Withdrawals ranged from 0.5 percent in the IDNT trial to 32 percent in the other study.

Results

Mortality (Table 12, Appendix Table C73 and Appendix Figure C16)

All-Cause Mortality

In the IDNT trial,[97,117] there was a nonsignificant reduction in risk of all-cause mortality (14.6 versus 16.3 percent; RR 0.90, 95% CI, 0.68 to 1.18). In the smaller study, only one death occurred, in an individual assigned to the CCB group.[55] In pooled results, risk with CCB treatment was nonsignificantly decreased for all-cause mortality (RR 0.90, 95% CI, 0.69 to 1.19).

Cardiovascular Mortality

In the IDNT trial,[97,117] there was a nonsignificant reduction in risk of cardiovascular mortality (6.5 versus 8.1 percent; RR 0.81, 95% CI, 0.53 to 1.22). In the smaller study, only one cardiovascular death occurred, in an individual assigned to the CCB group.[55] In pooled results, risk with CCB treatment was nonsignificantly decreased for cardiovascular mortality (RR 0.83, 95% CI, 0.55 to 1.25).

Vascular Outcomes (Table 12, Appendix Tables C73-C75 and Appendix Figure C16)

Myocardial Infarction

In the IDNT trial, there was a significant 41 percent reduction in risk of MI in CCB subjects compared with those assigned placebo (4.8 versus 8.1 percent; RR 0.59, 95% CI, 0.37 to 0.93). In the smaller study, there was only one MI, which occurred in an individual assigned to the placebo group.

Stroke

In the IDNT trial, participants assigned CCB had a nonsignificant reduction in risk of stroke compared with placebo (2.6 versus 4.6 percent; RR 0.58, 95% CI, 0.31 to 1.08).

Other Vascular Outcomes

In the IDNT trial, in the CCB group compared with the placebo group, there was a nonsignificant increase in risk of CHF (16.4 versus 12.7 percent; RR 1.30, 95% CI, 0.97 to 1.72). There was no significant difference between CCB and placebo for either of two composite vascular outcomes. For an outcome that included MI, CHF, neurologic deficit attributed to stroke, or unplanned revascularization, there was a nonsignificant 13 percent reduction in risk in the CCB group (28.4 versus. 32.5 percent; RR 0.87, 95% CI, 0.73 to 1.04). For an outcome that included death from cardiovascular causes, nonfatal MI, hospitalization for CHF, neurologic deficit, or lower limb amputation, there was a nonsignificant 11 percent reduction in risk in the CCB group (22.6 versus 25.3 percent; RR 0.89, 95% CI, 0.72 to 1.10).

Renal Outcomes (Table 12, Appendix Tables C76 and C77, and Appendix Figure C16)

End-Stage Renal Disease

In results reported only in the IDNT trial, in patients with CKD there was no significant difference between CCB and placebo groups in risk of ESRD (RR 1.03, 95% CI, 0.81 to 1.32).

Other Renal Outcomes

In results reported only in the IDNT trial, in patients with CKD there was no significant difference between CCB and placebo groups in risk of doubling of baseline creatinine (RR 1.07, 95% CI, 0.87 to 1.31), or in the composite renal outcome of doubling of serum creatinine, ESRD, or death (RR 1.05, 95% CI, 0.91 to 1.21).[97,117] The smaller of the studies reported a nonsignificant 63 percent reduction in risk of progression from microalbuminuria to macroalbuminuria in the CCB group versus the placebo group (7.7 versus 20.6 percent; RR 0.37, 95% CI, 0.08 to 1.65).[55]

Study Withdrawals and Adverse Events (Appendix Table C78)

There were few withdrawals in the larger study, just 0.4 percent of the CCB group and 0.7 percent of the placebo group.[97,117] It was reported that 61 percent of the study participants (including those in an ARB arm) had at least one serious adverse event, but the results were not presented by treatment group. Treatment was discontinued due to adverse events by 9.0 percent of the CCB group and 7.2 percent of the placebo group. Hyperkalemia was reported by 0.5 percent of the CCB group and 0.4 percent of the placebo group. There was one report of an early increase in serum creatinine suggestive of renal artery stenosis, but the group assignment of that patient was not given. In the smaller study, 36.6 percent of the CCB group and 30.6 percent of the placebo group withdrew.[55] Three of the withdrawals from the placebo group were a result of adverse events during the run-in phase; six were from adverse events during the randomized phase.

Summary

In two trials of patients with CKD and diabetes, treatment with CCB as compared with placebo was associated with nonsignificant reductions in risk of all-cause mortality, cardiovascular mortality, MI, stroke, and two different composite vascular outcomes. Risk of congestive heart failure was nonsignificantly higher for patients with CKD. The risk between treatment groups appeared similar for ESRD, doubling of creatinine, and a composite renal

outcome, including both of these events as well as death. The rate of withdrawals in the smaller study was high. In both trials, adverse event rates were difficult to interpret due to incomplete reporting. Results were limited in that nearly all were derived from only one trial. The multiple post-randomization exclusions from the smaller trial and its apparent nonsystematic reporting of outcomes lowered our confidence in its reported results. Because the followup of the IDNT trial was 2.6 years, it is not possible to determine from these results the longer term effects of CCB versus placebo in patients with CKD.

Table 12. Pooled clinical and renal outcomes, CCB versus placebo trials

Outcome	Number of Trials Reporting	Quality of the Studies	CCB Events/N (%)	Placebo Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
All-cause mortality	2	Fair	84/608 (13.8)	93/618 (15.0)	0.90 [0.69-1.19]	0%
Cardiovascular mortality	2	Fair	38/608 (6.3)	46/618 (7.4)	0.83 [0.55-1.25]	0%
Myocardial infarction	2	Fair	27/608 (4.4)	47/618 (7.6)	0.58 [0.37-0.92]	0%
Stroke	1	Good	15/567 (2.6)	26/569 (4.6)	0.58 [0.31-1.08]	NA
Congestive heart failure	1		93/567 (16.4)	72/569 (12.7)	1.30 [0.97-1.72]	NA
Composite vascular*	1	Good	161/567 (28.4)	185/569 (32.5)	0.87 [0.73-1.04]	NA
Lewis (A)[97]			128/567 (22.6)	144/569 (25.3)	0.89 [0.72-1.10]	
Lewis (B)[97]						
End-stage renal disease	1	Good	104/567 (18.3)	101/569 (17.8)	1.03 [0.81-1.32]	NA
Doubling of serum creatinine	1	Good	144/567 (25.4)	135/569 (23.7)	1.07 [0.87-1.31]	NA
Progression to macroalbuminuria	1	Fair	2/26 (7.7)	7/34 (20.6)	0.37 [0.08-0.65]	NA
Composite renal outcome**, Lewis[97]	1	Good	233/567 (41.1)	222/569 (39.0)	1.05 [0.91-1.21]	NA

CCB = calcium channel blocker; NA = not applicable; RR = relative risk reduction

*A = Myocardial infarction, heart failure, permanent neurologic deficit of at least 24-hour duration attributed to stroke, or unplanned (at time of randomization) coronary artery revascularization procedure (all before renal failure, death, or censorship).

*B= Death from cardiovascular causes, nonfatal myocardial infarction, heart failure resulting in hospitalization, permanent neurologic deficit caused by a cerebrovascular event, or lower limb amputation above the ankle.

**Doubling of baseline serum creatinine concentration, onset of end-stage renal disease (initiation of dialysis, renal transplantation, or serum creatinine concentration ≥ 6.0 mg/dL), or death from any cause

Diuretic Versus Placebo Trial

Overview

In patients with CKD, we found low strength of evidence that there is no difference between treatments in risk of all-cause mortality. We found insufficient evidence regarding whether treatments differ for risk of ESRD. There was a statistically significant reduction in risk of stroke in the diuretic group versus placebo. Our confidence in these estimates is limited because data are drawn from only one trial and there were few reported clinical events.

Description of Study

One trial met all eligibility criteria and randomized CKD patients (n=393) to diuretic versus placebo.[118] Detailed baseline characteristics are presented in Appendix Table C79.

The single eligible study was a subgroup analysis in patients with CKD from within the larger SHEP study (n=4,736), a randomized trial comparing chlorthalidone versus placebo in older patients with hypertension. Mean subject age was 74 years, and men constituted 76 percent of participants. Seventy-six percent of study participants were white, 20 percent were black, and 3 percent were Asian. The study was performed in the United States and followup duration was 5 years.

Renal Function

Participants included in this post hoc analysis were the subgroup from the larger study with a baseline creatinine of 1.35 mg/dL or higher, the level considered to represent the upper threshold of normal in the SHEP trial. Within this subgroup, no measures of baseline renal function were reported.

Baseline Comorbidities

For inclusion in the SHEP trial, participants were required to have isolated systolic hypertension, with a systolic blood pressure of 160 to 219 mm Hg, and a diastolic blood pressure less than 90 mm Hg. Mean baseline blood pressure within patients with CKD was 172/77 mm Hg. A history of myocardial infarction was reported by 5 percent, a history of stroke by 4 percent, and a history of diabetes by 12 percent. Patients were excluded from participation in SHEP for any recent myocardial infarction or stroke or for insulin-treated diabetes.

Study Quality (Appendix Table C140)

Study quality was rated as good. Concealment of treatment allocation was adequate and the study was reported to be double blind, though it is not clear whether open-label potassium supplementation for potassium levels <3.5 mmol/L could have compromised blinding. Analysis was performed according to intention-to-treat principles. Study withdrawals were not reported for the CKD subgroup, but were adequately reported for the overall SHEP trial.

Results

Mortality (Appendix Table C80 and Appendix Figure C17)

The risk of all-cause mortality was nonsignificantly higher in CKD study participants randomized to the diuretic group compared with placebo (17.1 versus 14.7 percent; RR 1.17, 95% CI, 0.74 to 1.85).

Vascular Outcomes (Appendix Tables C80-C82 and Appendix Figure C17)

Myocardial Infarction

The study did not report results for myocardial infarction.

Stroke

In subjects assigned to diuretic, there was a significant 51 percent reduction in the risk of stroke (6.5 versus 12.4 percent; RR 0.49, 95% CI, 0.24 to 0.99).

Other Vascular Outcomes

Two composite vascular outcomes were reported (Appendix Table C81 and C82), with a significant 37 percent reduction in the risk of any cardiovascular event (16.7 versus 26.6 percent; RR 0.63, 95% CI, 0.43 to 0.93), and a nonsignificant 38 percent reduction in the risk of fatal or nonfatal coronary heart disease (7.4 versus 11.9 percent; RR 0.62, 95% CI, 0.34 to 1.16).

Renal Outcomes

End-Stage Renal Disease

The study did not report on ESRD for the CKD subgroup.

Other Renal Outcomes

There were two renal deaths in the CKD subgroup, both in participants allocated to diuretic (0.9 percent). No other clinical renal outcomes were reported.

Study Withdrawals and Adverse Events (Appendix Table C83)

Neither study withdrawals nor adverse events data were reported within the CKD subgroup.

Summary

In this analysis of a subgroup of patients with CKD from a larger trial of older patients with systolic hypertension, diuretic treatment compared with placebo significantly reduced risk of stroke and of one of two composite vascular outcomes. There was no significant difference between treatment groups in all-cause mortality. Results were limited by the small number of patients with CKD, with insufficient statistical power to determine whether large magnitude differences in risk for clinical outcomes were statistically significant. Results also were limited in that this was a post hoc subgroup analysis without confirmation of findings in another study population. Further, results were not reported for several vascular events of interest, including cardiovascular mortality, MI and heart failure, and no clinical renal outcomes were reported.

ACE Inhibitor Versus Non-ACE Inhibitor Antihypertensive Therapy Trial

Overview

In patients with CKD, we found insufficient evidence that ACEI therapy as compared with non-ACEI antihypertensive therapy is associated with a reduced risk of all-cause mortality and low level of evidence that ACEI therapy compared with non-ACEI antihypertensive therapy does not significantly reduce the risk of ESRD. There was no statistically significant difference between treatment groups for risk of halving of GFR or for one reported composite renal outcome. Our confidence in these estimates is limited because data are drawn from only one trial and there were few reported clinical events.

Description of Study

We identified one trial that met all eligibility criteria and randomized 131 participants with CKD to ACEI versus non-ACEI hypertension treatment.[119] Detailed baseline characteristics are presented in Appendix Table C84.

Randomized subjects assigned to ACEI were treated with lisinopril or lisinopril in combination with another antihypertensive agent versus a non-ACEI antihypertensive treatment regimen. Prior to randomization, 139 hypertensive patients underwent a run-in period, during which they were to follow a 0.8 g/kg protein and 3–4 g salt intake per day, and non-ACEI antihypertensive agents were used to obtain diastolic blood pressure of 90 mm Hg or less. Only patients achieving this target on two or fewer drugs, judged compliant, and with stable renal function were eligible to proceed to randomization.

Mean age of randomized study participants was 51 years, and men constituted 66 percent of all subjects. Race/ethnicity of study participants was not reported, though the study was conducted in Italy. Mean followup was 1.9 years.

Renal Function

Participants were required to have creatinine clearance between 20 and 50 ml/min/1.73m^2 and were excluded if they had proteinuria of ≥1 gram/day. Among those enrolled, mean creatinine clearance was 36 ml/min/1.73m^2, mean GFR was 36 ml/min/1.73m^2, mean creatinine was 2.4 mg/dL, and mean proteinuria was 512 mg/day.

Baseline Comorbidities

All study participants had hypertension, with an untreated diastolic blood pressure of ≥95 mm Hg prior to run-in, and a stable treated diastolic blood pressure <90 mm Hg prior to randomization. Patients with malignant hypertension were excluded. Among subjects randomized, mean baseline blood pressure was 142/86 mm Hg. Patients with diabetes, heart failure or another major (undefined) cardiac disease, or a recent history of MI or stroke were excluded from study entry.

Study Quality (Appendix Table C140)

Study quality was rated as fair. This study was open-label and concealment of treatment allocation was unclear. Analyses were conducted according to the intention-to-treat principle. No information was reported regarding withdrawals.

Results

Mortality

No data were reported on mortality.

Vascular Outcomes (Appendix Table C85 and Appendix Figure C18)

Myocardial Infarction

The study reported just one myocardial infarction, in a subject assigned to non-ACEI antihypertensive treatment

Stroke

There were no reports of stroke.

Other Vascular Outcomes

There were no reports of heart failure or any composite vascular outcomes.

Renal Outcomes (Appendix Tables C86 and C87 and Appendix Figure C18)

End-Stage Renal Disease

There was a nonstatistically significant 61 percent reduction in risk of ESRD in those assigned to ACEI treatment as compared with those allocated to non-ACEI treatment (3.0 versus 7.6 percent; RR 0.39, 95% CI, 0.08 to 1.96).

Other Renal Outcomes

There was a nonstatistically significant 58 percent reduction in risk of halving of GFR in those assigned to ACEI treatment as compared with those allocated to non-ACEI treatment (4.5 versus 10.6 percent; RR 0.42, 95% CI, 0.11 to 1.56). Similarly, There was a nonstatistically significant 59 percent reduction in risk of the composite renal outcome of halving of GFR or need for dialysis in those assigned to ACEI treatment as compared with those allocated to non-ACEI treatment (7.6 versus 18.2 percent; RR 0.41, 95% CI, 0.15 to 1.10). However, there were only a small number of events for all these outcomes and none of these differences was clinically significant.

Study Withdrawals and Adverse Events (Appendix Table C88)

No data on study withdrawals were reported. Treatment was discontinued due to adverse events by 6.1 percent of the study participants assigned to the ACEI group and 4.6 percent in the non-ACEI antihypertensive therapy group. There was one incidence of hyperkalemia and one incidence of uncontrolled hypotension in the ACEI group. No hyperkalemia or hypotension events were reported for the non-ACEI antihypertensive therapy group.

Summary

In a single study of patients with hypertension and CKD, antihypertensive treatment with ACEIs in comparison to that without ACEIs was associated with nonsignificant reductions in the risk for MI, ESRD, halving of GFR, and a composite renal outcome including ESRD and GFR. Mortality data and other cardiovascular or renal outcomes were not reported, nor were study

withdrawals or serious adverse events. Results were limited by the small sample size, small number of clinical events, and short followup duration.

CCB Versus BB Trials (n=3)

Overview

In patients with CKD, we found low strength of evidence that treatment with CCB does not significantly reduce the risk of all-cause mortality compared with BB, and low strength of evidence that there is no difference between treatments in risk of ESRD. Participants assigned CCB were statistically significantly less likely to experience one composite vascular outcome. Our confidence in these estimates is limited by the small number of trials reporting different outcomes and the small number of clinical events.

Description of Studies

Three trials met all eligibility criteria and randomized participants with CKD (n=12,766, range 34 to 12,074) to CCB versus BB.[89,90,120,121] Detailed baseline characteristics of patients enrolled in the three trials are presented in Appendix Tables C80 and C81.

Among eligible trials, most data were derived from a subgroup analysis reported in a subset of 12,074 patients with undefined "renal dysfunction" from the larger ASCOT-BPLA trial (n=19,257).[121] In this study, participants were randomized to amlodipine versus atenolol. As needed to meet blood pressure targets (<140/90 mm Hg for patients without diabetes and <130/90 mm Hg for patients with diabetes), participants randomized to amlodipine could have had an ACEI added and subjects randomized to atenolol could have had a diuretic added. In the AASK trial, designed as a 3x2 factorial study, besides randomizing 658 participants to amlodipine versus metoprolol, an additional 436 were randomized to an ACEI, and all participants also were randomized to one of two blood pressure target groups as described elsewhere in this report.[89,90] In this trial, the amlodipine treatment arm was stopped early by recommendation of the data and safety monitoring board with patients switched to open label medication. Results presented here compare outcomes including followup until the time blinded amlodipine was discontinued. In the smallest trial,[120] 34 participants were randomized to one of two CCBs (verapamil or diltiazem) versus atenolol. This study also included an additional ACEI treatment arm that is reviewed elsewhere in this report.

The mean age of study participants across all three trials was 55 years (range 55 to 62) and men constituted 60 percent (range 44 to 61, n=2 trials) of all subjects studied. In the two trials that reported race/ethnicity,[89,90,120] 98 percent of participants were African American, including 100 percent of subjects in the AASK trial.[89,90] Two studies were conducted in the United States, and the large subgroup analysis was conducted in Europe. Median study duration ranged from 3 to 5.5 years.

Renal Function

Among eligible trials, one required that participants have impaired GFR (20 to 65 ml/min/1.73m^2)[89,90] and reported a mean baseline GFR of 46 ml/min/1.73m^2, a mean creatinine of 2.0 mg/dL, and mean proteinuria of 0.5 g/day. A second trial required that participants have both impaired creatinine clearance (<70 ml/min) and at least 2 g/day proteinuria, and reported a mean baseline creatinine clearance of 61 ml/min/1.73m^2, a mean creatinine of 1.9 mg/dL, and

mean proteinuria of 4.4 g/day.[120] The third study reported no information on the baseline renal function in its "renal dysfunction" subgroup.

Baseline Comorbidities

In all three studies, all participants were required to be hypertensive. In two trials reporting, mean baseline blood pressure was 150/95 mm Hg.[89,90,120] Patients with heart failure were excluded from all three trials, and patients with a history of MI[121] or of any documented coronary artery disease[120] were excluded in two trials. While one trial required that participants be diabetic,[120] a second trial excluded diabetic patients,[89,90] and the third study reported no information on participants' diabetes status.[121]

Study Quality (Appendix Table C140)

Study quality was rated good for two trials and fair for one trial. Two of the trials reported adequate treatment allocation concealment.[89,90,121] One study was open-label,[121] a second study was double blind with respect to medication assignment but not to blood pressure target.[89,90] Both reported that endpoint adjudicators were blinded to treatment allocation. The third study provided no information with respect to blinding.[120] Two of the three studies performed analyses according to the intention-to-treat principle. Withdrawals ranged from 0 to 11.5 percent between studies.

Results

Mortality (Table 13, Appendix Table C91, and Appendix Figure C19)

All-Cause Mortality

In two trials of CKD patients reporting mortality data, those randomized to CCB versus BB had a nonsignificant 38 percent reduction in risk of all-cause mortality (6.0 versus 9.2 percent; RR 0.62, 95% CI, 0.31 to 1.22; n=692 patients).[89,90,120]

Cardiovascular Mortality

One study reported cardiovascular deaths per patient year of followup (CCB 0.9 percent, BB 0.8 percent) but did not report the number and percentage of participants with this outcome by treatment group.[89,90] A second study reported cardiovascular deaths (9.6 percent) but did not report these outcomes by treatment group.[120]

Vascular Outcomes (Table 13, Appendix Tables C91-C93, and Appendix Figure C19)

Myocardial Infarction

One study reported fatal MI (7.7 percent), but did not report these outcomes by treatment group.[120]

Stroke

One study reported fatal strokes (1.9 percent), but did not report these outcomes by treatment group.[120]

Other Vascular Outcomes

No trials reported results for heart failure. Two trials reported results for a composite vascular endpoint. One reported that there was no significant difference in the rate of cardiovascular events (cardiovascular mortality or first cardiovascular hospitalization) per patient year (1.7 versus 2.9) between CCB and BB patients, but did not report the number of study participants with these events overall or by treatment group.[89,90] In the second study, though the main ASCOT-LLP study had defined six different composite vascular endpoints, results for the "renal dysfunction" subgroup were only reported for one, defined as cardiovascular mortality, nonfatal MI (symptomatic and silent), unstable angina, chronic stable angina, life threatening arrhythmias, silent nonfatal heart failure, nonfatal stroke, peripheral arterial disease, revascularization procedures, or retinal vascular thromboses.[121] Patients assigned to CCB were significantly less likely to experience this composite outcome than those assigned to BB (14.0 versus 16.0 percent; RR 0.87, 95% CI, 0.80 to 0.95; n=12,074 patients).

Renal Outcomes (Table 13, Appendix Tables C94 and C95, and Appendix Figure C19)

End-Stage Renal Disease

In one trial of patients with CKD, 9.6 percent of patients were reported to have started dialysis during the trial, but results were not reported by treatment group.[120] In a second trial, there was no significant difference in risk of ESRD between subjects randomized to CCB versus BB (16.6 versus 16.6 percent; RR 1.00, 95% CI, 0.70 to 1.44).[89,90]

Other Renal Outcomes

In one trial, there was no significant difference between treatment groups for the composite renal outcome of ESRD, death, or at least 50 percent decline in GFR (27.2 versus 26.5 percent; RR 1.02, 95% CI, 0.78 to 1.34). Similarly, there was no significant difference between treatment groups for a composite outcome of ESRD or death (22.5 versus 25.2 percent, RR 0.90, 95% CI, 0.67 to 1.20).[89,90] Doubling of serum creatinine, reported in one small study, was less frequent in the CCB group (11.1 percent versus 31.3 percent; $p<0.05$), a nonsignificant 64 percent reduction in risk (RR 0.36, 95% CI, 0.08 to 1.59).[120]

Study Withdrawals and Adverse Events (Appendix Table C96)

One study reported a withdrawal rate of 11.5 percent (six patients), but no withdrawal data were reported by treatment group.[120] Another study reported no withdrawals but noted that 23 patients in the CCB group and 30 in the BB group were no longer active study participants at the end of the study.[90] In the one study reporting withdrawals as a result of serious adverse events, there were no events in either group.[120] Specific adverse events were reported in two studies. In one study, impotence (16.7 percent versus 56.3 percent), insomnia (5.6 percent versus 37.5 percent), lethargy (0 percent versus 81.3 percent), exercise intolerance (0 percent versus 43.8 percent), and dry mouth (5.6 percent versus 81.0 percent) were less frequent in the CCB group than the BB group.[120] The second study reported percentage of patients experiencing the adverse event per patient year of followup. The results were similar for the two groups (hyperkalemia, CCB 0 versus BB 0.2 percent; angioedema, CCB 2.3 versus BB 2.7 percent; shortness of breath, CCB 44.4 versus BB 45.8 percent; syncope, CCB 2.3 versus BB 6.3 percent; dizziness, CCB 46.7 versus BB 47.8 percent; lightheadedness, CCB 48.1 versus BB 47.8 percent; edema, CCB

59.8 versus BB 51.0 percent; cough, CCB 46.3 versus BB 41.5 percent; and sexual dysfunction, CCB 25.7 versus BB 25.2 percent).[90]

Summary

In patients with CKD and hypertension, there was a nonsignificant 38 percent reduction in all-cause mortality with CCB compared with BB treatment. One of two trials reported a significant reduction in a composite vascular outcome, but this was the only one of six composite vascular endpoints collected in this trial that was reported for patients with renal dysfunction, raising uncertainty regarding whether this risk reduction is a consistent finding within this study. There was no significant difference between CCB and BB treatment groups in risk of ESRD or in risk of the composite renal outcome of ESRD, death, or greater than 50 percent decline in GFR. Both the composite outcome of ESRD or death and the risk of doubling creatinine appeared less likely in patients randomized to CCB, though results were not statistically significant. Results were limited in that most outcomes were not reported by treatment group in more than one study, and by the uncertainty regarding whether the patients in the ASCOT-BPLA study with “renal dysfunction” meet criteria for CKD.

Table 13. Pooled clinical and renal outcomes, CCB versus BB trials

Outcome	Number of Trials Reporting	Quality of the Studies	CCB Events/N (%)	BB Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
All-cause mortality	2	Fair	14/235 (6.0)	42/457 (9.2)	0.62 [0.31-1.22]	6%
Composite vascular outcome*, Dahlof, 2005[121]	1	Good	825/5893 (14.0)	989/6181 (16.0)	0.87 [0.80-0.95]	NA
End-stage renal disease	1	Good	36/217 (16.6)	73/441 (16.6)	1.00 [0.70-1.44]	NA
Doubling of serum creatinine	1	Fair	1/18 (5.6)	5/16 (31.3)	0.18 [0.02-1.37]	NA
Composite renal outcome**, AASK, Wright, 2002[90]	1	Good	59/217 (27.2)	117/441 (26.5)	1.02 [0.78-1.34]	NA

BB = beta blocker; CCB = calcium channel blocker; NA = not applicable; RR = relative risk reduction

* Cardiovascular mortality, nonfatal MI (symptomatic and silent), unstable angina, chronic stable angina, life threatening arrhythmias, silent non-fatal heart failure, non-fatal stroke, peripheral arterial disease, revascularization procedures, and retinal vascular thromboses

**GFR event (reduction in GFR by 50% or by 25 ml/min/1.73m^2 from baseline mean), ESRD (dialysis or transplantation), or death

CCB Monotherapy Versus Diuretic Trial

Overview

In patients with CKD, there was insufficient evidence regarding whether there is a difference between CCB and diuretic treatment for risk of all-cause mortality and low strength of evidence that there was no difference between CCB and diuretic treatment for risk of ESRD. There was no statistically significant difference between CCB and diuretic treatment groups in risk of stroke, CHF, or in multiple composite vascular or renal outcomes. Our confidence in these estimates is limited because they are based entirely on results reported from a post hoc analysis from a single large trial.

Description of Study

One study met all eligibility criteria and randomized 4,129 participants to CCB monotherapy versus diuretic monotherapy.[81-83] Detailed baseline characteristics are presented in Appendix Tables C97 and C98. The eligible study was a post hoc analysis performed within a subset of participants with CKD from the ALLHAT trial, a study of 23,261 subjects that was not originally limited to individuals with CKD, contained two additional antihypertensive treatment arms and, as part of a factorial design, also randomized participants to pravastatin versus control.

The CCB and diuretic utilized in this trial were amlodipine and chlorthalidone, respectively. The mean age among the 4,129 study participants assigned to CCB versus diuretic was 71 years, and men constituted 47 percent all study subjects. The most common race/ethnicity of trial participants was white non-Hispanic (57 percent), black (25 percent), and Hispanic (12 percent). The ALLHAT trial was performed primarily in the United States. The study duration was 4.9 years.

Renal Function

Patients with a baseline creatinine level >2 mg/dL were excluded from the main ALLHAT trial. Inclusion in the post-hoc analysis was limited to ALLHAT participants with a GFR <60 ml/min/ 1.73m^2. Within subjects in the CKD subgroup, mean baseline GFR was 50 ml/min/1.73m^2. No baseline data on albuminuria was reported.

Baseline Comorbidities

Enrollment was limited to patients with hypertension, with the mean blood pressure at baseline 147/83 mm Hg. Thirty-four percent of participants reported diabetes at baseline, 60 percent reported cardiovascular disease, and 30 percent reported coronary artery disease.

Study Quality (Appendix Table C140)

Study quality was rated as good. Allocation concealment was adequate. The trial was double blinded and analysis by the intention-to-treat principle was reported. No data regarding withdrawals was reported.

Results

Mortality

Neither all-cause mortality nor cardiovascular mortality data were reported.

Vascular Outcomes (Appendix Tables C99–C100 and Appendix Figure C20)

Myocardial Infarction

No data were reported for risk of MI as an isolated outcome.

Stroke

In patients with CKD, there was no significant difference between those assigned CCB versus diuretic treatment for risk of stroke (6.6 versus 6.0 percent; RR 1.10, 95% CI, 0.86 to 1.40). Among patients with diabetes, there was no statistically significant difference between treatment groups for risk of stroke

Other Vascular Outcomes

Similarly, in this CKD subgroup, there was no significant difference between those assigned CCB versus diuretic treatment for CHF (11.5 versus 9.9 percent; RR 1.16, 95% CI, 0.97 to 1.39). There also was no significant between-treatment difference for the composite vascular outcome of nonfatal MI or coronary heart disease death (RR 1.05, 95% CI, 0.89 to 1.24), or for the composite vascular outcome that included death from coronary heart disease, nonfatal MI, stroke, coronary revascularization procedures, hospitalized or treated angina, treated or hospitalized heart failure, or peripheral arterial disease requiring hospitalization or outpatient revascularization (RR 1.06, 95% CI, 0.98 to 1.16).

The ALLHAT trial reported additional results for CKD patients with diabetes. In this subgroup, risk of CHF was significantly greater in patients randomized to CCB treatment compared with diuretic treatment (RR 1.46, 95% CI, 1.12 to 1.89; n=1,387). There was no statistically significant difference between treatment groups for risk of the composite cardiovascular endpoint of nonfatal MI or coronary heart disease death. For the more comprehensive composite cardiovascular endpoint described above, risk of occurrence was significantly greater in patients randomized to CCB treatment compared with diuretic treatment (RR 1.20, 95% CI, 1.05 to 1.36; n=1,387).

Renal Outcomes (Appendix Tables C102 and C103 and Appendix Figure C20)

End-Stage Renal Disease

In CKD patients, CCB and diuretic treatments were comparable in CKD patients regarding the risk of ESRD, defined as death due to kidney disease, kidney transplantation, or start of long-term renal dialysis (RR 0.90, 95% CI 0.67 to 1.21). Results were similar in diabetics with CKD.

Other Renal Outcomes

In CKD patients, there was no statistically significant difference between CCB and diuretic treatment groups in risk of the composite renal outcome defined by ESRD or ≥50 percent decline in GFR (6 versus 7 percent, RR 0.86, 95% CI, 0.67 to 1.10). Results were similar in diabetics with CKD.

Study Withdrawals and Adverse Events

No study withdrawal or adverse event data were reported for the ALLHAT CKD subgroup.

Summary

Within the one eligible trial of patients with CKD, there was no apparent difference between the CCB and diuretic monotherapy treatment groups in risk of stroke, ESRD, or other composite clinical vascular or renal outcomes. Results were limited in that the study was a post hoc subgroup analysis. The ALLHAT study also did not report results for risk of mortality or risk of MI in the subgroup of CKD patients. In addition, mean followup did not extend beyond 5 years, so longer term effects of CCB monotherapy versus diuretic monotherapy cannot be determined from these data.

Strict Versus Standard Blood Pressure Target Treatment Trials (n=6)

Overview

In patients with CKD, we found a low strength of evidence regarding whether antihypertensive treatment targeting stricter blood pressure targets reduces risk of all-cause mortality compared with treatment targeting standard blood pressure control targets. We found a low strength of evidence regarding whether there was a difference between treatments for risk of ESRD. Our confidence in these estimates is limited by the small number of trials reporting different outcomes, the small number of clinical events, and heterogeneity between studies.

Description of Studies

Six trials met all eligibility criteria and randomized participants with CKD (n=2,520, range 77 to 1,094) to treatment aimed to reach different target blood pressures, i.e., "strict" versus "standard" blood pressure targets.[90,122-127] One study was not limited to individuals with CKD but presented subgroup results for the approximately 3 percent of participants whose baseline creatinine was >1.7 mg/dL.[126] Detailed baseline characteristics are presented in Appendix Tables C104 and C105.

In general, studies established blood pressure targets for their strict control group about 10-15 mm Hg lower than for their standard control group, though there was variability between trials in the absolute blood pressure targets selected. The most common treatment target, used in three trials, was a mean arterial blood pressure (MAP) of ≤92 mm Hg versus a MAP of 100 to 107.[90,123,125] Two trials set diastolic blood pressure (DBP) targets, <90 mm Hg for the strict target versus >90 mm Hg for the standard target in one trial,[126] and 65 to 80 mm Hg for the strict target versus 85 to 95 mm Hg for the standard target in the second trial.[124] The most recent trial compared treatment to achieve blood pressure <130/80 mm Hg versus a DBP target of <90 mm Hg.[122] The specific antihypertensive agents utilized to achieve these blood pressure targets varied between trials. The oldest trial, published in 1989,[126] used diuretics, adrenergic receptor blockers, and vasodilators, while all three trials published in the 1990s used ACEIs with or without diuretics as first-line treatment.[123-125] A trial published in 2002, structured as a 3 x 2 factorial design, assigned participants to initial treatment with either an ACEI, beta blocker or calcium channel blocker.[90] Finally, the most recent trial, published in 2005,[122] titrated all participants with an ACEI prior to randomization and then used a long-acting CCB to compare strict versus standard blood pressure control.

The mean age of study subjects was 53 years (range of study means 37 to 56; n=5 trials), and men constituted 63 percent (range 47 to 75; n=6 trials) of all patients evaluated. Among five trials reporting race/ethnicity, three were predominately[124,126] or entirely[90] comprised of

blacks/African Americans. In two other trials, more than 85 percent of participants were white.[123,125] All trials were conducted in the United States, except for one performed in Italy.[122] Mean or median study duration ranged from 19 months to 5 years, with all but one trial having a followup duration of at least 2 years.

Renal Function

Among the six trials, two required that participants have proteinuria to be included,[122,123] and one trial excluded participants with proteinuria.[90] Five trials required decreased GFR or creatinine clearance or elevation in serum creatinine for entry,[90,122,124-126] including one study that was a subgroup analysis of participants from a larger trial with baseline creatinine >1.7 mg/dL.[126] Measures of baseline renal function were reported in all but one trial.[126] Mean GFR was 43 ml/min/1.73m^2 (range 35 to 63), mean serum creatinine was 2.0 mg/dL (range 1.3 to 2.7), and mean proteinuria was 1.0 gm/day (range 0.36 to 2.85). Creatinine clearance, reported in only two trials, averaged 46.2 ml/min/1.73m^2.[122,125]

Baseline Comorbidities

In five trials reporting data, approximately 95 percent of study participants had a history of hypertension. In the sixth trial, though information on history of hypertension was not reported, approximately two-thirds of the subjects were receiving blood pressure lowering drugs at baseline.[122] Mean blood pressures at baseline were 142/89 mm Hg (MAP 106 mm Hg). Overall, few study participants had diabetes, though among individual trials one included only patients with type 1 diabetes,[123] two excluded all diabetic patients,[90,124] one had about 15 percent diabetic patients[126] and two studies provided no information regarding whether participants had a history of diabetes.[122,125] While only one trial reported baseline prevalence of cardiovascular disease, at 36 percent,[124] several reported exclusions of such participants, including exclusion of all subjects with recent MI or stroke,[122,124] exclusion of all participants with a history of any past MI or stroke,[123] and exclusion of any participants with clinical or overt heart failure.[90,122] One further trial documented enrollment of individuals with cardiovascular disease but did not report baseline prevalence.[126]

Study Quality (Appendix Table C140)

Among the six trials, study quality was rated as good in one trial and as fair in five trials. Allocation concealment was adequate in three trials and unclear in the remaining studies. Three trials were not blinded,[90,122,126] one was double blinded,[124] and blinding was unclear for two trials.[123,125] For the outcomes presented here, four of six trials analyzed results according to the intention-to-treat principal.[90,123-125] Three trials adequately described reasons for study withdrawal.[90,122,125] Percentages of study withdrawals ranged from 0 to 16 percent (n=4 trials).

Results

Mortality (Table 14, Appendix Table C106, and Appendix Figure C21)

All-Cause Mortality

Compared with standard blood pressure control, there was no significant reduction in risk of all-cause mortality with strict blood pressure control (RR 0.86, 95% CI, 0.68 to 1.09; n=4 trials, 1,803 patients). These results were driven almost entirely by two trials that, though they each

reported a 12 to 15 percent relative reduction in mortality with strict compared with standard blood pressure control, differed markedly in other respects. In the trial by Shulman, 35 percent of participants assigned strict blood pressure control versus 41 percent assigned standard control died during a 5-year followup period, compared with 6.9 percent versus 7.8 percent, respectively, in an approximately 4-year followup period, in the trial by Wright.[90,126] Other differences between these trials included the substantially higher baseline blood pressure, most of which had been untreated, among participants in the Shulman trial,[126] and lower blood pressure targets for both treatment groups, and use of ACEIs and BB only in the trial by Wright.[90]

Cardiovascular Mortality

Compared with standard blood pressure control, there was no significant reduction in risk of cardiovascular mortality with strict blood pressure control (RR 0.83, 95% CI, 0.54 to 1.26). Nearly all the weight contributing to this pooled estimate was derived from one trial, in which 20.1 percent versus 23.9 percent of participants experienced a cardiovascular death (RR 0.84, 95% CI, 0.55 to 1.29),[126] while fewer than 1 percent of participants died due to cardiovascular causes in the only other trial reporting this outcome.[122]

Vascular Outcomes (Table 14, Appendix Tables C106-C108, and Appendix Figure C21)

Myocardial Infarction

Incidence of fatal MI was reported in few trials and among these trials occurred in less than 5 percent of participants in all treatment groups. Based on these very limited data, there was no significant difference in risk of fatal MI (RR 1.01, 95% CI, 0.06 to 15.95; n=1 trial, 335 patients) between the strict and standard blood pressure control groups. However, the 95% CI estimating risk for this outcome is wide and cannot exclude either a clinically important benefit or harm.

Stroke

Similar findings were reported for stroke. As with MI, there was no evidence of reduced risk of fatal stroke (RR 1.09, 95% CI, 0.34 to 3.47; n=2 trials, 632 patients) between the strict and standard blood pressure control groups. Again, the 95% CI estimating risk is wide and cannot exclude either a clinically important benefit or harm.

Other Vascular Outcomes

Only one trial reported a composite vascular endpoint, in this case, a composite of cardiovascular mortality and first cardiovascular hospitalization. Incidence appeared similar between participants assigned to strict versus standard blood pressure control (2.3 percent versus 2.7 percent per patient year, respectively).

Renal Outcomes (Table 14, Appendix Tables C109 and C110, and Appendix Figure C21)

End-Stage Renal Disease

Though five trials reported outcomes for ESRD, results were reported separately by treatment group in only three trials. Among these trials, there was no significant reduction in risk for ESRD between strict and standard blood pressure control (16.8 percent versus 16.6 percent; RR 1.03, 95% CI, 0.77 to 1.38, n=3 trials, 1,506 patients).

Other Renal Outcomes

No trials comparing strict versus standard blood pressure targets reported results separately by treatment group for the individual outcomes of doubling of serum creatinine, halving of GFR, or progression from microalbuminuria to macroalbuminuria. Assignment to a strict blood pressure target group did not appear to decrease risk of experiencing any of several study-defined composite renal outcomes (Appendix Table C110), including ESRD, or death (RR 0.91, 95% CI, 0.73 to 1.13);[90] halving of GFR, ESRD, or death (RR 1.06, 95% CI, 0.89 to 1.27);[90] or 50 percent decline in GFR, doubled serum creatinine, ESRD, or death (RR 1.43, 95% CI, 0.63 to 3.23).[124]

Study Withdrawals and Adverse Events (Appendix Table C111)

Overall study withdrawals, reported in four trials, ranged from 0 to 16 percent, with results appearing to be similar between treatment groups in two trials reporting these data. In the only trial to report serious adverse events and withdrawals due to serious adverse events, incidence of these outcomes appeared possibly more frequent in the strict blood pressure control group.[122] Specific adverse events also were infrequently reported, with cough[90] and postural hypotension[123] each being significantly more frequent in the strict blood pressure target group compared with the standard blood pressure target group in one trial.

Subgroup Results

No trials reported outcomes stratified by any participant characteristic. In trials restricted to patients with diabetes, outcomes reported were limited to the finding of no significant difference in risk of conversion from microalbuminuria to macroalbuminuria in one trial (RR 0.70, 95% CI, 0.36 to 1.36). In one trial that excluded participants with cardiovascular disease, no results were reported by treatment group. In two trials restricted to participants with proteinuria, only one of which reported results by treatment group, there was no significant difference in risk of ESRD (RR 1.12, 95% CI 0.75 to 1.69), and clinical vascular events and deaths were rare. In trials restricted to participants with decreased eGFR or creatinine clearance or increased serum creatinine, there was no significant difference between strict and standard blood pressure control groups in all-cause mortality (RR 0.86, 95% CI, 0.68 to 1.09, n=4 trials), cardiovascular mortality, MI, fatal stroke, ESRD (RR 1.03, 95% CI, 0.77 to 1.38, n=3 trials), or any of four composite renal outcomes. In one trial restricted to African American participants, which also excluded patients with CHF, there was no significant difference between tight and standard blood pressure control groups for risk of mortality (RR 0.88, 95% CI, 0.58 to 1.35, ESRD (RR 0.92, 95% CI, 0.70 to 1.22), or either of two composite renal outcomes.

Summary (Appendix Table C140)

In individuals with CKD, compared with targeting standard blood pressure control, assignment to targeting strict control was associated with 14 percent and 17 percent relative reductions in risk of all-cause mortality and cardiovascular mortality, respectively, which were not statistically significant. There were no significant differences between treatment groups for the outcomes of MI, stroke, ESRD, or, in individual trials, for several composite renal outcomes. Findings for the mortality and ESRD outcomes were driven mostly by a single trial conducted more than 20 years ago that may have limited generalizability to current patient populations and available antihypertensive treatment options. Results for MI and stroke in particular were limited by small sample sizes and could not exclude either clinically meaningful benefits or harms. Overall results were further limited by heterogeneity in patient populations (i.e., baseline level of

renal function, comorbidities), and heterogeneity in blood pressure targets. Subgroup analyses, though limited, did not identify any comorbid conditions or category of renal function in which there was a significant difference between strict and standard blood pressure control for any clinical outcome. Reporting on study withdrawals and adverse effects was limited. Finally, no trial provided followup beyond 5 years; therefore, longer term effects of different blood pressure targets cannot be determined from these studies.

Table 14. Pooled clinical and renal outcomes, strict versus standard blood pressure target treatment trials

Outcome	Number of Trials Reporting	Quality of the Studies	Strict BP Events/N (%)	Usual BP Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
All-cause mortality	4	Fair	96/908 (10.6)	103/895 (11.5)	0.86 [0.68-1.09]	0%
Cardiovascular mortality	2	Fair	33/326 (10.1)	35/306 (11.4)	0.83 [0.54-1.26]	0%
Fatal MI	1	Fair	1/167 (0.6)	1/168 (0.6)	1.01 [0.06-15.95]	NA
Stroke, fatal	2	Fair	6/326 (1.8)	5/306 (1.6)	1.09 [0.34-3.47]	0%
End-stage renal disease	3	Fair	126/749 (16.8)	126/757 (16.6)	1.03 [0.77-1.38]	22%
Composite renal outcome*, Wright A[90]	1	Good	173/540 (32.0)	167/554 (30.1)	1.06 [0.89-1.27]	NA
Composite renal outcome*, Wright B[90]	1	Good	118/540 (21.9)	133/554 (24.0)	0.91 [0.73-1.13]	NA
Composite renal outcome**, Toto A[124]	1	Fair	12/42 (28.6)	7/35 (20.0)	1.43 [0.63-3.23]	NA
Composite renal outcome**, Toto B[124]	1	Fair	4/42 (9.5)	5/35 (14.3)	0.67 [0.19-2.29]	NA

BP = blood pressure; MI = myocardial infarction; NA = not applicable; RR = relative risk reduction

* (A) 50% or 25 mL/min reduction in GFR, ESRD (dialysis or transplantation), or death; (B) ESRD or death

** (A) 50% decline in GFR, doubled serum creatinine, ESRD, or death; (B) 50% decline in GFR or doubled serum creatinine.

Low Protein Diet Versus Usual Protein Diet Trials (n=6)

Overview

In patients with CKD, we found a low level of evidence that, compared with usual protein diets, a low protein did not significantly reduce risk of all-cause mortality nor increase risk of ESRD. We found no statistically significant difference between treatment groups in risk of doubling baseline creatinine, or halving GFR. Our confidence in these estimates is limited by the small number of trials reporting different outcomes, the small number of clinical events, and heterogeneity between studies.

Description of Studies

Six trials met all eligibility criteria and randomized 1,480 (range 63 to 585) participants with CKD to a low protein diet (typically 0.6 or 0.8 g protein per kg of ideal/lean body weight per day) versus a usual diet (typical protein intake less than 1.3 g/kg/day).[125,127-135] Detailed baseline characteristics are presented in Appendix Tables C112 and C113.

Mean participant age was 52 years (range 49 to 58; n=5 trials), and men constituted 59 percent (range 54 to 83; n=5 trials) of all study participants. In the one trial reporting ethnicity, 85 percent of participants were white. One study was conducted in the United States.[125,127,130,131] Of the remaining studies, two were conducted in Italy[132,133] and one each was conducted in Japan,[128] France,[129] and the United Kingdom.[134,135] Followup periods ranged from 2 to 3.5 years.

Renal Function

Two of the six eligible trials required that participants have albuminuria, with some limitation in the severity of their renal function. In one of these studies, all subjects had to have macroalbuminuria (UAER >200 µg/min) or proteinuria (urine protein excretion rate, i.e., urine protein excretion rate (UPER), >1 g/day) and serum creatinine <2.0 mg/dl (i.e., CKD stages 1–3).[128] In the second study, patients were required to have UAER >30 mg/day (i.e., at least microalbuminuria) and GFR of at least 15 ml/min (i.e., CKD stages 1-4).[129] The remaining four trials required that participants have either an elevated serum creatinine or a reduced GFR or creatinine clearance, and three also imposed limits on UPER. Thresholds for eligibility in these trials included creatinine 1.2 to 7.0 mg/dl in women and 1.4 to 7.0 mg/dl in men, with UPER less than 10 g/day (i.e., CKD stages 1-5);[131] creatinine 1.35 to 7.0 mg/dl in women and 1.5 to 7.0 mg/dl in men, with GFR <60 ml/min, and UPER <3 g/day (i.e., CKD stages 3-5);[133] creatinine clearance 15 to 70 ml/min and UPER <3 g/day (i.e., CKD stages 1-4);[132] and GFR 10 to 60 ml/min (i.e., CKD stages 3-5).[134,135] Among all six eligible trials, baseline mean UPER ranged from 0.28 g/day/1.73m^2 to 1.5 g/day (n=3 trials), mean UAER was reported in only one trial (366 mg/day), mean serum creatinine was 1.7 mg/dl (range 1.1 to 1.9, n=3 trials), and mean GFR was 45 ml/min/1.73m^2 (range 39 to 86, n=3 trials).

Baseline Comorbidities

Two trials enrolled only patients with diabetes,[128,129] two trials excluded patients with diabetes,[132,133] and two trials did not report baseline prevalence of diabetes[131,134,135] Among two trials reporting,[128,131] mean blood pressure was 132/80 mm Hg. One trial excluded all patients with CHF,[128] another trial excluded patients with either class III or IV CHF,[131] and two trials

excluded participants with a recent MI[128,133] or stroke.[128] However, no additional information on baseline cardiovascular morbidity was reported in any trial.

Study Quality (Appendix Table C140)

Study quality was rated as fair in all six trials. Allocation concealment was adequate in three studies and unclear in three studies. One trial reported that measures of GFR were blinded,[131] but the other trials were not reported as blinded. Five trials did not perform analyses using intention-to-treat principles, and it was unclear in one study.[131] Withdrawals were adequately described in all but two studies.[132,134,135] Study withdrawals ranged from 2 to 25 percent.

Results

Mortality (Table 15, Appendix Table C114, and Appendix Figure C22)

All-Cause Mortality

In the CKD patients studied in eligible trials, low protein diets were associated with a nonsignificant 42 percent reduction in risk of all-cause mortality compared with usual protein diets (1.9 versus 3.3 percent; RR 0.58, 95% CI, 0.29 to 1.16; n=4 trials).[128,131,133,135] All individual trials suggested a lower mortality risk with low protein diets, but the difference was not statistically significant in any trial.

Cardiovascular Mortality

Only one trial reported cardiovascular mortality, in which there were four such events (1.4 percent) in the low protein diet group and five cardiovascular deaths (1.7 percent) in the usual protein diet group.[131]

Vascular Outcomes (Table 15, Appendix Tables C114 and C115, and Appendix Figure C22)

Myocardial Infarction

One trial reported a single fatal MI (2.0 percent) in the usual protein diet group and none in the low protein diet group.[128]

Stroke

One trial reported two nonfatal strokes (0.7 percent) in the low protein diet group and none in the usual protein diet group.[131]

Other Vascular Outcomes

No other cardiovascular events were reported in any trial.

Renal Outcomes (Table 15, Appendix Tables C116 and C117, and Appendix Figure C22)

End-Stage Renal Disease

In three trials reporting, none of which had more than 10 cases of ESRD, low protein diets were associated with a nonstatistically significant 62 percent increase in risk of ESRD compared with usual protein diets (7.1 versus 4.1 percent; RR=1.62, 95% CI, 0.62 to 4.21; n=302

patients).[128,129,135] One additional trial reported that 12 participants (2.1 percent) developed ESRD, but did not report this result separately for the two treatment groups.[131]

Other Renal Outcomes

One trial reported no significant difference between low and usual protein diet groups in risk of doubling of plasma creatinine (RR 0.93, 95% CI, 0.53 to 1.64),[128] while a second trial reported no significant difference between these groups in risk of halving GFR (RR 0.71, 95% CI, 0.44 to 1.17).[132] One trial reported a significant 37 percent lower risk of the composite renal outcome of dialysis or doubling of plasma creatinine concentration in CKD subjects randomized to low protein diet versus usual protein diet (11.7 versus 18.6 percent; RR 0.63, 95% CI, 0.40 to 0.99).[133] A second trial reported that 60 patients reached a study stopping point due to "rapidly declining glomerular filtration rate."[131] Though it did not report this result separately for the two treatment groups, it did report that there was no significant difference in this outcome between the two groups. No other clinical renal events were reported in any trial.

Withdrawals and Adverse Events (Appendix Table C118)

Withdrawals were reported in 10.0 percent of randomized participants (range 1.9 to 27.7, n=6 trials). In the four trials that reported withdrawals by treatment group, withdrawals were 13.5 percent and 15.4 percent in low protein diet subjects and usual protein diet subjects, respectively. No data were reported on serious adverse events or withdrawals due to serious adverse events. One trial reported that 2.0 and 2.1 percent of participants in low protein diet and usual protein diet groups, respectively, stopped the trial due to a "serious medical condition."[131] In the low protein diet group, these conditions were pregnancy (n=1), stroke (n=2), acute renal failure (n=1), diabetes necessitating insulin (n=1), and cancer (n=1). In the usual protein diet group, these conditions were diabetes necessitating insulin (n=3), cardiomyopathy (n=1), cancer (n=1), and severe liver disease (n=1). In the same trial, additional outcomes reported as adverse events in the low protein diet group were weight loss (29 percent), weight gain (25 percent), and hyperkalemia (10 percent). Additional outcomes reported as adverse events in the usual protein diet group were weight loss (18 percent), weight gain (40 percent), and hyperkalemia (17 percent).

Subgroup Results

No trials reported outcomes stratified by any participant characteristic. In two small trials restricted to patients with diabetes, both of which also required participants to have albuminuria, there was no significant difference between low protein and usual protein treatment groups in risk of mortality or ESRD, though there were few clinical events. There also was no difference between treatment groups for doubling serum creatinine (RR 0.93, 95% CI, 0.53 to 1.64, n=1 trial). In two trials restricted to patients without diabetes, while there was no significant difference in risk of mortality, a significantly lower risk of experiencing a composite renal outcome (RR 0.63, 95% CI, 0.40 to 0.99) was seen in one trial reporting, and no ESRD events were reported. In one trial that excluded participants with CHF, there was no significant difference between low protein and usual protein treatment groups in risk of mortality or ESRD, though again there were few clinical events. No trials were either restricted to or excluded participants with hypertension or other cardiovascular conditions.

Summary

In six trials conducted in patients with CKD, low protein diets were associated with a nonsignificant 42 percent reduction in all-cause mortality compared with usual protein diets. In one trial reporting, the small number of cardiovascular deaths appeared similar in both diet intervention groups. No other vascular outcome was reported in more than two cases in any trial. In three trials reporting, all with fewer than 10 cases of ESRD, low protein diets were associated with a nonsignificant 62 percent increase in risk of ESRD compared with usual protein diets. One trial reported a significant 37 percent lower risk of the composite renal outcome of dialysis or doubling of plasma creatinine concentration in CKD subjects randomized to low protein diet versus usual protein diet. Applicability to patients with CKD stages 1–3 may be limited since at least four of six trials also included individuals in CKD stages 4–5. Withdrawals ranged widely between trials but did not appear greater in the low protein diet group in any trial. Results were limited by small sample sizes, few trials reporting clinical vascular or renal outcomes, and almost no events in the trials that reported these outcomes. Judging applicability was limited because of the variability in renal function reported between trials and scant data reported on comorbid conditions. Trials did not systematically report adverse events.

Other Dietary Intervention Trials (n=3)

Overview

In patients with CKD, we found a low level of evidence that, compared with a low protein diet, the CR-LIPE diet reduced risk of mortality or ESRD. There was a low level of evidence that diets altering phosphate intake impacted risk of ESRD and insufficient evidence regarding whether it impacted risk of mortality. There was insufficient evidence regarding whether a low triglyceride diet and pharmacological treatment to lower triglycerides differ regarding risk of mortality or ESRD. Our confidence in these estimates is limited because for each comparison data are drawn from only one trial and there were few reported clinical events.

Description of Studies

Three trials met all eligibility criteria and randomized participants with CKD to a diet intervention versus a control treatment group. Detailed baseline characteristics are presented in Appendix Tables C112 and C113.

Among the three trials, one randomized 191 participants to a carbohydrate restricted, low-iron-available, polyphenol-enriched diet (CR-LIPE) versus a low protein diet.[136] Mean age of study participants was 60 years and 53 percent of study participants were men. The study was conducted in the United States. Followup duration was 3.9 years.

A second trial randomized 57 participants to a triglyceride lowering diet versus gemfibrozil, a triglyceride lowering medication.[137] Mean age of study participants was 51 years and 75 percent of study subjects were men. The study was conducted in Sweden. Followup duration was 1 year.

The third trial randomized 98 participants to either a low protein-low phosphate diet, a low phosphate diet with phosphate binders, or an unrestricted diet.[138] Mean age of study participants was 45 years and 66 percent of study subjects were men. The study was conducted in the United Kingdom. Followup duration was 1.6 years.

Renal Function

For inclusion in the CR-LIPE versus low protein diet trial, participants were required to have GFR 15 to 75 ml/min and UPER 0.35 to 12 g/day. Baseline renal function was reported as mean GFR 63 ml/min, mean UPER 2.47 g/day, and mean creatinine 1.84 mg/dl.[136] For inclusion in the triglyceride lowering diet versus gemfibrozil trial, participants were required to have a GFR of 10 to 70 ml/min/1.73m^2. Baseline renal function was reported as mean GFR of 35.5 ml/min/1.73m^2, mean serum creatinine of 2.4 mg/dl, and mean UAER of 0.95 g/day.[137] For inclusion in the low protein low phosphate diet, low phosphate diet, or unrestricted diet trial, participants were required to have a serum creatinine between 1.7 and 10.2 mg/dl. At baseline, mean serum creatinine was 4.5 mg/dl, mean UPER was 3.15 g/day, and mean creatinine clearance was 26.8 ml/min/1.73m2.[138]

Baseline Comorbidities

For inclusion in the CR-LIPE versus low protein trial, participants were required to be diabetic.[136] No additional information was reported on comorbid conditions. For inclusion in the triglyceride lowering diet versus gemfibrozil trial, participants were required to be nondiabetic. No additional information was reported on comorbid conditions.[137] For the third trial, no information was reported on comorbid conditions.[138]

Study Quality (Appendix Table C140)

All three trials were rated as fair quality. Allocation concealment was adequate in one trial[138] and unclear in the other two studies. One study reported that study personnel were blinded to the aims of the study, but it was unclear if the outcome assessment was blinded.[136] The remaining two studies were unblinded. None of the studies analyzed by the intention-to-treat principle. Withdrawals ranged from 5.3 to 15.8 percent, and reasons for withdrawals were adequately explained in two of the three trials.[136,137]

Results

Mortality (Table 15, Appendix Table C114, Appendix Figure C22)

In one trial, reported all-cause mortality was 8.8 percent in CKD subjects assigned to the CR-LIPE diet compared with 17.7 percent in the low-protein diet group.[136] In a second trial, risk of all-cause mortality was not significantly different between treatment groups, at 3.0 percent, 13.3 percent, and 3.1 percent in the low protein-low phosphate, low phosphate-phosphate binding, and control diet groups.[138] The triglyceride lowering diet trial did not report mortality data.

Vascular Outcomes

Myocardial Infarction

No data were reported for MI.

Stroke

No studies reported on stroke.

Other Vascular Outcomes

No heart failure or composite vascular outcomes were reported.

Renal Outcomes (Table 15, Appendix Tables C116 and C117, and Appendix Figure C22)

End-Stage Renal Disease

In one trial, ESRD occurred in 11.0 percent of CKD subjects allocated to the CR-LIPE diet versus 21.5 percent assigned to the low protein diet group.[136] In a second trial, ESRD occurred in 54.8 percent, 48.3 percent, and 51.7 percent of the low protein-low phosphate diet group, low phosphate-phosphate binding group, and control diet group, respectively.[138] In the trial that compared a low triglyceride diet versus gemfibrozil, progression to ESRD was reported for 3.4 percent and 7.1 percent of these treatment groups, respectively.[137]

Other Renal Outcomes

In one study, participants randomized to a CR-LIPE diet appeared less likely than those assigned to a low protein diet to experience either a doubling in creatinine (20.9 versus 39.2 percent), or the composite renal outcome of renal replacement therapy or death (19.8 versus 39.2 percent, $p<0.05$).[136]

Withdrawals and Adverse Events (Appendix Table C118)

In the trial comparing the CR-LIPE diet and low protein diet, withdrawals by treatment group were 9.0 percent and 13.2 percent respectively.[136] In the trial comparing a low triglyceride diet to gemfibrozil, no withdrawals were reported in the diet group compared with 21.4 percent withdrawals in the gemfibrozil group, with all attributed to mild gastrointestinal symptoms.[137] In the third trial, 5.3 percent of the participants withdrew, but no data were reported according to treatment group.[138] No other adverse events data were reported from any trial.

Summary

In one trial, CKD patients randomized to a carbohydrate-restricted, low iron available, polyphenol-enriched diet (CR-LIPE) appeared to have lower all-cause mortality, lower risk of ESRD, and lower risk of the composite endpoint of ESRD or death compared with participants assigned to a low protein diet. In a second trial, study participants allocated to a low phosphate-phosphate binding diet appeared to have a higher risk of all-cause mortality than did patients assigned to either a low protein-low phosphate diet or to a control diet. There was no apparent difference between these three diet groups in risk of ESRD. In the third trial, results suggested that CKD patients randomized to a low triglyceride diet may have a lower risk of ESRD and fewer gastrointestinal side effects than patients assigned to gemfibrozil. Results were limited in that all trials were small, reported few clinical outcomes, and did not conduct their analyses according to an intention-to-treat principle.

Table 15. Pooled clinical and renal outcomes, dietary intervention trials

Outcome	Number of Trials Reporting	Quality of the Studies	Low Protein Diet Events /N (%)	Usual Protein Diet Events/N (%)	RR [95% CI]*	I^2 test for Heterogeneity
Low-protein diet versus usual protein diet (N=6)						
All-cause mortality	4	Fair	12/642 (1.9)	21/638 (3.3)	0.58 [0.29-1.16]	0%
Cardiovascular death	1	Fair	4/291 (1.4)	5/294 (1.7)	0.81 [0.22-2.98]	NA
Myocardial infarction, fatal	1	Fair	0/47 (0)	1/41 (2.4)	0.29 [0.01-6.97]	NA
Stroke, nonfatal	1	Fair	2/291 (0.7)	0/294 (0)	5.05 [0.24-104.76]	NA
End-stage renal disease	3	Fair	11/154 (7.1)	6/148 (4.1)	1.62 [0.62-4.21]	0%
Doubling of serum creatinine	1	Fair	16/47 (34.0)	15/41 (36.6)	0.93 [0.53-1.64]	NA
Halving of GFR**	1	Fair	18/63 (28.6)	26/65 (40.0)	0.71 [0.44-1.17]	NA
Composite renal outcome†	1	Fair	27/230 (11.7)	42/226 (18.6)	0.63 [0.40-0.99]	NA
Low-protein/low phosphate diet versus low phosphate diet (N=1)						
All-cause mortality	1	Fair	1/31 (3.2)	4/29 (13.8)	0.23 [0.03-1.97]	NA
End-stage renal disease	1	Fair	17/31 (54.8)	14/29 (48.3)	1.14 [0.69-1.86]	NA
Low-protein/low phosphate diet versus usual diet (N=1)						
All-cause mortality	1	Fair	1/31 (3.2)	1/29 (3.4)	0.94 [0.06-14.27]	NA
End-stage renal disease	1	Fair	17/31 (54.8)	15/29 (51.7)	1.06 [0.66-1.70]	NA
Low-protein versus other diet††						
All-cause mortality	1	Fair	14/79 (17.7)	8/91 (8.8)	2.02 [0.89-4.55]	NA
End-stage renal disease	1	Fair	17/79 (21.5)	10/91 (11.0)	1.96 [0.95-4.03]	NA
Doubling of serum creatinine	1	Fair	31/79 (39.2)	19/91 (20.9)	1.88 [1.16-3.05]	NA
Composite renal outcome§	1	Fair	31/79 (39.2)	18/91 (19.8)	1.98 [1.21-3.26]	NA
Low-triglyceride diet versus gemfibrozil (N=1)						
End-stage renal disease	1	Fair	1/29 (3.4)	2/28 (7.1)	0.48 [0.05-5.03]	NA

*RR = relative risk reduction; **GFR = reported as halving of creatinine clearance; NA = not applicable
†Need for dialysis or doubling of baseline plasma creatinine concentration.
††50% carbohydrate restricted, low-iron-available, polyphenol-enriched diet.
§Renal replacement therapy or death.

Glycemic Control Trials (n=2)

Overview

In diabetic patients with CKD, we found insufficient evidence regarding whether there is a difference between treatments in risk of mortality or ESRD. Our confidence in these estimates is limited by the small number of trials reporting different outcomes, the small number of clinical events, and heterogeneity between studies.

Description of Studies

Two trials met all eligibility criteria and randomized participants with diabetes and CKD to intensive versus standard glycemic control.[139,140] Detailed baseline characteristics are presented in Appendix Tables C119 and C120.

In the first study, conducted in 70 patients, those assigned intensive diabetes control (treatment targets HbA_{1c} ≤7.5percent, fasting blood glucose 72 to 108 mg/dL, and 2 hour postprandial blood glucose ≤180 mg/dL) were treated using insulin by continuous infusion or multiple daily injections. Frequent visits and medication adjustment were made as needed, and 24 hour/day consultation was available. Participants assigned to conventional therapy (no glycemic targets) generally were treated using two daily insulin injections, adjusted only for symptoms, along with conventional education about diet, exercise, and blood glucose monitoring. Standard control patients were seen every 3 months. No changes were made to the usual diabetic diet of participants in either treatment group, and all patients were treated to keep their blood pressure <160/95 mm Hg.[140] Mean age was 37 years, 73 percent of participants were male, and no data was reported on ethnicity.

In the second study, a subgroup analysis within 491 patients with microalbuminuria from a larger diabetes treatment trial (n=1,791), trial participants allocated to the intensive control group were started on maximal doses of oral therapy, and insulin was added as needed to achieve a target HbA_{1c} <6 percent.[139] Participants assigned to standard control were started on one-half of maximal doses of oral therapy and insulin was added as needed to achieve a target HbA_{1c} <9 percent. No data on age, gender, or ethnicity was reported for the subgroup with microalbuminuria.

Renal Function

Both trials were restricted to participants with microalbuminuria. In one study this was defined as UAER between 30 and 200 μg/min.[140] In the second trial, in which subgroup results were reported for conversion from microalbuminuria to macroalbuminuria, no definition of microalbuminuria was reported. Participants in this second trial further were restricted to those with serum creatinine ≤1.6 mg/dl.[139] Participant mean baseline GFR was 116.7 ml/min/1.73m^2 and mean UAER was 47.9 μg/min.

Baseline Comorbidities

Both trials were restricted to participants with diabetes. The first trial enrolled patients with baseline blood pressure <160/95 mm Hg and no evidence of diabetic macrovascular complications.[140] Participant mean HbA_{1c} was 10.1 percent. The second trial enrolled individuals with type 2 diabetes who had HbA_{1c} >7.5 percent, despite maximal doses of oral agents or on insulin.[139] In this second trial, no baseline characteristics were reported for the subgroup of

participants with microalbuminuria, though overall study excluded patients with a cardiovascular event during the previous 6 months, advanced CHF, or severe angina.

Results

Mortality (Appendix Table C121)

During median followup durations of about 5 years, neither trial reported results comparing intensive versus standard glycemic control within their CKD population for the outcome of mortality. One trial reported that one CKD patient died (2.7 percent) but did not report the group assignment of the patient.[140]

Vascular Outcomes

Myocardial Infarction

Neither trial reported on MI.

Stroke

Neither trial reported stroke outcomes.

Other Vascular Outcomes

Neither trial reported any composite vascular outcomes.

Renal Outcomes (Table 16, Appendix Table C122)

End-Stage Renal Disease

There were no reports of ESRD.

Other Renal Outcomes (Appendix Figure C23)

One trial reported that one patient experienced acute renal failure (2.7 percent) but did not report the group assignment of the patient.[140] In data from both trials, compared with conventional treatment, participants allocated to intensive diabetes treatment had a nonsignificant 31 percent relative reduction in risk of conversion from microalbuminuria to macroalbuminuria (8.7 versus 12.8 percent; RR 0.69, 95% CI, 0.42 to 1.12; n=561 patients). Neither study reported on any other renal outcomes.

Study Withdrawals and Adverse Events (Appendix Table C123)

Only one of the two trials reported study withdrawals,[140] with 13.9 percent versus 8.8 percent in the intensive versus conventional treatment groups, respectively. While it further noted that 4.3 percent (three of 70) of study participants withdrew due to serious adverse events, including one death, one leukemia, and one acute renal failure, it did not report these outcomes by treatment group. In one trial, neither incidence of severe hypoglycemia or diabetic ketoacidosis appeared to differ between CKD patients assigned to the two treatment groups.[139] In the second trial, risk of hypoglycemia was not reported for the CKD subgroup, but in the larger overall study population frequency of hypoglycemic events and frequency of severe hypoglycemic events was significantly greater in the intensive control group ($p<0.001$).[140]

Subgroup Results

No trials reported outcomes stratified by any participant characteristic. However, both trials were restricted to patients with diabetes and microalbuminuria, so all results reported above apply to these subgroups. No other subgroup results are available since no trials were restricted to patients with impaired eGFR, or with a history of hypertension or cardiovascular disease, and no trials excluded patients with these conditions. Since both trials were limited to participants with microalbuminuria, no data for patients with macroalbuminuria are available.

Summary

In diabetic individuals with CKD, compared with conventional treatment, assignment to intensive diabetes treatment was associated with an approximately 31 percent relative reduction in risk of conversion from microalbuminuria to macroalbuminuria that was not statistically significant. There were no data regarding the relative risk between these treatment strategies for all-cause or cardiovascular mortality, MI, stroke, ESRD, doubling of serum creatinine, halving of GFR, or any composite vascular or renal endpoint. Reporting on withdrawals and adverse effects associated with these treatment regimens in CKD patients was limited. Results were limited by the small number of trials, few outcomes reported, the heterogeneity of patient populations, and the heterogeneity in intensity of treatment regimens.

Table 16. Pooled clinical and renal outcomes, glycemic control trials

Outcome	Number of Trials Reporting	Quality of the Studies	Intensive Treatment Events/N (%)	Conventional Treatment Events/N (%)	Relative Risk [95% CI]	I^2 test for Heterogeneity
Intensive treatment versus conventional treatment trials (n=2)						
Progression from micro- to macroalbuminuria	2	Good	25/287	35/274	0.69 [0.42-1.12]	0%

HMG-CoA Reductase Inhibitors (Statins) Versus Control Trials (n=12)

Overview

In patients with CKD defined by impaired GFR, in comparison to control treatment, there is a high level of evidence that statins reduce risk of all-cause mortality. There is a low level of evidence that there is no difference between statins and control treatment for risk of ESRD. Compared with participants assigned to control, those randomized to statin had a statistically significantly lower risk of MI, stroke, and most composite cardiovascular outcomes, but no statistically significant difference in risk of cardiovascular mortality, CHF hospitalization, or a single composite renal outcome. Our confidence in these estimates is limited by the heterogeneity between studies and because all outcomes data are drawn from post hoc analyses.

Description of Studies

Twelve trials met all eligibility criteria and randomized participants with CKD (n=17,460, range 304 to 4,491) to statin therapy versus control.[62,83,141-149] One study, the CARE trial, was reported both by itself[148] and as part of a pooled subject-level meta-analysis of three trials of pravastatin versus placebo.[149] All but one study[62] were post hoc analyses performed within subsets of participants with CKD from larger trial populations not originally limited to subjects with CKD. Detailed baseline characteristics are presented in Appendix Tables C124 and C125.

Among eligible trials, 9,890 participants were randomized to pravastatin versus control, including 5,355 versus placebo (n=2 trials),[62,149] 2,978 versus diet (n=1 trial),[142] and 1,557 versus usual care (n=1 trial).[83] In addition, 4,902 participants were randomized to rosuvastatin versus placebo (n=2 trials),[146,150] and 1,549 participants were randomized to atorvastatin versus control, including 970 versus placebo (n=1 trial)[143] and 579 versus usual care (n=1 trial).[144] There also were several smaller studies, in which 505 participants were randomized to simvastatin versus placebo (n=1 trial),[145] 310 participants were randomized to fluvastatin versus placebo (n=1 trial),[147] and 304 participants were randomized to lovastatin versus placebo (n=1 trial).[141] The mean age of subjects was 65 years (range 51 to 71; n=10 trials), and men constituted 53 percent (range 24 to 82; n=10 trials) of all patients randomized. Among the six trials that reported race/ethnicity, 79 percent of participants were white. The majority of trials were multinational.[83,143,145-147,149,150] Mean or median study duration ranged from 1.9 to 5.4 years, with most trials having a followup of at least 4 years.

Renal Function

All studies except one were post hoc analyses from large statin trials, performed in subsets of participants with decreased GFR or creatinine clearance from the larger trial populations. Most of these analyses defined impaired GFR or creatinine clearance as <60 ml/min/1.73m^2,[83,141-144,149,150](i.e., CKD stage 3 or worse) or at least provided data for patients under this threshold.[145] No other trials based study eligibility on CKD stage or reported baseline distribution of participants by CKD stage. Instead, individual studies defined impairment as GFR <51 ml/min/1.73m^2,[146] and creatinine clearance of <55.9 ml/min[147] and <75 ml/min.[148] In trials reporting, mean baseline serum creatinine was 1.3 mg/dL (range 1.0 to 1.5, n=9 trials), mean GFR was 54 ml/min/1.73m^2 (range 50 to 56; n=10 trials), and mean creatinine clearance was 59 ml/min (range 47 to 61; n=2 trials). Most of the larger trials on which the post hoc analyses were

based excluded at least some patients with impaired renal function, with exclusion thresholds ranging from creatinine >1.5 to 1.8 mg/dL,[142,143,147,149] >2.0 mg/dL,[150] >2.5 mg/dL,[146,148] to >4.5 mg/dL.[149] One trial excluded participants with creatinine clearance less than 60 percent of the age-based normal.[62] Just one trial required participants to have microalbuminuria for inclusion,[62] and this was also the only trial to report mean baseline urinary albumin excretion (23 mg/24 hours).

Baseline Comorbidities

One trial was restricted to patients with diabetes,[143] and the mean prevalence of diabetes among 11 trials reporting was 22 percent (range 2 to 100). One trial was restricted to patients with hypertension,[83] while hypertensive patients were excluded from one trial.[62] The mean prevalence of hypertension was 49 percent among nine trials reporting. Mean systolic blood pressure was 136 mm Hg (range 131 to 146; n=10 trials) and mean diastolic blood pressure was 80 mm Hg (range 75 to 84; n=9 trials). Six trials were restricted to patients with coronary artery disease (secondary prevention studies),[144-149] including one restricted to patients with a history of myocardial infarction,[148] while patients with coronary artery disease were excluded from five trials (primary prevention studies).[141-143,149,150] The mean prevalence of coronary artery disease was 46 percent in 12 trials reporting. One trial was restricted to patients with CHF,[146] while patients with CHF were excluded from one trial.[62] The mean prevalence of CHF in four trials reporting was 39 percent. Mean baseline total cholesterol and low density lipoprotein (LDL) cholesterol were 220 mg/dL (range 189 to 265) and 142 mg/dL (range 109 to 192), respectively (n=12 trials).

Study Quality (Appendix Table C140)

Study quality was rated as good in eight trials and as fair in four trials. The method of allocation concealment was adequate in nine trials[83,142-146,148-150] but was unclear in three studies.[83,145,149] Nine trials were double blinded, of which eight explicitly stated that outcomes were adjudicated by blinded assessors.[62,141,143,145-147,149,150] Three trials were open label studies,[83,142,144] though one stated that outcomes were adjudicated by blinded assessors.[83] Analysis was by intention to treat in eleven studies[62,83,141-144,146-150] and not by intention to treat in one study.[145] None of the post hoc analyses reported the number of withdrawals within the subgroup of participants with impaired GFR. Only the trial that enrolled participants on the basis of microalbuminuria reported withdrawals (23 percent).[62]

Results

Mortality (Table 17, Appendix Table C126, and Appendix Figure C24)

All-Cause Mortality

In CKD patients assigned to statins versus control, there was a significant 20 percent reduction in all-cause mortality (7.1 versus 8.7 percent; RR 0.80, 95% CI, 0.68 to 0.95; n=8 trials, 13,964 patients).[62,142-145,147,149,150] However, in three trials that limited entry to patients with coronary artery disease, the 11 percent reduced all-cause mortality among patients randomized to statin treatment was not statistically significant (12.8 versus 14.3 percent; RR 0.89, 95% CI, 0.68 to 1.15; n=1,394 patients)[144,145,147] (Figure 8). In three trials that limited enrollment to patients without coronary artery disease, the 37 percent relative reduction in all-cause mortality was

statistically significant (2.1 versus 3.4 percent; RR 0.63, 95%CI, 0.44 to 0.90; n=7,215 patients)[142,143,150] (Figure 8).

Cardiovascular Mortality

In the four trials reporting data for cardiovascular mortality, there were few events (2.4 versus 3.4 percent for statin and control groups, respectively), with a nonsignificant 29 percent relative risk reduction in this outcome in participants randomized to statin treatment versus control (RR 0.71, 95% CI, 0.43 to 1.71; n=2,057 patients).[62,141,144,147] There also was no significant difference in risk of cardiovascular mortality between subjects assigned to statin versus control groups in two trials limited to patients with coronary artery disease (4.6 versus 6.6 percent; RR 0.69, 95% CI, 0.40 to 1.19; n=889 patients)[144,147] or in one trial limited to patients without coronary artery disease (0 versus 0.6 percent).[141]

Vascular Outcomes (Table 17, Appendix Tables C126–C128, and Appendix Figure C24)

Myocardial Infarction

In patients with CKD, assignment to statin treatment versus control was associated with a significant 28 percent reduction in risk of MI (RR 0.72, 95% CI, 0.54 to 0.98; n=2 trials, 2,015 patients).[141,148] In one secondary prevention trial, there was no statistically significant reduction in risk of MI between treatment groups (RR 0.74, 95% CI, 0.55 to 1.01; n=1,911 patients).[148] Similarly, in one primary prevention trial with few events, there was no significant reduction in risk of MI between treatment groups (RR 0.37, 95% CI, 0.07 to 1.78; n=304 patients).[141] Nonfatal MI was reported in one primary prevention and one secondary prevention trial. The primary prevention study alone demonstrated a significant reduction in the risk of nonfatal MI in the statin group compared with the placebo group (0.5 versus 1.2 percent; RR 0.40, 95% CI, 0.18 to 0.90). In the secondary prevention study, there was no significant reduction in risk of this outcome in statin subjects compared with those assigned to control (5.9 versus 9.9 percent; RR 0.60, 95% CI, 0.34 to 1.07).[144]

Stroke

In patients with CKD, assignment to statin treatment versus control significantly reduced the risk of stroke (1.4 versus 2.3 percent; RR 0.62, 95% CI, 0.41 to 0.95; n=6 trials, 10,369 patients).[62,142-144,148,150] The reduction in risk of stroke did not reach statistical significance in two secondary prevention trials (3.5 versus 5.0 percent; RR 0.71% 95% CI, 0.48 to 1.05; n=2,290 patients).[144,148] However, in three primary prevention trials, risk of stroke was significantly lower in statin patients than in those allocated to control (0.7 versus 1.6 percent; RR 0.43, 95% CI, 0.25 to 0.75; n=7,215 patients).[142,143,150]

Other Vascular Outcomes

In two trials reporting data, including one with fewer than 0.5 percent clinical events in either treatment group,[62] risk of hospitalization due to CHF in individuals with CKD was not significantly different between those who were randomized to statin treatment versus control (RR 0.7, 95% CI, 0.38 to 1.32; n=1,443 patients).[62,144] Nearly all trials reported multiple composite cardiovascular outcomes. For every composite cardiovascular outcome for every trial, the risk of the composite outcome was numerically lower (RR range 0.42 to 0.99) in study participants with CKD assigned to the statin group versus those allocated to control. This

difference was statistically significant in the majority of comparisons. Because the definition of the composite cardiovascular outcomes varied between trials, no pooled risk estimate was calculated

Renal Outcomes (Table 17, Appendix Tables C129 and C130, and Appendix Figure C24)

End-Stage Renal Disease

Only one trial reported results for ESRD.[83] In this trial of individuals with CKD with and without coronary artery disease there was no difference in risk of ESRD between study participants with CKD allocated to statin versus control treatment (4.1 versus 4.0 percent; RR 1.05, 95% CI, 0.64 to 1.73; n=1,557 patients).

Other Renal Outcomes

Similarly, this study reported no difference between treatment groups in the risk of experiencing the composite renal outcome of ESRD or ≥50 percent decline in renal function (6.4 versus 6.7 percent, RR 0.97, 95% CI, 0.66 to 1.43).[83] Only one trial reported on doubling of serum creatinine,[150] and there was no difference between groups for this rare outcome.

Study Withdrawals and Adverse Events (Appendix Table C131)

One trial provided data on withdrawals within patients with CKD, reporting 20 percent in the statin subjects and 26 percent in the placebo subjects.[62] However, the study included within these totals, 5 percent and 8 percent in each group withdrawn for "other medical reasons," which in part were comprised of subjects reaching study endpoints (i.e., cardiovascular mortality or hospitalization). A second trial reported no withdrawals among 1,711 subjects in both treatment groups.[148] No other post hoc analyses reported information on withdrawals for CKD patients.

Only five trials reported any data on adverse events within study participants with CKD. Four trials reported on the incidence of elevated creatine kinase, with two trials reporting only one control patient with creatine kinase exceeding ten times the upper limit of normal,[141,144] one trial reporting 0.7 and 0.3 percent of statin and control subjects, respectively, with creatine kinase levels exceeding three times the upper limit of normal,[148] and one trial reporting that 2.6 percent of participants in both treatment groups had a creatine kinase level greater than 500 IU.[142] In four trials reporting, rhabdomyolysis occurred in one of 2,913 (0.03 percent) statin subjects and four of 2,958 (0.1 percent) control group subjects.[141,144,148,150] Four trials reported incidence of abnormal liver function tests.[142,144,148,150] In all, the incidence was low, and in three trials that reported results for both statin and control groups,[142,148,150] there was no difference between these groups.

Subgroup Results

No trials reported outcomes stratified by any participant characteristic within CKD subjects. As noted above, in secondary prevention trials, compared with those assigned placebo, participants randomized to statins had no significant reduction in all-cause mortality (12.8 versus 14.3 percent; RR 0.89, 95% CI, 0.68 to 1.15; n=3 trials, 1,394 patients)[144,145,147] (Figure 8), cardiovascular mortality (RR 0.69, 95% CI, 0.40 to 1.19; n=2 trials, 889 patients), MI (RR 0.74, 95% CI, 0.55 to 1.01, n=1 trial, 1,711 patients), or stroke (RR 0.71, 95% CI, 0.48 to 1.05; n=2 trials, 2,290 patients), but were significantly less likely to experience a CHF hospitalization (RR

0.55, 95% CI, 0.39 to 0.77, n=1 trial, 3,107 patients). In addition, in primary prevention trials, compared with those assigned placebo, participants randomized to statins had a significant reduction in all-cause mortality (2.1 versus 3.4 percent; RR 0.63, 95% CI, 0.44 to 0.90; n=3 trials, 7,215 patients) (Figure 8), stroke (RR 0.43, 95% CI, 0.25 to 0.75; n=3 trials, 7,215 patients). None of these primary or secondary prevention trials reported any renal outcome measure.

In one trial limited to participants with diabetes, there was no significant between treatment difference in risk of all-cause mortality (RR 0.91, 95% CI, 0.55 to 1.51) or stroke (RR 0.40, 95% CI, 0.16 to 1.04), and mixed results for several composite vascular outcomes reported. In one trial limited to participants with hypertension, there was no difference between statins and placebo in risk of ESRD (RR 1.03, 95% CI, 0.64 to 1.67) or of a composite renal outcome, and no results were reported for mortality, MI, stroke, or other renal outcomes. In one trial limited to participants with CHF, there was no between treatment difference in risk of a composite vascular outcome and no results were reported for mortality, MI, stroke, CHF events, or any renal outcomes. In one trial that excluded patients with either CHF or hypertension, and was the only trial to require microalbuminuria for inclusion, participants randomized to statins did not have a significant reduction in risk of mortality (RR 1.49, 95% CI, 0.42 to 5.25), stroke (RR 1.74, 95% CI, 0.51 to 5.91), CHF hospitalization (RR 1.00, 95% CI, 0.06 to 15.86), or either of two composite vascular outcomes. No trials required macroalbuminuria for entry.

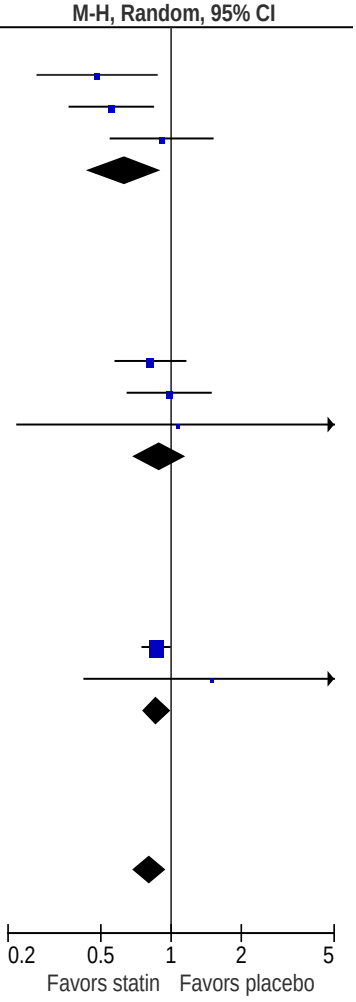
Summary

In individuals with CKD, statin treatment, as compared with control, was associated with significant relative reductions in risk of all-cause mortality (20 percent), MI (28 percent), and stroke (38 percent). Results appear to favor statin in both patients with and without a history of coronary artery disease, though results were statistically significant only for patients without coronary artery disease for mortality and stroke outcomes. Overall results were statistically nonsignificant but in favor of statin versus control for risk of hospitalization due to congestive heart failure. Risk for most composite vascular outcomes was significantly lower in CKD patients assigned statin treatment. In results available from only one trial, there was no difference between statin and control treatment groups regarding risk of ESRD or a composite outcome of ESRD or GFR decline by at least 50 percent. Only one trial reported on doubling of serum creatinine, but it had very few events.

While the magnitude of effect sizes favoring statins for many vascular outcomes, if real, seemed large enough to be clinically meaningful, results were limited by the small number of events in many studies and by small sample sizes in some others, in particular for analyses evaluating results in separate primary and secondary prevention subgroups. Results also were limited because, with one exception, studies were post hoc subgroup analyses from large statin trials that were not originally designed to evaluate CKD patients and renal outcomes. Consequently, there are almost no data on any renal outcome or on any vascular or renal outcome as a function of baseline albuminuria. Because most trials excluded patients with moderate and/or severely impaired renal function, available results may not be generalizable to these populations. Another limitation was that though composite vascular endpoints were reported in nearly all trials, the variability in their definitions prevented statistical pooling. Finally, few studies provided data on withdrawals or adverse events, so there was little information available regarding the relative tolerability and safety of statins versus control treatments in this population.

Figure 8. Statins versus placebo: Mortality by coronary artery disease (CAD) subgroups

Study or Subgroup	Statin Events	Statin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
7.15.1 Statins versus placebo: non-CAD patient studies						
Nakamura (MEGA) 2009	16	1471	34	1507	6.7%	0.48 [0.27, 0.87]
Ridker (JUPITER) 2010	34	1638	61	1629	12.1%	0.55 [0.37, 0.84]
Colhoun (CARDS) 2009	27	482	30	488	8.7%	0.91 [0.55, 1.51]
Subtotal (95% CI)		**3591**		**3624**	**27.5%**	**0.63 [0.44, 0.90]**
Total events	77		125			
Heterogeneity: Tau² = 0.04; Chi² = 3.22, df = 2 (P = 0.20); I² = 38%						
Test for overall effect: Z = 2.51 (P = 0.01)						
7.15.2 Statins versus placebo: CAD patient studies studies						
Koren (ALLIANCE) 2009	47	286	59	293	15.9%	0.82 [0.58, 1.15]
Chonchol (4S) 2007	37	245	40	260	12.2%	0.98 [0.65, 1.48]
Lemos (LIPS) 2005	3	150	3	160	1.0%	1.07 [0.22, 5.20]
Subtotal (95% CI)		**681**		**713**	**29.1%**	**0.89 [0.68, 1.15]**
Total events	87		102			
Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 2 (P = 0.78); I² = 0%						
Test for overall effect: Z = 0.91 (P = 0.36)						
7.15.3 Statins versus placebo: Mixed CAD and non-CAD patient studies						
Tonelli (WOS/C/LIP) 2004	322	2217	383	2274	41.7%	0.86 [0.75, 0.99]
Asselbergs (PREVEND) 2004	6	433	4	431	1.6%	1.49 [0.42, 5.25]
Subtotal (95% CI)		**2650**		**2705**	**43.3%**	**0.87 [0.76, 0.99]**
Total events	328		387			
Heterogeneity: Tau² = 0.00; Chi² = 0.72, df = 1 (P = 0.40); I² = 0%						
Test for overall effect: Z = 2.05 (P = 0.04)						
Total (95% CI)		**6922**		**7042**	**100.0%**	**0.80 [0.68, 0.95]**
Total events	492		614			
Heterogeneity: Tau² = 0.01; Chi² = 8.95, df = 7 (P = 0.26); I² = 22%						
Test for overall effect: Z = 2.64 (P = 0.008)						
Test for subgroup differences: Chi² = 2.84, df = 2 (P = 0.24), I² = 29.5%						



High-Dose Versus Low-Dose HMG-CoA Reductase Inhibitors Trials

Overview

In patients with CKD, there is a low level of evidence that there is no difference in risk of mortality between treatment with high versus low dose statin. There is insufficient evidence regarding whether there is a difference between high and low dose statin in risk of ESRD. Our confidence in these estimates is limited by the small number of trials reporting different outcomes and the small number of clinical events.

Description of Study

Two trials met all eligibility criteria and randomized participants with CKD to high versus low dose HMG-CoA reductase inhibitor treatment.[151,152] The first study was a post hoc analysis in 3,107 individuals with eGFR <60 ml/min/1.73m^2 from among the 10,003 enrolled in the TNT trial. The second study was a post hoc analysis in 1,686 individuals with a eGFR <60 ml/min/1.73m^2 from among the 12,064 enrolled in the SEARCH trial. Detailed baseline characteristics are presented in Appendix Tables C124 and C125.

Patients were randomized to atorvastatin 10 mg daily versus atorvastatin 80 mg daily in the TNT trial and to simvastatin 20 mg daily versus simvastatin 80 mg daily in the SEARCH trial. Only the TNT trial provided baseline characteristics for the CKD participants. The mean age of participants in the TNT post hoc analysis was 66 years, and men constituted 68 percent of patients. Ninety-five percent of study participants were white. Both trials were multinational. Mean or median study duration ranged from 5.0 to 6.7 years.

Renal Function

Study participants were required to have eGFR <60 ml/min/1.73m^2 (i.e., CKD stage 3 or worse), but did not otherwise report participant distribution by CKD stage. Mean eGFR was 53 ml/min/1.73m^2 in the TNT study. No other measures of renal function were reported.

Baseline Comorbidities

All participants in the TNT trial had coronary artery disease and hyperlipidemia while off cholesterol medications, while participants in the SEARCH trial had a history of myocardial infarction and either were taking or considered to have a clear indication for statin therapy. Additional comorbid conditions from TNT participants included hypertension (63 percent) and diabetes (18 percent). Mean baseline blood pressure was 133/78 mm Hg. In the TNT trial, all participants completed an 8 week open-label run-in of atorvastatin 10 mg daily, and only those with LDL cholesterol less than 130 mg/dL were considered for enrollment, mean baseline total cholesterol and LDL cholesterol were 176 mg/dL and 96 mg/dL, respectively. In the SEARCH trial, all participants completed a run-in period of treatment with 20 mg of simvastatin daily.

Study Quality (Appendix Table C140)

Study quality was rated as fair in one trial and good in one trial. Both trials reported that they were double blind. However, in the TNT post hoc analysis it was unclear whether allocation concealment was adequate, and analysis was not by intention to treat. Only 0.4 percent of TNT participants withdrew from the overall study, but withdrawals in the CKD subset were not reported. In the SEARCH trial, allocation concealment was adequate, analysis was intention to treat, and withdrawals were adequately reported.

Results

Mortality (Table 17, Appendix Table C126, and Appendix Figure C24)

In participants with CKD, only the TNT trial reported on this outcome. There was no significant difference between high and low dose statin groups regarding risk of all-cause mortality (7.0 versus 7.5 percent; RR 0.93, 95% CI, 0.72 to 1.20).

Vascular Outcomes (Table 17, Appendix Tables C126-C128, and Appendix Figure C24)

Myocardial Infarction

No results were reported for MI.

Stroke

No results were reported for stroke.

Other Vascular Outcomes

Risk for hospitalization due to CHF (3.1 versus 5.5 percent; RR 0.55, 95% CI, 0.39 to 0.77) and for all of the five defined composite vascular outcomes in the TNT trial was significantly lower in CKD patients assigned to high dose statin as compared with low dose statin. The composite vascular outcome was not different between groups in the SEARCH trial.

Renal Outcomes

End-Stage Renal Disease

No results were reported for ESRD.

Other Renal Outcomes

No results were reported for doubling of serum creatinine, halving of GFR, progression from microalbuminuria to macroalbuminuria, or for any composite renal outcome.

Withdrawals and Adverse Events (Appendix Table C131)

Only the TNT trial reported on these events. Less than 0.5 percent of participants with CKD withdrew from the study in both high and low dose statin groups. Treatment related adverse effects (8.7 versus 5.2 percent) and treatment discontinuations attributed to adverse effects (4.2 versus 1.9 percent) both were more common in study participants assigned high dose statins. Liver function abnormalities occurred in 1.4 versus 0.1 percent of patients on high versus low dose statin, respectively.

Summary

In individuals with CKD defined by reduced eGFR, high dose statin did not reduce all-cause mortality but significantly reduced risk of hospitalization attributed to CHF and risk of all defined composite vascular endpoints in the TNT trial, but did not reduce risk of the single reported composite vascular outcome in the SEARCH trial. There were no data reported for the individual outcomes of MI, stroke, ESRD, doubling of serum creatinine, halving of GFR, progression from microalbuminuria to macroalbuminuria, or for any composite renal outcome. Results were limited because they were based on two post hoc analyses, there were no data comparing treatment results in patients with albuminuria, and results were not reported for many vascular outcomes or any renal outcomes of clinical interest.

HMG-CoA Reductase Inhibitor Versus Bile Acid Sequestrant Trial

Overview

In patients with CKD, there is insufficient evidence regarding whether there is any difference between these treatments for the outcomes of mortality or ESRD. Our confidence in these estimates is limited because data are drawn from only one trial and there were few reported clinical events.

Description of Study

One trial met all eligibility criteria and randomized 86 participants with CKD to an HMG-CoA reductase inhibitor versus a bile acid sequestrant.[153] Detailed baseline characteristics are presented in Appendix Tables C124 and C125.

Participants were randomized to simvastatin versus cholestyramine. The mean age of subjects was 62 years. No data on gender or race/ethnicity was reported. Followup duration for this study, based in a single site in Italy, was 4 years.

Renal Function

The study did not base eligibility on CKD stage or report baseline distribution of participants by CKD stage. All participants were required to have microalbuminuria (urine albumin-to-creatinine ratio between 30 and 300 µg/mg) and at least a small measurable decline in GFR in the past 3 years. Mean GFR was 91 ml/min/1.73m2. Mean urine albumin/creatinine ratio was 83 µg/mg

Baseline Comorbidities

Eligible patients had treated hypertension and type 2 diabetes. Mean systolic blood pressure was 131 mm Hg and mean diastolic blood pressure was 76 mm Hg. No information on other comorbid conditions was reported.

Study Quality (Appendix Table C140)

Study quality was rated as fair. Though the adequacy of treatment allocation concealment was unclear, the study was double blinded and analysis was conducted using the intention-to-treat principle. Withdrawals were adequately described and five percent of participants withdrew from the study.

Results

Mortality

No information on mortality was reported.

Vascular Outcomes (Appendix Table C126)

Myocardial Infarction

The study reported that one participant experienced an MI, but did not indicate this patient's treatment group.

Stroke

No stroke outcomes were reported.

Other Vascular Outcomes

No information on CHF or any other vascular outcome was reported.

Renal Outcomes (Appendix Table C129)

End-Stage Renal Disease

No results were reported for ESRD.

Other Renal Outcomes

The study reported that conversion from microalbuminuria to macroalbuminuria occurred in 4 percent of participants randomized to simvastatin versus 15 percent of those assigned to

cholestyramine ($p<0.01$), but did not provide results for the number of participants experiencing these events in each treatment group or the denominators on which these calculations were derived. No results were reported for other renal outcomes.

Withdrawals and Adverse Events (Appendix Table C131)

Withdrawals, all due to adverse events, were reported in 2.3 percent (n=1) versus 7.0 percent (n=3) of CKD patients allocated to simvastatin and cholestyramine treatment, respectively. The study reported that these adverse events included renal cancer (n=2), and three- to four-fold increase of liver function tests above baseline levels (n=1), but did not indicate any patient's treatment group.

Summary

In patients with CKD defined by microalbuminuria, hypertension and diabetes, simvastatin significantly reduced risk of conversion to macroalbuminuria as compared with cholestyramine. There were no between-treatment group data for the endpoints of mortality, MI, stroke, CHF, ESRD, doubling of serum creatinine, halving of GFR, or for any composite vascular or renal outcome. Results were limited because they were based on a single small trial, and there were no between-treatment results for any vascular outcome or any other renal outcomes of clinical interest.

Gemfibrozil Versus Placebo or Control Trials (n=2)

Overview

In CKD patients defined by impaired GFR, we found a low level of evidence that there is no difference between gemfibrozil and placebo for risk of mortality. There was insufficient evidence regarding whether gemfibrozil and a low triglyceride diet differ for risk of mortality. There was insufficient evidence regarding whether gemfibrozil differs from either placebo or a low triglyceride diet for risk of ESRD. Our confidence in these estimates is limited because for each comparison data are drawn from only one trial and there were few reported clinical events.

Description of Studies

Two trials met all eligibility criteria and randomized participants with CKD to gemfibrozil versus a control treatment.[137,149,154] The largest of the two trials involved a post hoc analysis involving 470 participants with GFR <60 ml/min/1.73m^2 from the larger (n=2,531) VA-HIT trial. Detailed baseline characteristics are presented in Appendix Tables C124 and C125.

Participants in the post hoc VA-HIT trial analysis were randomized to gemfibrozil versus placebo. The mean age of participants in this analysis was 67 years, all participants were male U.S. veterans, and 91 percent of study participants were white. Followup for this multinational study was 5.3 years.[149,154] The second study randomized 57 nondiabetic patients to gemfibrozil versus a low triglyceride diet. The mean age of study participants was 51 years, and men constituted 75 percent of study participants. No data on race/ethnicity were reported. Followup for this single-site Swedish study was 1 year.[137]

Renal Function

In the VA-HIT post hoc analysis, participants were required to have GFR <60 ml/min/1.73m^2 (CKD stage 3 or worse).[149,154] All participants in the larger VA-HIT study had been required to

have baseline serum creatinine ≤2.0 mg/dL. Mean GFR was 52 ml/min/1.73m^2. Mean creatinine clearance was 60 ml/min/1.73m^2. The second study did not base eligibility on CKD stage. The second study enrolled patients with impaired GFR (10 to 70 ml/min/1.73m^2).[137] Mean GFR was 36 ml/min/1.73m^2 and mean albuminuria was 0.95 g/24 hours. Mean serum creatinine was 2.4 mg/dL. Neither study reported baseline distribution of participants by CKD stage

Baseline Comorbidities

All participants in the VA-HIT trial had coronary heart disease, LDL cholesterol ≤140 mg/dL, and HDL cholesterol ≤40 mg/dL. Additional comorbid conditions included hypertension (67 percent) and diabetes (30 percent). Mean baseline systolic blood pressure was 134 mm Hg, and mean diastolic blood pressure was 77 mm Hg. Mean total and LDL cholesterol were 176 mg/dL and 111 mg/dL, respectively. The second study excluded individuals with diabetes.[137] Mean baseline systolic blood pressure was 137 mm Hg, and mean diastolic blood pressure was 84 mm Hg. Mean total and LDL cholesterol were 244 mg/dL and 170 mg/dL, respectively. No other comorbidity data were reported.

Study Quality (Appendix Table C140)

Study quality of the VA-HIT post hoc analysis was rated as good. The adequacy of treatment allocation concealment in the first study was clear. The study was double blinded, including outcome adjudication by a blinded endpoint committee. Analysis was performed using the intention-to-treat principle. No study participants were reported as lost to followup.[149,154] Study quality of the second study was rated as fair. The adequacy of treatment allocation concealment in the second study was unclear. The study was open label, and analysis was not performed using the intention-to-treat principle. Withdrawals were adequately described, and 11 percent of study participants withdrew from the study.[137]

Results

Mortality (Table 17, Appendix Table C126, and Appendix Figure C24)

In the VA-HIT study, there was no significant difference in risk of all-cause mortality between CKD patients assigned to gemfibrozil versus placebo (10.0 versus 11.0 percent; RR 0.91, 95% CI, 0.52 to 1.62, n=399 patients).[149,154] The gemfibrozil versus low triglyceride diet trial did not report results for mortality.[137]

Vascular Outcomes (Table 17, Appendix Table C126-C128 and Appendix Figure C24)

Myocardial Infarction

No between-treatment results were reported for MI for either study.[137,149,154]

Stroke

No between-treatment results were reported for stroke for either study.[137,149,154]

Other Vascular Outcomes

In patients with CKD within the VA-HIT study, no between-treatment results were reported for the primary composite vascular outcome. For a second composite vascular outcome that included fatal CHD, nonfatal MI, and stroke, risk was significantly lower in participants assigned

to gemfibrozil versus placebo (24.0 versus 32.9 percent; RR 0.73, 95% CI, 0.54 to 0.97, n=470 patients).[149,154] The gemfibrozil versus low triglyceride diet trial did not report results for any vascular outcome.[137]

Renal Outcomes (Table 17, Appendix Table C129, and Appendix Figure C24)

End-Stage Renal Disease

In the VA-HIT study, no patient in either the gemfibrozil or placebo treatment groups experienced ESRD.[149,154] In the gemfibrozil versus low triglyceride diet trial, two of 28 (7.1 percent) CKD participants randomized to gemfibrozil and one of 29 (3.4 percent) allocated to diet developed ESRD.[137]

Other Renal Outcomes

Neither study reported results for doubling of serum creatinine, halving of GFR, or for any composite renal outcome.

Withdrawals and Side Effects (Appendix Table C131)

The VA-HIT trial reported no withdrawals and no cases of rhabdomyolysis or elevation of creatine kinase more than three times the upper limit of normal in either treatment group. The gemfibrozil versus low triglyceride diet trial reported withdrawals in 21.4 percent of gemfibrozil participants, all of which were attributed to “mild gastrointestinal symptoms,” while there were no withdrawals or gastrointestinal side effects reported in the diet group.

Summary

In male veterans with CKD defined by impaired GFR, coronary artery disease, LDL ≤140 mg/dL and HDL ≤40 mg/dL, gemfibrozil did not reduce all-cause mortality compared with placebo. In the one composite vascular endpoint reported of the two the study defined, gemfibrozil significantly reduced risk of fatal CHD, nonfatal MI, or stroke. In both studies, too few (or no) patients developed ESRD to effectively compare risk between gemfibrozil and either placebo or low triglyceride diet. The gemfibrozil versus diet study suggested an increased risk of gastrointestinal side effects with gemfibrozil, but the VA-HIT CKD study reported no information on the incidence of adverse gastrointestinal symptoms. Results were limited because they were based on small studies, with few reported outcomes and small numbers of clinical events. Results from the VA-HIT study were limited because they were a post hoc analysis from a larger trial not designed to look at CKD patients or renal outcomes. Studies are limited in that they do not also report results based on baseline albuminuria.

Table 17. Pooled clinical and renal outcomes, anti-lipid agents versus control trials

Outcome	Number of Trials Reporting	Quality of the Studies	Anti-lipid Events/N (%)	Control Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
HMG-CoA reductase inhibitors versus placebo (N=12)						
All-cause mortality	**8**	**Good**	**492/6922 (7.1)**	**614/7042 (8.7)**	**0.80 [0.68-0.95]**	**22%**
All-cause mortality; non-CAD patients	*3*	*Good*	*77/3591 (2.1)*	*125/3624 (3.4)*	*0.63 [0.44-0.90]*	*38%*
All-cause mortality; CAD patients	*3*	*Fair*	*87/681 (12.8)*	*102/713 (14.3)*	*0.89 [0.68-1.15]*	*0%*
All-cause mortality; CAD and non-CAD patients	*2*	*Fair*	*328/2650 (12.4)*	*387/2705 (14.3)*	*0.87 [0.76-0.99]*	*0%*
Cardiovascular mortality	**4**	**Fair**	**24/1014 (2.4)**	**35/1043 (3.4)**	**0.71 [0.43-1.17]**	**0%**
Cardiovascular mortality; non-CAD patients	*1*	*Fair*	*0/145*	*1/159 (0.6)*	*0.37 [0.01-8.90]*	*NA*
Cardiovascular mortality; CAD patients	*2*	*Fair*	*20/436 (4.6)*	*30/453 (6.6)*	*0.69 [0.40-1.19]*	*0%*
Cardiovascular mortality; CAD and non-CAD patients	*1*	*Fair*	*4/433 (0.9)*	*4/431 (0.9)*	*1.00 [0.28-3.95]*	*NA*
Myocardial infarction, any	**2**	**Fair**	**67/989 (6.8)**	**96/1026 (9.4)**	**0.72 [0.54-0.98]**	**0%**
Myocardial infarction, any; non-CAD patients	*1*	*Fair*	*2/145 (1.4)*	*6/159 (3.8)*	*0.37 [0.07-1.78]*	*NA*
Myocardial infarction, any; CAD patients	*1*	*Good*	*65/844 (7.7)*	*90/867 (10.4)*	*0.74 [0.55-1.01]*	*NA*
Myocardial infarction, nonfatal	**2**	**Good**	**25/1924 (1.3)**	**49/1922 (2.5)**	**0.52 [0.33-0.84]**	**0%**
Stroke, any	**6**	**Good**	**71/5154(1.4)**	**120/5215(2.3)**	**0.62 [0.41-0.95]**	**42%**
Stroke; non-CAD patients	*3*	*Good*	*24/3591 (0.7)*	*58/3624 (1.6)*	*0.43 [0.25-0.75]*	*24%*
Stroke; CAD patients	*2*	*Good*	*40/1130 (3.5)*	*58/1160 (5.0)*	*0.71 [0.48-1.05]*	*0%*
Stroke; CAD and non-CAD patients	*1*	*Fair*	*7/433 (1.6)*	*4/431 (0.9)*	*1.74 [0.51-5.91]*	*NA*
CHF hospitalization	**2**	**Fair**	**16/719 (2.2)**	**23/724 (3.2)**	**0.71 [0.38-1.32]**	**0%**
CHF hospitalization; CAD patients	*1*	*Good*	*15/286 (5.2)*	*22/293 (7.5)*	*0.70 [0.37-1.32]*	*NA*
CHF hospitalization; CAD and non-CAD patients	*1*	*Fair*	*1/433 (0.2)*	*1/431 (0.2)*	*1.00 [0.06-15.86]*	*NA*
Composite vascular outcomes						
Composite vascular outcome*; Kendrick[141] (AFCAPS), definition B[a]	1	Fair	8/145 (5.5)	21/159 (13.2)	0.42 [0.19-0.91]	NA
Composite vascular outcome; Kendrick[141] (AFCAPS), definition C[a]	1	Fair	7/145 (4.8)	18/159 (11.3)	0.43 [0.18-0.99]	NA
Composite vascular outcome; Nakamura[142] (MEGA), definition A[b]	1	Good	21/1471 (1.2)	40/1507 (5.7)	0.54 [0.32-0.91]	NA
Composite vascular outcome; Nakamura[142] (MEGA), definition B[b]	1	Good	25/1471 (3.7)	60/1507 (8.7)	0.43 [0.27-0.68]	NA
Composite vascular outcome; Nakamura[142] (MEGA), definition C[b]	1	Good	33/1471 (4.9)	71/1507 (10.3)	0.48 [0.32-0.72]	NA
Composite vascular outcome; Ridker (JUPITER), definition A[cx]	1	Good	40/1638 (2.4)	71/1629 (4.4)	0.56 [0.38-0.82]	NA
Composite vascular outcome; Ridker (JUPITER), definition B[c]	1	Good	64/1638 (3.9)	114/1629 (7.0)	0.56 [0.41-0.75]	NA

Table 17. Pooled clinical and renal outcomes, anti-lipid agents versus control trials (continued)

Outcome	Number of Trials Reporting	Quality of the Studies	Anti-lipid Events/N (%)	Control Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
Composite vascular outcome; Ridker (JUPITER), definition C[c]	1	Good	69/1638 (4.2)	127/1629 (7.8)	0.54 [0.41-0.72]	NA
Composite vascular outcome; Ridker (JUPITER), definition D[c]	1	Good	24/1638 (1.5)	40/1629 (2.5)	0.60 [0.36-0.99]	NA
Composite vascular outcome; Colhoun[143] (CARDS), definition A[d]	1	Good	25/482 (5.2)	42/488 (8.6)	0.63 [0.39-1.02]	NA
Composite vascular outcome; Colhoun[143] (CARDS), definition A-albuminuric patients[d]	1	Good	24/276 (8.7)	38/275 (13.8)	0.60 [0.37-0.97]	NA
Composite vascular outcome; Colhoun[143] (CARDS), definition B[d]	1	Good	18/482 (3.7)	27/488 (5.5)	0.67 [0.38-1.21]	NA
Composite vascular outcome; Koren[144] (ALLIANCE), definition A[e]	1	Good	78/286 (27.3)	105/293 (35.8)	0.76 [0.60-0.97]	NA
Composite vascular outcome; Koren[144] (ALLIANCE), definition B[e]	1	Good	73/286 (25.5)	85/293 (29.0)	0.88 [0.67-1.15]	NA
Composite vascular outcome; Koren[144] (ALLIANCE), definition C[e]	1	Good	32/286 (11.2)	54/293 (18.4)	0.61 [0.40-0.91]	NA
Composite vascular outcome; Chonchol[145] (4S), definition A[f]	1	Fair	53/245 (21.6)	77/260 (29.6)	0.73 [0.54-0.99]	NA
Composite vascular outcome; Kjekhus[146] (CORONA), definition A[g]	1	Good	288/791 (15.8)	309/844 (16.3)	0.99 [0.88-1.13]	NA
Composite vascular outcome; Lemos[147] (LIPS), definition A[h]	1	Fair	23/150 (15.3)	47/160 (29.4);	0.52 [0.33-0.82]	NA
Composite vascular outcome; Lemos[147] (LIPS), definition B[h]	1	Fair	7/150 (4.7)	13/160 (8.1)	0.57 [0.24-1.40]	NA
Composite vascular outcome; Lemos[147] (LIPS), definition C[h]	1	Fair	7/150 (4.7)	13/160 (8.1)	0.57 [0.24-1.40]	NA
Composite vascular outcome; Asselbergs[62] (PREVD), definition A[i]	1	Fair	21/433 (4.8)	24/431 (5.6)	0.87 [0.49-1.54]	NA
Composite vascular outcome; Asselbergs[62] (PREVD), definition B[i]	1	Fair	8/433 (1.8)	15/431 (3.5)	0.53 [0.23-1.24]	NA
Composite vascular outcome; Tonelli[149] (WOSCOPS/ CARE/ LIPID), definition A[j]	1	Good	492/2217 (22.2)	647/2274 (28.5)	0.78 [0.70-0.86]	NA
Composite vascular outcome; Tonelli[149] (WOSCOPS/ CARE/ LIPID), definition B[j]	1	Good	573/2217 (25.9)	730/2274 (32.1)	0.81 [0.73-0.88]	NA
Composite vascular outcome; Tonelli[148] (CARE), definition A[k]	1	Good	89/844 (10.5)	126/867 (14.5)	0.73 [0.56-0.94]	NA
Composite vascular outcome; Tonelli[148] (CARE), definition B[k]	1	Good	171/844 (20.3)	237/867 (27.0)	0.74 [0.62-0.88]	NA
End-stage renal disease	**1**	**Good**	**32/779 (4.1)**	**31/778 (4.0)**	**1.03 [0.64-1.67]**	**NA**
Composite renal outcome (ALLHAT)[l]	1	Good	50/779 (6.4)	52/778 (6.7)	0.96 [0.66-1.40]	NA
High- versus low-dose HMG-CoA reductase inhibitors (n=2)						
All-cause mortality	1	Fair	112/1602 (7.0)	113/1505 (7.5)	0.93 [0.72-1.20]	NA
CHF hospitalization	1	Fair	49/1602 (3.1)	84/1505 (5.6)	0.55 [0.39-0.77]	NA

Table 17. Pooled clinical and renal outcomes, anti-lipid agents versus control trials (continued)

Outcome	Number of Trials Reporting	Quality of the Studies	Anti-lipid Events/N (%)	Control Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
Composite vascular outcome; Shepard[151] (TNT), definition A[m]	1	Fair	149/1602 (9.3)	202/1505 (13.4)	0.69 [0.57-0.85]	NA
Composite vascular outcome; Shepard[151] (TNT), definition B[m]	1	Fair	489/1602 (30.5)	574/1505 (38.1)	0.80 [0.73-0.88]	NA
Composite vascular outcome; Shepard[151] (TNT), definition C[m]	1	Fair	110/1602 (6.9)	157/1505 (10.4)	0.66 [0.52-0.83]	NA
Composite vascular outcome; Shepard[151] (TNT), definition D[m]	1	Fair	356/1602 (22.2)	431/1505 (28.6)	0.78 [0.69-0.88]	NA
Composite vascular outcome; Shepard[151] (TNT), definition E[m]	1	Fair	74/1602 (4.6)	104/1505 (6.9)	0.67 [0.50-0.89]	NA
Composite vascular outcome; SEARCH trial[n]	1	Fair	265/820 (32.3)	292/866 (33.7)	0.96 [0.84-1.10]	NA
Gemfibrozil versus placebo trials (n=1)						
All-cause mortality	1	Good	20/199 (10)	22/200 (11.0)	0.91 [0.52-1.62]	NA
Composite vascular outcome; Tonelli[154] (VA-HIT), definition B[o]	1	Good	58/242 (24.0)	75/228 (32.9)	0.73 [0.54-0.97]	NA
End-stage renal disease	2	Fair	2/227 (0.9)	1/229 (0.4)	2.07 [0.20-21.58]	NA

CHF = congestive heart failure; NA = not applicable; RR = relative risk reduction

[a](B)Fatal and nonfatal cardiovascular events; (C) Fatal and nonfatal coronary events

[b](A)First occurrence of a CHD event, including fatal and nonfatal MI, angina pectoris, cardiac/sudden death, and coronary revascularization. Additional composite endpoints included; (B)first CHD event or ischemic stroke; (C) total CVD events, which was not defined

[c](A) nonfatal myocardial infarction, nonfatal stroke, hospital stay for unstable angina, arterial revascularization, or confirmed cardiovascular death; (B) same as A plus any death; (C) same as A plus any death plus venous thromboembolism; (D) non-fatal myocardial infarction, nonfatal stroke, or confirmed cardiovascular death

[d](A) Major cardiovascular disease, including acute CHD event (MI, including silent MI, unstable angina, acute CHD death, or resuscitated cardiac arrest), stroke, coronary revascularization, or death; (B) acute CHD event as defined above

[e](A) First primary cardiovascular event, including cardiac death, nonfatal MI, resuscitated cardiac arrest, cardiac revascularization, or unstable angina requiring hospitalization; (B) All-cause mortality, peripheral revascularization, hospitalization for CHF, or stroke; (C) Nonfatal MI or cardiac death

[f](A) Major coronary event, including coronary death, nonfatal MI, resuscitated cardiac arrest, ECG confirmed silent MI

[g](A) Cardiovascular death, nonfatal MI, or nonfatal stroke

[h](A) Adverse coronary atherosclerotic events, which included cardiac death, nonfatal MI, and all surgical or percutaneous coronary interventions not caused by restenosis after an index percutaneous coronary intervention; (B) Cardiac death or MI; (C) All-cause mortality or MI

[i](A) Cardiovascular mortality or hospitalization for any of the following: nonfatal MI, myocardial ischemia, CHF, PVD or stroke; (B) Hospitalization for nonfatal MI or myocardial ischemia

[j](A) Cardiovascular mortality or hospitalization for any of the following: nonfatal MI, myocardial ischemia, CHF, PVD or stroke; (B) Hospitalization for nonfatal MI or myocardial ischemia

[k](A) Death from coronary disease (including fatal MI, sudden death, death during a coronary intervention, and death from other coronary causes) or a symptomatic nonfatal biochemically confirmed myocardial infarction; (B) Major coronary events, defined as fatal coronary disease, nonfatal MI, CABG, or coronary angioplasty

[l](A) ESRD (start of long-term dialysis, death due to kidney disease, or kidney transplantation) or ≥50% decline in GFR; and (B) ESRD or ≥50% decline in GFR

[m](A) Major cardiovascular events, which included CHD death, nonfatal nonprocedure-related MI, resuscitation after cardiac arrest, and stroke; (B) Any cardiovascular event (defined as CHD death, nonfatal MI, resuscitation from cardiac arrest, revascularization procedure, documented angina, stroke, TIA, CABG, or CHF hospitalization); (C) Major coronary event (defined as CHD death, nonfatal nonprocedure-related MI, or resuscitation from cardiac arrest); (D) Any coronary event (defined as CHD death, nonfatal MI, resuscitation from cardiac arrest, revascularization procedure, or documented angina); and (E) Cerebrovascular event (stroke or TIA)

[n] first major vascular event, including coronary death, myocardial infarction, any stroke, or any arterial revascularization

[o](B) Major cardiovascular event, which included fatal CHD, nonfatal MI, and stroke

Intensive Multicomponent Intervention Trials (n=4)

Overview

In patients with CKD, we found a low strength of evidence that there is no difference between intensive, multicomponent treatment and conventional treatment for risk of all-cause mortality or ESRD. We found no statistically significant difference between treatment groups in risk of cardiovascular mortality, MI, or stroke. Risk of conversion from microalbuminuria was statistically significantly lower in the intensive treatment group. Our confidence in these estimates is limited by the small number of trials reporting different outcomes, the small number of clinical events, and heterogeneity between studies.

Description of Studies

Five reports of four unique trials met all eligibility criteria and randomized participants with CKD (n=892 patients, range 90 to 437) to an intensive multicomponent treatment intervention versus usual care.[155-159] Detailed baseline characteristics are presented in Appendix Tables C132 and C133.

In all eligible trials, the intensive treatment arm was implemented by a multidisciplinary research team, comprised of at least a physician, a nurse, and a dietitian. In three of these trials, conducted entirely in patients with diabetes, the research team met with the patients at least every three months and directly intervened in their care, treating them to achieve explicit targets for blood pressure (systolic <130 to 140 mm Hg, diastolic <80 to 85 mm Hg), diabetes (HbA_{1c} targets ranged from <6.5 to <8 percent), and lipid control (cholesterol <154 to 193 mg/dL, LDL <100 mg/dL, HDL >42 mg/dL, triglycerides <66 to 75 mg/dL).[155,156,158] The interventions were introduced in a stepwise fashion, including behavior modification and pharmacologic therapy, as necessary. In the fourth trial, the research team implementing the intensive treatment arm met with patients every 3 to 6 months and utilized a mix of direct intervention and letters sent with management recommendations to the patients' primary care providers.[159] In this latter trial, while improved blood pressure control was a stated aim, no explicit blood pressure target was reported, and the study did not discuss management of diabetes or lipids. An emphasis was placed on improving medication compliance and decreasing nephrotoxic drug exposure. In three trials, ACEIs or ARBs were to be initiated in all intensive treatment group participants,[155,156,159] and although the fourth trial did not state that these medications were mandated, it reported ACEI use in 95 percent of enrolled participants at followup.[158] Within the intensive treatment intervention groups, dietary recommendations in three trials included low protein,[155,158,159] with low potassium recommended in two trials.[155,159] Low fat[156] and low sodium[158] each were part of diet recommendations in one trial.

By comparison with the intensive intervention arms, all study participants assigned to control treatment groups were managed by their primary physician. In two trials, their management was left entirely to the discretion of their primary physician.[155,159] However, in two other trials their doctors were to target explicit goals for blood pressure, diabetes, and lipid control, aiming either for the same thresholds being used for treatment of the intensive treatment group,[158] or following national guidelines that were modestly less strict than the thresholds targeted for the intensive treatment group.[156]

The mean age of subjects was 65 years (range 55 to 68; n=4 trials) and men constituted 52 percent (range 34 to 74; n=4 trials) of all patients randomized. In the only trial that reported data

on ethnicity/race, 80 percent of participants were African American.[159] Two trials were conducted in Europe (including Scotland and Denmark),[156,158] one was conducted primarily in the United States,[159] and one was conducted in China.[155] Mean or median study durations ranged from 2 to 7.8 years.

Renal Function

No study based eligibility on CKD stage or reported baseline distribution of participants by CKD stage. Among the four eligible trials, two based participant eligibility on presence of albuminuria,[156,158] while two others determined eligibility based on impaired creatinine clearance and/or elevated serum creatinine.[155,159] In trials reporting these data, mean baseline creatinine clearance was 37.6 mL/min (range 34 to 55, n=2 trials),[158,159] mean baseline serum creatinine was 1.8 (range 0.9 to 2.1, n=2 trials),[156,159] and urinary albumin excretion rate ranged from a mean of 73.5 mg/24 hours in one trial[156] to a median of 755 mg/24 hours in a second trial.[158] In addition, one trial reported a baseline mean GFR of 117 ml/min/1.73m^2,[156] and another reported a mean albumin-to-creatinine ratio of 79 mg/mmol.[158]

Baseline Comorbidities

Hypertension prevalence was reported in three trials, within which 98 percent of participants had a diagnosis of hypertension.[155,158,159] Mean systolic and diastolic blood pressure measurements were 147 and 82 mm Hg, respectively (n=4 trials). Three trials were comprised entirely of type 2 diabetic patients,[155,156,158] with the fourth trial including 44 percent diabetic participants.[159] In the two diabetic trials reporting, mean baseline HbA_{1c} was 8.3 percent (range 7.9 to 8.6).[156,158] The prevalence of other comorbidities included coronary artery disease 35 percent (range 16 to 48, n=3 trials), CHF 30 percent (range 7 to 40, n=2 trials), MI 26 percent (range 2 to 37, n=2 trials), and stroke 16 percent (range 3 to 20, n=3 trials).

Study Quality (Appendix Table C140)

Among the four eligible trials, study quality was rated as good for one trial and as fair for three trials. Allocation concealment was adequate in three trials and unclear in the remaining study. All of these intensive multicomponent intervention trials were open label. Analysis by the intention-to-treat principle was performed in two trials. Reasons for study withdrawal were adequately described in all reports, and 2.6 percent (range 0 to 17) of randomized participants withdrew from trials overall.

Results

Mortality (Table 18, Appendix Table C134, and Appendix Figure C25)

All-Cause Mortality

Compared with control treatment, assignment of CKD patients to an intensive, multicomponent intervention did not significantly reduce risk of all-cause mortality (19.5 percent versus 23.3 percent; RR 0.86, 95% CI, 0.67 to 1.10; n=4 trials, 892 patients).

Cardiovascular Mortality

Assignment to the multicomponent treatment group was not associated with a significant difference in risk of cardiovascular mortality compared with control treatment (RR 1.07, 95% CI, 0.47 to 2.43; n=2 trials).

Vascular Outcomes (Table 18, Appendix Tables C134-C136, and Appendix Figure C25)

Myocardial Infarction

Compared with control treatment, allocation of patients with CKD to intensive, multicomponent treatment was not associated with a significant reduction in MI (RR 0.97, 95% CI, 0.25 to 3.78), fatal MI (RR 1.83, 95% CI, 0.17 to 19.47) or nonfatal MI (RR 0.50, 95% CI, 0.16 to 1.59). However, each of these outcomes was reported only in one trial with a small sample size and few events.

Stroke

Compared with control treatment, allocation of patients with CKD to intensive, multicomponent treatment was not associated with a significant reduction in fatal stroke (RR 0.31, 95% CI, 0.01 to 7.31). In contrast, participants assigned to intensive, multicomponent treatment had a significantly lower risk of nonfatal stroke (3.8 percent versus 13.8 percent; RR 0.27, 95% CI, 0.08 to 0.94). Again, this outcome was reported only in one trial with a small sample size and few events.

Other Vascular Outcomes

Two trials reported a composite vascular endpoint as a main outcome,[155,156] with a significant reduction in risk associated with intensive, multicomponent treatment in one of these trials (RR 0.54, 95% CI, 0.34 to 0.86, n=160 patients)[156] but not in the other (RR 1.07, 95% CI, 0.62 to 1.87).[155]

Renal Outcomes (Table 18, Appendix Tables C137 and C138, and Appendix Figure C25)

End-Stage Renal Disease

In three trials reporting, compared with control treatment, assignment of CKD patients to an intensive, multicomponent intervention was associated with a 53 percent relative reduction in risk of ESRD that was not statistically significant (6.9 versus 9.4 percent, RR 0.47, 95% CI, 0.10 to 2.20; n=3 trials, 455 patients). More than 80 percent of ESRD events occurred in one trial[155] and there was substantial heterogeneity between trials (I^2=43 percent).

Other Renal Outcomes

In the single trial reporting, intensive multicomponent treatment significantly reduced risk of progression of CKD patients from microalbuminuria to macroalbuminuria compared with conventional treatment (20.0 versus 38.8 percent, RR 0.52, 95% CI, 0.31 to 0.87; n=160 patients).[156] A composite renal outcome was reported in only one trial, and risk appeared no different between treatment groups (23.1 versus 23.8 percent).[155]

Study Withdrawals and Adverse Events (Appendix Table C139)

CKD patients allocated to intensive multicomponent treatment were no more likely to have withdrawn from treatment than those assigned to control treatment (0.9 versus 0.8 percent; n=3 trials, 687 patients). Adverse events data were only reported in one trial.[156] In this trial, risk of major hypoglycemic events that impaired consciousness and required help from another person was not higher in the intensive, multicomponent treatment group as compared with the

conventionally treated group (6.3 versus 15.0 percent, p=0.12). In this trial, there also was no between-group difference in the proportion of patients with at least one minor hypoglycemic event (48.8 versus 52.5 percent, p=0.50).

Subgroup Results

No trials reported outcomes stratified by any participant characteristic. In three trials restricted to patients with diabetes, all of which tested an intervention that explicitly targeted diabetes, blood pressure, and lipid control, there was no significant difference between intensive multicomponent and control treatment in risk of mortality (RR 0.86, 95% CI, 0.52 to 1.43), cardiovascular mortality, MI, or CHF hospitalization. However, risk of stroke was significantly reduced in one of these trials (RR 0.27, 95% CI, 0.08 to 0.94), a small study in which participants also were albuminuric. Also in this single trial, there was a significant reduction in risk of one reported composite vascular outcome, and of conversion from microalbuminuria to macroalbuminuria. There was no difference between treatment groups in risk of mortality (RR 0.99, 95% CI, 0.49 to 2.02), cardiovascular mortality, MI, or ESRD. In two trials in which decreased creatinine clearance or increased serum creatinine was required for inclusion, there was no significant difference between treatment groups in any of the few clinical outcomes reported.

Summary

In individuals with CKD, compared with usual care, assignment to intensive, multicomponent intervention was not associated with a significant reduction in risk of all-cause mortality. Further, there was no significant association between treatment groups and risk of MI, fatal stroke, and ESRD. In data from single trials only, there was a significantly reduced risk with intensive, multicomponent treatment for the outcomes of nonfatal stroke, a composite vascular endpoint, and conversion from microalbuminuria to macroalbuminuria. Results for all outcomes, with the possible exception of all-cause mortality, were limited by small sample sizes and few events and could not exclude either clinically meaningful benefits or harms. Overall results were further limited by heterogeneity in patient populations and in treatment protocols, including those for both the intensive intervention groups and the usual care groups. Reporting on study withdrawals and adverse effects was limited. Finally, no trial provided followup beyond 5 years; therefore, longer term effects of intensive, multicomponent interventions cannot be determined from these studies.

Table 18. Pooled clinical and renal outcomes, INT versus control treatment trials

Outcome	Number of Trials Reporting	Quality of the Studies	Intensive Events/N (%)	Control Events/N (%)	RR [95% CI]	I^2 Test for Heterogeneity
INT versus control treatment trials (N=4)						
All-cause mortality	4	Fair	85/437 (19.5)	106/455 (23.3)	0.86 [0.67-1.10]	0%
Cardiovascular mortality	2	Fair	11/127 (8.7)	10/123 (8.1)	1.07 [0.47-2.43]	0%
Myocardial infarction, any	1	Good	4/104 (3.8)	4/101 (4.0)	0.97 [0.25-3.78]	NA
Myocardial infarction, fatal	1	Fair	2/47 (4.25)	1/43 (2.3)	1.83 [0.17-19.47]	NA
Myocardial infarction, nonfatal	1	Fair	4/80 (5.0)	4/80 (10.0)	0.50 [0.16-1.59]	NA
Stroke, nonfatal	1	Fair	3/80 (3.8)	11/80 (13.8)	0.27 [0.08-0.94]	NA
Stroke, fatal	1	Fair	0/47 (0)	1/43(2.3)	0.31 [0.01-7.31]	NA
CHF hospitalization	1	Good	13/104(12.5)	15/101(14.8)	0.84 [0.42-1.68]	NA
Composite vascular outcome* Chan, 2009[155]	1	Good	4/104 (3.8)	4/101 (4.0)	0.97 [0.25-3.78]	NA
Composite vascular outcome** Gaede (A), 2003[156]	1	Fair	19/80 (23.8)	35/80 (43.8)	0.54 [0.34-0.86]	NA
End-stage renal disease	3	Fair	16/231 (6.9)	21/224 (9.4)	0.47 [0.10-2.20]	43%
Progression from micro to macroalbuminuria	1	Fair	16/80 (20.0)	31/80 (38.8)	0.52 [0.31-0.87]	NA
Composite renal outcome***, Chan, 2009[155]	1	Good	24/104(23.1)	24/101 (23.8)	0.97 [0.59-1.59]	NA

CHF = congestive heart failure; CI = confidence interval; INT = Intensive Multi-Component Intervention; NA = not applicable; RR = relative risk reduction;
*Hospitalization for heart failure, hospitalization for angina, hospitalization for arrhythmia, MI, coronary revascularization (PTCA/CABG), other revascularization, CVA or transient ischemic attack, and lower limb amputation.
** (A) death from cardiovascular causes, nonfatal MI, CABG, PCI, nonfatal stroke, amputation as a result of ischemia, or surgery for peripheral atherosclerotic artery disease.
***ESRD (defined as the need for dialysis, or plasma creatinine level ≥500 μmol/l) or death.

Strength of Evidence for Key Question 5

The strength of evidence for Key Question 5 is presented in Table 19.

Table 19. Strength of evidence for Key Question 5

Comparison	Outcome, Control	Number of Studies; Number of Subjects	Risk of Bias Design; Quality	Consistency	Directness	Precision	Strength of Evidence
ACEI Monotherapy Studies							
ACEI versus placebo (n=17)	All-cause mortality	16; 11,536	RCTs/good	Inconsistent	Direct	Precise	Moderate
	ESRD	7; 7490	RCTs/good	Consistent	Direct	Imprecise	Moderate
ACEI versus ARB (n=6)	All-cause mortality	4; 534	RCTs/fair	Consistent	Direct	Imprecise	Low
	ESRD	none	-	-	-	-	Insufficient
ACEI versus CCB (n=6)	All-cause mortality	5; 1307	RCTs/fair	Consistent	Direct	Imprecise	Low
	ESRD	3; 3823	RCTs/good	Inconsistent	Direct	Imprecise	Low
ACEI versus beta blocker (n=3)	All-cause mortality	3; 1080	RCTs/fair	Consistent	Direct	Imprecise	Low
	ESRD	3; 1080	RCTs/fair	Inconsistent	Direct	Imprecise	Low
ACEI versus diuretic (n=2)	All-cause mortality	1; 570	RCT/fair	Unknown	Direct	Imprecise	Insufficient
	ESRD	1; 4146	RCT/good	Unknown	Direct	Imprecise	Low
ARB Monotherapy Studies							
ARB versus placebo (n=4)	All-cause mortality	4; 5242	RCTs/good	Consistent	Direct	Precise	High
	ESRD	3; 4652	RCTs/good	Consistent	Direct	Precise	High
ARB versus CCB (n=3)	All-cause mortality	2; 1206	RCTs/fair	Unknown	Direct	Imprecise	Low
	ESRD	1; 1148	RCT/good	Unknown	Direct	Imprecise	Low
ACEI+ARB Versus Other Studies							
ACEI+ARB versus ACE (n=6)	All-cause mortality	3; 3059	RCTs/fair	Consistent	Direct	Precise	Moderate
	ESRD	1; 90	RCT/poor	Unknown	Direct	Imprecise	Insufficient
ACEI+ARB versus ARB (n=3)	All-cause mortality	1; 86	RCTs/fair	Unknown	Direct	Imprecise	Insufficient
	ESRD	none	-	-	-	-	Insufficient
ACEI+ARB versus ACEI or ARB (n=1)	All-cause mortality	1; 8933	RCT/good	Unknown	Direct	Precise	Moderate
	ESRD	1; 8933	RCT/good	Unknown	Direct	Imprecise	Low

Table 19. Strength of evidence for Key Question 5 (continued)

Comparison	Outcome, Control	Number of Studies; Number of Subjects	Risk of Bias Design; Quality	Consistency	Directness	Precision	Strength of Evidence
ACEI+ARB versus ACEI+aldosterone antagonist (n=1)	All-cause mortality	1; 53	RCT/poor	Unknown	Direct	Imprecise	Insufficient
	ESRD	none	-	-	-	-	Insufficient
ACEI+CCB or Diuretic Versus Other Studies							
ACEI+CCB versus ACE (n=1)	All-cause mortality	1; 207	RCT/poor	Unknown	Direct	Imprecise	Insufficient
	ESRD	none	-	-	-	-	Insufficient
ACEI+CCB versus CCB (n=1)	All-cause mortality	1; 207	RCT/poor	Unknown	Direct	Imprecise	Insufficient
	ESRD	none	-	-	-	-	Insufficient
ACEI+CCB versus ACEI+ diuretic (n=2)	All-cause mortality	1; 332	RCT/fair	Unknown	Direct	Imprecise	Insufficient
	ESRD	none	-	-	-	-	Insufficient
ACEI+ diuretic versus placebo (n=1)	All-cause mortality	1; 4519	RCT/good (post-hoc)	Unknown	Direct	Precise	Low
	ESRD	none	-	-	-	-	Insufficient
ACEI+ aldosterone antagonist versus ACE (n=1)	All-cause mortality	none	-	-	-	-	Insufficient
	ESRD	none	-	-	-	-	Insufficient
ARB Versus ARB Studies							
ARB (Telmisartan) versus different ARB (n=2)	All-cause mortality versus losartan	1; 860	RCT/poor	Inconsistent	Direct	Precise	Low
	All-cause mortality versus valsartan	1; 857	RCT/fair	Inconsistent	Direct	Imprecise	Low
	ESRD versus losartan	none	-	-	-	-	Insufficient
	ESRD versus valsartan	1; 857	RCTs/fair	Unknown	Direct	Imprecise	Insufficient
ARB (High Dose) versus ARB (Standard Dose)	All-cause mortality candesartan	1; 269	RCT/good	-	-	-	Insufficient
	ESRD candesartan	none	-	-	-	-	Insufficient

Table 19. Strength of evidence for Key Question 5 (continued)

Comparison	Outcome, Control	Number of Studies; Number of Subjects	Risk of Bias Design; Quality	Consistency	Directness	Precision	Strength of Evidence
	All-cause mortality Irbesartan	1; 389	RCT/fair	Unknown	Direct	Imprecise	Insufficient
	ESRD Irbesartan	none	-	-	-	-	Insufficient
	All-cause mortality Telmisartan	none	-	-	-	-	Insufficient
	ESRD Telmisartan	none	-	-	-	-	Insufficient
Aldosterone Antagonist Studies							
ACEI+ Aldosterone antagonist versus ACEI (n=1)	All-cause mortality	none	-	-	-	-	Insufficient
	ESRD	none	-	-	-	-	Insufficient
Aldosterone antagonist (+ACE/ ARB) versus placebo (+ACE/ ARB) (n=1)	All-cause mortality	1; 59	RCT/fair	Unknown	Direct	Imprecise	Insufficient
	ESRD	none	-	-	-	-	Insufficient
Miscellaneous Blood Pressure Control Versus Other Studies							
Beta blocker versus placebo (n=2)	All-cause mortality	2; 2173	RCT/fair (post-hoc)	Inconsistent	Direct	Precise	Low
	ESRD	none	-	-	-	-	Insufficient
CCB versus placebo (n=2)	All-cause mortality	2; 1226	RCTs/fair	Unknown	Direct	Imprecise	Low
	ESRD	1; 1136	RCT/good	Unknown	Direct	Imprecise	Low
CCB versus diuretic (n=1)	All-cause mortality	none	-	-	-	-	Insufficient
	ESRD	1; 4129	RCT/good (post-hoc)	Unknown	Direct	Imprecise	Low
CCB versus beta blocker (n=3)	All-cause mortality	2; 692	RCTs/fair	Consistent	Direct	Imprecise	Low
	ESRD	1; 658	RCT/good	Unknown	Direct	Imprecise	Low
Diuretic versus placebo (n=1)	All-cause mortality	1; 393	RCT/good (post-hoc)	Unknown	Direct	Imprecise	Low
	ESRD	none	-	-	-	-	Insufficient

Table 19. Strength of evidence for Key Question 5 (continued)

Comparison	Outcome, Control	Number of Studies; Number of Subjects	Risk of Bias Design; Quality	Consistency	Directness	Precision	Strength of Evidence
ACEI versus non-ACE (n=1)	All-cause mortality	none	-	-	-	-	Insufficient
	ESRD	1;	RCT/fair	Unknown	Direct	Imprecise	Low
Strict BP control versus Usual BP control (n=6)	All-cause mortality	4; 1803	RCTs/fair	Consistent	Direct	Imprecise	Low
	ESRD	3; 1506	RCTs/fair	Consistent	Direct	Imprecise	Low
Non-Blood Pressure Control Interventions Section: Anti-Lipid Treatment Trials							
HMG-CoA Reductase Inhibitors versus control (n=12)	All-cause mortality	8; 13964	RCTs/good	Consistent	Direct	Precise	High
	ESRD	1; 1557	RCT/good	Unknown	Direct	Imprecise	Low
High versus low-dose HMG-CoA Reductase Inhibitors (n=2)	All-cause mortality	1; 3107	RCT/good	Unknown	Direct	Imprecise	Low
	ESRD	none	-	-	-	-	Insufficient
Gemfibrozil versus Placebo (n=1)	All-cause mortality	1; 399	RCT/good	Unknown	Direct	Imprecise	Low
	ESRD	1; 399	RCT/good	Unknown	Direct	Imprecise	Insufficient
Gemfibrozil versus Low triglyceride diet (n=1)	All-cause mortality	none	-	-	-	-	Insufficient
	ESRD	1; 57	RCT/fair	Unknown	Direct	Imprecise	Insufficient
Non-Blood Pressure Control Interventions Section: Dietary Intervention and Weight Loss							
Low protein diet versus usual protein diet (n=6)	All-cause mortality	4; 1280	RCTs/fair	Consistent	Direct	Imprecise	Low
	ESRD	3:302	RCTs/fair	Consistent	Direct	Imprecise	Low
Low protein diet versus other diet (n=1)	All-cause mortality	1; 170	RCT/fair	Unknown	Direct	Imprecise	Low
	ESRD	1; 170	RCT/fair	Unknown	Direct	Imprecise	Low
Low protein-low phosphate diet versus low phosphate diet versus usual diet (n=1)	All-cause mortality	1; 98	RCT/fair	Unknown	Direct	Imprecise	Insufficient
	ESRD	1; 98	RCT/fair	Unknown	Direct	Imprecise	Low
Low triglyceride diet versus gemfibrozil trials (n=1)	All-cause mortality	none	-	-	-	-	Insufficient
	ESRD	1; 57	RCT/fair	Unknown	Direct	Imprecise	Insufficient

Table 19. Strength of evidence for Key Question 5 (continued)

Comparison	Outcome, Control	Number of Studies; Number of Subjects	Risk of Bias Design; Quality	Consistency	Directness	Precision	Strength of Evidence
Non-Blood Pressure Control Interventions Section: Glycemic Control Studies							
Intensive versus standard glycemic control studies (n=2)	All-cause mortality	none	-	-	-	-	Insufficient
	ESRD	none	-	-	-	-	Insufficient
Non-Blood Pressure Control Interventions Section: Intensive Multi-Component Intervention Studies							
Intensive multi-component intervention versus control studies (n=4)	All-cause mortality	4; 892	RCTs/fair	Consistent	Direct	Imprecise	Low
	ESRD	3; 455	RCTs/fair	Inconsistent	Direct	Imprecise	Low

ACEI = Angiotensin-converting Enzyme inhibitor; ARB= angiotensin II receptor blocker; BP = blood pressure; CCB = calcium channel blocker; ESRD = End-stage renal disease

Discussion

For CKD screening or monitoring to be of benefit, each would need to improve clinically important outcomes, presumably by leading to specific changes in treatment. However, we identified no RCTs that randomized individuals without known CKD to CKD screening, or those with CKD stages 1–3 to CKD monitoring, and collected and reported associated clinical outcomes.

With no direct link between screening or monitoring and clinical outcomes, concluding likely benefit of screening or monitoring requires, at minimum, the availability of accurate screening tests, and sufficient evidence that treatment for CKD stages 1–3 improves clinically important outcomes while limiting harms. For treatment benefits in CKD patients to be relevant to screening or monitoring, treatments also would need to improve these outcomes in individuals who would not otherwise receive them; i.e., patients without specific treatment indications in the absence of a CKD diagnosis. In patients with other treatment indications, diagnosis of CKD or of CKD progression might be beneficial if outcomes in these patients are significantly improved with a higher treatment dose or by treatment to a stricter target than indicated in individuals with no or less severe CKD. Finally, any treatment benefit would need to outstrip treatment harms and potential screening and monitoring harms, and applicability of treatment RCT results to screening or monitoring would be increased if subjects were identified for participation in these treatment trials through screening.

In this synthesis of RCT evidence, several treatments reduced risk of clinical events in patients with CKD stages 1–3. Compared with placebo, ACEI and ARB significantly reduced risk of ESRD in patients with proteinuria, nearly all of whom had concomitant diabetes and hypertension. While there was no significant reduction in risk of ESRD with ACEI or ARB in patients without proteinuria, because of the low rate of progression to ESRD in these patients, the present analysis had limited statistical power to detect such a difference. This is not direct evidence that testing patients with diabetes and hypertension for proteinuria will reduce ESRD risk, but it suggests, in patients not currently being treated with ACEI or ARB, that knowledge of these results might inform this treatment decision. Also compared with placebo, ACEI significantly reduced risk of mortality in patients with microalbuminuria who had cardiovascular disease or had diabetes and other cardiovascular risk factors. Though the relative reduction in mortality risk appeared slightly greater in patients with microalbuminuria compared with those without microalbuminuria, this difference was not statistically significant, suggesting that such patients may have an indication for ACEI regardless of CKD status.

In individuals with hyperlipidemia and impaired eGFR or creatinine clearance, we found that statins significantly reduced risk of mortality, MI, and stroke compared with placebo, including in patients without coronary artery disease. This is not direct evidence that testing patients with hyperlipidemia for eGFR will reduce risk of these outcomes, in part because some of these patients already have a clinical indication for statin treatment. Determining CKD status in these patients wouldn’t alter their management. Specifically, as previously documented, patients with hyperlipidemia and coronary artery disease randomized to statins have a significantly reduced risk of mortality compared with placebo,[160] They have an indication for statin treatment regardless of their CKD status. In contrast, also previously documented, hyperlipidemic patients without coronary artery disease taken as a whole did not have a significant mortality benefit from statins.[161] The current results suggest that, in patients with hyperlipidemia and no coronary artery

disease who are not currently being treated with a statin, knowledge of impaired eGFR might inform this treatment decision.

In individuals with CHF and impaired eGFR, beta blockers significantly reduced risk of mortality, MI, and CHF events compared with placebo. Patients in all eGFR strata had a significant reduction in risk of these clinical outcomes. Inconsistent results suggested possibly a greater relative risk reduction with beta blockers in patients with lower eGFR. However, as patients with systolic CHF already have an indication for beta blocker treatment, testing for eGFR is not likely to inform this treatment decision.

With regard to patients with CKD stages 1–3 already receiving treatments for conditions associated with CKD (e.g., ACEI for treatment of hypertension), no clear RCT evidence showed whether intensification of treatment improves clinical outcomes. We identified no eligible RCTs that compared clinical outcomes in CKD patients randomized to different fixed ACEI doses, though separate trials suggested that ramipril at 1.25 mg per day in patients with albuminuria lacks the mortality benefit of ramipril at 10 mg per day in patients with microalbuminuria. For other treatments in CKD patients, we did not find evidence of significant or consistent benefit in clinical outcomes in high versus low dose ARB, strict versus standard blood pressure control, high versus low dose statin, tight versus standard glycemic control, intensive multidisciplinary interventions versus standard care, and combination treatment versus monotherapy. While data limited to these latter trials suggests an absence of evidence for benefit from intensification of therapy as a justification for either CKD screening or monitoring, most had low statistical power to detect a significant difference in clinical outcomes.

In RCTs included in this evidence synthesis, many treatments reduced the risk of doubling of serum creatinine and progression from microalbuminuria to macroalbuminuria. However, these renal endpoints are not clinical outcomes. Although impaired GFR and albuminuria are unquestionably adverse prognostic markers, treatments that target and even improve these measures will not necessarily reduce risk of mortality, ESRD or important clinical vascular outcomes. Findings reported from the large ROADMAP study[162]—in which patients with diabetes and at least one additional CKD risk factor were randomized to ARB versus non-ARB blood pressure control—illustrated the potential danger of utilizing albuminuria as a surrogate marker for clinical outcomes in kidney disease. Though blood pressure control was significantly better and time to onset of microalbuminuria was significantly delayed in the ARB treatment group, these patients also experienced a significant increase in fatal cardiovascular events.

As we have noted, establishing the benefit of CKD screening and/or monitoring requires evidence of treatment benefit. Yet, treatment benefit does not by itself prove screening or monitoring benefit. First, the accuracy of available screening and monitoring measures for persistent CKD and progressive CKD, respectively, is uncertain. Second, only two of the dozens of RCTs included in this evidence synthesis reported that study participants were identified through screening.[26,27] Consequently, patients with CKD stages 1–3 enrolled in all these trials may not be representative of those who would be identified through systematic screening. For example, patients identified through screening may be earlier in their course of CKD, less likely to progress during treatment followup, and thus less likely to benefit from treatment intervention. In addition, formal diagnosis of CKD requires that impairment in kidney function or kidney damage persists for at least 3 months. The vast majority of trials included in this evidence synthesis categorized patients as having CKD based on one-time abnormalities. Other trials that required repeated or sustained kidney abnormalities for entry did not mandate persistence for 3 months. Study participants thus may have had transient impairments, been more likely to

improve regardless of treatment, and less likely to develop progressive CKD than patients with CKD confirmed over 3 months duration. Finally, we identified no evidence to quantify harms that may be associated with CKD screening and monitoring. Potential harms of systematic CKD screening could include adverse effects from screening and followup tests, including following false positive tests; psychological effects from labeling asymptomatic individuals as diseased; medication adverse effects; increased medical visits; and increased difficulty keeping health insurance coverage. Analogously, potential harms of systematic monitoring of patients with CKD stages 1–3 for worsening kidney function or damage could include adverse effects from monitoring and followup tests, including potentially unnecessary testing; medication adverse effects; and increased medical visits. Accurate information on screening and monitoring harms is needed to evaluate their overall impact in CKD.

Considering these issues, if there is a benefit from CKD screening, evidence suggests the likelihood of benefit is greatest in individuals with diabetes, cardiovascular disease, and possibly hyperlipidemia. For other populations with a high prevalence of CKD, such as patients with hypertension, obesity, and older age, evidence for benefit from screening appears weaker. Though also based only on indirect data, individuals under 50 years old and without diabetes, hypertension, cardiovascular disease, or obesity infrequently have CKD and seem least likely to benefit from CKD screening.

Finally, because of the imprecision and high intra-individual variability of eGFR and albuminuria, providers who monitor patients with CKD stages 1–3 for worsening kidney function and/or damage will identify both declines and improvements in these measures, including many that are transient and/or clinically insignificant. We identified no RCTs that assigned patients with CKD stages 1–3 to systematic monitoring versus control, or that modified treatment based on followup levels of eGFR or albuminuria and evaluated clinical outcomes. Rather, trials either assigned participants to a fixed dose to be maintained throughout the trial or titrated upward from an initial dose to achieve a specific target dose or clinical target (e.g., systolic blood pressure less than 140 mm Hg). Although treatment RCT results suggest that monitoring could inform decisions regarding whether to start ACEI or ARB treatment in patients with diabetes and hypertension who develop albuminuria, or statin treatment in patients with hyperlipidemia who develop impaired eGFR, considering uncertainty in the accuracy of monitoring tests for identifying CKD progression and uncertainty regarding possible monitoring harms, the relative benefits and harms of CKD monitoring are unclear.

Future Research Recommendations

Key Question 1. In asymptomatic adults with or without recognized risk factors for CKD incidence, progression, or complications, what direct evidence is there that systematic CKD screening improves clinical outcomes?

Knowledge Gaps

- No RCT evidence directly addresses whether systematic CKD screening improves clinical outcomes.
- Sensitivity and specificity of one-time measures of microalbuminuria, macroalbuminuria and eGFR for persistent (at least 3 months' duration) CKD is unknown; impact of patient factors on persistence also is unknown.
- Only two trials were performed in patients with CKD identified through screening.

Research Recommendations

- Long-term RCTs of systematic CKD screening versus usual care adequately powered to evaluate impact on clinical outcomes.
  - Target populations with high CKD prevalence and high risk for complications.
  - May test different screening measures (e.g., microalbuminuria, macroalbuminuria, eGFR, combination).
- Modeling studies evaluating efficacy and harms of different CKD screening strategies versus usual care. In addition to parameters in published models, consider impact of:
  - Variations in target populations.
  - Variations in screening measures and frequency.
  - Prevalence in target population of indications for and use of specific CKD treatments.
  - Yield of one-time screening tests based on actual association with persistent CKD.
  - Take into account potential screening harms.
- Determine eGFR and albuminuria from baseline and followup blood and urine available from large prospective cohorts or RCT/CCT control groups (or collect new samples).
  - Estimate the proportion of individuals with abnormal one-time abnormalities who meet criteria for CKD for at least 3 months.
  - Evaluate impact of patient factors on persistence (e.g., eGFR severity, albuminuria, age)

Key Question 2. What harms result from systematic CKD screening in asymptomatic adults with or without recognized risk factors for CKD incidence, progression or complications?

Knowledge Gaps

- No RCT evidence directly addresses whether systematic CKD screening increases harms.

Research Recommendations

- Long-term RCT comparing systematic CKD screening versus usual care to assess potential screening harms.
  - Potential harms should be predefined, and collected and reported in all study participants.
  - Potential harms may include adverse effects from screening/followup tests, including from false positive tests; psychological effects of labeling asymptomatic individuals as diseased; medication adverse effects; increased medical visits; increased costs; difficulty keeping health insurance.
- Prospectively collect predefined harms data (see above list) from all participants in large, observational CKD screening cohort studies.
- As above, conduct modeling studies evaluating the effectiveness and harms of different CKD screening strategies versus usual care.

Key Question 3. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what direct evidence is there that monitoring for worsening kidney function and/or kidney damage improves clinical outcomes?

Knowledge Gaps

- No RCT evidence directly addresses whether systematic CKD monitoring for worsened kidney function or damage improves clinical outcomes.
- Sensitivity and specificity of changes in eGFR and albuminuria for CKD progression is unknown.
- Limited RCT data address whether treatment relative risk reduction for clinical outcomes differs based on CKD severity that could inform decisions regarding whether to change treatment in patients identified by monitoring with worsened CKD severity..
- No RCT data address whether treatments have different relative risk reduction in clinical outcomes between patients with recently worsened kidney function or damage, as detectable by monitoring, compared with in those with stable CKD.

Research Recommendations

- Long-term RCTs of systematic CKD monitoring versus usual care adequately powered to evaluate impact on clinical outcomes.
  - Target populations with high risk for CKD complications.
  - Consider testing different monitoring measures, alone and in combination (e.g., quantitative microalbuminuria, macroalbuminuria, eGFR)
- Modeling studies evaluating efficacy and harms of different CKD monitoring strategies versus usual care. Parameters these models may include:
  - Variations in monitoring measures and frequency (quantitative albuminuria, eGFR, or a combination)
  - Variations in baseline CKD severity (i.e., stage, eGFR, quantitative albuminuria)

- Variations in CKD patient characteristics (e.g., diabetes, hypertension, age, cardiovascular disease, hyperlipidemia, race/ethnicity), including possible indication for specific CKD treatments and prevalence of use of these treatments
- Take into account potential monitoring harms

Key Question 4. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what harms result from monitoring for worsening kidney function and/or kidney damage?

Knowledge Gaps

- No RCT evidence directly addresses whether systematic CKD monitoring for worsening kidney function or damage increases harms.

Research Recommendations

- Long term RCT comparing systematic CKD monitoring versus usual care to assess potential monitoring harms.
  - Potential harms associated with monitoring should be predefined and collected and reported in all study participants.
  - Potential harms may include adverse effects from monitoring/followup tests, including from false positive (for progression) tests; medication adverse effects; increased medical visits; increased costs.
- Prospectively collect predefined harms data (see above list) from all participants in large, observational CKD monitoring cohort studies.
- As above, conduct modeling studies evaluating the effectiveness and harms of different CKD monitoring strategies versus usual care.

Key Question 5. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what direct evidence is there that treatment improves clinical outcomes?

Knowledge Gaps

- Limited RCT data address whether relative efficacy of treatments differs between patients with and without CKD.
- Limited RCT data address whether treatment risk reduction differs based on CKD severity.
- Limited RCT data address whether treatments improved outcomes in CKD subgroups in whom treatments were not already indicated.
- In RCTs of high versus low dose, combination versus monotherapy, and strict versus standard control, it was unclear whether intensification of treatment improves clinical outcomes.
- Effect of diet interventions on clinical outcomes in patients with CKD stages 1–3 is unclear because diet intervention RCTs were small, included both patients with CKD stages 1–3 and 4–5, and did not separate results by CKD stage or severity.
- In head-to-head RCTs, there was little evidence of a significant difference in mortality or any clinical vascular outcome between different active treatment groups.

- Trials used heterogeneous eligibility criteria for kidney function and damage, and rarely reported outcomes stratified by CKD stage or albuminuria category, impeding evidence synthesis.

Research Recommendations

- Post hoc analyses of ongoing or completed RCTs that already have or are collecting clinical outcomes.
  - Determine baseline eGFR and quantitative albuminuria, categorize participants by CKD stage and albuminuria category, and perform analyses to evaluate relative effectiveness of treatment versus control on clinical outcomes within these strata.
- Merge data from large scale treatment RCTs with Medicare data to identify incident ESRD cases occurring in post-trial followup period.
- Long-term RCTs of CKD treatment adequately powered to evaluate impact on clinical outcomes.
  - In addition to mortality, ESRD, and clinical vascular outcomes, additional clinical outcomes to consider for evaluation include quality of life, acute kidney injury complications (e.g., hospitalization), healthcare utilization, physical function, and cognitive function.
  - If composite outcomes reported, complete data also should be reported for individual composite components.
  - To increase trial relevance to a screened population, consider recruitment using population-based sampling.
  - Stratify results by CKD stage, albuminuria category, and other characteristics associated with CKD complications, including diabetes, hypertension, cardiovascular disease, older age, race/ethnicity, obesity, and hyperlipidemia.
  - Consider future RCTs of statins in patients with albuminuria, AECI, or ARB in patients with macroalbuminuria, ACEI or ARB in combination with other therapy, and of treatments other than ACEI or ARB.
  - Consider trials of dietary interventions restricted to patients with CKD stages 1–3.
  - Consider trials comparing system level interventions to aid providers in avoidance of nephrotoxic agents, medication renal dose adjustment, and other measures targeted to reduce CKD associated complications versus usual care.
- Patient level meta-analyses of treatment RCTs to evaluate the effect of treatments relative to control in relevant CKD subgroups.
- Analysis of administrative data to evaluate effect of nephrology referral on clinical outcomes, performing propensity analysis to account for factors associated with early referral.

Key Question 6. Among adults with CKD stages 1–3, whether detected by systematic screening or as part of routine care, what harms result from treatment?

Knowledge Gaps

- Withdrawals and adverse events were reported in few RCTs.

- Withdrawals often were not reported separately by treatment group; adverse events often did not appear predefined, systematically collected and reported, or separated by treatment group.

Research Recommendations

- In future RCTs, withdrawals and adverse effects should be predefined and collected and reported in all patients with CKD stages 1–3.
- Withdrawal and adverse effects may be reported stratified by CKD stage and albuminuria category, and other patient characteristics.

References

1. CDC. National Chronic Kidney Disease Fact Sheet 2010. 2010. Available at: www.cdc.gov/diabetes/pubs/pdf/kidney_Factsheet.pdf. Accessed November 12 2010.

2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. American Journal of Kidney Diseases. 2002 Feb;39(2 Suppl 1):S1-266. PMID 11904577.

3. Matsushita K, van der Velde M, Astor BC, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet. 2010 Jun 12;375(9731):2073-81. PMID 20483451.

4. Astor BC, Matsushita K, Gansevoort RT, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. A collaborative meta-analysis of kidney disease population cohorts. Kidney Int. 2011 Feb 2PMID 21289598.

5. Gansevoort RT, Matsushita K, van der Velde M, et al. Lower estimated GFR and higher albuminuria are associated with adverse kidney outcomes in both general and high-risk populations. A collaborative meta-analysis of general and high-risk population cohorts. Kidney Int. 2011 Feb 2PMID 21289597.

6. van der Velde M, Matsushita K, Coresh J, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. Kidney Int. 2011 Feb 9PMID 21307840.

7. Levey AS, de Jong PE, Coresh J, et al. The definition, classification and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. Kidney Int. 2010 Dec 8PMID 21150873.

8. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Annals of Internal Medicine. 2009 May 5;150(9):604-12. PMID 19414839.

9. USRDS. United States Renal Data System 2008 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2008. www.usrds.org/adr_2008.htm. Accessed on Jan. 2010 2010.

10. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. JAMA. 2007 Nov 7;298(17):2038-47. PMID 17986697.

11. Gilbertson DT, Liu J, Xue JL, et al. Projecting the number of patients with end-stage renal disease in the United States to the year 2015. Journal of the American Society of Nephrology. 2005 Dec;16(12):3736-41. PMID 16267160.

12. USRDS. United States Renal Data System 2010 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2010. www.usrds.org/adr_2010.htm2010.

13. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. New England Journal of Medicine. 2004 Sep 23;351(13):1296-305. PMID 15385656.

14. Weiner DE, Tabatabai S, Tighiouart H, et al. Cardiovascular outcomes and all-cause mortality: exploring the interaction between CKD and cardiovascular disease. American Journal of Kidney Diseases. 2006 Sep;48(3):392-401. PMID 16931212.

15. Ensrud KE, Lui L-Y, Taylor BC, et al. Renal function and risk of hip and vertebral fractures in older women. Archives of Internal Medicine. 2007 Jan 22;167(2):133-9. PMID 17242313.

16. Ishani A, Paudel M, Taylor BC, et al. Renal function and rate of hip bone loss in older men: the Osteoporotic Fractures in Men Study. Osteoporosis International. 2008 Nov;19(11):1549-56. PMID 18392664.

17. James MT, Quan H, Tonelli M, et al. CKD and risk of hospitalization and death with pneumonia. American Journal of Kidney Diseases. 2009 Jul;54(1):24-32. PMID 19447535.

18. Khatri M, Nickolas T, Moon YP, et al. CKD associates with cognitive decline. Journal of the American Society of Nephrology. 2009 Nov;20(11):2427-32. PMID 19729443.

19. Wilhelm-Leen ER, Hall YN, M KT, et al. Frailty and chronic kidney disease: the Third National Health and Nutrition Evaluation Survey. Am J Med. 2009 Jul;122(7):664-71 e2. PMID 19559169.

20. Rifkin DE, Katz R, Chonchol M, et al. Albuminuria, impaired kidney function and cardiovascular outcomes or mortality in the elderly. Nephrology Dialysis Transplantation. 2010 May;25(5):1560-7. PMID 20008829.

21. Ishani A, Grandits GA, Grimm RH, et al. Association of single measurements of dipstick proteinuria, estimated glomerular filtration rate, and hematocrit with 25-year incidence of end-stage renal disease in the multiple risk factor intervention trial. Journal of the American Society of Nephrology. 2006 May;17(5):1444-52. PMID 16611715.

22. Ninomiya T, Perkovic V, de Galan BE, et al. Albuminuria and kidney function independently predict cardiovascular and renal outcomes in diabetes. Journal of the American Society of Nephrology. 2009 Aug;20(8):1813-21. PMID 19443635.

23. Snyder JJ, Collins AJ. KDOQI hypertension, dyslipidemia, and diabetes care guidelines and current care patterns in the United States CKD population: National Health and Nutrition Examination Survey 1999-2004. Am J Nephrol. 2009;30(1):44-54. PMID 19202328.

24. Levey AS, Atkins R, Coresh J, et al. Chronic kidney disease as a global public health problem: approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. Kidney Int. 2007 Aug;72(3):247-59. PMID 17568785.

25. Executive summary: standards of medical care in diabetes--2011. Diabetes Care. 2011 Jan;34 Suppl 1:S4-10. PMID 21193627.

26. McCullough PA, Vassalotti JA, Collins AJ, et al. National Kidney Foundation's Kidney Early Evaluation Program (KEEP) annual data report 2009: executive summary. Am J Kidney Dis. 2010 Mar;55(3 Suppl 2):S1-3. PMID 20172443.

27. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002 Feb;39(2 Suppl 1):S1-266. PMID 11904577.

28. Renal Association T. Chronic Kidney Disease in Adults: UK Guidelines for Identification, Management and Referral of Adults. www.renal.org/CKDguide/full/SupportingEvidence1.htm.

29. American Diabetes Association. Standards of medical care in diabetes--2009. Diabetes Care. 2009 Jan;32 Suppl 1:S13-61. PMID 19118286.

30. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA. 2003 May 21;289(19):2560-72. PMID 12748199.

31. Levey AS, Cattran D, Friedman A, et al. Proteinuria as a surrogate outcome in CKD: report of a scientific workshop sponsored by the National Kidney Foundation and the US Food and Drug Administration. American Journal of Kidney Diseases. 2009 Aug;54(2):205-26. PMID 19577347.

32. Nelson RG, Tuttle KR. Prevention of diabetic kidney disease: negative clinical trials with renin-angiotensin system inhibitors. American Journal of Kidney Diseases. 2010 Mar;55(3):426-30. PMID 20005029.

33. Hogan M. KDIGO conference proposes changes to CKD classification, but not to the definition. Nephrology Times. 2009;2(12):9-10.

34. Moher D, Pham B, Lawson ML, et al. The inclusion of reports of randomised trials published in languages other than English in systematic reviews. Health Technol Assess. 2003;7(41):1-90. PMID 14670218.

35. Relevo R, Balshem H. Finding Evidence for Comparing Medical Interventions: Agency for Healthcare Research and Quality; 2011.

36. Cochrane Handbook for Systematic Reviews of Interventions. In: Higgins JPT, Green S, eds. Version 5.0.2 [updated September 2009] ed: The Cochrane Collaboration; 2008.

37. Schulz KF, Grimes DA. Allocation concealment in randomised trials: defending against deciphering. Lancet. 2002 Feb 16;359(9306):614-8. PMID 11867132.

38. Owens DK, Lohr KN, Atkins D, et al. AHRQ series paper 5: grading the strength of a body of evidence when comparing medical interventions--agency for healthcare research and quality and the effective health-care program. J Clin Epidemiol. 2010 May;63(5):513-23. PMID 19595577.

39. Review Manager. 5.0 ed. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration; 2008.

40. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. Bmj. 2003 Sep 6;327(7414):557-60. PMID 12958120.

41. Halbesma N, Kuiken DS, Brantsma AH, et al. Macroalbuminuria is a better risk marker than low estimated GFR to identify individuals at risk for accelerated GFR loss in population screening. J Am Soc Nephrol. 2006 Sep;17(9):2582-90. PMID 16899519.

42. USRDS. United States Renal Data System 2009 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2009. www.usrds.org/adr_2009.htm. Accessed on Jan. 2010 2010.

43. Ryan TP, Sloand JA, Winters PC, et al. Chronic kidney disease prevalence and rate of diagnosis. Am J Med. 2007 Nov;120(11):981-6. PMID 17976426.

44. CDC. CDC Chronic Kidney Disease (CKD) Surveillance Report. 2009. www.cdc.gov/features/dsChronicKidneyDisease/2010.

45. USRDS. United States Renal Data System 2006 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2006. www.usrds.org/adr_2006.htm. Accessed on Jan. 2010 2010.

46. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Annals of Internal Medicine. 2006 Aug 15;145(4):247-54. PMID 16908915.

47. Stevens LA, Schmid CH, Greene T, et al. Comparative performance of the CKD Epidemiology Collaboration (CKD-EPI) and the Modification of Diet in Renal Disease (MDRD) Study equations for estimating GFR levels above 60 mL/min/1.73 m2. Am J Kidney Dis. 2010 Sep;56(3):486-95. PMID 20557989.

48. Miller WG, Bruns DE, Hortin GL, et al. Current issues in measurement and reporting of urinary albumin excretion. Clin Chem. 2009 Jan;55(1):24-38. PMID 19028824.

49. Witte EC, Lambers Heerspink HJ, et al. First morning voids are more reliable than spot urine samples to assess microalbuminuria. J Am Soc Nephrol. 2009 Feb;20(2):436-43. PMID 19092125.

50. Gomes MB, Goncalves MF. Is there a physiological variability for albumin excretion rate? Study in patients with diabetes type 1 and non-diabetic individuals. Clin Chim Acta. 2001 Feb;304(1-2):117-23. PMID 11165206.

51. Coresh J, Astor BC, Greene T, et al. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. American Journal of Kidney Diseases. 2003 Jan;41(1):1-12. PMID 12500213.

52. Perkins BA, Ficociello LH, Silva KH, et al. Regression of microalbuminuria in type 1 diabetes. New England Journal of Medicine. 2003 Jun 5;348(23):2285-93. PMID 12788992.

53. Boulware LE, Jaar BG, Tarver-Carr ME, et al. Screening for proteinuria in US adults: a cost-effectiveness analysis. JAMA. 2003 Dec 17;290(23):3101-14. PMID 14679273.

54. Strippoli GFM, Bonifati C, Craig M, et al. Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists for preventing the progression of diabetic kidney disease. Cochrane Database of Systematic Reviews. 2006(4):CD006257. PMID 17054288.

55. Crepaldi G, Carta Q, Deferrari G, et al. Effects of lisinopril and nifedipine on the progression to overt albuminuria in IDDM patients with incipient nephropathy and normal blood pressure. The Italian Microalbuminuria Study Group in IDDM. Diabetes Care. 1998 Jan;21(1):104-10. PMID 9538979.

56. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators.[Erratum appears in Lancet 2000 Sep 2;356(9232):860]. Lancet. 2000 Jan 22;355(9200):253-9. PMID 10675071.

57. Laffel LM, McGill JB, Gans DJ. The beneficial effect of angiotensin-converting enzyme inhibition with captopril on diabetic nephropathy in normotensive IDDM patients with microalbuminuria. North American Microalbuminuria Study Group. American Journal of Medicine. 1995 Nov;99(5):497-504. PMID 7485207.

58. O'Hare P, Bilbous R, Mitchell T, et al. Low-dose ramipril reduces microalbuminuria in type 1 diabetic patients without hypertension: results of a randomized controlled trial. Diabetes Care. 2000 Dec;23(12):1823-9. PMID 11128360.

59. Ravid M, Savin H, Jutrin I, et al. Long-term stabilizing effect of angiotensin-converting enzyme inhibition on plasma creatinine and on proteinuria in normotensive type II diabetic patients. Annals of Internal Medicine. 1993 Apr 15;118(8):577-81. PMID 8452322.

60. Adler AI, Stevens RJ, Manley SE, et al. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney Int. 2003 Jan;63(1):225-32. PMID 12472787.

61. Perkovic V, Ninomiya T, Arima H, et al. Chronic kidney disease, cardiovascular events, and the effects of perindopril-based blood pressure lowering: data from the PROGRESS study. Journal of the American Society of Nephrology. 2007 Oct;18(10):2766-72. PMID 17804673.

62. Asselbergs FW, Diercks GFH, Hillege HL, et al. Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. Circulation. 2004 Nov 2;110(18):2809-16. PMID 15492322.

63. Marre M, Lievre M, Chatellier G, et al. Effects of low dose ramipril on cardiovascular and renal outcomes in patients with type 2 diabetes and raised excretion of urinary albumin: randomised, double blind, placebo controlled trial (the DIABHYCAR study).[Erratum appears in BMJ. 2004 Mar 20;328(7441):686]. BMJ. 2004 Feb 28;328(7438):495. PMID 14960504.

64. Katayama S, Kikkawa R, Isogai S, et al. Effect of captopril or imidapril on the progression of diabetic nephropathy in Japanese with type 1 diabetes mellitus: a randomized controlled study (JAPAN-IDDM).[Erratum appears in Diabetes Res Clin Pract 2002 Jul;57(1):71]. Diabetes Research & Clinical Practice. 2002 Feb;55(2):113-21. PMID 11796177.

65. Bojestig M, Karlberg BE, Lindstrom T, et al. Reduction of ACE activity is insufficient to decrease microalbuminuria in normotensive patients with type 1 diabetes. Diabetes Care. 2001 May;24(5):919-24. PMID 11347755.

66. Gerstein HC, Mann JF, Yi Q, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA. 2001 Jul 25;286(4):421-6. PMID 11466120.

67. Muirhead N, Feagan BF, Mahon J, et al. The effects of valsartan and captopril on reducing microalbuminuria in patients with type 2 diabetes mellitus: a placebo-controlled trial. Current Therapeutic Research - Clinical and Experimental 1999 1999 Dec;60(12):650-60.

68. Ruggenenti P, Perna A, Gherardi G, et al. Renoprotective properties of ACE-inhibition in non-diabetic nephropathies with non-nephrotic proteinuria. Lancet. 1999 Jul 31;354(9176):359-64. PMID 10437863.

69. Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy. The GISEN Group (Gruppo Italiano di Studi Epidemiologici in Nefrologia). Lancet. 1997 Jun 28;349(9069):1857-63. PMID 9217756.

70. Maschio G, Alberti D, Janin G, et al. Effect of the angiotensin-converting-enzyme inhibitor benazepril on the progression of chronic renal insufficiency. The Angiotensin-Converting-Enzyme Inhibition in Progressive Renal Insufficiency Study Group. New England Journal of Medicine. 1996 Apr 11;334(15):939-45. PMID 8596594.

71. Trevisan R, Tiengo A. Effect of low-dose ramipril on microalbuminuria in normotensive or mild hypertensive non-insulin-dependent diabetic patients. North-East Italy Microalbuminuria Study Group. American Journal of Hypertension. 1995 Sep;8(9):876-83. PMID 8541002.

72. Lewis EJ, Hunsicker LG, Bain RP, et al. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. The Collaborative Study Group.[Erratum appears in N Engl J Med 1993 Jan 13;330(2):152]. New England Journal of Medicine. 1993 Nov 11;329(20):1456-62. PMID 8413456.

73. Sano T, Kawamura T, Matsumae H, et al. Effects of long-term enalapril treatment on persistent micro-albuminuria in well-controlled hypertensive and normotensive NIDDM patients. Diabetes Care. 1994 May;17(5):420-4. PMID 8062609.

74. Yusuf S, Sleight P, Pogue J, et al. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. New England Journal of Medicine. 2000 Jan 20;342(3):145-53. PMID 10639539.

75. Mann JFE, Schmieder RE, McQueen M, et al. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. Lancet. 2008 Aug 16;372(9638):547-53. PMID 18707986.

76. Menne J, Farsang C, Deak L, et al. Valsartan in combination with lisinopril versus the respective high dose monotherapies in hypertensive patients with microalbuminuria: the VALERIA trial. Journal of Hypertension. 2008 Sep;26(9):1860-7. PMID 18698222.

77. Sengul AM, Altuntas Y, Kurklu A, et al. Beneficial effect of lisinopril plus telmisartan in patients with type 2 diabetes, microalbuminuria and hypertension. Diabetes Research & Clinical Practice. 2006 Feb;71(2):210-9. PMID 16112244.

78. Barnett AH, Bain SC, Bouter P, et al. Angiotensin-receptor blockade versus converting-enzyme inhibition in type 2 diabetes and nephropathy.[Erratum appears in N Engl J Med. 2005 Apr 21;352(16)1731]. New England Journal of Medicine. 2004 Nov 4;351(19):1952-61. PMID 15516696.

79. Lacourciere Y, Belanger A, Godin C, et al. Long-term comparison of losartan and enalapril on kidney function in hypertensive type 2 diabetics with early nephropathy. Kidney International. 2000 Aug;58(2):762-9. PMID 10916100.

80. Teo K, Yusuf S, Sleight P, et al. Rationale, design, and baseline characteristics of 2 large, simple, randomized trials evaluating telmisartan, ramipril, and their combination in high-risk patients: the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial/Telmisartan Randomized Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease (ONTARGET/TRANSCEND) trials. Am Heart J. 2004 Jul;148(1):52-61. PMID 15215792.

81. Rahman M, Pressel S, Davis BR, et al. Renal outcomes in high-risk hypertensive patients treated with an angiotensin-converting enzyme inhibitor or a calcium channel blocker vs a diuretic: a report from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Archives of Internal Medicine. 2005 Apr 25;165(8):936-46. PMID 15851647.

82. Rahman M, Pressel S, Davis BR, et al. Cardiovascular outcomes in high-risk hypertensive patients stratified by baseline glomerular filtration rate.[Summary for patients in Ann Intern Med. 2006 Feb 7;144(3):I33; PMID: 16461958]. Annals of Internal Medicine. 2006 Feb 7;144(3):172-80. PMID 16461961.

83. Rahman M, Baimbridge C, Davis BR, et al. Progression of kidney disease in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin versus usual care: a report from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). American Journal of Kidney Diseases. 2008 Sep;52(3):412-24. PMID 18676075.

84. Fogari R, Preti P, Zoppi A, et al. Effects of amlodipine fosinopril combination on microalbuminuria in hypertensive type 2 diabetic patients. American Journal of Hypertension. 2002 Dec;15(12):1042-9. PMID 12460699.

85. Agodoa LY, Appel L, Bakris GL, et al. Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial. JAMA. 2001 Jun 6;285(21):2719-28. PMID 11386927.

86. Marin R, Ruilope LM, Aljama P, et al. A random comparison of fosinopril and nifedipine GITS in patients with primary renal disease. Journal of Hypertension. 2001 Oct;19(10):1871-6. PMID 11593109.

87. Zucchelli P, Zuccala A, Borghi M, et al. Long-term comparison between captopril and nifedipine in the progression of renal insufficiency. Kidney International. 1992 Aug;42(2):452-8. PMID 1405330.

88. Zucchelli P, Zuccala A, Gaggi R. Comparison of the effects of ACE inhibitors and calcium channel blockers on the progression of renal failure. Nephrology Dialysis Transplantation. 1995 Oct;10 Suppl 9:46-51. PMID 8643208.

89. Wright JT, Jr., Kusek JW, Toto RD, et al. Design and baseline characteristics of participants in the African American Study of Kidney Disease and Hypertension (AASK) Pilot Study. Controlled Clinical Trials. 1996 Aug;17(4 Suppl):3S-16S. PMID 8889350.

90. Wright JT, Jr., Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial.[Erratum appears in JAMA. 2006 Jun 21;295(23):2726]. JAMA. 2002 Nov 20;288(19):2421-31. PMID 12435255.

91. Norris K, Bourgoigne J, Gassman J, et al. Cardiovascular outcomes in the African American Study of Kidney Disease and Hypertension (AASK) Trial. American Journal of Kidney Diseases. 2006 Nov;48(5):739-51. PMID 17059993.

92. van Essen GG, Apperloo AJ, Rensma PL, et al. Are angiotensin converting enzyme inhibitors superior to beta blockers in retarding progressive renal function decline? Kidney International - Supplement. 1997 Dec;63:S58-62. PMID 9407423.

93. Hannedouche T, Landais P, Goldfarb B, et al. Randomised controlled trial of enalapril and beta blockers in non-diabetic chronic renal failure. BMJ. 1994 Oct 1;309(6958):833-7. PMID 7950612.

94. Marre M, Puig JG, Kokot F, et al. Equivalence of indapamide SR and enalapril on microalbuminuria reduction in hypertensive patients with type 2 diabetes: the NESTOR Study. Journal of Hypertension. 2004 Aug;22(8):1613-22. PMID 15257186.

95. Makino H, Haneda M, Babazono T, et al. Prevention of transition from incipient to overt nephropathy with telmisartan in patients with type 2 diabetes. Diabetes Care. 2007 Jun;30(6):1577-8. PMID 17389334.

96. Parving HH, Lehnert H, Brochner-Mortensen J, et al. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. New England Journal of Medicine. 2001 Sep 20;345(12):870-8. PMID 11565519.

97. Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. New England Journal of Medicine. 2001 Sep 20;345(12):851-60. PMID 11565517.

98. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. New England Journal of Medicine. 2001 Sep 20;345(12):861-9. PMID 11565518.

99. Tobe SW, Clase CM, Gao P, et al. Cardiovascular and renal outcomes with telmisartan, ramipril, or both in people at high renal risk: results from the ONTARGET and TRANSCEND studies. Circulation. 2011 Mar 15;123(10):1098-107. PMID 21357827.

100. Saruta T, Hayashi K, Ogihara T, et al. Effects of candesartan and amlodipine on cardiovascular events in hypertensive patients with chronic kidney disease: subanalysis of the CASE-J Study. Hypertension Research - Clinical & Experimental. 2009 Jun;32(6):505-12. PMID 19390535.

101. Ogawa S, Takeuchi K, Mori T, et al. Effects of monotherapy of temocapril or candesartan with dose increments or combination therapy with both drugs on the suppression of diabetic nephropathy. Hypertension Research - Clinical & Experimental. 2007 Apr;30(4):325-34. PMID 17541211.

102. Fukui T, Rahman M, Hayashi K, et al. Candesartan Antihypertensive Survival Evaluation in Japan (CASE-J) trial of cardiovascular events in high-risk hypertensive patients: rationale, design, and methods. Hypertens Res. 2003 Dec;26(12):979-90. PMID 14717341.

103. Mehdi UF, Adams-Huet B, Raskin P, et al. Addition of angiotensin receptor blockade or mineralocorticoid antagonism to maximal angiotensin-converting enzyme inhibition in diabetic nephropathy. Journal of the American Society of Nephrology. 2009 Dec;20(12):2641-50. PMID 19926893.

104. Kanno Y, Takenaka T, Nakamura T, et al. Add-on angiotensin receptor blocker in patients who have proteinuric chronic kidney diseases and are treated with angiotensin-converting enzyme inhibitors. Clinical Journal of The American Society of Nephrology: CJASN. 2006 Jul;1(4):730-7. PMID 17699280.

105. Anand IS, Bishu K, Rector TS, et al. Proteinuria, chronic kidney disease, and the effect of an angiotensin receptor blocker in addition to an angiotensin-converting enzyme inhibitor in patients with moderate to severe heart failure. Circulation. 2009 Oct 20;120(16):1577-84. PMID 19805651.

106. Bakris GL, Toto RD, McCullough PA, et al. Effects of different ACE inhibitor combinations on albuminuria: results of the GUARD study. Kidney International. 2008 Jun;73(11):1303-9. PMID 18354383.

107. Bakris GL, Sarafidis PA, Weir MR, et al. Renal outcomes with different fixed-dose combination therapies in patients with hypertension at high risk for cardiovascular events (ACCOMPLISH): a prespecified secondary analysis of a randomised controlled trial. Lancet. 2010 Apr 3;375(9721):1173-81. PMID 20170948.

108. Jamerson KA, Bakris GL, Wun CC, et al. Rationale and design of the avoiding cardiovascular events through combination therapy in patients living with systolic hypertension (ACCOMPLISH) trial: the first randomized controlled trial to compare the clinical outcome effects of first-line combination therapies in hypertension. Am J Hypertens. 2004 Sep;17(9):793-801. PMID 15363822.

109. Mogensen CE, Viberti G, Halimi S, et al. Effect of low-dose perindopril/indapamide on albuminuria in diabetes: preterax in albuminuria regression: PREMIER. Hypertension. 2003 May;41(5):1063-71. PMID 12654706.

110. Lambers Heerspink HJ, Gansevoort RT, Brenner BM, et al. Comparison of different measures of urinary protein excretion for prediction of renal events. J Am Soc Nephrol. 2010 Aug;21(8):1355-60. PMID 20634296.

111. Burgess E, Muirhead N, Rene de Cotret P, et al. Supramaximal dose of candesartan in proteinuric renal disease. Journal of the American Society of Nephrology. 2009 Apr;20(4):893-900. PMID 19211712.

112. Bakris G, Burgess E, Weir M, et al. Telmisartan is more effective than losartan in reducing proteinuria in patients with diabetic nephropathy. Kidney International. 2008 Aug;74(3):364-9. PMID 18496508.

113. Galle J, Schwedhelm E, Pinnetti S, et al. Antiproteinuric effects of angiotensin receptor blockers: telmisartan versus valsartan in hypertensive patients with type 2 diabetes mellitus and overt nephropathy. Nephrology Dialysis Transplantation. 2008 Oct;23(10):3174-83. PMID 18450829.

114. van den Meiracker AH, Baggen RG, Pauli S, et al. Spironolactone in type 2 diabetic nephropathy: Effects on proteinuria, blood pressure and renal function. Journal of Hypertension. 2006 Nov;24(11):2285-92. PMID 17053552.

115. Ghali JK, Wikstrand J, Van Veldhuisen DJ, et al. The influence of renal function on clinical outcome and response to beta-blockade in systolic heart failure: insights from Metoprolol CR/XL Randomized Intervention Trial in Chronic HF (MERIT-HF). Journal of Cardiac Failure. 2009 May;15(4):310-8. PMID 19398079.

116. Cohen-Solal A, Kotecha D, van Veldhuisen DJ, et al. Efficacy and safety of nebivolol in elderly heart failure patients with impaired renal function: insights from the SENIORS trial. Eur J Heart Fail. 2009 Sep;11(9):872-80. PMID 19648605.

117. Berl T, Hunsicker LG, Lewis JB, et al. Cardiovascular outcomes in the Irbesartan Diabetic Nephropathy Trial of patients with type 2 diabetes and overt nephropathy.[Summary for patients in Ann Intern Med. 2003 Apr 1;138(7):I43; PMID: 12667050]. Annals of Internal Medicine. 2003 Apr 1;138(7):542-9. PMID 12667024.

118. Pahor M, Shorr RI, Somes GW, et al. Diuretic-based treatment and cardiovascular events in patients with mild renal dysfunction enrolled in the systolic hypertension in the elderly program. Archives of Internal Medicine. 1998 Jun 22;158(12):1340-5. PMID 9645829.

119. Cinotti GA, Zucchelli PC, Collaborative Study G. Effect of Lisinopril on the progression of renal insufficiency in mild proteinuric non-diabetic nephropathies. Nephrology Dialysis Transplantation. 2001 May;16(5):961-6. PMID 11328901.

120. Bakris GL, Copley JB, Vicknair N, et al. Calcium channel blockers versus other antihypertensive therapies on progression of NIDDM associated nephropathy. Kidney International. 1996 Nov;50(5):1641-50. PMID 8914031.

121. Dahlof B, Sever PS, Poulter NR, et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. Lancet. 2005 Sep 10-16;366(9489):895-906. PMID 16154016.

122. Ruggenenti P, Perna A, Loriga G, et al. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicentre, randomised controlled trial. Lancet. 2005 Mar 12-18;365(9463):939-46. PMID 15766995.

123. Lewis JB, Berl T, Bain RP, et al. Effect of intensive blood pressure control on the course of type 1 diabetic nephropathy. Collaborative Study Group. American Journal of Kidney Diseases. 1999 Nov;34(5):809-17. PMID 10561135.

124. Toto RD, Mitchell HC, Smith RD, et al. “Strict” blood pressure control and progression of renal disease in hypertensive nephrosclerosis. Kidney International. 1995 Sep;48(3):851-9. PMID 7474675.

125. Peterson JC, Adler S, Burkart JM, et al. Blood pressure control, proteinuria, and the progression of renal disease. The Modification of Diet in Renal Disease Study. Annals of Internal Medicine. 1995 Nov 15;123(10):754-62. PMID 7574193.

126. Shulman NB, Ford CE, Hall WD, et al. Prognostic value of serum creatinine and effect of treatment of hypertension on renal function. Results from the hypertension detection and follow-up program. The Hypertension Detection and Follow-up Program Cooperative Group. Hypertension. 1989 May;13(5 Suppl):I80-93. PMID 2490833.

127. Greene T, Bourgoignie JJ, Habwe V, et al. Baseline characteristics in the Modification of Diet in Renal Disease Study.[Republished from J Am Soc Nephrol 1993 May;3(11):1819-34]. Journal of the American Society of Nephrology. 1993 Nov;4(5):1221-36. PMID 8305650.

128. Koya D, Haneda M, Inomata S, et al. Long-term effect of modification of dietary protein intake on the progression of diabetic nephropathy: a randomised controlled trial. Diabetologia. 2009 Oct;52(10):2037-45. PMID 19652945.

129. Dussol B, Iovanna C, Raccah D, et al. A randomized trial of low-protein diet in type 1 and in type 2 diabetes mellitus patients with incipient and overt nephropathy. Journal of Renal Nutrition. 2005 Oct;15(4):398-406. PMID 16198932.

130. Klahr S, Levey AS, Beck GJ, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. New England Journal of Medicine. 1994 Mar 31;330(13):877-84. PMID 8114857.

131. Kopple JD, Levey AS, Greene T, et al. Effect of dietary protein restriction on nutritional status in the Modification of Diet in Renal Disease Study. Kidney International. 1997 Sep;52(3):778-91. PMID 9291200.

132. D'Amico G, Gentile MG, Fellin G, et al. Effect of dietary protein restriction on the progression of renal failure: a prospective randomized trial. Nephrology Dialysis Transplantation. 1994;9(11):1590-4. PMID 7870348.

133. Locatelli F, Alberti D, Graziani G, et al. Prospective, randomised, multicentre trial of effect of protein restriction on progression of chronic renal insufficiency. Northern Italian Cooperative Study Group. Lancet. 1991 Jun 1;337(8753):1299-304. PMID 1674294.

134. Rosman JB, ter Wee PM, Meijer S, et al. Prospective randomised trial of early dietary protein restriction in chronic renal failure. Lancet. 1984 Dec 8;2(8415):1291-6. PMID 6150320.

135. Rosman JB, Langer K, Brandl M, et al. Protein-restricted diets in chronic renal failure: a four year follow-up shows limited indications. Kidney International - Supplement. 1989 Nov;27:S96-102. PMID 2636680.

136. Facchini FS, Saylor KL. A low-iron-available, polyphenol-enriched, carbohydrate-restricted diet to slow progression of diabetic nephropathy. Diabetes. 2003 May;52(5):1204-9. PMID 12716753.

137. Samuelsson O, Attman PO, Knight-Gibson C, et al. Effect of gemfibrozil on lipoprotein abnormalities in chronic renal insufficiency: a controlled study in human chronic renal disease. Nephron. 1997;75(3):286-94. PMID 9069450.

138. Williams PS, Stevens ME, Fass G, et al. Failure of dietary protein and phosphate restriction to retard the rate of progression of chronic renal failure: a prospective, randomized, controlled trial. Quarterly Journal of Medicine. 1991 Oct;81(294):837-55. PMID 1801057.

139. Duckworth W, Abraira C, Moritz T, et al. Glucose control and vascular complications in veterans with type 2 diabetes. New England Journal of Medicine. 2009 Jan 8;360(2):129-39. PMID 19092145.

140. Intensive therapy and progression to clinical albuminuria in patients with insulin dependent diabetes mellitus and microalbuminuria. Microalbuminuria Collaborative Study Group, United Kingdom. BMJ. 1995 Oct 14;311(7011):973-7. PMID 7580637.

141. Kendrick J, Shlipak MG, Targher G, et al. Effect of lovastatin on primary prevention of cardiovascular events in mild CKD and kidney function loss: a post hoc analysis of the Air Force/Texas Coronary Atherosclerosis Prevention Study. American Journal of Kidney Diseases. 2010 Jan;55(1):42-9. PMID 19932541.

142. Nakamura H, Mizuno K, Ohashi Y, et al. Pravastatin and cardiovascular risk in moderate chronic kidney disease. Atherosclerosis. 2009 Oct;206(2):512-7. PMID 19423108.

143 Colhoun HM, Betteridge DJ, Durrington PN, et al. Effects of atorvastatin on kidney outcomes and cardiovascular disease in patients with diabetes: an analysis from the Collaborative Atorvastatin Diabetes Study (CARDS). American Journal of Kidney Diseases. 2009 Nov;54(5):810-9. PMID 19540640.

144. Koren MJ, Davidson MH, Wilson DJ, et al. Focused atorvastatin therapy in managed-care patients with coronary heart disease and CKD. American Journal of Kidney Diseases. 2009 May;53(5):741-50. PMID 19216014.

145. Chonchol M, Cook T, Kjekshus J, et al. Simvastatin for secondary prevention of all-cause mortality and major coronary events in patients with mild chronic renal insufficiency. American Journal of Kidney Diseases. 2007 Mar;49(3):373-82. PMID 17336698.

146. Kjekshus J, Apetrei E, Barrios V, et al. Rosuvastatin in older patients with systolic heart failure. New England Journal of Medicine. 2007 Nov 29;357(22):2248-61. PMID 17984166.

147. Lemos PA, Serruys PW, de Feyter P, et al. Long-term fluvastatin reduces the hazardous effect of renal impairment on four-year atherosclerotic outcomes (a LIPS substudy). American Journal of Cardiology. 2005 Feb 15;95(4):445-51. PMID 15695126.

148. Tonelli M, Moye L, Sacks FM, et al. Pravastatin for secondary prevention of cardiovascular events in persons with mild chronic renal insufficiency.[Summary for patients in Ann Intern Med. 2003 Jan 21;138(2):I28; PMID: 12529112]. Annals of Internal Medicine. 2003 Jan 21;138(2):98-104. PMID 12529091.

149. Tonelli M, Isles C, Curhan GC, et al. Effect of pravastatin on cardiovascular events in people with chronic kidney disease. Circulation. 2004 Sep 21;110(12):1557-63. PMID 15364796.

150. Ridker PM, MacFadyen J, Cressman M, et al. Efficacy of rosuvastatin among men and women with moderate chronic kidney disease and elevated high-sensitivity C-reactive protein: a secondary analysis from the JUPITER (Justification for the Use of Statins in Prevention-an Intervention Trial Evaluating Rosuvastatin) trial. J Am Coll Cardiol. 2010 Mar 23;55(12):1266-73. PMID 20206456.

151. Shepherd J, Kastelein JJP, Bittner V, et al. Intensive lipid lowering with atorvastatin in patients with coronary heart disease and chronic kidney disease: the TNT (Treating to New Targets) study. Journal of the American College of Cardiology. 2008 Apr 15;51(15):1448-54. PMID 18402899.

152. Armitage J, Bowman L, Wallendszus K, et al. Intensive lowering of LDL cholesterol with 80 mg versus 20 mg simvastatin daily in 12,064 survivors of myocardial infarction: a double-blind randomised trial. Lancet. 2010 Nov 13;376(9753):1658-69. PMID 21067805.

153. Tonolo G, Velussi M, Brocco E, et al. Simvastatin maintains steady patterns of GFR and improves AER and expression of slit diaphragm proteins in type II diabetes. Kidney International. 2006 Jul;70(1):177-86. PMID 16710349.

154. Tonelli M, Collins D, Robins S, et al. Effect of gemfibrozil on change in renal function in men with moderate chronic renal insufficiency and coronary disease. Am J Kidney Dis. 2004 Nov;44(5):832-9. PMID 15492949.

155. Chan JC, So W-Y, Yeung C-Y, et al. Effects of structured versus usual care on renal endpoint in type 2 diabetes: the SURE study: a randomized multicenter translational study. Diabetes Care. 2009 Jun;32(6):977-82. PMID 19460913.

156. Gaede P, Vedel P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. New England Journal of Medicine. 2003 Jan 30;348(5):383-93. PMID 12556541.

157. Gaede P, Vedel P, Parving HH, et al. Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study. Lancet. 1999 Feb 20;353(9153):617-22. PMID 10030326.

158. Joss N, Ferguson C, Brown C, et al. Intensified treatment of patients with type 2 diabetes mellitus and overt nephropathy. Qjm. 2004 Apr;97(4):219-27. PMID 15028852.

159. Harris LE, Luft FC, Rudy DW, et al. Effects of multidisciplinary case management in patients with chronic renal insufficiency. American Journal of Medicine. 1998 Dec;105(6):464-71. PMID 9870830.

160. Wilt TJ, Bloomfield HE, MacDonald R, et al. Effectiveness of statin therapy in adults with coronary heart disease. Arch Intern Med. 2004 Jul 12;164(13):1427-36. PMID 15249352.

161. Ray KK, Seshasai SR, Erqou S, et al. Statins and all-cause mortality in high-risk primary prevention: a meta-analysis of 11 randomized controlled trials involving 65,229 participants. Arch Intern Med. 2010 Jun 28;170(12):1024-31. PMID 20585067.

162. Haller H, Ito S, Izzo JL, Jr., et al. Olmesartan for the delay or prevention of microalbuminuria in type 2 diabetes. N Engl J Med. 2011 Mar 10;364(10):907-17. PMID 21388309.

Acronyms and Abbreviations

ACEI	Angiotensin converting enzyme inhibitors
AKI	Acute kidney injury
ARB	Angiotensin receptor blocker
ADA	American Diabetes Association
AHRQ	Agency for Healthcare Research and Quality
ALLHAT	Antihypertensive Lipid Lowering Treatment to Prevent Heart Attack
BB	Beta blocker
CCB	Calcium channel blocker
CCT	Controlled clinical trial
CHF	Congestive heart failure
CI	Confidence interval
CKD	Chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
DBP	Diastolic blood pressure
eGFR	Estimated glomerular filtration rate
ESRD	End-stage renal disease
GFR	Glomerular filtration rate
HbA_{1c}	Hemoglobin A_{1c}
HCTZ	Hydrochlorothiazide
JNC7	Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
KDIGO	Kidney Disease: Inspiring Global Outcomes
KDOQI	Kidney Disease Outcomes Quality Initiative
KEEP	Kidney Early Evaluation Program
LDL	Low density lipoprotein
MAP	Mean arterial blood pressure
MDRD	Modification of Diet in Renal Disease
MI	Myocardial infarction
NHANES	National Health and Nutrition Examination Survey
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
RCT	Randomized controlled trial
ROADMAP	Randomized Olmesartan and Diabetes Microalbuminuria Prevention
RR	Relative risk
TEP	Technical expert panel
UACR	Urinary albumin-creatinine ratio
UAER	Urinary albumin excretion rate
UPER	Urine protein excretion rate
USRDS	U.S. Renal Data System

Appendix A. Search Strings

Screening (KQ1, KQ2)

Database: Ovid MEDLINE(R)
Search Strategy:
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1 exp mass screening/ or screening.tw. or exp early diagnosis/
2 (expression screening or throughput screening or molecular screening or pharmaceutical screening or mutation screening or genetic screening).tw. or exp genetic screening/ or cancer screening.tw. or compound screening.tw. or drug screening.tw. or exp drug evaluation, preclinical/
3 1 not 2
4 (randomized controlled trial or controlled clinical trial).pt. or random*.ti,ab. or placebo.ab. or exp Double-Blind Method/
5 exp albuminuria/ or exp proteinuria/ or exp glomerular filtration rate/ or exp creatinine/ or exp kidney function tests/ or exp cystatins/ or exp kidney diseases/ or kidney$.ti. or nephr$.ti. or renal.ti. or exp kidney/
6 3 and 4 and 5
7 exp animals/ not humans.sh.
8 6 not 7
9 limit 8 to english language
10 limit 9 to yr="1985 -Current"
11 limit 10 to "all child (0 to 18 years)"
12 limit 10 to "all adult (19 plus years)"
13 11 not 12
14 10 not 13

Monitoring (KQ3, KQ4)

Database: Ovid MEDLINE(R)
Search Strategy:
---

1 monitoring.tw. or exp disease progression/
2 cardiac monitoring.tw. or exp drug monitoring/ or exp environmental monitoring/ or drug monitoring.tw. or exp blood glucose self-monitoring/ or exp blood gas monitoring, transcutaneous/ or exp clinical trials data monitoring committees/ or exp esophageal pH monitoring/ or exp monitoring, immunologic/ or exp uterine monitoring/ or exp monitoring, intraoperative/ or exp radiation monitoring/ or exp monitoring, physiologic/
3 1 not 2
4 (randomized controlled trial or controlled clinical trial).pt. or random*.ti,ab. or placebo.ab. or exp Double-Blind Method/
5 exp albuminuria/ or exp proteinuria/ or exp glomerular filtration rate/ or exp creatinine/ or exp kidney function tests/ or exp cystatins/ or exp kidney diseases/ or kidney$.ti. or nephr$.ti. or renal.ti. or exp kidney/
6 3 and 4 and 5

7 exp animals/ not humans.sh.
8 6 not 7
9 limit 8 to english language
10 limit 9 to yr="1985 -Current"
11 limit 10 to "all child (0 to 18 years)"
12 limit 10 to "all adult (19 plus years)"
13 11 not 12
14 10 not 13

Treatment (KQ5, KQ6)

Database: Ovid MEDLINE(R)
Search Strategy:
---

1 exp albuminuria/co, de, dh, dt, mo, pc, th or exp proteinuria/co, de, dh, dt, mo, pc, th or exp glomerular filtration rate/ or exp kidney diseases/co, de, dh, dt, mo, pc, th or exp kidney/co, de, dh, dt, mo, pc, th or exp diabetic nephropathies/co, de, dh, dt, mo, pc, th or exp kidney failure, chronic/co, de, dh, dt, mo, pc, th or exp chronic renal insufficiency/co, de, dh, dt, mo, pc, th or exp renal insufficiency/co, de, dh, dt, mo, pc, th or exp renal insufficiency, chronic/co, de, dh, dt, mo, pc, th
2 exp *renal replacement therapy/ or exp renal dialysis/ or exp *kidney neoplasms/ or *nephritis/ or exp *urinary tract infections/ or exp *urolithiasis/ or exp anuria/ or exp diabetes insipidus/ or exp fanconi syndrome/ or exp hepatorenal syndrome/ or exp hydronephrosis/ or exp kidney cortex necrosis/ or exp Kidney Diseases, Cystic/ or kidney papillary necrosis/ or exp nephritis/ or exp renal artery obstruction/ or exp Renal Tubular Transport, Inborn Errors/ or exp Tuberculosis, Renal/ or exp Zellweger syndrome/ or exp AIDS-Associated Nephropathy/ or exp Hyperoxaluria/ or exp Nephrocalcinosis/ or exp Perinephritis/ or exp Renal Osteodystrophy/
3 1 not 2
4 (randomized controlled trial or controlled clinical trial).pt. or random*.ti,ab. or placebo.ab. or exp Double-Blind Method/ or randomized controlled trials as topic/
5 3 and 4
6 exp animals/ not humans.sh.
7 5 not 6
8 limit 7 to english language
9 limit 8 to yr="1985 -Current"
10 limit 9 to "all child (0 to 18 years)"
11 limit 9 to "all adult (19 plus years)"
12 10 not 11
13 9 not 12

Appendix B. Excluded Studies

(Note that this set of references is different from those in the text, and the numbers are different.)

CKD Screening (KQ1, KQ2)

1. Microalbuminuria in type I diabetic patients. Prevalence and clinical characteristics. Microalbuminuria Collaborative Study Group. Diabetes Care 1992; 15(4):495-501. *Not a randomized trial*
2. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. New England Journal of Medicine 1993; 329(14):977-86. *Not an intervention for screening for CKD*
3. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the diabetes control and complications trial. Diabetes 1995; 44(8):968-83. *Not a randomized trial*
4. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet 2000; 355(9200):253-9. *Not an intervention for screening for CKD*
5. Abetimus: Abetimus sodium, LJP 394. Biodrugs 2003; 17(3):212-5. *Less than 1000 patients in study*
6. Accetta NA, Gladstone EH, DiSogra C, et al. Prevalence of estimated GFR reporting among US clinical laboratories. American Journal of Kidney Diseases 2008; 52(4):778-87. *Not a randomized trial*
7. Adler AI, Stevens RJ, Manley SE, et al. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney International 2003; 63(1):225-32. *Not an intervention for screening for CKD*
8. Agarwal A, Silver MR, Walczyk M, et al. Once-monthly darbepoetin alfa for maintaining hemoglobin levels in older patients with chronic kidney disease. Journal of the American Medical Directors Association 2007; 8(2):83-90. *Not a randomized trial*
9. Agodoa LY, Francis ME, Eggers PW. Association of analgesic use with prevalence of albuminuria and reduced GFR in US adults. American Journal of Kidney Diseases 2008; 51(4):573-83. *Not a randomized trial*
10. Agrawal A, Sautter MC, Jones NP. Effects of rosiglitazone maleate when added to a sulfonylurea regimen in patients with type 2 diabetes mellitus and mild to moderate renal impairment: a post hoc analysis. Clinical Therapeutics 2003; 25(11):2754-64. *Duration of follow-up less than 1 year*

11. Ahmedani MY, Hydrie MZI, Iqbal A, et al. Prevalence of microalbuminuria in type 2 diabetic patients in Karachi: Pakistan: a multi-center study.[Erratum appears in J Pak Med Assoc. 2005 Nov;55(11):523].[Erratum appears in J Pak Med Assoc. 2005 Dec;55(12):570]. JPMA - Journal of the Pakistan Medical Association 2005; 55(9):382-6. *Not a randomized trial*

12. Ahn CW, Song YD, Kim JH, et al. The validity of random urine specimen albumin measurement as a screening test for diabetic nephropathy. Yonsei Medical Journal 1999; 40(1):40-5. *Less than 1000 patients in study*

13. Akanji AO, Mainasara AS, Akinlade KS. Urinary iodine excretion in mothers and their breast-fed children in relation to other childhood nutritional parameters. European Journal of Clinical Nutrition 1996; 50(3):187-91. *Not an intervention for screening for CKD*

14. Al-Maskari F, El-Sadig M, Obineche E. Prevalence and determinants of microalbuminuria among diabetic patients in the United Arab Emirates. BMC Nephrology 2008; 9:1. *Not a randomized trial*

15. Alsuwaida A, Abdulkareem A, Alwakeel J. The Gulf Survey on Anemia Management (GSAM 2005). Saudi Journal of Kidney Diseases & Transplantation 2007; 18(2):206-14. *Patients already diagnosed with CKD*

16. Amato D, Alvarez-Aguilar C, Castaneda-Limones R, et al. Prevalence of chronic kidney disease in an urban Mexican population. Kidney International - Supplement 2005; (97):S11-7. *Not a randomized trial*

17. Andrassy J, Zeier M, Andrassy K. Do we need screening for thrombophilia prior to kidney transplantation? Nephrology Dialysis Transplantation 2004; 19 Suppl 4:iv64-8. *Not a randomized trial*

18. Atkins RC, Briganti EM, Zimmet PZ, et al. Association between albuminuria and proteinuria in the general population: the AusDiab Study. Nephrology Dialysis Transplantation 2003; 18(10):2170-4. *Not a randomized trial*

19. Atthobari J, Asselbergs FW, Boersma C, et al. Cost-effectiveness of screening for albuminuria with subsequent fosinopril treatment to prevent cardiovascular events: A pharmacoeconomic analysis linked to the prevention of renal and vascular endstage disease (PREVEND) study and the prevention of renal and vascular endstage disease intervention trial (PREVEND IT). Clinical Therapeutics 2006; 28(3):432-44. *Not an intervention for screening for CKD*

20. Atthobari J, Brantsma AH, Gansevoort RT, et al. The effect of statins on urinary albumin excretion and glomerular filtration rate: results from both a randomized clinical trial and an observational cohort study. Nephrology Dialysis Transplantation 2006; 21(11):3106-14. *Less than 1000 patients in study*

21. Atthobari J, Gansevoort RT, Visser ST, et al. The effect of screening for cardio-renal risk factors on drug use in the general population. British Journal of Clinical Pharmacology 2007; 64(6):810-8. *Not an intervention for screening for CKD*

22. Awai K, Imuta M, Utsunomiya D, et al. Contrast enhancement for whole-body screening using multidetector row helical CT: comparison between uniphasic and biphasic injection protocols. Radiation Medicine 2004; 22(5):303-9. *Less than 1000 patients in study*

23. Azizi M, Menard J, Peyrard S, et al. Assessment of patients' and physicians' compliance to an ACE inhibitor treatment based on urinary N-acetyl Ser-Asp-Lys-Pro determination in the Noninsulin-Dependent Diabetes, Hypertension, Microalbuminuria, Proteinuria, Cardiovascular Events, and Ramipril (DIABHYCAR) study. Diabetes Care 2006; 29(6):1331-6. *Not a randomized trial*

24. Bakris G. Inclusion of albuminuria in hypertension and heart guidelines. Kidney International - Supplement 2004; (92):S124-5. *Not a randomized trial*

25. Bakris G, Hester A, Weber M, et al. The diabetes subgroup baseline characteristics of the Avoiding Cardiovascular Events Through Combination Therapy in Patients Living With Systolic Hypertension (ACCOMPLISH) trial. J Cardiometab Syndr 2008; 3(4):229-33. *Not an intervention for screening for CKD*

26. Bakris GL, Fonseca V, Katholi RE, et al. Differential effects of beta-blockers on albuminuria in patients with type 2 diabetes. Hypertension 2005; 46(6):1309-15. *Not an intervention for screening for CKD*

27. Bang H, Mazumdar M, Newman G, et al. Screening for kidney disease in vascular patients: SCreening for Occult REnal Disease (SCORED) experience. Nephrology Dialysis Transplantation 2009; 24(8):2452-7. *Not a randomized trial*

28. Barbanel CS, Winkelman JW, Fischer GA, et al. Confirmation of the Department of Transportation criteria for a substituted urine specimen. Journal of Occupational & Environmental Medicine 2002; 44(5):407-16. *Not a randomized trial*

29. Barrett BJ, Katzberg RW, Thomsen HS, et al. Contrast-induced nephropathy in patients with chronic kidney disease undergoing computed tomography: a double-blind comparison of iodixanol and iopamidol.[Erratum appears in Invest Radiol. 2007 Feb;42(2):94 Note: Ni, Zhao-hui [added]]. Investigative Radiology 2006; 41(11):815-21. *Patients already diagnosed with CKD*

30. Baskar V, Kamalakannan D, Holland MR, et al. Uncertain clinical utility of contemporary strategies for microalbuminuria testing. Diabetes, Obesity & Metabolism 2003; 5(4):262-6. *Not a randomized trial*

31. Baxter GM, Aitchison F, Sheppard D, et al. Colour Doppler ultrasound in renal artery stenosis: intrarenal waveform analysis. British Journal of Radiology 1996; 69(825):810-5. *Not a randomized trial*

32. Beatovic S, Jaksic ED, Han RS. Measurement of renal function by calculation of fractional uptake of technetium-99m dimercaptosuccinic acid. Nucl Med Rev Cent East Eur 2004; 7(1):49-52. *Not an intervention for screening for CKD*

33. Beatty OL, Ritchie CM, Hadden DR, et al. Is a random urinary albumin concentration a useful screening test in insulin-treated diabetic patients? Irish Journal of Medical Science 1994; 163(9):406-9. *Not a randomized trial*

34. Beaulieu AJ, Gohh RY, Han H, et al. Enhanced reduction of fasting total homocysteine levels with supraphysiological versus standard multivitamin dose folic acid supplementation in renal transplant recipients. Arteriosclerosis, Thrombosis & Vascular Biology 1999; 19(12):2918-21. *Patients already diagnosed with CKD*

35. Beevers DG, Lip GY. Does non-malignant essential hypertension cause renal damage? A clinician's view. Journal of Human Hypertension 1996; 10(10):695-9. *Not a randomized trial*

36. Bellizzi V, Scalfi L, Terracciano V, et al. Early changes in bioelectrical estimates of body composition in chronic kidney disease. Journal of the American Society of Nephrology 2006; 17(5):1481-7. *Not a randomized trial*

37. Beresford TP, Blow FC, Hill E, et al. Comparison of CAGE questionnaire and computer-assisted laboratory profiles in screening for covert alcoholism. Lancet 1990; 336(8713):482-5. *Not an intervention for screening for CKD*

38. Berland LL, Koslin DB, Routh WD, et al. Renal artery stenosis: prospective evaluation of diagnosis with color duplex US compared with angiography. Work in progress. Radiology 1990; 174(2):421-3. *Not a randomized trial*

39. Berthoux P, Dejean C, Cecillon S, et al. High prevalence of hepatitis G virus (HGV) infection in renal transplantation. Nephrology Dialysis Transplantation 1998; 13(11):2909-13. *Not a randomized trial*

40. Beto JA, Bansal VK, Hart J, et al. Hemodialysis prognostic nutrition index as a predictor for morbidity and mortality in hemodialysis patients and its correlation to adequacy of dialysis. Council on Renal Nutrition National Research Question Collaborative Study Group. Journal of Renal Nutrition 1999; 9(1):2-8. *Patients already diagnosed with CKD*

41. Bobrie G, Clerson P, Menard J, et al. Masked hypertension: a systematic review. Journal of Hypertension 2008; 26(9):1715-25. *Not a randomized trial*

42. Boero R, Prodi E, Elia F, et al. How well are hypertension and albuminuria treated in type II diabetic patients? Journal of Human Hypertension 2003; 17(6):413-8. *Less than 1000 patients in study*

43. Bosmans JL, De Broe ME. Renovascular hypertension: diagnostic and therapeutic challenges. Jbr-Btr: Organe de la Societe Royale Belge de Radiologie 2004; 87(1):32-5. *Not a randomized trial*

44. Bostom AG, Carpenter MA, Kusek JW, et al. Rationale and design of the Folic Acid for Vascular Outcome Reduction In Transplantation (FAVORIT) trial. American Heart Journal 2006; 152(3):448.e1-7. *Patients already diagnosed with CKD*

45. Bostom AG, Shemin D, Gohh RY, et al. Treatment of hyperhomocysteinemia in hemodialysis patients and renal transplant recipients. Kidney International - Supplement 2001; 78:S246-52. *Patients already diagnosed with CKD*

46. Boucher BA, Coffey BC, Kuhl DA, et al. Algorithm for assessing renal dysfunction risk in critically ill trauma patients receiving aminoglycosides. American Journal of Surgery 1990; 160(5):473-80. *Not a randomized trial*

47. Bouhanick B, Berrut G, Chameau AM, et al. Predictive value of testing random urine sample to detect microalbuminuria in diabetic subjects during outpatient visit. Diabete et Metabolisme 1992; 18(1):54-8. *Less than 1000 patients in study*

48. Budde K, L Schmouder R, Nashan B, et al. Pharmacodynamics of single doses of the novel immunosuppressant FTY720 in stable renal transplant patients. American Journal of Transplantation 2003; 3(7):846-54. *Patients already diagnosed with CKD*

49. Budde RJ, Ke S, Levin VA. Activity of pp60c-src in 60 different cell lines derived from human tumors. Cancer Biochemistry Biophysics 1994; 14(3):171-5. *Not an intervention for screening for CKD*

50. Budney AJ, Hughes JR, Moore BA, et al. Marijuana abstinence effects in marijuana smokers maintained in their home environment. Archives of General Psychiatry 2001; 58(10):917-24. *Not a randomized trial*

51. Buhimschi CS, Norwitz ER, Funai E, et al. Urinary angiogenic factors cluster hypertensive disorders and identify women with severe preeclampsia. American Journal of Obstetrics & Gynecology 2005; 192(3):734-41. *Not a randomized trial*

52. Burrowes JD, Larive B, Chertow GM, et al. Self-reported appetite, hospitalization and death in haemodialysis patients: findings from the Hemodialysis (HEMO) Study. Nephrology Dialysis Transplantation 2005; 20(12):2765-74. *Patients already diagnosed with CKD*

53. Buturovic-Ponikvar J. Renal transplant artery stenosis. Nephrology Dialysis Transplantation 2003; 18 Suppl 5:v74-7. *Not a randomized trial*

54. Buxbaum J, Tagoe C, Gallo G, et al. The pathogenesis of transthyretin tissue deposition: lessons from transgenic mice. Amyloid 2003; 10 Suppl 1:2-6. *Not a randomized trial*

55. Canani LH, Costa LA, Crispim D, et al. The presence of allele D of angiotensin-converting enzyme polymorphism is associated with diabetic nephropathy in patients with less than 10 years duration of Type 2 diabetes. Diabetic Medicine 2005; 22(9):1167-72. *Not a randomized trial*

56. Cao C, Wan X, Chen Y, et al. Metabolic factors and microinflammatory state promote kidney injury in type 2 diabetes mellitus patients. Renal Failure 2009; 31(6):470-4. *Not a randomized trial*

57. Cardiel MH, Tumlin JA, Furie RA, et al. Abetimus sodium for renal flare in systemic lupus erythematosus: results of a randomized, controlled phase III trial. Arthritis & Rheumatism 2008; 58(8):2470-80. *Not an intervention for screening for CKD*

58. Carter JL, O'Riordan SE, Eaglestone GL, et al. Chronic kidney disease prevalence in a UK residential care home population. Nephrology Dialysis Transplantation 2008; 23(4):1257-64. *Not a randomized trial*

59. Cathelineau G, de Champvallins M, Bouallouche A, et al. Management of newly diagnosed non-insulin-dependent diabetes mellitus in the primary care setting: effects of 2 years of gliclazide treatment--the Diadem Study. Metabolism: Clinical & Experimental 1997; 46(12 Suppl 1):31-4. *Not a randomized trial*

60. Chadban SJ, Briganti EM, Kerr PG, et al. Prevalence of kidney damage in Australian adults: The AusDiab kidney study. Journal of the American Society of Nephrology 2003; 14(7 Suppl 2):S131-8. *Not a randomized trial*

61. Champion MC, Bending JJ, Rodger NW, et al. Conference on insulin pump therapy in diabetes. Multicenter study of effect on microvascular disease. Recruitment, Randomization, and baseline characteristics of the treatment groups. Diabetes 1985; 34 Suppl 3:13-6. *Less than 1000 patients in study*

62. Chan JC, So WY, Yeung CY, et al. Effects of structured versus usual care on renal endpoint in type 2 diabetes: the SURE study: a randomized multicenter translational study. Diabetes Care 2009; 32(6):977-82. *Not an intervention for screening for CKD*

63. Chan YL, Leung CB, Yu SC, et al. Comparison of non-breath-hold high resolution gadolinium-enhanced MRA with digital subtraction angiography in the evaluation on allograft renal artery stenosis. Clinical Radiology 2001; 56(2):127-32. *Patients already diagnosed with CKD*

64. Charytan DM, Wallentin L, Lagerqvist B, et al. Early angiography in patients with chronic kidney disease: a collaborative systematic review. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(6):1032-43. *Not an intervention for screening for CKD*

65. Chen N, Wang W, Huang Y, et al. Community-based study on CKD subjects and the associated risk factors. Nephrology Dialysis Transplantation 2009; 24(7):2117-23. *Not a randomized trial*

66. Chen Y-C, Chiu W-T, Wu M-S. Therapeutic effect of topical gamma-linolenic acid on refractory uremic pruritus. American Journal of Kidney Diseases 2006; 48(1):69-76. *Patients already diagnosed with CKD*

67. Chen Z-h, Wang G-h, Wang X-p, et al. Effects of warm-supplementing kidney yang (WSKY) capsule added on risperidone on cognition in chronic schizophrenic patients: a randomized, double-blind, placebo-controlled, multi-center clinical trial. Human Psychopharmacology 2008; 23(6):465-70. *Not an intervention for screening for CKD*

68. Cho ME, Kopp JB. HIV and the kidney: a status report after 20 years. Current HIV/AIDS Reports 2004; 1(3):109-15. *Not a randomized trial*

69. Chow FY, Briganti EM, Kerr PG, et al. Health-related quality of life in Australian adults with renal insufficiency: a population-based study. American Journal of Kidney Diseases 2003; 41(3):596-604. *Not a randomized trial*

70. Chow J, Bennett L. Pre-training assessment tool (JPAT)--a pilot study. Edtna-Erca Journal 2001; 27(1):37-41. *Not a randomized trial*

71. Christianson TJ, Bryant SC, Weymiller AJ, et al. A pen-and-paper coronary risk estimator for office use with patients with type 2 diabetes. Mayo Clin Proc 2006; 81(5):632-6. *Not a randomized trial*

72. Chumlea WC, Dwyer J, Bergen C, et al. Nutritional status assessed from anthropometric measures in the HEMO study. Journal of Renal Nutrition 2003; 13(1):31-8. *Patients already diagnosed with CKD*

73. Cohen A, Basch C. Steady state pharmacokinetics of naproxen in young and elderly healthy volunteers. Seminars in Arthritis & Rheumatism 1988; 17(3 Suppl 2):7-11. *Not an intervention for screening for CKD*

74. Cohen SD, Norris L, Acquaviva K, et al. Screening, diagnosis, and treatment of depression in patients with end-stage renal disease. Clinical Journal of The American Society of Nephrology: CJASN 2007; 2(6):1332-42. *Patients already diagnosed with CKD*

75. Col M, Ocaktan E, Ozdemir O, et al. Microalbuminuria: prevalence in hypertensives and diabetics. Acta Medica Austriaca 2004; 31(1):23-9. *Not a randomized trial*

76. Cole LA, Rinne KM, Mahajan SM, et al. Urinary screening tests for fetal Down syndrome: I. Fresh beta-core fragment. Prenatal Diagnosis 1999; 19(4):340-50. *Not an intervention for screening for CKD*

77. Collins AC, Vincent J, Newall RG, et al. An aid to the early detection and management of diabetic nephropathy: assessment of a new point of care microalbuminuria system in the diabetic clinic. Diabetic Medicine 2001; 18(11):928-32. *Less than 1000 patients in study*

78. Constantiner M, Sehgal AR, Humbert L, et al. A dipstick protein and specific gravity algorithm accurately predicts pathological proteinuria. American Journal of Kidney Diseases 2005; 45(5):833-41. *Not a randomized trial*

79. Cook JD, Hannon MW, Sr., Vo T, et al. Evaluation of freezing point depression osmolality for classifying random urine specimens defined as substituted under HHS/DOT criteria. Journal of Analytical Toxicology 2002; 26(7):424-9. *Less than 1000 patients in study*

80. Cortes-Sanabria L, Cabrera-Pivaral CE, Cueto-Manzano AM, et al. Improving care of patients with diabetes and CKD: a pilot study for a cluster-randomized trial. American Journal of Kidney Diseases 2008; 51(5):777-88. *Not an intervention for screening for CKD*

81. Craig JC, Barratt A, Cumming R, et al. Feasibility study of the early detection and treatment of renal disease by mass screening. Internal Medicine Journal 2002; 32(1-2):6-14. *Not an intervention for screening for CKD*

82. Craig KJ, Donovan K, Munnery M, et al. Identification and management of diabetic nephropathy in the diabetes clinic. Diabetes Care 2003; 26(6):1806-11. *Not a randomized trial*

83. Cueto-Manzano AM, Cortes-Sanabria L, Martinez-Ramirez HR, et al. Detection of early nephropathy in Mexican patients with type 2 diabetes mellitus. Kidney International - Supplement 2005; (97):S40-5. *Not a randomized trial*

84. Cukor D, Coplan J, Brown C, et al. Anxiety disorders in adults treated by hemodialysis: a single-center study. American Journal of Kidney Diseases 2008; 52(1):128-36. *Patients already diagnosed with CKD*

85. Curtis JJ, Barbeito R, Pirsch J, et al. Differences in bioavailability between oral cyclosporine formulations in maintenance renal transplant patients. American Journal of Kidney Diseases 1999; 34(5):869-74. *Patients already diagnosed with CKD*

86. Cusick M, Meleth AD, Agron E, et al. Associations of mortality and diabetes complications in patients with type 1 and type 2 diabetes: early treatment diabetic retinopathy study report no. 27. Diabetes Care 2005; 28(3):617-25. *Not a randomized trial*

87. Davidson MB, Wong A, Hamrahian AH, et al. Effect of spironolactone therapy on albuminuria in patients with type 2 diabetes treated with angiotensin-converting enzyme inhibitors. Endocrine Practice 2008; 14(8):985-92. *Less than 1000 patients in study*

88. Davis TM, Beilby J, Davis WA, et al. Prevalence, characteristics, and prognostic significance of HFE gene mutations in type 2 diabetes: the Fremantle Diabetes Study. Diabetes Care 2008; 31(9):1795-801. *Not a randomized trial*

89. De Cosmo S, Motterlini N, Prudente S, et al. Impact of the PPAR-gamma2 Pro12Ala polymorphism and ACE inhibitor therapy on new-onset microalbuminuria in type 2 diabetes: evidence from BENEDICT. Diabetes 2009; 58(12):2920-9. *Not a randomized trial*

90. de Silva R, Nikitin NP, Bhandari S, et al. Atherosclerotic renovascular disease in chronic heart failure: should we intervene? European Heart Journal 2005; 26(16):1596-605. *Not a randomized trial*

91. de Zeeuw D, Parving HH, Henning RH. Microalbuminuria as an early marker for cardiovascular disease. Journal of the American Society of Nephrology 2006; 17(8):2100-5. *Not a randomized trial*

92. Debatin JF, Spritzer CE, Grist TM, et al. Imaging of the renal arteries: value of MR angiography. AJR 1991; American Journal of Roentgenology. 157(5):981-90. *Less than 1000 patients in study*

93. Deepa M, Pradeepa R, Rema M, et al. The Chennai Urban Rural Epidemiology Study (CURES)--study design and methodology (urban component) (CURES-I). J Assoc Physicians India 2003; 51:863-70. *Not a randomized trial*

94. D'Elia JA, Weinrauch LA, Gleason RE, et al. Preliminary screening of the relationship of serum lipids to survival of chronic dialysis patients. Renal Failure 1993; 15(2):203-9. *Patients already diagnosed with CKD*

95. Dennen P, Douglas IS, Anderson R. Acute kidney injury in the intensive care unit: an update and primer for the intensivist. Critical Care Medicine; 38(1):261-75. *Not a randomized trial*

96. Desberg AL, Paushter DM, Lammert GK, et al. Renal artery stenosis: evaluation with color Doppler flow imaging. Radiology 1990; 177(3):749-53. *Less than 1000 patients in study*

97. Diaz VA, Mainous AG, 3rd, Carek PJ, et al. The association of vitamin D deficiency and insufficiency with diabetic nephropathy: implications for health disparities. J Am Board Fam Med 2009; 22(5):521-7. *Not a randomized trial*

98. Dieker JW, Sun Y-J, Jacobs CW, et al. Mimotopes for lupus-derived anti-DNA and nucleosome-specific autoantibodies selected from random peptide phage display libraries: facts and follies. Journal of Immunological Methods 2005; 296(1-2):83-93. *Not a randomized trial*

99. Doig JK, MacFadyen RJ, Sweet CS, et al. Haemodynamic and renal responses to oral losartan potassium during salt depletion or salt repletion in normal human volunteers. Journal of Cardiovascular Pharmacology 1995; 25(4):511-7. *Not an intervention for screening for CKD*

100. Dunn PJ, Jury DR. Random urine albumin:creatinine ratio measurements as a screening test for diabetic microalbuminuria--a five year follow up. New Zealand Medical Journal 1990; 103(902):562-4. *Not a randomized trial*

101. Ejerblad E, Fored CM, Lindblad P, et al. Obesity and risk for chronic renal failure. Journal of the American Society of Nephrology 2006; 17(6):1695-702. *Not a randomized trial*

102. Eleftheriadis T, Tsiaga P, Antoniadi G, et al. The value of serum antilipoarabinomannan antibody detection in the diagnosis of latent tuberculosis in hemodialysis patients. American Journal of Kidney Diseases 2005; 46(4):706-12. *Patients already diagnosed with CKD*

103. Elkohen M, Beregi JP, Deklunder G, et al. A prospective study of helical computed tomography angiography versus angiography for the detection of renal artery stenoses in hypertensive patients. Journal of Hypertension 1996; 14(4):525-8. *Less than 1000 patients in study*

104. Emamian SA, Nielsen MB, Pedersen JF. Can dipstick screening for hematuria identify individuals with structural renal abnormalities? A sonographic evaluation. Scandinavian Journal of Urology & Nephrology 1996; 30(1):25-7. *Not a randomized trial*

105. Ensom MHH, Chong G, Zhou D, et al. Estradiol in premenstrual asthma: a double-blind, randomized, placebo-controlled, crossover study. Pharmacotherapy 2003; 23(5):561-71. *Not an intervention for screening for CKD*

106. Escobedo J, Rana JS, Lombardero MS, et al. Association between albuminuria and duration of diabetes and myocardial dysfunction and peripheral arterial disease among patients with stable coronary artery disease in the BARI 2D study. Mayo Clin Proc 2010; 85(1):41-6. *Not a randomized trial*

107. Etard JF, Borel E. Epidemiological survey of urinary schistosomiasis in southeastern Mauritania. Tropical Medicine & Parasitology 1987; 38(1):27-30. *Not an intervention for screening for CKD*

108. Ethier J, Mendelssohn DC, Elder SJ, et al. Vascular access use and outcomes: an international perspective from the Dialysis Outcomes and Practice Patterns Study. Nephrology Dialysis Transplantation 2008; 23(10):3219-26. *Not a randomized trial*

109. Ewald B, Attia J. Which test to detect microalbuminuria in diabetic patients? A systematic review. Australian Family Physician 2004; 33(7):565-7. *Not a randomized trial*

110. Fabian J, Katz I, Gerntholtz T, et al. Chronic kidney disease in human immunodeficiency virus infection. Panminerva Medica 2007; 49(2):51-66. *Not a randomized trial*

111. Fagnani F, Souchet T, Labed D, et al. Management of hypertension and screening of renal complications by GPs in diabetic type 2 patients (France--2001). Diabetes & Metabolism 2003; 29(1):58-64. *Not a randomized trial*

112. Fava S, Azzopardi J, Hattersley AT, et al. Increased prevalence of proteinuria in diabetic sibs of proteinuric type 2 diabetic subjects. American Journal of Kidney Diseases 2000; 35(4):708-12. *Less than 1000 patients in study*

113. Fellstrom B, Holdaas H, Jardine AG, et al. Effect of rosuvastatin on outcomes in chronic haemodialysis patients: baseline data from the AURORA study. Kidney & Blood Pressure Research 2007; 30(5):314-22. *Patients already diagnosed with CKD*

114. Ferris M, Shoham DA, Pierre-Louis M, et al. High prevalence of unlabeled chronic kidney disease among inpatients at a tertiary-care hospital. American Journal of the Medical Sciences 2009; 337(2):93-7. *Not a randomized trial*

115. Fischbacher CM, Bhopal R, Rutter MK, et al. Microalbuminuria is more frequent in South Asian than in European origin populations: a comparative study in Newcastle, UK. Diabetic Medicine 2003; 20(1):31-6. *Not a randomized trial*

116. Fishbane S, Shapiro WB, Corry DB, et al. Cinacalcet HCl and concurrent low-dose vitamin D improves treatment of secondary hyperparathyroidism in dialysis patients compared with vitamin D alone: the ACHIEVE study results. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(6):1718-25. *Patients already diagnosed with CKD*

117. Flack JM, Grimm RH, Jr., Staffileno BA, et al. New salt-sensitivity metrics: variability-adjusted blood pressure change and the urinary sodium-to-creatinine ratio. Ethnicity & Disease 2002; 12(1):10-9. *Less than 1000 patients in study*

118. Fored CM, Nise G, Ejerblad E, et al. Absence of association between organic solvent exposure and risk of chronic renal failure: a nationwide population-based case-control study. Journal of the American Society of Nephrology 2004; 15(1):180-6. *Not a randomized trial*

119. Frankenfield DL, Rocco MV, Roman SH, et al. Survival advantage for adult Hispanic hemodialysis patients? Findings from the end-stage renal disease clinical performance measures project. Journal of the American Society of Nephrology 2003; 14(1):180-6. *Patients already diagnosed with CKD*

120. Freedman BI, Hicks PJ, Sale MM, et al. A leucine repeat in the carnosinase gene CNDP1 is associated with diabetic end-stage renal disease in European Americans. Nephrology Dialysis Transplantation 2007; 22(4):1131-5. *Not a randomized trial*

121. Freeman RB, Paya C, Pescovitz MD, et al. Risk factors for cytomegalovirus viremia and disease developing after prophylaxis in high-risk solid-organ transplant recipients. Transplantation 2004; 78(12):1765-73. *Not an intervention for screening for CKD*

122. Freemont AJ, Hoyland JA, Denton J, et al. The effects of lanthanum carbonate and calcium carbonate on bone abnormalities in patients with end-stage renal disease. Clinical Nephrology 2005; 64(6):428-37. *Patients already diagnosed with CKD*

123. Fujii H, Nakamura S, Kuroda S, et al. Relationship between renal artery stenosis and intrarenal damage in autopsy subjects with stroke. Nephrology Dialysis Transplantation 2006; 21(1):113-9. *Not a randomized trial*

124. Galassi A, Brancaccio D, Cozzolino M, et al. Awareness of hypertension and proteinuria in randomly selected patients in 11 Italian cities. A 2005 report of the National Kidney Foundation of Italy. Journal of Clinical Hypertension 2009; 11(3):138-43. *Not a randomized trial*

125. Gallant JE, Winston JA, DeJesus E, et al. The 3-year renal safety of a tenofovir disoproxil fumarate vs. a thymidine analogue-containing regimen in antiretroviral-naive patients. AIDS 2008; 22(16):2155-63. *Not an intervention for screening for CKD*

126. Gansevoort RT, Verhave JC, Hillege HL, et al. The validity of screening based on spot morning urine samples to detect subjects with microalbuminuria in the general population. Kidney International - Supplement 2005; (94):S28-35. *Not a randomized trial*

127. Garcia-Tsao G, Lim JK, Members of Veterans Affairs Hepatitis CRCP. Management and treatment of patients with cirrhosis and portal hypertension: recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program. American Journal of Gastroenterology 2009; 104(7):1802-29. *Not a randomized trial*

128. Garg AX, Kiberd BA, Clark WF, et al. Albuminuria and renal insufficiency prevalence guides population screening: results from the NHANES III. Kidney International 2002; 61(6):2165-75. *Not a randomized trial*

129. Gatling W, Knight C, Hill RD. Screening for early diabetic nephropathy: which sample to detect microalbuminuria? Diabetic Medicine 1985; 2(6):451-5. *Not a randomized trial*

130. Gatling W, Knight C, Mullee MA, et al. Microalbuminuria in diabetes: a population study of the prevalence and an assessment of three screening tests. Diabetic Medicine 1988; 5(4):343-7. *Not a randomized trial*

131. Gazis A, Page SR. Microalbuminuria screening in the UK: are we meeting European standards? Diabetic Medicine 1996; 13(8):764-7. *Not a randomized trial*

132. George S, Braithwaite RA. An investigation into the extent of possible dilution of specimens received for urinary drugs of abuse screening. Addiction 1995; 90(7):967-70. *Not a randomized trial*

133. Gerber LM, Johnston K, Alderman MH. Assessment of a new dipstick test in screening for microalbuminuria in patients with hypertension. American Journal of Hypertension 1998; 11(11 Pt 1):1321-7. *Not a randomized trial*

134. Ghahramani N, Shadrou S, Hollenbeak C. A systematic review of continuous renal replacement therapy and intermittent haemodialysis in management of patients with acute renal failure. Nephrology 2008; 13(7):570-8. *Patients already diagnosed with CKD*

135. Ghandour H, Bagley PJ, Shemin D, et al. Distribution of plasma folate forms in hemodialysis patients receiving high daily doses of L-folinic or folic acid. Kidney International 2002; 62(6):2246-9. *Patients already diagnosed with CKD*

136. Giordano M, Tirelli P, Ciarambino T, et al. Screening of depressive symptoms in young-old hemodialysis patients: relationship between Beck Depression Inventory and 15-item Geriatric Depression Scale. Nephron 2007; 106(4):c187-92. *Patients already diagnosed with CKD*

137. Giugliani R, Ferrari I, Greene LJ. An evaluation of four methods for the detection of heterozygous cystinuria. Clinica Chimica Acta 1987; 164(2):227-33. *Not a randomized trial*

138. Go RC, Desmond R, Roseman JM, et al. Prevalence and risk factors of microalbuminuria in a cohort of African-American women with gestational diabetes. Diabetes Care 2001; 24(10):1764-9. *Not a randomized trial*

139. Gok MA, Shenton BK, Buckley PE, et al. How to improve the quality of kidneys from non-heart-beating donors: a randomised controlled trial of thrombolysis in non-heart-beating donors. Transplantation 2003; 76(12):1714-9. *Not an intervention for screening for CKD*

140. Golan L, Birkmeyer JD, Welch HG. The cost-effectiveness of treating all patients with type 2 diabetes with angiotensin-converting enzyme inhibitors. Annals of Internal Medicine 1999; 131(9):660-7. *Not an intervention for screening for CKD*

141. Goldsmith DJ, Covic A. Coronary artery disease in uremia: Etiology, diagnosis, and therapy. Kidney International 2001; 60(6):2059-78. *Not a randomized trial*

142. Goldsmith DJ, Reidy J, Scoble J. Renal arterial intervention and angiotensin blockade in atherosclerotic nephropathy. American Journal of Kidney Diseases 2000; 36(4):837-43. *Not a randomized trial*

143. Groetzner J, Wittwer T, Kaczmarek I, et al. Conversion to sirolimus and mycophenolate can attenuate the progression of bronchiolitis obliterans syndrome and improves renal function after lung transplantation. Transplantation 2006; 81(3):355-60. *Not a randomized trial*

144. Gross JL, Zelmanovitz T, Oliveira J, et al. Screening for diabetic nephropathy: is measurement of urinary albumin-to-creatinine ratio worthwhile? Diabetes Care 1999; 22(9):1599-600. *Less than 1000 patients in study*

145. Group B. The BErgamo NEphrologic DIabetes Complications Trial (BENEDICT): design and baseline characteristics. Controlled Clinical Trials 2003; 24(4):442-61. *Not an intervention for screening for CKD*

146. Gupta R, Birnbaum Y, Uretsky BF. The renal patient with coronary artery disease: current concepts and dilemmas. Journal of the American College of Cardiology 2004; 44(7):1343-53. *Not a randomized trial*

147. Hall AM, Edwards SG, Lapsley M, et al. Subclinical tubular injury in HIV-infected individuals on antiretroviral therapy: a cross-sectional analysis. American Journal of Kidney Diseases 2009; 54(6):1034-42. *Not a randomized trial*

148. Hallan H, Romundstad S, Kvenild K, et al. Microalbuminuria in diabetic and hypertensive patients and the general population--consequences of various diagnostic criteria--the Nord-Trondelag Health Study (HUNT). Scandinavian Journal of Urology & Nephrology 2003; 37(2):151-8. *Not a randomized trial*

149. Hallett M, Burden S, Stewart D, et al. Sleep apnea in end-stage renal disease patients on hemodialysis and continuous ambulatory peritoneal dialysis. ASAIO Journal 1995; 41(3):M435-41. *Patients already diagnosed with CKD*

150. Hara N, Koike H, Ogino S, et al. Application of serum PSA to identify acute bacterial prostatitis in patients with fever of unknown origin or symptoms of acute pyelonephritis. Prostate 2004; 60(4):282-8. *Not a randomized trial*

151. Harding GKM, Zhanel GG, Nicolle LE, et al. Antimicrobial treatment in diabetic women with asymptomatic bacteriuria. New England Journal of Medicine 2002; 347(20):1576-83. *Not an intervention for screening for CKD*

152. Haug K, Bakke A, Daae LN, et al. Screening for hematuria, glucosuria and proteinuria in people aged 55-64. Technical, clinical and cost-benefit experience from a pilot study. Scandinavian Journal of Primary Health Care 1985; 3(1):31-4. *Not a randomized trial*

153. Herget-Rosenthal S, Marggraf G, Husing J, et al. Early detection of acute renal failure by serum cystatin C. Kidney International 2004; 66(3):1115-22. *Not an intervention for screening for CKD*

154. Hindmarsh JT. Microalbuminuria. Clinics in Laboratory Medicine 1988; 8(3):611-6. *Not a randomized trial*

155. Hor T, Baldwin D. Urinary albumin excretion in patients with diabetes after renal transplantation. Transplantation Proceedings 2006; 38(9):2879-82. *Not a randomized trial*

156. Howey JE, Browning MC, Fraser CG. Biologic variation of urinary albumin: consequences for analysis, specimen collection, interpretation of results, and screening programs. American Journal of Kidney Diseases 1989; 13(1):35-7. *Not a randomized trial*

157. Hoy WE, Wang Z, Baker PRA, et al. Reduction in natural death and renal failure from a systematic screening and treatment program in an Australian Aboriginal community. Kidney International - Supplement 2003; (83):S66-73. *Not a randomized trial*

158. Huestis MA, Cone EJ. Differentiating new marijuana use from residual drug excretion in occasional marijuana users. Journal of Analytical Toxicology 1998; 22(6):445-54. *Not an intervention for screening for CKD*

159. Hyndman ME, Manns BJ, Snyder FF, et al. Vitamin B12 decreases, but does not normalize, homocysteine and methylmalonic acid in end-stage renal disease: a link with glycine metabolism and possible explanation of hyperhomocysteinemia in end-stage renal disease. Metabolism: Clinical & Experimental 2003; 52(2):168-72. *Patients already diagnosed with CKD*

160. Incerti J, Zelmanovitz T, Camargo JL, et al. Evaluation of tests for microalbuminuria screening in patients with diabetes. Nephrology Dialysis Transplantation 2005; 20(11):2402-7. *Not a randomized trial*

161. Investigators RRTT, Bellomo R, Cass A, et al. Screening and study enrolment in the Randomized Evaluation of Normal vs. Augmented Level (RENAL) Replacement Therapy Trial. Blood Purification 2009; 27(2):199-205. *Not an intervention for screening for CKD*

162. Iso H, Shimamoto T, Yokota K, et al. Community-based education classes for hypertension control. A 1.5-year randomized controlled trial. Hypertension 1996; 27(4):968-74. *Not an intervention for screening for CKD*

163. Izzedine H, Hulot JS, Vittecoq D, et al. Long-term renal safety of tenofovir disoproxil fumarate in antiretroviral-naive HIV-1-infected patients. Data from a double-blind randomized active-controlled multicentre study. Nephrology Dialysis Transplantation 2005; 20(4):743-6. *Not an intervention for screening for CKD*

164. Jafar TH, Qadri Z, Hashmi S. Prevalence of microalbuminuria and associated electrocardiographic abnormalities in an Indo-Asian population. Nephrology Dialysis Transplantation 2009; 24(7):2111-6. *Not a randomized trial*

165. James MA, Fotherby MD, Potter JF. Screening tests for microalbuminuria in non-diabetic elderly subjects and their relation to blood pressure. Clinical Science 1995; 88(2):185-90. *Not a randomized trial*

166. Jansen JJ, Maassen JA, van der Woude FJ, et al. Mutation in mitochondrial tRNA(Leu(UUR)) gene associated with progressive kidney disease. Journal of the American Society of Nephrology 1997; 8(7):1118-24. *Not a randomized trial*

167. Johnson CA, McCarthy J, Bailie GR, et al. Analysis of renal bone disease treatment in dialysis patients. American Journal of Kidney Diseases 2002; 39(6):1270-7. *Not a randomized trial*

168. Johnson RK, Mortimer AJ. Routine pre-operative blood testing: is it necessary? Anaesthesia 2002; 57(9):914-7. *Not an intervention for screening for CKD*

169. Juarez FJ, Barrios Y, Cano L, et al. A randomized trial comparing two corticosteroid regimens combined with mycophenolate mofetil and cyclosporine for prevention of acute renal allograft rejection. Transplantation Proceedings 2006; 38(9):2866-8. *Patients already diagnosed with CKD*

170. Judge JS, Low V, Gajraj H, et al. The value of technetium-99M renography for the detection of renal artery stenosis in patients with aortic and lower limb vascular disease. Australian & New Zealand Journal of Surgery 1992; 62(4):261-5. *Not a randomized trial*

171. Jurkovitz C, Franch H, Shoham D, et al. Family members of patients treated for ESRD have high rates of undetected kidney disease. American Journal of Kidney Diseases 2002; 40(6):1173-8. *Not a randomized trial*

172. Justesen TI, Petersen JLA, Ekbom P, et al. Albumin-to-creatinine ratio in random urine samples might replace 24-h urine collections in screening for micro- and macroalbuminuria in pregnant woman with type 1 diabetes. Diabetes Care 2006; 29(4):924-5. *Not a randomized trial*

173. Kale K, Sawant S. Clinical significance and evaluation of proteinuria in NIDDM patients. Indian Journal of Medical Sciences 1999; 53(3):103-7. *Not a randomized trial*

174. Kapila K, Nampoory MRN, Johny KV, et al. Role of urinary cytology in detecting human polyoma bk virus in kidney transplant recipients. A preliminary report. Medical Principles & Practice 2007; 16(3):237-9. *Not a randomized trial*

175. Karaminia R, Tavallaii SA, Lorgard-Dezfuli-Nejad M, et al. Anxiety and depression: a comparison between renal transplant recipients and hemodialysis patients. Transplantation Proceedings 2007; 39(4):1082-4. *Patients already diagnosed with CKD*

176. Kelley DE, Bidot P, Freedman Z, et al. Efficacy and safety of acarbose in insulin-treated patients with type 2 diabetes. Diabetes Care 1998; 21(12):2056-61. *Not an intervention for screening for CKD*

177. Kimmel PL, Cukor D, Cohen SD, et al. Depression in end-stage renal disease patients: a critical review. Advances in Chronic Kidney Disease 2007; 14(4):328-34. *Not a randomized trial*

178. King CH, Wiper DW, 3rd, De Stigter KV, et al. Dose-finding study for praziquantel therapy of Schistosoma haematobium in Coast Province, Kenya. American Journal of Tropical Medicine & Hygiene 1989; 40(5):507-13. *Not an intervention for screening for CKD*

179. Kliewer MA, Tupler RH, Carroll BA, et al. Renal artery stenosis: analysis of Doppler waveform parameters and tardus-parvus pattern. Radiology 1993; 189(3):779-87. *Not a randomized trial*

180. Kocvara R, Plasgura P, Petrik A, et al. A prospective study of nonmedical prophylaxis after a first kidney stone. BJU International 1999; 84(4):393-8. *Not an intervention for screening for CKD*

181. Kouidi EJ, Grekas DM, Deligiannis AP. Effects of exercise training on noninvasive cardiac measures in patients undergoing long-term hemodialysis: a randomized controlled trial. American Journal of Kidney Diseases 2009; 54(3):511-21. *Patients already diagnosed with CKD*

182. Kovarik JM, Hartmann S, Figueiredo J, et al. Effect of food on everolimus absorption: quantification in healthy subjects and a confirmatory screening in patients with renal transplants. Pharmacotherapy 2002; 22(2):154-9. *Not an intervention for screening for CKD*

183. Kovarik JM, Moore R, Wolf P, et al. Screening for basiliximab exposure-response relationships in renal allotransplantation. Clinical Transplantation 1999; 13(1 Pt 1):32-8. *Patients already diagnosed with CKD*

184. Kristal B, Shasha SM, Labin L, et al. Estimation of quantitative proteinuria by using the protein-creatinine ratio in random urine samples. American Journal of Nephrology 1988; 8(3):198-203. *Not a randomized trial*

185. Krol E, Rutkowski B, Czarniak P, et al. Early detection of chronic kidney disease: results of the PolNef study. American Journal of Nephrology 2009; 29(3):264-73. *Not a randomized trial*

186. Kyle PM, Campbell S, Buckley D, et al. A comparison of the inactive urinary kallikrein:creatinine ratio and the angiotensin sensitivity test for the prediction of pre-eclampsia. British Journal of Obstetrics & Gynaecology 1996; 103(10):981-7. *Not an intervention for screening for CKD*

187. Lafolie P, Beck O, Blennow G, et al. Importance of creatinine analyses of urine when screening for abused drugs. Clinical Chemistry 1991; 37(11):1927-31. *Not an intervention for screening for CKD*

188. Lauritzen T, Christiansen JS, Brock A, et al. Repeated screening for albumin-creatinine ratio in an unselected population. The Ebeltoft Health Promotion Study, a randomized, population-based intervention trial on health test and health conversations with general practitioners. Journal of Diabetes & its Complications 1994; 8(3):146-9. *Not an intervention for screening for CKD*

189. Laville M, Anaemia CiDt. New strategies in anaemia management: ACORD (Anaemia CORrection in Diabetes) trial. Acta Diabetologica 2004; 41 Suppl 1:S18-22. *Not an intervention for screening for CKD*

190. Lawrie AS, McDonald SJ, Purdy G, et al. Prothrombin time derived fibrinogen determination on Sysmex CA-6000. Journal of Clinical Pathology 1998; 51(6):462-6. *Not an intervention for screening for CKD*

191. Leanos-Miranda A, Marquez-Acosta J, Romero-Arauz F, et al. Protein:creatinine ratio in random urine samples is a reliable marker of increased 24-hour protein excretion in hospitalized women with hypertensive disorders of pregnancy. Clinical Chemistry 2007; 53(9):1623-8. *Not a randomized trial*

192. Leedman PJ, Nankervis A, Goodwin M, et al. Assessment of the Albuscreen microalbuminuria kit in diabetic outpatients. Medical Journal of Australia 1987; 147(6):285-6. *Not a randomized trial*

193. Lehmann R, Borovicka J, Kunz P, et al. Evaluation of delayed gastric emptying in diabetic patients with autonomic neuropathy by a new magnetic resonance imaging technique and radio-opaque markers. Diabetes Care 1996; 19(10):1075-82. *Not an intervention for screening for CKD*

194. Leong SO, Lui KF, Ng WY, et al. The use of semi-quantitative urine test-strip (Micral Test) for microalbuminuria screening in patients with diabetes mellitus. Singapore Medical Journal 1998; 39(3):101-3. *Not a randomized trial*

195. Lewis EJ, Hunsicker LG, Rodby RA, et al. A clinical trial in type 2 diabetic nephropathy. American Journal of Kidney Diseases 2001; 38(4 Suppl 1):S191-4. *Patients already diagnosed with CKD*

196. Lewis WH, Yeger H, Bonetta L, et al. Homozygous deletion of a DNA marker from chromosome 11p13 in sporadic Wilms tumor. Genomics 1988; 3(1):25-31. *Not a randomized trial*

197. Lou HX, Vathsala A. Conversion from mycophenolate mofetil to azathioprine in high-risk renal allograft recipients on cyclosporine-based immunosuppression. Transplantation Proceedings 2004; 36(7):2090-1. *Patients already diagnosed with CKD*

198. Lu B, Song X, Dong X, et al. High prevalence of chronic kidney disease in population-based patients diagnosed with type 2 diabetes in downtown Shanghai. Journal of Diabetes & its Complications 2008; 22(2):96-103. *Not a randomized trial*

199. Lucas P, Blome S, Roche J. Intra-renal Doppler wave-form analysis as a screening test for renal artery stenosis. Australasian Radiology 1996; 40(3):276-82. *Not an intervention for screening for CKD*

200. Lum G. How effective are screening tests for microalbuminuria in random urine specimens? Annals of Clinical & Laboratory Science 2000; 30(4):406-11. *Not a randomized trial*

201. Macdougall IC, Matcham J, Gray SJ, et al. Correction of anaemia with darbepoetin alfa in patients with chronic kidney disease receiving dialysis. Nephrology Dialysis Transplantation 2003; 18(3):576-81. *Patients already diagnosed with CKD*

202. Malaguarnera M, Ferlito L, Gulizia G, et al. Use of interleukin-2 in advanced renal carcinoma: meta-analysis and review of the literature. European Journal of Clinical Pharmacology 2001; 57(4):267-73. *Not an intervention for screening for CKD*

203. Malik J, Slavikova M, Svobodova J, et al. Regular ultrasonographic screening significantly prolongs patency of PTFE grafts. Kidney International 2005; 67(4):1554-8. *Not an intervention for screening for CKD*

204. Malleson PN, Lockitch G, Mackinnon M, et al. Renal disease in chronic arthritis of childhood. A study of urinary N-acetyl-beta-glucosaminidase and beta 2-microglobulin excretion. Arthritis & Rheumatism 1990; 33(10):1560-6. *Not adult population*

205. Marcus J, Sarnak MJ, Menon V. Homocysteine lowering and cardiovascular disease risk: lost in translation. Canadian Journal of Cardiology 2007; 23(9):707-10. *Not a randomized trial*

206. Marshall SM. Screening for microalbuminuria: which measurement? Diabetic Medicine 1991; 8(8):706-11. *Not a randomized trial*

207. Matinlauri IH, Kyllonen LEJ, Eklund BH, et al. Weak humoral posttransplant alloresponse after a well-HLA-matched cadaveric kidney transplantation. Transplantation 2004; 78(2):198-204. *Patients already diagnosed with CKD*

208. McClellan WM, Ramirez SPB, Jurkovitz C. Screening for chronic kidney disease: unresolved issues. Journal of the American Society of Nephrology 2003; 14(7 Suppl 2):S81-7. *Not a randomized trial*

209. McCullough PA, Li S, Jurkovitz CT, et al. CKD and cardiovascular disease in screened high-risk volunteer and general populations: the Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES) 1999-2004. American Journal of Kidney Diseases 2008; 51(4 Suppl 2):S38-45. *Not a randomized trial*

210. McInnes GT, Semple PF. Hypertension: investigation, assessment and diagnosis. British Medical Bulletin 1994; 50(2):443-59. *Not a randomized trial*

211. McParland P, Pearce JM, Chamberlain GV. Doppler ultrasound and aspirin in recognition and prevention of pregnancy-induced hypertension. Lancet 1990; 335(8705):1552-5. *Not an intervention for screening for CKD*

212. Moore RR, Jr., Hirata-Dulas CA, Kasiske BL. Use of urine specific gravity to improve screening for albuminuria. Kidney International 1997; 52(1):240-3. *Not a randomized trial*

213. Morgenstern BZ, Butani L, Wollan P, et al. Validity of protein-osmolality versus protein-creatinine ratios in the estimation of quantitative proteinuria from random samples of urine in children. American Journal of Kidney Diseases 2003; 41(4):760-6. *Not adult population*

214. Mori S, Satoh T, Koide H, et al. Inhibition of Ras/Raf interaction by anti-oncogenic mutants of neurofibromin, the neurofibromatosis type 1 (NF1) gene product, in cell-free systems. Journal of Biological Chemistry 1995; 270(48):28834-8. *Not an intervention for screening for CKD*

215. Mori TA, Vandongen R, Masarei JR. Fish oil-induced changes in apolipoproteins in IDDM subjects. Diabetes Care 1990; 13(7):725-32. *Not an intervention for screening for CKD*

216. Mudun A, Falay O, Eryilmaz A, et al. Can exercise renography be an alternative to ACE inhibitor renography in hypertensive patients who are suspicious for renal artery stenosis? Clinical Nuclear Medicine 2004; 29(1):27-34. *Not a randomized trial*

217. Nakao N, Yoshimura A, Morita H, et al. Combination treatment of angiotensin-II receptor blocker and angiotensin-converting-enzyme inhibitor in non-diabetic renal disease (COOPERATE): a randomised controlled trial.[Erratum appears in Lancet. 2003 Apr 5;361(9364):1230].[Retraction in Lancet. 2009 Oct 10;374(9697):1226; PMID: 19819378]. Lancet 2003; 361(9352):117-24. *Less than 1000 patients in study*

218. Nankivell BJ, Chapman JR. The significance of subclinical rejection and the value of protocol biopsies. American Journal of Transplantation 2006; 6(9):2006-12. *Patients already diagnosed with CKD*

219. Nathan DM, Zinman B, Cleary PA, et al. Modern-day clinical course of type 1 diabetes mellitus after 30 years' duration: the diabetes control and complications trial/epidemiology of diabetes interventions and complications and Pittsburgh epidemiology of diabetes complications experience (1983-2005). Arch Intern Med 2009; 169(14):1307-16. *Not a randomized trial*

220. Newman DJ, Mattock MB, Dawnay ABS, et al. Systematic review on urine albumin testing for early detection of diabetic complications. Health Technology Assessment 2005; 9(30):iii-vi, xiii-163. *Not a randomized trial*

221. Ng LC, Teng LC, Ng ML, et al. Microalbuminuria measurements by two in-house ELISA methods. Malaysian Journal of Pathology 2000; 22(2):73-8. *Not a randomized trial*

222. O'Connor PJ, Spann SJ, Woolf SH. Care of adults with type 2 diabetes mellitus. A review of the evidence. Journal of Family Practice 1998; 47(5 Suppl):S13-22. *Not an intervention for screening for CKD*

223. Ogawa H, Xu FH, Uebaba K, et al. Antioxidative potentiality of a Kampo formulation measured by an ex vivo study. Journal of Alternative & Complementary Medicine 2009; 15(3):267-74. *Not an intervention for screening for CKD*

224. Ohmit SE, Flack JM, Peters RM, et al. Longitudinal Study of the National Kidney Foundation's (NKF) Kidney Early Evaluation Program (KEEP). Journal of the American Society of Nephrology 2003; 14(7 Suppl 2):S117-21. *Not a randomized trial*

225. Orakzai N, Hanbury DC, Farrington K. Screening for biochemical abnormalities in urolithiasis patients. Journal of Ayub Medical College, Abbottabad: JAMC 2004; 16(2):60-3. *Not a randomized trial*

226. Palmer AJ, Valentine WJ, Chen R, et al. A health economic analysis of screening and optimal treatment of nephropathy in patients with type 2 diabetes and hypertension in the USA. Nephrology Dialysis Transplantation 2008; 23(4):1216-23. *Not a randomized trial*

227. Paranjape SB, Thibonnier M. Development and therapeutic indications of orally-active non-peptide vasopressin receptor antagonists. Expert Opinion on Investigational Drugs 2001; 10(5):825-34. *Not a randomized trial*

228. Parikh CR, Gyamlani GG, Carvounis CP. Screening for microalbuminuria simplified by urine specific gravity. American Journal of Nephrology 2002; 22(4):315-9. *Less than 1000 patients in study*

229. Parving HH. Is antihypertensive treatment the same for NIDDM and IDDM patients? Diabetes Research & Clinical Practice 1998; 39 Suppl:S43-7. *Not a randomized trial*

230. Parving HH. Benefits and cost of antihypertensive treatment in incipient and overt diabetic nephropathy. Journal of Hypertension - Supplement 1998; 16(1):S99-101. *Not a randomized trial*

231. Parving HH, Rossing P. The use of antihypertensive agents in prevention and treatment of diabetic nephropathy. Current Opinion in Nephrology & Hypertension 1994; 3(3):292-300. *Not a randomized trial*

232. Pegoraro A, Singh A, Bakir AA, et al. Simplified screening for microalbuminuria. Annals of Internal Medicine 1997; 127(9):817-9. *Not a randomized trial*

233. Perroud B, Lee J, Valkova N, et al. Pathway analysis of kidney cancer using proteomics and metabolic profiling. Molecular Cancer 2006; 5:64. *Not an intervention for screening for CKD*

234. Persky AM, Ng C, Song MH, et al. Comparison of the acute pharmacodynamic responses after single doses of ephedrine or sibutramine in healthy, overweight volunteers. International Journal of Clinical Pharmacology & Therapeutics 2004; 42(8):442-8. *Not an intervention for screening for CKD*

235. Petersson B, Kristenson H, Trell E, et al. Screening and intervention for alcohol-related disease in middle-aged men: the Malmo Preventive Programme. Ciba Foundation Symposium 1985; 110:143-63. *Not an intervention for screening for CKD*

236. Pfab T, Franz U, Herfeld F, et al. Rapid immunochromatographic strip test for the detection of albuminuria and brief literature review on albuminuria screening. European Journal of Medical Research 2006; 11(1):3-6. *Not a randomized trial*

237. Phillips RA, Faulkner M, Gassman J, et al. Recruitment of African Americans with chronic renal insufficiency into a multicenter clinical trial: the african american study of kidney disease and hypertension. Journal of Clinical Hypertension 2004; 6(8):430-6. *Not an intervention for screening for CKD*

238. Plestina S, Stavljenic A, Ceovic S, et al. Haematological features of the population of the area of Croatia, Yugoslavia, endemic for Balkan nephropathy. IARC Scientific Publications 1991; (115):43-6. *Not a randomized trial*

239. Polkinghorne KR, Lau KKP, Saunder A, et al. Does monthly native arteriovenous fistula blood-flow surveillance detect significant stenosis--a randomized controlled trial. Nephrology Dialysis Transplantation 2006; 21(9):2498-506. *Not an intervention for screening for CKD*

240. Postma CT, van Aalen J, de Boo T, et al. Doppler ultrasound scanning in the detection of renal artery stenosis in hypertensive patients. British Journal of Radiology 1992; 65(778):857-60. *Not a randomized trial*

241. Prodjosudjadi W, Suhardjono, Suwitra K, et al. Detection and prevention of chronic kidney disease in Indonesia: initial community screening. Nephrology 2009; 14(7):669-74. *Not a randomized trial*

242. Pugia MJ, Lott JA, Luke KE, et al. Comparison of instrument-read dipsticks for albumin and creatinine in urine with visual results and quantitative methods. Journal of Clinical Laboratory Analysis 1998; 12(5):280-4. *Not a randomized trial*

243. Rabindranath KS, Butler JA, Macleod AM, et al. Physical measures for treating depression in dialysis patients. Cochrane Database of Systematic Reviews 2005; (2):CD004541. *Patients already diagnosed with CKD*

244. Ralston SH, Caine N, Richards I, et al. Screening for proteinuria in a rheumatology clinic: comparison of dipstick testing, 24 hour urine quantitative protein, and protein/creatinine ratio in random urine samples. Annals of the Rheumatic Diseases 1988; 47(9):759-63. *Not an intervention for screening for CKD*

245. Ravikovich E, Messersmith T, Mick G, et al. Effect of oral fluid intake on urinary albumin excretion in diabetes mellitus. Journal of Diabetes & its Complications 2002; 16(4):310-2. *Not a randomized trial*

246. Reach I, Luong N, Chastang C, et al. Dose effect relationship of reviparin in chronic hemodialysis: a crossover study versus nadroparin. Artificial Organs 2001; 25(7):591-5. *Not an intervention for screening for CKD*

247. Reddy PP, Mandell J. Prenatal diagnosis. Therapeutic implications. Urologic Clinics of North America 1998; 25(2):171-80. *Not adult population*

248. Reeves JH, Cumming AR, Gallagher L, et al. A controlled trial of low-molecular-weight heparin (dalteparin) versus unfractionated heparin as anticoagulant during continuous venovenous hemodialysis with filtration. Critical Care Medicine 1999; 27(10):2224-8. *Not an intervention for screening for CKD*

249. Regeniter A, Haenni V, Risch L, et al. Urine analysis performed by flow cytometry: reference range determination and comparison to morphological findings, dipstick chemistry and bacterial culture results--a multicenter study. Clinical Nephrology 2001; 55(5):384-92. *Not a randomized trial*

250. Reid A, Stohr W, Walker AS, et al. Severe renal dysfunction and risk factors associated with renal impairment in HIV-infected adults in Africa initiating antiretroviral therapy. Clinical Infectious Diseases 2008; 46(8):1271-81. *Not a randomized trial*

251. Ricos C, Jimenez CV, Hernandez A, et al. Biological variation in urine samples used for analyte measurements. Clinical Chemistry 1994; 40(3):472-7. *Not a randomized trial*

252. Roderick PJ, Atkins RJ, Smeeth L, et al. Detecting chronic kidney disease in older people; what are the implications?.[Erratum appears in Age Ageing. 2009 Sep;38(5):638 Note: Flectcher, Astrid E [corrected to Fletcher, Astrid E]]. Age & Ageing 2008; 37(2):179-86. *Not a randomized trial*

253. Romundstad S, Holmen J, Kvenild K, et al. Clinical relevance of microalbuminuria screening in self-reported non-diabetic/non-hypertensive persons identified in a large health screening--the Nord-Trondelag Health Study (HUNT), Norway. Clinical Nephrology 2003; 59(4):241-51. *Not a randomized trial*

254. Romundstad S, Holmen J, Kvenild K, et al. Microalbuminuria and all-cause mortality in 2,089 apparently healthy individuals: a 4.4-year follow-up study. The Nord-Trondelag Health Study (HUNT), Norway. American Journal of Kidney Diseases 2003; 42(3):466-73. *Not a randomized trial*

255. Sandler DP, Burr FR, Weinberg CR. Nonsteroidal anti-inflammatory drugs and the risk for chronic renal disease. Annals of Internal Medicine 1991; 115(3):165-72. *Not a randomized trial*

256. Saran AM, DuBose TD, Jr. Cardiovascular disease in chronic kidney disease. Therapeutic Advances in Cardiovascular Disease 2008; 2(6):425-34. *Not a randomized trial*

257. Saraux A, Fautrel B, Maillefert JF, et al. Laboratory and imaging studies used by French rheumatologists to evaluate patients with early arthritis. Journal of Rheumatology 2006; 33(5):897-902. *Not an intervention for screening for CKD*

258. Saw J, Levin A, Gin K. Coronary artery disease in chronic kidney disease patients: assessing the evidence for diagnosis, screening and revascularization. Canadian Journal of Cardiology 2004; 20(8):807-13. *Not a randomized trial*

259. Sawicki PT, Kaiser S, Heinemann L, et al. Prevalence of renal artery stenosis in diabetes mellitus--an autopsy study. Journal of Internal Medicine 1991; 229(6):489-92. *Not a randomized trial*

260. Scheid DC, McCarthy LH, Lawler FH, et al. Screening for microalbuminuria to prevent nephropathy in patients with diabetes: a systematic review of the evidence. Journal of Family Practice 2001; 50(8):661-8. *Not an intervention for screening for CKD*

261. Schreij G, van Es PN, Schiffers PM, et al. 'Captopril test', with blood pressure and peripheral renin as response variables in hypertensive patients with suspected renal artery stenosis. Journal of Human Hypertension 1995; 9(9):741-6. *Not an intervention for screening for CKD*

262. Schumacher G, Hilscher W, Mollering H, et al. Engineering enzymes for clinical diagnosis. Annales de Biologie Clinique 1993; 51(9):815-9. *Not an intervention for screening for CKD*

263. Schwab SJ, Dunn FL, Feinglos MN. Screening for microalbuminuria. A comparison of single sample methods of collection and techniques of albumin analysis. Diabetes Care 1992; 15(11):1581-4. *Not a randomized trial*

264. Servois V, Laissy JP, Feger C, et al. Two-dimensional time-of-flight magnetic resonance angiography of renal arteries without maximum intensity projection: a prospective comparison with angiography in 21 patients screened for renovascular hypertension. Cardiovascular & Interventional Radiology 1994; 17(3):138-42. *Not a randomized trial*

265. Shambesh MA, Craig PS, Macpherson CN, et al. An extensive ultrasound and serologic study to investigate the prevalence of human cystic echinococcosis in northern Libya. American Journal of Tropical Medicine & Hygiene 1999; 60(3):462-8. *Not an intervention for screening for CKD*

266. Shionoiri H, Kosaka T, Kita E, et al. Comparison of long-term therapeutic effect of an ACE inhibitor, temocapril, with that of a diuretic on microalbuminuria in non-diabetic essential hypertension. Hypertension Research - Clinical & Experimental 2000; 23(6):593-600. *Not an intervention for screening for CKD*

267. Siewert-Delle A. Long-term renal function in primary hypertension. An epidemiological and pathophysiological study. Scandinavian Journal of Urology & Nephrology Supplementum 1999; 199:1-36. *Not a randomized trial*

268. Sikka R, Waters J, Moore W, et al. Renal assessment practices and the effect of nurse case management of health maintenance organization patients with diabetes. Diabetes Care 1999; 22(1):1-6. *Less than 1000 patients in study*

269. Singh GR, White AV, Hoy WE. Renal ultrasound findings in an Australian Aboriginal population with high rates of renal disease. Nephrology 2005; 10(4):358-61. *Not a randomized trial*

270. Singh NP, Ingle GK, Saini VK, et al. Prevalence of low glomerular filtration rate, proteinuria and associated risk factors in North India using Cockcroft-Gault and Modification of Diet in Renal Disease equation: an observational, cross-sectional study. BMC Nephrology 2009; 10:4. *Not a randomized trial*

271. Skipper GE, Weinmann W, Thierauf A, et al. Ethyl glucuronide: a biomarker to identify alcohol use by health professionals recovering from substance use disorders. Alcohol & Alcoholism 2004; 39(5):445-9. *Not an intervention for screening for CKD*

272. Smaill F. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database of Systematic Reviews 2001; (2):CD000490. *Not an intervention for screening for CKD*

273. Smaill F, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database of Systematic Reviews 2007; (2):CD000490. *Not an intervention for screening for CKD*

274. Smith ML, Barnes AJ, Huestis MA. Identifying new cannabis use with urine creatinine-normalized THCCOOH concentrations and time intervals between specimen collections. Journal of Analytical Toxicology 2009; 33(4):185-9. *Not an intervention for screening for CKD*

275. Smith-Kielland A, Skuterud B, Olsen KM, et al. Urinary excretion of diazepam metabolites in healthy volunteers and drug users. Scandinavian Journal of Clinical & Laboratory Investigation 2001; 61(3):237-46. *Not an intervention for screening for CKD*

276. Snyder S, Pendergraph B. Detection and evaluation of chronic kidney disease. American Family Physician 2005; 72(9):1723-32. *Not a randomized trial*

277. Soonthornpun S, Leelawattana R, Thamprasit A, et al. Screening for microalbuminuria in type 2 diabetes: a reconsideration. Journal of the Medical Association of Thailand 2002; 85(5):604-11. *Not a randomized trial*

278. Springhart WP, Marguet CG, Sur RL, et al. Forced versus minimal intravenous hydration in the management of acute renal colic: a randomized trial. Journal of Endourology 2006; 20(10):713-6. *Not an intervention for screening for CKD*

279. Sumaili EK, Cohen EP, Zinga CV, et al. High prevalence of undiagnosed chronic kidney disease among at-risk population in Kinshasa, the Democratic Republic of Congo. BMC Nephrology 2009; 10:18. *Not a randomized trial*

280. Suri RS, Clark WF, Barrowman N, et al. Diabetes during diarrhea-associated hemolytic uremic syndrome: a systematic review and meta-analysis. Diabetes Care 2005; 28(10):2556-62. *Not an intervention for screening for CKD*

281. Takahashi H, Kinouchi M, Wuepper KD, et al. Cloning of human keratolinin cDNA: keratolinin is identical with a cysteine proteinase inhibitor, cystatin A, and is regulated by Ca2+, TPA, and cAMP. Journal of Investigative Dermatology 1997; 108(6):843-7. *Not an intervention for screening for CKD*

282. Tapp RJ, Shaw JE, Harper CA, et al. The prevalence of and factors associated with diabetic retinopathy in the Australian population. Diabetes Care 2003; 26(6):1731-7. *Not a randomized trial*

283. Thomsen HS, Morcos SK, Erley CM, et al. The ACTIVE Trial: comparison of the effects on renal function of iomeprol-400 and iodixanol-320 in patients with chronic kidney disease undergoing abdominal computed tomography. Investigative Radiology 2008; 43(3):170-8. *Not an intervention for screening for CKD*

284. Thomsen HS, Sos TA, Nielsen SL. Renovascular hypertension. Diagnosis and intervention. Acta Radiologica 1989; 30(2):113-20. *Not a randomized trial*

285. Torng S, Rigatto C, Rush DN, et al. The urine protein to creatinine ratio (P/C) as a predictor of 24-hour urine protein excretion in renal transplant patients. Transplantation 2001; 72(8):1453-6. *Not a randomized trial*

286. Toussaint ND, Lau KK, Strauss BJ, et al. Determination and validation of aortic calcification measurement from lateral bone densitometry in dialysis patients. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(1):119-27. *Patients already diagnosed with CKD*

287. Toyoda N, Nagai S, Terashima Y, et al. Analysis of mRNA with microsomal fractionation using a SAGE-based DNA microarray system facilitates identification of the genes encoding secretory proteins. Genome Research 2003; 13(7):1728-36. *Not an intervention for screening for CKD*

288. Tsai S-Y, Tseng H-F, Tan H-F, et al. End-stage renal disease in Taiwan: a case-control study. Journal of Epidemiology 2009; 19(4):169-76. *Not a randomized trial*

289. Tumlin JA, Finkel KW, Murray PT, et al. Fenoldopam mesylate in early acute tubular necrosis: a randomized, double-blind, placebo-controlled clinical trial. American Journal of Kidney Diseases 2005; 46(1):26-34. *Not an intervention for screening for CKD*

290. Tutone VK, Mark PB, Revanur V, et al. Random blood glucose measurements and survival in nondiabetic renal transplant recipients. Transplantation Proceedings 2004; 36(10):3006-11. *Patients already diagnosed with CKD*

291. van Kooten F, Ciabattoni G, Koudstaal PJ, et al. Increased thromboxane biosynthesis is associated with poststroke dementia. Stroke 1999; 30(8):1542-7. *Not an intervention for screening for CKD*

292. Vegter S, Perna A, Hiddema W, et al. Cost-effectiveness of ACE inhibitor therapy to prevent dialysis in nondiabetic nephropathy: influence of the ACE insertion/deletion polymorphism. Pharmacogenetics & Genomics 2009; 19(9):695-703. *Not a randomized trial*

293. Velazquez Lopez L, Sil Acosta MJ, Goycochea Robles MV, et al. Effect of protein restriction diet on renal function and metabolic control in patients with type 2 diabetes: a randomized clinical trial. Nutricion Hospitalaria 2008; 23(2):141-7. *Not an intervention for screening for CKD*

294. Viberti G, Kahn SE, Greene DA, et al. A diabetes outcome progression trial (ADOPT): an international multicenter study of the comparative efficacy of rosiglitazone, glyburide, and metformin in recently diagnosed type 2 diabetes. Diabetes Care 2002; 25(10):1737-43. *Not an intervention for screening for CKD*

295. Wachtell K, Olsen MH, Dahlof B, et al. Microalbuminuria in hypertensive patients with electrocardiographic left ventricular hypertrophy: the LIFE study. Journal of Hypertension 2002; 20(3):405-12. *Not a randomized trial*

296. Wanner C, Horl WH, Luley CH, et al. Effects of HMG-CoA reductase inhibitors in hypercholesterolemic patients on hemodialysis. Kidney International 1991; 39(4):754-60. *Patients already diagnosed with CKD*

297. Warrington SJ, Ravic M, Dawnay A. Renal and general tolerability of repeated doses of nimesulide in normal subjects. Drugs 1993; 46 Suppl 1:263-9. *Not an intervention for screening for CKD*

298. Waterman AD, Browne T, Waterman BM, et al. Attitudes and behaviors of African Americans regarding early detection of kidney disease. American Journal of Kidney Diseases 2008; 51(4):554-62. *Not a randomized trial*

299. Watson WJ. Screening for glycosuria during pregnancy. Southern Medical Journal 1990; 83(2):156-8. *Not a randomized trial*

300. Watts GF, Hodgson B, Morris RW, et al. Side-room tests to screen for microalbuminuria in diabetes mellitus. Diabetic Medicine 1988; 5(3):298-303. *Not a randomized trial*

301. Webb DJ, Newman DJ, Chaturvedi N, et al. The use of the Micral-Test strip to identify the presence of microalbuminuria in people with insulin dependent diabetes mellitus (IDDM) participating in the EUCLID study. Diabetes Research & Clinical Practice 1996; 31(1-3):93-102. *Not a randomized trial*

302. Weger M, Deutschmann H, Weger W, et al. Incomplete renal tubular acidosis in 'primary' osteoporosis. Osteoporosis International 1999; 10(4):325-9. *Not a randomized trial*

303. Whelton PK, Lee JY, Kusek JW, et al. Recruitment experience in the African American Study of Kidney Disease and Hypertension (AASK) Pilot Study. Controlled Clinical Trials 1996; 17(4 Suppl):17S-33S. *Not an intervention for screening for CKD*

304. Wilde HM, Banks D, Larsen CL, et al. Evaluation of the Bayer microalbumin/creatinine urinalysis dipstick. Clinica Chimica Acta 2008; 393(2):110-3. *Not a randomized trial*

305. Williams BT, Ketchum CH, Robinson CA, et al. Screening for slight albuminuria: a comparison of selected commercially available methods. Southern Medical Journal 1990; 83(12):1447-9. *Not a randomized trial*

306. Wilson RA, Norman DJ, Barry JM, et al. Noninvasive cardiac testing in the end-stage renal disease patient. Blood Purification 1994; 12(1):78-83. *Not an intervention for screening for CKD*

307. Wingo CS, Clapp WL. Proteinuria: potential causes and approach to evaluation. American Journal of the Medical Sciences 2000; 320(3):188-94. *Not a randomized trial*

308. Witting M, Kuo D. Screening with blood urea nitrogen before intravenous contrast. American Journal of Emergency Medicine 2003; 21(6):494-6. *Not a randomized trial*

309. Womer KL, Huang Y, Herren H, et al. Dendritic cell deficiency associated with development of BK viremia and nephropathy in renal transplant recipients. Transplantation 2010; 89(1):115-23. *Not an intervention for screening for CKD*

310. Woo J, Lau E, Swaminathan R, et al. Biochemical predictors for osteoporotic fractures in elderly Chinese--a longitudinal study. Gerontology 1990; 36(1):55-8. *Not an intervention for screening for CKD*

311. Woolhandler S, Pels RJ, Bor DH, et al. Dipstick urinalysis screening of asymptomatic adults for urinary tract disorders. I. Hematuria and proteinuria. JAMA 1989; 262(9):1214-9. *Not a randomized trial*

312. Wroe S. Zonisamide and renal calculi in patients with epilepsy: how big an issue? Current Medical Research & Opinion 2007; 23(8):1765-73. *Not a randomized trial*

313. Wu SY, Fisher DA, Huang WS, et al. Urinary compound W in pregnant women is a potential marker for fetal thyroid function. American Journal of Obstetrics & Gynecology 1998; 178(5):886-91. *Not an intervention for screening for CKD*

314. Xin G, Wang M, Jiao L-l, et al. Protein-to-creatinine ratio in spot urine samples as a predictor of quantitation of proteinuria. Clinica Chimica Acta 2004; 350(1-2):35-9. *Not a randomized trial*

315. Yanik B, Bavbek N, Yanik T, et al. The effect of alendronate, risedronate, and raloxifene on renal functions, based on the Cockcroft and Gault method, in postmenopausal women. Renal Failure 2007; 29(4):471-6. *Not an intervention for screening for CKD*

316. Ylinenjarvi K, Widersten M, Bjork I. Hydrophobic sequences can substitute for the wild-type N-terminal sequence of cystatin A (stefin A) in tight binding to cysteine proteinases selection of high-affinity N-terminal region variants by phage display. European Journal of Biochemistry 1999; 261(3):682-8. *Not an intervention for screening for CKD*

317. Yocum DE, Furst DE, Bensen WG, et al. Safety of tacrolimus in patients with rheumatoid arthritis: long-term experience. Rheumatology 2004; 43(8):992-9. *Not an intervention for screening for CKD*

318. Zarif L, Covic A, Iyengar S, et al. Inaccuracy of clinical phenotyping parameters for hypertensive nephrosclerosis. Nephrology Dialysis Transplantation 2000; 15(11):1801-7. *Not a randomized trial*

319. Zeller A, Sigle J-P, Battegay E, et al. Value of a standard urinary dipstick test for detecting microalbuminuria in patients with newly diagnosed hypertension. Swiss Medical Weekly 2005; 135(3-4):57-61. *Not a randomized trial*

320. Zelmanovitz T, Gross JL, Oliveira J, et al. Proteinuria is still useful for the screening and diagnosis of overt diabetic nephropathy. Diabetes Care 1998; 21(7):1076-9. *Not a randomized trial*

321. Zelmanovitz T, Gross JL, Oliveira JR, et al. The receiver operating characteristics curve in the evaluation of a random urine specimen as a screening test for diabetic nephropathy. Diabetes Care 1997; 20(4):516-9. *Not a randomized trial*

322. Zhang Q, Zhang Z, Xin D, et al. Suppression subtractive hybridization for identifying differentially expressed genes in renal cell carcinoma. Chinese Medical Journal 2001; 114(8):807-12. *Not an intervention for screening for CKD*

323. Zhao H, Li X, Johnson DE, et al. Identification of protease and rpoN-associated genes of uropathogenic Proteus mirabilis by negative selection in a mouse model of ascending urinary tract infection. Microbiology 1999; 145(Pt 1):185-95. *Not a randomized trial*

324. Ziegler D, Siekierka-Kleiser E, Meyer B, et al. Validation of a novel screening device (NeuroQuick) for quantitative assessment of small nerve fiber dysfunction as an early feature of diabetic polyneuropathy. Diabetes Care 2005; 28(5):1169-74. *Not an intervention for screening for CKD*

CKD Monitoring (KQ3, KQ4)

1. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. New England Journal of Medicine 1993; 329(14):977-86. *Intervention not related to monitoring of CKD*

2. Intensive therapy and progression to clinical albuminuria in patients with insulin dependent diabetes mellitus and microalbuminuria. Microalbuminuria Collaborative Study Group, United Kingdom. BMJ 1995; 311(7011):973-7. *Intervention not related to monitoring of CKD*

3. Effect of intensive therapy on the development and progression of diabetic nephropathy in the Diabetes Control and Complications Trial. The Diabetes Control and Complications (DCCT) Research Group. Kidney International 1995; 47(6):1703-20. *Intervention not related to monitoring of CKD*

4. The absence of a glycemic threshold for the development of long-term complications: the perspective of the Diabetes Control and Complications Trial. Diabetes 1996; 45(10):1289-98. *Intervention not related to monitoring of CKD*

5. Captopril reduces the risk of nephropathy in IDDM patients with microalbuminuria. The Microalbuminuria Captopril Study Group. Diabetologia 1996; 39(5):587-93. *Intervention not related to monitoring of CKD*

6. Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy. The GISEN Group (Gruppo Italiano di Studi Epidemiologici in Nefrologia). Lancet 1997; 349(9069):1857-63. *Intervention not related to monitoring of CKD*

7. Parenteral cidofovir for cytomegalovirus retinitis in patients with AIDS: the HPMPC peripheral cytomegalovirus retinitis trial. A randomized, controlled trial. Studies of Ocular complications of AIDS Research Group in Collaboration with the AIDS Clinical Trials Group. Annals of Internal Medicine 1997; 126(4):264-74. *Intervention not related to monitoring of CKD*

8. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators.[Erratum appears in Lancet 2000 Sep 2;356(9232):860]. Lancet 2000; 355(9200):253-9. *Intervention not related to monitoring of CKD*

9. Retinopathy and nephropathy in patients with type 1 diabetes four years after a trial of intensive therapy. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group.[Erratum appears in N Engl J Med 2000 May 4;342(18):1376]. New England Journal of Medicine 2000; 342(6):381-9. *Intervention not related to monitoring of CKD*

10. Angiotensin II receptor antagonists and heart failure: angiotensin-converting-enzyme inhibitors remain the first-line option. Prescrire International 2005; 14(79):180-6. *Intervention not related to monitoring of CKD*

11. Telmisartan did not prevent renal disease in patients without proteinuria.[Original report in Ann Intern Med. 2009 Jul 7;151(1):1-10, W1-2; PMID: 19451556]. Annals of Internal Medicine 2009; 151(1):I28. *Intervention not related to monitoring of CKD*

12. Abe M, Okada K, Kikuchi F, et al. Clinical investigation of the effects of pioglitazone on the improvement of insulin resistance and blood pressure in type 2-diabetic patients undergoing hemodialysis. Clinical Nephrology 2008; 70(3):220-8. *Less than 50 patients in study*

13. Abe M, Okada K, Maruyama T, et al. Comparison of the antiproteinuric effects of the calcium channel blockers benidipine and amlodipine administered in combination with angiotensin receptor blockers to hypertensive patients with stage 3-5 chronic kidney disease. Hypertension Research - Clinical & Experimental 2009; 32(4):270-5. *Intervention not related to monitoring of CKD*

14. Abe M, Okada K, Maruyama T, et al. Antiproteinuric and blood pressure-lowering effects of a fixed-dose combination of losartan and hydrochlorothiazide in hypertensive patients with stage 3 chronic kidney disease. Pharmacotherapy 2009; 29(9):1061-72. *Duration of follow-up less than 1 year*

15. Abouna GM, al-Abdullah IH, Kelly-Sullivan D, et al. Randomized clinical trial of antithymocyte globulin induction in renal transplantation comparing a fixed daily dose with dose adjustment according to T cell monitoring. Transplantation 1995; 59(11):1564-8. *Not patients with early CKD*

16. Acone D, Cante D, Cillo F, et al. Blood pressure and progression of renal failure in the elderly. Kidney International - Supplement 1996; 55:S75-7. *Less than 50 patients in study*

17. Adler AI, Stevens RJ, Manley SE, et al. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney International 2003; 63(1):225-32. *Not a randomized trial*

18. Agarwal R. Reproducibility of renal function measurements in adult men with diabetic nephropathy: research and clinical implications. American Journal of Nephrology 2007; 27(1):92-100. *Not a randomized trial*

19. Agarwal R. Vitamin D, proteinuria, diabetic nephropathy, and progression of CKD. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(9):1523-8. *Not a randomized trial*

20. Agarwal R. Blood pressure components and the risk for end-stage renal disease and death in chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(4):830-7. *Not a randomized trial*

21. Agarwal R, Acharya M, Tian J, et al. Antiproteinuric effect of oral paricalcitol in chronic kidney disease. Kidney International 2005; 68(6):2823-8. *Duration of follow-up less than 1 year*

22. Agha A, Amer W, Anwar E, et al. Reduction of microalbuminuria by using losartan in normotensive patients with type 2 diabetes mellitus: A randomized controlled trial. Saudi Journal of Kidney Diseases & Transplantation 2009; 20(3):429-35. *Duration of follow-up less than 1 year*

23. Agrawal A, Sautter MC, Jones NP. Effects of rosiglitazone maleate when added to a sulfonylurea regimen in patients with type 2 diabetes mellitus and mild to moderate renal impairment: a post hoc analysis. Clinical Therapeutics 2003; 25(11):2754-64. *Duration of follow-up less than 1 year*

24. Agrawal RP, Dogra R, Mohta N, et al. Beneficial effect of camel milk in diabetic nephropathy. Acta Bio-Medica de l Ateneo Parmense 2009; 80(2):131-4. *Duration of follow-up less than 1 year*

25. Ahern MJ, Harrison W, Hollingsworth P, et al. A randomised double-blind trial of cyclosporin and azathioprine in refractory rheumatoid arthritis. Australian & New Zealand Journal of Medicine 1991; 21(6):844-9. *Intervention not related to monitoring of CKD*

26. Ahmad J, Shafique S, Abidi SM, et al. Effect of 5-year enalapril therapy on progression of microalbuminuria and glomerular structural changes in type 1 diabetic subjects. Diabetes Research & Clinical Practice 2003; 60(2):131-8. *Intervention not related to monitoring of CKD*

27. Ahmad J, Siddiqui MA, Ahmad H. Effective postponement of diabetic nephropathy with enalapril in normotensive type 2 diabetic patients with microalbuminuria. Diabetes Care 1997; 20(10):1576-81. *Intervention not related to monitoring of CKD*

28. Aho PS, Niemi T, Lindgren L, et al. Endovascular vs open AAA repair: similar effects on renal proximal tubular function. Scandinavian Journal of Surgery: SJS 2004; 93(1):52-6. *Not a randomized trial*

29. Ahsan N, Hricik D, Matas A, et al. Prednisone withdrawal in kidney transplant recipients on cyclosporine and mycophenolate mofetil--a prospective randomized study. Steroid Withdrawal Study Group. Transplantation 1999; 68(12):1865-74. *Not patients with early CKD*

30. Akesson A, Wollheim FA, Thysell H, et al. Visceral improvement following combined plasmapheresis and immunosuppressive drug therapy in progressive systemic sclerosis. Scandinavian Journal of Rheumatology 1988; 17(5):313-23. *Not a randomized trial*

31. Akizawa T, Asano Y, Morita S, et al. Effect of a carbonaceous oral adsorbent on the progression of CKD: a multicenter, randomized, controlled trial. American Journal of Kidney Diseases 2009; 54(3):459-67. *Intervention not related to monitoring of CKD*

32. Akriviadis E, Botla R, Briggs W, et al. Pentoxifylline improves short-term survival in severe acute alcoholic hepatitis: a double-blind, placebo-controlled trial. Gastroenterology 2000; 119(6):1637-48. *Not patients with early CKD*

33. Albanis S, Ather HM, Papatsoris AG, et al. Inversion, hydration and diuresis during extracorporeal shock wave lithotripsy: does it improve the stone-free rate for lower pole stone clearance? Urologia Internationalis 2009; 83(2):211-6. *Not a randomized trial*

34. Albert I, Jais JP. The use of frailty models in genetic studies: application to the relationship between end-stage renal failure and mutation type in Alport syndrome. European Community Alport Syndrome Concerted Action Group (ECASCA). Journal of Epidemiology & Biostatistics 2000; 5(3):169-75. *Not a randomized trial*

35. Albert SG, Shapiro MJ, Brown WW, et al. Analysis of radiocontrast-induced nephropathy by dual-labeled radionuclide clearance. Investigative Radiology 1994; 29(6):618-23. *Duration of follow-up less than 1 year*

36. Al-Kateb H, Boright AP, Mirea L, et al. Multiple superoxide dismutase 1/splicing factor serine alanine 15 variants are associated with the development and progression of diabetic nephropathy: the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Genetics study. Diabetes 2008; 57(1):218-28. *Not a randomized trial*

37. Allon M, Robbin ML. Hemodialysis vascular access monitoring: current concepts. Hemodialysis International 2009; 13(2):153-62. *Not a randomized trial*

38. Amato RJ, Jac J, Hernandez-McClain J. Interferon-alpha in combination with either imatinib (Gleevec) or gefitinib (Iressa) in metastatic renal cell carcinoma: a phase II trial. Anti-Cancer Drugs 2008; 19(5):527-33. *Not a randomized trial*

39. Andersen S, Brochner-Mortensen J, Parving HH. Kidney function during and after withdrawal of long-term irbesartan treatment in patients with type 2 diabetes and microalbuminuria. Diabetes Care 2003; 26(12):3296-302. *Duration of follow-up less than 1 year*

40. Ansquer J-C, Foucher C, Rattier S, et al. Fenofibrate reduces progression to microalbuminuria over 3 years in a placebo-controlled study in type 2 diabetes: results from the Diabetes Atherosclerosis Intervention Study (DAIS). American Journal of Kidney Diseases 2005; 45(3):485-93. *Intervention not related to monitoring of CKD*

41. Aoki TT, Grecu EO, Prendergast JJ, et al. Effect of chronic intermittent intravenous insulin therapy on antihypertensive medication requirements in IDDM subjects with hypertension and nephropathy. Diabetes Care 1995; 18(9):1260-5. *Intervention not related to monitoring of CKD*

42. Appel LJ, Wright JT, Jr., Greene T, et al. Long-term effects of renin-angiotensin system-blocking therapy and a low blood pressure goal on progression of hypertensive chronic kidney disease in African Americans. Archives of Internal Medicine 2008; 168(8):832-9. *Intervention not related to monitoring of CKD*

43. Artz MA, Hilbrands LB, Borm G, et al. Blockade of the renin-angiotensin system increases graft survival in patients with chronic allograft nephropathy. Nephrology Dialysis Transplantation 2004; 19(11):2852-7. *Not patients with early CKD*

44. Assan R, Blanchet F, Feutren G, et al. Normal renal function 8 to 13 years after cyclosporin A therapy in 285 diabetic patients. Diabetes/Metabolism Research Reviews 2002; 18(6):464-72. *Not a randomized trial*

45. Astobieta A, Calvo R, Aguirre C, et al. Netilmicin kinetics in urology. International Journal of Clinical Pharmacology, Therapy, & Toxicology 1993; 31(11):557-60. *Not a randomized trial*

46. Atzpodien J, Kirchner H, Rebmann U, et al. Interleukin-2/interferon-alpha2a/13-retinoic acid-based chemoimmunotherapy in advanced renal cell carcinoma: results of a prospectively randomised trial of the German Cooperative Renal Carcinoma Chemoimmunotherapy Group (DGCIN). British Journal of Cancer 2006; 95(4):463-9. *Intervention not related to monitoring of CKD*

47. Aulitzky WE, Grosse-Wilde H, Westhoff U, et al. Enhanced serum levels of soluble HLA class I molecules are induced by treatment with recombinant interferon-gamma (IFN-gamma). Clinical & Experimental Immunology 1991; 86(2):236-9. *Not a randomized trial*

48. Axelsson J, Witasp A, Carrero JJ, et al. Circulating levels of visfatin/pre-B-cell colony-enhancing factor 1 in relation to genotype, GFR, body composition, and survival in patients with CKD. American Journal of Kidney Diseases 2007; 49(2):237-44. *Not a randomized trial*

49. Azizi M, Menard J, Peyrard S, et al. Assessment of patients' and physicians' compliance to an ACE inhibitor treatment based on urinary N-acetyl Ser-Asp-Lys-Pro determination in the Noninsulin-Dependent Diabetes, Hypertension, Microalbuminuria, Proteinuria, Cardiovascular Events, and Ramipril (DIABHYCAR) study. Diabetes Care 2006; 29(6):1331-6. *Not a randomized trial*

50. Bacoyiannis C, Dimopoulos MA, Kalofonos HP, et al. Vinblastine and interferon-gamma combination with and without 13-cis retinoic acid for patients with advanced renal cell carcinoma. Results of two phase II clinical trials. Oncology 2002; 63(2):130-8. *Not a randomized trial*

51. Baigent C, Landray M, Leaper C, et al. First United Kingdom Heart and Renal Protection (UK-HARP-I) study: biochemical efficacy and safety of simvastatin and safety of low-dose aspirin in chronic kidney disease. American Journal of Kidney Diseases 2005; 45(3):473-84. *Intervention not related to monitoring of CKD*

52. Baigent C, Landray M, Warren M. Statin therapy in kidney disease populations: potential benefits beyond lipid lowering and the need for clinical trials. Current Opinion in Nephrology & Hypertension 2004; 13(6):601-5. *Not a randomized trial*

53. Baker LR, Abrams L, Roe CJ, et al. 1,25(OH)2D3 administration in moderate renal failure: a prospective double-blind trial. Kidney International 1989; 35(2):661-9. *Less than 50 patients in study*

54. Baker LR, Abrams SM, Roe CJ, et al. Early therapy of renal bone disease with calcitriol: a prospective double-blind study. Kidney International - Supplement 1989; 27:S140-2. *Less than 50 patients in study*

55. Bakir AA, Share DS, Levy PS, et al. Focal segmental glomerulosclerosis in adult African Americans. Clinical Nephrology 1996; 46(5):306-11. *Not a randomized trial*

56. Bakris G, Hester A, Weber M, et al. The diabetes subgroup baseline characteristics of the Avoiding Cardiovascular Events Through Combination Therapy in Patients Living With Systolic Hypertension (ACCOMPLISH) trial. J Cardiometab Syndr 2008; 3(4):229-33. *Intervention not related to monitoring of CKD*

57. Bakris GL, Copley JB, Vicknair N, et al. Calcium channel blockers versus other antihypertensive therapies on progression of NIDDM associated nephropathy. Kidney International 1996; 50(5):1641-50. *Intervention not related to monitoring of CKD*

58. Bakris GL, Weir MR. Angiotensin-converting enzyme inhibitor-associated elevations in serum creatinine: is this a cause for concern? Archives of Internal Medicine 2000; 160(5):685-93. *Intervention not related to monitoring of CKD*

59. Bakris GL, Weir MR, Shanifar S, et al. Effects of blood pressure level on progression of diabetic nephropathy: results from the RENAAL study. Archives of Internal Medicine 2003; 163(13):1555-65. *Intervention not related to monitoring of CKD*

60. Ballardie FW, Roberts ISD. Controlled prospective trial of prednisolone and cytotoxics in progressive IgA nephropathy. Journal of the American Society of Nephrology 2002; 13(1):142-8. *Intervention not related to monitoring of CKD*

61. Banikazemi M, Bultas J, Waldek S, et al. Agalsidase-beta therapy for advanced Fabry disease: a randomized trial. Annals of Internal Medicine 2007; 146(2):77-86. *Intervention not related to monitoring of CKD*

62. Bannister KM, Weaver A, Clarkson AR, et al. Effect of angiotensin-converting enzyme and calcium channel inhibition on progression of IgA nephropathy. Contributions to Nephrology 1995; 111:184-92; discussion 92-3. *Intervention not related to monitoring of CKD*

63. Bansal N, Tighiouart H, Weiner D, et al. Anemia as a risk factor for kidney function decline in individuals with heart failure. American Journal of Cardiology 2007; 99(8):1137-42. *Intervention not related to monitoring of CKD*

64. Barichella M, Savardi C, Mauri A, et al. Diet with LPP for renal patients increases daily energy expenditure and improves motor function in parkinsonian patients with motor fluctuations. Nutritional Neuroscience 2007; 10(3-4):129-35. *Duration of follow-up less than 1 year*

65. Barlage S, Hauser IA, Elbracht R, et al. Monitoring of peripheral blood cytotoxic T-cells under fluvastatin treatment in renal transplant recipients. Journal of Biological Regulators & Homeostatic Agents 2005; 19(3-4):159-68. *Not a randomized trial*

66. Barratt J, Feehally J. Treatment of IgA nephropathy. Kidney International 2006; 69(11):1934-8. *Not a randomized trial*

67. Barrett BJ. Managing progressive renal disease before dialysis. Canadian Family Physician 1999; 45:977-84. *Not a randomized trial*

68. Barrett SV, Paul J, Hay A, et al. Does body mass index affect progression-free or overall survival in patients with ovarian cancer? Results from SCOTROC I trial. Annals of Oncology 2008; 19(5):898-902. *Intervention not related to monitoring of CKD*

69. Basile C, Ruggieri G, Vernaglione L, et al. The natural history of autogenous radio-cephalic wrist arteriovenous fistulas of haemodialysis patients: a prospective observational study. Nephrology Dialysis Transplantation 2004; 19(5):1231-6. *Not patients with early CKD*

70. Bax L, Mali WPTM, Buskens E, et al. The benefit of STent placement and blood pressure and lipid-lowering for the prevention of progression of renal dysfunction caused by Atherosclerotic ostial stenosis of the Renal artery. The STAR-study: rationale and study design. Journal of Nephrology 2003; 16(6):807-12. *Not a randomized trial*

71. Bazzato G, Scanferla F. Assessment of the best compatible dialysis system: feasible application for bioelectrical impedance. International Journal of Artificial Organs 1995; 18(11):712-5. *Not a randomized trial*

72. Beatovic S, Jaksic ED, Han RS. Measurement of renal function by calculation of fractional uptake of technetium-99m dimercaptosuccinic acid. Nucl Med Rev Cent East Eur 2004; 7(1):49-52. *Not adult population*

73. Bellasi A, Kooienga L, Block GA, et al. How long is the warranty period for nil or low coronary artery calcium in patients new to hemodialysis? Journal of Nephrology 2009; 22(2):255-62. *Not a randomized trial*

74. Bellizzi V, Scalfi L, Terracciano V, et al. Early changes in bioelectrical estimates of body composition in chronic kidney disease. Journal of the American Society of Nephrology 2006; 17(5):1481-7. *Not a randomized trial*

75. Bello E, Caramelo C, Martell N, et al. Impairment of renal vasodilation with l-arginine is related to more severe disease in untreated hypertensive patients. Hypertension 2001; 38(4):907-12. *Not a randomized trial*

76. Bellomo R, Auriemma S, Fabbri A, et al. The pathophysiology of cardiac surgery-associated acute kidney injury (CSA-AKI). International Journal of Artificial Organs 2008; 31(2):166-78. *Not a randomized trial*

77. Ben-Zvi I, Green Y, Nakhoul F, et al. Effects of diabetes mellitus, chronic renal failure and hemodialysis on serum and salivary antioxidant status. Nephron Clin Pract 2007; 105(3):c114-20. *Not a randomized trial*

78. Berenson JR. Recommendations for zoledronic acid treatment of patients with bone metastases. Oncologist 2005; 10(1):52-62. *Not a randomized trial*

79. Bergrem H, Goransson LG, Asmundsson P, et al. The Nephrocare project: referral, patient case-mix, follow-up and quality of renal care in Nordic renal centres. Scandinavian Journal of Urology & Nephrology 2009; 43(4):319-24. *Not a randomized trial*

80. Bertolissi M, Antonucci F, De Monte A, et al. Effects on renal function of a continuous infusion of nifedipine during cardiopulmonary bypass. Journal of Cardiothoracic & Vascular Anesthesia 1996; 10(2):238-42. *Less than 50 patients in study*

81. Besarab A, Frinak S, Yee J. What is so bad about a hemoglobin level of 12 to 13 g/dL for chronic kidney disease patients anyway? Advances in Chronic Kidney Disease 2009; 16(2):131-42. *Not a randomized trial*

82. Bhandari S, Brownjohn A, Turney J. Effective utilization of erythropoietin with intravenous iron therapy. Journal of Clinical Pharmacy & Therapeutics 1998; 23(1):73-8. *Not a randomized trial*

83. Bianchi S, Bigazzi R, Caiazza A, et al. A controlled, prospective study of the effects of atorvastatin on proteinuria and progression of kidney disease.[Erratum appears in Am J Kidney Dis. 2004 Jan;43(1):193]. American Journal of Kidney Diseases 2003; 41(3):565-70. *Intervention not related to monitoring of CKD*

84. Bianchi S, Bigazzi R, Campese VM. Antagonists of aldosterone and proteinuria in patients with CKD: an uncontrolled pilot study. American Journal of Kidney Diseases 2005; 46(1):45-51. *Duration of follow-up less than 1 year*

85. Biancofiore G, Esposito M, Bindi L, et al. Regional filter heparinization for continuous veno-venous hemofiltration in liver transplant recipients. Minerva Anestesiologica 2003; 69(6):527-34; 34-8. *Not a randomized trial*

86. Bibi G, Green Y, Nagler RM. Compositional and oxidative analysis in the saliva and serum of predialysis chronic kidney disease patients and end-stage renal failure patients on peritoneal dialysis. Therapeutic Apheresis & Dialysis: Official Peer-Reviewed Journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy 2008; 12(2):164-70. *Not a randomized trial*

87. Bilous R. Microvascular disease: what does the UKPDS tell us about diabetic nephropathy? Diabetic Medicine 2008; 25 Suppl 2:25-9. *Not a randomized trial*

88. Birnbaum BA, Jacobs JE, Langlotz CP, et al. Assessment of a bolus-tracking technique in helical renal CT to optimize nephrographic phase imaging. Radiology 1999; 211(1):87-94. *Not a randomized trial*

89. Ble A, Fink JC, Woodman RC, et al. Renal function, erythropoietin, and anemia of older persons: the InCHIANTI study. Archives of Internal Medicine 2005; 165(19):2222-7. *Not a randomized trial*

90. Blohme I, Idstrom JP, Andersson T. A study of the interaction between omeprazole and cyclosporine in renal transplant patients. British Journal of Clinical Pharmacology 1993; 35(2):156-60. *Intervention not related to monitoring of CKD*

91. Boccardo F, Rubagotti A, Canobbio L, et al. Interleukin-2, interferon-alpha and interleukin-2 plus interferon-alpha in renal cell carcinoma. A randomized phase II trial. Tumori 1998; 84(5):534-9. *Intervention not related to monitoring of CKD*

92. Body J-J, Diel I, Bell R. Profiling the safety and tolerability of bisphosphonates. Seminars in Oncology 2004; 31(5 Suppl 10):73-8. *Not a randomized trial*

93. Boger RH, Schwedhelm E, Maas R, et al. ADMA and oxidative stress may relate to the progression of renal disease: rationale and design of the VIVALDI study. Vasc Med 2005; 10 Suppl 1:S97-102. *Not a randomized trial*

94. Bohler T, Waiser J, Schutz M, et al. FTY 720A mediates reduction of lymphocyte counts in human renal allograft recipients by an apoptosis-independent mechanism. Transplant International 2000; 13 Suppl 1:S311-3. *Not a randomized trial*

95. Boldt J, Brosch C, Piper SN, et al. Influence of prophylactic use of pentoxifylline on postoperative organ function in elderly cardiac surgery patients. Critical Care Medicine 2001; 29(5):952-8. *Intervention not related to monitoring of CKD*

96. Bolondi L, Piscaglia F, Gatta A, et al. Effect of potassium canrenoate, an anti-aldosterone agent, on incidence of ascites and variceal progression in cirrhosis. Clinical Gastroenterology & Hepatology 2006; 4(11):1395-402. *Intervention not related to monitoring of CKD*

97. Bolton WK, Cattran DC, Williams ME, et al. Randomized trial of an inhibitor of formation of advanced glycation end products in diabetic nephropathy. American Journal of Nephrology 2004; 24(1):32-40. *Intervention not related to monitoring of CKD*

98. Bonello M, House AA, Cruz D, et al. Integration of blood volume, blood pressure, heart rate and bioimpedance monitoring for the achievement of optimal dry body weight during chronic hemodialysis. International Journal of Artificial Organs 2007; 30(12):1098-108. *Not a randomized trial*

99. Boogaard PJ, Houtsma AT, Journee HL, et al. Effects of exposure to elemental mercury on the nervous system and the kidneys of workers producing natural gas. Archives of Environmental Health 1996; 51(2):108-15. *Not a randomized trial*

100. Booth AD, Firth JD, Jayne DRW. Immunotherapy for autoimmune and inflammatory renal diseases. Expert Opinion on Biological Therapy 2003; 3(3):487-500. *Not a randomized trial*

101. Braden GL, von Oeyen PT, Germain MJ, et al. Ritodrine- and terbutaline-induced hypokalemia in preterm labor: mechanisms and consequences. Kidney International 1997; 51(6):1867-75. *Not a randomized trial*

102. Brennan DC, Barbeito R, Burke J, et al. Safety of Neoral conversion in maintenance renal transplant patients: A one-year, double-blind study. NOVARTIS OLN-353 Study Group. Kidney International 1999; 56(2):685-91. *Not patients with early CKD*

103. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. New England Journal of Medicine 2001; 345(12):861-9. *Intervention not related to monitoring of CKD*

104. Bretzel RG. Prevention and slowing down the progression of the diabetic nephropathy through antihypertensive therapy. Journal of Diabetes & its Complications 1997; 11(2):112-22. *Not a randomized trial*

105. Breyer JA, Bain RP, Evans JK, et al. Predictors of the progression of renal insufficiency in patients with insulin-dependent diabetes and overt diabetic nephropathy. The Collaborative Study Group. Kidney International 1996; 50(5):1651-8. *Not a randomized trial*

106. Brienza N, Giglio MT, Marucci M, et al. Does perioperative hemodynamic optimization protect renal function in surgical patients? A meta-analytic study. Critical Care Medicine 2009; 37(6):2079-90. *Not a randomized trial*

107. Brophy DF, Martin EJ, Gehr TWB, et al. Enhanced anticoagulant activity of enoxaparin in patients with ESRD as measured by thrombin generation time. American Journal of Kidney Diseases 2004; 44(2):270-7. *Not a randomized trial*

108. Buargub MA, Nabulsi MF, Shafeh TA. Prevalence and pattern of renal osteodystrophy in chronic hemodialysis patients: a cross sectional study of 103 patients. Saudi Journal of Kidney Diseases & Transplantation 2006; 17(3):401-7. *Not a randomized trial*

109. Budoff MJ, Kessler P, Gao YL, et al. The interscan variation of CT coronary artery calcification score: analysis of the Calcium Acetate Renagel Comparison (CARE)-2 study. Academic Radiology 2008; 15(1):58-61. *Intervention not related to monitoring of CKD*

110. Bukowski RM. Targeted therapy for cytokine-refractory metastatic renal cell carcinoma, and treatment in the community. Oncology 2006; 20(6 Suppl 5):25-8. *Not a randomized trial*

111. Bunke M, Sloan R, Brier M, et al. An improved glomerular filtration rate in cardiac transplant recipients with once-a-day cyclosporine dosing. Transplantation 1995; 59(4):537-40. *Intervention not related to monitoring of CKD*

112. Buraczynska M, Grzebalska A, Spasiewicz D, et al. Genetic polymorphisms of renin-angiotensin system and progression of interstitial nephritis. Annales Universitatis Mariae Curie-Sklodowska - Sectio d - Medicina 2002; 57(2):330-6. *Not a randomized trial*

113. Burgess E. Conservative treatment to slow deterioration of renal function: evidence-based recommendations. Kidney International - Supplement 1999; 70:S17-25. *Intervention not related to monitoring of CKD*

114. Bursztyn M, Motro M, Grossman E, et al. Accelerated coronary artery calcification in mildly reduced renal function of high-risk hypertensives: a 3-year prospective observation. Journal of Hypertension 2003; 21(10):1953-9. *Not a randomized trial*

115. Butler JA, Peveler RC, Roderick P, et al. Modifiable risk factors for non-adherence to immunosuppressants in renal transplant recipients: a cross-sectional study. Nephrology Dialysis Transplantation 2004; 19(12):3144-9. *Not a randomized trial*

116. Bybee KA, Lee JH, O'Keefe JH. Cumulative clinical trial data on atorvastatin for reducing cardiovascular events: the clinical impact of atorvastatin. Current Medical Research & Opinion 2008; 24(4):1217-29. *Not a randomized trial*

117. Calkins DS, Degioanni JJ, Tan MN, et al. Human performance and physiological function during a 24-hr exposure to 1% bromotrifluoromethane (Halon 1301). Fundamental & Applied Toxicology 1993; 20(2):240-7. *Not a randomized trial*

118. Campbell KL, Ash S, Bauer JD. The impact of nutrition intervention on quality of life in pre-dialysis chronic kidney disease patients. Clinical Nutrition 2008; 27(4):537-44. *Not a randomized trial*

119. Campistol JM, Inigo P, Larios S, et al. Role of transforming growth factor-beta1 in the progression of chronic allograft nephropathy. Nephrology Dialysis Transplantation 2001; 16 Suppl 1:114-6. *Not a randomized trial*

120. Cantarovich M. Renal protective strategies in heart transplant patients. Current Opinion in Cardiology 2007; 22(2):133-8. *Not a randomized trial*

121. Cantarovich M, Giannetti N, Routy J-P, et al. Long-term immunosuppression with anti-CD25 monoclonal antibodies in heart transplant patients with chronic kidney disease. Journal of Heart & Lung Transplantation 2009; 28(9):912-8. *Not a randomized trial*

122. Cao C, Wan X, Chen Y, et al. Metabolic factors and microinflammatory state promote kidney injury in type 2 diabetes mellitus patients. Renal Failure 2009; 31(6):470-4. *Not a randomized trial*

123. Carides GW, Shahinfar S, Dasbach EJ, et al. The impact of losartan on the lifetime incidence of end-stage renal disease and costs in patients with type 2 diabetes and nephropathy. Pharmacoeconomics 2006; 24(6):549-58. *Not a randomized trial*

124. Casey ET, Murad MH, Rizvi AZ, et al. Surveillance of arteriovenous hemodialysis access: a systematic review and meta-analysis. Journal of Vascular Surgery 2008; 48(5 Suppl):48S-54S. *Not a randomized trial*

125. Cass LM, Efthymiopoulos C, Marsh J, et al. Effect of renal impairment on the pharmacokinetics of intravenous zanamivir. Clinical Pharmacokinetics 1999; 36 Suppl 1:13-9. *Not a randomized trial*

126. Cathelineau G, de Champvallins M, Bouallouche A, et al. Management of newly diagnosed non-insulin-dependent diabetes mellitus in the primary care setting: effects of 2 years of gliclazide treatment--the Diadem Study. Metabolism: Clinical & Experimental 1997; 46(12 Suppl 1):31-4. *Not a randomized trial*

127. Cattran DC. Mycophenolate mofetil and cyclosporine therapy in membranous nephropathy. Seminars in Nephrology 2003; 23(3):272-7. *Not a randomized trial*

128. Cattran DC. Cyclosporine in the treatment of idiopathic focal segmental glomerulosclerosis. Seminars in Nephrology 2003; 23(2):234-41. *Not a randomized trial*

129. Cattran DC, Alexopoulos E, Heering P, et al. Cyclosporin in idiopathic glomerular disease associated with the nephrotic syndrome : workshop recommendations. Kidney International 2007; 72(12):1429-47. *Not a randomized trial*

130. Chan JC, So WY, Yeung CY, et al. Effects of structured versus usual care on renal endpoint in type 2 diabetes: the SURE study: a randomized multicenter translational study. Diabetes Care 2009; 32(6):977-82. *Intervention not related to monitoring of CKD*

131. Chapman AB. Improving clinical trial design for inquiries into the mechanisms of cyst growth in ADPKD. Kidney International 2009; 75(2):139-41. *Not a randomized trial*

132. Chaudhary UB, Haldas JR. Long-term complications of chemotherapy for germ cell tumours. Drugs 2003; 63(15):1565-77. *Not a randomized trial*

133. Chertow GM, Raggi P, Chasan-Taber S, et al. Determinants of progressive vascular calcification in haemodialysis patients. Nephrology Dialysis Transplantation 2004; 19(6):1489-96. *Not a randomized trial*

134. Chesterton LJ, Selby NM, Burton JO, et al. Cool dialysate reduces asymptomatic intradialytic hypotension and increases baroreflex variability. Hemodialysis International 2009; 13(2):189-96. *Not a randomized trial*

135. Chiang SS, Chen JB, Yang WC. Lanthanum carbonate (Fosrenol) efficacy and tolerability in the treatment of hyperphosphatemic patients with end-stage renal disease. Clinical Nephrology 2005; 63(6):461-70. *Intervention not related to monitoring of CKD*

136. Chiurchiu C, Remuzzi G, Ruggenenti P. Angiotensin-converting enzyme inhibition and renal protection in nondiabetic patients: the data of the meta-analyses. Journal of the American Society of Nephrology 2005; 16 Suppl 1:S58-63. *Not a randomized trial*

137. Choi KL, Elliott WJ. Antihypertensive, antiproteinuric therapy and myocardial infarction and stroke prevention. Current Hypertension Reports 2005; 7(5):367-73. *Not a randomized trial*

138. Chonchol M, Goldenberg I, Moss AJ, et al. Risk factors for sudden cardiac death in patients with chronic renal insufficiency and left ventricular dysfunction. American Journal of Nephrology 2007; 27(1):7-14. *Not a randomized trial*

139. Chrysant SG. Angiotensin II receptor blockers in the treatment of the cardiovascular disease continuum. Clinical Therapeutics 2008; 30 Pt 2:2181-90. *Not a randomized trial*

140. Chrysochou C, Randhawa H, Reeve R, et al. Determinants of renal functional outcome in lupus nephritis: a single centre retrospective study. Qjm 2008; 101(4):313-6. *Not a randomized trial*

141. Chu D, Lacouture ME, Fillos T, et al. Risk of hand-foot skin reaction with sorafenib: a systematic review and meta-analysis. Acta Oncologica 2008; 47(2):176-86. *Not a randomized trial*

142. Chu D, Lacouture ME, Weiner E, et al. Risk of hand-foot skin reaction with the multitargeted kinase inhibitor sunitinib in patients with renal cell and non-renal cell carcinoma: a meta-analysis. Clinical Genitourinary Cancer 2009; 7(1):11-9. *Not a randomized trial*

143. Cianci R, Gigante A, Polidori L, et al. In-stent restenosis of the renal artery in a single kidney patient: the role of ACEI in the therapeutic choice. Angiology 2009; 60(4):496-503. *Not a randomized trial*

144. Cianciaruso B, Pota A, Bellizzi V, et al. Effect of a low- versus moderate-protein diet on progression of CKD: follow-up of a randomized controlled trial. American Journal of Kidney Diseases 2009; 54(6):1052-61. *Intervention not related to monitoring of CKD*

145. Cianciaruso B, Pota A, Pisani A, et al. Metabolic effects of two low protein diets in chronic kidney disease stage 4-5--a randomized controlled trial. Nephrology Dialysis Transplantation 2008; 23(2):636-44. *Intervention not related to monitoring of CKD*

146. Cianciaruso B, Ravani P, Barrett BJ, et al. Italian randomized trial of hemoglobin maintenance to prevent or delay left ventricular hypertrophy in chronic kidney disease. J Nephrol 2008; 21(6):861-70. *Intervention not related to monitoring of CKD*

147. Ciancio G, Burke GW, Gaynor JJ, et al. A randomized trial of three renal transplant induction antibodies: early comparison of tacrolimus, mycophenolate mofetil, and steroid dosing, and newer immune-monitoring. Transplantation 2005; 80(4):457-65. *Not patients with early CKD*

148. Ciancio G, Burke GW, Gaynor JJ, et al. Randomized trial of mycophenolate mofetil versus enteric-coated mycophenolate sodium in primary renal transplant recipients given tacrolimus and daclizumab/thymoglobulin: one year follow-up. Transplantation 2008; 86(1):67-74. *Not patients with early CKD*

149. Ciancio G, Burke GW, Gaynor JJ, et al. A randomized long-term trial of tacrolimus/sirolimus versus tacrolimums/mycophenolate versus cyclosporine/sirolimus in renal transplantation: three-year analysis. Transplantation 2006; 81(6):845-52. *Not patients with early CKD*

150. Cicinnati VR, Yu Z, Klein CG, et al. Clinical trial: switch to combined mycophenolate mofetil and minimal dose calcineurin inhibitor in stable liver transplant patients--assessment of renal and allograft function, cardiovascular risk factors and immune monitoring. Alimentary Pharmacology & Therapeutics 2007; 26(9):1195-208. *Not patients with early CKD*

151. Cinotti GA, Zucchelli PC, Collaborative Study G. Effect of Lisinopril on the progression of renal insufficiency in mild proteinuric non-diabetic nephropathies. Nephrology Dialysis Transplantation 2001; 16(5):961-6. *Intervention not related to monitoring of CKD*

152. Citterio F, Sparacino V, Altieri P, et al. Addition of sirolimus to cyclosporine in long-term kidney transplant recipients to withdraw steroid. Transplantation Proceedings 2005; 37(2):827-9. *Not patients with early CKD*

153. Clark JI, Kancharla K, Qamar R, et al. Pilot study of sequential vinorelbine and cisplatin followed by docetaxel for selected IIIB and stage IV non-small cell lung cancer. Lung Cancer 2001; 34(2):271-7. *Not a randomized trial*

154. Clark PE, Hall MC, Miller A, et al. Phase II trial of combination interferon-alpha and thalidomide as first-line therapy in metastatic renal cell carcinoma. Urology 2004; 63(6):1061-5. *Not a randomized trial*

155. Cleland JG, Dargie HJ, Ball SG, et al. Effects of enalapril in heart failure: a double blind study of effects on exercise performance, renal function, hormones, and metabolic state. British Heart Journal 1985; 54(3):305-12. *Not a randomized trial*

156. Coburn JW, Elangovan L. Prevention of metabolic bone disease in the pre-end-stage renal disease setting. Journal of the American Society of Nephrology 1998; 9(12 Suppl):S71-7. *Not a randomized trial*

157. Coburn JW, Maung HM, Elangovan L, et al. Doxercalciferol safely suppresses PTH levels in patients with secondary hyperparathyroidism associated with chronic kidney disease stages 3 and 4. American Journal of Kidney Diseases 2004; 43(5):877-90. *Duration of follow-up less than 1 year*

158. Cody J, Daly C, Campbell M, et al. Recombinant human erythropoietin for chronic renal failure anaemia in pre-dialysis patients. Cochrane Database of Systematic Reviews 2001; (4):CD003266. *Not a randomized trial*

159. Cody J, Daly C, Campbell M, et al. Recombinant human erythropoietin for chronic renal failure anaemia in pre-dialysis patients. Cochrane Database of Systematic Reviews 2005; (3):CD003266. *Not a randomized trial*

160. Coen G, Mazzaferro S, Bonucci E, et al. Bone GLA protein in predialysis chronic renal failure. Effects of 1,25(OH)2D3 administration in a long-term follow-up. Kidney International 1985; 28(5):783-90. *Not a randomized trial*

161. Coen G, Mazzaferro S, Manni M, et al. No acceleration and possibly slower progression of renal failure during calcitriol treatment in predialysis chronic renal failure. Nephrology Dialysis Transplantation 1994; 9(10):1520. *Intervention not related to monitoring of CKD*

162. Cofan F, Gilabert R, Zambon D, et al. Effect of pravastatin treatment on the evolution of extracoronary atherosclerosis in renal transplant patients. Transplantation Proceedings 2002; 34(1):384-8. *Not patients with early CKD*

163. Colhoun HM, Betteridge DJ, Durrington PN, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet 2004; 364(9435):685-96. *Intervention not related to monitoring of CKD*

164. Collins AC, Vincent J, Newall RG, et al. An aid to the early detection and management of diabetic nephropathy: assessment of a new point of care microalbuminuria system in the diabetic clinic. Diabetic Medicine 2001; 18(11):928-32. *Not a randomized trial*

165. Conen D, Glynn RJ, Buring JE, et al. Association of renin-angiotensin and endothelial nitric oxide synthase gene polymorphisms with blood pressure progression and incident hypertension: prospective cohort study. Journal of Hypertension 2008; 26(9):1780-6. *Not a randomized trial*

166. Conil JM, Georges B, Fourcade O, et al. Intermittent administration of ceftazidime to burns patients: influence of glomerular filtration. International Journal of Clinical Pharmacology & Therapeutics 2007; 45(3):133-42. *Intervention not related to monitoring of CKD*

167. Cooper CJ, Murphy TP, Matsumoto A, et al. Stent revascularization for the prevention of cardiovascular and renal events among patients with renal artery stenosis and systolic hypertension: rationale and design of the CORAL trial. American Heart Journal 2006; 152(1):59-66. *Intervention not related to monitoring of CKD*

168. Coppo R, Peruzzi L, Amore A, et al. IgACE: a placebo-controlled, randomized trial of angiotensin-converting enzyme inhibitors in children and young people with IgA nephropathy and moderate proteinuria. Journal of the American Society of Nephrology 2007; 18(6):1880-8. *Not adult population*

169. Cortes-Sanabria L, Cabrera-Pivaral CE, Cueto-Manzano AM, et al. Improving care of patients with diabetes and CKD: a pilot study for a cluster-randomized trial. American Journal of Kidney Diseases 2008; 51(5):777-88. *Intervention not related to monitoring of CKD*

170. Cotter G, Dittrich HC, Weatherley BD, et al. The PROTECT pilot study: a randomized, placebo-controlled, dose-finding study of the adenosine A1 receptor antagonist rolofylline in patients with acute heart failure and renal impairment. Journal of Cardiac Failure 2008; 14(8):631-40. *Intervention not related to monitoring of CKD*

171. Couchoud C, Labeeuw M, Moranne O, et al. A clinical score to predict 6-month prognosis in elderly patients starting dialysis for end-stage renal disease. Nephrology Dialysis Transplantation 2009; 24(5):1553-61. *Not a randomized trial*

172. Coyle D, Rodby R, Soroka S, et al. Cost-effectiveness of irbesartan 300 mg given early versus late in patients with hypertension and a history of type 2 diabetes and renal disease: a Canadian perspective. Clinical Therapeutics 2007; 29(7):1508-23. *Not a randomized trial*

173. Coyne D, Acharya M, Qiu P, et al. Paricalcitol capsule for the treatment of secondary hyperparathyroidism in stages 3 and 4 CKD. American Journal of Kidney Diseases 2006; 47(2):263-76. *Intervention not related to monitoring of CKD*

174. Cravedi P, Ruggenenti P, Remuzzi G. Intensified inhibition of renin-angiotensin system: a way to improve renal protection? Current Hypertension Reports 2007; 9(5):430-6. *Not a randomized trial*

175. Crepaldi G, Carta Q, Deferrari G, et al. Effects of lisinopril and nifedipine on the progression to overt albuminuria in IDDM patients with incipient nephropathy and normal blood pressure. The Italian Microalbuminuria Study Group in IDDM. Diabetes Care 1998; 21(1):104-10. *Intervention not related to monitoring of CKD*

176. Cronberg S, Nordstrom L. Simplified monitoring of aminoglycoside treatment. Scandinavian Journal of Infectious Diseases Supplement 1990; 74:274-9. *Intervention not related to monitoring of CKD*

177. Cruzado JM, Rico J, Grinyo JM. The renin angiotensin system blockade in kidney transplantation: pros and cons. Transplant International 2008; 21(4):304-13. *Not a randomized trial*

178. Culp K, Flanigan M, Lowrie EG, et al. Modeling mortality risk in hemodialysis patients using laboratory values as time-dependent covariates. American Journal of Kidney Diseases 1996; 28(5):741-6. *Not a randomized trial*

179. Cummings DM, Amadio P, Jr., Nettler S, et al. Office-based evaluation of renal function in elderly patients receiving nonsteroidal anti-inflammatory drugs. Journal of the American Board of Family Practice 1988; 1(2):77-80. *Intervention not related to monitoring of CKD*

180. Cummings ST, Fraser CG. Total amylase and pancreatic isoamylase in serum and urine: considerations from data on biological variation. Annals of Clinical Biochemistry 1989; 26(Pt 4):335-40. *Not a randomized trial*

181. Cunningham MA, Huang XR, Dowling JP, et al. Prominence of cell-mediated immunity effectors in “pauci-immune” glomerulonephritis. Journal of the American Society of Nephrology 1999; 10(3):499-506. *Not a randomized trial*

182. Cupisti A, Licitra R, Chisari C, et al. Skeletal muscle and nutritional assessment in chronic renal failure patients on a protein-restricted diet. Journal of Internal Medicine 2004; 255(1):115-24. *Not a randomized trial*

183. Czupryniak L, Pawlowski M, Saryusz-Wolska M, et al. Circadian blood pressure variation and antihypertensive medication adjustment in normoalbuminuric type 2 diabetes patients. Kidney & Blood Pressure Research 2007; 30(3):182-6. *Not a randomized trial*

184. Dailey GE, Boden GH, Creech RH, et al. Effects of pulsatile intravenous insulin therapy on the progression of diabetic nephropathy. Metabolism: Clinical & Experimental 2000; 49(11):1491-5. *Intervention not related to monitoring of CKD*

185. D’Amico G, Gentile MG, Fellin G, et al. Effect of dietary protein restriction on the progression of renal failure: a prospective randomized trial. Nephrology Dialysis Transplantation 1994; 9(11):1590-4. *Intervention not related to monitoring of CKD*

186. Damman K, Navis G, Voors AA, et al. Worsening renal function and prognosis in heart failure: systematic review and meta-analysis. Journal of Cardiac Failure 2007; 13(8):599-608. *Intervention not related to monitoring of CKD*

187. Daumit GL, Hermann JA, Coresh J, et al. Use of cardiovascular procedures among black persons and white persons: a 7-year nationwide study in patients with renal disease. Annals of Internal Medicine 1999; 130(3):173-82. *Not a randomized trial*

188. Daumit GL, Hermann JA, Powe NR. Relation of gender and health insurance to cardiovascular procedure use in persons with progression of chronic renal disease. Medical Care 2000; 38(4):354-65. *Not a randomized trial*

189. Davidson MB, Karlan VJ, Hair TL. Effect of a pharmacist-managed diabetes care program in a free medical clinic. American Journal of Medical Quality 2000; 15(4):137-42. *Not a randomized trial*

190. Davis ID, MacRae Dell K, Sweeney WE, et al. Can progression of autosomal dominant or autosomal recessive polycystic kidney disease be prevented? Seminars in Nephrology 2001; 21(5):430-40. *Not a randomized trial*

191. Davis NB, Taber DA, Ansari RH, et al. Phase II trial of PS-341 in patients with renal cell cancer: a University of Chicago phase II consortium study. Journal of Clinical Oncology 2004; 22(1):115-9. *Not a randomized trial*

192. Davis R, Faulds D. Nadroparin calcium. A review of its pharmacology and clinical use in the prevention and treatment of thromboembolic disorders. Drugs & Aging 1997; 10(4):299-322. *Intervention not related to monitoring of CKD*

193. de Brito-Ashurst I, Varagunam M, Raftery MJ, et al. Bicarbonate supplementation slows progression of CKD and improves nutritional status. Journal of the American Society of Nephrology 2009; 20(9):2075-84. *Intervention not related to monitoring of CKD*

194. de Denus S, Tardif J-C, White M, et al. Quantification of the risk and predictors of hyperkalemia in patients with left ventricular dysfunction: a retrospective analysis of the Studies of Left Ventricular Dysfunction (SOLVD) trials. American Heart Journal 2006; 152(4):705-12. *Not a randomized trial*

195. de Denus S, Tardif J-C, White M, et al. Temporal variations in hematocrit values in patients with left ventricular dysfunction: Relationship with cause-specific mortality and morbidity and optimal monitoring--further insights from SOLVD. Canadian Journal of Cardiology 2008; 24(1):45-8. *Not a randomized trial*

196. de la Sierra A, Lluch MM, Coca A, et al. Fluid, ionic and hormonal changes induced by high salt intake in salt-sensitive and salt-resistant hypertensive patients. Clinical Science 1996; 91(2):155-61. *Intervention not related to monitoring of CKD*

197. De Marchi S, Cecchin E. Hepatic computed tomography for monitoring the iron status of haemodialysis patients with haemosiderosis treated with recombinant human erythropoietin. Clinical Science 1991; 81(1):113-21. *Not a randomized trial*

198. De Palo EF, Gatti R, Lancerin F, et al. Urinary insulin-like growth factor I in athletes, before and after physical exercise, and in sedentary subjects. Clinica Chimica Acta 2002; 322(1-2):51-7. *Not a randomized trial*

199. De Sadeleer C, Piepsz A, Ham HR. How good is the slope on the second exponential for estimating 51Cr-EDTA renal clearance? A Monte Carlo simulation. Nuclear Medicine Communications 2000; 21(5):455-8. *Not a randomized trial*

200. de Silva R, Nikitin NP, Bhandari S, et al. Atherosclerotic renovascular disease in chronic heart failure: should we intervene? European Heart Journal 2005; 26(16):1596-605. *Not a randomized trial*

201. De Vane GW, Czekala NM, Shideler SE, et al. Monitoring gonadotropin-releasing hormone administration by measurement of urinary steroid conjugates. Obstetrics & Gynecology 1986; 67(5):710-7. *Not a randomized trial*

202. de Vinuesa SG, Goicoechea M, Kanter J, et al. Insulin resistance, inflammatory biomarkers, and adipokines in patients with chronic kidney disease: effects of angiotensin II blockade. Journal of the American Society of Nephrology 2006; 17(12 Suppl 3):S206-12. *Not a randomized trial*

203. de Vries PJ, Verkooyen RP, Leguit P, et al. Prospective randomized study of once-daily versus thrice-daily netilmicin regimens in patients with intraabdominal infections. European Journal of Clinical Microbiology & Infectious Diseases 1990; 9(3):161-8. *Not patients with early CKD*

204. Deehan DJ, Heys SD, Broom J, et al. Renal impairment associated with the pre-operative administration of recombinant interleukin-2. Clinical Science 1994; 87(5):513-8. *Not patients with early CKD*

205. Deicher R, Horl WH. Anaemia as a risk factor for the progression of chronic kidney disease. Current Opinion in Nephrology & Hypertension 2003; 12(2):139-43. *Not a randomized trial*

206. Delmez JA, Yan G, Bailey J, et al. Cerebrovascular disease in maintenance hemodialysis patients: results of the HEMO Study. American Journal of Kidney Diseases 2006; 47(1):131-8. *Not patients with early CKD*

207. Dember LM, Hawkins PN, Hazenberg BPC, et al. Eprodisate for the treatment of renal disease in AA amyloidosis. New England Journal of Medicine 2007; 356(23):2349-60. *Intervention not related to monitoring of CKD*

208. Depner TA, Keshaviah PR, Ebben JP, et al. Multicenter clinical validation of an on-line monitor of dialysis adequacy. Journal of the American Society of Nephrology 1996; 7(3):464-71. *Not patients with early CKD*

209. Detournay B, Cros S, Charbonnel B, et al. Managing type 2 diabetes in France: the ECODIA survey. Diabetes & Metabolism 2000; 26(5):363-9. *Not a randomized trial*

210. Devins GM, Hollomby DJ, Barre PE, et al. Long-term knowledge retention following predialysis psychoeducational intervention. Nephron 2000; 86(2):129-34. *Not a randomized trial*

211. Devins GM, Mendelssohn DC, Barre PE, et al. Predialysis psychoeducational intervention and coping styles influence time to dialysis in chronic kidney disease. American Journal of Kidney Diseases 2003; 42(4):693-703. *Intervention not related to monitoring of CKD*

212. Devins GM, Mendelssohn DC, Barre PE, et al. Predialysis psychoeducational intervention extends survival in CKD: a 20-year follow-up. American Journal of Kidney Diseases 2005; 46(6):1088-98. *Intervention not related to monitoring of CKD*

213. Dijkman GA, Fernandez del Moral P, Debruyne FM, et al. Improved subjective responses to orchiectomy plus nilutamide (anandron) in comparison to orchiectomy plus placebo in metastatic prostate cancer. International Anandron Study Group. European Urology 1995; 27(3):196-201. *Not a randomized trial*

214. Dimopoulos MA, Richardson PG, Schlag R, et al. VMP (Bortezomib, Melphalan, and Prednisone) is active and well tolerated in newly diagnosed patients with multiple myeloma with moderately impaired renal function, and results in reversal of renal impairment: cohort analysis of the phase III VISTA study. Journal of Clinical Oncology 2009; 27(36):6086-93. *Intervention not related to monitoring of CKD*

215. Dittrich S, Kurschat K, Dahnert I, et al. Cyanotic nephropathy and use of non-ionic contrast agents during cardiac catherization in patients with cyanotic congenital heart disease. Cardiology in the Young 2000; 10(1):8-14. *Not a randomized trial*

216. Doehn C, Richter A, Lehmacher W, et al. Adjuvant autologous tumour cell-lysate vaccine versus no adjuvant treatment in patients with M0 renal cell carcinoma after radical nephrectomy: 3-year interim analysis of a German multicentre phase-III trial. Folia Biologica 2003; 49(2):69-73. *Intervention not related to monitoring of CKD*

217. Donadio JV, Bergstralh EJ, Bibus DM, et al. Is body size a biomarker for optimizing dosing of omega-3 polyunsaturated fatty acids in the treatment of patients with IgA nephropathy? Clinical Journal of The American Society of Nephrology: CJASN 2006; 1(5):933-9. *Intervention not related to monitoring of CKD*

218. Donadio JV, Grande JP. The role of fish oil/omega-3 fatty acids in the treatment of IgA nephropathy. Seminars in Nephrology 2004; 24(3):225-43. *Not a randomized trial*

219. Donadio JV, Jr., Grande JP, Bergstralh EJ, et al. The long-term outcome of patients with IgA nephropathy treated with fish oil in a controlled trial. Mayo Nephrology Collaborative Group. Journal of the American Society of Nephrology 1999; 10(8):1772-7. *Intervention not related to monitoring of CKD*

220. Donskov F. Interleukin-2 based immunotherapy in patients with metastatic renal cell carcinoma. Danish Medical Bulletin 2007; 54(4):249-65. *Not a randomized trial*

221. Dougados M, Awada H, Amor B. Cyclosporin in rheumatoid arthritis: a double blind, placebo controlled study in 52 patients. Annals of the Rheumatic Diseases 1988; 47(2):127-33. *Intervention not related to monitoring of CKD*

222. Dougados M, Duchesne L, Awada H, et al. Assessment of efficacy and acceptability of low dose cyclosporin in patients with rheumatoid arthritis. Annals of the Rheumatic Diseases 1989; 48(7):550-6. *Not patients with early CKD*

223. Douglas K, O'Malley PG, Jackson JL. Meta-analysis: the effect of statins on albuminuria. Annals of Internal Medicine 2006; 145(2):117-24. *Not a randomized trial*

224. Dries DL, Exner DV, Domanski MJ, et al. The prognostic implications of renal insufficiency in asymptomatic and symptomatic patients with left ventricular systolic dysfunction. Journal of the American College of Cardiology 2000; 35(3):681-9. *Not a randomized trial*

225. Drueke TB, Locatelli F, Clyne N, et al. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. New England Journal of Medicine 2006; 355(20):2071-84. *Not a randomized trial*

226. Dummer CD, Thome FS, Zingano B, et al. Acute effect of simvastatin on inflammation and oxidative stress in chronic kidney disease. Journal of Nephrology 2008; 21(6):900-8. *Duration of follow-up less than 1 year*

227. Dundas S, Todd WT. Clinical presentation, complications and treatment of infection with verocytotoxin-producing Escherichia coli. Challenges for the clinician. Symposium Series/The Society for Applied Microbiology 2000; (29):24S-30S. *Not a randomized trial*

228. Dworkin LD, Gong R, Tolbert E, et al. Hepatocyte growth factor ameliorates progression of interstitial fibrosis in rats with established renal injury. Kidney International 2004; 65(2):409-19. *Not human study*

229. Eardley KS, Lipkin GW. Atherosclerotic renal artery stenosis: is it worth diagnosing? Journal of Human Hypertension 1999; 13(4):217-20. *Not a randomized trial*

230. Ebbehoj E, Arildsen H, Hansen KW, et al. Effects of metoprolol on QT interval and QT dispersion in Type 1 diabetic patients with abnormal albuminuria. Diabetologia 2004; 47(6):1009-15. *Intervention not related to monitoring of CKD*

231. Ebbehoj E, Poulsen PL, Hansen KW, et al. Effects on heart rate variability of metoprolol supplementary to ongoing ACE-inhibitor treatment in Type I diabetic patients with abnormal albuminuria. Diabetologia 2002; 45(7):965-75. *Duration of follow-up less than 1 year*

232. Economides PA, Khaodhiar L, Caselli A, et al. The effect of vitamin E on endothelial function of micro- and macrocirculation and left ventricular function in type 1 and type 2 diabetic patients. Diabetes 2005; 54(1):204-11. *Intervention not related to monitoring of CKD*

233. Edwards MS, Corriere MA. Contemporary management of atherosclerotic renovascular disease. Journal of Vascular Surgery 2009; 50(5):1197-210. *Not a randomized trial*

234. Eidemak I, Haaber AB, Feldt-Rasmussen B, et al. Exercise training and the progression of chronic renal failure. Nephron 1997; 75(1):36-40. *Not a randomized trial*

235. Eitner F, Ackermann D, Hilgers R-D, et al. Supportive Versus Immunosuppressive Therapy of Progressive IgA nephropathy (STOP) IgAN trial: rationale and study protocol. Journal of Nephrology 2008; 21(3):284-9. *Not a randomized trial*

236. Ejerblad E, Fored CM, Lindblad P, et al. Obesity and risk for chronic renal failure. Journal of the American Society of Nephrology 2006; 17(6):1695-702. *Not a randomized trial*

237. El Kossi MMH, Ibrahim A, Lock TJ, et al. Impact of cardiac transplantation on kidney function: a single- center experience. Transplantation Proceedings 2003; 35(4):1527-31. *Not a randomized trial*

238. Elsasser-Beile U, Kolble N, Grussenmeyer T, et al. Correlation of clinical and immunological parameters of metastatic renal cell carcinoma patients undergoing therapy with interleukin 2, interferon-alpha and retinoic acid. Anticancer Research 1998; 18(3B):1883-90. *Not a randomized trial*

239. El-Sehemy MS, Al-Saaran AM, Baddour NM, et al. Comparative clinical prospective therapeutic study between cyclophosphamide, cyclosporine and azathioprine in the treatment of lupus nephritis. Egyptian Journal of Immunology/Egyptian Association of Immunologists 2006; 13(1):39-52. *Less than 50 patients in study*

240. Endo K, Miyashita Y, Sasaki H, et al. Probucol delays progression of diabetic nephropathy. Diabetes Research & Clinical Practice 2006; 71(2):156-63. *Intervention not related to monitoring of CKD*

241. Epstein M. The benefits of ACE inhibitors and calcium antagonists in slowing progressive renal failure: focus on fixed-dose combination antihypertensive therapy. Renal Failure 1996; 18(6):813-32. *Not a randomized trial*

242. Epstein M. Calcium antagonists and renal protection: emerging perspectives. Journal of Hypertension - Supplement 1998; 16(4):S17-25. *Not a randomized trial*

243. Epstein M. Aldosterone as a mediator of progressive renal dysfunction: evolving perspectives. Internal Medicine 2001; 40(7):573-83. *Not a randomized trial*

244. Epstein M. Aldosterone and the hypertensive kidney: its emerging role as a mediator of progressive renal dysfunction: a paradigm shift. Journal of Hypertension 2001; 19(5):829-42. *Not a randomized trial*

245. Escudier B, Eisen T, Stadler WM, et al. Sorafenib in advanced clear-cell renal-cell carcinoma.[Erratum appears in N Engl J Med. 2007 Jul 12;357(2):203]. New England Journal of Medicine 2007; 356(2):125-34. *Intervention not related to monitoring of CKD*

246. Esmail ZN, Loewen PS. Losartan as an alternative to ACE inhibitors in patients with renal dysfunction. Annals of Pharmacotherapy 1998; 32(10):1096-8. *Not a randomized trial*

247. Estacio RO, Coll JR, Tran ZV, et al. Effect of intensive blood pressure control with valsartan on urinary albumin excretion in normotensive patients with type 2 diabetes. American Journal of Hypertension 2006; 19(12):1241-8. *Intervention not related to monitoring of CKD*

248. Ewald B, Attia J. Which test to detect microalbuminuria in diabetic patients? A systematic review. Aust Fam Physician 2004; 33(7):565-7, 71. *Not a randomized trial*

249. Facchini FS, Saylor KL. A low-iron-available, polyphenol-enriched, carbohydrate-restricted diet to slow progression of diabetic nephropathy. Diabetes 2003; 52(5):1204-9. *Intervention not related to monitoring of CKD*

250. Fagnani F, Souchet T, Labed D, et al. Management of hypertension and screening of renal complications by GPs in diabetic type 2 patients (France--2001). Diabetes & Metabolism 2003; 29(1):58-64. *Not a randomized trial*

251. Farace F, Pallardy M, Angevin E, et al. Metastatic renal-cell carcinoma patients treated with interleukin 2 or interleukin 2 plus interferon gamma: immunological monitoring. International Journal of Cancer 1994; 57(6):814-21. *Not a randomized trial*

252. Farbakhsh K, Kasiske BL. Dyslipidemias in patients who have chronic kidney disease. Medical Clinics of North America 2005; 89(3):689-99. *Not a randomized trial*

253. Fassett RG, Ball MJ, Robertson IK, et al. The Lipid lowering and Onset of Renal Disease (LORD) Trial: a randomized double blind placebo controlled trial assessing the effect of atorvastatin on the progression of kidney disease. BMC Nephrology 2008; 9:4. *Not a randomized trial*

254. Faull RJ, Russ GR. Tubular expression of intercellular adhesion molecule-1 during renal allograft rejection. Transplantation 1989; 48(2):226-30. *Not a randomized trial*

255. Fayers PM, Cook PA, Machin D, et al. On the development of the Medical Research Council trial of alpha-interferon in metastatic renal carcinoma. Urological Working Party Renal Carcinoma Subgroup. Statistics in Medicine 1994; 13(21):2249-60. *Not a randomized trial*

256. Ferramosca E, Burke S, Chasan-Taber S, et al. Potential antiatherogenic and anti-inflammatory properties of sevelamer in maintenance hemodialysis patients. American Heart Journal 2005; 149(5):820-5. *Intervention not related to monitoring of CKD*

257. Ficarra V, Galfano A, Novara G, et al. Risk stratification and prognostication of renal cell carcinoma. World Journal of Urology 2008; 26(2):115-25. *Not a randomized trial*

258. Fifer MA, Molina CR, Quiroz AC, et al. Hemodynamic and renal effects of atrial natriuretic peptide in congestive heart failure. American Journal of Cardiology 1990; 65(3):211-6. *Intervention not related to monitoring of CKD*

259. Figlin RA, Thompson JA, Bukowski RM, et al. Multicenter, randomized, phase III trial of CD8(+) tumor-infiltrating lymphocytes in combination with recombinant interleukin-2 in metastatic renal cell carcinoma. Journal of Clinical Oncology 1999; 17(8):2521-9. *Intervention not related to monitoring of CKD*

260. Finn WF, Joy MS, Group LAMS. A long-term, open-label extension study on the safety of treatment with lanthanum carbonate, a new phosphate binder, in patients receiving hemodialysis. Current Medical Research & Opinion 2005; 21(5):657-64. *Not patients with early CKD*

261. Fischer U, Salzsieder E, Menzel R, et al. Primary health care of diabetic patients in a specialized outpatient setting: a DIABCARE-based analysis. Diabete et Metabolisme 1993; 19(1 Pt 2):188-94. *Not a randomized trial*

262. Fitts SS, Guthrie MR, Blagg CR. Exercise coaching and rehabilitation counseling improve quality of life for predialysis and dialysis patients. Nephron 1999; 82(2):115-21. *Less than 50 patients in study*

263. Flaherty KT. Sorafenib in renal cell carcinoma. Clinical Cancer Research 2007; 13(2 Pt 2):747s-52s. *Not a randomized trial*

264. Flaherty KT, Rosen MA, Heitjan DF, et al. Pilot study of DCE-MRI to predict progression-free survival with sorafenib therapy in renal cell carcinoma. Cancer Biology & Therapy 2008; 7(4):496-501. *Not a randomized trial*

265. Flechner SM. Sirolimus in kidney transplantation indications and practical guidelines: de novo sirolimus-based therapy without calcineurin inhibitors. Transplantation 2009; 87(8 Suppl):S1-6. *Not a randomized trial*

266. Fliser D, Haller H. Angiotensin II subtype 1-receptor antagonists in the treatment of diabetic nephropathy. Journal of Hypertension - Supplement 2001; 19(1):S57-60. *Not a randomized trial*

267. Floege J, Eitner F. Present and future therapy options in IgA-nephropathy. Journal of Nephrology 2005; 18(4):354-61. *Not a randomized trial*

268. Forastiere AA, Belliveau JF, Goren MP, et al. Pharmacokinetic and toxicity evaluation of five-day continuous infusion versus intermittent bolus cis-diamminedichloroplatinum(II) in head and neck cancer patients. Cancer Research 1988; 48(13):3869-74. *Not a randomized trial*

269. Fouque D, Aparicio M. Eleven reasons to control the protein intake of patients with chronic kidney disease. Nature Clinical Practice Nephrology 2007; 3(7):383-92. *Not a randomized trial*

270. Fouque D, Laville M. Low protein diets for chronic kidney disease in non diabetic adults. Cochrane Database of Systematic Reviews 2009; (3):CD001892. *Intervention not related to monitoring of CKD*

271. Fouque D, Laville M, Boissel JP. Low protein diets for chronic kidney disease in non diabetic adults. Cochrane Database of Systematic Reviews 2006; (2):CD001892. *Intervention not related to monitoring of CKD*

272. Fox CH, Brooks A, Zayas LE, et al. Primary care physicians' knowledge and practice patterns in the treatment of chronic kidney disease: an Upstate New York Practice-based Research Network (UNYNET) study. Journal of the American Board of Family Medicine: JABFM 2006; 19(1):54-61. *Not a randomized trial*

273. Freedman BI, Hicks PJ, Sale MM, et al. A leucine repeat in the carnosinase gene CNDP1 is associated with diabetic end-stage renal disease in European Americans. Nephrology Dialysis Transplantation 2007; 22(4):1131-5. *Not a randomized trial*

274. Fried LF, Duckworth W, Zhang JH, et al. Design of combination angiotensin receptor blocker and angiotensin-converting enzyme inhibitor for treatment of diabetic nephropathy (VA NEPHRON-D). Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(2):361-8. *Not a randomized trial*

275. Fried LF, Forrest KY, Ellis D, et al. Lipid modulation in insulin-dependent diabetes mellitus: effect on microvascular outcomes. Journal of Diabetes & its Complications 2001; 15(3):113-9. *Intervention not related to monitoring of CKD*

276. Fung MA, Warnock GL, Ao Z, et al. The effect of medical therapy and islet cell transplantation on diabetic nephropathy: an interim report. Transplantation 2007; 84(1):17-22. *Not a randomized trial*

277. Furumatsu Y, Nagasawa Y, Tomida K, et al. Effect of renin-angiotensin-aldosterone system triple blockade on non-diabetic renal disease: addition of an aldosterone blocker, spironolactone, to combination treatment with an angiotensin-converting enzyme inhibitor and angiotensin II receptor blocker. Hypertension Research - Clinical & Experimental 2008; 31(1):59-67. *Intervention not related to monitoring of CKD*

278. Furuta T, Hotta O, Horigome I, et al. Decreased CD4 lymphocyte count as a marker predicting high mortality rate in managing ANCA related rapidly progressive glomerulonephritis. Nephron 2002; 91(4):601-5. *Not a randomized trial*

279. Gaede P, Hansen HP, Parving H-H, et al. Impact of low-dose acetylsalicylic acid on kidney function in type 2 diabetic patients with elevated urinary albumin excretion rate. Nephrology Dialysis Transplantation 2003; 18(3):539-42. *Duration of follow-up less than 1 year*

280. Gaede P, Vedel P, Parving HH, et al. Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study. Lancet 1999; 353(9153):617-22. *Intervention not related to monitoring of CKD*

281. Gainer JV, Lipkowitz MS, Yu C, et al. Association of a CYP4A11 variant and blood pressure in black men. Journal of the American Society of Nephrology 2008; 19(8):1606-12. *Intervention not related to monitoring of CKD*

282. Garcia-Tsao G, Lim JK, Members of Veterans Affairs Hepatitis CRCP. Management and treatment of patients with cirrhosis and portal hypertension: recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program. American Journal of Gastroenterology 2009; 104(7):1802-29. *Not a randomized trial*

283. Gemperle O, Neuweiler J, Reutter FW, et al. Familial glomerulopathy with giant fibrillar (fibronectin-positive) deposits: 15-year follow-up in a large kindred. American Journal of Kidney Diseases 1996; 28(5):668-75. *Not a randomized trial*

284. Germain DP, Waldek S, Banikazemi M, et al. Sustained, long-term renal stabilization after 54 months of agalsidase beta therapy in patients with Fabry disease. Journal of the American Society of Nephrology 2007; 18(5):1547-57. *Intervention not related to monitoring of CKD*

285. Gerth WC, Remuzzi G, Viberti G, et al. Losartan reduces the burden and cost of ESRD: public health implications from the RENAAL study for the European Union. Kidney International - Supplement 2002; (82):S68-72. *Not a randomized trial*

286. Giatras I, Lau J, Levey AS. Effect of angiotensin-converting enzyme inhibitors on the progression of nondiabetic renal disease: a meta-analysis of randomized trials. Angiotensin-Converting-Enzyme Inhibition and Progressive Renal Disease Study Group. Annals of Internal Medicine 1997; 127(5):337-45. *Not a randomized trial*

287. Gillis BP, Caggiula AW, Chiavacci AT, et al. Nutrition intervention program of the Modification of Diet in Renal Disease Study: a self-management approach. Journal of the American Dietetic Association 1995; 95(11):1288-94. *Intervention not related to monitoring of CKD*

288. Glassock RJ. Glomerular therapeutics: looking back, looking forward. Heart Disease 2001; 3(4):276-81. *Not a randomized trial*

289. Gleave ME, Elhilali M, Fradet Y, et al. Interferon gamma-1b compared with placebo in metastatic renal-cell carcinoma. Canadian Urologic Oncology Group. New England Journal of Medicine 1998; 338(18):1265-71. *Intervention not related to monitoring of CKD*

290. Gonwa T, Mendez R, Yang HC, et al. Randomized trial of tacrolimus in combination with sirolimus or mycophenolate mofetil in kidney transplantation: results at 6 months. Transplantation 2003; 75(8):1213-20. *Not patients with early CKD*

291. Gonzalez Vitores AM, Encabo Duro G, Bermejo Fraile B, et al. Utility of tumor marker CA 72.4 in patients with chronic renal failure. International Journal of Biological Markers 1999; 14(2):118-21. *Not a randomized trial*

292. Gonzalgo ML, Eisenberger CF, Lee SM, et al. Prognostic significance of preoperative molecular serum analysis in renal cancer. Clinical Cancer Research 2002; 8(6):1878-81. *Not a randomized trial*

293. Gore ME, Escudier B. Emerging efficacy endpoints for targeted therapies in advanced renal cell carcinoma. Oncology 2006; 20(6 Suppl 5):19-24. *Not a randomized trial*

294. Gouva C, Nikolopoulos P, Ioannidis JPA, et al. Treating anemia early in renal failure patients slows the decline of renal function: a randomized controlled trial. Kidney International 2004; 66(2):753-60. *Intervention not related to monitoring of CKD*

295. Grabe DW, Garrison GD. Comparison of natural product use between primary care and nephrology patients. Annals of Pharmacotherapy 2004; 38(7-8):1169-72. *Not a randomized trial*

296. Gray DW, Richardson A, Hughes D, et al. A prospective, randomized, blind comparison of three biopsy techniques in the management of patients after renal transplantation. Transplantation 1992; 53(6):1226-32. *Not patients with early CKD*

297. Groetzner J, Wittwer T, Kaczmarek I, et al. Conversion to sirolimus and mycophenolate can attenuate the progression of bronchiolitis obliterans syndrome and improves renal function after lung transplantation. Transplantation 2006; 81(3):355-60. *Not a randomized trial*

298. Grootscholten C, Bajema IM, Florquin S, et al. Treatment with cyclophosphamide delays the progression of chronic lesions more effectively than does treatment with azathioprine plus methylprednisolone in patients with proliferative lupus nephritis. Arthritis & Rheumatism 2007; 56(3):924-37. *Intervention not related to monitoring of CKD*

299. Grootscholten C, Dieker JWC, McGrath FD, et al. A prospective study of anti-chromatin and anti-C1q autoantibodies in patients with proliferative lupus nephritis treated with cyclophosphamide pulses or azathioprine/methylprednisolone. Annals of the Rheumatic Diseases 2007; 66(5):693-6. *Intervention not related to monitoring of CKD*

300. Group ACEIiDNT. Should all patients with type 1 diabetes mellitus and microalbuminuria receive angiotensin-converting enzyme inhibitors? A meta-analysis of individual patient data. Annals of Internal Medicine 2001; 134(5):370-9. *Not a randomized trial*

301. Guitterez NV, Diaz A, Timmis GC, et al. Determinants of serum creatinine trajectory in acute contrast nephropathy. Journal of Interventional Cardiology 2002; 15(5):349-54. *Intervention not related to monitoring of CKD*

302. Gurley SB, Coffman TM. The renin-angiotensin system and diabetic nephropathy. Seminars in Nephrology 2007; 27(2):144-52. *Not a randomized trial*

303. Guy JM, Brammah TB, Holt L, et al. Urinary excretion of albumin and retinol binding protein in systemic lupus erythematosus. Annals of Clinical Biochemistry 1997; 34(Pt 6):668-74. *Not a randomized trial*

304. Guy M, Newall R, Borzomato J, et al. Use of a first-line urine protein-to-creatinine ratio strip test on random urines to rule out proteinuria in patients with chronic kidney disease. Nephrology Dialysis Transplantation 2009; 24(4):1189-93. *Not a randomized trial*

305. Haider DG, Fuhrmann H, Kovarik J, et al. Postprandial intradialytic dysglycaemia and diabetes in maintenance haemodialysis patients. European Journal of Clinical Investigation 2008; 38(10):721-7. *Not a randomized trial*

306. Hall AM, Edwards SG, Lapsley M, et al. Subclinical tubular injury in HIV-infected individuals on antiretroviral therapy: a cross-sectional analysis. American Journal of Kidney Diseases 2009; 54(6):1034-42. *Not a randomized trial*

307. Halstenson CE, Wong MO, Herman CS, et al. Effect of concomitant administration of piperacillin on the dispositions of isepamicin and gentamicin in patients with end-stage renal disease. Antimicrobial Agents & Chemotherapy 1992; 36(9):1832-6. *Not a randomized trial*

308. Han H, Bleyer AJ, Houser RF, et al. Dialysis and nutrition practices in Korean hemodialysis centers. Journal of Renal Nutrition 2002; 12(1):42-8. *Not a randomized trial*

309. Hansen HP, Gaede PH, Jensen BR, et al. Lack of impact of low-dose acetylsalicylic acid on kidney function in type 1 diabetic patients with microalbuminuria. Diabetes Care 2000; 23(12):1742-5. *Duration of follow-up less than 1 year*

310. Harris DCH, Rangan GK. Retardation of kidney failure -- applying principles to practice. Annals of the Academy of Medicine, Singapore 2005; 34(1):16-23. *Not a randomized trial*

311. Haupt MT, Jastremski MS, Clemmer TP, et al. Effect of ibuprofen in patients with severe sepsis: a randomized, double-blind, multicenter study. The Ibuprofen Study Group. Critical Care Medicine 1991; 19(11):1339-47. *Intervention not related to monitoring of CKD*

312. Havenetidis K, Bourdas D. Creatine supplementation: effects on urinary excretion and anaerobic performance. Journal of Sports Medicine & Physical Fitness 2003; 43(3):347-55. *Less than 50 patients in study*

313. Hayes JK, Stanley TH, Lind GH, et al. A double-blind study to evaluate the safety of recombinant human hemoglobin in surgical patients during general anesthesia. Journal of Cardiothoracic & Vascular Anesthesia 2001; 15(5):593-602. *Intervention not related to monitoring of CKD*

314. Hebert LA, Kusek JW, Greene T, et al. Effects of blood pressure control on progressive renal disease in blacks and whites. Modification of Diet in Renal Disease Study Group. Hypertension 1997; 30(3 Pt 1):428-35. *Intervention not related to monitoring of CKD*

315. Hebert LA, Wilmer WA, Falkenhain ME, et al. Renoprotection: one or many therapies? Kidney International 2001; 59(4):1211-26. *Intervention not related to monitoring of CKD*

316. Hedayat S, Kershner RP, Su G. Relationship of whole-blood FK506 concentrations to rejection and toxicity in liver and kidney transplants. Journal of Biopharmaceutical Statistics 1996; 6(4):411-24. *Not patients with early CKD*

317. Heering P, Morgera S, Schmitz FJ, et al. Cytokine removal and cardiovascular hemodynamics in septic patients with continuous venovenous hemofiltration. Intensive Care Medicine 1997; 23(3):288-96. *Not a randomized trial*

318. Herlitz H, Harris K, Risler T, et al. The effects of an ACE inhibitor and a calcium antagonist on the progression of renal disease: the Nephros Study. Nephrology Dialysis Transplantation 2001; 16(11):2158-65. *Intervention not related to monitoring of CKD*

319. Hernandez-Herrera G, Martin-Malo A, Rodriguez M, et al. Assessment of the length of each hemodialysis session by on-line dialysate urea monitoring. Nephron 2001; 89(1):37-42. *Not patients with early CKD*

320. Higashihara E, Nutahara K, Horie S, et al. The effect of eicosapentaenoic acid on renal function and volume in patients with ADPKD. Nephrology Dialysis Transplantation 2008; 23(9):2847-52. *Intervention not related to monitoring of CKD*

321. Hilton R, Tong CYW. Antiviral therapy for polyomavirus-associated nephropathy after renal transplantation. Journal of Antimicrobial Chemotherapy 2008; 62(5):855-9. *Not a randomized trial*

322. Himmelfarb J, Tolkoff Rubin N, Chandran P, et al. A multicenter comparison of dialysis membranes in the treatment of acute renal failure requiring dialysis. Journal of the American Society of Nephrology 1998; 9(2):257-66. *Not a randomized trial*

323. Hiremath S, Fergusson D, Doucette S, et al. Renin angiotensin system blockade in kidney transplantation: a systematic review of the evidence. American Journal of Transplantation 2007; 7(10):2350-60. *Not a randomized trial*

324. Hirth RA, Turenne MN, Wheeler JRC, et al. Provider monitoring and pay-for-performance when multiple providers affect outcomes: An application to renal dialysis. Health Services Research 2009; 44(5 Pt 1):1585-602. *Not a randomized trial*

325. Hogan TJ, Elliott WJ, Seto AH, et al. Antihypertensive treatment with and without benazepril in patients with chronic renal insufficiency: a US economic evaluation. Pharmacoeconomics 2002; 20(1):37-47. *Not a randomized trial*

326. Hollenberg NK. Aldosterone in the development and progression of renal injury. Kidney International 2004; 66(1):1-9. *Not a randomized trial*

327. Holm T, Andreassen AK, Aukrust P, et al. Omega-3 fatty acids improve blood pressure control and preserve renal function in hypertensive heart transplant recipients. European Heart Journal 2001; 22(5):428-36. *Less than 50 patients in study*

328. Hong SJ, Cho KS, Cho HY, et al. A prospective, multicenter, open-label trial of zoledronic acid in patients with hormone refractory prostate cancer. Yonsei Medical Journal 2007; 48(6):1001-8. *Not a randomized trial*

329. Hor T, Baldwin D. Urinary albumin excretion in patients with diabetes after renal transplantation. Transplantation Proceedings 2006; 38(9):2879-82. *Not patients with early CKD*

330. Hou FF, Zhang X, Zhang GH, et al. Efficacy and safety of benazepril for advanced chronic renal insufficiency. New England Journal of Medicine 2006; 354(2):131-40. *Intervention not related to monitoring of CKD*

331. Hu W, Liu C, Xie H, et al. Mycophenolate mofetil versus cyclophosphamide for inducing remission of ANCA vasculitis with moderate renal involvement. Nephrology Dialysis Transplantation 2008; 23(4):1307-12. *Less than 50 patients in study*

332. Huland E, Heinzer H, Huland H. Treatment of pulmonary metastatic renal-cell carcinoma in 116 patients using inhaled interleukin-2 (IL-2). Anticancer Research 1999; 19(4A):2679-83. *Not a randomized trial*

333. Hunsicker LG, Adler S, Caggiula A, et al. Predictors of the progression of renal disease in the Modification of Diet in Renal Disease Study. Kidney International 1997; 51(6):1908-19. *Not a randomized trial*

334. Huskey J, Lindenfeld J, Cook T, et al. Effect of simvastatin on kidney function loss in patients with coronary heart disease: findings from the Scandinavian Simvastatin Survival Study (4S). Atherosclerosis 2009; 205(1):202-6. *Intervention not related to monitoring of CKD*

335. Hutson TE, Davis ID, Machiels JP, et al. Efficacy and safety of pazopanib in patients with metastatic renal cell carcinoma. Journal of Clinical Oncology 2010; 28(3):475-80. *Not a randomized trial*

336. Iaria G, Pisani F, Iorio B, et al. Long-term results of kidney transplantation with cyclosporine- and everolimus-based immunosuppression. Transplantation Proceedings 2006; 38(4):1018-9. *Not patients with early CKD*

337. Ibsen H, Olsen MH, Wachtell K, et al. Reduction in albuminuria translates to reduction in cardiovascular events in hypertensive patients: losartan intervention for endpoint reduction in hypertension study. Hypertension 2005; 45(2):198-202. *Intervention not related to monitoring of CKD*

338. Ideura T, Shimazui M, Morita H, et al. Protein intake of more than 0.5 g/kg BW/day is not effective in suppressing the progression of chronic renal failure. Contributions to Nephrology 2007; 155:40-9. *Not a randomized trial*

339. Ihle BU, Whitworth JA, Shahinfar S, et al. Angiotensin-converting enzyme inhibition in nondiabetic progressive renal insufficiency: a controlled double-blind trial. American Journal of Kidney Diseases 1996; 27(4):489-95. *Intervention not related to monitoring of CKD*

340. Ikuerowo SO, Kuczyk MA, Mengel M, et al. Alteration of subcellular and cellular expression patterns of cyclin B1 in renal cell carcinoma is significantly related to clinical progression and survival of patients. International Journal of Cancer 2006; 119(4):867-74. *Not a randomized trial*

341. Imamura R, Ichimaru N, Moriyama T, et al. Long term efficacy of simvastatin in renal transplant recipients treated with cyclosporine or tacrolimus. Clinical Transplantation 2005; 19(5):616-21. *Not a randomized trial*

342. Inoue S, Tomino Y. Effects of calcium antagonists in hypertensive patients with renal dysfunction: a prospective, randomized, parallel trial comparing benidipine and nifedipine. Nephrology 2004; 9(5):265-71. *Intervention not related to monitoring of CKD*

343. Inrig JK, Patel UD, Gillespie BS, et al. Relationship between interdialytic weight gain and blood pressure among prevalent hemodialysis patients. American Journal of Kidney Diseases 2007; 50(1):108-18. *Not a randomized trial*

344. Investigators RS, Bellomo R, Cass A, et al. Design and challenges of the Randomized Evaluation of Normal versus Augmented Level Replacement Therapy (RENAL) Trial: high-dose versus standard-dose hemofiltration in acute renal failure. Blood Purification 2008; 26(5):407-16. *Not patients with early CKD*

345. Ishani A, Grandits GA, Grimm RH, et al. Association of single measurements of dipstick proteinuria, estimated glomerular filtration rate, and hematocrit with 25-year incidence of end-stage renal disease in the multiple risk factor intervention trial. Journal of the American Society of Nephrology 2006; 17(5):1444-52. *Not a randomized trial*

346. Ishani A, Paudel M, Taylor BC, et al. Renal function and rate of hip bone loss in older men: the Osteoporotic Fractures in Men Study. Osteoporosis International 2008; 19(11):1549-56. *Not a randomized trial*

347. Ishani A, Xue JL, Himmelfarb J, et al. Acute kidney injury increases risk of ESRD among elderly. Journal of the American Society of Nephrology 2009; 20(1):223-8. *Not a randomized trial*

348. Ishida H, Satou T, Tsuji K, et al. The breath ammonia measurement of the hemodialysis with a QCM-NH3 sensor. Bio-Medical Materials & Engineering 2008; 18(2):99-106. *Not a randomized trial*

349. Ishikawa J, Hoshide S, Shibasaki S, et al. The Japan Morning Surge-1 (JMS-1) study: protocol description.[Erratum appears in Hypertens Res. 2006 Sep;29(9):739]. Hypertension Research - Clinical & Experimental 2006; 29(3):153-9. *Intervention not related to monitoring of CKD*

350. Ix JH, Shlipak MG, Sarnak MJ, et al. Fetuin-A is not associated with mortality in chronic kidney disease. Kidney International 2007; 72(11):1394-9. *Not a randomized trial*

351. Jacobs C, Frei D, Perkins AC. Results of the European Survey on Anaemia Management 2003 (ESAM 2003): current status of anaemia management in dialysis patients, factors affecting epoetin dosage and changes in anaemia management over the last 5 years. Nephrology Dialysis Transplantation 2005; 20 Suppl 3:iii3-24. *Not a randomized trial*

352. Jafar TH, Schmid CH, Landa M, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease. A meta-analysis of patient-level data.[Erratum appears in Ann Intern Med 2002 Aug 20;137(4):299]. Annals of Internal Medicine 2001; 135(2):73-87. *Intervention not related to monitoring of CKD*

353. Jafar TH, Schmid CH, Stark PC, et al. The rate of progression of renal disease may not be slower in women compared with men: a patient-level meta-analysis. Nephrology Dialysis Transplantation 2003; 18(10):2047-53. *Not a randomized trial*

354. Jafar TH, Stark PC, Schmid CH, et al. Progression of chronic kidney disease: the role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: a patient-level meta-analysis. Annals of Internal Medicine 2003; 139(4):244-52. *Intervention not related to monitoring of CKD*

355. Jafar TH, Stark PC, Schmid CH, et al. Proteinuria as a modifiable risk factor for the progression of non-diabetic renal disease. Kidney International 2001; 60(3):1131-40. *Intervention not related to monitoring of CKD*

356. Jain L, Venitz J, Figg WD. Randomized discontinuation trial of sorafenib (BAY 43-9006). Cancer Biology & Therapy 2006; 5(10):1270-2. *Not a randomized trial*

357. Jandeleit-Dahm K, Cao Z, Cox AJ, et al. Role of hyperlipidemia in progressive renal disease: focus on diabetic nephropathy. Kidney International - Supplement 1999; 71:S31-6. *Not human study*

358. Jayne D. Challenges in the management of microscopic polyangiitis: past, present and future. Current Opinion in Rheumatology 2008; 20(1):3-9. *Not a randomized trial*

359. Jensen NF, Todd MM, Block RI, et al. The efficacy of routine central venous monitoring in major head and neck surgery: a retrospective review. Journal of Clinical Anesthesia 1995; 7(2):119-25. *Not a randomized trial*

360. Jeon SH, Chang SG, Kim JI. The role of adjuvant immunotherapy after radical nephrectomy and prognostic factors in pT3N0M0 renal cell carcinoma. Anticancer Research 1999; 19(6C):5593-7. *Not patients with early CKD*

361. Jerums G, Allen TJ, Campbell DJ, et al. Long-term renoprotection by perindopril or nifedipine in non-hypertensive patients with Type 2 diabetes and microalbuminuria. Diabetic Medicine 2004; 21(11):1192-9. *Intervention not related to monitoring of CKD*

362. Jin K-K, Chen L, Pan J-Y, et al. Acupressure therapy inhibits the development of diabetic complications in Chinese patients with type 2 diabetes. Journal of Alternative & Complementary Medicine 2009; 15(9):1027-32. *Intervention not related to monitoring of CKD*

363. Johnson CA, McCarthy J, Bailie GR, et al. Analysis of renal bone disease treatment in dialysis patients. American Journal of Kidney Diseases 2002; 39(6):1270-7. *Not a randomized trial*

364. Johnson DW. Evidence-based guide to slowing the progression of early renal insufficiency. Internal Medicine Journal 2004; 34(1-2):50-7. *Intervention not related to monitoring of CKD*

365. Johnson DW. Dietary protein restriction as a treatment for slowing chronic kidney disease progression: the case against. Nephrology 2006; 11(1):58-62. *Not a randomized trial*

366. Jorres A. Acute renal failure. Extracorporeal treatment strategies. Minerva Medica 2002; 93(5):329-4. *Not a randomized trial*

367. Jorres A. Extracorporeal treatment strategy in acute renal failure. International Journal of Artificial Organs 2002; 25(5):391-6. *Not a randomized trial*

368. Jose P, Skali H, Anavekar N, et al. Increase in creatinine and cardiovascular risk in patients with systolic dysfunction after myocardial infarction. Journal of the American Society of Nephrology 2006; 17(10):2886-91. *Intervention not related to monitoring of CKD*

369. Joss N, Jardine A, Gaffney D, et al. Influence of apolipoprotein E genotype on progression of diabetic nephropathy. Nephron. Experimental Nephrology 2005; 101(4):e127-33. *Not a randomized trial*

370. Jungers P, Choukroun G, Oualim Z, et al. Beneficial influence of recombinant human erythropoietin therapy on the rate of progression of chronic renal failure in predialysis patients. Nephrology Dialysis Transplantation 2001; 16(2):307-12. *Not a randomized trial*

371. Kadowaki D, Anraku M, Tasaki Y, et al. Effect of olmesartan on oxidative stress in hemodialysis patients. Hypertension Research - Clinical & Experimental 2007; 30(5):395-402. *Not patients with early CKD*

372. Kahan BD, Dunn J, Fitts C, et al. Reduced inter- and intrasubject variability in cyclosporine pharmacokinetics in renal transplant recipients treated with a microemulsion formulation in conjunction with fasting, low-fat meals, or high-fat meals. Transplantation 1995; 59(4):505-11. *Not patients with early CKD*

373. Kalpoe JS, Schippers EF, Eling Y, et al. Similar reduction of cytomegalovirus DNA load by oral valganciclovir and intravenous ganciclovir on pre-emptive therapy after renal and renal-pancreas transplantation. Antiviral Therapy 2005; 10(1):119-23. *Not a randomized trial*

374. Kamgar M, Nobakhthaghighi N, Shamshirsaz AA, et al. Impaired fibrinolytic activity in type II diabetes: correlation with urinary albumin excretion and progression of renal disease. Kidney International 2006; 69(10):1899-903. *Not a randomized trial*

375. Kamper AL, Holstein-Rathlou NH, Leyssac PP, et al. The influence of angiotensin-converting enzyme inhibition on renal tubular function in progressive chronic nephropathy. American Journal of Kidney Diseases 1996; 28(6):822-31. *Intervention not related to monitoring of CKD*

376. Kaneko K, Someya T, Nishizaki N, et al. Simplified quantification of urinary protein excretion using a novel dipstick in children. Pediatric Nephrology 2005; 20(6):834-6. *Not adult population*

377. Kanno Y, Okada H, Yamaji Y, et al. Angiotensin-converting-enzyme inhibitors slow renal decline in IgA nephropathy, independent of tubulointerstitial fibrosis at presentation. Qjm 2005; 98(3):199-203. *Intervention not related to monitoring of CKD*

378. Kaplan AA. Therapeutic apheresis for cancer related hemolytic uremic syndrome. Therapeutic Apheresis 2000; 4(3):201-6. *Intervention not related to monitoring of CKD*

379. Kaplan B, Wang Z, Keilani T, et al. The specificity of monoclonal fluorescence polarization immunoassay for cyclosporine in recipients of simultaneous pancreas-kidney transplants. Therapeutic Drug Monitoring 1995; 17(5):499-503. *Intervention not related to monitoring of CKD*

380. Kasahara J, Kobayashi K, Maeshima Y, et al. Clinical significance of serum oxidized low-density lipoprotein/beta2-glycoprotein I complexes in patients with chronic renal diseases. Nephron 2004; 98(1):c15-24. *Intervention not related to monitoring of CKD*

381. Kasimu H, Jakai T, Qilong C, et al. A brief evaluation for pre-estimating the severity of gallstone pancreatitis. Jop: Journal of the Pancreas [Electronic Resource] 2009; 10(2):147-51. *Intervention not related to monitoring of CKD*

382. Kasiske BL, Heim-Duthoy K, Rao KV, et al. The relationship between cyclosporine pharmacokinetic parameters and subsequent acute rejection in renal transplant recipients. Transplantation 1988; 46(5):716-22. *Not patients with early CKD*

383. Kasiske BL, Lakatua JD. The effects of dietary protein restriction on chronic progressive renal disease. Mineral & Electrolyte Metabolism 1997; 23(3-6):296-300. *Not a randomized trial*

384. Kasiske BL, Lakatua JD, Ma JZ, et al. A meta-analysis of the effects of dietary protein restriction on the rate of decline in renal function. American Journal of Kidney Diseases 1998; 31(6):954-61. *Not a randomized trial*

385. Katz-Brull R, Rofsky NM, Morrin MM, et al. Decreases in free cholesterol and fatty acid unsaturation in renal cell carcinoma demonstrated by breath-hold magnetic resonance spectroscopy. American Journal of Physiology - Renal Physiology 2005; 288(4):F637-41. *Intervention not related to monitoring of CKD*

386. Kaufman JS, O'Connor TZ, Zhang JH, et al. Randomized controlled trial of clopidogrel plus aspirin to prevent hemodialysis access graft thrombosis. Journal of the American Society of Nephrology 2003; 14(9):2313-21. *Not patients with early CKD*

387. Kaver I, Pecht M, Trainin N, et al. T lymphocyte subsets and function in the peripheral blood of patients with urological cancer. Oncology 1992; 49(2):108-13. *Not a randomized trial*

388. Kawasaka K, Tatsumi N. D-amino acid oxidase activity in urine obtained from patients with renal disorders. Clinical Nephrology 1998; 49(4):214-20. *Not a randomized trial*

389. Kell MJ. Utilization of plasma and urine methadone concentrations to optimize treatment in maintenance clinics: I. Measurement techniques for a clinical setting. Journal of Addictive Diseases 1994; 13(1):5-26. *Not a randomized trial*

390. Kent DM, Jafar TH, Hayward RA, et al. Progression risk, urinary protein excretion, and treatment effects of angiotensin-converting enzyme inhibitors in nondiabetic kidney disease. Journal of the American Society of Nephrology 2007; 18(6):1959-65. *Not a randomized trial*

391. Kershner RP, Fitzsimmons WE. Relationship of FK506 whole blood concentrations and efficacy and toxicity after liver and kidney transplantation. Transplantation 1996; 62(7):920-6. *Not patients with early CKD*

392. Khan DA, Ahmad TM, Qureshil AH, et al. Assessment of proteinuria by using protein: creatinine index in random urine sample. JPMA - Journal of the Pakistan Medical Association 2005; 55(10):428-31. *Not a randomized trial*

393. Khanna D, Clements PJ, Furst DE, et al. Recombinant human relaxin in the treatment of systemic sclerosis with diffuse cutaneous involvement: a randomized, double-blind, placebo-controlled trial. Arthritis & Rheumatism 2009; 60(4):1102-11. *Intervention not related to monitoring of CKD*

394. Khoury JA, Storch GA, Bohl DL, et al. Prophylactic versus preemptive oral valganciclovir for the management of cytomegalovirus infection in adult renal transplant recipients. American Journal of Transplantation 2006; 6(9):2134-43. *Intervention not related to monitoring of CKD*

395. Kimmel M, Butscheid M, Brenner S, et al. Improved estimation of glomerular filtration rate by serum cystatin C in preventing contrast induced nephropathy by N-acetylcysteine or zinc--preliminary results. Nephrology Dialysis Transplantation 2008; 23(4):1241-5. *Intervention not related to monitoring of CKD*

396. Kimmel PL, Mishkin GJ, Umana WO. Captopril and renal survival in patients with human immunodeficiency virus nephropathy. American Journal of Kidney Diseases 1996; 28(2):202-8. *Not a randomized trial*

397. Kincaid-Smith P, Fairley KF, Farish S, et al. Reduction of proteinuria by rosiglitazone in non-diabetic renal disease. Nephrology 2008; 13(1):58-62. *Intervention not related to monitoring of CKD*

398. Kincaid-Smith P, Fairley KF, Packham D. Dual blockade of the renin-angiotensin system compared with a 50% increase in the dose of angiotensin-converting enzyme inhibitor: effects on proteinuria and blood pressure. Nephrology Dialysis Transplantation 2004; 19(9):2272-4. *Intervention not related to monitoring of CKD*

399. Kinouchi T, Sakamoto J, Tsukamoto T, et al. Prospective randomized trial of natural interferon-alpha versus natural interferon-alpha plus cimetidine in advanced renal cell carcinoma with pulmonary metastasis. Journal of Cancer Research & Clinical Oncology 2006; 132(8):499-504. *Not patients with early CKD*

400. Klahr S. Role of dietary protein and blood pressure in the progression of renal disease. Kidney International 1996; 49(6):1783-6. *Not a randomized trial*

401. Klahr S. Prevention of progression of nephropathy. Nephrology Dialysis Transplantation 1997; 12 Suppl 2:63-6. *Not a randomized trial*

402. Klahr S, Breyer JA, Beck GJ, et al. Dietary protein restriction, blood pressure control, and the progression of polycystic kidney disease. Modification of Diet in Renal Disease Study Group.[Erratum appears in J Am Soc Nephrol 1995 Oct;6(4):1318]. Journal of the American Society of Nephrology 1995; 5(12):2037-47. *Not a randomized trial*

403. Kliem V, Fricke L, Wollbrink T, et al. Improvement in long-term renal graft survival due to CMV prophylaxis with oral ganciclovir: results of a randomized clinical trial. American Journal of Transplantation 2008; 8(5):975-83. *Intervention not related to monitoring of CKD*

404. Kobayashi Y, Hiki Y, Kokubo T, et al. Steroid therapy during the early stage of progressive IgA nephropathy. A 10-year follow-up study. Nephron 1996; 72(2):237-42. *Not patients with early CKD*

405. Koc E, Tunca M, Akgul EO, et al. Effects of etanercept on urine neopterin levels in patients with psoriasis in a controlled, open-label study. Journal of Dermatology 2009; 36(4):191-6. *Not patients with early CKD*

406. Koch KM, Koene RA, Messinger D, et al. The use of epoetin beta in anemic predialysis patients with chronic renal failure.[Erratum appears in Clin Nephrol 1995 Oct;44(4):278]. Clinical Nephrology 1995; 44(3):201-8. *Intervention not related to monitoring of CKD*

407. Kohen JA, Whitley KY, Kjellstrand CM. Continuous arteriovenous hemofiltration: a comparison with hemodialysis in acute renal failure. Transactions - American Society for Artificial Internal Organs 1985; 31:169-75. *Not patients with early CKD*

408. Kopple JD, Greene T, Chumlea WC, et al. Relationship between nutritional status and the glomerular filtration rate: results from the MDRD study. Kidney International 2000; 57(4):1688-703. *Not a randomized trial*

409. Kovesdy CP, Ahmadzadeh S, Anderson JE, et al. Association of activated vitamin D treatment and mortality in chronic kidney disease. Archives of Internal Medicine 2008; 168(4):397-403. *Not a randomized trial*

410. Kowey PR, Dickson TZ, Zhang Z, et al. Losartan and end-organ protection--lessons from the RENAAL study. Clinical Cardiology 2005; 28(3):136-42. *Not a randomized trial*

411. Koya D, Haneda M, Inomata S, et al. Long-term effect of modification of dietary protein intake on the progression of diabetic nephropathy: a randomised controlled trial. Diabetologia 2009; 52(10):2037-45. *Intervention not related to monitoring of CKD*

412. Krairittichai U, Chaisuvannarat V. Effects of dual blockade of renin-angiotensin system in type 2 diabetes mellitus patients with diabetic nephropathy. Journal of the Medical Association of Thailand 2009; 92(5):611-7. *Intervention not related to monitoring of CKD*

413. Kralovicova K, Spanik S, Halko J, et al. Do vancomycin serum levels predict failures of vancomycin therapy or nephrotoxicity in cancer patients? Journal of Chemotherapy 1997; 9(6):420-6. *Intervention not related to monitoring of CKD*

414. Kramer BK, Neumayer HH, Stahl R, et al. Graft function, cardiovascular risk factors, and sex hormones in renal transplant recipients on an immunosuppressive regimen of everolimus, reduced dose of cyclosporine, and basiliximab. Transplantation Proceedings 2005; 37(3):1601-4. *Not patients with early CKD*

415. Krane V, Wanner C. Dyslipidaemia in chronic kidney disease. Minerva Urologica e Nefrologica 2007; 59(3):299-316. *Not a randomized trial*

416. Kroencke TJ, Wasser MN, Pattynama PMT, et al. Gadobenate dimeglumine-enhanced MR angiography of the abdominal aorta and renal arteries. AJR 2002; American Journal of Roentgenology. 179(6):1573-82. *Intervention not related to monitoring of CKD*

417. Kshirsagar AV, Joy MS, Hogan SL, et al. Effect of ACE inhibitors in diabetic and nondiabetic chronic renal disease: a systematic overview of randomized placebo-controlled trials. American Journal of Kidney Diseases 2000; 35(4):695-707. *Not a randomized trial*

418. Kumar MSA, Xiao S-G, Fyfe B, et al. Steroid avoidance in renal transplantation using basiliximab induction, cyclosporine-based immunosuppression and protocol biopsies. Clinical Transplantation 2005; 19(1):61-9. *Not patients with early CKD*

419. Kuntz RA, Holt DW, Turner S, et al. Effects of conventional ultrafiltration on renal performance during adult cardiopulmonary bypass procedures. Journal of Extra-Corporeal Technology 2006; 38(2):144-53. *Intervention not related to monitoring of CKD*

420. Kuriyama S, Tomonari H, Yoshida H, et al. Reversal of anemia by erythropoietin therapy retards the progression of chronic renal failure, especially in nondiabetic patients. Nephron 1997; 77(2):176-85. *Intervention not related to monitoring of CKD*

421. Kutner NG. Quality of life and daily hemodialysis. Seminars in Dialysis 2004; 17(2):92-8. *Not patients with early CKD*

422. Laczika K, Staudinger T, Hollenstein U, et al. Renal tolerability of four different once-daily dose regimen of netilmicin in critical care patients. Wiener Klinische Wochenschrift 1997; 109(21):840-4. *Intervention not related to monitoring of CKD*

423. Laffel LM, McGill JB, Gans DJ. The beneficial effect of angiotensin-converting enzyme inhibition with captopril on diabetic nephropathy in normotensive IDDM patients with microalbuminuria. North American Microalbuminuria Study Group. American Journal of Medicine 1995; 99(5):497-504. *Intervention not related to monitoring of CKD*

424. Laing C, Unwin RJ. Are calcium antagonists effective in preventing complications of hypertension and progression of renal disease? Current Opinion in Nephrology & Hypertension 2000; 9(5):489-95. *Not a randomized trial*

425. Lalezari JP, Holland GN, Kramer F, et al. Randomized, controlled study of the safety and efficacy of intravenous cidofovir for the treatment of relapsing cytomegalovirus retinitis in patients with AIDS. Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology 1998; 17(4):339-44. *Intervention not related to monitoring of CKD*

426. Lamuraglia M, Escudier B, Chami L, et al. To predict progression-free survival and overall survival in metastatic renal cancer treated with sorafenib: pilot study using dynamic contrast-enhanced Doppler ultrasound.[Erratum appears in Eur J Cancer. 2007 May;43(8):1336]. European Journal of Cancer 2006; 42(15):2472-9. *Not patients with early CKD*

427. Lara PN, Jr., Quinn DI, Margolin K, et al. SU5416 plus interferon alpha in advanced renal cell carcinoma: a phase II California Cancer Consortium Study with biological and imaging correlates of angiogenesis inhibition. Clinical Cancer Research 2003; 9(13):4772-81. *Intervention not related to monitoring of CKD*

428. Laufs U, Custodis F, Bohm M. Who does not need a statin: too late in end-stage renal disease or heart failure? Heart 2008; 94(9):1138-40. *Not a randomized trial*

429. Lawrie AS, McDonald SJ, Purdy G, et al. Prothrombin time derived fibrinogen determination on Sysmex CA-6000. Journal of Clinical Pathology 1998; 51(6):462-6. *Intervention not related to monitoring of CKD*

430. Le Meur Y, Buchler M, Thierry A, et al. Individualized mycophenolate mofetil dosing based on drug exposure significantly improves patient outcomes after renal transplantation. American Journal of Transplantation 2007; 7(11):2496-503. *Not patients with early CKD*

431. Lea J, Cheek D, Thornley-Brown D, et al. Metabolic syndrome, proteinuria, and the risk of progressive CKD in hypertensive African Americans. American Journal of Kidney Diseases 2008; 51(5):732-40. *Intervention not related to monitoring of CKD*

432. Lea J, Greene T, Hebert L, et al. The relationship between magnitude of proteinuria reduction and risk of end-stage renal disease: results of the African American study of kidney disease and hypertension. Archives of Internal Medicine 2005; 165(8):947-53. *Intervention not related to monitoring of CKD*

433. Lee CP, Patel PM, Selby PJ, et al. Randomized phase II study comparing thalidomide with medroxyprogesterone acetate in patients with metastatic renal cell carcinoma. Journal of Clinical Oncology 2006; 24(6):898-903. *Not patients with early CKD*

434. Lee D, Levin A, Roger SD, et al. Longitudinal analysis of performance of estimated glomerular filtration rate as renal function declines in chronic kidney disease. Nephrology Dialysis Transplantation 2009; 24(1):109-16. *Not a randomized trial*

435. Lee JY, Kusek JW, Greene PG, et al. Assessing medication adherence by pill count and electronic monitoring in the African American Study of Kidney Disease and Hypertension (AASK) Pilot Study. American Journal of Hypertension 1996; 9(8):719-25. *Intervention not related to monitoring of CKD*

436. Leenen FHH, Coletta E, Davies RA. Prevention of renal dysfunction and hypertension by amlodipine after heart transplant. American Journal of Cardiology 2007; 100(3):531-5. *Intervention not related to monitoring of CKD*

437. Lehmkuhl HB, Arizon J, Vigano M, et al. Everolimus with reduced cyclosporine versus MMF with standard cyclosporine in de novo heart transplant recipients. Transplantation 2009; 88(1):115-22. *Not patients with early CKD*

438. Lely AT, van der Kleij FGH, Kistemaker TJ, et al. Impact of the preintervention rate of renal function decline on outcome of renoprotective intervention. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(1):54-60. *Intervention not related to monitoring of CKD*

439. Lemley KV, Abdullah I, Myers BD, et al. Evolution of incipient nephropathy in type 2 diabetes mellitus.[Erratum appears in Kidney Int 2000 Nov;58(5):2257]. Kidney International 2000; 58(3):1228-37. *Not a randomized trial*

440. Levey AS, Adler S, Caggiula AW, et al. Effects of dietary protein restriction on the progression of advanced renal disease in the Modification of Diet in Renal Disease Study. American Journal of Kidney Diseases 1996; 27(5):652-63. *Intervention not related to monitoring of CKD*

441. Levey AS, Greene T, Sarnak MJ, et al. Effect of dietary protein restriction on the progression of kidney disease: long-term follow-up of the Modification of Diet in Renal Disease (MDRD) Study. American Journal of Kidney Diseases 2006; 48(6):879-88. *Intervention not related to monitoring of CKD*

442. Levin NW, Fishbane S, Canedo FV, et al. Intravenous methoxy polyethylene glycol-epoetin beta for haemoglobin control in patients with chronic kidney disease who are on dialysis: a randomised non-inferiority trial (MAXIMA).[Erratum appears in Lancet. 2008 Feb 2;371(9610):386]. Lancet 2007; 370(9596):1415-21. *Not patients with early CKD*

443. Levine RJ, Hauth JC, Curet LB, et al. Trial of calcium to prevent preeclampsia. New England Journal of Medicine 1997; 337(2):69-76. *Intervention not related to monitoring of CKD*

444. Lewis EJ. The role of angiotensin II receptor blockers in preventing the progression of renal disease in patients with type 2 diabetes. American Journal of Hypertension 2002; 15(10 Pt 2):123S-8S. *Not a randomized trial*

445. Lewis EJ, Hunsicker LG, Rodby RA, et al. A clinical trial in type 2 diabetic nephropathy. American Journal of Kidney Diseases 2001; 38(4 Suppl 1):S191-4. *Intervention not related to monitoring of CKD*

446. Lezaic VD, Marinkovic J, Ristic S, et al. Conversion of azathioprine to mycophenolate mofetil and chronic graft failure progression. Transplantation Proceedings 2005; 37(2):734-6. *Not patients with early CKD*

447. Li PK, Mak TW, Wang AY, et al. The interaction of fluvastatin and cyclosporin A in renal transplant patients. International Journal of Clinical Pharmacology & Therapeutics 1995; 33(4):246-8. *Not patients with early CKD*

448. Lievre M, Marre M, Chatellier G, et al. The non-insulin-dependent diabetes, hypertension, microalbuminuria or proteinuria, cardiovascular events, and ramipril (DIABHYCAR) study: design, organization, and patient recruitment. DIABHYCAR Study Group. Controlled Clinical Trials 2000; 21(4):383-96. *Intervention not related to monitoring of CKD*

449. Lin JL, Lin-Tan DT, Yu CC, et al. Environmental exposure to lead and progressive diabetic nephropathy in patients with type II diabetes. Kidney International 2006; 69(11):2049-56. *Not a randomized trial*

450. Lin J-L, Lin-Tan D-T, Hsu K-H, et al. Environmental lead exposure and progression of chronic renal diseases in patients without diabetes. New England Journal of Medicine 2003; 348(4):277-86. *Intervention not related to monitoring of CKD*

451. Lin S-L, Chen Y-M, Chiang W-C, et al. Effect of pentoxifylline in addition to losartan on proteinuria and GFR in CKD: a 12-month randomized trial. American Journal of Kidney Diseases 2008; 52(3):464-74. *Intervention not related to monitoring of CKD*

452. Lin-Tan D-T, Lin J-L, Yen T-H, et al. Long-term outcome of repeated lead chelation therapy in progressive non-diabetic chronic kidney diseases. Nephrology Dialysis Transplantation 2007; 22(10):2924-31. *Intervention not related to monitoring of CKD*

453. Lipton A. The safety of zoledronic acid. Expert Opinion on Drug Safety 2007; 6(3):305-13. *Intervention not related to monitoring of CKD*

454. Lipton A, Zheng M, Seaman J. Zoledronic acid delays the onset of skeletal-related events and progression of skeletal disease in patients with advanced renal cell carcinoma. Cancer 2003; 98(5):962-9. *Intervention not related to monitoring of CKD*

455. Littlewood KJ, Greiner W, Baum D, et al. Adjunctive treatment with moxonidine versus nitrendipine for hypertensive patients with advanced renal failure: a cost-effectiveness analysis. BMC Nephrology 2007; 8:9. *Not a randomized trial*

456. Liu K-P, Lin C-Y, Chen H-J, et al. Renin-angiotensin system polymorphisms in Taiwanese primary vesicoureteral reflux. Pediatric Nephrology 2004; 19(6):594-601. *Not a randomized trial*

457. Liu M, Zhang W, Gu M, et al. Protective effects of sirolimus by attenuating connective tissue growth factor expression in human chronic allograft nephropathy. Transplantation Proceedings 2007; 39(5):1410-5. *Not patients with early CKD*

458. Llewelyn DEH, Garcia-Puig J. How different urinary albumin excretion rates can predict progression to nephropathy and the effect of treatment in hypertensive diabetics. Journal of the Renin-Angiotensin-Aldosterone System 2004; 5(3):141-5. *Intervention not related to monitoring of CKD*

459. Lobo PI, Cortez MS, Stevenson W, et al. Normocalcemic hyperparathyroidism associated with relatively low 1:25 vitamin D levels post-renal transplant can be successfully treated with oral calcitriol. Clinical Transplantation 1995; 9(4):277-81. *Not a randomized trial*

460. Locatelli F, Carbarns IR, Maschio G, et al. Long-term progression of chronic renal insufficiency in the AIPRI Extension Study. The Angiotensin-Converting-Enzyme Inhibition in Progressive Renal Insufficiency Study Group. Kidney International - Supplement 1997; 63:S63-6. *Intervention not related to monitoring of CKD*

461. Locatelli F, Del Vecchio L, Andrulli S, et al. The role of underlying nephropathy in the progression of renal disease. Kidney International - Supplement 2000; 75:S49-55. *Not a randomized trial*

462. Locatelli F, Del Vecchio L, Pozzoni P. Clinical benefits of slowing the progression of renal failure. Kidney International - Supplement 2005; (99):S152-6. *Not a randomized trial*

463. Locatelli F, Del Vecchio L, Pozzoni P, et al. Is it the agent or the blood pressure level that matters for renal and vascular protection in chronic nephropathies? Kidney International - Supplement 2005; (93):S15-9. *Not a randomized trial*

464. Locatelli F, Manzoni C, Marcelli D. Factors affecting progression of renal insufficiency. Mineral & Electrolyte Metabolism 1997; 23(3-6):301-5. *Not a randomized trial*

465. Locatelli F, Marcelli D, Comelli M, et al. Proteinuria and blood pressure as causal components of progression to end-stage renal failure. Northern Italian Cooperative Study Group. Nephrology Dialysis Transplantation 1996; 11(3):461-7. *Intervention not related to monitoring of CKD*

466. Locatelli F, Pozzi C, Del Vecchio L, et al. Role of proteinuria reduction in the progression of IgA nephropathy. Renal Failure 2001; 23(3-4):495-505. *Not patients with early CKD*

467. Locatelli F, Vecchio LD, Pozzi C. IgA glomerulonephritis: beyond angiotensin-converting enzyme inhibitors. Nature Clinical Practice Nephrology 2006; 2(1):24-31. *Not a randomized trial*

468. Locatelli F, Vecchio LD, Pozzoni P. The importance of early detection of chronic kidney disease. Nephrology Dialysis Transplantation 2002; 17 Suppl 11:2-7. *Not a randomized trial*

469. Lombardo F, Frijia F, Bongioanni P, et al. Diffusion tensor MRI and MR spectroscopy in long lasting upper motor neuron involvement in amyotrophic lateral sclerosis. Archives Italiennes de Biologie 2009; 147(3):69-82. *Intervention not related to monitoring of CKD*

470. Lonn E, Yusuf S, Dzavik V, et al. Effects of ramipril and vitamin E on atherosclerosis: the study to evaluate carotid ultrasound changes in patients treated with ramipril and vitamin E (SECURE). Circulation 2001; 103(7):919-25. *Intervention not related to monitoring of CKD*

471. Lopes RJ, Lourenco AP, Mascarenhas J, et al. Safety of spironolactone use in ambulatory heart failure patients. Clinical Cardiology 2008; 31(11):509-13. *Intervention not related to monitoring of CKD*

472. Lorber MI, Mulgaonkar S, Butt KMH, et al. Everolimus versus mycophenolate mofetil in the prevention of rejection in de novo renal transplant recipients: a 3-year randomized, multicenter, phase III study. Transplantation 2005; 80(2):244-52. *Not patients with early CKD*

473. Louis S, Audrain M, Cantarovich D, et al. Long-term cell monitoring of kidney recipients after an antilymphocyte globulin induction with and without steroids. Transplantation 2007; 83(6):712-21. *Not patients with early CKD*

474. Loukovaara S, Immonen I, Teramo KA, et al. Progression of retinopathy during pregnancy in type 1 diabetic women treated with insulin lispro. Diabetes Care 2003; 26(4):1193-8. *Intervention not related to monitoring of CKD*

475. Low CL, Bailie G, Morgan S, et al. Effect of a sliding scale protocol for heparin on the ability to maintain whole blood activated partial thromboplastin times within a desired range in hemodialysis patients. Clinical Nephrology 1996; 45(2):120-4. *Not patients with early CKD*

476. Luchner A, Hengstenberg C, Lowel H, et al. Effect of compensated renal dysfunction on approved heart failure markers: direct comparison of brain natriuretic peptide (BNP) and N-terminal pro-BNP. Hypertension 2005; 46(1):118-23. *Not a randomized trial*

477. Lumlertgul D, Noppakun K, Rojanasthien N, et al. Pharmacokinetic study of the combination of tacrolimus and fluconazole in renal transplant patients. Journal of the Medical Association of Thailand 2006; 89 Suppl 2:S73-8. *Not patients with early CKD*

478. MacDonald AS, Group RGS. A worldwide, phase III, randomized, controlled, safety and efficacy study of a sirolimus/cyclosporine regimen for prevention of acute rejection in recipients of primary mismatched renal allografts. Transplantation 2001; 71(2):271-80. *Not patients with early CKD*

479. MacGregor MS, Deighan CJ, Rodger RSC, et al. A prospective open-label randomised trial of quinapril and/or amlodipine in progressive non-diabetic renal failure. Nephron 2005; 101(3):c139-49. *Intervention not related to monitoring of CKD*

480. Magee GM, Bilous RW, Cardwell CR, et al. Is hyperfiltration associated with the future risk of developing diabetic nephropathy? A meta-analysis. Diabetologia 2009; 52(4):691-7. *Not a randomized trial*

481. Mahalati K, Lawen J, Kiberd B, et al. Is 3-hour cyclosporine blood level superior to trough level in early post-renal transplantation period? Journal of Urology 2000; 163(1):37-41. *Not patients with early CKD*

482. Mak G, Tan CY, Ben Khiaron O, et al. An evaluation of the effects of renal artery stenting in renovascular hypertension. Irish Medical Journal 2007; 100(3):397-8. *Not a randomized trial*

483. Makino H, Haneda M, Babazono T, et al. Microalbuminuria reduction with telmisartan in normotensive and hypertensive Japanese patients with type 2 diabetes: a post-hoc analysis of The Incipient to Overt: Angiotensin II Blocker, Telmisartan, Investigation on Type 2 Diabetic Nephropathy (INNOVATION) study. Hypertension Research - Clinical & Experimental 2008; 31(4):657-64. *Intervention not related to monitoring of CKD*

484. Malik J, Slavikova M, Svobodova J, et al. Regular ultrasonographic screening significantly prolongs patency of PTFE grafts. Kidney International 2005; 67(4):1554-8. *Not patients with early CKD*

485. Mallett C, House AA, Spence JD, et al. Longitudinal ultrasound evaluation of carotid atherosclerosis in one, two and three dimensions. Ultrasound in Medicine & Biology 2009; 35(3):367-75. *Intervention not related to monitoring of CKD*

486. Mallikaarjun S, Shoaf SE, Boulton DW, et al. Effects of hepatic or renal impairment on the pharmacokinetics of aripiprazole. Clinical Pharmacokinetics 2008; 47(8):533-42. *Intervention not related to monitoring of CKD*

487. Mancini D, Pinney S, Burkhoff D, et al. Use of rapamycin slows progression of cardiac transplantation vasculopathy. Circulation 2003; 108(1):48-53. *Intervention not related to monitoring of CKD*

488. Mani S, Poo WJ. Single institution experience with recombinant gamma-interferon in the treatment of patients with metastatic renal cell carcinoma. American Journal of Clinical Oncology 1996; 19(2):149-53. *Not a randomized trial*

489. Manikandan R, Srinivasan V, Rane A. Which is the real gold standard for small-volume renal tumors? Radical nephrectomy versus nephron-sparing surgery. Journal of Endourology 2004; 18(1):39-44. *Not a randomized trial*

490. Manley HJ. Role of angiotensin-converting-enzyme inhibition in patients with renal disease. American Journal of Health-System Pharmacy 2000; 57 Suppl 1:S12-8. *Not a randomized trial*

491. Mann JFE, Gerstein HC, Yi Q-L, et al. Progression of renal insufficiency in type 2 diabetes with and without microalbuminuria: results of the Heart Outcomes and Prevention Evaluation (HOPE) randomized study. American Journal of Kidney Diseases 2003; 42(5):936-42. *Not a randomized trial*

492. Mann JFE, Gerstein HC, Yi Q-L, et al. Development of renal disease in people at high cardiovascular risk: results of the HOPE randomized study. Journal of the American Society of Nephrology 2003; 14(3):641-7. *Not a randomized trial*

493. Mann JFE, Schmieder RE, Dyal L, et al. Effect of telmisartan on renal outcomes: a randomized trial.[Summary for patients in Ann Intern Med. 2009 Jul 7;151(1):I28; PMID: 19451555]. Annals of Internal Medicine 2009; 151(1):1-10. *Intervention not related to monitoring of CKD*

494. Manno C, Strippoli GFM, D'Altri C, et al. A novel simpler histological classification for renal survival in IgA nephropathy: a retrospective study. American Journal of Kidney Diseases 2007; 49(6):763-75. *Not a randomized trial*

495. Marcantoni C, Zanoli L, Rastelli S, et al. Stenting of renal artery stenosis in coronary artery disease (RAS-CAD) study: a prospective, randomized trial. Journal of Nephrology 2009; 22(1):13-6. *Intervention not related to monitoring of CKD*

496. Mariappan P, Smith G, Moussa SA, et al. One week of ciprofloxacin before percutaneous nephrolithotomy significantly reduces upper tract infection and urosepsis: a prospective controlled study. BJU International 2006; 98(5):1075-9. *Intervention not related to monitoring of CKD*

497. Markowitz CE, Spitsin S, Zimmerman V, et al. The treatment of multiple sclerosis with inosine. Journal of Alternative & Complementary Medicine 2009; 15(6):619-25. *Intervention not related to monitoring of CKD*

498. Martin PJ, Nelson BJ, Appelbaum FR, et al. Evaluation of a CD5-specific immunotoxin for treatment of acute graft-versus-host disease after allogeneic marrow transplantation. Blood 1996; 88(3):824-30. *Intervention not related to monitoring of CKD*

499. Martinez-Castelao A, Sarrias X, Bestard O, et al. Arterial elasticity measurement in renal transplant patients under anticalcineurin immunosuppression. Transplantation Proceedings 2005; 37(9):3788-90. *Not patients with early CKD*

500. Marto N, Bertolaccini ML, Calabuig E, et al. Anti-C1q antibodies in nephritis: correlation between titres and renal disease activity and positive predictive value in systemic lupus erythematosus. Annals of the Rheumatic Diseases 2005; 64(3):444-8. *Not a randomized trial*

501. Mas VR, Mas LA, Archer KJ, et al. Evaluation of gene panel mRNAs in urine samples of kidney transplant recipients as a non-invasive tool of graft function. Molecular Medicine 2007; 13(5-6):315-24. *Not a randomized trial*

502. Maschio G, Alberti D, Janin G, et al. Effect of the angiotensin-converting-enzyme inhibitor benazepril on the progression of chronic renal insufficiency. The Angiotensin-Converting-Enzyme Inhibition in Progressive Renal Insufficiency Study Group. New England Journal of Medicine 1996; 334(15):939-45. *Intervention not related to monitoring of CKD*

503. Masuda S-i, Tamura K, Wakui H, et al. Effects of angiotensin II type 1 receptor blocker on ambulatory blood pressure variability in hypertensive patients with overt diabetic nephropathy. Hypertension Research - Clinical & Experimental 2009; 32(11):950-5. *Intervention not related to monitoring of CKD*

504. Matsumura C, Kemmotsu O, Kawano Y, et al. Serum and urine inorganic fluoride levels following prolonged low-dose sevoflurane anesthesia combined with epidural block. Journal of Clinical Anesthesia 1994; 6(5):419-24. *Intervention not related to monitoring of CKD*

505. Matthews DR, Stratton IM, Aldington SJ, et al. Risks of progression of retinopathy and vision loss related to tight blood pressure control in type 2 diabetes mellitus: UKPDS 69. Archives of Ophthalmology 2004; 122(11):1631-40. *Intervention not related to monitoring of CKD*

506. Mauer M, Zinman B, Gardiner R, et al. Renal and retinal effects of enalapril and losartan in type 1 diabetes. New England Journal of Medicine 2009; 361(1):40-51. *Intervention not related to monitoring of CKD*

507. McClellan WM, Hodgin E, Pastan S, et al. A randomized evaluation of two health care quality improvement program (HCQIP) interventions to improve the adequacy of hemodialysis care of ESRD patients: feedback alone versus intensive intervention. Journal of the American Society of Nephrology 2004; 15(3):754-60. *Not patients with early CKD*

508. McClellan WM, Langston RD, Presley R. Medicare patients with cardiovascular disease have a high prevalence of chronic kidney disease and a high rate of progression to end-stage renal disease. Journal of the American Society of Nephrology 2004; 15(7):1912-9. *Not a randomized trial*

509. McClellan WM, Soucie JM, Krisher J, et al. Improving the care of patients treated with hemodialysis: a report from the Health Care Financing Administration's ESRD Core Indicators Project. American Journal of Kidney Diseases 1998; 31(4):584-92. *Not patients with early CKD*

510. McCormack PM, Cox JP, Marron J, et al. The antihypertensive efficacy of ketanserin in the elderly evaluated by ambulatory blood pressure measurement. Journal of Human Hypertension 1990; 4(5):565-70. *Intervention not related to monitoring of CKD*

511. McCormick PA, Greenslade L, Kibbler CC, et al. A prospective randomized trial of ceftazidime versus netilmicin plus mezlocillin in the empirical therapy of presumed sepsis in cirrhotic patients. Hepatology 1997; 25(4):833-6. *Intervention not related to monitoring of CKD*

512. McCullough PA, Agrawal V, Danielewicz E, et al. Accelerated atherosclerotic calcification and Monckeberg's sclerosis: a continuum of advanced vascular pathology in chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(6):1585-98. *Not a randomized trial*

513. McCullough PA, Bakris GL, Owen WF, Jr., et al. Slowing the progression of diabetic nephropathy and its cardiovascular consequences. American Heart Journal 2004; 148(2):243-51. *Not a randomized trial*

514. McDonald RA, Smith JM, Ho M, et al. Incidence of PTLD in pediatric renal transplant recipients receiving basiliximab, calcineurin inhibitor, sirolimus and steroids. American Journal of Transplantation 2008; 8(5):984-9. *Not adult population*

515. McGill JB. Improving microvascular outcomes in patients with diabetes through management of hypertension. Postgraduate Medicine 2009; 121(2):89-101. *Not a randomized trial*

516. McMahon LP, Roger SD, Levin A, et al. Development, prevention, and potential reversal of left ventricular hypertrophy in chronic kidney disease. Journal of the American Society of Nephrology 2004; 15(6):1640-7. *Intervention not related to monitoring of CKD*

517. Melis D, Parenti G, Gatti R, et al. Efficacy of ACE-inhibitor therapy on renal disease in glycogen storage disease type 1: a multicentre retrospective study. Clinical Endocrinology 2005; 63(1):19-25. *Not a randomized trial*

518. Menon V, Wang X, Sarnak MJ, et al. Long-term outcomes in nondiabetic chronic kidney disease. Kidney International 2008; 73(11):1310-5. *Not a randomized trial*

519. Mezzano D, Tagle R, Pais E, et al. Endothelial cell markers in chronic uremia: relationship with hemostatic defects and severity of renal failure. Thrombosis Research 1997; 88(6):465-72. *Not a randomized trial*

520. Midtvedt K, Fauchald P, Lien B, et al. Individualized T cell monitored administration of ATG versus OKT3 in steroid-resistant kidney graft rejection. Clinical Transplantation 2003; 17(1):69-74. *Not patients with early CKD*

521. Milas NC, Nowalk MP, Akpele L, et al. Factors associated with adherence to the dietary protein intervention in the Modification of Diet in Renal Disease Study. Journal of the American Dietetic Association 1995; 95(11):1295-300. *Not a randomized trial*

522. Miller PD, Bilezikian JP, Diaz-Curiel M, et al. Occurrence of hypercalciuria in patients with osteoporosis treated with teriparatide. Journal of Clinical Endocrinology & Metabolism 2007; 92(9):3535-41. *Not patients with early CKD*

523. Miyazaki Y, Cersosimo E, Triplitt C, et al. Rosiglitazone decreases albuminuria in type 2 diabetic patients. Kidney International 2007; 72(11):1367-73. *Intervention not related to monitoring of CKD*

524. Modine T, Decoene C, Al-Ruzzeh S, et al. Dobutamine improves thoracic aortic blood flow during off-pump coronary artery bypass surgery: results of a prospective randomised controlled trial. European Journal of Cardio-Thoracic Surgery 2005; 27(2):289-95. *Intervention not related to monitoring of CKD*

525. Mohanram A, Zhang Z, Shahinfar S, et al. Anemia and end-stage renal disease in patients with type 2 diabetes and nephropathy. Kidney International 2004; 66(3):1131-8. *Not a randomized trial*

526. Moist LM, Churchill DN, House AA, et al. Regular monitoring of access flow compared with monitoring of venous pressure fails to improve graft survival. Journal of the American Society of Nephrology 2003; 14(10):2645-53. *Not patients with early CKD*

527. Monier-Faugere MC, Malluche HH. Calcitriol pulse therapy in patients with end-stage renal failure. Current Opinion in Nephrology & Hypertension 1994; 3(6):615-9. *Not patients with early CKD*

528. Morita S, Fukuhara S, Akizawa T, et al. Prognostic factors for a composite end-point of renal outcomes in patients with chronic kidney disease. Therapeutic Apheresis & Dialysis: Official Peer-Reviewed Journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy 2006; 10(1):72-7. *Not a randomized trial*

529. Mosca A, Paleari R, Ceriotti F, et al. Biological variability of albumin excretion rate and albumin-to-creatinine ratio in hypertensive type 2 diabetic patients. Clinical Chemistry & Laboratory Medicine 2003; 41(9):1229-33. *Intervention not related to monitoring of CKD*

530. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. New England Journal of Medicine 2007; 356(2):115-24. *Not patients with early CKD*

531. Mpoy M, Vandeleene B, Ketelslegers JM, et al. Treatment of systemic hypertension in insulin-treated diabetes mellitus with rilmenidine. American Journal of Cardiology 1988; 61(7):91D-4D. *Intervention not related to monitoring of CKD*

532. Muhlhauser I, Bender R, Bott U, et al. Cigarette smoking and progression of retinopathy and nephropathy in type 1 diabetes. Diabetic Medicine 1996; 13(6):536-43. *Not a randomized trial*

533. Mulgaonkar S, Tedesco H, Oppenheimer F, et al. FTY720/cyclosporine regimens in de novo renal transplantation: a 1-year dose-finding study.[Erratum appears in Am J Transplant. 2006 Dec;6(12):3044]. American Journal of Transplantation 2006; 6(8):1848-57. *Not patients with early CKD*

534. Munger MA, Gardner SF, Ateshkadi A, et al. Misoprostol effects on diclofenac-induced cardiorenal changes in salt-sensitive patients with hypertension: the MEDIC Study. Pharmacotherapy 2008; 28(7):834-42. *Intervention not related to monitoring of CKD*

535. Myrup B, Mathiesen ER, Ronn B, et al. Endothelial function and serum lipids in the course of developing microalbuminuria in insulin-dependent diabetes mellitus. Diabetes Research 1994; 26(1):33-9. *Not a randomized trial*

536. Nakamura T, Sugaya T, Kawagoe Y, et al. Effect of pitavastatin on urinary liver-type fatty-acid-binding protein in patients with nondiabetic mild chronic kidney disease. American Journal of Nephrology 2006; 26(1):82-6. *Intervention not related to monitoring of CKD*

537. Nakamura T, Sugaya T, Kawagoe Y, et al. Effect of pitavastatin on urinary liver-type fatty acid-binding protein levels in patients with early diabetic nephropathy. Diabetes Care 2005; 28(11):2728-32. *Intervention not related to monitoring of CKD*

538. Nakano S, Ishii T, Kitazawa M, et al. Altered circadian blood pressure rhythm and progression of diabetic nephropathy in non-insulin dependent diabetes mellitus subjects: an average three year follow-up study. Journal of Investigative Medicine 1996; 44(5):247-53. *Not a randomized trial*

539. Nakao T, Kanazawa Y, Nagaoka Y, et al. Body protein index based on bioelectrical impedance analysis is a useful new marker assessing nutritional status: applications to patients with chronic renal failure on maintenance dialysis. Contributions to Nephrology 2007; 155:18-28. *Not patients with early CKD*

540. Nakao T, Yoshino M, Matsumoto H, et al. Low-density lipoprotein apheresis retards the progression of hyperlipidemic overt diabetic nephropathy. Kidney International - Supplement 1999; 71:S206-9. *Not a randomized trial*

541. Narenpitak S, Narenpitak A. Prevalence of chronic kidney disease in type 2 diabetes in primary health care unit of Udon Thani province, Thailand. Journal of the Medical Association of Thailand 2008; 91(10):1505-13. *Not a randomized trial*

542. Navaneethan SD, Nigwekar SU, Sehgal AR, et al. Aldosterone antagonists for preventing the progression of chronic kidney disease. Cochrane Database of Systematic Reviews 2009; (3):CD007004. *Not a randomized trial*

543. Navaneethan SD, Nigwekar SU, Sehgal AR, et al. Aldosterone antagonists for preventing the progression of chronic kidney disease: a systematic review and meta-analysis. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(3):542-51. *Not a randomized trial*

544. Navaneethan SD, Pansini F, Perkovic V, et al. HMG CoA reductase inhibitors (statins) for people with chronic kidney disease not requiring dialysis. Cochrane Database of Systematic Reviews 2009; (2):CD007784. *Not a randomized trial*

545. Negrier S, Escudier B, Lasset C, et al. Recombinant human interleukin-2, recombinant human interferon alfa-2a, or both in metastatic renal-cell carcinoma. Groupe Francais d'Immunotherapie. New England Journal of Medicine 1998; 338(18):1272-8. *Not patients with early CKD*

546. Neuhaus P, Blumhardt G, Bechstein WO, et al. Comparison of FK506- and cyclosporine-based immunosuppression in primary orthotopic liver transplantation. A single center experience. Transplantation 1995; 59(1):31-40. *Intervention not related to monitoring of CKD*

547. Neverov NI, Kaysen GA, Tareyeva IE. Effect of lipid-lowering therapy on the progression of renal disease in nondiabetic nephrotic patients. Contributions to Nephrology 1997; 120:68-78. *Intervention not related to monitoring of CKD*

548. Newman DJ, Mattock MB, Dawnay ABS, et al. Systematic review on urine albumin testing for early detection of diabetic complications. Health Technology Assessment 2005; 9(30):iii-vi, xiii-163. *Not a randomized trial*

549. Ng CS, Wang X, Faria SC, et al. Perfusion CT in patients with metastatic renal cell carcinoma treated with interferon. AJR 2010; 194(1):166-71. *Not patients with early CKD*

550. Nielsen FS, Jorgensen LN, Ipsen M, et al. Long-term comparison of human insulin analogue B10Asp and soluble human insulin in IDDM patients on a basal/bolus insulin regimen. Diabetologia 1995; 38(5):592-8. *Intervention not related to monitoring of CKD*

551. Niwa T, Aoyama I, Takayama F, et al. Urinary indoxyl sulfate is a clinical factor that affects the progression of renal failure. Mineral & Electrolyte Metabolism 1999; 25(1-2):118-22. *Not a randomized trial*

552. Niwa T, Tsukushi S, Ise M, et al. Indoxyl sulfate and progression of renal failure: effects of a low-protein diet and oral sorbent on indoxyl sulfate production in uremic rats and undialyzed uremic patients. Mineral & Electrolyte Metabolism 1997; 23(3-6):179-84. *Not human study*

553. Nohria A, Hasselblad V, Stebbins A, et al. Cardiorenal interactions: insights from the ESCAPE trial. Journal of the American College of Cardiology 2008; 51(13):1268-74. *Intervention not related to monitoring of CKD*

554. Norris KC, Greene T, Kopple J, et al. Baseline predictors of renal disease progression in the African American Study of Hypertension and Kidney Disease. Journal of the American Society of Nephrology 2006; 17(10):2928-36. *Intervention not related to monitoring of CKD*

555. Northridge DB, Jardine AG, Findlay IN, et al. Inhibition of the metabolism of atrial natriuretic factor causes diuresis and natriuresis in chronic heart failure. American Journal of Hypertension 1990; 3(9):682-7. *Intervention not related to monitoring of CKD*

556. Obialo CI, Conner AC, Lebon LF. Maintaining patency of tunneled hemodialysis catheters--efficacy of aspirin compared to warfarin. Scandinavian Journal of Urology & Nephrology 2003; 37(2):172-6. *Intervention not related to monitoring of CKD*

557. O'Hare AM, Kaufman JS, Covinsky KE, et al. Current guidelines for using angiotensin-converting enzyme inhibitors and angiotensin II-receptor antagonists in chronic kidney disease: is the evidence base relevant to older adults? Annals of Internal Medicine 2009; 150(10):717-24. *Not a randomized trial*

558. Oliveras A, Hurtado S, Vazquez S, et al. Efficacy and safety of doxazosin GITS in hypertensive renal transplant patients: comparison of 8 and 4 mg. Transplantation Proceedings 2003; 35(5):1732-5. *Not patients with early CKD*

559. Onuigbo MAC. Does concurrent renin-angiotensin-aldosterone blockade in (older) chronic kidney disease patients play a role in the acute renal failure epidemic in US hospitalized patients?--Three cases of severe acute renal failure encountered in a northwestern Wisconsin Nephrology practice. Hemodialysis International 2009; 13 Suppl 1:S24-9. *Not a randomized trial*

560. Onuigbo MAC. Reno-prevention vs. reno-protection: a critical re-appraisal of the evidence-base from the large RAAS blockade trials after ONTARGET--a call for more circumspection. Qjm 2009; 102(3):155-67. *Not a randomized trial*

561. Orth SR, Hallan SI. Smoking: a risk factor for progression of chronic kidney disease and for cardiovascular morbidity and mortality in renal patients--absence of evidence or evidence of absence? Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(1):226-36. *Not a randomized trial*

562. Ortiz MA, De Prado A, Donate T, et al. Angiotensin-converting enzyme polymorphism gene and evolution of nephropathy to end-stage renal disease. Nephrology 2003; 8(4):171-6. *Not a randomized trial*

563. Oudemans-van Straaten HM, Wester JPJ, de Pont ACJM, et al. Anticoagulation strategies in continuous renal replacement therapy: can the choice be evidence based? Intensive Care Medicine 2006; 32(2):188-202. *Not a randomized trial*

564. Oue T, Namba M, Nakajima H, et al. Risk factors for the progression of microalbuminuria in Japanese type 2 diabetic patients--a 10 year follow-up study. Diabetes Research & Clinical Practice 1999; 46(1):47-55. *Not a randomized trial*

565. Owada A, Nakao M, Koike J, et al. Effects of oral adsorbent AST-120 on the progression of chronic renal failure: a randomized controlled study. Kidney International - Supplement 1997; 63:S188-90. *Intervention not related to monitoring of CKD*

566. Owada A, Suda S, Hata T. Antiproteinuric effect of niceritrol, a nicotinic acid derivative, in chronic renal disease with hyperlipidemia: a randomized trial. American Journal of Medicine 2003; 114(5):347-53. *Intervention not related to monitoring of CKD*

567. Oyibo SO, Pritchard GM, McLay L, et al. Blood glucose overestimation in diabetic patients on continuous ambulatory peritoneal dialysis for end-stage renal disease. Diabetic Medicine 2002; 19(8):693-6. *Not patients with early CKD*

568. Paap CM, Simpson KS, Horton MW, et al. Multiple-dose pharmacokinetics of pentoxifylline and its metabolites during renal insufficiency. Annals of Pharmacotherapy 1996; 30(7-8):724-9. *Intervention not related to monitoring of CKD*

569. Padrik P, Leppik K, Arak A. Combination therapy with capecitabine and interferon alfa-2A in patients with advanced renal cell carcinoma: a phase II study. Urologic Oncology 2004; 22(5):387-92. *Not patients with early CKD*

570. Pakfetrat M, Nikoo MH, Malekmakan L, et al. A comparison of sodium bicarbonate infusion versus normal saline infusion and its combination with oral acetazolamide for prevention of contrast-induced nephropathy: a randomized, double-blind trial. International Urology & Nephrology 2009; 41(3):629-34. *Intervention not related to monitoring of CKD*

571. Paoletti E, Amidone M, Cassottana P, et al. Effect of sirolimus on left ventricular hypertrophy in kidney transplant recipients: a 1-year nonrandomized controlled trial. American Journal of Kidney Diseases 2008; 52(2):324-30. *Not a randomized trial*

572. Paoletti E, Cannella G. Update on erythropoietin treatment: should hemoglobin be normalized in patients with chronic kidney disease? Journal of the American Society of Nephrology 2006; 17(4 Suppl 2):S74-7. *Not a randomized trial*

573. Park CW, Yun SN, Yang CW, et al. Serum and urine soluble HLA class I antigen concentrations are increased in patients with hemorrhagic fever with renal syndrome. Korean Journal of Internal Medicine 1997; 12(1):52-7. *Not a randomized trial*

574. Parving HH. Is antihypertensive treatment the same for NIDDM and IDDM patients? Diabetes Research & Clinical Practice 1998; 39 Suppl:S43-7. *Not a randomized trial*

575. Parving HH. Benefits and cost of antihypertensive treatment in incipient and overt diabetic nephropathy. Journal of Hypertension - Supplement 1998; 16(1):S99-101. *Not a randomized trial*

576. Parving HH, Lehnert H, Brochner-Mortensen J, et al. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. New England Journal of Medicine 2001; 345(12):870-8. *Intervention not related to monitoring of CKD*

577. Parving HH, Lewis JB, Ravid M, et al. Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients: a global perspective. Kidney International 2006; 69(11):2057-63. *Not a randomized trial*

578. Parving HH, Rossing P. The use of antihypertensive agents in prevention and treatment of diabetic nephropathy. Current Opinion in Nephrology & Hypertension 1994; 3(3):292-300. *Not a randomized trial*

579. Pasero G, Priolo F, Marubini E, et al. Slow progression of joint damage in early rheumatoid arthritis treated with cyclosporin A. Arthritis & Rheumatism 1996; 39(6):1006-15. *Intervention not related to monitoring of CKD*

580. Pecherstorfer M, Rivkin S, Body J-J, et al. Long-term safety of intravenous ibandronic acid for up to 4 years in metastatic breast cancer: an open-label trial. Clinical Drug Investigation 2006; 26(6):315-22. *Intervention not related to monitoring of CKD*

581. Pedrinelli R, Dell'Omo G, Giampietro O, et al. Dissociation between albuminuria and insulinaemia in hypertensive and atherosclerotic men. Journal of Human Hypertension 1999; 13(2):129-34. *Not a randomized trial*

582. Pedrini MT, Levey AS, Lau J, et al. The effect of dietary protein restriction on the progression of diabetic and nondiabetic renal diseases: a meta-analysis. Annals of Internal Medicine 1996; 124(7):627-32. *Not a randomized trial*

583. Penno G, Chaturvedi N, Talmud PJ, et al. Effect of angiotensin-converting enzyme (ACE) gene polymorphism on progression of renal disease and the influence of ACE inhibition in IDDM patients: findings from the EUCLID Randomized Controlled Trial. EURODIAB Controlled Trial of Lisinopril in IDDM. Diabetes 1998; 47(9):1507-11. *Not a randomized trial*

584. Pereira TV, Nunes ACF, Rudnicki M, et al. Influence of ACE I/D gene polymorphism in the progression of renal failure in autosomal dominant polycystic kidney disease: a meta-analysis. Nephrology Dialysis Transplantation 2006; 21(11):3155-63. *Not a randomized trial*

585. Perkins RM, Aboudara MC, Uy AL, et al. Effect of pentoxifylline on GFR decline in CKD: a pilot, double-blind, randomized, placebo-controlled trial. American Journal of Kidney Diseases 2009; 53(4):606-16. *Intervention not related to monitoring of CKD*

586. Perrin NESS, Jaremko GA, Berg UB. The effects of candesartan on diabetes glomerulopathy: a double-blind, placebo-controlled trial. Pediatric Nephrology 2008; 23(6):947-54. *Intervention not related to monitoring of CKD*

587. Persson F, Rossing P, Hovind P, et al. Endothelial dysfunction and inflammation predict development of diabetic nephropathy in the Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria (IRMA 2) study. Scandinavian Journal of Clinical & Laboratory Investigation 2008; 68(8):731-8. *Intervention not related to monitoring of CKD*

588. Pescovitz MD. A cost too high to bear? Prophylaxis versus preemptive therapy to prevent post-transplantation cytomegalovirus. Kidney International 2007; 72(8):912-3. *Not patients with early CKD*

589. Petersen LJ, Petersen JR, Talleruphuus U, et al. A randomized and double-blind comparison of isradipine and spirapril as monotherapy and in combination on the decline in renal function in patients with chronic renal failure and hypertension. Clinical Nephrology 2001; 55(5):375-83. *Intervention not related to monitoring of CKD*

590. Peterson GE, de Backer T, Gabriel A, et al. Prevalence and correlates of left ventricular hypertrophy in the African American Study of Kidney Disease Cohort Study. Hypertension 2007; 50(6):1033-9. *Not a randomized trial*

591. Peterson JC, Adler S, Burkart JM, et al. Blood pressure control, proteinuria, and the progression of renal disease. The Modification of Diet in Renal Disease Study. Annals of Internal Medicine 1995; 123(10):754-62. *Intervention not related to monitoring of CKD*

592. Pfaller W, Thorwartl U, Nevinny-Stickel M, et al. Clinical value of fructose 1,6 bisphosphatase in monitoring renal proximal tubular injury. Kidney International - Supplement 1994; 47:S68-75. *Intervention not related to monitoring of CKD*

593. Pham P-TT, Pham P-CT, Wilkinson AH. Management of renal dysfunction in the liver transplant recipient. Current Opinion in Organ Transplantation 2009; 14(3):231-9. *Not a randomized trial*

594. Phillips CA, Molitch ME. The relationship between glucose control and the development and progression of diabetic nephropathy. Current Diabetes Reports 2002; 2(6):523-9. *Not a randomized trial*

595. Pierce HL, Stevermer JJ. Does losartan (Cozaar) slow the progression of renal disease in patients with type 2 diabetes and nephropathy? Journal of Family Practice 2001; 50(12):1083. *Intervention not related to monitoring of CKD*

596. Pimenta E, Gaddam KK, Oparil S, et al. Effects of dietary sodium reduction on blood pressure in subjects with resistant hypertension: results from a randomized trial. Hypertension 2009; 54(3):475-81. *Intervention not related to monitoring of CKD*

597. Pioro EP, Antel JP, Cashman NR, et al. Detection of cortical neuron loss in motor neuron disease by proton magnetic resonance spectroscopic imaging in vivo. Neurology 1994; 44(10):1933-8. *Intervention not related to monitoring of CKD*

598. Pisoni R, Ruggenenti P, Remuzzi G. Drug-induced thrombotic microangiopathy: incidence, prevention and management. Drug Safety 2001; 24(7):491-501. *Intervention not related to monitoring of CKD*

599. Plantinga LC, Jaar BG. Preventing repeat hospitalizations in dialysis patients: a call for action. Kidney International 2009; 76(3):249-51. *Not patients with early CKD*

600. Poirier LA, Brown AT, Fink LM, et al. Blood S-adenosylmethionine concentrations and lymphocyte methylenetetrahydrofolate reductase activity in diabetes mellitus and diabetic nephropathy. Metabolism: Clinical & Experimental 2001; 50(9):1014-8. *Not a randomized trial*

601. Polkinghorne KR, Lau KKP, Saunder A, et al. Does monthly native arteriovenous fistula blood-flow surveillance detect significant stenosis--a randomized controlled trial. Nephrology Dialysis Transplantation 2006; 21(9):2498-506. *Not patients with early CKD*

602. Ponticelli C, Rivolta E. Ciclosporin in minimal-change glomerulopathy and in focal segmental glomerular sclerosis. American Journal of Nephrology 1990; 10 Suppl 1:105-9. *Not a randomized trial*

603. Pontrelli P, Rossini M, Infante B, et al. Rapamycin inhibits PAI-1 expression and reduces interstitial fibrosis and glomerulosclerosis in chronic allograft nephropathy. Transplantation 2008; 85(1):125-34. *Not patients with early CKD*

604. Porta C. Maintenance biotherapy with interleukin-2 and interferon for metastatic renal cell cancer. Expert Review of Anticancer Therapy 2006; 6(1):141-52. *Not a randomized trial*

605. Portaluppi F, Vergnani L, Manfredini R, et al. Time-dependent effect of isradipine on the nocturnal hypertension in chronic renal failure. American Journal of Hypertension 1995; 8(7):719-26. *Intervention not related to monitoring of CKD*

606. Poschel KA, Bucha E, Esslinger HU, et al. Pharmacodynamics and pharmacokinetics of polyethylene glycol-hirudin in patients with chronic renal failure. Kidney International 2000; 58(6):2478-84. *Intervention not related to monitoring of CKD*

607. Poulsen PL, Ebbehoj E, Hansen KW, et al. High normo- or low microalbuminuria: basis for intervention in insulin-dependent diabetes mellitus. Kidney International - Supplement 1997; 63:S15-8. *Intervention not related to monitoring of CKD*

608. Poulsen PL, Hansen KW, Mogensen CE. Ambulatory blood pressure in the transition from normo- to microalbuminuria. A longitudinal study in IDDM patients. Diabetes 1994; 43(10):1248-53. *Not a randomized trial*

609. Pozzi C, Andrulli S, Del Vecchio L, et al. Corticosteroid effectiveness in IgA nephropathy: long-term results of a randomized, controlled trial. Journal of the American Society of Nephrology 2004; 15(1):157-63. *Not patients with early CKD*

610. Pozzi C, Del Vecchio L, Locatelli F. Can immunosuppressive therapy be useful in IgA nephropathy when the 'Point of No Return' has already been exceeded? Nephron 2002; 92(3):699-701. *Not a randomized trial*

611. Prisant LM, Loebl DH, Mulloy LL. Scleroderma renal crisis. Journal of Clinical Hypertension 2003; 5(2):168-70. *Not a randomized trial*

612. Rachmani R, Slavachevski I, Berla M, et al. Teaching and motivating patients to control their risk factors retards progression of cardiovascular as well as microvascular sequelae of Type 2 diabetes mellitus- a randomized prospective 8 years follow-up study. Diabetic Medicine 2005; 22(4):410-4. *Intervention not related to monitoring of CKD*

613. Rahman M, Baimbridge C, Davis BR, et al. Progression of kidney disease in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin versus usual care: a report from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). American Journal of Kidney Diseases 2008; 52(3):412-24. *Intervention not related to monitoring of CKD*

614. Ramin SM, Vidaeff AC, Yeomans ER, et al. Chronic renal disease in pregnancy. Obstetrics & Gynecology 2006; 108(6):1531-9. *Not a randomized trial*

615. Rammohan C, Fintel D. Dosing considerations and monitoring of low molecular weight heparins and glycoprotein IIb/IIIa antagonists in patients with renal insufficiency. Current Cardiology Reports 2003; 5(4):303-9. *Not a randomized trial*

616. Ranich T, Bhathena SJ, Velasquez MT. Protective effects of dietary phytoestrogens in chronic renal disease. Journal of Renal Nutrition 2001; 11(4):183-93. *Not a randomized trial*

617. Rasche FM, Keller F, Lepper PM, et al. High-dose intravenous immunoglobulin pulse therapy in patients with progressive immunoglobulin A nephropathy: a long-term follow-up. Clinical & Experimental Immunology 2006; 146(1):47-53. *Not a randomized trial*

618. Rasmussen K, Pedersen E. Monitoring of renal allografts by Doppler ultrasound: precision and reference values. Scandinavian Journal of Clinical & Laboratory Investigation 1990; 50(1):51-5. *Intervention not related to monitoring of CKD*

619. Ravid M, Neumann L, Lishner M. Plasma lipids and the progression of nephropathy in diabetes mellitus type II: effect of ACE inhibitors. Kidney International 1995; 47(3):907-10. *Intervention not related to monitoring of CKD*

620. Reach I, Luong N, Chastang C, et al. Dose effect relationship of reviparin in chronic hemodialysis: a crossover study versus nadroparin. Artificial Organs 2001; 25(7):591-5. *Not patients with early CKD*

621. Redman BG, Flaherty L, Martino S, et al. Effect of calcium replacement on the hemodynamic changes associated with high dose interleukin-2 therapy. American Journal of Clinical Oncology 1992; 15(4):340-3. *Intervention not related to monitoring of CKD*

622. Regazzi MB, Rinaldi M, Molinaro M, et al. Clinical pharmacokinetics of tacrolimus in heart transplant recipients. Therapeutic Drug Monitoring 1999; 21(1):2-7. *Not patients with early CKD*

623. Reichard P. Are there any glycemic thresholds for the serious microvascular diabetic complications? Journal of Diabetes & its Complications 1995; 9(1):25-30. *Intervention not related to monitoring of CKD*

624. Reichert LJ, Koene RA, Wetzels JF. Urinary excretion of beta 2-microglobulin predicts renal outcome in patients with idiopathic membranous nephropathy. Journal of the American Society of Nephrology 1995; 6(6):1666-9. *Not a randomized trial*

625. Reilly JP, Ramee SR. Vascular brachytherapy in renal artery restenosis. Current Opinion in Cardiology 2004; 19(4):332-5. *Not a randomized trial*

626. Remuzzi G, Macia M, Ruggenenti P. Prevention and treatment of diabetic renal disease in type 2 diabetes: the BENEDICT study. Journal of the American Society of Nephrology 2006; 17(4 Suppl 2):S90-7. *Intervention not related to monitoring of CKD*

627. Remuzzi G, Perico N, Gotti E, et al. The kidney transplant program at the Bergamo Center. Clinical Transplants 2000:179-91. *Not a randomized trial*

628. Repmann R, Goldschmidt AJW, Richter A. Adjuvant therapy of renal cell carcinoma patients with an autologous tumor cell lysate vaccine: a 5-year follow-up analysis.[Erratum appears in Anticancer Res. 2003;23:5370]. Anticancer Research 2003; 23(2A):969-74. *Not patients with early CKD*

629. Richer M, Robert S, Lebel M. Renal hemodynamics during norepinephrine and low-dose dopamine infusions in man. Critical Care Medicine 1996; 24(7):1150-6. *Intervention not related to monitoring of CKD*

630. Ricos C, Jimenez CV, Hernandez A, et al. Biological variation in urine samples used for analyte measurements. Clinical Chemistry 1994; 40(3):472-7. *Not a randomized trial*

631. Riess FC, Moshar S, Bader R, et al. Clinical outcome of patients with and without renal impairment undergoing a minimally invasive LIMA-to-LAD bypass operation. Heart Surgery Forum 2000; 3(4):313-8. *Intervention not related to monitoring of CKD*

632. Rini BI, Halabi S, Taylor J, et al. Cancer and Leukemia Group B 90206: A randomized phase III trial of interferon-alpha or interferon-alpha plus anti-vascular endothelial growth factor antibody (bevacizumab) in metastatic renal cell carcinoma. Clinical Cancer Research 2004; 10(8):2584-6. *Not patients with early CKD*

633. Rizzoni D, Porteri E, Boari GEM, et al. Prognostic significance of small-artery structure in hypertension. Circulation 2003; 108(18):2230-5. *Not a randomized trial*

634. Roderick PJ, Atkins RJ, Smeeth L, et al. Detecting chronic kidney disease in older people; what are the implications?.[Erratum appears in Age Ageing. 2009 Sep;38(5):638 Note: Flectcher, Astrid E [corrected to Fletcher, Astrid E]]. Age & Ageing 2008; 37(2):179-86. *Not a randomized trial*

635. Rodger RS, Muralikrishna GS, Halls DJ, et al. Ranitidine suppresses aluminium absorption in man. Clinical Science 1991; 80(5):505-8. *Not patients with early CKD*

636. Rodger RS, Sheldon WL, Watson MJ, et al. Zinc deficiency and hyperprolactinaemia are not reversible causes of sexual dysfunction in uraemia. Nephrology Dialysis Transplantation 1989; 4(10):888-92. *Intervention not related to monitoring of CKD*

637. Ronco C, Brendolan A, Milan M, et al. Impact of biofeedback-induced cardiovascular stability on hemodialysis tolerance and efficiency. Kidney International 2000; 58(2):800-8. *Not patients with early CKD*

638. Rosner GL, Stadler W, Ratain MJ. Randomized discontinuation design: application to cytostatic antineoplastic agents. Journal of Clinical Oncology 2002; 20(22):4478-84. *Intervention not related to monitoring of CKD*

639. Rossert J, Froissart M, Jacquot C. Anemia management and chronic renal failure progression. Kidney International - Supplement 2005; (99):S76-81. *Not a randomized trial*

640. Rossert J, Levin A, Roger SD, et al. Effect of early correction of anemia on the progression of CKD. American Journal of Kidney Diseases 2006; 47(5):738-50. *Intervention not related to monitoring of CKD*

641. Rossert JA, McClellan WM, Roger SD, et al. Contribution of anaemia to progression of renal disease: a debate. Nephrology Dialysis Transplantation 2002; 17 Suppl 1:60-6. *Not a randomized trial*

642. Roux C. The methodology of clinical trials of oral tiludronate in Paget's disease of bone. Bone 1995; 17(5 Suppl):497S-9S. *Not a randomized trial*

643. Roy JN, Barama A, Poirier C, et al. Cyp3A4, Cyp3A5, and MDR-1 genetic influences on tacrolimus pharmacokinetics in renal transplant recipients. Pharmacogenetics & Genomics 2006; 16(9):659-65. *Not a randomized trial*

644. Rudberg S, Rasmussen LM, Bangstad HJ, et al. Influence of insertion/deletion polymorphism in the ACE-I gene on the progression of diabetic glomerulopathy in type 1 diabetic patients with microalbuminuria. Diabetes Care 2000; 23(4):544-8. *Not a randomized trial*

645. Ruggenenti P, Fassi A, Ilieva AP, et al. Preventing microalbuminuria in type 2 diabetes. New England Journal of Medicine 2004; 351(19):1941-51. *Intervention not related to monitoring of CKD*

646. Ruggenenti P, Gaspari F, Perna A, et al. Cross sectional longitudinal study of spot morning urine protein:creatinine ratio, 24 hour urine protein excretion rate, glomerular filtration rate, and end stage renal failure in chronic renal disease in patients without diabetes.[Erratum appears in BMJ 1998 Nov 28;317(7171):1491]. BMJ 1998; 316(7130):504-9. *Not a randomized trial*

647. Ruggenenti P, Pagano E, Tammuzzo L, et al. Ramipril prolongs life and is cost effective in chronic proteinuric nephropathies. Kidney International 2001; 59(1):286-94. *Intervention not related to monitoring of CKD*

648. Ruggenenti P, Perna A, Gherardi G, et al. Chronic proteinuric nephropathies: outcomes and response to treatment in a prospective cohort of 352 patients with different patterns of renal injury. American Journal of Kidney Diseases 2000; 35(6):1155-65. *Intervention not related to monitoring of CKD*

649. Ruggenenti P, Perna A, Lesti M, et al. Pretreatment blood pressure reliably predicts progression of chronic nephropathies. GISEN Group. Kidney International 2000; 58(5):2093-101. *Not a randomized trial*

650. Ruggenenti P, Perna A, Loriga G, et al. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicentre, randomised controlled trial. Lancet 2005; 365(9463):939-46. *Intervention not related to monitoring of CKD*

651. Ruggenenti P, Perna A, Mosconi L, et al. Proteinuria predicts end-stage renal failure in non-diabetic chronic nephropathies. The "Gruppo Italiano di Studi Epidemiologici in Nefrologia" (GISEN). Kidney International - Supplement 1997; 63:S54-7. *Not patients with early CKD*

652. Ruggenenti P, Perna A, Remuzzi G, et al. Retarding progression of chronic renal disease: the neglected issue of residual proteinuria. Kidney International 2003; 63(6):2254-61. *Not patients with early CKD*

653. Ruggenenti P, Perna A, Zoccali C, et al. Chronic proteinuric nephropathies. II. Outcomes and response to treatment in a prospective cohort of 352 patients: differences between women and men in relation to the ACE gene polymorphism. Gruppo Italiano di Studi Epidemologici in Nefrologia (Gisen). Journal of the American Society of Nephrology 2000; 11(1):88-96. *Intervention not related to monitoring of CKD*

654. Ruilope LM, Casal MC, Guerrero L, et al. Sodium intake does not influence the effect of verapamil in hypertensive patients with mild renal insufficiency. Drugs 1992; 44 Suppl 1:94-8. *Intervention not related to monitoring of CKD*

655. Ruiz JC, Campistol JM, Grinyo JM, et al. Early cyclosporine a withdrawal in kidney-transplant recipients receiving sirolimus prevents progression of chronic pathologic allograft lesions. Transplantation 2004; 78(9):1312-8. *Not patients with early CKD*

656. Ruiz JC, Campistol JM, Mota A, et al. Early elimination of cyclosporine in kidney transplant recipients receiving sirolimus prevents progression of chronic pathologic allograft lesions. Transplantation Proceedings 2003; 35(5):1669-70. *Not patients with early CKD*

657. Rush DN, Cockfield SM, Nickerson PW, et al. Factors associated with progression of interstitial fibrosis in renal transplant patients receiving tacrolimus and mycophenolate mofetil. Transplantation 2009; 88(7):897-903. *Not patients with early CKD*

658. Ruzicka M, Burns KD, Culleton B, et al. Treatment of hypertension in patients with nondiabetic chronic kidney disease. Canadian Journal of Cardiology 2007; 23(7):595-601. *Not a randomized trial*

659. Sagawa M, Oka M, Chaboyer W. The utility of cognitive behavioural therapy on chronic haemodialysis patients' fluid intake: a preliminary examination. International Journal of Nursing Studies 2003; 40(4):367-73. *Not patients with early CKD*

660. Sahadevan M, Kasiske BL. Hyperlipidemia in kidney disease: causes and consequences. Current Opinion in Nephrology & Hypertension 2002; 11(3):323-9. *Not a randomized trial*

661. Saidi JA, Newhouse JH, Sawczuk IS. Radiologic follow-up of patients with T1-3a,b,c or T4N+M0 renal cell carcinoma after radical nephrectomy. Urology 1998; 52(6):1000-3. *Not patients with early CKD*

662. Salako BL, Finomo FO, Kadiri S, et al. Comparative effect of lisinopril and lacidipine on urinary albumin excretion in patients with type 11 diabetic nephropathy. African Journal of Medicine & Medical Sciences 2002; 31(1):53-7. *Intervention not related to monitoring of CKD*

663. Sands JJ, Jabyac PA, Miranda CL, et al. Intervention based on monthly monitoring decreases hemodialysis access thrombosis. ASAIO Journal 1999; 45(3):147-50. *Not patients with early CKD*

664. Sarapa N, Wickremasingha P, Ge N, et al. Lack of effect of DX-619, a novel des-fluoro(6)-quinolone, on glomerular filtration rate measured by serum clearance of cold iohexol. Antimicrobial Agents & Chemotherapy 2007; 51(6):1912-7. *Intervention not related to monitoring of CKD*

665. Sarnak MJ, Greene T, Wang X, et al. The effect of a lower target blood pressure on the progression of kidney disease: long-term follow-up of the modification of diet in renal disease study. Annals of Internal Medicine 2005; 142(5):342-51. *Intervention not related to monitoring of CKD*

666. Sattler FR, Cowan R, Nielsen DM, et al. Trimethoprim-sulfamethoxazole compared with pentamidine for treatment of Pneumocystis carinii pneumonia in the acquired immunodeficiency syndrome. A prospective, noncrossover study. Annals of Internal Medicine 1988; 109(4):280-7. *Intervention not related to monitoring of CKD*

667. Sav T, Tokgoz B, Sipahioglu MH, et al. Is there a difference between the allergic potencies of the iron sucrose and low molecular weight iron dextran? Renal Failure 2007; 29(4):423-6. *Intervention not related to monitoring of CKD*

668. Sawicki PT, Muhlhauser I, Didjurgeit U, et al. Intensified antihypertensive therapy is associated with improved survival in type 1 diabetic patients with nephropathy. Journal of Hypertension 1995; 13(8):933-8. *Intervention not related to monitoring of CKD*

669. Sawicki PT, Muhlhauser I, Didjurgeit U, et al. Effects of intensification of antihypertensive care in diabetic nephropathy. Journal of Diabetes & its Complications 1995; 9(4):315-7. *Intervention not related to monitoring of CKD*

670. Scarpioni R, Michieletti E, Cristinelli L, et al. Atherosclerotic renovascular disease: medical therapy versus medical therapy plus renal artery stenting in preventing renal failure progression: the rationale and study design of a prospective, multicenter and randomized trial (NITER). Journal of Nephrology 2005; 18(4):423-8. *Intervention not related to monitoring of CKD*

671. Schadewaldt P, Killius S, Kamalanathan L, et al. Renal excretion of galactose and galactitol in patients with classical galactosaemia, obligate heterozygous parents and healthy subjects. Journal of Inherited Metabolic Disease 2003; 26(5):459-79. *Not patients with early CKD*

672. Schaeffner ES, Kurth T, Bowman TS, et al. Blood pressure measures and risk of chronic kidney disease in men. Nephrology Dialysis Transplantation 2008; 23(4):1246-51. *Not a randomized trial*

673. Schetz M, Bove T, Morelli A, et al. Prevention of cardiac surgery-associated acute kidney injury. International Journal of Artificial Organs 2008; 31(2):179-89. *Intervention not related to monitoring of CKD*

674. Schiele J, Nowack R, Julian BA, et al. Treatment of immunoglobulin A nephropathy. Annales de Medecine Interne 1999; 150(2):127-36. *Intervention not related to monitoring of CKD*

675. Schjoedt KJ, Hansen HP, Tarnow L, et al. Long-term prevention of diabetic nephropathy: an audit. Diabetologia 2008; 51(6):956-61. *Not a randomized trial*

676. Schlosser K, Scigalla P. Biochemical markers as surrogates in clinical trials in patients with metastatic bone disease and osteoporosis. Scandinavian Journal of Clinical and Laboratory Investigation Supplement 1997; 227:21-8. *Intervention not related to monitoring of CKD*

677. Schluchter MD, Greene T, Beck GJ. Analysis of change in the presence of informative censoring: application to a longitudinal clinical trial of progressive renal disease. Statistics in Medicine 2001; 20(7):989-1007. *Not a randomized trial*

678. Schmieder RE, Langenfeld MR, Gatzka CD, et al. Impact of alpha- versus beta-blockers on hypertensive target organ damage: results of a double-blind, randomized, controlled clinical trial. American Journal of Hypertension 1997; 10(9 Pt 1):985-91. *Intervention not related to monitoring of CKD*

679. Schoffski P, Guillem V, Garcia M, et al. Phase II randomized study of Plitidepsin (Aplidin), alone or in association with L-carnitine, in patients with unresectable advanced renal cell carcinoma. Marine Drugs 2009; 7(1):57-70. *Intervention not related to monitoring of CKD*

680. Schrier RW. Treating high-risk diabetic hypertensive patients with comorbid conditions. American Journal of Kidney Diseases 2000; 36(3 Suppl 1):S10-7. *Not a randomized trial*

681. Schrier RW, Estacio RO. The effect of angiotensin-converting enzyme inhibitors on the progression of nondiabetic renal disease: a pooled analysis of individual-patient data from 11 randomized, controlled trials. Annals of Internal Medicine 2001; 135(2):138-9. *Intervention not related to monitoring of CKD*

682. Schrier RW, Estacio RO, Esler A, et al. Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes. Kidney International 2002; 61(3):1086-97. *Intervention not related to monitoring of CKD*

683. Schwartz MM, Korbet SM, Lewis EJ, et al. The prognosis and pathogenesis of severe lupus glomerulonephritis. Nephrology Dialysis Transplantation 2008; 23(4):1298-306. *Not a randomized trial*

684. Senitzer D, Greenstein SM, Louis P, et al. Monitoring serum IL-2R levels in cadaver renal transplantation: a prospective, blinded study. Transplantation Proceedings 1991; 23(1 Pt 2):1279-81. *Not patients with early CKD*

685. Seron D, Oppenheimer F, Pallardo LM, et al. Fluvastatin in the prevention of renal transplant vasculopathy: results of a prospective, randomized, double-blind, placebo-controlled trial. Transplantation 2008; 86(1):82-7. *Not patients with early CKD*

686. Shah A, Lettieri J, Blum R, et al. Pharmacokinetics of intravenous ciprofloxacin in normal and renally impaired subjects. Journal of Antimicrobial Chemotherapy 1996; 38(1):103-16. *Not a randomized trial*

687. Shah S, Paparello J, Danesh FR. Effects of statin therapy on the progression of chronic kidney disease. Advances in Chronic Kidney Disease 2005; 12(2):187-95. *Not a randomized trial*

688. Sharma M, Rao M, Jacob S, et al. A controlled trial of intermittent enteral nutrient supplementation in maintenance hemodialysis patients. Journal of Renal Nutrition 2002; 12(4):229-37. *Not patients with early CKD*

689. Shen Y, Fleming TR. Assessing effects on long-term survival after early termination of randomized trials. Lifetime Data Analysis 1999; 5(1):55-66. *Not a randomized trial*

690. Shigenaga A-i, Tamura K, Dejima T, et al. Effects of angiotensin II type 1 receptor blocker on blood pressure variability and cardiovascular remodeling in hypertensive patients on chronic peritoneal dialysis. Nephron 2009; 112(1):c31-40. *Not patients with early CKD*

691. Shin YS, Yang CW, Ahn HJ, et al. Clinical significance of anti-endothelial cell antibody in renal transplant recipients. Korean Journal of Internal Medicine 2001; 16(1):24-9. *Not patients with early CKD*

692. Siddiqi N, El Shahat O, Bokhari E, et al. The effect of use of dates on serum potassium in nondiabetic hemodialysis patients. Saudi Journal of Kidney Diseases & Transplantation 2009; 20(6):1018-22. *Not patients with early CKD*

693. Simeckova A, Zamrazil V, Cerovska J, et al. Does a relationship exist between ioduria, magnesiuria and calciuria? Journal of Trace Elements in Medicine & Biology 2000; 14(1):28-30. *Not a randomized trial*

694. Sinert R, Doty CI. Evidence-based emergency medicine review. Prevention of contrast-induced nephropathy in the emergency department. Annals of Emergency Medicine 2007; 50(3):335-45. *Not a randomized trial*

695. Singh-Franco D, Machado C, Tuteja S, et al. Trospium chloride for the treatment of overactive bladder with urge incontinence. Clinical Therapeutics 2005; 27(5):511-30. *Not a randomized trial*

696. Sirken GR, Shah C, Raja R. Slow-flow venous pressure for detection of arteriovenous graft malfunction. Kidney International 2003; 63(5):1894-8. *Not a randomized trial*

697. Siu Y-P, Leung K-T, Tong MK-H, et al. Use of allopurinol in slowing the progression of renal disease through its ability to lower serum uric acid level. American Journal of Kidney Diseases 2006; 47(1):51-9. *Intervention not related to monitoring of CKD*

698. Skipper GE, Weinmann W, Thierauf A, et al. Ethyl glucuronide: a biomarker to identify alcohol use by health professionals recovering from substance use disorders. Alcohol & Alcoholism 2004; 39(5):445-9. *Intervention not related to monitoring of CKD*

699. Slowik MM. Early education of patients with chronic renal insufficiency: the Healthy Start program. Case study of the anemic patient. Nephrology Nursing Journal: Journal of the American Nephrology Nurses' Association 2001; 28(6):643-6. *Not a randomized trial*

700. Smith RJH, Alexander J, Barlow PN, et al. New approaches to the treatment of dense deposit disease. Journal of the American Society of Nephrology 2007; 18(9):2447-56. *Not a randomized trial*

701. Smulders YM, van Eeden AE, Stehouwer CD, et al. Can reduction in hypertriglyceridaemia slow progression of microalbuminuria in patients with non-insulin-dependent diabetes mellitus? European Journal of Clinical Investigation 1997; 27(12):997-1002. *Intervention not related to monitoring of CKD*

702. Snyder S, Pendergraph B. Detection and evaluation of chronic kidney disease. American Family Physician 2005; 72(9):1723-32. *Not a randomized trial*

703. Solomkin JS, Fant WK, Rivera JO, et al. Randomized trial of imipenem/cilastatin versus gentamicin and clindamycin in mixed flora infections. American Journal of Medicine 1985; 78(6A):85-91. *Intervention not related to monitoring of CKD*

704. Solomon LR, Hendler ED. Prospective controlled study of androgen therapy in the anemia of chronic renal disease: effects on iron kinetics. Acta Haematologica 1988; 79(1):12-9. *Not a randomized trial*

705. Soroka N, Silverberg DS, Greemland M, et al. Comparison of a vegetable-based (soya) and an animal-based low-protein diet in predialysis chronic renal failure patients. Nephron 1998; 79(2):173-80. *Not patients with early CKD*

706. Souchet T, Durand Zaleski I, Hannedouche T, et al. An economic evaluation of Losartan therapy in type 2 diabetic patients with nephropathy: an analysis of the RENAAL study adapted to France. Diabetes & Metabolism 2003; 29(1):29-35. *Not patients with early CKD*

707. Sozen S, Gurocak S, Erdem O, et al. Cyclooxygenase-2 expression: does it have a probable role in tumorigenesis mechanisms of renal cell carcinoma? International Urology & Nephrology 2008; 40(2):295-301. *Not a randomized trial*

708. Stefoni S, Mosconi G, La Manna G, et al. Low-dosage ibopamine treatment in progressive renal failure: a long-term multicentre trial. American Journal of Nephrology 1996; 16(6):489-99. *Intervention not related to monitoring of CKD*

709. Stein WD, Yang J, Bates SE, et al. Bevacizumab reduces the growth rate constants of renal carcinomas: a novel algorithm suggests early discontinuation of bevacizumab resulted in a lack of survival advantage. Oncologist 2008; 13(10):1055-62. *Intervention not related to monitoring of CKD*

710. Stevenson JC, Hillard TC, Lees B, et al. Postmenopausal bone loss: does HRT always work? International Journal of Fertility & Menopausal Studies 1993; 38 Suppl 2:88-91. *Intervention not related to monitoring of CKD*

711. Stoves J, Inglis H, Newstead CG. A randomized study of oral vs intravenous iron supplementation in patients with progressive renal insufficiency treated with erythropoietin. Nephrology Dialysis Transplantation 2001; 16(5):967-74. *Not patients with early CKD*

712. Stoves J, Newstead CG, Baczkowski AJ, et al. A randomized controlled trial of immunosuppression conversion for the treatment of chronic allograft nephropathy. Nephrology Dialysis Transplantation 2004; 19(8):2113-20. *Not patients with early CKD*

713. Strippoli GFM, Bonifati C, Craig M, et al. Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists for preventing the progression of diabetic kidney disease. Cochrane Database of Systematic Reviews 2006; (4):CD006257. *Not a randomized trial*

714. Strippoli GFM, Craig MC, Schena FP, et al. Role of blood pressure targets and specific antihypertensive agents used to prevent diabetic nephropathy and delay its progression. Journal of the American Society of Nephrology 2006; 17(4 Suppl 2):S153-5. *Not a randomized trial*

715. Studies of Ocular Complications of ARGTACTG. The ganciclovir implant plus oral ganciclovir versus parenteral cidofovir for the treatment of cytomegalovirus retinitis in patients with acquired immunodeficiency syndrome: The Ganciclovir Cidofovir Cytomegalovirus Retinitis Trial. American Journal of Ophthalmology 2001; 131(4):457-67. *Intervention not related to monitoring of CKD*

716. Sumethkul V, Changsirikulchai S, Lothuvachai T, et al. Sirolimus attenuates the rate of progression of early chronic allograft nephropathy. Transplantation Proceedings 2006; 38(10):3470-2. *Not patients with early CKD*

717. Sundaram S, Mainali R, Norfolk ER, et al. Fibrillary glomerulopathy secondary to light chain deposition disease in a patient with monoclonal gammopathy. Annals of Clinical & Laboratory Science 2007; 37(4):370-4. *Intervention not related to monitoring of CKD*

718. Sunder-Plassmann G, Horl WH. Importance of iron supply for erythropoietin therapy. Nephrology Dialysis Transplantation 1995; 10(11):2070-6. *Not patients with early CKD*

719. Sussman SK. Nonvascular intervention in the genitourinary tract. Current Opinion in Radiology 1991; 3(5):669-80. *Intervention not related to monitoring of CKD*

720. Suzuki H, Moriwaki K, Nakamoto H, et al. Blood pressure reduction in the morning yields beneficial effects on progression of chronic renal insufficiency with regression of left ventricular hypertrophy. Clinical & Experimental Hypertension 2002; 24(1-2):51-63. *Intervention not related to monitoring of CKD*

721. Svensson M, Gustafsson F, Galatius S, et al. How prevalent is hyperkalemia and renal dysfunction during treatment with spironolactone in patients with congestive heart failure? Journal of Cardiac Failure 2004; 10(4):297-303. *Not a randomized trial*

722. Tabaei BP, Al-Kassab AS, Ilag LL, et al. Does microalbuminuria predict diabetic nephropathy? Diabetes Care 2001; 24(9):1560-6. *Not a randomized trial*

723. Takahashi T, Reed SD, Schulman KA. Cost-effectiveness of the oral adsorbent AST-120 versus placebo for chronic kidney disease. Nephrology 2008; 13(5):419-27. *Not a randomized trial*

724. Takei T, Otsubo S, Uchida K, et al. Effects of sevelamer on the progression of vascular calcification in patients on chronic haemodialysis. Nephron 2008; 108(4):c278-83. *Not patients with early CKD*

725. Talaulikar GS, Gallagher MP, Carney GM, et al. Switchover to generic cyclosporine in stable renal transplant recipients: a single unit experience. Nephrology 2004; 9(6):418-21. *Not patients with early CKD*

726. Tamura S, Ueki K, Ideura H, et al. Corticosteroid therapy in patients with IgA nephropathy and impaired renal function. Clinical Nephrology 2001; 55(3):192-5. *Not a randomized trial*

727. Tang IY, Murray PT. Prevention of perioperative acute renal failure: what works? Best Practice & Research 2004; Clinical Anaesthesiology. 18(1):91-111. *Intervention not related to monitoring of CKD*

728. Tang S, Ho YW, Leung CY, et al. Mycophenolate mofetil in the treatment of steroid-resistant primary focal segmental glomerulosclerosis. Journal of Nephrology 2005; 18(4):429-32. *Not patients with early CKD*

729. Teachey DT, Seif AE, Brown VI, et al. Targeting Notch signaling in autoimmune and lymphoproliferative disease. Blood 2008; 111(2):705-14. *Not human study*

730. Tedesco-Silva H, Jr., Vitko S, Pascual J, et al. 12-month safety and efficacy of everolimus with reduced exposure cyclosporine in de novo renal transplant recipients. Transplant International 2007; 20(1):27-36. *Not patients with early CKD*

731. Teschan PE, Beck GJ, Dwyer JT, et al. Effect of a ketoacid-aminoacid-supplemented very low protein diet on the progression of advanced renal disease: a reanalysis of the MDRD feasibility study. Clinical Nephrology 1998; 50(5):273-83. *Not patients with early CKD*

732. Textor SC. Renovascular hypertension update. Current Hypertension Reports 2006; 8(6):521-7. *Not a randomized trial*

733. Thall PF, Wooten LH, Tannir NM. Monitoring event times in early phase clinical trials: some practical issues. Clinical Trials 2005; 2(6):467-78. *Not a randomized trial*

734. Thomas DH, Taylor JD, Barnaby OS, et al. Determination of free catecholamines in urine by tandem affinity/ion-pair chromatography and flow injection analysis. Clinica Chimica Acta 2008; 398(1-2):63-9. *Intervention not related to monitoring of CKD*

735. Thomsen HS, Hvid-Jacobsen K, Nielsen SL. Alternating use of 123I and 131I hippuran for routine postoperative monitoring of transplanted kidneys is impracticable. Acta Radiologica 1987; 28(3):365-7. *Not patients with early CKD*

736. Tiseo M, Martelli O, Mancuso A, et al. Short hydration regimen and nephrotoxicity of intermediate to high-dose cisplatin-based chemotherapy for outpatient treatment in lung cancer and mesothelioma. Tumori 2007; 93(2):138-44. *Not a randomized trial*

737. Tobe S, Epstein M. The use of calcium antagonists in the treatment of hypertensive persons with kidney disease. Current Hypertension Reports 2002; 4(3):191-4. *Not a randomized trial*

738. Tobita I, Suzuki S, Kobayashi T, et al. A programme to encourage participation of haemodialysis patients in an exercise regimen. Journal of Renal Care 2009; 35(1):48-53. *Not patients with early CKD*

739. Tod M, Minozzi C, Beaucaire G, et al. Isepamicin in intensive care unit patients with nosocomial pneumonia: population pharmacokinetic-pharmacodynamic study. Journal of Antimicrobial Chemotherapy 1999; 44(1):99-108. *Not patients with early CKD*

740. Tofe Povedano S, Garcia De La Villa B. 24-hour and nighttime blood pressures in type 2 diabetic hypertensive patients following morning or evening administration of olmesartan. Journal of Clinical Hypertension 2009; 11(8):426-31. *Intervention not related to monitoring of CKD*

741. Tominaga Y, Kohara S, Namii Y, et al. Clonal analysis of nodular parathyroid hyperplasia in renal hyperparathyroidism. World Journal of Surgery 1996; 20(7):744-50; discussion 50-2. *Not a randomized trial*

742. Tonelli M, Sacks F, Pfeffer M, et al. Biomarkers of inflammation and progression of chronic kidney disease. Kidney International 2005; 68(1):237-45. *Intervention not related to monitoring of CKD*

743. Tong PCY, Ko GTC, Chan WB, et al. The efficacy and tolerability of fosinopril in Chinese type 2 diabetic patients with moderate renal insufficiency. Diabetes, Obesity & Metabolism 2006; 8(3):342-7. *Intervention not related to monitoring of CKD*

744. Toto RD. Lessons from the African-American Study of Kidney Disease and Hypertension: an update. Current Hypertension Reports 2006; 8(5):409-12. *Intervention not related to monitoring of CKD*

745. Trask PC, Bushmakin AG, Cappelleri JC, et al. Health-related quality of life during treatment for renal cell carcinoma: results from a phase II study of axitinib. Acta Oncologica 2008; 47(5):843-51. *Not patients with early CKD*

746. Trivedi H, Lu N, Andresen BT, et al. Slower decline of renal function after initiation of rosiglitazone in diabetics -- a pilot study. Clinical Nephrology 2009; 72(3):181-5. *Intervention not related to monitoring of CKD*

747. Tugwell P, Bombardier C, Gent M, et al. Low-dose cyclosporin versus placebo in patients with rheumatoid arthritis. Lancet 1990; 335(8697):1051-5. *Intervention not related to monitoring of CKD*

748. Tugwell P, Ludwin D, Gent M, et al. Interaction between cyclosporin A and nonsteroidal antiinflammatory drugs. Journal of Rheumatology 1997; 24(6):1122-5. *Intervention not related to monitoring of CKD*

749. Tumlin JA, Finkel KW, Murray PT, et al. Fenoldopam mesylate in early acute tubular necrosis: a randomized, double-blind, placebo-controlled clinical trial. American Journal of Kidney Diseases 2005; 46(1):26-34. *Intervention not related to monitoring of CKD*

750. Turner R. Hepatic and renal tolerability of long-term naproxen treatment in patients with rheumatoid arthritis. Seminars in Arthritis & Rheumatism 1988; 17(3 Suppl 2):29-35. *Intervention not related to monitoring of CKD*

751. Twyman S, Rowe D, Mansell P, et al. Longitudinal study of urinary albumin excretion in young diabetic patients--Wessex Diabetic Nephropathy Project. Diabetic Medicine 2001; 18(5):402-8. *Not a randomized trial*

752. Tylicki L, Rutkowski P, Renke M, et al. Triple pharmacological blockade of the renin-angiotensin-aldosterone system in nondiabetic CKD: an open-label crossover randomized controlled trial. American Journal of Kidney Diseases 2008; 52(3):486-93. *Intervention not related to monitoring of CKD*

753. Ulrich C, Bichel J, Euvrard S, et al. Topical immunomodulation under systemic immunosuppression: results of a multicentre, randomized, placebo-controlled safety and efficacy study of imiquimod 5% cream for the treatment of actinic keratoses in kidney, heart, and liver transplant patients. British Journal of Dermatology 2007; 157 Suppl 2:25-31. *Intervention not related to monitoring of CKD*

754. van Essen GG, Apperloo AJ, Rensma PL, et al. Are angiotensin converting enzyme inhibitors superior to beta blockers in retarding progressive renal function decline? Kidney International - Supplement 1997; 63:S58-62. *Intervention not related to monitoring of CKD*

755. Van Poppel H, Da Pozzo L, Albrecht W, et al. A prospective randomized EORTC intergroup phase 3 study comparing the complications of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. European Urology 2007; 51(6):1606-15. *Intervention not related to monitoring of CKD*

756. Vasavada N, Saha C, Agarwal R. A double-blind randomized crossover trial of two loop diuretics in chronic kidney disease. Kidney International 2003; 64(2):632-40. *Intervention not related to monitoring of CKD*

757. Vegter S, Perna A, Hiddema W, et al. Cost-effectiveness of ACE inhibitor therapy to prevent dialysis in nondiabetic nephropathy: influence of the ACE insertion/deletion polymorphism. Pharmacogenetics & Genomics 2009; 19(9):695-703. *Not a randomized trial*

758. Vercauteren SB, Bosmans JL, Elseviers MM, et al. A meta-analysis and morphological review of cyclosporine-induced nephrotoxicity in auto-immune diseases. Kidney International 1998; 54(2):536-45. *Not a randomized trial*

759. Vezyroglou G, Mitropoulos A, Antoniadis C. A metabolic syndrome in diffuse idiopathic skeletal hyperostosis. A controlled study.[Erratum appears in J Rheumatol 1997 Aug;24(8):1665]. Journal of Rheumatology 1996; 23(4):672-6. *Intervention not related to monitoring of CKD*

760. Viberti G, Kahn SE, Greene DA, et al. A diabetes outcome progression trial (ADOPT): an international multicenter study of the comparative efficacy of rosiglitazone, glyburide, and metformin in recently diagnosed type 2 diabetes. Diabetes Care 2002; 25(10):1737-43. *Intervention not related to monitoring of CKD*

761. Vidt DG, Cressman MD, Harris S, et al. Rosuvastatin-induced arrest in progression of renal disease. Cardiology 2004; 102(1):52-60. *Intervention not related to monitoring of CKD*

762. Vincenti F, Lantz M, Birnbaum J, et al. A phase I trial of humanized anti-interleukin 2 receptor antibody in renal transplantation. Transplantation 1997; 63(1):33-8. *Not patients with early CKD*

763. Vincenti F, Rostaing L, investigators D. Rationale and design of the DIRECT study: a comparative assessment of the hyperglycemic effects of tacrolimus and cyclosporine following renal transplantation. Contemporary Clinical Trials 2005; 26(1):17-24. *Not patients with early CKD*

764. Vitko S, Margreiter R, Weimar W, et al. Three-year efficacy and safety results from a study of everolimus versus mycophenolate mofetil in de novo renal transplant patients.[Erratum appears in Am J Transplant. 2006 Jan;6(1):243]. American Journal of Transplantation 2005; 5(10):2521-30. *Not patients with early CKD*

765. Vitko S, Tedesco H, Eris J, et al. Everolimus with optimized cyclosporine dosing in renal transplant recipients: 6-month safety and efficacy results of two randomized studies. American Journal of Transplantation 2004; 4(4):626-35. *Not patients with early CKD*

766. Vogt L, Kocks MJA, Laverman GD, et al. Renoprotection by blockade of the renin-angiotensin-aldosterone system in diabetic and non-diabetic chronic kidney disease. Specific involvement of intra-renal angiotensin-converting enzyme activity in therapy resistance? Minerva Medica 2004; 95(5):395-409. *Not a randomized trial*

767. Vonend O, Marsalek P, Russ H, et al. Moxonidine treatment of hypertensive patients with advanced renal failure. Journal of Hypertension 2003; 21(9):1709-17. *Not patients with early CKD*

768. Wade VL, Gleason BL. Dual blockade of the renin-angiotensin system in diabetic nephropathy. Annals of Pharmacotherapy 2004; 38(7-8):1278-82. *Not a randomized trial*

769. Wahbah AM, el-Hefny MO, Wafa EM, et al. Perioperative renal protection in patients with obstructive jaundice using drug combinations. Hepato-Gastroenterology 2000; 47(36):1691-4. *Intervention not related to monitoring of CKD*

770. Wallen NH, Andersson A, Hjemdahl P. Effects of treatment with oral isosorbide dinitrate on platelet function in vivo; a double-blind placebo-controlled study in patients with stable angina pectoris. British Journal of Clinical Pharmacology 1994; 38(1):63-70. *Intervention not related to monitoring of CKD*

771. Walser M, Hill S. Effect of ketoconazole plus low-dose prednisone on progression of chronic renal failure. American Journal of Kidney Diseases 1997; 29(4):503-13. *Intervention not related to monitoring of CKD*

772. Walters MR, Bolster A, Dyker AG, et al. Effect of perindopril on cerebral and renal perfusion in stroke patients with carotid disease. Stroke 2001; 32(2):473-8. *Intervention not related to monitoring of CKD*

773. Wang G, Lai FM-M, Lai K-B, et al. Urinary messenger RNA expression of podocyte-associated molecules in patients with diabetic nephropathy treated by angiotensin-converting enzyme inhibitor and angiotensin receptor blocker. European Journal of Endocrinology 2008; 158(3):317-22. *Intervention not related to monitoring of CKD*

774. Warrier I, Lusher JM. Development of anaphylactic shock in haemophilia B patients with inhibitors. Blood Coagulation & Fibrinolysis 1998; 9 Suppl 1:S125-8. *Intervention not related to monitoring of CKD*

775. Webb DJ, Newman DJ, Chaturvedi N, et al. The use of the Micral-Test strip to identify the presence of microalbuminuria in people with insulin dependent diabetes mellitus (IDDM) participating in the EUCLID study. Diabetes Research & Clinical Practice 1996; 31(1-3):93-102. *Not a randomized trial*

776. Webb JG, Pate GE, Humphries KH, et al. A randomized controlled trial of intravenous N-acetylcysteine for the prevention of contrast-induced nephropathy after cardiac catheterization: lack of effect. American Heart Journal 2004; 148(3):422-9. *Intervention not related to monitoring of CKD*

777. Weimer R, Susal C, Yildiz S, et al. Post-transplant sCD30 and neopterin as predictors of chronic allograft nephropathy: impact of different immunosuppressive regimens. American Journal of Transplantation 2006; 6(8):1865-74. *Intervention not related to monitoring of CKD*

778. Weinrauch LA, Bayliss G, Gleason RE, et al. A pilot study to assess utility of changes in elements of the Diabetes Impact Management Scale in evaluating diabetic patients for progressive nephropathy. Metabolism: Clinical & Experimental 2009; 58(4):492-6. *Intervention not related to monitoring of CKD*

779. Weinrauch LA, Burger AJ, Aepfelbacher F, et al. A pilot study to test the effect of pulsatile insulin infusion on cardiovascular mechanisms that might contribute to attenuation of renal compromise in type 1 diabetes mellitus patients with proteinuria. Metabolism: Clinical & Experimental 2007; 56(11):1453-7. *Intervention not related to monitoring of CKD*

780. Weinrauch LA, Kennedy FJ, Burger A, et al. Prospective evaluation of autonomic dysfunction in aggressive management of diabetic microangiopathy. American Journal of Hypertension 1999; 12(11 Pt 1):1135-9. *Intervention not related to monitoring of CKD*

781. Weir MR, Dengel DR, Behrens MT, et al. Salt-induced increases in systolic blood pressure affect renal hemodynamics and proteinuria. Hypertension 1995; 25(6):1339-44. *Intervention not related to monitoring of CKD*

782. Weir MR, Fink JC, Hanes DS, et al. Chronic allograft nephropathy: effect of cyclosporine reduction and addition of mycophenolate mofetil on progression of renal disease. Transplantation Proceedings 1999; 31(1-2):1286-7. *Intervention not related to monitoring of CKD*

783. Weiss MF, Rodby RA, Justice AC, et al. Free pentosidine and neopterin as markers of progression rate in diabetic nephropathy. Collaborative Study Group. Kidney International 1998; 54(1):193-202. *Not a randomized trial*

784. Welage LS, Mason NA, Hoffman EJ, et al. Influence of cellulose triacetate hemodialyzers on vancomycin pharmacokinetics. Journal of the American Society of Nephrology 1995; 6(4):1284-90. *Not patients with early CKD*

785. Wexler D, Silverberg D, Blum M, et al. Anaemia as a contributor to morbidity and mortality in congestive heart failure. Nephrology Dialysis Transplantation 2005; 20 Suppl 7:vii11-5. *Not a randomized trial*

786. White M, Lepage S, Lavoie J, et al. Effects of combined candesartan and ACE inhibitors on BNP, markers of inflammation and oxidative stress, and glucose regulation in patients with symptomatic heart failure. Journal of Cardiac Failure 2007; 13(2):86-94. *Intervention not related to monitoring of CKD*

787. Wiegmann TB, Herron KG, Chonko AM, et al. Effect of angiotensin-converting enzyme inhibition on renal function and albuminuria in normotensive type I diabetic patients. Diabetes 1992; 41(1):62-7. *Intervention not related to monitoring of CKD*

788. Wiland P, Szechcinski J. Proximal tubule damage in patients treated with gentamicin or amikacin. Polish Journal of Pharmacology 2003; 55(4):631-7. *Intervention not related to monitoring of CKD*

789. Williams ME, Lacson E, Jr., Teng M, et al. Hemodialyzed type I and type II diabetic patients in the US: Characteristics, glycemic control, and survival. Kidney International 2006; 70(8):1503-9. *Not patients with early CKD*

790. Wilmer WA, Hebert LA, Lewis EJ, et al. Remission of nephrotic syndrome in type 1 diabetes: long-term follow-up of patients in the Captopril Study. American Journal of Kidney Diseases 1999; 34(2):308-14. *Not patients with early CKD*

791. Wilson J, Wahbha MM, Martin PG, et al. The effect of nisoldipine on renal function in the long-term treatment of hypertension in patients with and without renal impairment. European Journal of Clinical Pharmacology 1989; 37(5):437-41. *Intervention not related to monitoring of CKD*

792. Wirta OR, Pasternack AI, Mustonen JT, et al. Urinary albumin excretion rate and its determinants after 6 years in non-insulin-dependent diabetic patients. Nephrology Dialysis Transplantation 1996; 11(3):449-56. *Not a randomized trial*

793. Womer KL, Huang Y, Herren H, et al. Dendritic cell deficiency associated with development of BK viremia and nephropathy in renal transplant recipients. Transplantation 2010; 89(1):115-23. *Not patients with early CKD*

794. Woo J, Sea MMM, Tong P, et al. Effectiveness of a lifestyle modification programme in weight maintenance in obese subjects after cessation of treatment with Orlistat. Journal of Evaluation in Clinical Practice 2007; 13(6):853-9. *Intervention not related to monitoring of CKD*

795. Woo KT, Lau YK, Chan CM, et al. ATRA therapy restores normal renal function and renal reserve and prevents renal failure. Annals of the Academy of Medicine, Singapore 2005; 34(1):52-9. *Not a randomized trial*

796. Woo KT, Lau YK, Zhao Y, et al. Disease progression, response to ACEI/ATRA therapy and influence of ACE gene in IgA nephritis. Cellular & Molecular Immunology 2007; 4(3):227-32. *Not patients with early CKD*

797. Woolerton J, Jury DR, Dunn PJ, et al. Urine albumin creatinine ratio and clinical correlates in a diabetic population. New Zealand Medical Journal 1987; 100(819):130-4. *Not a randomized trial*

798. Woolfson RG, Neild GH. Cyclosporin nephrotoxicity following cardiac transplantation. Nephrology Dialysis Transplantation 1997; 12(10):2054-6. *Not patients with early CKD*

799. Work J. Does vascular access monitoring work? Advances in Renal Replacement Therapy 2002; 9(2):85-90. *Not patients with early CKD*

800. Wright JT, Jr., Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial.[Erratum appears in JAMA. 2006 Jun 21;295(23):2726]. JAMA 2002; 288(19):2421-31. *Intervention not related to monitoring of CKD*

801. Wright S, Bogan A, Chokshi A. DaVita program advocates self-management of CKD. Nephrol News Issues 2009; 23(13):28-9. *Not a randomized trial*

802. Xu J, Lee ET, Devereux RB, et al. A longitudinal study of risk factors for incident albuminuria in diabetic American Indians: the Strong Heart Study. American Journal of Kidney Diseases 2008; 51(3):415-24. *Not a randomized trial*

803. Xu X, Wu Z, Zhou Q, et al. The role of determining the levels of serum collagen type IV in diagnosing early diabetic nephropathy. Renal Failure 2002; 24(6):747-53. *Intervention not related to monitoring of CKD*

804. Yang CW, Kim YO, Kim YS, et al. Clinical course of cytomegalovirus (CMV) viremia with and without ganciclovir treatment in CMV-seropositive kidney transplant recipients. Longitudinal follow-up of CMV pp65 antigenemia assay. American Journal of Nephrology 1998; 18(5):373-8. *Intervention not related to monitoring of CKD*

805. Yang JC, Haworth L, Sherry RM, et al. A randomized trial of bevacizumab, an anti-vascular endothelial growth factor antibody, for metastatic renal cancer. New England Journal of Medicine 2003; 349(5):427-34. *Intervention not related to monitoring of CKD*

806. Yee CS, Gordon C, Dostal C, et al. EULAR randomised controlled trial of pulse cyclophosphamide and methylprednisolone versus continuous cyclophosphamide and prednisolone followed by azathioprine and prednisolone in lupus nephritis. Annals of the Rheumatic Diseases 2004; 63(5):525-9. *Intervention not related to monitoring of CKD*

807. Yorioka N, Kiribayashi K, Naito T, et al. An oral adsorbent, AST-120, combined with a low-protein diet and RAS blocker, for chronic kidney disease. Journal of Nephrology 2008; 21(2):213-20. *Intervention not related to monitoring of CKD*

808. Zanardo G, Michielon P, Rosi P, et al. Effects of a continuous diltiazem infusion on renal function during cardiac surgery. Journal of Cardiothoracic & Vascular Anesthesia 1993; 7(6):711-6. *Intervention not related to monitoring of CKD*

809. Zhang A, Vertommen J, Van Gaal L, et al. Effects of pravastatin on lipid levels, in vitro oxidizability of non-HDL lipoproteins and microalbuminuria in IDDM patients. Diabetes Research & Clinical Practice 1995; 29(3):189-94. *Intervention not related to monitoring of CKD*

810. Zhang J, Ding EL, Song Y. Adverse effects of cyclooxygenase 2 inhibitors on renal and arrhythmia events: meta-analysis of randomized trials. JAMA 2006; 296(13):1619-32. *Not a randomized trial*

811. Zhu S, Liu Y, Wang L, et al. Transforming growth factor-beta1 is associated with kidney damage in patients with essential hypertension: renoprotective effect of ACE inhibitor and/or angiotensin II receptor blocker. Nephrology Dialysis Transplantation 2008; 23(9):2841-6. *Intervention not related to monitoring of CKD*

812. Zhu X, Stergiopoulos K, Wu S. Risk of hypertension and renal dysfunction with an angiogenesis inhibitor sunitinib: systematic review and meta-analysis. Acta Oncologica 2009; 48(1):9-17. *Not a randomized trial*

813. Ziakka S, Ursu M, Poulikakos D, et al. Predictive factors and therapeutic approach of renovascular disease: four years' follow-up. Renal Failure 2008; 30(10):965-70. *Not a randomized trial*

814. Zucchelli P, Cagnoli L, Pasquali S, et al. Clinical and morphologic evolution of idiopathic membranous nephropathy. Clinical Nephrology 1986; 25(6):282-8. *Not a randomized trial*

815. Zucchelli P, Ponticelli C, Cagnoli L, et al. Prognostic value of T lymphocyte subset ratio in idiopathic membranous nephropathy. American Journal of Nephrology 1988; 8(1):15-20. *Duration of follow-up less than 1 year*

816. Zucchelli P, Zuccala A, Gaggi R. Comparison of the effects of ACE inhibitors and calcium channel blockers on the progression of renal failure. Nephrology Dialysis Transplantation 1995; 10 Suppl 9:46-51. *Intervention not related to monitoring of CKD*

CKD Treatment (KQ5, KQ6)

1. The Diabetes Control and Complications Trial (DCCT). Design and methodologic considerations for the feasibility phase. The DCCT Research Group. Diabetes 1986; 35(5):530-45. *Not CKD treatment*

2. Dietary compliance in the trial of the European Study Group. A preliminary analysis. European Study Group for the Conservative Management of Chronic Renal Failure. Contributions to Nephrology 1990; 81:61-70. *Not CKD treatment*

3. Comparative study of the efficacy of dipyrone, diclofenac sodium and pethidine in acute renal colic. Collaborative Group of the Spanish Society of Clinical Pharmacology. European Journal of Clinical Pharmacology 1991; 40(6):543-6. *Not CKD treatment*

4. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. The SOLVD Investigators. New England Journal of Medicine 1991; 325(5):293-302. *Not CKD treatment*

5. Comparison between perindopril and nifedipine in hypertensive and normotensive diabetic patients with microalbuminuria. Melbourne Diabetic Nephropathy Study Group. BMJ 1991; 302(6770):210-6. *Not relevant to key questions*

6. Dietary compliance in the trial of the European Study Group. An interim analysis. European Study Group for the Conservative Management of Chronic Renal Failure. Contributions to Nephrology 1992; 98:133-41. *Not CKD treatment*

7. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. The SOLVD Investigators.[Erratum appears in N Engl J Med 1992 Dec 10;327(24):1768]. New England Journal of Medicine 1992; 327(10):685-91. *Not CKD treatment*

8. The Modification of Diet in Renal Disease Study: design, methods, and results from the feasibility study. American Journal of Kidney Diseases 1992; 20(1):18-33. *Not relevant to key questions*

9. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. New England Journal of Medicine 1993; 329(14):977-86. *Not early CKD*

10. Results of the North American trial of piperacillin/tazobactam compared with clindamycin and gentamicin in the treatment of severe intra-abdominal infections. Investigators of the Piperacillin/Tazobactam Intra-abdominal Infection Study Group. European Journal of Surgery, Acta Chirurgica, Supplement 1994; (573):61-6. *Not early CKD*

11. Reduction of dietary protein and phosphorus in the Modification of Diet in Renal Disease Feasibility Study. The MDRD Study Group. Journal of the American Dietetic Association 1994; 94(9):986-90; quiz 91-2. *Not CKD treatment*

12. The effect of age and renal function on the efficacy and toxicity of methotrexate in rheumatoid arthritis. Rheumatoid Arthritis Clinical Trial Archive Group. Journal of Rheumatology 1995; 22(2):218-23. *Not CKD treatment*

13. SOCA research group stops enrollment. Studies of the Ocular Complications of AIDS. AIDS Patient Care & Stds 1996; 10(3):188. *Not early CKD*

14. Effects of dietary protein restriction on the progression of moderate renal disease in the Modification of Diet in Renal Disease Study.[Erratum appears in J Am Soc Nephrol 1997 Mar;8(3):493]. Journal of the American Society of Nephrology 1996; 7(12):2616-26. *Not early CKD*

15. Short-term effects of protein intake, blood pressure, and antihypertensive therapy on glomerular filtration rate in the Modification of Diet in Renal Disease Study. Journal of the American Society of Nephrology 1996; 7(10):2097-109. *Not RCT or controlled trial*

16. Captopril reduces the risk of nephropathy in IDDM patients with microalbuminuria. The Microalbuminuria Captopril Study Group. Diabetologia 1996; 39(5):587-93. *Not relevant to key questions*

17. Effects of diet and antihypertensive therapy on creatinine clearance and serum creatinine concentration in the Modification of Diet in Renal Disease Study.[Erratum appears in J Am Soc Nephrol 1997 Aug;8(8):1354]. Journal of the American Society of Nephrology 1996; 7(4):556-66. *Not RCT or controlled trial*

18. Randomised placebo-controlled trial of lisinopril in normotensive patients with insulin-dependent diabetes and normoalbuminuria or microalbuminuria. The EUCLID Study Group. Lancet 1997; 349(9068):1787-92. *Not relevant to key questions*

19. Heart failure treatment with angiotensin-converting enzyme inhibitors in hospitalized Medicare patients in 10 large states. The Large State Peer Review Organization Consortium. Archives of Internal Medicine 1997; 157(10):1103-8. *Not RCT or controlled trial*

20. Parenteral cidofovir for cytomegalovirus retinitis in patients with AIDS: the HPMPC peripheral cytomegalovirus retinitis trial. A randomized, controlled trial. Studies of Ocular complications of AIDS Research Group in Collaboration with the AIDS Clinical Trials Group. Annals of Internal Medicine 1997; 126(4):264-74. *Not CKD treatment*

21. Benazepril and the kidney: new indication. No better than the other ACE inhibitors. Prescrire International 1998; 7(38):174-6. *Not relevant to key questions*

22. NESP researchers present latest data at ASN. Nephrology News & Issues 2000; 14(12):56. *Not RCT or controlled trial*

23. Summaries for patients. Weight-training exercises to counteract the negative effects of low-protein diets in people with kidney disease. Annals of Internal Medicine 2001; 135(11):S-60. *Not relevant to key questions*

24. Summaries for patients. Trial of a drug to decrease the risk for heart disease in patients with mild kidney failure. Annals of Internal Medicine 2001; 134(8):S-96. *Not RCT or controlled trial*

25. Effect of 3 years of antihypertensive therapy on renal structure in type 1 diabetic patients with albuminuria: the European Study for the Prevention of Renal Disease in Type 1 Diabetes (ESPRIT). Diabetes 2001; 50(4):843-50. *Sample size less than 50 patients*

26. Cinacalcet: AMG 073, Calcimimetics--Amgen/NPS Pharmaceuticals, KRN 1493, NPS 1493. Drugs in R & D 2003; 4(6):349-51. *Sample size less than 50 patients*

27. Summaries for patients. Oral administration of an antibiotic (norfloxacin) may help treat the cardiac and circulatory complications of liver failure. Annals of Internal Medicine 2003; 139(3):I62. *Not RCT or controlled trial*

28. Summaries for patients. Effects of blood pressure drugs in patients with diabetes and kidney disease.[Original report in Ann Intern Med. 2003 Apr 1;138(7):542-9; PMID: 12667024]. Annals of Internal Medicine 2003; 138(7):I43. *Not RCT or controlled trial*

29. Summaries for patients. Treating cholesterol in patients with mild kidney disease.[Original report in Ann Intern Med. 2003 Jan 21;138(2):98-104; PMID: 12529091]. Annals of Internal Medicine 2003; 138(2):I28. *Not RCT or controlled trial*

30. Bevacizumab (Avastin). Medical Letter on Drugs & Therapeutics 2004; 46(1184):47-8. *Not CKD treatment*

31. New Premier study suggest Preterax as a first-line antihypertensive. Cardiovascular Journal of Southern Africa 2004; 15(1):40-1. *Not CKD treatment*

32. Summaries for patients. Do the effects of blood pressure drugs differ by kidney function?.[Original report in Ann Intern Med. 2006 Feb 7;144(3):172-80; PMID: 16461961]. Annals of Internal Medicine 2006; 144(3):I33. *Not RCT or controlled trial*

33. Sorafenib: new drug. Second-line treatment of kidney cancer: better evaluated than sunitinib. Prescrire International 2007; 16(90):141-3. *Not relevant to key questions*

34. Sunitinib: new drug. For some gastrointestinal stromal tumours. Prescrire International 2007; 16(90):138-41. *Not early CKD*

35. Ruboxistaurin: LY 333531. Drugs in R & D 2007; 8(3):193-9. *Not RCT or controlled trial*

36. Type 2 diabetes and HbA1c targets. Prescrire International 2008; 17(98):254. *Not CKD treatment*

37. Telmisartan did not prevent renal disease in patients without proteinuria.[Original report in Ann Intern Med. 2009 Jul 7;151(1):1-10, W1-2; PMID: 19451556]. Annals of Internal Medicine 2009; 151(1):I28. *Not relevant to key questions*

38. Anti-HIV agents. Treatment interruption uncovers HIV's attack on the kidneys. Treatment Update 2009; 21(2):5-6. *Not early CKD*

39. Anemia therapy in kidney disease. What research reveals about ESA medication safety. Johns Hopkins Medical Letter, Health After 50 2010 Nov; 22(9):1-2. *Not RCT or controlled trial*

40. Using NSAIDs in cardiovascular disease. Drug & Therapeutics Bulletin 2010 Mar; 48(3):26-9. *Not early CKD*

41. Aarnoutse RE, Wasmuth J-C, Fatkenheuer G, et al. Administration of indinavir and low-dose ritonavir (800/100 mg twice daily) with food reduces nephrotoxic peak plasma levels of indinavir. Antiviral Therapy 2003; 8(4):309-14. *Not CKD treatment*

42. Abassi Z, Winaver J, Feuerstein GZ. The biochemical pharmacology of renin inhibitors: implications for translational medicine in hypertension, diabetic nephropathy and heart failure: expectations and reality. Biochemical Pharmacology 2009; 78(8):933-40. *Not RCT or controlled trial*

43. Abbott K, Basta E, Bakris GL. Blood pressure control and nephroprotection in diabetes. Journal of Clinical Pharmacology 2004; 44(4):431-8. *Not early CKD*

44. Abbott K, Smith A, Bakris GL. Effects of dihydropyridine calcium antagonists on albuminuria in patients with diabetes. Journal of Clinical Pharmacology 1996; 36(3):274-9. *Sample size less than 50 patients*

45. Abbott KC, Bakris GL. Treatment of the diabetic patient: focus on cardiovascular and renal risk reduction. Progress in Brain Research 2002; 139:289-98. *Not RCT or controlled trial*

46. Abbott KC, Bakris GL. What have we learned from the current trials? Medical Clinics of North America 2004; 88(1):189-207. *Not RCT or controlled trial*

47. Abboud H, Coyne D, Smolenski O, et al. A comparison of dosing regimens of paricalcitol capsule for the treatment of secondary hyperparathyroidism in CKD stages 3 and 4. American Journal of Nephrology 2006; 26(1):105-14. *Sample size less than 50 patients*

48. Abdel-Raheem MM, Hebert B, Potti A, et al. Hyperhomocysteinemia and the risk of thromboembolic phenomenon in patients with chronic renal failure. Thrombosis Research 2002; 105(4):299-302. *Not RCT or controlled trial*

49. Abdel-Rahman E, Bolton WK. Pimagedine: a novel therapy for diabetic nephropathy. Expert Opinion on Investigational Drugs 2002; 11(4):565-74. *Not relevant to key questions*

50. Abdin AA, Hassanien MA, Ibrahim EA, et al. Modulating effect of atorvastatin on paraoxonase 1 activity in type 2 diabetic Egyptian patients with or without nephropathy. Journal of Diabetes & its Complications 2010 Sep-Oct; 24(5):325-33. *Follow-up less than 6 months*

51. Abe K, Fujino Y, Sakakibara T. The effect of prostaglandin E1 during cardiopulmonary bypass on renal function after cardiac surgery. European Journal of Clinical Pharmacology 1993; 45(3):217-20. *Not CKD treatment*

52. Abe K, Sakakibara T, Yoshiya I. The effect of prostaglandin E1 on renal function after cardiac surgery involving cardiopulmonary bypass. Prostaglandins Leukotrienes & Essential Fatty Acids 1993; 49(2):627-31. *Sample size less than 50 patients*

53. Abe M, Okada K, Maruyama T, et al. Comparison of the antiproteinuric effects of the calcium channel blockers benidipine and amlodipine administered in combination with angiotensin receptor blockers to hypertensive patients with stage 3-5 chronic kidney disease. Hypertension Research - Clinical & Experimental 2009; 32(4):270-5. *Follow-up less than 6 months*

54. Abe M, Okada K, Maruyama T, et al. Antiproteinuric and blood pressure-lowering effects of a fixed-dose combination of losartan and hydrochlorothiazide in hypertensive patients with stage 3 chronic kidney disease. Pharmacotherapy 2009; 29(9):1061-72. *Follow-up less than 6 months*

55. Abe M, Okada K, Maruyama T, et al. Blood pressure-lowering and antiproteinuric effect of switching from high-dose angiotensin receptor blockers to normal-dose telmisartan and low-dose hydrochlorothiazide in hypertensive patients with chronic kidney disease. International Journal of Clinical Pharmacology & Therapeutics 2010 Mar; 48(3):206-13. *Not RCT or controlled trial*

56. Abels R. Rate of progression of chronic renal failure in predialysis patients treated with erythropoietin. Seminars in Nephrology 1990; 10(2 Suppl 1):20-5. *Not CKD treatment*

57. Abitbol CL, Chandar J, Onder AM, et al. Profiling proteinuria in pediatric patients. Pediatric Nephrology 2006; 21(7):995-1002. *Not RCT or controlled trial*

58. Abizaid AS, Clark CE, Mintz GS, et al. Effects of dopamine and aminophylline on contrast-induced acute renal failure after coronary angioplasty in patients with preexisting renal insufficiency. American Journal of Cardiology 1999; 83(2):260-3. *Not CKD treatment*

59. Abosaif NY, Tolba YA, Heap M, et al. The outcome of acute renal failure in the intensive care unit according to RIFLE: model application, sensitivity, and predictability. American Journal of Kidney Diseases 2005; 46(6):1038-48. *Not relevant to key questions*

60. Abouljoud MS, Levy MF, Klintmalm GB. Hyperlipidemia after liver transplantation: long-term results of the FK506/cyclosporine A US Multicenter Trial. US Multicenter Study Group. Transplantation Proceedings 1995; 27(1):1121-3. *Not early CKD*

61. Abouljoud MS, Levy MF, Klintmalm GB. Hyperlipidemia after liver transplantation: long-term results of the FK506/cyclosporine a US Multicenter trial. US Multicenter Study Group. Transplantation Proceedings 1995; 27(1):1121-3. *Not early CKD*

62. Abraham PA, Halstenson CE, Matzke GR, et al. Comparison of antihypertensive, renal hemodynamic, and humoral effects of pinacidil and hydralazine monotherapy. Journal of Clinical Hypertension 1987; 3(4):439-51. *Sample size less than 50 patients*

63. Abuissa H, O'Keefe J, Jr. The role of renin-angiotensin-aldosterone system-based therapy in diabetes prevention and cardiovascular and renal protection. Diabetes, Obesity & Metabolism 2008; 10(12):1157-66. *Not relevant to key questions*

64. Acanfora D, Lowenthal DT, Furgi G, et al. The effects of delapril in combination with indapamide on glomerular filtration rate in elderly hypertensive patients. American Journal of Therapeutics 1997; 4(11-12):405-8. *Sample size less than 50 patients*

65. Acbay O. Effects of low-dose losartan treatment on persistent microalbuminuria in normotensive type 1 diabetic subjects. Journal of Endocrinological Investigation 2001; 24(8):608-11. *Sample size less than 50 patients*

66. Accetta NA, Gladstone EH, DiSogra C, et al. Prevalence of estimated GFR reporting among US clinical laboratories. American Journal of Kidney Diseases 2008; 52(4):778-87. *Not CKD treatment*

67. Acchiardo SR, Hayden AJ. Is Na+ modeling necessary in high flux dialysis? ASAIO Transactions 1991; 37(3):M135-7. *Not CKD treatment*

68. Acharya GP, Davis TM, Ho M, et al. Factors affecting the pharmacokinetics of parenteral chloramphenicol in enteric fever. Journal of Antimicrobial Chemotherapy 1997; 40(1):91-8. *Sample size less than 50 patients*

69. Acker CG, Singh AR, Flick RP, et al. A trial of thyroxine in acute renal failure. Kidney International 2000; 57(1):293-8. *Not CKD treatment*

70. Ackerman Z, Cominelli F, Reynolds TB. Effect of misoprostol on ibuprofen-induced renal dysfunction in patients with decompensated cirrhosis: results of a double-blind placebo-controlled parallel group study. American Journal of Gastroenterology 2002; 97(8):2033-9. *Not CKD treatment*

71. Acton KJ, Shields R, Rith-Najarian S, et al. Applying the diabetes quality improvement project indicators in the Indian Health Service primary care setting. Diabetes Care 2001; 24(1):22-6. *Not RCT or controlled trial*

72. Adabag AS, Ishani A, Bloomfield HE, et al. Efficacy of N-acetylcysteine in preventing renal injury after heart surgery: a systematic review of randomized trials. European Heart Journal 2009; 30(15):1910-7. *Not early CKD*

73. Adabag AS, Ishani A, Koneswaran S, et al. Utility of N-acetylcysteine to prevent acute kidney injury after cardiac surgery: a randomized controlled trial. American Heart Journal 2008; 155(6):1143-9. *Not early CKD*

74. Adler AI, Stevens RJ, Manley SE, et al. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney International 2003; 63(1):225-32. *Not CKD treatment*

75. Adler SG, Schwartz S, Williams ME, et al. Phase 1 study of anti-CTGF monoclonal antibody in patients with diabetes and microalbuminuria. Clinical Journal of The American Society of Nephrology: CJASN 2010 Aug; 5(8):1420-8. *Not RCT or controlled trial*

76. Adnan T, Elif AA, Ayse K, et al. Clonidine as an adjuvant for lidocaine in axillary brachial plexus block in patients with chronic renal failure. Acta Anaesthesiologica Scandinavica 2005; 49(4):563-8. *Not relevant to key questions*

77. Adolph E, Holdt-Lehmann B, Chatterjee T, et al. Renal Insufficiency Following Radiocontrast Exposure Trial (REINFORCE): a randomized comparison of sodium bicarbonate versus sodium chloride hydration for the prevention of contrast-induced nephropathy. Coronary Artery Disease 2008; 19(6):413-9. *Not CKD treatment*

78. Agarwal A, Silver MR, Walczyk M, et al. Once-monthly darbepoetin alfa for maintaining hemoglobin levels in older patients with chronic kidney disease. Journal of the American Medical Directors Association 2007; 8(2):83-90. *Not RCT or controlled trial*

79. Agarwal R. Add-on angiotensin receptor blockade with maximized ACE inhibition. Kidney International 2001; 59(6):2282-9. *Sample size less than 50 patients*

80. Agarwal R. Is i.v. iron really superior in CKD patients not on dialysis? Kidney International 2006; 70(6):1188; author reply -9. *Not CKD treatment*

81. Agarwal R. Effects of statins on renal function. American Journal of Cardiology 2006; 97(5):748-55. *Not relevant to key questions*

82. Agarwal R. Anti-inflammatory effects of short-term pioglitazone therapy in men with advanced diabetic nephropathy. American Journal of Physiology - Renal Physiology 2006; 290(3):F600-5. *Follow-up less than 6 months*

83. Agarwal R. Nonhematological benefits of iron. American Journal of Nephrology 2007; 27(6):565-71. *Sample size less than 50 patients*

84. Agarwal R. Reproducibility of renal function measurements in adult men with diabetic nephropathy: research and clinical implications. American Journal of Nephrology 2007; 27(1):92-100. *Not RCT or controlled trial*

85. Agarwal R. Vitamin D, proteinuria, diabetic nephropathy, and progression of CKD. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(9):1523-8. *Not RCT or controlled trial*

86. Agarwal R. Blood pressure components and the risk for end-stage renal disease and death in chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(4):830-7. *Not CKD treatment*

87. Agarwal R. Are vitamin D receptor agonists like angiotensin-converting enzyme inhibitors without side effects? Kidney International 2010 Jun; 77(11):943-5. *Not RCT or controlled trial*

88. Agarwal R, Acharya M, Tian J, et al. Antiproteinuric effect of oral paricalcitol in chronic kidney disease. Kidney International 2005; 68(6):2823-8. *Sample size less than 50 patients*

89. Agarwal R, Curley TM. The role of statins in chronic kidney disease. American Journal of the Medical Sciences 2005; 330(2):69-81. *Follow-up less than 6 months*

90. Agarwal R, Gorski JC, Sundblad K, et al. Urinary protein binding does not affect response to furosemide in patients with nephrotic syndrome. Journal of the American Society of Nephrology 2000; 11(6):1100-5. *Sample size less than 50 patients*

91. Agarwal R, Light RP. Physical activity and hemodynamic reactivity in chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(6):1660-8. *Not CKD treatment*

92. Agarwal R, Rizkala AR, Bastani B, et al. A randomized controlled trial of oral versus intravenous iron in chronic kidney disease. American Journal of Nephrology 2006; 26(5):445-54. *Follow-up less than 6 months*

93. Agarwal R, Rizkala AR, Kaskas MO, et al. Iron sucrose causes greater proteinuria than ferric gluconate in non-dialysis chronic kidney disease. Kidney International 2007; 72(5):638-42. *Not RCT or controlled trial*

94. Agarwal R, Saha C, Battiwala M, et al. A pilot randomized controlled trial of renal protection with pioglitazone in diabetic nephropathy. Kidney International 2005; 68(1):285-92. *Not relevant to key questions*

95. Agarwal R, Siva S, Dunn SR, et al. Add-on angiotensin II receptor blockade lowers urinary transforming growth factor-beta levels. American Journal of Kidney Diseases 2002; 39(3):486-92. *Sample size less than 50 patients*

96. Agarwal R, Vasavada N, Sachs NG, et al. Oxidative stress and renal injury with intravenous iron in patients with chronic kidney disease. Kidney International 2004; 65(6):2279-89. *Not relevant to key questions*

97. Agarwal SK, Irshad M, Dash SC. Comparison of two schedules of hepatitis B vaccination in patients with mild, moderate and severe renal failure. Journal of the Association of Physicians of India 1999; 47(2):183-5. *Not CKD treatment*

98. Agewall S, Wikstrand J, Ljungman S, et al. Urinary albumin excretion is associated with the intima-media thickness of the carotid artery in hypertensive males with non-insulin-dependent diabetes mellitus. Journal of Hypertension 1995; 13(4):463-9. *Not CKD treatment*

99. Aggarwal HK, Nand N, Singh S, et al. Comparison of oral versus intravenous iron therapy in predialysis patients of chronic renal failure receiving recombinant human erythropoietin. Journal of the Association of Physicians of India 2003; 51:170-4. *Sample size less than 50 patients*

100. Agha A, Amer W, Anwar E, et al. Reduction of microalbuminuria by using losartan in normotensive patients with type 2 diabetes mellitus: A randomized controlled trial. Saudi Journal of Kidney Diseases & Transplantation 2009; 20(3):429-35. *Not CKD treatment*

101. Agnes E, Prost JF, Laher MS. Additional benefits of combining beta-blockade and renal vasodilation in the treatment of mild to moderate hypertension: Tertatolol International Multicentre Study results. Journal of Hypertension - Supplement 1989; 7(6):S270-1. *Not early CKD*

102. Agnoli GC, Borgatti R, Cacciari M, et al. Antagonistic effects of sulpiride--racemic and enantiomers--on renal response to low-dose dopamine infusion in normal women. Nephron 1989; 51(4):491-8. *Sample size less than 50 patients*

103. Agnoli GC, Borgatti R, Cacciari M, et al. Interactions between the renin-angiotensin system and prostanoids in modulating renal function in potassium-depleted healthy women. Prostaglandins Leukotrienes & Essential Fatty Acids 1994; 50(6):347-52. *Not CKD treatment*

104. Agnoli GC, Borgatti R, Cacciari M, et al. Urinary prostanoid excretion in healthy women with different degrees of induced potassium depletion. Prostaglandins Leukotrienes & Essential Fatty Acids 1992; 46(1):21-6. *Not CKD treatment*

105. Agnoli GC, Borgatti R, Cacciari M, et al. Renal function and urinary prostanoid excretions in salt-depleted women: comparative effects of enalapril and indomethacin treatments. Prostaglandins Leukotrienes & Essential Fatty Acids 1999; 60(2):87-93. *Not CKD treatment*

106. Agodoa L. Acute renal failure in the PACU. Journal of PeriAnesthesia Nursing 2002; 17(6):377-83. *Not CKD treatment*

107. Agodoa LY, Francis ME, Eggers PW. Association of analgesic use with prevalence of albuminuria and reduced GFR in US adults. American Journal of Kidney Diseases 2008; 51(4):573-83. *Not CKD treatment*

108. Agrawal RP, Dogra R, Mohta N, et al. Beneficial effect of camel milk in diabetic nephropathy. Acta Bio-Medica de l Ateneo Parmense 2009; 80(2):131-4. *Sample size less than 50 patients*

109. Aguilar D, Goldhaber SZ, Gans DJ, et al. Clinically unrecognized Q-wave myocardial infarction in patients with diabetes mellitus, systemic hypertension, and nephropathy. American Journal of Cardiology 2004; 94(3):337-9. *Not relevant to key questions*

110. Ahlmen M, Ahlmen J, Svalander C, et al. Cytotoxic drug treatment of reactive amyloidosis in rheumatoid arthritis with special reference to renal insufficiency. Clinical Rheumatology 1987; 6(1):27-38. *Sample size less than 50 patients*

111. Ahmad J, Shafique S, Abidi SMA, et al. Effect of 5-year enalapril therapy on progression of microalbuminuria and glomerular structural changes in type 1 diabetic subjects. Diabetes Research & Clinical Practice 2003; 60(2):131-8. *Not relevant to key questions*

112. Ahmad J, Siddiqui MA, Ahmad H. Effective postponement of diabetic nephropathy with enalapril in normotensive type 2 diabetic patients with microalbuminuria. Diabetes Care 1997; 20(10):1576-81. *Not relevant to key questions*

113. Ahmadi J, Benrazavi L. Substance use among Iranian nephrologic patients. American Journal of Nephrology 2002; 22(1):11-3. *Not CKD treatment*

114. Ahmed A. Use of angiotensin-converting enzyme inhibitors in patients with heart failure and renal insufficiency: how concerned should we be by the rise in serum creatinine? Journal of the American Geriatrics Society 2002; 50(7):1297-300. *Not relevant to key questions*

115. Ahmed A, Aronow WS, Fleg JL. Higher New York Heart Association classes and increased mortality and hospitalization in patients with heart failure and preserved left ventricular function. American Heart Journal 2006; 151(2):444-50. *Not RCT or controlled trial*

116. Ahmed A, Love TE, Sui X, et al. Effects of angiotensin-converting enzyme inhibitors in systolic heart failure patients with chronic kidney disease: a propensity score analysis. Journal of Cardiac Failure 2006; 12(7):499-506. *Not relevant to key questions*

117. Ai P, Yong G, Dingkun G, et al. Aqueous extract of Astragali Radix induces human natriuresis through enhancement of renal response to atrial natriuretic peptide. Journal of Ethnopharmacology 2008; 116(3):413-21. *Not CKD treatment*

118. Aitken HA, Burns JW, McArdle CS, et al. Effects of ketorolac trometamol on renal function. British Journal of Anaesthesia 1992; 68(5):481-5. *Not CKD treatment*

119. Akcicek F, Yalniz T, Basci A, et al. Diuretic effect of frusemide in patients with nephrotic syndrome: is it potentiated by intravenous albumin? BMJ 1995; 310(6973):162-3. *Follow-up less than 6 months*

120. Akesson A, Blom-Bulow B, Scheja A, et al. Long-term evaluation of penicillamine or cyclofenil in systemic sclerosis. Results from a two-year randomized study. Scandinavian Journal of Rheumatology 1992; 21(5):238-44. *Not CKD treatment*

121. Akesson-Johansson A, Lernestedt JO, Ringden O, et al. Sensitivity of cytomegalovirus to intravenous foscarnet treatment. Bone Marrow Transplantation 1986; 1(2):215-20. *Sample size less than 50 patients*

122. Akinsola W, Smith F, Alimi T, et al. Low protein/high calorie dietary regimen in the management of chronic renal failure. A preliminary study of Nigerian patients. African Journal of Medicine & Medical Sciences 1991; 20(1):53-9. *Sample size less than 50 patients*

123. Akizawa T, Asano Y, Morita S, et al. Effect of a carbonaceous oral adsorbent on the progression of CKD: a multicenter, randomized, controlled trial. American Journal of Kidney Diseases 2009; 54(3):459-67. *Not early CKD*

124. Akizawa T, Kino K, Koshikawa S, et al. Efficiency and biocompatibility of a polyethylene glycol grafted cellulosic membrane during hemodialysis. ASAIO Transactions 1989; 35(3):333-5. *Not CKD treatment*

125. Al Suwaidi J, Reddan DN, Williams K, et al. Prognostic implications of abnormalities in renal function in patients with acute coronary syndromes. Circulation 2002; 106(8):974-80. *Not CKD treatment*

126. Al-Ahmad A, Rand WM, Manjunath G, et al. Reduced kidney function and anemia as risk factors for mortality in patients with left ventricular dysfunction. Journal of the American College of Cardiology 2001; 38(4):955-62. *Not RCT or controlled trial*

127. Alaupovic P, Attman PO, Knight-Gibson C, et al. Effect of fluvastatin on apolipoprotein-defined lipoprotein subclasses in patients with chronic renal insufficiency. Kidney International 2006; 69(10):1865-71. *Sample size less than 50 patients*

128. Alavian S-M, Tabatabaei SV. The effect of diabetes mellitus on immunological response to hepatitis B virus vaccine in individuals with chronic kidney disease: A meta-analysis of current literature. Vaccine 2010 May 14; 28(22):3773-7. *Not RCT or controlled trial*

129. Al-Badr W, Martin KJ. Vitamin D and kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(5):1555-60. *Not human studies*

130. Albers M, Romiti M, Braganca Pereira CA, et al. A meta-analysis of infrainguinal arterial reconstruction in patients with end-stage renal disease. European Journal of Vascular & Endovascular Surgery 2001; 22(4):294-300. *Not RCT or controlled trial*

131. Albers M, Romiti M, De Luccia N, et al. An updated meta-analysis of infrainguinal arterial reconstruction in patients with end-stage renal disease. Journal of Vascular Surgery 2007; 45(3):536-42. *Follow-up less than 6 months*

132. Albert JM, Gadbury GL, Mascha EJ. Assessing treatment effect heterogeneity in clinical trials with blocked binary outcomes. Biometrical Journal 2005; 47(5):662-73. *Not relevant to key questions*

133. Albert SG, Shapiro MJ, Brown WW, et al. Analysis of radiocontrast-induced nephropathy by dual-labeled radionuclide clearance. Investigative Radiology 1994; 29(6):618-23. *Not CKD treatment*

134. Alberti D, Locatelli F, Graziani G, et al. Hypertension and chronic renal insufficiency: the experience of the Northern Italian Cooperative Study Group. American Journal of Kidney Diseases 1993; 21(5 Suppl 2):124-30. *Not RCT or controlled trial*

135. Albillos A, Garcia-Pagan JC, Iborra J, et al. Propranolol plus prazosin compared with propranolol plus isosorbide-5-mononitrate in the treatment of portal hypertension. Gastroenterology 1998; 115(1):116-23. *Not CKD treatment*

136. Albillos A, Lledo JL, Rossi I, et al. Continuous prazosin administration in cirrhotic patients: effects on portal hemodynamics and on liver and renal function. Gastroenterology 1995; 109(4):1257-65. *Follow-up less than 6 months*

137. Alborzi P, Patel NA, Peterson C, et al. Paricalcitol reduces albuminuria and inflammation in chronic kidney disease: a randomized double-blind pilot trial. Hypertension 2008; 52(2):249-55. *Sample size less than 50 patients*

138. Al-Dameh A, Bedford JJ, Leader JP, et al. Urinary aquaporin-2 levels in healthy volunteers. Nephrology 2003; 8(3):139-41. *Follow-up less than 6 months*

139. Alexander CM, Lyle PA, Keane WF, et al. Losartan and the United States costs of end-stage renal disease by baseline albuminuria in patients with type 2 diabetes and nephropathy. Kidney International - Supplement 2004; (92):S115-7. *Not RCT or controlled trial*

140. Ali A, Asif N, Yaqub S, et al. Spot urine protein: creatinine ratio versus 24 hour urine protein at various levels of GFR patients referred to a tertiary care hospital of Pakistan. JPMA - Journal of the Pakistan Medical Association 2008; 58(9):476-9. *Not relevant to key questions*

141. Ali F, Boldur A, Winchester JF, et al. A quick and simple estimate of creatinine clearance. Journal of Nephrology 2010 Jul-Aug; 23(4):408-14. *Not CKD treatment*

142. Ali ZA, Callaghan CJ, Lim E, et al. Remote ischemic preconditioning reduces myocardial and renal injury after elective abdominal aortic aneurysm repair: a randomized controlled trial. Circulation 2007; 116(11 Suppl):I98-105. *Not CKD treatment*

143. Alicic RZ, Saha SA, Short RA, et al. Should albuminuria be a focus of antihypertensive therapy goals? Current Hypertension Reports 2009 Oct; 11(5):354-62. *Not RCT or controlled trial*

144. Alimchandani A, Pai-dhungat JV. A study of gastric emptying in chronic renal failure. Journal of the Association of Physicians of India 1997; 45(11):835-8. *Sample size less than 50 patients*

145. Al-Kateb H, Boright AP, Mirea L, et al. Multiple superoxide dismutase 1/splicing factor serine alanine 15 variants are associated with the development and progression of diabetic nephropathy: the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Genetics study. Diabetes 2008; 57(1):218-28. *Not RCT or controlled trial*

146. Alkhalaf A, Klooster A, van Oeveren W, et al. A double-blind, randomized, placebo-controlled clinical trial on benfotiamine treatment in patients with diabetic nephropathy. Diabetes Care 2010 Jul; 33(7):1598-601. *Follow-up less than 6 months*

147. Allaqaband S, Tumuluri R, Malik AM, et al. Prospective randomized study of N-acetylcysteine, fenoldopam, and saline for prevention of radiocontrast-induced nephropathy. Catheterization & Cardiovascular Interventions 2002; 57(3):279-83. *Not CKD treatment*

148. Allen LA, Turer AT, Dewald T, et al. Continuous versus bolus dosing of Furosemide for patients hospitalized for heart failure. American Journal of Cardiology 2010 Jun 15; 105(12):1794-7. *Not CKD treatment*

149. Allen MJ, Ang VT, Bennett ED. Domperidone, a DA2-specific dopamine antagonist, has no effect on the renal or haemodynamic response to atrial natriuretic peptide in man. Clinical Science 1988; 75(6):569-75. *Sample size less than 50 patients*

150. Allen SJ, McBride WT, McMurray TJ, et al. Cell salvage alters the systemic inflammatory response after off-pump coronary artery bypass grafting surgery. Annals of Thoracic Surgery 2007; 83(2):578-85. *Sample size less than 50 patients*

151. Alli C, Lombardo M, Zanni D, et al. Albuminuria and transferrinuria in essential hypertension. Effects of antihypertensive therapy. American Journal of Hypertension 1996; 9(11):1068-76. *Sample size less than 50 patients*

152. Allison NL, Dubb JW, Ziemniak JA, et al. The effect of fenoldopam, a dopaminergic agonist, on renal hemodynamics. Clinical Pharmacology & Therapeutics 1987; 41(3):282-8. *Sample size less than 50 patients*

153. Al-Maskari F, El-Sadig M. Prevalence of risk factors for diabetic foot complications. BMC Family Practice 2007; 8:59. *Not RCT or controlled trial*

154. Almquist T, Forslund L, Rehnqvist N, et al. Prognostic implications of renal dysfunction in patients with stable angina pectoris. Journal of Internal Medicine 2006; 260(6):537-44. *Not CKD treatment*

155. al-Nahhas AM, Nimmon CC, Britton KE, et al. The effect of ramipril, a new angiotensin-converting enzyme inhibitor on cortical nephron flow and effective renal plasma flow in patients with essential hypertension. Nephron 1990; 54(1):47-52. *Sample size less than 50 patients*

156. Aloia JF. Role of calcitriol in the treatment of postmenopausal osteoporosis. Metabolism: Clinical & Experimental 1990; 39(4 Suppl 1):35-8. *Not CKD treatment*

157. Aloia JF, Patel M, Dimaano R, et al. Vitamin D intake to attain a desired serum 25-hydroxyvitamin D concentration. American Journal of Clinical Nutrition 2008; 87(6):1952-8. *Not CKD treatment*

158. Alonso A, Lau J, Jaber BL, et al. Prevention of radiocontrast nephropathy with N-acetylcysteine in patients with chronic kidney disease: a meta-analysis of randomized, controlled trials. American Journal of Kidney Diseases 2004; 43(1):1-9. *Not RCT or controlled trial*

159. Alper AB, Jr., Tomlin H, Sadhwani U, et al. Effects of the selective cyclooxygenase-2 inhibitor analgesic celecoxib on renal carbonic anhydrase enzyme activity: a randomized, controlled trial. American Journal of Therapeutics 2006; 13(3):229-35. *Not adult population*

160. al-Sahlawi KS, Tawfik OM. Comparative study of the efficacy of lysine acetylsalicylate, indomethacin and pethidine in acute renal colic. European Journal of Emergency Medicine 1996; 3(3):183-6. *Not CKD treatment*

161. Altay B, Horasanli K, Sarica K, et al. Double-blind, placebo-controlled, randomized clinical trial of sublingual or intramuscular piroxicam in the treatment of renal colic. A comparative study. Urologia Internationalis 2007; 79(1):73-5. *Sample size less than 50 patients*

162. Alvarez L, Puleo J, Balint JA. Investigation of gastrointestinal bleeding in patients with end stage renal disease. American Journal of Gastroenterology 1993; 88(1):30-3. *Not RCT or controlled trial*

163. Alvelos M, Ferreira A, Bettencourt P, et al. Effect of saline load and metoclopramide on the renal dopaminergic system in patients with heart failure and healthy controls. Journal of Cardiovascular Pharmacology 2005; 45(3):197-203. *Not RCT or controlled trial*

164. Alvelos M, Ferreira A, Bettencourt P, et al. The effect of dietary sodium restriction on neurohumoral activity and renal dopaminergic response in patients with heart failure. European Journal of Heart Failure 2004; 6(5):593-9. *Not CKD treatment*

165. al-Waili NS, Saloom KY. Intravenous tenoxicam to treat acute renal colic: comparison with buscopan compositum. JPMA - Journal of the Pakistan Medical Association 1998; 48(12):370-2. *Not CKD treatment*

166. Al-Waili NS, Saloom KY. Intramuscular piroxicam versus intramuscular diclofenac sodium in the treatment of acute renal colic: double-blind study. European Journal of Medical Research 1999; 4(1):23-6. *Not CKD treatment*

167. Amador-Licona N, Guizar-Mendoza J, Vargas E, et al. The short-term effect of a switch from glibenclamide to metformin on blood pressure and microalbuminuria in patients with type 2 diabetes mellitus. Archives of Medical Research 2000; 31(6):571-5. *Sample size less than 50 patients*

168. Amano J, Suzuki A, Sunamori M. Salutary effect of reduced glutathione on renal function in coronary artery bypass operation. Journal of the American College of Surgeons 1994; 179(6):714-20. *Not CKD treatment*

169. Amano J, Suzuki A, Sunamori M, et al. Effect of calcium antagonist diltiazem on renal function in open heart surgery. Chest 1995; 107(5):1260-5. *Sample size less than 50 patients*

170. Amaral CF, Campolina D, Dias MB, et al. Tourniquet ineffectiveness to reduce the severity of envenoming after Crotalus durissus snake bite in Belo Horizonte, Minas Gerais, Brazil. Toxicon 1998; 36(5):805-8. *Not CKD treatment*

171. Amaresan MS, Geetha R. Early diagnosis of CKD and its prevention. Journal of the Association of Physicians of India 2008; 56:41-6. *Not RCT or controlled trial*

172. Amato RJ. 5T4-modified vaccinia Ankara: progress in tumor-associated antigen-based immunotherapy. Expert Opinion on Biological Therapy 2010 Feb; 10(2):281-7. *Not CKD treatment*

173. Ambwani J, Ubhrani D, Saad R, et al. Could atrial natriuretic peptide be a useful drug therapy for high-risk patients after cardiac surgery? Interactive Cardiovascular & Thoracic Surgery 2009; 8(4):474-8. *Not CKD treatment*

174. Amini M, Salarifar M, Amirbaigloo A, et al. N-acetylcysteine does not prevent contrast-induced nephropathy after cardiac catheterization in patients with diabetes mellitus and chronic kidney disease: a randomized clinical trial. Trials [Electronic Resource] 2009; 10:45. *Not CKD treatment*

175. Aminorroaya A, Janghorbani M, Rezvanian H, et al. Comparison of the effect of pentoxifylline and captopril on proteinuria in patients with type 2 diabetes mellitus. Nephron 2005; 99(3):c73-7. *Sample size less than 50 patients*

176. Amrein PC, Fabian RL. Treatment of recurrent head and neck cancer with cisplatin and 5-fluorouracil vs. the same plus bleomycin and methotrexate. Laryngoscope 1992; 102(8):901-6. *Not CKD treatment*

177. An MM, Zou Z, Shen H, et al. Incidence and risk of significantly raised blood pressure in cancer patients treated with bevacizumab: an updated meta-analysis. European Journal of Clinical Pharmacology 2010 Aug; 66(8):813-21. *Not CKD treatment*

178. Anand A, Anand A, Anand N. Recombinant human erythropoietin for the correction of cancer associated anemia with and without concomitant cytotoxic chemotherapy. Cancer 1996; 77(9):1960-1. *Not RCT or controlled trial*

179. Anand IS, Deswal A, Kereiakes DJ, et al. Comparison of once-daily versus twice-daily dosing of valsartan in patients with chronic stable heart failure. Vascular Health & Risk Management 2010; 6:449-55. *Not CKD treatment*

180. Anastassiades E, Howarth D, Howarth JE, et al. Influence of azathioprine on the ferrokinetics of patients with renal failure before and after treatment with erythropoietin. Nephron 1994; 67(3):291-6. *Sample size less than 50 patients*

181. Anavekar NS, McMurray JJV, Velazquez EJ, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. New England Journal of Medicine 2004; 351(13):1285-95. *Follow-up less than 6 months*

182. Anavekar NS, Solomon SD, McMurray JJV, et al. Comparison of renal function and cardiovascular risk following acute myocardial infarction in patients with and without diabetes mellitus. American Journal of Cardiology 2008; 101(7):925-9. *Not CKD treatment*

183. Ancha HR, Spungen AM, Bauman WA, et al. Clinical trial: the efficacy and safety of routine bowel cleansing agents for elective colonoscopy in persons with spinal cord injury - a randomized prospective single-blind study. Alimentary Pharmacology & Therapeutics 2009 Dec 1; 30(11-12):1110-7. *Not CKD treatment*

184. Andel M, Grzeszczak W, Michalek J, et al. A multinational, multi-centre, observational, cross-sectional survey assessing diabetes secondary care in Central and Eastern Europe (DEPAC Survey). Diabetic Medicine 2008; 25(10):1195-203. *Not early CKD*

185. Anders HJ, Rihl M, Loch O, et al. Prediction of creatinine clearance from serum creatinine in patients with rheumatoid arthritis: comparison of six formulae and one nomogram. Clinical Rheumatology 2000; 19(1):26-9. *Not early CKD*

186. Andersen GS, Hartling OJ, Hein HO, et al. Changes in blood pressure, fluid volumes and glomerular filtration rate during long-term treatment with prizidilol, an antihypertensive drug with combined vasodilatator and beta-adrenoceptor blocking actions. Danish Medical Bulletin 1985; 32(5):280-3. *Sample size less than 50 patients*

187. Andersen K, Weinberger MH, Constance CM, et al. Comparative effects of aliskiren-based and ramipril-based therapy on the renin system during long-term (6 months) treatment and withdrawal in patients with hypertension. Journal of the Renin-Angiotensin-Aldosterone System 2009; 10(3):157-67. *Follow-up less than 6 months*

188. Andersen NH, Mogensen CE. Dual blockade of the renin angiotensin system in diabetic and nondiabetic kidney disease. Current Hypertension Reports 2004; 6(5):369-76. *Not RCT or controlled trial*

189. Andersen PE, Bolstad B, Berg KJ, et al. Iodixanol and ioxaglate in cardioangiography: a double-blind randomized phase III study. Clinical Radiology 1993; 48(4):268-72. *Not CKD treatment*

190. Andersen S, Blouch K, Bialek J, et al. Glomerular permselectivity in early stages of overt diabetic nephropathy. Kidney International 2000; 58(5):2129-37. *Sample size less than 50 patients*

191. Andersen S, Brochner-Mortensen J, Parving H-H, et al. Kidney function during and after withdrawal of long-term irbesartan treatment in patients with type 2 diabetes and microalbuminuria. Diabetes Care 2003; 26(12):3296-302. *Not RCT or controlled trial*

192. Andersen S, Mischak H, Zurbig P, et al. Urinary proteome analysis enables assessment of renoprotective treatment in type 2 diabetic patients with microalbuminuria. BMC Nephrology 2010; 11:29. *Not relevant to key questions*

193. Andersen S, Schalkwijk CG, Stehouwer CD, et al. Angiotensin II blockade is associated with decreased plasma leukocyte adhesion molecule levels in diabetic nephropathy. Diabetes Care 2000; 23(7):1031-2. *Not CKD treatment*

194. Andersen S, Tarnow L, Cambien F, et al. Renoprotective effects of losartan in diabetic nephropathy: interaction with ACE insertion/deletion genotype? Kidney International 2002; 62(1):192-8. *Follow-up less than 6 months*

195. Andersen S, Tarnow L, Rossing P, et al. Renoprotective effects of angiotensin II receptor blockade in type 1 diabetic patients with diabetic nephropathy. Kidney International 2000; 57(2):601-6. *Sample size less than 50 patients*

196. Anderson CM. Sodium chloride treatment of amphotericin B nephrotoxicity. Standard of care? Western Journal of Medicine 1995; 162(4):313-7. *Not CKD treatment*

197. Anderson J, Glynn LG, Newell J, et al. The impact of renal insufficiency and anaemia on survival in patients with cardiovascular disease: a cohort study. BMC Cardiovascular Disorders 2009; 9:51. *Not RCT or controlled trial*

198. Anderson JW, Blake JE, Turner J, et al. Effects of soy protein on renal function and proteinuria in patients with type 2 diabetes. American Journal of Clinical Nutrition 1998; 68(6 Suppl):1347S-53S. *Sample size less than 50 patients*

199. Anderson TJ, Sun Y-H, Hubacek J, et al. Effects of folinic acid on forearm blood flow in patients with end-stage renal disease. Nephrology Dialysis Transplantation 2006; 21(7):1927-33. *Sample size less than 50 patients*

200. Andersson LG, Jeppsson A, Bratteby LE, et al. Renal function during cardiopulmonary bypass: influence of the calcium entry blocker felodipine. Anesthesia & Analgesia 1996; 83(1):34-40. *Follow-up less than 6 months*

201. Anderton JL, Gill M, Notghi A. Renal haemodynamic effects of bunazosin retard and prazosin in mild to moderately hypertensive patients with normal or moderately impaired renal function. Nephrology Dialysis Transplantation 1994; 9(6):607-12. *Follow-up less than 6 months*

202. Anderton JL, Notghi A. An evaluation of the efficacy and safety of doxazosin in the treatment of hypertension associated with renal insufficiency. Journal of Human Hypertension 1990; 4 Suppl 3:52-7. *Sample size less than 50 patients*

203. Ando K, Ohtsu H, Arakawa Y, et al. Rationale and design of the Eplerenone combination Versus conventional Agents to Lower blood pressure on Urinary Antialbuminuric Treatment Effect (EVALUATE) trial: a double-blinded randomized placebo-controlled trial to evaluate the antialbuminuric effects of an aldosterone blocker in hypertensive patients with albuminuria. Hypertension Research - Clinical & Experimental 2010 Jun; 33(6):616-21. *Not RCT or controlled trial*

204. Ando Y, Minami H, Saka H, et al. Pharmacokinetic study of carboplatin given on a 5-day intravenous schedule. Japanese Journal of Cancer Research 1997; 88(5):517-21. *Not CKD treatment*

205. Andrew E, Berg KJ, Nossen JO, et al. Renal effects of iodixanol in patients: a comparison with other radiographic contrast media. Academic Radiology 1996; 3 Suppl 2:S440-3. *Not RCT or controlled trial*

206. Angeli P, Gatta A, Caregaro L, et al. Effects of iloprost, a prostacyclin analog derivative, on renal plasma flow, renal function, and renin-aldosterone system in humans. Clinical Pharmacology & Therapeutics 1988; 44(2):211-6. *Sample size less than 50 patients*

207. Angermann CE, Stork S, Costard-Jackle A, et al. Reduction of cyclosporine after introduction of mycophenolate mofetil improves chronic renal dysfunction in heart transplant recipients--the IMPROVED multi-centre study. European Heart Journal 2004; 25(18):1626-34. *Not early CKD*

208. Angevin E, Valteau-Couanet D, Farace F, et al. Phase I study of prolonged low-dose subcutaneous recombinant interleukin-2 (IL-2) in patients with advanced cancer. Journal of Immunotherapy with Emphasis on Tumor Immunology 1995; 18(3):188-95. *Follow-up less than 6 months*

209. Angoulvant D, Cucherat M, Rioufol G, et al. Preventing acute decrease in renal function induced by coronary angiography (PRECORD): a prospective randomized trial. Archives of cardiovascular diseases 2009; 102(11):761-7. *Not CKD treatment*

210. Angstwurm MW, Schottdorf J, Schopohl J, et al. Selenium replacement in patients with severe systemic inflammatory response syndrome improves clinical outcome. Critical Care Medicine 1999; 27(9):1807-13. *Sample size less than 50 patients*

211. Annuk M, Fellstrom B, Lind L. Cyclooxygenase inhibition improves endothelium-dependent vasodilatation in patients with chronic renal failure. Nephrology Dialysis Transplantation 2002; 17(12):2159-63. *Sample size less than 50 patients*

212. Anothaisintawee T, Rattanasiri S, Ingsathit A, et al. Prevalence of chronic kidney disease: a systematic review and meta-analysis. Clinical Nephrology 2009; 71(3):244-54. *Not relevant to key questions*

213. Anselmino M, Biondi-Zoccai G, Sheiban I. Letter regarding article by Solomon et al, “Cardiac Angiography in REnally Impaired Patients (CARE) study: a randomized double-blind trial of contrast-induced nephropathy in patients with chronic kidney disease”. Circulation 2008; 117(7):e166; author reply e7. *Not CKD treatment*

214. Ansquer JC, Foucher C, Aubonnet P, et al. Fibrates and microvascular complications in diabetes--insight from the FIELD study. Current Pharmaceutical Design 2009; 15(5):537-52. *Not CKD treatment*

215. Ansquer J-C, Dalton RN, Causse E, et al. Effect of fenofibrate on kidney function: a 6-week randomized crossover trial in healthy people. American Journal of Kidney Diseases 2008; 51(6):904-13. *Not CKD treatment*

216. Ansquer J-C, Foucher C, Rattier S, et al. Fenofibrate reduces progression to microalbuminuria over 3 years in a placebo-controlled study in type 2 diabetes: results from the Diabetes Atherosclerosis Intervention Study (DAIS). American Journal of Kidney Diseases 2005; 45(3):485-93. *Not relevant to key questions*

217. Anthony J, Rees AE, Davey DA. Indoramin in the treatment of pregnancy hypertension. A placebo-controlled trial comparing the efficacy of indoramin with alpha-methyldopa. South African Medical Journal 1990; Suid-Afrikaanse Tydskrif Vir Geneeskunde. 78(8):458-61. *Not CKD treatment*

218. Antonucci F, Calo L, Rizzolo M, et al. Nifedipine can preserve renal function in patients undergoing aortic surgery with infrarenal crossclamping. Nephron 1996; 74(4):668-73. *Not CKD treatment*

219. Antrum R, Gorst K, Galvin K, et al. A comparison of teicoplanin vs. cephradine and metronidazole in surgical prophylaxis: an interim analysis. Scandinavian Journal of Infectious Diseases Supplement 1990; 72:45-53. *Not CKD treatment*

220. Aoki J, Mintz GS, Weissman NJ, et al. Impact of mild or moderate renal insufficiency on the intravascular ultrasonic analysis of chronic vascular response to paclitaxel-eluting and bare-metal stents (from the TAXUS IV, V, and VI trials). American Journal of Cardiology 2008; 102(8):1009-16. *Not CKD treatment*

221. Aoki J, Ong ATL, Hoye A, et al. Five year clinical effect of coronary stenting and coronary artery bypass grafting in renal insufficient patients with multivessel coronary artery disease: insights from ARTS trial. European Heart Journal 2005; 26(15):1488-93. *Not RCT or controlled trial*

222. Apakkan Aksun S, Ozmen B, Ozmen D, et al. Serum and urinary nitric oxide in Type 2 diabetes with or without microalbuminuria: relation to glomerular hyperfiltration. Journal of Diabetes & its Complications 2003; 17(6):343-8. *Not early CKD*

223. Appel GB. COX-2 inhibitors and the kidney. Clinical & Experimental Rheumatology 2001; 19(6 Suppl 25):S37-40. *Not RCT or controlled trial*

224. Appel LJ, Middleton J, Miller ER, 3rd, et al. The rationale and design of the AASK cohort study. Journal of the American Society of Nephrology 2003; 14(7 Suppl 2):S166-72. *Not RCT or controlled trial*

225. Appel LJ, Wright JT, Jr., Greene T, et al. Intensive blood-pressure control in hypertensive chronic kidney disease. New England Journal of Medicine 2010 Sep 2; 363(10):918-29. *Not relevant to key questions*

226. Appel LJ, Wright JT, Jr., Greene T, et al. Long-term effects of renin-angiotensin system-blocking therapy and a low blood pressure goal on progression of hypertensive chronic kidney disease in African Americans. Archives of Internal Medicine 2008; 168(8):832-9. *Not CKD treatment*

227. Apperloo AJ, de Zeeuw D, de Jong PE. Short-term antiproteinuric response to antihypertensive treatment predicts long-term GFR decline in patients with non-diabetic renal disease. Kidney International - Supplement 1994; 45:S174-8. *Sample size less than 50 patients*

228. Apperloo AJ, de Zeeuw D, de Jong PE. A short-term antihypertensive treatment-induced fall in glomerular filtration rate predicts long-term stability of renal function. Kidney International 1997; 51(3):793-7. *Follow-up less than 6 months*

229. Apperloo AJ, de Zeeuw D, Sluiter HE, et al. Differential effects of enalapril and atenolol on proteinuria and renal haemodynamics in non-diabetic renal disease. BMJ 1991; 303(6806):821-4. *Sample size less than 50 patients*

230. Appleby C, Foley RN. Hypertension in end-stage renal disease. Minerva Urologica e Nefrologica 2002; 54(1):37-43. *Not RCT or controlled trial*

231. Apseloff G, Wilner KD, von Deutsch DA, et al. Tenidap sodium decreases renal clearance and increases steady-state concentrations of lithium in healthy volunteers. British Journal of Clinical Pharmacology 1995; 39 Suppl 1:25S-8S. *Sample size less than 50 patients*

232. Apseloff G, Wilner KD, von Deutsch DA, et al. Sertraline does not alter steady-state concentrations or renal clearance of lithium in healthy volunteers. Journal of Clinical Pharmacology 1992; 32(7):643-6. *Not CKD treatment*

233. Aranda P, Segura J, Ruilope LM, et al. Long-term renoprotective effects of standard versus high doses of telmisartan in hypertensive nondiabetic nephropathies. American Journal of Kidney Diseases 2005; 46(6):1074-9. *Sample size less than 50 patients*

234. Arcaro G, Zenere BM, Saggiani F, et al. ACE inhibitors improve endothelial function in type 1 diabetic patients with normal arterial pressure and microalbuminuria. Diabetes Care 1999; 22(9):1536-42. *Sample size less than 50 patients*

235. Arguedas JA, Perez MI, Wright JM. Treatment blood pressure targets for hypertension. Cochrane Database of Systematic Reviews 2009; (3):CD004349. *Not RCT or controlled trial*

236. Arguedas JA, Perez MI, Wright JM. Treatment blood pressure targets for hypertension. Cochrane Database of Systematic Reviews 2009; (3):CD004349. *Not RCT or controlled trial*

237. Arici M, Usalan C, Altun B, et al. Radiocontrast-induced nephrotoxicity and urinary alpha-glutathione S-transferase levels: effect of amlodipine administration. International Urology & Nephrology 2003; 35(2):255-61. *Not relevant to key questions*

238. Armstrong GD, Rowe PC, Goodyer P, et al. A phase I study of chemically synthesized verotoxin (Shiga-like toxin) Pk-trisaccharide receptors attached to chromosorb for preventing hemolytic-uremic syndrome. Journal of Infectious Diseases 1995; 171(4):1042-5. *Not RCT or controlled trial*

239. Armstrong LE, Pumerantz AC, Roti MW, et al. Fluid, electrolyte, and renal indices of hydration during 11 days of controlled caffeine consumption. International Journal of Sport Nutrition & Exercise Metabolism 2005; 15(3):252-65. *Not RCT or controlled trial*

240. Arns W, Gies M, Choi L, et al. Absorption characteristics of EC-MPS--an enteric-coated formulation of mycophenolic sodium. International Journal of Clinical Pharmacology & Therapeutics 2006; 44(8):375-85. *Not early CKD*

241. Aronoff GR. Therapeutic implications associated with renal studies of nabumetone. Journal of Rheumatology - Supplement 1992; 36:25-31. *Not CKD treatment*

242. Arora R, Clark L, Taylor M. Treatment of high-risk African American patients: left ventricular dysfunction, heart failure, renal disease, and postmyocardial infarction. Journal of Clinical Hypertension 2003; 5(1 Suppl 1):26-31. *Not RCT or controlled trial*

243. Arora S, Clarke K, Srinivasan V, et al. Effect of nesiritide on renal function in patients admitted for decompensated heart failure. Qjm 2007; 100(11):699-706. *Follow-up less than 6 months*

244. Arredondo A, Burke TA, Carides GW, et al. The impact of losartan on the lifetime incidence of ESRD and costs in Mexico. Revista de Investigacion Clinica 2005; 57(3):399-405. *Sample size less than 50 patients*

245. Arroyo V, Fernandez J, Mas A, et al. Molecular adsorbents recirculating system (MARS) and the failing liver: a negative editorial for a positive trial? Hepatology 2008; 47(6):2143-4. *Not CKD treatment*

246. Artz AS, Fergusson D, Drinka PJ, et al. Mechanisms of unexplained anemia in the nursing home. Journal of the American Geriatrics Society 2004; 52(3):423-7. *Not CKD treatment*

247. Arzilli F, Giovannetti R, Lenzi M, et al. Acute hemodynamic (systemic and renal) and humoral effects of three increasing doses of iloprost in essential hypertensives. American Journal of Hypertension 1989; 2(11 Pt 1):856-60. *Sample size less than 50 patients*

248. Arzilli F, Magagna A, Giovannetti R, et al. Acute dose-response curve of enalapril in renovascular hypertensives. American Journal of Hypertension 1988; 1(3 Pt 3):75S-8S. *Sample size less than 50 patients*

249. Ascione R, Lloyd CT, Underwood MJ, et al. On-pump versus off-pump coronary revascularization: evaluation of renal function. Annals of Thoracic Surgery 1999; 68(2):493-8. *Follow-up less than 6 months*

250. Ashworth A, Webb ST. Does the prophylactic administration of N-acetylcysteine prevent acute kidney injury following cardiac surgery? Interactive Cardiovascular & Thoracic Surgery 2010 Sep; 11(3):303-8. *Not CKD treatment*

251. Asif A, Epstein DL, Epstein M. Dopamine-1 receptor agonist: renal effects and its potential role in the management of radiocontrast-induced nephropathy. Journal of Clinical Pharmacology 2004; 44(12):1342-51. *Not relevant to key questions*

252. Aspelin P, Aubry P, Fransson S-G, et al. Nephrotoxic effects in high-risk patients undergoing angiography. New England Journal of Medicine 2003; 348(6):491-9. *Not CKD treatment*

253. Aspelin P, Aubry P, Fransson S-G, et al. Cost-effectiveness of iodixanol in patients at high risk of contrast-induced nephropathy. American Heart Journal 2005; 149(2):298-303. *Not RCT or controlled trial*

254. Asrani SK, Leise MD, West CP, et al. Use of sirolimus in liver transplant recipients with renal insufficiency: a systematic review and meta-analysis. Hepatology 2010 Oct; 52(4):1360-70. *Not CKD treatment*

255. Assadi F. Acetazolamide for prevention of contrast-induced nephropathy: a new use for an old drug. Pediatric Cardiology 2006; 27(2):238-42. *Not RCT or controlled trial*

256. Assan R, Blanchet F, Feutren G, et al. Normal renal function 8 to 13 years after cyclosporin A therapy in 285 diabetic patients. Diabetes/Metabolism Research Reviews 2002; 18(6):464-72. *Not CKD treatment*

257. Asselbergs FW, van der Harst P, van Roon AM, et al. Long-term effects of pravastatin and fosinopril on peripheral endothelial function in albuminuric subjects. Atherosclerosis 2008; 196(1):349-55. *Not RCT or controlled trial*

258. Asselbergs FW, van Gilst WH. Angiotensin converting enzyme inhibition in cardiovascular risk populations: a practical approach to identify the patient who will benefit most. Current Opinion in Cardiology 2007; 22(4):267-72. *Not CKD treatment*

259. Asselbergs FW, van Roon AM, Hillege HL, et al. Effects of fosinopril and pravastatin on carotid intima-media thickness in subjects with increased albuminuria. Stroke 2005; 36(3):649-53. *Sample size less than 50 patients*

260. Assy N, Kayal M, Mejirisky Y, et al. The changes in renal function after a single dose of intravenous furosemide in patients with compensated liver cirrhosis. BMC Gastroenterology 2006; 6:39. *Sample size less than 50 patients*

261. Astor BC, Levey AS, Stevens LA, et al. Method of glomerular filtration rate estimation affects prediction of mortality risk. Journal of the American Society of Nephrology 2009; 20(10):2214-22. *Not RCT or controlled trial*

262. Astor BC, Yi S, Hiremath L, et al. N-terminal prohormone brain natriuretic peptide as a predictor of cardiovascular disease and mortality in blacks with hypertensive kidney disease: the African American Study of Kidney Disease and Hypertension (AASK). Circulation 2008; 117(13):1685-92. *Not CKD treatment*

263. Athyros VG, Mikhailidis DP, Papageorgiou AA, et al. The effect of statins versus untreated dyslipidaemia on renal function in patients with coronary heart disease. A subgroup analysis of the Greek atorvastatin and coronary heart disease evaluation (GREACE) study. Journal of Clinical Pathology 2004; 57(7):728-34. *Not relevant to key questions*

264. Athyros VG, Papageorgiou AA, Elisaf M, et al. Statins and renal function in patients with diabetes mellitus. Current Medical Research & Opinion 2003; 19(7):615-7. *Not CKD treatment*

265. Atkins RC, Briganti EM, Lewis JB, et al. Proteinuria reduction and progression to renal failure in patients with type 2 diabetes mellitus and overt nephropathy. American Journal of Kidney Diseases 2005; 45(2):281-7. *Follow-up less than 6 months*

266. Atmaca A, Gedik O. Effects of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and their combination on microalbuminuria in normotensive patients with type 2 diabetes. Advances in Therapy 2006; 23(4):615-22. *Not relevant to key questions*

267. Atthobari J, Brantsma AH, Gansevoort RT, et al. The effect of statins on urinary albumin excretion and glomerular filtration rate: results from both a randomized clinical trial and an observational cohort study. Nephrology Dialysis Transplantation 2006; 21(11):3106-14. *Not RCT or controlled trial*

268. Atthobari J, Gansevoort RT, Visser ST, et al. The effect of screening for cardio-renal risk factors on drug use in the general population. British Journal of Clinical Pharmacology 2007; 64(6):810-8. *Not CKD treatment*

269. Aulitzky WE, Grosse-Wilde H, Westhoff U, et al. Enhanced serum levels of soluble HLA class I molecules are induced by treatment with recombinant interferon-gamma (IFN-gamma). Clinical & Experimental Immunology 1991; 86(2):236-9. *Not CKD treatment*

270. Aurell M, Bengtsson C, Bjorck S. Enalapril versus metoprolol in primary hypertension--effects on the glomerular filtration rate. Nephrology Dialysis Transplantation 1997; 12(11):2289-94. *Not early CKD*

271. Austen SK, Coombes JS, Fassett RG. Homocysteine and cardiovascular disease in renal disease. Nephrology 2003; 8(6):285-95. *Not CKD treatment*

272. Autier J, Escudier B, Wechsler J, et al. Prospective study of the cutaneous adverse effects of sorafenib, a novel multikinase inhibitor. Archives of Dermatology 2008; 144(7):886-92. *Not CKD treatment*

273. Aviles RJ, Askari AT, Lindahl B, et al. Troponin T levels in patients with acute coronary syndromes, with or without renal dysfunction.[Summary for patients in CMAJ. 2002 Sep 17;167(6):671; PMID: 12358205]. New England Journal of Medicine 2002; 346(26):2047-52. *Not RCT or controlled trial*

274. Axelsson J, Bergsten A, Qureshi AR, et al. Elevated resistin levels in chronic kidney disease are associated with decreased glomerular filtration rate and inflammation, but not with insulin resistance. Kidney International 2006; 69(3):596-604. *Not RCT or controlled trial*

275. Axelsson J, Witasp A, Carrero JJ, et al. Circulating levels of visfatin/pre-B-cell colony-enhancing factor 1 in relation to genotype, GFR, body composition, and survival in patients with CKD. American Journal of Kidney Diseases 2007; 49(2):237-44. *Not RCT or controlled trial*

276. Aybek Z, Turan T, Yonguc T, et al. Requirement of analgesia for extracorporeal shock wave lithotripsy and efficacy of a nonsteroidal antiinflammatory drug: piroxicam. European Urology 1998; 34(3):207-9. *Not CKD treatment*

277. Azadbakht L, Esmaillzadeh A. Soy-protein consumption and kidney-related biomarkers among type 2 diabetics: a crossover, randomized clinical trial. Journal of Renal Nutrition 2009; 19(6):479-86. *Follow-up less than 6 months*

278. Azadbakht L, Shakerhosseini R, Atabak S, et al. Beneficiary effect of dietary soy protein on lowering plasma levels of lipid and improving kidney function in type II diabetes with nephropathy. European Journal of Clinical Nutrition 2003; 57(10):1292-4. *Sample size less than 50 patients*

279. Azar RR, Prpic R, Ho KK, et al. Impact of end-stage renal disease on clinical and angiographic outcomes after coronary stenting. American Journal of Cardiology 2000; 86(5):485-9. *Sample size less than 50 patients*

280. Azevedo MJ, Pinotti AF, Gross JL, et al. Preserved left ventricular systolic and diastolic function in normoalbuminuric insulin-dependent diabetic patients with glomerular hyperfiltration. Diabetes Research & Clinical Practice 1994; 25(2):103-10. *Sample size less than 50 patients*

281. Azizi M, Bissery A, Lamarre-Cliche M, et al. Integrating drug pharmacokinetics for phenotyping individual renin response to angiotensin II blockade in humans. Hypertension 2004; 43(4):785-90. *Not relevant to key questions*

282. Azmus AD, Gottschall C, Manica A, et al. Effectiveness of acetylcysteine in prevention of contrast nephropathy. Journal of Invasive Cardiology 2005; 17(2):80-4. *Not RCT or controlled trial*

283. Baas AF, Janssen KJM, Prinssen M, et al. The Glasgow Aneurysm Score as a tool to predict 30-day and 2-year mortality in the patients from the Dutch Randomized Endovascular Aneurysm Management trial. Journal of Vascular Surgery 2008; 47(2):277-81. *Not CKD treatment*

284. Baba S, Group JMS. Nifedipine and enalapril equally reduce the progression of nephropathy in hypertensive type 2 diabetics. Diabetes Research & Clinical Practice 2001; 54(3):191-201. *Not early CKD*

285. Baba T, Boku A, Ishizaki T, et al. Renal effects of nicardipine in patients with mild-to-moderate essential hypertension. American Heart Journal 1986; 111(3):552-7. *Sample size less than 50 patients*

286. Baba T, Heinemann L, Berger M, et al. Effect of 4-hour hyperglycaemia and hyperinsulinaemia on plasma atrial natriuretic factor concentrations. Hormone & Metabolic Research 1995; 27(2):95-9. *Not CKD treatment*

287. Baba T, Ishizaki T, Ido Y, et al. Renal effects of nicardipine, a calcium entry blocker, in hypertensive type II diabetic patients with nephropathy. Diabetes 1986; 35(11):1206-14. *Sample size less than 50 patients*

288. Baba T, Ishizaki T, Murabayashi S, et al. Multiple oral doses of nicardipine, a calcium-entry blocker: effects on renal function, plasma renin activity, and aldosterone concentration in mild-to-moderate essential hypertension. Clinical Pharmacology & Therapeutics 1987; 42(2):232-9. *Follow-up less than 6 months*

289. Baba T, Murabayashi S, Aoyagi K, et al. Effects of dilevalol, an R, R-isomer of labetalol, on blood pressure and renal function in patients with mild-to-moderate essential hypertension. European Journal of Clinical Pharmacology 1988; 35(1):9-15. *Sample size less than 50 patients*

290. Baba T, Murabayashi S, Takebe K. Comparison of the renal effects of angiotensin converting enzyme inhibitor and calcium antagonist in hypertensive type 2 (non-insulin-dependent) diabetic patients with microalbuminuria: a randomised controlled trial. Diabetologia 1989; 32(1):40-4. *Sample size less than 50 patients*

291. Baba T, Murabayashi S, Tomiyama T, et al. Comparison of the renal effects of dilevalol and carteolol in patients with mild to moderate essential hypertension. European Journal of Clinical Pharmacology 1990; 38(3):305-7. *Sample size less than 50 patients*

292. Baba T, Tomiyama T, Murabayashi S, et al. Renal effects of bunazosin, a new alpha 1-adrenoceptor blocker, in patients with mild-to-moderate essential hypertension. Journal of Cardiovascular Pharmacology 1990; 15(5):826-30. *Not relevant to key questions*

293. Baber U, Toto RD, de Lemos JA. Statins and cardiovascular risk reduction in patients with chronic kidney disease and end-stage renal failure. American Heart Journal 2007; 153(4):471-7. *Not relevant to key questions*

294. Backlund M, Pere P, Lepantalo M, et al. Effect of intra-aortic magnesium on renal function during and after abdominal aortic surgery: a pilot study. Acta Anaesthesiologica Scandinavica 2000; 44(5):605-11. *Not early CKD*

295. Backman L, Ringden O, Tollemar J, et al. An increased risk of relapse in cyclosporin-treated compared with methotrexate-treated patients: long-term follow-up of a randomized trial. Bone Marrow Transplantation 1988; 3(5):463-71. *Not CKD treatment*

296. Badalamenti S, Salerno F, Lorenzano E, et al. Renal effects of dietary supplementation with fish oil in cyclosporine-treated liver transplant recipients. Hepatology 1995; 22(6):1695-71. *Follow-up less than 6 months*

297. Badalamenti S, Salerno F, Salmeron JM, et al. Lack of renal effects of fish oil administration in patients with advanced cirrhosis and impaired glomerular filtration. Hepatology 1997; 25(2):313-6. *Follow-up less than 6 months*

298. Bader BD, Berger ED, Heede MB, et al. What is the best hydration regimen to prevent contrast media-induced nephrotoxicity? Clinical Nephrology 2004; 62(1):1-7. *Not CKD treatment*

299. Bagshaw SM, Delaney A, Haase M, et al. Loop diuretics in the management of acute renal failure: a systematic review and meta-analysis. Critical Care & Resuscitation 2007; 9(1):60-8. *Not RCT or controlled trial*

300. Bagshaw SM, Delaney A, Jones D, et al. Diuretics in the management of acute kidney injury: a multinational survey. Contributions to Nephrology 2007; 156:236-49. *Not RCT or controlled trial*

301. Bagshaw SM, Ghali WA. Acetylcysteine for prevention of contrast-induced nephropathy after intravascular angiography: a systematic review and meta-analysis. BMC Medicine 2004; 2:38. *Not relevant to key questions*

302. Bagshaw SM, Ghali WA. Theophylline for prevention of contrast-induced nephropathy: a systematic review and meta-analysis. Archives of Internal Medicine 2005; 165(10):1087-93. *Not early CKD*

303. Bagshaw SM, Gibney RTN, McAlister FA, et al. The SPARK Study: a phase II randomized blinded controlled trial of the effect of furosemide in critically ill patients with early acute kidney injury. Trials [Electronic Resource] 2010; 11:50. *Not RCT or controlled trial*

304. Bagshaw SM, McAlister FA, Manns BJ, et al. Acetylcysteine in the prevention of contrast-induced nephropathy: a case study of the pitfalls in the evolution of evidence. Archives of Internal Medicine 2006; 166(2):161-6. *Not RCT or controlled trial*

305. Baigent C, Landray M. Which cardiovascular risk factors matter in chronic kidney disease? Nephrology Dialysis Transplantation 2007; 22(1):9-11. *Not CKD treatment*

306. Baigent C, Landray M, Warren M. Statin therapy in kidney disease populations: potential benefits beyond lipid lowering and the need for clinical trials. Current Opinion in Nephrology & Hypertension 2004; 13(6):601-5. *Not RCT or controlled trial*

307. Bailey RR, Carlson RV, Walker RJ, et al. Effect of oral penbutolol on renal haemodynamics of hypertensive patients with renal insufficiency. New Zealand Medical Journal 1985; 98(785):683-5. *Follow-up less than 6 months*

308. Bailey RR, Nairn PL, Walker RJ. Effect of doxazosin on blood pressure and renal haemodynamics of hypertensive patients with renal failure. New Zealand Medical Journal 1986; 99(815):942-5. *Sample size less than 50 patients*

309. Bailey SR. Past and present attempts to prevent radiocontrast nephropathy. Reviews in Cardiovascular Medicine 2001; 2 Suppl 1:S14-8. *Not CKD treatment*

310. Bain R, Rohde R, Hunsicker LG, et al. A controlled clinical trial of angiotensin-converting enzyme inhibition in type I diabetic nephropathy: study design and patient characteristics. The Collaborative Study Group. Journal of the American Society of Nephrology 1992; 3(4 Suppl):S97-103. *Not RCT or controlled trial*

311. Bainbridge AD, Meredith PA, Elliott HL. A clinical pharmacological assessment of doxazosin and enalapril in combination. British Journal of Clinical Pharmacology 1993; 36(6):599-602. *Sample size less than 50 patients*

312. Baker CSR, Wragg A, Kumar S, et al. A rapid protocol for the prevention of contrast-induced renal dysfunction: the RAPPID study. Journal of the American College of Cardiology 2003; 41(12):2114-8. *Not CKD treatment*

313. Baker J, Cotter JD, Gerrard DF, et al. Effects of indomethacin and celecoxib on renal function in athletes. Medicine & Science in Sports & Exercise 2005; 37(5):712-7. *Not RCT or controlled trial*

314. Baker LR, Abrams L, Roe CJ, et al. 1,25(OH)2D3 administration in moderate renal failure: a prospective double-blind trial. Kidney International 1989; 35(2):661-9. *Sample size less than 50 patients*

315. Baker LR, Abrams SM, Roe CJ, et al. Early therapy of renal bone disease with calcitriol: a prospective double-blind study. Kidney International - Supplement 1989; 27:S140-2. *Sample size less than 50 patients*

316. Bakris G. Inclusion of albuminuria in hypertension and heart guidelines. Kidney International - Supplement 2004; (92):S124-5. *Not RCT or controlled trial*

317. Bakris G, Viberti G, Weston WM, et al. Rosiglitazone reduces urinary albumin excretion in type II diabetes. Journal of Human Hypertension 2003; 17(1):7-12. *Sample size less than 50 patients*

318. Bakris GL. Effects of diltiazem or lisinopril on massive proteinuria associated with diabetes mellitus. Annals of Internal Medicine 1990; 112(9):707-8. *Sample size less than 50 patients*

319. Bakris GL. Role for beta-blockers in the management of diabetic kidney disease. American Journal of Hypertension 2003; 16(9 Pt 2):7S-12S. *Not RCT or controlled trial*

320. Bakris GL. ACE inhibitors and ARBs: are they better than other agents to slow nephropathy progression? Journal of Clinical Hypertension 2007; 9(6):413-5. *Not relevant to key questions*

321. Bakris GL, Barnhill BW, Sadler R. Treatment of arterial hypertension in diabetic humans: importance of therapeutic selection. Kidney International 1992; 41(4):912-9. *Sample size less than 50 patients*

322. Bakris GL, Fonseca V, Katholi RE, et al. Differential effects of beta-blockers on albuminuria in patients with type 2 diabetes. Hypertension 2005; 46(6):1309-15. *Not relevant to key questions*

323. Bakris GL, Mangrum A, Copley JB, et al. Effect of calcium channel or beta-blockade on the progression of diabetic nephropathy in African Americans. Hypertension 1997; 29(3):744-50. *Sample size less than 50 patients*

324. Bakris GL, Ruilope L, Locatelli F, et al. Treatment of microalbuminuria in hypertensive subjects with elevated cardiovascular risk: results of the IMPROVE trial. Kidney International 2007; 72(7):879-85. *Not RCT or controlled trial*

325. Bakris GL, Ruilope L, Locatelli F, et al. Rationale and design of a study to evaluate management of proteinuria in patients at high risk for vascular events: the IMPROVE trial. Journal of Human Hypertension 2006; 20(9):693-700. *Not relevant to key questions*

326. Bakris GL, Siomos M, Richardson D, et al. ACE inhibition or angiotensin receptor blockade: impact on potassium in renal failure. VAL-K Study Group. Kidney International 2000; 58(5):2084-92. *Sample size less than 50 patients*

327. Bakris GL, Slataper R, Vicknair N, et al. ACE inhibitor mediated reductions in renal size and microalbuminuria in normotensive, diabetic subjects. Journal of Diabetes & its Complications 1994; 8(1):2-6. *Sample size less than 50 patients*

328. Bakris GL, Starke U, Heifets M, et al. Renal effects of oral prostaglandin supplementation after ibuprofen in diabetic subjects: a double-blind, placebo-controlled, multicenter trial. Journal of the American Society of Nephrology 1995; 5(9):1684-8. *Sample size less than 50 patients*

329. Bakris GL, Toto RD, McCullough PA. Rationale and design of a study comparing two fixed-dose combination regimens to reduce albuminuria in patients with type II diabetes and hypertension. Journal of Human Hypertension 2005; 19(2):139-44. *Not relevant to key questions*

330. Bakris GL, Weir MR. Angiotensin-converting enzyme inhibitor-associated elevations in serum creatinine: is this a cause for concern? Archives of Internal Medicine 2000; 160(5):685-93. *Not relevant to key questions*

331. Bakris GL, Weir MR, DeQuattro V, et al. Effects of an ACE inhibitor/calcium antagonist combination on proteinuria in diabetic nephropathy. Kidney International 1998; 54(4):1283-9. *Sample size less than 50 patients*

332. Bakris GL, Weir MR, Secic M, et al. Differential effects of calcium antagonist subclasses on markers of nephropathy progression. Kidney International 2004; 65(6):1991-2002. *Not early CKD*

333. Bakris GL, Weir MR, Shanifar S, et al. Effects of blood pressure level on progression of diabetic nephropathy: results from the RENAAL study. Archives of Internal Medicine 2003; 163(13):1555-65. *Not CKD treatment*

334. Bakris GL, Williams M, Dworkin L, et al. Preserving renal function in adults with hypertension and diabetes: a consensus approach. National Kidney Foundation Hypertension and Diabetes Executive Committees Working Group. American Journal of Kidney Diseases 2000; 36(3):646-61. *Not relevant to key questions*

335. Balakrishnan VS, Coles GA, Williams JD. A potential role for endogenous adenosine in control of human glomerular and tubular function. American Journal of Physiology 1993; 265(4 Pt 2):F504-10. *Not CKD treatment*

336. Balakrishnan VS, Coles GA, Williams JD. Functional role of endogenous adenosine in human chronic renal disease. Experimental Nephrology 1996; 4(1):26-36. *Sample size less than 50 patients*

337. Balakrishnan VS, Rao M, Menon V, et al. Resistance training increases muscle mitochondrial biogenesis in patients with chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2010 Jun; 5(6):996-1002. *Follow-up less than 6 months*

338. Balamuthusamy S, Srinivasan L, Verma M, et al. Renin angiotensin system blockade and cardiovascular outcomes in patients with chronic kidney disease and proteinuria: a meta-analysis.[Erratum appears in Am Heart J. 2009 Mar;157(3):501 Note: Jalandara, Nishant [corrected to Jalandhara, Nishant]]. American Heart Journal 2008; 155(5):791-805. *Not CKD treatment*

339. Balderramo DC, Verdu MB, Ramacciotti CF, et al. Renoprotective effect of high periprocedural doses of oral N-acetylcysteine in patients scheduled to undergo a same-day angiography. Revista de la Facultad de Ciencias Medicas de Cordoba 2004; 61(2):13-9. *Sample size less than 50 patients*

340. Baldwin L, Henderson A, Hickman P. Effect of postoperative low-dose dopamine on renal function after elective major vascular surgery. Annals of Internal Medicine 1994; 120(9):744-7. *Not CKD treatment*

341. Banach M, Mikhailidis DP, Kjeldsen SE, et al. Time for new indications for statins? Medical Science Monitor 2009; 15(12):MS1-5. *Not RCT or controlled trial*

342. Banerjee D, Materson BJ. Blood pressure-independent impact of antihypertensive agents on cardiovascular and renal disease. Current Hypertension Reports 2002; 4(6):445-52. *Not relevant to key questions*

343. Bangstad HJ, Osterby R, Dahl-Jorgensen K, et al. Improvement of blood glucose control in IDDM patients retards the progression of morphological changes in early diabetic nephropathy. Diabetologia 1994; 37(5):483-90. *Sample size less than 50 patients*

344. Bangstad HJ, Osterby R, Dahl-Jorgensen K, et al. Early glomerulopathy is present in young, type 1 (insulin-dependent) diabetic patients with microalbuminuria. Diabetologia 1993; 36(6):523-9. *Sample size less than 50 patients*

345. Banikazemi M, Bultas J, Waldek S, et al. Agalsidase-beta therapy for advanced Fabry disease: a randomized trial. Annals of Internal Medicine 2007; 146(2):77-86. *Sample size less than 50 patients*

346. Bansal N, Tighiouart H, Weiner D, et al. Anemia as a risk factor for kidney function decline in individuals with heart failure. American Journal of Cardiology 2007; 99(8):1137-42. *Not relevant to key questions*

347. Baranska-Kosakowska A, Zakliczynski M, Przybylski R, et al. Role of N-acetylcysteine on renal function in patients after orthotopic heart transplantation undergoing coronary angiography. Transplantation Proceedings 2007; 39(9):2853-5. *Not CKD treatment*

348. Barba G, Vallance PJ, Strazzullo P, et al. Effects of sodium intake on the pressor and renal responses to nitric oxide synthesis inhibition in normotensive individuals with different sodium sensitivity. Journal of Hypertension 2000; 18(5):615-21. *Sample size less than 50 patients*

349. Barber TJ, Hughes A, Dinsmore WW, et al. How does HIV impact on non-AIDS events in the era of HAART? International Journal of STD & AIDS 2009; 20(1):1-3. *Not CKD treatment*

350. Barichella M, Savardi C, Mauri A, et al. Diet with LPP for renal patients increases daily energy expenditure and improves motor function in parkinsonian patients with motor fluctuations. Nutritional Neuroscience 2007; 10(3-4):129-35. *Not RCT or controlled trial*

351. Barit D, Cooper ME. Diabetic patients and kidney protection: an attainable target. Journal of Hypertension - Supplement 2008; 26(2):S3-7. *Not relevant to key questions*

352. Barit D, Cooper ME. Diabetic patients and kidney protection: an attainable target. Journal of Hypertension 2008; 26 Suppl 2:S3-7. *Follow-up less than 6 months*

353. Barletta G, Lazzeri C, Vecchiarino S, et al. Low-dose C-type natriuretic peptide does not affect cardiac and renal function in humans. Hypertension 1998; 31(3):802-8. *Sample size less than 50 patients*

354. Barlovic DP, Zaletel J, Prezelj J. Adipocytokines are associated with renal function in patients with normal range glomerular filtration rate and type 2 diabetes. Cytokine 2009; 46(1):142-5. *Not early CKD*

355. Barman Balfour JA, Scott LJ. Cinacalcet hydrochloride. Drugs 2005; 65(2):271-81. *Not CKD treatment*

356. Barnett A. Preventing renal complications in type 2 diabetes: results of the diabetics exposed to telmisartan and enalapril trial. Journal of the American Society of Nephrology 2006; 17(4 Suppl 2):S132-5. *Not RCT or controlled trial*

357. Barnett A. Prevention of loss of renal function over time in patients with diabetic nephropathy. American Journal of Medicine 2006; 119(5 Suppl 1):S40-7. *Follow-up less than 6 months*

358. Barnett AH. The role of angiotensin II receptor antagonists in the management of diabetes. Blood Pressure Supplement 2001; 1:21-6. *Not RCT or controlled trial*

359. Barnett AH. Preventing renal complications in diabetic patients: the Diabetics Exposed to Telmisartan And enalaprIL (DETAIL) study. Acta Diabetologica 2005; 42 Suppl 1:S42-9. *Not CKD treatment*

360. Baron F, Frere P, Baudoux E, et al. Low incidence of acute graft-versus-host disease after non-myeloablative stem cell transplantation with CD8-depleted peripheral blood stem cells: an update. Haematologica 2003; 88(7):835-7. *Not CKD treatment*

361. Barone R, Borson-Chazot F, Valkema R, et al. Patient-specific dosimetry in predicting renal toxicity with (90)Y-DOTATOC: relevance of kidney volume and dose rate in finding a dose-effect relationship. Journal of Nuclear Medicine 2005; 46 Suppl 1:99S-106S. *Not relevant to key questions*

362. Barone R, Pauwels S, De Camps J, et al. Metabolic effects of amino acid solutions infused for renal protection during therapy with radiolabelled somatostatin analogues. Nephrology Dialysis Transplantation 2004; 19(9):2275-81. *Sample size less than 50 patients*

363. Barr J, Zaloga GP, Haupt MT, et al. Cation metabolism during propofol sedation with and without EDTA in patients with impaired renal function. Intensive Care Medicine 2000; 26 Suppl 4:S433-42. *Not CKD treatment*

364. Barrantes F, Feng Y, Ivanov O, et al. Acute kidney injury predicts outcomes of non-critically ill patients. Mayo Clinic Proceedings 2009; 84(5):410-6. *Not CKD treatment*

365. Barras MA, Duffull SB, Atherton JJ, et al. Modelling the occurrence and severity of enoxaparin-induced bleeding and bruising events. British Journal of Clinical Pharmacology 2009 Nov; 68(5):700-11. *Not CKD treatment*

366. Barratt TM, Chantler C, Lederman S, et al. Assessment of renal function. American Journal of Kidney Diseases 1986; 7(4):347-9. *Not CKD treatment*

367. Barrett BJ. Contrast-induced nephropathy: we need all the data to discern the truth. American Journal of Kidney Diseases 2009; 54(4):587-9. *Not RCT or controlled trial*

368. Barrett SV, Paul J, Hay A, et al. Does body mass index affect progression-free or overall survival in patients with ovarian cancer? Results from SCOTROC I trial. Annals of Oncology 2008; 19(5):898-902. *Not CKD treatment*

369. Barri YM, Wilcox CS. Salt intake determines the renal response to L-arginine infusion in normal human subjects. Kidney International 1998; 53(5):1299-304. *Not CKD treatment*

370. Barrios V, Escobar C. Diabetes and hypertension. What is new? Minerva Cardioangiologica 2009 Dec; 57(6):705-22. *Not CKD treatment*

371. Barros Silva GE, Costa RS, Ravinal RC, et al. Evaluation of erythrocyte dysmorphism by light microscopy with lowering of the condenser lens: A simple and efficient method. Nephrology 2010 Mar; 15(2):171-7. *Not CKD treatment*

372. Barton M, Mullins JJ, Bailey MA, et al. Role of endothelin receptors for renal protection and survival in hypertension: waiting for clinical trials. Hypertension 2006; 48(5):834-7. *Not RCT or controlled trial*

373. Basic-Jukic N, Kes P, Mokos I, et al. Do we need more intensive enzyme replacement therapy for Anderson-Fabry disease? Medical Hypotheses 2009; 72(4):476-7. *Not RCT or controlled trial*

374. Baskurt M, Okcun B, Abaci O, et al. N-acetylcysteine versus N-acetylcysteine + theophylline for the prevention of contrast nephropathy. European Journal of Clinical Investigation 2009; 39(9):793-9. *Not CKD treatment*

375. Battershill AJ, Scott LJ. Telmisartan: a review of its use in the management of hypertension. Drugs 2006; 66(1):51-83. *Not RCT or controlled trial*

376. Bauer JH, Gaddy P. Effects of enalapril alone, and in combination with hydrochlorothiazide, on renin-angiotensin-aldosterone, renal function, salt and water excretion, and body fluid composition. American Journal of Kidney Diseases 1985; 6(4):222-32. *Sample size less than 50 patients*

377. Bauer JH, Reams G, Gaddy P. Renal function and hemodynamics during treatment with enalapril in primary hypertension. Nephron 1986; 44 Suppl 1:83-6. *Sample size less than 50 patients*

378. Bauer JH, Reams GP. Hemodynamic and renal function in essential hypertension during treatment with enalapril. American Journal of Medicine 1985; 79(3C):10-3. *Sample size less than 50 patients*

379. Bauer JH, Reams GP, Hewett J, et al. A randomized, double-blind, placebo-controlled trial to evaluate the effect of enalapril in patients with clinical diabetic nephropathy. American Journal of Kidney Diseases 1992; 20(5):443-57. *Sample size less than 50 patients*

380. Bauer JH, Reams GP, Lau A. A comparison of betaxolol and nadolol on renal function in essential hypertension. American Journal of Kidney Diseases 1987; 10(2):109-12. *Sample size less than 50 patients*

381. Bauer LA, Black DJ, Lill JS, et al. Levofloxacin and ciprofloxacin decrease procainamide and N-acetylprocainamide renal clearances. Antimicrobial Agents & Chemotherapy 2005; 49(4):1649-51. *Not RCT or controlled trial*

382. Bayerle-Eder M, Fuchsjager-Mayrl G, Sieder A, et al. Effect of pravastatin on responsiveness to N-monomethyl-L-arginine in patients with hypercholesterolaemia. Atherosclerosis 2002; 160(1):177-84. *Not early CKD*

383. Bayerle-Eder M, Langenberger H, Pleiner J, et al. Endothelin ETA receptor-subtype specific antagonism does not mitigate the acute systemic or renal effects of exogenous angiotensin II in humans. European Journal of Clinical Investigation 2002; 32(4):230-5. *Not early CKD*

384. Bayliss J, Canepa-Anson R, Norell M, et al. The renal response to neuroendocrine inhibition in chronic heart failure: double-blind comparison of captopril and prazosin. European Heart Journal 1986; 7(10):877-84. *Follow-up less than 6 months*

385. Beatty OL, Ritchie CM, Hadden DR, et al. Is a random urinary albumin concentration a useful screening test in insulin-treated diabetic patients? Irish Journal of Medical Science 1994; 163(9):406-9. *Not RCT or controlled trial*

386. Bech JN, Nielsen CB, Ivarsen P, et al. Dietary sodium affects systemic and renal hemodynamic response to NO inhibition in healthy humans. American Journal of Physiology 1998; 274(5 Pt 2):F914-23. *Not CKD treatment*

387. Bech JN, Nielsen CB, Pedersen EB. Effects of systemic NO synthesis inhibition on RPF, GFR, UNa, and vasoactive hormones in healthy humans. American Journal of Physiology 1996; 270(5 Pt 2):F845-51. *Not CKD treatment*

388. Bech JN, Nielsen EH, Pedersen RS, et al. Enhanced sodium retention after acute nitric oxide blockade in mildly sodium loaded patients with essential hypertension. American Journal of Hypertension 2007; 20(3):287-95. *Sample size less than 50 patients*

389. Beck GJ, Berg RL, Coggins CH, et al. Design and statistical issues of the Modification of Diet in Renal Disease Trial. The Modification of Diet in Renal Disease Study Group. Controlled Clinical Trials 1991; 12(5):566-86. *Not CKD treatment*

390. Beckebaum S, Cicinnati V, Brokalaki E, et al. CNI-sparing regimens within the liver transplant setting: experiences of a single center. Clinical Transplants 2004:215-20. *Not relevant to key questions*

391. Beckebaum S, Cicinnati VR, Klein CG, et al. Impact of combined mycophenolate mofetil and low-dose calcineurin inhibitor therapy on renal function, cardiovascular risk factors, and graft function in liver transplant patients: preliminary results of an open prospective study. Transplantation Proceedings 2004; 36(9):2671-4. *Sample size less than 50 patients*

392. Beckebaum S, Klein CG, Sotiropoulos GC, et al. Combined mycophenolate mofetil and minimal dose calcineurin inhibitor therapy in liver transplant patients: clinical results of a prospective randomized study. Transplantation Proceedings 2009; 41(6):2567-9. *Not CKD treatment*

393. Beck-Nielsen H, Olesen T, Mogensen CE, et al. Effect of near normoglycemia for 5 years on progression of early diabetic retinopathy and renal involvement. Diabetes Research 1990; 15(4):185-90. *Sample size less than 50 patients*

394. Beck-Nielsen H, Richelsen B, Mogensen CE, et al. Effect of insulin pump treatment for one year on renal function and retinal morphology in patients with IDDM. Diabetes Care 1985; 8(6):585-9. *Sample size less than 50 patients*

395. Beeks E, van der Klauw MM, Kroon AA, et al. Alpha-adducin Gly460Trp polymorphism and renal hemodynamics in essential hypertension. Hypertension 2004; 44(4):419-23. *Not CKD treatment*

396. Beermann B, Eriksson LO, Kallner M. A double blind comparison of naproxen and sulindac in female patients with heart failure. Scandinavian Journal of Rheumatology - Supplement 1986; 62:32-5. *Sample size less than 50 patients*

397. Beevers DG, Lip GY. The protective effect of blocking angiotensin in both type I and type II diabetics with nephropathy. Journal of Human Hypertension 2001; 15(12):837-9. *Not RCT or controlled trial*

398. Behets GJ, Verberckmoes SC, D'Haese PC, et al. Lanthanum carbonate: a new phosphate binder. Current Opinion in Nephrology & Hypertension 2004; 13(4):403-9. *Not relevant to key questions*

399. Bektas F, Eken C, Karadeniz O, et al. Intravenous paracetamol or morphine for the treatment of renal colic: a randomized, placebo-controlled trial. Annals of Emergency Medicine 2009; 54(4):568-74. *Not CKD treatment*

400. Bell N, Hawkins V, Holliman D, et al. Trandolapril and human diabetic neuropathy. Lancet 1999; 353(9156):927. *Not RCT or controlled trial*

401. Bellinghieri G, Mazzaglia G, Savica V, et al. Effects of manidipine and nifedipine on blood pressure and renal function in patients with chronic renal failure: a multicenter randomized controlled trial. Renal Failure 2003; 25(5):681-9. *Not CKD treatment*

402. Bellizzi V, Di Iorio BR, De Nicola L, et al. Very low protein diet supplemented with ketoanalogs improves blood pressure control in chronic kidney disease. Kidney International 2007; 71(3):245-51. *Not RCT or controlled trial*

403. Bellizzi V, Scalfi L, Terracciano V, et al. Early changes in bioelectrical estimates of body composition in chronic kidney disease. Journal of the American Society of Nephrology 2006; 17(5):1481-7. *Follow-up less than 6 months*

404. Bello E, Caramelo C, Martell N, et al. Impairment of renal vasodilation with l-arginine is related to more severe disease in untreated hypertensive patients. Hypertension 2001; 38(4):907-12. *Not CKD treatment*

405. Bellomo R, Auriemma S, Fabbri A, et al. The pathophysiology of cardiac surgery-associated acute kidney injury (CSA-AKI). International Journal of Artificial Organs 2008; 31(2):166-78. *Not CKD treatment*

406. Bellomo R, Chapman M, Finfer S, et al. Low-dose dopamine in patients with early renal dysfunction: a placebo-controlled randomised trial. Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group. Lancet 2000; 356(9248):2139-43. *Follow-up less than 6 months*

407. Bellomo R, Ronco C, Kellum JA, et al. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Critical Care 2004; 8(4):R204-12. *Not CKD treatment*

408. Belonje AMS, de Boer RA, Voors AA. Recombinant human Epo treatment: beneficial in chronic kidney disease, chronic heart failure, or both? Editorial to: "Correction of anemia with erythropoietin in chronic kidney disease (stage 3 or 4): effects on cardiac performance by Pappas et al.". Cardiovascular Drugs & Therapy 2008; 22(1):1-2. *Not CKD treatment*

409. Benavente D, Chue CD, Ferro CJ. The importance of renin-angiotensin blockade in patients with cardio-renal disease. Journal of Renal Care 2010 May; 36 Suppl 1:97-105. *Not CKD treatment*

410. Benck U, Clorius JH, Zuna I, et al. Renal hemodynamic changes during smoking: effects of adrenoreceptor blockade. European Journal of Clinical Investigation 1999; 29(12):1010-8. *Not CKD treatment*

411. Benck U, Haeckel S, Clorius JH, et al. Proteinuria-lowering effect of heparin therapy in diabetic nephropathy without affecting the renin-angiotensin-aldosterone system. Clinical Journal of The American Society of Nephrology: CJASN 2007; 2(1):58-67. *Sample size less than 50 patients*

412. Bender A, Samtleben W, Elstner M, et al. Long-term creatine supplementation is safe in aged patients with Parkinson disease. Nutrition Research 2008; 28(3):172-8. *Not CKD treatment*

413. Bender R. The effect of cholesterol-lowering therapy on the progression of diabetic nephropathy is unproved.[Erratum appears in Diabetologia 1996 Aug;39(8):1004]. Diabetologia 1996; 39(3):368-70. *Not RCT or controlled trial*

414. Bending JJ, Dodds RA, Keen H, et al. Renal response to restricted protein intake in diabetic nephropathy. Diabetes 1988; 37(12):1641-6. *Follow-up less than 6 months*

415. Bending JJ, Viberti GC, Watkins PJ, et al. Intermittent clinical proteinuria and renal function in diabetes: evolution and the effect of glycaemic control. British Medical Journal Clinical Research Ed. 1986; 292(6513):83-6. *Sample size less than 50 patients*

416. Benincosa LJ, Sagawa K, Massey LK, et al. Effects of acute caffeine ingestion and menopause on sulfate homeostasis in women. Life Sciences 1995; 57(16):1497-505. *Sample size less than 50 patients*

417. Benndorf RA, Appel D, Maas R, et al. Telmisartan improves endothelial function in patients with essential hypertension. Journal of Cardiovascular Pharmacology 2007; 50(4):367-71. *Not RCT or controlled trial*

418. Bennett WM. Side effects of erythropoietin therapy. American Journal of Kidney Diseases 1991; 18(4 Suppl 1):84-6. *Not relevant to key questions*

419. Bennett WM. A multicenter clinical trial of epoetin beta for anemia of end-stage renal disease. Journal of the American Society of Nephrology 1991; 1(7):990-8. *Not early CKD*

420. Benoehr P, Krueth P, Bokemeyer C, et al. Nephroprotection by theophylline in patients with cisplatin chemotherapy: a randomized, single-blinded, placebo-controlled trial. Journal of the American Society of Nephrology 2005; 16(2):452-8. *Not RCT or controlled trial*

421. Benohr P, Grenz A, Hartmann JT, et al. Cystatin C--a marker for assessment of the glomerular filtration rate in patients with cisplatin chemotherapy. Kidney & Blood Pressure Research 2006; 29(1):32-5. *Not relevant to key questions*

422. Benzoni D, Geoffroy J, Waeber B, et al. Atrial natriuretic peptide and urinary prostaglandins in man. British Journal of Clinical Pharmacology 1989; 28(4):397-402. *Sample size less than 50 patients*

423. Berenson JR. Recommendations for zoledronic acid treatment of patients with bone metastases. Oncologist 2005; 10(1):52-62. *Not RCT or controlled trial*

424. Berg KJ, Forre O, Djoseland O, et al. Renal side effects of high and low cyclosporin A doses in patients with rheumatoid arthritis. Clinical Nephrology 1989; 31(5):232-8. *Not CKD treatment*

425. Berg KJ, Talseth T. Acute renal effects of sulindac and indomethacin in chronic renal failure. Clinical Pharmacology & Therapeutics 1985; 37(4):447-52. *Sample size less than 50 patients*

426. Berger ED, Setzler BA, Werz U, et al. Blood pressure reduction is necessary for the reduction of proteinuria in diabetic nephropathy--comparison of different antihypertensive agents. Nephrology Dialysis Transplantation 1999; 14 Suppl 4:28-9. *Sample size less than 50 patients*

427. Berger PB, Best PJM, Topol EJ, et al. The relation of renal function to ischemic and bleeding outcomes with 2 different glycoprotein IIb/IIIa inhibitors: the do Tirofiban and ReoPro Give Similar Efficacy Outcome (TARGET) trial. American Heart Journal 2005; 149(5):869-75. *Not relevant to key questions*

428. Berghmans T, Klastersky J, Markiewicz E, et al. Cisplatin-carboplatin-gemcitabine or ifosfamide-gemcitabine in advanced non-small cell lung carcinoma: two pilot studies. Anticancer Research 1999; 19(6C):5651-5. *Not early CKD*

429. Bergman A, Odar-Cederlof I, Westman L, et al. Effects of human atrial natriuretic peptide in patients after coronary artery bypass surgery. Journal of Cardiothoracic & Vascular Anesthesia 1996; 10(4):490-6. *Sample size less than 50 patients*

430. Bergman ASF, Odar-Cederlof I, Westman L, et al. Diltiazem infusion for renal protection in cardiac surgical patients with preexisting renal dysfunction. Journal of Cardiothoracic & Vascular Anesthesia 2002; 16(3):294-9. *Follow-up less than 6 months*

431. Bergner R, Diel IJ, Henrich D, et al. Differences in nephrotoxicity of intravenous bisphosphonates for the treatment of malignancy-related bone disease. Onkologie 2006; 29(11):534-40. *Not relevant to key questions*

432. Bergstrom J, Alvestrand A, Bucht H, et al. Progression of chronic renal failure in man is retarded with more frequent clinical follow-ups and better blood pressure control. Clinical Nephrology 1986; 25(1):1-6. *Sample size less than 50 patients*

433. Bergstrom J, Alvestrand A, Bucht H, et al. What is the role of controls in an outpatient department on progression of renal disease? Blood Purification 1988; 6(6):336-42. *Not relevant to key questions*

434. Bergstrom J, Alvestrand A, Bucht H, et al. Stockholm clinical study on progression of chronic renal failure--an interim report. Kidney International - Supplement 1989; 27:S110-4. *Sample size less than 50 patients*

435. Bergstrom J, Alvestrand A, Bucht H, et al. Is chronic renal disease always progressive? Contributions to Nephrology 1989; 75:60-7. *Sample size less than 50 patients*

436. Bergus GR. Pain relief for renal colic. Journal of Family Practice 1996; 43(5):438-40. *Not CKD treatment*

437. Beri A, Sural N, Mahajan SB. Non-atheroprotective effects of statins: a systematic review. American Journal of Cardiovascular Drugs 2009; 9(6):361-70. *Not RCT or controlled trial*

438. Beringer PM, Hidayat L, Heed A, et al. GFR estimates using cystatin C are superior to serum creatinine in adult patients with cystic fibrosis. Journal of Cystic Fibrosis 2009; 8(1):19-25. *Sample size less than 50 patients*

439. Beringer PM, Kriengkauykiat J, Zhang X, et al. Lack of effect of P-glycoprotein inhibition on renal clearance of dicloxacillin in patients with cystic fibrosis. Pharmacotherapy 2008; 28(7):883-94. *Not human studies*

440. Berl T, Hunsicker LG, Lewis JB, et al. Impact of achieved blood pressure on cardiovascular outcomes in the Irbesartan Diabetic Nephropathy Trial. Journal of the American Society of Nephrology 2005; 16(7):2170-9. *Follow-up less than 6 months*

441. Bernard S, Fouque D, Laville M, et al. Effects of low-protein diet supplemented with ketoacids on plasma lipids in adult chronic renal failure. Mineral & Electrolyte Metabolism 1996; 22(1-3):143-6. *Sample size less than 50 patients*

442. Bernardi M, De Palma R, Trevisani F, et al. Effects of a new loop diuretic (muzolimine) in cirrhosis with ascites: comparison with furosemide. Hepatology 1986; 6(3):400-5. *Sample size less than 50 patients*

443. Bernardi M, De Palma R, Trevisani F, et al. Comparative pharmacodynamics of furosemide and muzolimine in cirrhosis. Study on renal sodium and potassium handling and renin-aldosterone axis. Zeitschrift fur Kardiologie 1985; 74 Suppl 2:129-34. *Sample size less than 50 patients*

444. Bernardi M, D'Intino PE, Trevisani F, et al. Effects of prolonged ingestion of graded doses of licorice by healthy volunteers. Life Sciences 1994; 55(11):863-72. *Not CKD treatment*

445. Bernasconi AR, Liste A, Del Pino N, et al. Folic acid 5 or 15 mg/d similarly reduces plasma homocysteine in patients with moderate-advanced chronic renal failure. Nephrology 2006; 11(2):137-41. *Not RCT or controlled trial*

446. Bernhard J, Beaufrere B, Laville M, et al. Adaptive response to a low-protein diet in predialysis chronic renal failure patients. Journal of the American Society of Nephrology 2001; 12(6):1249-54. *Sample size less than 50 patients*

447. Bersten AD, Holt AW. Vasoactive drugs and the importance of renal perfusion pressure. New Horizons 1995; 3(4):650-61. *Not RCT or controlled trial*

448. Berthold H, del Pozo E. Antidiuretic effect of Sandostatin (SMS 201-995) in healthy volunteers. Acta Endocrinologica 1989; 120(6):708-14. *Sample size less than 50 patients*

449. Bertolissi M, Antonucci F, De Monte A, et al. Effects on renal function of a continuous infusion of nifedipine during cardiopulmonary bypass. Journal of Cardiothoracic & Vascular Anesthesia 1996; 10(2):238-42. *Sample size less than 50 patients*

450. Bertolotto M, Quaia E, Gasparini C, et al. Resistive index in patients with renal colic: differences after medical treatment with indomethacin and ketorolac. Radiologia Medica 2003; 106(4):370-5. *Not relevant to key questions*

451. Bertoluci MC, Uebel D, Schmidt A, et al. Urinary TGF-beta1 reduction related to a decrease of systolic blood pressure in patients with type 2 diabetes and clinical diabetic nephropathy. Diabetes Research & Clinical Practice 2006; 72(3):258-64. *Follow-up less than 6 months*

452. Bertram D, Summers R. Serum creatinine levels during cardiac surgery: absence of effect by aminoglycosides. Journal of Clinical Pharmacy & Therapeutics 1993; 18(3):165-70. *Not RCT or controlled trial*

453. Besarab A, Frinak S, Yee J. What is so bad about a hemoglobin level of 12 to 13 g/dL for chronic kidney disease patients anyway? Advances in Chronic Kidney Disease 2009; 16(2):131-42. *Not CKD treatment*

454. Besarab A, Horl WH, Silverberg D. Iron metabolism, iron deficiency, thrombocytosis, and the cardiorenal anemia syndrome. Oncologist 2009; 14 Suppl 1:22-33. *Not CKD treatment*

455. Best PJM, Berger PB, Davis BR, et al. Impact of mild or moderate chronic kidney disease on the frequency of restenosis: results from the PRESTO trial. Journal of the American College of Cardiology 2004; 44(9):1786-91. *Sample size less than 50 patients*

456. Best PJM, Steinhubl SR, Berger PB, et al. The efficacy and safety of short- and long-term dual antiplatelet therapy in patients with mild or moderate chronic kidney disease: results from the Clopidogrel for the Reduction of Events During Observation (CREDO) trial. American Heart Journal 2008; 155(4):687-93. *Not CKD treatment*

457. Best R, Walker BR. Additional value of measurement of urinary cortisone and unconjugated cortisol metabolites in assessing the activity of 11 beta-hydroxysteroid dehydrogenase in vivo. Clinical Endocrinology 1997; 47(2):231-6. *Sample size less than 50 patients*

458. Bestle MH, Olsen NV, Christensen P, et al. Cardiovascular, endocrine, and renal effects of urodilatin in normal humans. American Journal of Physiology 1999; 276(3 Pt 2):R684-95. *Sample size less than 50 patients*

459. Beyer I, Compte N, Busuioc A, et al. Anemia and transfusions in geriatric patients: a time for evaluation. Hematology 2010 Apr; 15(2):116-21. *Not CKD treatment*

460. Beyer KH, Jr., Gelarden RT, Vary JE, et al. Novel multivalent effects of pyrazinoylguanidine in patients with azotemia. Clinical Pharmacology & Therapeutics 1990; 47(5):629-38. *Not CKD treatment*

461. Bhatnagar V, Garcia EP, O'Connor DT, et al. CYP3A4 and CYP3A5 polymorphisms and blood pressure response to amlodipine among African-American men and women with early hypertensive renal disease. American Journal of Nephrology 2010; 31(2):95-103. *Not relevant to key questions*

462. Bhatnagar V, O'Connor DT, Brophy VH, et al. G-protein-coupled receptor kinase 4 polymorphisms and blood pressure response to metoprolol among African Americans: sex-specificity and interactions. American Journal of Hypertension 2009; 22(3):332-8. *Not CKD treatment*

463. Bhatnagar V, O'Connor DT, Schork NJ, et al. Angiotensin-converting enzyme gene polymorphism predicts the time-course of blood pressure response to angiotensin converting enzyme inhibition in the AASK trial. Journal of Hypertension 2007; 25(10):2082-92. *Not early CKD*

464. Bhatnagar V, O'Connor DT, Schork NJ, et al. Angiotensin-converting enzyme gene polymorphism predicts the time-course of blood pressure response to angiotensin converting enzyme inhibition in the AASK trial. Journal of Hypertension 2007; 25(10):2082-92. *Follow-up less than 6 months*

465. Bhattacharya N. Placental umbilical cord blood transfusion: a new method of treatment of patients with diabetes and microalbuminuria in the background of anemia. Clinical & Experimental Obstetrics & Gynecology 2006; 33(3):164-8. *Not RCT or controlled trial*

466. Bianchi S, Bigazzi R, Baldari G, et al. Long-term effects of enalapril and nicardipine on urinary albumin excretion in patients with chronic renal insufficiency: a 1-year follow-up. American Journal of Nephrology 1991; 11(2):131-7. *Sample size less than 50 patients*

467. Bianchi S, Bigazzi R, Baldari G, et al. Microalbuminuria in patients with essential hypertension. Effects of an angiotensin converting enzyme inhibitor and of a calcium channel blocker. American Journal of Hypertension 1991; 4(4 Pt 1):291-6. *Sample size less than 50 patients*

468. Bianchi S, Bigazzi R, Baldari G, et al. Microalbuminuria in patients with essential hypertension: effects of several antihypertensive drugs. American Journal of Medicine 1992; 93(5):525-8. *Follow-up less than 6 months*

469. Bianchi S, Bigazzi R, Caiazza A, et al. A controlled, prospective study of the effects of atorvastatin on proteinuria and progression of kidney disease.[Erratum appears in Am J Kidney Dis. 2004 Jan;43(1):193]. American Journal of Kidney Diseases 2003; 41(3):565-70. *Not relevant to key questions*

470. Bianchi S, Bigazzi R, Campese VM. Antagonists of aldosterone and proteinuria in patients with CKD: an uncontrolled pilot study. American Journal of Kidney Diseases 2005; 46(1):45-51. *Follow-up less than 6 months*

471. Bianchi S, Bigazzi R, Campese VM. Long-term effects of spironolactone on proteinuria and kidney function in patients with chronic kidney disease. Kidney International 2006; 70(12):2116-23. *Not relevant to key questions*

472. Biancofiore G, Della Rocca G, Bindi L, et al. Use of fenoldopam to control renal dysfunction early after liver transplantation. Liver Transplantation 2004; 10(8):986-92. *Sample size less than 50 patients*

473. Bibbins-Domingo K, Lin F, Vittinghoff E, et al. Renal insufficiency as an independent predictor of mortality among women with heart failure. Journal of the American College of Cardiology 2004; 44(8):1593-600. *Not RCT or controlled trial*

474. Bichet DG, Kortas C, Mettauer B, et al. Modulation of plasma and platelet vasopressin by cardiac function in patients with heart failure. Kidney International 1986; 29(6):1188-96. *Sample size less than 50 patients*

475. Bichu P, Nistala R, Khan A, et al. Angiotensin receptor blockers for the reduction of proteinuria in diabetic patients with overt nephropathy: results from the AMADEO study. Vascular Health & Risk Management 2009; 5(1):129-40. *Not CKD treatment*

476. Bidiville J, Waeber G, Porchet M, et al. Hemodynamic, renal, and endocrine effects of 4-h infusions of human atrial natriuretic peptide in normal volunteers. Fundamental & Clinical Pharmacology 1988; 2(5):413-29. *Sample size less than 50 patients*

477. Bierkens AF, Maes RM, Hendrikx JM, et al. The use of local anesthesia in second generation extracorporeal shock wave lithotripsy: eutectic mixture of local anesthetics. Journal of Urology 1991; 146(2):287-9. *Not CKD treatment*

478. Bigazzi R, Bianchi S, Baldari D, et al. Long-term effects of a converting enzyme inhibitor and a calcium channel blocker on urinary albumin excretion in patients with essential hypertension. American Journal of Hypertension 1993; 6(2):108-13. *Sample size less than 50 patients*

479. Biggi A, Musiari L, Iori M, et al. Contribution of bradykinin B2 receptors to the inhibition by valsartan of systemic and renal effects of exogenous angiotensin II in salt-repleted humans. Journal of Pharmacology & Experimental Therapeutics 2010 Sep 1; 334(3):911-6. *Not CKD treatment*

480. Billstrom A, Hietala SO, Lithner F, et al. Nephrotoxicity of contrast media in patients with diabetes mellitus. A comparative urographic and angiographic study with iohexol and metrizoate. Acta Radiologica 1989; 30(5):509-15. *Not CKD treatment*

481. Bilo H, Kluitman E, van Ballegooie E, et al. Long term use of captopril or nifedipine in normotensive microalbuminuric patients with insulin-dependent diabetes mellitus. Diabetes Research 1993; 23(3):115-22. *Sample size less than 50 patients*

482. Bilous R. Microvascular disease: what does the UKPDS tell us about diabetic nephropathy? Diabetic Medicine 2008; 25 Suppl 2:25-9. *Not CKD treatment*

483. Bilous R, Chaturvedi N, Sjolie AK, et al. Effect of candesartan on microalbuminuria and albumin excretion rate in diabetes: three randomized trials. Annals of Internal Medicine 2009; 151(1):11-20. *Not RCT or controlled trial*

484. Binet I, Wallnofer A, Weber C, et al. Renal hemodynamics and pharmacokinetics of bosentan with and without cyclosporine A. Kidney International 2000; 57(1):224-31. *Not CKD treatment*

485. Biollaz J, Bidiville J, Diezi J, et al. Site of the action of a synthetic atrial natriuretic peptide evaluated in humans. Kidney International 1987; 32(4):537-46. *Sample size less than 50 patients*

486. Biollaz J, Nussberger J, Porchet M, et al. Four-hour infusions of synthetic atrial natriuretic peptide in normal volunteers. Hypertension 1986; 8(6 Pt 2):II96-105. *Sample size less than 50 patients*

487. Biondi-Zoccai GGL, Lotrionte M, Abbate A, et al. Compliance with QUOROM and quality of reporting of overlapping meta-analyses on the role of acetylcysteine in the prevention of contrast associated nephropathy: case study. BMJ 2006; 332(7535):202-9. *Sample size less than 50 patients*

488. Bito H, Ikeda K. Renal and hepatic function in surgical patients after low-flow sevoflurane or isoflurane anesthesia. Anesthesia & Analgesia 1996; 82(1):173-6. *Not CKD treatment*

489. Bito H, Ikeuchi Y, Ikeda K. Effects of low-flow sevoflurane anesthesia on renal function: comparison with high-flow sevoflurane anesthesia and low-flow isoflurane anesthesia. Anesthesiology 1997; 86(6):1231-7. *Not CKD treatment*

490. Bjorck S, Aurell M. Angiotensin-converting enzyme inhibitors in diabetes: effect on the kidney and on blood pressure. Journal of the American Society of Nephrology 1990; 1(5 Suppl 2):S59-63. *Not CKD treatment*

491. Bjorck S, Mulec H, Johnsen SA, et al. Renal protective effect of enalapril in diabetic nephropathy. BMJ 1992; 304(6823):339-43. *Sample size less than 50 patients*

492. Bjorck S, Mulec H, Johnsen SA, et al. Contrasting effects of enalapril and metoprolol on proteinuria in diabetic nephropathy.[Erratum appears in BMJ 1990 May 5;300(6733):1170]. BMJ 1990; 300(6729):904-7. *Follow-up less than 6 months*

493. Black C, Sharma P, Scotland G, et al. Early referral strategies for management of people with markers of renal disease: a systematic review of the evidence of clinical effectiveness, cost-effectiveness and economic analysis. Health Technology Assessment 2010 Apr; 14(21):1-184. *Not relevant to key questions*

494. Blake GM, Moore AEB, Park-Holohan SJ, et al. A direct in vivo measurement of 99mTc-methylene diphosphonate protein binding. Nuclear Medicine Communications 2003; 24(7):829-35. *Not CKD treatment*

495. Blanchard J, Sawers SJ, Jonkman JH, et al. Comparison of the urinary metabolite profile of caffeine in young and elderly males. British Journal of Clinical Pharmacology 1985; 19(2):225-32. *Sample size less than 50 patients*

496. Blaser J, Simmen HP, Thurnheer U, et al. Nephrotoxicity, high frequency ototoxicity, efficacy and serum kinetics of once versus thrice daily dosing of netilmicin in patients with serious infections. Journal of Antimicrobial Chemotherapy 1995; 36(5):803-14. *Not CKD treatment*

497. Blau A, Herzog D, Shechter P, et al. Calcium channel blocker nisoldipine in chronic renal failure. Renal Failure 1990; 12(2):113-9. *Not early CKD*

498. Ble A, Fink JC, Woodman RC, et al. Renal function, erythropoietin, and anemia of older persons: the InCHIANTI study. Archives of Internal Medicine 2005; 165(19):2222-7. *Not relevant to key questions*

499. Bleie O, Semb AG, Grundt H, et al. Homocysteine-lowering therapy does not affect inflammatory markers of atherosclerosis in patients with stable coronary artery disease. Journal of Internal Medicine 2007; 262(2):244-53. *Not CKD treatment*

500. Bliss DZ, Stein TP, Schleifer CR, et al. Supplementation with gum arabic fiber increases fecal nitrogen excretion and lowers serum urea nitrogen concentration in chronic renal failure patients consuming a low-protein diet. American Journal of Clinical Nutrition 1996; 63(3):392-8. *Sample size less than 50 patients*

501. Block GA, Persky MS, Ketteler M, et al. A randomized double-blind pilot study of serum phosphorus normalization in chronic kidney disease: a new paradigm for clinical outcomes studies in nephrology. Hemodialysis International 2009; 13(3):360-2. *Not RCT or controlled trial*

502. Boccalandro F, Amhad M, Smalling RW, et al. Oral acetylcysteine does not protect renal function from moderate to high doses of intravenous radiographic contrast. Catheterization & Cardiovascular Interventions 2003; 58(3):336-41. *Not CKD treatment*

503. Bochud M, Staessen JA, Maillard M, et al. Ethnic differences in proximal and distal tubular sodium reabsorption are heritable in black and white populations. Journal of Hypertension 2009; 27(3):606-12. *Not early CKD*

504. Bocksch W, Fateh-Moghadam S, Mueller E, et al. Percutaneous coronary intervention in patients with end-stage renal disease. Kidney & Blood Pressure Research 2005; 28(5-6):275-9. *Not relevant to key questions*

505. Boddy AV, Griffin MJ, Sludden J, et al. Pharmacological study of paclitaxel duration of infusion combined with GFR-based carboplatin in the treatment of ovarian cancer. Cancer Chemotherapy & Pharmacology 2001; 48(1):15-21. *Not early CKD*

506. Bodei L, Cremonesi M, Zoboli S, et al. Receptor-mediated radionuclide therapy with 90Y-DOTATOC in association with amino acid infusion: a phase I study. European Journal of Nuclear Medicine & Molecular Imaging 2003; 30(2):207-16. *Not CKD treatment*

507. Bodmer CW, Lake D, Savage MW, et al. Hand vein responses to noradrenaline in normotensive patients with insulin-dependent diabetes mellitus and microalbuminuria: effects of alpha-adrenoceptor blockade with doxazosin. Current Medical Research & Opinion 1999; 15(3):169-76. *Sample size less than 50 patients*

508. Bodnar L, Wcislo G, Gasowska-Bodnar A, et al. Renal protection with magnesium subcarbonate and magnesium sulphate in patients with epithelial ovarian cancer after cisplatin and paclitaxel chemotherapy: a randomised phase II study. European Journal of Cancer 2008; 44(17):2608-14. *Not CKD treatment*

509. Body J-J, Diel I, Bell R. Profiling the safety and tolerability of bisphosphonates. Seminars in Oncology 2004; 31(5 Suppl 10):73-8. *Follow-up less than 6 months*

510. Boelaert J, Lijnen P, Robbens E, et al. Impairment of renal function due to sulphinpyrazone after coronary artery bypass surgery: a prospective double-blind study. Journal of Cardiovascular Pharmacology 1986; 8(2):386-91. *Not CKD treatment*

511. Boero R, Prodi E, Elia F, et al. How well are hypertension and albuminuria treated in type II diabetic patients? Journal of Human Hypertension 2003; 17(6):413-8. *Not relevant to key questions*

512. Boero R, Rollino C, Massara C, et al. The verapamil versus amlodipine in nondiabetic nephropathies treated with trandolapril (VVANNTT) study. American Journal of Kidney Diseases 2003; 42(1):67-75. *Not relevant to key questions*

513. Boero R, Rollino C, Massara C, et al. Verapamil versus amlodipine in proteinuric non-diabetic nephropathies treated with trandolapril (VVANNTT study): design of a prospective randomized multicenter trial. Journal of Nephrology 2001; 14(1):15-8. *Not CKD treatment*

514. Boerrigter G, Costello-Boerrigter LC, Abraham WT, et al. Cardiac resynchronization therapy improves renal function in human heart failure with reduced glomerular filtration rate. Journal of Cardiac Failure 2008; 14(7):539-46. *Not CKD treatment*

515. Boers M, Bensen WG, Ludwin D, et al. Cyclosporine nephrotoxicity in rheumatoid arthritis: no effect of short term misoprostol treatment. Journal of Rheumatology 1992; 19(4):534-7. *Not CKD treatment*

516. Boers M, Dijkmans BA, Breedveld FC, et al. No effect of misoprostol on renal function of rheumatoid patients treated with diclofenac. British Journal of Rheumatology 1991; 30(1):56-9. *Sample size less than 50 patients*

517. Boers M, Dijkmans BA, van Rijthoven AW, et al. Reversible nephrotoxicity of cyclosporine in rheumatoid arthritis. Journal of Rheumatology 1990; 17(1):38-42. *Not CKD treatment*

518. Boesgaard S, Aldershvile J, Poulsen HE, et al. N-acetylcysteine inhibits angiotensin converting enzyme in vivo. Journal of Pharmacology & Experimental Therapeutics 1993; 265(3):1239-44. *Not human studies*

519. Boesken WH, Kult J. High-dose torasemide, given once daily intravenously for one week, in patients with advanced chronic renal failure. Clinical Nephrology 1997; 48(1):22-8. *Sample size less than 50 patients*

520. Boey O, Van Hooland S, Woestenburg A, et al. Methotrexate should not be used for patients with end-stage kidney disease. Acta Clinica Belgica 2006; 61(4):166-9. *Not CKD treatment*

521. Boger RH, Schwedhelm E, Maas R, et al. ADMA and oxidative stress may relate to the progression of renal disease: rationale and design of the VIVALDI study. Vascular Medicine 2005; 10 Suppl 1:S97-102. *Not RCT or controlled trial*

522. Bog-Hansen E, Lindblad U, Ranstam J, et al. Impaired glucose metabolism and obesity in Swedish patients with borderline isolated systolic hypertension: Skaraborg Hypertension and Diabetes Project. Diabetes, Obesity & Metabolism 2001; 3(1):25-31. *Not RCT or controlled trial*

523. Bohe J, Ding H, Qing DP, et al. IGF-I binding proteins, IGF-I binding protein mRNA and IGF-I receptor mRNA in rats with acute renal failure given IGF-I. Kidney International 1998; 54(4):1070-82. *Not human studies*

524. Bohler J, Woitas R, Keller E, et al. Effect of nifedipine and captopril on glomerular hyperfiltration in normotensive man. American Journal of Kidney Diseases 1992; 20(2):132-9. *Sample size less than 50 patients*

525. Bokemeyer C, Fels LM, Dunn T, et al. Silibinin protects against cisplatin-induced nephrotoxicity without compromising cisplatin or ifosfamide anti-tumour activity. British Journal of Cancer 1996; 74(12):2036-41. *Not CKD treatment*

526. Boldt J, Brenner T, Lehmann A, et al. Influence of two different volume replacement regimens on renal function in elderly patients undergoing cardiac surgery: comparison of a new starch preparation with gelatin. Intensive Care Medicine 2003; 29(5):763-9. *Sample size less than 50 patients*

527. Boldt J, Brosch C, Rohm K, et al. Is albumin administration in hypoalbuminemic elderly cardiac surgery patients of benefit with regard to inflammation, endothelial activation, and long-term kidney function? Anesthesia & Analgesia 2008; 107(5):1496-503. *Not RCT or controlled trial*

528. Boldt J, Mayer J, Brosch C, et al. Volume replacement with a balanced hydroxyethyl starch (HES) preparation in cardiac surgery patients. Journal of Cardiothoracic & Vascular Anesthesia 2010 Jun; 24(3):399-407. *Not CKD treatment*

529. Boldt J, Muller M, Heesen M, et al. The effects of pentoxifylline on circulating adhesion molecules in critically ill patients with acute renal failure treated by continuous veno-venous hemofiltration. Intensive Care Medicine 1996; 22(4):305-11. *Not CKD treatment*

530. Boldt J, Suttner S, Brosch C, et al. Cardiopulmonary bypass priming using a high dose of a balanced hydroxyethyl starch versus an albumin-based priming strategy. Anesthesia & Analgesia 2009; 109(6):1752-62. *Not CKD treatment*

531. Boldt J, Suttner S, Brosch C, et al. The influence of a balanced volume replacement concept on inflammation, endothelial activation, and kidney integrity in elderly cardiac surgery patients. Intensive Care Medicine 2009; 35(3):462-70. *Not CKD treatment*

532. Bolognese L, Falsini G, Grotti S, et al. The contrast media and nephrotoxicity following coronary revascularization by primary angioplasty for acute myocardial infarction study: design and rationale of the CONTRAST-AMI study. Journal of Cardiovascular Medicine 2010 Mar; 11(3):199-206. *Not CKD treatment*

533. Bolognesi M, Sacerdoti D, Merkel C, et al. Effects of chronic therapy with nadolol on portal hemodynamics and on splanchnic impedance indices using Doppler sonography: comparison between acute and chronic effects. Journal of Hepatology 1997; 26(2):305-11. *Sample size less than 50 patients*

534. Bolton WK, Cattran DC, Williams ME, et al. Randomized trial of an inhibitor of formation of advanced glycation end products in diabetic nephropathy. American Journal of Nephrology 2004; 24(1):32-40. *Not CKD treatment*

535. Bomback AS, Kshirsagar AV, Amamoo MA, et al. Change in proteinuria after adding aldosterone blockers to ACE inhibitors or angiotensin receptor blockers in CKD: a systematic review. American Journal of Kidney Diseases 2008; 51(2):199-211. *Not CKD treatment*

536. Bommer J, Jaber BL. Ultrapure dialysate: facts and myths. Seminars in Dialysis 2006; 19(2):115-9. *Not early CKD*

537. Bond GG, Reeve GR, Ott MG, et al. Mortality among a sample of chemical company employees. American Journal of Industrial Medicine 1985; 7(2):109-21. *Not early CKD*

538. Boner G, Cooper ME, McCarroll K, et al. Adverse effects of left ventricular hypertrophy in the reduction of endpoints in NIDDM with the angiotensin II antagonist losartan (RENAAL) study. Diabetologia 2005; 48(10):1980-7. *Not RCT or controlled trial*

539. Bonne JF, Fournier A, Massy Z, et al. Overview of randomised trials of ACE inhibitors. Lancet 2006; 368(9542):1152-3. *Follow-up less than 6 months*

540. Bonner G, Lederle RM, Scholze J, et al. Therapeutic safety of perindopril in the treatment of mild hypertension with concomitant nephropathy. Arzneimittel-Forschung 1993; 43(8):852-5. *Follow-up less than 6 months*

541. Bonney SL, Northington RS, Hedrich DA, et al. Renal safety of two analgesics used over the counter: ibuprofen and aspirin. Clinical Pharmacology & Therapeutics 1986; 40(4):373-7. *Not CKD treatment*

542. Boogaard PJ, Houtsma AT, Journee HL, et al. Effects of exposure to elemental mercury on the nervous system and the kidneys of workers producing natural gas. Archives of Environmental Health 1996; 51(2):108-15. *Not CKD treatment*

543. Boonen S, Sellmeyer DE, Lippuner K, et al. Renal safety of annual zoledronic acid infusions in osteoporotic postmenopausal women. Kidney International 2008; 74(5):641-8. *Not CKD treatment*

544. Boor P, Casper S, Celec P, et al. Renal, vascular and cardiac fibrosis in rats exposed to passive smoking and industrial dust fibre amosite. Journal of Cellular & Molecular Medicine 2009 Nov-Dec; 13(11-12):4484-91. *Not human studies*

545. Borcea V, Morcos M, Isermann B, et al. Influence of ramipril on the course of plasma thrombomodulin in patients with diabetes mellitus. Vasa 1999; 28(3):172-80. *Not RCT or controlled trial*

546. Borzecki AM, Wong AT, Hickey EC, et al. Hypertension control: how well are we doing? Archives of Internal Medicine 2003; 163(22):2705-11. *Not CKD treatment*

547. Boscheri A, Weinbrenner C, Botzek B, et al. Failure of ascorbic acid to prevent contrast-media induced nephropathy in patients with renal dysfunction. Clinical Nephrology 2007; 68(5):279-86. *Sample size less than 50 patients*

548. Bostom AG, Culleton BF. Hyperhomocysteinemia in chronic renal disease. Journal of the American Society of Nephrology 1999; 10(4):891-900. *Not RCT or controlled trial*

549. Botker HE, Jensen HK, Krusell LR, et al. Renal effects of xamoterol in patients with moderate heart failure. Cardiovascular Drugs & Therapy 1993; 7(1):111-6. *Sample size less than 50 patients*

550. Bouhanick B. Equivalent effects of nicardipine and captopril on urinary albumin excretion of type 2, non-insulin-dependent diabetic subjects with mild to moderate hypertension. Therapie 1996; 51(1):41-7. *Follow-up less than 6 months*

551. Boulware LE, Troll MU, Jaar BG, et al. Identification and referral of patients with progressive CKD: a national study. American Journal of Kidney Diseases 2006; 48(2):192-204. *Not relevant to key questions*

552. Bouzas-Mosquera A, Vazquez-Rodriguez JM, Peteiro J. Sodium bicarbonate vs sodium chloride in preventing contrast medium-induced nephropathy. JAMA 2009; 301(4):378-9; author reply 9-80. *Not CKD treatment*

553. Bouzidi N, Mekki K, Boukaddoum A, et al. Effects of omega-3 polyunsaturated fatty-acid supplementation on redox status in chronic renal failure patients with dyslipidemia. Journal of Renal Nutrition 2010 Sep; 20(5):321-8. *Follow-up less than 6 months*

554. Bove T, Landoni G, Calabro MG, et al. Renoprotective action of fenoldopam in high-risk patients undergoing cardiac surgery: a prospective, double-blind, randomized clinical trial. Circulation 2005; 111(24):3230-5. *Not CKD treatment*

555. Bowden RG, Wilson RL, Deike E, et al. Fish oil supplementation lowers C-reactive protein levels independent of triglyceride reduction in patients with end-stage renal disease. Nutrition in Clinical Practice 2009; 24(4):508-12. *Sample size less than 50 patients*

556. Bowling CB, Pitt B, Ahmed MI, et al. Hypokalemia and outcomes in patients with chronic heart failure and chronic kidney disease: findings from propensity-matched studies. Circulation: Heart Failure 2010 Mar; 3(2):253-60. *Not CKD treatment*

557. Boyden TF, Gurm HS. Does gadolinium-based angiography protect against contrast-induced nephropathy?: a systematic review of the literature. Catheterization & Cardiovascular Interventions 2008; 71(5):687-93. *Not CKD treatment*

558. Boyle JA. Controlled trials of amphotericin B lipid complex. Clinical Infectious Diseases 2000; 31(4):1117-8. *Not relevant to key questions*

559. Braden GL, von Oeyen PT, Germain MJ, et al. Ritodrine- and terbutaline-induced hypokalemia in preterm labor: mechanisms and consequences. Kidney International 1997; 51(6):1867-75. *Sample size less than 50 patients*

560. Bradley RT, Ebbs P, Young WY, et al. Specialty practice in dietetics: empirical models and results.[Erratum appears in J Am Diet Assoc 1993 Mar;93(3):271].[Erratum appears in J Am Diet Assoc 1993 Apr;93(4):402]. Journal of the American Dietetic Association 1993; 93(2):203-10. *Not RCT or controlled trial*

561. Brady CB, Gaziano JM, Cxypoliski RA, et al. Homocysteine lowering and cognition in CKD: the Veterans Affairs homocysteine study. American Journal of Kidney Diseases 2009; 54(3):440-9. *Not early CKD*

562. Braith RW, Mills RM, Wilcox CS, et al. High-dose angiotensin-converting enzyme inhibition restores body fluid homeostasis in heart-transplant recipients. Journal of the American College of Cardiology 2003; 41(3):426-32. *Sample size less than 50 patients*

563. Bramlage P, Durand-Zaleski I, Desai N, et al. The value of irbesartan in the management of hypertension. Expert Opinion on Pharmacotherapy 2009; 10(11):1817-31. *Not RCT or controlled trial*

564. Brancati FL, Cusumano AM. Epidemiology and prevention of diabetic nephropathy. Current Opinion in Nephrology & Hypertension 1995; 4(3):223-9. *Not relevant to key questions*

565. Branch RA. Prevention of amphotericin B-induced renal impairment. A review on the use of sodium supplementation. Archives of Internal Medicine 1988; 148(11):2389-94. *Not CKD treatment*

566. Brandao-Neto J, Silva CA, Shuhama T, et al. Renal handling of zinc in insulin-dependent diabetes mellitus patients. BioMetals 2001; 14(1):75-80. *Not CKD treatment*

567. Brandli DW, Sarkissian E, Ng SC, et al. Individual variability in concentrations of urinary sulindac sulfide. Clinical Pharmacology & Therapeutics 1991; 50(6):650-5. *Not CKD treatment*

568. Brandstrom E, Grzegorczyk A, Jacobsson L, et al. GFR measurement with iohexol and 51Cr-EDTA. A comparison of the two favoured GFR markers in Europe. Nephrology Dialysis Transplantation 1998; 13(5):1176-82. *Sample size less than 50 patients*

569. Brandt JR, Avner ED, Hickman RO, et al. Safety and efficacy of erythropoietin in children with chronic renal failure. Pediatric Nephrology 1999; 13(2):143-7. *Sample size less than 50 patients*

570. Brar SS, Hiremath S, Dangas G, et al. Sodium bicarbonate for the prevention of contrast induced-acute kidney injury: a systematic review and meta-analysis. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(10):1584-92. *Not RCT or controlled trial*

571. Brar SS, Shen AY-J, Jorgensen MB, et al. Sodium bicarbonate vs sodium chloride for the prevention of contrast medium-induced nephropathy in patients undergoing coronary angiography: a randomized trial. JAMA 2008; 300(9):1038-46. *Not CKD treatment*

572. Brater DC, Anderson S, Baird B, et al. Effects of ibuprofen, naproxen, and sulindac on prostaglandins in men. Kidney International 1985; 27(1):66-73. *Sample size less than 50 patients*

573. Brater DC, Leinfelder J, Anderson SA. Clinical pharmacology of torasemide, a new loop diuretic. Clinical Pharmacology & Therapeutics 1987; 42(2):187-92. *Sample size less than 50 patients*

574. Brater DC, Rudy DR, Voelker JR, et al. Pharmacokinetics and pharmacodynamics of torasemide in patients with chronic renal insufficiency--preliminary evaluation. Cardiovascular Drugs & Therapy 1993; 7 Suppl 1:69-73. *Sample size less than 50 patients*

575. Braunstein JB, Anderson GF, Gerstenblith G, et al. Noncardiac comorbidity increases preventable hospitalizations and mortality among Medicare beneficiaries with chronic heart failure. Journal of the American College of Cardiology 2003; 42(7):1226-33. *Not CKD treatment*

576. Brenner BM. Remission of renal disease: recounting the challenge, acquiring the goal. Journal of Clinical Investigation 2002; 110(12):1753-8. *Not RCT or controlled trial*

577. Brenner BM, Cooper ME, de Zeeuw D, et al. The losartan renal protection study--rationale, study design and baseline characteristics of RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan). Journal of the Renin-Angiotensin-Aldosterone System 2000; 1(4):328-35. *Not RCT or controlled trial*

578. Brenner P, Meyer M, Reichenspurner H, et al. Significance of prophylactic urodilatin (INN: ularitide) infusion for the prevention of acute renal failure in patients after heart transplantation. European Journal of Medical Research 1995; 1(3):137-43. *Sample size less than 50 patients*

579. Brenner RM, Chertow GM. The rise and fall of atrial natriuretic peptide for acute renal failure. Current Opinion in Nephrology & Hypertension 1997; 6(5):474-6. *Not RCT or controlled trial*

580. Bretzel RG. Prevention and slowing down the progression of the diabetic nephropathy through antihypertensive therapy. Journal of Diabetes & its Complications 1997; 11(2):112-22. *Not RCT or controlled trial*

581. Breyer JA, Hunsicker LG, Bain RP, et al. Angiotensin converting enzyme inhibition in diabetic nephropathy. The Collaborative Study Group. Kidney International - Supplement 1994; 45:S156-60. *Not CKD treatment*

582. Brichard S, Ketelslegers JM, Lambert AE. Renal function, glycemic control and perindopril in diabetic patients. Clinical & Experimental Hypertension - Part A, Theory & Practice 1989; 11 Suppl 2:545-54. *Sample size less than 50 patients*

583. Brichard S, Ketelslegers JM, Lambert AE. Renal function, glycaemic control and perindopril in diabetic patients. Archives des Maladies du Coeur et des Vaisseaux 1989; 82 Spec No 1:57-61. *Sample size less than 50 patients*

584. Brichard SM, Santoni JP, Thomas JR, et al. Long term reduction of microalbuminuria after 1 year of angiotensin converting enzyme inhibition by perindopril in hypertensive insulin-treated diabetic patients. Diabete et Metabolisme 1990; 16(1):30-6. *Sample size less than 50 patients*

585. Brienza N, Giglio MT, Marucci M, et al. Does perioperative hemodynamic optimization protect renal function in surgical patients? A meta-analytic study. Critical Care Medicine 2009; 37(6):2079-90. *Not CKD treatment*

586. Brienza N, Malcangi V, Dalfino L, et al. A comparison between fenoldopam and low-dose dopamine in early renal dysfunction of critically ill patients. Critical Care Medicine 2006; 34(3):707-14. *Sample size less than 50 patients*

587. Briganti EM, Branley P, Chadban SJ, et al. Smoking is associated with renal impairment and proteinuria in the normal population: the AusDiab kidney study. Australian Diabetes, Obesity and Lifestyle Study. American Journal of Kidney Diseases 2002; 40(4):704-12. *Not CKD treatment*

588. Briggs DE, French JA. Levetiracetam safety profiles and tolerability in epilepsy patients. Expert Opinion on Drug Safety 2004; 3(5):415-24. *Not CKD treatment*

589. Briguori C, Airoldi F, D'Andrea D, et al. Renal Insufficiency Following Contrast Media Administration Trial (REMEDIAL): a randomized comparison of 3 preventive strategies. Circulation 2007; 115(10):1211-7. *Not CKD treatment*

590. Briguori C, Colombo A, Airoldi F, et al. N-Acetylcysteine versus fenoldopam mesylate to prevent contrast agent-associated nephrotoxicity. Journal of the American College of Cardiology 2004; 44(4):762-5. *Not CKD treatment*

591. Briguori C, Colombo A, Violante A, et al. Standard vs double dose of N-acetylcysteine to prevent contrast agent associated nephrotoxicity. European Heart Journal 2004; 25(3):206-11. *Not CKD treatment*

592. Briguori C, Manganelli F, Scarpato P, et al. Acetylcysteine and contrast agent-associated nephrotoxicity. Journal of the American College of Cardiology 2002; 40(2):298-303. *Not early CKD*

593. Briguori C, Marenzi G. Contrast-induced nephropathy: pharmacological prophylaxis. Kidney International - Supplement 2006; (100):S30-8. *Not relevant to key questions*

594. Brinkmann A, Seeling W, Wolf CF, et al. Ibuprofen does not impair renal function in patients undergoing infrarenal aortic surgery with epidural anaesthesia. Intensive Care Medicine 1998; 24(4):322-8. *Sample size less than 50 patients*

595. Brinkworth GD, Buckley JD, Noakes M, et al. Renal function following long-term weight loss in individuals with abdominal obesity on a very-low-carbohydrate diet vs high-carbohydrate diet. Journal of the American Dietetic Association 2010 Apr; 110(4):633-8. *Not CKD treatment*

596. Brocco E, Velussi M, Cernigoi AM, et al. Evidence of a threshold value of glycated hemoglobin to improve the course of renal function in type 2 diabetes with typical diabetic glomerulopathy. Journal of Nephrology 2001; 14(6):461-71. *Not RCT or controlled trial*

597. Brockenbrough AT, Dittrich MO, Page ST, et al. Transdermal androgen therapy to augment EPO in the treatment of anemia of chronic renal disease. American Journal of Kidney Diseases 2006; 47(2):251-62. *Not relevant to key questions*

598. Bromage PR, el-Faqih S, Husain I, et al. Epinephrine and fentanyl as adjuvants to 0.5% bupivacaine for epidural analgesia. Regional Anesthesia 1989; 14(4):189-94. *Not CKD treatment*

599. Bronas UG. Exercise training and reduction of cardiovascular disease risk factors in patients with chronic kidney disease. Advances in Chronic Kidney Disease 2009; 16(6):449-58. *Not RCT or controlled trial*

600. Brooks D, Charleston J, Dowie D, et al. Predictors of participant adherence and retention in the African American Study of Kidney Disease and Hypertension. Nephrology Nursing Journal: Journal of the American Nephrology Nurses' Association 2008; 35(2):133-42. *Not RCT or controlled trial*

601. Brow TD, Kakkar VV, Das SK. The significance of creatine kinase in cardiac patients with acute limb ischaemia. Journal of Cardiovascular Surgery 1999; 40(5):637-44. *Not CKD treatment*

602. Brown J. Effects of interrupting the renin-angiotensin system on sodium excretion in man. Journal of Physiology 1988; 395:17-40. *Sample size less than 50 patients*

603. Brown J, O'Flynn MA. Acute effects of physiological increments of alpha-atrial natriuretic peptide in man. Kidney International 1989; 36(4):645-52. *Sample size less than 50 patients*

604. Brown LC, Brown EA, Greenhalgh RM, et al. Renal function and abdominal aortic aneurysm (AAA): the impact of different management strategies on long-term renal function in the UK EndoVascular Aneurysm Repair (EVAR) Trials. Annals of Surgery 2010 May; 251(5):966-75. *Not CKD treatment*

605. Brown WV. Safety of statins. Current Opinion in Lipidology 2008; 19(6):558-62. *Not relevant to key questions*

606. Bruce R, Daniels A, Cundy T. Renal function changes in diabetic nephropathy induced by bezafibrate. Nephron 1996; 73(3):490. *Sample size less than 50 patients*

607. Bruce R, Rutland M, Cundy T. Glomerular hyperfiltration in young Polynesians with type 2 diabetes. Diabetes Research & Clinical Practice 1994; 25(3):155-60. *Sample size less than 50 patients*

608. Brugts JJ, Boersma E, Chonchol M, et al. The cardioprotective effects of the angiotensin-converting enzyme inhibitor perindopril in patients with stable coronary artery disease are not modified by mild to moderate renal insufficiency: insights from the EUROPA trial. Journal of the American College of Cardiology 2007; 50(22):2148-55. *Not RCT or controlled trial*

609. Brunton C, Varghese Z, Moorhead JF. Lipopheresis in the nephrotic syndrome. Kidney International - Supplement 1999; 71:S6-9. *Sample size less than 50 patients*

610. Bruun NE, Dige-Pedersen H, Skott P. Normal responses of atrial natriuretic factor and renal tubular function to sodium loading in hypertension-prone humans. Blood Pressure 2000; 9(4):206-13. *Not early CKD*

611. Bruun NE, Ibsen H, Nielsen F, et al. Lack of effect of nifedipine on counterregulatory mechanisms in essential hypertension. Hypertension 1986; 8(8):655-61. *Sample size less than 50 patients*

612. Bruun NE, Ibsen H, Skott P, et al. Lithium clearance and renal tubular sodium handling during acute and long-term nifedipine treatment in essential hypertension. Clinical Science 1988; 75(6):609-13. *Follow-up less than 6 months*

613. Bruun NE, Skott P, Giese J. Renal and endocrine effects of physiological variations of atrial natriuretic factor in normal humans. American Journal of Physiology 1991; 260(1 Pt 2):R217-24. *Not CKD treatment*

614. Bryan AG, Bolsin SN, Vianna PT, et al. Modification of the diuretic and natriuretic effects of a dopamine infusion by fluid loading in preoperative cardiac surgical patients. Journal of Cardiothoracic & Vascular Anesthesia 1995; 9(2):158-63. *Follow-up less than 6 months*

615. Bucchi F, Bodzenta A, de Gaetano G, et al. Effects of 1 gram oral or intravenous aspirin on urinary excretion of thromboxane B2 and 6-keto-PGF1 alpha in healthy subjects. Prostaglandins 1986; 32(5):691-701. *Sample size less than 50 patients*

616. Buchet JP, Lauwerys R, Roels H, et al. Renal effects of cadmium body burden of the general population.[Erratum appears in Lancet 1991 Jun 22;337(8756):1554]. Lancet 1990; 336(8717):699-702. *Not CKD treatment*

617. Buckalew VM, Jr. End-stage renal disease: can dietary protein restriction prevent it? Southern Medical Journal 1994; 87(10):1034-7. *Not RCT or controlled trial*

618. Buclin T, Pechere-Bertschi A, Sechaud R, et al. Sinistrin clearance for determination of glomerular filtration rate: a reappraisal of various approaches using a new analytical method. Journal of Clinical Pharmacology 1997; 37(8):679-92. *Sample size less than 50 patients*

619. Buclin T, Sechaud R, Bertschi AP, et al. Estimation of glomerular filtration rate by sinistrin clearance using various approaches. Renal Failure 1998; 20(2):267-76. *Not CKD treatment*

620. Budoff MJ, Kessler P, Gao YL, et al. The interscan variation of CT coronary artery calcification score: analysis of the Calcium Acetate Renagel Comparison (CARE)-2 study. Academic Radiology 2008; 15(1):58-61. *Not RCT or controlled trial*

621. Bueter M, Dubb SS, Gill A, et al. Renal cytokines improve early after bariatric surgery. British Journal of Surgery 2010 Dec; 97(12):1838-44. *Not CKD treatment*

622. Bunke M, Sloan R, Brier M, et al. An improved glomerular filtration rate in cardiac transplant recipients with once-a-day cyclosporine dosing. Transplantation 1995; 59(4):537-40. *Sample size less than 50 patients*

623. Burgess E. Conservative treatment to slow deterioration of renal function: evidence-based recommendations. Kidney International - Supplement 1999; 70:S17-25. *Not RCT or controlled trial*

624. Burgess ED, Carides GW, Gerth WC, et al. Losartan reduces the costs associated with nephropathy and end-stage renal disease from type 2 diabetes: Economic evaluation of the RENAAL study from a Canadian perspective. Canadian Journal of Cardiology 2004; 20(6):613-8. *Not CKD treatment*

625. Burgess W, Merten GJ, Rittase RA. Sodium bicarbonate vs sodium chloride in preventing contrast medium-induced nephropathy. JAMA 2009; 301(4):377; author reply 9-80. *Not CKD treatment*

626. Burnier M, Brunner HR. Angiotensin II receptor antagonists in hypertension. Kidney International - Supplement 1998; 68:S107-11. *Not RCT or controlled trial*

627. Burnier M, Hagman M, Nussberger J, et al. Short-term and sustained renal effects of angiotensin II receptor blockade in healthy subjects. Hypertension 1995; 25(4 Pt 1):602-9. *Sample size less than 50 patients*

628. Burnier M, Mooser V, Wauters JP, et al. Bolus injections of synthetic atrial natriuretic peptide in patients with chronic renal failure or nephrotic syndrome. Journal of Cardiovascular Pharmacology 1989; 13(5):682-90. *Not CKD treatment*

629. Burnier M, Rutschmann B, Nussberger J, et al. Salt-dependent renal effects of an angiotensin II antagonist in healthy subjects. Hypertension 1993; 22(3):339-47. *Sample size less than 50 patients*

630. Burns KEA, Chu MWA, Novick RJ, et al. Perioperative N-acetylcysteine to prevent renal dysfunction in high-risk patients undergoing cabg surgery: a randomized controlled trial. JAMA 2005; 294(3):342-50. *Not CKD treatment*

631. Burodom A. Renal response to egg white protein loading in healthy young adults. Journal of the Medical Association of Thailand 2010 Jul; 93(7):824-9. *Not CKD treatment*

632. Bursztyn M, Kobrin I, Fidel J, et al. Improved kidney function with cilazapril in hypertensive type II diabetics with chronic renal failure. Journal of Cardiovascular Pharmacology 1991; 18(3):337-41. *Sample size less than 50 patients*

633. Bursztyn M, Motro M, Grossman E, et al. Accelerated coronary artery calcification in mildly reduced renal function of high-risk hypertensives: a 3-year prospective observation. Journal of Hypertension 2003; 21(10):1953-9. *Not CKD treatment*

634. Burton CJ, Tomson CR. Can the use of low-dose dopamine for treatment of acute renal failure be justified? Postgraduate Medical Journal 1999; 75(883):269-74. *Not CKD treatment*

635. Bus SA, Maas M, de Lange A, et al. Elevated plantar pressures in neuropathic diabetic patients with claw/hammer toe deformity. Journal of Biomechanics 2005; 38(9):1918-25. *Not relevant to key questions*

636. Busch M, Franke S, Wolf G, et al. Serum levels of the advanced glycation end products Nepsilon-carboxymethyllysine and pentosidine are not influenced by treatment with the angiotensin receptor II type 1 blocker irbesartan in patients with type 2 diabetic nephropathy and hypertension. Nephron 2008; 108(4):c291-7. *Not early CKD*

637. Buter H, Navis G, Dullaart RP, et al. Time course of the antiproteinuric and renal haemodynamic responses to losartan in microalbuminuric IDDM. Nephrology Dialysis Transplantation 2001; 16(4):771-5. *Sample size less than 50 patients*

638. Butler J, Emerman C, Peacock WF, et al. The efficacy and safety of B-type natriuretic peptide (nesiritide) in patients with renal insufficiency and acutely decompensated congestive heart failure. Nephrology Dialysis Transplantation 2004; 19(2):391-9. *Not relevant to key questions*

639. Bybee KA, Lee JH, O'Keefe JH. Cumulative clinical trial data on atorvastatin for reducing cardiovascular events: the clinical impact of atorvastatin. Current Medical Research & Opinion 2008; 24(4):1217-29. *Not CKD treatment*

640. Caglar K, Yilmaz MI, Saglam M, et al. Short-term treatment with sevelamer increases serum fetuin-a concentration and improves endothelial dysfunction in chronic kidney disease stage 4 patients. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(1):61-8. *Follow-up less than 6 months*

641. Cahill CJ, Pain JA, Bailey ME. Bile salts, endotoxin and renal function in obstructive jaundice. Surgery, Gynecology & Obstetrics 1987; 165(6):519-22. *Sample size less than 50 patients*

642. Caidahl K, Eden S, Bengtsson BA. Cardiovascular and renal effects of growth hormone. Clinical Endocrinology 1994; 40(3):393-400. *Not CKD treatment*

643. Caillot D, Reny G, Solary E, et al. A controlled trial of the tolerance of amphotericin B infused in dextrose or in Intralipid in patients with haematological malignancies. Journal of Antimicrobial Chemotherapy 1994; 33(3):603-13. *Not CKD treatment*

644. Caimmi P-P, Pagani L, Micalizzi E, et al. Fenoldopam for renal protection in patients undergoing cardiopulmonary bypass. Journal of Cardiothoracic & Vascular Anesthesia 2003; 17(4):491-4. *Not CKD treatment*

645. Callahan MB, LeSage L, Johnstone S. A model for patient participation in quality of life measurement to improve rehabilitation outcomes. Nephrology News & Issues 1999; 13(1):33-7. *Not RCT or controlled trial*

646. Callis A, Magnan de Bornier B, Serrano JJ, et al. Activity of citrulline malate on acid-base balance and blood ammonia and amino acid levels. Study in the animal and in man. Arzneimittel-Forschung 1991; 41(6):660-3. *Not CKD treatment*

647. Camacho P, Pitale S, Abraira C. Beneficial and detrimental effects of intensive glycaemic control, with emphasis on type 2 diabetes mellitus. Drugs & Aging 2000; 17(6):463-76. *Not relevant to key questions*

648. Camargo EG, Weinert LS, Lavinsky J, et al. The effect of aspirin on the antiproteinuric properties of enalapril in microalbuminuric type 2 diabetic patients: a randomized, double-blind, placebo-controlled study. Diabetes Care 2007; 30(7):e66. *Sample size less than 50 patients*

649. Camisasca P, Avanzini F, Alli C, et al. Overall cardiovascular risk still ignored in general practice care of hypertension. Journal of Cardiovascular Risk 2002; 9(3):147-52. *Not relevant to key questions*

650. Camp MJ, Wingard JR, Gilmore CE, et al. Efficacy of low-dose dopamine in preventing amphotericin B nephrotoxicity in bone marrow transplant patients and leukemia patients. Antimicrobial Agents & Chemotherapy 1998; 42(12):3103-6. *Not CKD treatment*

651. Campbell DR, Flemming BK, Mason WF, et al. A comparative study of the nephrotoxicity of iohexol, iopamidol and ioxaglate in peripheral angiography. Canadian Association of Radiologists Journal 1990; 41(3):133-7. *Not CKD treatment*

652. Campbell KL, Ash S, Bauer JD. The impact of nutrition intervention on quality of life in pre-dialysis chronic kidney disease patients. Clinical Nutrition 2008; 27(4):537-44. *Not early CKD*

653. Campbell KL, Ash S, Davies PSW, et al. Randomized controlled trial of nutritional counseling on body composition and dietary intake in severe CKD. American Journal of Kidney Diseases 2008; 51(5):748-58. *Not early CKD*

654. Campbell MS, Rai J, Kozin E, et al. Effects of sirolimus vs. calcineurin inhibitors on renal dysfunction after orthotopic liver transplantation. Clinical Transplantation 2007; 21(3):377-84. *Sample size less than 50 patients*

655. Campbell RC, Sui X, Filippatos G, et al. Association of chronic kidney disease with outcomes in chronic heart failure: a propensity-matched study. Nephrology Dialysis Transplantation 2009; 24(1):186-93. *Not CKD treatment*

656. Campbell RC, Sui X, Filippatos G, et al. Association of chronic kidney disease with outcomes in chronic heart failure: a propensity-matched study. Nephrology Dialysis Transplantation 2009; 24(1):186-93. *Not CKD treatment*

657. Campbell WW, Joseph LJO, Ostlund RE, Jr., et al. Resistive training and chromium picolinate: effects on inositols and liver and kidney functions in older adults. International Journal of Sport Nutrition & Exercise Metabolism 2004; 14(4):430-42. *Not RCT or controlled trial*

658. Campo C, Garcia-Vallejo O, Barrios V, et al. The natriuretic effect of nifedipine gastrointestinal therapeutic system remains despite the presence of mild-to-moderate renal failure. Journal of Hypertension 1997; 15(12 Pt 2):1803-8. *Follow-up less than 6 months*

659. Cangiano JL, Figueroa J, Palmer R. Renal hemodynamic effects of nabumetone, sulindac, and placebo in patients with osteoarthritis. Clinical Therapeutics 1999; 21(3):503-12. *Not CKD treatment*

660. Cantaluppi V, Assenzio B, Pasero D, et al. Polymyxin-B hemoperfusion inactivates circulating proapoptotic factors. Intensive Care Medicine 2008; 34(9):1638-45. *Not RCT or controlled trial*

661. Cantarovich F, Rangoonwala B, Lorenz H, et al. High-dose furosemide for established ARF: a prospective, randomized, double-blind, placebo-controlled, multicenter trial. American Journal of Kidney Diseases 2004; 44(3):402-9. *Not CKD treatment*

662. Cantarovich M. Renal protective strategies in heart transplant patients. Current Opinion in Cardiology 2007; 22(2):133-8. *Not RCT or controlled trial*

663. Cantarovich M, Besner JG, Fitchett DH, et al. Efficacy and side-effects of cyclosporine dose monitoring with levels 6 h after the morning dose in heart transplant patients. Clinical Transplantation 1997; 11(5 Pt 1):399-405. *Sample size less than 50 patients*

664. Cantarovich M, Yoshida EM, Peltekian KM, et al. Poor prediction of the glomerular filtration rate using current formulas in de novo liver transplant patients. Transplantation 2006; 82(3):433-6. *Not CKD treatment*

665. Cantor TL. Lack of evidence for administering vitamin D analogs to kidney failure patients to improve survivability. Clinical Nephrology 2009; 72(2):97-104. *Not early CKD*

666. Cao Y, Zhao J, Yang Z, et al. CD4+FOXP3+ regulatory T cell depletion by low-dose cyclophosphamide prevents recurrence in patients with large condylomata acuminata after laser therapy. Clinical Immunology 2010 Jul; 136(1):21-9. *Not CKD treatment*

667. Capek M, Schnack C, Ludvik B, et al. Effects of captopril treatment versus placebo on renal function in type 2 diabetic patients with microalbuminuria: a long-term study. Clinical Investigator 1994; 72(12):961-6. *Sample size less than 50 patients*

668. Capes SE, Gerstein HC, Negassa A, et al. Enalapril prevents clinical proteinuria in diabetic patients with low ejection fraction. Diabetes Care 2000; 23(3):377-80. *Not CKD treatment*

669. Cappelli P, Di Liberato L, Stuard S, et al. N-3 polyunsaturated fatty acid supplementation in chronic progressive renal disease. Journal of Nephrology 1997; 10(3):157-62. *Sample size less than 50 patients*

670. Cappuccio FP, Antonios TF, Markandu ND, et al. Acute natriuretic effect of nifedipine on different sodium intakes in essential hypertension: evidence for distal tubular effect? Journal of Human Hypertension 1994; 8(8):627-30. *Not CKD treatment*

671. Caravaca F, Cubero JJ, Jimenez F, et al. Effect of the mode of calcitriol administration on PTH-ionized calcium relationship in uraemic patients with secondary hyperparathyroidism. Nephrology Dialysis Transplantation 1995; 10(5):665-70. *Sample size less than 50 patients*

672. Carbonell N, Blasco M, Sanjuan R, et al. Intravenous N-acetylcysteine for preventing contrast-induced nephropathy: a randomised trial. International Journal of Cardiology 2007; 115(1):57-62. *Not CKD treatment*

673. Carbonell N, Sanjuan R, Blasco M, et al. N-acetylcysteine: short-term clinical benefits after coronary angiography in high-risk renal patients. Revista Espanola de Cardiologia 2010 Jan; 63(1):12-9. *Not relevant to key questions*

674. Carcoana OV, Hines RL. Is renal dose dopamine protective or therapeutic? Yes. Critical Care Clinics 1996; 12(3):677-85. *Not CKD treatment*

675. Carcoana OV, Mathew JP, Davis E, et al. Mannitol and dopamine in patients undergoing cardiopulmonary bypass: a randomized clinical trial. Anesthesia & Analgesia 2003; 97(5):1222-9. *Not CKD treatment*

676. Cardiel MH. Abetimus sodium: a new therapy for delaying the time to, and reducing the incidence of, renal flare and/or major systemic lupus erythematosus flares in patients with systemic lupus erythematosus who have a history of renal disease. Expert Opinion on Investigational Drugs 2005; 14(1):77-88. *Not RCT or controlled trial*

677. Carella MJ, Gossain VV, Jones J. The effects of a low-dose regimen of fosinopril on elevated urinary albumin excretion in normotensive type 1 diabetic patients. Journal of Medicine 1999; 30(5-6):305-20. *Sample size less than 50 patients*

678. Carides GW, Shahinfar S, Dasbach EJ, et al. The impact of losartan on the lifetime incidence of end-stage renal disease and costs in patients with type 2 diabetes and nephropathy. Pharmacoeconomics 2006; 24(6):549-58. *Not relevant to key questions*

679. Carlsen JE, Jensen HA, Rehling M, et al. Long term haemodynamic effects of pinacidil and hydralazine in arterial hypertension. Drugs 1988; 36 Suppl 7:55-63. *Sample size less than 50 patients*

680. Carlson K, Hjorth M, Knudsen LM, et al. Toxicity in standard melphalan-prednisone therapy among myeloma patients with renal failure--a retrospective analysis and recommendations for dose adjustment. British Journal of Haematology 2005; 128(5):631-5. *Not RCT or controlled trial*

681. Carr AA, Kowey PR, Devereux RB, et al. Hospitalizations for new heart failure among subjects with diabetes mellitus in the RENAAL and LIFE studies. American Journal of Cardiology 2005; 96(11):1530-6. *Not RCT or controlled trial*

682. Carraro M, Malalan F, Antonione R, et al. Effects of a dimeric vs a monomeric nonionic contrast medium on renal function in patients with mild to moderate renal insufficiency: a double-blind, randomized clinical trial. European Radiology 1998; 8(1):144-7. *Not CKD treatment*

683. Carraro M, Mancini W, Artero M, et al. Dose effect of nitrendipine on urinary enzymes and microproteins following non-ionic radiocontrast administration. Nephrology Dialysis Transplantation 1996; 11(3):444-8. *Not CKD treatment*

684. Carraro M, Stacul F, Collari P, et al. Contrast media nephrotoxicity: urinary protein and enzyme pattern in patients with or without saline infusion during digital subtracting angiography. Contributions to Nephrology 1993; 101:251-4. *Not CKD treatment*

685. Carrier M, Leblanc M-H, Perrault LP, et al. Basiliximab and rabbit anti-thymocyte globulin for prophylaxis of acute rejection after heart transplantation: a non-inferiority trial. Journal of Heart & Lung Transplantation 2007; 26(3):258-63. *Not RCT or controlled trial*

686. Carrier M, Pelletier GB, White M, et al. Effect of pentoxifylline on renal toxicity of cyclosporine: preliminary results. Transplantation Proceedings 1994; 26(5):2745-6. *Sample size less than 50 patients*

687. Carrier M, Pelletier GB, White M, et al. Effect of pentoxifylline on renal toxicity of cyclosporine: results of a clinical trial after heart transplantation. Journal of Heart & Lung Transplantation 1996; 15(12):1179-83. *Not CKD treatment*

688. Carstens J, Greisen J, Jensen KT, et al. Renal effects of a urodilatin infusion in patients with liver cirrhosis, with and without ascites. Journal of the American Society of Nephrology 1998; 9(8):1489-98. *Not CKD treatment*

689. Carstens J, Gronbaek H, Larsen HK, et al. Effects of urodilatin on natriuresis in cirrhosis patients with sodium retention. BMC Gastroenterology 2007; 7:1. *Follow-up less than 6 months*

690. Carstens J, Jensen KT, Pedersen EB. Effect of urodilatin infusion on renal haemodynamics, tubular function and vasoactive hormones. Clinical Science 1997; 92(4):397-407. *Sample size less than 50 patients*

691. Carstens J, Jensen KT, Pedersen EB. Metabolism and action of urodilatin infusion in healthy volunteers. Clinical Pharmacology & Therapeutics 1998; 64(1):73-86. *Follow-up less than 6 months*

692. Carstens J, Pedersen EB. Renal effects of urodilatin in healthy subjects are independent of blockade of the cyclooxygenase and angiotensin II receptor. Scandinavian Journal of Clinical & Laboratory Investigation 2008; 68(1):2-10. *Not RCT or controlled trial*

693. Carswell CI, Goa KL. Losartan in diabetic nephropathy. Drugs 2003; 63(4):407-14; discussion 15-6. *Not RCT or controlled trial*

694. Carter JL, O'Riordan SE, Eaglestone GL, et al. Chronic kidney disease prevalence in a UK residential care home population. Nephrology Dialysis Transplantation 2008; 23(4):1257-64. *Not RCT or controlled trial*

695. Caruso D, D'Avino M, Acampora C, et al. Effects of losartan and chlorthalidone on blood pressure and renal vascular resistance index in non-diabetic patients with essential hypertension and normal renal function. Journal of Cardiovascular Pharmacology 2004; 44(5):520-4. *Not RCT or controlled trial*

696. Casas JP, Chua W, Loukogeorgakis S, et al. Effect of inhibitors of the renin-angiotensin system and other antihypertensive drugs on renal outcomes: systematic review and meta-analysis. Lancet 2005; 366(9502):2026-33. *Not RCT or controlled trial*

697. Castaneda C, Gordon PL, Parker RC, et al. Resistance training to reduce the malnutrition-inflammation complex syndrome of chronic kidney disease. American Journal of Kidney Diseases 2004; 43(4):607-16. *Not relevant to key questions*

698. Castaneda C, Gordon PL, Uhlin KL, et al. Resistance training to counteract the catabolism of a low-protein diet in patients with chronic renal insufficiency. A randomized, controlled trial. Annals of Internal Medicine 2001; 135(11):965-76. *Sample size less than 50 patients*

699. Castellani S, Scarti L, Chen JL, et al. The antihypertensive and renal activities of potassium canrenoate are associated with increased renal prostaglandin excretion. Clinical Science 1989; 77(2):217-22. *Sample size less than 50 patients*

700. Castellani S, Scarti L, Masotti G, et al. Selective stimulation of renal PGE2 by potassium canrenoate in essential hypertension. Progress in Clinical & Biological Research 1989; 301:297-301. *Sample size less than 50 patients*

701. Castellano M, Beschi M, Agabiti-Rosei E, et al. Renal and hemodynamic effects of atrial natriuretic peptide infusion are not mediated by peripheral dopaminergic mechanisms. American Journal of Hypertension 1991; 4(4 Pt 1):385-8. *Not CKD treatment*

702. Castellino P, Hunt W, DeFronzo RA. Regulation of renal hemodynamics by plasma amino acid and hormone concentrations. Kidney International - Supplement 1987; 22:S15-20. *Not relevant to key questions*

703. Castro-Gonzalez I, Miranda-Becerra D, Montano-Benavides S. Evaluation of phosphorus, protein, and n-3 fatty-acid content in 15 marine fish species identifies the species most beneficial to renal patients. Journal of Renal Nutrition 2009; 19(6):462-8. *Not human studies*

704. Catella-Lawson F, McAdam B, Morrison BW, et al. Effects of specific inhibition of cyclooxygenase-2 on sodium balance, hemodynamics, and vasoactive eicosanoids. Journal of Pharmacology & Experimental Therapeutics 1999; 289(2):735-41. *Sample size less than 50 patients*

705. Cattaneo D, Remuzzi G. Lipid oxidative stress and the anti-inflammatory properties of statins and ACE inhibitors. Journal of Renal Nutrition 2005; 15(1):71-6. *Sample size less than 50 patients*

706. Cattran DC, Alexopoulos E, Heering P, et al. Cyclosporin in idiopathic glomerular disease associated with the nephrotic syndrome : workshop recommendations. Kidney International 2007; 72(12):1429-47. *Not RCT or controlled trial*

707. Cavalcanti AB, Goncalves AR, Almeida CS, et al. Teicoplanin versus vancomycin for proven or suspected infection. Cochrane Database of Systematic Reviews 2010; (6):CD007022. *Not CKD treatment*

708. Cavaliere G, Arrigo G, D'Amico G, et al. Tubular nephrotoxicity after intravenous urography with ionic high-osmolal and nonionic low-osmolal contrast media in patients with chronic renal insufficiency. Nephron 1987; 46(2):128-33. *Sample size less than 50 patients*

709. Cavatorta A, Buzio C, Pucci F, et al. Effects of antihypertensive drugs on glomerular function in normotensive and hypertensive subjects: hormonal aspects. Journal of Hypertension - Supplement 1991; 9(6):S218-9. *Sample size less than 50 patients*

710. Cazzola M. Erythropoietin pathophysiology and erythropoietin deficiency anemia. Hematology Journal 2004; 5 Suppl 3:S100-3. *Sample size less than 50 patients*

711. Celik JB, Gormus N, Topal A, et al. Effect of off-pump and on-pump coronary artery bypass grafting on renal function. Renal Failure 2005; 27(2):183-8. *Not RCT or controlled trial*

712. Centonza L, Castoldi G, Busca G, et al. Behavioural stress blunts the creatinine clearance increase induced by a protein load in healthy subjects. Journal of Nephrology 2001; 14(5):403-9. *Not RCT or controlled trial*

713. Cetina L, Rivera L, Candelaria M, et al. Chemoradiation with gemcitabine for cervical cancer in patients with renal failure. Anti-Cancer Drugs 2004; 15(8):761-6. *Not relevant to key questions*

714. Cetinkaya R, Odabas AR, Selcuk Y. Anti-proteinuric effects of combination therapy with enalapril and losartan in patients with nephropathy due to type 2 diabetes. International Journal of Clinical Practice 2004; 58(5):432-5. *Not CKD treatment*

715. Ceyhan C, Akar H, Tekten T, et al. Microalbuminuria is associated with reduced cardiac cyclic variation of integrated backscatter signal in severe hypertension. Echocardiography 2004; 21(6):495-501. *Sample size less than 50 patients*

716. Chalmers J, Joshi R, Kengne A-P, et al. Blood pressure lowering with fixed combination perindopril-indapamide: key findings from ADVANCE. Journal of Hypertension - Supplement 2008; 26(2):S11-5. *Not RCT or controlled trial*

717. Chalmers N, Jackson RW. Comparison of iodixanol and iohexol in renal impairment. British Journal of Radiology 1999; 72(859):701-3. *Not CKD treatment*

718. Chan C, Maurer J, Cardella C, et al. A randomized controlled trial of verapamil on cyclosporine nephrotoxicity in heart and lung transplant recipients. Transplantation 1997; 63(10):1435-40. *Sample size less than 50 patients*

719. Chan JC, Cheung CK, Cheung MY, et al. Abnormal albuminuria as a predictor of mortality and renal impairment in Chinese patients with NIDDM. Diabetes Care 1995; 18(7):1013-6. *Not RCT or controlled trial*

720. Chan JC, Critchley JA, Tomlinson B, et al. Antihypertensive and anti-albuminuric effects of losartan potassium and felodipine in Chinese elderly hypertensive patients with or without non-insulin-dependent diabetes mellitus. American Journal of Nephrology 1997; 17(1):72-80. *Sample size less than 50 patients*

721. Chan JC, Ko GT, Leung DH, et al. Long-term effects of angiotensin-converting enzyme inhibition and metabolic control in hypertensive type 2 diabetic patients. Kidney International 2000; 57(2):590-600. *Not relevant to key questions*

722. Chan JCN, Scott R, Arjona Ferreira JC, et al. Safety and efficacy of sitagliptin in patients with type 2 diabetes and chronic renal insufficiency. Diabetes, Obesity & Metabolism 2008; 10(7):545-55. *Not CKD treatment*

723. Chan JCN, Wat NMS, So W-Y, et al. Renin angiotensin aldosterone system blockade and renal disease in patients with type 2 diabetes. An Asian perspective from the RENAAL Study. Diabetes Care 2004; 27(4):874-9. *Not relevant to key questions*

724. Chan MY, Becker RC, Sim L-L, et al. Reperfusion strategy and mortality in ST-elevation myocardial infarction among patients with and without impaired renal function. Annals of the Academy of Medicine, Singapore 2010 Mar; 39(3):179-84. *Not CKD treatment*

725. Chandra P, Binongo JNG, Ziegler TR, et al. Cholecalciferol (vitamin D3) therapy and vitamin D insufficiency in patients with chronic kidney disease: a randomized controlled pilot study. Endocrine Practice 2008; 14(1):10-7. *Not CKD treatment*

726. Chang GJ, Mahanty HD, Quan D, et al. Experience with the use of sirolimus in liver transplantation--use in patients for whom calcineurin inhibitors are contraindicated. Liver Transplantation 2000; 6(6):734-40. *Not early CKD*

727. Chanu P, Gieschke R, Charoin J-E, et al. Population pharmacokinetic/pharmacodynamic model for C.E.R.A. in both ESA-naive and ESA-treated chronic kidney disease patients with renal anemia. Journal of Clinical Pharmacology 2010 May; 50(5):507-20. *Not RCT or controlled trial*

728. Chapman JR, Griffiths D, Harding NG, et al. Reversibility of cyclosporin nephrotoxicity after three months' treatment. Lancet 1985; 1(8421):128-30. *Follow-up less than 6 months*

729. Charloux A, Chaouat A, Piquard F, et al. Renal hyporesponsiveness to brain natriuretic peptide: both generation and renal activity of cGMP are decreased in patients with pulmonary hypertension. Peptides 2006; 27(11):2993-9. *Not relevant to key questions*

730. Chartapisak W, Opastiraku S, Willis NS, et al. Prevention and treatment of renal disease in Henoch-Schonlein purpura: a systematic review. Archives of Disease in Childhood 2009; 94(2):132-7. *Not CKD treatment*

731. Charytan C, Coburn JW, Chonchol M, et al. Cinacalcet hydrochloride is an effective treatment for secondary hyperparathyroidism in patients with CKD not receiving dialysis. American Journal of Kidney Diseases 2005; 46(1):58-67. *Follow-up less than 6 months*

732. Charytan C, Qunibi W, Bailie GR, et al. Comparison of intravenous iron sucrose to oral iron in the treatment of anemic patients with chronic kidney disease not on dialysis. Nephron 2005; 100(3):c55-62. *Not RCT or controlled trial*

733. Charytan D, Forman JP, Cutlip DE. Risk of target lesion revascularization after coronary stenting in patients with and without chronic kidney disease. Nephrology Dialysis Transplantation 2007; 22(9):2578-85. *Sample size less than 50 patients*

734. Charytan DM, Kuntz RE, Chhabra A, et al. Relationship of chronic kidney disease to cardiovascular death and myocardial infarction following coronary stenting. Journal of Nephrology 2006; 19(6):764-70. *Not early CKD*

735. Chase HP, Garg SK, Harris S, et al. Angiotensin-converting enzyme inhibitor treatment for young normotensive diabetic subjects: a two-year trial. Annals of Ophthalmology 1993; 25(8):284-9. *Sample size less than 50 patients*

736. Chattington PD, Anderson JV, Rees LH, et al. Atrial natriuretic peptide in type 2 diabetes mellitus: response to a physiological mixed meal and relationship to renal function. Diabetic Medicine 1998; 15(5):375-9. *Sample size less than 50 patients*

737. Chaturvedi N. Modulation of the renin-angiotensin system and retinopathy. Heart 2000; 84 Suppl 1:i29-31:discussion i50. *Not relevant to key questions*

738. Chauveau P, Chadefaux B, Coude M, et al. Long-term folic acid (but not pyridoxine) supplementation lowers elevated plasma homocysteine level in chronic renal failure. Mineral & Electrolyte Metabolism 1996; 22(1-3):106-9. *Sample size less than 50 patients*

739. Chawla V, Greene T, Beck GJ, et al. Hyperlipidemia and long-term outcomes in nondiabetic chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2010 Sep; 5(9):1582-7. *Not relevant to key questions*

740. Cheer SM, McClellan K. Manidipine: a review of its use in hypertension. Drugs 2001; 61(12):1777-99. *Not RCT or controlled trial*

741. Chellingsworth MC, Kendall MJ. Effects of nifedipine, verapamil and diltiazem on renal function. British Journal of Clinical Pharmacology 1988; 25(5):599-602. *Sample size less than 50 patients*

742. Chemla ES, Morsy M. Randomized clinical trial comparing decellularized bovine ureter with expanded polytetrafluoroethylene for vascular access. British Journal of Surgery 2009; 96(1):34-9. *Not CKD treatment*

743. Chen BH. COX-2 inhibitors and renal function in elderly people. CMAJ Canadian Medical Association Journal 2000; 163(5):604. *Not relevant to key questions*

744. Chen BH. Combination treatment effective option for hypertensive, diabetic patients with microalbuminuria. CMAJ Canadian Medical Association Journal 2001; 164(6):861. *Not RCT or controlled trial*

745. Chen DT, Wynia MK, Moloney RM, et al. U.S. physician knowledge of the FDA-approved indications and evidence base for commonly prescribed drugs: results of a national survey. Pharmacoepidemiology & Drug Safety 2009 Nov; 18(11):1094-100. *Not CKD treatment*

746. Chen HC, Hsieh MT, Chang SS, et al. Long-term reno-cardiovascular effects of orally administered aconiti tuber in humans. American Journal of Chinese Medicine 1990; 18(1-2):25-33. *Not CKD treatment*

747. Chen HH, Redfield MM, Nordstrom LJ, et al. Angiotensin II AT1 receptor antagonism prevents detrimental renal actions of acute diuretic therapy in human heart failure. American Journal of Physiology - Renal Physiology 2003; 284(5):F1115-9. *Sample size less than 50 patients*

748. Chen HH, Sundt TM, Cook DJ, et al. Low dose nesiritide and the preservation of renal function in patients with renal dysfunction undergoing cardiopulmonary-bypass surgery: a double-blind placebo-controlled pilot study. Circulation 2007; 116(11 Suppl):I134-8. *Follow-up less than 6 months*

749. Chen HH, Tarng DC, Lee KF, et al. Epoetin alfa and darbepoetin alfa: effects on ventricular hypertrophy in patients with chronic kidney disease. Journal of Nephrology 2008; 21(4):543-9. *Not CKD treatment*

750. Chen HX. Expanding the clinical development of bevacizumab. Oncologist 2004; 9 Suppl 1:27-35. *Not CKD treatment*

751. Chen JLT, Lerner D, Ruthazer R, et al. Association of physical activity with mortality in chronic kidney disease. Journal of Nephrology 2008; 21(2):243-52. *Not early CKD*

752. Chen SL, Zhang J, Yei F, et al. Clinical outcomes of contrast-induced nephropathy in patients undergoing percutaneous coronary intervention: a prospective, multicenter, randomized study to analyze the effect of hydration and acetylcysteine. International Journal of Cardiology 2008; 126(3):407-13. *Not CKD treatment*

753. Chen X, Zheng F, Chen P, et al. An open-label, randomized, controlled, 4-week comparative clinical trial of barnidipine hydrochloride, a calcium-channel blocker, and benazepril, an angiotensin-converting enzyme inhibitor, in Chinese patients with renal parenchymal hypertension. Journal of International Medical Research 2006; 34(2):121-8. *Not CKD treatment*

754. Chen Y, Lipkowitz MS, Salem RM, et al. Progression of chronic kidney disease: Adrenergic genetic influence on glomerular filtration rate decline in hypertensive nephrosclerosis. American Journal of Nephrology 2010; 32(1):23-30. *Not relevant to key questions*

755. Cheng H-C, Kao A-W, Chuang C-H, et al. The efficacy of high- and low-dose intravenous omeprazole in preventing rebleeding for patients with bleeding peptic ulcers and comorbid illnesses. Digestive Diseases & Sciences 2005; 50(7):1194-201. *Not RCT or controlled trial*

756. Cheng IK, Lam KS, Janus ED, et al. Treatment of hyperlipidaemia in patients with non-insulin-dependent diabetes mellitus with progressive nephropathy. Contributions to Nephrology 1997; 120:79-87. *Not RCT or controlled trial*

757. Cheng IK, Ma JT, Yeh GR, et al. Comparison of captopril and enalapril in the treatment of hypertension in patients with non-insulin dependent diabetes mellitus and nephropathy. International Urology & Nephrology 1990; 22(3):295-303. *Sample size less than 50 patients*

758. Cheng JWM. Ambrisentan for the management of pulmonary arterial hypertension. Clinical Therapeutics 2008; 30(5):825-33. *Not RCT or controlled trial*

759. Cheng S, Coyne D. Paricalcitol capsules for the control of secondary hyperparathyroidism in chronic kidney disease. Expert Opinion on Pharmacotherapy 2006; 7(5):617-21. *Not relevant to key questions*

760. Cheng Y-F, Strid S, Borga O, et al. Active renal secretion of NXY-059, a novel neuroprotectant, is mediated via an organic acid transporter. Journal of Clinical Pharmacology 2007; 47(7):909-14. *Sample size less than 50 patients*

761. Chen-Scarabelli C, Scarabelli TM. Chronic renal insufficiency is an independent predictor of mortality in implantable cardioverter-defibrillator recipients. Pacing & Clinical Electrophysiology 2007; 30(3):371-6. *Not RCT or controlled trial*

762. Chernausek SD, Backeljauw PF, Frane J, et al. Long-term treatment with recombinant insulin-like growth factor (IGF)-I in children with severe IGF-I deficiency due to growth hormone insensitivity. Journal of Clinical Endocrinology & Metabolism 2007; 92(3):902-10. *Not human studies*

763. Cherney DZI, Miller JA, Scholey JW, et al. The effect of cyclooxygenase-2 inhibition on renal hemodynamic function in humans with type 1 diabetes. Diabetes 2008; 57(3):688-95. *Not RCT or controlled trial*

764. Chertow GM, Dillon M, Burke SK, et al. A randomized trial of sevelamer hydrochloride (RenaGel) with and without supplemental calcium. Strategies for the control of hyperphosphatemia and hyperparathyroidism in hemodialysis patients. Clinical Nephrology 1999; 51(1):18-26. *Not early CKD*

765. Cheung R, Lewanczuk RZ, Rodger NW, et al. The effect of valsartan and captopril on lipid parameters in patients with type II diabetes mellitus and nephropathy. International Journal of Clinical Practice 1999; 53(8):584-92. *Not CKD treatment*

766. Chew DP, Bhatt DL, Kimball W, et al. Bivalirudin provides increasing benefit with decreasing renal function: a meta-analysis of randomized trials. American Journal of Cardiology 2003; 92(8):919-23. *Not CKD treatment*

767. Chew DP, Lincoff AM, Gurm H, et al. Bivalirudin versus heparin and glycoprotein IIb/IIIa inhibition among patients with renal impairment undergoing percutaneous coronary intervention (a subanalysis of the REPLACE-2 trial). American Journal of Cardiology 2005; 95(5):581-5. *Sample size less than 50 patients*

768. Chi Y. Multiple testing procedures based on weighted Kaplan-Meier statistics for right-censored survival data. Statistics in Medicine 2005; 24(1):23-35. *Not CKD treatment*

769. Chiarelli F, Di Marzio D, Santilli F, et al. Effects of irbesartan on intracellular antioxidant enzyme expression and activity in adolescents and young adults with early diabetic angiopathy. Diabetes Care 2005; 28(7):1690-7. *Follow-up less than 6 months*

770. Chin HJ, Song YR, Lee JJ, et al. Moderately decreased renal function negatively affects the health-related quality of life among the elderly Korean population: a population-based study. Nephrology Dialysis Transplantation 2008; 23(9):2810-7. *Not CKD treatment*

771. Chiolero A, Maillard M, Nussberger J, et al. Proximal sodium reabsorption: An independent determinant of blood pressure response to salt. Hypertension 2000; 36(4):631-7. *Sample size less than 50 patients*

772. Chiurchiu C, Remuzzi G, Ruggenenti P. Angiotensin-converting enzyme inhibition and renal protection in nondiabetic patients: the data of the meta-analyses. Journal of the American Society of Nephrology 2005; 16 Suppl 1:S58-63. *Not relevant to key questions*

773. Chmielewski M, Carrero JJ, Nordfors L, et al. Lipid disorders in chronic kidney disease: reverse epidemiology and therapeutic approach. Journal of Nephrology 2008; 21(5):635-44. *Not early CKD*

774. Chmielewski M, Carrero JJ, Stenvinkel P, et al. Metabolic abnormalities in chronic kidney disease that contribute to cardiovascular disease, and nutritional initiatives that may diminish the risk. Current Opinion in Lipidology 2009; 20(1):3-9. *Follow-up less than 6 months*

775. Cho H-Y, Blum RA, Sunderland T, et al. Pharmacokinetic and pharmacodynamic modeling of a copper-selective chelator (TETA) in healthy adults. Journal of Clinical Pharmacology 2009; 49(8):916-28. *Not CKD treatment*

776. Cho JE, Shim JK, Chang JH, et al. Effect of nicardipine on renal function after robot-assisted laparoscopic radical prostatectomy. Urology 2009; 73(5):1056-60. *Not CKD treatment*

777. Chodjania Y, Tharaux P-L, Ragueneau I, et al. Renal and vascular effects of S21402, a dual inhibitor of angiotensin-converting enzyme and neutral endopeptidase, in healthy subjects with hypovolemia. Clinical Pharmacology & Therapeutics 2002; 71(6):468-78. *Sample size less than 50 patients*

778. Choi KC, Lee J, Kim SW, et al. Cimetidine improves the accuracy of creatinine clearance as an indicator for glomerular filtration rate. Korean Journal of Internal Medicine 1993; 8(1):28-33. *Sample size less than 50 patients*

779. Choi KL, Elliott WJ. Antihypertensive, antiproteinuric therapy and myocardial infarction and stroke prevention. Current Hypertension Reports 2005; 7(5):367-73. *Follow-up less than 6 months*

780. Chonchol M, Goldenberg I, Moss AJ, et al. Risk factors for sudden cardiac death in patients with chronic renal insufficiency and left ventricular dysfunction. American Journal of Nephrology 2007; 27(1):7-14. *Follow-up less than 6 months*

781. Choudhury D, Tuncel M, Levi M. Disorders of lipid metabolism and chronic kidney disease in the elderly. Seminars in Nephrology 2009 Nov; 29(6):610-20. *Not RCT or controlled trial*

782. Christensen CK, Christiansen JS, Christensen T, et al. The effect of six months continuous subcutaneous insulin infusion on kidney function and size in insulin-dependent diabetics. Diabetic Medicine 1986; 3(1):29-32. *Sample size less than 50 patients*

783. Christensen CK, Christiansen JS, Schmitz A, et al. Effect of continuous subcutaneous insulin infusion on kidney function and size in IDDM patients: a 2 year controlled study. Journal of Diabetic Complications 1987; 1(3):91-5. *Sample size less than 50 patients*

784. Christensen CK, Krusell LR. Acute and long-term effect of antihypertensive treatment on exercise induced microalbuminuria in essential hypertension. Journal of Clinical Hypertension 1987; 3(4):704-12. *Sample size less than 50 patients*

785. Christensen CK, Mogensen CE. Acute and long-term effect of antihypertensive treatment on exercise-induced albuminuria in incipient diabetic nephropathy. Scandinavian Journal of Clinical & Laboratory Investigation 1986; 46(6):553-9. *Sample size less than 50 patients*

786. Christensen PK, Akram K, Konig KB, et al. Autoregulation of glomerular filtration rate in patients with type 2 diabetes during isradipine therapy. Diabetes Care 2003; 26(1):156-62. *Sample size less than 50 patients*

787. Christensen PK, Hansen HP, Parving HH. Impaired autoregulation of GFR in hypertensive non-insulin dependent diabetic patients. Kidney International 1997; 52(5):1369-74. *Sample size less than 50 patients*

788. Christensen PK, Hommel EE, Clausen P, et al. Impaired autoregulation of the glomerular filtration rate in patients with nondiabetic nephropathies. Kidney International 1999; 56(4):1517-23. *Sample size less than 50 patients*

789. Christensen PK, Lund S, Parving HH. Autoregulated glomerular filtration rate during candesartan treatment in hypertensive type 2 diabetic patients. Kidney International 2001; 60(4):1435-42. *Sample size less than 50 patients*

790. Christensen PK, Lund S, Parving HH. The impact of glycaemic control on autoregulation of glomerular filtration rate in patients with non-insulin dependent diabetes. Scandinavian Journal of Clinical & Laboratory Investigation 2001; 61(1):43-50. *Sample size less than 50 patients*

791. Christiansen H, Segura J, Ruilope LM. Renal endpoints in hypertension trials. Clinical & Experimental Hypertension 2004; 26(7-8):721-6. *Not relevant to key questions*

792. Christiansen JS, Feldt-Rasmussen B, Parving HH. Short-term inhibition of prostaglandin synthesis has no effect on the elevated glomerular filtration rate of early insulin-dependent diabetes. Diabetic Medicine 1985; 2(1):17-20. *Sample size less than 50 patients*

793. Chrysant SG. Angiotensin II receptor blockers in the treatment of the cardiovascular disease continuum. Clinical Therapeutics 2008; 30 Pt 2:2181-90. *Not CKD treatment*

794. Chrysant SG, Chrysant GS. Pharmacological and clinical profile of moexipril: a concise review. Journal of Clinical Pharmacology 2004; 44(8):827-36. *Not CKD treatment*

795. Chrysochou C, Kalra PA. Current management of atherosclerotic renovascular disease--what have we learned from ASTRAL? Nephron 2010; 115(1):c73-81. *Not RCT or controlled trial*

796. Chrysostomou A, Pedagogos E, MacGregor L, et al. Double-blind, placebo-controlled study on the effect of the aldosterone receptor antagonist spironolactone in patients who have persistent proteinuria and are on long-term angiotensin-converting enzyme inhibitor therapy, with or without an angiotensin II receptor blocker. Clinical Journal of The American Society of Nephrology: CJASN 2006; 1(2):256-62. *Not RCT or controlled trial*

797. Chu D, Lacouture ME, Fillos T, et al. Risk of hand-foot skin reaction with sorafenib: a systematic review and meta-analysis. Acta Oncologica 2008; 47(2):176-86. *Not CKD treatment*

798. Chuang F-R, Chen T-C, Wang IK, et al. Comparison of iodixanol and iohexol in patients undergoing intravenous pyelography: a prospective controlled study. Renal Failure 2009; 31(3):181-8. *Not CKD treatment*

799. Chuang LM, Jou TS, Wu HP, et al. Effect of treatment of borderline hypertension on microalbuminuria in non-insulin-dependent diabetes mellitus. Journal of the Formosan Medical Association 1991; 90(6):531-5. *Not relevant to key questions*

800. Chung F-M, Yang Y-H, Shieh T-Y, et al. Effect of alcohol consumption on estimated glomerular filtration rate and creatinine clearance rate. Nephrology Dialysis Transplantation 2005; 20(8):1610-6. *Follow-up less than 6 months*

801. Cianciaruso B, Pota A, Bellizzi V, et al. Effect of a low- versus moderate-protein diet on progression of CKD: follow-up of a randomized controlled trial. American Journal of Kidney Diseases 2009; 54(6):1052-61. *Not early CKD*

802. Cianciaruso B, Pota A, Bellizzi V, et al. Effect of a low- versus moderate-protein diet on progression of CKD: follow-up of a randomized controlled trial. American Journal of Kidney Diseases 2009; 54(6):1052-61. *Not early CKD*

803. Cianciaruso B, Pota A, Pisani A, et al. Metabolic effects of two low protein diets in chronic kidney disease stage 4-5--a randomized controlled trial. Nephrology Dialysis Transplantation 2008; 23(2):636-44. *Not RCT or controlled trial*

804. Cianciaruso B, Ravani P, Barrett BJ, et al. Italian randomized trial of hemoglobin maintenance to prevent or delay left ventricular hypertrophy in chronic kidney disease. Journal of Nephrology 2008; 21(6):861-70. *Follow-up less than 6 months*

805. Cianciolo G, La Manna G, Coli L, et al. 5-methyltetrahydrofolate administration is associated with prolonged survival and reduced inflammation in ESRD patients. American Journal of Nephrology 2008; 28(6):941-8. *Not early CKD*

806. Cianciolo G, La Manna G, Coli L, et al. 5-methyltetrahydrofolate administration is associated with prolonged survival and reduced inflammation in ESRD patients. American Journal of Nephrology 2008; 28(6):941-8. *Not RCT or controlled trial*

807. Ciavarella A, Di Mizio G, Stefoni S, et al. Reduced albuminuria after dietary protein restriction in insulin-dependent diabetic patients with clinical nephropathy. Diabetes Care 1987; 10(4):407-13. *Sample size less than 50 patients*

808. Ciavarella A, Vannini P, Flammini M, et al. Effect of long-term near-normoglycemia on the progression of diabetic nephropathy. Diabete et Metabolisme 1985; 11(1):3-8. *Sample size less than 50 patients*

809. Ciavarella D. The use of protein A columns in the treatment of cancer and allied diseases. International Journal of Clinical & Laboratory Research 1992; 21(3):210-3. *Not CKD treatment*

810. Cicconetti A, Bartoli A, Ripari F, et al. COX-2 selective inhibitors: a literature review of analgesic efficacy and safety in oral-maxillofacial surgery. Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics 2004; 97(2):139-46. *Not CKD treatment*

811. Cicek M, Koroglu A, Demirbilek S, et al. Comparison of propofol-alfentanil and propofol-remifentanil anaesthesia in percutaneous nephrolithotripsy. European Journal of Anaesthesiology 2005; 22(9):683-8. *Not RCT or controlled trial*

812. Cicinnati VR, Yu Z, Klein CG, et al. Clinical trial: switch to combined mycophenolate mofetil and minimal dose calcineurin inhibitor in stable liver transplant patients--assessment of renal and allograft function, cardiovascular risk factors and immune monitoring. Alimentary Pharmacology & Therapeutics 2007; 26(9):1195-208. *Sample size less than 50 patients*

813. Cifkova R, Nilsson PM. Statins and hypertension. Journal of Hypertension 2009; 27(3):662-5. *Sample size less than 50 patients*

814. Cinquegrani MP, Liang CS. Indomethacin attenuates the hypotensive action of hydralazine. Clinical Pharmacology & Therapeutics 1986; 39(5):564-70. *Sample size less than 50 patients*

815. Claas GJ, Julg B, Goebel FD, et al. Metabolic and anthropometric changes one year after switching from didanosine/stavudine to tenofovir in HIV-infected patients. European Journal of Medical Research 2007; 12(2):54-60. *Sample size less than 50 patients*

816. Claria J, Kent JD, Lopez-Parra M, et al. Effects of celecoxib and naproxen on renal function in nonazotemic patients with cirrhosis and ascites. Hepatology 2005; 41(3):579-87. *Not RCT or controlled trial*

817. Claris-Appiani A, Assael BM, Tirelli AS, et al. Lack of glomerular hemodynamic stimulation after infusion of branched-chain amino acids. Kidney International 1988; 33(1):91-4. *Sample size less than 50 patients*

818. Clark WF, Forzley BR, Sontrop JM, et al. TTP/HUS: observational studies generate hypotheses that lead to randomized controlled trials. Kidney International - Supplement 2009; (112):S50-1. *Not early CKD*

819. Clarke WL. The Diabetes Control and Complications Trial: new challenges for the primary physician. Virginia Medical Quarterly 1994; 121(3):185-8. *Not RCT or controlled trial*

820. Clasen W, Khartabil T, Imm S, et al. Torasemide for diuretic treatment of advanced chronic renal failure. Arzneimittel-Forschung 1988; 38(1A):209-11. *Sample size less than 50 patients*

821. Clavijo LC, Pinto TL, Kuchulakanti PK, et al. Effect of a rapid intra-arterial infusion of dextrose 5% prior to coronary angiography on frequency of contrast-induced nephropathy in high-risk patients. American Journal of Cardiology 2006; 97(7):981-3. *Not CKD treatment*

822. Cleland JG, Dargie HJ, Gillen G, et al. Captopril in heart failure: a double-blind study of the effects on renal function. Journal of Cardiovascular Pharmacology 1986; 8(4):700-6. *Sample size less than 50 patients*

823. Cleland JG, Dargie HJ, Pettigrew A, et al. The effects of captopril on serum digoxin and urinary urea and digoxin clearances in patients with congestive heart failure. American Heart Journal 1986; 112(1):130-5. *Sample size less than 50 patients*

824. Cleland JG, Gillen G, Dargie HJ. The effects of frusemide and angiotensin-converting enzyme inhibitors and their combination on cardiac and renal haemodynamics in heart failure. European Heart Journal 1988; 9(2):132-41. *Sample size less than 50 patients*

825. Cleland JG, Shah D, Krikler S, et al. Effects of lisinopril on cardiorespiratory, neuroendocrine, and renal function in patients with asymptomatic left ventricular dysfunction. British Heart Journal 1993; 69(6):512-5. *Follow-up less than 6 months*

826. Cleland JG, Shah D, Krikler S, et al. Angiotensin-converting enzyme inhibitors, left ventricular dysfunction, and early heart failure. American Journal of Cardiology 1992; 70(10):55C-61C. *Sample size less than 50 patients*

827. Clement JG, Bailey DG, Madill HD, et al. The acetylcholinesterase oxime reactivator HI-6 in man: pharmacokinetics and tolerability in combination with atropine. Biopharmaceutics & Drug Disposition 1995; 16(5):415-25. *Sample size less than 50 patients*

828. Cleveringa FGW, Welsing PMJ, van den Donk M, et al. Cost-effectiveness of the diabetes care protocol, a multifaceted computerized decision support diabetes management intervention that reduces cardiovascular risk. Diabetes Care 2010; 33(2):258-63. *Not CKD treatment*

829. Clifton GG, Cook ME, Poland M, et al. The renal function and blood pressure effects of dilevalol in the normotensive and hypertensive elderly. Journal of Clinical Pharmacology 1989; 29(7):603-8. *Sample size less than 50 patients*

830. Clifton GG, Cook ME, Wallin JD. Effects of dilevalol on renal function. American Journal of Cardiology 1989; 63(19):75I-8I. *Sample size less than 50 patients*

831. Clyne N, Jogestrand T. Effect of erythropoietin treatment on physical exercise capacity and on renal function in predialytic uremic patients. Nephron 1992; 60(4):390-6. *Not early CKD*

832. Coburn JW, Maung HM. Use of active vitamin D sterols in patients with chronic kidney disease, stages 3 and 4. Kidney International - Supplement 2003; (85):S49-53. *Not early CKD*

833. Coburn JW, Maung HM, Elangovan L, et al. Doxercalciferol safely suppresses PTH levels in patients with secondary hyperparathyroidism associated with chronic kidney disease stages 3 and 4. American Journal of Kidney Diseases 2004; 43(5):877-90. *Not CKD treatment*

834. Coca A. Manidipine plus delapril in patients with Type 2 diabetes and hypertension: reducing cardiovascular risk and end-organ damage. Expert Review of Cardiovascular Therapy 2007; 5(2):147-59. *Not RCT or controlled trial*

835. Coca SG. Acute kidney injury in elderly persons. American Journal of Kidney Diseases 2010 Jul; 56(1):122-31. *Not RCT or controlled trial*

836. Coca SG. Long-term outcomes of acute kidney injury. Current Opinion in Nephrology & Hypertension 2010 May; 19(3):266-72. *Not RCT or controlled trial*

837. Cochrane R, Regan L. Undetected gynaecological disorders in women with renal disease. Human Reproduction 1997; 12(4):667-70. *Not early CKD*

838. Coco M, Glicklich D, Faugere MC, et al. Prevention of bone loss in renal transplant recipients: a prospective, randomized trial of intravenous pamidronate. Journal of the American Society of Nephrology 2003; 14(10):2669-76. *Not early CKD*

839. Cody J, Daly C, Campbell M, et al. Recombinant human erythropoietin for chronic renal failure anaemia in pre-dialysis patients. Cochrane Database of Systematic Reviews 2001; (4):CD003266. *Not CKD treatment*

840. Cody J, Daly C, Campbell M, et al. Recombinant human erythropoietin for chronic renal failure anaemia in pre-dialysis patients. Cochrane Database of Systematic Reviews 2005; (3):CD003266. *Not relevant to key questions*

841. Coen G, Mazzaferro S, Bonucci E, et al. Bone GLA protein in predialysis chronic renal failure. Effects of 1,25(OH)2D3 administration in a long-term follow-up. Kidney International 1985; 28(5):783-90. *Sample size less than 50 patients*

842. Coggins CH, Breyer Lewis J, Caggiula AW, et al. Differences between women and men with chronic renal disease. Nephrology Dialysis Transplantation 1998; 13(6):1430-7. *Not relevant to key questions*

843. Coggins CH, Dwyer JT, Greene T, et al. Serum lipid changes associated with modified protein diets: results from the feasibility phase of the Modification of Diet in Renal Disease Study. American Journal of Kidney Diseases 1994; 23(4):514-23. *Not RCT or controlled trial*

844. Cogliati AA, Vellutini R, Nardini A, et al. Fenoldopam infusion for renal protection in high-risk cardiac surgery patients: a randomized clinical study. Journal of Cardiothoracic & Vascular Anesthesia 2007; 21(6):847-50. *Not RCT or controlled trial*

845. Cohen AF, Harkin N, Posner J. Cardiovascular effects of a novel enkephalin analogue, 443C81, in humans. Journal of Cardiovascular Pharmacology 1990; 16(3):455-60. *Not CKD treatment*

846. Cohen D, Dodds R, Viberti G. Effect of protein restriction in insulin dependent diabetics at risk of nephropathy. British Medical Journal Clinical Research Ed. 1987; 294(6575):795-8. *Sample size less than 50 patients*

847. Cohen E, Hafner R, Rotenberg Z, et al. Comparison of ketorolac and diclofenac in the treatment of renal colic. European Journal of Clinical Pharmacology 1998; 54(6):455-8. *Not CKD treatment*

848. Cohen EP, Irving AA, Drobyski WR, et al. Captopril to mitigate chronic renal failure after hematopoietic stem cell transplantation: a randomized controlled trial. International Journal of Radiation Oncology, Biology, Physics 2008; 70(5):1546-51. *Not CKD treatment*

849. Cohen JA, Jeffers BW, Stabler S, et al. Increasing homocysteine levels and diabetic autonomic neuropathy. Autonomic Neuroscience-Basic & Clinical 2001; 87(2-3):268-73. *Not early CKD*

850. Cohen SD, Norris L, Acquaviva K, et al. Screening, diagnosis, and treatment of depression in patients with end-stage renal disease. Clinical Journal of The American Society of Nephrology: CJASN 2007; 2(6):1332-42. *Not relevant to key questions*

851. Cole RS, Palfrey EL, Smith SE, et al. Indomethacin as prophylaxis against ureteral colic following extracorporeal shock wave lithotripsy. Journal of Urology 1989; 141(1):9-12. *Not CKD treatment*

852. Collins AC, Vincent J, Newall RG, et al. An aid to the early detection and management of diabetic nephropathy: assessment of a new point of care microalbuminuria system in the diabetic clinic. Diabetic Medicine 2001; 18(11):928-32. *Not CKD treatment*

853. Colson P, Capdevilla X, Barlet H, et al. Effects of halothane and isoflurane on transient renal dysfunction associated with infrarenal aortic cross-clamping. Journal of Cardiothoracic & Vascular Anesthesia 1992; 6(3):295-8. *Not CKD treatment*

854. Colson P, Capdevilla X, Cuchet D, et al. Does choice of the anesthetic influence renal function during infrarenal aortic surgery? Anesthesia & Analgesia 1992; 74(4):481-5. *Not CKD treatment*

855. Colson P, Ribstein J, Mimran A, et al. Effect of angiotensin converting enzyme inhibition on blood pressure and renal function during open heart surgery. Anesthesiology 1990; 72(1):23-7. *Not CKD treatment*

856. Colson P, Ribstein J, Seguin JR, et al. Mechanisms of renal hemodynamic impairment during infrarenal aortic cross-clamping. Anesthesia & Analgesia 1992; 75(1):18-23. *Not CKD treatment*

857. Coltamai L, Maillard M, Simon A, et al. Comparative vascular and renal tubular effects of angiotensin II receptor blockers combined with a thiazide diuretic in humans. Journal of Hypertension 2010 Mar; 28(3):520-6. *Follow-up less than 6 months*

858. Compton A. A practical cost analysis of bivalirudin. Pharmacotherapy 2002; 22(6 Pt 2):119S-27S. *Not early CKD*

859. Conant EF, Fox KR, Miller WT. Pulmonary edema as a complication of interleukin-2 therapy. AJR 1989; American Journal of Roentgenology. 152(4):749-52. *Sample size less than 50 patients*

860. Conen D, Buerkle G, Perruchoud AP, et al. Hypertension is an independent risk factor for contrast nephropathy after percutaneous coronary intervention. International Journal of Cardiology 2006; 110(2):237-41. *Sample size less than 50 patients*

861. Conen D, Glynn RJ, Buring JE, et al. Association of renin-angiotensin and endothelial nitric oxide synthase gene polymorphisms with blood pressure progression and incident hypertension: prospective cohort study. Journal of Hypertension 2008; 26(9):1780-6. *Not RCT or controlled trial*

862. Conil JM, Georges B, Fourcade O, et al. Intermittent administration of ceftazidime to burns patients: influence of glomerular filtration. International Journal of Clinical Pharmacology & Therapeutics 2007; 45(3):133-42. *Not RCT or controlled trial*

863. Connell JM, Whitworth JA, Davies DL, et al. Effects of ACTH and cortisol administration on blood pressure, electrolyte metabolism, atrial natriuretic peptide and renal function in normal man. Journal of Hypertension 1987; 5(4):425-33. *Sample size less than 50 patients*

864. Constantiner M, Sehgal AR, Humbert L, et al. A dipstick protein and specific gravity algorithm accurately predicts pathological proteinuria. American Journal of Kidney Diseases 2005; 45(5):833-41. *Not relevant to key questions*

865. Conte G, Dal Canton A, Imperatore P, et al. Acute increase in plasma osmolality as a cause of hyperkalemia in patients with renal failure. Kidney International 1990; 38(2):301-7. *Sample size less than 50 patients*

866. Contreras F, de la Parte MA, Cabrera J, et al. Role of angiotensin II AT1 receptor blockers in the treatment of arterial hypertension. American Journal of Therapeutics 2003; 10(6):401-8. *Not CKD treatment*

867. Contreras G, Greene T, Agodoa LY, et al. Blood pressure control, drug therapy, and kidney disease. Hypertension 2005; 46(1):44-50. *Not early CKD*

868. Contreras I, Reiser KM, Martinez N, et al. Effects of aspirin or basic amino acids on collagen cross-links and complications in NIDDM. Diabetes Care 1997; 20(5):832-5. *Follow-up less than 6 months*

869. Conway SP, Pond MN, Watson A, et al. Intravenous colistin sulphomethate in acute respiratory exacerbations in adult patients with cystic fibrosis. Thorax 1997; 52(11):987-93. *Not CKD treatment*

870. Conzen PF, Kharasch ED, Czerner SFA, et al. Low-flow sevoflurane compared with low-flow isoflurane anesthesia in patients with stable renal insufficiency. Anesthesiology 2002; 97(3):578-84. *Not CKD treatment*

871. Conzen PF, Nuscheler M, Melotte A, et al. Renal function and serum fluoride concentrations in patients with stable renal insufficiency after anesthesia with sevoflurane or enflurane. Anesthesia & Analgesia 1995; 81(3):569-75. *Sample size less than 50 patients*

872. Cook DJ, Crowther MA. Thromboprophylaxis in the intensive care unit: focus on medical-surgical patients. Critical Care Medicine 2010; 38(2 Suppl):S76-82. *Not RCT or controlled trial*

873. Cook ME, Wallin JD, Clifton GG, et al. Renal function effects of dilevalol, a nonselective beta-adrenergic blocking drug with beta-2 agonist activity. Clinical Pharmacology & Therapeutics 1988; 43(4):393-9. *Not relevant to key questions*

874. Cook ME, Wallin JD, Thakur VD, et al. Comparative effects of nabumetone, sulindac, and ibuprofen on renal function. Journal of Rheumatology 1997; 24(6):1137-44. *Sample size less than 50 patients*

875. Cook RJ, Neerhut R, Thomas DG. Does combined epidural lignocaine and fentanyl provide better anaesthesia for ESWL than lignocaine alone? Anaesthesia & Intensive Care 1991; 19(3):357-64. *Not CKD treatment*

876. Cooper ME. Renal protection and angiotensin converting enzyme inhibition in microalbuminuric type I and type II diabetic patients. Journal of Hypertension - Supplement 1996; 14(6):S11-4. *Not RCT or controlled trial*

877. Copley JB, Rosario R. Hypertension: a review and rationale of treatment. Disease-A-Month 2005; 51(10-11):548-614. *Follow-up less than 6 months*

878. Cordell WH, Larson TA, Lingeman JE, et al. Indomethacin suppositories versus intravenously titrated morphine for the treatment of ureteral colic. Annals of Emergency Medicine 1994; 23(2):262-9. *Not CKD treatment*

879. Cordell WH, Wright SW, Wolfson AB, et al. Comparison of intravenous ketorolac, meperidine, and both (balanced analgesia) for renal colic. Annals of Emergency Medicine 1996; 28(2):151-8. *Not CKD treatment*

880. Cordonnier DJ, Pinel N, Barro C, et al. Expansion of cortical interstitium is limited by converting enzyme inhibition in type 2 diabetic patients with glomerulosclerosis. The Diabiopsies Group. Journal of the American Society of Nephrology 1999; 10(6):1253-63. *Sample size less than 50 patients*

881. Coresh J, Astor BC, McQuillan G, et al. Calibration and random variation of the serum creatinine assay as critical elements of using equations to estimate glomerular filtration rate. American Journal of Kidney Diseases 2002; 39(5):920-9. *Not RCT or controlled trial*

882. Coresh J, Toto RD, Kirk KA, et al. Creatinine clearance as a measure of GFR in screenees for the African-American Study of Kidney Disease and Hypertension pilot study. American Journal of Kidney Diseases 1998; 32(1):32-42. *Not CKD treatment*

883. Cornish SM, Candow DG, Jantz NT, et al. Conjugated linoleic acid combined with creatine monohydrate and whey protein supplementation during strength training. International Journal of Sport Nutrition & Exercise Metabolism 2009; 19(1):79-96. *Not CKD treatment*

884. Cortes-Sanabria L, Cabrera-Pivaral CE, Cueto-Manzano AM, et al. Improving care of patients with diabetes and CKD: a pilot study for a cluster-randomized trial. American Journal of Kidney Diseases 2008; 51(5):777-88. *Not CKD treatment*

885. Cosenzi A, Carraro M, Sacerdote A, et al. Nifedipine reduces postexercise proteinuria in young volunteers. Renal Physiology & Biochemistry 1995; 18(6):306-10. *Sample size less than 50 patients*

886. Cosgrove SE, Vigliani GA, Fowler VG, Jr., et al. Initial low-dose gentamicin for Staphylococcus aureus bacteremia and endocarditis is nephrotoxic. Clinical Infectious Diseases 2009; 48(6):713-21. *Not RCT or controlled trial*

887. Cosman F, Nieves J, Herbert J, et al. High-dose glucocorticoids in multiple sclerosis patients exert direct effects on the kidney and skeleton. Journal of Bone & Mineral Research 1994; 9(7):1097-105. *Not CKD treatment*

888. Costa P, Ottino GM, Matani A, et al. Low-dose dopamine during cardiopulmonary bypass in patients with renal dysfunction. Journal of Cardiothoracic Anesthesia 1990; 4(4):469-73. *Sample size less than 50 patients*

889. Costa S, Nucci M. Can we decrease amphotericin nephrotoxicity? Current Opinion in Critical Care 2001; 7(6):379-83. *Not early CKD*

890. Costello-Boerrigter LC, Smith WB, Boerrigter G, et al. Vasopressin-2-receptor antagonism augments water excretion without changes in renal hemodynamics or sodium and potassium excretion in human heart failure. American Journal of Physiology - Renal Physiology 2006; 290(2):F273-8. *Sample size less than 50 patients*

891. Cotter G, Dittrich HC, Weatherley BD, et al. The PROTECT pilot study: a randomized, placebo-controlled, dose-finding study of the adenosine A1 receptor antagonist rolofylline in patients with acute heart failure and renal impairment. Journal of Cardiac Failure 2008; 14(8):631-40. *Not CKD treatment*

892. Cotter G, Metra M, Weatherley BD, et al. Physician-determined worsening heart failure: a novel definition for early worsening heart failure in patients hospitalized for acute heart failure--association with signs and symptoms, hospitalization duration, and 60-day outcomes. Cardiology 2010; 115(1):29-36. *Not CKD treatment*

893. Cotter G, Weissgarten J, Metzkor E, et al. Increased toxicity of high-dose furosemide versus low-dose dopamine in the treatment of refractory congestive heart failure. Clinical Pharmacology & Therapeutics 1997; 62(2):187-93. *Sample size less than 50 patients*

894. Courtney AE, Maxwell AP. Critiques of clinical guidelines in nephrology: anaemia. Nephron 2008; 110(2):c115-25. *Not CKD treatment*

895. Courtney MJ, Pannu N. Calcific uremic arteriolopathy should be treated conservatively. Seminars in Dialysis 2010 Jan-Feb; 23(1):34-7. *Not RCT or controlled trial*

896. Couverchel L, Maugars Y, Prost A. Outcomes of thirty-four rheumatoid arthritis patients with renal amyloidosis, including twelve given alkylating agents. Revue du Rhumatisme 1995; 62(2):79-85. *Not RCT or controlled trial*

897. Cox JP, O'Boyle CA, Mee F, et al. The antihypertensive efficacy of verapamil in the elderly evaluated by ambulatory blood pressure measurement. Journal of Human Hypertension 1988; 2(1):41-7. *Sample size less than 50 patients*

898. Coyle LC, Rodriguez A, Jeschke RE, et al. Acetylcysteine In Diabetes (AID): a randomized study of acetylcysteine for the prevention of contrast nephropathy in diabetics. American Heart Journal 2006; 151(5):1032.e9-12. *Sample size less than 50 patients*

899. Coyne D, Acharya M, Qiu P, et al. Paricalcitol capsule for the treatment of secondary hyperparathyroidism in stages 3 and 4 CKD. American Journal of Kidney Diseases 2006; 47(2):263-76. *Not relevant to key questions*

900. Coyne DW. From anemia trials to clinical practice: understanding the risks and benefits when setting goals for therapy. Seminars in Dialysis 2008; 21(3):212-6. *Not relevant to key questions*

901. Coyne DW. Managing anemia in for-profit dialysis chains: when ethics and business conflict. Seminars in Dialysis 2009; 22(1):18-21. *Not CKD treatment*

902. Coyne T, Olson M, Bradham K, et al. Dietary satisfaction correlated with adherence in the Modification of Diet in Renal Disease Study. Journal of the American Dietetic Association 1995; 95(11):1301-6. *Not CKD treatment*

903. Craig JC. Can ACE inhibitor therapy prevent end-stage renal failure? Medical Journal of Australia 2001; 175(5):276. *Not RCT or controlled trial*

904. Craig JC, Barratt A, Cumming R, et al. Feasibility study of the early detection and treatment of renal disease by mass screening. Internal Medicine Journal 2002; 32(1-2):6-14. *Not RCT or controlled trial*

905. Craig JC, Irwig LM, Knight JF, et al. Does treatment of vesicoureteric reflux in childhood prevent end-stage renal disease attributable to reflux nephropathy? Pediatrics 2000; 105(6):1236-41. *Not adult population*

906. Craig KJ, Donovan K, Munnery M, et al. Identification and management of diabetic nephropathy in the diabetes clinic. Diabetes Care 2003; 26(6):1806-11. *Not CKD treatment*

907. Cravedi P, Remuzzi G. Treating the kidney to cure the heart. Kidney International - Supplement 2008; (111):S2-3. *Not CKD treatment*

908. Cravedi P, Ruggenenti P, Remuzzi G. Intensified inhibition of renin-angiotensin system: a way to improve renal protection? Current Hypertension Reports 2007; 9(5):430-6. *Not CKD treatment*

909. Cribier B, Couilliet D, Meyer P, et al. The severity of histopathological changes of leukocytoclastic vasculitis is not predictive of extracutaneous involvement. American Journal of Dermatopathology 1999; 21(6):532-6. *Not CKD treatment*

910. Crofford LJ. Specific cyclooxygenase-2 inhibitors: what have we learned since they came into widespread clinical use? Current Opinion in Rheumatology 2002; 14(3):225-30. *Not RCT or controlled trial*

911. Crofford OB. Diabetes control and complications. Annual Review of Medicine 1995; 46:267-79. *Not CKD treatment*

912. Cronberg S, Nordstrom L. Simplified monitoring of aminoglycoside treatment. Scandinavian Journal of Infectious Diseases Supplement 1990; 74:274-9. *Not CKD treatment*

913. Cronin RE. Contrast-induced nephropathy: pathogenesis and prevention. Pediatric Nephrology 2010 Feb; 25(2):191-204. *Not CKD treatment*

914. Crook ED, Preddie DC. Therapeutic controversies in hypertension management: angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers for diabetic nephropathy? A case for ACE inhibitors. Ethnicity & Disease 2002; 12(4):S3-49-52. *Not RCT or controlled trial*

915. Crook ED, Velusamy L. Are low target blood pressure goals justified in persons with diabetes mellitus? Current Hypertension Reports 2003; 5(3):231-8. *Not RCT or controlled trial*

916. Croom KF, Curran MP, Goa KL, et al. Irbesartan: a review of its use in hypertension and in the management of diabetic nephropathy. Drugs 2004; 64(9):999-1028. *Not RCT or controlled trial*

917. Crowe AV, Howse M, Vinjamuri S, et al. The antiproteinuric effect of losartan is systemic blood pressure dependent. Nephrology Dialysis Transplantation 2003; 18(10):2160-4. *Sample size less than 50 patients*

918. Crowther MA, Cook DJ. Preventing venous thromboembolism in critically ill patients. Seminars in Thrombosis & Hemostasis 2008; 34(5):469-74. *Not CKD treatment*

919. Cruickshank JK, Anderson NM, Wadsworth J, et al. Treating hypertension in black compared with white non-insulin dependent diabetics: a double blind trial of verapamil and metoprolol. BMJ 1988; 297(6657):1155-9. *Follow-up less than 6 months*

920. Cruickshanks KJ, Ritter LL, Klein R, et al. The association of microalbuminuria with diabetic retinopathy. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. Ophthalmology 1993; 100(6):862-7. *Not RCT or controlled trial*

921. Cserti C, Haspel R, Stowell C, et al. Light-chain removal by plasmapheresis in myeloma-associated renal failure. Transfusion 2007; 47(3):511-4. *Not RCT or controlled trial*

922. Cuculich PS, Sanchez JM, Kerzner R, et al. Poor prognosis for patients with chronic kidney disease despite ICD therapy for the primary prevention of sudden death. Pacing & Clinical Electrophysiology 2007; 30(2):207-13. *Sample size less than 50 patients*

923. Cummings DM, Amadio P, Jr., Nettler S, et al. Office-based evaluation of renal function in elderly patients receiving nonsteroidal anti-inflammatory drugs. Journal of the American Board of Family Practice 1988; 1(2):77-80. *Follow-up less than 6 months*

924. Cummings MH, Watts GF, Tavakolian A, et al. Prevalence of microalbuminuria, lipoprotein (a) and coronary artery disease in the lipid clinic. Journal of Clinical Pathology 1996; 49(1):19-23. *Not RCT or controlled trial*

925. Cunningham J, Danese M, Olson K, et al. Effects of the calcimimetic cinacalcet HCl on cardiovascular disease, fracture, and health-related quality of life in secondary hyperparathyroidism. Kidney International 2005; 68(4):1793-800. *Sample size less than 50 patients*

926. Cuocolo A, Volpe M, Mele AF, et al. Effects of atrial natriuretic peptide on glomerular filtration rate in essential hypertension: a radionuclide study. European Journal of Nuclear Medicine 1991; 18(1):32-7. *Sample size less than 50 patients*

927. Curry C, Kelly AM. Intravenous tenoxicam for the treatment of renal colic. New Zealand Medical Journal 1995; 108(1001):229-30. *Not CKD treatment*

928. Curtis JJ, Laskow DA, Jones PA, et al. Captopril-induced fall in glomerular filtration rate in cyclosporine-treated hypertensive patients. Journal of the American Society of Nephrology 1993; 3(9):1570-4. *Follow-up less than 6 months*

929. Curtis JR. Interventions in chronic renal failure. BMJ 1990; 301(6753):622-4. *Not RCT or controlled trial*

930. Curtis JR. Randomised controlled trial of hydroquinine in muscle cramps. Lancet 1997; 349(9061):1325; author reply 6. *Not RCT or controlled trial*

931. Curtiss FR. Antihypertensive drug effects on renal function and myocardial infarction and implications of the ALLHAT study results. Journal of Managed Care Pharmacy 2003; 9(1):93-4. *Not CKD treatment*

932. Curtiss FR, Fairman KA. No TREATment with darbepoetin dosed to hemoglobin 13 grams per deciliter in type 2 diabetes with pre-dialysis chronic kidney disease--safety warnings for erythropoiesis-stimulating agents. Journal of Managed Care Pharmacy 2009; 15(9):759-65. *Not RCT or controlled trial*

933. Cushner HM, Copley JB, Lindberg JS, et al. Calcium citrate, a nonaluminum-containing phosphate-binding agent for treatment of CRF.[Erratum appears in Kidney Int 1988 May;33(5):1047]. Kidney International 1988; 33(1):95-9. *Follow-up less than 6 months*

934. Cusson JR, du Souich P, Le Morvan P, et al. Effect of ketoprofen on blood pressure, endocrine and renal responses to chronic dosing with captopril in patients with essential hypertension. Blood Pressure 1992; 1(3):162-7. *Sample size less than 50 patients*

935. Czapla K, Rodger RS, Halls DJ, et al. Ranitidine reduces aluminium toxicity in patients with renal failure. Nephrology Dialysis Transplantation 1992; 7(12):1246-8. *Not CKD treatment*

936. Czupryniak L, Pawlowski M, Saryusz-Wolska M, et al. Circadian blood pressure variation and antihypertensive medication adjustment in normoalbuminuric type 2 diabetes patients. Kidney & Blood Pressure Research 2007; 30(3):182-6. *Sample size less than 50 patients*

937. Dahl-Jorgensen K, Bjoro T, Kierulf P, et al. Long-term glycemic control and kidney function in insulin-dependent diabetes mellitus. Kidney International 1992; 41(4):920-3. *Sample size less than 50 patients*

938. Dailey GE, Boden GH, Creech RH, et al. Effects of pulsatile intravenous insulin therapy on the progression of diabetic nephropathy. Metabolism: Clinical & Experimental 2000; 49(11):1491-5. *Sample size less than 50 patients*

939. Dal Canton A, Fuiano G, Conte G, et al. Mechanism of increased plasma urea after diuretic therapy in uraemic patients. Clinical Science 1985; 68(3):255-61. *Follow-up less than 6 months*

940. Dalla Vestra M, Pozza G, Mosca A, et al. Effect of lercanidipine compared with ramipril on albumin excretion rate in hypertensive Type 2 diabetic patients with microalbuminuria: DIAL study (diabete, ipertensione, albuminuria, lercanidipina). Diabetes, Nutrition & Metabolism - Clinical & Experimental 2004; 17(5):259-66. *Follow-up less than 6 months*

941. Dalla Vestra M, Simioni N, Masiero A. Aliskiren: a new inhibitor of renin-angiotensin aldosterone system activity. Minerva Endocrinologica 2009 Dec; 34(4):333-8. *Not RCT or controlled trial*

942. Dalton RN, Chetty R, Stuart M, et al. Effects of the Src inhibitor saracatinib (AZD0530) on renal function in healthy subjects. Anticancer Research 2010 Jul; 30(7):2935-42. *Not early CKD*

943. Damasceno A, Santos A, Pestana M, et al. Acute hypotensive, natriuretic, and hormonal effects of nifedipine in salt-sensitive and salt-resistant black normotensive and hypertensive subjects. Journal of Cardiovascular Pharmacology 1999; 34(3):346-53. *Sample size less than 50 patients*

944. D'Ambra MN, Akins CW, Blackstone EH, et al. Aprotinin in primary valve replacement and reconstruction: a multicenter, double-blind, placebo-controlled trial. Journal of Thoracic & Cardiovascular Surgery 1996; 112(4):1081-9. *Not CKD treatment*

945. D'Ambrosio G, Filippi A, Labriola R, et al. Identification of patients with asymptomatic left ventricular dysfunction: 'real practice' results in primary care. Family Practice 2010 Aug; 27(4):359-62. *Not early CKD*

946. D'Amico G, Gentile MG. Pharmacological and dietary treatment of lipid abnormalities in nephrotic patients. Kidney International - Supplement 1991; 31:S65-9. *Not RCT or controlled trial*

947. D'Amico G, Gentile MG. Effect of dietary manipulation on the lipid abnormalities and urinary protein loss in nephrotic patients. Mineral & Electrolyte Metabolism 1992; 18(2-5):203-6. *Sample size less than 50 patients*

948. Damman K, Navis G, Voors AA, et al. Worsening renal function and prognosis in heart failure: systematic review and meta-analysis. Journal of Cardiac Failure 2007; 13(8):599-608. *Sample size less than 50 patients*

949. Damman K, Voors AA, Hillege HL, et al. Congestion in chronic systolic heart failure is related to renal dysfunction and increased mortality. European Journal of Heart Failure 2010 Sep; 12(9):974-82. *Not CKD treatment*

950. Dana R, Kachhwaha VS. Comparison of oral and intravenous hydration and diuretic, choice for protecting cisplatin induced nephrotoxicity. Indian Journal of Cancer 1996; 33(4):168-70. *Not CKD treatment*

951. Darko W, Medicis JJ, Smith A, et al. Mississippi mud no more: cost-effectiveness of pharmacokinetic dosage adjustment of vancomycin to prevent nephrotoxicity. Pharmacotherapy 2003; 23(5):643-50. *Not CKD treatment*

952. Darling JR, Murray JM, McBride DR, et al. Serum glutathione S-transferase concentrations and creatinine clearance after sevoflurane anaesthesia. Anaesthesia 1997; 52(2):121-6. *Not CKD treatment*

953. Darragh AS. The effects of isoxicam and piroxicam on renal function in healthy subjects. British Journal of Clinical Practice 1985; 39(4):144-7. *Not early CKD*

954. Dasgupta A, Steinhubl SR, Bhatt DL, et al. Clinical outcomes of patients with diabetic nephropathy randomized to clopidogrel plus aspirin versus aspirin alone (a post hoc analysis of the clopidogrel for high atherothrombotic risk and ischemic stabilization, management, and avoidance [CHARISMA] trial). American Journal of Cardiology 2009; 103(10):1359-63. *Not CKD treatment*

955. Daugirdas JT. Proposed controlled trials of phosphate reduction in CKD: which whey should we go? Kidney International 2010 May; 77(10):929-30; author reply 30. *Not RCT or controlled trial*

956. Daumit GL, Hermann JA, Coresh J, et al. Use of cardiovascular procedures among black persons and white persons: a 7-year nationwide study in patients with renal disease. Annals of Internal Medicine 1999; 130(3):173-82. *Not RCT or controlled trial*

957. Daumit GL, Hermann JA, Powe NR. Relation of gender and health insurance to cardiovascular procedure use in persons with progression of chronic renal disease. Medical Care 2000; 38(4):354-65. *Not early CKD*

958. Daumit GL, Powe NR. Factors influencing access to cardiovascular procedures in patients with chronic kidney disease: race, sex, and insurance. Seminars in Nephrology 2001; 21(4):367-76. *Not RCT or controlled trial*

959. Davidson IJ. Renal impact of fluid management with colloids: a comparative review. European Journal of Anaesthesiology 2006; 23(9):721-38. *Follow-up less than 6 months*

960. Davidson MB, Karlan VJ, Hair TL. Effect of a pharmacist-managed diabetes care program in a free medical clinic. American Journal of Medical Quality 2000; 15(4):137-42. *Sample size less than 50 patients*

961. Davidson MB, Wong A, Hamrahian AH, et al. Effect of spironolactone therapy on albuminuria in patients with type 2 diabetes treated with angiotensin-converting enzyme inhibitors. Endocrine Practice 2008; 14(8):985-92. *Not RCT or controlled trial*

962. Davis KL, Nappi JM. The cardiovascular effects of eplerenone, a selective aldosterone-receptor antagonist. Clinical Therapeutics 2003; 25(11):2647-68. *Not relevant to key questions*

963. Davis ME, Pemberton CJ, Yandle TG, et al. Urocortin 2 infusion in healthy humans: hemodynamic, neurohormonal, and renal responses. Journal of the American College of Cardiology 2007; 49(4):461-71. *Not relevant to key questions*

964. Davis ME, Pemberton CJ, Yandle TG, et al. Urocortin 2 infusion in human heart failure. European Heart Journal 2007; 28(21):2589-97. *Not early CKD*

965. de Boer IH, Kestenbaum B. Vitamin D in chronic kidney disease: is the jury in? Kidney International 2008; 74(8):985-7. *Not CKD treatment*

966. de Brito-Ashurst I, Varagunam M, Raftery MJ, et al. Bicarbonate supplementation slows progression of CKD and improves nutritional status. Journal of the American Society of Nephrology 2009; 20(9):2075-84. *Not CKD treatment*

967. De Caprio L, De Rosa ML, Di Palma A, et al. Regression of left ventricular hypertrophy and improvement of renal hemodynamics in hypertensive patients treated with quinapril. Cardiovascular Drugs & Therapy 1994; 8(5):735-40. *Follow-up less than 6 months*

968. De Cesaris R, Ranieri G, Andriani A, et al. Effects of benazepril and nicardipine on microalbuminuria in normotensive and hypertensive patients with diabetes. Clinical Pharmacology & Therapeutics 1996; 60(4):472-8. *Not relevant to key questions*

969. De Cesaris R, Ranieri G, Filitti V, et al. Effects of atenolol and enalapril on kidney function in hypertensive diabetic patients. Journal of Cardiovascular Pharmacology 1993; 22(2):208-14. *Sample size less than 50 patients*

970. De Cosmo S, Earle K, Morocutti A, et al. Glucose-induced changes in renal haemodynamics in proteinuric type 1 (insulin-dependent) diabetic patients: inhibition by acetylsalicilic acid infusion. Diabetologia 1993; 36(7):622-7. *Sample size less than 50 patients*

971. De Cosmo S, Motterlini N, Prudente S, et al. Impact of the PPAR-gamma2 Pro12Ala polymorphism and ACE inhibitor therapy on new-onset microalbuminuria in type 2 diabetes: evidence from BENEDICT. Diabetes 2009; 58(12):2920-9. *Not CKD treatment*

972. de Denus S, Tardif J-C, White M, et al. Temporal variations in hematocrit values in patients with left ventricular dysfunction: Relationship with cause-specific mortality and morbidity and optimal monitoring--further insights from SOLVD. Canadian Journal of Cardiology 2008; 24(1):45-8. *Not CKD treatment*

973. De Feo ML, La Villa G, Lazzeri C, et al. Urinary endothelin-1 excretion is enhanced by low-dose infusion of brain natriuretic peptide in normal humans. Hypertension 1997; 29(1 Pt 1):70-4. *Sample size less than 50 patients*

974. de Gaetano G, Bucchi F, Gambino MC, et al. Does oral aspirin spare the kidney? Lancet 1986; 1(8483):736. *Not RCT or controlled trial*

975. de Galan BE, Perkovic V, Ninomiya T, et al. Lowering blood pressure reduces renal events in type 2 diabetes. Journal of the American Society of Nephrology 2009; 20(4):883-92. *Follow-up less than 6 months*

976. de Graeff PA, Kingma JH, Viersma JW, et al. Acute and chronic effects of ramipril and captopril in congestive heart failure. International Journal of Cardiology 1989; 23(1):59-67. *Sample size less than 50 patients*

977. De Jager J, Kooy A, Lehert P, et al. Effects of short-term treatment with metformin on markers of endothelial function and inflammatory activity in type 2 diabetes mellitus: a randomized, placebo-controlled trial. Journal of Internal Medicine 2005; 257(1):100-9. *Follow-up less than 6 months*

978. De Jong PE, Navis G, de Zeeuw D. Renoprotective therapy: titration against urinary protein excretion. Lancet 1999; 354(9176):352-3. *Not RCT or controlled trial*

979. de la Rosette JJMCH, Tsakiris P, Ferrandino MN, et al. Beyond prone position in percutaneous nephrolithotomy: a comprehensive review. European Urology 2008; 54(6):1262-9. *Not RCT or controlled trial*

980. de La Sierra A, Ruilope LM. Treatment of hypertension in diabetes mellitus. Current Hypertension Reports 2000; 2(3):335-42. *Not RCT or controlled trial*

981. de Lasson L, Hansen HE, Juhl B, et al. A randomised, clinical study of the effect of low-dose dopamine on central and renal haemodynamics in infrarenal aortic surgery.[Erratum appears in Eur J Vasc Endovasc Surg 1997 Oct;14(4):323]. European Journal of Vascular & Endovascular Surgery 1995; 10(1):82-90. *Sample size less than 50 patients*

982. de Lasson L, Hansen HE, Juhl B, et al. Effect of felodipine on renal function and vasoactive hormones in infrarenal aortic surgery. British Journal of Anaesthesia 1997; 79(6):719-25. *Sample size less than 50 patients*

983. de Leeuw PW. Renal function in the elderly: results from the European Working Party on High Blood Pressure in the Elderly trial. American Journal of Medicine 1991; 90(3A):45S-9S. *Not CKD treatment*

984. de Leeuw PW, Ruilope LM, Palmer CR, et al. Clinical significance of renal function in hypertensive patients at high risk: results from the INSIGHT trial. Archives of Internal Medicine 2004; 164(22):2459-64. *Not RCT or controlled trial*

985. De Leeuw PW, Thijs L, Birkenhager WH, et al. Prognostic significance of renal function in elderly patients with isolated systolic hypertension: results from the Syst-Eur trial. Journal of the American Society of Nephrology 2002; 13(9):2213-22. *Not CKD treatment*

986. De Luca L, Tomai F, Verdoia M, et al. Evaluation and management of special subgroups after primary percutaneous coronary intervention. American Heart Journal 2010 Dec; 160(6 Suppl):S22-7. *Not CKD treatment*

987. de Mello VDF, Zelmanovitz T, Azevedo MJ, et al. Long-term effect of a chicken-based diet versus enalapril on albuminuria in type 2 diabetic patients with microalbuminuria. Journal of Renal Nutrition 2008; 18(5):440-7. *Not CKD treatment*

988. de Mello VDF, Zelmanovitz T, Perassolo MS, et al. Withdrawal of red meat from the usual diet reduces albuminuria and improves serum fatty acid profile in type 2 diabetes patients with macroalbuminuria. American Journal of Clinical Nutrition 2006; 83(5):1032-8. *Not RCT or controlled trial*

989. De Nicola L, Bellizzi V, Minutolo R, et al. Randomized, double-blind, placebo-controlled study of arginine supplementation in chronic renal failure. Kidney International 1999; 56(2):674-84. *Sample size less than 50 patients*

990. De Nicola L, Libetta C, Memoli B, et al. Acute renal and immunological effects of low-dose cyclosporin in humans. Nephrology Dialysis Transplantation 1995; 10(9):1739-44. *Not CKD treatment*

991. de Oliveira MM, Conti CF, Valbuza JS, et al. The pharmacological treatment for uremic restless legs syndrome: evidence-based review. Movement Disorders 2010 Jul 30; 25(10):1335-42. *Not early CKD*

992. de Pablos-Velasco PL, Pazos Toral F, Esmatjes JE, et al. Losartan titration versus diuretic combination in type 2 diabetic patients. Journal of Hypertension 2002; 20(4):715-9. *Follow-up less than 6 months*

993. De Rosa ML, Cardace P, Rossi M, et al. Comparative effects of chronic ACE inhibition and AT1 receptor blocked losartan on cardiac hypertrophy and renal function in hypertensive patients. Journal of Human Hypertension 2002; 16(2):133-40. *Not early CKD*

994. De Rosa ML, de Cristofaro A, Rossi M, et al. Irbesartan effects on renal function in patients with renal impairment and hypertension: a drug-withdrawal study. Journal of Cardiovascular Pharmacology 2001; 38(3):482-9. *Not CKD treatment*

995. De Rosa ML, Maddaluno G, Lionetti F, et al. Effects of enalapril and isradipine alone and in combination on blood pressure, renal function and echocardiographic parameters in mild hypertension. International Journal of Cardiology 2000; 74(1):77-84. *Not early CKD*

996. de Saint-Aurin RG, Kloeckner M, Annane D. Crystalloids versus colloids for fluid resuscitation in critically-ill patients. Acta Clinica Belgica - Supplementum 2007; (2):412-6. *Not CKD treatment*

997. De Santo NG, Anastasio P, Spitali L, et al. Renal reserve is normal in adults born with unilateral renal agenesis and is not related to hyperfiltration or renal failure. Mineral & Electrolyte Metabolism 1997; 23(3-6):283-6. *Sample size less than 50 patients*

998. De Shong D, Mathis AS. Lessons in formulary management: the case of fenoldopam for radiographic contrast material-induced nephropathy. Pharmacotherapy 2004; 24(6):819-20; author reply 20. *Follow-up less than 6 months*

999. de Smet MD, Rubin BI, Whitcup SM, et al. Combined use of cyclosporine and ketoconazole in the treatment of endogenous uveitis. American Journal of Ophthalmology 1992; 113(6):687-90. *Not CKD treatment*

1000. de Vinuesa SG, Goicoechea M, Kanter J, et al. Insulin resistance, inflammatory biomarkers, and adipokines in patients with chronic kidney disease: effects of angiotensin II blockade. Journal of the American Society of Nephrology 2006; 17(12 Suppl 3):S206-12. *Follow-up less than 6 months*

1001. de Vries PJ, Verkooyen RP, Leguit P, et al. Prospective randomized study of once-daily versus thrice-daily netilmicin regimens in patients with intraabdominal infections. European Journal of Clinical Microbiology & Infectious Diseases 1990; 9(3):161-8. *Not CKD treatment*

1002. De Vriese AS, Coster RV, Smet J, et al. Linezolid-induced inhibition of mitochondrial protein synthesis. Clinical Infectious Diseases 2006; 42(8):1111-7. *Sample size less than 50 patients*

1003. De Vriese AS, Verbeke F, Schrijvers BF, et al. Is folate a promising agent in the prevention and treatment of cardiovascular disease in patients with renal failure? Kidney International 2002; 61(4):1199-209. *Not RCT or controlled trial*

1004. de Vroege R, Stooker W, van Oeveren W, et al. The impact of heparin coated circuits upon metabolism in vital organs: effect upon cerebral and renal function during and after cardiopulmonary bypass. ASAIO Journal 2005; 51(1):103-9. *Not CKD treatment*

1005. de Zeeuw D, Agarwal R, Amdahl M, et al. Selective vitamin D receptor activation with paricalcitol for reduction of albuminuria in patients with type 2 diabetes (VITAL study): a randomised controlled trial. Lancet 2010 Nov 6; 376(9752):1543-51. *Follow-up less than 6 months*

1006. de Zeeuw D, Gansevoort RT, Dullaart RP, et al. Angiotensin II antagonism improves the lipoprotein profile in patients with nephrotic syndrome. Journal of Hypertension - Supplement 1995; 13(1):S53-8. *Follow-up less than 6 months*

1007. de Zeeuw D, Remuzzi G, Parving H-H, et al. Albuminuria, a therapeutic target for cardiovascular protection in type 2 diabetic patients with nephropathy. Circulation 2004; 110(8):921-7. *Not relevant to key questions*

1008. de Zeeuw D, Remuzzi G, Parving H-H, et al. Proteinuria, a target for renoprotection in patients with type 2 diabetic nephropathy: lessons from RENAAL. Kidney International 2004; 65(6):2309-20. *Not CKD treatment*

1009. Decatris M, Santhanam S, O'Byrne K. Potential of interferon-alpha in solid tumours: part 1. Biodrugs 2002; 16(4):261-81. *Not CKD treatment*

1010. Dedov I, Shestakova M, Vorontzov A, et al. A randomized, controlled study of sulodexide therapy for the treatment of diabetic nephropathy. Nephrology Dialysis Transplantation 1997; 12(11):2295-300. *Sample size less than 50 patients*

1011. Deehan DJ, Heys SD, Broom J, et al. Pre-operative recombinant interleukin-2 and increased nephrotoxicity. Biochemical Society Transactions 1994; 22(4):425S. *Not RCT or controlled trial*

1012. Deehan DJ, Heys SD, Broom J, et al. Renal impairment associated with the pre-operative administration of recombinant interleukin-2. Clinical Science 1994; 87(5):513-8. *Follow-up less than 6 months*

1013. Deerochanawong C, Kornthong P, Phongwiratchai S, et al. Effects on urinary albumin excretion and renal function changes by delapril and manidipine in normotensive type 2 diabetic patients with microalbuminuria. Journal of the Medical Association of Thailand 2001; 84(2):234-41. *Sample size less than 50 patients*

1014. Deferrari G, Ravera M, Deferrari L, et al. Renal and cardiovascular protection in type 2 diabetes mellitus: angiotensin II receptor blockers. Journal of the American Society of Nephrology 2002; 13 Suppl 3:S224-9. *Not RCT or controlled trial*

1015. Degiannis D, Mowat AM, Tsakiris D, et al. The effect of random blood transfusions on immunoglobulin production by peripheral blood mononuclear cells from uraemic patients. Clinical & Experimental Immunology 1988; 73(1):155-9. *Not RCT or controlled trial*

1016. Dehne MG, Klein TF, Muhling J, et al. Impairment of renal function after cardiopulmonary bypass is not influenced by dopexamine. Renal Failure 2001; 23(2):217-30. *Not CKD treatment*

1017. Dehne MG, Muhling J, Sablotzki A, et al. Hydroxyethyl starch (HES) does not directly affect renal function in patients with no prior renal impairment. Journal of Clinical Anesthesia 2001; 13(2):103-11. *Not early CKD*

1018. Deicher R, Horl WH. Differentiating factors between erythropoiesis-stimulating agents: a guide to selection for anaemia of chronic kidney disease. Drugs 2004; 64(5):499-509. *Not CKD treatment*

1019. Deighan CJ, Caslake MJ, McConnell M, et al. Comparative effects of cerivastatin and fenofibrate on the atherogenic lipoprotein phenotype in proteinuric renal disease. Journal of the American Society of Nephrology 2001; 12(2):341-8. *Sample size less than 50 patients*

1020. Del Vecchio L, Pozzi M, Salvetti A, et al. Efficacy and tolerability of manidipine in the treatment of hypertension in patients with non-diabetic chronic kidney disease without glomerular disease. Prospective, randomized, double-blind study of parallel groups in comparison with enalapril. Journal of Nephrology 2004; 17(2):261-9. *Not relevant to key questions*

1021. Delahanty LM. Implications of the diabetes control and complications trial for renal outcomes and medical nutrition therapy. Journal of Renal Nutrition 1998; 8(2):59-63. *Not relevant to key questions*

1022. Delic-Brkljacic D, Galesic K, Ivanac G, et al. Influence of ATII blockers and calcium channel blockers on renal vascular resistance in patients with essential hypertension. Collegium Antropologicum 2009; 33(4):1129-38. *Not RCT or controlled trial*

1023. Delles C, Jacobi J, Schlaich MP, et al. Assessment of endothelial function of the renal vasculature in human subjects. American Journal of Hypertension 2002; 15(1 Pt 1):3-9. *Not early CKD*

1024. Delles C, Klingbeil AU, Schneider MP, et al. Direct comparison of the effects of valsartan and amlodipine on renal hemodynamics in human essential hypertension. American Journal of Hypertension 2003; 16(12):1030-5. *Sample size less than 50 patients*

1025. Delmas A, Leone M, Rousseau S, et al. Clinical review: Vasopressin and terlipressin in septic shock patients. Critical Care 2005; 9(2):212-22. *Not CKD treatment*

1026. DeMarco PJ, Weisman MH, Seibold JR, et al. Predictors and outcomes of scleroderma renal crisis: the high-dose versus low-dose D-penicillamine in early diffuse systemic sclerosis trial. Arthritis & Rheumatism 2002; 46(11):2983-9. *Not RCT or controlled trial*

1027. Demarie BK, Bakris GL. Effects of different calcium antagonists on proteinuria associated with diabetes mellitus. Annals of Internal Medicine 1990; 113(12):987-8. *Sample size less than 50 patients*

1028. Dember LM, Hawkins PN, Hazenberg BPC, et al. Eprodisate for the treatment of renal disease in AA amyloidosis. New England Journal of Medicine 2007; 356(23):2349-60. *Not RCT or controlled trial*

1029. Dengel DR, Brown MD, Ferrell RE, et al. A preliminary study on T-786C endothelial nitric oxide synthase gene and renal hemodynamic and blood pressure responses to dietary sodium. Physiological Research 2007; 56(4):393-401. *Not relevant to key questions*

1030. Denig P, Haaijer-Ruskamp FM, Zijsling DH. Impact of a drug bulletin on the knowledge, perception of drug utility, and prescribing behavior of physicians. DICP 1990; 24(1):87-93. *Not CKD treatment*

1031. Dennis VW. Decoding the modification of diet in renal disease study. Cleveland Clinic Journal of Medicine 1994; 61(4):254-7. *Not RCT or controlled trial*

1032. Deo R, Lin F, Vittinghoff E, et al. Kidney dysfunction and sudden cardiac death among women with coronary heart disease. Hypertension 2008; 51(6):1578-82. *Not CKD treatment*

1033. Depre M, Van Hecken A, Verbesselt R, et al. Pharmacokinetic and pharmacodynamic interaction between the lipoxygenase inhibitor MK-0591 and the cyclooxygenase inhibitor ibuprofen in man. International Journal of Clinical Pharmacology Research 1998; 18(2):53-61. *Sample size less than 50 patients*

1034. DeQuattro V, Lee DP. Equivalent reduction of proteinuria in hypertensives by either nifedipine GITS or enalapril: disparate effects on neurohormones and ambulatory blood pressure and the influence of salt. Cardiology 1997; 88 Suppl 3:38-42. *Sample size less than 50 patients*

1035. Deray G. Amphotericin B nephrotoxicity. Journal of Antimicrobial Chemotherapy 2002; 49 Suppl 1:37-41. *Not early CKD*

1036. Deray G, Bellin MF, Boulechfar H, et al. Nephrotoxicity of contrast media in high-risk patients with renal insufficiency: comparison of low- and high-osmolar contrast agents. American Journal of Nephrology 1991; 11(4):309-12. *Not CKD treatment*

1037. Deray G, Khayat D, Cacoub P, et al. The effects of diltiazem on methotrexate-induced nephrotoxicity. European Journal of Clinical Pharmacology 1989; 37(4):337-40. *Not CKD treatment*

1038. Derlatka P, Bidzinski M, Stachurska E, et al. Nadroparine activated fibrinolysis and improvement of glomerular filtration rate in patients with FIGO IIB-IIIB cervical cancer treated with radiochemotherapy. Gynecologic Oncology 2007; 104(1):24-31. *Not relevant to key questions*

1039. Despas F, Detis N, Dumonteil N, et al. Excessive sympathetic activation in heart failure with chronic renal failure: role of chemoreflex activation. Journal of Hypertension 2009; 27(9):1849-54. *Follow-up less than 6 months*

1040. Detrenis S, Meschi M, del Mar Jordana Sanchez M, et al. Contrast medium induced nephropathy in urological practice. Journal of Urology 2007; 178(4 Pt 1):1164-70. *Follow-up less than 6 months*

1041. Deyneli O, Yavuz D, Velioglu A, et al. Effects of ACE inhibition and angiotensin II receptor blockade on glomerular basement membrane protein excretion and charge selectivity in type 2 diabetic patients. Journal of the Renin-Angiotensin-Aldosterone System 2006; 7(2):98-103. *Not early CKD*

1042. Dhaene M, Sabot JP, Philippart Y, et al. Effects of acute protein loads of different sources on glomerular filtration rate. Kidney International - Supplement 1987; 22:S25-8. *Sample size less than 50 patients*

1043. D'Haens G, Lemmens L, Geboes K, et al. Intravenous cyclosporine versus intravenous corticosteroids as single therapy for severe attacks of ulcerative colitis. Gastroenterology 2001; 120(6):1323-9. *Not early CKD*

1044. Dharmarajan TS. Anemia and response to epoetin alfa: the cause of anemia matters! Journal of the American Geriatrics Society 2008; 56(8):1574-5. *Not relevant to key questions*

1045. Dharmarajan TS, Widjaja D. Adverse consequences with use of erythropoiesis-stimulating agents in anemia prompt release of guidelines to ensure safe use and maximize benefit. Geriatrics 2008; 63(6):13-29. *Not CKD treatment*

1046. Dhaun N, Macintyre IM, Melville V, et al. Blood pressure-independent reduction in proteinuria and arterial stiffness after acute endothelin-a receptor antagonism in chronic kidney disease. Hypertension 2009; 54(1):113-9. *Sample size less than 50 patients*

1047. Di Iorio B, Gaudiano G, Altieri C, et al. Aluminum urinary excretion in patients with chronic renal failure in treatment with conservative conventional therapy and with ketoanalogs: research on fasting patients and after a pharmacological load. Nephron 1995; 71(3):371-2. *Not CKD treatment*

1048. Di Iorio BR, Minutolo R, De Nicola L, et al. Supplemented very low protein diet ameliorates responsiveness to erythropoietin in chronic renal failure. Kidney International 2003; 64(5):1822-8. *Not early CKD*

1049. Di Lullo L, Addesse R, Comegna C, et al. Effects of fluvastatin treatment on lipid profile, C-reactive protein trend, and renal function in dyslipidemic patients with chronic renal failure. Advances in Therapy 2005; 22(6):601-12. *Sample size less than 50 patients*

1050. Di Mario U, Bacci S, Morano S, et al. Selective decrement of anionic immunoglobulin clearance after induced renal hemodynamic changes in diabetic patients. American Journal of Physiology 1992; 262(3 Pt 2):F381-8. *Not CKD treatment*

1051. Diabetes Prevention Program Research G. Changes in albumin excretion in the diabetes prevention program. Diabetes Care 2009; 32(4):720-5. *Not RCT or controlled trial*

1052. Diaz-Mitoma F, Harding GK, Louie TJ, et al. Prospective randomized comparison of imipenem/cilastatin and cefotaxime for treatment of lung, soft tissue, and renal infections. Reviews of Infectious Diseases 1985; 7 Suppl 3:S452-7. *Sample size less than 50 patients*

1053. Diaz-Sandoval LJ, Kosowsky BD, Losordo DW. Acetylcysteine to prevent angiography-related renal tissue injury (the APART trial). American Journal of Cardiology 2002; 89(3):356-8. *Not early CKD*

1054. Dick IM, St John A, Heal S, et al. The effect of estrogen deficiency on bone mineral density, renal calcium and phosphorus handling and calcitropic hormones in the rat. Calcified Tissue International 1996; 59(3):174-8. *Sample size less than 50 patients*

1055. Didjurgeit U, Kruse J, Schmitz N, et al. A time-limited, problem-orientated psychotherapeutic intervention in Type 1 diabetic patients with complications: a randomized controlled trial. Diabetic Medicine 2002; 19(10):814-21. *Sample size less than 50 patients*

1056. DiDomenico RJ, Eyrich HM. Did contrast nephropathyin RAPPID really occur? Journal of the American College of Cardiology 2003; 42(12):2167; author reply -9. *Not CKD treatment*

1057. Diercks GF, Janssen WM, van Boven AJ, et al. Rationale, design, and baseline characteristics of a trial of prevention of cardiovascular and renal disease with fosinopril and pravastatin in nonhypertensive, nonhypercholesterolemic subjects with microalbuminuria (the Prevention of REnal and Vascular ENdstage Disease Intervention Trial [PREVEND IT]). American Journal of Cardiology 2000; 86(6):635-8. *Not RCT or controlled trial*

1058. Dilek K, Usta M, Ersoy A, et al. Long-term effects of losartan on proteinuria and renal function in patients with renal amyloidosis. Scandinavian Journal of Urology & Nephrology 2002; 36(6):443-6. *Sample size less than 50 patients*

1059. Dilger K, Herrlinger C, Peters J, et al. Effects of celecoxib and diclofenac on blood pressure, renal function, and vasoactive prostanoids in young and elderly subjects. Journal of Clinical Pharmacology 2002; 42(9):985-94. *Not CKD treatment*

1060. Dillman RO. The clinical experience with interleukin-2 in cancer therapy. Cancer Biotherapy 1994; 9(3):183-209. *Not CKD treatment*

1061. Dillman RO, Wiemann M, Nayak SK, et al. Interferon-gamma or granulocyte-macrophage colony-stimulating factor administered as adjuvants with a vaccine of irradiated autologous tumor cells from short-term cell line cultures: a randomized phase 2 trial of the cancer biotherapy research group. Journal of Immunotherapy 2003; 26(4):367-73. *Not CKD treatment*

1062. Dimopoulos M, Alegre A, Stadtmauer EA, et al. The efficacy and safety of lenalidomide plus dexamethasone in relapsed and/or refractory multiple myeloma patients with impaired renal function. Cancer 2010 Aug 15; 116(16):3807-14. *Not CKD treatment*

1063. Dimopoulos MA, Richardson PG, Schlag R, et al. VMP (Bortezomib, Melphalan, and Prednisone) is active and well tolerated in newly diagnosed patients with multiple myeloma with moderately impaired renal function, and results in reversal of renal impairment: cohort analysis of the phase III VISTA study. Journal of Clinical Oncology 2009; 27(36):6086-93. *Not CKD treatment*

1064. Dinits-Pensy M, Forrest GN, Cross AS, et al. The use of vaccines in adult patients with renal disease. American Journal of Kidney Diseases 2005; 46(6):997-1011. *Not relevant to key questions*

1065. Dittrich HC, Gupta DK, Hack TC, et al. The effect of KW-3902, an adenosine A1 receptor antagonist, on renal function and renal plasma flow in ambulatory patients with heart failure and renal impairment. Journal of Cardiac Failure 2007; 13(8):609-17. *Not early CKD*

1066. Dittrich S, Kurschat K, Dahnert I, et al. Renal function after cardiopulmonary bypass surgery in cyanotic congenital heart disease. International Journal of Cardiology 2000; 73(2):173-9. *Not early CKD*

1067. Dittrich S, Kurschat K, Dahnert I, et al. Cyanotic nephropathy and use of non-ionic contrast agents during cardiac catherization in patients with cyanotic congenital heart disease. Cardiology in the Young 2000; 10(1):8-14. *Sample size less than 50 patients*

1068. Dixey JJ, Noormohamed FH, Lant AF, et al. The effects of naproxen and sulindac on renal function and their interaction with hydrochlorothiazide and piretanide in man. British Journal of Clinical Pharmacology 1987; 23(1):55-63. *Sample size less than 50 patients*

1069. Dixey JJ, Noormohamed FH, Lant AF, et al. Effect of maximal hydration on the renal responses to pretreatment with nonsteroidal anti-inflammatory drugs and probenecid in man. British Journal of Clinical Pharmacology 1988; 25(5):614-7. *Follow-up less than 6 months*

1070. Dixey JJ, Noormohamed FH, Pawa JS, et al. The influence of nonsteroidal anti-inflammatory drugs and probenecid on the renal response to and kinetics of piretanide in man. Clinical Pharmacology & Therapeutics 1988; 44(5):531-9. *Sample size less than 50 patients*

1071. Djabarouti S, Duffau P, Lazaro E, et al. Therapeutic drug monitoring of mycophenolate mofetil and enteric-coated mycophenolate sodium in patients with systemic lupus erythematosus. Expert Opinion on Pharmacotherapy 2010 Apr; 11(5):689-99. *Not CKD treatment*

1072. Doggrell SA. Sarpogrelate: cardiovascular and renal clinical potential. Expert Opinion on Investigational Drugs 2004; 13(7):865-74. *Not CKD treatment*

1073. Dogra G, Irish A, Chan D, et al. A randomized trial of the effect of statin and fibrate therapy on arterial function in CKD. American Journal of Kidney Diseases 2007; 49(6):776-85. *Not RCT or controlled trial*

1074. Dogra GK, Watts GF, Chan DC, et al. Statin therapy improves brachial artery vasodilator function in patients with Type 1 diabetes and microalbuminuria. Diabetic Medicine 2005; 22(3):239-42. *Not RCT or controlled trial*

1075. Doig JK, MacFadyen RJ, Sweet CS, et al. Haemodynamic and renal responses to oral losartan potassium during salt depletion or salt repletion in normal human volunteers. Journal of Cardiovascular Pharmacology 1995; 25(4):511-7. *Sample size less than 50 patients*

1076. Dolecek TA, Olson MB, Caggiula AW, et al. Registered dietitian time requirements in the Modification of Diet in Renal Disease Study. Journal of the American Dietetic Association 1995; 95(11):1307-12. *Not CKD treatment*

1077. Dolegowska B, Pikula E, Safranow K, et al. Metabolism of eicosanoids and their action on renal function during ischaemia and reperfusion: the effect of alprostadil. Prostaglandins Leukotrienes & Essential Fatty Acids 2006; 75(6):403-11. *Not RCT or controlled trial*

1078. Don BR, Kaysen GA, Hutchison FN, et al. The effect of angiotensin-converting enzyme inhibition and dietary protein restriction in the treatment of proteinuria. American Journal of Kidney Diseases 1991; 17(1):10-7. *Sample size less than 50 patients*

1079. Donadio C, Lucchesi A, Tramonti G, et al. Creatinine clearance can be predicted from plasma creatinine and body composition analysis by means of electrical bioimpedance. Renal Failure 1998; 20(2):285-93. *Not CKD treatment*

1080. Donadio C, Lucchesi A, Tramonti G, et al. Glomerular and tubular effects of contrast media diatrizoate and iopromide. Renal Failure 1996; 18(4):657-66. *Sample size less than 50 patients*

1081. Dones L, Wiltshaw E, Birkhead BG, et al. Towards an assessment of toxicity in the treatment of ovarian cancer. Cancer Chemotherapy & Pharmacology 1987; 20(3):213-8. *Not relevant to key questions*

1082. Dong F, Cheng J, Lin S, et al. The clinical research on serum cystatin-C alteration on stage II chronic kidney disease with gubenquduyishen decoction treatment. Journal of Ethnopharmacology 2010 Oct 5; 131(3):581-4. *Not CKD treatment*

1083. Donnelly R, Elliott HL, Meredith PA, et al. Clinical studies with the potassium channel activator cromakalim in normotensive and hypertensive subjects. Journal of Cardiovascular Pharmacology 1990; 16(5):790-5. *Sample size less than 50 patients*

1084. Donnelly R, Molyneaux LM, Willey KA, et al. Comparative effects of indapamide and captopril on blood pressure and albumin excretion rate in diabetic microalbuminuria. American Journal of Cardiology 1996; 77(6):26B-30B. *Follow-up less than 6 months*

1085. Donnelly S. Why is erythropoietin made in the kidney? The kidney functions as a 'critmeter' to regulate the hematocrit. Advances in Experimental Medicine & Biology 2003; 543:73-87. *Not CKD treatment*

1086. Donner KM, Hiltunen TP, Suonsyrja T, et al. CYP2C9 genotype modifies activity of the renin-angiotensin-aldosterone system in hypertensive men. Journal of Hypertension 2009; 27(10):2001-9. *Not CKD treatment*

1087. Doorenbos CJ, Iestra JA, Papapoulos SE, et al. Atrial natriuretic peptide and chronic renal effects of changes in dietary protein and sodium intake in man. Clinical Science 1990; 78(6):565-72. *Sample size less than 50 patients*

1088. Dorio PJ, Lee FT, Jr., Henseler KP, et al. Using a saline chaser to decrease contrast media in abdominal CT. AJR 2003; American Journal of Roentgenology. 180(4):929-34. *Not CKD treatment*

1089. Dorner GT, Pehamberger H, Kornek G, et al. Cisplatin-induced renal effects and thromboxane A2 receptor blockade. European Journal of Clinical Investigation 1997; 27(10):836-9. *Not CKD treatment*

1090. Dougados M, Awada H, Amor B. Cyclosporin in rheumatoid arthritis: a double blind, placebo controlled study in 52 patients. Annals of the Rheumatic Diseases 1988; 47(2):127-33. *Follow-up less than 6 months*

1091. Dougados M, Duchesne L, Awada H, et al. Assessment of efficacy and acceptability of low dose cyclosporin in patients with rheumatoid arthritis. Annals of the Rheumatic Diseases 1989; 48(7):550-6. *Not CKD treatment*

1092. Doughty RN, White HD. Carvedilol: use in chronic heart failure. Expert Review of Cardiovascular Therapy 2007; 5(1):21-31. *Not early CKD*

1093. Douglas JG, Agodoa L. ACE inhibition is effective and renoprotective in hypertensive nephrosclerosis: the African American Study of Kidney Disease and Hypertension (AASK) trial. Kidney International - Supplement 2003; (83):S74-6. *Not early CKD*

1094. Douglas K, O'Malley PG, Jackson JL. Meta-analysis: the effect of statins on albuminuria. Annals of Internal Medicine 2006; 145(2):117-24. *Sample size less than 50 patients*

1095. Drager LF, Andrade L, Barros de Toledo JF, et al. Renal effects of N-acetylcysteine in patients at risk for contrast nephropathy: decrease in oxidant stress-mediated renal tubular injury. Nephrology Dialysis Transplantation 2004; 19(7):1803-7. *Not relevant to key questions*

1096. Dragu R, Behar S, Sandach A, et al. Should primary percutaneous coronary intervention be the preferred method of reperfusion therapy for patients with renal failure and ST-elevation acute myocardial infarction? American Journal of Cardiology 2006; 97(8):1142-5. *Follow-up less than 6 months*

1097. Dreicer R. Locally advanced and metastatic bladder cancer. Current Treatment Options in Oncology 2001; 2(5):431-6. *Not early CKD*

1098. Drescher P, Pereira F, Will JA, et al. Nephrotoxicity from contrast media: attenuation with theophylline. Radiology 1995; 197(2):547-8. *Not RCT or controlled trial*

1099. Drion I. B-vitamin therapy for diabetic nephropathy. JAMA 2010 Aug 11; 304(6):636; author reply -7. *Not CKD treatment*

1100. Drueke TB, Landais P. Paricalcitol for treatment of secondary hyperparathyroidism in CKD patients. American Journal of Kidney Diseases 2006; 47(6):1083; author reply -4. *Not RCT or controlled trial*

1101. Druml W. Supplements of keto acids in patients with chronic renal failure--more than modulators of nitrogen economy. Wiener Klinische Wochenschrift 2001; 113(17-18):638-40. *Not relevant to key questions*

1102. Dugandzic RM, Sketris IS, Belitsky P, et al. Effect of coadministration of acyclovir and cyclosporine on kidney function and cyclosporine concentrations in renal transplant patients. DICP 1991; 25(3):316-7. *Not early CKD*

1103. Dullaart RP, Beusekamp BJ, Meijer S, et al. Long-term effects of linoleic-acid-enriched diet on albuminuria and lipid levels in type 1 (insulin-dependent) diabetic patients with elevated urinary albumin excretion. Diabetologia 1992; 35(2):165-72. *Sample size less than 50 patients*

1104. Dullaart RP, Beusekamp BJ, Meijer S, et al. Long-term effects of protein-restricted diet on albuminuria and renal function in IDDM patients without clinical nephropathy and hypertension. Diabetes Care 1993; 16(2):483-92. *Sample size less than 50 patients*

1105. Dumas M, de Gislain C, d'Athis P, et al. Evaluation of the effect of furosemide on ultrafilterable platinum kinetics in patients treated with cis-diamminedichloroplatinum. Cancer Chemotherapy & Pharmacology 1989; 23(1):37-40. *Sample size less than 50 patients*

1106. Dumas M, de Gislain C, d'Athis P, et al. Influence of hydration on ultrafilterable platinum kinetics and kidney function in patients treated with cis-diamminedichloroplatinum(II). Cancer Chemotherapy & Pharmacology 1990; 26(4):278-82. *Not CKD treatment*

1107. Dumler F. Dietary sodium intake and arterial blood pressure. Journal of Renal Nutrition 2009; 19(1):57-60. *Not CKD treatment*

1108. Dummer CD, Thome FS, Zingano B, et al. Acute effect of simvastatin on inflammation and oxidative stress in chronic kidney disease. Journal of Nephrology 2008; 21(6):900-8. *Sample size less than 50 patients*

1109. Dunn CJ, Markham A. Epoetin beta. A review of its pharmacological properties and clinical use in the management of anaemia associated with chronic renal failure. Drugs 1996; 51(2):299-318. *Not RCT or controlled trial*

1110. Duong MH, MacKenzie TA, Malenka DJ. N-acetylcysteine prophylaxis significantly reduces the risk of radiocontrast-induced nephropathy: comprehensive meta-analysis. Catheterization & Cardiovascular Interventions 2005; 64(4):471-9. *Sample size less than 50 patients*

1111. Dupont AG. Effects of carvedilol on renal function. European Journal of Clinical Pharmacology 1990; 38 Suppl 2:S96-100. *Follow-up less than 6 months*

1112. Dupont AG, Gerlo E, Van der Niepen P, et al. Renal pharmacodynamic effects of torasemide and furosemide in normal man. Arzneimittel-Forschung 1988; 38(1A):172-5. *Sample size less than 50 patients*

1113. Dupont AG, Van der Niepen P, Taeymans Y, et al. Effect of carvedilol on ambulatory blood pressure, renal hemodynamics, and cardiac function in essential hypertension. Journal of Cardiovascular Pharmacology 1987; 10 Suppl 11:S130-6. *Follow-up less than 6 months*

1114. Dupont AG, Van der Niepen P, Volckaert A, et al. Improved renal function during chronic lisinopril treatment in moderate to severe primary hypertension. Journal of Cardiovascular Pharmacology 1987; 10 Suppl 7:S148-50. *Sample size less than 50 patients*

1115. Dupuis J, Lalonde G, Bichet D, et al. Captopril does not prevent nitroglycerin tolerance in heart failure. Canadian Journal of Cardiology 1990; 6(7):281-6. *Not CKD treatment*

1116. Dural O, Kanbak M, Ciliv G, et al. Comparison of halothane, enflurane and isoflurane kidney effects through alanine aminopeptidase/urine creatinine values. Anaesthesia & Intensive Care 1995; 23(2):162-4. *Sample size less than 50 patients*

1117. Durand D, Ader JL, Rey JP, et al. Inducing hyperkalemia by converting enzyme inhibitors and heparin. Kidney International - Supplement 1988; 25:S196-7. *Sample size less than 50 patients*

1118. Duranteau J, Pussard E, Edouard A, et al. Flosequinan does not affect systemic and regional vascular responses to simulated orthostatic stress in healthy volunteers. British Journal of Clinical Pharmacology 1992; 34(3):207-14. *Not CKD treatment*

1119. Durham JD, Caputo C, Dokko J, et al. A randomized controlled trial of N-acetylcysteine to prevent contrast nephropathy in cardiac angiography. Kidney International 2002; 62(6):2202-7. *Not CKD treatment*

1120. Durie BGM, Kyle RA, Belch A, et al. Myeloma management guidelines: a consensus report from the Scientific Advisors of the International Myeloma Foundation. Hematology Journal 2003; 4(6):379-98. *Sample size less than 50 patients*

1121. Dussaule JC, Michel C, Peraldi MN, et al. Inhibition of neutral endopeptidase stimulates renal sodium excretion in patients with chronic renal failure. Clinical Science 1993; 84(1):31-9. *Sample size less than 50 patients*

1122. Dussol B, Morange S, Loundoun A, et al. A randomized trial of saline hydration to prevent contrast nephropathy in chronic renal failure patients. Nephrology Dialysis Transplantation 2006; 21(8):2120-6. *Not CKD treatment*

1123. Dyadyk AI, Bagriy AE, Lebed IA, et al. ACE inhibitors captopril and enalapril induce regression of left ventricular hypertrophy in hypertensive patients with chronic renal failure. Nephrology Dialysis Transplantation 1997; 12(5):945-51. *Not CKD treatment*

1124. Eadington DW, Freestone S, Waugh CJ, et al. Lithium pretreatment affects renal and systemic responses to angiotensin II infusion in normal man. Clinical Science 1992; 82(5):543-9. *Sample size less than 50 patients*

1125. Eadington DW, Frier BM, Swainson CP. Renal tubular responses to low-dose infusion of angiotensin II in type 1 diabetes mellitus; relation to chronic glycaemic control. Nephrology Dialysis Transplantation 1994; 9(9):1264-70. *Sample size less than 50 patients*

1126. Eadington DW, Swainson CP, Lee MR. Oral carbidopa has no effect on the renal response to angiotensin II in normal man. Clinical Science 1991; 80(2):149-54. *Sample size less than 50 patients*

1127. Easthope SE, Jarvis B. Candesartan cilexetil: an update of its use in essential hypertension. Drugs 2002; 62(8):1253-87. *Not relevant to key questions*

1128. Ebbehoj E, Arildsen H, Hansen KW, et al. Effects of metoprolol on QT interval and QT dispersion in Type 1 diabetic patients with abnormal albuminuria. Diabetologia 2004; 47(6):1009-15. *Not relevant to key questions*

1129. Ebbehoj E, Poulsen PL, Hansen KW, et al. Effects on heart rate variability of metoprolol supplementary to ongoing ACE-inhibitor treatment in Type I diabetic patients with abnormal albuminuria. Diabetologia 2002; 45(7):965-75. *Sample size less than 50 patients*

1130. Ebell MH. NSAIDs vs. opiates for pain in acute renal colic. American Family Physician 2004; 70(9):1682. *Sample size less than 50 patients*

1131. Ebert TJ, Arain SR. Renal responses to low-flow desflurane, sevoflurane, and propofol in patients. Anesthesiology 2000; 93(6):1401-6. *Not early CKD*

1132. Ebert TJ, Groban L, Muzi M, et al. ANP-mediated volume depletion attenuates renal responses in humans. American Journal of Physiology 1992; 263(6 Pt 2):R1303-8. *Sample size less than 50 patients*

1133. Ecder T. Influence of protein-restricted diets on proteinuria and endothelial dysfunction. Journal of Renal Nutrition 2009; 19(5 Suppl):S13-4. *Not RCT or controlled trial*

1134. Echevarria J, Seas C, Cruz M, et al. Oral rehydration solution to prevent nephrotoxicity of amphotericin B. American Journal of Tropical Medicine & Hygiene 2006; 75(6):1108-12. *Not RCT or controlled trial*

1135. Eckardt KU. Anaemia in end-stage renal disease: pathophysiological considerations. Nephrology Dialysis Transplantation 2001; 16 Suppl 7:2-8. *Not RCT or controlled trial*

1136. Eckardt KU, Cardiovascular risk Reduction by Early Anemia Treatment with Epoetin Beta T. The CREATE trial--building the evidence. Nephrology Dialysis Transplantation 2001; 16 Suppl 2:16-8. *Not CKD treatment*

1137. Edwards NC, Steeds RP, Ferro CJ, et al. The treatment of coronary artery disease in patients with chronic kidney disease. Qjm 2006; 99(11):723-36. *Not RCT or controlled trial*

1138. Edwards NC, Steeds RP, Stewart PM, et al. Effect of spironolactone on left ventricular mass and aortic stiffness in early-stage chronic kidney disease: a randomized controlled trial. Journal of the American College of Cardiology 2009; 54(6):505-12. *Not CKD treatment*

1139. Efrati S, Dishy V, Averbukh M, et al. The effect of N-acetylcysteine on renal function, nitric oxide, and oxidative stress after angiography. Kidney International 2003; 64(6):2182-7. *Not relevant to key questions*

1140. Egan B, Gleim G, Panish J. Use of losartan in diabetic patients in the primary care setting: review of the results in LIFE and RENAAL. Current Medical Research & Opinion 2004; 20(12):1909-17. *Not RCT or controlled trial*

1141. Eggers KM, Lagerqvist B, Venge P, et al. Prognostic value of biomarkers during and after non-ST-segment elevation acute coronary syndrome. Journal of the American College of Cardiology 2009; 54(4):357-64. *Not CKD treatment*

1142. Egleston BL, Wong Y-N. Sensitivity analysis to investigate the impact of a missing covariate on survival analyses using cancer registry data. Statistics in Medicine 2009; 28(10):1498-511. *Not CKD treatment*

1143. Eguchi A, Takei T, Yoshida T, et al. Combined cyclosporine and prednisolone therapy in adult patients with the first relapse of minimal-change nephrotic syndrome. Nephrology Dialysis Transplantation 2010; 25(1):124-9. *Follow-up less than 6 months*

1144. Ehrich JHH, Geerlings C, Zivicnjak M, et al. Steroid-resistant idiopathic childhood nephrosis: overdiagnosed and undertreated. Nephrology Dialysis Transplantation 2007; 22(8):2183-93. *Not RCT or controlled trial*

1145. Ehrlich M, Grabenwoger M, Cartes-Zumelzu F, et al. Operations on the thoracic aorta and hypothermic circulatory arrest: is aprotinin safe? Journal of Thoracic & Cardiovascular Surgery 1998; 115(1):220-5. *Sample size less than 50 patients*

1146. Eidemak I, Haaber AB, Feldt-Rasmussen B, et al. Exercise training and the progression of chronic renal failure. Nephron 1997; 75(1):36-40. *Sample size less than 50 patients*

1147. Eijkelkamp WBA, Zhang Z, Brenner BM, et al. Renal function and risk for cardiovascular events in type 2 diabetic patients with hypertension: the RENAAL and LIFE studies. Journal of Hypertension 2007; 25(4):871-6. *Not RCT or controlled trial*

1148. Eijkelkamp WBA, Zhang Z, Remuzzi G, et al. Albuminuria is a target for renoprotective therapy independent from blood pressure in patients with type 2 diabetic nephropathy: post hoc analysis from the Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) trial. Journal of the American Society of Nephrology 2007; 18(5):1540-6. *Not RCT or controlled trial*

1149. Eikelboom JW, Hankey GJ. Associations of homocysteine, C-reactive protein and cardiovascular disease in patients with renal disease. Current Opinion in Nephrology & Hypertension 2001; 10(3):377-83. *Not CKD treatment*

1150. Eisenberger U, Sollinger D, Stickel F, et al. Relationship between renal resistance index and renal function in liver transplant recipients after cessation of calcineurin inhibitor. Clinical Transplantation 2009; 23(4):499-504. *Not CKD treatment*

1151. Eisenstein EL. DRIVE it home: making the case for prospective economic data collection in randomized clinical trials. Kidney International 2008; 74(12):1507-9. *Not RCT or controlled trial*

1152. Eiskjaer H, Nielsen CB, Pedersen EB. Pressure-dependent, enhanced natriuretic response to low-dose, atrial natriuretic peptide infusion in essential hypertension. Journal of Internal Medicine 1994; 236(6):665-74. *Not RCT or controlled trial*

1153. Eiskjaer H, Nielsen CB, Pedersen EB. Pressure-dependent distal tubular action of atrial natriuretic peptide in healthy humans. Journal of Hypertension 1996; 14(1):99-106. *Not early CKD*

1154. Eiskjaer H, Nielsen CB, Sorensen SS, et al. Renal and hormonal actions of atrial natriuretic peptide during angiotensin II or noradrenaline infusion in man. European Journal of Clinical Investigation 1996; 26(7):584-95. *Not CKD treatment*

1155. Eiskjaer H, Pedersen EB. Dose-response study of atrial natriuretic peptide bolus injection in healthy man. European Journal of Clinical Investigation 1993; 23(1):37-45. *Follow-up less than 6 months*

1156. Eiskjaer H, Pedersen EB, Rasmussen LM, et al. Sustained release verapamil in renal hypertension. European Journal of Clinical Pharmacology 1988; 33(6):549-55. *Sample size less than 50 patients*

1157. Eiskjaer H, Pedersen EB, Rasmussen LM, et al. Verapamil sustained-release in renal parenchymal hypertension: effect on blood pressure, kidney function, angiotensin II, aldosterone, arginine vasopressin, atrial natriuretic peptide, and lipoproteins. Journal of Cardiovascular Pharmacology 1989; 13 Suppl 4:S17-22. *Sample size less than 50 patients*

1158. Eiskjaer H, Schmiegelow M, Jespersen B, et al. Renal and hormonal effects and tolerance of an ANP analogue in healthy man. European Journal of Clinical Pharmacology 1991; 41(6):547-54. *Sample size less than 50 patients*

1159. Eiskjaer H, Sorensen SS, Danielsen H, et al. Glomerular and tubular antinatriuretic actions of low-dose angiotensin II infusion in man. Journal of Hypertension 1992; 10(9):1033-40. *Sample size less than 50 patients*

1160. Ejaz AA, Beaver TM, Shimada M, et al. Uric acid: a novel risk factor for acute kidney injury in high-risk cardiac surgery patients? American Journal of Nephrology 2009; 30(5):425-9. *Not RCT or controlled trial*

1161. Ejerblad E, Fored CM, Lindblad P, et al. Obesity and risk for chronic renal failure. Journal of the American Society of Nephrology 2006; 17(6):1695-702. *Sample size less than 50 patients*

1162. Ekinci EI, Thomas G, Thomas D, et al. Effects of salt supplementation on the albuminuric response to telmisartan with or without hydrochlorothiazide therapy in hypertensive patients with type 2 diabetes are modulated by habitual dietary salt intake. Diabetes Care 2009; 32(8):1398-403. *Follow-up less than 6 months*

1163. Eknoyan G. Emergence of quantification in clinical investigation and the quest for certainty in therapeutics: the road from Hammurabi to Kefauver. Advances in Chronic Kidney Disease 2005; 12(1):88-95. *Not RCT or controlled trial*

1164. Ekundayo OJ, Muchimba M, Aban IB, et al. Multimorbidity due to diabetes mellitus and chronic kidney disease and outcomes in chronic heart failure. American Journal of Cardiology 2009; 103(1):88-92. *Not CKD treatment*

1165. Ekundayo OJ, Muchimba M, Aban IB, et al. Multimorbidity due to diabetes mellitus and chronic kidney disease and outcomes in chronic heart failure. American Journal of Cardiology 2009; 103(1):88-92. *Not CKD treatment*

1166. El Kossi MMH, Ibrahim A, Lock TJ, et al. Impact of cardiac transplantation on kidney function: a single- center experience. Transplantation Proceedings 2003; 35(4):1527-31. *Not CKD treatment*

1167. Elapavaluru S, Kellum JA. Why do patients die of acute kidney injury? Acta Clinica Belgica - Supplementum 2007; (2):326-31. *Not CKD treatment*

1168. Eliahou HE, Cohen D, Ben-David A, et al. The calcium channel blocker nisoldipine delays progression of chronic renal failure in humans (preliminary communication). Cardiovascular Drugs & Therapy 1988; 1(5):523-8. *Sample size less than 50 patients*

1169. Eliahou HE, Cohen D, Hellberg B, et al. Effect of the calcium channel blocker nisoldipine on the progression of chronic renal failure in man. American Journal of Nephrology 1988; 8(4):285-90. *Sample size less than 50 patients*

1170. Elkayam U, Janmohamed M, Hatamizadeh P, et al. Impact of acute serum creatinine elevation in patients treated with nesiritide. Clinical Cardiology 2009; 32(4):215-9. *Not CKD treatment*

1171. Ellis CN, Fradin MS, Messana JM, et al. Cyclosporine for plaque-type psoriasis. Results of a multidose, double-blind trial. New England Journal of Medicine 1991; 324(5):277-84. *Not CKD treatment*

1172. Ellis M, Bernsen R, Ali-Zadeh H, et al. A safety and feasibility study comparing an intermittent high dose with a daily standard dose of liposomal amphotericin B for persistent neutropenic fever. Journal of Medical Microbiology 2009; 58(Pt 11):1474-85. *Not CKD treatment*

1173. el-Sayed YM. Correlation between nephrotoxicity and pharmacokinetic parameters of gentamicin. Journal of Clinical Pharmacy & Therapeutics 1994; 19(4):267-71. *Not CKD treatment*

1174. Elsendoorn TJ, Weijl NI, Mithoe S, et al. Chemotherapy-induced chromosomal damage in peripheral blood lymphocytes of cancer patients supplemented with antioxidants or placebo. Mutation Research 2001; 498(1-2):145-58. *Not early CKD*

1175. Elseviers MM, Waller I, Nenoy D, et al. Evaluation of diagnostic criteria for analgesic nephropathy in patients with end-stage renal failure: results of the ANNE study. Analgesic Nephropathy Network of Europe. Nephrology Dialysis Transplantation 1995; 10(6):808-14. *Follow-up less than 6 months*

1176. el-Sherif AE, Foda R, Norlen LJ, et al. Treatment of renal colic by prostaglandin synthetase inhibitors and avafortan (analgesic antispasmodic). British Journal of Urology 1990; 66(6):602-5. *Not CKD treatment*

1177. Elung-Jensen T, Heisterberg J, Kamper A-L, et al. Blood pressure response to conventional and low-dose enalapril in chronic renal failure. British Journal of Clinical Pharmacology 2003; 55(2):139-46. *Sample size less than 50 patients*

1178. Elung-Jensen T, Heisterberg J, Sonne J, et al. Enalapril dosage in progressive chronic nephropathy: a randomised, controlled trial. European Journal of Clinical Pharmacology 2005; 61(2):87-96. *Not relevant to key questions*

1179. Elung-Jensen T, Strandgaard S, Kamper A-L. Longitudinal observations on circadian blood pressure variation in chronic kidney disease stages 3-5. Nephrology Dialysis Transplantation 2008; 23(9):2873-8. *Sample size less than 50 patients*

1180. Elving LD, Wetzels JF, van Lier HJ, et al. Captopril and atenolol are equally effective in retarding progression of diabetic nephropathy. Results of a 2-year prospective, randomized study. Diabetologia 1994; 37(6):604-9. *Sample size less than 50 patients*

1181. Ely H. Is pentoxifylline the drug of the decade? Journal of the American Academy of Dermatology 1994; 30(4):639-42. *Not RCT or controlled trial*

1182. Emery P. Cyclooxygenase-2: a major therapeutic advance? American Journal of Medicine 2001; 110(1A):42S-5S. *Not RCT or controlled trial*

1183. Endemann D, Marienhagen J, Stubanus M, et al. Volume independent stimulation of renin secretion by a single dose of amiloride in man. Arzneimittel-Forschung 2002; 52(9):677-83. *Sample size less than 50 patients*

1184. Endre ZH, Walker RJ, Pickering JW, et al. Early intervention with erythropoietin does not affect the outcome of acute kidney injury (the EARLYARF trial). Kidney International 2010 Jun; 77(11):1020-30. *Not CKD treatment*

1185. Engeler DS, Ackermann DK, Osterwalder JJ, et al. A double-blind, placebo controlled comparison of the morphine sparing effect of oral rofecoxib and diclofenac for acute renal colic. Journal of Urology 2005; 174(3):933-6. *Not relevant to key questions*

1186. Engoren M. Does erythrocyte blood transfusion prevent acute kidney injury? Propensity-matched case control analysis. Anesthesiology 2010 Nov; 113(5):1126-33. *Not CKD treatment*

1187. Ensrud KE, Lui L-Y, Taylor BC, et al. Renal function and risk of hip and vertebral fractures in older women. Archives of Internal Medicine 2007; 167(2):133-9. *Not CKD treatment*

1188. Epstein M. Effects of ACE inhibitors and calcium antagonists on progression of chronic renal disease. Blood Pressure Supplement 1995; 2:108-12. *Not CKD treatment*

1189. Epstein M. The benefits of ACE inhibitors and calcium antagonists in slowing progressive renal failure: focus on fixed-dose combination antihypertensive therapy. Renal Failure 1996; 18(6):813-32. *Not RCT or controlled trial*

1190. Epstein M. Calcium antagonists and renal protection: emerging perspectives. Journal of Hypertension - Supplement 1998; 16(4):S17-25. *Not RCT or controlled trial*

1191. Epstein M. Aldosterone as a determinant of cardiovascular and renal dysfunction. Journal of the Royal Society of Medicine 2001; 94(8):378-83. *Not RCT or controlled trial*

1192. Epstein M. Aldosterone as a mediator of progressive renal disease: pathogenetic and clinical implications. American Journal of Kidney Diseases 2001; 37(4):677-88. *Not RCT or controlled trial*

1193. Epstein M. Recent landmark clinical trials: how do they modify the therapeutic paradigm? American Journal of Hypertension 2002; 15(7 Pt 2):82S-4S. *Not RCT or controlled trial*

1194. Epstein M, Campese VM. Evolving role of calcium antagonists in the management of hypertension. Medical Clinics of North America 2004; 88(1):149-65. *Not relevant to key questions*

1195. Epstein M, Leary E, Laskey R, et al. Atorvastatin does not induce glomerular or tubular dysfunction even at high doses. Journal of the CardioMetabolic Syndrome 2007; 2(3):163-7. *Sample size less than 50 patients*

1196. Epstein M, Tobe S. What is the optimal strategy to intensify blood pressure control and prevent progression of renal failure? Current Hypertension Reports 2001; 3(5):422-8. *Not RCT or controlled trial*

1197. Epstein M, Williams GH, Weinberger M, et al. Selective aldosterone blockade with eplerenone reduces albuminuria in patients with type 2 diabetes. Clinical Journal of The American Society of Nephrology: CJASN 2006; 1(5):940-51. *Follow-up less than 6 months*

1198. Eray O, Cete Y, Oktay C, et al. Intravenous single-dose tramadol versus meperidine for pain relief in renal colic. European Journal of Anaesthesiology 2002; 19(5):368-70. *Not CKD treatment*

1199. Erdine S, Ari O, Zanchetti A, et al. ESH-ESC guidelines for the management of hypertension. Herz 2006; 31(4):331-8. *Not early CKD*

1200. Erdogan A, Davidson CJ. Recent clinical trials of iodixanol. Reviews in Cardiovascular Medicine 2003; 4 Suppl 5:S43-50. *Not CKD treatment*

1201. Eriksson LO, Beermann B, Kallner M. Renal function and tubular transport effects of sulindac and naproxen in chronic heart failure. Clinical Pharmacology & Therapeutics 1987; 42(6):646-54. *Sample size less than 50 patients*

1202. Eriksson LO, Sturfelt G, Thysell H, et al. Effects of sulindac and naproxen on prostaglandin excretion in patients with impaired renal function and rheumatoid arthritis. American Journal of Medicine 1990; 89(3):313-21. *Not CKD treatment*

1203. Erley CM, Bader B, Scheu M, et al. Renal hemodynamics in essential hypertensives treated with losartan. Clinical Nephrology 1995; 43 Suppl 1:S8-11. *Sample size less than 50 patients*

1204. Erley CM, Duda SH, Rehfuss D, et al. Prevention of radiocontrast-media-induced nephropathy in patients with pre-existing renal insufficiency by hydration in combination with the adenosine antagonist theophylline. Nephrology Dialysis Transplantation 1999; 14(5):1146-9. *Follow-up less than 6 months*

1205. Erley CM, Duda SH, Schlepckow S, et al. Adenosine antagonist theophylline prevents the reduction of glomerular filtration rate after contrast media application. Kidney International 1994; 45(5):1425-31. *Not CKD treatment*

1206. Erley CM, Haefele U, Heyne N, et al. Microalbuminuria in essential hypertension. Reduction by different antihypertensive drugs. Hypertension 1993; 21(6 Pt 1):810-5. *Sample size less than 50 patients*

1207. Erley CM, Harrer U, Kramer BK, et al. Renal hemodynamics and reduction of proteinuria by a vasodilating beta blocker versus an ACE inhibitor. Kidney International 1992; 41(5):1297-303. *Sample size less than 50 patients*

1208. Ermolenko VM, Kukhtevich AV, Dedov II, et al. Parlodel treatment of uremic hypogonadism in men. Nephron 1986; 42(1):19-22. *Sample size less than 50 patients*

1209. Erstad BL, Gales BJ, Rappaport WD. The use of albumin in clinical practice. Archives of Internal Medicine 1991; 151(5):901-11. *Not CKD treatment*

1210. Eschbach JW, Abdulhadi MH, Browne JK, et al. Recombinant human erythropoietin in anemic patients with end-stage renal disease. Results of a phase III multicenter clinical trial. Annals of Internal Medicine 1989; 111(12):992-1000. *Not early CKD*

1211. Escobedo J, Rana JS, Lombardero MS, et al. Association between albuminuria and duration of diabetes and myocardial dysfunction and peripheral arterial disease among patients with stable coronary artery disease in the BARI 2D study. Mayo Clinic Proceedings 2010; 85(1):41-6. *Not CKD treatment*

1212. Escudier B, Lethiec JL, Angevin E, et al. Totally implanted catheters to reduce catheter-related infections in patients receiving interleukin-2: a 2-year experience. Supportive Care in Cancer 1995; 3(5):297-300. *Not CKD treatment*

1213. Eskens FALM, Sleijfer S. The use of bevacizumab in colorectal, lung, breast, renal and ovarian cancer: where does it fit? European Journal of Cancer 2008; 44(16):2350-6. *Not CKD treatment*

1214. Esmail ZN, Loewen PS. Losartan as an alternative to ACE inhibitors in patients with renal dysfunction. Annals of Pharmacotherapy 1998; 32(10):1096-8. *Not RCT or controlled trial*

1215. Esnault VL, Potiron-Josse M, Testa A, et al. Captopril but not acebutolol, prazosin or indomethacin decreases postexercise proteinuria. Nephron 1991; 58(4):437-42. *Sample size less than 50 patients*

1216. Esnault VLM. Radiocontrast media-induced nephrotoxicity in patients with renal failure: rationale for a new double-blind, prospective, randomized trial testing calcium channel antagonists. Nephrology Dialysis Transplantation 2002; 17(8):1362-4. *Not RCT or controlled trial*

1217. Esnault VLM, Brown EA, Apetrei E, et al. The effects of amlodipine and enalapril on renal function in adults with hypertension and nondiabetic nephropathies: a 3-year, randomized, multicenter, double-blind, placebo-controlled study. Clinical Therapeutics 2008; 30(3):482-98. *Not CKD treatment*

1218. Esnault VLM, Ekhlas A, Delcroix C, et al. Diuretic and enhanced sodium restriction results in improved antiproteinuric response to RAS blocking agents. Journal of the American Society of Nephrology 2005; 16(2):474-81. *Not relevant to key questions*

1219. Esnault VLM, Ekhlas A, Nguyen J-M, et al. Diuretic uptitration with half dose combined ACEI + ARB better decreases proteinuria than combined ACEI + ARB uptitration. Nephrology Dialysis Transplantation 2010 Jul; 25(7):2218-24. *Follow-up less than 6 months*

1220. Estacio RO, Coll JR, Tran ZV, et al. Effect of intensive blood pressure control with valsartan on urinary albumin excretion in normotensive patients with type 2 diabetes. American Journal of Hypertension 2006; 19(12):1241-8. *Not CKD treatment*

1221. Estacio RO, Regensteiner JG, Wolfel EE, et al. The association between diabetic complications and exercise capacity in NIDDM patients. Diabetes Care 1998; 21(2):291-5. *Not RCT or controlled trial*

1222. Estacio RO, Savage S, Nagel NJ, et al. Baseline characteristics of participants in the Appropriate Blood Pressure Control in Diabetes trial. Controlled Clinical Trials 1996; 17(3):242-57. *Not RCT or controlled trial*

1223. Euser AM, Zoccali C, Jager KJ, et al. Cohort studies: prospective versus retrospective. Nephron 2009; 113(3):c214-7. *Not RCT or controlled trial*

1224. Evans DA, Buring J, Mayrent S, et al. Qualitative overview of randomized trials of aminoglycosides. American Journal of Medicine 1986; 80(6B):39-43. *Not relevant to key questions*

1225. Eyileten T, Sonmez A, Saglam M, et al. Effect of renin-angiotensin-aldosterone system (RAAS) blockade on visfatin levels in diabetic nephropathy. Nephrology 2010 Mar; 15(2):225-9. *Follow-up less than 6 months*

1226. Fabrizi F, Ganeshan SV, Dixit V, et al. Meta-analysis: the adjuvant role of granulocyte macrophage-colony stimulating factor on immunological response to hepatitis B virus vaccine in end-stage renal disease. Alimentary Pharmacology & Therapeutics 2006; 24(5):789-96. *Sample size less than 50 patients*

1227. Faddy SC. Significant statistical heterogeneity in a meta-analysis of the usefulness of acetylcysteine for prevention of contrast nephropathy. American Journal of Cardiology 2004; 94(3):414. *Not relevant to key questions*

1228. Faenza A, Catena F, Nardo B, et al. Kidney preservation with university of Wisconsin and Celsior solution: a prospective multicenter randomized study. Transplantation 2001; 72(7):1274-7. *Not CKD treatment*

1229. Fagher B, Henningsen N, Hulthen L, et al. Antihypertensive and renal effects of enalapril and slow-release verapamil in essential hypertension. A double-blind, randomized study. European Journal of Clinical Pharmacology 1990; 39 Suppl 1:S41-3. *Sample size less than 50 patients*

1230. Fagnani F, Souchet T, Labed D, et al. Management of hypertension and screening of renal complications by GPs in diabetic type 2 patients (France--2001). Diabetes & Metabolism 2003; 29(1):58-64. *Not RCT or controlled trial*

1231. Fakeye TO, Adegoke AO, Omoyeni OC, et al. Effects of water extract of Hibiscus sabdariffa, Linn (Malvaceae) 'Roselle' on excretion of a diclofenac formulation. Phytotherapy Research 2007; 21(1):96-8. *Not relevant to key questions*

1232. Falardeau P, Champagne P, Poyet P, et al. Neovastat, a naturally occurring multifunctional antiangiogenic drug, in phase III clinical trials. Seminars in Oncology 2001; 28(6):620-5. *Not early CKD*

1233. Falkiewicz K, Nahaczewska W, Boratynska M, et al. Tacrolimus decreases tubular phosphate wasting in renal allograft recipients. Transplantation Proceedings 2003; 35(6):2213-5. *Not CKD treatment*

1234. Fallo F, Gregianin M, Bui F, et al. Comparison of the antihypertensive and renal effects of tertatolol and nadolol in hypertensive patients with mild renal impairment. European Journal of Clinical Pharmacology 1991; 40(3):309-11. *Follow-up less than 6 months*

1235. Fanti P, Asmis R, Stephenson TJ, et al. Positive effect of dietary soy in ESRD patients with systemic inflammation--correlation between blood levels of the soy isoflavones and the acute-phase reactants. Nephrology Dialysis Transplantation 2006; 21(8):2239-46. *Not RCT or controlled trial*

1236. Farbakhsh K, Kasiske BL. Dyslipidemias in patients who have chronic kidney disease. Medical Clinics of North America 2005; 89(3):689-99. *Not RCT or controlled trial*

1237. Farbom P, Wahlstrand B, Almgren P, et al. Interaction between renal function and microalbuminuria for cardiovascular risk in hypertension: the nordic diltiazem study. Hypertension 2008; 52(1):115-22. *Not early CKD*

1238. Farkas G, Degi R, Voros P. Long-term effects of fetal islet transplantation on complication of diabetes, as compared with effects of intensive insulin therapy. Transplantation Proceedings 1995; 27(6):3145. *Not RCT or controlled trial*

1239. Farker K, Merkel U, Schweer H, et al. Effects of short-term treatment with diclofenac-colestyramine on renal function and urinary prostanoid excretion in patients with type-2 diabetes. European Journal of Clinical Pharmacology 2002; 58(2):85-91. *Sample size less than 50 patients*

1240. Farker K, Nassr N, Huck F, et al. Dipyrone and diclofenac do not influence creatinine-clearance, inulin-clearance or PAH-clearance in healthy male volunteers. International Journal of Clinical Pharmacology & Therapeutics 1995; 33(3):125-30. *Sample size less than 50 patients*

1241. Farquhar W, Kenney L. Renal effects of ibuprofen during sodium restriction in the aged. Journal of the American Geriatrics Society 2000; 48(1):106-8. *Not CKD treatment*

1242. Farquhar WB, Kenney WL. Age and renal prostaglandin inhibition during exercise and heat stress. Journal of Applied Physiology 1999; 86(6):1936-43. *Not CKD treatment*

1243. Farquhar WB, Morgan AL, Zambraski EJ, et al. Effects of acetaminophen and ibuprofen on renal function in the stressed kidney. Journal of Applied Physiology 1999; 86(2):598-604. *Not CKD treatment*

1244. Farvid MS, Jalali M, Siassi F, et al. Comparison of the effects of vitamins and/or mineral supplementation on glomerular and tubular dysfunction in type 2 diabetes. Diabetes Care 2005; 28(10):2458-64. *Sample size less than 50 patients*

1245. Fassbinder W, Quarder O, Waltz A. Treatment with carvedilol is associated with a significant reduction in microalbuminuria: a multicentre randomised study. International Journal of Clinical Practice 1999; 53(7):519-22. *Follow-up less than 6 months*

1246. Fassett RG, Ball MJ, Robertson IK, et al. Baseline serum lipids and renal function in chronic kidney disease patients entering the LORD trial. International Journal of Clinical Pharmacology & Therapeutics 2006; 44(11):580-8. *Not early CKD*

1247. Fassett RG, Ball MJ, Robertson IK, et al. The Lipid lowering and Onset of Renal Disease (LORD) Trial: a randomized double blind placebo controlled trial assessing the effect of atorvastatin on the progression of kidney disease. BMC Nephrology 2008; 9:4. *Not relevant to key questions*

1248. Fassett RG, Gobe GC, Peake JM, et al. Omega-3 polyunsaturated fatty acids in the treatment of kidney disease. American Journal of Kidney Diseases 2010 Oct; 56(4):728-42. *Not CKD treatment*

1249. Fassett RG, Robertson IK, Ball MJ, et al. Effects of atorvastatin on arterial stiffness in chronic kidney disease: a randomised controlled trial. Journal of Atherosclerosis & Thrombosis 2010 Mar 31; 17(3):235-41. *Sample size less than 50 patients*

1250. Fauli A, Gomar C, Campistol JM, et al. Kidney-specific proteins in patients receiving aprotinin at high- and low-dose regimens during coronary artery bypass graft with cardiopulmonary bypass. European Journal of Anaesthesiology 2005; 22(9):666-71. *Sample size less than 50 patients*

1251. Fauvel JP, Najem R, Maakel N, et al. Effects of moxonidine on stress-induced peak blood pressure and renal function: a randomized, double-blind, placebo-controlled crossover study. Journal of Cardiovascular Pharmacology 1998; 32(3):495-9. *Follow-up less than 6 months*

1252. Fauvel JP, Najem R, Ryon B, et al. Effects of rilmenidine on stress-induced peak blood pressure and renal function. Journal of Cardiovascular Pharmacology 1999; 34(1):41-5. *Follow-up less than 6 months*

1253. Fauvel JP, Velon S, Berra N, et al. Effects of losartan on renal function in patients with essential hypertension. Journal of Cardiovascular Pharmacology 1996; 28(2):259-63. *Sample size less than 50 patients*

1254. Fava S, Azzopardi J, Hattersley AT, et al. Increased prevalence of proteinuria in diabetic sibs of proteinuric type 2 diabetic subjects. American Journal of Kidney Diseases 2000; 35(4):708-12. *Not RCT or controlled trial*

1255. Favre H, Miescher PA, Lemoine R. Use of cyclosporine in the treatment of autoimmune disorders. Transplantation Proceedings 1994; 26(6):3194-6. *Not RCT or controlled trial*

1256. Fedoruk LM, Wang H, Conaway MR, et al. Statin therapy improves outcomes after valvular heart surgery. Annals of Thoracic Surgery 2008; 85(5):1521-5; discussion 5-6. *Not CKD treatment*

1257. Feindt PR, Walcher S, Volkmer I, et al. Effects of high-dose aprotinin on renal function in aortocoronary bypass grafting. Annals of Thoracic Surgery 1995; 60(4):1076-80. *Sample size less than 50 patients*

1258. Feiten SF, Draibe SA, Watanabe R, et al. Short-term effects of a very-low-protein diet supplemented with ketoacids in nondialyzed chronic kidney disease patients. European Journal of Clinical Nutrition 2005; 59(1):129-36. *Not CKD treatment*

1259. Feldt-Rasmussen B. The development of nephropathy in insulin-dependent diabetes mellitus is associated with poor glycemic control. Transplantation Proceedings 1994; 26(2):371-2. *Sample size less than 50 patients*

1260. Feldt-Rasmussen B, El Nahas M. Potential role of growth factors with particular focus on growth hormone and insulin-like growth factor-1 in the management of chronic kidney disease. Seminars in Nephrology 2009; 29(1):50-8. *Not relevant to key questions*

1261. Feldt-Rasmussen B, Jensen T, Dieperink H, et al. Nephrotoxicity of cyclosporin A in patients with newly diagnosed type 1 diabetes mellitus. Diabetic Medicine 1990; 7(5):429-33. *Sample size less than 50 patients*

1262. Feldt-Rasmussen B, Mathiesen ER, Deckert T. Effect of two years of strict metabolic control on progression of incipient nephropathy in insulin-dependent diabetes. Lancet 1986; 2(8519):1300-4. *Sample size less than 50 patients*

1263. Feldt-Rasmussen B, Mathiesen ER, Hegedus L, et al. Kidney function during 12 months of strict metabolic control in insulin-dependent diabetic patients with incipient nephropathy. New England Journal of Medicine 1986; 314(11):665-70. *Sample size less than 50 patients*

1264. Felisart J, Rimola A, Arroyo V, et al. Cefotaxime is more effective than is ampicillin-tobramycin in cirrhotics with severe infections. Hepatology 1985; 5(3):457-62. *Not early CKD*

1265. Fellstrom B, Holdaas H, Jardine AG, et al. Cardiovascular disease in patients with renal disease: the role of statins. Current Medical Research & Opinion 2009; 25(1):271-85. *Follow-up less than 6 months*

1266. Feramisco JD, Berger TG, Steinhoff M. Innovative management of pruritus. Dermatologic Clinics 2010 Jul; 28(3):467-78. *Not CKD treatment*

1267. Ferder L, Daccordi H, Martello M, et al. Angiotensin converting enzyme inhibitors versus calcium antagonists in the treatment of diabetic hypertensive patients. Hypertension 1992; 19(2 Suppl):II237-42. *Sample size less than 50 patients*

1268. Ferdinand KC, Taylor C. The management of hypertension with angiotensin receptor blockers in special populations. Clinical Cornerstone 2009; 9 Suppl 3:S5-17. *Not CKD treatment*

1269. Ferguson JA, Sundblad KJ, Becker PK, et al. Role of duration of diuretic effect in preventing sodium retention. Clinical Pharmacology & Therapeutics 1997; 62(2):203-8. *Sample size less than 50 patients*

1270. Fernandez PG, Snedden W, Vasdev S, et al. Bevantolol attenuates thiazide stimulated renin secretion and catecholamine release in diuretic resistant hypertensives. Canadian Journal of Cardiology 1989; 5(2):93-7. *Sample size less than 50 patients*

1271. Fernandez R, Puig JG, Rodriguez-Perez JC, et al. Effect of two antihypertensive combinations on metabolic control in type-2 diabetic hypertensive patients with albuminuria: a randomised, double-blind study. Journal of Human Hypertension 2001; 15(12):849-56. *Follow-up less than 6 months*

1272. Fernandez-Andrade C, Russo D, Iversen B, et al. Comparison of losartan and amlodipine in renally impaired hypertensive patients. Kidney International - Supplement 1998; 68:S120-4. *Sample size less than 50 patients*

1273. Ferrari P, Gadient G, Cozzio A, et al. Reduced plasma cyclic GMP but normal renal responses to atrial natriuretic factor in pre-hypertension. Blood Pressure 1996; 5(1):16-26. *Follow-up less than 6 months*

1274. Ferrari P, Marti H-P, Pfister M, et al. Additive antiproteinuric effect of combined ACE inhibition and angiotensin II receptor blockade. Journal of Hypertension 2002; 20(1):125-30. *Sample size less than 50 patients*

1275. Ferrario F, Barone MT, Landoni G, et al. Acetylcysteine and non-ionic isosmolar contrast-induced nephropathy--a randomized controlled study. Nephrology Dialysis Transplantation 2009; 24(10):3103-7. *Not CKD treatment*

1276. Ferretti A, Judd JT, Ballard-Barbash R, et al. Effect of fish oil supplementation on the excretion of the major metabolite of prostaglandin E in healthy male subjects. Lipids 1991; 26(7):500-3. *Not CKD treatment*

1277. Ferri C, Baldoncini R, Bellini C, et al. Hormonal and renal responses to atrial natriuretic peptide infusion in low-renin hypertension. American Journal of Nephrology 1995; 15(3):222-9. *Sample size less than 50 patients*

1278. Ferris M, Shoham DA, Pierre-Louis M, et al. High prevalence of unlabeled chronic kidney disease among inpatients at a tertiary-care hospital. American Journal of the Medical Sciences 2009; 337(2):93-7. *Not CKD treatment*

1279. Feutren G, von Graffenried B. Pharmacology of cyclosporin A (Sandimmun) and clinical experience in inflammatory bowel diseases. Schweizerische Medizinische Wochenschrift 1991; Journal Suisse de Medecine. 121(20):748-53. *Not CKD treatment*

1280. Fiaccadori E, Maggiore U, Rotelli C, et al. Effects of different energy intakes on nitrogen balance in patients with acute renal failure: a pilot study. Nephrology Dialysis Transplantation 2005; 20(9):1976-80. *Not relevant to key questions*

1281. Field TS, Rochon P, Lee M, et al. Computerized clinical decision support during medication ordering for long-term care residents with renal insufficiency. Journal of the American Medical Informatics Association 2009; 16(4):480-5. *Not CKD treatment*

1282. Field TS, Rochon P, Lee M, et al. Computerized clinical decision support during medication ordering for long-term care residents with renal insufficiency. Journal of the American Medical Informatics Association 2009; 16(4):480-5. *Not CKD treatment*

1283. Fifer MA, Molina CR, Quiroz AC, et al. Hemodynamic and renal effects of atrial natriuretic peptide in congestive heart failure. American Journal of Cardiology 1990; 65(3):211-6. *Not CKD treatment*

1284. Fine J-D, Johnson LB, Weiner M, et al. Cause-specific risks of childhood death in inherited epidermolysis bullosa. Journal of Pediatrics 2008; 152(2):276-80. *Not CKD treatment*

1285. Fischbach R, Landwehr P, Lackner K, et al. Iodixanol vs iopamidol in intravenous DSA of the abdominal aorta and lower extremity arteries: a comparative phase-III trial. European Radiology 1996; 6(1):9-13. *Not CKD treatment*

1286. Fischer D, Cline K, Plone MA, et al. Results of a randomized crossover study comparing once-daily and thrice-daily sevelamer dosing. American Journal of Kidney Diseases 2006; 48(3):437-44. *Not relevant to key questions*

1287. Fischer U, Salzsieder E, Menzel R, et al. Primary health care of diabetic patients in a specialized outpatient setting: a DIABCARE-based analysis. Diabete et Metabolisme 1993; 19(1 Pt 2):188-94. *Not RCT or controlled trial*

1288. Fischer UM, Tossios P, Mehlhorn U. Renal protection by radical scavenging in cardiac surgery patients. Current Medical Research & Opinion 2005; 21(8):1161-4. *Not relevant to key questions*

1289. Fishbane S, Chittineni H, Packman M, et al. Oral paricalcitol in the treatment of patients with CKD and proteinuria: a randomized trial. American Journal of Kidney Diseases 2009; 54(4):647-52. *Not early CKD*

1290. Fishbane S, Miyawaki N, Szczech LA. Hypothesis: an erythropoietin honeymoon phase exists. Kidney International 2010 Oct; 78(7):646-9. *Not CKD treatment*

1291. Fishbane S, Pannier A, Liogier X, et al. Pharmacokinetic and pharmacodynamic properties of methoxy polyethylene glycol-epoetin beta are unaffected by the site of subcutaneous administration. Journal of Clinical Pharmacology 2007; 47(11):1390-7. *Not RCT or controlled trial*

1292. Fisher AR, Jones P, Barlow P, et al. The influence of mannitol on renal function during and after open-heart surgery. Perfusion 1998; 13(3):181-6. *Not CKD treatment*

1293. Fisher CJ, Jr., Opal SM, Lowry SF, et al. Role of interleukin-1 and the therapeutic potential of interleukin-1 receptor antagonist in sepsis. Circulatory Shock 1994; 44(1):1-8. *Not RCT or controlled trial*

1294. Fitchett D. Have angiotensin receptor blockers lived up to expectations? Canadian Journal of Cardiology 2005; 21(7):569-75. *Sample size less than 50 patients*

1295. Flaa A, Aksnes TA, Strand A, et al. Complications of hypertension and the role of angiotensin receptor blockers in hypertension trials. Expert Review of Cardiovascular Therapy 2007; 5(3):451-61. *Not human studies*

1296. Flaa A, Kjeldsen SE. Are all the hypertensives made equal? Herz 2006; 31(4):323-30. *Not RCT or controlled trial*

1297. Flack JM. Effect of ramipril versus amlodipine on renal outcomes in hypertensive nephrosclerosis. Current Hypertension Reports 2002; 4(3):183-4. *Not RCT or controlled trial*

1298. Flack JM. Maximising antihypertensive effects of angiotensin II receptor blockers with thiazide diuretic combination therapy: focus on irbesartan/hydrochlorothiazide. International Journal of Clinical Practice 2007; 61(12):2093-102. *Not relevant to key questions*

1299. Flack JR, Molyneaux L, Willey K, et al. Regression of microalbuminuria: results of a controlled study, indapamide versus captopril. Journal of Cardiovascular Pharmacology 1993; 22 Suppl 6:S75-7. *Follow-up less than 6 months*

1300. Flapan AD, Davies E, Waugh C, et al. Posture determines the nature of the interaction between angiotensin converting enzyme inhibitors and loop diuretics in patients with chronic cardiac failure. International Journal of Cardiology 1991; 33(3):377-83. *Follow-up less than 6 months*

1301. Fleisch M, Sutsch G, Yan XW, et al. Systemic, pulmonary, and renal hemodynamic effects of endothelin ET(A/B)-receptor blockade in patients with maintained left ventricular function. Journal of Cardiovascular Pharmacology 2000; 36(3):302-9. *Not early CKD*

1302. Fleming JS, Persaud L, Zivanovic MA. A general equation for estimating glomerular filtration rate from a single plasma sample.[Erratum appears in Nucl Med Commun. 2005 Oct;26(10):933]. Nuclear Medicine Communications 2005; 26(8):743-8. *Sample size less than 50 patients*

1303. Fleming JS, Persaud L, Zivanovic MA. Quality control of slope-intercept measurements of glomerular filtration rate using single-sample estimates. Nuclear Medicine Communications 2005; 26(8):737-42. *Follow-up less than 6 months*

1304. Flesch M, Knipp S, Kessler G, et al. ARTA: AT1-receptor blocker therapy in patients undergoing coronary artery bypass grafting. Clinical Research in Cardiology 2009; 98(1):33-43. *Not CKD treatment*

1305. Fliser D, Dikow R, Demukaj S, et al. Opposing effects of angiotensin II on muscle and renal blood flow under euglycemic conditions. Journal of the American Society of Nephrology 2000; 11(11):2001-6. *Sample size less than 50 patients*

1306. Fliser D, Haller H. Angiotensin II subtype 1-receptor antagonists in the treatment of diabetic nephropathy. Journal of Hypertension - Supplement 2001; 19(1):S57-60. *Not RCT or controlled trial*

1307. Fliser D, Rett K, Hubinger A, et al. Influence of ACE inhibition on glucose tolerance in patients with stable chronic renal failure. Nephrology Dialysis Transplantation 1995; 10(5):643-7. *Sample size less than 50 patients*

1308. Fliser D, Ritz E. Serum cystatin C concentration as a marker of renal dysfunction in the elderly. American Journal of Kidney Diseases 2001; 37(1):79-83. *Not RCT or controlled trial*

1309. Fliser D, Schroter M, Neubeck M, et al. Coadministration of thiazides increases the efficacy of loop diuretics even in patients with advanced renal failure. Kidney International 1994; 46(2):482-8. *Not early CKD*

1310. Fliser D, Zurbruggen I, Mutschler E, et al. Coadministration of albumin and furosemide in patients with the nephrotic syndrome. Kidney International 1999; 55(2):629-34. *Sample size less than 50 patients*

1311. Flordal PA, Ljungstrom KG. Renal effects of high dose desmopressin and dextran. A study in normal subjects and in patients undergoing total hip replacement. Acta Anaesthesiologica Scandinavica 1993; 37(1):1-6. *Sample size less than 50 patients*

1312. Fluck RJ, Raine AE. ACE inhibitors in non-diabetic renal disease. British Heart Journal 1994; 72(3 Suppl):S46-51. *Not RCT or controlled trial*

1313. Fogari R, Corradi L, Zoppi A, et al. Addition of manidipine improves the antiproteinuric effect of candesartan in hypertensive patients with type II diabetes and microalbuminuria. American Journal of Hypertension 2007; 20(10):1092-6. *Not RCT or controlled trial*

1314. Fogari R, Derosa G, Zoppi A, et al. Effect of telmisartan-amlodipine combination at different doses on urinary albumin excretion in hypertensive diabetic patients with microalbuminuria. American Journal of Hypertension 2007; 20(4):417-22. *Not CKD treatment*

1315. Fogari R, Mugellini A, Zoppi A, et al. Effect of successful hypertension control by manidipine or lisinopril on albuminuria and left ventricular mass in diabetic hypertensive patients with microalbuminuria. European Journal of Clinical Pharmacology 2005; 61(7):483-90. *Not CKD treatment*

1316. Fogari R, Zoppi A, Corradi L, et al. Long-term effects of ramipril and nitrendipine on albuminuria in hypertensive patients with type II diabetes and impaired renal function. Journal of Human Hypertension 1999; 13(1):47-53. *Not relevant to key questions*

1317. Foley RN. Do we know the correct hemoglobin target for anemic patients with chronic kidney disease? Clinical Journal of The American Society of Nephrology: CJASN 2006; 1(4):678-84. *Not relevant to key questions*

1318. Foley RN. Target hemoglobin trials in chronic kidney disease: design and interpretation issues. Pediatric Nephrology 2009; 24(12):2279-85. *Not CKD treatment*

1319. Fontsere N, Bonal J, Navarro M, et al. A comparison of prediction equations for estimating glomerular filtration rate in adult patients with chronic kidney disease stages 4-5. Effect of nutritional status and age. Nephron 2006; 104(4):c160-8. *Not RCT or controlled trial*

1320. Forbes JM, Soulis T, Thallas V, et al. Renoprotective effects of a novel inhibitor of advanced glycation. Diabetologia 2001; 44(1):108-14. *Not human studies*

1321. Ford I, Bezlyak V, Stott DJ, et al. Reduced glomerular filtration rate and its association with clinical outcome in older patients at risk of vascular events: secondary analysis. PLoS Medicine / Public Library of Science 2009; 6(1):e16. *Not CKD treatment*

1322. Foreman BH, Chambliss ML. Clinical inquiries. Are ARBs or ACE inhibitors preferred for nephropathy in diabetes? Journal of Family Practice 2004; 53(3):241-2. *Not early CKD*

1323. Fornos JA, Andres NF, Andres JC, et al. A pharmacotherapy follow-up program in patients with type-2 diabetes in community pharmacies in Spain. Pharmacy World & Science 2006; 28(2):65-72. *Not relevant to key questions*

1324. Forrester DL, Britton J, Lewis SA, et al. Impact of adopting low sodium diet on biomarkers of inflammation and coagulation: a randomised controlled trial. Journal of Nephrology 2010 Jan-Feb; 23(1):49-54. *Not CKD treatment*

1325. Forsblom C, Hiukka A, Leinonen ES, et al. Effects of long-term fenofibrate treatment on markers of renal function in type 2 diabetes: the FIELD Helsinki substudy. Diabetes Care 2010; 33(2):215-20. *Not CKD treatment*

1326. Forsyth DR, Roberts CJ. Nitrendipine and renal tubular function in human volunteers. Journal of Clinical Pharmacology 1992; 32(3):284-9. *Not CKD treatment*

1327. Forzley BR, Sontrop JM, Macnab JJ, et al. Treating TTP/HUS with plasma exchange: a single centre's 25-year experience. British Journal of Haematology 2008; 143(1):100-6. *Not CKD treatment*

1328. Foucan L, Bourhis V, Bangou J, et al. A randomized trial of captopril for microalbuminuria in normotensive adults with sickle cell anemia. American Journal of Medicine 1998; 104(4):339-42. *Sample size less than 50 patients*

1329. Foucher C, Brugere L, Ansquer J-C. Fenofibrate, homocysteine and renal function. Current Vascular Pharmacology 2010 Sep; 8(5):589-603. *Not RCT or controlled trial*

1330. Fouque D, Aparicio M. Eleven reasons to control the protein intake of patients with chronic kidney disease. Nature Clinical Practice Nephrology 2007; 3(7):383-92. *Not CKD treatment*

1331. Fouque D, Guebre-Egziabher F. Do low-protein diets work in chronic kidney disease patients? Seminars in Nephrology 2009; 29(1):30-8. *Not RCT or controlled trial*

1332. Fouque D, Laville M. Low protein diets for chronic kidney disease in non diabetic adults. Cochrane Database of Systematic Reviews 2009; (3):CD001892. *Not RCT or controlled trial*

1333. Fouque D, Laville M, Boissel JP. Low protein diets for chronic kidney disease in non diabetic adults. Cochrane Database of Systematic Reviews 2006; (2):CD001892. *Not RCT or controlled trial*

1334. Fouque D, Le Bouc Y, Laville M, et al. Insulin-like growth factor-1 and its binding proteins during a low-protein diet in chronic renal failure. Journal of the American Society of Nephrology 1995; 6(5):1427-33. *Sample size less than 50 patients*

1335. Fouque D, Wang P, Laville M, et al. Low protein diets delay end-stage renal disease in non-diabetic adults with chronic renal failure. Nephrology Dialysis Transplantation 2000; 15(12):1986-92. *Not relevant to key questions*

1336. Fouque D, Wang P, Laville M, et al. Low protein diets delay end-stage renal disease in non diabetic adults with chronic renal failure. Cochrane Database of Systematic Reviews 2000; (2):CD001892. *Not relevant to key questions*

1337. Fouque D, Wang P, Laville M, et al. Low protein diets for chronic renal failure in non diabetic adults. Cochrane Database of Systematic Reviews 2001; (2):CD001892. *Not relevant to key questions*

1338. Fournier A, Moriniere PH, Oprisiu R, et al. 1-alpha-Hydroxyvitamin D3 derivatives in the treatment of renal bone diseases: justification and optimal modalities of administration. Nephron 1995; 71(3):254-83. *Not CKD treatment*

1339. Fox CH, Brooks A, Zayas LE, et al. Primary care physicians' knowledge and practice patterns in the treatment of chronic kidney disease: an Upstate New York Practice-based Research Network (UNYNET) study. Journal of the American Board of Family Medicine: JABFM 2006; 19(1):54-61. *Follow-up less than 6 months*

1340. Fox KAA, Antman EM, Montalescot G, et al. The impact of renal dysfunction on outcomes in the ExTRACT-TIMI 25 trial. Journal of the American College of Cardiology 2007; 49(23):2249-55. *Follow-up less than 6 months*

1341. Fox KAA, Bassand J-P, Mehta SR, et al. Influence of renal function on the efficacy and safety of fondaparinux relative to enoxaparin in non ST-segment elevation acute coronary syndromes. Annals of Internal Medicine 2007; 147(5):304-10. *Not CKD treatment*

1342. Franceschini N, Joy MS, Kshirsagar A. Cinacalcet HCl: a calcimimetic agent for the management of primary and secondary hyperparathyroidism. Expert Opinion on Investigational Drugs 2003; 12(8):1413-21. *Not CKD treatment*

1343. Frank H, Schobel H-P, Vitkowsky J, et al. Effects of angiotensin II receptor antagonism on the renal hemodynamic response to cardiovascular stress. Kidney International 2003; 63(2):617-23. *Sample size less than 50 patients*

1344. Frank H, Werner D, Lorusso V, et al. Simultaneous hemodialysis during coronary angiography fails to prevent radiocontrast-induced nephropathy in chronic renal failure. Clinical Nephrology 2003; 60(3):176-82. *Not CKD treatment*

1345. Franklin SC, Moulton M, Sicard GA, et al. Insulin-like growth factor I preserves renal function postoperatively. American Journal of Physiology 1997; 272(2 Pt 2):F257-9. *Follow-up less than 6 months*

1346. Franklin SS, Smith RD. Comparison of effects of enalapril plus hydrochlorothiazide versus standard triple therapy on renal function in renovascular hypertension. American Journal of Medicine 1985; 79(3C):14-23. *Follow-up less than 6 months*

1347. Franklin SS, Smith RD. A comparison of enalapril plus hydrochlorothiazide with standard triple therapy in renovascular hypertension. Nephron 1986; 44 Suppl 1:73-82. *Not CKD treatment*

1348. Frassetto LA, Nash E, Morris RC, Jr., et al. Comparative effects of potassium chloride and bicarbonate on thiazide-induced reduction in urinary calcium excretion. Kidney International 2000; 58(2):748-52. *Not early CKD*

1349. Frederick PR, Frankenfield DL, Biddle MG, et al. Changes in dialysis units' quality improvement practices from 1994 to 1996. Anna Journal 1998; 25(5):469-78. *Not RCT or controlled trial*

1350. Fredman B, Jedeikin R, Olsfanger D, et al. The opioid-sparing effect of diclofenac sodium in outpatient extracorporeal shock wave lithotripsy (ESWL). Journal of Clinical Anesthesia 1993; 5(2):141-4. *Not CKD treatment*

1351. Fredman B, Zohar E, Golan E, et al. Diclofenac does not decrease renal blood flow or glomerular filtration in elderly patients undergoing orthopedic surgery. Anesthesia & Analgesia 1999; 88(1):149-54. *Not CKD treatment*

1352. Freedman BI, Wuerth JP, Cartwright K, et al. Design and baseline characteristics for the aminoguanidine Clinical Trial in Overt Type 2 Diabetic Nephropathy (ACTION II). Controlled Clinical Trials 1999; 20(5):493-510. *Not RCT or controlled trial*

1353. Freeman RV, Mehta RH, Al Badr W, et al. Influence of concurrent renal dysfunction on outcomes of patients with acute coronary syndromes and implications of the use of glycoprotein IIb/IIIa inhibitors. Journal of the American College of Cardiology 2003; 41(5):718-24. *Not CKD treatment*

1354. Freestone S, Jeffrey RF, Bonner CV, et al. Effect of lithium on the renal actions of alpha-human atrial natriuretic peptide in normal man. Clinical Science 1990; 78(4):371-5. *Sample size less than 50 patients*

1355. Freestone S, McAuslane JA, Prescott LF. Effects of tenoxicam on renal function and the disposition of inulin and p-aminohippurate in healthy volunteers and patients with chronic renal failure. British Journal of Clinical Pharmacology 1991; 32(4):495-500. *Sample size less than 50 patients*

1356. Frei U, Wagner K. Renal function in liver transplant patients receiving FK506 or cyclosporin A immunosuppressive therapy. Transplantation Proceedings 1994; 26(6):3270-1. *Not early CKD*

1357. Freidlin B, Korn EL. A testing procedure for survival data with few responders. Statistics in Medicine 2002; 21(1):65-78. *Not RCT or controlled trial*

1358. Frenken LA, van Lier HJ, Jordans JG, et al. Identification of the component part in an epoetin alfa preparation that causes pain after subcutaneous injection. American Journal of Kidney Diseases 1993; 22(4):553-6. *Sample size less than 50 patients*

1359. Freudenberger RS, Kim J, Tawfik I, et al. Optimal medical therapy is superior to transplantation for the treatment of class I, II, and III heart failure: a decision analytic approach. Circulation 2006; 114(1 Suppl):I62-6. *Not RCT or controlled trial*

1360. Freudenthaler S, Benohr P, Grenz A, et al. Do alterations of endogenous angiotensin II levels regulate erythropoietin production in humans? British Journal of Clinical Pharmacology 2003; 56(4):378-87. *Sample size less than 50 patients*

1361. Fricker AF, Nussberger J, Meilenbrock S, et al. Effect of indomethacin on the renal response to angiotensin II receptor blockade in healthy subjects. Kidney International 1998; 54(6):2089-97. *Sample size less than 50 patients*

1362. Fridman K, Andersson OK, Wysocki M, et al. Acute effects of candesartan cilexetil (the new angiotensin II antagonist) on systemic and renal haemodynamics in hypertensive patients. European Journal of Clinical Pharmacology 1998; 54(7):497-501. *Sample size less than 50 patients*

1363. Fried LF, Forrest KY, Ellis D, et al. Lipid modulation in insulin-dependent diabetes mellitus: effect on microvascular outcomes. Journal of Diabetes & its Complications 2001; 15(3):113-9. *Sample size less than 50 patients*

1364. Friedman AN. Omega-3 fatty acid supplementation in advanced kidney disease. Seminars in Dialysis 2010 Jul-Aug; 23(4):396-400. *Not RCT or controlled trial*

1365. Friedman AN, Hunsicker LG, Selhub J, et al. C-reactive protein as a predictor of total arteriosclerotic outcomes in type 2 diabetic nephropathy. Kidney International 2005; 68(2):773-8. *Not relevant to key questions*

1366. Friedman AN, Yu Z, Juliar BE, et al. Independent influence of dietary protein on markers of kidney function and disease in obesity. Kidney International 2010 Oct; 78(7):693-7. *Follow-up less than 6 months*

1367. Friedrich JO, Adhikari N, Herridge MS, et al. Meta-analysis: low-dose dopamine increases urine output but does not prevent renal dysfunction or death. Annals of Internal Medicine 2005; 142(7):510-24. *Not relevant to key questions*

1368. Frimodt-Moller M, Hoj Nielsen A, Strandgaard S, et al. Feasibility of combined treatment with enalapril and candesartan in advanced chronic kidney disease. Nephrology Dialysis Transplantation 2010 Mar; 25(3):842-7. *Follow-up less than 6 months*

1369. Frohling PT, Krupki F, Kokot F, et al. What are the most important factors in the progression of renal failure? Kidney International - Supplement 1989; 27:S106-9. *Not early CKD*

1370. Frossard V, Ketterer N, Rosselet A, et al. Early intensification and autologous stem cell transplantation in patients with systemic AL amyloidosis: a single-centre experience. Annals of Hematology 2009; 88(7):681-5. *Not CKD treatment*

1371. Frumento RJ, Logginidou HG, Wahlander S, et al. Dexmedetomidine infusion is associated with enhanced renal function after thoracic surgery. Journal of Clinical Anesthesia 2006; 18(6):422-6. *Not early CKD*

1372. Fuiano G, Esposito C, Sepe V, et al. Effects of hypercholesterolemia of renal hemodynamics: study in patients with nephrotic syndrome. Nephron 1996; 73(3):430-5. *Sample size less than 50 patients*

1373. Fuiano G, Mancuso D, Indolfi C, et al. Early detection of progressive renal dysfunction in patients with coronary artery disease. Kidney International 2005; 68(6):2773-80. *Not relevant to key questions*

1374. Fujii N, Hamano T, Mikami S, et al. Risedronate, an effective treatment for glucocorticoid-induced bone loss in CKD patients with or without concomitant active vitamin D (PRIUS-CKD). Nephrology Dialysis Transplantation 2007; 22(6):1601-7. *Not RCT or controlled trial*

1375. Fujisaki T, Hida M, Hiraga S, et al. Cellular proliferation and secretion in secondary hyperparathyroidism during renal failure. Nephron 1997; 77(1):68-75. *Sample size less than 50 patients*

1376. Fujita T, Ando K, Nishimura H, et al. Antiproteinuric effect of the calcium channel blocker cilnidipine added to renin-angiotensin inhibition in hypertensive patients with chronic renal disease. Kidney International 2007; 72(12):1543-9. *Not RCT or controlled trial*

1377. Fukuoka N, Aibiki M. Recommended dose of arbekacin, an aminoglycoside against methicillin-resistant Staphylococcus aureus, does not achieve desired serum concentration in critically ill patients with lowered creatinine clearance. Journal of Clinical Pharmacy & Therapeutics 2008; 33(5):521-7. *Not CKD treatment*

1378. Fullerton T, Sica DA, Blum RA. Evaluation of the renal protective effect of misoprostol in elderly, osteoarthritic patients at risk for nonsteroidal anti-inflammatory drug-induced renal dysfunction. Journal of Clinical Pharmacology 1993; 33(12):1225-32. *Not CKD treatment*

1379. Fung JWH, Szeto CC, Chan WWM, et al. Effect of N-acetylcysteine for prevention of contrast nephropathy in patients with moderate to severe renal insufficiency: a randomized trial. American Journal of Kidney Diseases 2004; 43(5):801-8. *Not early CKD*

1380. Fung MA, Warnock GL, Ao Z, et al. The effect of medical therapy and islet cell transplantation on diabetic nephropathy: an interim report. Transplantation 2007; 84(1):17-22. *Sample size less than 50 patients*

1381. Furey SA, Vargas R, McMahon FG. Renovascular effects of nonprescription ibuprofen in elderly hypertensive patients with mild renal impairment. Pharmacotherapy 1993; 13(2):143-8. *Not CKD treatment*

1382. Furumatsu Y, Nagasawa Y, Tomida K, et al. Effect of renin-angiotensin-aldosterone system triple blockade on non-diabetic renal disease: addition of an aldosterone blocker, spironolactone, to combination treatment with an angiotensin-converting enzyme inhibitor and angiotensin II receptor blocker. Hypertension Research - Clinical & Experimental 2008; 31(1):59-67. *Not CKD treatment*

1383. Gabrielsen A, Bie P, Holstein-Rathlou NH, et al. Neuroendocrine and renal effects of intravascular volume expansion in compensated heart failure. American Journal of Physiology - Regulatory Integrative & Comparative Physiology 2001; 281(2):R459-67. *Not early CKD*

1384. Gadano A, Moreau R, Vachiery F, et al. Natriuretic response to the combination of atrial natriuretic peptide and terlipressin in patients with cirrhosis and refractory ascites. Journal of Hepatology 1997; 26(6):1229-34. *Not CKD treatment*

1385. Gaede P, Hansen HP, Parving H-H, et al. Impact of low-dose acetylsalicylic acid on kidney function in type 2 diabetic patients with elevated urinary albumin excretion rate. Nephrology Dialysis Transplantation 2003; 18(3):539-42. *Sample size less than 50 patients*

1386. Gaede P, Poulsen HE, Parving HH, et al. Double-blind, randomised study of the effect of combined treatment with vitamin C and E on albuminuria in Type 2 diabetic patients. Diabetic Medicine 2001; 18(9):756-60. *Sample size less than 50 patients*

1387. Gaede P, Vedel P, Parving HH, et al. Elevated levels of plasma von Willebrand factor and the risk of macro- and microvascular disease in type 2 diabetic patients with microalbuminuria. Nephrology Dialysis Transplantation 2001; 16(10):2028-33. *Not RCT or controlled trial*

1388. Gaedeke J, Neumayer H-H, Peters H. Pharmacological management of renal fibrotic disease. Expert Opinion on Pharmacotherapy 2006; 7(4):377-86. *Not relevant to key questions*

1389. Gainer JV, Morrow JD, Loveland A, et al. Effect of bradykinin-receptor blockade on the response to angiotensin-converting-enzyme inhibitor in normotensive and hypertensive subjects. New England Journal of Medicine 1998; 339(18):1285-92. *Sample size less than 50 patients*

1390. Galassi A, Brancaccio D, Cozzolino M, et al. Awareness of hypertension and proteinuria in randomly selected patients in 11 Italian cities. A 2005 report of the National Kidney Foundation of Italy. Journal of Clinical Hypertension 2009; 11(3):138-43. *Not CKD treatment*

1391. Galera SC, Fechine FV, Teixeira MJ, et al. The safety of oral use of L-glutamine in middle-aged and elderly individuals. Nutrition 2010 Apr; 26(4):375-81. *Follow-up less than 6 months*

1392. Gall MA, Rossing P, Skott P, et al. Placebo-controlled comparison of captopril, metoprolol, and hydrochlorothiazide therapy in non-insulin-dependent diabetic patients with primary hypertension. American Journal of Hypertension 1992; 5(5 Pt 1):257-65. *Sample size less than 50 patients*

1393. Gallagher DJ, Milowsky MI, Iasonos A, et al. Sequential adjuvant chemotherapy after surgical resection of high-risk urothelial carcinoma. Cancer 2009; 115(22):5193-201. *Not CKD treatment*

1394. Gallagher H, de Lusignan S, Harris K, et al. Quality-improvement strategies for the management of hypertension in chronic kidney disease in primary care: a systematic review. British Journal of General Practice 2010 Jun; 60(575):258-65. *Not RCT or controlled trial*

1395. Gallagher JC, Rapuri P, Smith L. Falls are associated with decreased renal function and insufficient calcitriol production by the kidney. Journal of Steroid Biochemistry & Molecular Biology 2007; 103(3-5):610-3. *Not RCT or controlled trial*

1396. Gallagher PM, Carrithers JA, Godard MP, et al. Beta-hydroxy-beta-methylbutyrate ingestion, part II: effects on hematology, hepatic and renal function. Medicine & Science in Sports & Exercise 2000; 32(12):2116-9. *Not early CKD*

1397. Gallant JE, Winston JA, DeJesus E, et al. The 3-year renal safety of a tenofovir disoproxil fumarate vs. a thymidine analogue-containing regimen in antiretroviral-naive patients. AIDS 2008; 22(16):2155-63. *Not CKD treatment*

1398. Gallicchio L, Helzlsouer KJ, Chow W-H, et al. Circulating 25-hydroxyvitamin D and the risk of rarer cancers: Design and methods of the Cohort Consortium Vitamin D Pooling Project of Rarer Cancers. American Journal of Epidemiology 2010 Jul 1; 172(1):10-20. *Not CKD treatment*

1399. Galsky MD, Iasonos A, Mironov S, et al. Phase II trial of dose-dense doxorubicin plus gemcitabine followed by paclitaxel plus carboplatin in patients with advanced urothelial carcinoma and impaired renal function. Cancer 2007; 109(3):549-55. *Not CKD treatment*

1400. Gambaro G, Kinalska I, Oksa A, et al. Oral sulodexide reduces albuminuria in microalbuminuric and macroalbuminuric type 1 and type 2 diabetic patients: the Di.N.A.S. randomized trial. Journal of the American Society of Nephrology 2002; 13(6):1615-25. *Not CKD treatment*

1401. Gambini G, Rossi S, Valori C. Absence of effects of ketanserin on renal prostacyclin and thromboxane A2 in essential hypertension. European Heart Journal 1991; 12(4):550-3. *Sample size less than 50 patients*

1402. Gandhi MR, Brown P, Romanowski CA, et al. The use of theophylline, an adenosine antagonist in the prevention of contrast media induced nephrotoxicity.[Republished from Br J Radiol 1992 May;65(773):459]. British Journal of Radiology 1992; 65(777):838. *Not RCT or controlled trial*

1403. Gandhi SK, Ryder DH, Brown NJ. Losartan blocks aldosterone and renal vascular responses to angiotensin II in humans. Hypertension 1996; 28(6):961-6. *Sample size less than 50 patients*

1404. Gandra SR, Finkelstein FO, Bennett AV, et al. Impact of erythropoiesis-stimulating agents on energy and physical function in nondialysis CKD patients with anemia: a systematic review. American Journal of Kidney Diseases 2010 Mar; 55(3):519-34. *Not RCT or controlled trial*

1405. Ganguli A, Kohli HS, Khullar M, et al. Lipid peroxidation products formation with various intravenous iron preparations in chronic kidney disease. Renal Failure 2009; 31(2):106-10. *Not CKD treatment*

1406. Gansevoort RT, de Zeeuw D, de Jong PE. Is the antiproteinuric effect of ACE inhibition mediated by interference in the renin-angiotensin system? Kidney International 1994; 45(3):861-7. *Not relevant to key questions*

1407. Gansevoort RT, de Zeeuw D, de Jong PE. Additive antiproteinuric effect of ACE inhibition and a low-protein diet in human renal disease. Nephrology Dialysis Transplantation 1995; 10(4):497-504. *Sample size less than 50 patients*

1408. Gansevoort RT, de Zeeuw D, Shahinfar S, et al. Effects of the angiotensin II antagonist losartan in hypertensive patients with renal disease. Journal of Hypertension - Supplement 1994; 12(2):S37-42. *Follow-up less than 6 months*

1409. Gansevoort RT, Verhave JC, Hillege HL, et al. The validity of screening based on spot morning urine samples to detect subjects with microalbuminuria in the general population. Kidney International - Supplement 2005; (94):S28-35. *Not CKD treatment*

1410. Gao Y, Lu R, Wang X, et al. A clinical trial of tang shen ning for treatment of diabetic nephropathy. Journal of Traditional Chinese Medicine 1998; 18(4):247-52. *Not relevant to key questions*

1411. Garattini L, Brunetti M, Salvioni F, et al. Economic evaluation of ACE inhibitor treatment of nephropathy in patients with insulin-dependent diabetes mellitus in Italy. Pharmacoeconomics 1997; 12(1):67-75. *Not RCT or controlled trial*

1412. Garcia CA, Abell-Aleff PC, Gamb SI, et al. Ultrastructural analysis of amyloidoma. Ultrastructural Pathology 2009; 33(3):123-7. *Not CKD treatment*

1413. Garcia de Vinuesa S, Luno J, Gomez-Campdera F, et al. Effect of strict blood pressure control on proteinuria in renal patients treated with different antihypertensive drugs. Nephrology Dialysis Transplantation 2001; 16 Suppl 1:78-81. *Sample size less than 50 patients*

1414. Garcia-Donaire JA, Segura J, Ruilope LM. An update of irbesartan and renin-angiotensin system blockade in diabetic nephropathy. Expert Opinion on Pharmacotherapy 2005; 6(9):1587-96. *Sample size less than 50 patients*

1415. Gare M, Haviv YS, Ben-Yehuda A, et al. The renal effect of low-dose dopamine in high-risk patients undergoing coronary angiography. Journal of the American College of Cardiology 1999; 34(6):1682-8. *Not CKD treatment*

1416. Garg AX, Kiberd BA, Clark WF, et al. Albuminuria and renal insufficiency prevalence guides population screening: results from the NHANES III. Kidney International 2002; 61(6):2165-75. *Not relevant to key questions*

1417. Garg JP, Ellis R, Elliott WJ, et al. Angiotensin receptor blockade and arterial compliance in chronic kidney disease: a pilot study. American Journal of Nephrology 2005; 25(4):393-9. *Not relevant to key questions*

1418. Garg P, Charytan DM, Novack L, et al. Impact of moderate renal insufficiency on restenosis and adverse clinical events after sirolimus-eluting and bare metal stent implantation (from the SIRIUS trials). American Journal of Cardiology 2010 Nov 15; 106(10):1436-42. *Not CKD treatment*

1419. Garini G, Mazzi A, Allegri L, et al. Effectiveness of dietary protein augmentation associated with angiotensin-converting enzyme inhibition in the management of the nephrotic syndrome. Mineral & Electrolyte Metabolism 1996; 22(1-3):123-7. *Sample size less than 50 patients*

1420. Garneata L. Pharmaco-economic evaluation of keto acid/amino acid-supplemented protein-restricted diets. Journal of Renal Nutrition 2009; 19(5 Suppl):S19-21. *Not early CKD*

1421. Garneata L, Mircescu G. Nutritional intervention in uremia--myth or reality? Journal of Renal Nutrition 2010 Sep; 20(5 Suppl):S31-4. *Not RCT or controlled trial*

1422. Garovic V, Textor SC. Renovascular hypertension: current concepts. Seminars in Nephrology 2005; 25(4):261-71. *Sample size less than 50 patients*

1423. Garty M, Perry G, Shmueli H, et al. Effect of cimetidine on digoxin disposition in peptic ulcer patients. European Journal of Clinical Pharmacology 1986; 30(4):489-91. *Sample size less than 50 patients*

1424. Garufi C, Levi F, Giunta S, et al. Chronomodulated 5-day infusion of floxuridine and L-folinic acid in patients with advanced malignancies: a feasibility and tolerability study. Journal of Infusional Chemotherapy 1995; 5(3 Suppl 1):134-7. *Sample size less than 50 patients*

1425. Garwood S, Swamidoss CP, Davis EA, et al. A case series of low-dose fenoldopam in seventy cardiac surgical patients at increased risk of renal dysfunction. Journal of Cardiothoracic & Vascular Anesthesia 2003; 17(1):17-21. *Not RCT or controlled trial*

1426. Gaspari F, Perico N, Ruggenenti P, et al. Plasma clearance of nonradioactive iohexol as a measure of glomerular filtration rate. Journal of the American Society of Nephrology 1995; 6(2):257-63. *Sample size less than 50 patients*

1427. Gassman JJ, Greene T, Wright JT, Jr., et al. Design and statistical aspects of the African American Study of Kidney Disease and Hypertension (AASK). Journal of the American Society of Nephrology 2003; 14(7 Suppl 2):S154-65. *Not relevant to key questions*

1428. Gates GF. Filtration fraction and its implications for radionuclide renography using diethylenetriaminepentaacetic acid and mercaptoacetyltriglycine. Clinical Nuclear Medicine 2004; 29(4):231-7. *Sample size less than 50 patients*

1429. Gatling W, Knight C, Hill RD. Screening for early diabetic nephropathy: which sample to detect microalbuminuria? Diabetic Medicine 1985; 2(6):451-5. *Not RCT or controlled trial*

1430. Gatot I, Abramov D, Tsodikov V, et al. Should we give prophylactic renal-dose dopamine after coronary artery bypass surgery? Journal of Cardiac Surgery 2004; 19(2):128-33. *Not relevant to key questions*

1431. Gatti AM, Rivasi F. Biocompatibility of micro- and nanoparticles. Part I: in liver and kidney. Biomaterials 2002; 23(11):2381-7. *Not CKD treatment*

1432. Gaudry SE, Sitar DS, Smyth DD, et al. Gender and age as factors in the inhibition of renal clearance of amantadine by quinine and quinidine. Clinical Pharmacology & Therapeutics 1993; 54(1):23-7. *Follow-up less than 6 months*

1433. Gaweda AE, Jacobs AA, Aronoff GR, et al. Model predictive control of erythropoietin administration in the anemia of ESRD. American Journal of Kidney Diseases 2008; 51(1):71-9. *Not early CKD*

1434. Gay F, Palumbo A. Multiple myeloma: management of adverse events. Medical Oncology 2010 Sep; 27(3):646-53. *Not CKD treatment*

1435. Gayet-Ageron A, Ananworanich J, Jupimai T, et al. No change in calculated creatinine clearance after tenofovir initiation among Thai patients. Journal of Antimicrobial Chemotherapy 2007; 59(5):1034-7. *Not CKD treatment*

1436. Gazis A, Page SR. Microalbuminuria screening in the UK: are we meeting European standards? Diabetic Medicine 1996; 13(8):764-7. *Not RCT or controlled trial*

1437. Gelber RP, Kurth T, Kausz AT, et al. Association between body mass index and CKD in apparently healthy men. American Journal of Kidney Diseases 2005; 46(5):871-80. *Not RCT or controlled trial*

1438. Geluk CA, Asselbergs FW, Hillege HL, et al. Impact of statins in microalbuminuric subjects with the metabolic syndrome: a substudy of the PREVEND Intervention Trial. European Heart Journal 2005; 26(13):1314-20. *Sample size less than 50 patients*

1439. Gentile MG, Ciceri R, Manna GM, et al. The role of fibre in the treatment of secondary hyperlipidaemia in nephrotic patients. European Journal of Clinical Nutrition 1995; 49 Suppl 3:S239-41. *Sample size less than 50 patients*

1440. Gentilini P, La Villa G, Marra F, et al. Pharmacokinetics and pharmacodynamics of torasemide and furosemide in patients with diuretic resistant ascites. Journal of Hepatology 1996; 25(4):481-90. *Sample size less than 50 patients*

1441. Gentilini P, Romanelli RG, La Villa G, et al. Effects of low-dose captopril on renal hemodynamics and function in patients with cirrhosis of the liver. Gastroenterology 1993; 104(2):588-94. *Follow-up less than 6 months*

1442. Genuth S. Insights from the diabetes control and complications trial/epidemiology of diabetes interventions and complications study on the use of intensive glycemic treatment to reduce the risk of complications of type 1 diabetes. Endocrine Practice 2006; 12 Suppl 1:34-41. *Not relevant to key questions*

1443. Georges B, Conil J-M, Seguin T, et al. Population pharmacokinetics of ceftazidime in intensive care unit patients: influence of glomerular filtration rate, mechanical ventilation, and reason for admission. Antimicrobial Agents & Chemotherapy 2009; 53(10):4483-9. *Sample size less than 50 patients*

1444. Gerbes AL, Gulberg V, Gines P, et al. Therapy of hyponatremia in cirrhosis with a vasopressin receptor antagonist: a randomized double-blind multicenter trial. Gastroenterology 2003; 124(4):933-9. *Not CKD treatment*

1445. Gerhardt T, Terjung B, Knipper P, et al. Renal impairment after liver transplantation - a pilot trial of calcineurin inhibitor-free vs. calcineurin inhibitor sparing immunosuppression in patients with mildly impaired renal function after liver transplantation. European Journal of Medical Research 2009; 14(5):210-5. *Sample size less than 50 patients*

1446. Germain DP, Waldek S, Banikazemi M, et al. Sustained, long-term renal stabilization after 54 months of agalsidase beta therapy in patients with Fabry disease. Journal of the American Society of Nephrology 2007; 18(5):1547-57. *Follow-up less than 6 months*

1447. Gerrah R, Ehrlich S, Tshori S, et al. Beneficial effect of aspirin on renal function in patients with renal insufficiency postcardiac surgery. Journal of Cardiovascular Surgery 2004; 45(6):545-50. *Not CKD treatment*

1448. Gerstein HC. Diabetes and the HOPE study: implications for macrovascular and microvascular disease. International Journal of Clinical Practice 2001; Supplement.(117):8-12. *Not CKD treatment*

1449. Gerstein HC. Reduction of cardiovascular events and microvascular complications in diabetes with ACE inhibitor treatment: HOPE and MICRO-HOPE. Diabetes/Metabolism Research Reviews 2002; 18 Suppl 3:S82-5. *Not relevant to key questions*

1450. Gerstein HC, Bosch J, Pogue J, et al. Rationale and design of a large study to evaluate the renal and cardiovascular effects of an ACE inhibitor and vitamin E in high-risk patients with diabetes. The MICRO-HOPE Study. Microalbuminuria, cardiovascular, and renal outcomes. Heart Outcomes Prevention Evaluation. Diabetes Care 1996; 19(11):1225-8. *Not RCT or controlled trial*

1451. Gerth WC, Remuzzi G, Viberti G, et al. Losartan reduces the burden and cost of ESRD: public health implications from the RENAAL study for the European Union. Kidney International - Supplement 2002; (82):S68-72. *Not CKD treatment*

1452. Ghebremariam YT, Engelbrecht G, Tyler M, et al. Vaccinia virus complement control protein (VCP) improves kidney structure and function following ischemia/reperfusion injury in rats. Journal of Surgical Research 2010 Apr; 159(2):747-54. *Not human studies*

1453. Gheith O, Sheashaa H, Abdelsalam M, et al. Efficacy and safety of Monascus purpureus Went rice in subjects with secondary hyperlipidemia. Clinical & Experimental Nephrology 2008; 12(3):189-94. *Not CKD treatment*

1454. Gheith O, Sheashaa H, Abdelsalam M, et al. Efficacy and safety of Monascus purpureus Went rice in children and young adults with secondary hyperlipidemia: a preliminary report. European Journal of Internal Medicine 2009; 20(3):e57-61. *Not CKD treatment*

1455. Gheith OA, Sobh MA-K, Mohamed KE-S, et al. Impact of treatment of dyslipidemia on renal function, fat deposits and scarring in patients with persistent nephrotic syndrome. Nephron 2002; 91(4):612-9. *Sample size less than 50 patients*

1456. Giamarellou H, Yiallouros K, Petrikkos G, et al. Comparative kinetics and efficacy of amikacin administered once or twice daily in the treatment of systemic gram-negative infections. Journal of Antimicrobial Chemotherapy 1991; 27 Suppl C:73-9. *Not CKD treatment*

1457. Giannini C, Lombardo F, Curro F, et al. Effects of high-dose vitamin E supplementation on oxidative stress and microalbuminuria in young adult patients with childhood onset type 1 diabetes mellitus. Diabetes/Metabolism Research Reviews 2007; 23(7):539-46. *Not RCT or controlled trial*

1458. Giatras I, Lau J, Levey AS. Effect of angiotensin-converting enzyme inhibitors on the progression of nondiabetic renal disease: a meta-analysis of randomized trials. Angiotensin-Converting-Enzyme Inhibition and Progressive Renal Disease Study Group. Annals of Internal Medicine 1997; 127(5):337-45. *Not RCT or controlled trial*

1459. Gibson CM, Dumaine RL, Gelfand EV, et al. Association of glomerular filtration rate on presentation with subsequent mortality in non-ST-segment elevation acute coronary syndrome; observations in 13,307 patients in five TIMI trials. European Heart Journal 2004; 25(22):1998-2005. *Sample size less than 50 patients*

1460. Gilbert DN, Lee BL, Dworkin RJ, et al. A randomized comparison of the safety and efficacy of once-daily gentamicin or thrice-daily gentamicin in combination with ticarcillin-clavulanate. American Journal of Medicine 1998; 105(3):182-91. *Not CKD treatment*

1461. Gilbert RE, Kim SA, Tuttle KR, et al. Effect of ruboxistaurin on urinary transforming growth factor-beta in patients with diabetic nephropathy and type 2 diabetes. Diabetes Care 2007; 30(4):995-6. *Not CKD treatment*

1462. Gilbert S, Zuo C, Epstein FH. Effect of specific and non-specific inhibition of COX-2 on renal oxygenation before and after water diuresis. Nephron. Physiology 2005; 99(4):p101-4. *Not relevant to key questions*

1463. Gille J, Spieth K, Kaufmann R. Metronomic low-dose chemotherapy as antiangiogenic therapeutic strategy for cancer. Journal der Deutschen Dermatologischen Gesellschaft 2005; 3(1):26-32. *Not RCT or controlled trial*

1464. Gillespie EA, Gillespie BW, Stevens MJ. Painful diabetic neuropathy: impact of an alternative approach. Diabetes Care 2007; 30(4):999-1001. *Not RCT or controlled trial*

1465. Gillis BP, Averbach FM, Caggiula AW, et al. Features of the nutrient database and analysis system for the Modification of Diet in Renal Disease Study.[Erratum appears in Control Clin Trials 1994 Aug;15(4):326]. Controlled Clinical Trials 1994; 15(1):44-58. *Not RCT or controlled trial*

1466. Gillis BP, Caggiula AW, Chiavacci AT, et al. Nutrition intervention program of the Modification of Diet in Renal Disease Study: a self-management approach. Journal of the American Dietetic Association 1995; 95(11):1288-94. *Not CKD treatment*

1467. Ginifer C, Kelly AM. Administration of rectal indomethacin does not reduce the requirement for intravenous narcotic analgesia in acute renal colic. European Journal of Emergency Medicine 1996; 3(2):92-4. *Not CKD treatment*

1468. Ginsberg AM, Laurenzi MW, Rouse DJ, et al. Assessment of the effects of the nitroimidazo-oxazine PA-824 on renal function in healthy subjects. Antimicrobial Agents & Chemotherapy 2009; 53(9):3726-33. *Follow-up less than 6 months*

1469. Giordano M, Castellino P, McConnell EL, et al. Effect of amino acid infusion on renal hemodynamics in humans: a dose-response study. American Journal of Physiology 1994; 267(5 Pt 2):F703-8. *Sample size less than 50 patients*

1470. Giordano M, Sanders LR, Castellino P, et al. Effect of alpha-adrenergic blockers, ACE inhibitors, and calcium channel antagonists on renal function in hypertensive non-insulin-dependent diabetic patients. Nephron 1996; 72(3):447-53. *Sample size less than 50 patients*

1471. Giovannetti S, Barsotti G, Cupisti A, et al. Oral activated charcoal in patients with uremic pruritus. Nephron 1995; 70(2):193-6. *Sample size less than 50 patients*

1472. Girbes AR, Smit AJ, Meijer S, et al. Lithium and the renal response to gludopa, fenoldopam and dopamine. British Journal of Clinical Pharmacology 1990; 30(4):652-3. *Not RCT or controlled trial*

1473. Girbes AR, Smit AJ, Meijer S, et al. Renal and endocrine effects of fenoldopam and metoclopramide in normal man. Nephron 1990; 56(2):179-85. *Sample size less than 50 patients*

1474. Girbes AR, van Veldhuisen DJ, Smit AJ, et al. Renal and neurohumoral effects of ibopamine and metoclopramide in normal man. British Journal of Clinical Pharmacology 1991; 31(6):701-4. *Sample size less than 50 patients*

1475. Girndt M, Pietsch M, Kohler H. Tetanus immunization and its association to hepatitis B vaccination in patients with chronic renal failure. American Journal of Kidney Diseases 1995; 26(3):454-60. *Sample size less than 50 patients*

1476. Gisclon LG, Boyd RA, Williams RL, et al. The effect of probenecid on the renal elimination of cimetidine. Clinical Pharmacology & Therapeutics 1989; 45(4):444-52. *Not RCT or controlled trial*

1477. Giugliano D, Acampora R, Marfella R, et al. Hemodynamic and metabolic effects of transdermal clonidine in patients with hypertension and non-insulin-dependent diabetes mellitus. American Journal of Hypertension 1998; 11(2):184-9. *Sample size less than 50 patients*

1478. Giustina A, Bossoni S, Cimino A, et al. Picotamide, a dual TXB synthetase inhibitor and TXB receptor antagonist, reduces exercise-induced albuminuria in microalbuminuric patients with NIDDM. Diabetes 1993; 42(1):178-82. *Sample size less than 50 patients*

1479. Giustina A, Bossoni S, Macca C, et al. Isradipine decreases exercise-induced albuminuria in patients with essential hypertension. Renal Failure 1993; 15(4):509-14. *Sample size less than 50 patients*

1480. Giustina A, Perini P, Desenzani P, et al. Long-term treatment with the dual antithromboxane agent picotamide decreases microalbuminuria in normotensive type 2 diabetic patients. Diabetes 1998; 47(3):423-30. *Sample size less than 50 patients*

1481. Givertz MM, Massie BM, Fields TK, et al. The effects of KW-3902, an adenosine A1-receptor antagonist,on diuresis and renal function in patients with acute decompensated heart failure and renal impairment or diuretic resistance. Journal of the American College of Cardiology 2007; 50(16):1551-60. *Not CKD treatment*

1482. Glasser SP. Angiotensin converting enzyme inhibitors: are they preferred first-line therapy? Current Hypertension Reports 2000; 2(4):392-7. *Not RCT or controlled trial*

1483. Glassock RJ. Uremia (end-stage renal disease): how cost-effective are preventive strategies? Journal of Renal Nutrition 2010 Sep; 20(5 Suppl):S131-4. *Not RCT or controlled trial*

1484. Gleiter CH, Becker T, Schreeb KH, et al. Fenoterol but not dobutamine increases erythropoietin production in humans. Clinical Pharmacology & Therapeutics 1997; 61(6):669-76. *Sample size less than 50 patients*

1485. Glorioso N, Manunta P, Troffa C, et al. Effects of nitrendipine on blood pressure, renin-angiotensin system, and kidney function in essential hypertension. Journal of Cardiovascular Pharmacology 1988; 12 Suppl 4:S142-5. *Sample size less than 50 patients*

1486. Glynn LG, Buckley B, Reddan D, et al. Multimorbidity and risk among patients with established cardiovascular disease: a cohort study. British Journal of General Practice 2008; 58(552):488-94. *Not CKD treatment*

1487. Glynn LG, Reddan D, Newell J, et al. Chronic kidney disease and mortality and morbidity among patients with established cardiovascular disease: a West of Ireland community-based cohort study. Nephrology Dialysis Transplantation 2007; 22(9):2586-94. *Sample size less than 50 patients*

1488. Gobburu JVS, Sekar VJ. Application of modeling and simulation to integrate clinical pharmacology knowledge across a new drug application. International Journal of Clinical Pharmacology & Therapeutics 2002; 40(7):281-8. *Not early CKD*

1489. Goddard J, Johnston NR, Cumming AD, et al. Fractional urinary excretion of endothelin-1 is reduced by acute ETB receptor blockade. American Journal of Physiology - Renal Physiology 2007; 293(5):F1433-8. *Not relevant to key questions*

1490. Goddard J, Johnston NR, Hand MF, et al. Endothelin-A receptor antagonism reduces blood pressure and increases renal blood flow in hypertensive patients with chronic renal failure: a comparison of selective and combined endothelin receptor blockade. Circulation 2004; 109(9):1186-93. *Not CKD treatment*

1491. Goenka N, Kotonya C, Penney MD, et al. Thiazolidinediones and the renal and hormonal response to water immersion-induced volume expansion in type 2 diabetes mellitus. American Journal of Physiology - Endocrinology & Metabolism 2008; 294(4):E733-9. *Not CKD treatment*

1492. Goeters C, Reinhardt C, Gronau E, et al. Minimal flow sevoflurane and isoflurane anaesthesia and impact on renal function. European Journal of Anaesthesiology 2001; 18(1):43-50. *Not early CKD*

1493. Goicoechea M, de Vinuesa SG, Lahera V, et al. Effects of atorvastatin on inflammatory and fibrinolytic parameters in patients with chronic kidney disease. Journal of the American Society of Nephrology 2006; 17(12 Suppl 3):S231-5. *Not relevant to key questions*

1494. Goicoechea M, de Vinuesa SG, Verdalles U, et al. Effect of allopurinol in chronic kidney disease progression and cardiovascular risk. Clinical Journal of The American Society of Nephrology: CJASN 2010 Aug; 5(8):1388-93. *Not CKD treatment*

1495. Goicoechea M, Liu S, Best B, et al. Greater tenofovir-associated renal function decline with protease inhibitor-based versus nonnucleoside reverse-transcriptase inhibitor-based therapy. Journal of Infectious Diseases 2008; 197(1):102-8. *Follow-up less than 6 months*

1496. Golan L, Birkmeyer JD, Welch HG. The cost-effectiveness of treating all patients with type 2 diabetes with angiotensin-converting enzyme inhibitors. Annals of Internal Medicine 1999; 131(9):660-7. *Not CKD treatment*

1497. Goldberg DI, Dillon MA, Slatopolsky EA, et al. Effect of RenaGel, a non-absorbed, calcium- and aluminium-free phosphate binder, on serum phosphorus, calcium, and intact parathyroid hormone in end-stage renal disease patients. Nephrology Dialysis Transplantation 1998; 13(9):2303-10. *Follow-up less than 6 months*

1498. Goldenberg I, Chonchol M, Guetta V. Reversible acute kidney injury following contrast exposure and the risk of long-term mortality. American Journal of Nephrology 2009; 29(2):136-44. *Not CKD treatment*

1499. Goldenberg I, Moss AJ, McNitt S, et al. Relations among renal function, risk of sudden cardiac death, and benefit of the implanted cardiac defibrillator in patients with ischemic left ventricular dysfunction. American Journal of Cardiology 2006; 98(4):485-90. *Not RCT or controlled trial*

1500. Goldenberg I, Shechter M, Matetzky S, et al. Oral acetylcysteine as an adjunct to saline hydration for the prevention of contrast-induced nephropathy following coronary angiography. A randomized controlled trial and review of the current literature. European Heart Journal 2004; 25(3):212-8. *Not CKD treatment*

1501. Goldfarb B, Pardoux CM. Exploring series of multivariate censored temporal data through fuzzy coding and correspondence analysis. Statistics in Medicine 2006; 25(10):1741-50. *Not RCT or controlled trial*

1502. Goldfarb S, Spinler S, Berns JS, et al. Low-osmolality contrast media and the risk of contrast-associated nephrotoxicity. Investigative Radiology 1993; 28 Suppl 5:S7-10; discussion S1-2. *Not CKD treatment*

1503. Goldfarb S, Walker BR, Agus ZS. The uricosuric effect of oxaprozin in humans. Journal of Clinical Pharmacology 1985; 25(2):144-8. *Sample size less than 50 patients*

1504. Goldfarb-Rumyantzev AS, Pappas L. Prediction of renal insufficiency in Pima Indians with nephropathy of type 2 diabetes mellitus. American Journal of Kidney Diseases 2002; 40(2):252-64. *Not CKD treatment*

1505. Goldsmith D. 2009: a requiem for rHuEPOs--but should we nail down the coffin in 2010? Clinical Journal of The American Society of Nephrology: CJASN 2010 May; 5(5):929-35. *Not RCT or controlled trial*

1506. Goldsmith DJ, Covic A. Coronary artery disease in uremia: Etiology, diagnosis, and therapy. Kidney International 2001; 60(6):2059-78. *Not early CKD*

1507. Goldstein DJ, Wang O, Gitter BD, et al. Dose-response study of the analgesic effect of lanepitant in patients with painful diabetic neuropathy. Clinical Neuropharmacology 2001; 24(1):16-22. *Not CKD treatment*

1508. Golightly LK, O'Fallon CL, Moran WD, et al. Pharmacist monitoring of drug therapy in patients with abnormal serum creatinine levels. Hospital Pharmacy 1993; 28(8):725-7. *Sample size less than 50 patients*

1509. Golper TA, Illingworth DR, Morris CD, et al. Lovastatin in the treatment of multifactorial hyperlipidemia associated with proteinuria. American Journal of Kidney Diseases 1989; 13(4):312-20. *Sample size less than 50 patients*

1510. Gomes VO, Poli de Figueredo CE, Caramori P, et al. N-acetylcysteine does not prevent contrast induced nephropathy after cardiac catheterisation with an ionic low osmolality contrast medium: a multicentre clinical trial. Heart 2005; 91(6):774-8. *Not relevant to key questions*

1511. Gonzalez GL, Manrique CM, Sowers JR. High cardiovascular risk in patients with diabetes and the cardiometabolic syndrome: mandate for statin therapy. Journal of the CardioMetabolic Syndrome 2006; 1(3):178-83. *Not RCT or controlled trial*

1512. Gonzalez RP, Falimirski M, Holevar MR, et al. Surgical management of renal trauma: is vascular control necessary? Journal of Trauma-Injury Infection & Critical Care 1999; 47(6):1039-42; discussion 42-4. *Not CKD treatment*

1513. Gonzalez-Abraldes J, Albillos A, Banares R, et al. Randomized comparison of long-term losartan versus propranolol in lowering portal pressure in cirrhosis. Gastroenterology 2001; 121(2):382-8. *Not early CKD*

1514. Gonzalez-Ortiz M, Mora-Martinez JM, Martinez-Abundis E, et al. Effect of valsartan on renal handling of uric acid in healthy subjects. Journal of Nephrology 2000; 13(2):126-8. *Not early CKD*

1515. Good J, Frost G, Oakley CM, et al. The renal effects of dopamine and dobutamine in stable chronic heart failure. Postgraduate Medical Journal 1992; 68 Suppl 2:S7-11. *Not CKD treatment*

1516. Good JM, Brady AJ, Noormohamed FH, et al. Effect of intense angiotensin II suppression on the diuretic response to furosemide during chronic ACE inhibition. Circulation 1994; 90(1):220-4. *Sample size less than 50 patients*

1517. Goodman WG, Frazao JM, Goodkin DA, et al. A calcimimetic agent lowers plasma parathyroid hormone levels in patients with secondary hyperparathyroidism. Kidney International 2000; 58(1):436-45. *Not early CKD*

1518. Gookin JL, McWhorter D, Vaden S, et al. Outcome assessment of a computer-animated model for learning about the regulation of glomerular filtration rate. Advances in Physiology Education 2010 Jun; 34(2):97-105. *Not CKD treatment*

1519. Goonasekera CD, Dillon MJ. Random zero sphygmomanometer versus automatic oscillometric blood pressure monitor; is either the instrument of choice? Journal of Human Hypertension 1995; 9(11):885-9. *Not CKD treatment*

1520. Gordon AC, Russell JA, Walley KR, et al. The effects of vasopressin on acute kidney injury in septic shock. Intensive Care Medicine 2010 Jan; 36(1):83-91. *Not CKD treatment*

1521. Gordon EJ, Prohaska TR, Gallant MP, et al. Longitudinal analysis of physical activity, fluid intake, and graft function among kidney transplant recipients. Transplant International 2009; 22(10):990-8. *Not RCT or controlled trial*

1522. Gorse GJ, Bernstein JM, Cronin RE, et al. A comparison of netilmicin and tobramycin therapy in patients with renal impairment. Scandinavian Journal of Infectious Diseases 1992; 24(4):503-14. *Not CKD treatment*

1523. Goswami K, Gachhui R, Bandopadhyay A. Hepatorenal dysfunctions in lead pollution. Journal of Environmental Science & Engineering 2005; 47(1):75-80. *Sample size less than 50 patients*

1524. Goto F, Kato S, Sudo I. Treatment of intraoperative hypertension with enflurane, nicardipine, or human atrial natriuretic peptide: haemodynamic and renal effects. Canadian Journal of Anaesthesia 1992; 39(9):932-7. *Not CKD treatment*

1525. Gottesman RF, Sozio SM. Management of symptomatic carotid stenosis in individuals with CKD. Journal of the American Society of Nephrology 2010; 21(1):9-11. *Not RCT or controlled trial*

1526. Gottlieb SS. Adenosine A1 antagonists and the cardiorenal syndrome. Current Heart Failure Reports 2008; 5(2):105-9. *Not CKD treatment*

1527. Gottlieb SS, Brater DC, Thomas I, et al. BG9719 (CVT-124), an A1 adenosine receptor antagonist, protects against the decline in renal function observed with diuretic therapy.[Erratum appears in Circulation 2002 Sep 24;106(13):1743]. Circulation 2002; 105(11):1348-53. *Follow-up less than 6 months*

1528. Gottlieb SS, Skettino SL, Wolff A, et al. Effects of BG9719 (CVT-124), an A1-adenosine receptor antagonist, and furosemide on glomerular filtration rate and natriuresis in patients with congestive heart failure. Journal of the American College of Cardiology 2000; 35(1):56-9. *Sample size less than 50 patients*

1529. Gould MM, Mohamed-Ali V, Goubet SA, et al. Associations of urinary albumin excretion rate with vascular disease in europid nondiabetic subjects. Journal of Diabetes & its Complications 1994; 8(3):180-8. *Not RCT or controlled trial*

1530. Gouva C, Nikolopoulos P, Ioannidis JPA, et al. Treating anemia early in renal failure patients slows the decline of renal function: a randomized controlled trial. Kidney International 2004; 66(2):753-60. *Not relevant to key questions*

1531. Govindarajan G, Saab G, Whaley-Connell A. Outcomes of carotid revascularization in patients with chronic kidney disease. Advances in Chronic Kidney Disease 2008; 15(4):347-54. *Not CKD treatment*

1532. Graber SE, Krantz SB. Erythropoietin: biology and clinical use. Hematology - Oncology Clinics of North America 1989; 3(3):369-400. *Not relevant to key questions*

1533. Gradman AH. Evolving understanding of the renin-angiotensin-aldosterone system: pathophysiology and targets for therapeutic intervention. American Heart Journal 2009; 157(6 Suppl):S1-6. *Not RCT or controlled trial*

1534. Graiff C, Bezza M, Ziller F, et al. Caerulein in the treatment of biliary and renal colic. Peptides 1985; 6 Suppl 3:47-51. *Not CKD treatment*

1535. Grande L, Rimola A, Cugat E, et al. Effect of venovenous bypass on perioperative renal function in liver transplantation: results of a randomized, controlled trial. Hepatology 1996; 23(6):1418-28. *Not CKD treatment*

1536. Grant MC, Kon Z, Joshi A, et al. Is aprotinin safe to use in a cohort at increased risk for thrombotic events: results from a randomized, prospective trial in off-pump coronary artery bypass. Annals of Thoracic Surgery 2008; 86(3):815-22; discussion -22. *Sample size less than 50 patients*

1537. Gras J, Llenas J, Jansat JM, et al. Almotriptan, a new anti-migraine agent: a review. CNS Drug Reviews 2002; 8(3):217-34. *Not CKD treatment*

1538. Grases F, Garcia-Gonzalez R, Redondo E, et al. Effects of escin on indinavir crystallization time in the urine of patients with HIV-I infection: a multicenter, randomized, open-label, controlled, four-period crossover trial. Clinical Therapeutics 2004; 26(12):2045-55. *Follow-up less than 6 months*

1539. Grassegger A, Schuler G, Hessenberger G, et al. Interferon-gamma in the treatment of systemic sclerosis: a randomized controlled multicentre trial. British Journal of Dermatology 1998; 139(4):639-48. *Sample size less than 50 patients*

1540. Greenbaum R, Zucchelli P, Caspi A, et al. Comparison of the pharmacokinetics of fosinoprilat with enalaprilat and lisinopril in patients with congestive heart failure and chronic renal insufficiency. British Journal of Clinical Pharmacology 2000; 49(1):23-31. *Follow-up less than 6 months*

1541. Greenberg B, Thomas I, Banish D, et al. Effects of multiple oral doses of an A1 adenosine antagonist, BG9928, in patients with heart failure: results of a placebo-controlled, dose-escalation study. Journal of the American College of Cardiology 2007; 50(7):600-6. *Not RCT or controlled trial*

1542. Greene T, Daugirdas JT, Depner TA, et al. Solute clearances and fluid removal in the frequent hemodialysis network trials. American Journal of Kidney Diseases 2009; 53(5):835-44. *Not early CKD*

1543. Greenstone MA, Shaw AB. Alternate day corticosteroid causes alternate day hyperglycaemia. Postgraduate Medical Journal 1987; 63(743):761-4. *Not RCT or controlled trial*

1544. Greenwood V. ARBs vs ACE inhibitors for preventing diabetic nephropathy. Journal of Family Practice 2005; 54(5):453; discussion -4. *Not RCT or controlled trial*

1545. Gregory DD, Sarnak MJ, Konstam MA, et al. Impact of chronic kidney disease and anemia on hospitalization expense in patients with left ventricular dysfunction. American Journal of Cardiology 2003; 92(11):1300-5. *Not CKD treatment*

1546. Greminger P, Foerster E, Vetter H, et al. Minoxidil and captopril in severe hypertension. Klinische Wochenschrift 1986; 64(7):327-32. *Sample size less than 50 patients*

1547. Gretz N, Strauch M. Statistical problems in designing, conducting, and analysing nutritional trials in patients with chronic renal failure. Contributions to Nephrology 1986; 53:82-91. *Not RCT or controlled trial*

1548. Grima KM. Therapeutic apheresis in hematological and oncological diseases. Journal of Clinical Apheresis 2000; 15(1-2):28-52. *Not relevant to key questions*

1549. Grimm RH, Jr., Svendsen KH, Kasiske B, et al. Proteinuria is a risk factor for mortality over 10 years of follow-up. MRFIT Research Group. Multiple Risk Factor Intervention Trial. Kidney International - Supplement 1997; 63:S10-4. *Not RCT or controlled trial*

1550. Groban L, Ebert TJ, Kreis DU, et al. Hemodynamic, renal, and hormonal responses to incremental ANF infusions in humans. American Journal of Physiology 1989; 256(5 Pt 2):F780-6. *Sample size less than 50 patients*

1551. Groetzner J, Kaczmarek I, Landwehr P, et al. Renal recovery after conversion to a calcineurin inhibitor-free immunosuppression in late cardiac transplant recipients. European Journal of Cardio-Thoracic Surgery 2004; 25(3):333-41. *Sample size less than 50 patients*

1552. Groetzner J, Kaczmarek I, Schulz U, et al. Mycophenolate and sirolimus as calcineurin inhibitor-free immunosuppression improves renal function better than calcineurin inhibitor-reduction in late cardiac transplant recipients with chronic renal failure.[Erratum appears in Transplantation. 2009 Apr 27;87(8):1264]. Transplantation 2009; 87(5):726-33. *Not CKD treatment*

1553. Groetzner J, Meiser B, Landwehr P, et al. Mycophenolate mofetil and sirolimus as calcineurin inhibitor-free immunosuppression for late cardiac-transplant recipients with chronic renal failure. Transplantation 2004; 77(4):568-74. *Not CKD treatment*

1554. Groetzner J, Meiser BM, Schirmer J, et al. Tacrolimus or cyclosporine for immunosuppression after cardiac transplantation: which treatment reveals more side effects during long-term follow-up? Transplantation Proceedings 2001; 33(1-2):1461-4. *Not CKD treatment*

1555. Groetzner J, Wittwer T, Kaczmarek I, et al. Conversion to sirolimus and mycophenolate can attenuate the progression of bronchiolitis obliterans syndrome and improves renal function after lung transplantation. Transplantation 2006; 81(3):355-60. *Sample size less than 50 patients*

1556. Groggel GC, Cheung AK, Ellis-Benigni K, et al. Treatment of nephrotic hyperlipoproteinemia with gemfibrozil. Kidney International 1989; 36(2):266-71. *Sample size less than 50 patients*

1557. Gross AS, McLachlan AJ, Minns I, et al. Simultaneous administration of a cocktail of markers to measure renal drug elimination pathways: absence of a pharmacokinetic interaction between fluconazole and sinistrin, p-aminohippuric acid and pindolol. British Journal of Clinical Pharmacology 2001; 51(6):547-55. *Not CKD treatment*

1558. Gross JL, Zelmanovitz T, Moulin CC, et al. Effect of a chicken-based diet on renal function and lipid profile in patients with type 2 diabetes: a randomized crossover trial. Diabetes Care 2002; 25(4):645-51. *Sample size less than 50 patients*

1559. Gross P, Schirutschke H, Barnett K. Should we prescribe blood pressure lowering drugs to every patient with advanced chronic kidney disease? A comment on two recent meta-analyses. Polskie Archiwum Medycyny Wewnetrznej 2009 Oct; 119(10):644-7. *Not RCT or controlled trial*

1560. Grossman E, Messerli FH. Why beta-blockers are not cardioprotective in elderly patients with hypertension. Current Cardiology Reports 2002; 4(6):468-73. *Not RCT or controlled trial*

1561. Grossman PD, Burroughs M, Guthmann RA. Clinical inquiries. What interventions reduce the risk of contrast nephropathy for high-risk patients? Journal of Family Practice 2005; 54(4):365-7. *Not RCT or controlled trial*

1562. Grossman RM, Chevret S, Abi-Rached J, et al. Long-term safety of cyclosporine in the treatment of psoriasis. Archives of Dermatology 1996; 132(6):623-9. *Not CKD treatment*

1563. Grostern RJ, Bryar PJ, Zimbric ML, et al. Toxicity and dose-response studies of 1alpha-hydroxyvitamin D2 in a retinoblastoma xenograft model. Archives of Ophthalmology 2002; 120(5):607-12. *Not human studies*

1564. Groth S, Nielsen H, Sorensen JB, et al. Acute and long-term nephrotoxicity of cis-platinum in man. Cancer Chemotherapy & Pharmacology 1986; 17(2):191-6. *Not CKD treatment*

1565. Group ACEIiPRDS. Summaries for patients. Using a type of blood pressure medicine, angiotensin-converting enzyme inhibitors, to prevent worsening of kidney disease unrelated to diabetes. Annals of Internal Medicine 2001; 135(2):S-21. *Not RCT or controlled trial*

1566. Group ACEIiDNT. Should all patients with type 1 diabetes mellitus and microalbuminuria receive angiotensin-converting enzyme inhibitors? A meta-analysis of individual patient data. Annals of Internal Medicine 2001; 134(5):370-9. *Not relevant to key questions*

1567. Group AS, Cushman WC, Evans GW, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. New England Journal of Medicine 2010 Apr 29; 362(17):1575-85. *Not CKD treatment*

1568. Group B. The BErgamo NEphrologic DIabetes Complications Trial (BENEDICT): design and baseline characteristics. Controlled Clinical Trials 2003; 24(4):442-61. *Not RCT or controlled trial*

1569. Group PS. Dissociation between blood pressure reduction and fall in proteinuria in primary renal disease: a randomized double-blind trial. Journal of Hypertension 2002; 20(4):729-37. *Not CKD treatment*

1570. Grover-Paez F, Villegas Rivera G, Guillen Ortiz R. Sildenafil citrate diminishes microalbuminuria and the percentage of A1c in male patients with type 2 diabetes. Diabetes Research & Clinical Practice 2007; 78(1):136-40. *Follow-up less than 6 months*

1571. Gruberg L, Waksman R, Ajani AE, et al. The effect of intracoronary radiation for the treatment of recurrent in-stent restenosis in patients with chronic renal failure. Journal of the American College of Cardiology 2001; 38(4):1049-53. *Not RCT or controlled trial*

1572. Gruss E, Tomas JF, Bernis C, et al. Nephroprotective effect of cilastatin in allogeneic bone marrow transplantation. Results from a retrospective analysis. Bone Marrow Transplantation 1996; 18(4):761-5. *Not RCT or controlled trial*

1573. Gualano B, Ugrinowitsch C, Novaes RB, et al. Effects of creatine supplementation on renal function: a randomized, double-blind, placebo-controlled clinical trial. European Journal of Applied Physiology 2008; 103(1):33-40. *Not CKD treatment*

1574. Guasch A. Improving renal outcomes in chronic anemia: learning from paroxysmal nocturnal hemoglobinuria. American Journal of Hematology 2010 Aug; 85(8):551-2. *Not RCT or controlled trial*

1575. Guasch A, Parham M, Zayas CF, et al. Contrasting effects of calcium channel blockade versus converting enzyme inhibition on proteinuria in African Americans with non-insulin-dependent diabetes mellitus and nephropathy. Journal of the American Society of Nephrology 1997; 8(5):793-8. *Sample size less than 50 patients*

1576. Guastalla JP, Vermorken JB, Wils JA, et al. Phase II trial for intraperitoneal cisplatin plus intravenous sodium thiosulphate in advanced ovarian carcinoma patients with minimal residual disease after cisplatin-based chemotherapy--a phase II study of the EORTC Gynaecological Cancer Cooperative Group. European Journal of Cancer 1994; 30A(1):45-9. *Not CKD treatment*

1577. Gubern JM, Sancho JJ, Simo J, et al. A randomized trial on the effect of mannitol on postoperative renal function in patients with obstructive jaundice. Surgery 1988; 103(1):39-44. *Sample size less than 50 patients*

1578. Gudbjornsdottir S, Friberg P, Elam M, et al. The effect of metformin and insulin on sympathetic nerve activity, norepinephrine spillover and blood pressure in obese, insulin resistant, normoglycemic, hypertensive men. Blood Pressure 1994; 3(6):394-403. *Sample size less than 50 patients*

1579. Gude E, Gullestad L, Arora S, et al. Benefit of early conversion from CNI-based to everolimus-based immunosuppression in heart transplantation. Journal of Heart & Lung Transplantation 2010 Jun; 29(6):641-7. *Not CKD treatment*

1580. Guerin C, Girard R, Selli JM, et al. Initial versus delayed acute renal failure in the intensive care unit. A multicenter prospective epidemiological study. Rhone-Alpes Area Study Group on Acute Renal Failure.[Erratum appears in Am J Respir Crit Care Med 2001 Mar;163(3 Pt 1):793-4]. American Journal of Respiratory & Critical Care Medicine 2000; 161(3 Pt 1):872-9. *Not RCT or controlled trial*

1581. Guerra JG, Casalino E, Palomino JC, et al. Imipenem/cilastatin vs. gentamicin/clindamycin for the treatment of moderate to severe infections in hospitalized patients. Reviews of Infectious Diseases 1985; 7 Suppl 3:S463-70. *Not early CKD*

1582. Guerrero-Romero F, Rodriguez-Moran M, Paniagua-Sierra JR, et al. Pentoxifylline reduces proteinuria in insulin-dependent and non insulin-dependent diabetic patients. Clinical Nephrology 1995; 43(2):116-21. *Follow-up less than 6 months*

1583. Guglielmi G, de Terlizzi F, Aucella F, et al. Quantitative ultrasound technique at the phalanges in discriminating between uremic and osteoporotic patients. European Journal of Radiology 2006; 60(1):108-14. *Not RCT or controlled trial*

1584. Guh J-Y. Proteinuria versus albuminuria in chronic kidney disease. Nephrology 2010 Jun; 15 Suppl 2:53-6. *Not CKD treatment*

1585. Guillet C. Overview of novel renal properties of tertatolol. Cardiology 1993; 83 Suppl 1:64-9. *Sample size less than 50 patients*

1586. Guillevin L, Le Thi Huong Du, Godeau P, et al. Clinical findings and prognosis of polyarteritis nodosa and Churg-Strauss angiitis: a study in 165 patients. British Journal of Rheumatology 1988; 27(4):258-64. *Not RCT or controlled trial*

1587. Guitterez NV, Diaz A, Timmis GC, et al. Determinants of serum creatinine trajectory in acute contrast nephropathy. Journal of Interventional Cardiology 2002; 15(5):349-54. *Not CKD treatment*

1588. Guizar JM, Kornhauser C, Malacara JM, et al. Renal functional reserve in patients with recently diagnosed Type 2 diabetes mellitus with and without microalbuminuria. Nephron 2001; 87(3):223-30. *Not RCT or controlled trial*

1589. Gulel O, Keles T, Eraslan H, et al. Prophylactic acetylcysteine usage for prevention of contrast nephropathy after coronary angiography. Journal of Cardiovascular Pharmacology 2005; 46(4):464-7. *Follow-up less than 6 months*

1590. Gullestad L, Iversen M, Mortensen S-A, et al. Everolimus with reduced calcineurin inhibitor in thoracic transplant recipients with renal dysfunction: a multicenter, randomized trial. Transplantation 2010 Apr 15; 89(7):864-72. *Not CKD treatment*

1591. Gulmann C, Rudberg S, Osterby R. Renal arterioles in patients with type I diabetes and microalbuminuria before and after treatment with antihypertensive drugs. Virchows Archiv 1999; 434(6):523-8. *Sample size less than 50 patients*

1592. Guney I, Selcuk NY, Altintepe L, et al. Antifibrotic effects of aldosterone receptor blocker (spironolactone) in patients with chronic kidney disease. Renal Failure 2009; 31(9):779-84. *Sample size less than 50 patients*

1593. Gunning TC, Brown MR, Swygert TH, et al. Perioperative renal function in patients undergoing orthotopic liver transplantation. A randomized trial of the effects of verapamil. Transplantation 1991; 51(2):422-7. *Not CKD treatment*

1594. Gunst J, Schetz M. Clinical benefits of tight glycaemic control: effect on the kidney. Best Practice & Research 2009; Clinical Anaesthesiology. 23(4):431-9. *Not RCT or controlled trial*

1595. Guo LL, Pan Y, Jin HM. Adiponectin is positively associated with insulin resistance in subjects with type 2 diabetic nephropathy and effects of angiotensin II type 1 receptor blocker losartan. Nephrology Dialysis Transplantation 2009; 24(6):1876-83. *Not relevant to key questions*

1596. Gupta AK, Rocher LL, Schmaltz SP, et al. Short-term changes in renal function, blood pressure, and electrolyte levels in patients receiving cyclosporine for dermatologic disorders. Archives of Internal Medicine 1991; 151(2):356-62. *Not CKD treatment*

1597. Gupta R, Birnbaum Y, Uretsky BF. The renal patient with coronary artery disease: current concepts and dilemmas. Journal of the American College of Cardiology 2004; 44(7):1343-53. *Follow-up less than 6 months*

1598. Gupta RK, Kapoor A, Tewari S, et al. Captopril for prevention of contrast-induced nephropathy in diabetic patients: a randomised study. Indian Heart Journal 1999; 51(5):521-6. *Not early CKD*

1599. Gupta RK, Kjeldsen SE, Krause L, et al. Hemodynamic effects of quinapril, a novel angiotensin-converting enzyme inhibitor. Clinical Pharmacology & Therapeutics 1990; 48(1):41-9. *Sample size less than 50 patients*

1600. Gupta SK, Parker RA, Robbins GK, et al. The effects of highly active antiretroviral therapy on albuminuria in HIV-infected persons: results from a randomized trial. Nephrology Dialysis Transplantation 2005; 20(10):2237-42. *Not CKD treatment*

1601. Gupta SK, Smurzynski M, Franceschini N, et al. The effects of HIV type-1 viral suppression and non-viral factors on quantitative proteinuria in the highly active antiretroviral therapy era. Antiviral Therapy 2009; 14(4):543-9. *Not RCT or controlled trial*

1602. Gurley SB, Coffman TM. The renin-angiotensin system and diabetic nephropathy. Seminars in Nephrology 2007; 27(2):144-52. *Not RCT or controlled trial*

1603. Gurm HS, Lincoff AM, Kleiman NS, et al. Double jeopardy of renal insufficiency and anemia in patients undergoing percutaneous coronary interventions. American Journal of Cardiology 2004; 94(1):30-4. *Not CKD treatment*

1604. Guru V, Fremes SE. The role of N-acetylcysteine in preventing radiographic contrast-induced nephropathy. Clinical Nephrology 2004; 62(2):77-83. *Not CKD treatment*

1605. Gutzwiller J-P, Tschopp S, Bock A, et al. Glucagon-like peptide 1 induces natriuresis in healthy subjects and in insulin-resistant obese men. Journal of Clinical Endocrinology & Metabolism 2004; 89(6):3055-61. *Not relevant to key questions*

1606. Guy M, Newall R, Borzomato J, et al. Use of a first-line urine protein-to-creatinine ratio strip test on random urines to rule out proteinuria in patients with chronic kidney disease. Nephrology Dialysis Transplantation 2009; 24(4):1189-93. *Not CKD treatment*

1607. Guy M, Newall R, Borzomato J, et al. Diagnostic accuracy of the urinary albumin: creatinine ratio determined by the CLINITEK Microalbumin and DCA 2000+ for the rule-out of albuminuria in chronic kidney disease. Clinica Chimica Acta 2009; 399(1-2):54-8. *Not CKD treatment*

1608. Guy M, Newall R, Borzomato J, et al. Use of a first-line urine protein-to-creatinine ratio strip test on random urines to rule out proteinuria in patients with chronic kidney disease. Nephrology Dialysis Transplantation 2009; 24(4):1189-93. *Not CKD treatment*

1609. Haanpaa ML, Gourlay GK, Kent JL, et al. Treatment considerations for patients with neuropathic pain and other medical comorbidities. Mayo Clinic Proceedings 2010 Mar; 85(3 Suppl):S15-25. *Not CKD treatment*

1610. Haase M, Haase-Fielitz A, Bagshaw SM, et al. Phase II, randomized, controlled trial of high-dose N-acetylcysteine in high-risk cardiac surgery patients. Critical Care Medicine 2007; 35(5):1324-31. *Not RCT or controlled trial*

1611. Haase M, Haase-Fielitz A, Bellomo R, et al. Sodium bicarbonate to prevent increases in serum creatinine after cardiac surgery: a pilot double-blind, randomized controlled trial. Critical Care Medicine 2009; 37(1):39-47. *Not RCT or controlled trial*

1612. Haase M, Haase-Fielitz A, Ratnaike S, et al. N-Acetylcysteine does not artifactually lower plasma creatinine concentration. Nephrology Dialysis Transplantation 2008; 23(5):1581-7. *Follow-up less than 6 months*

1613. Hadjadj S, Gourdy P, Zaoui P, et al. Effect of raloxifene -- a selective oestrogen receptor modulator -- on kidney function in post-menopausal women with Type 2 diabetes: results from a randomized, placebo-controlled pilot trial. Diabetic Medicine 2007; 24(8):906-10. *Not relevant to key questions*

1614. Hadj-Aissa A, Bankir L, Fraysse M, et al. Influence of the level of hydration on the renal response to a protein meal. Kidney International 1992; 42(5):1207-16. *Sample size less than 50 patients*

1615. Hadjibabaie M, Alimoghaddam K, Shamshiri AR, et al. Continuous bladder irrigation prevents hemorrhagic cystitis after allogeneic hematopoietic cell transplantation. Urologic Oncology 2008; 26(1):43-6. *Sample size less than 50 patients*

1616. Haffner CA, Kendall MJ, Struthers AD, et al. Effects of captopril and enalapril on renal function in elderly patients with chronic heart failure. Postgraduate Medical Journal 1995; 71(835):287-92. *Follow-up less than 6 months*

1617. Hafner J, Keusch G, Wahl C, et al. Uremic small-artery disease with medial calcification and intimal hyperplasia (so-called calciphylaxis): a complication of chronic renal failure and benefit from parathyroidectomy. Journal of the American Academy of Dermatology 1995; 33(6):954-62. *Not RCT or controlled trial*

1618. Hager B, Betschart M, Krapf R. Effect of postoperative intravenous loop diuretic on renal function after major surgery. Schweizerische Medizinische Wochenschrift 1996; Journal Suisse de Medecine. 126(16):666-73. *Follow-up less than 6 months*

1619. Hagg E, Carlberg BC, Hillorn VS, et al. Magnesium therapy in type 1 diabetes. A double blind study concerning the effects on kidney function and serum lipid levels. Magnesium Research 1999; 12(2):123-30. *Sample size less than 50 patients*

1620. Haghi D, Papavassiliu T, Hach C, et al. Utility of combined parameters of common carotid intima-media thickness or albuminuria in diagnosis of coronary artery disease in women. International Journal of Cardiology 2005; 105(2):134-40. *Follow-up less than 6 months*

1621. Haight AE, Kaste SC, Goloubeva OG, et al. Nephrotoxicity of iopamidol in pediatric, adolescent, and young adult patients who have undergone allogeneic bone marrow transplantation. Radiology 2003; 226(2):399-404. *Not CKD treatment*

1622. Hailpern SM, Melamed ML, Cohen HW, et al. Moderate chronic kidney disease and cognitive function in adults 20 to 59 years of age: Third National Health and Nutrition Examination Survey (NHANES III). Journal of the American Society of Nephrology 2007; 18(7):2205-13. *Not CKD treatment*

1623. Haines AP, Sanders TA, Imeson JD, et al. Effects of a fish oil supplement on platelet function, haemostatic variables and albuminuria in insulin-dependent diabetics. Thrombosis Research 1986; 43(6):643-55. *Sample size less than 50 patients*

1624. Hale WA, Nashelsky J, Wilson SA. Clinical inquiries. Does screening for microalbuminuria in diabetes prevent complications? Journal of Family Practice 2003; 52(3):229-31. *Not RCT or controlled trial*

1625. Halimi JM, Asmar R, Ribstein J. Optimal nephroprotection: use, misuse and misconceptions about blockade of the renin-angiotensin system. Lessons from the ONTARGET and other recent trials. Diabetes & Metabolism 2009; 35(6):425-30. *Not RCT or controlled trial*

1626. Halkin A, Mehran R, Casey CW, et al. Impact of moderate renal insufficiency on restenosis and adverse clinical events after paclitaxel-eluting and bare metal stent implantation: results from the TAXUS-IV Trial. American Heart Journal 2005; 150(6):1163-70. *Not relevant to key questions*

1627. Hall AM, Edwards SG, Lapsley M, et al. Subclinical tubular injury in HIV-infected individuals on antiretroviral therapy: a cross-sectional analysis. American Journal of Kidney Diseases 2009; 54(6):1034-42. *Not RCT or controlled trial*

1628. Hall WD, Kusek JW, Kirk KA, et al. Short-term effects of blood pressure control and antihypertensive drug regimen on glomerular filtration rate: the African-American Study of Kidney Disease and Hypertension Pilot Study. American Journal of Kidney Diseases 1997; 29(5):720-8. *Follow-up less than 6 months*

1629. Hallab M, Gallois Y, Chatellier G, et al. Comparison of reduction in microalbuminuria by enalapril and hydrochlorothiazide in normotensive patients with insulin dependent diabetes. BMJ 1993; 306(6871):175-82. *Sample size less than 50 patients*

1630. Hallan H, Romundstad S, Kvenild K, et al. Microalbuminuria in diabetic and hypertensive patients and the general population--consequences of various diagnostic criteria--the Nord-Trondelag Health Study (HUNT). Scandinavian Journal of Urology & Nephrology 2003; 37(2):151-8. *Not CKD treatment*

1631. Hallen B, Guilbaud O, Stromberg S, et al. Single-dose pharmacokinetics of terodiline, including a stable isotope technique for improvement of statistical evaluations. Biopharmaceutics & Drug Disposition 1988; 9(3):229-50. *Sample size less than 50 patients*

1632. Haller H, Viberti GC, Mimran A, et al. Preventing microalbuminuria in patients with diabetes: rationale and design of the Randomised Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) study. Journal of Hypertension 2006; 24(2):403-8. *Not relevant to key questions*

1633. Halpenny M, Lakshmi S, O'Donnell A, et al. Fenoldopam: renal and splanchnic effects in patients undergoing coronary artery bypass grafting. Anaesthesia 2001; 56(10):953-60. *Sample size less than 50 patients*

1634. Halpenny M, Rushe C, Breen P, et al. The effects of fenoldopam on renal function in patients undergoing elective aortic surgery. European Journal of Anaesthesiology 2002; 19(1):32-9. *Not early CKD*

1635. Halperin AK, Cubeddu LX. The role of calcium channel blockers in the treatment of hypertension. American Heart Journal 1986; 111(2):363-82. *Not RCT or controlled trial*

1636. Halperin M, Lan KK, Wright EC, et al. Stochastic curtailing for comparison of slopes in longitudinal studies. Controlled Clinical Trials 1987; 8(4):315-26. *Not RCT or controlled trial*

1637. Hamazaki T, Takazakura E, Osawa K, et al. Reduction in microalbuminuria in diabetics by eicosapentaenoic acid ethyl ester. Lipids 1990; 25(9):541-5. *Sample size less than 50 patients*

1638. Hamilton RA, Kane MP, Demers J. Angiotensin-converting enzyme inhibitors and type 2 diabetic nephropathy: a meta-analysis. Pharmacotherapy 2003; 23(7):909-15. *Not RCT or controlled trial*

1639. Hammond PJ, Wade AF, Gwilliam ME, et al. Amino acid infusion blocks renal tubular uptake of an indium-labelled somatostatin analogue. British Journal of Cancer 1993; 67(6):1437-9. *Not CKD treatment*

1640. Hampl H, Steinmuller T, Frohling P, et al. Long-term results of total parathyroidectomy without autotransplantation in patients with and without renal failure. Mineral & Electrolyte Metabolism 1999; 25(3):161-70. *Not early CKD*

1641. Han SS, Kim KW, Na KY, et al. Quality of life and mortality from a nephrologist's view: a prospective observational study. BMC Nephrology 2009; 10:39. *Not CKD treatment*

1642. Haneda M, Kikkawa R, Sakai H, et al. Antiproteinuric effect of candesartan cilexetil in Japanese subjects with type 2 diabetes and nephropathy. Diabetes Research & Clinical Practice 2004; 66(1):87-95. *Not relevant to key questions*

1643. Hannedouche T, Chanard J, Baumelou B, et al. Evaluation of the safety and efficacy of telmisartan and enalapril, with the potential addition of frusemide, in moderate-renal failure patients with mild-to-moderate hypertension. Journal of the Renin-Angiotensin-Aldosterone System 2001; 2(4):246-54. *Follow-up less than 6 months*

1644. Hannedouche T, Natov S, Ikeni A, et al. Does lithium affect renal sodium handling and renal haemodynamics in normal man? Nephrology Dialysis Transplantation 1990; 5(12):1007-12. *Not CKD treatment*

1645. Hannedouche TP, Natov S, Boitard C, et al. Angiotensin converting enzyme inhibition and chronic cyclosporine-induced renal dysfunction in type 1 diabetes. Nephrology Dialysis Transplantation 1996; 11(4):673-8. *Follow-up less than 6 months*

1646. Hannisdal E, Kildahl-Andersen O, Grottum KA, et al. Prognostic factors in multiple myeloma in a population-based trial. European Journal of Haematology 1990; 45(4):198-202. *Not CKD treatment*

1647. Hans B, Hans SS, Mittal VK, et al. Renal functional response to dopamine during and after arteriography in patients with chronic renal insufficiency. Radiology 1990; 176(3):651-4. *Not CKD treatment*

1648. Hans SS, Hans BA, Dhillon R, et al. Effect of dopamine on renal function after arteriography in patients with pre-existing renal insufficiency. American Surgeon 1998; 64(5):432-6. *Not CKD treatment*

1649. Hansen HP, Christensen PK, Tauber-Lassen E, et al. Low-protein diet and kidney function in insulin-dependent diabetic patients with diabetic nephropathy. Kidney International 1999; 55(2):621-8. *Sample size less than 50 patients*

1650. Hansen HP, Gaede PH, Jensen BR, et al. Lack of impact of low-dose acetylsalicylic acid on kidney function in type 1 diabetic patients with microalbuminuria. Diabetes Care 2000; 23(12):1742-5. *Sample size less than 50 patients*

1651. Hansen HP, Rossing K, Jacobsen P, et al. The acute effect of smoking on systemic haemodynamics, kidney and endothelial functions in insulin-dependent diabetic patients with microalbuminuria. Scandinavian Journal of Clinical & Laboratory Investigation 1996; 56(5):393-9. *Follow-up less than 6 months*

1652. Hansen HP, Rossing P, Tarnow L, et al. Increased glomerular filtration rate after withdrawal of long-term antihypertensive treatment in diabetic nephropathy. Kidney International 1995; 47(6):1726-31. *Not relevant to key questions*

1653. Hansen JM, Fogh-Andersen N, Christensen NJ, et al. Cyclosporine-induced hypertension and decline in renal function in healthy volunteers. Journal of Hypertension 1997; 15(3):319-26. *Sample size less than 50 patients*

1654. Hansen KW, Klein F, Christensen PD, et al. Effects of captopril on ambulatory blood pressure, renal and cardiac function in microalbuminuric type 1 diabetic patients. Diabete et Metabolisme 1994; 20(5):485-93. *Sample size less than 50 patients*

1655. Hansen KW, Pedersen MM, Christiansen JS, et al. Acute renal effects of angiotensin converting enzyme inhibition in microalbuminuric type 1 diabetic patients. Acta Diabetologica 1993; 30(3):149-53. *Sample size less than 50 patients*

1656. Hansen PM, Mathiesen ER, Kofoed-Enevoldsen A, et al. Possible effect of angiotensin-converting enzyme inhibition on glomerular charge selectivity. Journal of Diabetes & its Complications 1995; 9(3):158-62. *Sample size less than 50 patients*

1657. Hansen RA, Chin H, Blalock S, et al. Predialysis chronic kidney disease: evaluation of quality of life in clinic patients receiving comprehensive anemia care. Research In Social & Administrative Pharmacy 2009; 5(2):143-53. *Not early CKD*

1658. Hansen TK, Moller J, Thomsen K, et al. Effects of growth hormone on renal tubular handling of sodium in healthy humans. American Journal of Physiology - Endocrinology & Metabolism 2001; 281(6):E1326-32. *Not early CKD*

1659. Hanssen KF, Dahl-Jorgensen K, Brinchmann-Hansen O. The influence of strict control on diabetic complications. Acta Endocrinologica. Supplementum 1985; 272:57-60. *Sample size less than 50 patients*

1660. Hansson L. Effects of angiotensin-converting enzyme inhibition versus conventional antihypertensive therapy on the glomerular filtration rate. Cardiology 1995; 86 Suppl 1:30-3. *Not CKD treatment*

1661. Hara K, Koga H, Kohno S, et al. The administration regimen of isepamicin in patients with chronic respiratory tract infection. Chemotherapy 1995; 41(6):462-9. *Sample size less than 50 patients*

1662. Hardiek KJ, Katholi RE, Robbs RS, et al. Renal effects of contrast media in diabetic patients undergoing diagnostic or interventional coronary angiography. Journal of Diabetes & its Complications 2008; 22(3):171-7. *Not RCT or controlled trial*

1663. Harding MB, Davidson CJ, Pieper KS, et al. Comparison of cardiovascular and renal toxicity after cardiac catheterization using a nonionic versus ionic radiographic contrast agent. American Journal of Cardiology 1991; 68(10):1117-9. *Not CKD treatment*

1664. Haria M, Plosker GL, Markham A. Felodipine/metoprolol: a review of the fixed dose controlled release formulation in the management of essential hypertension. Drugs 2000; 59(1):141-57. *Not CKD treatment*

1665. Harman C. Putting clinical trials on trial. Nature Reviews Nephrology 2009; 5(6):301. *Not RCT or controlled trial*

1666. Harman-Boehm I. Angiotensin receptor blockers do not have an advantage over angiotensin-converting inhibitors [corrected]. Israel Medical Association Journal: Imaj 2004; 6(5):296-8. *Not CKD treatment*

1667. Harmankaya O, Seber S, Yilmaz M. Combination of pentoxifylline with angiotensin converting enzyme inhibitors produces an additional reduction in microalbuminuria in hypertensive type 2 diabetic patients. Renal Failure 2003; 25(3):465-70. *Not relevant to key questions*

1668. Harper PL, Williamson L, Park G, et al. A pilot study of antithrombin replacement in intensive care management: the effects on mortality, coagulation and renal function. Transfusion Medicine 1991; 1(2):121-8. *Not CKD treatment*

1669. Harris DCH, Rangan GK. Retardation of kidney failure -- applying principles to practice. Annals of the Academy of Medicine, Singapore 2005; 34(1):16-23. *Not RCT or controlled trial*

1670. Harris LE, Luft FC, Rudy DW, et al. Clinical correlates of functional status in patients with chronic renal insufficiency. American Journal of Kidney Diseases 1993; 21(2):161-6. *Not RCT or controlled trial*

1671. Harris RZ, Salfi M, Sullivan JT, et al. Pharmacokinetics of cinacalcet hydrochloride when administered with ketoconazole. Clinical Pharmacokinetics 2007; 46(6):495-501. *Not relevant to key questions*

1672. Harten J, Crozier JEM, McCreath B, et al. Effect of intraoperative fluid optimisation on renal function in patients undergoing emergency abdominal surgery: a randomised controlled pilot study (ISRCTN 11799696). International Journal Of Surgery 2008; 6(3):197-204. *Not CKD treatment*

1673. Hartmann JT, Fels LM, Franzke A, et al. Comparative study of the acute nephrotoxicity from standard dose cisplatin +/- ifosfamide and high-dose chemotherapy with carboplatin and ifosfamide. Anticancer Research 2000; 20(5C):3767-73. *Not RCT or controlled trial*

1674. Hartmann JT, Fels LM, Knop S, et al. A randomized trial comparing the nephrotoxicity of cisplatin/ifosfamide-based combination chemotherapy with or without amifostine in patients with solid tumors. Investigational New Drugs 2000; 18(3):281-9. *Not early CKD*

1675. Hartmann JT, Knop S, Fels LM, et al. The use of reduced doses of amifostine to ameliorate nephrotoxicity of cisplatin/ifosfamide-based chemotherapy in patients with solid tumors. Anti-Cancer Drugs 2000; 11(1):1-6. *Not early CKD*

1676. Harvey JN, Worth DP, Brown J, et al. The effect of oral fenoldopam (SKF 82526-J), a peripheral dopamine receptor agonist, on blood pressure and renal function in normal man. British Journal of Clinical Pharmacology 1985; 19(1):21-7. *Sample size less than 50 patients*

1677. Harvey JN, Worth DP, Brown J, et al. Studies with fenoldopam, a dopamine receptor DA1 agonist, in essential hypertension. British Journal of Clinical Pharmacology 1986; 21(1):53-61. *Sample size less than 50 patients*

1678. Harwood PJ, Giannoudis PV. The safety and efficacy of linezolid in orthopaedic practice for the treatment of infection due to antibiotic-resistant organisms. Expert Opinion on Drug Safety 2004; 3(5):405-14. *Not CKD treatment*

1679. Hasebe N, Kikuchi K, Group NCS. Controlled-release nifedipine and candesartan low-dose combination therapy in patients with essential hypertension: the NICE Combi (Nifedipine and Candesartan Combination) Study. Journal of Hypertension 2005; 23(2):445-53. *Sample size less than 50 patients*

1680. Hashim H, Malmberg L, Graugaard-Jensen C, et al. Desmopressin, as a “designer-drug,” in the treatment of overactive bladder syndrome. Neurourology & Urodynamics 2009; 28(1):40-6. *Not CKD treatment*

1681. Hashizume M, Kitano S, Yamaga H, et al. Haptoglobin to protect against renal damage from ethanolamine oleate sclerosant. Lancet 1988; 2(8606):340-1. *Follow-up less than 6 months*

1682. Hassan Y, Al-Ramahi RJ, Aziz NA, et al. Impact of a renal drug dosing service on dose adjustment in hospitalized patients with chronic kidney disease. Annals of Pharmacotherapy 2009; 43(10):1598-605. *Not RCT or controlled trial*

1683. Hassan Y, Al-Ramahi RJ, Aziz NA, et al. Adverse drug events in hospitalized patients with chronic kidney disease. International Journal of Clinical Pharmacology & Therapeutics 2010 Sep; 48(9):571-6. *Not RCT or controlled trial*

1684. Hasselblad V, Gattis Stough W, Shah MR, et al. Relation between dose of loop diuretics and outcomes in a heart failure population: results of the ESCAPE trial. European Journal of Heart Failure 2007; 9(10):1064-9. *Follow-up less than 6 months*

1685. Hasselgren B, Edgar B, Johnsson G, et al. The acute haemodynamic and renal effects of oral felodipine and ramipril in healthy subjects. European Journal of Clinical Pharmacology 1993; 45(4):327-32. *Sample size less than 50 patients*

1686. Haug K, Bakke A, Daae LN, et al. Screening for hematuria, glucosuria and proteinuria in people aged 55-64. Technical, clinical and cost-benefit experience from a pilot study. Scandinavian Journal of Primary Health Care 1985; 3(1):31-4. *Not CKD treatment*

1687. Hausmann DF, Nutz V, Rommelsheim K, et al. Anabolic steroids in polytrauma patients. Influence on renal nitrogen and amino acid losses: a double-blind study. Jpen: Journal of Parenteral & Enteral Nutrition 1990; 14(2):111-4. *Not CKD treatment*

1688. Hawkey CJ. Cyclooxygenase inhibition: between the devil and the deep blue sea. Gut 2002; 50 Suppl 3:III25-30. *Not early CKD*

1689. Hawkins MJ. Interleukin-2 antitumor and effector cell responses. Seminars in Oncology 1993; 20(6 Suppl 9):52-9. *Not RCT or controlled trial*

1690. Hawkins RG, Houston MC. Is population-wide diuretic use directly associated with the incidence of end-stage renal disease in the United States? A hypothesis. American Journal of Hypertension 2005; 18(6):744-9. *Not relevant to key questions*

1691. Hayakawa T, Shouzu A, Nishikawa M, et al. Effects of beraprost and cilostazol and renal function on serum thrombomodulin levels in diabetic patients. Arzneimittel-Forschung 2000; 50(6):535-8. *Not CKD treatment*

1692. Hayami S, Ishigooka M, Suzuki Y, et al. Comparison of the nephrotoxicity between ioversol and iohexol. International Urology & Nephrology 1996; 28(5):615-9. *Sample size less than 50 patients*

1693. Hayashi K, Kumagai H, Saruta T. Effect of efonidipine and ACE inhibitors on proteinuria in human hypertension with renal impairment. American Journal of Hypertension 2003; 16(2):116-22. *Not relevant to key questions*

1694. Hayashi K, Matsuda H, Honda M, et al. Impact of calcium antagonists on bleeding time in patients with chronic renal failure. Journal of Human Hypertension 2002; 16(3):199-203. *Not CKD treatment*

1695. Hayashi M, Numaguchi M, Watabe H, et al. Cisplatin-induced nephrotoxicity and the protective effect of fosfomycin on it as demonstrated by using a crossover study of urinary metabolite levels. Acta Obstetricia et Gynecologica Scandinavica 1997; 76(6):590-5. *Not CKD treatment*

1696. Hayashi Y, Ohtani M, Sawa Y, et al. Synthetic human alpha-atrial natriuretic peptide improves the management of postoperative hypertension and renal dysfunction after the repair of abdominal aortic aneurysm. Journal of Cardiovascular Pharmacology 2003; 42(5):636-41. *Not CKD treatment*

1697. Hayashida N, Isomura T, Sato T, et al. Effects of minimal-dose aprotinin on coronary artery bypass grafting. Journal of Thoracic & Cardiovascular Surgery 1997; 114(2):261-9. *Not CKD treatment*

1698. Hayashino Y, Fukuhara S, Akiba T, et al. Diabetes, glycaemic control and mortality risk in patients on haemodialysis: the Japan Dialysis Outcomes and Practice Pattern Study. Diabetologia 2007; 50(6):1170-7. *Not relevant to key questions*

1699. Hayes C, Alam A, Black-Peart J, et al. Mitigating the cardiovascular risk of anemia in patients with type 2 diabetes and CKD: Does darbepoetin help? The TREAT Trial. Current Diabetes Reports 2010 Apr; 10(2):87-9. *Not RCT or controlled trial*

1700. Hayes TG, Falchook GS, Varadhachary A. Phase IB trial of oral talactoferrin in the treatment of patients with metastatic solid tumors. Investigational New Drugs 2010 Apr; 28(2):156-62. *Not CKD treatment*

1701. Haynes WG. Hyperhomocysteinemia, vascular function and atherosclerosis: effects of vitamins. Cardiovascular Drugs & Therapy 2002; 16(5):391-9. *Not RCT or controlled trial*

1702. Haynes WG, Hand MF, Dockrell ME, et al. Physiological role of nitric oxide in regulation of renal function in humans. American Journal of Physiology 1997; 272(3 Pt 2):F364-71. *Not RCT or controlled trial*

1703. He FJ, Marciniak M, Carney C, et al. Effects of potassium chloride and potassium bicarbonate on endothelial function, cardiovascular risk factors, and bone turnover in mild hypertensives. Hypertension 2010; 55(3):681-8. *Follow-up less than 6 months*

1704. He J, Whelton PK. Elevated systolic blood pressure as a risk factor for cardiovascular and renal disease. Journal of Hypertension - Supplement 1999; 17(2):S7-13. *Not RCT or controlled trial*

1705. Head JE, Bryant BJ, Grills BL, et al. Effects of short-term use of ibuprofen or acetaminophen on bone resorption in healthy men: a double-blind, placebo-controlled pilot study. Bone 2001; 29(5):437-41. *Not early CKD*

1706. Heaney RP. Calcium intake and disease prevention. Arquivos Brasileiros de Endocrinologia e Metabologia 2006; 50(4):685-93. *Not RCT or controlled trial*

1707. Hebert LA. Renoprotective therapy: how good can it get? Kidney International 2000; 57(1):343-4. *Not RCT or controlled trial*

1708. Hebert LA, Bain RP, Verme D, et al. Remission of nephrotic range proteinuria in type I diabetes. Collaborative Study Group. Kidney International 1994; 46(6):1688-93. *Not relevant to key questions*

1709. Hebert LA, Birmingham DJ, Shidham G, et al. Random spot urine protein/creatinine ratio is unreliable for estimating 24-hour proteinuria in individual systemic lupus erythematosus nephritis patients. Nephron 2009; 113(3):c177-82. *Not CKD treatment*

1710. Hebert LA, Kusek JW, Greene T, et al. Effects of blood pressure control on progressive renal disease in blacks and whites. Modification of Diet in Renal Disease Study Group. Hypertension 1997; 30(3 Pt 1):428-35. *Not RCT or controlled trial*

1711. Hebert LA, Wilmer WA, Falkenhain ME, et al. Renoprotection: one or many therapies? Kidney International 2001; 59(4):1211-26. *Not relevant to key questions*

1712. Hebert MJ, Masse M, Vigneault N, et al. Soluble Fas is a marker of coronary artery disease in patients with end-stage renal disease. American Journal of Kidney Diseases 2001; 38(6):1271-6. *Not early CKD*

1713. Heeg JE, de Jong PE, van der Hem GK, et al. Efficacy and variability of the antiproteinuric effect of ACE inhibition by lisinopril. Kidney International 1989; 36(2):272-9. *Sample size less than 50 patients*

1714. Heeg JE, de Jong PE, van der Hem GK, et al. Angiotensin II does not acutely reverse the reduction of proteinuria by long-term ACE inhibition. Kidney International 1991; 40(4):734-41. *Sample size less than 50 patients*

1715. Heeg JE, de Jong PE, Vriesendorp R, et al. Additive antiproteinuric effect of the NSAID indomethacin and the ACE inhibitor lisinopril. American Journal of Nephrology 1990; 10 Suppl 1:94-7. *Sample size less than 50 patients*

1716. Heemskerk S, Masereeuw R, Moesker O, et al. Alkaline phosphatase treatment improves renal function in severe sepsis or septic shock patients. Critical Care Medicine 2009; 37(2):417-23. *Not RCT or controlled trial*

1717. Heerspink HL, Greene T, Lewis JB, et al. Effects of sulodexide in patients with type 2 diabetes and persistent albuminuria. Nephrology Dialysis Transplantation 2008; 23(6):1946-54. *Not RCT or controlled trial*

1718. Heinemann L, Janicke I, Bender R, et al. Effects of enalapril and nitrendipine on exercise albuminuria in normotensive type I diabetic patients with incipient nephropathy. Hormone & Metabolic Research 1996; 28(10):549-52. *Follow-up less than 6 months*

1719. Heise D, Waeschle RM, Schlobohm J, et al. Utility of cystatin C for assessment of renal function after cardiac surgery. Nephron 2009; 112(2):c107-14. *Not CKD treatment*

1720. Heise T, Magnusson K, Grobel B, et al. A cross-over evaluation of different methods and devices to measure blood pressure in type 1 diabetic patients with nephropathy. Blood Pressure Monitoring 2000; 5(3):175-80. *Sample size less than 50 patients*

1721. Helaly MA, Sheashaa HA, Hatata ESZ, et al. Endothelial dysfunction in geriatric diabetic patients: the role of microalbuminuria in elderly type 2 diabetic patients? A randomized controlled study. International Urology & Nephrology 2007; 39(1):333-8. *Follow-up less than 6 months*

1722. Helenglass G, Powles RL, McElwain TJ, et al. Melphalan and total body irradiation (TBI) versus cyclophosphamide and TBI as conditioning for allogeneic matched sibling bone marrow transplants for acute myeloblastic leukaemia in first remission. Bone Marrow Transplantation 1988; 3(1):21-9. *Sample size less than 50 patients*

1723. Hemmelder MH, de Zeeuw D, de Jong PE. Antiproteinuric efficacy of verapamil in comparison to trandolapril in non-diabetic renal disease. Nephrology Dialysis Transplantation 1999; 14(1):98-104. *Follow-up less than 6 months*

1724. Hemmelder MH, de Zeeuw D, Gansevoort RT, et al. Blood pressure reduction initiates the antiproteinuric effect of ACE inhibition. Kidney International 1996; 49(1):174-80. *Sample size less than 50 patients*

1725. Hemmelgarn BR, Ghali WA, Quan H, et al. Poor long-term survival after coronary angiography in patients with renal insufficiency. American Journal of Kidney Diseases 2001; 37(1):64-72. *Not RCT or controlled trial*

1726. Hemmelgarn BR, Manns BJ, Zhang J, et al. Association between multidisciplinary care and survival for elderly patients with chronic kidney disease. Journal of the American Society of Nephrology 2007; 18(3):993-9. *Sample size less than 50 patients*

1727. Heng AE, Cellarier E, Aublet-Cuvelier B, et al. Is treatment with N-acetylcysteine to prevent contrast-induced nephropathy when using bicarbonate hydration out of date? Clinical Nephrology 2008; 70(6):475-84. *Not CKD treatment*

1728. Henrich WL. Optimal cardiovascular therapy for patients with ESRD over the next several years. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4 Suppl 1:S106-9. *Not RCT or controlled trial*

1729. Henry H, 2nd, Nordan J, Tomlin EM. Comparison of butorphanol tartrate and meperidine in moderate to severe renal colic. Urology 1987; 29(3):339-45. *Not CKD treatment*

1730. Henry HH, 2nd. Urological applications of butorphanol tartrate: postoperative pain and renal colic. Acute Care 1988; 12 Suppl 1:22-30. *Not RCT or controlled trial*

1731. Herbert MK, Ginzel S, Muhlschlegel S, et al. Concomitant treatment with urodilatin (ularitide) does not improve renal function in patients with acute renal failure after major abdominal surgery--a randomized controlled trial. Wiener Klinische Wochenschrift 1999; 111(4):141-7. *Sample size less than 50 patients*

1732. Hering R, Wrigge H, Vorwerk R, et al. The effects of prone positioning on intraabdominal pressure and cardiovascular and renal function in patients with acute lung injury. Anesthesia & Analgesia 2001; 92(5):1226-31. *Not early CKD*

1733. Herlitz H, Harris K, Risler T, et al. The effects of an ACE inhibitor and a calcium antagonist on the progression of renal disease: the Nephros Study. Nephrology Dialysis Transplantation 2001; 16(11):2158-65. *Not early CKD*

1734. Herman WH, Shahinfar S, Carides GW, et al. Losartan reduces the costs associated with diabetic end-stage renal disease: the RENAAL study economic evaluation. Diabetes Care 2003; 26(3):683-7. *Not CKD treatment*

1735. Hermans MP, Brichard SM, Colin I, et al. Long-term reduction of microalbuminuria after 3 years of angiotensin-converting enzyme inhibition by perindopril in hypertensive insulin-treated diabetic patients. American Journal of Medicine 1992; 92(4B):102S-7S. *Sample size less than 50 patients*

1736. Hernandez C, Rodriguez B, Losada E, et al. Normoalbuminuric type 1 diabetic patients with retinopathy have an impaired tubular response to desmopressin: its relationship with plasma endothelin-1. Journal of Clinical Endocrinology & Metabolism 2009; 94(6):2060-5. *Not RCT or controlled trial*

1737. Hernberg M. Lymphocyte subsets as prognostic markers for cancer patients receiving immunomodulative therapy. Medical Oncology 1999; 16(3):145-53. *Not CKD treatment*

1738. Herselman MG, Albertse EC, Lombard CJ, et al. Supplemented low-protein diets--are they superior in chronic renal failure? South African Medical Journal 1995; Suid-Afrikaanse Tydskrif Vir Geneeskunde. 85(5):361-5. *Sample size less than 50 patients*

1739. Herzog S, Cunze T, Martin M, et al. Pulsatile vs. continuous parenteral tocolysis: comparison of side effects. European Journal of Obstetrics, Gynecology, & Reproductive Biology 1999; 85(2):199-204. *Not CKD treatment*

1740. Hesselvik F, Brodin B, Carlsson C, et al. Cryoprecipitate infusion fails to improve organ function in septic shock. Critical Care Medicine 1987; 15(5):475-83. *Sample size less than 50 patients*

1741. Hetherington JW, Philp NH. Diclofenac sodium versus pethidine in acute renal colic. British Medical Journal Clinical Research Ed. 1986; 292(6515):237-8. *Not CKD treatment*

1742. Heydendael VMR, Spuls PI, Ten Berge IJM, et al. Cyclosporin trough levels: is monitoring necessary during short-term treatment in psoriasis? A systematic review and clinical data on trough levels. British Journal of Dermatology 2002; 147(1):122-9. *Not CKD treatment*

1743. Hiemstra TF, Walsh M, Mahr A, et al. Mycophenolate mofetil vs azathioprine for remission maintenance in antineutrophil cytoplasmic antibody-associated vasculitis: a randomized controlled trial. JAMA 2010 Dec 1; 304(21):2381-8. *Not CKD treatment*

1744. Higashi Y, Oshima T, Ono N, et al. Intravenous administration of L-arginine inhibits angiotensin-converting enzyme in humans. Journal of Clinical Endocrinology & Metabolism 1995; 80(7):2198-202. *Sample size less than 50 patients*

1745. Higashi Y, Oshima T, Sasaki S, et al. Angiotensin-converting enzyme inhibition, but not calcium antagonism, improves a response of the renal vasculature to L-arginine in patients with essential hypertension. Hypertension 1998; 32(1):16-24. *Sample size less than 50 patients*

1746. Higuchi H, Arimura S, Sumikura H, et al. Urine concentrating ability after prolonged sevoflurane anaesthesia. British Journal of Anaesthesia 1994; 73(2):239-40. *Sample size less than 50 patients*

1747. Higuchi H, Wada H, Usui Y, et al. Effects of probenecid on renal function in surgical patients anesthetized with low-flow sevoflurane. Anesthesiology 2001; 94(1):21-31. *Not early CKD*

1748. Hill AJ, Feneck RO, Walesby RK. A comparison of fenoldopam and nitroprusside in the control of hypertension following coronary artery surgery. Journal of Cardiothoracic & Vascular Anesthesia 1993; 7(3):279-84. *Sample size less than 50 patients*

1749. Hillege HL, Girbes AR, de Kam PJ, et al. Renal function, neurohormonal activation, and survival in patients with chronic heart failure. Circulation 2000; 102(2):203-10. *Not early CKD*

1750. Hillege HL, van Gilst WH, van Veldhuisen DJ, et al. Accelerated decline and prognostic impact of renal function after myocardial infarction and the benefits of ACE inhibition: the CATS randomized trial. European Heart Journal 2003; 24(5):412-20. *Not early CKD*

1751. Hilleman DE. Role of angiotensin-converting-enzyme inhibitors in the treatment of hypertension. American Journal of Health-System Pharmacy 2000; 57 Suppl 1:S8-11. *Not RCT or controlled trial*

1752. Hillmen P, Elebute M, Kelly R, et al. Long-term effect of the complement inhibitor eculizumab on kidney function in patients with paroxysmal nocturnal hemoglobinuria.[Erratum appears in Am J Hematol. 2010 Nov;85(11):911]. American Journal of Hematology 2010 Aug; 85(8):553-9. *Not CKD treatment*

1753. Hillock RJ, Frampton CM, Yandle TG, et al. B-type natriuretic peptide infusions in acute myocardial infarction. Heart 2008; 94(5):617-22. *Not early CKD*

1754. Hilmi IA, Peng Z, Planinsic RM, et al. N-acetylcysteine does not prevent hepatorenal ischaemia-reperfusion injury in patients undergoing orthotopic liver transplantation. Nephrology Dialysis Transplantation 2010 Jul; 25(7):2328-33. *Not CKD treatment*

1755. Himmelfarb J, Hakim RM. Oxidative stress in uremia. Current Opinion in Nephrology & Hypertension 2003; 12(6):593-8. *Not CKD treatment*

1756. Himmelmann A, Hansson L, Hansson BG, et al. ACE inhibition preserves renal function better than beta-blockade in the treatment of essential hypertension. Blood Pressure 1995; 4(2):85-90. *Not CKD treatment*

1757. Himmelmann A, Hansson L, Hansson BG, et al. Long-term renal preservation in essential hypertension. Angiotensin converting enzyme inhibition is superior to beta-blockade. American Journal of Hypertension 1996; 9(9):850-3. *Not relevant to key questions*

1758. Hirakata H, Tsubakihara Y, Gejyo F, et al. Maintaining high hemoglobin levels improved the left ventricular mass index and quality of life scores in pre-dialysis Japanese chronic kidney disease patients. Clinical & Experimental Nephrology 2010 Feb; 14(1):28-35. *Not CKD treatment*

1759. Hirosawa A, Niitani H, Hayashibara K, et al. Effects of sodium thiosulfate in combination therapy of cis-dichlorodiammineplatinum and vindesine. Cancer Chemotherapy & Pharmacology 1989; 23(4):255-8. *Not CKD treatment*

1760. Hirschberg R. Biologically active peptides in acute renal failure: recent clinical trials. Nephrology Dialysis Transplantation 1997; 12(8):1563-6. *Not RCT or controlled trial*

1761. Hirschberg R, Brunori G, Kopple JD, et al. Effects of insulin-like growth factor I on renal function in normal men. Kidney International 1993; 43(2):387-97. *Not adult population*

1762. Hirschberg R, Kopple JD. Role of growth hormone in the amino acid-induced acute rise in renal function in man. Kidney International 1987; 32(3):382-7. *Sample size less than 50 patients*

1763. Hirschberg RR, Zipser RD, Slomowitz LA, et al. Glucagon and prostaglandins are mediators of amino acid-induced rise in renal hemodynamics. Kidney International 1988; 33(6):1147-55. *Sample size less than 50 patients*

1764. Hjorth M, Holmberg E, Rodjer S, et al. Impact of active and passive exclusions on the results of a clinical trial in multiple myeloma. The Myeloma Group of Western Sweden. British Journal of Haematology 1992; 80(1):55-61. *Not CKD treatment*

1765. Hladunewich MA, Derby GC, Lafayette RA, et al. Effect of L-arginine therapy on the glomerular injury of preeclampsia: a randomized controlled trial. Obstetrics & Gynecology 2006; 107(4):886-95. *Sample size less than 50 patients*

1766. Hlatky MA. Underuse of evidence-based therapies. Circulation 2004; 110(6):644-5. *Not CKD treatment*

1767. Ho J-d, Liou S-W, Lin H-C. Retinal vein occlusion and the risk of stroke development: a five-year follow-up study. American Journal of Ophthalmology 2009; 147(2):283-90.e2. *Follow-up less than 6 months*

1768. Ho KM, Morgan DJ. Use of isotonic sodium bicarbonate to prevent radiocontrast nephropathy in patients with mild pre-existing renal impairment: a meta-analysis. Anaesthesia & Intensive Care 2008; 36(5):646-53. *Sample size less than 50 patients*

1769. Ho KM, Morgan DJR. Meta-analysis of N-acetylcysteine to prevent acute renal failure after major surgery. American Journal of Kidney Diseases 2009; 53(1):33-40. *Not early CKD*

1770. Ho KM, Power BM. Benefits and risks of furosemide in acute kidney injury. Anaesthesia 2010 Mar; 65(3):283-93. *Not CKD treatment*

1771. Ho KM, Sheridan DJ. Meta-analysis of frusemide to prevent or treat acute renal failure. BMJ 2006; 333(7565):420. *Not relevant to key questions*

1772. Hobbs H, Stevens P, Klebe B, et al. Referral patterns to renal services: what has changed in the past 4 years? Nephrology Dialysis Transplantation 2009; 24(11):3411-9. *Not RCT or controlled trial*

1773. Hochman JS, Shah NR. What price pain relief?.[Erratum appears in Circulation. 2006 Aug 22;114(8):e364]. Circulation 2006; 113(25):2868-70. *Not RCT or controlled trial*

1774. Hodge EE, Reich DJ, Clavien PA, et al. Use of mycophenolate mofetil in liver transplant recipients experiencing renal dysfunction on cyclosporine or tacrolimus-randomized, prospective, multicenter study results. Transplantation Proceedings 2002; 34(5):1546-7. *Sample size less than 50 patients*

1775. Hoek FJ, Korevaar JC, Dekker FW, et al. Estimation of residual glomerular filtration rate in dialysis patients from the plasma cystatin C level. Nephrology Dialysis Transplantation 2007; 22(6):1633-8. *Follow-up less than 6 months*

1776. Hoffer LJ, Saboohi F, Golden M, et al. Cobalamin dose regimen for maximum homocysteine reduction in end-stage renal disease. Metabolism: Clinical & Experimental 2005; 54(6):835-40. *Not RCT or controlled trial*

1777. Hoffler D, Koeppe P. Temocillin pharmacokinetics in normal and impaired renal function. Drugs 1985; 29 Suppl 5:135-9. *Sample size less than 50 patients*

1778. Hogan SE, L'Allier P, Chetcuti S, et al. Current role of sodium bicarbonate-based preprocedural hydration for the prevention of contrast-induced acute kidney injury: a meta-analysis. American Heart Journal 2008; 156(3):414-21. *Not CKD treatment*

1779. Hoieggen A, Alderman MH, Kjeldsen SE, et al. The impact of serum uric acid on cardiovascular outcomes in the LIFE study. Kidney International 2004; 65(3):1041-9. *Not early CKD*

1780. Hojs R, Bevc S, Ekart R, et al. Serum cystatin C-based equation compared to serum creatinine-based equations for estimation of glomerular filtration rate in patients with chronic kidney disease. Clinical Nephrology 2008; 70(1):10-7. *Sample size less than 50 patients*

1781. Holdaas H, Hartmann A, Berg KJ, et al. Contrasting effects of angiotensin converting inhibitor and alpha-1-antagonist on albuminuria in insulin-dependent diabetes mellitus patients with nephropathy. Journal of Internal Medicine 1995; 237(1):63-71. *Sample size less than 50 patients*

1782. Holdaas H, Hartmann A, Berg KJ, et al. Renal effects of losartan and amlodipine in hypertensive patients with non-diabetic nephropathy. Nephrology Dialysis Transplantation 1998; 13(12):3096-102. *Follow-up less than 6 months*

1783. Holdaas H, Hartmann A, Lien MG, et al. Contrasting effects of lisinopril and nifedipine on albuminuria and tubular transport functions in insulin dependent diabetics with nephropathy. Journal of Internal Medicine 1991; 229(2):163-70. *Sample size less than 50 patients*

1784. Holdaas H, Wanner C, Abletshauser C, et al. The renal safety profile of fluvastatin: results of a pooled analysis. Renal Failure 2006; 28(6):487-92. *Not relevant to key questions*

1785. Holdgate A, Oh CM. Is there a role for antimuscarinics in renal colic? A randomized controlled trial. Journal of Urology 2005; 174(2):572-5; discussion 5. *Sample size less than 50 patients*

1786. Holdgate A, Pollock T. Systematic review of the relative efficacy of non-steroidal anti-inflammatory drugs and opioids in the treatment of acute renal colic. BMJ 2004; 328(7453):1401. *Not CKD treatment*

1787. Holdgate A, Pollock T. Nonsteroidal anti-inflammatory drugs (NSAIDs) versus opioids for acute renal colic. Cochrane Database of Systematic Reviews 2004; (1):CD004137. *Not RCT or controlled trial*

1788. Holdgate A, Pollock T. Nonsteroidal anti-inflammatory drugs (NSAIDs) versus opioids for acute renal colic. Cochrane Database of Systematic Reviews 2005; (2):CD004137. *Follow-up less than 6 months*

1789. Holl MG, Allen LH. Comparative effects of meals high in protein, sucrose, or starch on human mineral metabolism and insulin secretion. American Journal of Clinical Nutrition 1988; 48(5):1219-25. *Sample size less than 50 patients*

1790. Hollenberg NK. Non-insulin-dependent diabetes mellitus, nephropathy, and the renin system. Journal of Hypertension - Supplement 1997; 15(7):S7-13. *Not RCT or controlled trial*

1791. Hollenberg NK, Parving H-H, Viberti G, et al. Albuminuria response to very high-dose valsartan in type 2 diabetes mellitus. Journal of Hypertension 2007; 25(9):1921-6. *Not relevant to key questions*

1792. Holmberg B, Brannstrom M, Bucht B, et al. Safety and efficacy of atorvastatin in patients with severe renal dysfunction. Scandinavian Journal of Urology & Nephrology 2005; 39(6):503-10. *Sample size less than 50 patients*

1793. Holme I, Fayyad R, Faergeman O, et al. Cardiovascular outcomes and their relationships to lipoprotein components in patients with and without chronic kidney disease: results from the IDEAL trial. Journal of Internal Medicine 2010 Jun; 267(6):567-75. *Not RCT or controlled trial*

1794. Holmes CL, Walley KR. Bad medicine: low-dose dopamine in the ICU. Chest 2003; 123(4):1266-75. *Not CKD treatment*

1795. Holmes DI, Abdel Wahab N, Mason RM. Identification of glucose-regulated genes in human mesangial cells by mRNA differential display. Biochemical & Biophysical Research Communications 1997; 238(1):179-84. *Not RCT or controlled trial*

1796. Holmes SJ, Espiner EA, Richards AM, et al. Renal, endocrine, and hemodynamic effects of human brain natriuretic peptide in normal man. Journal of Clinical Endocrinology & Metabolism 1993; 76(1):91-6. *Not CKD treatment*

1797. Homma K, Hayashi K, Kanda T, et al. Beneficial action of candesartan cilexetil plus amlodipine or ACE inhibitors in chronic nondiabetic renal disease. Journal of Human Hypertension 2004; 18(12):879-84. *Sample size less than 50 patients*

1798. Hommel E, Andersen P, Gall MA, et al. Plasma lipoproteins and renal function during simvastatin treatment in diabetic nephropathy. Diabetologia 1992; 35(5):447-51. *Sample size less than 50 patients*

1799. Hommel E, Mathiesen E, Arnold-Larsen S, et al. Effects of indomethacin on kidney function in type 1 (insulin-dependent) diabetic patients with nephropathy. Diabetologia 1987; 30(2):78-81. *Sample size less than 50 patients*

1800. Hommel E, Mathiesen E, Edsberg B, et al. Acute reduction of arterial blood pressure reduces urinary albumin excretion in type 1 (insulin-dependent) diabetic patients with incipient nephropathy. Diabetologia 1986; 29(4):211-5. *Sample size less than 50 patients*

1801. Hommel E, Parving HH, Mathiesen E, et al. Effect of captopril on kidney function in insulin-dependent diabetic patients with nephropathy. British Medical Journal Clinical Research Ed. 1986; 293(6545):467-70. *Sample size less than 50 patients*

1802. Hon G, Vaziri ND, Kaupke CJ, et al. Lack of a fast-acting effect of erythropoietin on arterial blood pressure and endothelin level. Artificial Organs 1995; 19(2):188-91. *Sample size less than 50 patients*

1803. Honing ML, Hijmering ML, Ballard DE, et al. Selective ET(A) receptor antagonism with ABT-627 attenuates all renal effects of endothelin in humans. Journal of the American Society of Nephrology 2000; 11(8):1498-504. *Not early CKD*

1804. Honore PM, Joannes-Boyau O, Boer W, et al. Acute kidney injury in the ICU: time has come for an early biomarker kit! Acta Clinica Belgica - Supplementum 2007; (2):318-21. *Not CKD treatment*

1805. Hoogenberg K, Sluiter WJ, Navis G, et al. Exogenous norepinephrine induces an enhanced microproteinuric response in microalbuminuric insulin-dependent diabetes mellitus. Journal of the American Society of Nephrology 1998; 9(4):643-54. *Sample size less than 50 patients*

1806. Hoogenberg K, Smit AJ, Girbes AR. Effects of low-dose dopamine on renal and systemic hemodynamics during incremental norepinephrine infusion in healthy volunteers. Critical Care Medicine 1998; 26(2):260-5. *Not CKD treatment*

1807. Hoogeveen EK, Kostense PJ, Jager A, et al. Serum homocysteine level and protein intake are related to risk of microalbuminuria: the Hoorn Study. Kidney International 1998; 54(1):203-9. *Not RCT or controlled trial*

1808. Hoogkamer JF, Kleinbloesem CH, Nokhodian A, et al. Pharmacokinetics of imidapril and its active metabolite imidaprilat following single dose and during steady state in patients with chronic renal failure. European Journal of Clinical Pharmacology 1998; 54(1):59-61. *Sample size less than 50 patients*

1809. Hoogwerf BJ, Young JB. The HOPE study. Ramipril lowered cardiovascular risk, but vitamin E did not. Cleveland Clinic Journal of Medicine 2000; 67(4):287-93. *Not early CKD*

1810. Hooper AH, Tindall H, Barker MJ, et al. Renal scintigraphy and survival of indium-111-labelled platelets in patients with diabetic nephropathy. Nuclear Medicine Communications 1986; 7(5):349-54. *Sample size less than 50 patients*

1811. Hoos A, Levey DL. Vaccination with heat shock protein-peptide complexes: from basic science to clinical applications. Expert Review of Vaccines 2003; 2(3):369-79. *Not CKD treatment*

1812. Hopper AH, Tindall H, Davies JA. Administration of aspirin-dipyridamole reduces proteinuria in diabetic nephropathy. Nephrology Dialysis Transplantation 1989; 4(2):140-3. *Sample size less than 50 patients*

1813. Hopper AH, Tindall H, Urquhart S, et al. Reduction of exercise-induced albuminuria by aspirin-dipyridamole in patients with diabetes mellitus. Hormone & Metabolic Research 1987; 19(5):201-3. *Sample size less than 50 patients*

1814. Hoque R, Rahman MS, Iqbal M. Effect of enalapril and losartan on proteinuria in type 2 diabetic nephropathy patients. Bangladesh Medical Research Council Bulletin 2009; 35(2):44-8. *Sample size less than 50 patients*

1815. Horita Y, Hayashida K, Fukuchi K, et al. Acetazolamide assisted Tc-99m MAG3 renography to assess renal blood flow reserve. Annals of Nuclear Medicine 2003; 17(2):139-44. *Not CKD treatment*

1816. Horl WH. A need for an individualized approach to end-stage renal disease patients. Nephrology Dialysis Transplantation 2002; 17 Suppl 6:17-21. *Not early CKD*

1817. Horl WH. Anemia: What can we learn from a secondary analysis of CHOIR? Nature Reviews Nephrology 2010 May; 6(5):251-2. *Not RCT or controlled trial*

1818. Horl WH, Steinhauer HB, Riegel W, et al. Effect of different dialyzer membranes on plasma levels of granulocyte elastase. Kidney International - Supplement 1988; 24:S90-1. *Sample size less than 50 patients*

1819. Hornberger J, Wrone E. When to base clinical policies on observational versus randomized trial data. Annals of Internal Medicine 1997; 127(8 Pt 2):697-703. *Not RCT or controlled trial*

1820. Hornberger JC, Garber AM, Jeffery JR. Mortality, hospital admissions, and medical costs of end-stage renal disease in the United States and Manitoba, Canada. Medical Care 1997; 35(7):686-700. *Not early CKD*

1821. Hoste EAJ, De Waele JJ, Gevaert SA, et al. Sodium bicarbonate for prevention of contrast-induced acute kidney injury: a systematic review and meta-analysis. Nephrology Dialysis Transplantation 2010 Mar; 25(3):747-58. *Not CKD treatment*

1822. Hotu C, Bagg W, Collins J, et al. A community-based model of care improves blood pressure control and delays progression of proteinuria, left ventricular hypertrophy and diastolic dysfunction in Maori and Pacific patients with type 2 diabetes and chronic kidney disease: a randomized controlled trial. Nephrology Dialysis Transplantation 2010 Oct; 25(10):3260-6. *Not relevant to key questions*

1823. Hou FF, Xie D, Zhang X, et al. Renoprotection of Optimal Antiproteinuric Doses (ROAD) Study: a randomized controlled study of benazepril and losartan in chronic renal insufficiency. Journal of the American Society of Nephrology 2007; 18(6):1889-98. *Follow-up less than 6 months*

1824. Hou FF, Zhang X, Zhang GH, et al. Efficacy and safety of benazepril for advanced chronic renal insufficiency. New England Journal of Medicine 2006; 354(2):131-40. *Not RCT or controlled trial*

1825. Houben AJ, Krekels MM, Schaper NC, et al. Microvascular effects of atrial natriuretic peptide (ANP) in man: studies during high and low salt diet. Cardiovascular Research 1998; 39(2):442-50. *Sample size less than 50 patients*

1826. House AA, Eliasziw M, Cattran DC, et al. Effect of B-vitamin therapy on progression of diabetic nephropathy: a randomized controlled trial. JAMA 2010 Apr 28; 303(16):1603-9. *Not CKD treatment*

1827. Hovind P, Tarnow L, Parving H-H. Remission and regression of diabetic nephropathy. Current Hypertension Reports 2004; 6(5):377-82. *Not CKD treatment*

1828. Howard K, White S, Salkeld G, et al. Cost-effectiveness of screening and optimal management for diabetes, hypertension, and chronic kidney disease: a modeled analysis. Value in Health 2010 Mar-Apr; 13(2):196-208. *Not relevant to key questions*

1829. Hoy W, McDonald SP. Albuminuria: marker or target in indigenous populations. Kidney International - Supplement 2004; (92):S25-31. *Not CKD treatment*

1830. Hoy WE, Wang Z, Baker PRA, et al. Reduction in natural death and renal failure from a systematic screening and treatment program in an Australian Aboriginal community. Kidney International - Supplement 2003; (83):S66-73. *Not RCT or controlled trial*

1831. Hoy WE, Wang Z, Baker PRA, et al. Secondary prevention of renal and cardiovascular disease: results of a renal and cardiovascular treatment program in an Australian aboriginal community. Journal of the American Society of Nephrology 2003; 14(7 Suppl 2):S178-85. *Not RCT or controlled trial*

1832. Hoy WE, Wang Z, VanBuynder P, et al. The natural history of renal disease in Australian Aborigines. Part 1. Changes in albuminuria and glomerular filtration rate over time. Kidney International 2001; 60(1):243-8. *Not RCT or controlled trial*

1833. Hricik DE, Levine BS, Adrogue HJ, et al. Evaluation of enalapril/diltiazem ER in hypertensive patients with coexisting renal dysfunction. Enalapril/Diltiazem ER in Hypertensive Renal Disease Group. Journal of Human Hypertension 1996; 10(11):769-74. *Follow-up less than 6 months*

1834. Hsia HC, Lin HC, Tsai YT, et al. The effects of chronic administration of indomethacin and misoprostol on renal function in cirrhotic patients with and without ascites. Scandinavian Journal of Gastroenterology 1995; 30(12):1194-9. *Sample size less than 50 patients*

1835. Hsu CY. Does treatment of non-malignant hypertension reduce the incidence of renal dysfunction? A meta-analysis of 10 randomised, controlled trials. Journal of Human Hypertension 2001; 15(2):99-106. *Not relevant to key questions*

1836. Hu YJ, Chen Y, Zhang YQ, et al. The protective role of selenium on the toxicity of cisplatin-contained chemotherapy regimen in cancer patients. Biological Trace Element Research 1997; 56(3):331-41. *Sample size less than 50 patients*

1837. Hu Y-Y, Ye S-D, Zhao L-L, et al. Hydrochloride pioglitazone decreases urinary TGF-beta1 excretion in type 2 diabetics. European Journal of Clinical Investigation 2010 Jul; 40(7):571-4. *Not CKD treatment*

1838. Huang M, Yu J, Hu W. Effect of yitangning granule on glycometabolism and urinary micro albumin of diabetes B patients. Journal of Traditional Chinese Medicine 2004; 24(4):270-3. *Follow-up less than 6 months*

1839. Huber W, Eckel F, Hennig M, et al. Prophylaxis of contrast material-induced nephropathy in patients in intensive care: acetylcysteine, theophylline, or both? A randomized study. Radiology 2006; 239(3):793-804. *Sample size less than 50 patients*

1840. Huber W, Ilgmann K, Page M, et al. Effect of theophylline on contrast material-nephropathy in patients with chronic renal insufficiency: controlled, randomized, double-blinded study. Radiology 2002; 223(3):772-9. *Not early CKD*

1841. Huber W, Schipek C, Ilgmann K, et al. Effectiveness of theophylline prophylaxis of renal impairment after coronary angiography in patients with chronic renal insufficiency. American Journal of Cardiology 2003; 91(10):1157-62. *Not CKD treatment*

1842. Huggins JT, Sahn SA. Causes and management of pleural fibrosis. Respirology 2004; 9(4):441-7. *Not RCT or controlled trial*

1843. Huitema AD, Mathot RA, Tibben MM, et al. Validation of techniques for the prediction of carboplatin exposure: application of Bayesian methods. Clinical Pharmacology & Therapeutics 2000; 67(6):621-30. *Not RCT or controlled trial*

1844. Huledal G, Jonzon B, Malmenas M, et al. Renal effects of the cyclooxygenase-inhibiting nitric oxide donator AZD3582 compared with rofecoxib and naproxen during normal and low sodium intake. Clinical Pharmacology & Therapeutics 2005; 77(5):437-50. *Not CKD treatment*

1845. Humphrey LL, Ballard DJ. Renal complications in non-insulin-dependent diabetes mellitus. Clinics in Geriatric Medicine 1990; 6(4):807-25. *Not relevant to key questions*

1846. Humphreys MR, Lingeman JE, Terry C, et al. Renal injury and the application of polysaccharide hemospheres: a laparoscopic experimental model. Journal of Endourology 2008; 22(6):1375-81. *Not CKD treatment*

1847. Hunsicker LG. Emerging trends for prevention and treatment of diabetic nephropathy: blockade of the RAAS and BP control. Journal of Managed Care Pharmacy 2004; 10(5 Suppl A):S12-7. *Not RCT or controlled trial*

1848. Hunsicker LG, Adler S, Caggiula A, et al. Predictors of the progression of renal disease in the Modification of Diet in Renal Disease Study. Kidney International 1997; 51(6):1908-19. *Not RCT or controlled trial*

1849. Hunter DW, Chamsuddin A, Bjarnason H, et al. Preventing contrast-induced nephropathy with fenoldopam. Techniques in Vascular & Interventional Radiology 2001; 4(1):53-6. *Not early CKD*

1850. Huntress JD, Papadakos PJ. The role of calcium-channel antagonists in solid organ transplantation. New Horizons 1996; 4(1):129-33. *Not RCT or controlled trial*

1851. Hurst M, Jarvis B. Perindopril: an updated review of its use in hypertension. Drugs 2001; 61(6):867-96. *Not RCT or controlled trial*

1852. Hussain SA, Moffitt DD, Glaholm JG, et al. A phase I-II study of synchronous chemoradiotherapy for poor prognosis locally advanced bladder cancer. Annals of Oncology 2001; 12(7):929-35. *Not early CKD*

1853. Hussain SA, Stocken DD, Riley P, et al. A phase I/II study of gemcitabine and fractionated cisplatin in an outpatient setting using a 21-day schedule in patients with advanced and metastatic bladder cancer. British Journal of Cancer 2004; 91(5):844-9. *Not relevant to key questions*

1854. Huxtable L, Raney CRK, Khera GS. Should intravenous N-acetylcysteine be considered standard of care for prevention of radio-contrast-induced nephropathy? Journal of the American College of Cardiology 2003; 42(12):2169; author reply -70. *Not relevant to key questions*

1855. Huybregts RAJM, Morariu AM, Rakhorst G, et al. Attenuated renal and intestinal injury after use of a mini-cardiopulmonary bypass system. Annals of Thoracic Surgery 2007; 83(5):1760-6. *Not CKD treatment*

1856. Huyen VTT, Phan DV, Thang P, et al. Antidiabetic effect of Gynostemma pentaphyllum tea in randomly assigned type 2 diabetic patients. Hormone & Metabolic Research 2010 May; 42(5):353-7. *Not CKD treatment*

1857. Hwang WYK, Koh LP, Ng HJ, et al. A randomized trial of amifostine as a cytoprotectant for patients receiving myeloablative therapy for allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplantation 2004; 34(1):51-6. *Not CKD treatment*

1858. Hyndman ME, Manns BJ, Snyder FF, et al. Vitamin B12 decreases, but does not normalize, homocysteine and methylmalonic acid in end-stage renal disease: a link with glycine metabolism and possible explanation of hyperhomocysteinemia in end-stage renal disease. Metabolism: Clinical & Experimental 2003; 52(2):168-72. *Not early CKD*

1859. Hynes DM, Stroupe KT, Greer JW, et al. Potential cost savings of erythropoietin administration in end-stage renal disease. American Journal of Medicine 2002; 112(3):169-75. *Not RCT or controlled trial*

1860. Hynninen MS, Niemi TT, Poyhia R, et al. N-acetylcysteine for the prevention of kidney injury in abdominal aortic surgery: a randomized, double-blind, placebo-controlled trial. Anesthesia & Analgesia 2006; 102(6):1638-45. *Not relevant to key questions*

1861. Hynynen M, Palojoki R, Heinonen J, et al. Renal and vascular effects of atrial natriuretic factor during cardiopulmonary bypass. Chest 1991; 100(5):1203-9. *Not CKD treatment*

1862. Ibbotson T, Goa KL. Darbepoetin alfa. Drugs 2001; 61(14):2097-104; discussion 105-6. *Not RCT or controlled trial*

1863. Ibrahim A, Scher N, Williams G, et al. Approval summary for zoledronic acid for treatment of multiple myeloma and cancer bone metastases. Clinical Cancer Research 2003; 9(7):2394-9. *Not CKD treatment*

1864. Ibrahim H, Mondress M, Tello A, et al. An alternative formula to the Cockcroft-Gault and the modification of diet in renal diseases formulas in predicting GFR in individuals with type 1 diabetes. Journal of the American Society of Nephrology 2005; 16(4):1051-60. *Not relevant to key questions*

1865. Ibrahim HN, Rogers T, Tello A, et al. The performance of three serum creatinine-based formulas in estimating GFR in former kidney donors. American Journal of Transplantation 2006; 6(6):1479-85. *Not CKD treatment*

1866. Ibrahim S, Derde MP, Kaufman L, et al. Safety, pharmacokinetics and efficacy of once-a-day netilmicin and amikacin versus their conventional schedules in patients suffering from pelvic inflammatory disease. Renal Failure 1990; 12(3):199-203. *Not CKD treatment*

1867. Ichai C, Passeron C, Carles M, et al. Prolonged low-dose dopamine infusion induces a transient improvement in renal function in hemodynamically stable, critically ill patients: a single-blind, prospective, controlled study. Critical Care Medicine 2000; 28(5):1329-35. *Sample size less than 50 patients*

1868. Ichai C, Soubielle J, Carles M, et al. Comparison of the renal effects of low to high doses of dopamine and dobutamine in critically ill patients: a single-blind randomized study. Critical Care Medicine 2000; 28(4):921-8. *Not early CKD*

1869. Ichihara A, Kaneshiro Y, Sakoda M, et al. Add-on amlodipine improves arterial function and structure in hypertensive patients treated with an angiotensin receptor blocker. Journal of Cardiovascular Pharmacology 2007; 49(3):161-6. *Follow-up less than 6 months*

1870. Ichihara A, Kaneshiro Y, Takemitsu T, et al. Benefits of candesartan on arterial and renal damage of non-diabetic hypertensive patients treated with calcium channel blockers. American Journal of Nephrology 2006; 26(5):462-8. *Follow-up less than 6 months*

1871. Ifudu O, Dawood M, Homel P. Erythropoietin-induced elevation in blood pressure is immediate and dose dependent. Nephron 1998; 79(4):486-7. *Not RCT or controlled trial*

1872. Ifudu O, Homel P. Effect of serum parathyroid hormone and aluminum levels on the response to erythropoietin in uremia. Nephron 1998; 79(4):477-8. *Not RCT or controlled trial*

1873. Igarashi M, Hirata A, Kadomoto Y, et al. Dual blockade of angiotensin II with enalapril and losartan reduces proteinuria in hypertensive patients with type 2 diabetes. Endocrine Journal 2006; 53(4):493-501. *Sample size less than 50 patients*

1874. Iglesias J, Marik PE, Levine JS, et al. Elevated serum levels of the type I and type II receptors for tumor necrosis factor-alpha as predictive factors for ARF in patients with septic shock. American Journal of Kidney Diseases 2003; 41(1):62-75. *Not CKD treatment*

1875. Iguchi M, Katoh Y, Koike H, et al. Randomized trial of trigger point injection for renal colic. International Journal of Urology 2002; 9(9):475-9. *Not CKD treatment*

1876. Ihle BU, Becker GJ, Whitworth JA, et al. The effect of protein restriction on the progression of renal insufficiency. New England Journal of Medicine 1989; 321(26):1773-7. *Not early CKD*

1877. Ihle BU, Whitworth JA, Shahinfar S, et al. Angiotensin-converting enzyme inhibition in nondiabetic progressive renal insufficiency: a controlled double-blind trial. American Journal of Kidney Diseases 1996; 27(4):489-95. *Not early CKD*

1878. Iino Y, Hayashi M, Kawamura T, et al. Interim evidence of the renoprotective effect of the angiotensin II receptor antagonist losartan versus the calcium channel blocker amlodipine in patients with chronic kidney disease and hypertension: a report of the Japanese Losartan Therapy Intended for Global Renal Protection in Hypertensive Patients (JLIGHT) Study. Clinical & Experimental Nephrology 2003; 7(3):221-30. *Not relevant to key questions*

1879. Iino Y, Hayashi M, Kawamura T, et al. Renoprotective effect of losartan in comparison to amlodipine in patients with chronic kidney disease and hypertension--a report of the Japanese Losartan Therapy Intended for the Global Renal Protection in Hypertensive Patients (JLIGHT) study. Hypertension Research - Clinical & Experimental 2004; 27(1):21-30. *Not relevant to key questions*

1880. Ikeda K, Terashima M, Kawamura H, et al. Pharmacokinetics of cisplatin in combined cisplatin and 5-fluorouracil therapy: a comparative study of three different schedules of cisplatin administration. Japanese Journal of Clinical Oncology 1998; 28(3):168-75. *Not CKD treatment*

1881. Ikeda T, Nakayama D, Gomi T, et al. Captopril, an angiotensin I-converting enzyme inhibitor, decreases proteinuria in hypertensive patients with renal diseases. Nephron 1989; 52(1):72-5. *Sample size less than 50 patients*

1882. Ilag LL, Martin CL, Tabaei BP, et al. Improving diabetes processes of care in managed care. Diabetes Care 2003; 26(10):2722-7. *Not relevant to key questions*

1883. Imai E, Ito S, Haneda M, et al. Olmesartan reducing incidence of endstage renal disease in diabetic nephropathy trial (ORIENT): rationale and study design. Hypertension Research - Clinical & Experimental 2006; 29(9):703-9. *Not early CKD*

1884. Imai H, Hotta O, Yoshimura M, et al. Deoxyspergualin, an immunosuppressant, in patients suffering from nephropathies with crescent formation: an open-label trial to evaluate safety and efficacy. Clinical & Experimental Nephrology 2006; 10(1):40-54. *Sample size less than 50 patients*

1885. Imai Y, Suzuki H, Saito T, et al. The effect of pravastatin on renal function and lipid metabolism in patients with renal dysfunction with hypertension and hyperlipidemia. Pravastatin and Renal Function Research Group. Clinical & Experimental Hypertension 1999; 21(8):1345-55. *Not relevant to key questions*

1886. Imamura Y, Murayama N, Okudaira N, et al. Prediction of fluoroquinolone-induced elevation in serum creatinine levels: a case of drug-endogenous substance interaction involving the inhibition of renal secretion. Clinical Pharmacology & Therapeutics 2011 Jan; 89(1):81-8. *Not CKD treatment*

1887. Imanishi M, Yoshioka K, Okumura M, et al. Mechanism of decreased albuminuria caused by angiotensin converting enzyme inhibitor in early diabetic nephropathy. Kidney International - Supplement 1997; 63:S198-200. *Sample size less than 50 patients*

1888. Imbasciati E, Gusmano R, Edefonti A, et al. Controlled trial of methylprednisolone pulses and low dose oral prednisone for the minimal change nephrotic syndrome. British Medical Journal Clinical Research Ed. 1985; 291(6505):1305-8. *Not early CKD*

1889. Indermitte J, Burkolter S, Drewe J, et al. Risk factors associated with a high velocity of the development of hyperkalaemia in hospitalised patients. Drug Safety 2007; 30(1):71-80. *Not relevant to key questions*

1890. Innes A, Gemmell HG, Smith FW, et al. The short term effects of oral labetalol in patients with chronic renal disease and hypertension. Journal of Human Hypertension 1992; 6(3):211-4. *Follow-up less than 6 months*

1891. Inoue S, Tomino Y. Effects of calcium antagonists in hypertensive patients with renal dysfunction: a prospective, randomized, parallel trial comparing benidipine and nifedipine. Nephrology 2004; 9(5):265-71. *Not early CKD*

1892. Insua A, Ribstein J, Mimran A. Comparative effect of captopril and nifedipine in normotensive patients with incipient diabetic nephropathy. Postgraduate Medical Journal 1988; 64 Suppl 3:59-62; discussion 90-2. *Follow-up less than 6 months*

1893. Inthorn D, Hoffmann JN, Hartl WH, et al. Antithrombin III supplementation in severe sepsis: beneficial effects on organ dysfunction. Shock 1997; 8(5):328-34. *Not CKD treatment*

1894. Investigators ACTT. Rationale, design, and baseline characteristics of the Acetylcystein for Contrast-Induced nephropaThy (ACT) Trial: a pragmatic randomized controlled trial to evaluate the efficacy of acetylcysteine for the prevention of contrast-induced nephropathy. Trials [Electronic Resource] 2009; 10:38. *Not CKD treatment*

1895. Investigators DT, Dagenais GR, Gerstein HC, et al. Effects of ramipril and rosiglitazone on cardiovascular and renal outcomes in people with impaired glucose tolerance or impaired fasting glucose: results of the Diabetes REduction Assessment with ramipril and rosiglitazone Medication (DREAM) trial. Diabetes Care 2008; 31(5):1007-14. *Not CKD treatment*

1896. Ip-Yam PC, Murphy S, Baines M, et al. Renal function and proteinuria after cardiopulmonary bypass: the effects of temperature and mannitol. Anesthesia & Analgesia 1994; 78(5):842-7. *Sample size less than 50 patients*

1897. Irish A, Dogra G, Mori T, et al. Preventing AVF thrombosis: the rationale and design of the Omega-3 fatty acids (Fish Oils) and Aspirin in Vascular access OUtcomes in REnal Disease (FAVOURED) study. BMC Nephrology 2009; 10:1. *Not CKD treatment*

1898. Irwin MG, Roulson CJ, Jones RD, et al. Peri-operative administration of rectal diclofenac sodium. The effect on renal function in patients undergoing minor orthopaedic surgery. European Journal of Anaesthesiology 1995; 12(4):403-6. *Sample size less than 50 patients*

1899. Isakova T, Gutierrez O, Shah A, et al. Postprandial mineral metabolism and secondary hyperparathyroidism in early CKD.[Erratum appears in J Am Soc Nephrol. 2009 Jan;20(1):229]. Journal of the American Society of Nephrology 2008; 19(3):615-23. *Sample size less than 50 patients*

1900. Isakova T, Gutierrez OM, Wolf M. A blueprint for randomized trials targeting phosphorus metabolism in chronic kidney disease. Kidney International 2009; 76(7):705-16. *Not RCT or controlled trial*

1901. Isakova T, Gutierrez OM, Wolf M. A blueprint for randomized trials targeting phosphorus metabolism in chronic kidney disease. Kidney International 2009; 76(7):705-16. *Not RCT or controlled trial*

1902. Isbel NM, Haluska B, Johnson DW, et al. Increased targeting of cardiovascular risk factors in patients with chronic kidney disease does not improve atheroma burden or cardiovascular function. American Heart Journal 2006; 151(3):745-53. *Not relevant to key questions*

1903. Iseki K, Osato S, Onoyama K, et al. Role of calcium supplementation in patients with mild renal failure. Contributions to Nephrology 1991; 90:155-60. *Sample size less than 50 patients*

1904. Isenbarger DW, Kent SM, O'Malley PG. Meta-analysis of randomized clinical trials on the usefulness of acetylcysteine for prevention of contrast nephropathy. American Journal of Cardiology 2003; 92(12):1454-8. *Not CKD treatment*

1905. Ishani A, Blackwell T, Jamal SA, et al. The effect of raloxifene treatment in postmenopausal women with CKD. Journal of the American Society of Nephrology 2008; 19(7):1430-8. *Follow-up less than 6 months*

1906. Ishani A, Grandits GA, Grimm RH, et al. Association of single measurements of dipstick proteinuria, estimated glomerular filtration rate, and hematocrit with 25-year incidence of end-stage renal disease in the multiple risk factor intervention trial. Journal of the American Society of Nephrology 2006; 17(5):1444-52. *Not RCT or controlled trial*

1907. Ishani A, Herzog CA, Collins AJ, et al. Cardiac medications and their association with cardiovascular events in incident dialysis patients: cause or effect? Kidney International 2004; 65(3):1017-25. *Not relevant to key questions*

1908. Ishani A, Paudel M, Taylor BC, et al. Renal function and rate of hip bone loss in older men: the Osteoporotic Fractures in Men Study. Osteoporosis International 2008; 19(11):1549-56. *Not CKD treatment*

1909. Ishani A, Xue JL, Himmelfarb J, et al. Acute kidney injury increases risk of ESRD among elderly. Journal of the American Society of Nephrology 2009; 20(1):223-8. *Not CKD treatment*

1910. Ishani A, Xue JL, Himmelfarb J, et al. Acute kidney injury increases risk of ESRD among elderly. Journal of the American Society of Nephrology 2009; 20(1):223-8. *Not CKD treatment*

1911. Ishibashi F. Glomerular clearance and tubular reabsorption of transferrin in microtransferrinuric patients with non-insulin-dependent diabetes. Diabetes Research & Clinical Practice 1994; 25(3):169-75. *Not CKD treatment*

1912. Ishikawa J, Hoshide S, Shibasaki S, et al. Relationship between morning hypertension identified by home blood pressure monitoring and brain natriuretic peptide and estimated glomerular filtration rate: the Japan Morning Surge 1 (JMS-1) Study. Journal of Clinical Hypertension 2008; 10(1):34-42. *Not RCT or controlled trial*

1913. Ishimitsu T, Akashiba A, Kameda T, et al. Benazepril slows progression of renal dysfunction in patients with non-diabetic renal disease. Nephrology 2007; 12(3):294-8. *Not RCT or controlled trial*

1914. Ishimitsu T, Numabe A, Masuda T, et al. Angiotensin-II receptor antagonist combined with calcium channel blocker or diuretic for essential hypertension. Hypertension Research - Clinical & Experimental 2009; 32(11):962-8. *Sample size less than 50 patients*

1915. Ishimura E, Nishizawa Y, Okuno S, et al. Diabetes mellitus increases the severity of anemia in non-dialyzed patients with renal failure. Journal of Nephrology 1998; 11(2):83-6. *Sample size less than 50 patients*

1916. Isles C, Main J, O'Connell J, et al. Survival associated with renovascular disease in Glasgow and Newcastle: a collaborative study. Scottish Medical Journal 1990; 35(3):70-3. *Not RCT or controlled trial*

1917. Ismail T, Ayres R, Kiff P, et al. Enisoprost in liver transplantation. Transplantation 1995; 59(9):1298-301. *Follow-up less than 6 months*

1918. Ismail-Beigi F, Craven T, Banerji MA, et al. Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial.[Erratum appears in Lancet. 2010 Oct 30;376(9751):1466]. Lancet 2010 Aug 7; 376(9739):419-30. *Not relevant to key questions*

1919. Isnard F, Tilleul P, Laporte J-P, et al. A benefit for renal function after early switch to liposomal amphotericin B from conventional formulation in empirical antifungal treatment. Nephrology Dialysis Transplantation 2007; 22(10):3090-1. *Not relevant to key questions*

1920. Isomaa B, Henricsson M, Almgren P, et al. The metabolic syndrome influences the risk of chronic complications in patients with type II diabetes. Diabetologia 2001; 44(9):1148-54. *Not CKD treatment*

1921. Ito S. Usefulness of RAS inhibition depends on baseline albuminuria. Nature Reviews Nephrology 2010; 6(1):10-1. *Not RCT or controlled trial*

1922. Ito S, Nakura N, Le Breton S, et al. Efficacy and safety of aliskiren in Japanese hypertensive patients with renal dysfunction. Hypertension Research - Clinical & Experimental 2010; 33(1):62-6. *Follow-up less than 6 months*

1923. Itoh K. Comparison of methods for determination of glomerular filtration rate: Tc-99m-DTPA renography, predicted creatinine clearance method and plasma sample method. Annals of Nuclear Medicine 2003; 17(7):561-5. *Not CKD treatment*

1924. Itoh K, Tsushima S, Tsukamoto E, et al. Reappraisal of single-sample and gamma camera methods for determination of the glomerular filtration rate with 99mTc-DTPA. Annals of Nuclear Medicine 2000; 14(3):143-50. *Not early CKD*

1925. Ivanovski O, Nikolov IG, Drueke BT, et al. Atherosclerosis and vascular calcification in uraemia - a new experimental model. Makedonska Akademija na Naukite i Umetnostite Oddelenie Za Bioloshki i Meditsinski Nauki Prilozi 2007; 28(2):11-24. *Not CKD treatment*

1926. Ivanyi B. Development of chronic renal failure in patients with multiple myeloma. Archives of Pathology & Laboratory Medicine 1993; 117(8):837-40. *Sample size less than 50 patients*

1927. Ives NJ, Wheatley K, Stowe RL, et al. Continuing uncertainty about the value of percutaneous revascularization in atherosclerotic renovascular disease: a meta-analysis of randomized trials. Nephrology Dialysis Transplantation 2003; 18(2):298-304. *Not relevant to key questions*

1928. Ix JH, McCulloch CE, Chertow GM. Theophylline for the prevention of radiocontrast nephropathy: a meta-analysis. Nephrology Dialysis Transplantation 2004; 19(11):2747-53. *Sample size less than 50 patients*

1929. Ix JH, Shlipak MG, Sarnak MJ, et al. Fetuin-A is not associated with mortality in chronic kidney disease. Kidney International 2007; 72(11):1394-9. *Not RCT or controlled trial*

1930. Iyengar A, Damle H, Kulkarni C, et al. Steroid sparing effect of a herbal preparation in steroid-dependent nephrotic syndrome. Pediatric Nephrology 2006; 21(7):1031-3. *Sample size less than 50 patients*

1931. Iyengar SK, Adler SG. The application of the HapMap to diabetic nephropathy and other causes of chronic renal failure. Seminars in Nephrology 2007; 27(2):223-36. *Not relevant to key questions*

1932. Izhar M, Alausa T, Folker A, et al. Effects of COX inhibition on blood pressure and kidney function in ACE inhibitor-treated blacks and hispanics. Hypertension 2004; 43(3):573-7. *Not RCT or controlled trial*

1933. Izumi K, Eishi K, Yamachika S, et al. The efficacy of human atrial natriuretic peptide in patients with renal dysfunction undergoing cardiac surgery. Annals of Thoracic & Cardiovascular Surgery 2008; 14(5):294-302. *Not CKD treatment*

1934. Izzedine H, Hulot JS, Launay-Vacher V, et al. Renal safety of adefovir dipivoxil in patients with chronic hepatitis B: two double-blind, randomized, placebo-controlled studies. Kidney International 2004; 66(3):1153-8. *Not early CKD*

1935. Izzo JL, Jr., Purkayastha D, Hall D, et al. Comparative efficacy and safety of amlodipine/benazepril combination therapy and amlodipine monotherapy in severe hypertension. Journal of Human Hypertension 2010 Jun; 24(6):403-9. *Not CKD treatment*

1936. Jackson GH. Renal safety of ibandronate. Oncologist 2005; 10 Suppl 1:14-8. *Not relevant to key questions*

1937. Jacobi J, Schmieder RE. Nephroprotection by antihypertensive therapy. Basic Research in Cardiology 1998; 93 Suppl 2:109-19. *Not RCT or controlled trial*

1938. Jacobs DR, Jr., Gross MD, Steffen L, et al. The effects of dietary patterns on urinary albumin excretion: results of the Dietary Approaches to Stop Hypertension (DASH) Trial. American Journal of Kidney Diseases 2009; 53(4):638-46. *Not CKD treatment*

1939. Jacobs ML, Derkx FH, Stijnen T, et al. Effect of long-acting somatostatin analog (Somatulin) on renal hyperfiltration in patients with IDDM. Diabetes Care 1997; 20(4):632-6. *Sample size less than 50 patients*

1940. Jacobsen BA, Fjeldborg P. Renal haemodynamics during propranolol treatment in patients with arterial hypertension and chronic renal failure. Scandinavian Journal of Clinical & Laboratory Investigation 1986; 46(3):289-92. *Follow-up less than 6 months*

1941. Jacobsen P, Andersen S, Jensen BR, et al. Additive effect of ACE inhibition and angiotensin II receptor blockade in type I diabetic patients with diabetic nephropathy. Journal of the American Society of Nephrology 2003; 14(4):992-9. *Sample size less than 50 patients*

1942. Jacobsen P, Andersen S, Rossing K, et al. Dual blockade of the renin-angiotensin system in type 1 patients with diabetic nephropathy. Nephrology Dialysis Transplantation 2002; 17(6):1019-24. *Follow-up less than 6 months*

1943. Jacobsen P, Andersen S, Rossing K, et al. Dual blockade of the renin-angiotensin system versus maximal recommended dose of ACE inhibition in diabetic nephropathy. Kidney International 2003; 63(5):1874-80. *Sample size less than 50 patients*

1944. Jacobsen P, Parving H-H. Beneficial impact on cardiovascular risk factors by dual blockade of the renin-angiotensin system in diabetic nephropathy. Kidney International - Supplement 2004; (92):S108-10. *Not CKD treatment*

1945. Jacobson P, Uberti J, Davis W, et al. Tacrolimus: a new agent for the prevention of graft-versus-host disease in hematopoietic stem cell transplantation. Bone Marrow Transplantation 1998; 22(3):217-25. *Not CKD treatment*

1946. Jacobson SH, Ostenson CG. Effects of alpha 2-adrenergic blockade on renal hemodynamics in patients with insulin dependent diabetes mellitus. Diabetes Research & Clinical Practice 1991; 14(3):197-203. *Sample size less than 50 patients*

1947. Jaehde U, Sorgel F, Reiter A, et al. Effect of probenecid on the distribution and elimination of ciprofloxacin in humans. Clinical Pharmacology & Therapeutics 1995; 58(5):532-41. *Sample size less than 50 patients*

1948. Jaehde U, Sorgel F, Stephan U, et al. Effect of an antacid containing magnesium and aluminum on absorption, metabolism, and mechanism of renal elimination of pefloxacin in humans. Antimicrobial Agents & Chemotherapy 1994; 38(5):1129-33. *Follow-up less than 6 months*

1949. Jafar TH, Schmid CH, Landa M, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease. A meta-analysis of patient-level data.[Erratum appears in Ann Intern Med 2002 Aug 20;137(4):299]. Annals of Internal Medicine 2001; 135(2):73-87. *Not relevant to key questions*

1950. Jafar TH, Schmid CH, Stark PC, et al. The rate of progression of renal disease may not be slower in women compared with men: a patient-level meta-analysis. Nephrology Dialysis Transplantation 2003; 18(10):2047-53. *Not RCT or controlled trial*

1951. Jafar TH, Stark PC, Schmid CH, et al. Progression of chronic kidney disease: the role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: a patient-level meta-analysis. Annals of Internal Medicine 2003; 139(4):244-52. *Not RCT or controlled trial*

1952. Jafar TH, Stark PC, Schmid CH, et al. Proteinuria as a modifiable risk factor for the progression of non-diabetic renal disease. Kidney International 2001; 60(3):1131-40. *Not RCT or controlled trial*

1953. Jager A, Kostense PJ, Nijpels G, et al. Microalbuminuria is strongly associated with NIDDM and hypertension, but not with the insulin resistance syndrome: the Hoorn Study. Diabetologia 1998; 41(6):694-700. *Not CKD treatment*

1954. Jakobsen JA. Renal experience with Visipaque. European Radiology 1996; 6 Suppl 2:S16-9. *Not RCT or controlled trial*

1955. Jakobsen JA, Berg KJ, Brodahl U, et al. Renal effects of nonionic contrast media after cardioangiography. Acta Radiologica 1994; 35(2):191-6. *Not CKD treatment*

1956. Jakobsen JA, Berg KJ, Kjaersgaard P, et al. Angiography with nonionic X-ray contrast media in severe chronic renal failure: renal function and contrast retention. Nephron 1996; 73(4):549-56. *Sample size less than 50 patients*

1957. Jakobsen JA, Kolbenstvedt AN, Berg KJ. Renal effects of iopentol and iohexol after intravenous injection. Acta Radiologica 1991; 32(4):320-4. *Not CKD treatment*

1958. Jakobsen JA, Kolbenstvedt AN, Levorstad K, et al. Renal effects of nonionic contrast media after intravenous cardiac, and lumbar aortic injections. Investigative Radiology 1990; 25 Suppl 1:S135-6. *Sample size less than 50 patients*

1959. Jamal SA, Bauer DC, Ensrud KE, et al. Alendronate treatment in women with normal to severely impaired renal function: an analysis of the fracture intervention trial. Journal of Bone & Mineral Research 2007; 22(4):503-8. *Not relevant to key questions*

1960. Jamal SA, Fitchett D, Lok CE, et al. The effects of calcium-based versus non-calcium-based phosphate binders on mortality among patients with chronic kidney disease: a meta-analysis. Nephrology Dialysis Transplantation 2009; 24(10):3168-74. *Not RCT or controlled trial*

1961. Jamar F, Barone R, Mathieu I, et al. 86Y-DOTA0)-D-Phe1-Tyr3-octreotide (SMT487)--a phase 1 clinical study: pharmacokinetics, biodistribution and renal protective effect of different regimens of amino acid co-infusion. European Journal of Nuclear Medicine & Molecular Imaging 2003; 30(4):510-8. *Not CKD treatment*

1962. James S, Budaj A, Aylward P, et al. Ticagrelor versus clopidogrel in acute coronary syndromes in relation to renal function: results from the Platelet Inhibition and Patient Outcomes (PLATO) trial. Circulation 2010 Sep 14; 122(11):1056-67. *Not CKD treatment*

1963. Jamieson MJ, Webster J, Fowler G, et al. A comparison of the chronic effects of oral xamoterol and enalapril on blood pressure and renal function in mild to moderate heart failure. British Journal of Clinical Pharmacology 1991; 31(3):305-12. *Follow-up less than 6 months*

1964. Jamison RL, Hartigan P, Kaufman JS, et al. Effect of homocysteine lowering on mortality and vascular disease in advanced chronic kidney disease and end-stage renal disease: a randomized controlled trial.[Erratum appears in JAMA. 2008 Jul 9;300(2):170]. JAMA 2007; 298(10):1163-70. *Sample size less than 50 patients*

1965. Jamison RL, Shih M-C, Humphries DE, et al. Effect of the MTHFR C677T and A1298C polymorphisms on survival in patients with advanced CKD and ESRD: a prospective study. American Journal of Kidney Diseases 2009; 53(5):779-89. *Not CKD treatment*

1966. Jandeleit-Dahm K, Cao Z, Cox AJ, et al. Role of hyperlipidemia in progressive renal disease: focus on diabetic nephropathy. Kidney International - Supplement 1999; 71:S31-6. *Not human studies*

1967. Jansen JJ, Maassen JA, van der Woude FJ, et al. Mutation in mitochondrial tRNA(Leu(UUR)) gene associated with progressive kidney disease. Journal of the American Society of Nephrology 1997; 8(7):1118-24. *Not RCT or controlled trial*

1968. Jansen PM, Danser AHJ, Imholz BP, et al. Aldosterone-receptor antagonism in hypertension. Journal of Hypertension 2009; 27(4):680-91. *Not RCT or controlled trial*

1969. Janssen JJ, Gans RO, van der Meulen J, et al. Comparison between the effects of amlodipine and lisinopril on proteinuria in nondiabetic renal failure: a double-blind, randomized prospective study. American Journal of Hypertension 1998; 11(9):1074-9. *Sample size less than 50 patients*

1970. Janssen van Doorn K, Spapen H, Geers C, et al. Sepsis-related acute kidney injury: a protective effect of drotrecogin alpha (activated) treatment?.[Erratum appears in Acta Anaesthesiol Scand. 2009 Feb;53(2):275. Note: van Doorn, K J [corrected to Janssen van Doorn, K]]. Acta Anaesthesiologica Scandinavica 2008; 52(9):1259-64. *Sample size less than 50 patients*

1971. Janssen-Heijnen MLG, van Spronsen DJ, Lemmens VEPP, et al. A population-based study of severity of comorbidity among patients with non-Hodgkin's lymphoma: prognostic impact independent of International Prognostic Index. British Journal of Haematology 2005; 129(5):597-606. *Not relevant to key questions*

1972. Januzzi JL, Cannon CP, DiBattiste PM, et al. Effects of renal insufficiency on early invasive management in patients with acute coronary syndromes (The TACTICS-TIMI 18 Trial). American Journal of Cardiology 2002; 90(11):1246-9. *Not CKD treatment*

1973. Januzzi JL, Jr., Snapinn SM, DiBattiste PM, et al. Benefits and safety of tirofiban among acute coronary syndrome patients with mild to moderate renal insufficiency: results from the Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) trial. Circulation 2002; 105(20):2361-6. *Not CKD treatment*

1974. Jardine AG, Connell JM, Northridge D, et al. The atriopeptidase inhibitor UK 69,578 increases atrial natriuretic factor and causes a natriuresis in normal humans. American Journal of Hypertension 1990; 3(9):661-7. *Not CKD treatment*

1975. Jardine MJ, Ninomiya T, Perkovic V, et al. Aspirin is beneficial in hypertensive patients with chronic kidney disease: a post-hoc subgroup analysis of a randomized controlled trial. Journal of the American College of Cardiology 2010 Sep 14; 56(12):956-65. *Not CKD treatment*

1976. Jarnberg P-O. Renal protection strategies in the perioperative period. Best Practice & Research 2004; Clinical Anaesthesiology. 18(4):645-60. *Not RCT or controlled trial*

1977. Jasani NB, O'Conner RE, Bouzoukis JK. Comparison of hydromorphone and meperidine for ureteral colic. Academic Emergency Medicine 1994; 1(6):539-43. *Not CKD treatment*

1978. Jaschevatzky OE, Rosenberg RP, Shalit A, et al. Protein/creatinine ratio in random urine specimens for quantitation of proteinuria in preeclampsia. Obstetrics & Gynecology 1990; 75(4):604-6. *Not CKD treatment*

1979. Jawa A, Nachimuthu S, Pendergrass M, et al. Beta-blockers have a beneficial effect upon endothelial function and microalbuminuria in African-American subjects with diabetes and hypertension. Journal of Diabetes & its Complications 2008; 22(5):303-8. *Not CKD treatment*

1980. Jean R, Ducasse JL, Montastruc JL, et al. Treatment of acute renal colic in a French emergency department: a comparison of simulated cases and real cases in acute pain assessment and management. European Journal of Clinical Pharmacology 2001; 57(9):685-9. *Not early CKD*

1981. Jeevanandam V, Russell H, Mather P, et al. Donor tricuspid annuloplasty during orthotopic heart transplantation: long-term results of a prospective controlled study. Annals of Thoracic Surgery 2006; 82(6):2089-95; discussion 95. *Follow-up less than 6 months*

1982. Jeffres MN, Isakow W, Doherty JA, et al. A retrospective analysis of possible renal toxicity associated with vancomycin in patients with health care-associated methicillin-resistant Staphylococcus aureus pneumonia. Clinical Therapeutics 2007; 29(6):1107-15. *Follow-up less than 6 months*

1983. Jeffrey RF, MacDonald TM, Freestone S, et al. The effect of carbidopa and lithium on the systemic and renal response to acute intravenous saline loading in normal man. Nephrology Dialysis Transplantation 1989; 4(4):271-7. *Not CKD treatment*

1984. Jeffrey RF, MacDonald TM, Lee MR. A comparison of the renal actions of gamma-L-glutamyl-L-dopa and gamma-L-glutamyl-L-tyrosine in normal man. Clinical Science 1988; 74(1):37-40. *Sample size less than 50 patients*

1985. Jenkins DA, Cowan P, Patrick AW, et al. Renal responses to nifedipine and captopril in hypertensive insulin-dependent diabetic men: a randomized cross-over study. Nephrology Dialysis Transplantation 1993; 8(3):200-5. *Follow-up less than 6 months*

1986. Jenkins DJ, Kendall CW, Vidgen E, et al. High-protein diets in hyperlipidemia: effect of wheat gluten on serum lipids, uric acid, and renal function. American Journal of Clinical Nutrition 2001; 74(1):57-63. *Not early CKD*

1987. Jensen HV, Plenge P, Mellerup ET, et al. Lithium prophylaxis of manic-depressive disorder: daily lithium dosing schedule versus every second day. Acta Psychiatrica Scandinavica 1995; 92(1):69-74. *Follow-up less than 6 months*

1988. Jensen JS, Feldt-Rasmussen B, Borch-Johnsen K, et al. Increased transvascular lipoprotein transport in diabetes: association with albuminuria and systolic hypertension. Journal of Clinical Endocrinology & Metabolism 2005; 90(8):4441-5. *Not early CKD*

1989. Jensen KT, Carstens J, Pedersen EB. Effect of BNP on renal hemodynamics, tubular function and vasoactive hormones in humans. American Journal of Physiology 1998; 274(1 Pt 2):F63-72. *Sample size less than 50 patients*

1990. Jensen T, Stender S, Goldstein K, et al. Partial normalization by dietary cod-liver oil of increased microvascular albumin leakage in patients with insulin-dependent diabetes and albuminuria. New England Journal of Medicine 1989; 321(23):1572-7. *Sample size less than 50 patients*

1991. Jentzer JC, DeWald TA, Hernandez AF. Combination of loop diuretics with thiazide-type diuretics in heart failure. Journal of the American College of Cardiology 2010 Nov 2; 56(19):1527-34. *Not CKD treatment*

1992. Jeppsson A, Ekroth R, Friberg P, et al. Renal effects of amino acid infusion in cardiac surgery. Journal of Cardiothoracic & Vascular Anesthesia 2000; 14(1):51-5. *Sample size less than 50 patients*

1993. Jeppsson A, Ekroth R, Friberg P, et al. Renal effects of alpha-ketoglutarate early after coronary operations. Annals of Thoracic Surgery 1998; 65(3):684-90. *Not CKD treatment*

1994. Jeppsson A, Ekroth R, Kirno K, et al. Insulin and amino acid infusion after cardiac operations: effects on systemic and renal perfusion. Journal of Thoracic & Cardiovascular Surgery 1997; 113(3):594-602. *Sample size less than 50 patients*

1995. Jerums G, Allen TJ, Campbell DJ, et al. Long-term renoprotection by perindopril or nifedipine in non-hypertensive patients with Type 2 diabetes and microalbuminuria. Diabetic Medicine 2004; 21(11):1192-9. *Not relevant to key questions*

1996. Jerums G, Allen TJ, Campbell DJ, et al. Long-term comparison between perindopril and nifedipine in normotensive patients with type 1 diabetes and microalbuminuria. American Journal of Kidney Diseases 2001; 37(5):890-9. *Sample size less than 50 patients*

1997. Jerums G, Allen TJ, Gilbert RE, et al. Natural history of early diabetic nephropathy: what are the effects of therapeutic intervention? Melbourne Diabetic Nephropathy Study Group. Journal of Diabetes & its Complications 1995; 9(4):308-14. *Not RCT or controlled trial*

1998. Jerums G, Murray RM, Seeman E, et al. Lack of effect of gliclazide on early diabetic nephropathy and retinopathy: a two-year controlled study. Diabetes Research & Clinical Practice 1987; 3(2):71-80. *Sample size less than 50 patients*

1999. Jespersen B, Randlov A, Abrahamsen J, et al. Acute cardiovascular effect of 1,25-dihydroxycholecalciferol in essential hypertension. American Journal of Hypertension 1998; 11(6 Pt 1):659-66. *Sample size less than 50 patients*

2000. Jevnikar AM, Finnie KJ, Dennis B, et al. Nephrotoxicity of high- and low-osmolality contrast media. Nephron 1988; 48(4):300-5. *Sample size less than 50 patients*

2001. Ji H, Yao S, Luo Q, et al. TCM treatment of rheumatoid arthritis by supplementing the kidney and invigorating the blood circulation. Journal of Traditional Chinese Medicine 2002; 22(4):252-5. *Not RCT or controlled trial*

2002. Jiang F, Jones GT, Dusting GJ. Failure of antioxidants to protect against angiotensin II-induced aortic rupture in aged apolipoprotein(E)-deficient mice. British Journal of Pharmacology 2007; 152(6):880-90. *Sample size less than 50 patients*

2003. Jin HM, Pan Y. Renoprotection provided by losartan in combination with pioglitazone is superior to renoprotection provided by losartan alone in patients with type 2 diabetic nephropathy. Kidney & Blood Pressure Research 2007; 30(4):203-11. *Not RCT or controlled trial*

2004. Jin H-M, Pan Y. Angiotensin type-1 receptor blockade with losartan increases insulin sensitivity and improves glucose homeostasis in subjects with type 2 diabetes and nephropathy. Nephrology Dialysis Transplantation 2007; 22(7):1943-9. *Follow-up less than 6 months*

2005. Jin K-K, Chen L, Pan J-Y, et al. Acupressure therapy inhibits the development of diabetic complications in Chinese patients with type 2 diabetes. Journal of Alternative & Complementary Medicine 2009; 15(9):1027-32. *Not CKD treatment*

2006. Jin X. A clinical investigation on 30 cases of senile benign renal arteriolosclerosis treated by huang qi gu jing yin. Journal of Traditional Chinese Medicine 2001; 21(3):177-80. *Not early CKD*

2007. Jin Z. Chai ling tang in the treatment of steroid-dependent nephrosis syndrome. Journal of Traditional Chinese Medicine 1994; 14(4):254-8. *Not CKD treatment*

2008. Jindal RM, Popescu I, Emre S, et al. Serum lipid changes in liver transplant recipients in a prospective trial of cyclosporine versus FK506. Transplantation 1994; 57(9):1395-8. *Not early CKD*

2009. Jo S-H, Koo B-K, Park J-S, et al. Prevention of radiocontrast medium-induced nephropathy using short-term high-dose simvastatin in patients with renal insufficiency undergoing coronary angiography (PROMISS) trial--a randomized controlled study. American Heart Journal 2008; 155(3):499.e1-8. *Not CKD treatment*

2010. Jo S-H, Koo B-K, Park J-S, et al. N-acetylcysteine versus AScorbic acid for preventing contrast-Induced nephropathy in patients with renal insufficiency undergoing coronary angiography NASPI study-a prospective randomized controlled trial. American Heart Journal 2009; 157(3):576-83. *Not early CKD*

2011. Jo S-H, Koo B-K, Youn T-J, et al. Conclusion of recent 'osmolality trials' in preventing contrast-induced nephropathy by NAC--what is the standard? Nephrology Dialysis Transplantation 2008; 23(7):2424; author reply -5. *Sample size less than 50 patients*

2012. Joannidis M. Medical therapy of acute kidney injury. Acta Clinica Belgica - Supplementum 2007; (2):353-6. *Not CKD treatment*

2013. Jodrell DI. Formula-based dosing for carboplatin. European Journal of Cancer 1999; 35(9):1299-301. *Not RCT or controlled trial*

2014. Joffe HV, Kwong RY, Gerhard-Herman MD, et al. Beneficial effects of eplerenone versus hydrochlorothiazide on coronary circulatory function in patients with diabetes mellitus. Journal of Clinical Endocrinology & Metabolism 2007; 92(7):2552-8. *Not RCT or controlled trial*

2015. Johansson BL, Borg K, Fernqvist-Forbes E, et al. Beneficial effects of C-peptide on incipient nephropathy and neuropathy in patients with Type 1 diabetes mellitus. Diabetic Medicine 2000; 17(3):181-9. *Sample size less than 50 patients*

2016. Johansson BL, Kernell A, Sjoberg S, et al. Influence of combined C-peptide and insulin administration on renal function and metabolic control in diabetes type 1. Journal of Clinical Endocrinology & Metabolism 1993; 77(4):976-81. *Sample size less than 50 patients*

2017. Johnson AG, Crawford GA, Kelly D, et al. Arginine vasopressin and osmolality in the elderly. Journal of the American Geriatrics Society 1994; 42(4):399-404. *Not RCT or controlled trial*

2018. Johnson CA. Use of androgens in patients with renal failure. Seminars in Dialysis 2000; 13(1):36-9. *Not CKD treatment*

2019. Johnson DW. Evidence-based guide to slowing the progression of early renal insufficiency. Internal Medicine Journal 2004; 34(1-2):50-7. *Not CKD treatment*

2020. Johnson DW. Dietary protein restriction as a treatment for slowing chronic kidney disease progression: the case against. Nephrology 2006; 11(1):58-62. *Not relevant to key questions*

2021. Johnson DW, Armstrong K, Campbell SB, et al. Metabolic syndrome in severe chronic kidney disease: Prevalence, predictors, prognostic significance and effects of risk factor modification. Nephrology 2007; 12(4):391-8. *Not RCT or controlled trial*

2022. Johnson DW, Forman C, Vesey DA. Novel renoprotective actions of erythropoietin: new uses for an old hormone. Nephrology 2006; 11(4):306-12. *Not CKD treatment*

2023. Johnson DW, Hawley CM, Rosser B, et al. Oxpentifylline versus placebo in the treatment of erythropoietin-resistant anaemia: a randomized controlled trial. BMC Nephrology 2008; 9:8. *Not RCT or controlled trial*

2024. Johnston CS, Day CS, Swan PD. Postprandial thermogenesis is increased 100% on a high-protein, low-fat diet versus a high-carbohydrate, low-fat diet in healthy, young women. Journal of the American College of Nutrition 2002; 21(1):55-61. *Not early CKD*

2025. Johnston GD, Passmore AP. The effects of cilazapril alone and in combination with frusemide in healthy subjects. British Journal of Clinical Pharmacology 1989; 27 Suppl 2:235S-42S. *Not CKD treatment*

2026. Jones D, Bellomo R. Renal-dose dopamine: from hypothesis to paradigm to dogma to myth and, finally, superstition? Journal of Intensive Care Medicine 2005; 20(4):199-211. *Not relevant to key questions*

2027. Jones E, Goldman M. Lipid formulations of amphotericin B. Cleveland Clinic Journal of Medicine 1998; 65(8):423-7. *Not CKD treatment*

2028. Jones M, Ibels L, Schenkel B, et al. Impact of epoetin alfa on clinical end points in patients with chronic renal failure: a meta-analysis. Kidney International 2004; 65(3):757-67. *Not early CKD*

2029. Jones RB, Tervaert JWC, Hauser T, et al. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. New England Journal of Medicine 2010 Jul 15; 363(3):211-20. *Not CKD treatment*

2030. Jones RD, Endre Z, Miles W, et al. Tenoxicam i.v. for major gynaecological surgery--effects on renal function. Anaesthesia & Intensive Care 2000; 28(5):501-9. *Sample size less than 50 patients*

2031. Jones SL, Kontessis P, Wiseman M, et al. Protein intake and blood glucose as modulators of GFR in hyperfiltering diabetic patients. Kidney International 1992; 41(6):1620-8. *Sample size less than 50 patients*

2032. Jonsson O, Herlitz H, Lindholm E, et al. Prophylaxis against bone loss in Kock reservoir patients with reduced glomerular filtration rate. Scandinavian Journal of Urology & Nephrology 2005; 39(3):200-5. *Sample size less than 50 patients*

2033. Jonsson PE, Olsson AM, Petersson BA, et al. Intravenous indomethacin and oxycone-papaverine in the treatment of acute renal colic. A double-blind study. British Journal of Urology 1987; 59(5):396-400. *Follow-up less than 6 months*

2034. Jorgensen JO, Pedersen SA, Thuesen L, et al. Beneficial effects of growth hormone treatment in GH-deficient adults. Lancet 1989; 1(8649):1221-5. *Not CKD treatment*

2035. Jose P, Skali H, Anavekar N, et al. Increase in creatinine and cardiovascular risk in patients with systolic dysfunction after myocardial infarction. Journal of the American Society of Nephrology 2006; 17(10):2886-91. *Sample size less than 50 patients*

2036. Josephson CD, Castillejo M-I, Grima K, et al. ABO-mismatched platelet transfusions: strategies to mitigate patient exposure to naturally occurring hemolytic antibodies. Transfusion & Apheresis Science 2010 Feb; 42(1):83-8. *Not CKD treatment*

2037. Joss N, Jardine A, Gaffney D, et al. Influence of apolipoprotein E genotype on progression of diabetic nephropathy. Nephron. Experimental Nephrology 2005; 101(4):e127-33. *Not CKD treatment*

2038. Joy MS. Darbepoetin alfa: a novel erythropoiesis-stimulating protein. Annals of Pharmacotherapy 2002; 36(7-8):1183-92. *Not RCT or controlled trial*

2039. Juergens CP, Winter JP, Nguyen-Do P, et al. Nephrotoxic effects of iodixanol and iopromide in patients with abnormal renal function receiving N-acetylcysteine and hydration before coronary angiography and intervention: a randomized trial. Internal Medicine Journal 2009; 39(1):25-31. *Not CKD treatment*

2040. Juhanson P, Kepp K, Org E, et al. N-acetyltransferase 8, a positional candidate for blood pressure and renal regulation: resequencing, association and in silico study. BMC Medical Genetics 2008; 9:25. *Not CKD treatment*

2041. Juhlin T, Bjorkman S, Gunnarsson B, et al. Acute administration of diclofenac, but possibly not long term low dose aspirin, causes detrimental renal effects in heart failure patients treated with ACE-inhibitors. European Journal of Heart Failure 2004; 6(7):909-16. *Not relevant to key questions*

2042. Juhlin T, Bjorkman S, Hoglund P. Cyclooxygenase inhibition causes marked impairment of renal function in elderly subjects treated with diuretics and ACE-inhibitors. European Journal of Heart Failure 2005; 7(6):1049-56. *Not RCT or controlled trial*

2043. Juhlin T, Erhardt LR, Ottosson H, et al. Treatments with losartan or enalapril are equally sensitive to deterioration in renal function from cyclooxygenase inhibition. European Journal of Heart Failure 2007; 9(2):191-6. *Not relevant to key questions*

2044. Juhlin T, Jonsson BAG, Hoglund P. Renal effects of aspirin are clearly dose-dependent and are of clinical importance from a dose of 160 mg. European Journal of Heart Failure 2008; 10(9):892-8. *Not CKD treatment*

2045. Julier K, da Silva R, Garcia C, et al. Preconditioning by sevoflurane decreases biochemical markers for myocardial and renal dysfunction in coronary artery bypass graft surgery: a double-blinded, placebo-controlled, multicenter study. Anesthesiology 2003; 98(6):1315-27. *Not CKD treatment*

2046. Jungers P, Chauveau P, Ployard F, et al. Comparison of ketoacids and low protein diet on advanced chronic renal failure progression. Kidney International - Supplement 1987; 22:S67-71. *Sample size less than 50 patients*

2047. Jungers P, Choukroun G, Oualim Z, et al. Beneficial influence of recombinant human erythropoietin therapy on the rate of progression of chronic renal failure in predialysis patients. Nephrology Dialysis Transplantation 2001; 16(2):307-12. *Not RCT or controlled trial*

2048. Jungmann E, Haak T, Althoff PH, et al. Dopaminergic effects on kidney function and responsiveness of aldosterone, plasma renin activity, prolactin, catecholamines, and blood pressure to stimulation in patients with prolactinoma. Comparison of the efficacy of pergolide and bromocriptine therapy. Arzneimittel-Forschung 1988; 38(2):296-300. *Sample size less than 50 patients*

2049. Jungmann E, Malanyn M, Mortasawi N, et al. Effect of 1-year treatment with nitrendipine versus enalapril on urinary albumin and alpha 1-microglobulin excretion in microalbuminuric patients with type 1 diabetes mellitus. A randomized, single-blind comparative study. Arzneimittel-Forschung 1994; 44(3):313-7. *Sample size less than 50 patients*

2050. Jungmann E, Usadel KH. Effect of captopril on renal functional reserve in type 1 (insulin-dependent) diabetes mellitus. Diabetologia 1991; 34(11):843-4. *Not early CKD*

2051. Jungmann E, Walter-Schrader MC, Haak T, et al. Impaired renal responsiveness to human atrial natriuretic peptide (hANP) in normotensive patients with type 1 diabetes mellitus. Klinische Wochenschrift 1988; 66(12):527-32. *Sample size less than 50 patients*

2052. Junyent M, Martinez M, Borras M, et al. Predicting cardiovascular disease morbidity and mortality in chronic kidney disease in Spain. The rationale and design of NEFRONA: a prospective, multicenter, observational cohort study. BMC Nephrology 2010; 11:14. *Not RCT or controlled trial*

2053. Jurkovitz C, Franch H, Shoham D, et al. Family members of patients treated for ESRD have high rates of undetected kidney disease. American Journal of Kidney Diseases 2002; 40(6):1173-8. *Not CKD treatment*

2054. Kaasjager KA, Koomans HA, Rabelink TJ. Effectiveness of enalapril versus nifedipine to antagonize blood pressure and the renal response to endothelin in humans. Hypertension 1995; 25(4 Pt 1):620-5. *Not RCT or controlled trial*

2055. Kaasjager KA, Koomans HA, Rabelink TJ. Endothelin-1-induced vasopressor responses in essential hypertension. Hypertension 1997; 30(1 Pt 1):15-21. *Sample size less than 50 patients*

2056. Kabat-Koperska J, Motyl W, Domanski L, et al. Methods of GFR determination--creatinine clearance after cimetidine administration in clinical practice. Acta Medica Austriaca 2004; 31(2):51-5. *Follow-up less than 6 months*

2057. Kadam S, Kulshrestha S, Swaminathan S. B-vitamin therapy for diabetic nephropathy. JAMA 2010 Aug 11; 304(6):636; author reply -7. *Not CKD treatment*

2058. Kadhim HM, Ismail SH, Hussein KI, et al. Effects of melatonin and zinc on lipid profile and renal function in type 2 diabetic patients poorly controlled with metformin. Journal of Pineal Research 2006; 41(2):189-93. *Not RCT or controlled trial*

2059. Kageyama S, Brown J, Causon R, et al. DOPA decarboxylase inhibition does not influence the diuretic and natriuretic response to exogenous alpha-atrial natriuretic peptide in man. European Journal of Clinical Pharmacology 1990; 38(3):223-7. *Not CKD treatment*

2060. Kahn D, Ben-Haim S, Bushnell DL, et al. Captopril-enhanced 99Tcm-MAG3 renal scintigraphy in subjects with suspected renovascular hypertension. Nuclear Medicine Communications 1994; 15(7):515-28. *Sample size less than 50 patients*

2061. Kaisar MO, Isbel NM, Johnson DW. Recent clinical trials of pharmacologic cardiovascular interventions in patients with chronic kidney disease. Reviews on Recent Clinical Trials 2008; 3(2):79-88. *Not CKD treatment*

2062. Kalaitzidis RG, Bakris GL. Should proteinuria reduction be the criterion for antihypertensive drug selection for patients with kidney disease? Current Opinion in Nephrology & Hypertension 2009; 18(5):386-91. *Not RCT or controlled trial*

2063. Kalambokis G, Economou M, Fotopoulos A, et al. Effects of nitric oxide inhibition by methylene blue in cirrhotic patients with ascites. Digestive Diseases & Sciences 2005; 50(10):1771-7. *Not relevant to key questions*

2064. Kalambokis G, Fotopoulos A, Economou M, et al. Effects of a 7-day treatment with midodrine in non-azotemic cirrhotic patients with and without ascites. Journal of Hepatology 2007; 46(2):213-21. *Sample size less than 50 patients*

2065. Kalantarinia K, Okusa MD. The renin-angiotensin system and its blockade in diabetic renal and cardiovascular disease. Current Diabetes Reports 2006; 6(1):8-16. *Follow-up less than 6 months*

2066. Kalantar-Zadeh K, Kovesdy CP. Clinical outcomes with active versus nutritional vitamin D compounds in chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(9):1529-39. *Not RCT or controlled trial*

2067. Kalayjian RC, Franceschini N, Gupta SK, et al. Suppression of HIV-1 replication by antiretroviral therapy improves renal function in persons with low CD4 cell counts and chronic kidney disease. AIDS 2008; 22(4):481-7. *Not CKD treatment*

2068. Kale K, Sawant S. Clinical significance and evaluation of proteinuria in NIDDM patients. Indian Journal of Medical Sciences 1999; 53(3):103-7. *Not relevant to key questions*

2069. Kamali F, Edwards C. Possible role of metabolite in flosequinan-related mortality. Clinical Pharmacokinetics 1995; 29(6):396-403. *Not RCT or controlled trial*

2070. Kamiyama N, Ogawa R, Hamada H, et al. Preventive effect of N-acetylcysteine on contrast-induced nephropathy following coronary angiography and angioplasty. Yakugaku Zasshi - Journal of the Pharmaceutical Society of Japan 2008; 128(9):1333-9. *Not CKD treatment*

2071. Kammerl MC, Grimm D, Nabel C, et al. Effects of growth hormone on renal renin gene expression in normal rats and rats with myocardial infarction. Nephrology Dialysis Transplantation 2000; 15(6):786-90. *Not human studies*

2072. Kamper AL, Holstein-Rathlou NH, Leyssac PP, et al. The influence of angiotensin-converting enzyme inhibition on renal tubular function in progressive chronic nephropathy. American Journal of Kidney Diseases 1996; 28(6):822-31. *Not RCT or controlled trial*

2073. Kamper AL, Nielsen OJ. Effect of enalapril on haemoglobin and serum erythropoietin in patients with chronic nephropathy. Scandinavian Journal of Clinical & Laboratory Investigation 1990; 50(6):611-8. *Not relevant to key questions*

2074. Kamper AL, Strandgaard S, Leyssac PP. Effect of enalapril on the progression of chronic renal failure. A randomized controlled trial. American Journal of Hypertension 1992; 5(7):423-30. *Not relevant to key questions*

2075. Kamper AL, Strandgaard S, Leyssac PP. Late outcome of a controlled trial of enalapril treatment in progressive chronic renal failure. Hard end-points and influence of proteinuria. Nephrology Dialysis Transplantation 1995; 10(7):1182-8. *Not early CKD*

2076. Kanbay M, Covic A, Coca SG, et al. Sodium bicarbonate for the prevention of contrast-induced nephropathy: a meta-analysis of 17 randomized trials. International Urology & Nephrology 2009; 41(3):617-27. *Sample size less than 50 patients*

2077. Kanbay M, Kasapoglu B, Akcay A. Sodium bicarbonate vs sodium chloride in preventing contrast medium-induced nephropathy. JAMA 2009; 301(4):378; author reply 9-80. *Not CKD treatment*

2078. Kandarpa K, Becker GJ, Hunink MG, et al. Transcatheter interventions for the treatment of peripheral atherosclerotic lesions: part I. Journal of Vascular & Interventional Radiology 2001; 12(6):683-95. *Not CKD treatment*

2079. Kandula P, Shah R, Singh N, et al. Statins for prevention of contrast-induced nephropathy in patients undergoing non-emergent percutaneous coronary intervention. Nephrology 2010 Mar; 15(2):165-70. *Not CKD treatment*

2080. Kaneshiro Y, Ichihara A, Sakoda M, et al. Add-on benefits of amlodipine and thiazide in nondiabetic chronic kidney disease stage 1/2 patients treated with valsartan. Kidney & Blood Pressure Research 2009; 32(1):51-8. *Not early CKD*

2081. Kang YS, Han KH, Han SY, et al. Characteristics of population with normal serum creatinine impaired renal function and: the validation of a MDRD formula in a healthy general population. Clinical Nephrology 2005; 63(4):258-66. *Sample size less than 50 patients*

2082. Kanno Y, Takenaka T, Nakamura T, et al. Add-on angiotensin receptor blocker in patients who have proteinuric chronic kidney diseases and are treated with angiotensin-converting enzyme inhibitors. Clinical Journal of The American Society of Nephrology: CJASN 2006; 1(4):730-7. *Follow-up less than 6 months*

2083. Kantarci F, Mihmanli I, Adaletli I, et al. The effect of fluid intake on renal length measurement in adults. Journal of Clinical Ultrasound 2006; 34(3):128-33. *Not relevant to key questions*

2084. Kantor TG. Use of diclofenac in analgesia. American Journal of Medicine 1986; 80(4B):64-9. *Not RCT or controlled trial*

2085. Kaplan AA. Therapeutic apheresis for cancer related hemolytic uremic syndrome. Therapeutic Apheresis 2000; 4(3):201-6. *Not early CKD*

2086. Kaplan NM. The place of diuretics in preventing cardiovascular events. Journal of Human Hypertension 2004; 18 Suppl 2:S29-32. *Not RCT or controlled trial*

2087. Kaplan-Pavlovcic S, Nadja C. Captopril renography and duplex Doppler sonography in the diagnosis of renovascular hypertension. Nephrology Dialysis Transplantation 1998; 13(2):313-7. *Sample size less than 50 patients*

2088. Kapoor A, Figlin RA. Targeted inhibition of mammalian target of rapamycin for the treatment of advanced renal cell carcinoma. Cancer 2009; 115(16):3618-30. *Not CKD treatment*

2089. Kapoor A, Kumar S, Gulati S, et al. The role of theophylline in contrast-induced nephropathy: a case-control study. Nephrology Dialysis Transplantation 2002; 17(11):1936-41. *Not CKD treatment*

2090. Kapoor A, Sinha N, Sharma RK, et al. Use of dopamine in prevention of contrast induced acute renal failure--a randomised study. International Journal of Cardiology 1996; 53(3):233-6. *Not CKD treatment*

2091. Karabina SA, Pappas H, Miltiadous G, et al. Compositional lipoprotein changes and low-density lipoprotein susceptibility to oxidation in chronic renal failure patients with heavy proteinuria. Nephron 2003; 95(3):c77-83. *Not CKD treatment*

2092. Karalliedde J, Smith A, DeAngelis L, et al. Valsartan improves arterial stiffness in type 2 diabetes independently of blood pressure lowering. Hypertension 2008; 51(6):1617-23. *Not CKD treatment*

2093. Kario K, Hoshide S, Shimizu M, et al. Effect of dosing time of angiotensin II receptor blockade titrated by self-measured blood pressure recordings on cardiorenal protection in hypertensives: the Japan Morning Surge-Target Organ Protection (J-TOP) study. Journal of Hypertension 2010 Jul; 28(7):1574-83. *Not relevant to key questions*

2094. Kario K, Matsui Y, Shibasaki S, et al. An alpha-adrenergic blocker titrated by self-measured blood pressure recordings lowered blood pressure and microalbuminuria in patients with morning hypertension: the Japan Morning Surge-1 Study. Journal of Hypertension 2008; 26(6):1257-65. *Not CKD treatment*

2095. Karnik AM, Bashir R, Khan FA, et al. Renal involvement in the systemic inflammatory reaction syndrome. Renal Failure 1998; 20(1):103-16. *Not CKD treatment*

2096. Karthik S, Lisbon A. Low-dose dopamine in the intensive care unit. Seminars in Dialysis 2006; 19(6):465-71. *Not RCT or controlled trial*

2097. Kasiakou SK, Sermaides GJ, Michalopoulos A, et al. Continuous versus intermittent intravenous administration of antibiotics: a meta-analysis of randomised controlled trials. The Lancet Infectious Diseases 2005; 5(9):581-9. *Follow-up less than 6 months*

2098. Kasiske BL. Questions and answers from controlled clinical trials of antihypertensive therapy in progressive renal disease. American Journal of Hypertension 1992; 5(10):778-9. *Not RCT or controlled trial*

2099. Kasiske BL, Kalil RS, Ma JZ, et al. Effect of antihypertensive therapy on the kidney in patients with diabetes: a meta-regression analysis. Annals of Internal Medicine 1993; 118(2):129-38. *Not RCT or controlled trial*

2100. Kasiske BL, Lakatua JD. The effects of dietary protein restriction on chronic progressive renal disease. Mineral & Electrolyte Metabolism 1997; 23(3-6):296-300. *Not RCT or controlled trial*

2101. Kasiske BL, Lakatua JD, Ma JZ, et al. A meta-analysis of the effects of dietary protein restriction on the rate of decline in renal function. American Journal of Kidney Diseases 1998; 31(6):954-61. *Not RCT or controlled trial*

2102. Kasiske BL, Velosa JA, Halstenson CE, et al. The effects of lovastatin in hyperlipidemic patients with the nephrotic syndrome. American Journal of Kidney Diseases 1990; 15(1):8-15. *Sample size less than 50 patients*

2103. Kassimatis TI, Goldsmith DJA. New hope for chronic kidney disease patients after the JUPITER trial: myth or reality? Journal of the American College of Cardiology 2010 Aug 3; 56(6):529. *Not RCT or controlled trial*

2104. Kassimatis TI, Konstantinopoulos PA. The role of statins in chronic kidney disease (CKD): friend or foe? Pharmacology & Therapeutics 2009; 122(3):312-23. *Not early CKD*

2105. Kastarinen H, Vasunta RL, Ukkola O, et al. Glomerular filtration rate is related to dipping pattern in ambulatory blood pressure monitoring--a cross-sectional population-based study. Journal of Human Hypertension 2010 Apr; 24(4):247-53. *Not CKD treatment*

2106. Kastarinen M, Juutilainen A, Kastarinen H, et al. Risk factors for end-stage renal disease in a community-based population: 26-year follow-up of 25,821 men and women in eastern Finland. Journal of Internal Medicine 2010 Jun; 267(6):612-20. *Not CKD treatment*

2107. Katavetin P, Eiam-Ong S, Suwanwalaikorn S. Pioglitazone reduces urinary protein and urinary transforming growth factor-beta excretion in patients with type 2 diabetes and overt nephropathy. Journal of the Medical Association of Thailand 2006; 89(2):170-7. *Not RCT or controlled trial*

2108. Katayama K, Nomura S, Ishikawa H, et al. Comparison between valsartan and valsartan plus cilnidipine in type II diabetics with normo- and microalbuminuria. Kidney International 2006; 70(1):151-6. *Not CKD treatment*

2109. Katayama S, Kawamori R, Iwamoto Y, et al. In half of hypertensive diabetics, co-administration of a calcium channel blocker and an angiotensin-converting enzyme inhibitor achieved a target blood pressure of <130/80 mmHg: the azelnidipine and temocapril in hypertensive patients with type 2 diabetes (ATTEST) study. Hypertension Research - Clinical & Experimental 2008; 31(8):1499-508. *Not CKD treatment*

2110. Katayama Y, Haraoka J, Hirabayashi H, et al. A randomized controlled trial of hydrocortisone against hyponatremia in patients with aneurysmal subarachnoid hemorrhage. Stroke 2007; 38(8):2373-5. *Not RCT or controlled trial*

2111. Katholi RE, Taylor GJ, McCann WP, et al. Nephrotoxicity from contrast media: attenuation with theophylline. Radiology 1995; 195(1):17-22. *Not CKD treatment*

2112. Katholi RE, Taylor GJ, Woods WT, et al. Nephrotoxicity of nonionic low-osmolality versus ionic high-osmolality contrast media: a prospective double-blind randomized comparison in human beings. Radiology 1993; 186(1):183-7. *Not CKD treatment*

2113. Katholi RE, Woods WT, Jr., Taylor GJ, et al. Oxygen free radicals and contrast nephropathy. American Journal of Kidney Diseases 1998; 32(1):64-71. *Not CKD treatment*

2114. Katiyar CK, Arora D, Mehrotra R, et al. Management of chronic hepatitis B with New Livfit in end stage renal disease. Indian Journal of Physiology & Pharmacology 2005; 49(1):83-8. *Sample size less than 50 patients*

2115. Katzman PL, DiBona GF, Hokfelt B, et al. Acute renal tubular and hemodynamic effects of the calcium antagonist felodipine in healthy volunteers. Journal of the American Society of Nephrology 1991; 2(5):1000-6. *Sample size less than 50 patients*

2116. Katzman PL, Henningsen NC, Fagher B, et al. Renal and endocrine effects of long-term converting enzyme inhibition as compared with calcium antagonism in essential hypertension. Journal of Cardiovascular Pharmacology 1990; 15(3):360-4. *Sample size less than 50 patients*

2117. Kawamori R, Kamado K, Kamada T. Recent progress in the treatment of diabetic nephropathy: importance of strict glycemic control on the regression of diabetic nephropathy. Journal of Diabetic Complications 1991; 5(2-3):88-90. *Sample size less than 50 patients*

2118. Kawamoto R, Kohara K, Tabara Y, et al. An association between body mass index and estimated glomerular filtration rate. Hypertension Research - Clinical & Experimental 2008; 31(8):1559-64. *Not CKD treatment*

2119. Kawamoto R, Kohara K, Tabara Y, et al. An association between decreased estimated glomerular filtration rate and arterial stiffness. Internal Medicine 2008; 47(7):593-8. *Not CKD treatment*

2120. Kay J, Chow WH, Chan TM, et al. Acetylcysteine for prevention of acute deterioration of renal function following elective coronary angiography and intervention: a randomized controlled trial. JAMA 2003; 289(5):553-8. *Not CKD treatment*

2121. Kaya K, Oguz M, Akar AR, et al. The effect of sodium nitroprusside infusion on renal function during reperfusion period in patients undergoing coronary artery bypass grafting: a prospective randomized clinical trial. European Journal of Cardio-Thoracic Surgery 2007; 31(2):290-7. *Sample size less than 50 patients*

2122. Kaysen GA, Gambertoglio J, Felts J, et al. Albumin synthesis, albuminuria and hyperlipemia in nephrotic patients. Kidney International 1987; 31(6):1368-76. *Sample size less than 50 patients*

2123. Keane WF, Hirata-Dulas CA, Bullock ML, et al. Adjunctive therapy with intravenous human immunoglobulin G improves survival of patients with acute renal failure. Journal of the American Society of Nephrology 1991; 2(4):841-7. *Not CKD treatment*

2124. Keane WF, Lyle PA, Reduction of Endpoints in NwtAIIRALs. Recent advances in management of type 2 diabetes and nephropathy: lessons from the RENAAL study. American Journal of Kidney Diseases 2003; 41(3 Suppl 1):S22-5. *Not RCT or controlled trial*

2125. Keeley EC, McCullough PA. Coronary revascularization in patients with end-stage renal disease: risks, benefits, and optimal strategies. Reviews in Cardiovascular Medicine 2003; 4(3):125-30. *Not CKD treatment*

2126. Keeley EC, McCullough PA. Coronary revascularization in patients with coronary artery disease and chronic kidney disease. Advances in Chronic Kidney Disease 2004; 11(3):254-60. *Not CKD treatment*

2127. Keeton GR, Smit RvZ, Bryer A. Renal outcome of type 2 diabetes in South Africa--a 12-year follow-up study. South African Medical Journal 2004; Suid-Afrikaanse Tydskrif Vir Geneeskunde. 94(9):771-5. *Not RCT or controlled trial*

2128. Kefer JM, Hanet CE, Boitte S, et al. Acetylcysteine, coronary procedure and prevention of contrast-induced worsening of renal function: which benefit for which patient? Acta Cardiologica 2003; 58(6):555-60. *Not relevant to key questions*

2129. Keilani T, Danesh FR, Schlueter WA, et al. A subdepressor low dose of ramipril lowers urinary protein excretion without increasing plasma potassium. American Journal of Kidney Diseases 1999; 33(3):450-7. *Sample size less than 50 patients*

2130. Keilani T, Schlueter WA, Levin ML, et al. Improvement of lipid abnormalities associated with proteinuria using fosinopril, an angiotensin-converting enzyme inhibitor. Annals of Internal Medicine 1993; 118(4):246-54. *Follow-up less than 6 months*

2131. Keithi-Reddy SR, Addabbo F, Patel TV, et al. Association of anemia and erythropoiesis stimulating agents with inflammatory biomarkers in chronic kidney disease. Kidney International 2008; 74(6):782-90. *Sample size less than 50 patients*

2132. Keithi-Reddy SR, Singh AK. Hemoglobin target in chronic kidney disease: a pediatric perspective. Pediatric Nephrology 2009; 24(3):431-4. *Sample size less than 50 patients*

2133. Kekec Z, Yilmaz U, Sozuer E. The effectiveness of tenoxicam vs isosorbide dinitrate plus tenoxicam in the treatment of acute renal colic. BJU International 2000; 85(7):783-5. *Not early CKD*

2134. Kell MJ. Utilization of plasma and urine methadone concentrations to optimize treatment in maintenance clinics: I. Measurement techniques for a clinical setting. Journal of Addictive Diseases 1994; 13(1):5-26. *Not RCT or controlled trial*

2135. Kellum JA. Prophylactic fenoldopam for renal protection? No, thank you, not for me--not yet at least. Critical Care Medicine 2005; 33(11):2681-3. *Not RCT or controlled trial*

2136. Kellum JA, Leblanc M, Venkataraman R. Acute renal failure. Clinical Evidence 2002; (7):757-74. *Not RCT or controlled trial*

2137. Kelly AM, Dwamena B, Cronin P, et al. Meta-analysis: effectiveness of drugs for preventing contrast-induced nephropathy.[Erratum appears in Ann Intern Med. 2008 Aug 5;149(3):219]. Annals of Internal Medicine 2008; 148(4):284-94. *Not CKD treatment*

2138. Kelly DJ, Edgley AJ, Zhang Y, et al. Protein kinase C-beta inhibition attenuates the progression of nephropathy in non-diabetic kidney disease. Nephrology Dialysis Transplantation 2009; 24(6):1782-90. *Not CKD treatment*

2139. Keltai M, Tonelli M, Mann JFE, et al. Renal function and outcomes in acute coronary syndrome: impact of clopidogrel. European Journal of Cardiovascular Prevention & Rehabilitation 2007; 14(2):312-8. *Sample size less than 50 patients*

2140. Kemp G, Rose P, Lurain J, et al. Amifostine pretreatment for protection against cyclophosphamide-induced and cisplatin-induced toxicities: results of a randomized control trial in patients with advanced ovarian cancer. Journal of Clinical Oncology 1996; 14(7):2101-12. *Not CKD treatment*

2141. Kennedy C, Rickards D, Lee S, et al. A double-blind study comparing the efficiency, tolerance and renal effects of iopromide and iopamidol. British Journal of Radiology 1988; 61(724):288-93. *Not relevant to key questions*

2142. Kennedy L, Solano MP, Meneghini L, et al. Anti-glycation and anti-albuminuric effects of GLY-230 in human diabetes. American Journal of Nephrology 2010; 31(2):110-6. *Not CKD treatment*

2143. Kenny GN. Potential renal, haematological and allergic adverse effects associated with nonsteroidal anti-inflammatory drugs. Drugs 1992; 44 Suppl 5:31-6; discussion 7. *Not CKD treatment*

2144. Kent DM, Jafar TH, Hayward RA, et al. Progression risk, urinary protein excretion, and treatment effects of angiotensin-converting enzyme inhibitors in nondiabetic kidney disease. Journal of the American Society of Nephrology 2007; 18(6):1959-65. *Not RCT or controlled trial*

2145. Kentsch M, Ludwig D, Drummer C, et al. Haemodynamic and renal effects of urodilatin bolus injections in patients with congestive heart failure. European Journal of Clinical Investigation 1992; 22(10):662-9. *Sample size less than 50 patients*

2146. Kentsch M, Ludwig D, Drummer C, et al. Haemodynamic and renal effects of urodilatin in healthy volunteers. European Journal of Clinical Investigation 1992; 22(5):319-25. *Sample size less than 50 patients*

2147. Keown PA. Quality of life in end-stage renal disease patients during recombinant human erythropoietin therapy. The Canadian Erythropoietin Study Group. Contributions to Nephrology 1991; 88:81-6; discussion 7-9. *Not early CKD*

2148. Kerr E, Craig D, McGuinness B, et al. Reduced estimated glomerular filtration rate in Alzheimer's disease. International Journal of Geriatric Psychiatry 2009 Sep; 24(9):927-32. *Not CKD treatment*

2149. Kerstens MN, Buter H, Navis GJ, et al. 11beta-hydroxysteroid dehydrogenase activity in proteinuric patients and the effect of angiotensin-II receptor blockade. European Journal of Clinical Investigation 2002; 32(7):513-8. *Sample size less than 50 patients*

2150. Kerstetter JE, O'Brien KO, Insogna KL. Dietary protein affects intestinal calcium absorption. American Journal of Clinical Nutrition 1998; 68(4):859-65. *Sample size less than 50 patients*

2151. Kestenbaum B, Gillen DL, Sherrard DJ, et al. Calcium channel blocker use and mortality among patients with end-stage renal disease. Kidney International 2002; 61(6):2157-64. *Not early CKD*

2152. Ketelhut R, Bramlage P. Candesartan cilexetil/hydrochlorothiazide treatment in high-risk patients with type 2 diabetes mellitus and microalbuminuria: the CHILI T2D study. Clinical Drug Investigation 2010; 30(5):301-11. *Not RCT or controlled trial*

2153. Khajehdehi P, Roozbeh J, Mostafavi H. A comparative randomized and placebo-controlled short-term trial of aspirin and dipyridamole for overt type-2 diabetic nephropathy. Scandinavian Journal of Urology & Nephrology 2002; 36(2):145-8. *Follow-up less than 6 months*

2154. Khan DA, Ahmad TM, Qureshil AH, et al. Assessment of proteinuria by using protein: creatinine index in random urine sample. JPMA - Journal of the Pakistan Medical Association 2005; 55(10):428-31. *Not relevant to key questions*

2155. Khan NA, Campbell NR, Frost SD, et al. Risk of intraoperative hypotension with loop diuretics: a randomized controlled trial. American Journal of Medicine 2010 Nov; 123(11):1059.e1-8. *Not CKD treatment*

2156. Khan NA, Hemmelgarn BR, Tonelli M, et al. Prognostic value of troponin T and I among asymptomatic patients with end-stage renal disease: a meta-analysis. Circulation 2005; 112(20):3088-96. *Sample size less than 50 patients*

2157. Khan NA, Ma I, Thompson CR, et al. Kidney function and mortality among patients with left ventricular systolic dysfunction. Journal of the American Society of Nephrology 2006; 17(1):244-53. *Not relevant to key questions*

2158. Khan NA, McAlister FA, Rabkin SW, et al. The 2006 Canadian Hypertension Education Program recommendations for the management of hypertension: Part II - Therapy. Canadian Journal of Cardiology 2006; 22(7):583-93. *Follow-up less than 6 months*

2159. Khan NA, Susa D, van den Berg JW, et al. Amelioration of renal ischaemia-reperfusion injury by synthetic oligopeptides related to human chorionic gonadotropin. Nephrology Dialysis Transplantation 2009; 24(9):2701-8. *Not CKD treatment*

2160. Khandekar JD, Elson PJ, DeWys WD, et al. Comparative activity and toxicity of cis-diamminedichloroplatinum (DDP) and a combination of doxorubicin, cyclophosphamide, and DDP in disseminated transitional cell carcinomas of the urinary tract. Journal of Clinical Oncology 1985; 3(4):539-45. *Follow-up less than 6 months*

2161. Kharasch ED, Frink EJ, Jr., Artru A, et al. Long-duration low-flow sevoflurane and isoflurane effects on postoperative renal and hepatic function. Anesthesia & Analgesia 2001; 93(6):1511-20. *Not CKD treatment*

2162. Kharasch ED, Frink EJ, Jr., Zager R, et al. Assessment of low-flow sevoflurane and isoflurane effects on renal function using sensitive markers of tubular toxicity. Anesthesiology 1997; 86(6):1238-53. *Not CKD treatment*

2163. Khoury Z, Schlicht JR, Como J, et al. The effect of prophylactic nifedipine on renal function in patients administered contrast media. Pharmacotherapy 1995; 15(1):59-65. *Sample size less than 50 patients*

2164. Kiberd BA. Atorvastatin has no beneficial effect on cardiovascular outcomes in patients with advanced chronic kidney disease. Nature Clinical Practice Nephrology 2006; 2(7):354-5. *Not RCT or controlled trial*

2165. Kielstein JT, Salpeter SR, Bode-Boeger SM, et al. Symmetric dimethylarginine (SDMA) as endogenous marker of renal function--a meta-analysis. Nephrology Dialysis Transplantation 2006; 21(9):2446-51. *Follow-up less than 6 months*

2166. Kielstein JT, Simmel S, Bode-Boger SM, et al. Subpressor dose asymmetric dimethylarginine modulates renal function in humans through nitric oxide synthase inhibition. Kidney & Blood Pressure Research 2004; 27(3):143-7. *Not early CKD*

2167. Kim BJ, Sung KC, Kim BS, et al. Effect of N-acetylcysteine on cystatin C-based renal function after elective coronary angiography (ENABLE Study): a prospective, randomized trial. International Journal of Cardiology 2010 Feb 4; 138(3):239-45. *Follow-up less than 6 months*

2168. Kim H, Rosenberg SA, Steinberg SM, et al. A randomized double-blinded comparison of the antiemetic efficacy of ondansetron and droperidol in patients receiving high-dose interleukin-2. Journal of Immunotherapy with Emphasis on Tumor Immunology 1994; 16(1):60-5. *Not CKD treatment*

2169. Kim JY, Lee KC, Kim HS, et al. Effect of diltiazem on kidney function during laparoscopic surgery. Surgical Endoscopy 2009; 23(8):1785-90. *Not CKD treatment*

2170. Kim KH, Lee MS, Kang KW, et al. Role of acupressure in symptom management in patients with end-stage renal disease: a systematic review. Journal of Palliative Medicine 2010 Jul; 13(7):885-92. *Not CKD treatment*

2171. Kim K-S, Fan WH, Kim Y-D, et al. Effectiveness of open-label losartan/hydrochlorothiazide combination therapy in Asian patients with hypertension not controlled with ACE inhibitor or ARB monotherapy. Hypertension Research - Clinical & Experimental 2009; 32(6):520-6. *Not CKD treatment*

2172. Kimel M, Leidy NK, Mannix S, et al. Does epoetin alfa improve health-related quality of life in chronically ill patients with anemia? Summary of trials of cancer, HIV/AIDS, and chronic kidney disease. Value in Health 2008; 11(1):57-75. *Follow-up less than 6 months*

2173. Kimmel M, Butscheid M, Brenner S, et al. Improved estimation of glomerular filtration rate by serum cystatin C in preventing contrast induced nephropathy by N-acetylcysteine or zinc--preliminary results. Nephrology Dialysis Transplantation 2008; 23(4):1241-5. *Not RCT or controlled trial*

2174. Kimmel PL, Barisoni L, Kopp JB. Pathogenesis and treatment of HIV-associated renal diseases: lessons from clinical and animal studies, molecular pathologic correlations, and genetic investigations. Annals of Internal Medicine 2003; 139(3):214-26. *Not CKD treatment*

2175. Kimmelstiel CD, Perrone R, Kilcoyne L, et al. Effects of renal neutral endopeptidase inhibition on sodium excretion, renal hemodynamics and neurohormonal activation in patients with congestive heart failure. Cardiology 1996; 87(1):46-53. *Sample size less than 50 patients*

2176. Kimura G, Uzu T, Nakamura S, et al. High sodium sensitivity and glomerular hypertension/hyperfiltration in primary aldosteronism. Journal of Hypertension 1996; 14(12):1463-8. *Sample size less than 50 patients*

2177. Kinbara T, Hayano T, Ohtani N, et al. Efficacy of N-acetylcysteine and aminophylline in preventing contrast-induced nephropathy. Journal of Cardiology 2010 Mar; 55(2):174-9. *Not CKD treatment*

2178. Kincaid-Smith P, Fairley K, Packham D. Randomized controlled crossover study of the effect on proteinuria and blood pressure of adding an angiotensin II receptor antagonist to an angiotensin converting enzyme inhibitor in normotensive patients with chronic renal disease and proteinuria.[Erratum appears in Nephrol Dial Transplant 2002 Jun;17(6):1153]. Nephrology Dialysis Transplantation 2002; 17(4):597-601. *Follow-up less than 6 months*

2179. Kincaid-Smith P, Fairley KF, Farish S, et al. Reduction of proteinuria by rosiglitazone in non-diabetic renal disease. Nephrology 2008; 13(1):58-62. *Sample size less than 50 patients*

2180. Kincaid-Smith P, Fairley KF, Packham D. Dual blockade of the renin-angiotensin system compared with a 50% increase in the dose of angiotensin-converting enzyme inhibitor: effects on proteinuria and blood pressure. Nephrology Dialysis Transplantation 2004; 19(9):2272-4. *Not CKD treatment*

2181. Kindler J, Schunkert H, Gassmann M, et al. Therapeutic efficacy and tolerance of ramipril in hypertensive patients with renal failure. Journal of Cardiovascular Pharmacology 1989; 13 Suppl 3:S55-8. *Sample size less than 50 patients*

2182. Kini AA, Sharma SK. Managing the high-risk patient: experience with fenoldopam, a selective dopamine receptor agonist, in prevention of radiocontrast nephropathy during percutaneous coronary intervention. Reviews in Cardiovascular Medicine 2001; 2 Suppl 1:S19-25. *Not CKD treatment*

2183. Kinoshita Y, Yahata K, Yoshioka T, et al. Long-term renal preservation after brain death maintained with vasopressin and epinephrine. Transplant International 1990; 3(1):15-8. *Sample size less than 50 patients*

2184. Kinouchi K, Ichihara A, Sakoda M, et al. Safety and benefits of a tablet combining losartan and hydrochlorothiazide in Japanese diabetic patients with hypertension. Hypertension Research - Clinical & Experimental 2009; 32(12):1143-7. *Sample size less than 50 patients*

2185. Kinouchi K, Ichihara A, Sakoda M, et al. Effects of telmisartan on arterial stiffness assessed by the cardio-ankle vascular index in hypertensive patients. Kidney & Blood Pressure Research 2010; 33(4):304-12. *Not CKD treatment*

2186. Kirch W, Stroemer K, Hoogkamer JF, et al. The influence of prostaglandin inhibition by indomethacin on blood pressure and renal function in hypertensive patients treated with cilazapril. British Journal of Clinical Pharmacology 1989; 27 Suppl 2:297S-301S. *Sample size less than 50 patients*

2187. Kirchhoff KT, Hammes BJ, Kehl KA, et al. Effect of a disease-specific planning intervention on surrogate understanding of patient goals for future medical treatment. Journal of the American Geriatrics Society 2010 Jul; 58(7):1233-40. *Not CKD treatment*

2188. Kirsten R, Heintz B, Nelson K, et al. Magnesium pyridoxal 5-phosphate glutamate reduces hyperlipidaemia in patients with chronic renal insufficiency. European Journal of Clinical Pharmacology 1988; 34(2):133-7. *Sample size less than 50 patients*

2189. Kitazato H, Fujita H, Shimotomai T, et al. Effects of chronic intake of vegetable protein added to animal or fish protein on renal hemodynamics. Nephron 2002; 90(1):31-6. *Not early CKD*

2190. Kiya Y, Miura S-I, Fujino M, et al. Clinical and pharmacotherapeutic relevance of the double-chain domain of the angiotensin II type 1 receptor blocker olmesartan. Clinical & Experimental Hypertension 2010 Jan; 32(2):129-36. *Not CKD treatment*

2191. Kjaersgaard P, Jakobsen JA, Nossen JO, et al. Determination of glomerular filtration rate with Visipaque in patients with severely reduced renal function. European Radiology 1996; 6(6):865-71. *Sample size less than 50 patients*

2192. Klag MJ, Whelton PK, Randall BL, et al. End-stage renal disease in African-American and white men. 16-year MRFIT findings. JAMA 1997; 277(16):1293-8. *Not RCT or controlled trial*

2193. Klahr S. Primary and secondary results of the modification of diet in renal disease study. Mineral & Electrolyte Metabolism 1996; 22(1-3):138-42. *Not relevant to key questions*

2194. Klahr S. Prevention of progression of nephropathy. Nephrology Dialysis Transplantation 1997; 12 Suppl 2:63-6. *Not RCT or controlled trial*

2195. Kleber FX. Socioeconomic aspects of ACE inhibition in the secondary prevention in cardiovascular diseases. American Journal of Hypertension 1994; 7(9 Pt 2):112S-6S. *Not CKD treatment*

2196. Klein F, Juhl B, Christiansen JS. Unchanged renal haemodynamics following high dose ascorbic acid administration in normoalbuminuric IDDM patients. Scandinavian Journal of Clinical & Laboratory Investigation 1995; 55(1):53-9. *Follow-up less than 6 months*

2197. Klein H, Abassi Z, Keiser HR. Effects of angiotensin II and phenylephrine on urinary endothelin in normal female volunteers. Metabolism: Clinical & Experimental 1995; 44(1):115-8. *Follow-up less than 6 months*

2198. Klein IHHT, Abrahams A, van Ede T, et al. Different effects of tacrolimus and cyclosporine on renal hemodynamics and blood pressure in healthy subjects. Transplantation 2002; 73(5):732-6. *Not early CKD*

2199. Klein IHHT, Ligtenberg G, Oey PL, et al. Enalapril and losartan reduce sympathetic hyperactivity in patients with chronic renal failure. Journal of the American Society of Nephrology 2003; 14(2):425-30. *Sample size less than 50 patients*

2200. Klein L, Massie BM, Leimberger JD, et al. Admission or changes in renal function during hospitalization for worsening heart failure predict postdischarge survival: results from the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF). Circulation: Heart Failure 2008; 1(1):25-33. *Not RCT or controlled trial*

2201. Klein R. Is intensive management of blood pressure to prevent visual loss in persons with type 2 diabetes indicated? Archives of Ophthalmology 2004; 122(11):1707-9. *Not CKD treatment*

2202. Klein R, Klein BE, Moss SE, et al. Blood pressure and hypertension in diabetes. American Journal of Epidemiology 1985; 122(1):75-89. *Not RCT or controlled trial*

2203. Klein R, Moss SE, Sinaiko AR, et al. The relation of ambulatory blood pressure and pulse rate to retinopathy in type 1 diabetes mellitus: the renin-angiotensin system study. Ophthalmology 2006; 113(12):2231-6. *Not CKD treatment*

2204. Kloke HJ, Huysmans FT, Wetzels JF, et al. Antihypertensive effects of nitrendipine and cilazapril alone, and in combination in hypertensive patients with chronic renal failure. British Journal of Clinical Pharmacology 1989; 27 Suppl 2:289S-96S. *Sample size less than 50 patients*

2205. Kloke HJ, Wetzels JF, van Hamersvelt HW, et al. Effects of nitrendipine and cilazapril on renal hemodynamics and albuminuria in hypertensive patients with chronic renal failure. Journal of Cardiovascular Pharmacology 1990; 16(6):924-30. *Follow-up less than 6 months*

2206. Klotz U, Arvela P, Rosenkranz B. Famotidine, a new H2-receptor antagonist, does not affect hepatic elimination of diazepam or tubular secretion of procainamide. European Journal of Clinical Pharmacology 1985; 28(6):671-5. *Sample size less than 50 patients*

2207. Klow NE, Levorstad K, Berg KJ, et al. Iodixanol in cardioangiography in patients with coronary artery disease. Tolerability, cardiac and renal effects. Acta Radiologica 1993; 34(1):72-7. *Not CKD treatment*

2208. Klutsch K, Grosswendt J, Haecker W. Single dose comparison of torasemide and furosemide in patients with advanced renal failure. Arzneimittel-Forschung 1988; 38(1A):200-4. *Not relevant to key questions*

2209. Knauf H, Bailey MA, Hasenfuss G, et al. The influence of cardiovascular and antiinflammatory drugs on thiazide-induced hemodynamic and saluretic effects. European Journal of Clinical Pharmacology 2006; 62(11):885-92. *Not relevant to key questions*

2210. Knauf H, Mutschler E. Diuretic effectiveness of hydrochlorothiazide and furosemide alone and in combination in chronic renal failure. Journal of Cardiovascular Pharmacology 1995; 26(3):394-400. *Sample size less than 50 patients*

2211. Knauf H, Wenk E, Scholmerich J, et al. Prediction of diuretic mobilization of cirrhotic ascites by pretreatment fractional sodium excretion. Klinische Wochenschrift 1990; 68(11):545-51. *Not CKD treatment*

2212. Knight EL, Glynn RJ, McIntyre KM, et al. Predictors of decreased renal function in patients with heart failure during angiotensin-converting enzyme inhibitor therapy: results from the studies of left ventricular dysfunction (SOLVD). American Heart Journal 1999; 138(5 Pt 1):849-55. *Not CKD treatment*

2213. Knudsen ST, Andersen NH, Poulsen SH, et al. Pulse pressure lowering effect of dual blockade with candesartan and lisinopril vs. high-dose ACE inhibition in hypertensive type 2 diabetic subjects: a CALM II study post-hoc analysis. American Journal of Hypertension 2008; 21(2):172-6. *Not CKD treatment*

2214. Knupp CA, Hak LJ, Coakley DF, et al. Disposition of didanosine in HIV-seropositive patients with normal renal function or chronic renal failure: influence of hemodialysis and continuous ambulatory peritoneal dialysis. Clinical Pharmacology & Therapeutics 1996; 60(5):535-42. *Sample size less than 50 patients*

2215. Ko DT, Juurlink DN, Mamdani MM, et al. Appropriateness of spironolactone prescribing in heart failure patients: a population-based study. Journal of Cardiac Failure 2006; 12(3):205-10. *Not relevant to key questions*

2216. Ko GTC, Tsang C-C, Chan HCK. Stabilization and regression of albuminuria in Chinese patients with type 2 diabetes: a one-year randomized study of valsartan versus enalapril. Advances in Therapy 2005; 22(2):155-62. *Sample size less than 50 patients*

2217. Ko JS, Gwak MS, Choi SJ, et al. The effects of desflurane and propofol-remifentanil on postoperative hepatic and renal functions after right hepatectomy in liver donors. Liver Transplantation 2008; 14(8):1150-8. *Not early CKD*

2218. Ko JS, Gwak MS, Choi SJ, et al. The effects of desflurane and sevoflurane on hepatic and renal functions after right hepatectomy in living donors*. Transplant International 2010 Jul; 23(7):736-44. *Not CKD treatment*

2219. Kobashigawa JA, Meiser BM. Review of major clinical trials with mycophenolate mofetil in cardiac transplantation. Transplantation 2005; 80(2 Suppl):S235-43. *Follow-up less than 6 months*

2220. Kobayashi M, To H, Tokue A, et al. Cisplatin-induced vomiting depends on circadian timing. Chronobiology International 2001; 18(5):851-63. *Not early CKD*

2221. Kobayashi M, Wood PA, Hrushesky WJM. Circadian chemotherapy for gynecological and genitourinary cancers. Chronobiology International 2002; 19(1):237-51. *Not early CKD*

2222. Kobayashi S. Applications of LDL-apheresis in nephrology. Clinical & Experimental Nephrology 2008; 12(1):9-15. *Not relevant to key questions*

2223. Kober A, Dobrovits M, Djavan B, et al. Local active warming: an effective treatment for pain, anxiety and nausea caused by renal colic. Journal of Urology 2003; 170(3):741-4. *Not CKD treatment*

2224. Kobori H, Urushihara M, Xu JH, et al. Urinary angiotensinogen is correlated with blood pressure in men (Bogalusa Heart Study). Journal of Hypertension 2010 Jul; 28(7):1422-8. *Not CKD treatment*

2225. Kocakulak M, Askin G, Kucukaksu S, et al. Pulsatile flow improves renal function in high-risk cardiac operations. Blood Purification 2005; 23(4):263-7. *Not relevant to key questions*

2226. Kocakulak M, Kucukaksu S, Piskin E. Pulsatile roller pump perfusion is safe in high risk patients. International Journal of Artificial Organs 2004; 27(5):433-9. *Not CKD treatment*

2227. Koch G, Fransson L, Karlegard L, et al. Responses of glomerular filtration, renal blood flow and salt-water handling to acute cardioselective and non-selective beta-adrenoceptor blockade in essential hypertension. European Journal of Clinical Pharmacology 1989; 36(4):343-5. *Sample size less than 50 patients*

2228. Koch JA, Plum J, Grabensee B, et al. Prostaglandin E1 (PGE1)--prophylaxis against radiocontrast-induced nephrotoxicity in patients with pre-existing renal dysfunction. PGE1 Study Group. Nephrology Dialysis Transplantation 1999; 14 Suppl 4:15. *Follow-up less than 6 months*

2229. Koch JA, Plum J, Grabensee B, et al. Prostaglandin E1: a new agent for the prevention of renal dysfunction in high risk patients caused by radiocontrast media? PGE1 Study Group. Nephrology Dialysis Transplantation 2000; 15(1):43-9. *Not CKD treatment*

2230. Koch KM, Koene RA, Messinger D, et al. The use of epoetin beta in anemic predialysis patients with chronic renal failure.[Erratum appears in Clin Nephrol 1995 Oct;44(4):278]. Clinical Nephrology 1995; 44(3):201-8. *Not RCT or controlled trial*

2231. Koenig K, Padalino P, Alexandrides G, et al. Bioavailability of potassium and magnesium, and citraturic response from potassium-magnesium citrate. Journal of Urology 1991; 145(2):330-4. *Not CKD treatment*

2232. Kohlmann O, Jr., Roca-Cusachs A, Laurent S, et al. Fixed-dose manidipine/delapril versus losartan/hydrochlorothiazide in hypertensive patients with type 2 diabetes and microalbuminuria. Advances in Therapy 2009; 26(3):313-24. *Not RCT or controlled trial*

2233. Kohzuki M, Yasujima M, Kanazawa M, et al. Effects of recombinant human erythropoietin on blood pressure and renal function in SHR with chronic renal failure. Clinical & Experimental Pharmacology & Physiology - Supplement 1995; 22(1):S165-6. *Not RCT or controlled trial*

2234. Kojima S, Shida M, Yokoyama H. Comparison between cilnidipine and amlodipine besilate with respect to proteinuria in hypertensive patients with renal diseases. Hypertension Research - Clinical & Experimental 2004; 27(6):379-85. *Not early CKD*

2235. Kokubo Y, Nakamura S, Okamura T, et al. Relationship between blood pressure category and incidence of stroke and myocardial infarction in an urban Japanese population with and without chronic kidney disease: the Suita Study. Stroke 2009; 40(8):2674-9. *Not RCT or controlled trial*

2236. Koller-Strametz J, Wolzt M, Fuchs C, et al. Renal hemodynamic effects of L-arginine and sodium nitroprusside in heart transplant recipients. Kidney International 1999; 55(5):1871-7. *Sample size less than 50 patients*

2237. Kolonko A, Wiecek A, Kokot F. The nonselective adenosine antagonist theophylline does prevent renal dysfunction induced by radiographic contrast agents. Journal of Nephrology 1998; 11(3):151-6. *Not CKD treatment*

2238. Komajda M, Genevray B, Grosgogeat Y. Long-term experience with tertatolol in hypertension. American Journal of Nephrology 1986; 6 Suppl 2:106-12. *Not relevant to key questions*

2239. Komajda M, Lutiger B, Madeira H, et al. Tolerability of carvedilol and ACE-Inhibition in mild heart failure. Results of CARMEN (Carvedilol ACE-Inhibitor Remodelling Mild CHF EvaluatioN). European Journal of Heart Failure 2004; 6(4):467-75. *Not adult population*

2240. Komajda M, Wimart MC. Angiotensin converting enzyme inhibition: from viper to patient. Heart 2000; 84 Suppl 1:i11-4:discussion i50. *Not CKD treatment*

2241. Komenda P, Zalunardo N, Burnett S, et al. Conservative outpatient renoprotective protocol in patients with low GFR undergoing contrast angiography: a case series. Clinical & Experimental Nephrology 2007; 11(3):209-13. *Not relevant to key questions*

2242. Komers R, Komersova K, Kazdova L, et al. Effect of ACE inhibition and angiotensin AT1 receptor blockade on renal and blood pressure response to L-arginine in humans. Journal of Hypertension 2000; 18(1):51-9. *Sample size less than 50 patients*

2243. Komers R, Simkova R, Kazdova L, et al. Effects of ACE inhibition and AT1-receptor blockade on haemodynamic responses to L-arginine in Type 1 diabetes. Journal of the Renin-Angiotensin-Aldosterone System 2004; 5(1):33-8. *Not relevant to key questions*

2244. Komisarof JA, Gilkey GM, Peters DM, et al. N-acetylcysteine for patients with prolonged hypotension as prophylaxis for acute renal failure (NEPHRON). Critical Care Medicine 2007; 35(2):435-41. *Not CKD treatment*

2245. Kong KL, Tyler JE, Willatts SM, et al. Isoflurane sedation for patients undergoing mechanical ventilation: metabolism to inorganic fluoride and renal effects. British Journal of Anaesthesia 1990; 64(2):159-62. *Not CKD treatment*

2246. Konishi K, Nakano S, Tsuda S-i, et al. AST-120 (Kremezin) initiated in early stage chronic kidney disease stunts the progression of renal dysfunction in type 2 diabetic subjects. Diabetes Research & Clinical Practice 2008; 81(3):310-5. *Not CKD treatment*

2247. Kontessis P, Jones S, Dodds R, et al. Renal, metabolic and hormonal responses to ingestion of animal and vegetable proteins. Kidney International 1990; 38(1):136-44. *Sample size less than 50 patients*

2248. Kontessis PA, Bossinakou I, Sarika L, et al. Renal, metabolic, and hormonal responses to proteins of different origin in normotensive, nonproteinuric type I diabetic patients. Diabetes Care 1995; 18(9):1233. *Follow-up less than 6 months*

2249. Kontessis PS, Jones SL, Barrow SE, et al. Effect of selective inhibition of thromboxane synthesis on renal function in diabetic nephropathy. Journal of Laboratory & Clinical Medicine 1993; 121(3):415-23. *Sample size less than 50 patients*

2250. Kooienga L, Fried L, Scragg R, et al. The effect of combined calcium and vitamin D3 supplementation on serum intact parathyroid hormone in moderate CKD. American Journal of Kidney Diseases 2009; 53(3):408-16. *Not CKD treatment*

2251. Kooman JP, Daemen MJ, Wijnen R, et al. Morphological changes of the venous system in uremic patients. A histopathologic study. Nephron 1995; 69(4):454-8. *Sample size less than 50 patients*

2252. Koopmans PP, Thien T, Thomas CM, et al. The effects of sulindac and indomethacin on the anti-hypertensive and diuretic action of hydrochlorothiazide in patients with mild to moderate essential hypertension. British Journal of Clinical Pharmacology 1986; 21(4):417-23. *Sample size less than 50 patients*

2253. Kopf D, Schmitz H, Beyer J, et al. A double-blind trial of perindopril and nitrendipine in incipient diabetic nephropathy. Diabetes, Nutrition & Metabolism - Clinical & Experimental 2001; 14(5):245-52. *Sample size less than 50 patients*

2254. Koppert W, Frotsch K, Huzurudin N, et al. The effects of paracetamol and parecoxib on kidney function in elderly patients undergoing orthopedic surgery. Anesthesia & Analgesia 2006; 103(5):1170-6. *Not early CKD*

2255. Kopple JD, Berg R, Houser H, et al. Nutritional status of patients with different levels of chronic renal insufficiency. Modification of Diet in Renal Disease (MDRD) Study Group. Kidney International - Supplement 1989; 27:S184-94. *Not relevant to key questions*

2256. Kopple JD, Greene T, Chumlea WC, et al. Relationship between nutritional status and the glomerular filtration rate: results from the MDRD study. Kidney International 2000; 57(4):1688-703. *Not early CKD*

2257. Kopple JD, Kalantar-Zadeh K, Mehrotra R. Risks of chronic metabolic acidosis in patients with chronic kidney disease. Kidney International - Supplement 2005; (95):S21-7. *Not relevant to key questions*

2258. Koretz RL. Does nutritional intervention in protein-energy malnutrition improve morbidity or mortality? Journal of Renal Nutrition 1999; 9(3):119-21. *Not RCT or controlled trial*

2259. Korkor AB, Bretzmann C. Effect of fish oil on vitamin D absorption. American Journal of Kidney Diseases 2009; 53(2):356. *Not CKD treatment*

2260. Kossmann S, Magner-Krezel Z, Sobieraj R, et al. The assessment of nephrotoxic effect of organophosphorous pesticides based on the determination of the activity of some selected enzymes in urine. Przeglad Lekarski 1997; 54(10):707-11. *Not RCT or controlled trial*

2261. Kostapanos MS, Milionis HJ, Saougos VG, et al. Dose-dependent effect of rosuvastatin treatment on urinary protein excretion. Journal of Cardiovascular Pharmacology & Therapeutics 2007; 12(4):292-7. *Not CKD treatment*

2262. Kotlyar E, Keogh AM, Thavapalachandran S, et al. Prehydration alone is sufficient to prevent contrast-induced nephropathy after day-only angiography procedures--a randomised controlled trial. Heart, Lung & Circulation 2005; 14(4):245-51. *Not relevant to key questions*

2263. Koufaki P, Mercer TH, Naish PF. Effects of exercise training on aerobic and functional capacity of end-stage renal disease patients. Clinical Physiology & Functional Imaging 2002; 22(2):115-24. *Not early CKD*

2264. Kovesdy CP, Kalantar-Zadeh K. Why is protein-energy wasting associated with mortality in chronic kidney disease? Seminars in Nephrology 2009; 29(1):3-14. *Not CKD treatment*

2265. Kowey PR, Dickson TZ, Zhang Z, et al. Losartan and end-organ protection--lessons from the RENAAL study. Clinical Cardiology 2005; 28(3):136-42. *Not relevant to key questions*

2266. Krairittichai U, Chaisuvannarat V. Effects of dual blockade of renin-angiotensin system in type 2 diabetes mellitus patients with diabetic nephropathy. Journal of the Medical Association of Thailand 2009; 92(5):611-7. *Follow-up less than 6 months*

2267. Kramer BK, Preuner J, Ebenburger A, et al. Lack of renoprotective effect of theophylline during aortocoronary bypass surgery. Nephrology Dialysis Transplantation 2002; 17(5):910-5. *Not early CKD*

2268. Kramer H. The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) Grant Initiative: moving clinical practice forward. American Journal of Kidney Diseases 2010 Mar; 55(3):411-4. *Not RCT or controlled trial*

2269. Kramer HJ, Uhl W, Ladstetter B, et al. Influence of asimadoline, a new kappa-opioid receptor agonist, on tubular water absorption and vasopressin secretion in man. British Journal of Clinical Pharmacology 2000; 50(3):227-35. *Not early CKD*

2270. Krantz SB. Review of patients' responses to epoetin alfa therapy. Pharmacotherapy 1990; 10(2 (Pt 2)):15S-21S. *Not relevant to key questions*

2271. Krasuski RA, Beard BM, Geoghagan JD, et al. Optimal timing of hydration to erase contrast-associated nephropathy: the OTHER CAN study. Journal of Invasive Cardiology 2003; 15(12):699-702. *Not CKD treatment*

2272. Krekels MM, Spiering W, Schaper NC, et al. Dissociation between the renal effects of angiotensin I and II in sodium-restricted normal subjects. Cardiovascular Research 1998; 38(1):215-20. *Sample size less than 50 patients*

2273. Krempf M, Ranganathan S, Remy JP, et al. Effect of long-acting somatostatin analog (SMS 201-995) on high glomerular filtration rate in insulin dependent diabetic patients. International Journal of Clinical Pharmacology, Therapy, & Toxicology 1990; 28(7):309-11. *Sample size less than 50 patients*

2274. Krespi PG, Makris TK, Hatzizacharias AN, et al. Moxonidine effect on microalbuminuria, thrombomodulin, and plasminogen activator inhibitor-1 levels in patients with essential hypertension. Cardiovascular Drugs & Therapy 1998; 12(5):463-7. *Not RCT or controlled trial*

2275. Kresyn VI, Aryaev VL, Kostev FI. Litonit: evaluation of clinical effectiveness. Alcohol & Alcoholism 1993; 28(3):333-7. *Not RCT or controlled trial*

2276. Kreutz R, Kruse HJ, Overlack A, et al. Effects of sympathetic inhibition on blood pressure and renal responses to central hypervolaemia in normal humans. Acta Physiologica Scandinavica 1996; 156(1):1-7. *Sample size less than 50 patients*

2277. Krijnen P, van Jaarsveld BC, Man in ‘t Veld AJ, et al. Reproducibility and validity of quality of life measurements in hypertensive patients on stable medication. Netherlands Journal of Medicine 1997; 50(4):137-52. *Not RCT or controlled trial*

2278. Krikken JA, Gansevoort RT, Dullaart RPF, et al. Lower HDL-C and apolipoprotein A-I are related to higher glomerular filtration rate in subjects without kidney disease. Journal of Lipid Research 2010 Jul; 51(7):1982-90. *Not early CKD*

2279. Krikken JA, Waanders F, Dallinga-Thie GM, et al. Antiproteinuric therapy decreases LDL-cholesterol as well as HDL-cholesterol in non-diabetic proteinuric patients: relationships with cholesteryl ester transfer protein mass and adiponectin. Expert Opinion on Therapeutic Targets 2009; 13(5):497-504. *Not CKD treatment*

2280. Krimholtz MJ, Karalliedde J, Thomas S, et al. Targeting albumin excretion rate in the treatment of the hypertensive diabetic patient with renal disease. Journal of the American Society of Nephrology 2005; 16 Suppl 1:S42-7. *Not relevant to key questions*

2281. Krishna GG, Kapoor SC. Preservation of renal reserve in chronic renal disease. American Journal of Kidney Diseases 1991; 17(1):18-24. *Sample size less than 50 patients*

2282. Krishna GG, Newell G, Miller E, et al. Protein-induced glomerular hyperfiltration: role of hormonal factors. Kidney International 1988; 33(2):578-83. *Sample size less than 50 patients*

2283. Kristjansson A, Mansson W. Renal function in the setting of urinary diversion. World Journal of Urology 2004; 22(3):172-7. *Not relevant to key questions*

2284. Kristjansson A, Wallin L, Mansson W. Renal function up to 16 years after conduit (refluxing or anti-reflux anastomosis) or continent urinary diversion. 1. Glomerular filtration rate and patency of uretero-intestinal anastomosis.[Erratum appears in Br Urol 1995 Dec;76(6):815]. British Journal of Urology 1995; 76(5):539-45. *Not CKD treatment*

2285. Kron BG, Sjostrom PA, Karlberg BE, et al. Acute tolerance to furosemide. Pretreatment with captopril or prazosin does not influence diuresis and natriuresis. Scandinavian Journal of Urology & Nephrology 1994; 28(4):337-44. *Not CKD treatment*

2286. Kronenberg F, Kuen E, Ritz E, et al. Lipoprotein(a) serum concentrations and apolipoprotein(a) phenotypes in mild and moderate renal failure. Journal of the American Society of Nephrology 2000; 11(1):105-15. *Not RCT or controlled trial*

2287. Kruger W, Sobottka I, Stockschlader M, et al. Fatal outcome of disseminated candidosis after allogeneic bone marrow transplantation under treatment with liposomal and conventional amphotericin-B. A report of 4 cases with determination of the Mic values. Scandinavian Journal of Infectious Diseases 1996; 28(3):313-6. *Not CKD treatment*

2288. Krum H, Aw T-J, Liew D, et al. Blood pressure effects of COX-2 inhibitors. Journal of Cardiovascular Pharmacology 2006; 47 Suppl 1:S43-8. *Not RCT or controlled trial*

2289. Krum H, Schlaich M, Whitbourn R, et al. Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study. Lancet 2009; 373(9671):1275-81. *Not RCT or controlled trial*

2290. Krusell LR, Christensen CK, Pedersen OL. Alpha-adrenoceptor blockade in patients with mild to moderate hypertension: long-term renal effects of doxazosin. Journal of Cardiovascular Pharmacology 1992; 20(3):440-4. *Sample size less than 50 patients*

2291. Kshirsagar AV, Joy MS, Hogan SL, et al. Effect of ACE inhibitors in diabetic and nondiabetic chronic renal disease: a systematic overview of randomized placebo-controlled trials. American Journal of Kidney Diseases 2000; 35(4):695-707. *Not relevant to key questions*

2292. Kshirsagar AV, Poole C, Mottl A, et al. N-acetylcysteine for the prevention of radiocontrast induced nephropathy: a meta-analysis of prospective controlled trials. Journal of the American Society of Nephrology 2004; 15(3):761-9. *Sample size less than 50 patients*

2293. Kshirsagar AV, Shoham DA, Bang H, et al. The effect of cholesterol reduction with cholestyramine on renal function. American Journal of Kidney Diseases 2005; 46(5):812-9. *Not RCT or controlled trial*

2294. Kuan Y, Surman J, Frystyk J, et al. Lack of effect of IGF-I on the glomerular filtration rate in non-diabetic patients with advanced chronic kidney disease. Growth Hormone & Igf Research 2009; 19(3):219-25. *Not CKD treatment*

2295. Kuduvalli M, Grayson AD, Au J, et al. A multi-centre additive and logistic risk model for in-hospital mortality following aortic valve replacement. European Journal of Cardio-Thoracic Surgery 2007; 31(4):607-13. *Not RCT or controlled trial*

2296. Kulik A, Ruel M. Statins and coronary artery bypass graft surgery: preoperative and postoperative efficacy and safety. Expert Opinion on Drug Safety 2009; 8(5):559-71. *Not RCT or controlled trial*

2297. Kulka PJ, Tryba M, Zenz M. Preoperative alpha2-adrenergic receptor agonists prevent the deterioration of renal function after cardiac surgery: results of a randomized, controlled trial. Critical Care Medicine 1996; 24(6):947-52. *Sample size less than 50 patients*

2298. Kult J, Hacker W, Glocke M. Comparison of efficacy and tolerance of different oral doses of torasemide and furosemide in patients with advanced chronic renal failure. Arzneimittel-Forschung 1988; 38(1A):212-4. *Follow-up less than 6 months*

2299. Kumar A. Influence of radish consumption on urinary calcium oxalate excretion. Nepal Medical College Journal: NMCJ 2004; 6(1):41-4. *Not relevant to key questions*

2300. Kumar NS, Singh AK, Mishra RN, et al. Comparative study of angiotensin converting enzyme inhibitor and calcium channel blocker in the treatment of steroid-resistant idiopathic nephrotic syndrome. Journal of the Association of Physicians of India 2004; 52:454-8. *Not early CKD*

2301. Kumar R, Kapoor R, Mandhani A, et al. Optimum duration of splinting after endopyelotomy. Journal of Endourology 1999; 13(2):89-92. *Not CKD treatment*

2302. Kumar S, Masood N, Shaikh AJ. Old disease, new targets--part-I, solid malignancies. JPMA - Journal of the Pakistan Medical Association 2009 Jun; 59(6):398-405. *Not early CKD*

2303. Kunz R, Friedrich C, Wolbers M, et al. Meta-analysis: effect of monotherapy and combination therapy with inhibitors of the renin angiotensin system on proteinuria in renal disease. Annals of Internal Medicine 2008; 148(1):30-48. *Not RCT or controlled trial*

2304. Kunz R, Wolbers M, Glass T, et al. The COOPERATE trial: a letter of concern. Lancet 2008; 371(9624):1575-6. *Not CKD treatment*

2305. Kuriyama S, Tomonari H, Tokudome G, et al. Antiproteinuric effects of combined antihypertensive therapies in patients with overt type 2 diabetic nephropathy. Hypertension Research - Clinical & Experimental 2002; 25(6):849-55. *Sample size less than 50 patients*

2306. Kuriyama S, Tomonari H, Yoshida H, et al. Reversal of anemia by erythropoietin therapy retards the progression of chronic renal failure, especially in nondiabetic patients. Nephron 1997; 77(2):176-85. *Not early CKD*

2307. Kurman MR. Recent clinical trials with levamisole. Annals of the New York Academy of Sciences 1993; 685:269-77. *Not RCT or controlled trial*

2308. Kurnik BR, Allgren RL, Genter FC, et al. Prospective study of atrial natriuretic peptide for the prevention of radiocontrast-induced nephropathy. American Journal of Kidney Diseases 1998; 31(4):674-80. *Not CKD treatment*

2309. Kurnik BR, Weisberg LS, Askenase AD, et al. Mannitol stimulates atrial natriuretic peptide release in humans. American Journal of Kidney Diseases 1991; 17(1):62-8. *Sample size less than 50 patients*

2310. Kurokawa K, Chan JCN, Cooper ME, et al. Renin angiotensin aldosterone system blockade and renal disease in patients with type 2 diabetes: a subanalysis of Japanese patients from the RENAAL study. Clinical & Experimental Nephrology 2006; 10(3):193-200. *Sample size less than 50 patients*

2311. Kurth T, de Jong PE, Cook NR, et al. Kidney function and risk of cardiovascular disease and mortality in women: a prospective cohort study.[Erratum appears in BMJ. 2009;339:b2769]. BMJ 2009; 338:b2392. *Not RCT or controlled trial*

2312. Kurth T, de Jong PE, Cook NR, et al. Kidney function and risk of cardiovascular disease and mortality in women: a prospective cohort study.[Erratum appears in BMJ. 2009;339:b2769]. BMJ 2009; 338:b2392. *Not RCT or controlled trial*

2313. Kusek JW, Coyne T, de Velasco A, et al. Recruitment experience in the full-scale phase of the Modification of Diet in Renal Disease Study. Controlled Clinical Trials 1993; 14(6):538-57. *Not relevant to key questions*

2314. Kusek JW, Hirschman GH, Agodoa L, et al. Nephrology clinical trials supported by the kidney programs of the National Institutes of Health. Clinical Nephrology 1992; 38 Suppl 1:S61-3. *Not CKD treatment*

2315. Kusek JW, Lee JY, Charleston J, et al. Participant satisfaction in the African American Study of Kidney Disease and Hypertension (AASK) Pilot Study. Controlled Clinical Trials 1996; 17(4 Suppl):47S-54S. *Not RCT or controlled trial*

2316. Kusek JW, Lee JY, Smith DE, et al. Effect of blood pressure control and antihypertensive drug regimen on quality of life: the African American Study of Kidney Disease and Hypertension (AASK) Pilot Study. Controlled Clinical Trials 1996; 17(4 Suppl):40S-6S. *Not relevant to key questions*

2317. Kutner N. Quality of life assessment in a recent haemoglobin trial in CKD (CHOIR). Nephrology Dialysis Transplantation 2007; 22(7):2099. *Not CKD treatment*

2318. Kutner NG, Johansen KL, Kaysen GA, et al. The comprehensive dialysis study (CDS): a USRDS special study. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(3):645-50. *Not early CKD*

2319. Kvetny J, Gregersen G, Pedersen RS. Randomized placebo-controlled trial of perindopril in normotensive, normoalbuminuric patients with type 1 diabetes mellitus. Qjm 2001; 94(2):89-94. *Not early CKD*

2320. Kwong Y-TD, Stevens LA, Selvin E, et al. Imprecision of urinary iothalamate clearance as a gold-standard measure of GFR decreases the diagnostic accuracy of kidney function estimating equations. American Journal of Kidney Diseases 2010 Jul; 56(1):39-49. *Not CKD treatment*

2321. Kyle RA, Gertz MA, Greipp PR, et al. A trial of three regimens for primary amyloidosis: colchicine alone, melphalan and prednisone, and melphalan, prednisone, and colchicine. New England Journal of Medicine 1997; 336(17):1202-7. *Not CKD treatment*

2322. La Villa G, Barletta G, Pantaleo P, et al. Hemodynamic, renal, and endocrine effects of acute inhibition of nitric oxide synthase in compensated cirrhosis. Hepatology 2001; 34(1):19-27. *Not early CKD*

2323. La Villa G, Fronzaroli C, Lazzeri C, et al. Cardiovascular and renal effects of low dose brain natriuretic peptide infusion in man. Journal of Clinical Endocrinology & Metabolism 1994; 78(5):1166-71. *Not CKD treatment*

2324. La Villa G, Lazzeri C, Pascale A, et al. Cardiovascular and renal effects of low-dose atrial natriuretic peptide in compensated cirrhosis. American Journal of Gastroenterology 1997; 92(5):852-7. *Not CKD treatment*

2325. La Villa G, Marra F, Laffi G, et al. Effects of rhein on renal arachidonic acid metabolism and renal function in patients with congestive heart failure. European Journal of Clinical Pharmacology 1989; 37(1):1-5. *Sample size less than 50 patients*

2326. La Villa G, Stefani L, Lazzeri C, et al. Acute effects of physiological increments of brain natriuretic peptide in humans. Hypertension 1995; 26(4):628-33. *Sample size less than 50 patients*

2327. Labrecque M, Dostaler LP, Rousselle R, et al. Efficacy of nonsteroidal anti-inflammatory drugs in the treatment of acute renal colic. A meta-analysis. Archives of Internal Medicine 1994; 154(12):1381-7. *Not RCT or controlled trial*

2328. Lacourciere Y, Nadeau A, Poirier L, et al. Comparative effects of converting enzyme inhibition and conventional therapy in hypertensive non-insulin dependent diabetics with normal renal function. Clinical & Investigative Medicine - Medecine Clinique et Experimentale 1991; 14(6):652-60. *Not early CKD*

2329. Laczy B, Cseh J, Mohas M, et al. Effects of pentoxifylline and pentosan polysulphate combination therapy on diabetic neuropathy in type 2 diabetes mellitus. Acta Diabetologica 2009; 46(2):105-11. *Not CKD treatment*

2330. Laerum E, Ommundsen OE, Gronseth JE, et al. Intramuscular diclofenac versus intravenous indomethacin in the treatment of acute renal colic. European Urology 1996; 30(3):358-62. *Not CKD treatment*

2331. Laffi G, Marra F, Carloni V, et al. Thromboxane-receptor blockade increases water diuresis in cirrhotic patients with ascites. Gastroenterology 1992; 103(3):1017-21. *Not CKD treatment*

2332. Lainchbury JG, Richards AM, Nicholls MG, et al. The effects of pathophysiological increments in brain natriuretic peptide in left ventricular systolic dysfunction. Hypertension 1997; 30(3 Pt 1):398-404. *Follow-up less than 6 months*

2333. Lainchbury JG, Troughton RW, Lewis LK, et al. Hemodynamic, hormonal, and renal effects of short-term adrenomedullin infusion in healthy volunteers. Journal of Clinical Endocrinology & Metabolism 2000; 85(3):1016-20. *Not early CKD*

2334. Laine L, White WB, Rostom A, et al. COX-2 selective inhibitors in the treatment of osteoarthritis. Seminars in Arthritis & Rheumatism 2008; 38(3):165-87. *Not CKD treatment*

2335. Laing C, Unwin RJ. Are calcium antagonists effective in preventing complications of hypertension and progression of renal disease? Current Opinion in Nephrology & Hypertension 2000; 9(5):489-95. *Not relevant to key questions*

2336. Laisalmi M, Teppo AM, Koivusalo AM, et al. The effect of ketorolac and sevoflurane anesthesia on renal glomerular and tubular function. Anesthesia & Analgesia 2001; 93(5):1210-3. *Not early CKD*

2337. Laisalmi-Kokki M, Pesonen E, Kokki H, et al. Potentially detrimental effects of N-acetylcysteine on renal function in knee arthroplasty. Free Radical Research 2009; 43(7):691-6. *Not CKD treatment*

2338. Lajer H, Daugaard G. Cisplatin and hypomagnesemia. Cancer Treatment Reviews 1999; 25(1):47-58. *Not CKD treatment*

2339. Lalezari JP, Drew WL, Glutzer E, et al. (S)-1-[3-hydroxy-2-(phosphonylmethoxy)propyl]cytosine (cidofovir): results of a phase I/II study of a novel antiviral nucleotide analogue. Journal of Infectious Diseases 1995; 171(4):788-96. *Sample size less than 50 patients*

2340. Lalezari JP, Holland GN, Kramer F, et al. Randomized, controlled study of the safety and efficacy of intravenous cidofovir for the treatment of relapsing cytomegalovirus retinitis in patients with AIDS. Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology 1998; 17(4):339-44. *Not CKD treatment*

2341. Laliberte M-C, Normandeau M, Lord A, et al. Use of over-the-counter medications and natural products in patients with moderate and severe chronic renal insufficiency. American Journal of Kidney Diseases 2007; 49(2):245-56. *Not RCT or controlled trial*

2342. Lalonde L, Normandeau M, Lamarre D, et al. Evaluation of a training and communication-network nephrology program for community pharmacists. Pharmacy World & Science 2008; 30(6):924-33. *Not CKD treatment*

2343. Lam KS, Cheng IK, Janus ED, et al. Cholesterol-lowering therapy may retard the progression of diabetic nephropathy. Diabetologia 1995; 38(5):604-9. *Sample size less than 50 patients*

2344. Lam YW, Boyd RA, Chin SK, et al. Effect of probenecid on the pharmacokinetics and pharmacodynamics of procainamide. Journal of Clinical Pharmacology 1991; 31(5):429-32. *Not CKD treatment*

2345. Lamb EJ, Fluck RJ, Venton TR, et al. Effects of parathyroid hormone and 1,25(OH2)D3 on protein glycation in moderate uraemia. Nephron 1996; 74(2):295-300. *Not RCT or controlled trial*

2346. Lambers Heerspink HJ, Agarwal R, Coyne DW, et al. The selective vitamin D receptor activator for albuminuria lowering (VITAL) study: study design and baseline characteristics. American Journal of Nephrology 2009; 30(3):280-6. *Not early CKD*

2347. Lambers Heerspink HJ, Fowler MJ, Volgi J, et al. Rationale for and study design of the sulodexide trials in Type 2 diabetic, hypertensive patients with microalbuminuria or overt nephropathy. Diabetic Medicine 2007; 24(11):1290-5. *Not RCT or controlled trial*

2348. Lambert KE. Recombinant human erythropoietin. Canadian Nurse 1990; 86(10):27-8. *Not early CKD*

2349. Lameire N. Contrast-induced nephropathy in the critically-ill patient: focus on emergency screening and prevention. Acta Clinica Belgica - Supplementum 2007; (2):346-52. *Not CKD treatment*

2350. Landersdorfer CB, Kirkpatrick CMJ, Kinzig M, et al. Competitive inhibition of renal tubular secretion of gemifloxacin by probenecid. Antimicrobial Agents & Chemotherapy 2009; 53(9):3902-7. *Sample size less than 50 patients*

2351. Landersdorfer CB, Kirkpatrick CMJ, Kinzig M, et al. Inhibition of flucloxacillin tubular renal secretion by piperacillin. British Journal of Clinical Pharmacology 2008; 66(5):648-59. *Not RCT or controlled trial*

2352. Landmann R, Keilholz U, Scheibenbogen C, et al. Relationship between soluble tumor necrosis factor (TNF) receptors and TNF alpha during immunotherapy with interleukin-2 and/or interferon alpha. Cancer Immunology, Immunotherapy 1994; 38(2):113-8. *Not CKD treatment*

2353. Landoni G, Bignami E, Gonfalini M, et al. Fenoldopam in cardiac surgery-associated acute kidney injury. International Journal of Artificial Organs 2008; 31(6):561. *Not CKD treatment*

2354. Landoni G, Biondi-Zoccai GGL, Tumlin JA, et al. Beneficial impact of fenoldopam in critically ill patients with or at risk for acute renal failure: a meta-analysis of randomized clinical trials. American Journal of Kidney Diseases 2007; 49(1):56-68. *Not RCT or controlled trial*

2355. Landray M, Baigent C, Leaper C, et al. The second United Kingdom Heart and Renal Protection (UK-HARP-II) Study: a randomized controlled study of the biochemical safety and efficacy of adding ezetimibe to simvastatin as initial therapy among patients with CKD. American Journal of Kidney Diseases 2006; 47(3):385-95. *Not RCT or controlled trial*

2356. Lane C, Brown M, Dunsmuir W, et al. Can spot urine protein/creatinine ratio replace 24 h urine protein in usual clinical nephrology? Nephrology 2006; 11(3):245-9. *Follow-up less than 6 months*

2357. Lang CC, Choy AM, Balfour DJ, et al. Prazosin attenuates the natriuretic response to atrial natriuretic factor in man. Kidney International 1992; 42(2):433-41. *Sample size less than 50 patients*

2358. Lang CC, Choy AM, Rahman AR, et al. Renal effects of low dose prazosin in patients with congestive heart failure. European Heart Journal 1993; 14(9):1245-52. *Not CKD treatment*

2359. Lang CC, Rahman AR, Balfour DJ, et al. Effect of noradrenaline on renal sodium and water handling in euhydrated and overhydrated man. Clinical Science 1993; 85(4):487-94. *Not RCT or controlled trial*

2360. Lang CC, Rahman AR, Balfour DJ, et al. Enalapril blunts the antinatriuretic effect of circulating noradrenaline in man. Journal of Hypertension 1993; 11(5):565-71. *Sample size less than 50 patients*

2361. Lang CC, Rahman AR, Choy AM, et al. Renal interactions between the renin-angiotensin system and the sympathetic nervous system in man. Journal of Hypertension - Supplement 1991; 9(6):S206-7. *Sample size less than 50 patients*

2362. Lang SM, Schiffl H. Losartan and anaemia of end-stage renal disease. Lancet 1998; 352(9141):1708. *Not early CKD*

2363. Langer M, Junge W, Keysser R, et al. Renal and hepatic tolerance of nonionic and ionic contrast media in intravenous digital subtraction angiography. Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin - Erganzungsband 1989; 128:95-100. *Not CKD treatment*

2364. Langer M, Langer R, Felix R, et al. Analysis of renal and hepatic impairment by ionic and nonionic contrast media. Investigative Radiology 1990; 25 Suppl 1:S125-6. *Follow-up less than 6 months*

2365. Langer M, Langer R, Zwicker C, et al. Clinical and nephrologic tolerance of iopromide and iotrolan in computed tomography. Investigative Radiology 1991; 26 Suppl 1:S83-5; discussion S8-91. *Sample size less than 50 patients*

2366. Langston RD, Presley R, Flanders WD, et al. Renal insufficiency and anemia are independent risk factors for death among patients with acute myocardial infarction. Kidney International 2003; 64(4):1398-405. *Not CKD treatment*

2367. Langtry HD, Gillis JC, Davis R. Topiramate. A review of its pharmacodynamic and pharmacokinetic properties and clinical efficacy in the management of epilepsy. Drugs 1997; 54(5):752-73. *Not CKD treatment*

2368. Larkin JMG, Kaye SB. Potential clinical applications of epothilones: a review of phase II studies. Annals of Oncology 2007; 18 Suppl 5:v28-34. *Sample size less than 50 patients*

2369. Larochelle P, Cusson JR, du Souich P, et al. Renal effects of a nonhypotensive i.v. dose of felodipine. Journal of Clinical Pharmacology 1993; 33(8):732-7. *Sample size less than 50 patients*

2370. Larsen M, Hommel E, Parving HH, et al. Protective effect of captopril on the blood-retina barrier in normotensive insulin-dependent diabetic patients with nephropathy and background retinopathy. Graefes Archive for Clinical & Experimental Ophthalmology 1990; 228(6):505-9. *Sample size less than 50 patients*

2371. Lasaridis AN, Sarafidis PA. Diabetic nephropathy and antihypertensive treatment: what are the lessons from clinical trials? American Journal of Hypertension 2003; 16(8):689-97. *Not RCT or controlled trial*

2372. Lash JP, Wang X, Greene T, et al. Quality of life in the African American Study of Kidney Disease and Hypertension: effects of blood pressure management. American Journal of Kidney Diseases 2006; 47(6):956-64. *Not CKD treatment*

2373. Lassnigg A, Donner E, Grubhofer G, et al. Lack of renoprotective effects of dopamine and furosemide during cardiac surgery. Journal of the American Society of Nephrology 2000; 11(1):97-104. *Not CKD treatment*

2374. Lastra-Gonzalez G, Manrique CM, Govindarajan G, et al. Insights into the emerging cardiometabolic prevention and management of diabetes mellitus. Expert Opinion on Pharmacotherapy 2005; 6(13):2209-21. *Not RCT or controlled trial*

2375. Laszlo J, Goldstein D, Vugrin D, et al. Does maintenance therapy with alpha interferon stabilize cancer growth? A pilot study. Journal of Biological Response Modifiers 1986; 5(4):294-9. *Sample size less than 50 patients*

2376. Latinwo LM, Ikediobi CO, Singh NP, et al. Comparative studies of in vivo genotoxic effects of cadmium chloride in rat brain, kidney and liver cells. Cellular & Molecular Biology 1997; 43(2):203-10. *Not human studies*

2377. Lau HS, Hyneck ML, Berardi RR, et al. Kinetics, dynamics, and bioavailability of bumetanide in healthy subjects and patients with chronic renal failure. Clinical Pharmacology & Therapeutics 1986; 39(6):635-45. *Sample size less than 50 patients*

2378. Lau LL, Halliday MI, Smye MG, et al. Extraperitoneal approach reduces intestinal and renal dysfunction in elective abdominal aortic aneurysm repair. International Angiology 2001; 20(4):282-7. *Not early CKD*

2379. Laufs U, Custodis F, Bohm M. Who does not need a statin: too late in end-stage renal disease or heart failure? Heart 2008; 94(9):1138-40. *Not CKD treatment*

2380. Laufs U, Custodis F, Bohm M. Who does not need a statin: too late in end-stage renal disease or heart failure? Postgraduate Medical Journal 2009; 85(1002):187-9. *Not RCT or controlled trial*

2381. Laurent S. Evidence for benefits of perindopril in hypertension and its complications. American Journal of Hypertension 2005; 18(9 Pt 2):155S-62S. *Sample size less than 50 patients*

2382. Lauridsen TG, Vase H, Bech JN, et al. Direct effect of methylprednisolone on renal sodium and water transport via the principal cells in the kidney. European Journal of Endocrinology 2010 May; 162(5):961-9. *Not early CKD*

2383. Lauridsen TG, Vase H, Starklint J, et al. Protein-enriched diet increases water absorption via the aquaporin-2 water channels in healthy humans. Nephrology Dialysis Transplantation 2010 Aug; 25(8):2502-10. *Not early CKD*

2384. Lauschke A, Teichgraber UKM, Frei U, et al. 'Low-dose' dopamine worsens renal perfusion in patients with acute renal failure. Kidney International 2006; 69(9):1669-74. *Sample size less than 50 patients*

2385. Laverman GD, Navis G, Henning RH, et al. Dual renin-angiotensin system blockade at optimal doses for proteinuria. Kidney International 2002; 62(3):1020-5. *Sample size less than 50 patients*

2386. Laviades C, Varo N, Diez J. Transforming growth factor beta in hypertensives with cardiorenal damage. Hypertension 2000; 36(4):517-22. *Sample size less than 50 patients*

2387. Laville M, Anaemia CiDt. New strategies in anaemia management: ACORD (Anaemia CORrection in Diabetes) trial. Acta Diabetologica 2004; 41 Suppl 1:S18-22. *Not CKD treatment*

2388. Lavrijssen AT, Kroon AA, Fuss-Lejeune M, et al. Renal haemodynamics and sodium excretory capacity during urapidil treatment in patients with essential hypertension. Journal of Hypertension 2000; 18(7):963-9. *Sample size less than 50 patients*

2389. Lawendy N, Krishnaswami S, Wang R, et al. Effect of CP-690,550, an orally active janus kinase inhibitor, on renal function in healthy adult volunteers. Journal of Clinical Pharmacology 2009; 49(4):423-9. *Not early CKD*

2390. Lawlor DK, Moist L, DeRose G, et al. Prevention of contrast-induced nephropathy in vascular surgery patients. Annals of Vascular Surgery 2007; 21(5):593-7. *Follow-up less than 6 months*

2391. Lazarus JM, Bourgoignie JJ, Buckalew VM, et al. Achievement and safety of a low blood pressure goal in chronic renal disease. The Modification of Diet in Renal Disease Study Group. Hypertension 1997; 29(2):641-50. *Not relevant to key questions*

2392. Lazzeri C, Tosti Guerra C, Vecchiarino S, et al. C-type natriuretic peptide does not affect plasma and urinary adrenomedullin in man. Clinical Physiology 1999; 19(1):68-75. *Sample size less than 50 patients*

2393. Lazzeri M, Barbanti G, Beneforti P, et al. Vesical-renal reflex: diuresis and natriuresis activated by intravesical capsaicin. Scandinavian Journal of Urology & Nephrology 1995; 29(1):39-43. *Sample size less than 50 patients*

2394. Le Bricon T, Erlich D, Bengoufa D, et al. Sodium dodecyl sulfate-agarose gel electrophoresis of urinary proteins: application to multiple myeloma. Clinical Chemistry 1998; 44(6 Pt 1):1191-7. *Not RCT or controlled trial*

2395. Lea J, Greene T, Hebert L, et al. The relationship between magnitude of proteinuria reduction and risk of end-stage renal disease: results of the African American study of kidney disease and hypertension. Archives of Internal Medicine 2005; 165(8):947-53. *Not RCT or controlled trial*

2396. Leary WP. Renal excretory actions of antihypertensive agents. Effects of rilmenidine. American Journal of Medicine 1989; 87(3C):63S-6S. *Not relevant to key questions*

2397. Leary WP, Reyes AJ, Wynne RD, et al. Renal excretory actions of furosemide, of hydrochlorothiazide and of the vasodilator flosequinan in healthy subjects. Journal of International Medical Research 1990; 18(2):120-41. *Not CKD treatment*

2398. Leavey SF, Weitzel WF. Endocrine abnormalities in chronic renal failure. Endocrinology & Metabolism Clinics of North America 2002; 31(1):107-19. *Not RCT or controlled trial*

2399. Leblond V, Sutton L, Jacquiaud C, et al. Evaluation of renal function in 60 long-term survivors of bone marrow transplantation. Journal of the American Society of Nephrology 1995; 6(6):1661-5. *Not CKD treatment*

2400. Lebovitz HE, Wiegmann TB, Cnaan A, et al. Renal protective effects of enalapril in hypertensive NIDDM: role of baseline albuminuria. Kidney International - Supplement 1994; 45:S150-5. *Not relevant to key questions*

2401. Lebrec D, Thabut D, Oberti F, et al. Pentoxifylline does not decrease short-term mortality but does reduce complications in patients with advanced cirrhosis. Gastroenterology 2010 May; 138(5):1755-62. *Not early CKD*

2402. Lecomte JM, Baumer P, Lim C, et al. Stereoselective protection of exogenous and endogenous atrial natriuretic factor by enkephalinase inhibitors in mice and humans. European Journal of Pharmacology 1990; 179(1-2):65-73. *Sample size less than 50 patients*

2403. Ledderhos C, Brauer H, Gens A, et al. Cardiorespiratory and renal responses to arterial chemoreceptor stimulation in early hypertension. International Journal of Clinical Pharmacology & Therapeutics 1996; 34(11):470-6. *Sample size less than 50 patients*

2404. Lee A, Cooper MC, Craig JC, et al. Effects of nonsteroidal anti-inflammatory drugs on post-operative renal function in normal adults. Cochrane Database of Systematic Reviews 2001; (2):CD002765. *Not CKD treatment*

2405. Lee A, Cooper MC, Craig JC, et al. Effects of nonsteroidal anti-inflammatory drugs on postoperative renal function in adults with normal renal function. Cochrane Database of Systematic Reviews 2004; (2):CD002765. *Not CKD treatment*

2406. Lee A, Cooper MG, Craig JC, et al. The effects of nonsteroidal anti-inflammatory drugs (NSAIDs) on postoperative renal function: a meta-analysis. Anaesthesia & Intensive Care 1999; 27(6):574-80. *Not RCT or controlled trial*

2407. Lee A, Cooper MG, Craig JC, et al. Effects of nonsteroidal anti-inflammatory drugs on post-operative renal function in adults. Cochrane Database of Systematic Reviews 2000; (4):CD002765. *Not early CKD*

2408. Lee A, Cooper MG, Craig JC, et al. Effects of nonsteroidal anti-inflammatory drugs on postoperative renal function in adults with normal renal function. Cochrane Database of Systematic Reviews 2007; (2):CD002765. *Not relevant to key questions*

2409. Lee C, Gnanasegaram D, Maloba M. Best evidence topic report. Rectal or intravenous non-steroidal anti-inflammatory drugs in acute renal colic. Emergency Medicine Journal 2005; 22(9):653-4. *Not relevant to key questions*

2410. Lee CC, Sharp SJ, Wexler DJ, et al. Dietary intake of eicosapentaenoic and docosahexaenoic acid and diabetic nephropathy: cohort analysis of the diabetes control and complications trial. Diabetes Care 2010 Jul; 33(7):1454-6. *Not CKD treatment*

2411. Lee CYW, Chen HH, Lisy O, et al. Pharmacodynamics of a novel designer natriuretic peptide, CD-NP, in a first-in-human clinical trial in healthy subjects. Journal of Clinical Pharmacology 2009; 49(6):668-73. *Not CKD treatment*

2412. Lee D, Levin A, Roger SD, et al. Longitudinal analysis of performance of estimated glomerular filtration rate as renal function declines in chronic kidney disease. Nephrology Dialysis Transplantation 2009; 24(1):109-16. *Not CKD treatment*

2413. Lee HC, Mitchell HC, Van Dreal P, et al. Hyperfiltration and conservation of renal function in hypertensive nephrosclerosis patients. American Journal of Kidney Diseases 1993; 21(4 Suppl 1):68-74. *Not RCT or controlled trial*

2414. Lee HK, Kim YJ, Jeong JU, et al. Desmopressin improves platelet dysfunction measured by in vitro closure time in uremic patients. Nephron 2010; 114(4):c248-52. *Sample size less than 50 patients*

2415. Lee JY, Greene PG, Douglas M, et al. Appointment attendance, pill counts, and achievement of goal blood pressure in the African American Study of Kidney Disease and Hypertension Pilot Study. Controlled Clinical Trials 1996; 17(4 Suppl):34S-9S. *Follow-up less than 6 months*

2416. Lee JY, Kusek JW, Greene PG, et al. Assessing medication adherence by pill count and electronic monitoring in the African American Study of Kidney Disease and Hypertension (AASK) Pilot Study. American Journal of Hypertension 1996; 9(8):719-25. *Follow-up less than 6 months*

2417. Lee M, Saver JL, Chang K-H, et al. Impact of microalbuminuria on incident stroke: a meta-analysis. Stroke 2010 Nov; 41(11):2625-31. *Not relevant to key questions*

2418. Lee M, Saver JL, Chang K-H, et al. Low glomerular filtration rate and risk of stroke: meta-analysis. BMJ 2010; 341:c4249. *Not CKD treatment*

2419. Lee RT, Lee TH, Poole WK, et al. Rate of disappearance of creatine kinase-MB after acute myocardial infarction: clinical determinants of variability. American Heart Journal 1988; 116(6 Pt 1):1493-9. *Follow-up less than 6 months*

2420. Lee RWC, Di Giantomasso D, May C, et al. Vasoactive drugs and the kidney. Best Practice & Research 2004; Clinical Anaesthesiology. 18(1):53-74. *Not CKD treatment*

2421. Lee T-M, Chang N-C. Effect of nicorandil on proteinuria in well controlled hypertensive patients. Journal of Hypertension 2009; 27(3):618-25. *Not RCT or controlled trial*

2422. Lee T-M, Lin M-S, Tsai C-H, et al. Add-on and withdrawal effect of pravastatin on proteinuria in hypertensive patients treated with AT receptor blockers. Kidney International 2005; 68(2):779-87. *Not relevant to key questions*

2423. Lee T-M, Su S-F, Tsai C-H. Effect of pravastatin on proteinuria in patients with well-controlled hypertension. Hypertension 2002; 40(1):67-73. *Not relevant to key questions*

2424. Lee VS, Rusinek H, Bokacheva L, et al. Renal function measurements from MR renography and a simplified multicompartmental model. American Journal of Physiology - Renal Physiology 2007; 292(5):F1548-59. *Not RCT or controlled trial*

2425. Lee WT, Padayachi K, Collins JF, et al. A comparison of oral and intravenous alfacalcidol in the treatment of uremic hyperparathyroidism. Journal of the American Society of Nephrology 1994; 5(6):1344-8. *Not early CKD*

2426. Lee YH, Lee WC, Chen MT, et al. Acupuncture in the treatment of renal colic. Journal of Urology 1992; 147(1):16-8. *Not CKD treatment*

2427. Leehey DJ, Braun BI, Tholl DA, et al. Can pharmacokinetic dosing decrease nephrotoxicity associated with aminoglycoside therapy. Journal of the American Society of Nephrology 1993; 4(1):81-90. *Sample size less than 50 patients*

2428. Leehey DJ, Moinuddin I, Bast JP, et al. Aerobic exercise in obese diabetic patients with chronic kidney disease: a randomized and controlled pilot study. Cardiovascular Diabetology 2009; 8:62. *Follow-up less than 6 months*

2429. Leehey DJ, Palubiak DJ, Chebrolu S, et al. Sodium ferric gluconate causes oxidative stress but not acute renal injury in patients with chronic kidney disease: a pilot study. Nephrology Dialysis Transplantation 2005; 20(1):135-40. *Not relevant to key questions*

2430. Leeman M, van de Borne P, Collart F, et al. Bisoprolol and atenolol in essential hypertension: effects on systemic and renal hemodynamics and on ambulatory blood pressure. Journal of Cardiovascular Pharmacology 1993; 22(6):785-91. *Sample size less than 50 patients*

2431. Leenen FH, Smith DL, Farkas RM, et al. Cardiovascular effects of indapamide in hypertensive patients with or without renal failure. A dose-response curve. American Journal of Medicine 1988; 84(1B):76-85. *Sample size less than 50 patients*

2432. Leenen FHH, Coletta E, Davies RA. Prevention of renal dysfunction and hypertension by amlodipine after heart transplant. American Journal of Cardiology 2007; 100(3):531-5. *Follow-up less than 6 months*

2433. Leenen FHH, Nwachuku CE, Black HR, et al. Clinical events in high-risk hypertensive patients randomly assigned to calcium channel blocker versus angiotensin-converting enzyme inhibitor in the antihypertensive and lipid-lowering treatment to prevent heart attack trial. Hypertension 2006; 48(3):374-84. *Not RCT or controlled trial*

2434. Lefebvre P, Duh MS, Buteau S, et al. Medical costs of untreated anemia in elderly patients with predialysis chronic kidney disease. Journal of the American Society of Nephrology 2006; 17(12):3497-502. *Sample size less than 50 patients*

2435. Lefebvre P, Vekeman F, Sarokhan B, et al. Relationship between hemoglobin level and quality of life in anemic patients with chronic kidney disease receiving epoetin alfa. Current Medical Research & Opinion 2006; 22(10):1929-37. *Not RCT or controlled trial*

2436. Legault L, Ogilvie RI, Cardella CJ, et al. Calcium antagonists in heart transplant recipients: effects on cardiac and renal function and cyclosporine pharmacokinetics. Canadian Journal of Cardiology 1993; 9(5):398-404. *Follow-up less than 6 months*

2437. Legroux-Crespel E, Cledes J, Misery L. A comparative study on the effects of naltrexone and loratadine on uremic pruritus. Dermatology 2004; 208(4):326-30. *Sample size less than 50 patients*

2438. Lehmkuhl HB, Arizon J, Vigano M, et al. Everolimus with reduced cyclosporine versus MMF with standard cyclosporine in de novo heart transplant recipients. Transplantation 2009; 88(1):115-22. *Not early CKD*

2439. Leitersdorf E, Muratti EN, Eliav O, et al. Efficacy and safety of triple therapy (fluvastatin-bezafibrate-cholestyramine) for severe familial hypercholesterolemia. American Journal of Cardiology 1995; 76(2):84A-8A. *Follow-up less than 6 months*

2440. Lely AT, van der Kleij FGH, Kistemaker TJ, et al. Impact of the preintervention rate of renal function decline on outcome of renoprotective intervention. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(1):54-60. *Not CKD treatment*

2441. Lema G, Urzua J, Jalil R, et al. Renal protection in patients undergoing cardiopulmonary bypass with preoperative abnormal renal function. Anesthesia & Analgesia 1998; 86(1):3-8. *Sample size less than 50 patients*

2442. Lemaire SA, Jones MM, Conklin LD, et al. Randomized comparison of cold blood and cold crystalloid renal perfusion for renal protection during thoracoabdominal aortic aneurysm repair. Journal of Vascular Surgery 2009; 49(1):11-9; discussion 9. *Not CKD treatment*

2443. Lemann J, Bidani AK, Bain RP, et al. Use of the serum creatinine to estimate glomerular filtration rate in health and early diabetic nephropathy. Collaborative Study Group of Angiotensin Converting Enzyme Inhibition in Diabetic Nephropathy. American Journal of Kidney Diseases 1990; 16(3):236-43. *Not CKD treatment*

2444. Lemann J, Jr., Pleuss JA, Hornick L, et al. Dietary NaCl-restriction prevents the calciuria of KCl-deprivation and blunts the calciuria of KHCO3-deprivation in healthy adults. Kidney International 1995; 47(3):899-906. *Sample size less than 50 patients*

2445. Lemley KV, Abdullah I, Myers BD, et al. Evolution of incipient nephropathy in type 2 diabetes mellitus.[Erratum appears in Kidney Int 2000 Nov;58(5):2257]. Kidney International 2000; 58(3):1228-37. *Not RCT or controlled trial*

2446. Lemmer JH, Jr., Stanford W, Bonney SL, et al. Aprotinin for coronary artery bypass grafting: effect on postoperative renal function. Annals of Thoracic Surgery 1995; 59(1):132-6. *Not CKD treatment*

2447. Lemos PA, Arampatzis CA, Hoye A, et al. Impact of baseline renal function on mortality after percutaneous coronary intervention with sirolimus-eluting stents or bare metal stents. American Journal of Cardiology 2005; 95(2):167-72. *Sample size less than 50 patients*

2448. Lenaerts A, Codden T, Henry J-P, et al. Comparative pilot study of repeated large volume paracentesis vs the combination on clonidine-spironolactone in the treatment of cirrhosis-associated refractory ascites. Gastroenterologie Clinique et Biologique 2005; 29(11):1137-42. *Sample size less than 50 patients*

2449. Lennert T, Luft FC. Kidneys on vacation: the notion of renal work and the introduction of nonpharmacological therapies. American Journal of Kidney Diseases 1997; 29(5):777-80. *Not RCT or controlled trial*

2450. Leoncini G, Martinoli C, Viazzi F, et al. Changes in renal resistive index and urinary albumin excretion in hypertensive patients under long-term treatment with lisinopril or nifedipine GITS. Nephron 2002; 90(2):169-73. *Sample size less than 50 patients*

2451. Leopold JA. Small-molecule glycoprotein IIb/IIIa antagonists and bleeding risk in women: too much of a good thing? Circulation 2006; 114(13):1344-6. *Not CKD treatment*

2452. Lepor NE. A review of contemporary prevention strategies for radiocontrast nephropathy: a focus on fenoldopam and N-acetylcysteine. Reviews in Cardiovascular Medicine 2003; 4 Suppl 1:S15-20. *Not CKD treatment*

2453. Lerner SA, Schmitt BA, Seligsohn R, et al. Comparative study of ototoxicity and nephrotoxicity in patients randomly assigned to treatment with amikacin or gentamicin. American Journal of Medicine 1986; 80(6B):98-104. *Not early CKD*

2454. Lernfelt B, Landahl S, Johansson P, et al. Haemodynamic and renal effects of felodipine in young and elderly subjects. European Journal of Clinical Pharmacology 1998; 54(8):595-601. *Sample size less than 50 patients*

2455. Leung T-K, Luk AOY, So WY, et al. Development and validation of equations estimating glomerular filtration rates in Chinese patients with type 2 diabetes. Kidney International 2010 Apr; 77(8):729-35. *Not CKD treatment*

2456. Leung WYS, So W-Y, Tong PCY, et al. The renoprotective effects of structured care in a clinical trial setting in type 2 diabetic patients with nephropathy. Nephrology Dialysis Transplantation 2004; 19(10):2519-25. *Not CKD treatment*

2457. Levey AS, Adler S, Caggiula AW, et al. Effects of dietary protein restriction on the progression of advanced renal disease in the Modification of Diet in Renal Disease Study. American Journal of Kidney Diseases 1996; 27(5):652-63. *Not early CKD*

2458. Levey AS, Berg RL, Gassman JJ, et al. Creatinine filtration, secretion and excretion during progressive renal disease. Modification of Diet in Renal Disease (MDRD) Study Group. Kidney International - Supplement 1989; 27:S73-80. *Not relevant to key questions*

2459. Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Annals of Internal Medicine 1999; 130(6):461-70. *Not RCT or controlled trial*

2460. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate.[Erratum appears in Ann Intern Med. 2008 Oct 7;149(7):519]. Annals of Internal Medicine 2006; 145(4):247-54. *Not CKD treatment*

2461. Levey AS, Gassman JJ, Hall PM, et al. Assessing the progression of renal disease in clinical studies: effects of duration of follow-up and regression to the mean. Modification of Diet in Renal Disease (MDRD) Study Group. Journal of the American Society of Nephrology 1991; 1(9):1087-94. *Not relevant to key questions*

2462. Levey AS, Greene T, Schluchter MD, et al. Glomerular filtration rate measurements in clinical trials. Modification of Diet in Renal Disease Study Group and the Diabetes Control and Complications Trial Research Group. Journal of the American Society of Nephrology 1993; 4(5):1159-71. *Not CKD treatment*

2463. Levey AS, Mulrow CD. An editorial update: what level of blood pressure control in chronic kidney disease? Annals of Internal Medicine 2005; 143(1):79-81. *Not CKD treatment*

2464. Levin A. The treatment of anemia in chronic kidney disease: understandings in 2006. Current Opinion in Nephrology & Hypertension 2007; 16(3):267-71. *Sample size less than 50 patients*

2465. Levin A. Understanding recent haemoglobin trials in CKD: methods and lesson learned from CREATE and CHOIR.[Erratum appears in Nephrol Dial Transplant. 2007 Mar;22(3):977]. Nephrology Dialysis Transplantation 2007; 22(2):309-12. *Not CKD treatment*

2466. Levin A, Duncan L, Djurdjev O, et al. A randomized placebo-controlled double-blind trial of lipid-lowering strategies in patients with renal insufficiency: diet modification with or without fenofibrate. Clinical Nephrology 2000; 53(2):140-6. *Sample size less than 50 patients*

2467. Levine CB, Fahrbach KR, Frame D, et al. Effect of amlodipine on systolic blood pressure. Clinical Therapeutics 2003; 25(1):35-57. *Not RCT or controlled trial*

2468. Levy B, Nace L, Bollaert PE, et al. Comparison of systemic and regional effects of dobutamine and dopexamine in norepinephrine-treated septic shock. Intensive Care Medicine 1999; 25(9):942-8. *Sample size less than 50 patients*

2469. Levy EM. Angiotensin converting enzyme inhibitors: first line therapy in patients with diabetic hypertension? Current Opinion in Nephrology & Hypertension 1999; 8(3):333-4. *Not RCT or controlled trial*

2470. Levy P-Y, Corey R, Berger P, et al. Etiologic diagnosis of 204 pericardial effusions. Medicine 2003; 82(6):385-91. *Not CKD treatment*

2471. Levy R, DellaValle A, Atav AS, et al. The relationship between glomerular filtration rate and survival in patients treated with an implantable cardioverter defibrillator. Clinical Cardiology 2008; 31(6):265-9. *Not CKD treatment*

2472. Lewandowski B, Bernacka K, Kucharewicz B, et al. Assessment of beta-2-microglobulin concentration in serum and urine in rheumatoid arthritis. Roczniki Akademii Medycznej W Bialymstoku 1996; 41(2):482-91. *Not CKD treatment*

2473. Lewerin C, Ljungman S, Nilsson-Ehle H. Glomerular filtration rate as measured by serum cystatin C is an important determinant of plasma homocysteine and serum methylmalonic acid in the elderly. Journal of Internal Medicine 2007; 261(1):65-73. *Not relevant to key questions*

2474. Lewis D, Haynes R, Landray MJ. Lipids in chronic kidney disease. Journal of Renal Care 2010 May; 36 Suppl 1:27-33. *Not RCT or controlled trial*

2475. Lewis EJ. Therapeutic interventions in the progression of diabetic nephropathy. American Journal of Hypertension 1994; 7(9 Pt 2):93S-5S. *Not CKD treatment*

2476. Lewis EJ. The role of angiotensin II receptor blockers in preventing the progression of renal disease in patients with type 2 diabetes. American Journal of Hypertension 2002; 15(10 Pt 2):123S-8S. *Not RCT or controlled trial*

2477. Lewis EJ, Hunsicker LG, Rodby RA, et al. A clinical trial in type 2 diabetic nephropathy. American Journal of Kidney Diseases 2001; 38(4 Suppl 1):S191-4. *Not RCT or controlled trial*

2478. Lewis EJ, Lewis JB. Treatment of diabetic nephropathy with angiotensin II receptor antagonist. Clinical & Experimental Nephrology 2003; 7(1):1-8. *Not CKD treatment*

2479. Lewis HM, Wilkins MR, Kendall MJ, et al. Carbidopa does not affect the renal response to atrial natriuretic factor in man. Clinical Science 1989; 77(3):281-5. *Not CKD treatment*

2480. Lewis J, Agodoa L, Cheek D, et al. Comparison of cross-sectional renal function measurements in African Americans with hypertensive nephrosclerosis and of primary formulas to estimate glomerular filtration rate.[Erratum appears in Am J Kidney Dis 2002 Feb;39(2):444]. American Journal of Kidney Diseases 2001; 38(4):744-53. *Not RCT or controlled trial*

2481. Lewis J, Greene T, Appel L, et al. A comparison of iothalamate-GFR and serum creatinine-based outcomes: acceleration in the rate of GFR decline in the African American Study of Kidney Disease and Hypertension. Journal of the American Society of Nephrology 2004; 15(12):3175-83. *Sample size less than 50 patients*

2482. Lewis NP, Ferguson DR. The effect of enalapril on the renal response to tilting in humans. British Journal of Clinical Pharmacology 1989; 27(2):191-7. *Sample size less than 50 patients*

2483. Lherm T, Troche G, Rossignol M, et al. Renal effects of low-dose dopamine in patients with sepsis syndrome or septic shock treated with catecholamines. Intensive Care Medicine 1996; 22(3):213-9. *Sample size less than 50 patients*

2484. Li G, Yin L, Liu T, et al. Role of probucol in preventing contrast-induced acute kidney injury after coronary interventional procedure. American Journal of Cardiology 2009; 103(4):512-4. *Not CKD treatment*

2485. Li G-S, Jiang W-L, Yue X-D, et al. Effect of astilbin on experimental diabetic nephropathy in vivo and in vitro. Planta Medica 2009 Nov; 75(14):1470-5. *Not RCT or controlled trial*

2486. Li H, Liu L-t, Zhao W-m, et al. Effect of traditional and integrative regimens on quality of life and early renal impairment in elderly patients with isolated systolic hypertension. Chinese Journal of Integrative Medicine 2010 Jun; 16(3):216-21. *Follow-up less than 6 months*

2487. Li J, Schluchter MD. Conditional mixed models adjusting for non-ignorable drop-out with administrative censoring in longitudinal studies. Statistics in Medicine 2004; 23(22):3489-503. *Not RCT or controlled trial*

2488. Li J, Wu HM, Zhang L, et al. Heparin and related substances for preventing diabetic kidney disease. Cochrane Database of Systematic Reviews 2010; (9):CD005631. *Not CKD treatment*

2489. Li Kam Wa TC, Freestone S, Samson RR, et al. A comparison of the renal and neuroendocrine effects of two 5-hydroxytryptamine renal prodrugs in normal man. Clinical Science 1993; 85(5):607-14. *Follow-up less than 6 months*

2490. Li Kam Wa TC, Freestone S, Samson RR, et al. The antinatriuretic action of gamma-L-glutamyl-5-hydroxy-L-tryptophan is dependent on its decarboxylation to 5-hydroxytryptamine in normal man. British Journal of Clinical Pharmacology 1994; 38(3):265-9. *Sample size less than 50 patients*

2491. Li Kam Wa TC, Freestone S, Samson RR, et al. Renal metabolism and effects of the glutamyl derivatives of L-dopa and 5-hydroxytryptophan in man. Clinical Science 1996; 91(2):177-85. *Not CKD treatment*

2492. Li Q, Zhang C-L, Fu Z-L, et al. Development of formulae for accurate measurement of the glomerular filtration rate by renal dynamic imaging. Nuclear Medicine Communications 2007; 28(5):407-13. *Not CKD treatment*

2493. Li X, Tian J, Wu J, et al. A comparison of a standard-dose prednisone regimen and mycophenolate mofetil combined with a lower prednisone dose in Chinese adults with idiopathic nephrotic syndrome who were carriers of hepatitis B surface antigen: a prospective cohort study. Clinical Therapeutics 2009; 31(4):741-50. *Not RCT or controlled trial*

2494. Li X-S, Zheng W-Y, Lou S-X, et al. Effect of Ginkgo leaf extract on vascular endothelial function in patients with early stage diabetic nephropathy. Chinese Journal of Integrative Medicine 2009; 15(1):26-9. *Not early CKD*

2495. Li X-Y, Xu M, Wang J-G, et al. Serum C-reactive protein (CRP) and microalbuminuria in relation to fasting and 2-h postload plasma glucose in a Chinese population. Clinical Endocrinology 2009; 70(5):691-7. *Not RCT or controlled trial*

2496. Li Y, Tang X, Zhang J, et al. Nutritional support for acute kidney injury. Cochrane Database of Systematic Reviews 2010; (1):CD005426. *Not early CKD*

2497. Libertino JA, Beckmann CF. Surgery and percutaneous angioplasty in the management of renovascular hypertension. Urologic Clinics of North America 1994; 21(2):235-43. *Not RCT or controlled trial*

2498. Licata G, Scaglione R, Ganguzza A, et al. Effects of amlodipine on renal haemodynamics in mild to moderate hypertensive patients. A randomized controlled study versus placebo. European Journal of Clinical Pharmacology 1993; 45(4):307-11. *Sample size less than 50 patients*

2499. Licata G, Scaglione R, Guillet C, et al. Double-blind controlled study of rilmenidine versus hydrochlorothiazide in mild hypertension: clinical and renal haemodynamic evaluation. Journal of Human Hypertension 1993; 7(2):153-7. *Sample size less than 50 patients*

2500. Licker M, Bednarkiewicz M, Neidhart P, et al. Preoperative inhibition of angiotensin-converting enzyme improves systemic and renal haemodynamic changes during aortic abdominal surgery. British Journal of Anaesthesia 1996; 76(5):632-9. *Sample size less than 50 patients*

2501. Lieberman SA, Holloway L, Marcus R, et al. Interactions of growth hormone and parathyroid hormone in renal phosphate, calcium, and calcitriol metabolism and bone remodeling in postmenopausal women. Journal of Bone & Mineral Research 1994; 9(11):1723-8. *Sample size less than 50 patients*

2502. Lievre M, Marre M, Chatellier G, et al. The non-insulin-dependent diabetes, hypertension, microalbuminuria or proteinuria, cardiovascular events, and ramipril (DIABHYCAR) study: design, organization, and patient recruitment. DIABHYCAR Study Group. Controlled Clinical Trials 2000; 21(4):383-96. *Not RCT or controlled trial*

2503. Ligtenberg G, Blankestijn PJ, Oey PL, et al. Reduction of sympathetic hyperactivity by enalapril in patients with chronic renal failure. New England Journal of Medicine 1999; 340(17):1321-8. *Sample size less than 50 patients*

2504. Lim SC, Koh AFY, Goh SK, et al. Angiotensin receptor antagonist vs. angiotensin-converting enzyme inhibitor in Asian subjects with type 2 diabetes and albuminuria - a randomized crossover study. Diabetes, Obesity & Metabolism 2007; 9(4):477-82. *Sample size less than 50 patients*

2505. Lim VS. Recombinant human erythropoietin in predialysis patients. American Journal of Kidney Diseases 1991; 18(4 Suppl 1):34-7. *Not relevant to key questions*

2506. Lim VS, DeGowin RL, Zavala D, et al. Recombinant human erythropoietin treatment in pre-dialysis patients. A double-blind placebo-controlled trial. Annals of Internal Medicine 1989; 110(2):108-14. *Follow-up less than 6 months*

2507. Lim VS, Wolfson M, Yarasheski KE, et al. Leucine turnover in patients with nephrotic syndrome: evidence suggesting body protein conservation. Journal of the American Society of Nephrology 1998; 9(6):1067-73. *Not RCT or controlled trial*

2508. Lim VS, Zavala DC, Flanigan MJ, et al. Blunted peripheral tissue responsiveness to thyroid hormone in uremic patients. Kidney International 1987; 31(3):808-14. *Sample size less than 50 patients*

2509. Lim W, Dentali F, Eikelboom JW, et al. Meta-analysis: low-molecular-weight heparin and bleeding in patients with severe renal insufficiency. Annals of Internal Medicine 2006; 144(9):673-84. *Not RCT or controlled trial*

2510. Lin C-C, Chuang F-R, Lee C-H, et al. The renal-sparing efficacy of basiliximab in adult living donor liver transplantation. Liver Transplantation 2005; 11(10):1258-64. *Follow-up less than 6 months*

2511. Lin J, Bonventre JV. Prevention of radiocontrast nephropathy. Current Opinion in Nephrology & Hypertension 2005; 14(2):105-10. *Not relevant to key questions*

2512. Lin JL, Ho HH, Yu CC. Chelation therapy for patients with elevated body lead burden and progressive renal insufficiency. A randomized, controlled trial. Annals of Internal Medicine 1999; 130(1):7-13. *Sample size less than 50 patients*

2513. Lin JL, Lin-Tan DT, Yu CC, et al. Environmental exposure to lead and progressive diabetic nephropathy in patients with type II diabetes. Kidney International 2006; 69(11):2049-56. *Not relevant to key questions*

2514. Lin JL, Tan DT, Hsu KH, et al. Environmental lead exposure and progressive renal insufficiency. Archives of Internal Medicine 2001; 161(2):264-71. *Not CKD treatment*

2515. Lin JL, Yu CC, Lin-Tan DT, et al. Lead chelation therapy and urate excretion in patients with chronic renal diseases and gout. Kidney International 2001; 60(1):266-71. *Sample size less than 50 patients*

2516. Lin J-L, Lin-Tan D-T, Hsu K-H, et al. Environmental lead exposure and progression of chronic renal diseases in patients without diabetes. New England Journal of Medicine 2003; 348(4):277-86. *Not CKD treatment*

2517. Lin J-L, Lin-Tan D-T, Li Y-J, et al. Low-level environmental exposure to lead and progressive chronic kidney diseases. American Journal of Medicine 2006; 119(8):707.e1-9. *Not relevant to key questions*

2518. Lin S. New research areas for keto acid/amino acid-supplemented protein diets. Journal of Renal Nutrition 2009; 19(5 Suppl):S30-2. *Not RCT or controlled trial*

2519. Lin S-L, Chen Y-M, Chiang W-C, et al. Effect of pentoxifylline in addition to losartan on proteinuria and GFR in CKD: a 12-month randomized trial. American Journal of Kidney Diseases 2008; 52(3):464-74. *Not RCT or controlled trial*

2520. Lind L, Wengle B, Sorensen OH, et al. Delayed hypersensitivity in primary and secondary hyperparathyroidism. Treatment with active vitamin D. Experimental & Clinical Endocrinology 1990; 95(2):271-4. *Not CKD treatment*

2521. Lindeman RD, Romero L, Liang HC, et al. Prevalence of proteinuria/microalbuminuria in an elderly urban, biethnic community. Geriatric Nephrology & Urology 1998; 8(3):123-30. *Not RCT or controlled trial*

2522. Lindenfeld J, Borer J, Armstrong PW. Losartan potassium (Cozaar). Circulation 2002; 105(16):e9100. *Not relevant to key questions*

2523. Lindsay RM, Spanner E, Heidenheim AP, et al. A multicenter study of short hour dialysis using AN69S. Preliminary results. ASAIO Transactions 1991; 37(3):M465-7. *Not CKD treatment*

2524. Lindsay RM, Spanner E, Heidenheim AP, et al. The influence of dialysis membrane upon protein catabolic rate. ASAIO Transactions 1991; 37(3):M134-5. *Not CKD treatment*

2525. Linnebjerg H, Kothare PA, Park S, et al. Effect of renal impairment on the pharmacokinetics of exenatide. British Journal of Clinical Pharmacology 2007; 64(3):317-27. *Sample size less than 50 patients*

2526. Lin-Tan D-T, Lin J-L, Yen T-H, et al. Long-term outcome of repeated lead chelation therapy in progressive non-diabetic chronic kidney diseases. Nephrology Dialysis Transplantation 2007; 22(10):2924-31. *Not RCT or controlled trial*

2527. Lintott CJ, Scott RS, Bremer JM, et al. Fluvastatin for dyslipoproteinemia, with or without concomitant chronic renal insufficiency. American Journal of Cardiology 1995; 76(2):97A-101A. *Sample size less than 50 patients*

2528. Liou HH, Chiang SS, Wu SC, et al. Intravenous infusion or nebulization of salbutamol for treatment of hyperkalemia in patients with chronic renal failure. Chung Hua i Hsueh Tsa Chih - Chinese Medical Journal 1994; 53(5):276-81. *Sample size less than 50 patients*

2529. Liou HH, Huang TP, Campese VM. Effect of long-term therapy with captopril on proteinuria and renal function in patients with non-insulin-dependent diabetes and with non-diabetic renal diseases. Nephron 1995; 69(1):41-8. *Sample size less than 50 patients*

2530. Lipkin GW, Dawnay AB, Harwood SM, et al. Enhanced natriuretic response to neutral endopeptidase inhibition in patients with moderate chronic renal failure. Kidney International 1997; 52(3):792-801. *Sample size less than 50 patients*

2531. Lips P, Wiersinga A, van Ginkel FC, et al. The effect of vitamin D supplementation on vitamin D status and parathyroid function in elderly subjects. Journal of Clinical Endocrinology & Metabolism 1988; 67(4):644-50. *Not CKD treatment*

2532. Lipton A. The safety of zoledronic acid. Expert Opinion on Drug Safety 2007; 6(3):305-13. *Sample size less than 50 patients*

2533. Lishner M, Lang R, Jutrin I, et al. Analgesic effect of ceruletide compared with pentazocine in biliary and renal colic: a prospective, controlled, double-blind study. Drug Intelligence & Clinical Pharmacy 1985; 19(6):433-6. *Follow-up less than 6 months*

2534. Lissoni P, Malugani F, Malysheva O, et al. Neuroimmunotherapy of untreatable metastatic solid tumors with subcutaneous low-dose interleukin-2, melatonin and naltrexone: modulation of interleukin-2-induced antitumor immunity by blocking the opioid system. Neuroendocrinology Letters 2002; 23(4):341-4. *Not CKD treatment*

2535. Lit YZ, Meyer T. Managing diabetic nephropathy: recent studies. Current Opinion in Nephrology & Hypertension 2006; 15(2):111-6. *Not RCT or controlled trial*

2536. Littlewood KJ, Greiner W, Baum D, et al. Adjunctive treatment with moxonidine versus nitrendipine for hypertensive patients with advanced renal failure: a cost-effectiveness analysis. BMC Nephrology 2007; 8:9. *Not RCT or controlled trial*

2537. Littlewood TJ, Alikhan R. The use of intravenous iron in patients with cancer-related anaemia. British Journal of Haematology 2008; 141(6):751-6. *Sample size less than 50 patients*

2538. Litz RJ, Hubler M, Lorenz W, et al. Renal responses to desflurane and isoflurane in patients with renal insufficiency. Anesthesiology 2002; 97(5):1133-6. *Not CKD treatment*

2539. Liu B-C, Chen L, Sun J, et al. Connective tissue growth factor-mediated angiotensin II-induced hypertrophy of proximal tubular cells. Nephron. Experimental Nephrology 2006; 103(1):e16-26. *Not RCT or controlled trial*

2540. Liu C, Chen H, Zhou C, et al. Potent potentiating diuretic effects of prednisone in congestive heart failure. Journal of Cardiovascular Pharmacology 2006; 48(4):173-6. *Not CKD treatment*

2541. Liu C, Liu G, Zhou C, et al. Potent diuretic effects of prednisone in heart failure patients with refractory diuretic resistance. Canadian Journal of Cardiology 2007; 23(11):865-8. *Not RCT or controlled trial*

2542. Liu Q, Garner P, Wang Y, et al. Drugs and herbs given to prevent hepatotoxicity of tuberculosis therapy: systematic review of ingredients and evaluation studies. BMC Public Health 2008; 8:365. *Not CKD treatment*

2543. Liu R, Nair D, Ix J, et al. N-acetylcysteine for the prevention of contrast-induced nephropathy. A systematic review and meta-analysis. Journal of General Internal Medicine 2005; 20(2):193-200. *Not RCT or controlled trial*

2544. Liu X, Du J, Cai J, et al. Clinical systematic observation of Kangxin capsule curing vascular dementia of senile kidney deficiency and blood stagnation type. Journal of Ethnopharmacology 2007; 112(2):350-5. *Not RCT or controlled trial*

2545. Livio M, Mannucci PM, Vigano G, et al. Conjugated estrogens for the management of bleeding associated with renal failure. New England Journal of Medicine 1986; 315(12):731-5. *Sample size less than 50 patients*

2546. Ljungman S, Wikstrand J, Hartford M, et al. Effects of long-term antihypertensive treatment and aging on renal function and albumin excretion in primary hypertension. American Journal of Hypertension 1993; 6(7 Pt 1):554-63. *Sample size less than 50 patients*

2547. Ljutic D, Perkovic D, Rumboldt Z, et al. Comparison of ondansetron with metoclopramide in the symptomatic relief of uremia-induced nausea and vomiting. Kidney & Blood Pressure Research 2002; 25(1):61-4. *Sample size less than 50 patients*

2548. Llanos A, Cieza J, Bernardo J, et al. Effect of salt supplementation on amphotericin B nephrotoxicity. Kidney International 1991; 40(2):302-8. *Not CKD treatment*

2549. Lloret J, Vila A, Puig X, et al. Nifedipine in the treatment of renal colic. Methods & Findings in Experimental & Clinical Pharmacology 1986; 8(9):575-9. *Sample size less than 50 patients*

2550. Lobo ED, Heathman M, Kuan H-Y, et al. Effects of varying degrees of renal impairment on the pharmacokinetics of duloxetine: analysis of a single-dose phase I study and pooled steady-state data from phase II/III trials. Clinical Pharmacokinetics 2010 May 1; 49(5):311-21. *Not RCT or controlled trial*

2551. Locatelli F. Controlled study of protein-restricted diet in chronic renal failure. Contributions to Nephrology 1989; 75:141-6. *Not relevant to key questions*

2552. Locatelli F. Dietary compliance in patients with chronic renal failure: experience in a northern Italy trial. Contributions to Nephrology 1990; 81:102-6. *Not CKD treatment*

2553. Locatelli F, Aljama P, Canaud B, et al. Target haemoglobin to aim for with erythropoiesis-stimulating agents: a position statement by ERBP following publication of the Trial to reduce cardiovascular events with Aranesp therapy (TREAT) study. Nephrology Dialysis Transplantation 2010 Sep; 25(9):2846-50. *Not CKD treatment*

2554. Locatelli F, Canaud B, Eckardt K-U, et al. Oxidative stress in end-stage renal disease: an emerging threat to patient outcome. Nephrology Dialysis Transplantation 2003; 18(7):1272-80. *Not early CKD*

2555. Locatelli F, Carbarns IR, Maschio G, et al. Long-term progression of chronic renal insufficiency in the AIPRI Extension Study. The Angiotensin-Converting-Enzyme Inhibition in Progressive Renal Insufficiency Study Group. Kidney International - Supplement 1997; 63:S63-6. *Not relevant to key questions*

2556. Locatelli F, Covic A, Macdougall IC, et al. ORAMA: a study to investigate EBPG impact on renal anaemia - design and baseline data. Journal of Nephrology 2008; 21(4):592-603. *Not CKD treatment*

2557. Locatelli F, Del Vecchio L, Andrulli S, et al. The role of underlying nephropathy in the progression of renal disease. Kidney International - Supplement 2000; 75:S49-55. *Not CKD treatment*

2558. Locatelli F, Del Vecchio L, Marai P, et al. The renoprotective effect of antihypertensive drugs. Journal of Nephrology 1998; 11(6):330-6. *Not RCT or controlled trial*

2559. Locatelli F, Del Vecchio L, Pozzoni P. Clinical benefits of slowing the progression of renal failure. Kidney International - Supplement 2005; (99):S152-6. *Not relevant to key questions*

2560. Locatelli F, Del Vecchio L, Pozzoni P. Anemia and cardiovascular risk: the lesson of the CREATE Trial. Journal of the American Society of Nephrology 2006; 17(12 Suppl 3):S262-6. *Not RCT or controlled trial*

2561. Locatelli F, Del Vecchio L, Pozzoni P. Treating anemia at different stages of renal disease. Journal of Nephrology 2007; 20 Suppl 12:S33-8. *Not relevant to key questions*

2562. Locatelli F, Del Vecchio L, Pozzoni P, et al. Is it the agent or the blood pressure level that matters for renal and vascular protection in chronic nephropathies? Kidney International - Supplement 2005; (93):S15-9. *Not RCT or controlled trial*

2563. Locatelli F, Manzoni C, Marcelli D. Factors affecting progression of renal insufficiency. Mineral & Electrolyte Metabolism 1997; 23(3-6):301-5. *Not RCT or controlled trial*

2564. Locatelli F, Manzoni C, Marcelli D. Treatment of hypertension in chronic renal insufficiency. Journal of Nephrology 1997; 10(4):220-3. *Not RCT or controlled trial*

2565. Locatelli F, Marcelli D, Comelli M, et al. Proteinuria and blood pressure as causal components of progression to end-stage renal failure. Northern Italian Cooperative Study Group. Nephrology Dialysis Transplantation 1996; 11(3):461-7. *Not RCT or controlled trial*

2566. Locatelli F, Marcelli D, Tentori F, et al. Controlled trials on low-protein diet: effects on chronic renal insufficiency progression. Renal Failure 1993; 15(3):407-13. *Not RCT or controlled trial*

2567. Locatelli F, Olivares J, Walker R, et al. Novel erythropoiesis stimulating protein for treatment of anemia in chronic renal insufficiency. Kidney International 2001; 60(2):741-7. *Not CKD treatment*

2568. Locatelli F, Vecchio LD, Pozzoni P. The importance of early detection of chronic kidney disease. Nephrology Dialysis Transplantation 2002; 17 Suppl 11:2-7. *Not relevant to key questions*

2569. Locatelli MC, D'Antona A, Labianca R, et al. A phase II study of combination chemotherapy in advanced ovarian carcinoma with cisplatin and cyclophosphamide plus reduced glutathione as potential protective agent against cisplatin toxicity. Tumori 1993; 79(1):37-9. *Not CKD treatment*

2570. Lodise TP, Lomaestro B, Graves J, et al. Larger vancomycin doses (at least four grams per day) are associated with an increased incidence of nephrotoxicity. Antimicrobial Agents & Chemotherapy 2008; 52(4):1330-6. *Not CKD treatment*

2571. Loeb M, Neupane B, Walter SD, et al. Environmental risk factors for community-acquired pneumonia hospitalization in older adults. Journal of the American Geriatrics Society 2009; 57(6):1036-40. *Not CKD treatment*

2572. Loef BG, Epema AH, Navis G, et al. Off-pump coronary revascularization attenuates transient renal damage compared with on-pump coronary revascularization. Chest 2002; 121(4):1190-4. *Not early CKD*

2573. Loef BG, Henning RH, Epema AH, et al. Effect of dexamethasone on perioperative renal function impairment during cardiac surgery with cardiopulmonary bypass. British Journal of Anaesthesia 2004; 93(6):793-8. *Not relevant to key questions*

2574. Logan A. BENEDICT in the treatment of hypertension. Current Hypertension Reports 2005; 7(2):121-3. *Not RCT or controlled trial*

2575. London GM. Efficacy of indapamide 1.5 mg, sustained release, in the lowering of systolic blood pressure. Journal of Human Hypertension 2004; 18 Suppl 2:S9-S14. *Not RCT or controlled trial*

2576. London GM, Pannier B, Guerin AP, et al. Cardiac hypertrophy, aortic compliance, peripheral resistance, and wave reflection in end-stage renal disease. Comparative effects of ACE inhibition and calcium channel blockade. Circulation 1994; 90(6):2786-96. *Not early CKD*

2577. Lopes NH, da Silva Paulitsch F, Pereira A, et al. Mild chronic kidney dysfunction and treatment strategies for stable coronary artery disease. Journal of Thoracic & Cardiovascular Surgery 2009; 137(6):1443-9. *Not CKD treatment*

2578. Lopes T, Dias JS, Marcelino J, et al. An assessment of the clinical efficacy of intranasal desmopressin spray in the treatment of renal colic. BJU International 2001; 87(4):322-5. *Not CKD treatment*

2579. Lopez LM, Santiago TM. Isradipine--another calcium-channel blocker for the treatment of hypertension and angina. Annals of Pharmacotherapy 1992; 26(6):789-99. *Not relevant to key questions*

2580. Lopez MC, Belizan JM, Villar J, et al. The measurement of diastolic blood pressure during pregnancy: which Korotkoff phase should be used? American Journal of Obstetrics & Gynecology 1994; 170(2):574-8. *Not RCT or controlled trial*

2581. Lopez-Suarez A, Beltran-Robles M, Elvira-Gonzalez J, et al. Comparison of the MDRD and the CKD-EPI equations to estimate the glomerular filtration rate in the general population. Medicina Clinica 2010 May 15; 134(14):617-23. *Not early CKD*

2582. Lorenzano E, Badalamenti S, Scotti A, et al. Renal effects of imidazole-2-hydroxybenzoate in patients with compensated liver cirrhosis. International Journal of Clinical Pharmacology, Therapy, & Toxicology 1992; 30(7):225-9. *Sample size less than 50 patients*

2583. Lottenberg R, Hassell KL. An evidence-based approach to the treatment of adults with sickle cell disease. Hematology 2005:58-65. *Not adult population*

2584. Loudon JAZ, Groom KM, Bennett PR. Prostaglandin inhibitors in preterm labour. Best Practice & Research in Clinical Obstetrics & Gynaecology 2003; 17(5):731-44. *Not CKD treatment*

2585. Loup R, Favre L, Vallotton MB. Effect of noradrenaline, vasopressin and angiotensin II on renal prostaglandins in man. Clinical Science 1986; 70(4):371-7. *Sample size less than 50 patients*

2586. Lovell HG. Angiotensin converting enzyme inhibitors in normotensive diabetic patients with microalbuminuria. Cochrane Database of Systematic Reviews 2000; (2):CD002183. *Not relevant to key questions*

2587. Lovell HG. Angiotensin converting enzyme inhibitors in normotensive diabetic patients with microalbuminuria. Cochrane Database of Systematic Reviews 2001; (1):CD002183. *Not relevant to key questions*

2588. Lovell HG. WITHDRAWN: Angiotensin converting enzyme inhibitors in normotensive diabetic patients with microalbuminuria. Cochrane Database of Systematic Reviews 2006; (1):CD002183. *Sample size less than 50 patients*

2589. Lu M, Cohen MH, Rieves D, et al. FDA report: Ferumoxytol for intravenous iron therapy in adult patients with chronic kidney disease. American Journal of Hematology 2010 May; 85(5):315-9. *Follow-up less than 6 months*

2590. Lubrano R, Marandola M, Antonucci A, et al. Hypotensive anesthesia with propofol and remifentanil: protective effect of alpha-tocopherol on renal function. Journal of Clinical Anesthesia 2008; 20(3):164-9. *Not CKD treatment*

2591. Lucarini AR, Arrighi P, Favilla S, et al. The influence of dopamine-1 receptor blockade on the humoral and renal effects of low-dose atrial natriuretic factor in human hypertensives. Journal of Hypertension - Supplement 1989; 7(6):S230-1. *Sample size less than 50 patients*

2592. Lucarini AR, Salvetti A. Haemodynamic (systemic and renal) and humoral interactions between nicardipine and domperidone in hypertensives. Journal of Hypertension - Supplement 1987; 5(5):S571-4. *Sample size less than 50 patients*

2593. Lucarini AR, Salvetti A. Systemic and renal hemodynamic effects of celiprolol in essential hypertensives. American Journal of Cardiology 1988; 61(5):45C-8C. *Sample size less than 50 patients*

2594. Luchner A, Hengstenberg C, Lowel H, et al. Effect of compensated renal dysfunction on approved heart failure markers: direct comparison of brain natriuretic peptide (BNP) and N-terminal pro-BNP. Hypertension 2005; 46(1):118-23. *Not RCT or controlled trial*

2595. Luchsinger A, Velasco M, Urbina A, et al. Comparative effects of dopaminergic agonists on cardiovascular, renal, and renin-angiotensin systems in hypertensive patients. Journal of Clinical Pharmacology 1992; 32(1):55-60. *Sample size less than 50 patients*

2596. Lucker PW, Venitz J, Hey B, et al. Pharmacodynamic and pharmacokinetic correlation of muzolimine with and without aluminium hydroxide. Zeitschrift fur Kardiologie 1985; 74 Suppl 2:141-4. *Sample size less than 50 patients*

2597. Ludlow M, Luxton G, Mathew T. Effects of fluoridation of community water supplies for people with chronic kidney disease. Nephrology Dialysis Transplantation 2007; 22(10):2763-7. *Sample size less than 50 patients*

2598. Luft FC. STOPPING at the CAPPP of good HOPE. Nephrology Dialysis Transplantation 2000; 15(4):451-2. *Not RCT or controlled trial*

2599. Luft FC. Hypertensive nephrosclerosis: update. Current Opinion in Nephrology & Hypertension 2004; 13(2):147-54. *Not CKD treatment*

2600. Luik PT, Hoogenberg K, Van Der Kleij FGH, et al. Short-term moderate sodium restriction induces relative hyperfiltration in normotensive normoalbuminuric Type I diabetes mellitus. Diabetologia 2002; 45(4):535-41. *Sample size less than 50 patients*

2601. Luippold G, Benohr P, Piesch C, et al. Urinary dopamine excretion in healthy volunteers: effect of sodium diet and acute water load. Pflugers Archiv - European Journal of Physiology 2000; 440(1):28-33. *Not early CKD*

2602. Luippold G, Schneider S, Stefanescu A, et al. Dopamine D2-like receptors and amino acid-induced glomerular hyperfiltration in humans. British Journal of Clinical Pharmacology 2001; 51(5):415-21. *Not early CKD*

2603. Luke DR, Sarnoski TP, Bell N, et al. Influence of pentoxifylline on renal function in HIV-seropositive patients. Renal Failure 1993; 15(2):181-8. *Sample size less than 50 patients*

2604. Luke RG, Boyle JA. Renal effects of amphotericin B lipid complex. American Journal of Kidney Diseases 1998; 31(5):780-5. *Not CKD treatment*

2605. Luksch A, Polak K, Matulla B, et al. Glucose and insulin exert additive ocular and renal vasodilator effects on healthy humans. Diabetologia 2001; 44(1):95-103. *Not early CKD*

2606. Lumlertgul D, Keoplung M, Sitprija V, et al. Furosemide and dopamine in malarial acute renal failure. Nephron 1989; 52(1):40-4. *Not CKD treatment*

2607. Lumlertgul D, Wongmekiat O, Sirivanichai C, et al. Intrarenal infusion of gallopamil in acute renal failure. A preliminary report. Drugs 1991; 42 Suppl 1:44-50. *Not CKD treatment*

2608. Lund B, Hansen OP, Hansen HH, et al. Combination therapy with carboplatin/cisplatin/ifosfamide/etoposide in ovarian cancer. Seminars in Oncology 1992; 19(1 Suppl 1):26-9. *Not CKD treatment*

2609. Lundby B, Berg KJ, Lien HH, et al. A double blind study to evaluate the tolerability of gadodiamide injection and its effect on renal function in patients undergoing cerebral magnetic resonance imaging. British Journal of Radiology 1993; 66(790):871-6. *Not CKD treatment*

2610. Lungershausen YK, Howe PR, Clifton PM, et al. Evaluation of an omega-3 fatty acid supplement in diabetics with microalbuminuria. Annals of the New York Academy of Sciences 1997; 827:369-81. *Follow-up less than 6 months*

2611. Luno J, Barrio V, Goicoechea MA, et al. Effects of dual blockade of the renin-angiotensin system in primary proteinuric nephropathies. Kidney International - Supplement 2002; (82):S47-52. *Sample size less than 50 patients*

2612. Luntz SP, Unnebrink K, Seibert-Grafe M, et al. HEGPOL: randomized, placebo controlled, multicenter, double-blind clinical trial to investigate hepatoprotective effects of glycine in the postoperative phase of liver transplantation [ISRCTN69350312]. BMC Surgery 2005; 5:18. *Not relevant to key questions*

2613. Luss H, Mitrovic V, Seferovic PM, et al. Renal effects of ularitide in patients with decompensated heart failure. American Heart Journal 2008; 155(6):1012.e1-8. *Not CKD treatment*

2614. Luts L, Bergenfelz A, Alumets J, et al. Parathyroid function and histology in patients with parathyroid adenoma: correlation of clinical and morphologic findings. World Journal of Surgery 1997; 21(5):553-63. *Not RCT or controlled trial*

2615. Lynch AI, Boerwinkle E, Davis BR, et al. Antihypertensive pharmacogenetic effect of fibrinogen-beta variant -455G>A on cardiovascular disease, end-stage renal disease, and mortality: the GenHAT study. Pharmacogenetics & Genomics 2009; 19(6):415-21. *Not CKD treatment*

2616. Lyubimova NV, Topchieva SV, Averinova SG, et al. Modern methods for diagnosis and monitoring of nephrotoxicity during antitumor therapy with platinum derivatives. Bulletin of Experimental Biology & Medicine 2000; 130(9):886-91. *Not early CKD*

2617. Ma WW, Jimeno A. Temsirolimus. Drugs of Today 2007; 43(10):659-69. *Not RCT or controlled trial*

2618. Ma X. Clinical analysis for the acupuncture treatment in 42 cases of gouty renal damage. Journal of Traditional Chinese Medicine 2004; 24(3):185-7. *Sample size less than 50 patients*

2619. Ma YC, Zuo L, Chen JH, et al. Improved GFR estimation by combined creatinine and cystatin C measurements. Kidney International 2007; 72(12):1535-42. *Not RCT or controlled trial*

2620. Ma Y-C, Zuo L, Chen J-H, et al. Modified glomerular filtration rate estimating equation for Chinese patients with chronic kidney disease.[Erratum appears in J Am Soc Nephrol. 2006 Dec;17(12):3540]. Journal of the American Society of Nephrology 2006; 17(10):2937-44. *Not RCT or controlled trial*

2621. Maccariello ER, Genelhu de Abreu Fagundes V, Francischetti EA. The effects of isradipine and spirapril as monotherapy and combined therapy on blood pressure, renal hemodynamics, natriuresis, and urinary kallikrein in hypertensive nephropathy. American Journal of Hypertension 1997; 10(5 Pt 1):541-5. *Follow-up less than 6 months*

2622. Maccubbin D, Tipping D, Kuznetsova O, et al. Hypophosphatemic effect of niacin in patients without renal failure: a randomized trial. Clinical Journal of The American Society of Nephrology: CJASN 2010 Apr; 5(4):582-9. *Not CKD treatment*

2623. Macdonald JH, Marcora SM, Jibani MM, et al. Nandrolone decanoate as anabolic therapy in chronic kidney disease: a randomized phase II dose-finding study. Nephron 2007; 106(3):c125-35. *Follow-up less than 6 months*

2624. MacDonald TM. Metoclopramide, domperidone and dopamine in man: actions and interactions. European Journal of Clinical Pharmacology 1991; 40(3):225-30. *Sample size less than 50 patients*

2625. MacDonald TM, Jeffrey RF, Lee MR. The renal and haemodynamic effects of a 10 h infusion of glutamyl-L-dopa in normal man. British Journal of Clinical Pharmacology 1989; 27(6):811-22. *Not CKD treatment*

2626. Macdougall IC. How to improve survival in pre-dialysis patients. Nephron 2000; 85 Suppl 1:15-22. *Not RCT or controlled trial*

2627. Macdougall IC, Robson R, Opatrna S, et al. Pharmacokinetics and pharmacodynamics of intravenous and subcutaneous continuous erythropoietin receptor activator (C.E.R.A.) in patients with chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2006; 1(6):1211-5. *Not RCT or controlled trial*

2628. Macdougall IC, Steering Committee of the Ct, Group CS. CREATE: new strategies for early anaemia management in renal insufficiency. Nephrology Dialysis Transplantation 2003; 18 Suppl 2:ii13-6. *Not early CKD*

2629. Macdougall IC, Walker R, Provenzano R, et al. C.E.R.A. corrects anemia in patients with chronic kidney disease not on dialysis: results of a randomized clinical trial. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(2):337-47. *Not CKD treatment*

2630. Macedo E, Abdulkader R, Castro I, et al. Lack of protection of N-acetylcysteine (NAC) in acute renal failure related to elective aortic aneurysm repair-a randomized controlled trial. Nephrology Dialysis Transplantation 2006; 21(7):1863-9. *Sample size less than 50 patients*

2631. MacGregor DA, Butterworth JFt, Zaloga CP, et al. Hemodynamic and renal effects of dopexamine and dobutamine in patients with reduced cardiac output following coronary artery bypass grafting. Chest 1994; 106(3):835-41. *Sample size less than 50 patients*

2632. MacGregor GA. Blood pressure, angiotensin-converting enzyme (ACE) inhibitors, and the kidney. American Journal of Medicine 1992; 92(4B):20S-7S. *Not relevant to key questions*

2633. MacGregor MS, Deighan CJ, Rodger RSC, et al. A prospective open-label randomised trial of quinapril and/or amlodipine in progressive non-diabetic renal failure. Nephron 2005; 101(3):c139-49. *Sample size less than 50 patients*

2634. Macisaac RJ, Jerums G, Weekes AJ, et al. Patterns of glycaemic control in Australian primary care (NEFRON 8).[Erratum appears in Intern Med J. 2009 Dec;39(12):862]. Internal Medicine Journal 2009 Aug; 39(8):512-8. *Not CKD treatment*

2635. Mackay IG, Macnicol AM, Smith HJ, et al. Intrinsic sympathomimetic activity of cardioselective beta-adrenoceptor blockers and effects on renal function. British Journal of Clinical Pharmacology 1985; 20(3):197-203. *Sample size less than 50 patients*

2636. MacKinnon M, Leenen FHH, Ruzicka M. Does ALLHAT change the management of hypertension in chronic kidney disease? Current Hypertension Reports 2005; 7(6):474-83. *Not RCT or controlled trial*

2637. MacKinnon M, Shurraw S, Akbari A, et al. Combination therapy with an angiotensin receptor blocker and an ACE inhibitor in proteinuric renal disease: a systematic review of the efficacy and safety data. American Journal of Kidney Diseases 2006; 48(1):8-20. *Not relevant to key questions*

2638. MacLean CH, Mojica WA, Morton SC, et al. Effects of omega-3 fatty acids on lipids and glycemic control in type II diabetes and the metabolic syndrome and on inflammatory bowel disease, rheumatoid arthritis, renal disease, systemic lupus erythematosus, and osteoporosis. Evidence Report: Technology Assessment 2004; (89):1-4. *Follow-up less than 6 months*

2639. MacLeod MJ, McLay J. Drug treatment of hypertension complicating diabetes mellitus. Drugs 1998; 56(2):189-202. *Not RCT or controlled trial*

2640. MacNeill BD, Harding SA, Bazari H, et al. Prophylaxis of contrast-induced nephropathy in patients undergoing coronary angiography. Catheterization & Cardiovascular Interventions 2003; 60(4):458-61. *Not relevant to key questions*

2641. Madero M, Sarnak MJ, Wang X, et al. Uric acid and long-term outcomes in CKD. American Journal of Kidney Diseases 2009; 53(5):796-803. *Follow-up less than 6 months*

2642. Madero M, Sarnak MJ, Wang X, et al. Body mass index and mortality in CKD. American Journal of Kidney Diseases 2007; 50(3):404-11. *Sample size less than 50 patients*

2643. Madkour H, Gadallah M, Riveline B, et al. Comparison between the effects of indapamide and hydrochlorothiazide on creatinine clearance in patients with impaired renal function and hypertension. American Journal of Nephrology 1995; 15(3):251-5. *Not relevant to key questions*

2644. Madkour H, Gadallah M, Riveline B, et al. Indapamide is superior to thiazide in the preservation of renal function in patients with renal insufficiency and systemic hypertension. American Journal of Cardiology 1996; 77(6):23B-5B. *Not CKD treatment*

2645. Madore F, Lazarus JM, Brady HR. Therapeutic plasma exchange in renal diseases. Journal of the American Society of Nephrology 1996; 7(3):367-86. *Not RCT or controlled trial*

2646. Madsen JK, Jensen JW, Sandermann J, et al. Effect of nitrendipine on renal function and on hormonal parameters after intravascular iopromide. Acta Radiologica 1998; 39(4):375-80. *Sample size less than 50 patients*

2647. Madsen JK, Zachariae H, Pedersen EB. Effects of the calcium antagonist felodipine on renal haemodynamics, tubular sodium handling, and blood pressure in cyclosporin-treated dermatological patients. Nephrology Dialysis Transplantation 1997; 12(3):480-4. *Not CKD treatment*

2648. Magee GM, Bilous RW, Cardwell CR, et al. Is hyperfiltration associated with the future risk of developing diabetic nephropathy? A meta-analysis. Diabetologia 2009; 52(4):691-7. *Not relevant to key questions*

2649. Mahajan A, Simoni J, Sheather SJ, et al. Daily oral sodium bicarbonate preserves glomerular filtration rate by slowing its decline in early hypertensive nephropathy. Kidney International 2010 Aug; 78(3):303-9. *Not CKD treatment*

2650. Mahajan SK, Sharma VK, Thakral S. Effect of enalapril on renal profile and right ventricular dimensions in chronic cor pulmonale. Journal of the Association of Physicians of India 1996; 44(5):323-4. *Sample size less than 50 patients*

2651. Mahesh B, Yim B, Robson D, et al. Does furosemide prevent renal dysfunction in high-risk cardiac surgical patients? Results of a double-blinded prospective randomised trial. European Journal of Cardio-Thoracic Surgery 2008; 33(3):370-6. *Sample size less than 50 patients*

2652. Mahmood A, Gosling P, Vohra RK. Randomized clinical trial comparing the effects on renal function of hydroxyethyl starch or gelatine during aortic aneurysm surgery. British Journal of Surgery 2007; 94(4):427-33. *Not relevant to key questions*

2653. Mahmud N, O'Toole D, O'Hare N, et al. Evaluation of renal function following treatment with 5-aminosalicylic acid derivatives in patients with ulcerative colitis. Alimentary Pharmacology & Therapeutics 2002; 16(2):207-15. *Not early CKD*

2654. Maillard M, Burnier M. Comparative cardiovascular safety of traditional nonsteroidal anti-inflammatory drugs. Expert Opinion on Drug Safety 2006; 5(1):83-94. *Not relevant to key questions*

2655. Mainra R, Gallo K, Moist L. Effect of N-acetylcysteine on renal function in patients with chronic kidney disease. Nephrology 2007; 12(5):510-3. *Sample size less than 50 patients*

2656. Maioli M, Toso A, Leoncini M, et al. Sodium bicarbonate versus saline for the prevention of contrast-induced nephropathy in patients with renal dysfunction undergoing coronary angiography or intervention. Journal of the American College of Cardiology 2008; 52(8):599-604. *Not early CKD*

2657. Maione A, Nicolucci A, Craig JC, et al. Protocol of the Long-term Impact of RAS Inhibition on Cardiorenal Outcomes (LIRICO) randomized trial. Journal of Nephrology 2007; 20(6):646-55. *Not CKD treatment*

2658. Maisch NM, Pezzillo KK. HMG-CoA reductase inhibitors for the prevention of nephropathy. Annals of Pharmacotherapy 2004; 38(2):342-5. *Sample size less than 50 patients*

2659. Majumdar SR, Kjellstrand CM, Tymchak WJ, et al. Forced euvolemic diuresis with mannitol and furosemide for prevention of contrast-induced nephropathy in patients with CKD undergoing coronary angiography: a randomized controlled trial. American Journal of Kidney Diseases 2009; 54(4):602-9. *Not CKD treatment*

2660. Mak RH, Cheung W. Therapeutic strategy for cachexia in chronic kidney disease. Current Opinion in Nephrology & Hypertension 2007; 16(6):542-6. *Not CKD treatment*

2661. Maki DD, Ma JZ, Louis TA, et al. Long-term effects of antihypertensive agents on proteinuria and renal function. Archives of Internal Medicine 1995; 155(10):1073-80. *Not relevant to key questions*

2662. Makino H, Haneda M, Babazono T, et al. The telmisartan renoprotective study from incipient nephropathy to overt nephropathy--rationale, study design, treatment plan and baseline characteristics of the incipient to overt: angiotensin II receptor blocker, telmisartan, Investigation on Type 2 Diabetic Nephropathy (INNOVATION) Study. Journal of International Medical Research 2005; 33(6):677-86. *Not human studies*

2663. Makino H, Haneda M, Babazono T, et al. Microalbuminuria reduction with telmisartan in normotensive and hypertensive Japanese patients with type 2 diabetes: a post-hoc analysis of The Incipient to Overt: Angiotensin II Blocker, Telmisartan, Investigation on Type 2 Diabetic Nephropathy (INNOVATION) study. Hypertension Research - Clinical & Experimental 2008; 31(4):657-64. *Not CKD treatment*

2664. Malaguarnera M, Vacante M, Russo C, et al. A single dose of rasburicase in elderly patients with hyperuricaemia reduces serum uric acid levels and improves renal function. Expert Opinion on Pharmacotherapy 2009; 10(5):737-42. *Not RCT or controlled trial*

2665. Malandrino S, Angelini M, Baldini L, et al. Effects of suprofen on renal function in patients with rheumatoid arthritis. International Journal of Clinical Pharmacology Research 1987; 7(4):259-63. *Follow-up less than 6 months*

2666. Malani AK, Ammar H, Yassin MH. Progression of chronic kidney disease: can it be prevented or arrested? American Journal of Medicine 2007; 120(3):e29; author reply e31. *Not RCT or controlled trial*

2667. Malhis M, Al-Bitar S, Al-Deen Zaiat K. The role of theophylline in prevention of radiocontrast media-induced nephropathy. Saudi Journal of Kidney Diseases & Transplantation 2010 Mar; 21(2):276-83. *Not CKD treatment*

2668. Mallamaci F, Leonardis D, Bellizzi V, et al. Does high salt intake cause hyperfiltration in patients with essential hypertension? Journal of Human Hypertension 1996; 10(3):157-61. *Sample size less than 50 patients*

2669. Maller R, Ahrne H, Holmen C, et al. Once- versus twice-daily amikacin regimen: efficacy and safety in systemic gram-negative infections. Scandinavian Amikacin Once Daily Study Group. Journal of Antimicrobial Chemotherapy 1993; 31(6):939-48. *Not CKD treatment*

2670. Maller R, Isaksson B, Nilsson L, et al. A study of amikacin given once versus twice daily in serious infections. Journal of Antimicrobial Chemotherapy 1988; 22(1):75-9. *Sample size less than 50 patients*

2671. Malleson PN, Lockitch G, Mackinnon M, et al. Renal disease in chronic arthritis of childhood. A study of urinary N-acetyl-beta-glucosaminidase and beta 2-microglobulin excretion. Arthritis & Rheumatism 1990; 33(10):1560-6. *Not CKD treatment*

2672. Mallett C, House AA, Spence JD, et al. Longitudinal ultrasound evaluation of carotid atherosclerosis in one, two and three dimensions. Ultrasound in Medicine & Biology 2009; 35(3):367-75. *Sample size less than 50 patients*

2673. Mallick NP. Dietary protein and progression of chronic renal disease. BMJ 1994; 309(6962):1101-2. *Not CKD treatment*

2674. Malmstrom H, Rasmussen S, Simonsen E. Intraperitoneal high-dose cisplatin and etoposide with systemic thiosulfate protection in second-line treatment of advanced ovarian cancer. Gynecologic Oncology 1993; 49(2):166-71. *Not CKD treatment*

2675. Malnick SDH, Somin M. The VALIDD study. Lancet 2007; 370(9591):931; author reply -2. *Sample size less than 50 patients*

2676. Malvy D, Maingourd C, Pengloan J, et al. Effects of severe protein restriction with ketoanalogues in advanced renal failure. Journal of the American College of Nutrition 1999; 18(5):481-6. *Not early CKD*

2677. Man in’t Veld AJ. Clinical overview of irbesartan: expanding the therapeutic window in hypertension. Journal of Hypertension - Supplement 1997; 15(7):S27-33. *Not relevant to key questions*

2678. Manasia AR, Leibowitz AB, Miller CM, et al. Postoperative intravenous infusion of alprostadil (PGE1) does not improve renal function in hepatic transplant recipients. Journal of the American College of Surgeons 1996; 182(4):347-52. *Sample size less than 50 patients*

2679. Manche A, Galea J, Busuttil W. Tolerance to ACE inhibitors after cardiac surgery. European Journal of Cardio-Thoracic Surgery 1999; 15(1):55-60. *Not CKD treatment*

2680. Mancia G. ADVANCE: a new era in diabetes and hypertension. Introduction. Journal of Hypertension - Supplement 2008; 26(2):S1. *Not RCT or controlled trial*

2681. Mandhani A, Kapoor R, Zaman W, et al. Is a 2-week duration sufficient for stenting in endopyelotomy? Journal of Urology 2003; 169(3):886-9. *Not CKD treatment*

2682. Manley HJ. Role of angiotensin-converting-enzyme inhibition in patients with renal disease. American Journal of Health-System Pharmacy 2000; 57 Suppl 1:S12-8. *Not relevant to key questions*

2683. Manley KJ, Fraenkel MB, Mayall BC, et al. Probiotic treatment of vancomycin-resistant enterococci: a randomised controlled trial. Medical Journal of Australia 2007; 186(9):454-7. *Follow-up less than 6 months*

2684. Manlucu J, Tonelli M, Ray JG, et al. Dose-reducing H2 receptor antagonists in the presence of low glomerular filtration rate: a systematic review of the evidence. Nephrology Dialysis Transplantation 2005; 20(11):2376-84. *Follow-up less than 6 months*

2685. Mann JF. Ace inhibition in chronic renal failure: a step forward. Nephrology Dialysis Transplantation 1996; 11(6):932-3. *Not RCT or controlled trial*

2686. Mann JF. What are the short-term and long-term consequences of anaemia in CRF patients? Nephrology Dialysis Transplantation 1999; 14 Suppl 2:29-36. *Not RCT or controlled trial*

2687. Mann JF. Valsartan and the kidney: present and future. Journal of Cardiovascular Pharmacology 1999; 33 Suppl 1:S37-40; discussion S1-3. *Not RCT or controlled trial*

2688. Mann JF. Should the results of the HOPE study affect nephrological practice? For the HOPE investigators. Nephrology Dialysis Transplantation 2000; 15(4):453-4. *Not relevant to key questions*

2689. Mann JF, Gerstein HC, Pogue J, et al. Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. Annals of Internal Medicine 2001; 134(8):629-36. *Not relevant to key questions*

2690. Mann JF, Hilgers KF, Veelken R, et al. Effect of antihypertensive therapy on the progression of non-diabetic renal disease. Clinical Nephrology 1992; 38 Suppl 1:S74-7. *Not relevant to key questions*

2691. Mann JF, Reisch C, Bergbreiter R, et al. Effects of WY 47987 (atrial natriuretic factor 102-126) in patients with renal insufficiency: a placebo-controlled, randomised study. Nephrology Dialysis Transplantation 1989; 4(9):776-81. *Sample size less than 50 patients*

2692. Mann JFE. Cardiovascular risk in patients with mild renal insufficiency: implications for the use of ACE inhibitors. Presse Medicale 2005; 34(18):1303-8. *Not relevant to key questions*

2693. Mann JFE, Gerstein HC, Yi Q-L, et al. Development of renal disease in people at high cardiovascular risk: results of the HOPE randomized study. Journal of the American Society of Nephrology 2003; 14(3):641-7. *Not relevant to key questions*

2694. Mann JFE, Green D, Jamerson K, et al. Avosentan for overt diabetic nephropathy. Journal of the American Society of Nephrology 2010; 21(3):527-35. *Not CKD treatment*

2695. Mann JFE, Lonn EM, Yi Q, et al. Effects of vitamin E on cardiovascular outcomes in people with mild-to-moderate renal insufficiency: results of the HOPE study. Kidney International 2004; 65(4):1375-80. *Not CKD treatment*

2696. Manns B, Stevens L, Miskulin D, et al. A systematic review of sevelamer in ESRD and an analysis of its potential economic impact in Canada and the United States. Kidney International 2004; 66(3):1239-47. *Not CKD treatment*

2697. Manske CL, Wang Y, Rector T, et al. Coronary revascularisation in insulin-dependent diabetic patients with chronic renal failure. Lancet 1992; 340(8826):998-1002. *Not CKD treatment*

2698. Mansour G, Mansour J. Autoregulated glomerular filtration rate during candesartan treatment in hypertensive type 2 diabetic patients. Current Hypertension Reports 2002; 4(6):437-8. *Not RCT or controlled trial*

2699. Mansson W, Ahlgren G, White T. Glomerular filtration rate up to 10 years after urinary diversion of different types. A comparative study of ileal and colonic conduit, refluxing and antirefluxing ureteral anastomosis and continent caecal reservoir. Scandinavian Journal of Urology & Nephrology 1989; 23(3):195-200. *Not CKD treatment*

2700. Mansy H, Goodship TH, Tapson JS, et al. Effect of a high protein diet in patients with the nephrotic syndrome. Clinical Science 1989; 77(4):445-51. *Sample size less than 50 patients*

2701. Marathias KP, Vassili M, Robola A, et al. Preoperative intravenous hydration confers renoprotection in patients with chronic kidney disease undergoing cardiac surgery. Artificial Organs 2006; 30(8):615-21. *Follow-up less than 6 months*

2702. Marchais SJ, Boussac I, Guerin AP, et al. Arteriosclerosis and antihypertensive response to calcium antagonists in end-stage renal failure. Journal of Cardiovascular Pharmacology 1991; 18 Suppl 1:S74-8. *Not early CKD*

2703. Marcus J, Sarnak MJ, Menon V. Homocysteine lowering and cardiovascular disease risk: lost in translation. Canadian Journal of Cardiology 2007; 23(9):707-10. *Not RCT or controlled trial*

2704. Marcus LS, Hart D, Packer M, et al. Hemodynamic and renal excretory effects of human brain natriuretic peptide infusion in patients with congestive heart failure. A double-blind, placebo-controlled, randomized crossover trial. Circulation 1996; 94(12):3184-9. *Not CKD treatment*

2705. Marcus R, Butterfield G, Holloway L, et al. Effects of short term administration of recombinant human growth hormone to elderly people. Journal of Clinical Endocrinology & Metabolism 1990; 70(2):519-27. *Sample size less than 50 patients*

2706. Marenzi G, Assanelli E, Marana I, et al. N-acetylcysteine and contrast-induced nephropathy in primary angioplasty. New England Journal of Medicine 2006; 354(26):2773-82. *Sample size less than 50 patients*

2707. Marier J-F, Lee J, Kambhampati SRP, et al. Effect of repeated oral administrations of the oral adsorbent AST-120 on serum creatinine and other markers of renal function. A randomized controlled study in patients with chronic kidney disease. American Journal of Nephrology 2006; 26(2):136-41. *Not RCT or controlled trial*

2708. Marik PE. Low-dose dopamine: a systematic review. Intensive Care Medicine 2002; 28(7):877-83. *Not early CKD*

2709. Marik PE, Iglesias J. Low-dose dopamine does not prevent acute renal failure in patients with septic shock and oliguria. NORASEPT II Study Investigators. American Journal of Medicine 1999; 107(4):387-90. *Follow-up less than 6 months*

2710. Marin R, Ruilope LM, Aljama P, et al. A random comparison of fosinopril and nifedipine GITS in patients with primary renal disease. Journal of Hypertension 2001; 19(10):1871-6. *Not early CKD*

2711. Marincola FM, White DE, Wise AP, et al. Combination therapy with interferon alfa-2a and interleukin-2 for the treatment of metastatic cancer. Journal of Clinical Oncology 1995; 13(5):1110-22. *Not RCT or controlled trial*

2712. Maroni BJ, Tom K, Masud T, et al. How is lean body mass conserved with the very-low protein diet regimen? Mineral & Electrolyte Metabolism 1996; 22(1-3):54-7. *Follow-up less than 6 months*

2713. Marre M. Microalbuminuria and ACE inhibition in non-hypertensive diabetics. Journal of Diabetic Complications 1990; 4(2):84-5. *Sample size less than 50 patients*

2714. Marre M. Recent advance in the treatment of diabetic nephropathy: angiotensin I converting enzyme (ACE) inhibitors. Journal of Diabetic Complications 1991; 5(2-3):91. *Sample size less than 50 patients*

2715. Marre M, Chatellier G, Leblanc H, et al. Prevention of diabetic nephropathy with enalapril in normotensive diabetics with microalbuminuria. BMJ 1988; 297(6656):1092-5. *Sample size less than 50 patients*

2716. Marre M, Hallab M, Billiard A, et al. Small doses of ramipril to reduce microalbuminuria in diabetic patients with incipient nephropathy independently of blood pressure changes. Journal of Cardiovascular Pharmacology 1991; 18 Suppl 2:S165-8. *Sample size less than 50 patients*

2717. Marre M, Leblanc H, Suarez L, et al. Converting enzyme inhibition and kidney function in normotensive diabetic patients with persistent microalbuminuria. British Medical Journal Clinical Research Ed. 1987; 294(6585):1448-52. *Sample size less than 50 patients*

2718. Marre M, Lievre M, Chatellier G, et al. ACE inhibitors and diabetics with albuminuria. The DIABHYCAR Study Group. Lancet 1995; 346(8990):1638. *Not RCT or controlled trial*

2719. Marre M, Lievre M, Vasmant D, et al. Determinants of elevated urinary albumin in the 4,937 type 2 diabetic subjects recruited for the DIABHYCAR Study in Western Europe and North Africa. Diabetes Care 2000; 23 Suppl 2:B40-8. *Not RCT or controlled trial*

2720. Marrocco-Trischitta MM, Melissano G, Kahlberg A, et al. Glomerular filtration rate after left renal vein division and reconstruction during infrarenal aortic aneurysm repair. Journal of Vascular Surgery 2007; 45(3):481-6. *Not RCT or controlled trial*

2721. Marsell R, Grundberg E, Krajisnik T, et al. Fibroblast growth factor-23 is associated with parathyroid hormone and renal function in a population-based cohort of elderly men. European Journal of Endocrinology 2008; 158(1):125-9. *Not CKD treatment*

2722. Marshall MR, Song Q, Ma TM, et al. Evolving connectionist system versus algebraic formulas for prediction of renal function from serum creatinine. Kidney International 2005; 67(5):1944-54. *Not RCT or controlled trial*

2723. Marshall SM. Screening for microalbuminuria: which measurement? Diabetic Medicine 1991; 8(8):706-11. *Not CKD treatment*

2724. Marshall SM. HOPE for all people with diabetes? Heart Outcomes Prevention Evaluation. Diabetic Medicine 2000; 17 Suppl 2:9-10. *Not relevant to key questions*

2725. Marshall SM, Shearing PA, Shelley JH, et al. The effect of bromhexine on albumin excretion in insulin dependent diabetes. Diabete et Metabolisme 1991; 17(3):332-6. *Sample size less than 50 patients*

2726. Marso SP, Ellis SG, Tuzcu M, et al. The importance of proteinuria as a determinant of mortality following percutaneous coronary revascularization in diabetics. Journal of the American College of Cardiology 1999; 33(5):1269-77. *Not RCT or controlled trial*

2727. Marti H-P, Frey FJ. Nephrotoxicity of rapamycin: an emerging problem in clinical medicine. Nephrology Dialysis Transplantation 2005; 20(1):13-5. *Not RCT or controlled trial*

2728. Martin KJ. The first human cell line-derived erythropoietin, epoetin-delta (Dynepo), in the management of anemia in patients with chronic kidney disease. Clinical Nephrology 2007; 68(1):26-31. *Not RCT or controlled trial*

2729. Martin KJ, Gonzalez EA, Gellens ME, et al. Therapy of secondary hyperparathyroidism with 19-nor-1alpha,25-dihydroxyvitamin D2. American Journal of Kidney Diseases 1998; 32(2 Suppl 2):S61-6. *Sample size less than 50 patients*

2730. Martin P, Tindall H, Rice P, et al. Effects of pimobendan (UDCG 115) on renal function in healthy volunteers. Journal of International Medical Research 1992; 20(3):267-72. *Sample size less than 50 patients*

2731. Martinez I, Saracho R, Montenegro J, et al. The importance of dietary calcium and phosphorous in the secondary hyperparathyroidism of patients with early renal failure. American Journal of Kidney Diseases 1997; 29(4):496-502. *Follow-up less than 6 months*

2732. Martinez Martin FJ. Manidipine in hypertensive patients with metabolic syndrome: the MARIMBA study. Expert Review of Cardiovascular Therapy 2009; 7(7):863-9. *Follow-up less than 6 months*

2733. Martinez-de-Anda A, Valdivia AG, Jaramillo-Juarez F, et al. Effects of aflatoxin chronic intoxication in renal function of laying hens. Poultry Science 2010 Aug; 89(8):1622-8. *Not human studies*

2734. Martinez-Martin FJ, Saiz-Satjes M. Add-on manidipine versus amlodipine in diabetic patients with hypertension and microalbuminuria: the AMANDHA study. Expert Review of Cardiovascular Therapy 2008; 6(10):1347-55. *Not CKD treatment*

2735. Martino G, Frusciante V, Varraso A, et al. Efficacy of 51Cr-EDTA clearance to tailor a carboplatin therapeutic regimen in ovarian cancer patients. Anticancer Research 1999; 19(6C):5587-91. *Sample size less than 50 patients*

2736. Martins D, Norris K. Combating diabetic nephropathy with drug therapy. Current Diabetes Reports 2001; 1(2):148-56. *Not RCT or controlled trial*

2737. Masala A, Faedda R, Alagna S, et al. Use of testosterone to prevent cyclophosphamide-induced azoospermia. Annals of Internal Medicine 1997; 126(4):292-5. *Sample size less than 50 patients*

2738. Maschio G, Alberti D, Locatelli F, et al. Angiotensin-converting enzyme inhibitors and kidney protection: the AIPRI trial. The ACE Inhibition in Progressive Renal Insufficiency (AIPRI) Study Group. Journal of Cardiovascular Pharmacology 1999; 33 Suppl 1:S16-20; discussion S41-3. *Not relevant to key questions*

2739. Massarella JW, Nazareno LA, Passe S, et al. The effect of probenecid on the pharmacokinetics of zalcitabine in HIV-positive patients. Pharmaceutical Research 1996; 13(3):449-52. *Sample size less than 50 patients*

2740. Massy ZA. Therapy of hyperhomocysteinemia in chronic kidney disease. Seminars in Nephrology 2006; 26(1):24-7. *Follow-up less than 6 months*

2741. Masud T, Young VR, Chapman T, et al. Adaptive responses to very low protein diets: the first comparison of ketoacids to essential amino acids. Kidney International 1994; 45(4):1182-92. *Sample size less than 50 patients*

2742. Masuda M, Yamada T, Mine T, et al. Comparison of usefulness of sodium bicarbonate versus sodium chloride to prevent contrast-induced nephropathy in patients undergoing an emergent coronary procedure. American Journal of Cardiology 2007; 100(5):781-6. *Not early CKD*

2743. Masuda M, Yamada T, Okuyama Y, et al. Sodium bicarbonate improves long-term clinical outcomes compared with sodium chloride in patients with chronic kidney disease undergoing an emergent coronary procedure. Circulation Journal 2008; 72(10):1610-4. *Not CKD treatment*

2744. Masuda S-i, Tamura K, Wakui H, et al. Effects of angiotensin II type 1 receptor blocker on ambulatory blood pressure variability in hypertensive patients with overt diabetic nephropathy. Hypertension Research - Clinical & Experimental 2009; 32(11):950-5. *Sample size less than 50 patients*

2745. Mathew A, Eliasziw M, Devereaux PJ, et al. Carotid endarterectomy benefits patients with CKD and symptomatic high-grade stenosis. Journal of the American Society of Nephrology 2010; 21(1):145-52. *Not RCT or controlled trial*

2746. Mathew JT, Patni H, Chaudhary AN, et al. Aldosterone induces mesangial cell apoptosis both in vivo and in vitro. American Journal of Physiology - Renal Physiology 2008; 295(1):F73-81. *Not CKD treatment*

2747. Mathiesen ER, Hommel E, Giese J, et al. Efficacy of captopril in postponing nephropathy in normotensive insulin dependent diabetic patients with microalbuminuria. BMJ 1991; 303(6794):81-7. *Not relevant to key questions*

2748. Mathiesen ER, Hommel E, Hansen HP, et al. Randomised controlled trial of long term efficacy of captopril on preservation of kidney function in normotensive patients with insulin dependent diabetes and microalbuminuria. BMJ 1999; 319(7201):24-5. *Sample size less than 50 patients*

2749. Mathiesen ER, Hommel E, Olsen UB, et al. Elevated urinary prostaglandin excretion and the effect of indomethacin on renal function in incipient diabetic nephropathy. Diabetic Medicine 1988; 5(2):145-9. *Sample size less than 50 patients*

2750. Mathur RP, Dash SC, Gupta N, et al. Effects of correction of metabolic acidosis on blood urea and bone metabolism in patients with mild to moderate chronic kidney disease: a prospective randomized single blind controlled trial. Renal Failure 2006; 28(1):1-5. *Not RCT or controlled trial*

2751. Mathur VS. Pathophysiology of radiocontrast nephropathy and use of fenoldopam for its prevention. Reviews in Cardiovascular Medicine 2001; 2 Suppl 1:S4-8. *Not CKD treatment*

2752. Mathur VS. The role of the DA1 receptor agonist fenoldopam in the management of critically ill, transplant, and hypertensive patients. Reviews in Cardiovascular Medicine 2003; 4 Suppl 1:S35-40. *Not CKD treatment*

2753. Mathur VS, Swan SK, Lambrecht LJ, et al. The effects of fenoldopam, a selective dopamine receptor agonist, on systemic and renal hemodynamics in normotensive subjects. Critical Care Medicine 1999; 27(9):1832-7. *Follow-up less than 6 months*

2754. Matikainen N, Kahri J, Taskinen M-R. Reviewing statin therapy in diabetes--towards the best practise. Primary care diabetes 2010 Apr; 4(1):9-15. *Not CKD treatment*

2755. Matin SF. Laparoscopic approaches to urologic malignancies. Current Treatment Options in Oncology 2003; 4(5):373-83. *Not CKD treatment*

2756. Matos JPS, de Lourdes Rodrigues M, Ismerim VL, et al. Effects of dual blockade of the renin angiotensin system in hypertensive type 2 diabetic patients with nephropathy. Clinical Nephrology 2005; 64(3):180-9. *Not RCT or controlled trial*

2757. Matsuda H, Hayashi K, Homma K, et al. Differing anti-proteinuric action of candesartan and losartan in chronic renal disease. Hypertension Research - Clinical & Experimental 2003; 26(11):875-80. *Follow-up less than 6 months*

2758. Matsuda H, Hayashi K, Saruta T. Distinct time courses of renal protective action of angiotensin receptor antagonists and ACE inhibitors in chronic renal disease. Journal of Human Hypertension 2003; 17(4):271-6. *Not CKD treatment*

2759. Matsumoto H, Nakao T, Okada T, et al. Favorable outcome of low-dose cyclosporine after pulse methylprednisolone in Japanese adult minimal-change nephrotic syndrome. Internal Medicine 2004; 43(8):668-73. *Not RCT or controlled trial*

2760. Matsumura C, Kemmotsu O, Kawano Y, et al. Serum and urine inorganic fluoride levels following prolonged low-dose sevoflurane anesthesia combined with epidural block. Journal of Clinical Anesthesia 1994; 6(5):419-24. *Sample size less than 50 patients*

2761. Matthews DR, Stratton IM, Aldington SJ, et al. Risks of progression of retinopathy and vision loss related to tight blood pressure control in type 2 diabetes mellitus: UKPDS 69. Archives of Ophthalmology 2004; 122(11):1631-40. *Not CKD treatment*

2762. Matuszkiewicz-Rowinska J. KDIGO clinical practice guidelines for the diagnosis, evaluation, prevention, and treatment of mineral and bone disorders in chronic kidney disease. Polskie Archiwum Medycyny Wewnetrznej 2010 Jul; 120(7-8):300-6. *Not RCT or controlled trial*

2763. Matz GJ. Aminoglycoside ototoxicity. American Journal of Otolaryngology 1986; 7(2):117-9. *Not relevant to key questions*

2764. Mauer M, Zinman B, Gardiner R, et al. ACE-I and ARBs in early diabetic nephropathy. Journal of the Renin-Angiotensin-Aldosterone System 2002; 3(4):262-9. *Not early CKD*

2765. Mauer M, Zinman B, Gardiner R, et al. Renal and retinal effects of enalapril and losartan in type 1 diabetes. New England Journal of Medicine 2009; 361(1):40-51. *Not relevant to key questions*

2766. Mauer M, Zinman B, Gardiner R, et al. Renal and retinal effects of enalapril and losartan in type 1 diabetes. New England Journal of Medicine 2009; 361(1):40-51. *Not relevant to key questions*

2767. Mauri JM, Valles M. Effects of recombinant interleukin-2 and revaccination for hepatitis B in previously vaccinated, non-responder, chronic uraemic patients. Collaborative Group of Girona. Nephrology Dialysis Transplantation 1997; 12(4):729-32. *Not CKD treatment*

2768. Mauro LS, Kuhl DA, Kirchhoff JR, et al. Impact of oral bases on aluminum absorption. American Journal of Therapeutics 2001; 8(1):21-5. *Not early CKD*

2769. Mayer AF, Schroeder C, Heusser K, et al. Influences of norepinephrine transporter function on the distribution of sympathetic activity in humans. Hypertension 2006; 48(1):120-6. *Not early CKD*

2770. Mayer SA, Solomon RA, Fink ME, et al. Effect of 5% albumin solution on sodium balance and blood volume after subarachnoid hemorrhage. Neurosurgery 1998; 42(4):759-67; discussion 67-8. *Not CKD treatment*

2771. Mazze RS, Bergenstal R, Ginsberg B. Intensified diabetes management: lessons from the diabetes control and complications trial. International Journal of Clinical Pharmacology & Therapeutics 1995; 33(1):43-51. *Not RCT or controlled trial*

2772. Mazzeo AT, Brophy GM, Gilman CB, et al. Safety and tolerability of cyclosporin a in severe traumatic brain injury patients: results from a prospective randomized trial. Journal of Neurotrauma 2009; 26(12):2195-206. *Not CKD treatment*

2773. McAlister FA, Levine M, Zarnke KB, et al. The 2000 Canadian recommendations for the management of hypertension: Part one--therapy. Canadian Journal of Cardiology 2001; 17(5):543-59. *Not early CKD*

2774. McAuliffe AV, Brooks BA, Fisher EJ, et al. Administration of ascorbic acid and an aldose reductase inhibitor (tolrestat) in diabetes: effect on urinary albumin excretion. Nephron 1998; 80(3):277-84. *Sample size less than 50 patients*

2775. McBride WT, Allen S, Gormley SMC, et al. Methylprednisolone favourably alters plasma and urinary cytokine homeostasis and subclinical renal injury at cardiac surgery. Cytokine 2004; 27(2-3):81-9. *Sample size less than 50 patients*

2776. McCance-Katz EF, Rainey PM, Jatlow P, et al. Methadone effects on zidovudine disposition (AIDS Clinical Trials Group 262). Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology 1998; 18(5):435-43. *Not CKD treatment*

2777. McCarthy ML, Stoukides CA. Estrogen therapy of uremic bleeding. Annals of Pharmacotherapy 1994; 28(1):60-2. *Not relevant to key questions*

2778. McClean DR, Ikram H, Garlick AH, et al. The clinical, cardiac, renal, arterial and neurohormonal effects of omapatrilat, a vasopeptidase inhibitor, in patients with chronic heart failure. Journal of the American College of Cardiology 2000; 36(2):479-86. *Not early CKD*

2779. McClellan WM, Knight DF, Karp H, et al. Early detection and treatment of renal disease in hospitalized diabetic and hypertensive patients: important differences between practice and published guidelines. American Journal of Kidney Diseases 1997; 29(3):368-75. *Not RCT or controlled trial*

2780. McClellan WM, Langston RD, Presley R. Medicare patients with cardiovascular disease have a high prevalence of chronic kidney disease and a high rate of progression to end-stage renal disease. Journal of the American Society of Nephrology 2004; 15(7):1912-9. *Not CKD treatment*

2781. McClellan WM, Ramirez SPB, Jurkovitz C. Screening for chronic kidney disease: unresolved issues. Journal of the American Society of Nephrology 2003; 14(7 Suppl 2):S81-7. *Not CKD treatment*

2782. McConaghy JR. What is the best treatment for slowing the progression to end-stage renal disease (ESRD) in African Americans with hypertensive nephropathy? Journal of Family Practice 2001; 50(9):744. *Not RCT or controlled trial*

2783. McCormack PL, Wagstaff AJ. Lacidipine: a review of its use in the management of hypertension. Drugs 2003; 63(21):2327-56. *Not RCT or controlled trial*

2784. McCormack PM, Cox JP, Marron J, et al. The antihypertensive efficacy of ketanserin in the elderly evaluated by ambulatory blood pressure measurement. Journal of Human Hypertension 1990; 4(5):565-70. *Sample size less than 50 patients*

2785. McCormick BB, Sydor A, Akbari A, et al. The effect of pentoxifylline on proteinuria in diabetic kidney disease: a meta-analysis. American Journal of Kidney Diseases 2008; 52(3):454-63. *Not CKD treatment*

2786. McCormick PA, Greenslade L, Kibbler CC, et al. A prospective randomized trial of ceftazidime versus netilmicin plus mezlocillin in the empirical therapy of presumed sepsis in cirrhotic patients. Hepatology 1997; 25(4):833-6. *Not CKD treatment*

2787. McCullough PA. Evaluation and treatment of coronary artery disease in patients with end-stage renal disease. Kidney International - Supplement 2005; (95):S51-8. *Not RCT or controlled trial*

2788. McCullough PA. Multimodality prevention of contrast-induced acute kidney injury. American Journal of Kidney Diseases 2008; 51(2):169-72. *Not CKD treatment*

2789. McCullough PA. Prevention of cardiorenal syndromes. Contributions to Nephrology 2010; 165:101-11. *Not RCT or controlled trial*

2790. McCullough PA, Agrawal V, Danielewicz E, et al. Accelerated atherosclerotic calcification and Monckeberg's sclerosis: a continuum of advanced vascular pathology in chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(6):1585-98. *Not CKD treatment*

2791. McCullough PA, Bertrand ME, Brinker JA, et al. A meta-analysis of the renal safety of isosmolar iodixanol compared with low-osmolar contrast media. Journal of the American College of Cardiology 2006; 48(4):692-9. *Not relevant to key questions*

2792. McCullough PA, Franklin BA, Leifer E, et al. Impact of reduced kidney function on cardiopulmonary fitness in patients with systolic heart failure. American Journal of Nephrology 2010; 32(3):226-33. *Not CKD treatment*

2793. McCullough PA, Li S, Jurkovitz CT, et al. CKD and cardiovascular disease in screened high-risk volunteer and general populations: the Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES) 1999-2004. American Journal of Kidney Diseases 2008; 51(4 Suppl 2):S38-45. *Not CKD treatment*

2794. McDiarmid SV, Colonna JO, 2nd, Shaked A, et al. A comparison of renal function in cyclosporine- and FK-506-treated patients after primary orthotopic liver transplantation. Transplantation 1993; 56(4):847-53. *Follow-up less than 6 months*

2795. McDonald V, Leandro M. Rituximab in non-haematological disorders of adults and its mode of action. British Journal of Haematology 2009; 146(3):233-46. *Not CKD treatment*

2796. McGee WT, Mailloux P, Jodka P, et al. The pulmonary artery catheter in critical care. Seminars in Dialysis 2006; 19(6):480-91. *Follow-up less than 6 months*

2797. McGill JB. Improving microvascular outcomes in patients with diabetes through management of hypertension. Postgraduate Medicine 2009; 121(2):89-101. *Not RCT or controlled trial*

2798. McGowan T, Vaccaro NM, Beaver JS, et al. Pharmacokinetic and pharmacodynamic profiles of extended dosing of epoetin alfa in anemic patients who have chronic kidney disease and are not on dialysis. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(4):1006-14. *Sample size less than 50 patients*

2799. McGregor DO, Dellow WJ, Robson RA, et al. Betaine supplementation decreases post-methionine hyperhomocysteinemia in chronic renal failure. Kidney International 2002; 61(3):1040-6. *Sample size less than 50 patients*

2800. McInnes GT. Angiotensin II antagonism in clinical practice: experience with valsartan. Journal of Cardiovascular Pharmacology 1999; 33 Suppl 1:S29-32; discussion S41-3. *Not RCT or controlled trial*

2801. McInnes GT. The expanding role of angiotensin receptor blockers in the management of the elderly hypertensive. Current Medical Research & Opinion 2003; 19(5):452-5. *Not relevant to key questions*

2802. McKee MD, Cecco SA, Niemela JE, et al. Effects of interleukin 2 therapy on lymphocyte magnesium levels. Journal of Laboratory & Clinical Medicine 2002; 139(1):5-12. *Not early CKD*

2803. McKenna F, Davison AM. Renin and beta-blockade: prorenin and aldosterone may explain the controversy. Clinical Nephrology 1986; 25(3):149-54. *Sample size less than 50 patients*

2804. McKenna K, Smith D, Barrett P, et al. Angiotensin-converting enzyme inhibition by quinapril blocks the albuminuric effect of atrial natriuretic peptide in Type 1 diabetes and microalbuminuria. Diabetic Medicine 2000; 17(3):219-24. *Sample size less than 50 patients*

2805. McKinnon PS, Paladino JA, Schentag JJ. Evaluation of area under the inhibitory curve (AUIC) and time above the minimum inhibitory concentration (T>MIC) as predictors of outcome for cefepime and ceftazidime in serious bacterial infections. International Journal of Antimicrobial Agents 2008; 31(4):345-51. *Not early CKD*

2806. McLachlan S-A, Cameron D, Murray R, et al. Safety of oral ibandronate in the treatment of bone metastases from breast cancer : long-term follow-up experience. Clinical Drug Investigation 2006; 26(1):43-8. *Not CKD treatment*

2807. McMahon LP, Mason K, Skinner SL, et al. Effects of haemoglobin normalization on quality of life and cardiovascular parameters in end-stage renal failure. Nephrology Dialysis Transplantation 2000; 15(9):1425-30. *Sample size less than 50 patients*

2808. McMurray J. Angiotensin receptor blockers and myocardial infarction: analysis of evidence is incomplete and inaccurate. BMJ 2005; 330(7502):1269; author reply 70-1. *Not RCT or controlled trial*

2809. McMurray J, Seidelin PH, Struthers AD. Evidence for a proximal and distal nephron action of atrial natriuretic factor in man. Nephron 1989; 51(1):39-43. *Not CKD treatment*

2810. McMurray J, Struthers AD. Effects of angiotensin II and atrial natriuretic peptide alone and in combination on urinary water and electrolyte excretion in man. Clinical Science 1988; 74(4):419-25. *Not RCT or controlled trial*

2811. McMurray JJ, Seidelin PH, Brown RA, et al. Noradrenaline attenuates the natriuretic effect of atrial natriuretic factor in man. British Journal of Clinical Pharmacology 1989; 27(1):7-12. *Not CKD treatment*

2812. McNabb WR, Noormohamed FH, Lant AF. The effects of enalapril on blood pressure and the kidney in normotensive subjects under altered sodium balance. Journal of Hypertension 1986; 4(1):39-47. *Sample size less than 50 patients*

2813. McParland P, Pearce JM, Chamberlain GV. Doppler ultrasound and aspirin in recognition and prevention of pregnancy-induced hypertension. Lancet 1990; 335(8705):1552-5. *Not early CKD*

2814. McQueen MJ, Lonn E, Gerstein HC, et al. The HOPE (Heart Outcomes Prevention Evaluation) Study and its consequences. Scandinavian Journal of Clinical and Laboratory Investigation Supplement 2005; 240:143-56. *Not RCT or controlled trial*

2815. Mechl Z, Kerpel-Fronius S, Decker A, et al. Comparative evaluation of two administration schedules of cis-dichlorodiammineplatinum (DDP) in ovarian and head and neck cancers: a CMEA chemotherapy group study. Neoplasma 1987; 34(1):37-43. *Follow-up less than 6 months*

2816. Medina HJ, Galvin EM, Dirckx M, et al. Remifentanil as a single drug for extracorporeal shock wave lithotripsy: a comparison of infusion doses in terms of analgesic potency and side effects. Anesthesia & Analgesia 2005; 101(2):365-70. *Follow-up less than 6 months*

2817. Meeme A, Kasozi H. Effect of glycaemic control on glomerular filtration rate in diabetes mellitus patients. African Health Sciences 2009 Aug 1; 9 Suppl 1:S23-6. *Not RCT or controlled trial*

2818. Mehdi U, Toto RD. Anemia, diabetes, and chronic kidney disease. Diabetes Care 2009; 32(7):1320-6. *Not RCT or controlled trial*

2819. Mehdi UF, Adams-Huet B, Raskin P, et al. Addition of angiotensin receptor blockade or mineralocorticoid antagonism to maximal angiotensin-converting enzyme inhibition in diabetic nephropathy. Journal of the American Society of Nephrology 2009; 20(12):2641-50. *Duplicate listings*

2820. Mehls O, Haas S. Effects of recombinant human growth hormone in catabolic adults with chronic renal failure. Growth Hormone & Igf Research 2000; 10 Suppl B:S31-7. *Not relevant to key questions*

2821. Mehls O, Knoller N, Oh J, et al. Daily but not pulse calcitriol therapy improves growth in experimental uremia. Pediatric Nephrology 2000; 14(7):658-63. *Not human studies*

2822. Mehran R, Ashby DT. Radiocontrast-induced acute renal failure: allocations and outcomes. Reviews in Cardiovascular Medicine 2001; 2 Suppl 1:S9-13. *Not CKD treatment*

2823. Mehran R, Nikolsky E, Kirtane AJ, et al. Ionic low-osmolar versus nonionic iso-osmolar contrast media to obviate worsening nephropathy after angioplasty in chronic renal failure patients: the ICON (Ionic versus non-ionic Contrast to Obviate worsening Nephropathy after angioplasty in chronic renal failure patients) study. Jacc: Cardiovascular Interventions 2009 May; 2(5):415-21. *Not CKD treatment*

2824. Mehran R, Nikolsky E, Lansky AJ, et al. Impact of chronic kidney disease on early (30-day) and late (1-year) outcomes of patients with acute coronary syndromes treated with alternative antithrombotic treatment strategies: an ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) substudy. Jacc: Cardiovascular Interventions 2009; 2(8):748-57. *Not CKD treatment*

2825. Mehrotra R, De Gaudio R, Palazzo M. Antibiotic pharmacokinetic and pharmacodynamic considerations in critical illness. Intensive Care Medicine 2004; 30(12):2145-56. *Not RCT or controlled trial*

2826. Mehrotra R, Kermah DA, Salusky IB, et al. Chronic kidney disease, hypovitaminosis D, and mortality in the United States. Kidney International 2009; 76(9):977-83. *Not RCT or controlled trial*

2827. Mehta RL. Timed and targeted therapy for acute kidney injury: a glimpse of the future. Kidney International 2010 Jun; 77(11):947-9. *Not early CKD*

2828. Mehta RL, Pascual MT, Soroko S, et al. Diuretics, mortality, and nonrecovery of renal function in acute renal failure. JAMA 2002; 288(20):2547-53. *Not CKD treatment*

2829. Meier P, Ko DT, Tamura A, et al. Sodium bicarbonate-based hydration prevents contrast-induced nephropathy: a meta-analysis. BMC Medicine 2009; 7:23. *Not early CKD*

2830. Meisinger E, Strauch M. Controlled trial of two keto acid supplements on renal function, nutritional status, and bone metabolism in uremic patients. Kidney International - Supplement 1987; 22:S170-3. *Not RCT or controlled trial*

2831. Melin B, Jimenez C, Koulmann N, et al. Hyperhydration induced by glycerol ingestion: hormonal and renal responses. Canadian Journal of Physiology & Pharmacology 2002; 80(6):526-32. *Not early CKD*

2832. Melis D, Parenti G, Gatti R, et al. Efficacy of ACE-inhibitor therapy on renal disease in glycogen storage disease type 1: a multicentre retrospective study. Clinical Endocrinology 2005; 63(1):19-25. *Sample size less than 50 patients*

2833. Mellor JA, Kingdom J, Cafferkey M, et al. Vancomycin toxicity: a prospective study. Journal of Antimicrobial Chemotherapy 1985; 15(6):773-80. *Sample size less than 50 patients*

2834. Meloni C, Morosetti M, Suraci C, et al. Severe dietary protein restriction in overt diabetic nephropathy: benefits or risks? Journal of Renal Nutrition 2002; 12(2):96-101. *Not relevant to key questions*

2835. Meloni C, Tatangelo P, Cipriani S, et al. Adequate protein dietary restriction in diabetic and nondiabetic patients with chronic renal failure. Journal of Renal Nutrition 2004; 14(4):208-13. *Not relevant to key questions*

2836. Mena AC, Pulido EG, Guillen-Ponce C. Understanding the molecular-based mechanism of action of the tyrosine kinase inhibitor: sunitinib. Anti-Cancer Drugs 2010; 21 Suppl 1:S3-11. *Not CKD treatment*

2837. Mendelssohn DC, Muirhead N, Manns BJ. Managing anemia. What do we do now? Views from Canada. Nephrology News & Issues 2007; 21(7):55-7. *Follow-up less than 6 months*

2838. Menon V, Greene T, Pereira AA, et al. Glycosylated hemoglobin and mortality in patients with nondiabetic chronic kidney disease. Journal of the American Society of Nephrology 2005; 16(11):3411-7. *Follow-up less than 6 months*

2839. Menon V, Greene T, Pereira AA, et al. Relationship of phosphorus and calcium-phosphorus product with mortality in CKD. American Journal of Kidney Diseases 2005; 46(3):455-63. *Follow-up less than 6 months*

2840. Menon V, Greene T, Wang X, et al. C-reactive protein and albumin as predictors of all-cause and cardiovascular mortality in chronic kidney disease. Kidney International 2005; 68(2):766-72. *Not relevant to key questions*

2841. Menon V, Kopple JD, Wang X, et al. Effect of a very low-protein diet on outcomes: long-term follow-up of the Modification of Diet in Renal Disease (MDRD) Study. American Journal of Kidney Diseases 2009; 53(2):208-17. *Not CKD treatment*

2842. Menon V, Li L, Wang X, et al. Adiponectin and mortality in patients with chronic kidney disease. Journal of the American Society of Nephrology 2006; 17(9):2599-606. *Sample size less than 50 patients*

2843. Menon V, Sarnak MJ, Greene T, et al. Relationship between homocysteine and mortality in chronic kidney disease. Circulation 2006; 113(12):1572-7. *Sample size less than 50 patients*

2844. Menon V, Shlipak MG, Wang X, et al. Cystatin C as a risk factor for outcomes in chronic kidney disease. Annals of Internal Medicine 2007; 147(1):19-27. *Follow-up less than 6 months*

2845. Menon V, Tighiouart H, Vaughn NS, et al. Serum bicarbonate and long-term outcomes in CKD. American Journal of Kidney Diseases 2010 Nov; 56(5):907-14. *Not RCT or controlled trial*

2846. Menon V, Wang X, Greene T, et al. Relationship between C-reactive protein, albumin, and cardiovascular disease in patients with chronic kidney disease. American Journal of Kidney Diseases 2003; 42(1):44-52. *Not CKD treatment*

2847. Menon V, Wang X, Greene T, et al. Homocysteine in chronic kidney disease: Effect of low protein diet and repletion with B vitamins. Kidney International 2005; 67(4):1539-46. *Not relevant to key questions*

2848. Menon V, Wang X, Sarnak MJ, et al. Long-term outcomes in nondiabetic chronic kidney disease. Kidney International 2008; 73(11):1310-5. *Not CKD treatment*

2849. Mercieri M, Mercieri A, Tritapepe L, et al. High-dose aprotinin with gentamicin-vancomycin antibiotic prophylaxis increases blood concentrations of creatinine and cystatin C in patients undergoing coronary artery bypass grafting. British Journal of Anaesthesia 1999; 82(4):531-6. *Follow-up less than 6 months*

2850. Meredith PA, Elliott HL, Pasanisi F, et al. Verapamil pharmacokinetics and apparent hepatic and renal blood flow. British Journal of Clinical Pharmacology 1985; 20(2):101-6. *Sample size less than 50 patients*

2851. Meredith PA, Pasanisi F, Elliott HL, et al. The effect of nisoldipine on apparent liver blood flow and effective renal plasma flow. British Journal of Clinical Pharmacology 1985; 20(3):235-7. *Sample size less than 50 patients*

2852. Merion RM. Prostaglandins in liver transplantation. Advances in Experimental Medicine & Biology 1997; 433:13-8. *Not CKD treatment*

2853. Merkel C, Gatta A, Donada C, et al. Long-term effect of nadolol or nadolol plus isosorbide-5-mononitrate on renal function and ascites formation in patients with cirrhosis. GTIP Gruppo Triveneto per l'Ipertensione Portale. Hepatology 1995; 22(3):808-13. *Not CKD treatment*

2854. Merten GJ, Burgess WP, Gray LV, et al. Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized controlled trial. JAMA 2004; 291(19):2328-34. *Not relevant to key questions*

2855. Mesotten D, Swinnen JV, Vanderhoydonc F, et al. Contribution of circulating lipids to the improved outcome of critical illness by glycemic control with intensive insulin therapy. Journal of Clinical Endocrinology & Metabolism 2004; 89(1):219-26. *Not relevant to key questions*

2856. Messa P, Macario F, Yaqoob M, et al. The OPTIMA study: assessing a new cinacalcet (Sensipar/Mimpara) treatment algorithm for secondary hyperparathyroidism. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(1):36-45. *Not CKD treatment*

2857. Messerli FH. Combinations in the treatment of hypertension: ACE inhibitors and calcium antagonists. American Journal of Hypertension 1999; 12(8 Pt 2):86S-90S. *Not RCT or controlled trial*

2858. Metra M, Dei Cas L. Clinical efficacy of ibopamine in patients with chronic heart failure. Clinical Cardiology 1995; 18(3 Suppl I):I22-31. *Not CKD treatment*

2859. Metz U, Graben N, Maruhn D, et al. Urinary enzyme excretion after a single dose of phenacetin and paracetamol (acetaminophen) during antidiuresis and during water diuresis. Clinica Chimica Acta 1986; 160(2):151-5. *Sample size less than 50 patients*

2860. Meyer M, Pfarr E, Schirmer G, et al. Therapeutic use of the natriuretic peptide ularitide in acute renal failure. Renal Failure 1999; 21(1):85-100. *Not CKD treatment*

2861. Meyer M, Wiebe K, Wahlers T, et al. Urodilatin (INN:ularitide) as a new drug for the therapy of acute renal failure following cardiac surgery. Clinical & Experimental Pharmacology & Physiology 1997; 24(5):374-6. *Not CKD treatment*

2862. Meyer RD. Risk factors and comparisons of clinical nephrotoxicity of aminoglycosides. American Journal of Medicine 1986; 80(6B):119-25. *Not relevant to key questions*

2863. Meyrier A, Dratwa M, Sennesael J, et al. Fixed low-dose perindopril-indapamide combination in hypertensive patients with chronic renal failure. American Journal of Hypertension 1998; 11(9):1087-92. *Sample size less than 50 patients*

2864. Mezzano D, Tagle R, Pais E, et al. Endothelial cell markers in chronic uremia: relationship with hemostatic defects and severity of renal failure. Thrombosis Research 1997; 88(6):465-72. *Not RCT or controlled trial*

2865. Miao L, Sun J, Yuan H, et al. Combined therapy of low-dose tacrolimus and prednisone in nephrotic syndrome with slight mesangial proliferation. Nephrology 2006; 11(5):449-54. *Not RCT or controlled trial*

2866. Miao X-H, Wang C-G, Hu B-Q, et al. TGF-beta1 immunohistochemistry and promoter methylation in chronic renal failure rats treated with Uremic Clearance Granules. Folia Histochemica et Cytobiologica 2010 Jan; 48(2):284-91. *Not human studies*

2867. Miceli JJ, Wilner KD, Swan SK, et al. Pharmacokinetics, safety, and tolerability of intramuscular ziprasidone in healthy volunteers. Journal of Clinical Pharmacology 2005; 45(6):620-30. *Not relevant to key questions*

2868. Michael M, Elliott EJ, Craig JC, et al. Interventions for hemolytic uremic syndrome and thrombotic thrombocytopenic purpura: a systematic review of randomized controlled trials. American Journal of Kidney Diseases 2009; 53(2):259-72. *Not CKD treatment*

2869. Michael M, Elliott EJ, Ridley GF, et al. Interventions for haemolytic uraemic syndrome and thrombotic thrombocytopenic purpura. Cochrane Database of Systematic Reviews 2009; (1):CD003595. *Not early CKD*

2870. Michalopoulos A, Geroulanos S, Rosmarakis ES, et al. Frequency, characteristics, and predictors of microbiologically documented nosocomial infections after cardiac surgery. European Journal of Cardio-Thoracic Surgery 2006; 29(4):456-60. *Not relevant to key questions*

2871. Mielniczuk LM, Pfeffer MA, Lewis EF, et al. Acute decline in renal function, inflammation, and cardiovascular risk after an acute coronary syndrome. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(11):1811-7. *Not CKD treatment*

2872. Mielniczuk LM, Pfeffer MA, Lewis EF, et al. Estimated glomerular filtration rate, inflammation, and cardiovascular events after an acute coronary syndrome. American Heart Journal 2008; 155(4):725-31. *Not CKD treatment*

2873. Mihatsch MJ, Helmchen U, Casanova P, et al. Kidney biopsy findings in cyclosporine-treated patients with insulin-dependent diabetes mellitus. Klinische Wochenschrift 1991; 69(8):354-9. *Not CKD treatment*

2874. Mihmanli I, Besirli K, Kurugoglu S, et al. Cephalic vein and hemodialysis fistula: surgeon's observation versus color Doppler ultrasonographic findings. Journal of Ultrasound in Medicine 2001; 20(3):217-22. *Not early CKD*

2875. Milas NC, Nowalk MP, Akpele L, et al. Factors associated with adherence to the dietary protein intervention in the Modification of Diet in Renal Disease Study. Journal of the American Dietetic Association 1995; 95(11):1295-300. *Not CKD treatment*

2876. Miller CC, 3rd, Grimm JC, Estrera AL, et al. Postoperative renal function preservation with nonischemic femoral arterial cannulation for thoracoabdominal aortic repair. Journal of Vascular Surgery 2010; 51(1):38-42. *Not RCT or controlled trial*

2877. Miller ER, 3rd, Juraschek SP, Appel LJ, et al. The effect of n-3 long-chain polyunsaturated fatty acid supplementation on urine protein excretion and kidney function: meta-analysis of clinical trials. American Journal of Clinical Nutrition 2009; 89(6):1937-45. *Not CKD treatment*

2878. Miller HI, Dascalu A, Rassin TA, et al. Effects of an acute dose of L-arginine during coronary angiography in patients with chronic renal failure: a randomized, parallel, double-blind clinical trial. American Journal of Nephrology 2003; 23(2):91-5. *Follow-up less than 6 months*

2879. Miller JA. Impact of hyperglycemia on the renin angiotensin system in early human type 1 diabetes mellitus. Journal of the American Society of Nephrology 1999; 10(8):1778-85. *Sample size less than 50 patients*

2880. Miller MA, Texter M, Gmerek A, et al. Quinapril hydrochloride effects on renal function in patients with renal dysfunction and hypertension: a drug-withdrawal study. Cardiovascular Drugs & Therapy 1994; 8(2):271-5. *Sample size less than 50 patients*

2881. Miller PD, Roux C, Boonen S, et al. Safety and efficacy of risedronate in patients with age-related reduced renal function as estimated by the Cockcroft and Gault method: a pooled analysis of nine clinical trials. Journal of Bone & Mineral Research 2005; 20(12):2105-15. *Not RCT or controlled trial*

2882. Miller PD, Schwartz EN, Chen P, et al. Teriparatide in postmenopausal women with osteoporosis and mild or moderate renal impairment. Osteoporosis International 2007; 18(1):59-68. *Not relevant to key questions*

2883. Miller SB, Moulton M, O'Shea M, et al. Effects of IGF-I on renal function in end-stage chronic renal failure. Kidney International 1994; 46(1):201-7. *Not early CKD*

2884. Millis JM, McDiarmid SV, Hiatt JR, et al. Randomized prospective trial of OKT3 for early prophylaxis of rejection after liver transplantation. Transplantation 1989; 47(1):82-8. *Not CKD treatment*

2885. Millward SF, Burbridge BE, Hartman NG, et al. Nephrotoxicity of ioxaglate and ioversol assessed by glomerular filtration rate: a pilot study. Canadian Association of Radiologists Journal 1996; 47(1):24-9. *Sample size less than 50 patients*

2886. Mimran A, Alfaro V. Candesartan: nephroprotective effects and treatment of diabetic nephropathy. Drugs of Today 2003; 39(6):439-50. *Not RCT or controlled trial*

2887. Mimran A, Insua A, Ribstein J, et al. Comparative effect of captopril and nifedipine in normotensive patients with incipient diabetic nephropathy. Diabetes Care 1988; 11(10):850-3. *Follow-up less than 6 months*

2888. Mimran A, Insua A, Ribstein J, et al. Contrasting effects of captopril and nifedipine in normotensive patients with incipient diabetic nephropathy. Journal of Hypertension 1988; 6(11):919-23. *Follow-up less than 6 months*

2889. Mimran A, Ribstein J, DuCailar G. Angiotensin II receptor antagonists and hypertension. Clinical & Experimental Hypertension 1999; 21(5-6):847-58. *Not RCT or controlled trial*

2890. Mimura T, Takenaka T, Kanno Y, et al. Vascular compliance is secured under angiotensin inhibition in non-diabetic chronic kidney diseases. Journal of Human Hypertension 2008; 22(1):38-47. *Not RCT or controlled trial*

2891. Miner SES, Dzavik V, Nguyen-Ho P, et al. N-acetylcysteine reduces contrast-associated nephropathy but not clinical events during long-term follow-up. American Heart Journal 2004; 148(4):690-5. *Not RCT or controlled trial*

2892. Mineshita S, Toyoshima A, Yazaki T. Influence of phenacetin and its metabolites on renal function. Nippon Jinzo Gakkai Shi 1989; Japanese Journal of Nephrology. 31(6):629-33. *Sample size less than 50 patients*

2893. Minetti EE, Cozzi MG, Guidi E. Long- versus short-term effects of two different ACE inhibitors on renal haemodynamics: preliminary results from an ongoing trial. Nephrology Dialysis Transplantation 1995; 10 Suppl 6:18-21. *Sample size less than 50 patients*

2894. Minutolo R, Andreucci M, Balletta MM, et al. Effect of posture on sodium excretion and diuretic efficacy in nephrotic patients. American Journal of Kidney Diseases 2000; 36(4):719-27. *Not RCT or controlled trial*

2895. Miralles R, Cami J, Gutierrez J, et al. Diclofenac versus dipyrone in acute renal colic: a double-blind controlled trial. European Journal of Clinical Pharmacology 1987; 33(5):527-8. *Not CKD treatment*

2896. Miranda ME. The influence of allopurinol on renal deterioration in familial nepropathy associated with hyperuricemia (FNAH). The Spanish Group for the Study of FNAH. Advances in Experimental Medicine & Biology 1994; 370:61-4. *Not CKD treatment*

2897. Mircescu G, Garneata L, Stancu SH, et al. Effects of a supplemented hypoproteic diet in chronic kidney disease. Journal of Renal Nutrition 2007; 17(3):179-88. *Not RCT or controlled trial*

2898. Misra D, Leibowitz K, Gowda RM, et al. Role of N-acetylcysteine in prevention of contrast-induced nephropathy after cardiovascular procedures: a meta-analysis. Clinical Cardiology 2004; 27(11):607-10. *Not relevant to key questions*

2899. Mitaka C, Kudo T, Jibiki M, et al. Effects of human atrial natriuretic peptide on renal function in patients undergoing abdominal aortic aneurysm repair. Critical Care Medicine 2008; 36(3):745-51. *Not RCT or controlled trial*

2900. Mitchell HC, Smith RD, Cutler RE, et al. Racial differences in the renal response to blood pressure lowering during chronic angiotensin-converting enzyme inhibition: a prospective double-blind randomized comparison of fosinopril and lisinopril in older hypertensive patients with chronic renal insufficiency. American Journal of Kidney Diseases 1997; 29(6):897-906. *Sample size less than 50 patients*

2901. Mitrovic V, Seferovic P, Dodic S, et al. Cardio-renal effects of the A1 adenosine receptor antagonist SLV320 in patients with heart failure. Circulation: Heart Failure 2009; 2(6):523-31. *Not CKD treatment*

2902. Mittleman KD. Influence of angiotensin II blockade during exercise in the heat. European Journal of Applied Physiology & Occupational Physiology 1996; 72(5-6):542-7. *Not CKD treatment*

2903. Mix TCH, Brenner RM, Cooper ME, et al. Rationale--Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT): evolving the management of cardiovascular risk in patients with chronic kidney disease.[Erratum appears in Am Heart J. 2005 Jul;150(1):53]. American Heart Journal 2005; 149(3):408-13. *Not relevant to key questions*

2904. Miyagawa K, Dohi Y, Nakazawa A, et al. Renoprotective effect of calcium channel blockers in combination with an angiotensin receptor blocker in elderly patients with hypertension. A randomized crossover trial between benidipine and amlodipine. Clinical & Experimental Hypertension 2010 Jan; 32(1):1-7. *Not CKD treatment*

2905. Miyazaki Y, Cersosimo E, Triplitt C, et al. Rosiglitazone decreases albuminuria in type 2 diabetic patients. Kidney International 2007; 72(11):1367-73. *Follow-up less than 6 months*

2906. Miyoshi H, Ohshiba S, Matsumoto A, et al. Haptoglobin prevents renal dysfunction associated with intravariceal infusion of ethanolamine oleate. American Journal of Gastroenterology 1991; 86(11):1638-41. *Not CKD treatment*

2907. Mocan MZ, Mocan H, Gacar MN, et al. Effect of essential amino acid supplementation in acute renal failure. International Urology & Nephrology 1995; 27(4):503-10. *Not CKD treatment*

2908. Mocroft A, Wyatt C, Szczech L, et al. Interruption of antiretroviral therapy is associated with increased plasma cystatin C. AIDS 2009; 23(1):71-82. *Not CKD treatment*

2909. Mocroft A, Wyatt C, Szczech L, et al. Interruption of antiretroviral therapy is associated with increased plasma cystatin C. AIDS 2009; 23(1):71-82. *Not CKD treatment*

2910. Modesti PA, Vanni S, Morabito M, et al. Role of endothelin-1 in exposure to high altitude: Acute Mountain Sickness and Endothelin-1 (ACME-1) study. Circulation 2006; 114(13):1410-6. *Sample size less than 50 patients*

2911. Modi GK. The death knell for dopamine? National Medical Journal of India 2001; 14(2):88-9. *Not CKD treatment*

2912. Modi NB, Novotny W, Reimann JD, et al. Pharmacokinetics and pharmacodynamics of sibrafiban, an orally administered IIb/IIIa antagonist, in patients with acute coronary syndrome. Journal of Clinical Pharmacology 1999; 39(7):675-84. *Not CKD treatment*

2913. Moe SM, Cunningham J, Bommer J, et al. Long-term treatment of secondary hyperparathyroidism with the calcimimetic cinacalcet HCl. Nephrology Dialysis Transplantation 2005; 20(10):2186-93. *Follow-up less than 6 months*

2914. Moe SM, Saifullah A, LaClair RE, et al. A randomized trial of cholecalciferol versus doxercalciferol for lowering parathyroid hormone in chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2010 Feb; 5(2):299-306. *Follow-up less than 6 months*

2915. Mogensen CE. The reno-protective role of AT(1)-receptor blockers. Journal of Human Hypertension 2002; 16 Suppl 3:S52-8. *Not relevant to key questions*

2916. Mogensen CE, Neldam S, Tikkanen I, et al. Randomised controlled trial of dual blockade of renin-angiotensin system in patients with hypertension, microalbuminuria, and non-insulin dependent diabetes: the candesartan and lisinopril microalbuminuria (CALM) study. BMJ 2000; 321(7274):1440-4. *Follow-up less than 6 months*

2917. Mohammed SF, Korinek J, Chen HH, et al. Nesiritide in acute decompensated heart failure: current status and future perspectives. Reviews in Cardiovascular Medicine 2008; 9(3):151-8. *Not CKD treatment*

2918. Mohanram A, Zhang Z, Shahinfar S, et al. Anemia and end-stage renal disease in patients with type 2 diabetes and nephropathy. Kidney International 2004; 66(3):1131-8. *Not CKD treatment*

2919. Mohanram A, Zhang Z, Shahinfar S, et al. The effect of losartan on hemoglobin concentration and renal outcome in diabetic nephropathy of type 2 diabetes. Kidney International 2008; 73(5):630-6. *Not CKD treatment*

2920. Mohideen P, Bornemann M, Sugihara J, et al. The metabolic effects of troglitazone in patients with diabetes and end-stage renal disease. Endocrine 2005; 28(2):181-6. *Not relevant to key questions*

2921. Mohrke W, Knauf H, Mutschler E. Pharmacokinetics and pharmacodynamics of triamterene and hydrochlorothiazide and their combination in healthy volunteers. International Journal of Clinical Pharmacology & Therapeutics 1997; 35(10):447-52. *Not CKD treatment*

2922. Moist L, Nesrallah G, Kortas C, et al. Plasma exchange in rapidly progressive renal failure due to multiple myeloma. A retrospective case series. American Journal of Nephrology 1999; 19(1):45-50. *Not RCT or controlled trial*

2923. Moist L, Sontrop JM, Gallo K, et al. Effect of N-acetylcysteine on serum creatinine and kidney function: results of a randomized controlled trial. American Journal of Kidney Diseases 2010 Oct; 56(4):643-50. *Follow-up less than 6 months*

2924. Molenaar IQ, Begliomini B, Grazi GL, et al. The effect of aprotinin on renal function in orthotopic liver transplantation. Transplantation 2001; 71(2):247-52. *Not CKD treatment*

2925. Molina CR, Fowler MB, McCrory S, et al. Hemodynamic, renal and endocrine effects of atrial natriuretic peptide infusion in severe heart failure. Journal of the American College of Cardiology 1988; 12(1):175-86. *Sample size less than 50 patients*

2926. Molitch ME, Steffes M, Sun W, et al. Development and progression of renal insufficiency with and without albuminuria in adults with type 1 diabetes in the diabetes control and complications trial and the epidemiology of diabetes interventions and complications study. Diabetes Care 2010 Jul; 33(7):1536-43. *Not relevant to key questions*

2927. Molitch ME, Steffes MW, Cleary PA, et al. Baseline analysis of renal function in the Diabetes Control and Complications Trial. The Diabetes Control and Complications Trial Research Group [corrected].[Erratum appears in Kidney Int 1993 May;43(5):1196]. Kidney International 1993; 43(3):668-74. *Not RCT or controlled trial*

2928. Mollee PN, Wechalekar AD, Pereira DL, et al. Autologous stem cell transplantation in primary systemic amyloidosis: the impact of selection criteria on outcome. Bone Marrow Transplantation 2004; 33(3):271-7. *Not CKD treatment*

2929. Molnar Z, Szakmany T, Koszegi T. Prophylactic N-acetylcysteine decreases serum CRP but not PCT levels and microalbuminuria following major abdominal surgery. A prospective, randomised, double-blinded, placebo-controlled clinical trial. Intensive Care Medicine 2003; 29(5):749-55. *Not CKD treatment*

2930. Molyneaux LM, Willey KA, Yue DK. Indapamide is as effective as captopril in the control of microalbuminuria in diabetes. Journal of Cardiovascular Pharmacology 1996; 27(3):424-7. *Sample size less than 50 patients*

2931. Molzahn AE, Hibbert MP, Gaudet D, et al. Managing chronic kidney disease in a nurse-run, physician-monitored clinic: the CanPREVENT experience. Canadian Journal of Nursing Research 2008; 40(3):96-112. *Not RCT or controlled trial*

2932. Momeni A, Shahidi S, Seirafian S, et al. Effect of allopurinol in decreasing proteinuria in type 2 diabetic patients. Iranian journal of Kidney Diseases 2010 Apr; 4(2):128-32. *Sample size less than 50 patients*

2933. Monaco M, Di Tommaso L, Mottola M, et al. Clinical outcome for on-pump myocardial revascularization in patients with mild renal dysfunction. Thoracic & Cardiovascular Surgeon 2005; 53(1):46-51. *Not relevant to key questions*

2934. Mondorf A, Mondorf W, Banzer S. A multiple-center comparative study of the kidney tolerance of ceftazidime versus cefotaxime and tobramycin. Chemioterapia 1987; 6(2 Suppl):331-2. *Follow-up less than 6 months*

2935. Mondorf AW, Bonsiepe C, Mondorf W. Randomized multi center study comparing nephrotoxicity of ceftazidime versus the combination of piperacillin and netilmicin with and without furosemide. Advances in Experimental Medicine & Biology 1989; 252:307-12. *Not early CKD*

2936. Monier-Faugere MC, Malluche HH. Calcitriol pulse therapy in patients with end-stage renal failure. Current Opinion in Nephrology & Hypertension 1994; 3(6):615-9. *Not early CKD*

2937. Montanari A, Carra N, Perinotto P, et al. Renal hemodynamic control by endothelin and nitric oxide under angiotensin II blockade in man. Hypertension 2002; 39(2 Pt 2):715-20. *Not early CKD*

2938. Montanari A, Tateo E, Fasoli E, et al. Angiotensin II blockade does not prevent renal effects of L-NAME in sodium-repleted humans. Hypertension 1997; 30(3 Pt 2):557-62. *Sample size less than 50 patients*

2939. Montori VM. Should patients with type 2 diabetes focus on glycemic control to reduce their cardiovascular risk? Polskie Archiwum Medycyny Wewnetrznej 2008; 118(9):502-7. *Not CKD treatment*

2940. Moore AEB, Hain SF, Blake GM, et al. Validation of ultrafiltration as a method of measuring free 99mTc-MDP. Journal of Nuclear Medicine 2003; 44(6):891-7. *Not CKD treatment*

2941. Moore KB, McKenna K, Tormey WP, et al. The albuminuric action of atrial natriuretic peptide is not modified by ACE-inhibition with perindopril in Type 2 diabetes. Diabetic Medicine 2003; 20(9):713-6. *Sample size less than 50 patients*

2942. Moore MJ, O'Sullivan B, Tannock IF. Are treatment strategies of urologic oncologists influenced by the opinions of their colleagues? British Journal of Cancer 1990; 62(6):988-91. *Not CKD treatment*

2943. Moore NN, Lapsley M, Norden AG, et al. Does N-acetylcysteine prevent contrast-induced nephropathy during endovascular AAA repair? A randomized controlled pilot study. Journal of Endovascular Therapy: Official Journal of the International Society of Endovascular Specialists 2006; 13(5):660-6. *Sample size less than 50 patients*

2944. Moore RD, Lerner SA, Levine DP. Nephrotoxicity and ototoxicity of aztreonam versus aminoglycoside therapy in seriously ill nonneutropenic patients. Journal of Infectious Diseases 1992; 165(4):683-8. *Not CKD treatment*

2945. Moore RD, Smith CR, Holloway JJ, et al. Cefotaxime vs nafcillin and tobramycin for the treatment of serious infection. Comparative cost-effectiveness. Archives of Internal Medicine 1986; 146(6):1153-7. *Not CKD treatment*

2946. Moore RD, Steinberg EP, Powe NR, et al. Nephrotoxicity of high-osmolality versus low-osmolality contrast media: randomized clinical trial. Radiology 1992; 182(3):649-55. *Not CKD treatment*

2947. Moore WV, Donaldson DL, Chonko AM, et al. Ambulatory blood pressure in type I diabetes mellitus. Comparison to presence of incipient nephropathy in adolescents and young adults. Diabetes 1992; 41(9):1035-41. *Not RCT or controlled trial*

2948. Mor E, Patel T, Glabman S, et al. Comparison of short and long-term renal function in liver transplant patients receiving cyclosporin or FK 506. Transplant International 1994; 7 Suppl 1:S77-80. *Not RCT or controlled trial*

2949. Mora C, Macia M, Navarro JF. Renal failure, anaemia, cytokines and inflammation. Nephrology Dialysis Transplantation 2001; 16(7):1524-5. *Not RCT or controlled trial*

2950. Morales E, Valero MA, Leon M, et al. Beneficial effects of weight loss in overweight patients with chronic proteinuric nephropathies. American Journal of Kidney Diseases 2003; 41(2):319-27. *Sample size less than 50 patients*

2951. Morales JM, Grinyo JM, Campistol JM, et al. Improved renal function, with similar proteinuria, after two years of early tacrolimus withdrawal from a regimen of sirolimus plus tacrolimus. Transplantation 2008; 86(4):620-2. *Not CKD treatment*

2952. Morariu AM, Loef BG, Aarts LPHJ, et al. Dexamethasone: benefit and prejudice for patients undergoing on-pump coronary artery bypass grafting: a study on myocardial, pulmonary, renal, intestinal, and hepatic injury. Chest 2005; 128(4):2677-87. *Not RCT or controlled trial*

2953. Morcos M, Borcea V, Isermann B, et al. Effect of alpha-lipoic acid on the progression of endothelial cell damage and albuminuria in patients with diabetes mellitus: an exploratory study. Diabetes Research & Clinical Practice 2001; 52(3):175-83. *Sample size less than 50 patients*

2954. Moreau ME, Garbacki N, Molinaro G, et al. The kallikrein-kinin system: current and future pharmacological targets. Journal of Pharmacological Sciences 2005; 99(1):6-38. *Not RCT or controlled trial*

2955. Moreau P, Milpied N, Fayette N, et al. Reduced renal toxicity and improved clinical tolerance of amphotericin B mixed with intralipid compared with conventional amphotericin B in neutropenic patients. Journal of Antimicrobial Chemotherapy 1992; 30(4):535-41. *Sample size less than 50 patients*

2956. Moreau R, Lebrec D. Acute kidney injury: new concepts. Hepatorenal syndrome: the role of vasopressors. Nephron. Physiology 2008; 109(4):p73-9. *Not CKD treatment*

2957. Moreira RO, Trujillo FR, Meirelles RM, et al. Use of optical coherence tomography (OCT) and indirect ophthalmoscopy in the diagnosis of macular edema in diabetic patients. International Ophthalmology 2001; 24(6):331-6. *Not CKD treatment*

2958. Morelli A, Ricci Z, Bellomo R, et al. Prophylactic fenoldopam for renal protection in sepsis: a randomized, double-blind, placebo-controlled pilot trial. Critical Care Medicine 2005; 33(11):2451-6. *Not relevant to key questions*

2959. Morgan T, Anderson A, Bertram D, et al. Effect of candesartan and lisinopril alone and in combination on blood pressure and microalbuminuria. Journal of the Renin-Angiotensin-Aldosterone System 2004; 5(2):64-71. *Not CKD treatment*

2960. Morganti A. Randomized clinical trials on surrogate end points: are they useful for evaluating cardiovascular and renal disease protection in hypertension? The case for yes. Journal of the American Society of Nephrology 2006; 17(4 Suppl 2):S141-4. *Not relevant to key questions*

2961. Morgera S, Woydt R, Kern H, et al. Low-dose prostacyclin preserves renal function in high-risk patients after coronary bypass surgery. Critical Care Medicine 2002; 30(1):107-12. *Not early CKD*

2962. Mori TA, Burke V, Puddey I, et al. The effects of [omega]3 fatty acids and coenzyme Q10 on blood pressure and heart rate in chronic kidney disease: a randomized controlled trial. Journal of Hypertension 2009; 27(9):1863-72. *Follow-up less than 6 months*

2963. Morikawa S, Sone T, Tsuboi H, et al. Renal protective effects and the prevention of contrast-induced nephropathy by atrial natriuretic peptide.[Erratum appears in J Am Coll Cardiol. 2009 Sep 15;54(12):1122]. Journal of the American College of Cardiology 2009; 53(12):1040-6. *Not RCT or controlled trial*

2964. Morillas RM, Planas R, Cabre E, et al. Propranolol plus isosorbide-5-mononitrate for portal hypertension in cirrhosis: long-term hemodynamic and renal effects. Hepatology 1994; 20(6):1502-8. *Not CKD treatment*

2965. Morimoto S, Yano Y, Maki K, et al. Renal and vascular protective effects of cilnidipine in patients with essential hypertension. Journal of Hypertension 2007; 25(10):2178-83. *Not RCT or controlled trial*

2966. Morimoto S, Yano Y, Maki K, et al. Renal and vascular protective effects of telmisartan in patients with essential hypertension. Hypertension Research - Clinical & Experimental 2006; 29(8):567-72. *Not RCT or controlled trial*

2967. Morita S, Fukuhara S, Akizawa T, et al. Study design and methods for a clinical trial of an oral carbonaceous adsorbent used to prevent the progression of chronic kidney disease (CAP-KD). Clinical & Experimental Nephrology 2005; 9(3):219-27. *Not CKD treatment*

2968. Morris ST, McMurray JJ, Rodger RS, et al. Impaired endothelium-dependent vasodilatation in uraemia. Nephrology Dialysis Transplantation 2000; 15(8):1194-200. *Sample size less than 50 patients*

2969. Mortelmans LJM, Desruelles D, Baert JA, et al. Use of tramadol drip in controlling renal colic pain. Journal of Endourology 2006; 20(12):1010-5. *Not RCT or controlled trial*

2970. Mortensen BM, Aarseth HP, Ganss R, et al. 24,25-dihydroxy vitamin D3 treatment inhibits parathyroid-stimulated adenylate cyclase in iliac crest biopsies from uremic patients. Bone 1993; 14(2):125-31. *Sample size less than 50 patients*

2971. Mosconi L, Ruggenenti P, Perna A, et al. Nitrendipine and enalapril improve albuminuria and glomerular filtration rate in non-insulin dependent diabetes. Kidney International - Supplement 1996; 55:S91-3. *Sample size less than 50 patients*

2972. Motovska Z, Widimsky P, Petr R, et al. Factors influencing clopidogrel efficacy in patients with stable coronary artery disease undergoing elective percutaneous coronary intervention: statin's advantage and the smoking "paradox". Journal of Cardiovascular Pharmacology 2009; 53(5):368-72. *Not CKD treatment*

2973. Motwani JG, Fenwick MK, McAlpine HM, et al. Effectiveness of captopril in reversing renal vasoconstriction after Q-wave acute myocardial infarction. American Journal of Cardiology 1993; 71(4):281-6. *Sample size less than 50 patients*

2974. Motwani JG, Fenwick MK, Morton JJ, et al. Furosemide-induced natriuresis is augmented by ultra-low-dose captopril but not by standard doses of captopril in chronic heart failure. Circulation 1992; 86(2):439-45. *Sample size less than 50 patients*

2975. Motwani JG, Fenwick MK, Morton JJ, et al. Determinants of the initial effects of captopril on blood pressure, glomerular filtration rate, and natriuresis in mild-to-moderate chronic congestive heart failure secondary to coronary artery disease. American Journal of Cardiology 1994; 73(16):1191-6. *Sample size less than 50 patients*

2976. Motwani JG, Fenwick MK, Struthers AD. Comparison of three methods of glomerular filtration rate measurement with and without captopril pretreatment in groups of patients with left ventricular dysfunction. European Heart Journal 1992; 13(9):1195-200. *Not CKD treatment*

2977. Motwani JG, Lang CC, Cramb G, et al. Natriuretic response to neutral endopeptidase inhibition is blunted by enalapril in healthy men. Hypertension 1995; 25(4 Pt 1):637-42. *Sample size less than 50 patients*

2978. Motwani JG, Struthers AD. Interactive effects of indomethacin, angiotensin II and frusemide on renal haemodynamics and natriuresis in man. British Journal of Clinical Pharmacology 1994; 37(4):355-61. *Not CKD treatment*

2979. Moudgal VV, Sobel JD. Selecting antifungal agents for the treatment of invasive fungal infections in patients with renal failure. Current Opinion in Investigational Drugs 2004; 5(8):873-8. *Follow-up less than 6 months*

2980. Moulder JE, Fish BL, Cohen EP. ACE inhibitors and AII receptor antagonists in the treatment and prevention of bone marrow transplant nephropathy. Current Pharmaceutical Design 2003; 9(9):737-49. *Not relevant to key questions*

2981. Moulin B, Fillastre JP, Godin M, et al. Renal hemodynamics and sodium excretion after acute and chronic administration of cicletanine in normotensive and hypertensive subjects. Journal of Cardiovascular Pharmacology 1995; 25(2):292-9. *Sample size less than 50 patients*

2982. Mourad G, Haecker W, Mion C. Dose-dependent salidiuretic efficacy of torasemide in comparison to furosemide and placebo in advanced renal failure. Arzneimittel-Forschung 1988; 38(1A):205-8. *Sample size less than 50 patients*

2983. Mourad JJ, Le Jeune S. Evaluation of high dose of perindopril/indapamide fixed combination in reducing blood pressure and improving end-organ protection in hypertensive patients. Current Medical Research & Opinion 2009; 25(9):2271-80. *Not RCT or controlled trial*

2984. Moyses C, Higgins TJ. Safety of long-term use of lisinopril for congestive heart failure. American Journal of Cardiology 1992; 70(10):91C-7C. *Not CKD treatment*

2985. Mueck AO, Seeger H, Petersen G, et al. Effect of two oral contraceptives with different ethinyl estradiol and levonorgestrel concentrations on the urinary excretion of biochemical vasoactive markers. Contraception 2001; 64(6):357-62. *Not early CKD*

2986. Mueller AR, Platz KP, Blumhardt G, et al. The optimal immunosuppressant after liver transplantation according to diagnosis: cyclosporine A or FK506? Clinical Transplantation 1995; 9(3 Pt 1):176-84. *Not CKD treatment*

2987. Mueller C. Prevention of contrast-induced nephropathy with volume supplementation. Kidney International - Supplement 2006; (100):S16-9. *Not RCT or controlled trial*

2988. Mueller C, Buerkle G, Buettner HJ, et al. Prevention of contrast media-associated nephropathy: randomized comparison of 2 hydration regimens in 1620 patients undergoing coronary angioplasty. Archives of Internal Medicine 2002; 162(3):329-36. *Not early CKD*

2989. Mueller C, Buerkle G, Perruchoud AP, et al. Female sex and risk of contrast nephropathy after percutaneous coronary intervention. Canadian Journal of Cardiology 2004; 20(5):505-9. *Not relevant to key questions*

2990. Mueller C, Laule-Kilian K, Scholer A, et al. B-type natriuretic peptide for acute dyspnea in patients with kidney disease: insights from a randomized comparison. Kidney International 2005; 67(1):278-84. *Not CKD treatment*

2991. Mueller C, Seidensticker P, Buettner HJ, et al. Incidence of contrast nephropathy in patients receiving comprehensive intravenous and oral hydration. Swiss Medical Weekly 2005; 135(19-20):286-90. *Follow-up less than 6 months*

2992. Muir A, Davidson R, Silverstone T, et al. Two regimens of lithium prophylaxis and renal function. Acta Psychiatrica Scandinavica 1989; 80(6):579-83. *Sample size less than 50 patients*

2993. Muirhead N. A rationale for an individualized haemoglobin target. Nephrology Dialysis Transplantation 2002; 17 Suppl 6:2-7. *Not RCT or controlled trial*

2994. Mukhopadhyay S, Singh M, Cater JI, et al. Nebulised antipseudomonal antibiotic therapy in cystic fibrosis: a meta-analysis of benefits and risks. Thorax 1996; 51(4):364-8. *Not RCT or controlled trial*

2995. Mulec H, Johnsen SA, Bjorck S. Long-term enalapril treatment in diabetic nephropathy. Kidney International - Supplement 1994; 45:S141-4. *Not relevant to key questions*

2996. Mulec H, Johnson SA, Bjorck S. Relation between serum cholesterol and diabetic nephropathy. Lancet 1990; 335(8704):1537-8. *Not RCT or controlled trial*

2997. Mulhauser I, Prange K, Sawicki PT, et al. Effects of dietary sodium on blood pressure in IDDM patients with nephropathy. Diabetologia 1996; 39(2):212-9. *Sample size less than 50 patients*

2998. Munger MA, Gardner SF, Ateshkadi A, et al. Misoprostol effects on diclofenac-induced cardiorenal changes in salt-sensitive patients with hypertension: the MEDIC Study. Pharmacotherapy 2008; 28(7):834-42. *Not CKD treatment*

2999. Munkhaugen J, Lydersen S, Romundstad PR, et al. Kidney function and future risk for adverse pregnancy outcomes: a population-based study from HUNT II, Norway. Nephrology Dialysis Transplantation 2009; 24(12):3744-50. *Not RCT or controlled trial*

3000. Munoz M, Breymann C, Garcia-Erce JA, et al. Efficacy and safety of intravenous iron therapy as an alternative/adjunct to allogeneic blood transfusion. Vox Sanguinis 2008; 94(3):172-83. *Not RCT or controlled trial*

3001. Munoz-Garcia B, Moreno JA, Lopez-Franco O, et al. Tumor necrosis factor-like weak inducer of apoptosis (TWEAK) enhances vascular and renal damage induced by hyperlipidemic diet in ApoE-knockout mice. Arteriosclerosis, Thrombosis & Vascular Biology 2009; 29(12):2061-8. *Follow-up less than 6 months*

3002. Murakami R, Tajima H, Kumazaki T. Effect of iomeprol on renal function immediately after abdominal angiography. Acta Radiologica 1996; 37(6):962-5. *Sample size less than 50 patients*

3003. Murakami R, Tajima H, Kumazaki T, et al. Effect of iodixanol on renal function immediately after abdominal angiography. Clinical comparison with iomeprol and ioxaglate. Acta Radiologica 1998; 39(4):368-71. *Sample size less than 50 patients*

3004. Murayama S, Hirano T, Sakaue T, et al. Low-dose candesartan cilexetil prevents early kidney damage in type 2 diabetic patients with mildly elevated blood pressure. Hypertension Research - Clinical & Experimental 2003; 26(6):453-8. *Not RCT or controlled trial*

3005. Murdoch D, Sager J. Will targeted therapy hold its promise? An evidence-based review. Current Opinion in Oncology 2008; 20(1):104-11. *Follow-up less than 6 months*

3006. Murgia MG, Jordan S, Kahan BD. The side effect profile of sirolimus: a phase I study in quiescent cyclosporine-prednisone-treated renal transplant patients. Kidney International 1996; 49(1):209-16. *Not early CKD*

3007. Muriel C, Ortiz P. Efficacy of two different intramuscular doses of dipyrone in acute renal colic. Cooperative Study Group. Methods & Findings in Experimental & Clinical Pharmacology 1993; 15(7):465-9. *Not CKD treatment*

3008. Muriel-Villoria C, Zungri-Telo E, Diaz-Curiel M, et al. Comparison of the onset and duration of the analgesic effect of dipyrone, 1 or 2 g, by the intramuscular or intravenous route, in acute renal colic. European Journal of Clinical Pharmacology 1995; 48(2):103-7. *Follow-up less than 6 months*

3009. Murphy PT, Casey MC, Walker F, et al. The role of plasmapheresis in myeloma patients with renal failure. Clinical & Laboratory Haematology 1994; 16(4):407. *Not CKD treatment*

3010. Murray MD, Black PK, Kuzmik DD, et al. Acute and chronic effects of nonsteroidal antiinflammatory drugs on glomerular filtration rate in elderly patients. American Journal of the Medical Sciences 1995; 310(5):188-97. *Sample size less than 50 patients*

3011. Murray MD, Greene PK, Brater DC, et al. Effects of flurbiprofen on renal function in patients with moderate renal insufficiency. British Journal of Clinical Pharmacology 1992; 33(4):385-93. *Sample size less than 50 patients*

3012. Muscheites J, Wigger M, Drueckler E, et al. Cinacalcet for secondary hyperparathyroidism in children with end-stage renal disease. Pediatric Nephrology 2008; 23(10):1823-9. *Not CKD treatment*

3013. Musleh GS, Patel NC, Grayson AD, et al. Off-pump coronary artery bypass surgery does not reduce gastrointestinal complications. European Journal of Cardio-Thoracic Surgery 2003; 23(2):170-4. *Not CKD treatment*

3014. Musso P, Cox I, Vidano E, et al. Cardiac troponin elevations in chronic renal failure: prevalence and clinical significance. Clinical Biochemistry 1999; 32(2):125-30. *Not CKD treatment*

3015. Myint L, Tin Nu S, Myint Aye M, et al. Heparin therapy in Russell's viper bite victims with impending dic (a controlled trial). Southeast Asian Journal of Tropical Medicine & Public Health 1989; 20(2):271-7. *Sample size less than 50 patients*

3016. Myles PS, Buckland MR, Schenk NJ, et al. Effect of "renal-dose" dopamine on renal function following cardiac surgery. Anaesthesia & Intensive Care 1993; 21(1):56-61. *Not RCT or controlled trial*

3017. Myrup B, Hansen PM, Jensen T, et al. Effect of low-dose heparin on urinary albumin excretion in insulin-dependent diabetes mellitus. Lancet 1995; 345(8947):421-2. *Sample size less than 50 patients*

3018. Na KY, Han JS, Kim YS, et al. Does albumin preinfusion potentiate diuretic action of furosemide in patients with nephrotic syndrome? Journal of Korean Medical Science 2001; 16(4):448-54. *Sample size less than 50 patients*

3019. Naeije R, Degaute JP. Redistribution of cardiac output to the kidneys by tertatolol does not involve prostaglandins. American Journal of Hypertension 1989; 2(11 Pt 2):241S-4S. *Sample size less than 50 patients*

3020. Naeije R, Fiasse A, Carlier E, et al. Systemic and renal haemodynamic effects of angiotensin converting enzyme inhibition by zabicipril in young and in old normal men. European Journal of Clinical Pharmacology 1993; 44(1):35-9. *Sample size less than 50 patients*

3021. Nagai T. The effect of pancreatic elastase on diabetic nephropathy. Diabetes Research & Clinical Practice 1994; 24(3):161-5. *Not RCT or controlled trial*

3022. Nagaya N, Miyatake K, Uematsu M, et al. Hemodynamic, renal, and hormonal effects of ghrelin infusion in patients with chronic heart failure. Journal of Clinical Endocrinology & Metabolism 2001; 86(12):5854-9. *Sample size less than 50 patients*

3023. Nagaya N, Satoh T, Nishikimi T, et al. Hemodynamic, renal, and hormonal effects of adrenomedullin infusion in patients with congestive heart failure. Circulation 2000; 101(5):498-503. *Sample size less than 50 patients*

3024. Nagler A, Ackerstein A, Ben-Shahar M, et al. Continuous interleukin-2 infusion combined with cyclophosphamide- based combination chemotherapy in the treatment of hemato-oncological malignancies. Results of a phase I-II study. Acta Haematologica 1998; 100(2):63-8. *Sample size less than 50 patients*

3025. Nair KS, Pabico RC, Truglia JA, et al. Mechanism of glomerular hyperfiltration after a protein meal in humans. Role of hormones and amino acids. Diabetes Care 1994; 17(7):711-5. *Not CKD treatment*

3026. Nakamura K, Okamura T, Hayakawa T, et al. Chronic kidney disease is a risk factor for cardiovascular death in a community-based population in Japan: NIPPON DATA90. Circulation Journal 2006; 70(8):954-9. *Follow-up less than 6 months*

3027. Nakamura M, Arakawa N, Kato M. Renal, hormonal, and hemodynamic effects of low-dose infusion of atrial natriuretic factor in acute myocardial infarction. American Heart Journal 1990; 120(5):1078-85. *Not CKD treatment*

3028. Nakamura T, Fujiwara N, Kawagoe Y, et al. Effects of telmisartan and enalapril on renoprotection in patients with mild to moderate chronic kidney disease. European Journal of Clinical Investigation 2010 Sep; 40(9):790-6. *Sample size less than 50 patients*

3029. Nakamura T, Fujiwara N, Sugaya T, et al. Effect of red wine on urinary protein, 8-hydroxydeoxyguanosine, and liver-type fatty acid-binding protein excretion in patients with diabetic nephropathy. Metabolism: Clinical & Experimental 2009; 58(8):1185-90. *Sample size less than 50 patients*

3030. Nakamura T, Inoue T, Fujiwara N, et al. Additional renoprotective effects of azelnidipine combined with angiotensin receptor blockers in patients with diabetic nephropathy. Clinical Nephrology 2008; 70(5):385-92. *Not RCT or controlled trial*

3031. Nakamura T, Inoue T, Sugaya T, et al. Renoprotective effect of telmisartan in patients with chronic kidney disease. Clinical & Experimental Hypertension 2008; 30(7):662-72. *Sample size less than 50 patients*

3032. Nakamura T, Kanno Y, Takenaka T, et al. An angiotensin receptor blocker reduces the risk of congestive heart failure in elderly hypertensive patients with renal insufficiency. Hypertension Research - Clinical & Experimental 2005; 28(5):415-23. *Not relevant to key questions*

3033. Nakamura T, Kawagoe Y, Matsuda T, et al. Oral ADSORBENT AST-120 decreases carotid intima-media thickness and arterial stiffness in patients with chronic renal failure. Kidney & Blood Pressure Research 2004; 27(2):121-6. *Not relevant to key questions*

3034. Nakamura T, Matsuda T, Kawagoe Y, et al. Effect of pioglitazone on carotid intima-media thickness and arterial stiffness in type 2 diabetic nephropathy patients. Metabolism: Clinical & Experimental 2004; 53(10):1382-6. *Follow-up less than 6 months*

3035. Nakamura T, Sato E, Fujiwara N, et al. Comparative effects of benidipine and amlodipine on proteinuria, urinary 8-OHdG, urinary L-FABP, and inflammatory and atherosclerosis markers in early-stage chronic kidney disease. American Journal of the Medical Sciences 2010; 339(2):157-63. *Sample size less than 50 patients*

3036. Nakamura T, Sato E, Fujiwara N, et al. Co-administration of ezetimibe enhances proteinuria-lowering effects of pitavastatin in chronic kidney disease patients partly via a cholesterol-independent manner. Pharmacological Research 2010 Jan; 61(1):58-61. *Sample size less than 50 patients*

3037. Nakamura T, Sugaya T, Kawagoe Y, et al. Effect of pitavastatin on urinary liver-type fatty-acid-binding protein in patients with nondiabetic mild chronic kidney disease. American Journal of Nephrology 2006; 26(1):82-6. *Not RCT or controlled trial*

3038. Nakamura T, Sugaya T, Kawagoe Y, et al. Effect of erythropoietin on urinary liver-type fatty-acid-binding protein in patients with chronic renal failure and anemia. American Journal of Nephrology 2006; 26(3):276-80. *Sample size less than 50 patients*

3039. Nakamura T, Sugaya T, Kawagoe Y, et al. Azelnidipine reduces urinary protein excretion and urinary liver-type fatty acid binding protein in patients with hypertensive chronic kidney disease. American Journal of the Medical Sciences 2007; 333(6):321-6. *Follow-up less than 6 months*

3040. Nakamura T, Sugaya T, Kawagoe Y, et al. Effect of pitavastatin on urinary liver-type fatty acid-binding protein levels in patients with early diabetic nephropathy. Diabetes Care 2005; 28(11):2728-32. *Sample size less than 50 patients*

3041. Nakamura T, Ushiyama C, Hirokawa K, et al. Effect of cerivastatin on urinary albumin excretion and plasma endothelin-1 concentrations in type 2 diabetes patients with microalbuminuria and dyslipidemia. American Journal of Nephrology 2001; 21(6):449-54. *Not relevant to key questions*

3042. Nakamura T, Ushiyama C, Osada S, et al. Pioglitazone reduces urinary podocyte excretion in type 2 diabetes patients with microalbuminuria. Metabolism: Clinical & Experimental 2001; 50(10):1193-6. *Sample size less than 50 patients*

3043. Nakamura T, Ushiyama C, Shimada N, et al. Effect of the antiplatelet drug dilazep dihydrochloride on urinary podocytes in patients in the early stage of diabetic nephropathy. Diabetes Care 2000; 23(8):1168-71. *Not RCT or controlled trial*

3044. Nakamura T, Ushiyama C, Suzuki S, et al. Comparison between the angiotensin II receptor antagonist candesartan cilexetil and the angiotensin-converting enzyme inhibitor trandolapril in microalbuminuria of patients with early diabetic nephropathy. Nephron 2000; 86(2):247. *Follow-up less than 6 months*

3045. Nakamura T, Ushiyama C, Suzuki Y, et al. Hemoperfusion with polymyxin B immobilized fibers for urinary albumin excretion in septic patients with trauma. ASAIO Journal 2002; 48(3):244-8. *Not early CKD*

3046. Nakano S, Takekoshi H, Nakano M. Chlorella pyrenoidosa supplementation reduces the risk of anemia, proteinuria and edema in pregnant women. Plant Foods for Human Nutrition 2010 Mar; 65(1):25-30. *Not early CKD*

3047. Nakano T, Ninomiya T, Sumiyoshi S, et al. Association of kidney function with coronary atherosclerosis and calcification in autopsy samples from Japanese elders: the Hisayama study. American Journal of Kidney Diseases 2010; 55(1):21-30. *Not RCT or controlled trial*

3048. Nakao N, Seno H, Kasuga H, et al. Effects of combination treatment with losartan and trandolapril on office and ambulatory blood pressures in non-diabetic renal disease: a COOPERATE-ABP substudy. American Journal of Nephrology 2004; 24(5):543-8. *Not RCT or controlled trial*

3049. Nakao N, Yoshimura A, Morita H, et al. Combination treatment of angiotensin-II receptor blocker and angiotensin-converting-enzyme inhibitor in non-diabetic renal disease (COOPERATE): a randomised controlled trial.[Erratum appears in Lancet. 2003 Apr 5;361(9364):1230].[Retraction in Lancet. 2009 Oct 10;374(9697):1226; PMID: 19819378]. Lancet 2003; 361(9352):117-24. *Not CKD treatment*

3050. Nakao N, Yoshimura A, Morita H, et al. Combination treatment of angiotensin-II receptor blocker and angiotensin-converting-enzyme inhibitor in non-diabetic renal disease (COOPERATE): a randomised controlled trial.[Erratum appears in Lancet. 2003 Apr 5;361(9364):1230].[Retraction in Lancet. 2009 Oct 10;374(9697):1226; PMID: 19819378]. Lancet 2003; 361(9352):117-24. *Not CKD treatment*

3051. Nakao T, Yoshino M, Matsumoto H, et al. Low-density lipoprotein apheresis retards the progression of hyperlipidemic overt diabetic nephropathy. Kidney International - Supplement 1999; 71:S206-9. *Sample size less than 50 patients*

3052. Nakayama Y, Nonoguchi H, Kohda Y, et al. Different Mechanisms for the Progression of CKD with ACE Gene Polymorphisms. Nephron 2009; 111(4):c240-6. *Not RCT or controlled trial*

3053. Nallamothu BK, Shojania KG, Saint S, et al. Is acetylcysteine effective in preventing contrast-related nephropathy? A meta-analysis. American Journal of Medicine 2004; 117(12):938-47. *Not relevant to key questions*

3054. Nalysnyk L, Fahrbach K, Reynolds MW, et al. Adverse events in coronary artery bypass graft (CABG) trials: a systematic review and analysis. Heart 2003; 89(7):767-72. *Not CKD treatment*

3055. Nanayakkara PWB, Kiefte-de Jong JC, Stehouwer CDA, et al. Association between global leukocyte DNA methylation, renal function, carotid intima-media thickness and plasma homocysteine in patients with stage 2-4 chronic kidney disease. Nephrology Dialysis Transplantation 2008; 23(8):2586-92. *Not CKD treatment*

3056. Nanayakkara PWB, Kiefte-de Jong JC, ter Wee PM, et al. Randomized placebo-controlled trial assessing a treatment strategy consisting of pravastatin, vitamin E, and homocysteine lowering on plasma asymmetric dimethylarginine concentration in mild to moderate CKD. American Journal of Kidney Diseases 2009; 53(1):41-50. *Not CKD treatment*

3057. Nanayakkara PWB, Teerlink T, Stehouwer CDA, et al. Plasma asymmetric dimethylarginine (ADMA) concentration is independently associated with carotid intima-media thickness and plasma soluble vascular cell adhesion molecule-1 (sVCAM-1) concentration in patients with mild-to-moderate renal failure. Kidney International 2005; 68(5):2230-6. *Sample size less than 50 patients*

3058. Nanayakkara PWB, van Guldener C, ter Wee PM, et al. Effect of a treatment strategy consisting of pravastatin, vitamin E, and homocysteine lowering on carotid intima-media thickness, endothelial function, and renal function in patients with mild to moderate chronic kidney disease: results from the Anti-Oxidant Therapy in Chronic Renal Insufficiency (ATIC) Study. Archives of Internal Medicine 2007; 167(12):1262-70. *Not RCT or controlled trial*

3059. Nangaku M, Fliser D. Erythropoiesis-stimulating agents: past and future. Kidney International - Supplement 2007; (107):S1-3. *Not RCT or controlled trial*

3060. Nankervis A, Nicholls K, Kilmartin G, et al. Effects of perindopril on renal histomorphometry in diabetic subjects with microalbuminuria: a 3-year placebo-controlled biopsy study. Metabolism: Clinical & Experimental 1998; 47(12 Suppl 1):12-5. *Sample size less than 50 patients*

3061. Nash RA, Etzioni R, Storb R, et al. Tacrolimus (FK506) alone or in combination with methotrexate or methylprednisolone for the prevention of acute graft-versus-host disease after marrow transplantation from HLA-matched siblings: a single-center study. Blood 1995; 85(12):3746-53. *Sample size less than 50 patients*

3062. Natov S, Hannedouche T, Schmitt F, et al. Are the renal haemodynamic and natriuretic effects of calcium antagonists and angiotensin converting inhibitors additive? Journal of Hypertension - Supplement 1991; 9(6):S392-3. *Sample size less than 50 patients*

3063. Naughton F, Wijeysundera D, Karkouti K, et al. N-acetylcysteine to reduce renal failure after cardiac surgery: a systematic review and meta-analysis. Canadian Journal of Anaesthesia 2008; 55(12):827-35. *Not CKD treatment*

3064. Navaneethan SD, Nigwekar SU, Sehgal AR, et al. Aldosterone antagonists for preventing the progression of chronic kidney disease. Cochrane Database of Systematic Reviews 2009; (3):CD007004. *Not RCT or controlled trial*

3065. Navaneethan SD, Nigwekar SU, Sehgal AR, et al. Aldosterone antagonists for preventing the progression of chronic kidney disease: a systematic review and meta-analysis. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(3):542-51. *Follow-up less than 6 months*

3066. Navaneethan SD, Pansini F, Strippoli GFM. Statins in patients with chronic kidney disease: evidence from systematic reviews and randomized clinical trials. PLoS Medicine / Public Library of Science 2006; 3(5):e123. *Not relevant to key questions*

3067. Navaneethan SD, Singh S, Appasamy S, et al. Sodium bicarbonate therapy for prevention of contrast-induced nephropathy: a systematic review and meta-analysis. American Journal of Kidney Diseases 2009; 53(4):617-27. *Not CKD treatment*

3068. Navarro JF, Mora C, Muros M, et al. Additive antiproteinuric effect of pentoxifylline in patients with type 2 diabetes under angiotensin II receptor blockade: a short-term, randomized, controlled trial. Journal of the American Society of Nephrology 2005; 16(7):2119-26. *Follow-up less than 6 months*

3069. Navarro JF, Mora C, Muros M, et al. Effects of pentoxifylline administration on urinary N-acetyl-beta-glucosaminidase excretion in type 2 diabetic patients: a short-term, prospective, randomized study. American Journal of Kidney Diseases 2003; 42(2):264-70. *Sample size less than 50 patients*

3070. Navarro JF, Mora C, Rivero A, et al. Urinary protein excretion and serum tumor necrosis factor in diabetic patients with advanced renal failure: effects of pentoxifylline administration. American Journal of Kidney Diseases 1999; 33(3):458-63. *Sample size less than 50 patients*

3071. Naviglio S, Pirozzi F. Renin-Angiotensin system blockade for diabetic nephropathy prevention. American Journal of Cardiology 2010 May 15; 105(10):1505. *Not RCT or controlled trial*

3072. Navis G, de Jong PE, Donker AJ, et al. Moderate sodium restriction in hypertensive subjects: renal effects of ACE-inhibition. Kidney International 1987; 31(3):815-9. *Follow-up less than 6 months*

3073. Naylor CD, Detsky AS, O'Rourke K, et al. Does treatment with essential amino acids and hypertonic glucose improve survival in acute renal failure?: A meta-analysis. Renal Failure 1987; 10(3-4):141-52. *Not relevant to key questions*

3074. Nazir FS, Overell JR, Bolster A, et al. Effect of perindopril on cerebral and renal perfusion on normotensives in mild early ischaemic stroke: a randomized controlled trial. Cerebrovascular Diseases 2005; 19(2):77-83. *Follow-up less than 6 months*

3075. Nazir FS, Overell JR, Bolster A, et al. The effect of losartan on global and focal cerebral perfusion and on renal function in hypertensives in mild early ischaemic stroke. Journal of Hypertension 2004; 22(5):989-95. *Not CKD treatment*

3076. Negri AL. Prevention of progressive fibrosis in chronic renal diseases: antifibrotic agents. Journal of Nephrology 2004; 17(4):496-503. *Not relevant to key questions*

3077. Negrier S, Perol D, Ravaud A, et al. Randomized study of intravenous versus subcutaneous interleukin-2, and IFNalpha in patients with good prognosis metastatic renal cancer. Clinical Cancer Research 2008; 14(18):5907-12. *Not CKD treatment*

3078. Nellemann B, Gormsen LC, Dollerup J, et al. Simvastatin reduces plasma osteoprotegerin in type 2 diabetic patients with microalbuminuria. Diabetes Care 2007; 30(12):3122-4. *Not RCT or controlled trial*

3079. Nelson CE, Nylander C, Olsson AM, et al. Rectal v. intravenous administration of indomethacin in the treatment of renal colic. Acta Chirurgica Scandinavica 1988; 154(4):253-5. *Not relevant to key questions*

3080. Nergelius G, Vinge E, Bengtsson HI, et al. No effect of diclofenac on the pharmacokinetics of cloxacillin. Pharmacology & Toxicology 1997; 81(1):26-30. *Not CKD treatment*

3081. Neri S, Bruno CM, Leotta C, et al. Early endothelial alterations in non-insulin-dependent diabetes mellitus. International Journal of Clinical & Laboratory Research 1998; 28(2):100-3. *Not CKD treatment*

3082. Nesher G, Sonnenblick M, Dwolatzky T. Protective effect of misoprostol on indomethacin induced renal dysfunction in elderly patients. Journal of Rheumatology 1995; 22(4):713-6. *Sample size less than 50 patients*

3083. Netelenbos JC, Asscheman H, Lips P, et al. Absence of effect of 24,25-dihydroxyvitamin D3 in primary hyperparathyroidism. Journal of Clinical Endocrinology & Metabolism 1986; 63(1):246-8. *Sample size less than 50 patients*

3084. Neuberger JM, Mamelok RD, Neuhaus P, et al. Delayed introduction of reduced-dose tacrolimus, and renal function in liver transplantation: the 'ReSpECT' study. American Journal of Transplantation 2009; 9(2):327-36. *Not RCT or controlled trial*

3085. Neuhaus PJ. Optimised first-line FK506-based protocols in liver transplantation: experience from the University Hospital Rudolf Virchow, Berlin. Transplantation Proceedings 1994; 26(6):3264-6. *Not RCT or controlled trial*

3086. Neuhofer W, Pittrow D. Endothelin receptor selectivity in chronic kidney disease: rationale and review of recent evidence. European Journal of Clinical Investigation 2009; 39 Suppl 2:50-67. *Not early CKD*

3087. Neumann DR, Esselstyn CB, Jr., Madera A, et al. Parathyroid detection in secondary hyperparathyroidism with 123I/99mTc-sestamibi subtraction single photon emission computed tomography. Journal of Clinical Endocrinology & Metabolism 1998; 83(11):3867-71. *Not CKD treatment*

3088. Neumayer HH, Gellert J, Luft FC. Calcium antagonists and renal protection. Renal Failure 1993; 15(3):353-8. *Not RCT or controlled trial*

3089. Neumayer HH, Junge W, Kufner A, et al. Prevention of radiocontrast-media-induced nephrotoxicity by the calcium channel blocker nitrendipine: a prospective randomised clinical trial. Nephrology Dialysis Transplantation 1989; 4(12):1030-6. *Not CKD treatment*

3090. Neumayer HH, Kunzendorf U. Renal protection with the calcium antagonists. Journal of Cardiovascular Pharmacology 1991; 18 Suppl 1:S11-8. *Not relevant to key questions*

3091. Neuringer JR, Levey AS. Strategies to slow the progression of renal disease. Seminars in Nephrology 1994; 14(3):261-73. *Not RCT or controlled trial*

3092. New JP, Marshall SM, Bilous RW. Renal autoregulation is normal in newly diagnosed, normotensive, NIDDM patients. Diabetologia 1998; 41(2):206-11. *Sample size less than 50 patients*

3093. Newell DR, Eeles RA, Gumbrell LA, et al. Carboplatin and etoposide pharmacokinetics in patients with testicular teratoma. Cancer Chemotherapy & Pharmacology 1989; 23(6):367-72. *Not CKD treatment*

3094. Newman PJ, Quinn AC, Hall GM, et al. Circulating fluoride changes and hepatorenal function following sevoflurane anaesthesia. Anaesthesia 1994; 49(11):936-9. *Not CKD treatment*

3095. Newman TJ, Dreslinski GR, Tadros SS. Safety profile of aztreonam in clinical trials. Reviews of Infectious Diseases 1985; 7 Suppl 4:S648-55. *Not RCT or controlled trial*

3096. Ng TMH, Shurmur SW, Silver M, et al. Comparison of N-acetylcysteine and fenoldopam for preventing contrast-induced nephropathy (CAFCIN). International Journal of Cardiology 2006; 109(3):322-8. *Follow-up less than 6 months*

3097. Ngan HY, Choo YC, Cheung M, et al. A randomized study of high-dose versus low-dose cis-platinum combined with cyclophosphamide in the treatment of advanced ovarian cancer. Hong Kong Ovarian Carcinoma Study Group. Chemotherapy 1989; 35(3):221-7. *Not CKD treatment*

3098. Ngugi NN, McLigeyo SO, Kayima JK. Treatment of hyperkalaemia by altering the transcellular gradient in patients with renal failure: effect of various therapeutic approaches. East African Medical Journal 1997; 74(8):503-9. *Follow-up less than 6 months*

3099. Nguyen M, Chung EP. Telithromycin: the first ketolide antimicrobial. Clinical Therapeutics 2005; 27(8):1144-63. *Not CKD treatment*

3100. Nguyen SA, Suranyi P, Ravenel JG, et al. Iso-osmolality versus low-osmolality iodinated contrast medium at intravenous contrast-enhanced CT: effect on kidney function. Radiology 2008; 248(1):97-105. *Not RCT or controlled trial*

3101. Nguyen TC, Stegmayr B, Busund R, et al. Plasma therapies in thrombotic syndromes. International Journal of Artificial Organs 2005; 28(5):459-65. *Follow-up less than 6 months*

3102. Niccoli L, Bellino S, Cantini F. Renal tolerability of three commonly employed non-steroidal anti-inflammatory drugs in elderly patients with osteoarthritis. Clinical & Experimental Rheumatology 2002; 20(2):201-7. *Not early CKD*

3103. Nicholls MG, Arakawa K. Angiotensin-converting enzyme inhibitors in congestive heart failure. Journal of Cardiovascular Pharmacology 1987; 9 Suppl 3:S19-21. *Not relevant to key questions*

3104. Nicholls SJ, Tuzcu EM, Hsu A, et al. Comparison of coronary atherosclerotic volume in patients with glomerular filtration rates < or = 60 versus > 60 ml/min/1.73 m(2): a meta-analysis of intravascular ultrasound studies. American Journal of Cardiology 2007; 99(6):813-6. *Not relevant to key questions*

3105. Nichols GA, Arondekar B, Herman WH. Complications of dysglycemia and medical costs associated with nondiabetic hyperglycemia. American Journal of Managed Care 2008; 14(12):791-8. *Not CKD treatment*

3106. Nicholson ML, Baker DM, Hopkinson BR, et al. Randomized controlled trial of the effect of mannitol on renal reperfusion injury during aortic aneurysm surgery. British Journal of Surgery 1996; 83(9):1230-3. *Sample size less than 50 patients*

3107. Nieburg I, Kahan T. Cardiovascular risk factors are not treated to target in hypertensive patients in primary care. Blood Pressure 2010 Jun; 19(3):176-81. *Not CKD treatment*

3108. Nielsen CB, Bech JN, Pedersen EB. Effects of prostacyclin on renal haemodynamics, renal tubular function and vasoactive hormones in healthy humans. A placebo-controlled dose-response study. British Journal of Clinical Pharmacology 1997; 44(5):471-6. *Sample size less than 50 patients*

3109. Nielsen CB, Eiskjaer H, Pedersen EB. Enhanced renal production of cyclic GMP and reduced free water clearance during sodium nitroprusside infusion in healthy man. European Journal of Clinical Investigation 1993; 23(6):375-81. *Sample size less than 50 patients*

3110. Nielsen CB, Pedersen EB. Effect of pinacidil on renal haemodynamics, tubular function and plasma levels of angiotensin II, aldosterone and atrial natriuretic peptide in healthy man. European Journal of Clinical Pharmacology 1993; 45(1):29-35. *Sample size less than 50 patients*

3111. Nielsen CB, Pedersen EB. Abnormal distal tubular sodium reabsorption during dopamine infusion in patients with essential hypertension evaluated by the lithium clearance methods. Clinical Nephrology 1997; 47(5):304-9. *Sample size less than 50 patients*

3112. Nielsen FS. Diabetic nephropathy in non-insulin dependent diabetes mellitus. Cardiovascular risk factors and antihypertensive treatment. Danish Medical Bulletin 2000; 47(4):249-70. *Not relevant to key questions*

3113. Nielsen FS, Gaede P, Vedel P, et al. White coat hypertension in NIDDM patients with and without incipient and overt diabetic nephropathy. Diabetes Care 1997; 20(5):859-63. *Follow-up less than 6 months*

3114. Nielsen FS, Rossing P, Gall MA, et al. Impact of lisinopril and atenolol on kidney function in hypertensive NIDDM subjects with diabetic nephropathy. Diabetes 1994; 43(9):1108-13. *Sample size less than 50 patients*

3115. Nielsen FS, Rossing P, Gall MA, et al. Long-term effect of lisinopril and atenolol on kidney function in hypertensive NIDDM subjects with diabetic nephropathy. Diabetes 1997; 46(7):1182-8. *Sample size less than 50 patients*

3116. Nielsen FS, Rossing P, Gall MA, et al. Lisinopril improves endothelial dysfunction in hypertensive NIDDM subjects with diabetic nephropathy. Scandinavian Journal of Clinical & Laboratory Investigation 1997; 57(5):427-34. *Sample size less than 50 patients*

3117. Nielsen HK, Krusell L, Baelum J, et al. Renal effects of acute exposure to toluene. A controlled clinical trial. Acta Medica Scandinavica 1985; 218(3):317-21. *Sample size less than 50 patients*

3118. Nielsen HK, Thomsen K, Eriksen EF, et al. The effects of high-dose glucocorticoid administration on serum bone gamma carboxyglutamic acid-containing protein, serum alkaline phosphatase and vitamin D metabolites in normal subjects. Bone & Mineral 1988; 4(1):105-13. *Follow-up less than 6 months*

3119. Nielsen OM, Engell HC. Effects of maintaining normal plasma colloid osmotic pressure on renal function and excretion of sodium and water after major surgery. A randomized study. Danish Medical Bulletin 1985; 32(3):182-5. *Sample size less than 50 patients*

3120. Nielsen S, Dollerup J, Nielsen B, et al. Losartan reduces albuminuria in patients with essential hypertension. An enalapril controlled 3 months study. Nephrology Dialysis Transplantation 1997; 12 Suppl 2:19-23. *Sample size less than 50 patients*

3121. Nielsen S, Dollerup J, Nielsen B, et al. Combination of enalapril and low-dose thiazide reduces normoalbuminuria in essential hypertension. Journal of Hypertension 1998; 16(10):1539-44. *Follow-up less than 6 months*

3122. Nielsen S, Hove KY, Dollerup J, et al. Losartan modifies glomerular hyperfiltration and insulin sensitivity in type 1 diabetes. Diabetes, Obesity & Metabolism 2001; 3(6):463-71. *Sample size less than 50 patients*

3123. Nielsen S, Schmitz A, Bacher T, et al. Transcapillary escape rate and albuminuria in Type II diabetes. Effects of short-term treatment with low-molecular weight heparin. Diabetologia 1999; 42(1):60-7. *Not RCT or controlled trial*

3124. Nielsen S, Schmitz O, Moller N, et al. Renal function and insulin sensitivity during simvastatin treatment in type 2 (non-insulin-dependent) diabetic patients with microalbuminuria. Diabetologia 1993; 36(10):1079-86. *Sample size less than 50 patients*

3125. Nielsen SE, Sugaya T, Tarnow L, et al. Tubular and glomerular injury in diabetes and the impact of ACE inhibition. Diabetes Care 2009; 32(9):1684-8. *Not RCT or controlled trial*

3126. Niemczyk S, Sikorska H, Wiecek A, et al. A super-agonist of growth hormone-releasing hormone causes rapid improvement of nutritional status in patients with chronic kidney disease. Kidney International 2010 Mar; 77(5):450-8. *Not early CKD*

3127. Nigwekar SU, Kandula P, Hix JK, et al. Off-pump coronary artery bypass surgery and acute kidney injury: a meta-analysis of randomized and observational studies. American Journal of Kidney Diseases 2009; 54(3):413-23. *Not RCT or controlled trial*

3128. Nigwekar SU, Navaneethan SD, Parikh CR, et al. Atrial natriuretic peptide for preventing and treating acute kidney injury. Cochrane Database of Systematic Reviews 2009; (4):CD006028. *Not RCT or controlled trial*

3129. Nigwekar SU, Navaneethan SD, Parikh CR, et al. Atrial natriuretic peptide for management of acute kidney injury: a systematic review and meta-analysis. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(2):261-72. *Not CKD treatment*

3130. Nigwekar SU, Navaneethan SD, Parikh CR, et al. Atrial natriuretic peptide for management of acute kidney injury: a systematic review and meta-analysis. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(2):261-72. *Not CKD treatment*

3131. Nikolov IG, Mozar A, Drueke TB, et al. Impact of disturbances of calcium and phosphate metabolism on vascular calcification and clinical outcomes in patients with chronic kidney disease. Blood Purification 2009; 27(4):350-9. *Not CKD treatment*

3132. Nikolsky E, Mehran R, Dangas G, et al. Development and validation of a prognostic risk score for major bleeding in patients undergoing percutaneous coronary intervention via the femoral approach. European Heart Journal 2007; 28(16):1936-45. *Follow-up less than 6 months*

3133. Nilsen L, Djoseland O, Rootwelt K, et al. Effects of short-term treatment with naproxen on kidney function in insulin-dependent diabetic patients with microalbuminuria. Scandinavian Journal of Clinical & Laboratory Investigation 1991; 51(7):591-7. *Sample size less than 50 patients*

3134. Nilsen OG, Sellevold OF, Romfo OS, et al. Pharmacokinetics and effects on renal function following cilazapril and hydrochlorothiazide alone and in combination in healthy subjects and hypertensive patients. British Journal of Clinical Pharmacology 1989; 27 Suppl 2:323S-8S. *Not relevant to key questions*

3135. Ninomiya T, Perkovic V, de Galan BE, et al. Albuminuria and kidney function independently predict cardiovascular and renal outcomes in diabetes. Journal of the American Society of Nephrology 2009; 20(8):1813-21. *Not early CKD*

3136. Ninomiya T, Perkovic V, Gallagher M, et al. Lower blood pressure and risk of recurrent stroke in patients with chronic kidney disease: PROGRESS trial. Kidney International 2008; 73(8):963-70. *Not CKD treatment*

3137. Ninomiya Y, Arakawa M. Renal effects of prostaglandin E1 in type 2 (non-insulin-dependent) diabetic patients with subclinical nephropathy. Diabetes Research 1989; 10(3):129-34. *Follow-up less than 6 months*

3138. Nishimura M, Sasaki T, Ohishi A, et al. Angiotensin-converting enzyme inhibitors and probucol suppress the time-dependent increase in urinary Type IV collagen excretion of Type II diabetes mellitus patients with early diabetic nephropathy. Clinical Nephrology 2001; 56(2):96-103. *Not early CKD*

3139. Nishizawa Y, Shoji T. Does paricalcitol reduce proteinuria in patients with chronic kidney disease? Nature Clinical Practice Nephrology 2006; 2(7):352-3. *Not RCT or controlled trial*

3140. Nissel R, Fischer D-C, Puhlmann A, et al. Short-term growth hormone treatment and microcirculation: effects in patients with chronic kidney disease. Microvascular Research 2009; 78(2):246-52. *Not RCT or controlled trial*

3141. Nitsch D, Felber Dietrich D, von Eckardstein A, et al. Prevalence of renal impairment and its association with cardiovascular risk factors in a general population: results of the Swiss SAPALDIA study. Nephrology Dialysis Transplantation 2006; 21(4):935-44. *Not adult population*

3142. Nitsch D, Lawlor DA, Patel R, et al. The association of renal impairment with all-cause and cardiovascular disease mortality. Nephrology Dialysis Transplantation 2010 Apr; 25(4):1191-9. *Not CKD treatment*

3143. Nix DE, Thomas JK, Symonds WT, et al. Assessment of the enzymuria resulting from gentamicin alone and combinations of gentamicin with various beta-lactam antibiotics. Annals of Pharmacotherapy 1997; 31(6):696-703. *Not CKD treatment*

3144. Nohria A, Hasselblad V, Stebbins A, et al. Cardiorenal interactions: insights from the ESCAPE trial. Journal of the American College of Cardiology 2008; 51(13):1268-74. *Not CKD treatment*

3145. Nolan CR, Califano JR, Butzin CA. Influence of calcium acetate or calcium citrate on intestinal aluminum absorption. Kidney International 1990; 38(5):937-41. *Not CKD treatment*

3146. Nolasco F, Cameron JS, Heywood EF, et al. Adult-onset minimal change nephrotic syndrome: a long-term follow-up. Kidney International 1986; 29(6):1215-23. *Follow-up less than 6 months*

3147. Nolin TD, Ouseph R, Himmelfarb J, et al. Multiple-dose pharmacokinetics and pharmacodynamics of N-acetylcysteine in patients with end-stage renal disease. Clinical Journal of The American Society of Nephrology: CJASN 2010 Sep; 5(9):1588-94. *Follow-up less than 6 months*

3148. Noone M, Pomeroy L, Sage R, et al. Prospective study of amikacin versus netilmicin in the treatment of severe infection in hospitalized patients. American Journal of Medicine 1989; 86(6 Pt 2):809-13. *Not CKD treatment*

3149. Noormohamed FH, Fuller GN, Lant AF. Effect of salt balance on the renal and hemodynamic actions of benazepril in normal men. Journal of Clinical Pharmacology 1989; 29(10):928-37. *Sample size less than 50 patients*

3150. Noormohamed FH, Lant AF. Renal handling of lithium and the effects of mannitol and arginine vasopressin in man. Clinical Science 1995; 89(1):27-36. *Sample size less than 50 patients*

3151. Nordal KP, Dahl E. Low dose calcitriol versus placebo in patients with predialysis chronic renal failure. Journal of Clinical Endocrinology & Metabolism 1988; 67(5):929-36. *Sample size less than 50 patients*

3152. Nordenstrom E, Westerdahl J, Bergenfelz A. Effect on bone density of postoperative calcium and vitamin-D supplementation in patients with primary hyperparathyroidism: A retrospective study. Langenbecks Archives of Surgery 2009; 394(3):461-7. *Not CKD treatment*

3153. Norgaard K, Feldt-Rasmussen B. Sodium retention and insulin treatment in insulin-dependent diabetes mellitus. Acta Diabetologica 1994; 31(1):19-25. *Sample size less than 50 patients*

3154. Norgaard K, Jensen T, Christensen P, et al. A comparison of spirapril and isradipine in patients with diabetic nephropathy and hypertension. Blood Pressure 1993; 2(4):301-8. *Sample size less than 50 patients*

3155. Norgaard K, Jensen T, Skott P, et al. Effects of insulin on renal haemodynamics and sodium handling in normal subjects. Scandinavian Journal of Clinical & Laboratory Investigation 1991; 51(4):367-76. *Sample size less than 50 patients*

3156. Norlund L, Fex G, Lanke J, et al. Reference intervals for the glomerular filtration rate and cell-proliferation markers: serum cystatin C and serum beta 2-microglobulin/cystatin C-ratio. Scandinavian Journal of Clinical & Laboratory Investigation 1997; 57(6):463-70. *Not RCT or controlled trial*

3157. Norman RW, Butler GJ, MacDiarmid SA, et al. 111Indium-oxine-labeled leukocytes and 67gallium-citrate as indicators of renal injury following extracorporeal shock wave lithotripsy. Journal of Urology 1992; 148(3 Pt 2):1022-4. *Sample size less than 50 patients*

3158. Norris K, Vaughn C. The role of renin-angiotensin-aldosterone system inhibition in chronic kidney disease. Expert Review of Cardiovascular Therapy 2003; 1(1):51-63. *Not early CKD*

3159. Norris KC, Greene T, Kopple J, et al. Baseline predictors of renal disease progression in the African American Study of Hypertension and Kidney Disease. Journal of the American Society of Nephrology 2006; 17(10):2928-36. *Not RCT or controlled trial*

3160. North RA, Taylor RS, Schellenberg JC. Evaluation of a definition of pre-eclampsia. British Journal of Obstetrics & Gynaecology 1999; 106(8):767-73. *Not RCT or controlled trial*

3161. Northridge DB, Jardine AG, Findlay IN, et al. Inhibition of the metabolism of atrial natriuretic factor causes diuresis and natriuresis in chronic heart failure. American Journal of Hypertension 1990; 3(9):682-7. *Not CKD treatment*

3162. Nosrati SM, Khwaja S, el-Shahawy M, et al. Effect of angiotensin converting enzyme inhibition by perindopril on proteinuria of primary renal diseases. American Journal of Nephrology 1997; 17(6):511-7. *Sample size less than 50 patients*

3163. Nossen JO, Jakobsen JA, Kjaersgaard P, et al. Elimination of the non-ionic X-ray contrast media iodixanol and iohexol in patients with severely impaired renal function. Scandinavian Journal of Clinical & Laboratory Investigation 1995; 55(4):341-50. *Sample size less than 50 patients*

3164. Notghi A, Fiskerstrand CE, Burnet ME, et al. Effect of nifedipine and mefruside on renal function and platelet function in hypertensive patients. Current Medical Research & Opinion 1987; 10(7):441-9. *Sample size less than 50 patients*

3165. Nouri-Majalan N, Ardakani EF, Forouzannia K, et al. Effects of allopurinol and vitamin E on renal function in patients with cardiac coronary artery bypass grafts. Vascular Health & Risk Management 2009; 5(2):489-94. *Follow-up less than 6 months*

3166. Nowack R, Fliser D, Richter J, et al. Effects of angiotensin-converting enzyme inhibition on renal sodium handling after furosemide injection. Clinical Investigator 1993; 71(8):622-7. *Sample size less than 50 patients*

3167. Nyberg G, Blohme G, Norden G. Impact of metabolic control in progression of clinical diabetic nephropathy. Diabetologia 1987; 30(2):82-6. *Sample size less than 50 patients*

3168. Nyman U, Almen T, Aspelin P, et al. Contrast-medium-Induced nephropathy correlated to the ratio between dose in gram iodine and estimated GFR in ml/min. Acta Radiologica 2005; 46(8):830-42. *Not RCT or controlled trial*

3169. Nyman U, Elmstahl B, Leander P, et al. Are gadolinium-based contrast media really safer than iodinated media for digital subtraction angiography in patients with azotemia? Radiology 2002; 223(2):311-8; discussion 28-9. *Not early CKD*

3170. Obasaju CK, Johnson SW, Rogatko A, et al. Evaluation of carboplatin pharmacokinetics in the absence and presence of paclitaxel. Clinical Cancer Research 1996; 2(3):549-52. *Sample size less than 50 patients*

3171. Obata R, Bito H, Ohmura M, et al. The effects of prolonged low-flow sevoflurane anesthesia on renal and hepatic function. Anesthesia & Analgesia 2000; 91(5):1262-8. *Not early CKD*

3172. Ochoa A, Pellizzon G, Addala S, et al. Abbreviated dosing of N-acetylcysteine prevents contrast-induced nephropathy after elective and urgent coronary angiography and intervention. Journal of Interventional Cardiology 2004; 17(3):159-65. *Not early CKD*

3173. O'Connell DP, Ragsdale NV, Boyd DG, et al. Differential human renal tubular responses to dopamine type 1 receptor stimulation are determined by blood pressure status. Hypertension 1997; 29(1 Pt 1):115-22. *Sample size less than 50 patients*

3174. O'Connell JE, Jardine AG, Davies DL, et al. Renal and hormonal effects of chronic inhibition of neutral endopeptidase (EC 3.4.24.11) in normal man. Clinical Science 1993; 85(1):19-26. *Follow-up less than 6 months*

3175. O'Connor PJ, Spann SJ, Woolf SH. Care of adults with type 2 diabetes mellitus. A review of the evidence. Journal of Family Practice 1998; 47(5 Suppl):S13-22. *Not RCT or controlled trial*

3176. Odabas AR, Cetinkaya R, Selcuk Y, et al. Effect of losartan treatment on the proteinuria in normotensive patients having proteinuria due to secondary amyloidosis. Upsala Journal of Medical Sciences 2001; 106(3):183-8. *Sample size less than 50 patients*

3177. Oddoze C, Morange S, Portugal H, et al. Cystatin C is not more sensitive than creatinine for detecting early renal impairment in patients with diabetes. American Journal of Kidney Diseases 2001; 38(2):310-6. *Not RCT or controlled trial*

3178. O'Doherty DP, Gertz BJ, Tindale W, et al. Effects of five daily 1 h infusions of alendronate in Paget's disease of bone. Journal of Bone & Mineral Research 1992; 7(1):81-7. *Not CKD treatment*

3179. O'Doherty DP, McCloskey EV, Vasikaran S, et al. The effects of intravenous alendronate in Paget's disease of bone. Journal of Bone & Mineral Research 1995; 10(7):1094-100. *Sample size less than 50 patients*

3180. O'Donnell MJ, Rowe BR, Lawson N, et al. Comparison of the effects of an angiotensin converting enzyme inhibitor and a calcium antagonist in hypertensive, macroproteinuric diabetic patients: a randomised double-blind study. Journal of Human Hypertension 1993; 7(4):333-9. *Sample size less than 50 patients*

3181. O'Donnell MJ, Rowe BR, Lawson N, et al. Placebo-controlled trial of lisinopril in normotensive diabetic patients with incipient nephropathy. Journal of Human Hypertension 1993; 7(4):327-32. *Sample size less than 50 patients*

3182. Odvina CV, Mason RP, Pak CYC. Prevention of thiazide-induced hypokalemia without magnesium depletion by potassium-magnesium-citrate. American Journal of Therapeutics 2006; 13(2):101-8. *Not RCT or controlled trial*

3183. Ogawa O, Hayashi C, Nakaniwa T, et al. Arterial stiffness is associated with diabetic retinopathy in type 2 diabetes. Diabetes Research & Clinical Practice 2005; 68(2):162-6. *Not relevant to key questions*

3184. Ogawa S, Mori T, Nako K, et al. Reduced albuminuria with sarpogrelate is accompanied by a decrease in monocyte chemoattractant protein-1 levels in type 2 diabetes. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(2):362-8. *Not RCT or controlled trial*

3185. Ogawa S, Mori T, Nako K, et al. Combination therapy with renin-angiotensin system inhibitors and the calcium channel blocker azelnidipine decreases plasma inflammatory markers and urinary oxidative stress markers in patients with diabetic nephropathy. Hypertension Research - Clinical & Experimental 2008; 31(6):1147-55. *Sample size less than 50 patients*

3186. Ogawa S, Mori T, Nako K, et al. Angiotensin II type 1 receptor blockers reduce urinary oxidative stress markers in hypertensive diabetic nephropathy. Hypertension 2006; 47(4):699-705. *Follow-up less than 6 months*

3187. Ogawa S, Takeuchi K, Mori T, et al. Spironolactone further reduces urinary albumin excretion and plasma B-type natriuretic peptide levels in hypertensive type II diabetes treated with angiotensin-converting enzyme inhibitor. Clinical & Experimental Pharmacology & Physiology 2006; 33(5-6):477-9. *Not RCT or controlled trial*

3188. Ogawa Y, Haneda T, Hirayama T, et al. Effects of lisinopril and nitrendipine on urinary albumin excretion and renal function in patients with mild to moderate essential hypertension. Hypertension Research - Clinical & Experimental 2000; 23(6):607-12. *Sample size less than 50 patients*

3189. Ogihara T, Kaneko Y, Ikeda M, et al. Clinical evaluation of delapril in Japan. Report from the Japan Study Group on Delapril. American Journal of Hypertension 1991; 4(1 Pt 2):42S-5S. *Not CKD treatment*

3190. O'Hanlon JJ, Beers H, Huss BK, et al. A comparison of the effect of intramuscular diclofenac, ketorolac or piroxicam on post-operative pain following laparoscopy. European Journal of Anaesthesiology 1996; 13(4):404-7. *Not CKD treatment*

3191. O'Hara JF, Jr., Hsu THS, Sprung J, et al. The effect of dopamine on renal function in solitary partial nephrectomy surgery.[Erratum appears in J Urol 2002 Mar;167(3):1408]. Journal of Urology 2002; 167(1):24-8. *Not early CKD*

3192. O'Hare AM, Kaufman JS, Covinsky KE, et al. Current guidelines for using angiotensin-converting enzyme inhibitors and angiotensin II-receptor antagonists in chronic kidney disease: is the evidence base relevant to older adults? Annals of Internal Medicine 2009; 150(10):717-24. *Not RCT or controlled trial*

3193. O'Hare AM, Vittinghoff E, Hsia J, et al. Renal insufficiency and the risk of lower extremity peripheral arterial disease: results from the Heart and Estrogen/Progestin Replacement Study (HERS). Journal of the American Society of Nephrology 2004; 15(4):1046-51. *Not CKD treatment*

3194. Ohkubo Y, Kishikawa H, Araki E, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. Diabetes Research & Clinical Practice 1995; 28(2):103-17. *Not CKD treatment*

3195. Ohls RK, Dai A. Long-acting erythropoietin: clinical studies and potential uses in neonates. Clinics in Perinatology 2004; 31(1):77-89. *Sample size less than 50 patients*

3196. Ohmit SE, Flack JM, Peters RM, et al. Longitudinal Study of the National Kidney Foundation's (NKF) Kidney Early Evaluation Program (KEEP). Journal of the American Society of Nephrology 2003; 14(7 Suppl 2):S117-21. *Not CKD treatment*

3197. Ohnmacht GA, Phan GQ, Mavroukakis SA, et al. A prospective, randomized, double-blind, placebo-controlled trial evaluating the effect of nystatin on the development of oral irritation in patients receiving high-dose intravenous interleukin-2. Journal of Immunotherapy 2001; 24(2):188-92. *Not CKD treatment*

3198. Okamoto H, Nagatomo A, Kunitoh H, et al. Prediction of carboplatin clearance calculated by patient characteristics or 24-hour creatinine clearance: a comparison of the performance of three formulae. Cancer Chemotherapy & Pharmacology 1998; 42(4):307-12. *Not CKD treatment*

3199. O'Keefe JH, Bybee KA, Lavie CJ. Intensive lipid intervention in the post-ENHANCE era. Mayo Clinic Proceedings 2008; 83(8):867-9. *Not CKD treatment*

3200. Oksa A, Spustova V, Krivosikova Z, et al. Effects of long-term cholecalciferol supplementation on mineral metabolism and calciotropic hormones in chronic kidney disease. Kidney & Blood Pressure Research 2008; 31(5):322-9. *Not CKD treatment*

3201. Olbricht CJ, Wanner C, Thiery J, et al. Simvastatin in nephrotic syndrome. Simvastatin in Nephrotic Syndrome Study Group. Kidney International - Supplement 1999; 71:S113-6. *Not CKD treatment*

3202. Oldemeyer JB, Biddle WP, Wurdeman RL, et al. Acetylcysteine in the prevention of contrast-induced nephropathy after coronary angiography. American Heart Journal 2003; 146(6):E23. *Not RCT or controlled trial*

3203. Olencki T, Finke J, Tubbs R, et al. Immunomodulatory effects of interleukin-2 and interleukin-4 in patients with malignancy. Journal of Immunotherapy with Emphasis on Tumor Immunology 1996; 19(1):69-80. *Not CKD treatment*

3204. Olgaard K, Lewin E. Reply to Dr S.C. Palmer and co-workers. Nephrology Dialysis Transplantation 2008; 23(8):2709-10. *Not CKD treatment*

3205. Olgaard K, Storm T, van Wowern N, et al. Glucocorticoid-induced osteoporosis in the lumbar spine, forearm, and mandible of nephrotic patients: a double-blind study on the high-dose, long-term effects of prednisone versus deflazacort. Calcified Tissue International 1992; 50(6):490-7. *Sample size less than 50 patients*

3206. Oliveira RB, Cancela ALE, Graciolli FG, et al. Early control of PTH and FGF23 in normophosphatemic CKD patients: a new target in CKD-MBD therapy? Clinical Journal of The American Society of Nephrology: CJASN 2010 Feb; 5(2):286-91. *Follow-up less than 6 months*

3207. Oliver WC, Jr., Nuttall GA, Cherry KJ, et al. A comparison of fenoldopam with dopamine and sodium nitroprusside in patients undergoing cross-clamping of the abdominal aorta. Anesthesia & Analgesia 2006; 103(4):833-40. *Not CKD treatment*

3208. Olsen KM, Rudis MI, Rebuck JA, et al. Effect of once-daily dosing vs. multiple daily dosing of tobramycin on enzyme markers of nephrotoxicity. Critical Care Medicine 2004; 32(8):1678-82. *Not CKD treatment*

3209. Olsen ME, Thomsen T, Hassager C, et al. Hemodynamic and renal effects of indomethacin in losartan-treated hypertensive individuals. American Journal of Hypertension 1999; 12(2 Pt 1):209-16. *Sample size less than 50 patients*

3210. Olsen MH, Wachtell K, Bella JN, et al. Albuminuria predicts cardiovascular events independently of left ventricular mass in hypertension: a LIFE substudy. Journal of Human Hypertension 2004; 18(6):453-9. *Not CKD treatment*

3211. Olsen MH, Wachtell K, Borch-Johnsen K, et al. A blood pressure independent association between glomerular albumin leakage and electrocardiographic left ventricular hypertrophy. The LIFE Study. Losartan Intervention For Endpoint reduction. Journal of Human Hypertension 2002; 16(8):591-5. *Not relevant to key questions*

3212. Olsen MH, Wachtell K, Ibsen H, et al. Reductions in albuminuria and in electrocardiographic left ventricular hypertrophy independently improve prognosis in hypertension: the LIFE study. Journal of Hypertension 2006; 24(4):775-81. *Sample size less than 50 patients*

3213. Olsen NV, Fogh-Andersen N, Strandgaard S, et al. Endogenous versus exogenous lithium clearance for evaluation of dopamine-induced changes in renal tubular function. Clinical Science 1996; 90(6):511-5. *Sample size less than 50 patients*

3214. Olsen NV, Jensen NG, Hansen JM, et al. Non-steroidal anti-inflammatory drugs and renal response to exercise: a comparison of indomethacin and nabumetone. Clinical Science 1999; 97(4):457-65. *Sample size less than 50 patients*

3215. Olsen NV, Lang-Jensen T, Hansen JM, et al. Effects of acute beta-adrenoceptor blockade with metoprolol on the renal response to dopamine in normal humans. British Journal of Clinical Pharmacology 1994; 37(4):347-53. *Not CKD treatment*

3216. Olsen NV, Olsen MH, Bonde J, et al. Dopamine natriuresis in salt-repleted, water-loaded humans: a dose-response study. British Journal of Clinical Pharmacology 1997; 43(5):509-20. *Sample size less than 50 patients*

3217. Olsen NV, Olsen MH, Fogh-Andersen N, et al. Lithium clearance method and the renal response to low-dose dopamine in man: a randomized, controlled study. Clinical Science 1993; 84(2):237-42. *Sample size less than 50 patients*

3218. Olthof MR, Brink EJ, Katan MB, et al. Choline supplemented as phosphatidylcholine decreases fasting and postmethionine-loading plasma homocysteine concentrations in healthy men. American Journal of Clinical Nutrition 2005; 82(1):111-7. *Sample size less than 50 patients*

3219. Omar MA, Motala AA, Seedat MA, et al. Effects of captopril and prazosin on renal function in diabetes. South African Medical Journal 1993; Suid-Afrikaanse Tydskrif Vir Geneeskunde. 83(5):365. *Not RCT or controlled trial*

3220. Omari BO, Nelson RJ, Robertson JM. Effect of right atrial appendectomy on the release of atrial natriuretic hormone. Journal of Thoracic & Cardiovascular Surgery 1991; 102(2):272-9. *Not CKD treatment*

3221. O'Meara E, Clayton T, McEntegart MB, et al. Clinical correlates and consequences of anemia in a broad spectrum of patients with heart failure: results of the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) Program. Circulation 2006; 113(7):986-94. *Not RCT or controlled trial*

3222. Onat A, Hergenc G, Uyarel H, et al. Association between mild renal dysfunction and insulin resistance or metabolic syndrome in a random nondiabetic population sample. Kidney & Blood Pressure Research 2007; 30(2):88-96. *Not relevant to key questions*

3223. Onbasili AO, Yeniceriglu Y, Agaoglu P, et al. Trimetazidine in the prevention of contrast-induced nephropathy after coronary procedures. Heart 2007; 93(6):698-702. *Not CKD treatment*

3224. O'Neill JO, Taylor DO, Starling RC. Immunosuppression for cardiac transplantation--the past, present and future. Transplantation Proceedings 2004; 36(2 Suppl):309S-13S. *Sample size less than 50 patients*

3225. Ong-Ajyooth L, Vareesangthip K, Khonputsa P, et al. Prevalence of chronic kidney disease in Thai adults: a national health survey. BMC Nephrology 2009; 10:35. *Not CKD treatment*

3226. Onorati F, Presta P, Fuiano G, et al. A randomized trial of pulsatile perfusion using an intra-aortic balloon pump versus nonpulsatile perfusion on short-term changes in kidney function during cardiopulmonary bypass during myocardial reperfusion. American Journal of Kidney Diseases 2007; 50(2):229-38. *Not relevant to key questions*

3227. Onuigbo MAC. Does concurrent renin-angiotensin-aldosterone blockade in (older) chronic kidney disease patients play a role in the acute renal failure epidemic in US hospitalized patients?--Three cases of severe acute renal failure encountered in a northwestern Wisconsin Nephrology practice. Hemodialysis International 2009; 13 Suppl 1:S24-9. *Not CKD treatment*

3228. Onuigbo MAC. Reno-prevention vs. reno-protection: a critical re-appraisal of the evidence-base from the large RAAS blockade trials after ONTARGET--a call for more circumspection. Qjm 2009; 102(3):155-67. *Not CKD treatment*

3229. Onwude JL, Lilford RJ, Hjartardottir H, et al. A randomised double blind placebo controlled trial of fish oil in high risk pregnancy. British Journal of Obstetrics & Gynaecology 1995; 102(2):95-100. *Not CKD treatment*

3230. Ooi JSM, Ramzisham ARM, Zamrin MD. Is 6% hydroxyethyl starch 130/0.4 safe in coronary artery bypass graft surgery? Asian Cardiovascular & Thoracic Annals 2009; 17(4):368-72. *Not CKD treatment*

3231. Oosterlinck W, Philp NH, Charig C, et al. A double-blind single dose comparison of intramuscular ketorolac tromethamine and pethidine in the treatment of renal colic. Journal of Clinical Pharmacology 1990; 30(4):336-41. *Not CKD treatment*

3232. Ordonez JD, Hiatt RA, Killebrew EJ, et al. The increased risk of coronary heart disease associated with nephrotic syndrome. Kidney International 1993; 44(3):638-42. *Not RCT or controlled trial*

3233. O'Reilly PH, Brooman PJ, Martin PJ, et al. Accuracy and reproducibility of a new contrast clearance method for the determination of glomerular filtration rate. British Medical Journal Clinical Research Ed. 1986; 293(6541):234-6. *Follow-up less than 6 months*

3234. Oriana S, Bohm S, Spatti G, et al. A preliminary clinical experience with reduced glutathione as protector against cisplatin-toxicity. Tumori 1987; 73(4):337-40. *Sample size less than 50 patients*

3235. O'Riordan E, Foley RN. Effects of anaemia on cardiovascular status. Nephrology Dialysis Transplantation 2000; 15 Suppl 3:19-22. *Not early CKD*

3236. Orita Y, Okada M, Harada S, et al. Skim soy protein enhances GFR as much as beefsteak protein in healthy human subjects. Clinical & Experimental Nephrology 2004; 8(2):103-8. *Not CKD treatment*

3237. Ortapamuk H, Naldoken S, Tekdogan UY, et al. Differential renal function in the prediction of recovery in adult obstructed kidneys after pyeloplasty. Annals of Nuclear Medicine 2003; 17(8):663-8. *Not CKD treatment*

3238. Orth SR, Hallan SI. Smoking: a risk factor for progression of chronic kidney disease and for cardiovascular morbidity and mortality in renal patients--absence of evidence or evidence of absence? Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(1):226-36. *Not RCT or controlled trial*

3239. Ortiz A, Oliveira JP, Wanner C, et al. Recommendations and guidelines for the diagnosis and treatment of Fabry nephropathy in adults. Nature Clinical Practice Nephrology 2008; 4(6):327-36. *Not CKD treatment*

3240. Ortiz MA, De Prado A, Donate T, et al. Angiotensin-converting enzyme polymorphism gene and evolution of nephropathy to end-stage renal disease. Nephrology 2003; 8(4):171-6. *Sample size less than 50 patients*

3241. Os I, Gudmundsdottir H, Kjeldsen SE, et al. Treatment of isolated systolic hypertension in diabetes mellitus type 2. Diabetes, Obesity & Metabolism 2006; 8(4):381-7. *Not RCT or controlled trial*

3242. Osei SY, Price DA, Laffel LM, et al. Effect of angiotensin II antagonist eprosartan on hyperglycemia-induced activation of intrarenal renin-angiotensin system in healthy humans. Hypertension 2000; 36(1):122-6. *Not early CKD*

3243. Oster HS, Hoffman M, Prutchi-Sagiv S, et al. Erythropoietin in clinical practice: current use, effect on survival, and future directions. Israel Medical Association Journal: Imaj 2006; 8(10):703-6. *Not CKD treatment*

3244. Ostermann M, Alvarez G, Sharpe MD, et al. Frusemide administration in critically ill patients by continuous compared to bolus therapy. Nephron 2007; 107(2):c70-6. *Sample size less than 50 patients*

3245. Osterziel KJ, Dietz R, Harder K, et al. Comparison of captopril with enalapril in the treatment of heart failure: influence on hemodynamics and measures of renal function. Cardiovascular Drugs & Therapy 1992; 6(2):173-80. *Sample size less than 50 patients*

3246. Osterziel KJ, Dietz R, Lemmer B. Circadian rhythm of blood pressure in congestive heart failure and effects of ACE inhibitors. Chronobiology International 1991; 8(5):420-31. *Sample size less than 50 patients*

3247. O'Toole L, Stewart M, Padfield P, et al. Effect of the insertion/deletion polymorphism of the angiotensin-converting enzyme gene on response to angiotensin-converting enzyme inhibitors in patients with heart failure. Journal of Cardiovascular Pharmacology 1998; 32(6):988-94. *Sample size less than 50 patients*

3248. Ott C, Ritt M, Titze SI, et al. Rosuvastatin does not affect intrarenal hemodynamics in patients with hypercholesterolemia. Journal of Nephrology 2009; 22(5):675-81. *Sample size less than 50 patients*

3249. Ottesen LH, Aagaard NK, Kiszka-Kanowitz M, et al. Effects of a long-acting formulation of octreotide on renal function and renal sodium handling in cirrhotic patients with portal hypertension: a randomized, double-blind, controlled trial. Hepatology 2001; 34(3):471-7. *Not early CKD*

3250. Oudemans-van Straaten HM. Strategies to prevent contrast nephropathy. Minerva Cardioangiologica 2005; 53(5):445-63. *Sample size less than 50 patients*

3251. Oudit GY, Liu GC, Zhong J, et al. Human recombinant ACE2 reduces the progression of diabetic nephropathy. Diabetes 2010; 59(2):529-38. *Not human studies*

3252. Ovartlarnporn M, Jongjaroenprasert W. Advancing age and renal impairment as important predisposing factors of gatifloxacin-induced hyperglycemia in non-diabetes patients. Journal of the Medical Association of Thailand 2007; 90(3):569-73. *Not relevant to key questions*

3253. Overbosch D, van Gulpen C, Mattie H. Renal clearance of temocillin in volunteers. Drugs 1985; 29 Suppl 5:128-34. *Sample size less than 50 patients*

3254. Overman GP, Teter CJ, Guthrie SK. Acamprosate for the adjunctive treatment of alcohol dependence. Annals of Pharmacotherapy 2003; 37(7-8):1090-9. *Not CKD treatment*

3255. Owada A, Nakao M, Koike J, et al. Effects of oral adsorbent AST-120 on the progression of chronic renal failure: a randomized controlled study. Kidney International - Supplement 1997; 63:S188-90. *Sample size less than 50 patients*

3256. Owada A, Suda S, Hata T. Effect of long-term administration of prostaglandin I(2) in incipient diabetic nephropathy. Nephron 2002; 92(4):788-96. *Sample size less than 50 patients*

3257. Owada A, Suda S, Hata T. Antiproteinuric effect of niceritrol, a nicotinic acid derivative, in chronic renal disease with hyperlipidemia: a randomized trial. American Journal of Medicine 2003; 114(5):347-53. *Sample size less than 50 patients*

3258. Owan TE, Chen HH, Frantz RP, et al. The effects of nesiritide on renal function and diuretic responsiveness in acutely decompensated heart failure patients with renal dysfunction. Journal of Cardiac Failure 2008; 14(4):267-75. *Not CKD treatment*

3259. Ozcan EE, Guneri S, Akdeniz B, et al. Sodium bicarbonate, N-acetylcysteine, and saline for prevention of radiocontrast-induced nephropathy. A comparison of 3 regimens for protecting contrast-induced nephropathy in patients undergoing coronary procedures. A single-center prospective controlled trial. American Heart Journal 2007; 154(3):539-44. *Follow-up less than 6 months*

3260. Ozcan S, Yilmaz E, Buyukkocak U, et al. Comparison of three analgesics for extracorporeal shock wave lithotripsy. Scandinavian Journal of Urology & Nephrology 2002; 36(4):281-5. *Not CKD treatment*

3261. Ozdal OL, Ozden C, Benli K, et al. Effect of short-term finasteride therapy on peroperative bleeding in patients who were candidates for transurethral resection of the prostate (TUR-P): a randomized controlled study. Prostate Cancer & Prostatic Diseases 2005; 8(3):215-8. *Not RCT or controlled trial*

3262. Ozdener F, Ozdemir V. Fasidotril Eli Lilly. Current Opinion in Investigational Drugs 2003; 4(9):1113-9. *Not CKD treatment*

3263. Ozhan H, Erden I, Ordu S, et al. Efficacy of short-term high-dose atorvastatin for prevention of contrast-induced nephropathy in patients undergoing coronary angiography. Angiology 2010 Oct; 61(7):711-4. *Not CKD treatment*

3264. Pacher R, Stanek B, Globits S, et al. Effects of two different enalapril dosages on clinical, haemodynamic and neurohumoral response of patients with severe congestive heart failure. European Heart Journal 1996; 17(8):1223-32. *Not early CKD*

3265. Pacher R, Stanek B, Hulsmann M, et al. Effect of prostaglandin E1 infusion in severe chronic heart failure. Prostaglandins 1997; 53(4):221-35. *Not CKD treatment*

3266. Packard DP, Milton JE, Shuler LA, et al. Implications of chronic kidney disease for dietary treatment in cardiovascular disease. Journal of Renal Nutrition 2006; 16(3):259-68. *Follow-up less than 6 months*

3267. Padillo FJ, Briceno J, Cruz A, et al. Randomized clinical trial of the effect of intravenous fluid administration on hormonal and renal dysfunction in patients with obstructive jaundice undergoing endoscopic drainage. British Journal of Surgery 2005; 92(1):39-43. *Sample size less than 50 patients*

3268. Pageaux G-P, Rostaing L, Calmus Y, et al. Mycophenolate mofetil in combination with reduction of calcineurin inhibitors for chronic renal dysfunction after liver transplantation. Liver Transplantation 2006; 12(12):1755-60. *Sample size less than 50 patients*

3269. Pagliaro LC, Sharma P. Review of metastatic bladder cancer. Minerva Urologica e Nefrologica 2006; 58(1):53-71. *Not relevant to key questions*

3270. Pain JA, Cahill CJ, Gilbert JM, et al. Prevention of postoperative renal dysfunction in patients with obstructive jaundice: a multicentre study of bile salts and lactulose. British Journal of Surgery 1991; 78(4):467-9. *Not CKD treatment*

3271. Pais RC, Abdel-Mageed A, Ghim TT, et al. Phase I study of recombinant human interleukin-2 for pediatric malignancies: feasibility of outpatient therapy. A Pediatric Oncology Group Study. Journal of Immunotherapy 1992; 12(2):138-46. *Not adult population*

3272. Palazzuoli A, Gallotta M, Iovine F, et al. Anaemia in heart failure: a common interaction with renal insufficiency called the cardio-renal anaemia syndrome. International Journal of Clinical Practice 2008; 62(2):281-6. *Not CKD treatment*

3273. Palazzuoli A, Silverberg D, Iovine F, et al. Erythropoietin improves anemia exercise tolerance and renal function and reduces B-type natriuretic peptide and hospitalization in patients with heart failure and anemia. American Heart Journal 2006; 152(6):1096.e9-15. *Not CKD treatment*

3274. Palla R, Marchitiello M, Tuoni M, et al. Enzymuria in aminoglycoside-induced kidney damage. Comparative study of gentamicin, amikacin, sisomicin and netilmicin. International Journal of Clinical Pharmacology Research 1985; 5(5):351-5. *Sample size less than 50 patients*

3275. Palla R, Parrini M, Panichi V, et al. Acute effects of calcitonin gene related peptide on renal haemodynamics and renin and angiotensin II secretion in patients with renal disease. International Journal of Tissue Reactions 1995; 17(1):43-9. *Sample size less than 50 patients*

3276. Palmas W, Moran A, Pickering T, et al. Ambulatory pulse pressure and progression of urinary albumin excretion in older patients with type 2 diabetes mellitus. Hypertension 2006; 48(2):301-8. *Sample size less than 50 patients*

3277. Palmer AJ, Annemans L, Roze S, et al. An economic evaluation of the Irbesartan in Diabetic Nephropathy Trial (IDNT) in a UK setting. Journal of Human Hypertension 2004; 18(10):733-8. *Not CKD treatment*

3278. Palmer AJ, Valentine WJ, Chen R, et al. A health economic analysis of screening and optimal treatment of nephropathy in patients with type 2 diabetes and hypertension in the USA. Nephrology Dialysis Transplantation 2008; 23(4):1216-23. *Sample size less than 50 patients*

3279. Palmer AJ, Valentine WJ, Ray JA. Irbesartan treatment of patients with type 2 diabetes, hypertension and renal disease: a UK health economics analysis. International Journal of Clinical Practice 2007; 61(10):1626-33. *Not RCT or controlled trial*

3280. Palmer SC, McGregor DO, Macaskill P, et al. Meta-analysis: vitamin D compounds in chronic kidney disease. Annals of Internal Medicine 2007; 147(12):840-53. *Not relevant to key questions*

3281. Palmer SC, Nand K, Strippoli GF. Interventions for minimal change disease in adults with nephrotic syndrome. Cochrane Database of Systematic Reviews 2008; (1):CD001537. *Not relevant to key questions*

3282. Palmer SC, Navaneethan SD, Craig JC, et al. Meta-analysis: erythropoiesis-stimulating agents in patients with chronic kidney disease. Annals of Internal Medicine 2010 Jul 6; 153(1):23-33. *Not CKD treatment*

3283. Palumbo A, Gay F. How to treat elderly patients with multiple myeloma: combination of therapy or sequencing. Hematology 2009:566-77. *Not RCT or controlled trial*

3284. Pan Y, Guo LL, Jin HM. Low-protein diet for diabetic nephropathy: a meta-analysis of randomized controlled trials. American Journal of Clinical Nutrition 2008; 88(3):660-6. *Not CKD treatment*

3285. Panetta CJ, Herzog CA, Henry TD. Acute coronary syndromes in patients with renal disease: what are the issues? Current Cardiology Reports 2006; 8(4):296-300. *Sample size less than 50 patients*

3286. Paniagua JA, Lopez-Miranda J, Perez-Martinez P, et al. Oxidized-LDL levels are changed during short-term serum glucose variations and lowered with statin treatment in early Type 2 diabetes: a study of endothelial function and microalbuminuria. Diabetic Medicine 2005; 22(12):1647-56. *Sample size less than 50 patients*

3287. Paniagua R, Claure R, Amato D, et al. Effects of oral administration of zinc and diiodohydroxyquinolein on plasma zinc levels of uremic patients. Nephron 1995; 69(2):147-50. *Sample size less than 50 patients*

3288. Panichi V, Andreini B, De Pietro S, et al. Calcitriol oral therapy for the prevention of secondary hyperparathyroidism in patients with predialytic renal failure. Clinical Nephrology 1998; 49(4):245-50. *Sample size less than 50 patients*

3289. Panichi V, Paoletti S, Mantuano E, et al. In vivo and in vitro effects of simvastatin on inflammatory markers in pre-dialysis patients. Nephrology Dialysis Transplantation 2006; 21(2):337-44. *Not CKD treatment*

3290. Pannu N, Manns B, Lee H, et al. Systematic review of the impact of N-acetylcysteine on contrast nephropathy. Kidney International 2004; 65(4):1366-74. *Not relevant to key questions*

3291. Pannu N, Tonelli M. Strategies to reduce the risk of contrast nephropathy: an evidence-based approach. Current Opinion in Nephrology & Hypertension 2006; 15(3):285-90. *Follow-up less than 6 months*

3292. Pannu N, Wiebe N, Tonelli M, et al. Prophylaxis strategies for contrast-induced nephropathy. JAMA 2006; 295(23):2765-79. *Not relevant to key questions*

3293. Panos GZ, Betsi GI, Falagas ME. Systematic review: are antibiotics detrimental or beneficial for the treatment of patients with Escherichia coli O157:H7 infection? Alimentary Pharmacology & Therapeutics 2006; 24(5):731-42. *Not RCT or controlled trial*

3294. Pantaleo P, Marra F, Vizzutti F, et al. Effects of dietary supplementation with arachidonic acid on platelet and renal function in patients with cirrhosis. Clinical Science 2004; 106(1):27-34. *Not CKD treatment*

3295. Paoletti E, Cannella G. Update on erythropoietin treatment: should hemoglobin be normalized in patients with chronic kidney disease? Journal of the American Society of Nephrology 2006; 17(4 Suppl 2):S74-7. *Not relevant to key questions*

3296. Papaioannou GI, Seip RL, Grey NJ, et al. Brachial artery reactivity in asymptomatic patients with type 2 diabetes mellitus and microalbuminuria (from the Detection of Ischemia in Asymptomatic Diabetics-brachial artery reactivity study). American Journal of Cardiology 2004; 94(3):294-9. *Not CKD treatment*

3297. Papavasiliou EC, Gouva C, Siamopoulos KC, et al. Erythrocyte PAF-acetylhydrolase activity in various stages of chronic kidney disease: effect of long-term therapy with erythropoietin. Kidney International 2005; 68(1):246-55. *Sample size less than 50 patients*

3298. Papavasiliou EC, Gouva C, Siamopoulos KC, et al. PAF-acetylhydrolase activity in plasma of patients with chronic kidney disease. Effect of long-term therapy with erythropoietin. Nephrology Dialysis Transplantation 2006; 21(5):1270-7. *Not RCT or controlled trial*

3299. Pappas KD, Gouva CD, Katopodis KP, et al. Correction of anemia with erythropoietin in chronic kidney disease (stage 3 or 4): effects on cardiac performance. Cardiovascular Drugs & Therapy 2008; 22(1):37-44. *Not RCT or controlled trial*

3300. Paran H, Neufeld D, Mayo A, et al. Preliminary report of a prospective randomized study of octreotide in the treatment of severe acute pancreatitis. Journal of the American College of Surgeons 1995; 181(2):121-4. *Not CKD treatment*

3301. Paredes J, Hong WK, Felder TB, et al. Prospective randomized trial of high-dose cisplatin and fluorouracil infusion with or without sodium diethyldithiocarbamate in recurrent and/or metastatic squamous cell carcinoma of the head and neck. Journal of Clinical Oncology 1988; 6(6):955-62. *Not CKD treatment*

3302. Parfrey P. Anaemia in chronic renal disease: lessons learned since Seville 1994. Nephrology Dialysis Transplantation 2001; 16 Suppl 7:41-5. *Not RCT or controlled trial*

3303. Parfrey PS, Harnett JD. The management of cardiac disease in chronic uremia. Current Opinion in Nephrology & Hypertension 1994; 3(2):145-54. *Not CKD treatment*

3304. Parikh CR, McSweeney P, Schrier RW. Acute renal failure independently predicts mortality after myeloablative allogeneic hematopoietic cell transplant. Kidney International 2005; 67(5):1999-2005. *Not CKD treatment*

3305. Parissis JT, Rafouli-Stergiou P, Paraskevaidis I, et al. Levosimendan: from basic science to clinical practice. Heart Failure Reviews 2009; 14(4):265-75. *Not CKD treatment*

3306. Park GD, Goldberg MJ, Spector R, et al. The effects of activated charcoal on digoxin and digitoxin clearance. Drug Intelligence & Clinical Pharmacy 1985; 19(12):937-41. *Sample size less than 50 patients*

3307. Park JS, Kim SB. C-reactive protein as a cardiovascular risk factor and its therapeutic implications in end-stage renal disease patients. Nephrology 2003; 8 Suppl:S40-4. *Not CKD treatment*

3308. Park M, Coca SG, Nigwekar SU, et al. Prevention and treatment of acute kidney injury in patients undergoing cardiac surgery: a systematic review. American Journal of Nephrology 2010; 31(5):408-18. *Not CKD treatment*

3309. Parkash R, Stevenson WG, Epstein LM, et al. Predicting early mortality after implantable defibrillator implantation: a clinical risk score for optimal patient selection. American Heart Journal 2006; 151(2):397-403. *Not RCT or controlled trial*

3310. Parker MR, Willatts SM. A pilot study to investigate the effects of an infusion of aminophylline on renal function following major abdominal surgery. Anaesthesia 2001; 56(7):670-5. *Not RCT or controlled trial*

3311. Parks RW, Diamond T, McCrory DC, et al. Prospective study of postoperative renal function in obstructive jaundice and the effect of perioperative dopamine. British Journal of Surgery 1994; 81(3):437-9. *Not CKD treatment*

3312. Parrinello G, Paterna S, Torres D, et al. One-year renal and cardiac effects of bisoprolol versus losartan in recently diagnosed hypertensive patients: a randomized, double-blind study. Clinical Drug Investigation 2009; 29(9):591-600. *Not CKD treatment*

3313. Parsons DS, Harris DC. A review of quality of life in chronic renal failure. Pharmacoeconomics 1997; 12(2 Pt 1):140-60. *Not RCT or controlled trial*

3314. Parvanova A, Chiurchiu C, Ruggenenti P, et al. Inhibition of the renin-angiotensin system and cardio-renal protection: focus on losartan and angiotensin receptor blockade. Expert Opinion on Pharmacotherapy 2005; 6(11):1931-42. *Not relevant to key questions*

3315. Parvez Z, Ramamurthy S, Patel NB, et al. Enzyme markers of contrast media-induced renal failure. Investigative Radiology 1990; 25 Suppl 1:S133-4. *Sample size less than 50 patients*

3316. Parving HH. Protein restriction and renal failure in diabetes mellitus. New England Journal of Medicine 1991; 324(24):1743-4. *Not RCT or controlled trial*

3317. Parving HH. Is antihypertensive treatment the same for NIDDM and IDDM patients? Diabetes Research & Clinical Practice 1998; 39 Suppl:S43-7. *Not RCT or controlled trial*

3318. Parving HH. Benefits and cost of antihypertensive treatment in incipient and overt diabetic nephropathy. Journal of Hypertension - Supplement 1998; 16(1):S99-101. *Not RCT or controlled trial*

3319. Parving HH. Diabetic hypertensive patients. Is this a group in need of particular care and attention? Diabetes Care 1999; 22 Suppl 2:B76-9. *Not RCT or controlled trial*

3320. Parving HH. Blockade of the renin-angiotensin-aldosterone system and renal protection in diabetes mellitus. Journal of the Renin-Angiotensin-Aldosterone System 2000; 1(1):30-1. *Not RCT or controlled trial*

3321. Parving HH, Hommel E, Damkjaer Nielsen M, et al. Effect of captopril on blood pressure and kidney function in normotensive insulin dependent diabetics with nephropathy. BMJ 1989; 299(6698):533-6. *Sample size less than 50 patients*

3322. Parving HH, Hommel E, Jensen BR, et al. Long-term beneficial effect of ACE inhibition on diabetic nephropathy in normotensive type 1 diabetic patients. Kidney International 2001; 60(1):228-34. *Sample size less than 50 patients*

3323. Parving HH, Hommel E, Smidt UM. Protection of kidney function and decrease in albuminuria by captopril in insulin dependent diabetics with nephropathy. BMJ 1988; 297(6656):1086-91. *Sample size less than 50 patients*

3324. Parving HH, Mogensen CE, Thomas MC, et al. Poor prognosis in proteinuric type 2 diabetic patients with retinopathy: insights from the RENAAL study. Qjm 2005; 98(2):119-26. *Not early CKD*

3325. Parving HH, Rossing P. The use of antihypertensive agents in prevention and treatment of diabetic nephropathy. Current Opinion in Nephrology & Hypertension 1994; 3(3):292-300. *Not RCT or controlled trial*

3326. Parving HH, Tarnow L, Nielsen FS, et al. Cyclosporine nephrotoxicity in type 1 diabetic patients. A 7-year follow-up study. Diabetes Care 1999; 22(3):478-83. *Sample size less than 50 patients*

3327. Parving HH, Tarnow L, Rossing P. Renal protection in diabetes: an emerging role for calcium antagonists. Journal of Hypertension - Supplement 1996; 14(4):S21-5. *Not RCT or controlled trial*

3328. Parving HH, Tarnow L, Rossing P. Renal protection in diabetes--an emerging role for calcium antagonists. Cardiology 1997; 88 Suppl 3:56-62. *Not RCT or controlled trial*

3329. Parving H-H, Andersen S, Jacobsen P, et al. Angiotensin receptor blockers in diabetic nephropathy: renal and cardiovascular end points. Seminars in Nephrology 2004; 24(2):147-57. *Not CKD treatment*

3330. Parving H-H, Brenner BM, McMurray JJV, et al. Aliskiren Trial in Type 2 Diabetes Using Cardio-Renal Endpoints (ALTITUDE): rationale and study design. Nephrology Dialysis Transplantation 2009; 24(5):1663-71. *Not CKD treatment*

3331. Parving H-H, de Zeeuw D, Cooper ME, et al. ACE gene polymorphism and losartan treatment in type 2 diabetic patients with nephropathy. Journal of the American Society of Nephrology 2008; 19(4):771-9. *Not CKD treatment*

3332. Parving H-H, Persson F, Lewis JB, et al. Aliskiren combined with losartan in type 2 diabetes and nephropathy.[Reprint in Ugeskr Laeger. 2009 Mar 9;171(11):881-4; PMID: 19291865]. New England Journal of Medicine 2008; 358(23):2433-46. *Follow-up less than 6 months*

3333. Pasquali S, Cagnoli L, Rovinetti C, et al. Plasma exchange therapy in rapidly progressive renal failure due to multiple myeloma. International Journal of Artificial Organs 1985; 8 Suppl 2:27-30. *Sample size less than 50 patients*

3334. Passa P, Chatellier G. The DIAB-HYCAR Study. Diabetologia 1996; 39(12):1662-7. *Not RCT or controlled trial*

3335. Passa P, Leblanc H, Chevrel A, et al. Discontinuing ACE inhibition in patients with diabetic nephropathy. BMJ 1991; 302(6777):658. *Not RCT or controlled trial*

3336. Passariello N, Sepe J, Marrazzo G, et al. Effect of aldose reductase inhibitor (tolrestat) on urinary albumin excretion rate and glomerular filtration rate in IDDM subjects with nephropathy. Diabetes Care 1993; 16(5):789-95. *Sample size less than 50 patients*

3337. Passfall J, Pai J, Spies KP, et al. Effect of water and bicarbonate loading in patients with chronic renal failure. Clinical Nephrology 1997; 47(2):92-8. *Sample size less than 50 patients*

3338. Passmore AP, Copeland S, Johnston GD. The effects of ibuprofen and indomethacin on renal function in the presence and absence of frusemide in healthy volunteers on a restricted sodium diet. British Journal of Clinical Pharmacology 1990; 29(3):311-9. *Not CKD treatment*

3339. Passmore AP, Kondowe GB, Johnston GD. Renal and cardiovascular effects of caffeine: a dose-response study. Clinical Science 1987; 72(6):749-56. *Sample size less than 50 patients*

3340. Pasternack A, Vanttinen T, Solakivi T, et al. Normalization of lipoprotein lipase and hepatic lipase by gemfibrozil results in correction of lipoprotein abnormalities in chronic renal failure. Clinical Nephrology 1987; 27(4):163-8. *Sample size less than 50 patients*

3341. Pastors JG, Franz MJ, Warshaw H, et al. How effective is medical nutrition therapy in diabetes care? Journal of the American Dietetic Association 2003; 103(7):827-31. *Not RCT or controlled trial*

3342. Patel A. Acute renal failure from contrast medium: ... and remember simple and cheap measures. BMJ 2006; 333(7569):653-4. *Not RCT or controlled trial*

3343. Patel UD, Greiner MA, Fonarow GC, et al. Associations between worsening renal function and 30-day outcomes among Medicare beneficiaries hospitalized with heart failure. American Heart Journal 2010 Jul; 160(1):132-8.e1. *Not CKD treatment*

3344. Patel Z, Bhattacharjee LI, Shah BV. The role of dietary protein restriction in Indian patients with chronic renal failure. Journal of the Association of Physicians of India 2000; 48(11):1078-81. *Sample size less than 50 patients*

3345. Paterna S, Parrinello G, Scaglione R, et al. Effect of long-term losartan administration on renal haemodynamics and function in hypertensive patients. Cardiovascular Drugs & Therapy 2000; 14(5):529-32. *Sample size less than 50 patients*

3346. Patil AJ, Bhagwat VR, Patil JA, et al. Occupational lead exposure in battery manufacturing workers, silver jewelry workers, and spray painters in western Maharashtra (India): effect on liver and kidney function. Journal of Basic & Clinical Physiology & Pharmacology 2007; 18(2):87-100. *Not RCT or controlled trial*

3347. Patrono C, Davi G. Antiplatelet agents in the prevention of diabetic vascular complications. Diabetes-Metabolism Reviews 1993; 9(3):177-88. *Not RCT or controlled trial*

3348. Pattou FN, Pellissier LC, Noel C, et al. Supernumerary parathyroid glands: frequency and surgical significance in treatment of renal hyperparathyroidism. World Journal of Surgery 2000; 24(11):1330-4. *Not early CKD*

3349. Paulsen L, Holm C, Bech JN, et al. Effects of statins on renal sodium and water handling: acute and short-term effects of atorvastatin on renal haemodynamics, tubular function, vasoactive hormones, blood pressure and pulse rate in healthy, normocholesterolemic humans. Nephrology Dialysis Transplantation 2008; 23(5):1556-61. *Follow-up less than 6 months*

3350. Paulsen L, Holst LM, Bech JN, et al. Glomerular filtration rate and blood pressure are unchanged by increased sodium intake in atorvastatin-treated healthy men. Scandinavian Journal of Clinical & Laboratory Investigation 2009; 69(3):323-9. *Sample size less than 50 patients*

3351. Paulsen L, Matthesen SK, Bech JN, et al. Acute effects of atorvastatin on glomerular filtration rate, tubular function, blood pressure, and vasoactive hormones in patients with type 2 diabetes. Journal of Clinical Pharmacology 2010 Jul; 50(7):816-22. *Not CKD treatment*

3352. Pavlik I, Suchy J, Pacik D, et al. Comparison of cizolirtine citrate and metamizol sodium in the treatment of adult acute renal colic: a randomized, double-blind, clinical pilot study. Clinical Therapeutics 2004; 26(7):1061-72. *Sample size less than 50 patients*

3353. Pechere-Bertschi A, Maillard M, Stalder H, et al. Renal hemodynamic and tubular responses to salt in women using oral contraceptives. Kidney International 2003; 64(4):1374-80. *Sample size less than 50 patients*

3354. Pecis M, Azevedo MJ, Gross JL. Glomerular hyperfiltration is associated with blood pressure abnormalities in normotensive normoalbuminuric IDDM patients. Diabetes Care 1997; 20(8):1329-33. *Follow-up less than 6 months*

3355. Pecis M, de Azevedo MJ, Gross JL. Chicken and fish diet reduces glomerular hyperfiltration in IDDM patients. Diabetes Care 1994; 17(7):665-72. *Sample size less than 50 patients*

3356. Pedersen EB, Madsen JK, Sorensen SS, et al. Improvement in renal function by felodipine during cyclosporine treatment in acute and short-term studies. Kidney International - Supplement 1996; 55:S94-6. *Not early CKD*

3357. Pedersen EB, Thomsen IM, Fjordside LS. Effect of BQ-123, an endothelin antagonist, on renal hemodynamics, tubular function, vasoactive hormones, and blood pressure in healthy humans: a dose response study. American Journal of Hypertension 2005; 18(12 Pt 1):1578-85. *Not relevant to key questions*

3358. Pedersen LM, Milman N. Microalbuminuria in patients with lung cancer. European Journal of Cancer 1998; 34(1):76-80. *Not CKD treatment*

3359. Pedersen MM, Christiansen JS, Mogensen CE. Reduction of glomerular hyperfiltration in normoalbuminuric IDDM patients by 6 mo of aldose reductase inhibition. Diabetes 1991; 40(5):527-31. *Sample size less than 50 patients*

3360. Pedersen MM, Hansen KW, Schmitz A, et al. Effects of ACE inhibition supplementary to beta blockers and diuretics in early diabetic nephropathy. Kidney International 1992; 41(4):883-90. *Sample size less than 50 patients*

3361. Pedersen MM, Mogensen CE, Jorgensen FS, et al. Renal effects from limitation of high dietary protein in normoalbuminuric diabetic patients. Kidney International - Supplement 1989; 27:S115-21. *Sample size less than 50 patients*

3362. Pedersen MM, Schmitz A, Pedersen EB, et al. Acute and long-term renal effects of angiotensin converting enzyme inhibition in normotensive, normoalbuminuric insulin-dependent diabetic patients. Diabetic Medicine 1988; 5(6):562-9. *Sample size less than 50 patients*

3363. Pedersen RS, Bentzen H, Bech JN, et al. Effect of an acute oral ibuprofen intake on urinary aquaporin-2 excretion in healthy humans. Scandinavian Journal of Clinical & Laboratory Investigation 2001; 61(8):631-40. *Not early CKD*

3364. Pedrinelli R, Dell'Omo G, Giampietro O, et al. Dissociation between albuminuria and insulinaemia in hypertensive and atherosclerotic men. Journal of Human Hypertension 1999; 13(2):129-34. *Not CKD treatment*

3365. Pedrinelli R, Ebel M, Catapano G, et al. Pressor, renal and endocrine effects of L-arginine in essential hypertensives. European Journal of Clinical Pharmacology 1995; 48(3-4):195-201. *Sample size less than 50 patients*

3366. Pedrinelli R, Panarace G, Spessot M, et al. Low dose atrial natriuretic factor in primary aldosteronism: renal, hemodynamic, and vascular effects. Hypertension 1989; 14(2):156-63. *Not CKD treatment*

3367. Pedrini MT, Levey AS, Lau J, et al. The effect of dietary protein restriction on the progression of diabetic and nondiabetic renal diseases: a meta-analysis. Annals of Internal Medicine 1996; 124(7):627-32. *Not RCT or controlled trial*

3368. Peixoto AJ, Orias M. Is there a role for direct renin inhibitors in chronic kidney disease? Current Opinion in Nephrology & Hypertension 2009; 18(5):397-403. *Not RCT or controlled trial*

3369. Peloquin CA, Berning SE, Nitta AT, et al. Aminoglycoside toxicity: daily versus thrice-weekly dosing for treatment of mycobacterial diseases. Clinical Infectious Diseases 2004; 38(11):1538-44. *Not CKD treatment*

3370. Peng T, Hu Z, Xia Q, et al. A comparative study of the renoprotective effects of benidipine and valsartan in primary hypertensive patients with proteinuria. Arzneimittel-Forschung 2009; 59(12):647-50. *Not relevant to key questions*

3371. Penno G, Chaturvedi N, Talmud PJ, et al. Effect of angiotensin-converting enzyme (ACE) gene polymorphism on progression of renal disease and the influence of ACE inhibition in IDDM patients: findings from the EUCLID Randomized Controlled Trial. EURODIAB Controlled Trial of Lisinopril in IDDM. Diabetes 1998; 47(9):1507-11. *Not CKD treatment*

3372. Pentheroudakis G, Twelves C. Capecitabine (Xeloda): from the laboratory to the patient's home. Clinical Colorectal Cancer 2002; 2(1):16-23. *Not CKD treatment*

3373. Percheron C, Colette C, Astre C, et al. Effects of moderate changes in protein intake on urinary albumin excretion in type I diabetic patients. Nutrition 1995; 11(4):345-9. *Sample size less than 50 patients*

3374. Pereira CN, Machado FR, Guimaraes HP, et al. Hemodynamics and renal function during administration of low-dose dopamine in severely ill patients. Sao Paulo Medical Journal = Revista Paulista de Medicina 2004; 122(4):141-6. *Not RCT or controlled trial*

3375. Perez J, Taura P, Rueda J, et al. Role of dopamine in renal dysfunction during laparoscopic surgery. Surgical Endoscopy 2002; 16(9):1297-301. *Not early CKD*

3376. Perez N, Spizzirri F, Rahman R, et al. Steroids in the hemolytic uremic syndrome. Pediatric Nephrology 1998; 12(2):101-4. *Not CKD treatment*

3377. Perez-Maraver M, Carrera MJ, Micalo T, et al. Renoprotective effect of diltiazem in hypertensive type 2 diabetic patients with persistent microalbuminuria despite ACE inhibitor treatment. Diabetes Research & Clinical Practice 2005; 70(1):13-9. *Sample size less than 50 patients*

3378. Perez-Valdivieso JR, Bes-Rastrollo M, Monedero P, et al. Prognosis and serum creatinine levels in acute renal failure at the time of nephrology consultation: an observational cohort study. BMC Nephrology 2007; 8:14. *Not early CKD*

3379. Pergola PE, Gartenberg G, Fu M, et al. A randomized controlled study comparing once-weekly to every-2-week and every-4-week dosing of epoetin alfa in CKD patients with anemia. Clinical Journal of The American Society of Nephrology: CJASN 2010 Apr; 5(4):598-606. *Not CKD treatment*

3380. Perinotto P, Biggi A, Carra N, et al. Angiotensin II and prostaglandin interactions on systemic and renal effects of L-NAME in humans. Journal of the American Society of Nephrology 2001; 12(8):1706-12. *Not early CKD*

3381. Perkins RM, Aboudara MC, Uy AL, et al. Effect of pentoxifylline on GFR decline in CKD: a pilot, double-blind, randomized, placebo-controlled trial. American Journal of Kidney Diseases 2009; 53(4):606-16. *Not CKD treatment*

3382. Perkovic V, Verdon C, Ninomiya T, et al. The relationship between proteinuria and coronary risk: a systematic review and meta-analysis. PLoS Medicine / Public Library of Science 2008; 5(10):e207. *Not CKD treatment*

3383. Perna A, Ruggenenti P, Testa A, et al. ACE genotype and ACE inhibitors induced renoprotection in chronic proteinuric nephropathies1. Kidney International 2000; 57(1):274-81. *Not CKD treatment*

3384. Perneger TV, Klag MJ, Whelton PK. Cause of death in patients with end-stage renal disease: death certificates vs registry reports. American Journal of Public Health 1993; 83(12):1735-8. *Not early CKD*

3385. Perrin NESS, Jaremko GA, Berg UB. The effects of candesartan on diabetes glomerulopathy: a double-blind, placebo-controlled trial. Pediatric Nephrology 2008; 23(6):947-54. *Sample size less than 50 patients*

3386. Persson B, Andersson OK, Wysocki M, et al. Renal and hemodynamic effects of isradipine in essential hypertension. American Journal of Medicine 1989; 86(4A):60-4. *Sample size less than 50 patients*

3387. Persson B, Andersson OK, Wysocki M, et al. Calcium antagonism in essential hypertension: effect on renal haemodynamics and microalbuminuria. Journal of Internal Medicine 1992; 231(3):247-52. *Sample size less than 50 patients*

3388. Persson B, Granerus G, Wysocki M, et al. Acute systemic and renal haemodynamic effects and long-term antihypertensive action of cadralazine in patients pretreated with beta-blockers and diuretics. European Journal of Clinical Pharmacology 1987; 31(5):513-8. *Sample size less than 50 patients*

3389. Persson F, Rossing P, Hovind P, et al. Endothelial dysfunction and inflammation predict development of diabetic nephropathy in the Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria (IRMA 2) study. Scandinavian Journal of Clinical & Laboratory Investigation 2008; 68(8):731-8. *Not CKD treatment*

3390. Persson F, Rossing P, Reinhard H, et al. Renal effects of aliskiren compared with and in combination with irbesartan in patients with type 2 diabetes, hypertension, and albuminuria. Diabetes Care 2009; 32(10):1873-9. *Sample size less than 50 patients*

3391. Persson F, Rossing P, Reinhard H, et al. Optimal antiproteinuric dose of aliskiren in type 2 diabetes mellitus: a randomised crossover trial. Diabetologia 2010 Aug; 53(8):1576-80. *Follow-up less than 6 months*

3392. Persson NH, Bergqvist D, Melander A, et al. Comparison of a narcotic (oxicone) and a non-narcotic anti-inflammatory analgesic (indoprofen) in the treatment of renal colic. Acta Chirurgica Scandinavica 1985; 151(2):105-8. *Follow-up less than 6 months*

3393. Perttunen K, Kalso E, Heinonen J, et al. IV diclofenac in post-thoracotomy pain. British Journal of Anaesthesia 1992; 68(5):474-80. *Not CKD treatment*

3394. Perttunen K, Nilsson E, Kalso E. I.v. diclofenac and ketorolac for pain after thoracoscopic surgery. British Journal of Anaesthesia 1999; 82(2):221-7. *Not CKD treatment*

3395. Perumal K, Fischer MJ, Mrtek R. Efficacy of furosemide in ARF. American Journal of Kidney Diseases 2005; 45(4):786; author reply -7. *Follow-up less than 6 months*

3396. Petchey WG, Hickman IJ, Duncan E, et al. The role of 25-hydroxyvitamin D deficiency in promoting insulin resistance and inflammation in patients with chronic kidney disease: a randomised controlled trial. BMC Nephrology 2009; 10:41. *Not RCT or controlled trial*

3397. Peters PJ, Moore DM, Mermin J, et al. Antiretroviral therapy improves renal function among HIV-infected Ugandans. Kidney International 2008; 74(7):925-9. *Not early CKD*

3398. Peters RM, Flack JM. Salt sensitivity and hypertension in African Americans: implications for cardiovascular nurses. Progress in Cardiovascular Nursing 2000; 15(4):138-44. *Not RCT or controlled trial*

3399. Petersen LJ, Petersen JR, Talleruphuus U, et al. A randomized and double-blind comparison of isradipine and spirapril as monotherapy and in combination on the decline in renal function in patients with chronic renal failure and hypertension. Clinical Nephrology 2001; 55(5):375-83. *Sample size less than 50 patients*

3400. Peterson GE, de Backer T, Gabriel A, et al. Prevalence and correlates of left ventricular hypertrophy in the African American Study of Kidney Disease Cohort Study. Hypertension 2007; 50(6):1033-9. *Sample size less than 50 patients*

3401. Peterson K. ACE inhibitors and renoprotection. Journal of Family Practice 1996; 42(5):453. *Not RCT or controlled trial*

3402. Petrica L, Petrica M, Vlad A, et al. Nephro- and neuroprotective effects of rosiglitazone versus glimepiride in normoalbuminuric patients with type 2 diabetes mellitus: a randomized controlled trial. Wiener Klinische Wochenschrift 2009; 121(23-24):765-75. *Sample size less than 50 patients*

3403. Petrovich Z, Yu C, Giannotta SL, et al. Survival and pattern of failure in brain metastasis treated with stereotactic gamma knife radiosurgery. Journal of Neurosurgery 2002; 97(5 Suppl):499-506. *Not CKD treatment*

3404. Petry A, Wulf H, Baumgartel M. The influence of ketanserin or urapidil on haemodynamics, stress response and kidney function during operations for myocardial revascularisation. Anaesthesia 1995; 50(4):312-6. *Sample size less than 50 patients*

3405. Pettinger WA, Lee HC, Reisch J, et al. Long-term improvement in renal function after short-term strict blood pressure control in hypertensive nephrosclerosis. Hypertension 1989; 13(6 Pt 2):766-72. *Not relevant to key questions*

3406. Peuckmann V, Elsner F, Krumm N, et al. Pharmacological treatments for fatigue associated with palliative care. Cochrane Database of Systematic Reviews 2010; 11:CD006788. *Not CKD treatment*

3407. Pfaller W, Thorwartl U, Nevinny-Stickel M, et al. Clinical value of fructose 1,6 bisphosphatase in monitoring renal proximal tubular injury. Kidney International - Supplement 1994; 47:S68-75. *Not CKD treatment*

3408. Pfeffer MA, Burdmann EA, Chen C-Y, et al. A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease. New England Journal of Medicine 2009; 361(21):2019-32. *Not CKD treatment*

3409. Pfeffer MA, Burdmann EA, Chen C-Y, et al. A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease. New England Journal of Medicine 2009; 361(21):2019-32. *Not CKD treatment*

3410. Pfeffer MA, Burdmann EA, Chen C-Y, et al. Baseline characteristics in the Trial to Reduce Cardiovascular Events With Aranesp Therapy (TREAT). American Journal of Kidney Diseases 2009; 54(1):59-69. *Not CKD treatment*

3411. Pfeffer MA, Committee TE. An ongoing study of anemia correction in chronic kidney disease. New England Journal of Medicine 2007; 356(9):959-61. *Not relevant to key questions*

3412. Pfeffer MA, Solomon SD, Singh AK, et al. Uncertainty in the treatment of anemia in chronic kidney disease. Reviews in Cardiovascular Medicine 2005; 6 Suppl 3:S35-41. *Not human studies*

3413. Pham P-TT, Pham P-CT, Wilkinson AH. Management of renal dysfunction in the liver transplant recipient. Current Opinion in Organ Transplantation 2009; 14(3):231-9. *Not CKD treatment*

3414. Phillips E, Hinck B, Pedro R, et al. Celecoxib in the management of acute renal colic: a randomized controlled clinical trial. Urology 2009; 74(5):994-9. *Follow-up less than 6 months*

3415. Phillips PJ, Phillipou G, Bowen KM, et al. Diabetic microalbuminuria and cilazapril. American Journal of Medicine 1993; 94(4A):58S-60S. *Sample size less than 50 patients*

3416. Phillips RA, Faulkner M, Gassman J, et al. Recruitment of African Americans with chronic renal insufficiency into a multicenter clinical trial: the african american study of kidney disease and hypertension. Journal of Clinical Hypertension 2004; 6(8):430-6. *Not CKD treatment*

3417. Phrommintikul A, Haas SJ, Elsik M, et al. Mortality and target haemoglobin concentrations in anaemic patients with chronic kidney disease treated with erythropoietin: a meta-analysis. Lancet 2007; 369(9559):381-8. *Sample size less than 50 patients*

3418. Piccoli A. Elementary clinical decision analysis in evidence-based nephrology. Journal of Nephrology 2000; 13(6):419-32. *Not RCT or controlled trial*

3419. Pichler J, Risch L, Hefti U, et al. Glomerular filtration rate estimates decrease during high altitude expedition but increase with Lake Louise acute mountain sickness scores. Acta Physiologica 2008; 192(3):443-50. *Not RCT or controlled trial*

3420. Pichler RH, de Boer IH. Dual renin-angiotensin-aldosterone system blockade for diabetic kidney disease. Current Diabetes Reports 2010 Aug; 10(4):297-305. *Not relevant to key questions*

3421. Pickering JW, Endre ZH. Back-calculating baseline creatinine with MDRD misclassifies acute kidney injury in the intensive care unit. Clinical Journal of The American Society of Nephrology: CJASN 2010 Jul; 5(7):1165-73. *Not CKD treatment*

3422. Pickering TG. Cardiorenal protection in diabetes. Heart Disease 2000; 2(2):S18-22. *Not RCT or controlled trial*

3423. Pickles CJ, Broughton Pipkin F, Symonds EM. A randomised placebo controlled trial of labetalol in the treatment of mild to moderate pregnancy induced hypertension. British Journal of Obstetrics & Gynaecology 1992; 99(12):964-8. *Not CKD treatment*

3424. Pickup JC, Collins AC, Walker JD, et al. Patterns of hyperinsulinaemia in type 1 diabetic patients with and without nephropathy. Diabetic Medicine 1989; 6(8):685-91. *Sample size less than 50 patients*

3425. Pidgeon GB, Richards AM, Nicholls MG, et al. Acute effects of intravenous ouabain in healthy volunteers. Clinical Science 1994; 86(4):391-7. *Not CKD treatment*

3426. Piecha G, Adamczak M, Chudek J, et al. Indapamide decreases plasma adiponectin concentration in patients with essential hypertension. Kidney & Blood Pressure Research 2007; 30(3):187-94. *Sample size less than 50 patients*

3427. Pierce HL, Stevermer JJ. Does losartan (Cozaar) slow the progression of renal disease in patients with type 2 diabetes and nephropathy? Journal of Family Practice 2001; 50(12):1083. *Not RCT or controlled trial*

3428. Pieta J, Millar T, Zacharias J, et al. Effect of pergolide on restless legs and leg movements in sleep in uremic patients. Sleep 1998; 21(6):617-22. *Not early CKD*

3429. Pijls LTJ, de Vries H, van Eijk JTM, et al. Protein restriction, glomerular filtration rate and albuminuria in patients with type 2 diabetes mellitus: a randomized trial. European Journal of Clinical Nutrition 2002; 56(12):1200-7. *Sample size less than 50 patients*

3430. Pimenta E, Oparil S. Role of aliskiren in cardio-renal protection and use in hypertensives with multiple risk factors. Vascular Health & Risk Management 2009; 5(1):453-63. *Not RCT or controlled trial*

3431. Pines A, Fisman EZ. ACE Inhibition with moexipril: a review of potential effects beyond blood pressure control. American Journal of Cardiovascular Drugs 2003; 3(5):351-60. *Follow-up less than 6 months*

3432. Pinkau T, Ndrepepa G, Kastrati A, et al. Glycoprotein IIb/IIIa receptor inhibition with abciximab during percutaneous coronary interventions increases the risk of bleeding in patients with impaired renal function. Cardiology 2008; 111(4):247-53. *Follow-up less than 6 months*

3433. Pinol C, Cobos A, Cases A, et al. Nitrendipine and enalapril in the treatment of diabetic hypertensive patients with microalbuminuria. Kidney International - Supplement 1996; 55:S85-7. *Sample size less than 50 patients*

3434. Pinto JR, Bending JJ, Dodds RA, et al. Effect of low protein diet on the renal response to meat ingestion in diabetic nephropathy. European Journal of Clinical Investigation 1991; 21(2):175-83. *Sample size less than 50 patients*

3435. Piozzi R, Ribeiro DA, Padovan LEM, et al. Genotoxicity and cytotoxicity in multiple organs induced by titanium miniplates in Wistar rats. Journal of Biomedical Materials Research 2009; Part A. 88(2):342-7. *Not early CKD*

3436. Piper SN, Kumle B, Maleck WH, et al. Diltiazem may preserve renal tubular integrity after cardiac surgery. Canadian Journal of Anaesthesia 2003; 50(3):285-92. *Not CKD treatment*

3437. Piquard F, Richard R, Charloux A, et al. Hormonal, renal, hemodynamic responses to acute neutral endopeptidase inhibition in heart transplant patients. Journal of Applied Physiology 2002; 93(2):569-75. *Not early CKD*

3438. Pisoni R, Ruggenenti P, Remuzzi G. Drug-induced thrombotic microangiopathy: incidence, prevention and management. Drug Safety 2001; 24(7):491-501. *Not early CKD*

3439. Pistrosch F, Herbrig K, Kindel B, et al. Rosiglitazone improves glomerular hyperfiltration, renal endothelial dysfunction, and microalbuminuria of incipient diabetic nephropathy in patients. Diabetes 2005; 54(7):2206-11. *Sample size less than 50 patients*

3440. Pitt B. Revascularization in patients with chronic kidney disease: the state of the ARTS. European Heart Journal 2005; 26(15):1456-7. *Follow-up less than 6 months*

3441. Pitt B, Segal R, Martinez FA, et al. Randomised trial of losartan versus captopril in patients over 65 with heart failure (Evaluation of Losartan in the Elderly Study, ELITE). Lancet 1997; 349(9054):747-52. *Not early CKD*

3442. Pivalizza EG, Abramson DC, Harvey A. Perioperative hypercoagulability in uremic patients: a viscoelastic study. Journal of Clinical Anesthesia 1997; 9(6):442-5. *Sample size less than 50 patients*

3443. Platz KP, Mueller AR, Jonas S, et al. Toxicity versus rejection--or why conversions between cyclosporine A and FK506 were performed after liver transplantation. Clinical Transplantation 1995; 9(3 Pt 1):146-54. *Not RCT or controlled trial*

3444. Plosker GL, Sorkin EM. Quinapril. A reappraisal of its pharmacology and therapeutic efficacy in cardiovascular disorders. Drugs 1994; 48(2):227-52. *Not CKD treatment*

3445. Plum J, Bunten B, Nemeth R, et al. Effects of the angiotensin II antagonist valsartan on blood pressure, proteinuria, and renal hemodynamics in patients with chronic renal failure and hypertension. Journal of the American Society of Nephrology 1998; 9(12):2223-34. *Sample size less than 50 patients*

3446. Plum J, Bunten B, Nemeth R, et al. Treatment with the angiotensin II antagonist valsartan in patients with chronic renal failure and hypertension. Nephrology Dialysis Transplantation 1999; 14 Suppl 4:25-7. *Sample size less than 50 patients*

3447. Plusa SM, Clark NW. Prevention of postoperative renal dysfunction in patients with obstructive jaundice: a comparison of mannitol-induced diuresis and oral sodium taurocholate. Journal of the Royal College of Surgeons of Edinburgh 1991; 36(5):303-5. *Not CKD treatment*

3448. Pohl MA. Changing the course of diabetic nephropathy: angiotensin-converting enzyme inhibition in type I diabetic renal disease. Cleveland Clinic Journal of Medicine 1994; 61(1):38-42. *Not RCT or controlled trial*

3449. Pohl MA, Blumenthal S, Cordonnier DJ, et al. Independent and additive impact of blood pressure control and angiotensin II receptor blockade on renal outcomes in the irbesartan diabetic nephropathy trial: clinical implications and limitations. Journal of the American Society of Nephrology 2005; 16(10):3027-37. *Not RCT or controlled trial*

3450. Poirier SJ. Reducing complications in type 2 diabetes. American Family Physician 1998; 57(6):1238-9. *Not RCT or controlled trial*

3451. Poletti P-A, Saudan P, Platon A, et al. I.v. N-acetylcysteine and emergency CT: use of serum creatinine and cystatin C as markers of radiocontrast nephrotoxicity. AJR 2007; American Journal of Roentgenology. 189(3):687-92. *Not CKD treatment*

3452. Polonia J, Boaventura I, Gama G, et al. Influence of non-steroidal anti-inflammatory drugs on renal function and 24h ambulatory blood pressure-reducing effects of enalapril and nifedipine gastrointestinal therapeutic system in hypertensive patients. Journal of Hypertension 1995; 13(8):925-31. *Follow-up less than 6 months*

3453. Pomerleau J, Verdy M, Garrel DR, et al. Effect of protein intake on glycaemic control and renal function in type 2 (non-insulin-dependent) diabetes mellitus. Diabetologia 1993; 36(9):829-34. *Sample size less than 50 patients*

3454. Ponticelli C, Edefonti A, Ghio L, et al. Cyclosporin versus cyclophosphamide for patients with steroid-dependent and frequently relapsing idiopathic nephrotic syndrome: a multicentre randomized controlled trial. Nephrology Dialysis Transplantation 1993; 8(12):1326-32. *Not early CKD*

3455. Ponticelli C, Rizzoni G, Edefonti A, et al. A randomized trial of cyclosporine in steroid-resistant idiopathic nephrotic syndrome. Kidney International 1993; 43(6):1377-84. *Sample size less than 50 patients*

3456. Pool JL. Is it time to move to multidrug combinations? American Journal of Hypertension 2003; 16(11 Pt 2):36S-40S. *Not CKD treatment*

3457. Poortmans JR, Auquier H, Renaut V, et al. Effect of short-term creatine supplementation on renal responses in men. European Journal of Applied Physiology & Occupational Physiology 1997; 76(6):566-7. *Sample size less than 50 patients*

3458. Porayko MK, Gonwa TA, Klintmalm GB, et al. Comparing nephrotoxicity of FK 506 and cyclosporine regimens after liver transplantation: preliminary results from US Multicenter trial. U.S. Multicenter Liver Study Group. Transplantation Proceedings 1995; 27(1):1114-6. *Not early CKD*

3459. Porayko MK, Textor SC, Krom RA, et al. Nephrotoxic effects of primary immunosuppression with FK-506 and cyclosporine regimens after liver transplantation. Mayo Clinic Proceedings 1994; 69(2):105-11. *Sample size less than 50 patients*

3460. Porayko MK, Textor SC, Krom RA, et al. Nephrotoxicity of FK 506 and cyclosporine when used as primary immunosuppression in liver transplant recipients. Transplantation Proceedings 1993; 25(1 Pt 1):665-8. *Not RCT or controlled trial*

3461. Pordy R, Woittiez A. Steady-state trough plasma mibefradil concentrations and correlation to blood pressure response in hypertensive patients with chronic renal disease. International Journal of Clinical Pharmacology Research 1998; 18(3):105-8. *Not RCT or controlled trial*

3462. Portaluppi F, Vergnani L, Manfredini R, et al. Time-dependent effect of isradipine on the nocturnal hypertension in chronic renal failure. American Journal of Hypertension 1995; 8(7):719-26. *Sample size less than 50 patients*

3463. Porter GA. Contrast-associated nephropathy: presentation, pathophysiology and management. Mineral & Electrolyte Metabolism 1994; 20(4):232-43. *Not CKD treatment*

3464. Porter GA, Norton TL, Legg V. Using urinary biomarkers to evaluate renal effects of a Cox-2 NSAID in volunteers. Renal Failure 1999; 21(3-4):311-7. *Sample size less than 50 patients*

3465. Porzano AM, Baldoncini R, De Siati L, et al. Effects of short-time insulin suppression on renal sodium excretion in type II diabetic hypertensives. Diabetes Research 1993; 22(1):3-10. *Sample size less than 50 patients*

3466. Poschel KA, Bucha E, Esslinger HU, et al. Pharmacodynamics and pharmacokinetics of polyethylene glycol-hirudin in patients with chronic renal failure. Kidney International 2000; 58(6):2478-84. *Not RCT or controlled trial*

3467. Posen S, Clifton-Bligh P, Reeve TS, et al. Is parathyroidectomy of benefit in primary hyperparathyroidism? Quarterly Journal of Medicine 1985; 54(215):241-51. *Not CKD treatment*

3468. Post FA, Moyle GJ, Stellbrink HJ, et al. Randomized comparison of renal effects, efficacy, and safety with once-daily abacavir/lamivudine versus tenofovir/emtricitabine, administered with efavirenz, in antiretroviral-naive, HIV-1-infected adults: 48-week results from the ASSERT study. Journal of Acquired Immune Deficiency Syndromes: JAIDS 2010 Sep 1; 55(1):49-57. *Not early CKD*

3469. Postma MJ, Kruidhof H, de Jong-van den Berg LTW, et al. Pharmacoeconomic aspects of losartan treatment to delay progression of renal disease in patients with Type 2 diabetes. Expert Opinion on Pharmacotherapy 2003; 4(9):1543-50. *Not relevant to key questions*

3470. Potena L, Bianchi IG, Magnani G, et al. Cyclosporine lowering with everolimus or mycophenolate to preserve renal function in heart recipients: a randomized study. Transplantation 2010; 89(2):263-5. *Sample size less than 50 patients*

3471. Potter K, Hankey GJ, Green DJ, et al. Homocysteine or renal impairment: which is the real cardiovascular risk factor? Arteriosclerosis, Thrombosis & Vascular Biology 2008; 28(6):1158-64. *Not human studies*

3472. Pouleur H. Neurohormonal and hemodynamic effects of ibopamine. Clinical Cardiology 1995; 18(3 Suppl I):I17-21. *Not CKD treatment*

3473. Poulsen PL. ACE inhibitor intervention in Type 1 diabetes with low grade microalbuminuria. Journal of the Renin-Angiotensin-Aldosterone System 2003; 4(1):17-26. *Sample size less than 50 patients*

3474. Poulsen PL, Ebbehoj E, Mogensen CE. Lisinopril reduces albuminuria during exercise in low grade microalbuminuric type 1 diabetic patients: a double blind randomized study. Journal of Internal Medicine 2001; 249(5):433-40. *Sample size less than 50 patients*

3475. Poulsen PL, Ebbehoj E, Nosadini R, et al. Early ACE-i intervention in microalbuminuric patients with type 1 diabetes: effects on albumin excretion, 24 h ambulatory blood pressure, and renal function. Diabetes & Metabolism 2001; 27(2 Pt 1):123-8. *Sample size less than 50 patients*

3476. Powe NR. Measuring effectiveness and outcomes of interventions for renal disease. Current Opinion in Nephrology & Hypertension 1996; 5(3):230-5. *Not RCT or controlled trial*

3477. Powe NR, Moore RD, Steinberg EP. Adverse reactions to contrast media: factors that determine the cost of treatment. AJR 1993; American Journal of Roentgenology. 161(5):1089-95. *Not CKD treatment*

3478. Power DA, Duggan J, Brady HR. Renal-dose (low-dose) dopamine for the treatment of sepsis-related and other forms of acute renal failure: ineffective and probably dangerous. Clinical & Experimental Pharmacology & Physiology - Supplement 1999; 26:S23-8. *Not RCT or controlled trial*

3479. Power I, Cumming AD, Pugh GC. Effect of diclofenac on renal function and prostacyclin generation after surgery. British Journal of Anaesthesia 1992; 69(5):451-6. *Sample size less than 50 patients*

3480. Praga M, Andrade CF, Luno J, et al. Antiproteinuric efficacy of losartan in comparison with amlodipine in non-diabetic proteinuric renal diseases: a double-blind, randomized clinical trial. Nephrology Dialysis Transplantation 2003; 18(9):1806-13. *Follow-up less than 6 months*

3481. Praga M, Hernandez E, Andres A, et al. Effects of body-weight loss and captopril treatment on proteinuria associated with obesity. Nephron 1995; 70(1):35-41. *Sample size less than 50 patients*

3482. Prakash S, Pande DP, Sharma S, et al. Randomized, double-blind, placebo-controlled trial to evaluate efficacy of ketodiet in predialytic chronic renal failure. Journal of Renal Nutrition 2004; 14(2):89-96. *Not CKD treatment*

3483. Pratley RE, Rosenstock J, Pi-Sunyer FX, et al. Management of type 2 diabetes in treatment-naive elderly patients: benefits and risks of vildagliptin monotherapy. Diabetes Care 2007; 30(12):3017-22. *Not relevant to key questions*

3484. Predel HG, Kuklinski P, Kramer HJ. Intranasal application of atrial natriuretic peptide and 1-deamino-d-arginine vasopressin in healthy volunteers. Hemodynamic, hormonal, and renal excretory effects. American Journal of Hypertension 1992; 5(9):657-60. *Sample size less than 50 patients*

3485. Preiss DJ, Godber IM, Lamb EJ, et al. The influence of a cooked-meat meal on estimated glomerular filtration rate. Annals of Clinical Biochemistry 2007; 44(Pt 1):35-42. *Not RCT or controlled trial*

3486. Prescott LF, Freestone S, McAuslane JA. Reassessment of the single intravenous injection method with inulin for measurement of the glomerular filtration rate in man. Clinical Science 1991; 80(2):167-76. *Sample size less than 50 patients*

3487. Prescott LF, Mattison P, Menzies DG, et al. The comparative effects of paracetamol and indomethacin on renal function in healthy female volunteers. British Journal of Clinical Pharmacology 1990; 29(4):403-12. *Not CKD treatment*

3488. Presta P, Onorati F, Fuiano L, et al. Can pulsatile cardiopulmonary bypass prevent perioperative renal dysfunction during myocardial revascularization in elderly patients? Nephron 2009; 111(4):c229-35. *Not CKD treatment*

3489. Preston RA, Afshartous D, Alonso AB. Effects of selective vs. nonselective cyclooxygenase inhibition on dynamic renal potassium excretion: a randomized trial. Clinical Pharmacology & Therapeutics 2008; 84(2):208-11. *Not CKD treatment*

3490. Preston RA, Afshartous D, Garg D, et al. Mechanisms of impaired potassium handling with dual renin-angiotensin-aldosterone blockade in chronic kidney disease. Hypertension 2009; 53(5):754-60. *Not CKD treatment*

3491. Preston RA, Materson BJ, Reda DJ, et al. Proteinuria in mild to moderate hypertension: results of the VA cooperative study of six antihypertensive agents and placebo. Department of Veterans Affairs Cooperative Study Group on Antihypertensive Agents. Clinical Nephrology 1997; 47(5):310-5. *Not early CKD*

3492. Price DA, Fisher NDL, Lansang MC, et al. Renal perfusion in blacks: alterations caused by insuppressibility of intrarenal renin with salt. Hypertension 2002; 40(2):186-9. *Not CKD treatment*

3493. Price DA, Hollenberg NK. Angiotensin receptor blockers in diabetic nephropathy. Current Diabetes Reports 2001; 1(3):267-74. *Not RCT or controlled trial*

3494. Pridjian AK, Bove EL, Beekman RH, 3rd, et al. Comparison of a low osmolarity nonionic radiographic contrast agent with a standard medium on renal function in cyanotic and normal dogs. Catheterization & Cardiovascular Diagnosis 1994; 31(1):90-3. *Sample size less than 50 patients*

3495. Prins JM, Buller HR, Kuijper EJ, et al. Once versus thrice daily gentamicin in patients with serious infections. Lancet 1993; 341(8841):335-9. *Not CKD treatment*

3496. Prisant LM. Diabetes mellitus and hypertension: a mandate for intense treatment according to new guidelines. American Journal of Therapeutics 2003; 10(5):363-9. *Not RCT or controlled trial*

3497. Prisant LM, Louard RJ. Controversies surrounding the treatment of the hypertensive patient with diabetes. Current Hypertension Reports 1999; 1(6):512-20. *Not RCT or controlled trial*

3498. Pritchard G, Lyons D, Webster J, et al. Do trandolapril and indomethacin influence renal function and renal functional reserve in hypertensive patients? British Journal of Clinical Pharmacology 1997; 44(2):145-9. *Follow-up less than 6 months*

3499. Prodjosudjadi W, Suhardjono, Suwitra K, et al. Detection and prevention of chronic kidney disease in Indonesia: initial community screening. Nephrology 2009; 14(7):669-74. *Not RCT or controlled trial*

3500. Pronovost PH, Brady HR, Gunning ME, et al. Clinical features, predictors of disease progression and results of renal transplantation in fibrillary/immunotactoid glomerulopathy. Nephrology Dialysis Transplantation 1996; 11(5):837-42. *Not RCT or controlled trial*

3501. Provenzano R, Bhaduri S, Singh AK, et al. Extended epoetin alfa dosing as maintenance treatment for the anemia of chronic kidney disease: the PROMPT study. Clinical Nephrology 2005; 64(2):113-23. *Not CKD treatment*

3502. Provenzano R, Garcia-Mayol L, Suchinda P, et al. Once-weekly epoetin alfa for treating the anemia of chronic kidney disease. Clinical Nephrology 2004; 61(6):392-405. *Sample size less than 50 patients*

3503. Prowle JR, Echeverri JE, Ligabo EV, et al. Fluid balance and acute kidney injury. Nature Reviews Nephrology 2010 Feb; 6(2):107-15. *Not early CKD*

3504. Puig JG, Marre M, Kokot F, et al. Efficacy of indapamide SR compared with enalapril in elderly hypertensive patients with type 2 diabetes. American Journal of Hypertension 2007; 20(1):90-7. *Not RCT or controlled trial*

3505. Puig JG, Mateos FA, Ramos TH, et al. Albumin excretion rate and metabolic modifications in patients with essential hypertension. Effects of two angiotensin converting enzyme inhibitors. American Journal of Hypertension 1994; 7(1):46-51. *Sample size less than 50 patients*

3506. Puigmule M, Lopez-Hellin J, Sune G, et al. Differential proteomic analysis of cyclosporine A-induced toxicity in renal proximal tubule cells. Nephrology Dialysis Transplantation 2009; 24(9):2672-86. *Not CKD treatment*

3507. Pull ter Gunne AJ, Bruining HA, Obertop H. Haemodynamics and ‘optimal’ hydration in aortic cross clamping. Netherlands Journal of Surgery 1990; 42(4):113-7. *Not CKD treatment*

3508. Puolakka PAE, Rintala S, Yli-Hankala A, et al. The effect of parecoxib on kidney function at laparoscopic hysterectomy. Renal Failure 2009; 31(4):284-9. *Sample size less than 50 patients*

3509. Puscas I, Coltau M, Baican M, et al. Omeprazole has a dual mechanism of action: it inhibits both H(+)K(+)ATPase and gastric mucosa carbonic anhydrase enzyme in humans (in vitro and in vivo experiments). Journal of Pharmacology & Experimental Therapeutics 1999; 290(2):530-4. *Not CKD treatment*

3510. Pylypchuk G, Beaubien E. Diabetic nephropathy. Prevention and early referral. Canadian Family Physician 2000; 46:636-42. *Not RCT or controlled trial*

3511. Qiu Z, Chen X, Xu M, et al. Evaluation of preoperative intra-aortic balloon pump in coronary patients with severe left ventricular dysfunction undergoing OPCAB surgery: early and mid-term outcomes. Journal Of Cardiothoracic Surgery 2009; 4:39. *Not CKD treatment*

3512. Quan DJ, McQueen KD. dDAVP in enuresis. DICP 1990; 24(12):1179-80. *Not RCT or controlled trial*

3513. Qureshi F, Tahir M, Sami W. Protective role of vitamin C and E against sodium arsenate induced changes in developing kidney of albino mice. Journal of Ayub Medical College, Abbottabad: JAMC 2009 Oct-Dec; 21(4):63-9. *Not human studies*

3514. Raab C, Weidmann E, Schmidt A, et al. The effects of interleukin-2 treatment on endothelin and the activation of the hypothalamic-pituitary-adrenal axis. Clinical Endocrinology 1999; 50(1):37-44. *Not CKD treatment*

3515. Raal FJ, Kalk WJ, Lawson M, et al. Effect of moderate dietary protein restriction on the progression of overt diabetic nephropathy: a 6-mo prospective study. American Journal of Clinical Nutrition 1994; 60(4):579-85. *Sample size less than 50 patients*

3516. Rab A, Dallinger S, Polak K, et al. Specific endothelin ET(A) receptor antagonism does not modulate insulin-induced hemodynamic effects in the human kidney, eye, or forearm. Journal of Pharmacology & Experimental Therapeutics 2004; 309(2):692-6. *Not CKD treatment*

3517. Rabbani N, Alam SS, Riaz S, et al. High-dose thiamine therapy for patients with type 2 diabetes and microalbuminuria: a randomised, double-blind placebo-controlled pilot study. Diabetologia 2009; 52(2):208-12. *Not CKD treatment*

3518. Rabelink AJ, Hene RJ, Erkelens DW, et al. Effects of simvastatin and cholestyramine on lipoprotein profile in hyperlipidaemia of nephrotic syndrome. Lancet 1988; 2(8624):1335-8. *Sample size less than 50 patients*

3519. Rabelink TJ, Kaasjager KA, Boer P, et al. Effects of endothelin-1 on renal function in humans: implications for physiology and pathophysiology. Kidney International 1994; 46(2):376-81. *Not RCT or controlled trial*

3520. Rabelink TJ, Koomans HA, van de Stolpe A, et al. Effects of atrial natriuretic peptide on distal tubule function in humans. Kidney International 1990; 37(3):996-1001. *Not CKD treatment*

3521. Rachmani R, Levi Z, Slavachevski I, et al. Teaching patients to monitor their risk factors retards the progression of vascular complications in high-risk patients with Type 2 diabetes mellitus--a randomized prospective study. Diabetic Medicine 2002; 19(5):385-92. *Not early CKD*

3522. Rachmani R, Levi Z, Slavachevsky I, et al. Effect of an alpha-adrenergic blocker, and ACE inhibitor and hydrochlorothiazide on blood pressure and on renal function in type 2 diabetic patients with hypertension and albuminuria. A randomized cross-over study. Nephron 1998; 80(2):175-82. *Follow-up less than 6 months*

3523. Rachmani R, Ravid M. Risk factors for nephropathy in type 2 diabetes mellitus. Comprehensive Therapy 1999; 25(6-7):366-9. *Not RCT or controlled trial*

3524. Rachmani R, Slavachevski I, Berla M, et al. Teaching and motivating patients to control their risk factors retards progression of cardiovascular as well as microvascular sequelae of Type 2 diabetes mellitus- a randomized prospective 8 years follow-up study. Diabetic Medicine 2005; 22(4):410-4. *Not early CKD*

3525. Rachmani R, Slavachevsky I, Amit M, et al. The effect of spironolactone, cilazapril and their combination on albuminuria in patients with hypertension and diabetic nephropathy is independent of blood pressure reduction: a randomized controlled study.[Retraction in Diabet Med. 2006 Jul;23(7):818; PMID: 16842490]. Diabetic Medicine 2004; 21(5):471-5. *Sample size less than 50 patients*

3526. Radermacher J, Koch KM. Treatment of renal anemia by erythropoietin substitution. The effects on the cardiovascular system. Clinical Nephrology 1995; 44 Suppl 1:S56-60. *Not early CKD*

3527. Radovancevic B, Frazier OH. Treatment of moderate heart allograft rejection with cyclosporine. Journal of Heart Transplantation 1986; 5(4):307-11. *Sample size less than 50 patients*

3528. Ragsdale NV, Lynd M, Chevalier RL, et al. Selective peripheral dopamine-1 receptor stimulation. Differential responses to sodium loading and depletion in humans. Hypertension 1990; 15(6 Pt 2):914-21. *Not CKD treatment*

3529. Rahman AR, Motwani JG, Lang CC, et al. Circulating angiotensin II and renal sodium handling in man: a dose-response study. Clinical Science 1993; 85(2):147-56. *Sample size less than 50 patients*

3530. Rahman IA, Mascaro JG, Steeds RP, et al. Remote ischemic preconditioning in human coronary artery bypass surgery: from promise to disappointment? Circulation 2010 Sep 14; 122(11 Suppl):S53-9. *Not CKD treatment*

3531. Rahman M. Initial findings of the AASK: African Americans with hypertensive kidney disease benefit from an ACE inhibitor. Cleveland Clinic Journal of Medicine 2003; 70(4):304-5. *Not relevant to key questions*

3532. Rahman M, El-Meanawy A, Romanello J. The African American Study of Kidney Disease: do these results indicate that 140/90 mm hg is good enough? Current Hypertension Reports 2005; 7(5):363-6. *Not relevant to key questions*

3533. Raimondo ML, Dagher L, Papatheodoridis GV, et al. Long-term mycophenolate mofetil monotherapy in combination with calcineurin inhibitors for chronic renal dysfunction after liver transplantation. Transplantation 2003; 75(2):186-90. *Sample size less than 50 patients*

3534. Ralph CJ, Tanser SJ, Macnaughton PD, et al. A randomised controlled trial investigating the effects of dopexamine on gastrointestinal function and organ dysfunction in the critically ill.[Erratum appears in Intensive Care Med 2002 Jul;28(7):1001]. Intensive Care Medicine 2002; 28(7):884-90. *Not CKD treatment*

3535. Ram CV. Ketanserin in essential hypertension. Effects of blood pressure on renal hemodynamics. American Journal of Hypertension 1988; 1(3 Pt 3):309S-11S. *Follow-up less than 6 months*

3536. Raman GV, Campbell SK, Farrer A, et al. Modifying effects of amlodipine on cyclosporin A-induced changes in renal function in patients with psoriasis. Journal of Hypertension - Supplement 1998; 16(4):S39-41. *Sample size less than 50 patients*

3537. Ramel A, Jonsson PV, Bjornsson S, et al. Differences in the glomerular filtration rate calculated by two creatinine-based and three cystatin-C-based formulae in hospitalized elderly patients. Nephron 2008; 108(1):c16-22. *Not relevant to key questions*

3538. Ramin SM, Vidaeff AC, Yeomans ER, et al. Chronic renal disease in pregnancy. Obstetrics & Gynecology 2006; 108(6):1531-9. *Not relevant to key questions*

3539. Ramires JA, Tsanaclis A, Gimenez HC, et al. Acute effects of dobutamine and dopamine on renal and respiratory functions in patients on prolonged mechanical ventilation. Brazilian Journal of Medical & Biological Research 1991; 24(1):35-42. *Sample size less than 50 patients*

3540. Rammohan C, Fintel D. Dosing considerations and monitoring of low molecular weight heparins and glycoprotein IIb/IIIa antagonists in patients with renal insufficiency. Current Cardiology Reports 2003; 5(4):303-9. *Not CKD treatment*

3541. Randell TT, Hockerstedt KA. Triiodothyronine treatment in brain-dead multiorgan donors--a controlled study. Transplantation 1992; 54(4):736-8. *Sample size less than 50 patients*

3542. Ranganathan N, Friedman EA, Tam P, et al. Probiotic dietary supplementation in patients with stage 3 and 4 chronic kidney disease: a 6-month pilot scale trial in Canada. Current Medical Research & Opinion 2009; 25(8):1919-30. *Sample size less than 50 patients*

3543. Ranganathan S, Krempf M, Feraille E, et al. Short term effect of an aldose reductase inhibitor on urinary albumin excretion rate (UAER) and glomerular filtration rate (GFR) in type 1 diabetic patients with incipient nephropathy. Diabete et Metabolisme 1993; 19(2):257-61. *Sample size less than 50 patients*

3544. Rangemark C, Lind H, Lindholm L, et al. Lisinopril reduces postexercise albuminuria more effectively than atenolol in primary hypertension. European Journal of Clinical Pharmacology 1996; 49(4):267-71. *Follow-up less than 6 months*

3545. Ranich T, Bhathena SJ, Velasquez MT. Protective effects of dietary phytoestrogens in chronic renal disease. Journal of Renal Nutrition 2001; 11(4):183-93. *Not CKD treatment*

3546. Ranieri G, Andriani A, Lamontanara G, et al. Effects of lisinopril and amlodipine on microalbuminuria and renal function in patients with hypertension. Clinical Pharmacology & Therapeutics 1994; 56(3):323-30. *Sample size less than 50 patients*

3547. Ranpura V, Hapani S, Chuang J, et al. Risk of cardiac ischemia and arterial thromboembolic events with the angiogenesis inhibitor bevacizumab in cancer patients: a meta-analysis of randomized controlled trials. Acta Oncologica 2010 Apr; 49(3):287-97. *Not CKD treatment*

3548. Ranucci M, Soro G, Barzaghi N, et al. Fenoldopam prophylaxis of postoperative acute renal failure in high-risk cardiac surgery patients. Annals of Thoracic Surgery 2004; 78(4):1332-7; discussion 7-8. *Not RCT or controlled trial*

3549. Rapini RP, Herbert AA, Drucker CR. Acquired perforating dermatosis. Evidence for combined transepidermal elimination of both collagen and elastic fibers. Archives of Dermatology 1989; 125(8):1074-8. *Sample size less than 50 patients*

3550. Rappelli A, Dessi-Fulgheri P, Madeddu P, et al. Studies on the natriuretic effect of nifedipine in hypertensive patients: increase in levels of plasma atrial natriuretic factor without participation of the renal kallikrein-kinin system. Journal of Hypertension - Supplement 1987; 5(4):S61-5. *Sample size less than 50 patients*

3551. Rasaratnam B, Kaye D, Jennings G, et al. The effect of selective intestinal decontamination on the hyperdynamic circulatory state in cirrhosis. A randomized trial. Annals of Internal Medicine 2003; 139(3):186-93. *Not CKD treatment*

3552. Rashid ST, Salman M, Myint F, et al. Prevention of contrast-induced nephropathy in vascular patients undergoing angiography: a randomized controlled trial of intravenous N-acetylcysteine. Journal of Vascular Surgery 2004; 40(6):1136-41. *Not relevant to key questions*

3553. Rasmussen A, Jespersen L. Reduced tubular reabsorption of phosphate during post-operative glucose infusions in humans. European Journal of Clinical Investigation 1985; 15(3):157-60. *Sample size less than 50 patients*

3554. Rasmussen A, Kimose HH, Hessov I. Severity of postoperative hypophosphatemia in relation to glucose administration and renal handling of phosphate. Acta Chirurgica Scandinavica 1988; 154(11-12):617-21. *Follow-up less than 6 months*

3555. Rasmussen S, Leth A, Ibsen H, et al. Converting enzyme inhibition in mild and moderate essential hypertension. II. Acta Medica Scandinavica 1986; 219(1):29-36. *Sample size less than 50 patients*

3556. Rathod A, Badheka A, Kizilbash M, et al. Renal disease and cardiac mortality in survivors of sudden cardiac death. Acta Cardiologica 2010 Jun; 65(3):323-8. *Not CKD treatment*

3557. Ratner RE. Diabetes control and complications. Where do we go from here? Online Journal of Current Clinical Trials 1993; Doc No 68:[996 words; 6 paragraphs]. *Not RCT or controlled trial*

3558. Ravera M, Ratto E, Vettoretti S, et al. Prevention and treatment of diabetic nephropathy: the program for irbesartan mortality and morbidity evaluation. Journal of the American Society of Nephrology 2005; 16 Suppl 1:S48-52. *Not relevant to key questions*

3559. Ravid M, Brosh D, Levi Z, et al. Use of enalapril to attenuate decline in renal function in normotensive, normoalbuminuric patients with type 2 diabetes mellitus. A randomized, controlled trial. Annals of Internal Medicine 1998; 128(12 Pt 1):982-8. *Not relevant to key questions*

3560. Ravid M, Lang R, Rachmani R, et al. Long-term renoprotective effect of angiotensin-converting enzyme inhibition in non-insulin-dependent diabetes mellitus. A 7-year follow-up study. Archives of Internal Medicine 1996; 156(3):286-9. *Not relevant to key questions*

3561. Ravid M, Neumann L, Lishner M. Plasma lipids and the progression of nephropathy in diabetes mellitus type II: effect of ACE inhibitors. Kidney International 1995; 47(3):907-10. *Not CKD treatment*

3562. Ravid M, Savin H, Jutrin I, et al. Long-term effect of ACE inhibition on development of nephropathy in diabetes mellitus type II. Kidney International - Supplement 1994; 45:S161-4. *Not relevant to key questions*

3563. Ravva P, Gastonguay MR, Tensfeldt TG, et al. Population pharmacokinetic analysis of varenicline in adult smokers. British Journal of Clinical Pharmacology 2009 Nov; 68(5):669-81. *Not CKD treatment*

3564. Rayner B. Advances in the treatment of diabetic renal disease: focus on losartan. Current Medical Research & Opinion 2004; 20(3):333-40. *Not RCT or controlled trial*

3565. Rayner BL, Trinder YA, Baines D, et al. Effect of losartan versus candesartan on uric acid, renal function, and fibrinogen in patients with hypertension and hyperuricemia associated with diuretics. American Journal of Hypertension 2006; 19(2):208-13. *Follow-up less than 6 months*

3566. Reams G, Villarreal D, Wu Z, et al. Urinary angiotensin II: a marker of renal tissue activity? Nephron 1994; 67(4):450-8. *Not RCT or controlled trial*

3567. Reams GP, Bauer JH. Enalapril versus triple-drug therapy in the treatment of renovascular hypertension. Drugs 1985; 30 Suppl 1:59-69. *Sample size less than 50 patients*

3568. Reams GP, Lau A, Bauer JH. Short-term and long-term renal response to nifedipine monotherapy. American Journal of Hypertension 1989; 2(3 Pt 1):188-90. *Not CKD treatment*

3569. Reams GP, Lau A, Hamory A, et al. Amlodipine therapy corrects renal abnormalities encountered in the hypertensive state. American Journal of Kidney Diseases 1987; 10(6):446-51. *Sample size less than 50 patients*

3570. Reddan D, Laville M, Garovic VD. Contrast-induced nephropathy and its prevention: What do we really know from evidence-based findings? Journal of Nephrology 2009; 22(3):333-51. *Not RCT or controlled trial*

3571. Reddan DN, Frankenfield DL, Klassen PS, et al. Regional variability in anaemia management and haemoglobin in the US. Nephrology Dialysis Transplantation 2003; 18(1):147-52. *Not early CKD*

3572. Reddan DN, O'Shea JC, Sarembock IJ, et al. Treatment effects of eptifibatide in planned coronary stent implantation in patients with chronic kidney disease (ESPRIT Trial). American Journal of Cardiology 2003; 91(1):17-21. *Follow-up less than 6 months*

3573. Redman BG, Flaherty L, Martino S, et al. Effect of calcium replacement on the hemodynamic changes associated with high dose interleukin-2 therapy. American Journal of Clinical Oncology 1992; 15(4):340-3. *Not CKD treatment*

3574. Regamey F, Maillard M, Nussberger J, et al. Renal hemodynamic and natriuretic effects of concomitant Angiotensin-converting enzyme and neutral endopeptidase inhibition in men. Hypertension 2002; 40(3):266-72. *Sample size less than 50 patients*

3575. Regazzi MB, Rinaldi M, Molinaro M, et al. Clinical pharmacokinetics of tacrolimus in heart transplant recipients. Therapeutic Drug Monitoring 1999; 21(1):2-7. *Not CKD treatment*

3576. Reich DJ, Clavien PA, Hodge EE, et al. Mycophenolate mofetil for renal dysfunction in liver transplant recipients on cyclosporine or tacrolimus: randomized, prospective, multicenter pilot study results. Transplantation 2005; 80(1):18-25. *Follow-up less than 6 months*

3577. Reichard P, Nilsson BY, Rosenqvist U. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. New England Journal of Medicine 1993; 329(5):304-9. *Not early CKD*

3578. Reichard P, Pihl M, Rosenqvist U, et al. Complications in IDDM are caused by elevated blood glucose level: the Stockholm Diabetes Intervention Study (SDIS) at 10-year follow up. Diabetologia 1996; 39(12):1483-8. *Sample size less than 50 patients*

3579. Reichard P, Rosenqvist U. Nephropathy is delayed by intensified insulin treatment in patients with insulin-dependent diabetes mellitus and retinopathy. Journal of Internal Medicine 1989; 226(2):81-7. *Not relevant to key questions*

3580. Reichel H, Grussinger A, Knehans A, et al. Long-term therapy with cyclosporin A does not influence serum concentrations of vitamin D metabolites in patients with multiple sclerosis. Clinical Investigator 1992; 70(7):595-9. *Not CKD treatment*

3581. Reichert LJ, Koene RA, Wetzels JF. Acute haemodynamic and proteinuric effects of prednisolone in patients with a nephrotic syndrome. Nephrology Dialysis Transplantation 1999; 14(1):91-7. *Sample size less than 50 patients*

3582. Reid A, Stohr W, Walker AS, et al. Severe renal dysfunction and risk factors associated with renal impairment in HIV-infected adults in Africa initiating antiretroviral therapy. Clinical Infectious Diseases 2008; 46(8):1271-81. *Not CKD treatment*

3583. Reimann IW, Golbs E, Fischer C, et al. Influence of intravenous acetylsalicylic acid and sodium salicylate on human renal function and lithium clearance. European Journal of Clinical Pharmacology 1985; 29(4):435-41. *Sample size less than 50 patients*

3584. Reisler RB, Han C, Burman WJ, et al. Grade 4 events are as important as AIDS events in the era of HAART. Journal of Acquired Immune Deficiency Syndromes: JAIDS 2003; 34(4):379-86. *Not relevant to key questions*

3585. Remuzzi G, Macia M, Ruggenenti P. Prevention and treatment of diabetic renal disease in type 2 diabetes: the BENEDICT study. Journal of the American Society of Nephrology 2006; 17(4 Suppl 2):S90-7. *Sample size less than 50 patients*

3586. Remuzzi G, Ruggenenti P, Perna A, et al. Continuum of renoprotection with losartan at all stages of type 2 diabetic nephropathy: a post hoc analysis of the RENAAL trial results. Journal of the American Society of Nephrology 2004; 15(12):3117-25. *Not relevant to key questions*

3587. Renke M, Knap N, Tylicki L, et al. Atorvastatin attenuates oxidative stress in patients with chronic kidney disease. Medical Science Monitor 2010 Feb 26; 16(3):LE3-. *Not relevant to key questions*

3588. Renke M, Rutkowski P, Tylicki L, et al. Combination treatment and renal function in patients with chronic kidney disease. Journal of the Renin-Angiotensin-Aldosterone System 2010 Jun; 11(2):146-7. *Not relevant to key questions*

3589. Renke M, Tylicki L, Knap N, et al. Spironolactone attenuates oxidative stress in patients with chronic kidney disease. Hypertension 2008; 52(5):e132-3; author reply e4. *Not CKD treatment*

3590. Renke M, Tylicki L, Knap N, et al. High-dose angiotensin-converting enzyme inhibitor attenuates oxidative stress in patients with chronic kidney disease. Nephrology Dialysis Transplantation 2009; 24(2):689-90. *Sample size less than 50 patients*

3591. Renke M, Tylicki L, Rutkowski P, et al. Effect of pentoxifylline on proteinuria, markers of tubular injury and oxidative stress in non-diabetic patients with chronic kidney disease - placebo controlled, randomized, cross-over study. Acta Biochimica Polonica 2010; 57(1):119-23. *Sample size less than 50 patients*

3592. Renke M, Tylicki L, Rutkowski P, et al. The effect of N-acetylcysteine on proteinuria and markers of tubular injury in non-diabetic patients with chronic kidney disease. A placebo-controlled, randomized, open, cross-over study. Kidney & Blood Pressure Research 2008; 31(6):404-10. *Sample size less than 50 patients*

3593. Renke M, Tylicki L, Rutkowski P, et al. The effect of N-acetylcysteine on blood pressure and markers of cardiovascular risk in non-diabetic patients with chronic kidney disease: a placebo-controlled, randomized, cross-over study. Medical Science Monitor 2010; 16(7):PI13-8. *Sample size less than 50 patients*

3594. Renke M, Tylicki L, Rutkowski P, et al. Low-dose dual blockade of the renin-angiotensin system improves tubular status in non-diabetic proteinuric patients. Scandinavian Journal of Urology & Nephrology 2005; 39(6):511-7. *Not CKD treatment*

3595. Reriani M, Raichlin E, Prasad A, et al. Long-term administration of endothelin receptor antagonist improves coronary endothelial function in patients with early atherosclerosis. Circulation 2010 Sep 7; 122(10):958-66. *Not CKD treatment*

3596. Resnick B, Sabol V, Galik E, et al. The impact of anemia on nursing home residents. Clinical Nursing Research 2010 May; 19(2):113-30. *Not CKD treatment*

3597. Reuse C, Leeman M, Degaute JP, et al. Preserved renal perfusion during beta blockade by tertatolol with and without cyclooxygenase inhibition in normal humans. Journal of Clinical Pharmacology 1988; 28(4):312-6. *Sample size less than 50 patients*

3598. Revicki DA. Relationship between health utility and psychometric health status measures. Medical Care 1992; 30(5 Suppl):MS274-82. *Not CKD treatment*

3599. Revicki DA, Brown RE, Feeny DH, et al. Health-related quality of life associated with recombinant human erythropoietin therapy for predialysis chronic renal disease patients. American Journal of Kidney Diseases 1995; 25(4):548-54. *Not CKD treatment*

3600. Rexrode KM, Buring JE, Glynn RJ, et al. Analgesic use and renal function in men. JAMA 2001; 286(3):315-21. *Not RCT or controlled trial*

3601. Reyes AJ. Effects of diuretics on renal excretory function. European Heart Journal 1992; 13 Suppl G:15-21. *Follow-up less than 6 months*

3602. Ribeiro AB. Angiotensin II antagonists--therapeutic benefits spanning the cardiovascular disease continuum from hypertension to heart failure and diabetic nephropathy. Current Medical Research & Opinion 2006; 22(1):1-16. *Sample size less than 50 patients*

3603. Ribeiro AB, Gavras H. Angiotensin II antagonists: clinical experience in the treatment of hypertension, prevention of cardiovascular outcomes and renal protection in diabetic nephropathy and proteinuria. Arquivos Brasileiros de Endocrinologia e Metabologia 2006; 50(2):327-33. *Sample size less than 50 patients*

3604. Riben PD, Horsman GB, Rayner E, et al. Emergence of tobramycin-resistant S. epidermidis possessing aminoglycoside modifying enzymes and bacteremic superinfection during empiric therapy of febrile neutropenic episodes. Clinical & Investigative Medicine - Medecine Clinique et Experimentale 1985; 8(4):272-85. *Sample size less than 50 patients*

3605. Ribstein J, Codis P, duCailar G, et al. Effects of captopril and nitrendipine on the response to acute volume expansion in essential hypertension. Journal of Hypertension - Supplement 1988; 6(4):S473-5. *Sample size less than 50 patients*

3606. Ribstein J, Du Cailar G, Brouard R, et al. Comparative renal and cardiac effects of tertatolol and enalapril in essential hypertension. Cardiology 1993; 83 Suppl 1:57-63. *Follow-up less than 6 months*

3607. Ricci Z, Ronco C. 'Renal-dose' fenoldopam for early-stage renal dysfunction in critically ill patients. Nature Clinical Practice Nephrology 2006; 2(10):548-9. *Not CKD treatment*

3608. Richards AM, Crozier IG, Espiner EA, et al. Acute inhibition of endopeptidase 24.11 in essential hypertension: SCH 34826 enhances atrial natriuretic peptide and natriuresis without lowering blood pressure. Journal of Cardiovascular Pharmacology 1992; 20(5):735-41. *Sample size less than 50 patients*

3609. Richards AM, Espiner EA, Ikram H, et al. Atrial natriuretic factor in hypertension: bioactivity at normal plasma levels. Hypertension 1989; 14(3):261-8. *Sample size less than 50 patients*

3610. Richards AM, Nicholls MG, Espiner EA, et al. Effects of alpha-human atrial natriuretic peptide in essential hypertension. Hypertension 1985; 7(5):812-7. *Sample size less than 50 patients*

3611. Richards AM, Tonolo G, Montorsi P, et al. Low dose infusions of 26- and 28-amino acid human atrial natriuretic peptides in normal man. Journal of Clinical Endocrinology & Metabolism 1988; 66(3):465-72. *Sample size less than 50 patients*

3612. Richards AM, Wittert G, Espiner EA, et al. Prolonged inhibition of endopeptidase 24.11 in normal man: renal, endocrine and haemodynamic effects. Journal of Hypertension 1991; 9(10):955-62. *Not CKD treatment*

3613. Richards AM, Wittert GA, Crozier IG, et al. Chronic inhibition of endopeptidase 24.11 in essential hypertension: evidence for enhanced atrial natriuretic peptide and angiotensin II. Journal of Hypertension 1993; 11(4):407-16. *Follow-up less than 6 months*

3614. Richards M, Espiner E, Frampton C, et al. Inhibition of endopeptidase EC 24.11 in humans. Renal and endocrine effects. Hypertension 1990; 16(3):269-76. *Sample size less than 50 patients*

3615. Richer M, Robert S, Lebel M. Renal hemodynamics during norepinephrine and low-dose dopamine infusions in man. Critical Care Medicine 1996; 24(7):1150-6. *Sample size less than 50 patients*

3616. Richmond H, Zwerner J, Kim Y, et al. Nephrogenic systemic fibrosis: relationship to gadolinium and response to photopheresis.[Erratum appears in Arch Dermatol. 2007 Dec;143(12):1565]. Archives of Dermatology 2007; 143(8):1025-30. *Follow-up less than 6 months*

3617. Riechers G, Futerova M, Hanisch M, et al. Effects of muzolimine and of a combination of hydrochlorothiazide/triamterene in healthy subjects and in nephrotic patients. Zeitschrift fur Kardiologie 1985; 74 Suppl 2:103-8. *Follow-up less than 6 months*

3618. Riedl M, Hass M, Oberbauer R, et al. The effects of prolonged substitution of recombinant human growth hormone on renal functional reserve in growth hormone-deficient adults. Journal of the American Society of Nephrology 1995; 6(5):1434-8. *Not CKD treatment*

3619. Riegger GA, Kahles HW, Elsner D, et al. Effects of acetylsalicylic acid on renal function in patients with chronic heart failure. American Journal of Medicine 1991; 90(5):571-5. *Not CKD treatment*

3620. Righetti M. Hopeful for a second HOPE-2 post hoc analysis. Nephrology Dialysis Transplantation 2008; 23(7):2428-9; author reply 9-30. *Not relevant to key questions*

3621. Righetti M. Protective effect of vitamin B therapy on bone and cardiovascular disease. Recent Patents on Cardiovascular Drug Discovery 2009; 4(1):37-44. *Not human studies*

3622. Rigler R, Pramanik A, Jonasson P, et al. Specific binding of proinsulin C-peptide to human cell membranes. Proceedings of the National Academy of Sciences of the United States of America 1999; 96(23):13318-23. *Not CKD treatment*

3623. Rinaldi M, Pellegrini C, Martinelli L, et al. FK506 effectiveness in reducing acute rejection after heart transplantation: a prospective randomized study. Journal of Heart & Lung Transplantation 1997; 16(10):1001-10. *Sample size less than 50 patients*

3624. Rinaldi S, Adembri C, Grechi S, et al. Low-dose hydrocortisone during severe sepsis: effects on microalbuminuria. Critical Care Medicine 2006; 34(9):2334-9. *Not CKD treatment*

3625. Ring-Larsen H, Henriksen JH, Wilken C, et al. Diuretic treatment in decompensated cirrhosis and congestive heart failure: effect of posture. British Medical Journal Clinical Research Ed. 1986; 292(6532):1351-3. *Sample size less than 50 patients*

3626. Ripley E. Complementary effects of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in slowing the progression of chronic kidney disease. American Heart Journal 2009; 157(6 Suppl):S7-S16. *Not early CKD*

3627. Rippin J, Bain SC, Barnett AH, et al. Rationale and design of diabetics exposed to telmisartan and enalapril (DETAIL) study. Journal of Diabetes & its Complications 2002; 16(3):195-200. *Not RCT or controlled trial*

3628. Ristikankare A, Kuitunen T, Kuitunen A, et al. Lack of renoprotective effect of i.v. N-acetylcysteine in patients with chronic renal failure undergoing cardiac surgery. British Journal of Anaesthesia 2006; 97(5):611-6. *Not CKD treatment*

3629. Ritchie C, Ekundayo OJ, Muchimba M, et al. Effects of diabetes mellitus in patients with heart failure and chronic kidney disease: a propensity-matched study of multimorbidity in chronic heart failure. International Journal of Cardiology 2009; 134(3):330-5. *Not RCT or controlled trial*

3630. Ritchie C, Ekundayo OJ, Muchimba M, et al. Effects of diabetes mellitus in patients with heart failure and chronic kidney disease: a propensity-matched study of multimorbidity in chronic heart failure.[Erratum appears in Int J Cardiol. 2010 Jan 7;138(1):106]. International Journal of Cardiology 2009; 134(3):330-5. *Not CKD treatment*

3631. Ritter JM, Ludgin JR, Scharschmidt LA, et al. Effects of a stable prostaglandin analogue, L-644,122, in healthy and hypertensive men. European Journal of Clinical Pharmacology 1985; 28(6):685-8. *Sample size less than 50 patients*

3632. Ritz E. Should all patients with chronic kidney disease take a statin? A commentary to a meta-analysis of randomized control trials. Polskie Archiwum Medycyny Wewnetrznej 2008; 118(10):541-2. *Not CKD treatment*

3633. Ritz E, Kuster S, Schmidt-Gayk H, et al. Low-dose calcitriol prevents the rise in 1,84-iPTH without affecting serum calcium and phosphate in patients with moderate renal failure (prospective placebo-controlled multicentre trial). Nephrology Dialysis Transplantation 1995; 10(12):2228-34. *Sample size less than 50 patients*

3634. Ritz E, Laville M, Bilous RW, et al. Target level for hemoglobin correction in patients with diabetes and CKD: primary results of the Anemia Correction in Diabetes (ACORD) Study.[Erratum appears in Am J Kidney Dis. 2007 Apr;49(4):562]. American Journal of Kidney Diseases 2007; 49(2):194-207. *Not RCT or controlled trial*

3635. Ritz E, Rychlik I, Miltenberger-Miltenyi G. Optimizing antihypertensive therapy in patients with diabetic nephropathy. Journal of Hypertension - Supplement 1998; 16(7):S17-22. *Not RCT or controlled trial*

3636. Ritz E, Rychlik I, Schomig M, et al. Blood pressure in diabetic nephropathy--current controversies. Journal of Internal Medicine 2001; 249(3):215-23. *Not relevant to key questions*

3637. Ritz E, Schmieder RE, Pollock CA. Renal protection in diabetes: lessons from ONTARGET. Cardiovascular Diabetology 2010; 9:60. *Not RCT or controlled trial*

3638. Ritz E, Viberti GC, Ruilope LM, et al. Determinants of urinary albumin excretion within the normal range in patients with type 2 diabetes: the Randomised Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) study. Diabetologia 2010 Jan; 53(1):49-57. *Not CKD treatment*

3639. Rius F, Pizarro E, Castells I, et al. Renal function changes in hypertensive patients with non-insulin- dependent diabetes mellitus. Kidney International - Supplement 1996; 55:S88-90. *Not RCT or controlled trial*

3640. Rix M, Eskildsen P, Olgaard K. Effect of 18 months of treatment with alfacalcidol on bone in patients with mild to moderate chronic renal failure. Nephrology Dialysis Transplantation 2004; 19(4):870-6. *Not CKD treatment*

3641. Rizos CV, Elisaf MS, Liberopoulos EN. Are the pleiotropic effects of telmisartan clinically relevant? Current Pharmaceutical Design 2009; 15(24):2815-32. *Not RCT or controlled trial*

3642. Rizos E, Bairaktari E, Ganotakis E, et al. Effect of ciprofibrate on lipoproteins, fibrinogen, renal function, and hepatic enzymes. Journal of Cardiovascular Pharmacology & Therapeutics 2002; 7(4):219-26. *Not CKD treatment*

3643. Rizzoni D, Porteri E, Boari GEM, et al. Prognostic significance of small-artery structure in hypertension. Circulation 2003; 108(18):2230-5. *Not CKD treatment*

3644. Roberto AJ, Krieger JL, Beam MA. Enhancing web-based kidney disease prevention messages for Hispanics using targeting and tailoring. Journal of Health Communication 2009; 14(6):525-40. *Not RCT or controlled trial*

3645. Roberts DG, Gerber JG, Barnes JS, et al. Sulindac is not renal sparing in man. Clinical Pharmacology & Therapeutics 1985; 38(3):258-65. *Sample size less than 50 patients*

3646. Roberts JT. Chemotherapy for metastatic bladder cancer. Clinical Oncology 2005; 17(7):514-23. *Not CKD treatment*

3647. Roberts JT, Ali HH, Shorten GD. Using the bubble inclinometer to measure laryngeal tilt and predict difficulty of laryngoscopy. Journal of Clinical Anesthesia 1993; 5(4):306-9. *Not CKD treatment*

3648. Roberts JT, Ali HH, Shorten GD. Using the laryngeal indices caliper to predict difficulty of laryngoscopy with a Macintosh #3 laryngoscope. Journal of Clinical Anesthesia 1993; 5(4):302-5. *Not CKD treatment*

3649. Roberts MA, Hare DL. JUPITER “moderate CKD” subgroup is not truly “moderate” chronic kidney disease. Journal of the American College of Cardiology 2010 Aug 3; 56(6):528; author reply 30. *Not RCT or controlled trial*

3650. Roberts WL, Calcote CB, Cook CB, et al. Comparison of four commercial urinary albumin (microalbumin) methods: implications for detecting diabetic nephropathy using random urine specimens. Clinica Chimica Acta 1998; 273(1):21-33. *Not RCT or controlled trial*

3651. Robertson L, Waugh N, Robertson A. Protein restriction for diabetic renal disease. Cochrane Database of Systematic Reviews 2007; (4):CD002181. *Not early CKD*

3652. Robiner WN, Yozwiak JA, Bearman DL, et al. Barriers to clinical research participation in a diabetes randomized clinical trial. Social Science & Medicine 2009; 68(6):1069-74. *Follow-up less than 6 months*

3653. Robinson T, Gariballa S, Fancourt G, et al. The acute effects of a single dopamine infusion in elderly patients with congestive cardiac failure. British Journal of Clinical Pharmacology 1994; 37(3):261-3. *Not CKD treatment*

3654. Robinson TM, Sewell DA, Casey A, et al. Dietary creatine supplementation does not affect some haematological indices, or indices of muscle damage and hepatic and renal function. British Journal of Sports Medicine 2000; 34(4):284-8. *Sample size less than 50 patients*

3655. Robson R. The use of bivalirudin in patients with renal impairment. Journal of Invasive Cardiology 2000; 12 Suppl F:33F-6. *Not RCT or controlled trial*

3656. Robson RA, Bridgman PG, Wells JE, et al. The effect of celiprolol on glomerular filtration rate and renal blood flow in patients with chronic renal impairment and healthy volunteers. British Journal of Clinical Pharmacology 1992; 33(4):454-7. *Sample size less than 50 patients*

3657. Roca-Cusachs A, Triposkiadis F. Antihypertensive effect of manidipine. Drugs 2005; 65 Suppl 2:11-9. *Not RCT or controlled trial*

3658. Rocco MV, Gassman JJ, Wang SR, et al. Cross-sectional study of quality of life and symptoms in chronic renal disease patients: the Modification of Diet in Renal Disease Study. American Journal of Kidney Diseases 1997; 29(6):888-96. *Not RCT or controlled trial*

3659. Rocco S, Opocher G, Carpene G, et al. Atrial natriuretic peptide infusion in primary aldosteronism. Renal, hemodynamic and hormonal effects. American Journal of Hypertension 1990; 3(9):668-73. *Not CKD treatment*

3660. Rocha R, Funder JW. The pathophysiology of aldosterone in the cardiovascular system. Annals of the New York Academy of Sciences 2002; 970:89-100. *Not CKD treatment*

3661. Rock G, Shumak K, Kelton J, et al. Thrombotic thrombocytopenic purpura: outcome in 24 patients with renal impairment treated with plasma exchange. Canadian Apheresis Study Group. Transfusion 1992; 32(8):710-4. *Not CKD treatment*

3662. Rockemann MG, Seeling W, Bischof C, et al. Prophylactic use of epidural mepivacaine/morphine, systemic diclofenac, and metamizole reduces postoperative morphine consumption after major abdominal surgery. Anesthesiology 1996; 84(5):1027-34. *Not CKD treatment*

3663. Rodby RA, Ali A, Rohde RD, et al. Renal scanning 99mTc diethylene-triamine pentaacetic acid glomerular filtration rate (GFR) determination compared with iothalamate clearance GFR in diabetics. The Collaborative Study Group for The study of Angiotensin-Converting Enzyme Inhibition in Diabetic Nephropathy. American Journal of Kidney Diseases 1992; 20(6):569-73. *Not CKD treatment*

3664. Rodby RA, Chiou CF, Borenstein J, et al. The cost-effectiveness of irbesartan in the treatment of hypertensive patients with type 2 diabetic nephropathy. Clinical Therapeutics 2003; 25(7):2102-19. *Not relevant to key questions*

3665. Rodby RA, Firth LM, Lewis EJ. An economic analysis of captopril in the treatment of diabetic nephropathy. The Collaborative Study Group. Diabetes Care 1996; 19(10):1051-61. *Not CKD treatment*

3666. Rodby RA, Rohde R, Evans J, et al. The study of the effect of intensity of blood pressure management on the progression of type 1 diabetic nephropathy: study design and baseline patient characteristics. Collaborative Study Group. Journal of the American Society of Nephrology 1995; 5(10):1775-81. *Not relevant to key questions*

3667. Rodby RA, Rohde RD, Clarke WR, et al. The Irbesartan type II diabetic nephropathy trial: study design and baseline patient characteristics. For the Collaborative Study Group. Nephrology Dialysis Transplantation 2000; 15(4):487-97. *Not RCT or controlled trial*

3668. Roderick PJ, Atkins RJ, Smeeth L, et al. Detecting chronic kidney disease in older people; what are the implications?.[Erratum appears in Age Ageing. 2009 Sep;38(5):638 Note: Flectcher, Astrid E [corrected to Fletcher, Astrid E]]. Age & Ageing 2008; 37(2):179-86. *Follow-up less than 6 months*

3669. Rodicio JL. Does antihypertensive therapy protect the kidney in essential hypertension? Journal of Hypertension - Supplement 1996; 14(2):S69-75; discussion S-6. *Not RCT or controlled trial*

3670. Rodjer S, Alestig K, Bergmark J, et al. Treatment of septicaemia in immunocompromised patients with ceftazidime or with tobramycin and cefuroxime, with special reference to renal effects. Journal of Antimicrobial Chemotherapy 1987; 20(1):109-16. *Not relevant to key questions*

3671. Rodondi LC, Flaherty JF, Schoenfeld P, et al. Influence of coadministration on the pharmacokinetics of mezlocillin and cefotaxime in healthy volunteers and in patients with renal failure. Clinical Pharmacology & Therapeutics 1989; 45(5):527-34. *Sample size less than 50 patients*

3672. Rodondi N, Yerly P, Gabriel A, et al. Microalbuminuria, but not cystatin C, is associated with carotid atherosclerosis in middle-aged adults. Nephrology Dialysis Transplantation 2007; 22(4):1107-14. *Follow-up less than 6 months*

3673. Rodriguez-Iturbe B, Herrera J, Garcia R. Relationship between glomerular filtration rate and renal blood flow at different levels of protein-induced hyperfiltration in man. Clinical Science 1988; 74(1):11-5. *Sample size less than 50 patients*

3674. Rodriguez-Iturbe B, Herrera J, Gutkowska J, et al. Atrial natriuretic factor increases after a protein meal in man. Clinical Science 1988; 75(5):495-8. *Sample size less than 50 patients*

3675. Rodriguez-Moran M, Gonzalez-Gonzalez G, Bermudez-Barba MV, et al. Effects of pentoxifylline on the urinary protein excretion profile of type 2 diabetic patients with microproteinuria: a double-blind, placebo-controlled randomized trial. Clinical Nephrology 2006; 66(1):3-10. *Sample size less than 50 patients*

3676. Rodriguez-Moran M, Guerrero-Romero F. Pentoxifylline is as effective as captopril in the reduction of microalbuminuria in non-hypertensive type 2 diabetic patients--a randomized, equivalent trial. Clinical Nephrology 2005; 64(2):91-7. *Not CKD treatment*

3677. Rodriquez A, Martin A, Oterino JA, et al. Renal function in compensated hepatic cirrhosis: effects of an amino acid infusion and relationship with nitric acid. Digestive Diseases 1999; 17(4):235-40. *Not early CKD*

3678. Roehrborn CG. Acute relief or future prevention: is urology ready for preventive health care? Urology 2000; 56(5 Suppl 1):12-9. *Not early CKD*

3679. Roelen DL, Frolich M, Papapoulos SE. Renal responsiveness to synthetic human parathyroid hormone 1-38 in healthy subjects. European Journal of Clinical Investigation 1989; 19(3):311-5. *Sample size less than 50 patients*

3680. Roger SD, Levin A. Epoetin trials: randomised controlled trials don't always mimic observational data. Nephrology Dialysis Transplantation 2007; 22(3):684-6. *Follow-up less than 6 months*

3681. Roger SD, McMahon LP, Clarkson A, et al. Effects of early and late intervention with epoetin alpha on left ventricular mass among patients with chronic kidney disease (stage 3 or 4): results of a randomized clinical trial. Journal of the American Society of Nephrology 2004; 15(1):148-56. *Not CKD treatment*

3682. Roger SD, Suranyi MG, Walker RG, et al. A randomised, cross-over study comparing injection site pain with subcutaneous epoetin beta and subcutaneous darbepoetin alfa in patients with chronic kidney disease. Current Medical Research & Opinion 2008; 24(8):2181-7. *Not CKD treatment*

3683. Rogers NM, Coates PTH. Calcific uraemic arteriolopathy: an update. Current Opinion in Nephrology & Hypertension 2008; 17(6):629-34. *Not CKD treatment*

3684. Roglic G, Colhoun HM, Stevens LK, et al. Parental history of hypertension and parental history of diabetes and microvascular complications in insulin-dependent diabetes mellitus: the EURODIAB IDDM Complications Study. Diabetic Medicine 1998; 15(5):418-26. *Not RCT or controlled trial*

3685. Rohrer JE. Outcomes research in nephrology. Seminars in Nephrology 2003; 23(3):250-4. *Not CKD treatment*

3686. Rojanasthien N, Kumsorn B, Atikachai B, et al. Protective effects of fosfomycin on cisplatin-induced nephrotoxicity in patients with lung cancer. International Journal of Clinical Pharmacology & Therapeutics 2001; 39(3):121-5. *Not early CKD*

3687. Rokoss MJ, Teo KK. Ramipril in the treatment of vascular diseases. Expert Opinion on Pharmacotherapy 2005; 6(11):1911-9. *Not relevant to key questions*

3688. Rolleman EJ, Valkema R, de Jong M, et al. Safe and effective inhibition of renal uptake of radiolabelled octreotide by a combination of lysine and arginine. European Journal of Nuclear Medicine & Molecular Imaging 2003; 30(1):9-15. *Not CKD treatment*

3689. Romanelli G, Giustina A, Agabiti-Rosei E, et al. Short-term effect of captopril and nifedipine on micro-albuminuria induced by exercise in hypertensive diabetic patients. Journal of Hypertension - Supplement 1989; 7(6):S312-3. *Sample size less than 50 patients*

3690. Romanelli G, Giustina A, Bossoni S, et al. Short-term administration of captopril and nifedipine and exercise-induced albuminuria in normotensive diabetic patients with early-stage nephropathy. Diabetes 1990; 39(11):1333-8. *Follow-up less than 6 months*

3691. Romanelli G, Giustina A, Cimino A, et al. Short term effect of captopril on microalbuminuria induced by exercise in normotensive diabetics. BMJ 1989; 298(6669):284-8. *Follow-up less than 6 months*

3692. Romanelli G, Giustina A, Cravarezza P, et al. Albuminuria induced by exercise in hypertensive type I and type II diabetic patients: a randomised, double-blind study on the effects of acute administration of captopril and nifedipine. Journal of Human Hypertension 1991; 5(3):167-73. *Sample size less than 50 patients*

3693. Romero R, Salinas I, Lucas A, et al. Renal function changes in microalbuminuric normotensive type II diabetic patients treated with angiotensin-converting enzyme inhibitors. Diabetes Care 1993; 16(4):597-600. *Sample size less than 50 patients*

3694. Romero R, Salinas I, Lucas A, et al. Comparative effects of captopril versus nifedipine on proteinuria and renal function of type 2 diabetic patients. Diabetes Research & Clinical Practice 1992; 17(3):191-8. *Sample size less than 50 patients*

3695. Romundstad S, Holmen J, Hallan H, et al. Microalbuminuria, cardiovascular disease and risk factors in a nondiabetic/nonhypertensive population. The Nord-Trondelag Health Study (HUNT, 1995-97), Norway. Journal of Internal Medicine 2002; 252(2):164-72. *Not CKD treatment*

3696. Romundstad S, Holmen J, Kvenild K, et al. Clinical relevance of microalbuminuria screening in self-reported non-diabetic/non-hypertensive persons identified in a large health screening--the Nord-Trondelag Health Study (HUNT), Norway. Clinical Nephrology 2003; 59(4):241-51. *Not CKD treatment*

3697. Ronco C, Bellomo R. Prevention of acute renal failure in the critically ill. Nephron 2003; 93(1):C13-20. *Not CKD treatment*

3698. Rooke GA, Ebert T, Muzi M, et al. The hemodynamic and renal effects of sevoflurane and isoflurane in patients with coronary artery disease and chronic hypertension. Sevoflurane Ischemia Study Group. Anesthesia & Analgesia 1996; 82(6):1159-65. *Not CKD treatment*

3699. Roozbeh J, Banihashemi MA, Ghezlou M, et al. Captopril and combination therapy of captopril and pentoxifylline in reducing proteinuria in diabetic nephropathy. Renal Failure 2010 Jan; 32(2):172-8. *Not relevant to key questions*

3700. Rosa EM, Viecceli C, Jr. Interesting findings in the VALERIA trial. Journal of Hypertension 2009; 27(4):902; author reply -3. *Not CKD treatment*

3701. Rose GW, Kanno Y, Ikebukuro H, et al. Cilnidipine is as effective as benazepril for control of blood pressure and proteinuria in hypertensive patients with benign nephrosclerosis. Hypertension Research - Clinical & Experimental 2001; 24(4):377-83. *Sample size less than 50 patients*

3702. Rose PG. Amifostine cytoprotection with chemotherapy for advanced ovarian carcinoma. Seminars in Oncology 1996; 23(4 Suppl 8):83-9. *Not CKD treatment*

3703. Rosei EA, Rizzoni D, Muiesan ML, et al. Effects of candesartan cilexetil and enalapril on inflammatory markers of atherosclerosis in hypertensive patients with non-insulin-dependent diabetes mellitus. Journal of Hypertension 2005; 23(2):435-44. *Follow-up less than 6 months*

3704. Rosenberg ME, Hostetter TH. Comparative effects of antihypertensives on proteinuria: angiotensin-converting enzyme inhibitor versus alpha 1-antagonist. American Journal of Kidney Diseases 1991; 18(4):472-82. *Sample size less than 50 patients*

3705. Rosenberg PH, Veering BT, Urmey WF. Maximum recommended doses of local anesthetics: a multifactorial concept. Regional Anesthesia & Pain Medicine 2004; 29(6):564-75; discussion 24. *Not RCT or controlled trial*

3706. Rosenstock JL, Bruno R, Kim JK, et al. The effect of withdrawal of ACE inhibitors or angiotensin receptor blockers prior to coronary angiography on the incidence of contrast-induced nephropathy. International Urology & Nephrology 2008; 40(3):749-55. *Not CKD treatment*

3707. Rosenthal JH. Therapeutic experience with cilazapril. Journal of Cardiovascular Pharmacology 1994; 24 Suppl 2:S65-9. *Not RCT or controlled trial*

3708. Rosman JB, Donker-Willenborg MA. Dietary compliance and its assessment in the Groningen trial on protein restriction in renal failure. Contributions to Nephrology 1990; 81:95-101. *Not RCT or controlled trial*

3709. Rosman JB, ter Wee PM, Piers-Becht GP, et al. Early protein restriction in chronic renal failure. Proceedings of the European Dialysis & Transplant Association - European Renal Association 1985; 21:567-73. *Not CKD treatment*

3710. Rossat J, Maillard M, Nussberger J, et al. Renal effects of selective cyclooxygenase-2 inhibition in normotensive salt-depleted subjects. Clinical Pharmacology & Therapeutics 1999; 66(1):76-84. *Sample size less than 50 patients*

3711. Rosseel PM, Santman FW, Bouter H, et al. Postcardiac surgery low cardiac output syndrome: dopexamine or dopamine? Intensive Care Medicine 1997; 23(9):962-8. *Not CKD treatment*

3712. Rossert J, Fouqueray B, Boffa JJ. Anemia management and the delay of chronic renal failure progression. Journal of the American Society of Nephrology 2003; 14(7 Suppl 2):S173-7. *Not relevant to key questions*

3713. Rossert J, Froissart M. Role of anemia in progression of chronic kidney disease. Seminars in Nephrology 2006; 26(4):283-9. *Not RCT or controlled trial*

3714. Rossert J, Froissart M, Jacquot C. Anemia management and chronic renal failure progression. Kidney International - Supplement 2005; (99):S76-81. *Not relevant to key questions*

3715. Rossert J, Gassmann-Mayer C, Frei D, et al. Prevalence and predictors of epoetin hyporesponsiveness in chronic kidney disease patients. Nephrology Dialysis Transplantation 2007; 22(3):794-800. *Not RCT or controlled trial*

3716. Rossert J, Levin A, Roger SD, et al. Effect of early correction of anemia on the progression of CKD. American Journal of Kidney Diseases 2006; 47(5):738-50. *Sample size less than 50 patients*

3717. Rossert JA, McClellan WM, Roger SD, et al. Contribution of anaemia to progression of renal disease: a debate. Nephrology Dialysis Transplantation 2002; 17 Suppl 1:60-6. *Not RCT or controlled trial*

3718. Rossing K, Christensen PK, Andersen S, et al. Comparative effects of Irbesartan on ambulatory and office blood pressure: a substudy of ambulatory blood pressure from the Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria study. Diabetes Care 2003; 26(3):569-74. *Sample size less than 50 patients*

3719. Rossing K, Christensen PK, Hansen BV, et al. Optimal dose of candesartan for renoprotection in type 2 diabetic patients with nephropathy: a double-blind randomized cross-over study. Diabetes Care 2003; 26(1):150-5. *Sample size less than 50 patients*

3720. Rossing K, Christensen PK, Jensen BR, et al. Dual blockade of the renin-angiotensin system in diabetic nephropathy: a randomized double-blind crossover study. Diabetes Care 2002; 25(1):95-100. *Sample size less than 50 patients*

3721. Rossing K, Jacobsen P, Pietraszek L, et al. Renoprotective effects of adding angiotensin II receptor blocker to maximal recommended doses of ACE inhibitor in diabetic nephropathy: a randomized double-blind crossover trial. Diabetes Care 2003; 26(8):2268-74. *Sample size less than 50 patients*

3722. Rossing K, Mischak H, Parving H-H, et al. Impact of diabetic nephropathy and angiotensin II receptor blockade on urinary polypeptide patterns. Kidney International 2005; 68(1):193-205. *Not relevant to key questions*

3723. Rossing K, Schjoedt KJ, Jensen BR, et al. Enhanced renoprotective effects of ultrahigh doses of irbesartan in patients with type 2 diabetes and microalbuminuria. Kidney International 2005; 68(3):1190-8. *Follow-up less than 6 months*

3724. Rossing K, Schjoedt KJ, Smidt UM, et al. Beneficial effects of adding spironolactone to recommended antihypertensive treatment in diabetic nephropathy: a randomized, double-masked, cross-over study. Diabetes Care 2005; 28(9):2106-12. *Follow-up less than 6 months*

3725. Rossing P, Hansen BV, Nielsen FS, et al. Fish oil in diabetic nephropathy. Diabetes Care 1996; 19(11):1214-9. *Sample size less than 50 patients*

3726. Rossing P, Tarnow L, Boelskifte S, et al. Differences between nisoldipine and lisinopril on glomerular filtration rates and albuminuria in hypertensive IDDM patients with diabetic nephropathy during the first year of treatment. Diabetes 1997; 46(3):481-7. *Not relevant to key questions*

3727. Roth D, Smith RD, Schulman G, et al. Effects of recombinant human erythropoietin on renal function in chronic renal failure predialysis patients. American Journal of Kidney Diseases 1994; 24(5):777-84. *Not early CKD*

3728. Rothele E, Krumme B, Rump LC. Design of the prospective randomized study for the treatment of patients with thrombotic microangiopathy. PRODROMI Study Group. Therapeutic Apheresis 2000; 4(5):327-31. *Not early CKD*

3729. Rother KI, Brown RJ, Morales MM, et al. Effect of ingested interferon-alpha on beta-cell function in children with new-onset type 1 diabetes.[Erratum appears in Diabetes Care. 2009 Sep;32(9):1751]. Diabetes Care 2009; 32(7):1250-5. *Not CKD treatment*

3730. Rousso P, Buclin T, Nussberger J, et al. Effects of a dual inhibitor of angiotensin converting enzyme and neutral endopeptidase, MDL 100,240, on endocrine and renal functions in healthy volunteers. Journal of Hypertension 1999; 17(3):427-37. *Follow-up less than 6 months*

3731. Rozen-Zvi B, Gafter-Gvili A, Paul M, et al. Intravenous versus oral iron supplementation for the treatment of anemia in CKD: systematic review and meta-analysis. American Journal of Kidney Diseases 2008; 52(5):897-906. *Not CKD treatment*

3732. Ruben E-C, Manuel V-R, Agustin O-R, et al. Ciprofloxacin utility as antifibrotic in the skin of patients with scleroderma. Journal of Dermatology 2010 Apr; 37(4):323-9. *Not CKD treatment*

3733. Rubenstein MH, Harrell LC, Sheynberg BV, et al. Are patients with renal failure good candidates for percutaneous coronary revascularization in the new device era? Circulation 2000; 102(24):2966-72. *Not RCT or controlled trial*

3734. Rubin MR, Volek JS, Gomez AL, et al. Safety measures of L-carnitine L-tartrate supplementation in healthy men. Journal of Strength & Conditioning Research 2001; 15(4):486-90. *Not early CKD*

3735. Rucinska EJ, Small R, Irvin J. High-risk patients treated with enalapril maleate: safety considerations. International Journal of Cardiology 1989; 22(2):249-59. *Not RCT or controlled trial*

3736. Rucker D, Tonelli M, Coles MG, et al. Vitamin D insufficiency and treatment with oral vitamin D3 in northern-dwelling patients with chronic kidney disease. Journal of Nephrology 2009; 22(1):75-82. *Sample size less than 50 patients*

3737. Rudberg S, Dahlquist G, Aperia A, et al. Reduction of protein intake decreases glomerular filtration rate in young type 1 (insulin-dependent) diabetic patients mainly in hyperfiltering patients. Diabetologia 1988; 31(12):878-83. *Sample size less than 50 patients*

3738. Rudberg S, Osterby R, Bangstad HJ, et al. Effect of angiotensin converting enzyme inhibitor or beta blocker on glomerular structural changes in young microalbuminuric patients with Type I (insulin-dependent) diabetes mellitus. Diabetologia 1999; 42(5):589-95. *Sample size less than 50 patients*

3739. Rudis MI, Zarowitz BJ. Low-dose dopamine in acute oliguric renal failure. American Journal of Medicine 1997; 102(3):320-2. *Not early CKD*

3740. Rudnick MR, Davidson C, Laskey W, et al. Nephrotoxicity of iodixanol versus ioversol in patients with chronic kidney disease: the Visipaque Angiography/Interventions with Laboratory Outcomes in Renal Insufficiency (VALOR) Trial. American Heart Journal 2008; 156(4):776-82. *Not RCT or controlled trial*

3741. Rudnick MR, Goldfarb S, Wexler L, et al. Nephrotoxicity of ionic and nonionic contrast media in 1196 patients: a randomized trial. The Iohexol Cooperative Study. Kidney International 1995; 47(1):254-61. *Not RCT or controlled trial*

3742. Rudy DW, Voelker JR, Greene PK, et al. Loop diuretics for chronic renal insufficiency: a continuous infusion is more efficacious than bolus therapy. Annals of Internal Medicine 1991; 115(5):360-6. *Not early CKD*

3743. Ruedin P, Rizzoli R, Slosman D, et al. Effects of oral calcitriol on bone mineral density in patients with end-stage renal failure. Kidney International 1994; 45(1):245-52. *Not early CKD*

3744. Ruggenenti P, Fassi A, Ilieva AP, et al. Preventing microalbuminuria in type 2 diabetes. New England Journal of Medicine 2004; 351(19):1941-51. *Not RCT or controlled trial*

3745. Ruggenenti P, Flores C, Aros C, et al. Renal and metabolic effects of insulin lispro in type 2 diabetic subjects with overt nephropathy. Diabetes Care 2003; 26(2):502-9. *Sample size less than 50 patients*

3746. Ruggenenti P, Gaspari F, Perna A, et al. Cross sectional longitudinal study of spot morning urine protein:creatinine ratio, 24 hour urine protein excretion rate, glomerular filtration rate, and end stage renal failure in chronic renal disease in patients without diabetes.[Erratum appears in BMJ 1998 Nov 28;317(7171):1491]. BMJ 1998; 316(7130):504-9. *Not RCT or controlled trial*

3747. Ruggenenti P, Iliev I, Costa GM, et al. Preventing left ventricular hypertrophy by ACE inhibition in hypertensive patients with type 2 diabetes: a prespecified analysis of the Bergamo Nephrologic Diabetes Complications Trial (BENEDICT). Diabetes Care 2008; 31(8):1629-34. *Not CKD treatment*

3748. Ruggenenti P, Mise N, Pisoni R, et al. Diverse effects of increasing lisinopril doses on lipid abnormalities in chronic nephropathies. Circulation 2003; 107(4):586-92. *Sample size less than 50 patients*

3749. Ruggenenti P, Mosconi L, Bianchi L, et al. Long-term treatment with either enalapril or nitrendipine stabilizes albuminuria and increases glomerular filtration rate in non-insulin-dependent diabetic patients. American Journal of Kidney Diseases 1994; 24(5):753-61. *Sample size less than 50 patients*

3750. Ruggenenti P, Mosconi L, Sangalli F, et al. Glomerular size-selective dysfunction in NIDDM is not ameliorated by ACE inhibition or by calcium channel blockade. Kidney International 1999; 55(3):984-94. *Sample size less than 50 patients*

3751. Ruggenenti P, Pagano E, Tammuzzo L, et al. Ramipril prolongs life and is cost effective in chronic proteinuric nephropathies. Kidney International 2001; 59(1):286-94. *Not RCT or controlled trial*

3752. Ruggenenti P, Perna A, Benini R, et al. In chronic nephropathies prolonged ACE inhibition can induce remission: dynamics of time-dependent changes in GFR. Investigators of the GISEN Group. Gruppo Italiano Studi Epidemiologici in Nefrologia. Journal of the American Society of Nephrology 1999; 10(5):997-1006. *Not relevant to key questions*

3753. Ruggenenti P, Perna A, Benini R, et al. Effects of dihydropyridine calcium channel blockers, angiotensin-converting enzyme inhibition, and blood pressure control on chronic, nondiabetic nephropathies. Gruppo Italiano di Studi Epidemiologici in Nefrologia (GISEN). Journal of the American Society of Nephrology 1998; 9(11):2096-101. *Not relevant to key questions*

3754. Ruggenenti P, Perna A, Ganeva M, et al. Impact of blood pressure control and angiotensin-converting enzyme inhibitor therapy on new-onset microalbuminuria in type 2 diabetes: a post hoc analysis of the BENEDICT trial. Journal of the American Society of Nephrology 2006; 17(12):3472-81. *Not early CKD*

3755. Ruggenenti P, Perna A, Gherardi G, et al. Chronic proteinuric nephropathies: outcomes and response to treatment in a prospective cohort of 352 patients with different patterns of renal injury. American Journal of Kidney Diseases 2000; 35(6):1155-65. *Not RCT or controlled trial*

3756. Ruggenenti P, Perna A, Lesti M, et al. Pretreatment blood pressure reliably predicts progression of chronic nephropathies. GISEN Group. Kidney International 2000; 58(5):2093-101. *Not RCT or controlled trial*

3757. Ruggenenti P, Perna A, Loriga G, et al. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicentre, randomised controlled trial. Lancet 2005; 365(9463):939-46. *Not relevant to key questions*

3758. Ruggenenti P, Perna A, Mosconi L, et al. Proteinuria predicts end-stage renal failure in non-diabetic chronic nephropathies. The “Gruppo Italiano di Studi Epidemiologici in Nefrologia” (GISEN). Kidney International - Supplement 1997; 63:S54-7. *Not RCT or controlled trial*

3759. Ruggenenti P, Perna A, Mosconi L, et al. Urinary protein excretion rate is the best independent predictor of ESRF in non-diabetic proteinuric chronic nephropathies. “Gruppo Italiano di Studi Epidemiologici in Nefrologia” (GISEN). Kidney International 1998; 53(5):1209-16. *Not RCT or controlled trial*

3760. Ruggenenti P, Perna A, Remuzzi G, et al. Retarding progression of chronic renal disease: the neglected issue of residual proteinuria. Kidney International 2003; 63(6):2254-61. *Not relevant to key questions*

3761. Ruggenenti P, Remuzzi G. Primary prevention of renal failure in diabetic patients: the Bergamo Nephrologic Diabetes Complication Trial. Journal of Hypertension - Supplement 1998; 16(1):S95-7. *Not early CKD*

3762. Ruggenenti P, Remuzzi G. Proteinuria: Is the ONTARGET renal substudy actually off target? Nature Reviews Nephrology 2009; 5(8):436-7. *Not RCT or controlled trial*

3763. Rugiu C, Oldrizzi L, Maschio G. Effects of an oral protein load on glomerular filtration rate in patients with solitary kidneys. Kidney International - Supplement 1987; 22:S29-31. *Sample size less than 50 patients*

3764. Ruhnau KJ, Meissner HP, Finn JR, et al. Effects of 3-week oral treatment with the antioxidant thioctic acid (alpha-lipoic acid) in symptomatic diabetic polyneuropathy. Diabetic Medicine 1999; 16(12):1040-3. *Sample size less than 50 patients*

3765. Ruilope L. RAS blockade: new possibilities in the treatment of complications of diabetes. Heart 2000; 84 Suppl 1:i32-4:discussion i50. *Not relevant to key questions*

3766. Ruilope LM. Renoprotection and renin-angiotensin system blockade in diabetes mellitus. American Journal of Hypertension 1997; 10(12 Pt 2):325S-31S. *Not RCT or controlled trial*

3767. Ruilope LM. Lessons from trials in hypertensive type 2 diabetic patients. Current Hypertension Reports 2003; 5(4):322-8. *Not RCT or controlled trial*

3768. Ruilope LM. New ADVANCEs in guidelines. Journal of Hypertension - Supplement 2008; 26(2):S16-8. *Not CKD treatment*

3769. Ruilope LM. New ADVANCEs in guidelines. Journal of Hypertension 2008; 26 Suppl 2:S16-8. *Not RCT or controlled trial*

3770. Ruilope LM. Angiotensin receptor blockers: RAAS blockade and renoprotection. Current Medical Research & Opinion 2008; 24(5):1285-93. *Not CKD treatment*

3771. Ruilope LM, Alcazar JM, Hernandez E, et al. Long-term influences of antihypertensive therapy on microalbuminuria in essential hypertension. Kidney International - Supplement 1994; 45:S171-3. *Sample size less than 50 patients*

3772. Ruilope LM, Aldigier JC, Ponticelli C, et al. Safety of the combination of valsartan and benazepril in patients with chronic renal disease. European Group for the Investigation of Valsartan in Chronic Renal Disease. Journal of Hypertension 2000; 18(1):89-95. *Follow-up less than 6 months*

3773. Ruilope LM, Araque A, Lahera V, et al. Antihypertensive effect of nitrendipine in the hypertensive patient with renal impairment. Renal Failure 1993; 15(3):359-63. *Not RCT or controlled trial*

3774. Ruilope LM, Casal MC, Guerrero L, et al. Sodium intake does not influence the effect of verapamil in hypertensive patients with mild renal insufficiency. Drugs 1992; 44 Suppl 1:94-8. *Sample size less than 50 patients*

3775. Ruilope LM, Lahera V, Alcazar JM, et al. Randomly allocated study of the effects of standard therapy versus ACE inhibition on micro-albuminuria in essential hypertension. Journal of Hypertension - Supplement 1994; 12(4):S59-63. *Sample size less than 50 patients*

3776. Ruilope LM, Miranda B, Garcia-Robles R, et al. Effects of nisoldipine on renal function in normal volunteers and essential hypertensive patients. Journal of Cardiovascular Pharmacology 1989; 13(1):90-3. *Sample size less than 50 patients*

3777. Ruilope LM, Rodicio J, Garcia Robles R, et al. Influence of a low sodium diet on the renal response to amino acid infusions in humans. Kidney International 1987; 31(4):992-9. *Follow-up less than 6 months*

3778. Ruilope LM, Schiffrin EL. Blood pressure control and benefits of antihypertensive therapy: does it make a difference which agents we use? Hypertension 2001; 38(3 Pt 2):537-42. *Not RCT or controlled trial*

3779. Ruilope LM, Zanchetti A, Julius S, et al. Prediction of cardiovascular outcome by estimated glomerular filtration rate and estimated creatinine clearance in the high-risk hypertension population of the VALUE trial. Journal of Hypertension 2007; 25(7):1473-9. *Not RCT or controlled trial*

3780. Rule AD, Rodeheffer RJ, Larson TS, et al. Limitations of estimating glomerular filtration rate from serum creatinine in the general population.[Erratum appears in Mayo Clin Proc. 2006 Dec;81(12):1639]. Mayo Clinic Proceedings 2006; 81(11):1427-34. *Not relevant to key questions*

3781. Ruml LA, Gonzalez G, Taylor R, et al. Effect of varying doses of potassium-magnesium citrate on thiazide-induced hypokalemia and magnesium loss. American Journal of Therapeutics 1999; 6(1):45-50. *Sample size less than 50 patients*

3782. Rupoli L, Fruscio M, Gradnik R, et al. Cardiovascular and renal effects of single administration of three different doses of isradipine in hypertensive patients. Dose-response curves of the different effects. American Journal of Medicine 1989; 86(4A):65-6. *Sample size less than 50 patients*

3783. Rusinek H, Lee VS, Johnson G. Optimal dose of Gd-DTPA in dynamic MR studies. Magnetic Resonance in Medicine 2001; 46(2):312-6. *Not RCT or controlled trial*

3784. Russel JA. The current management of septic shock. Minerva Medica 2008; 99(5):431-58. *Sample size less than 50 patients*

3785. Russell CD. Optimum sample times for single-injection, multisample renal clearance methods. Journal of Nuclear Medicine 1993; 34(10):1761-5. *Not RCT or controlled trial*

3786. Russo D, Minutolo R, Cianciaruso B, et al. Early effects of contrast media on renal hemodynamics and tubular function in chronic renal failure. Journal of the American Society of Nephrology 1995; 6(5):1451-8. *Not CKD treatment*

3787. Russo D, Testa A, Della Volpe L, et al. Randomised prospective study on renal effects of two different contrast media in humans: protective role of a calcium channel blocker. Nephron 1990; 55(3):254-7. *Sample size less than 50 patients*

3788. Ruzicka M, Burns KD, Culleton B, et al. Treatment of hypertension in patients with nondiabetic chronic kidney disease. Canadian Journal of Cardiology 2007; 23(7):595-601. *Follow-up less than 6 months*

3789. Rybak MJ, Abate BJ, Kang SL, et al. Prospective evaluation of the effect of an aminoglycoside dosing regimen on rates of observed nephrotoxicity and ototoxicity. Antimicrobial Agents & Chemotherapy 1999; 43(7):1549-55. *Not CKD treatment*

3790. Ryckwaert F, Colson P, Ribstein J, et al. Haemodynamic and renal effects of intravenous enalaprilat during coronary artery bypass graft surgery in patients with ischaemic heart dysfunction. British Journal of Anaesthesia 2001; 86(2):169-75. *Sample size less than 50 patients*

3791. Sa Carvalho M, Henderson R, Shimakura S, et al. Survival of hemodialysis patients: modeling differences in risk of dialysis centers. International Journal for Quality in Health Care 2003; 15(3):189-96. *Not early CKD*

3792. Sackner-Bernstein JD, Skopicki HA, Aaronson KD. Risk of worsening renal function with nesiritide in patients with acutely decompensated heart failure.[Erratum appears in Circulation. 2005 May 3;111(17):2274]. Circulation 2005; 111(12):1487-91. *Not relevant to key questions*

3793. Sadeghi HM, Stone GW, Grines CL, et al. Impact of renal insufficiency in patients undergoing primary angioplasty for acute myocardial infarction. Circulation 2003; 108(22):2769-75. *Not RCT or controlled trial*

3794. Safdar B, Degutis LC, Landry K, et al. Intravenous morphine plus ketorolac is superior to either drug alone for treatment of acute renal colic. Annals of Emergency Medicine 2006; 48(2):173-81. *Not early CKD*

3795. Sahani DV, Soulez G, Chen K-M, et al. A comparison of the efficacy and safety of iopamidol-370 and iodixanol-320 in patients undergoing multidetector-row computed tomography. Investigative Radiology 2007; 42(12):856-61. *Follow-up less than 6 months*

3796. Saikawa T, Sasaki J, Biro S, et al. Is the reno-protective effect of valsartan dose dependent? A comparative study of 80 and 160 mg day(-1). Hypertension Research - Clinical & Experimental 2010 Sep; 33(9):886-91. *Not early CKD*

3797. Saito F, Fujita H, Takahashi A, et al. Renoprotective effect and cost-effectiveness of using benidipine, a calcium channel blocker, to lower the dose of angiotensin receptor blocker in hypertensive patients with albuminuria. Hypertension Research - Clinical & Experimental 2007; 30(1):39-47. *Not RCT or controlled trial*

3798. Sakai H, Watanabe S, Inoue I, et al. Effect of urokinase on preservation of renal function in patients with diabetic nephropathy. Journal of Diabetic Complications 1991; 5(2-3):95-7. *Sample size less than 50 patients*

3799. Saklayen MG, Gyebi LK, Tasosa J, et al. Effects of additive therapy with spironolactone on proteinuria in diabetic patients already on ACE inhibitor or ARB therapy: results of a randomized, placebo-controlled, double-blind, crossover trial. Journal of Investigative Medicine 2008; 56(4):714-9. *Not RCT or controlled trial*

3800. Salako BL, Finomo FO, Kadiri S, et al. Comparative effect of lisinopril and lacidipine on urinary albumin excretion in patients with type 11 diabetic nephropathy. African Journal of Medicine & Medical Sciences 2002; 31(1):53-7. *Sample size less than 50 patients*

3801. Salazar MR, Carbajal HA, Marillet AG, et al. Glomerular filtration rate, cardiovascular risk factors and insulin resistance. Medicina 2009; 69(5):541-6. *Not CKD treatment*

3802. Salerno F, Lorenzano E, Maggi A, et al. Effects of imidazole-salicylate on renal function and the diuretic action of furosemide in cirrhotic patients with ascites. Journal of Hepatology 1993; 19(2):279-84. *Not CKD treatment*

3803. Salerno M, Di Salvo M, Furnari R, et al. Comparison of muzolimine and furosemide in heart failure. Zeitschrift fur Kardiologie 1985; 74 Suppl 2:32-3. *Sample size less than 50 patients*

3804. Salvetti A, Leonetti G, Bernini GP, et al. Antihypertensive and renal effects of tertatolol, a new beta-blocking agent, in hypertensive patients. American Journal of Nephrology 1986; 6 Suppl 2:45-9. *Sample size less than 50 patients*

3805. Sambhi MP. Saluretic and diuretic effects of antihypertensive nitrendipine monotherapy in man. Angiology 1988; 39(1 Pt 2):106-12. *Sample size less than 50 patients*

3806. Sampath S, Moran JL, Graham PL, et al. The efficacy of loop diuretics in acute renal failure: assessment using Bayesian evidence synthesis techniques. Critical Care Medicine 2007; 35(11):2516-24. *Not RCT or controlled trial*

3807. Samuelsson O, Attman P-O, Knight-Gibson C, et al. Fluvastatin improves lipid abnormalities in patients with moderate to advanced chronic renal insufficiency. American Journal of Kidney Diseases 2002; 39(1):67-75. *Sample size less than 50 patients*

3808. Samuelsson O, Hedner T, Ljungman S, et al. A comparative study of lisinopril and atenolol on low degree urinary albumin excretion, renal function and haemodynamics in uncomplicated, primary hypertension. European Journal of Clinical Pharmacology 1992; 43(5):469-75. *Follow-up less than 6 months*

3809. Samy AK, Murray G, MacBain G. Glasgow aneurysm score. Cardiovascular Surgery 1994; 2(1):41-4. *Not RCT or controlled trial*

3810. San Miguel JF, Blade Creixenti J, Garcia-Sanz R. Treatment of multiple myeloma. Haematologica 1999; 84(1):36-58. *Not CKD treatment*

3811. Sanahuja J, Corbera G, Garau J, et al. Intramuscular diclofenac sodium versus intravenous Baralgin in the treatment of renal colic. DICP 1990; 24(4):361-4. *Not CKD treatment*

3812. Sanchez EQ, Martin AP, Ikegami T, et al. Sirolimus conversion after liver transplantation: improvement in measured glomerular filtration rate after 2 years.[Erratum appears in Transplant Proc. 2006 Jan-Feb;38(1):342 Note: Klintmaim, GB [corrected to Klintmalm, GB]]. Transplantation Proceedings 2005; 37(10):4416-23. *Sample size less than 50 patients*

3813. Sanchez Garcia M, Alvarez Gonzaez M, Velo Plaza M. Dopamine dose and renal damage. Lancet 2001; 357(9269):1707-8. *Not early CKD*

3814. Sanchez RA, Marco E, Gilbert HB, et al. Natriuretic effect and changes in renal haemodynamics induced by enalapril in essential hypertension. Drugs 1985; 30 Suppl 1:49-58. *Sample size less than 50 patients*

3815. Sanchez RA, Migliorini M, Giannone C, et al. Plasma renin activity levels influence the effect of converting enzyme inhibitors in preserving renal function in hypertension. Journal of Hypertension 1996; 14(8):1025-31. *Sample size less than 50 patients*

3816. Sanchez RA, Traballi CA, Gilbert BH, et al. Effect of cilazapril in hypertensive patients with renal impairment. Journal of Cardiovascular Pharmacology 1991; 17(2):222-7. *Sample size less than 50 patients*

3817. Sanchez-Alcaraz A, Vargas A, Quintana MB, et al. Therapeutic drug monitoring of tobramycin: once-daily versus twice-daily dosage schedules. Journal of Clinical Pharmacy & Therapeutics 1998; 23(5):367-73. *Sample size less than 50 patients*

3818. Sanchez-Carpena J, Dominguez-Hervella F, Garcia I, et al. Comparison of intravenous dexketoprofen and dipyrone in acute renal colic. European Journal of Clinical Pharmacology 2007; 63(8):751-60. *Not early CKD*

3819. Sanchorawala V, Wright DG, Seldin DC, et al. High-dose intravenous melphalan and autologous stem cell transplantation as initial therapy or following two cycles of oral chemotherapy for the treatment of AL amyloidosis: results of a prospective randomized trial. Bone Marrow Transplantation 2004; 33(4):381-8. *Not relevant to key questions*

3820. Sandage B, Sabounjian L, Shipley J, et al. Predictive power of an in vitro system to assess drug interactions of an antimuscarinic medication: a comparison of in vitro and in vivo drug-drug interaction studies of trospium chloride with digoxin. Journal of Clinical Pharmacology 2006; 46(7):776-84. *Not RCT or controlled trial*

3821. Sanders PW. Management of paraproteinemic renal disease. Current Opinion in Nephrology & Hypertension 2005; 14(2):97-103. *Not RCT or controlled trial*

3822. Sandhu C, Belli A-M, Oliveira DB. The role of N-acetylcysteine in the prevention of contrast-induced nephrotoxicity. Cardiovascular & Interventional Radiology 2006; 29(3):344-7. *Not RCT or controlled trial*

3823. Sandhu DP, Iacovou JW, Fletcher MS, et al. A comparison of intramuscular ketorolac and pethidine in the alleviation of renal colic. British Journal of Urology 1994; 74(6):690-3. *Sample size less than 50 patients*

3824. Sandhu S, Wiebe N, Fried LF, et al. Statins for improving renal outcomes: a meta-analysis. Journal of the American Society of Nephrology 2006; 17(7):2006-16. *Not relevant to key questions*

3825. Sanjay S, Annigeri RA, Seshadri R, et al. The comparison of the diuretic and natriuretic efficacy of continuous and bolus intravenous furosemide in patients with chronic kidney disease. Nephrology 2008; 13(3):247-50. *Not early CKD*

3826. San-Miguel JF, Richardson PG, Sonneveld P, et al. Efficacy and safety of bortezomib in patients with renal impairment: results from the APEX phase 3 study. Leukemia 2008; 22(4):842-9. *Not CKD treatment*

3827. Sano T, Hotta N, Kawamura T, et al. Effects of long-term enalapril treatment on persistent microalbuminuria in normotensive type 2 diabetic patients: results of a 4-year, prospective, randomized study. Diabetic Medicine 1996; 13(2):120-4. *Not relevant to key questions*

3828. Santoso JT, Lucci JA, 3rd, Coleman RL, et al. Saline, mannitol, and furosemide hydration in acute cisplatin nephrotoxicity: a randomized trial. Cancer Chemotherapy & Pharmacology 2003; 52(1):13-8. *Not CKD treatment*

3829. Sar F, Saler T, Ecebay A, et al. The efficacy of n-acetylcysteine in preventing contrast-induced nephropathy in type 2 diabetic patients without nephropathy. Journal of Nephrology 2010 Jul-Aug; 23(4):478-82. *Not CKD treatment*

3830. Sarafidis PA, Bakris GL. Protection of the kidney by thiazolidinediones: an assessment from bench to bedside. Kidney International 2006; 70(7):1223-33. *Not relevant to key questions*

3831. Sarafidis PA, Bakris GL. Renin-angiotensin blockade and kidney disease. Lancet 2008; 372(9638):511-2. *Not relevant to key questions*

3832. Sarafidis PA, Lasaridis AN. Diabetic nephropathy: Endothelin antagonism for diabetic nephropathy. Nature Reviews Nephrology 2010 Aug; 6(8):447-9. *Not relevant to key questions*

3833. Sarafidis PA, Stafylas PC, Georgianos PI, et al. Effect of thiazolidinediones on albuminuria and proteinuria in diabetes: a meta-analysis. American Journal of Kidney Diseases 2010 May; 55(5):835-47. *Not relevant to key questions*

3834. Sarafidis PA, Stafylas PC, Kanaki AI, et al. Effects of renin-angiotensin system blockers on renal outcomes and all-cause mortality in patients with diabetic nephropathy: an updated meta-analysis. American Journal of Hypertension 2008; 21(8):922-9. *Not relevant to key questions*

3835. Saran R, Novak JE, Desai A, et al. Impact of vitamin E on plasma asymmetric dimethylarginine (ADMA) in chronic kidney disease (CKD): a pilot study. Nephrology Dialysis Transplantation 2003; 18(11):2415-20. *Sample size less than 50 patients*

3836. Sarapa N, Wickremasingha P, Ge N, et al. Lack of effect of DX-619, a novel des-fluoro(6)-quinolone, on glomerular filtration rate measured by serum clearance of cold iohexol. Antimicrobial Agents & Chemotherapy 2007; 51(6):1912-7. *Sample size less than 50 patients*

3837. Sarnak MJ, Coronado BE, Greene T, et al. Cardiovascular disease risk factors in chronic renal insufficiency. Clinical Nephrology 2002; 57(5):327-35. *Not RCT or controlled trial*

3838. Sarnak MJ, Greene T, Wang X, et al. The effect of a lower target blood pressure on the progression of kidney disease: long-term follow-up of the modification of diet in renal disease study. Annals of Internal Medicine 2005; 142(5):342-51. *Not relevant to key questions*

3839. Sarnak MJ, Wang S-R, Beck GJ, et al. Homocysteine, cysteine, and B vitamins as predictors of kidney disease progression. American Journal of Kidney Diseases 2002; 40(5):932-9. *Not CKD treatment*

3840. Sarraf M, Masoumi A, Schrier RW. Cardiorenal syndrome in acute decompensated heart failure. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(12):2013-26. *Not CKD treatment*

3841. Saruta T, Hayashi K, Ogihara T, et al. Effects of candesartan and amlodipine on cardiovascular events in hypertensive patients with chronic kidney disease: subanalysis of the CASE-J Study.[Erratum appears in Hypertens Res. 2009 Dec;32(12):1157]. Hypertension Research - Clinical & Experimental 2009; 32(6):505-12. *Duplicate listings*

3842. Sasaki H, Saiki A, Endo K, et al. Protective effects of efonidipine, a T- and L-type calcium channel blocker, on renal function and arterial stiffness in type 2 diabetic patients with hypertension and nephropathy. Journal of Atherosclerosis & Thrombosis 2009; 16(5):568-75. *Sample size less than 50 patients*

3843. Sassard J, Geoffroy J, Ferry N, et al. Compared effects of isoxicam and indomethacin on the urinary excretion of prostaglandins in degenerative articular diseases. Prostaglandins Leukotrienes & Essential Fatty Acids 1989; 38(2):107-11. *Sample size less than 50 patients*

3844. Sasso FC, Carbonara O, Persico M, et al. Irbesartan reduces the albumin excretion rate in microalbuminuric type 2 diabetic patients independently of hypertension: a randomized double-blind placebo-controlled crossover study. Diabetes Care 2002; 25(11):1909-13. *Not relevant to key questions*

3845. Sato A, Hayashi K, Naruse M, et al. Effectiveness of aldosterone blockade in patients with diabetic nephropathy. Hypertension 2003; 41(1):64-8. *Sample size less than 50 patients*

3846. Sato A, Hayashi K, Saruta T. Antiproteinuric effects of mineralocorticoid receptor blockade in patients with chronic renal disease. American Journal of Hypertension 2005; 18(1):44-9. *Not relevant to key questions*

3847. Sato A, Tabata M, Hayashi K, et al. Effects of the angiotensin II type 1 receptor antagonist candesartan, compared with angiotensin-converting enzyme inhibitors, on the urinary excretion of albumin and type IV collagen in patients with diabetic nephropathy. Clinical & Experimental Nephrology 2003; 7(3):215-20. *Not relevant to key questions*

3848. Satoh N, Kimoto S, Hiraki Y. Studies of an aspect of renal function with the aid of dynamic CT and renogram. Acta Medica Okayama 1991; 45(3):187-93. *Not CKD treatment*

3849. Sav T, Tokgoz B, Sipahioglu MH, et al. Is there a difference between the allergic potencies of the iron sucrose and low molecular weight iron dextran? Renal Failure 2007; 29(4):423-6. *Not CKD treatment*

3850. Savage S, Nagel NJ, Estacio RO, et al. Clinical factors associated with urinary albumin excretion in type II diabetes. American Journal of Kidney Diseases 1995; 25(6):836-44. *Not CKD treatment*

3851. Savage S, Schrier RW. Progressive renal insufficiency: the role of angiotensin converting enzyme inhibitors. Advances in Internal Medicine 1992; 37:85-101. *Not relevant to key questions*

3852. Savolainen H. Studies on urinary proteoglycan excretion in occupational cadmium exposure. Pharmacology & Toxicology 1994; 75(2):113-4. *Not RCT or controlled trial*

3853. Sawara Y, Takei T, Uchida K, et al. Effects of lipid-lowering therapy with rosuvastatin on atherosclerotic burden in patients with chronic kidney disease. Internal Medicine 2008; 47(17):1505-10. *Not CKD treatment*

3854. Sawicki PT. Stabilization of glomerular filtration rate over 2 years in patients with diabetic nephropathy under intensified therapy regimens. Diabetes Treatment and Teaching Programmes Working Group. Nephrology Dialysis Transplantation 1997; 12(9):1890-9. *Sample size less than 50 patients*

3855. Sawicki PT, Muhlhauser I, Bender R, et al. Effects of smoking on blood pressure and proteinuria in patients with diabetic nephropathy. Journal of Internal Medicine 1996; 239(4):345-52. *Sample size less than 50 patients*

3856. Sawicki PT, Muhlhauser I, Didjurgeit U, et al. Intensified antihypertensive therapy is associated with improved survival in type 1 diabetic patients with nephropathy. Journal of Hypertension 1995; 13(8):933-8. *Not RCT or controlled trial*

3857. Sawicki PT, Muhlhauser I, Didjurgeit U, et al. Effects of intensification of antihypertensive care in diabetic nephropathy. Journal of Diabetes & its Complications 1995; 9(4):315-7. *Not RCT or controlled trial*

3858. Sax PE, Gallant JE, Klotman PE. Renal safety of tenofovir disoproxil fumarate. AIDS Reader 2007; 17(2):90-2. *Sample size less than 50 patients*

3859. Saxenhofer H, Raselli A, Weidmann P, et al. Urodilatin, a natriuretic factor from kidneys, can modify renal and cardiovascular function in men. American Journal of Physiology 1990; 259(5 Pt 2):F832-8. *Not CKD treatment*

3860. Scaglione R, Argano C, Corrao S, et al. Transforming growth factor beta1 and additional renoprotective effect of combination ACE inhibitor and angiotensin II receptor blocker in hypertensive subjects with minor renal abnormalities: a 24-week randomized controlled trial. Journal of Hypertension 2005; 23(3):657-64. *Sample size less than 50 patients*

3861. Scaglione R, Ganguzza A, Corrao S, et al. Effects of cilazapril on renal haemodynamics and function in hypertensive patients: a randomised controlled study versus hydrochlorothiazide. Blood Pressure 1995; 4(6):363-8. *Sample size less than 50 patients*

3862. Scaglione R, Indovina A, Parrinello G, et al. Antihypertensive efficacy and effects of nitrendipine on cardiac and renal hemodynamics in mild to moderate hypertensive patients: randomized controlled trial versus hydrochlorothiazide. Cardiovascular Drugs & Therapy 1992; 6(2):141-6. *Follow-up less than 6 months*

3863. Scanferla F, Toffoletto PP, Roncali D, et al. Associated effect of hepatic hydroxymethylglutaryl coenzyme A reductase + angiotensin converting enzyme inhibitors on the progression of renal failure in hypertensive subjects. American Journal of Hypertension 1991; 4(10 Pt 1):868. *Sample size less than 50 patients*

3864. Scarsi KK, Bjornson DC. The use of ACE inhibitors as renoprotective agents in Medicaid patients with diabetes. Annals of Pharmacotherapy 2000; 34(9):1002-6. *Not RCT or controlled trial*

3865. Schachinger V, Zeiher AM. Stem cells and cardiovascular and renal disease: today and tomorrow. Journal of the American Society of Nephrology 2005; 16 Suppl 1:S2-6. *Sample size less than 50 patients*

3866. Schaefer K, Scheer J, Asmus G, et al. The treatment of uraemic hyperphosphataemia with calcium acetate and calcium carbonate: a comparative study. Nephrology Dialysis Transplantation 1991; 6(3):170-5. *Not early CKD*

3867. Schaefer RM, Schaefer L, Heidland A. Recombinant human erythropoietin for anaemia associated with chronic renal failure in predialysis patients. Przeglad Lekarski 1992; 49(1-2):41-2. *Not early CKD*

3868. Schaeffner ES, Kurth T, Bowman TS, et al. Blood pressure measures and risk of chronic kidney disease in men. Nephrology Dialysis Transplantation 2008; 23(4):1246-51. *Not RCT or controlled trial*

3869. Schaeffner ES, van der Giet M, Gaedeke J, et al. The Berlin initiative study: the methodology of exploring kidney function in the elderly by combining a longitudinal and cross-sectional approach. European Journal of Epidemiology 2010 Mar; 25(3):203-10. *Not CKD treatment*

3870. Schefer T, Wolber T, Binggeli C, et al. Long-term predictors of mortality in ICD patients with non-ischaemic cardiac disease: impact of renal function. Europace 2008; 10(9):1052-9. *Not CKD treatment*

3871. Scheid DC, McCarthy LH, Lawler FH, et al. Screening for microalbuminuria to prevent nephropathy in patients with diabetes: a systematic review of the evidence. Journal of Family Practice 2001; 50(8):661-8. *Not relevant to key questions*

3872. Scherberich JE, Fischer A, Rautschka E, et al. Nephrotoxicity of high and low osmolar contrast media: case control studies following digital subtraction angiography in potential risk patients. Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin - Erganzungsband 1989; 128:91-4. *Not CKD treatment*

3873. Scherberich JE, Mondorf WA. Nephrotoxic potential of antiinfective drugs as assessed by tissue-specific proteinuria of renal antigens. International Journal of Clinical Pharmacology & Therapeutics 1998; 36(3):152-8. *Not CKD treatment*

3874. Schetz M. Diuretics in acute renal failure? Contributions to Nephrology 2004; 144:166-81. *Not CKD treatment*

3875. Schetz M, Bove T, Morelli A, et al. Prevention of cardiac surgery-associated acute kidney injury. International Journal of Artificial Organs 2008; 31(2):179-89. *Not CKD treatment*

3876. Schetz M, Vanhorebeek I, Wouters PJ, et al. Tight blood glucose control is renoprotective in critically ill patients. Journal of the American Society of Nephrology 2008; 19(3):571-8. *Sample size less than 50 patients*

3877. Schiffl H, Schollmeyer P. Metabolic consequences of long-term thiazide-based antihypertensive treatment of renal hypertension. Cardiology 1985; 72 Suppl 1:54-6. *Not CKD treatment*

3878. Schiffl H, Sitter T, Lang S, et al. Bioincompatible membranes place patients with acute renal failure at increased risk of infection. ASAIO Journal 1995; 41(3):M709-12. *Not CKD treatment*

3879. Schiffmann R, Ries M, Timmons M, et al. Long-term therapy with agalsidase alfa for Fabry disease: safety and effects on renal function in a home infusion setting. Nephrology Dialysis Transplantation 2006; 21(2):345-54. *Not relevant to key questions*

3880. Schindler C. ACE-inhibitor, AT1-receptor-antagonist, or both? A clinical pharmacologist's perspective after publication of the results of ONTARGET. Therapeutic Advances in Cardiovascular Disease 2008; 2(4):233-48. *Not relevant to key questions*

3881. Schjoedt KJ, Andersen S, Rossing P, et al. Aldosterone escape during blockade of the renin-angiotensin-aldosterone system in diabetic nephropathy is associated with enhanced decline in glomerular filtration rate. Diabetologia 2004; 47(11):1936-9. *Not early CKD*

3882. Schjoedt KJ, Astrup AS, Persson F, et al. Optimal dose of lisinopril for renoprotection in type 1 diabetic patients with diabetic nephropathy: a randomised crossover trial. Diabetologia 2009; 52(1):46-9. *Not RCT or controlled trial*

3883. Schjoedt KJ, Christensen PK, Jorsal A, et al. Autoregulation of glomerular filtration rate during spironolactone treatment in hypertensive patients with type 1 diabetes: a randomized crossover trial. Nephrology Dialysis Transplantation 2009; 24(11):3343-9. *Sample size less than 50 patients*

3884. Schjoedt KJ, Hansen HP, Tarnow L, et al. Long-term prevention of diabetic nephropathy: an audit. Diabetologia 2008; 51(6):956-61. *Follow-up less than 6 months*

3885. Schjoedt KJ, Jacobsen P, Rossing K, et al. Dual blockade of the renin-angiotensin-aldosterone system in diabetic nephropathy: the role of aldosterone. Hormone & Metabolic Research 2005; 37 Suppl 1:4-8. *Not relevant to key questions*

3886. Schjoedt KJ, Rossing K, Juhl TR, et al. Beneficial impact of spironolactone in diabetic nephropathy. Kidney International 2005; 68(6):2829-36. *Follow-up less than 6 months*

3887. Schjoedt KJ, Rossing K, Juhl TR, et al. Beneficial impact of spironolactone on nephrotic range albuminuria in diabetic nephropathy. Kidney International 2006; 70(3):536-42. *Not RCT or controlled trial*

3888. Schlaich MP, Jacobi J, John S, et al. Is l-arginine infusion an adequate tool to assess endothelium-dependent vasodilation of the human renal vasculature? Clinical Science 2000; 99(4):293-302. *Not early CKD*

3889. Schlaich MP, Sobotka PA, Krum H, et al. Renal denervation as a therapeutic approach for hypertension: novel implications for an old concept. Hypertension 2009; 54(6):1195-201. *Not RCT or controlled trial*

3890. Schlieper G, Brandenburg V, Ketteler M, et al. Sodium thiosulfate in the treatment of calcific uremic arteriolopathy. Nature Reviews Nephrology 2009; 5(9):539-43. *Not CKD treatment*

3891. Schluchter MD. Estimating correlation between alternative measures of disease progression in a longitudinal study. Modification of Diet in Renal Disease Study. Statistics in Medicine 1990; 9(10):1175-88. *Not CKD treatment*

3892. Schluchter MD, Greene T, Beck GJ. Analysis of change in the presence of informative censoring: application to a longitudinal clinical trial of progressive renal disease. Statistics in Medicine 2001; 20(7):989-1007. *Not RCT or controlled trial*

3893. Schlueter W, Keilani T, Batlle DC. Metabolic effects of converting enzyme inhibitors: focus on the reduction of cholesterol and lipoprotein(a) by fosinopril. American Journal of Cardiology 1993; 72(20):37H-44H. *Sample size less than 50 patients*

3894. Schmetterer L, Dallinger S, Bobr B, et al. Systemic and renal effects of an ET(A) receptor subtype-specific antagonist in healthy subjects. British Journal of Pharmacology 1998; 124(5):930-4. *Sample size less than 50 patients*

3895. Schmid CH, Landa M, Jafar TH, et al. Constructing a database of individual clinical trials for longitudinal analysis. Controlled Clinical Trials 2003; 24(3):324-40. *Not RCT or controlled trial*

3896. Schmid CH, Stark PC, Berlin JA, et al. Meta-regression detected associations between heterogeneous treatment effects and study-level, but not patient-level, factors. Journal of Clinical Epidemiology 2004; 57(7):683-97. *Not RCT or controlled trial*

3897. Schmidt A, Bayerle-Eder M, Pleiner H, et al. The renal and systemic hemodynamic effects of a nitric oxide-synthase inhibitor are reversed by a selective endothelin(a) receptor antagonist in men. Nitric Oxide 2001; 5(4):370-6. *Not early CKD*

3898. Schmidt A, Pleiner J, Schaller G, et al. Renal hemodynamic effects of somatostatin are not related to inhibition of endogenous insulin release. Kidney International 2002; 61(5):1788-93. *Not early CKD*

3899. Schmidt BMW, Sammer U, Fleischmann I, et al. Rapid nongenomic effects of aldosterone on the renal vasculature in humans. Hypertension 2006; 47(4):650-5. *Not RCT or controlled trial*

3900. Schmidt P, Pang D, Nykamp D, et al. N-acetylcysteine and sodium bicarbonate versus N-acetylcysteine and standard hydration for the prevention of radiocontrast-induced nephropathy following coronary angiography. Annals of Pharmacotherapy 2007; 41(1):46-50. *Sample size less than 50 patients*

3901. Schmieder RE. Nephroprotection by antihypertensive agents. Journal of Cardiovascular Pharmacology 1994; 24 Suppl 2:S55-64. *Not RCT or controlled trial*

3902. Schmieder RE. Optimizing therapeutic strategies to achieve renal and cardiovascular risk reduction in diabetic patients with angiotensin receptor blockers. Journal of Hypertension 2005; 23(5):905-11. *Sample size less than 50 patients*

3903. Schmieder RE, Gatzka C, Schobel H, et al. Renal hemodynamic response to stress is influenced by ACE-inhibitors. Clinical Nephrology 1994; 42(6):381-8. *Sample size less than 50 patients*

3904. Schmieder RE, Klingbeil AU, Fleischmann EH, et al. Additional antiproteinuric effect of ultrahigh dose candesartan: a double-blind, randomized, prospective study. Journal of the American Society of Nephrology 2005; 16(10):3038-45. *Sample size less than 50 patients*

3905. Schmieder RE, Ruddel H, Schlebusch H, et al. Impact of antihypertensive therapy with isradipine and metoprolol on early markers of hypertensive nephropathy. American Journal of Hypertension 1992; 5(5 Pt 1):318-21. *Sample size less than 50 patients*

3906. Schmieder RE, Schobel HP, Gatzka CE, et al. Effects of angiotensin converting enzyme inhibitor on renal haemodynamics during mental stress. Journal of Hypertension 1996; 14(10):1201-7. *Sample size less than 50 patients*

3907. Schmieder RE, Veelken R, Schobel H, et al. Glomerular hyperfiltration during sympathetic nervous system activation in early essential hypertension. Journal of the American Society of Nephrology 1997; 8(6):893-900. *Sample size less than 50 patients*

3908. Schmitt F, Martinez F, Brillet G, et al. Acute renal effects of AT1-receptor blockade after exogenous angiotensin II infusion in healthy subjects. Journal of Cardiovascular Pharmacology 1998; 31(2):314-21. *Follow-up less than 6 months*

3909. Schmitt F, Natov S, Martinez F, et al. Renal effects of angiotensin I-receptor blockade and angiotensin convertase inhibition in man. Clinical Science 1996; 90(3):205-13. *Not RCT or controlled trial*

3910. Schmitt R, Coca S, Kanbay M, et al. Recovery of kidney function after acute kidney injury in the elderly: a systematic review and meta-analysis. American Journal of Kidney Diseases 2008; 52(2):262-71. *Not RCT or controlled trial*

3911. Schmitz A, Pedersen MM, Mogensen CE. Effects of felodipine on urinary albumin excretion and metabolic control in hypertensive non-insulin-dependent diabetics. American Journal of Hypertension 1990; 3(8 Pt 1):611-7. *Sample size less than 50 patients*

3912. Schmitz A, Pedersen MM, Moller A, et al. Some aspects of antihypertensive and diuretic treatment in noninsulin-dependent diabetic patients. Journal of Diabetic Complications 1990; 4(2):79-81. *Sample size less than 50 patients*

3913. Schmoelz M, Schelling G, Dunker M, et al. Comparison of systemic and renal effects of dopexamine and dopamine in norepinephrine-treated septic shock. Journal of Cardiothoracic & Vascular Anesthesia 2006; 20(2):173-8. *Not RCT or controlled trial*

3914. Schnack C, Capek M, Banyai M, et al. Long-term treatment with nifedipine reduces urinary albumin excretion and glomerular filtration rate in normotensive type 1 diabetic patients with microalbuminuria. Acta Diabetologica 1994; 31(1):14-8. *Sample size less than 50 patients*

3915. Schnack C, Hoffmann W, Hopmeier P, et al. Renal and metabolic effects of 1-year treatment with ramipril or atenolol in NIDDM patients with microalbuminuria. Diabetologia 1996; 39(12):1611-6. *Not relevant to key questions*

3916. Schnapp P. Acute natriuretic effect of nifedipine in elderly males with essential hypertension. International Journal of Clinical Pharmacology, Therapy, & Toxicology 1989; 27(9):442-4. *Sample size less than 50 patients*

3917. Schneider CA, Ferrannini E, Defronzo R, et al. Effect of pioglitazone on cardiovascular outcome in diabetes and chronic kidney disease. Journal of the American Society of Nephrology 2008; 19(1):182-7. *Follow-up less than 6 months*

3918. Schneider LM, Roubin GS. Minimal contrast use in carotid stenting: avoiding contrast pitfalls. Journal of Invasive Cardiology 2007; 19(1):37-8. *Sample size less than 50 patients*

3919. Schneider MP, Klingbeil AU, Schlaich MP, et al. Impaired sodium excretion during mental stress in mild essential hypertension. Hypertension 2001; 37(3):923-7. *Not early CKD*

3920. Schohn DC, Jahn HA, Maareck M. Long term effects of sustained release verapamil on the renal and systemic haemodynamic parameters in hypertensive patients with mild to severe chronic renal failure. Drugs 1993; 46 Suppl 2:113-9; discussion 9-20. *Sample size less than 50 patients*

3921. Schorr U, Distler A, Sharma AM. Effect of sodium chloride- and sodium bicarbonate-rich mineral water on blood pressure and metabolic parameters in elderly normotensive individuals: a randomized double-blind crossover trial. Journal of Hypertension 1996; 14(1):131-5. *Not early CKD*

3922. Schou M, Gabrielsen A, Bruun NE, et al. Angiotensin II attenuates the natriuresis of water immersion in humans. American Journal of Physiology - Regulatory Integrative & Comparative Physiology 2002; 283(1):R187-96. *Not CKD treatment*

3923. Schouten LMT, Niessen LW, van de Pas JWAM, et al. Cost-effectiveness of a quality improvement collaborative focusing on patients with diabetes. Medical Care 2010 Oct; 48(10):884-91. *Not CKD treatment*

3924. Schram MT, van Ittersum FJ, Spoelstra-de Man A, et al. Aggressive antihypertensive therapy based on hydrochlorothiazide, candesartan or lisinopril as initial choice in hypertensive type II diabetic individuals: effects on albumin excretion, endothelial function and inflammation in a double-blind, randomized clinical trial. Journal of Human Hypertension 2005; 19(6):429-37. *Not RCT or controlled trial*

3925. Schrier RW. Treating high-risk diabetic hypertensive patients with comorbid conditions. American Journal of Kidney Diseases 2000; 36(3 Suppl 1):S10-7. *Not RCT or controlled trial*

3926. Schrier RW. Aggressively preventing diabetes. Nature Reviews Nephrology 2010 Jun; 6(6):313. *Not CKD treatment*

3927. Schrier RW. Fluid administration in critically ill patients with acute kidney injury. Clinical Journal of The American Society of Nephrology: CJASN 2010 Apr; 5(4):733-9. *Not CKD treatment*

3928. Schrier RW, Burke TJ. Role of calcium-channel blockers in preventing acute and chronic renal injury. Journal of Cardiovascular Pharmacology 1991; 18 Suppl 6:S38-43. *Not relevant to key questions*

3929. Schrier RW, Estacio RO. The effect of angiotensin-converting enzyme inhibitors on the progression of nondiabetic renal disease: a pooled analysis of individual-patient data from 11 randomized, controlled trials. Annals of Internal Medicine 2001; 135(2):138-9. *Not RCT or controlled trial*

3930. Schrier RW, Estacio RO, Esler A, et al. Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes. Kidney International 2002; 61(3):1086-97. *Not relevant to key questions*

3931. Schrier RW, Estacio RO, Jeffers B. Appropriate Blood Pressure Control in NIDDM (ABCD) Trial. Diabetologia 1996; 39(12):1646-54. *Not RCT or controlled trial*

3932. Schroth RJ, Hitchon CA, Uhanova J, et al. Hepatitis B vaccination for patients with chronic renal failure. Cochrane Database of Systematic Reviews 2004; (3):CD003775. *Not CKD treatment*

3933. Schucker JJ, Ward KE. Hyperphosphatemia and phosphate binders. American Journal of Health-System Pharmacy 2005; 62(22):2355-61. *Follow-up less than 6 months*

3934. Schulman G. A nexus of progression of chronic kidney disease: charcoal, tryptophan and profibrotic cytokines. Blood Purification 2006; 24(1):143-8. *Sample size less than 50 patients*

3935. Schulman G, Agarwal R, Acharya M, et al. A multicenter, randomized, double-blind, placebo-controlled, dose-ranging study of AST-120 (Kremezin) in patients with moderate to severe CKD. American Journal of Kidney Diseases 2006; 47(4):565-77. *Not relevant to key questions*

3936. Schultz MJ, Baas MC, van der Sluijs HP, et al. N-acetylcysteine and other preventive measures for contrast-induced nephropathy in the intensive care unit. Current Medicinal Chemistry 2006; 13(21):2565-70. *Not RCT or controlled trial*

3937. Schutzer K-M, Svensson MK, Zetterstrand S, et al. Reversible elevations of serum creatinine levels but no effect on glomerular filtration during treatment with the direct thrombin inhibitor AZD0837. European Journal of Clinical Pharmacology 2010 Sep; 66(9):903-10. *Not early CKD*

3938. Schwab SJ, Dunn FL, Feinglos MN. Screening for microalbuminuria. A comparison of single sample methods of collection and techniques of albumin analysis. Diabetes Care 1992; 15(11):1581-4. *Not CKD treatment*

3939. Schwab SJ, Hlatky MA, Pieper KS, et al. Contrast nephrotoxicity: a randomized controlled trial of a nonionic and an ionic radiographic contrast agent. New England Journal of Medicine 1989; 320(3):149-53. *Sample size less than 50 patients*

3940. Schwartz AB, Prior JE, Mintz GS, et al. Cardiovascular hemodynamic effects of correction of anemia of chronic renal failure with recombinant-human erythropoietin. Transplantation Proceedings 1991; 23(2):1827-30. *Not relevant to key questions*

3941. Schwartz JI, Vandormael K, Malice MP, et al. Comparison of rofecoxib, celecoxib, and naproxen on renal function in elderly subjects receiving a normal-salt diet. Clinical Pharmacology & Therapeutics 2002; 72(1):50-61. *Not CKD treatment*

3942. Schwartz MM, Lewis EJ, Leonard-Martin T, et al. Renal pathology patterns in type II diabetes mellitus: relationship with retinopathy. The Collaborative Study Group. Nephrology Dialysis Transplantation 1998; 13(10):2547-52. *Sample size less than 50 patients*

3943. Schwartz RP. Recent advances in the management of diabetes mellitus. Indian Journal of Pediatrics 1997; 64(1):33-41. *Not RCT or controlled trial*

3944. Schwartz Sorensen S, Eiskjaer H, Orskov H, et al. Effect of intravenous glucagon infusion on renal haemodynamics and renal tubular handling of sodium in healthy humans. Scandinavian Journal of Clinical & Laboratory Investigation 1993; 53(1):25-34. *Sample size less than 50 patients*

3945. Schweizer A, Hohn L, Morel DR, et al. Aprotinin does not impair renal haemodynamics and function after cardiac surgery. British Journal of Anaesthesia 2000; 84(1):16-22. *Not early CKD*

3946. Schwenk MH. Ferumoxytol: a new intravenous iron preparation for the treatment of iron deficiency anemia in patients with chronic kidney disease. Pharmacotherapy 2010 Jan; 30(1):70-9. *Follow-up less than 6 months*

3947. Schwietzer GK, Hartmann A, Kober G, et al. Chronic angiotensin-converting enzyme inhibition may improve sodium excretion in cardiac transplant hypertension. Transplantation 1995; 59(7):999-1004. *Sample size less than 50 patients*

3948. Scorza R, Rivolta R, Mascagni B, et al. Effect of iloprost infusion on the resistance index of renal vessels of patients with systemic sclerosis. Journal of Rheumatology 1997; 24(10):1944-8. *Sample size less than 50 patients*

3949. Scott DA, Hore PJ, Cannata J, et al. A comparison of albumin, polygeline and crystalloid priming solutions for cardiopulmonary bypass in patients having coronary artery bypass graft surgery. Perfusion 1995; 10(6):415-24. *Not CKD treatment*

3950. Sculier JP, Paesmans M, Thiriaux J, et al. A comparison of methods of calculation for estimating carboplatin AUC with a retrospective pharmacokinetic-pharmacodynamic analysis in patients with advanced non-small cell lung cancer. European Lung Cancer Working Party. European Journal of Cancer 1999; 35(9):1314-9. *Not CKD treatment*

3951. Sear JW. Kidney dysfunction in the postoperative period. British Journal of Anaesthesia 2005; 95(1):20-32. *Not RCT or controlled trial*

3952. Sebekova K, Ramuscak A, Boor P, et al. The selective TP receptor antagonist, S18886 (terutroban), attenuates renal damage in the double transgenic rat model of hypertension. American Journal of Nephrology 2008; 28(1):47-53. *Follow-up less than 6 months*

3953. Seddon M, Curzen N. Coronary revascularisation in chronic kidney disease. Part II: acute coronary syndromes. Journal of Renal Care 2010 May; 36 Suppl 1:118-26. *Not RCT or controlled trial*

3954. Sedlis SP, Jurkovitz CT, Hartigan PM, et al. Optimal medical therapy with or without percutaneous coronary intervention for patients with stable coronary artery disease and chronic kidney disease. American Journal of Cardiology 2009; 104(12):1647-53. *Not CKD treatment*

3955. Sedrakyan A. Improving clinical outcomes in coronary artery bypass graft surgery. American Journal of Health-System Pharmacy 2005; 62(18 Suppl 4):S19-23. *Not relevant to key questions*

3956. Segall L, Oprisiu R, Fournier A, et al. Antihypertensive treatment and stroke prevention in patients with and without chronic kidney disease: a review of controlled trials. Journal of Nephrology 2008; 21(3):374-83. *Not CKD treatment*

3957. Segura J, Garcia-Donaire JA, Ruilope LM. Calcium channel blockers and renal protection: insights from the latest clinical trials. Journal of the American Society of Nephrology 2005; 16 Suppl 1:S64-6. *Not relevant to key questions*

3958. Segura J, Praga M, Campo C, et al. Combination is better than monotherapy with ACE inhibitor or angiotensin receptor antagonist at recommended doses. Journal of the Renin-Angiotensin-Aldosterone System 2003; 4(1):43-7. *Sample size less than 50 patients*

3959. Seidelin PH, McMurray JJ, Struthers AD. Mechanisms of the antinatriuretic action of physiological doses of angiotensin II in man. Clinical Science 1989; 76(6):653-8. *Not CKD treatment*

3960. Seiler S. Anemia of chronic renal failure: new treatment alternative. Cannt Journal 2000; 10(3):35-9. *Not CKD treatment*

3961. Sekkarie M, Cosma M, Mendelssohn D. Nonreferral and nonacceptance to dialysis by primary care physicians and nephrologists in Canada and the United States. American Journal of Kidney Diseases 2001; 38(1):36-41. *Not CKD treatment*

3962. Selamet U, Kovaliv YB, Savage CO, et al. ANCA-associated vasculitis: new options beyond steroids and cytotoxic drugs. Expert Opinion on Investigational Drugs 2007; 16(5):689-703. *Sample size less than 50 patients*

3963. Selvin E, Manzi J, Stevens LA, et al. Calibration of serum creatinine in the National Health and Nutrition Examination Surveys (NHANES) 1988-1994, 1999-2004. American Journal of Kidney Diseases 2007; 50(6):918-26. *Sample size less than 50 patients*

3964. Semplicini A, Ceolotto G, Sartori M, et al. Regulation of glomerular filtration in essential hypertension: role of abnormal Na+ transport and atrial natriuretic peptide. Journal of Nephrology 2002; 15(5):489-96. *Sample size less than 50 patients*

3965. Sener M, Torgay A, Akpek E, et al. The effect of anesthetic technique on early postoperative renal function after donor nephrectomy: a preliminary report. Transplantation Proceedings 2005; 37(5):2023-7. *Not relevant to key questions*

3966. Seng WK, Hwang S-J, Han DC, et al. Losartan reduces the costs of diabetic end-stage renal disease: an Asian perspective. Nephrology 2005; 10(5):520-4. *Sample size less than 50 patients*

3967. Serri O, Beauregard H, Brazeau P, et al. Somatostatin analogue, octreotide, reduces increased glomerular filtration rate and kidney size in insulin-dependent diabetes. JAMA 1991; 265(7):888-92. *Not CKD treatment*

3968. Seth AK. Management of hepatitis C in HIV infected and other immunocompromised individuals. Tropical Gastroenterology 2006; 27(3):111-7. *Sample size less than 50 patients*

3969. Seyon RA, Jensen LA, Ferguson IA, et al. Efficacy of N-acetylcysteine and hydration versus placebo and hydration in decreasing contrast-induced renal dysfunction in patients undergoing coronary angiography with or without concomitant percutaneous coronary intervention. Heart & Lung 2007; 36(3):195-204. *Not RCT or controlled trial*

3970. Seyss C, Foote EF. Calcium-channel blockers for prophylaxis of radiocontrast-associated nephrotoxicity. Annals of Pharmacotherapy 1995; 29(2):187-8. *Not CKD treatment*

3971. Sezai A, Hata M, Niino T, et al. Continuous low-dose infusion of human atrial natriuretic peptide in patients with left ventricular dysfunction undergoing coronary artery bypass grafting: the NU-HIT (Nihon University working group study of low-dose Human ANP Infusion Therapy during cardiac surgery) for left ventricular dysfunction. Journal of the American College of Cardiology 2010 Apr 27; 55(17):1844-51. *Not CKD treatment*

3972. Sezai A, Hata M, Niino T, et al. Influence of continuous infusion of low-dose human atrial natriuretic peptide on renal function during cardiac surgery: a randomized controlled study. Journal of the American College of Cardiology 2009; 54(12):1058-64. *Not CKD treatment*

3973. Sgouros J, Maraveyas A. Excess premature (3-month) mortality in advanced pancreatic cancer could be related to fatal vascular thromboembolic events. A hypothesis based on a systematic review of phase III chemotherapy studies in advanced pancreatic cancer. Acta Oncologica 2008; 47(3):337-46. *Sample size less than 50 patients*

3974. Shaefer MS. Current topics in immunotherapy and the role of the pharmacist on a solid organ transplant service. Pharmacotherapy 1991; 11(6):136S-41S. *Not CKD treatment*

3975. Shafqat J, Juntti-Berggren L, Zhong Z, et al. Proinsulin C-peptide and its analogues induce intracellular Ca2+ increases in human renal tubular cells. Cellular & Molecular Life Sciences 2002; 59(7):1185-9. *Not CKD treatment*

3976. Shah A, Lettieri J, Blum R, et al. Pharmacokinetics of intravenous ciprofloxacin in normal and renally impaired subjects. Journal of Antimicrobial Chemotherapy 1996; 38(1):103-16. *Sample size less than 50 patients*

3977. Shah HN, Hegde SS, Shah JN, et al. Safety and efficacy of supracostal access in tubeless percutaneous nephrolithotomy.[Erratum appears in J Endourol. 2007 Jan;21(1):118 Note: Shah, Hemendra [corrected to Shah, Hemendra N]; Hegde, Sunil [corrected to Hegde, Sunil S]; Shah, Jignesh [corrected to Shah, Jignesh N]; Bansal, Manish [corrected to Bansal, Manish B]]. Journal of Endourology 2006; 20(12):1016-21. *Not early CKD*

3978. Shah S, Paparello J, Danesh FR. Effects of statin therapy on the progression of chronic kidney disease. Advances in Chronic Kidney Disease 2005; 12(2):187-95. *Follow-up less than 6 months*

3979. Shah SV. Progress toward novel treatments for chronic kidney disease. Journal of Renal Nutrition 2010 Sep; 20(5 Suppl):S122-6. *Not relevant to key questions*

3980. Shaheen FA, Mansuri NA, al-Shaikh AM, et al. Reversible uremic deafness: is it correlated with the degree of anemia? Annals of Otology, Rhinology & Laryngology 1997; 106(5):391-3. *Not CKD treatment*

3981. Shahinfar S, Dickson TZ, Ahmed T, et al. Losartan in patients with type 2 diabetes and proteinuria: observations from the RENAAL Study. Kidney International - Supplement 2002; (82):S64-7. *Not RCT or controlled trial*

3982. Shahinfar S, Lyle PA, Zhang Z, et al. Losartan: lessons learned from the RENAAL study. Expert Opinion on Pharmacotherapy 2006; 7(5):623-30. *Not relevant to key questions*

3983. Shand BI. Haemorheological effects of losartan and enalapril in patients with renal parenchymal disease and hypertension. Journal of Human Hypertension 2000; 14(5):305-9. *Sample size less than 50 patients*

3984. Shara NM, Umans JG, Wang W, et al. Assessing the impact of different imputation methods on serial measures of renal function: the Strong Heart Study. Kidney International 2007; 71(7):701-5. *Sample size less than 50 patients*

3985. Sharma AK, Arora M, Goyle A, et al. Lipid peroxide levels in chronic renal failure. Journal of the Association of Physicians of India 1999; 47(3):296-7. *Not RCT or controlled trial*

3986. Sharma AM, Hollander A, Koster J, et al. Telmisartan in patients with mild/moderate hypertension and chronic kidney disease. Clinical Nephrology 2005; 63(4):250-7. *Not RCT or controlled trial*

3987. Sharma K, Eltayeb BO, McGowan TA, et al. Captopril-induced reduction of serum levels of transforming growth factor-beta1 correlates with long-term renoprotection in insulin-dependent diabetic patients.[Erratum appears in Am J Kidney Dis 2000 Mar;35(3):572]. American Journal of Kidney Diseases 1999; 34(5):818-23. *Sample size less than 50 patients*

3988. Sharma SK, Kini A. Effect of nonionic radiocontrast agents on the occurrence of contrast-induced nephropathy in patients with mild-moderate chronic renal insufficiency: pooled analysis of the randomized trials. Catheterization & Cardiovascular Interventions 2005; 65(3):386-93. *Not relevant to key questions*

3989. Shehata N, Kouroukis C, Kelton JG. A review of randomized controlled trials using therapeutic apheresis. Transfusion Medicine Reviews 2002; 16(3):200-29. *Not CKD treatment*

3990. Sheinfeld GR, Bakris GL. Benefits of combination angiotensin-converting enzyme inhibitor and calcium antagonist therapy for diabetic patients. American Journal of Hypertension 1999; 12(8 Pt 2):80S-5S. *Not RCT or controlled trial*

3991. Shemin D, Bostom AG, Selhub J. Treatment of hyperhomocysteinemia in end-stage renal disease. American Journal of Kidney Diseases 2001; 38(4 Suppl 1):S91-4. *Not early CKD*

3992. Shenker Y. Atrial natriuretic hormone effect on renal function and aldosterone secretion in sodium depletion. American Journal of Physiology 1988; 255(6 Pt 2):R867-73. *Sample size less than 50 patients*

3993. Shepherd J, Hunninghake DB, Stein EA, et al. Safety of rosuvastatin. American Journal of Cardiology 2004; 94(7):882-8. *Follow-up less than 6 months*

3994. Shepherd J, Kastelein JJP, Bittner V, et al. Effect of intensive lipid lowering with atorvastatin on renal function in patients with coronary heart disease: the Treating to New Targets (TNT) study. Clinical Journal of The American Society of Nephrology: CJASN 2007; 2(6):1131-9. *Not CKD treatment*

3995. Shepherd J, Kastelein JP, Bittner VA, et al. Intensive lipid lowering with atorvastatin in patients with coronary artery disease, diabetes, and chronic kidney disease. Mayo Clinic Proceedings 2008; 83(8):870-9. *Not relevant to key questions*

3996. Sheu BS, Huang JJ, Yang HB, et al. The selection of triple therapy for Helicobacter pylori eradication in chronic renal insufficiency. Alimentary Pharmacology & Therapeutics 2003; 17(10):1283-90. *Not CKD treatment*

3997. Shiba T, Inoue M, Tada H, et al. Delapril versus manidipine in hypertensive therapy to halt the type-2-diabetes-mellitus-associated nephropathy. Diabetes Research & Clinical Practice 2000; 47(2):97-104. *Sample size less than 50 patients*

3998. Shibasaki T, Nakano H, Matsuda H, et al. Pravastatin administration to hyperlipidemia in patients with nephrotic syndrome. Nippon Jinzo Gakkai Shi 1993; Japanese Journal of Nephrology. 35(11):1243-8. *Not RCT or controlled trial*

3999. Shibasaki Y, Nishiue T, Masaki H, et al. Impact of the angiotensin II receptor antagonist, losartan, on myocardial fibrosis in patients with end-stage renal disease: assessment by ultrasonic integrated backscatter and biochemical markers. Hypertension Research - Clinical & Experimental 2005; 28(10):787-95. *Not RCT or controlled trial*

4000. Shichiri M, Kishikawa H, Ohkubo Y, et al. Long-term results of the Kumamoto Study on optimal diabetes control in type 2 diabetic patients. Diabetes Care 2000; 23 Suppl 2:B21-9. *Not early CKD*

4001. Shiga Microalbuminuria Reduction Trial G, Uzu T, Sawaguchi M, et al. Reduction of microalbuminuria in patients with type 2 diabetes: the Shiga Microalbuminuria Reduction Trial (SMART). Diabetes Care 2007; 30(6):1581-3. *Not RCT or controlled trial*

4002. Shiga Microalbuminuria Reduction Trial G, Uzu T, Sawaguchi M, et al. Impact of renin-angiotensin system inhibition on microalbuminuria in type 2 diabetes: a post hoc analysis of the Shiga Microalbuminuria Reduction Trial (SMART). Hypertension Research - Clinical & Experimental 2008; 31(6):1171-6. *Follow-up less than 6 months*

4003. Shiga T, Hashiguchi M, Urae A, et al. Effect of cimetidine and probenecid on pilsicainide renal clearance in humans. Clinical Pharmacology & Therapeutics 2000; 67(3):222-8. *Not early CKD*

4004. Shigihara T, Sato A, Hayashi K, et al. Effect of combination therapy of angiotensin-converting enzyme inhibitor plus calcium channel blocker on urinary albumin excretion in hypertensive microalbuminuric patients with type II diabetes. Hypertension Research - Clinical & Experimental 2000; 23(3):219-26. *Sample size less than 50 patients*

4005. Shih YC, Kauf TL. Reconciling decision models with the real world. An application to anaemia of renal failure. Pharmacoeconomics 1999; 15(5):481-93. *Not CKD treatment*

4006. Shiigai T, Hattori K, Iwamoto H, et al. Long-term enalapril therapy in patients with chronic renal failure on a low-protein diet. A prospective randomized comparison with metoprolol. Nephron 1998; 79(2):148-53. *Sample size less than 50 patients*

4007. Shik J, Parfrey PS. The clinical epidemiology of cardiovascular disease in chronic kidney disease. Current Opinion in Nephrology & Hypertension 2005; 14(6):550-7. *Not relevant to key questions*

4008. Shilliday I, Allison ME. Diuretics in acute renal failure. Renal Failure 1994; 16(1):3-17. *Not CKD treatment*

4009. Shilliday IR, Allison ME. Intraplatelet calcium levels in patients with acute renal failure before and after the administration of loop diuretics.[Erratum appears in Nephrol Dial Transplant 2001 Sep;16(9):1964]. Nephrology Dialysis Transplantation 2001; 16(3):552-5. *Not early CKD*

4010. Shilliday IR, Quinn KJ, Allison ME. Loop diuretics in the management of acute renal failure: a prospective, double-blind, placebo-controlled, randomized study. Nephrology Dialysis Transplantation 1997; 12(12):2592-6. *Not CKD treatment*

4011. Shimizu H, Ohtani K, Tanaka Y, et al. Increased plasma thrombin-antithrombin III complex levels in non-insulin dependent diabetic patients with albuminuria are reduced by ethyl icosapentatenoate. Thrombosis & Haemostasis 1995; 74(5):1231-4. *Not CKD treatment*

4012. Shimizu H, Ohtani K, Tanaka Y, et al. Long-term effect of eicosapentaenoic acid ethyl (EPA-E) on albuminuria of non-insulin dependent diabetic patients. Diabetes Research & Clinical Practice 1995; 28(1):35-40. *Not early CKD*

4013. Shionoiri H, Sugimoto K, Kosaka T, et al. Long-term therapy with an ACE inhibitor, temocapril, reduces microalbuminuria in essential hypertension. Hypertension Research - Clinical & Experimental 1998; 21(2):81-7. *Not relevant to key questions*

4014. Shirley DG, Walter SJ, Noormohamed FH. Natriuretic effect of caffeine: assessment of segmental sodium reabsorption in humans. Clinical Science 2002; 103(5):461-6. *Sample size less than 50 patients*

4015. Shirley DG, Walter SJ, Skinner J, et al. The natriuretic effect of lithium in man: is the proximal tubule involved? Scandinavian Journal of Clinical & Laboratory Investigation 1995; 55(7):635-42. *Not CKD treatment*

4016. Shlipak MG, Massie BM. The clinical challenge of cardiorenal syndrome. Circulation 2004; 110(12):1514-7. *Not relevant to key questions*

4017. Shlipak MG, Smith GL, Rathore SS, et al. Renal function, digoxin therapy, and heart failure outcomes: evidence from the digoxin intervention group trial. Journal of the American Society of Nephrology 2004; 15(8):2195-203. *Sample size less than 50 patients*

4018. Shlipak MG, Stehman-Breen C, Vittinghoff E, et al. Creatinine levels and cardiovascular events in women with heart disease: do small changes matter? American Journal of Kidney Diseases 2004; 43(1):37-44. *Not CKD treatment*

4019. Shobha TR, Prakash O. Glycosuria in organophosphate and carbamate poisoning. Journal of the Association of Physicians of India 2000; 48(12):1197-9. *Not early CKD*

4020. Shoemaker WC, Appel PL, Kram HB. Oxygen transport measurements to evaluate tissue perfusion and titrate therapy: dobutamine and dopamine effects. Critical Care Medicine 1991; 19(5):672-88. *Not CKD treatment*

4021. Shoji T, Wada A, Inoue K, et al. Prospective randomized study evaluating the efficacy of the spherical adsorptive carbon AST-120 in chronic kidney disease patients with moderate decrease in renal function. Nephron 2007; 105(3):c99-107. *Not RCT or controlled trial*

4022. Shroff R, Knott C, Rees L. The virtues of vitamin D--but how much is too much? Pediatric Nephrology 2010 Sep; 25(9):1607-20. *Not RCT or controlled trial*

4023. Shurraw S, Tonelli M. Statins for treatment of dyslipidemia in chronic kidney disease. Peritoneal Dialysis International 2006; 26(5):523-39. *Sample size less than 50 patients*

4024. Shy BD, Gupta A, Hoffman RS. Sodium bicarbonate vs sodium chloride in preventing contrast medium-induced nephropathy. JAMA 2009; 301(4):377-8; author reply 9-80. *Not CKD treatment*

4025. Shyu KG, Cheng JJ, Kuan P. Acetylcysteine protects against acute renal damage in patients with abnormal renal function undergoing a coronary procedure. Journal of the American College of Cardiology 2002; 40(8):1383-8. *Not CKD treatment*

4026. Sibai BM. Risk factors, pregnancy complications, and prevention of hypertensive disorders in women with pregravid diabetes mellitus. Journal of Maternal-Fetal Medicine 2000; 9(1):62-5. *Not early CKD*

4027. Sibai BM. Imitators of severe preeclampsia. Obstetrics & Gynecology 2007; 109(4):956-66. *Not RCT or controlled trial*

4028. Sica DA. ALLHAT: is the final answer in? Heart Disease 2003; 5(3):171-5. *Not RCT or controlled trial*

4029. Sidharta PN, Wagner FD, Bohnemeier H, et al. Pharmacodynamics and pharmacokinetics of the urotensin II receptor antagonist palosuran in macroalbuminuric, diabetic patients. Clinical Pharmacology & Therapeutics 2006; 80(3):246-56. *Not RCT or controlled trial*

4030. Siebenhofer A, Plank J, Horvath K, et al. Angiotensin receptor blockers as anti-hypertensive treatment for patients with diabetes mellitus: meta-analysis of controlled double-blind randomized trials. Diabetic Medicine 2004; 21(1):18-25. *Not CKD treatment*

4031. Siegel J, Jorgenson J, Johnson PE, et al. Use and prescribing patterns for erythropoiesis-stimulating agents in inpatient and outpatient hospital settings. American Journal of Health-System Pharmacy 2008; 65(18):1711-9. *Not CKD treatment*

4032. Siegers CP, Andresen S, Keogh JP. Does cimetidine improve prospects for cancer patients?. A reappraisal of the evidence to date. Digestion 1999; 60(5):415-21. *Not RCT or controlled trial*

4033. Siewert-Delle A, Ljungman S, Andersson OK, et al. Does treated primary hypertension lead to end-stage renal disease? A 20-year follow-up of the Primary Prevention Study in Goteborg, Sweden. Nephrology Dialysis Transplantation 1998; 13(12):3084-90. *Not RCT or controlled trial*

4034. Siewert-Delle A, Ljungman S, Hartford M, et al. Effects of intensified blood-pressure reduction on renal function and albumin excretion in primary hypertension. Addition of felodipine or ramipril to long-term treatment with beta-blockade. American Journal of Hypertension 1995; 8(2):113-23. *Sample size less than 50 patients*

4035. Siewert-Delle A, Ljungman S, Hartford M, et al. Effect of 14 years of antihypertensive treatment on renal function and urinary albumin excretion in primary hypertension. American Journal of Hypertension 1996; 9(9):841-9. *Sample size less than 50 patients*

4036. Sikka R, Waters J, Moore W, et al. Renal assessment practices and the effect of nurse case management of health maintenance organization patients with diabetes. Diabetes Care 1999; 22(1):1-6. *Not RCT or controlled trial*

4037. Sikole A, Efremov DG, Dimovski A, et al. Hemoglobin F levels in end-stage renal disease patients after correction of anemia with erythropoietin. Nephron 1993; 65(3):482-4. *Sample size less than 50 patients*

4038. Silver MA, Yancy CW. Using homeostatic peptides in decompensated heart failure a reasonable paradigm but a flawed practice? Journal of the American College of Cardiology 2007; 50(19):1841-3. *Follow-up less than 6 months*

4039. Silverberg DS, Wexler D, Blum M, et al. The effect of correction of anaemia in diabetics and non-diabetics with severe resistant congestive heart failure and chronic renal failure by subcutaneous erythropoietin and intravenous iron. Nephrology Dialysis Transplantation 2003; 18(1):141-6. *Not RCT or controlled trial*

4040. Silverberg DS, Wexler D, Iaina A, et al. The interaction between heart failure and other heart diseases, renal failure, and anemia. Seminars in Nephrology 2006; 26(4):296-306. *Follow-up less than 6 months*

4041. Silverberg DS, Wexler D, Iaina A, et al. Anaemia management in cardio renal disease. Journal of Renal Care 2010 May; 36 Suppl 1:86-96. *Not RCT or controlled trial*

4042. Sima AAF. Diabetic neuropathy in type 1 and type 2 diabetes and the effects of C-peptide. Journal of the Neurological Sciences 2004; 220(1-2):133-6. *Not relevant to key questions*

4043. Simon AH, Lima PR, Almerinda M, et al. Renal haemodynamic responses to a chicken or beef meal in normal individuals. Nephrology Dialysis Transplantation 1998; 13(9):2261-4. *Sample size less than 50 patients*

4044. Simon SR, Trinacty CM, Soumerai SB, et al. Improving diabetes care among patients overdue for recommended testing: a randomized controlled trial of automated telephone outreach. Diabetes Care 2010 Jul; 33(7):1452-3. *Not CKD treatment*

4045. Sinert R, Doty CI. Evidence-based emergency medicine review. Prevention of contrast-induced nephropathy in the emergency department. Annals of Emergency Medicine 2007; 50(3):335-45. *Not RCT or controlled trial*

4046. Singer DR, Markandu ND, Miller MA, et al. Potassium channel stimulation in normal subjects and in patients with essential hypertension: an acute study with cromakalim (BRL 34915). Journal of Hypertension - Supplement 1989; 7(6):S294-5. *Sample size less than 50 patients*

4047. Singer DR, Shirley DG, Markandu ND, et al. How important are suppression of aldosterone and stimulation of atrial natriuretic peptide secretion in the natriuretic response to an acute sodium load in man? Clinical Science 1991; 80(4):293-9. *Sample size less than 50 patients*

4048. Singer I, Epstein M. Potential of dopamine A-1 agonists in the management of acute renal failure. American Journal of Kidney Diseases 1998; 31(5):743-55. *Not CKD treatment*

4049. Singer P. High-dose amino acid infusion preserves diuresis and improves nitrogen balance in non-oliguric acute renal failure. Wiener Klinische Wochenschrift 2007; 119(7-8):218-22. *Not early CKD*

4050. Singh A, Gupta U, Sagar S, et al. Comparative bioequivalence study of furosemide in patients with edema of renal origin. International Journal of Clinical Pharmacology, Therapy, & Toxicology 1987; 25(3):136-8. *Sample size less than 50 patients*

4051. Singh A, Patel T, Hertel J, et al. Safety of ferumoxytol in patients with anemia and CKD. American Journal of Kidney Diseases 2008; 52(5):907-15. *Not RCT or controlled trial*

4052. Singh AK. The target hemoglobin in patients with chronic kidney disease. Nephrology News & Issues 2006; 20(13):29-30. *Sample size less than 50 patients*

4053. Singh AK. The controversy surrounding hemoglobin and erythropoiesis-stimulating agents: what should we do now? American Journal of Kidney Diseases 2008; 52(6 Suppl):S5-13. *Not early CKD*

4054. Singh AK. Does TREAT give the boot to ESAs in the treatment of CKD anemia? Journal of the American Society of Nephrology 2010; 21(1):2-6. *Not RCT or controlled trial*

4055. Singh AK. What is causing the mortality in treating the anemia of chronic kidney disease: erythropoietin dose or hemoglobin level? Current Opinion in Nephrology & Hypertension 2010 Sep; 19(5):420-4. *Not RCT or controlled trial*

4056. Singh AK. Diabetes, anemia and CKD: Why TREAT? Current Diabetes Reports 2010 Aug; 10(4):291-6. *Not RCT or controlled trial*

4057. Singh AK, Szczech L, Tang KL, et al. Anaemia of CKD--the CHOIR study revisited. Nephrology Dialysis Transplantation 2007; 22(7):1806-10. *Not RCT or controlled trial*

4058. Singh AK, Szczech L, Tang KL, et al. Correction of anemia with epoetin alfa in chronic kidney disease. New England Journal of Medicine 2006; 355(20):2085-98. *Not CKD treatment*

4059. Singh N, Limaye AP, Forrest G, et al. Combination of voriconazole and caspofungin as primary therapy for invasive aspergillosis in solid organ transplant recipients: a prospective, multicenter, observational study. Transplantation 2006; 81(3):320-6. *Sample size less than 50 patients*

4060. Singh NP, Aggarwal L, Singh T, et al. Anaemia, iron studies and erythropoietin in patients of chronic renal failure. Journal of the Association of Physicians of India 1999; 47(3):284-90. *Sample size less than 50 patients*

4061. Singh NP, Ingle GK, Saini VK, et al. Prevalence of low glomerular filtration rate, proteinuria and associated risk factors in North India using Cockcroft-Gault and Modification of Diet in Renal Disease equation: an observational, cross-sectional study. BMC Nephrology 2009; 10:4. *Not RCT or controlled trial*

4062. Singh V, Deedwania P. Reducing morbidity and mortality in high risk patients with statins. Vascular Health & Risk Management 2009; 5(2):495-507. *Not RCT or controlled trial*

4063. Singh-Franco D, Machado C, Tuteja S, et al. Trospium chloride for the treatment of overactive bladder with urge incontinence. Clinical Therapeutics 2005; 27(5):511-30. *Follow-up less than 6 months*

4064. Sinsakul M, Sika M, Rodby R, et al. A randomized trial of a 6-week course of celecoxib on proteinuria in diabetic kidney disease. American Journal of Kidney Diseases 2007; 50(6):946-51. *Not RCT or controlled trial*

4065. Siragy HM. Angiotensin receptor blockers: how important is selectivity? American Journal of Hypertension 2002; 15(11):1006-14. *Not relevant to key questions*

4066. Siragy HM. Comparing angiotensin II receptor blockers on benefits beyond blood pressure. Advances in Therapy 2010 May; 27(5):257-84. *Not RCT or controlled trial*

4067. Sirivella S, Gielchinsky I, Parsonnet V. Mannitol, furosemide, and dopamine infusion in postoperative renal failure complicating cardiac surgery. Annals of Thoracic Surgery 2000; 69(2):501-6. *Not early CKD*

4068. Sisillo E, Ceriani R, Bortone F, et al. N-acetylcysteine for prevention of acute renal failure in patients with chronic renal insufficiency undergoing cardiac surgery: a prospective, randomized, clinical trial. Critical Care Medicine 2008; 36(1):81-6. *Not RCT or controlled trial*

4069. Sitprija V, Lumlertgul D. Angiotensin converting enzyme inhibitor and chronic renal failure. Journal of the Medical Association of Thailand 1993; 76(7):359-67. *Sample size less than 50 patients*

4070. Sjoland JA, Pedersen RS, Jespersen J, et al. Intraperitoneal heparin ameliorates the systemic inflammatory response in PD patients. Nephron 2005; 100(4):c105-10. *Not relevant to key questions*

4071. Sketch MH, Jr., Whelton A, Schollmayer E, et al. Prevention of contrast media-induced renal dysfunction with prostaglandin E1: a randomized, double-blind, placebo-controlled study. American Journal of Therapeutics 2001; 8(3):155-62. *Follow-up less than 6 months*

4072. Skott P, Hommel E, Bruun NE, et al. Effects of acetazolamide on kidney function in type 1 (insulin-dependent) diabetic patients with diabetic nephropathy. Diabetologia 1988; 31(11):806-10. *Follow-up less than 6 months*

4073. Skov AR, Toubro S, Bulow J, et al. Changes in renal function during weight loss induced by high vs low-protein low-fat diets in overweight subjects. International Journal of Obesity & Related Metabolic Disorders: Journal of the International Association for the Study of Obesity 1999; 23(11):1170-7. *Not early CKD*

4074. Skovgaard N, Holm J, Hemmingsen L, et al. Urinary protein excretion following intravenously administered ionic and non-ionic contrast media in man. Acta Radiologica 1989; 30(5):517-9. *Sample size less than 50 patients*

4075. Skroeder NR, Jacobson SH, Lins LE, et al. Biocompatibility of dialysis membranes is of no importance for objective or subjective symptoms during or after hemodialysis. ASAIO Transactions 1990; 36(3):M637-9. *Not CKD treatment*

4076. Slagman MCJ, Navis G, Laverman GD. Dual blockade of the renin-angiotensin-aldosterone system in cardiac and renal disease. Current Opinion in Nephrology & Hypertension 2010 Mar; 19(2):140-52. *Not relevant to key questions*

4077. Slagman MCJ, Sinkeler SJ, Hemmelder MH, et al. Erythropoietin is reduced by combination of diuretic therapy and RAAS blockade in proteinuric renal patients with preserved renal function. Nephrology Dialysis Transplantation 2010 Oct; 25(10):3256-60. *Follow-up less than 6 months*

4078. Slataper R, Vicknair N, Sadler R, et al. Comparative effects of different antihypertensive treatments on progression of diabetic renal disease. Archives of Internal Medicine 1993; 153(8):973-80. *Sample size less than 50 patients*

4079. Slaven GM, Walker RJ, Zacharias M, et al. Tenoxicam does not alter renal function during anaesthesia in normal individuals. Australian & New Zealand Journal of Medicine 1998; 28(6):772-6. *Not CKD treatment*

4080. Slotman GJ, Kerstein MD, Bone RC, et al. The effects of prostaglandin E1 on non-pulmonary organ function during clinical acute respiratory failure. The Prostaglandin E1 Study Group. Journal of Trauma-Injury Infection & Critical Care 1992; 32(4):480-8; discussion 8-9. *Not CKD treatment*

4081. Slowik MM. Early education of patients with chronic renal insufficiency: the Healthy Start program. Case study of the anemic patient. Nephrology Nursing Journal: Journal of the American Nephrology Nurses' Association 2001; 28(6):643-6. *Not relevant to key questions*

4082. Small EJ, Halabi S, Kantoff P, et al. Activities and accomplishments of the cancer and leukemia group B genitourinary committee. Clinical Cancer Research 2006; 12(11 Pt 2):3596s-600s. *Follow-up less than 6 months*

4083. Smalley RV, Guaspari A, Haase-Statz S, et al. Allopurinol: intravenous use for prevention and treatment of hyperuricemia.[Erratum appears in J Clin Oncol 2000 May;18(10):2188]. Journal of Clinical Oncology 2000; 18(8):1758-63. *Not early CKD*

4084. Smebye ML, Iversen EK, Hoieggen A, et al. Effect of hemoglobin levels on cardiovascular outcomes in patients with isolated systolic hypertension and left ventricular hypertrophy (from the LIFE study). American Journal of Cardiology 2007; 100(5):855-9. *Not relevant to key questions*

4085. Smilde TDJ, Linssen GCM, Gallemann D, et al. Influence of renal dysfunction on the pharmacokinetics of the selective Na+/H+ exchange inhibitor EMD 87 580 in patients with chronic heart failure. International Journal of Clinical Pharmacology & Therapeutics 2005; 43(11):507-16. *Sample size less than 50 patients*

4086. Smit AJ, Meijer S, Wesseling H, et al. Effect of metoclopramide on dopamine-induced changes in renal function in healthy controls and in patients with renal disease. Clinical Science 1988; 75(4):421-8. *Sample size less than 50 patients*

4087. Smith AC, Toto R, Bakris GL. Differential effects of calcium channel blockers on size selectivity of proteinuria in diabetic glomerulopathy. Kidney International 1998; 54(3):889-96. *Sample size less than 50 patients*

4088. Smith DG, Nguyen AB, Peak CN, et al. Markov modeling analysis of health and economic outcomes of therapy with valsartan versus amlodipine in patients with type 2 diabetes and microalbuminuria. Journal of Managed Care Pharmacy 2004; 10(1):26-32. *Not CKD treatment*

4089. Smith DH, Johnson ES, Thorp ML, et al. Outcomes predicted by phosphorous in chronic kidney disease: a retrospective CKD-inception cohort study. Nephrology Dialysis Transplantation 2010; 25(1):166-74. *Not RCT or controlled trial*

4090. Smith DHG. Treatment of hypertension with an angiotensin II-receptor antagonist compared with an angiotensin-converting enzyme inhibitor: a review of clinical studies of telmisartan and enalapril. Clinical Therapeutics 2002; 24(10):1484-501. *Not relevant to key questions*

4091. Smith HJ, Levorstad K, Berg KJ, et al. High dose urography in patients with renal failure. A double blind investigation of iohexol and metrizoate. Acta Radiologica: Diagnosis 1985; 26(2):213-20. *Sample size less than 50 patients*

4092. Smith MC, Austen JL, Carey JT, et al. Prednisone improves renal function and proteinuria in human immunodeficiency virus-associated nephropathy. American Journal of Medicine 1996; 101(1):41-8. *Sample size less than 50 patients*

4093. Smith MNA, Best D, Sheppard SV, et al. The effect of mannitol on renal function after cardiopulmonary bypass in patients with established renal dysfunction. Anaesthesia 2008; 63(7):701-4. *Not early CKD*

4094. Smith SR, Coffman TM, Svetkey LP. Effect of low-dose aspirin on thromboxane production and the antihypertensive effect of captopril. Journal of the American Society of Nephrology 1993; 4(5):1133-9. *Follow-up less than 6 months*

4095. Smolander J, Vogt B, Maillard M, et al. Dose-dependent acute and sustained renal effects of the endothelin receptor antagonist avosentan in healthy subjects. Clinical Pharmacology & Therapeutics 2009; 85(6):628-34. *Not CKD treatment*

4096. Snetselaar L. MDRD study enters clinical phases ... as the recruitment of patients begins. Modification of Diet and Renal Disease. Nephrology News & Issues 1990; 4(3):14-5. *Not RCT or controlled trial*

4097. Snir N, Moskovitz B, Nativ O, et al. Papaverine hydrochloride for the treatment of renal colic: an old drug revisited. A prospective, randomized study. Journal of Urology 2008; 179(4):1411-4. *Not CKD treatment*

4098. Sobh MA, Moustafa FE, Sally SM, et al. A prospective, randomized therapeutic trial for schistosomal specific nephropathy. Kidney International 1989; 36(5):904-7. *Sample size less than 50 patients*

4099. Sobue S, Tan K, Layton G, et al. The effects of renal impairment on the pharmacokinetics and safety of fosfluconazole and fluconazole following a single intravenous bolus injection of fosfluconazole. British Journal of Clinical Pharmacology 2004; 57(6):773-84. *Not relevant to key questions*

4100. Sochman J. N-acetylcysteine somewhere between Scylla and Charybdis. Journal of the American College of Cardiology 2010 Sep 21; 56(13):1067; author reply -8. *Not RCT or controlled trial*

4101. Sola-Vera J, Minana J, Ricart E, et al. Randomized trial comparing albumin and saline in the prevention of paracentesis-induced circulatory dysfunction in cirrhotic patients with ascites. Hepatology 2003; 37(5):1147-53. *Not CKD treatment*

4102. Solerte SB, Fioravanti M, Bozzetti A, et al. Pentoxifylline, albumin excretion rate and proteinuria in type I and type II diabetic patients with microproteinuria. Results of a short-term randomized study. Acta Diabetologica Latina 1986; 23(2):171-7. *Not relevant to key questions*

4103. Solerte SB, Fioravanti M, Patti AL, et al. Pentoxifylline, total urinary protein excretion rate and arterial blood pressure in long-term insulin-dependent diabetic patients with overt nephropathy. Acta Diabetologica Latina 1987; 24(3):229-39. *Sample size less than 50 patients*

4104. Solini A, Vergnani L, Ricci F, et al. Glycosaminoglycans delay the progression of nephropathy in NIDDM. Diabetes Care 1997; 20(5):819-23. *Follow-up less than 6 months*

4105. Solmazgul E, Uzun G, Cermik H, et al. Hyperbaric oxygen therapy attenuates renal ischemia/reperfusion injury in rats. Urologia Internationalis 2007; 78(1):82-5. *Not early CKD*

4106. Solomon LR, Atherton JC, Bobinski H, et al. Effect of a meal containing protein on lithium clearance and plasma immunoreactive atrial natriuretic peptide in man. Clinical Science 1988; 75(2):151-7. *Not RCT or controlled trial*

4107. Solomon LR, Atherton JC, Bobinski H, et al. Effect of low dose infusion of atrial natriuretic peptide on renal function in man. Clinical Science 1988; 75(4):403-10. *Sample size less than 50 patients*

4108. Solomon LR, Hendler ED. Prospective controlled study of androgen therapy in the anemia of chronic renal disease: effects on iron kinetics. Acta Haematologica 1988; 79(1):12-9. *Follow-up less than 6 months*

4109. Solomon R, Werner C, Mann D, et al. Effects of saline, mannitol, and furosemide to prevent acute decreases in renal function induced by radiocontrast agents. New England Journal of Medicine 1994; 331(21):1416-20. *Not CKD treatment*

4110. Solomon RJ, Mehran R, Natarajan MK, et al. Contrast-induced nephropathy and long-term adverse events: cause and effect? Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(7):1162-9. *Not CKD treatment*

4111. Solomon RJ, Natarajan MK, Doucet S, et al. Cardiac Angiography in Renally Impaired Patients (CARE) study: a randomized double-blind trial of contrast-induced nephropathy in patients with chronic kidney disease. Circulation 2007; 115(25):3189-96. *Not RCT or controlled trial*

4112. Solomon SD, Lin J, Solomon CG, et al. Influence of albuminuria on cardiovascular risk in patients with stable coronary artery disease. Circulation 2007; 116(23):2687-93. *Sample size less than 50 patients*

4113. Solomon SD, Rice MM, A Jablonski K, et al. Renal function and effectiveness of angiotensin-converting enzyme inhibitor therapy in patients with chronic stable coronary disease in the Prevention of Events with ACE inhibition (PEACE) trial. Circulation 2006; 114(1):26-31. *Follow-up less than 6 months*

4114. Solomon SD, Uno H, Lewis EF, et al. Erythropoietic response and outcomes in kidney disease and type 2 diabetes. New England Journal of Medicine 2010 Sep 16; 363(12):1146-55. *Follow-up less than 6 months*

4115. Soma J, Saito T, Taguma Y, et al. High prevalence and adverse effect of hepatitis C virus infection in type II diabetic-related nephropathy. Journal of the American Society of Nephrology 2000; 11(4):690-9. *Not early CKD*

4116. Soma J, Sato K, Saito H, et al. Effect of tranilast in early-stage diabetic nephropathy. Nephrology Dialysis Transplantation 2006; 21(10):2795-9. *Not CKD treatment*

4117. Somlo G, Doroshow JH, Lev-Ran A, et al. Effect of low-dose prophylactic dopamine on high-dose cisplatin-induced electrolyte wasting, ototoxicity, and epidermal growth factor excretion: a randomized, placebo-controlled, double-blind trial. Journal of Clinical Oncology 1995; 13(5):1231-7. *Sample size less than 50 patients*

4118. Sommer P, Kromann-Andersen B, Lendorf A, et al. Analgesic effect and tolerance of Voltaren and Ketogan in acute renal or ureteric colic. British Journal of Urology 1989; 63(1):4-6. *Not CKD treatment*

4119. Song H, Tasaki H, Yashiro A, et al. Chlamydia pneumoniae infection and accelerated development of coronary artery disease in patients with chronic renal failure. Clinical Nephrology 2001; 56(5):346-52. *Not early CKD*

4120. Song JH, Cha SH, Lee HJ, et al. Effect of low-dose dual blockade of renin-angiotensin system on urinary TGF-beta in type 2 diabetic patients with advanced kidney disease. Nephrology Dialysis Transplantation 2006; 21(3):683-9. *Not relevant to key questions*

4121. Song M-K, Ward SE, Happ MB, et al. Randomized controlled trial of SPIRIT: an effective approach to preparing African-American dialysis patients and families for end of life. Research in Nursing & Health 2009; 32(3):260-73. *Not CKD treatment*

4122. Song T-t, Jiang Y-h, Lan X-z. Clinical observation on chemical damage of nephron and the preventive and therapeutic effects of Baoshen Mixture on it. Chinese Journal of Integrative Medicine 2007; 13(2):115-9. *Sample size less than 50 patients*

4123. Song YR, Lee T, You SJ, et al. Prevention of acute kidney injury by erythropoietin in patients undergoing coronary artery bypass grafting: a pilot study. American Journal of Nephrology 2009; 30(3):253-60. *Not CKD treatment*

4124. Sonkodi S, Mogyorosi A. Treatment of diabetic nephropathy with angiotensin II blockers. Nephrology Dialysis Transplantation 2003; 18 Suppl 5:v21-3. *Not RCT or controlled trial*

4125. Sonpavde G, Hutson TE, Galsky MD, et al. Problems with the randomized discontinuation design. Journal of Clinical Oncology 2006; 24(28):4669-70; author reply 70-1. *Not relevant to key questions*

4126. Soraas CL, Wachtell K, Okin PM, et al. Lack of regression of left ventricular hypertrophy is associated with higher incidence of revascularization in hypertension: The LIFE Study. Blood Pressure 2010 Jun; 19(3):145-51. *Not CKD treatment*

4127. Sorensen SS, Jensen JD, Madsen JK, et al. Effect of isradipine on renal haemodynamics and systemic blood pressure changes induced by intravenous infusion of endothelin in healthy humans. Nephrology Dialysis Transplantation 1995; 10(8):1324-31. *Sample size less than 50 patients*

4128. Sorensen SS, Lauridsen IN, Thomsen K, et al. Effect of two regimens of intravenous amino acid infusion on renal haemodynamics, renal tubular function and sodium and water homeostatic hormones in healthy humans. Nephrology Dialysis Transplantation 1991; 6(6):410-9. *Not CKD treatment*

4129. Sorensen SS, Madsen JK, Pedersen EB. Systemic and renal effect of intravenous infusion of endothelin-1 in healthy human volunteers. American Journal of Physiology 1994; 266(3 Pt 2):F411-8. *Sample size less than 50 patients*

4130. Sorensen SS, Thomsen OO, Danielsen H, et al. Effect of verapamil on renal plasma flow, glomerular filtration rate and plasma angiotensin II, aldosterone and arginine vasopressin in essential hypertension. European Journal of Clinical Pharmacology 1985; 29(3):257-61. *Sample size less than 50 patients*

4131. Sorensen VB, Rossing P, Tarnow L, et al. Effects of nisoldipine and lisinopril on microvascular dysfunction in hypertensive Type I diabetes patients with nephropathy. Clinical Science 1998; 95(6):709-17. *Sample size less than 50 patients*

4132. Sorger JI, Kirk PG, Ruhnke CJ, et al. Once daily, high dose versus divided, low dose gentamicin for open fractures. Clinical Orthopaedics & Related Research 1999; (366):197-204. *Not CKD treatment*

4133. Sorkine P, Nagar H, Weinbroum A, et al. Administration of amphotericin B in lipid emulsion decreases nephrotoxicity: results of a prospective, randomized, controlled study in critically ill patients. Critical Care Medicine 1996; 24(8):1311-5. *Not CKD treatment*

4134. Sorof J, Berne C, Siewert-Delle A, et al. Effect of rosuvastatin or atorvastatin on urinary albumin excretion and renal function in type 2 diabetic patients. Diabetes Research & Clinical Practice 2006; 72(1):81-7. *Not RCT or controlled trial*

4135. Sorrenti G, Grimaldi M, Canova N, et al. Glycosaminoglycans as a possible tool for micro- and macroalbuminuria in diabetic patients. A pilot study. Journal of International Medical Research 1997; 25(2):81-6. *Sample size less than 50 patients*

4136. Sort P, Navasa M, Arroyo V, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. New England Journal of Medicine 1999; 341(6):403-9. *Not CKD treatment*

4137. Sosman JA, Kohler PC, Hank JA, et al. Repetitive weekly cycles of interleukin-2. II. Clinical and immunologic effects of dose, schedule, and addition of indomethacin. Journal of the National Cancer Institute 1988; 80(18):1451-61. *Follow-up less than 6 months*

4138. Souchet T, Durand Zaleski I, Hannedouche T, et al. An economic evaluation of Losartan therapy in type 2 diabetic patients with nephropathy: an analysis of the RENAAL study adapted to France. Diabetes & Metabolism 2003; 29(1):29-35. *Not relevant to key questions*

4139. Soupart A, Buisson L, Prospert F, et al. Indirect evidence to suggest that prolactin induces salt retention in cirrhosis. Journal of Hepatology 1994; 21(3):347-52. *Sample size less than 50 patients*

4140. Spangberg-Viklund B, Berglund J, Nikonoff T, et al. Does prophylactic treatment with felodipine, a calcium antagonist, prevent low-osmolar contrast-induced renal dysfunction in hydrated diabetic and nondiabetic patients with normal or moderately reduced renal function? Scandinavian Journal of Urology & Nephrology 1996; 30(1):63-8. *Sample size less than 50 patients*

4141. Spapen HD, Diltoer MW, Nguyen DN, et al. Effects of N-acetylcysteine on microalbuminuria and organ failure in acute severe sepsis: results of a pilot study. Chest 2005; 127(4):1413-9. *Not RCT or controlled trial*

4142. Spargias K, Adreanides E, Giamouzis G, et al. Iloprost for prevention of contrast-mediated nephropathy in high-risk patients undergoing a coronary procedure. Results of a randomized pilot study. European Journal of Clinical Pharmacology 2006; 62(8):589-95. *Not relevant to key questions*

4143. Spargias K, Alexopoulos E, Kyrzopoulos S, et al. Ascorbic acid prevents contrast-mediated nephropathy in patients with renal dysfunction undergoing coronary angiography or intervention.[Erratum appears in Circulation. 2005 Jan 25;111(3):379 Note: Iacovis, Panagiotis [corrected to Iokovis,Panagiotis]]. Circulation 2004; 110(18):2837-42. *Not relevant to key questions*

4144. Spasovski G, Massy Z, Vanholder R. Phosphate metabolism in chronic kidney disease: from pathophysiology to clinical management. Seminars in Dialysis 2009; 22(4):357-62. *Not RCT or controlled trial*

4145. Spector R, Park GD. Regression to the mean: a potential source of error in clinical pharmacological studies. Drug Intelligence & Clinical Pharmacy 1985; 19(12):916-9. *Not RCT or controlled trial*

4146. Spence JD. The arthritic patient with hypertension: selection of an NSAID. Scandinavian Journal of Rheumatology - Supplement 1986; 62:36-40. *Not early CKD*

4147. Spence JD. Management of resistant hypertension in patients with carotid stenosis: high prevalence of renovascular hypertension. Cerebrovascular Diseases 2000; 10(4):249-54. *Not early CKD*

4148. Spence JD. Treatment options for renovascular hypertension. Expert Opinion on Pharmacotherapy 2002; 3(4):411-6. *Not early CKD*

4149. Spence JD, Bang H, Chambless LE, et al. Vitamin Intervention For Stroke Prevention trial: an efficacy analysis. Stroke 2005; 36(11):2404-9. *Not early CKD*

4150. Spencer A, Roberts A, Kennedy N, et al. Renal safety of zoledronic acid with thalidomide in patients with myeloma: a pharmacokinetic and safety sub-study. BMC Clinical Pharmacology 2008; 8:2. *Not CKD treatment*

4151. Spencer EM, Willatts SM, Prys-Roberts C. Plasma inorganic fluoride concentrations during and after prolonged (greater than 24 h) isoflurane sedation: effect on renal function. Anesthesia & Analgesia 1991; 73(6):731-7. *Not CKD treatment*

4152. Spicer J, Quatan N, Plunkett T, et al. Cellular immunotherapy for cancer: current concepts and clinical perspectives Monitoring immune responses and clinical trials: part II. Clinical Oncology 2004; 16(6):395-404. *Not RCT or controlled trial*

4153. Spieker LE, Noll G, Luscher TF. Therapeutic potential for endothelin receptor antagonists in cardiovascular disorders. American Journal of Cardiovascular Drugs 2001; 1(4):293-303. *Not relevant to key questions*

4154. Spigt MG, Knottnerus JA, Westerterp KR, et al. The effects of 6 months of increased water intake on blood sodium, glomerular filtration rate, blood pressure, and quality of life in elderly (aged 55-75) men. Journal of the American Geriatrics Society 2006; 54(3):438-43. *Not RCT or controlled trial*

4155. Spinazzi A, Pozzi Mucelli R. [Administration of iodinated contrast in patients with pre-existing renal failure: a review]. Radiologia Medica 2004; 107(1-2):88-97. *Not CKD treatment*

4156. Spinler SA, Inverso SM, Cohen M, et al. Safety and efficacy of unfractionated heparin versus enoxaparin in patients who are obese and patients with severe renal impairment: analysis from the ESSENCE and TIMI 11B studies. American Heart Journal 2003; 146(1):33-41. *Not CKD treatment*

4157. Spinowitz B, Germain M, Benz R, et al. A randomized study of extended dosing regimens for initiation of epoetin alfa treatment for anemia of chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(4):1015-21. *Not RCT or controlled trial*

4158. Spinowitz BS, Kausz AT, Baptista J, et al. Ferumoxytol for treating iron deficiency anemia in CKD. Journal of the American Society of Nephrology 2008; 19(8):1599-605. *Follow-up less than 6 months*

4159. Spinowitz BS, Pratt RD, Epoetin Delta Study G. Epoetin delta is effective for the management of anaemia associated with chronic kidney disease. Current Medical Research & Opinion 2006; 22(12):2507-13. *Not relevant to key questions*

4160. Spitalewitz S, Porush JG, Cattran D, et al. Treatment of hyperlipidemia in the nephrotic syndrome: the effects of pravastatin therapy. American Journal of Kidney Diseases 1993; 22(1):143-50. *Sample size less than 50 patients*

4161. Spitalewitz S, Weber MA, Reiser IW. Medical and non-medical approaches to renovascular hypertension. Cardiologia 1997; 42(3):237-43. *Not RCT or controlled trial*

4162. Stabler SP, Estacio R, Jeffers BW, et al. Total homocysteine is associated with nephropathy in non-insulin-dependent diabetes mellitus. Metabolism: Clinical & Experimental 1999; 48(9):1096-101. *Not RCT or controlled trial*

4163. Stachenfeld NS, DiPietro L, Palter SF, et al. Estrogen influences osmotic secretion of AVP and body water balance in postmenopausal women. American Journal of Physiology 1998; 274(1 Pt 2):R187-95. *Sample size less than 50 patients*

4164. Stachenfeld NS, Silva C, Keefe DL, et al. Effects of oral contraceptives on body fluid regulation. Journal of Applied Physiology 1999; 87(3):1016-25. *Follow-up less than 6 months*

4165. Stack AG. Coronary artery disease and peripheral vascular disease in chronic kidney disease: an epidemiological perspective. Cardiology Clinics 2005; 23(3):285-98. *Not relevant to key questions*

4166. Stacul F, Carraro M, Magnaldi S, et al. Contrast agent nephrotoxicity: comparison of ionic and nonionic contrast agents. AJR 1987; American Journal of Roentgenology. 149(6):1287-9. *Not RCT or controlled trial*

4167. Stacul F, Thomsen HS. Safety profile of new non-ionic contrast media: renal tolerance. European Journal of Radiology 1996; 23 Suppl 1:S6-9. *Not RCT or controlled trial*

4168. Stadler DD, Chenard CA, Rebouche CJ. Effect of dietary macronutrient content on carnitine excretion and efficiency of carnitine reabsorption. American Journal of Clinical Nutrition 1993; 58(6):868-72. *Sample size less than 50 patients*

4169. Staessen J. Low-level lead exposure, renal function and blood pressure. Verhandelingen - Koninklijke Academie voor Geneeskunde van Belgie 1995; 57(6):527-74. *Not CKD treatment*

4170. Staessen J, Lauwerys R. Health effects of environmental exposure to cadmium in a population study. Journal of Human Hypertension 1993; 7(2):195-9. *Not RCT or controlled trial*

4171. Staessen J, Yeoman WB, Fletcher AE, et al. Blood cadmium in London civil servants. International Journal of Epidemiology 1990; 19(2):362-6. *Not CKD treatment*

4172. Staessen JA. Antiproteinuric effects of cilnidipine. Kidney International 2008; 73(9):1095; author reply -6. *Sample size less than 50 patients*

4173. Staessen JA, Lauwerys RR, Buchet JP, et al. Impairment of renal function with increasing blood lead concentrations in the general population. The Cadmibel Study Group. New England Journal of Medicine 1992; 327(3):151-6. *Not CKD treatment*

4174. Staessen JA, Lauwerys RR, Ide G, et al. Renal function and historical environmental cadmium pollution from zinc smelters. Lancet 1994; 343(8912):1523-7. *Not RCT or controlled trial*

4175. Staessen JA, Li Y, Richart T. Oral renin inhibitors. Lancet 2006; 368(9545):1449-56. *Not CKD treatment*

4176. Stafford-Smith M. Evidence-based renal protection in cardiac surgery. Seminars in Cardiothoracic & Vascular Anesthesia 2005; 9(1):65-76. *Not CKD treatment*

4177. Stafford-Smith M, Shaw A, Swaminathan M. Cardiac surgery and acute kidney injury: emerging concepts. Current Opinion in Critical Care 2009; 15(6):498-502. *Not RCT or controlled trial*

4178. Stafylas PC, Sarafidis PA, Lasaridis AN, et al. Cost-effectiveness of losartan in diabetic nephropathy: a Greek perspective. Journal of Nephrology 2007; 20(6):703-15. *Sample size less than 50 patients*

4179. Staniloae CS, Doucet S, Sharma SK, et al. N-Acetylcysteine added to volume expansion with sodium bicarbonate does not further prevent contrast-induced nephropathy: results from the cardiac angiography in renally impaired patients study. Journal of Interventional Cardiology 2009 Jun; 22(3):261-5. *Not CKD treatment*

4180. Stankov G, Schmieder G, Zerle G, et al. Double-blind study with dipyrone versus tramadol and butylscopolamine in acute renal colic pain. World Journal of Urology 1994; 12(3):155-61. *Not CKD treatment*

4181. Stanton R. Intensive treatment of diabetic nephropathy. Current Diabetes Reports 2004; 4(6):433-4. *Not CKD treatment*

4182. Starklint J, Bech JN, Nyvad O, et al. Increased urinary aquaporin-2 excretion in response to furosemide in patients with chronic heart failure. Scandinavian Journal of Clinical & Laboratory Investigation 2006; 66(1):55-66. *Sample size less than 50 patients*

4183. Stefanidis I, Kytoudis K, Papathanasiou AA, et al. XbaI GLUT1 gene polymorphism and the risk of type 2 diabetes with nephropathy. Disease Markers 2009; 27(1):29-35. *Not RCT or controlled trial*

4184. Stefoni S, Mosconi G, La Manna G, et al. Low-dosage ibopamine treatment in progressive renal failure: a long-term multicentre trial. American Journal of Nephrology 1996; 16(6):489-99. *Not early CKD*

4185. Stegmayr BG, Brannstrom M, Bucht S, et al. Low-dose atorvastatin in severe chronic kidney disease patients: a randomized, controlled endpoint study. Scandinavian Journal of Urology & Nephrology 2005; 39(6):489-97. *Not RCT or controlled trial*

4186. Stein A, Ben Dov D, Finkel B, et al. Single-dose intramuscular ketorolac versus diclofenac for pain management in renal colic. American Journal of Emergency Medicine 1996; 14(4):385-7. *Not CKD treatment*

4187. Stein CM, Longmire AW, Minton TA, et al. Cyclosporine-induced alterations in renal function are not associated with lipid peroxidation. Transplantation 1994; 58(3):386-8. *Sample size less than 50 patients*

4188. Stein EA, Amerena J, Ballantyne CM, et al. Long-term efficacy and safety of rosuvastatin 40 mg in patients with severe hypercholesterolemia. American Journal of Cardiology 2007; 100(9):1387-96. *Not relevant to key questions*

4189. Stein G, Sierakowski B, Jansa U, et al. Spirapril in chronic renal failure. Blood Pressure Supplement 1994; 2:54-60. *Sample size less than 50 patients*

4190. Steinberg EP, Moore RD, Brinker JA, et al. Nephrotoxicity of low osmolality contrast media versus high osmolality media. Investigative Radiology 1991; 26 Suppl 1:S86; discussion S8-91. *Not RCT or controlled trial*

4191. Steinberg MH, McCarthy WF, Castro O, et al. The risks and benefits of long-term use of hydroxyurea in sickle cell anemia: A 17.5 year follow-up. American Journal of Hematology 2010 Jun; 85(6):403-8. *Not CKD treatment*

4192. Steiner G. How can we improve the management of vascular risk in type 2 diabetes: insights from FIELD. Cardiovascular Drugs & Therapy 2009; 23(5):403-8. *Not RCT or controlled trial*

4193. Steinmetz OM, Panzer U, Stahl RAK, et al. Statin therapy in patients with chronic kidney disease: to use or not to use. European Journal of Clinical Investigation 2006; 36(8):519-27. *Not relevant to key questions*

4194. Stenlof K, Rossner S, Vercruysse F, et al. Topiramate in the treatment of obese subjects with drug-naive type 2 diabetes. Diabetes, Obesity & Metabolism 2007; 9(3):360-8. *Not CKD treatment*

4195. Stenvinkel P. Chronic kidney disease: a public health priority and harbinger of premature cardiovascular disease. Journal of Internal Medicine 2010 Nov; 268(5):456-67. *Not CKD treatment*

4196. Stenvinkel P, Carrero JJ, Axelsson J, et al. Emerging biomarkers for evaluating cardiovascular risk in the chronic kidney disease patient: how do new pieces fit into the uremic puzzle? Clinical Journal of The American Society of Nephrology: CJASN 2008; 3(2):505-21. *Not relevant to key questions*

4197. Stephenson JM, Kenny S, Stevens LK, et al. Proteinuria and mortality in diabetes: the WHO Multinational Study of Vascular Disease in Diabetes. Diabetic Medicine 1995; 12(2):149-55. *Not CKD treatment*

4198. Stergiou GS, Nasothimiou EG. Does dosing antihypertensive drugs at night alter renal or cardiovascular outcome: do we have the evidence? Current Opinion in Nephrology & Hypertension 2008; 17(5):464-9. *Not CKD treatment*

4199. Stevens MA, McCullough PA, Tobin KJ, et al. A prospective randomized trial of prevention measures in patients at high risk for contrast nephropathy: results of the P.R.I.N.C.E. Study. Prevention of Radiocontrast Induced Nephropathy Clinical Evaluation. Journal of the American College of Cardiology 1999; 33(2):403-11. *Not CKD treatment*

4200. Stevens PE. Blind Pew sends a black spot: the current haemoglobin controversy. Blood Purification 2008; 26(1):54-8. *Not CKD treatment*

4201. Stewart CP, Christian P, Schulze KJ, et al. Antenatal micronutrient supplementation reduces metabolic syndrome in 6- to 8-year-old children in rural Nepal. Journal of Nutrition 2009; 139(8):1575-81. *Not RCT or controlled trial*

4202. Stichtenoth DO, Marhauer V, Tsikas D, et al. Effects of specific COX-2-inhibition on renin release and renal and systemic prostanoid synthesis in healthy volunteers. Kidney International 2005; 68(5):2197-207. *Not early CKD*

4203. Stieglmayr S, Khayyat AH, Bodlaj G, et al. Comparable outcomes in type 2 diabetic patients with diabetic or vascular nephropathy treated by hemodialysis. Nephron 2010; 114(2):c104-7. *Not CKD treatment*

4204. Stier CT, Jr., Chander PN, Rocha R. Aldosterone as a mediator in cardiovascular injury. Cardiology in Review 2002; 10(2):97-107. *Not RCT or controlled trial*

4205. Stock JL, Coderre JA, Posillico JT. Effects of estrogen on mineral metabolism in postmenopausal women as evaluated by multiple assays measuring parathyrin bioactivity. Clinical Chemistry 1989; 35(1):18-22. *Sample size less than 50 patients*

4206. Stock PG, Ascher NL, Osorio RW, et al. Standard sequential immunosuppression with Minnesota antilymphoblast globulin and cyclosporine vs FK 506: a comparison of early nephrotoxicity. Transplantation Proceedings 1993; 25(1 Pt 1):675-6. *Not RCT or controlled trial*

4207. Stockwell MA, Scott A, Day A, et al. Colloid solutions in the critically ill. A randomised comparison of albumin and polygeline 2. Serum albumin concentration and incidences of pulmonary oedema and acute renal failure. Anaesthesia 1992; 47(1):7-9. *Not CKD treatment*

4208. Stojiljkovic L, Behnia R. Role of renin angiotensin system inhibitors in cardiovascular and renal protection: a lesson from clinical trials. Current Pharmaceutical Design 2007; 13(13):1335-45. *Sample size less than 50 patients*

4209. Stokes GS, Monaghan JC, Pillai DN. Comparison of the effects on urinary sodium excretion of indomethacin and of carbidopa in normal volunteers given an intravenous saline infusion. Clinical Science 1997; 92(4):409-14. *Sample size less than 50 patients*

4210. Stoll DM, King LE, Jr., McNeil L, et al. Human urinary epidermal growth factor excretion: age, sex, and race dependence. Journal of Clinical Endocrinology & Metabolism 1988; 67(2):361-7. *Not RCT or controlled trial*

4211. Stone GW, McCullough PA, Tumlin JA, et al. Fenoldopam mesylate for the prevention of contrast-induced nephropathy: a randomized controlled trial. JAMA 2003; 290(17):2284-91. *Not relevant to key questions*

4212. Stone GW, Tumlin JA, Madyoon H, et al. Design and rationale of CONTRAST--a prospective, randomized, placebo-controlled trial of fenoldopam mesylate for the prevention of radiocontrast nephropathy. Reviews in Cardiovascular Medicine 2001; 2 Suppl 1:S31-6. *Not CKD treatment*

4213. Stone WJ, Graber SE, Krantz SB, et al. Treatment of the anemia of predialysis patients with recombinant human erythropoietin: a randomized, placebo-controlled trial. American Journal of the Medical Sciences 1988; 296(3):171-9. *Sample size less than 50 patients*

4214. Stoof TJ, Korstanje MJ, Bilo HJ, et al. Does fish oil protect renal function in cyclosporin-treated psoriasis patients? Journal of Internal Medicine 1989; 226(6):437-41. *Sample size less than 50 patients*

4215. Stornello M, Valvo EV, Puglia N, et al. Angiotensin converting enzyme inhibition with a low dose of enalapril in normotensive diabetics with persistent proteinuria. Journal of Hypertension - Supplement 1988; 6(4):S464-6. *Sample size less than 50 patients*

4216. Stornello M, Valvo EV, Scapellato L. Angiotensin converting enzyme inhibition in normotensive type II diabetics with persistent mild proteinuria. Journal of Hypertension - Supplement 1989; 7(6):S314-5. *Sample size less than 50 patients*

4217. Stornello M, Valvo EV, Scapellato L. Hemodynamic, renal, and humoral effects of the calcium entry blocker nicardipine and converting enzyme inhibitor captopril in hypertensive type II diabetic patients with nephropathy. Journal of Cardiovascular Pharmacology 1989; 14(6):851-5. *Sample size less than 50 patients*

4218. Stornello M, Valvo EV, Scapellato L. Comparative effects of enalapril, atenolol and chlorthalidone on blood pressure and kidney function of diabetic patients affected by arterial hypertension and persistent proteinuria. Nephron 1991; 58(1):52-7. *Sample size less than 50 patients*

4219. Stornello M, Valvo EV, Scapellato L. Persistent albuminuria in normotensive non-insulin-dependent (type II) diabetic patients: comparative effects of angiotensin-converting enzyme inhibitors and beta-adrenoceptor blockers. Clinical Science 1992; 82(1):19-23. *Sample size less than 50 patients*

4220. Stornello M, Valvo EV, Vasques E, et al. Systemic and renal effects of chronic angiotensin converting enzyme inhibition with captopril in hypertensive diabetic patients. Journal of Hypertension - Supplement 1989; 7(7):S65-7. *Sample size less than 50 patients*

4221. Story DA, Tosolini A, Bellomo R, et al. Plasma acid-base changes in chronic renal failure: a Stewart analysis. International Journal of Artificial Organs 2005; 28(10):961-5. *Not relevant to key questions*

4222. Stouthard JM, Levi M, Hack CE, et al. Interleukin-6 stimulates coagulation, not fibrinolysis, in humans. Thrombosis & Haemostasis 1996; 76(5):738-42. *Not CKD treatment*

4223. Stouthard JM, van der Poll T, Endert E, et al. Effects of acute and chronic interleukin-6 administration on thyroid hormone metabolism in humans. Journal of Clinical Endocrinology & Metabolism 1994; 79(5):1342-6. *Not CKD treatment*

4224. Stoves J, Inglis H, Newstead CG. A randomized study of oral vs intravenous iron supplementation in patients with progressive renal insufficiency treated with erythropoietin. Nephrology Dialysis Transplantation 2001; 16(5):967-74. *Not CKD treatment*

4225. Strasser T, Schiffl H. Generation of leukotriene B4 by hemodialyzer membranes: a novel index of biocompatibility. Klinische Wochenschrift 1991; 69(17):808-12. *Not CKD treatment*

4226. Strazzullo P, Cappuccio FP, Trevisan M, et al. Erythrocyte sodium/lithium countertransport and renal lithium clearance in a random sample of untreated middle-aged men. Clinical Science 1989; 77(3):337-42. *Not relevant to key questions*

4227. Stricker K, Yu S, Krammer G. A 6-week, multicentre, randomised, double-blind, double-dummy, active-controlled, clinical safety study of lumiracoxib and rofecoxib in osteoarthritis patients. BMC Musculoskeletal Disorders 2008; 9:118. *Not early CKD*

4228. Strippoli GFM, Bonifati C, Craig M, et al. Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists for preventing the progression of diabetic kidney disease. Cochrane Database of Systematic Reviews 2006; (4):CD006257. *Not RCT or controlled trial*

4229. Strippoli GFM, Craig JC. Hypothesis versus association: the optimal hemoglobin target debate. American Journal of Kidney Diseases 2005; 46(5):970-3. *Not early CKD*

4230. Strippoli GFM, Craig JC, Manno C, et al. Hemoglobin targets for the anemia of chronic kidney disease: a meta-analysis of randomized, controlled trials. Journal of the American Society of Nephrology 2004; 15(12):3154-65. *Not relevant to key questions*

4231. Strippoli GFM, Craig M, Craig JC. Antihypertensive agents for preventing diabetic kidney disease. Cochrane Database of Systematic Reviews 2005; (4):CD004136. *Sample size less than 50 patients*

4232. Strippoli GFM, Craig M, Deeks JJ, et al. Effects of angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists on mortality and renal outcomes in diabetic nephropathy: systematic review. BMJ 2004; 329(7470):828. *Not RCT or controlled trial*

4233. Strippoli GFM, Craig M, Schena FP, et al. Antihypertensive agents for primary prevention of diabetic nephropathy. Journal of the American Society of Nephrology 2005; 16(10):3081-91. *Not RCT or controlled trial*

4234. Strippoli GFM, Craig MC, Schena FP, et al. Role of blood pressure targets and specific antihypertensive agents used to prevent diabetic nephropathy and delay its progression. Journal of the American Society of Nephrology 2006; 17(4 Suppl 2):S153-5. *Not relevant to key questions*

4235. Strippoli GFM, Navaneethan SD, Johnson DW, et al. Effects of statins in patients with chronic kidney disease: meta-analysis and meta-regression of randomised controlled trials. BMJ 2008; 336(7645):645-51. *Follow-up less than 6 months*

4236. Strippoli GFM, Palmer S, Tong A, et al. Meta-analysis of biochemical and patient-level effects of calcimimetic therapy. American Journal of Kidney Diseases 2006; 47(5):715-26. *Not relevant to key questions*

4237. Strippoli GFM, Tognoni G, Navaneethan SD, et al. Haemoglobin targets: we were wrong, time to move on. Lancet 2007; 369(9559):346-50. *Not RCT or controlled trial*

4238. Strohmaier WL, Bichler KH, Koch J, et al. Protective effect of verapamil on shock wave induced renal tubular dysfunction. Journal of Urology 1993; 150(1):27-9. *Sample size less than 50 patients*

4239. Strohmaier WL, Koch J, Balk N, et al. Limitation of shock-wave-induced renal tubular dysfunction by nifedipine. European Urology 1994; 25(2):99-104. *Sample size less than 50 patients*

4240. Strojek K, Grzeszczak W, Gorska J, et al. Lowering of microalbuminuria in diabetic patients by a sympathicoplegic agent: novel approach to prevent progression of diabetic nephropathy? Journal of the American Society of Nephrology 2001; 12(3):602-5. *Sample size less than 50 patients*

4241. Strumberg D. Preclinical and clinical development of the oral multikinase inhibitor sorafenib in cancer treatment. Drugs of Today 2005; 41(12):773-84. *Not RCT or controlled trial*

4242. Studies of Ocular Complications of ARGTACTG. The ganciclovir implant plus oral ganciclovir versus parenteral cidofovir for the treatment of cytomegalovirus retinitis in patients with acquired immunodeficiency syndrome: The Ganciclovir Cidofovir Cytomegalovirus Retinitis Trial. American Journal of Ophthalmology 2001; 131(4):457-67. *Not early CKD*

4243. Stumpe KO, Overlack A. A new trial of the efficacy, tolerability, and safety of angiotensin-converting enzyme inhibition in mild systemic hypertension with concomitant diseases and therapies. Perindopril Therapeutic Safety Study Group (PUTS). American Journal of Cardiology 1993; 71(17):32E-7E. *Follow-up less than 6 months*

4244. Sturgiss SN, Wilkinson R, Davison JM. Renal reserve during human pregnancy. American Journal of Physiology 1996; 271(1 Pt 2):F16-20. *Sample size less than 50 patients*

4245. Sturrock ND, Lang CC, Baylis PH, et al. Sequential effects of cyclosporine therapy on blood pressure, renal function and neurohormones. Kidney International 1994; 45(4):1203-10. *Not RCT or controlled trial*

4246. Sturrock ND, Lang CC, Clark G, et al. Acute haemodynamic and renal effects of cyclosporin and indomethacin in man. Nephrology Dialysis Transplantation 1994; 9(8):1149-56. *Follow-up less than 6 months*

4247. Sturrock ND, Lang CC, MacFarlane LJ, et al. Serial changes in blood pressure, renal function, endothelin and lipoprotein (a) during the first 9 days of cyclosporin therapy in males. Journal of Hypertension 1995; 13(6):667-73. *Follow-up less than 6 months*

4248. Sturrock ND, Lang CC, Struthers AD. Cyclosporin-induced hypertension precedes renal dysfunction and sodium retention in man. Journal of Hypertension 1993; 11(11):1209-16. *Sample size less than 50 patients*

4249. Sturrock ND, Lang CC, Struthers AD. Indomethacin and cyclosporin together produce marked renal vasoconstriction in humans. Journal of Hypertension 1994; 12(8):919-24. *Sample size less than 50 patients*

4250. Subira M, Martino R, Gomez L, et al. Low-dose amphotericin B lipid complex vs. conventional amphotericin B for empirical antifungal therapy of neutropenic fever in patients with hematologic malignancies--a randomized, controlled trial. European Journal of Haematology 2004; 72(5):342-7. *Not early CKD*

4251. Subira M, Martino R, Sureda A, et al. Safety and efficacy of low-dose amphotericin B lipid complex for empirical antifungal therapy of neutropenic fever in patients with hematologic malignancies. Methods & Findings in Experimental & Clinical Pharmacology 2001; 23(9):505-10. *Not early CKD*

4252. Sulikowska B, Olejniczak H, Muszynska M, et al. Effect of sulodexide on albuminuria, NAG excretion and glomerular filtration response to dopamine in diabetic patients. American Journal of Nephrology 2006; 26(6):621-8. *Not adult population*

4253. Suliman ME, Lindholm B, Barany P, et al. Homocysteine-lowering is not a primary target for cardiovascular disease prevention in chronic kidney disease patients. Seminars in Dialysis 2007; 20(6):523-9. *Not RCT or controlled trial*

4254. Sullivan DH, Walls RC. The risk of life-threatening complications in a select population of geriatric patients: the impact of nutritional status. Journal of the American College of Nutrition 1995; 14(1):29-36. *Not RCT or controlled trial*

4255. Sumaili EK, Krzesinski J-M, Zinga CV, et al. Prevalence of chronic kidney disease in Kinshasa: results of a pilot study from the Democratic Republic of Congo. Nephrology Dialysis Transplantation 2009; 24(1):117-22. *Sample size less than 50 patients*

4256. Sumeray M, Robertson C, Lapsley M, et al. Low dose dopamine infusion reduces renal tubular injury following cardiopulmonary bypass surgery. Journal of Nephrology 2001; 14(5):397-402. *Sample size less than 50 patients*

4257. Summers MJ, Oliver KR, Coombes JS, et al. Effect of atorvastatin on cognitive function in patients from the Lipid Lowering and Onset of Renal Disease (LORD) trial. Pharmacotherapy 2007; 27(2):183-90. *Sample size less than 50 patients*

4258. Sundar S, Gupta LB, Makharia MK, et al. Oral treatment of visceral leishmaniasis with miltefosine. Annals of Tropical Medicine & Parasitology 1999; 93(6):589-97. *Not early CKD*

4259. Sunder-Plassmann G, Horl WH. Importance of iron supply for erythropoietin therapy. Nephrology Dialysis Transplantation 1995; 10(11):2070-6. *Not early CKD*

4260. Sunderrajan S, Reams G, Bauer JH. Renal effects of diltiazem in primary hypertension. Hypertension 1986; 8(3):238-42. *Sample size less than 50 patients*

4261. Supervia A, Pedro-Botet J, Nogues X, et al. Piroxicam fast-dissolving dosage form vs diclofenac sodium in the treatment of acute renal colic: a double-blind controlled trial. British Journal of Urology 1998; 81(1):27-30. *Not CKD treatment*

4262. Sutherland DE. The case for pancreas transplantation. Diabetes & Metabolism 1996; 22(2):132-8. *Not RCT or controlled trial*

4263. Sutters M, Duncan R, Peart WS. Effect of dietary salt restriction on renal sensitivity to vasopressin in man. Clinical Science 1995; 89(1):37-43. *Not RCT or controlled trial*

4264. Sutton L, Sayer GP, Bajuk B, et al. Do very sick neonates born at term have antenatal risks? 1. Infants ventilated primarily for problems of adaptation to extra-uterine life. Acta Obstetricia et Gynecologica Scandinavica 2001; 80(10):905-16. *Not RCT or controlled trial*

4265. Suzuki H, Kanno Y, Ikeda N, et al. Selection of the dose of angiotensin converting enzyme inhibitor for patients with diabetic nephropathy depends on the presence or absence of left ventricular hypertrophy. Hypertension Research - Clinical & Experimental 2002; 25(6):865-73. *Not relevant to key questions*

4266. Suzuki H, Moriwaki K, Kanno Y, et al. Comparison of the effects of an ACE inhibitor and alphabeta blocker on the progression of renal failure with left ventricular hypertrophy: preliminary report. Hypertension Research - Clinical & Experimental 2001; 24(2):153-8. *Not RCT or controlled trial*

4267. Suzuki H, Moriwaki K, Nakamoto H, et al. Blood pressure reduction in the morning yields beneficial effects on progression of chronic renal insufficiency with regression of left ventricular hypertrophy. Clinical & Experimental Hypertension 2002; 24(1-2):51-63. *Sample size less than 50 patients*

4268. Suzuki M, Hirasawa Y, Hirashima K, et al. Dose-finding, double-blind, clinical trial of recombinant human erythropoietin (Chugai) in Japanese patients with end-stage renal disease. Research Group for Clinical Assessment of rhEPO. Contributions to Nephrology 1989; 76:179-92; discussion 212-8. *Not early CKD*

4269. Suzuki S, Hinokio Y, Ohtomo M, et al. The effects of coenzyme Q10 treatment on maternally inherited diabetes mellitus and deafness, and mitochondrial DNA 3243 (A to G) mutation. Diabetologia 1998; 41(5):584-8. *Sample size less than 50 patients*

4270. Svarstad E, Helland S, Morken T, et al. Renal effects of maintenance low-dose cyclosporin A treatment in psoriasis. Nephrology Dialysis Transplantation 1994; 9(10):1462-7. *Sample size less than 50 patients*

4271. Svendsen KB, Bech JN, Sorensen TB, et al. A comparison of the effects of etodolac and ibuprofen on renal haemodynamics, tubular function, renin, vasopressin and urinary excretion of albumin and alpha-glutathione-S-transferase in healthy subjects: a placebo-controlled cross-over study. European Journal of Clinical Pharmacology 2000; 56(5):383-8. *Not early CKD*

4272. Svensson M, Christensen JH, Solling J, et al. The effect of n-3 fatty acids on plasma lipids and lipoproteins and blood pressure in patients with CRF. American Journal of Kidney Diseases 2004; 44(1):77-83. *Follow-up less than 6 months*

4273. Swan SK, Hursting MJ. The pharmacokinetics and pharmacodynamics of argatroban: effects of age, gender, and hepatic or renal dysfunction. Pharmacotherapy 2000; 20(3):318-29. *Not CKD treatment*

4274. Swan SK, Rudy DW, Lasseter KC, et al. Effect of cyclooxygenase-2 inhibition on renal function in elderly persons receiving a low-salt diet. A randomized, controlled trial. Annals of Internal Medicine 2000; 133(1):1-9. *Not early CKD*

4275. Sward K, Valsson F, Odencrants P, et al. Recombinant human atrial natriuretic peptide in ischemic acute renal failure: a randomized placebo-controlled trial.[Erratum appears in Crit Care Med. 2006 Jun;34(6):1862]. Critical Care Medicine 2004; 32(6):1310-5. *Not relevant to key questions*

4276. Swedberg K. Effect of ACE-inhibition on renal function in severe congestive heart failure. Zeitschrift fur Kardiologie 1991; 80 Suppl 2:50-4. *Not relevant to key questions*

4277. Swenson J, Olgun S, Radjavi A, et al. Clinical efficacy of buprenorphine to minimize distress in MRL/lpr mice. European Journal of Pharmacology 2007; 567(1-2):67-76. *Sample size less than 50 patients*

4278. Swift PA, MacGregor GA. Renoprotection in Type 2 diabetes: blockade of the renin-angiotensin system with angiotensin II receptor blockers. Journal of the Renin-Angiotensin-Aldosterone System 2001; 2(3):170-3. *Not RCT or controlled trial*

4279. Swygert TH, Roberts LC, Valek TR, et al. Effect of intraoperative low-dose dopamine on renal function in liver transplant recipients. Anesthesiology 1991; 75(4):571-6. *Not CKD treatment*

4280. Szczech LA, Barnhart HX, Inrig JK, et al. Secondary analysis of the CHOIR trial epoetin-alpha dose and achieved hemoglobin outcomes. Kidney International 2008; 74(6):791-8. *Not adult population*

4281. Szczech LA, Barnhart HX, Sapp S, et al. A secondary analysis of the CHOIR trial shows that comorbid conditions differentially affect outcomes during anemia treatment. Kidney International 2010 Feb; 77(3):239-46. *Not CKD treatment*

4282. Szczech LA, Best PJ, Crowley E, et al. Outcomes of patients with chronic renal insufficiency in the bypass angioplasty revascularization investigation. Circulation 2002; 105(19):2253-8. *Not relevant to key questions*

4283. Szepietowski JC, Bielicka E, Wasik F, et al. Microalbuminuria as a subclinical marker of renal impairment in subjects with psoriasis vulgaris. Journal of the European Academy of Dermatology & Venereology 2000; 14(6):513-4. *Not CKD treatment*

4284. Szucs TD, Sandoz MS, Keusch GW. The cost-effectiveness of losartan in type 2 diabetics with nephropathy in Switzerland--an analysis of the RENAAL study. Swiss Medical Weekly 2004; 134(31-32):440-7. *Follow-up less than 6 months*

4285. Taal MW, Brenner BM. Renoprotective benefits of RAS inhibition: from ACEI to angiotensin II antagonists. Kidney International 2000; 57(5):1803-17. *Not RCT or controlled trial*

4286. Tadros GM, Malik JA, Manske CL, et al. Iso-osmolar radio contrast iodixanol in patients with chronic kidney disease. Journal of Invasive Cardiology 2005; 17(4):211-5. *Not RCT or controlled trial*

4287. Tagliaferri F, Sirovich I, Stipa F, et al. Systemic specific active immunotherapy for solid tumors. An overview about cancer vaccinetherapy. Recenti Progressi in Medicina 1994; 85(12):591-6. *Not RCT or controlled trial*

4288. Tahir H, Jackson LL, Warnock DG. Antiproteinuric therapy and fabry nephropathy: sustained reduction of proteinuria in patients receiving enzyme replacement therapy with agalsidase-beta. Journal of the American Society of Nephrology 2007; 18(9):2609-17. *Sample size less than 50 patients*

4289. Takabatake T, Ohta H, Sasaki T, et al. Renal effects of manidipine hydrochloride. A new calcium antagonist in hypertensive patients. European Journal of Clinical Pharmacology 1993; 45(4):321-5. *Sample size less than 50 patients*

4290. Takahashi A, Shiga T, Shoda M, et al. Impact of renal dysfunction on appropriate therapy in implantable cardioverter defibrillator patients with non-ischaemic dilated cardiomyopathy. Europace 2009; 11(11):1476-82. *Not CKD treatment*

4291. Takahashi T, Reed SD, Schulman KA. Cost-effectiveness of the oral adsorbent AST-120 versus placebo for chronic kidney disease. Nephrology 2008; 13(5):419-27. *Not CKD treatment*

4292. Takahashi T, Yano M, Minami J, et al. Sarpogrelate hydrochloride, a serotonin2A receptor antagonist, reduces albuminuria in diabetic patients with early-stage diabetic nephropathy. Diabetes Research & Clinical Practice 2002; 58(2):123-9. *Not CKD treatment*

4293. Takebayashi K, Matsumoto S, Aso Y, et al. Aldosterone blockade attenuates urinary monocyte chemoattractant protein-1 and oxidative stress in patients with type 2 diabetes complicated by diabetic nephropathy. Journal of Clinical Endocrinology & Metabolism 2006; 91(6):2214-7. *Sample size less than 50 patients*

4294. Takeda H, Ohta K, Hagiwara M, et al. Genetic predisposing factors in non-insulin dependent diabetes with persistent albuminuria. Tokai Journal of Experimental & Clinical Medicine 1992; 17(5-6):199-203. *Not CKD treatment*

4295. Takeuchi K, Abe K, Yasujima M, et al. No adverse effect of non-steroidal anti-inflammatory drugs, sulindac and diclofenac sodium, on blood pressure control with a calcium antagonist, nifedipine, in elderly hypertensive patients. Tohoku Journal of Experimental Medicine 1991; 165(3):201-8. *Sample size less than 50 patients*

4296. Takimoto CH, Remick SC, Sharma S, et al. Dose-escalating and pharmacological study of oxaliplatin in adult cancer patients with impaired renal function: a National Cancer Institute Organ Dysfunction Working Group Study. Journal of Clinical Oncology 2003; 21(14):2664-72. *Sample size less than 50 patients*

4297. Taliercio CP, Vlietstra RE, Ilstrup DM, et al. A randomized comparison of the nephrotoxicity of iopamidol and diatrizoate in high risk patients undergoing cardiac angiography. Journal of the American College of Cardiology 1991; 17(2):384-90. *Not CKD treatment*

4298. Tam SC, Tang LS, Lai CK, et al. Role of atrial natriuretic peptide in the increase in glomerular filtration rate induced by a protein meal. Clinical Science 1990; 78(5):481-5. *Not relevant to key questions*

4299. Tammara V, Mahmood I, Yu DK, et al. A limited sampling method for the estimation of vigabatrin maximum plasma concentration and area under the curve. Therapeutic Drug Monitoring 1997; 19(1):79-82. *Sample size less than 50 patients*

4300. Tamsma JT, Beverdam FH, Leuven JA, et al. Decreased interstitial apolipoprotein A-I levels in IDDM patients with diabetic nephropathy. Diabetes 1995; 44(5):501-5. *Sample size less than 50 patients*

4301. Tamsma JT, van der Woude FJ, Lemkes HH. Effect of sulphated glycosaminoglycans on albuminuria in patients with overt diabetic (type 1) nephropathy. Nephrology Dialysis Transplantation 1996; 11(1):182-5. *Follow-up less than 6 months*

4302. Tamura A, Goto Y, Miyamoto K, et al. Efficacy of single-bolus administration of sodium bicarbonate to prevent contrast-induced nephropathy in patients with mild renal insufficiency undergoing an elective coronary procedure. American Journal of Cardiology 2009; 104(7):921-5. *Not CKD treatment*

4303. Tamura Y, Ikeda O, Nakasone Y, et al. Effect of sodium thiosulfate on cisplatin removal after intra-arterial embolization with a lipiodol-platinum suspension for hepatocellular carcinoma. Acta Radiologica 2010 May; 51(4):383-8. *Not CKD treatment*

4304. Tamura Y, Kosuga M, Yamashita M, et al. Renoprotective effects of angiotensin II receptor blocker, candesartan cilexetil, in patients with stage 4-5 chronic kidney disease. Clinical & Experimental Nephrology 2008; 12(4):256-63. *Not CKD treatment*

4305. Tan F, Mukherjee JJ, Lee KO, et al. Dual blockade of the renin-angiotensin-aldosterone system is safe and effective in reducing albuminuria in Asian type 2 diabetic patients with nephropathy. Singapore Medical Journal 2010 Feb; 51(2):151-6. *Follow-up less than 6 months*

4306. Tan JK, Haberman HF, Coldman AJ. Identifying effective treatments for uremic pruritus. Journal of the American Academy of Dermatology 1991; 25(5 Pt 1):811-8. *Not CKD treatment*

4307. Tan K, Chow W-S, Wong Y, et al. Effect of losartan on plasma C-reactive protein in type 2 diabetic patients with microabluminuria. Diabetes Care 2002; 25(7):1254-5. *Not relevant to key questions*

4308. Tan KCB, Chow W-S, Ai VHG, et al. Effects of angiotensin II receptor antagonist on endothelial vasomotor function and urinary albumin excretion in type 2 diabetic patients with microalbuminuria. Diabetes/Metabolism Research Reviews 2002; 18(1):71-6. *Not relevant to key questions*

4309. Tang AT, El-Gamel A, Keevil B, et al. The effect of 'renal-dose' dopamine on renal tubular function following cardiac surgery: assessed by measuring retinol binding protein (RBP). European Journal of Cardio-Thoracic Surgery 1999; 15(5):717-21; discussion 21-2. *Not CKD treatment*

4310. Tang ATM, Knott J, Nanson J, et al. A prospective randomized study to evaluate the renoprotective action of beating heart coronary surgery in low risk patients. European Journal of Cardio-Thoracic Surgery 2002; 22(1):118-23. *Not CKD treatment*

4311. Tang IY, Murray PT. Prevention of perioperative acute renal failure: what works? Best Practice & Research 2004; Clinical Anaesthesiology. 18(1):91-111. *Not relevant to key questions*

4312. Tang J, Wingerchuk DM, Crum BA, et al. Alpha-lipoic acid may improve symptomatic diabetic polyneuropathy. Neurologist 2007; 13(3):164-7. *Follow-up less than 6 months*

4313. Tanihara S, Hayakawa T, Oki I, et al. Proteinuria is a prognostic marker for cardiovascular mortality: NIPPON DATA 80, 1980-1999. Journal of Epidemiology 2005; 15(4):146-53. *Not RCT or controlled trial*

4314. Taniwaki H, Ishimura E, Kawagishi T, et al. Intrarenal hemodynamic changes after captopril test in patients with type 2 diabetes: a duplex Doppler sonography study. Diabetes Care 2003; 26(1):132-7. *Follow-up less than 6 months*

4315. Tannehill SP, Mehta MP, Larson M, et al. Effect of amifostine on toxicities associated with sequential chemotherapy and radiation therapy for unresectable non-small-cell lung cancer: results of a phase II trial. Journal of Clinical Oncology 1997; 15(8):2850-7. *Sample size less than 50 patients*

4316. Tannenbaum H, Davis P, Russell AS, et al. An evidence-based approach to prescribing NSAIDs in musculoskeletal disease: a Canadian consensus. Canadian NSAID Consensus Participants. CMAJ Canadian Medical Association Journal 1996; 155(1):77-88. *Not CKD treatment*

4317. Tapp RJ, Zimmet PZ, Harper CA, et al. Diagnostic thresholds for diabetes: the association of retinopathy and albuminuria with glycaemia. Diabetes Research & Clinical Practice 2006; 73(3):315-21. *Follow-up less than 6 months*

4318. Tarnow L, Rossing P, Jensen C, et al. Long-term renoprotective effect of nisoldipine and lisinopril in type 1 diabetic patients with diabetic nephropathy. Diabetes Care 2000; 23(12):1725-30. *Sample size less than 50 patients*

4319. Tarnow L, Sato A, Ali S, et al. Effects of nisoldipine and lisinopril on left ventricular mass and function in diabetic nephropathy. Diabetes Care 1999; 22(3):491-4. *Not CKD treatment*

4320. Tasanarong A, Piyayotai D, Thitiarchakul S. Protection of radiocontrast induced nephropathy by vitamin E (alpha tocopherol): a randomized controlled pilot study. Journal of the Medical Association of Thailand 2009; 92(10):1273-81. *Not CKD treatment*

4321. Taskin F, Akdilli A, Karaman C, et al. Mammographically detected breast arterial calcifications: indicators for arteriosclerotic diseases? European Journal of Radiology 2006; 60(2):250-5. *Not RCT or controlled trial*

4322. Tassies D, Reverter JC, Cases A, et al. Effect of recombinant human erythropoietin treatment on circulating reticulated platelets in uremic patients: association with early improvement in platelet function. American Journal of Hematology 1998; 59(2):105-9. *Not early CKD*

4323. Tataranni G, Malacarne F, Farinelli R, et al. Beneficial effects of verapamil in renal-risk surgical patients. Renal Failure 1994; 16(3):383-90. *Sample size less than 50 patients*

4324. Tauxe WN, Mochizuki T, McCauley J, et al. A comparison of the renal effects (ERPF, GFR, and FF) of FK 506 and cyclosporine in patients with liver transplantation. Transplantation Proceedings 1991; 23(6):3146-7. *Not CKD treatment*

4325. Tauzin-Fin P, Delort-Laval S, Krol-Houdek MC, et al. Effect of balanced analgesia with buprenorphine on pain response and general anaesthesia requirement during lithotripsy procedures. European Journal of Anaesthesiology 1998; 15(2):147-52. *Not CKD treatment*

4326. Taverner D, Mackay IG, Craig K, et al. The effects of selective beta-adrenoceptor antagonists and partial agonist activity on renal function during exercise in normal subjects and those with moderate renal impairment. British Journal of Clinical Pharmacology 1991; 32(3):387-91. *Sample size less than 50 patients*

4327. Taylor A, Jr., Manatunga A, Morton K, et al. Multicenter trial validation of a camera-based method to measure Tc-99m mercaptoacetyltriglycine, or Tc-99m MAG3, clearance. Radiology 1997; 204(1):47-54. *Sample size less than 50 patients*

4328. Team DT, Mugyenyi P, Walker AS, et al. Routine versus clinically driven laboratory monitoring of HIV antiretroviral therapy in Africa (DART): a randomised non-inferiority trial. Lancet 2010; 375(9709):123-31. *Not CKD treatment*

4329. Tefekli A, Altunrende F, Tepeler K, et al. Tubeless percutaneous nephrolithotomy in selected patients: a prospective randomized comparison. International Urology & Nephrology 2007; 39(1):57-63. *Sample size less than 50 patients*

4330. Teirstein PS, Price MJ, Mathur VS, et al. Differential effects between intravenous and targeted renal delivery of fenoldopam on renal function and blood pressure in patients undergoing cardiac catheterization. American Journal of Cardiology 2006; 97(7):1076-81. *Sample size less than 50 patients*

4331. Teixeira SR, Tappenden KA, Carson L, et al. Isolated soy protein consumption reduces urinary albumin excretion and improves the serum lipid profile in men with type 2 diabetes mellitus and nephropathy. Journal of Nutrition 2004; 134(8):1874-80. *Not RCT or controlled trial*

4332. Tejani A. Cyclosporine therapy for nephrotic syndrome. Nephron 1997; 77(4):488. *Not RCT or controlled trial*

4333. Tejedor A, Torres AM, Castilla M, et al. Cilastatin protection against cyclosporin A-induced nephrotoxicity: clinical evidence. Current Medical Research & Opinion 2007; 23(3):505-13. *Not relevant to key questions*

4334. Telishevka M, Chenett L, McKee M. Towards an understanding of the high death rate among young people with diabetes in Ukraine. Diabetic Medicine 2001; 18(1):3-9. *Not RCT or controlled trial*

4335. ten Dam MA, Zwiers A, Crusius JB, et al. Tubular reabsorption of pepsinogen isozymogens in man studied by the inhibition of tubular protein reabsorption with dibasic amino acids. Clinical Science 1991; 80(2):161-6. *Sample size less than 50 patients*

4336. Tepel M, van der Giet M, Schwarzfeld C, et al. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. New England Journal of Medicine 2000; 343(3):180-4. *Not early CKD*

4337. Tepel M, Zidek W. Acetylcysteine for radiocontrast nephropathy. Current Opinion in Critical Care 2001; 7(6):390-2. *Not early CKD*

4338. Tepel M, Zidek W. Acetylcysteine and contrast media nephropathy. Current Opinion in Nephrology & Hypertension 2002; 11(5):503-6. *Not CKD treatment*

4339. Tepel M, Zidek W. N-Acetylcysteine in nephrology; contrast nephropathy and beyond. Current Opinion in Nephrology & Hypertension 2004; 13(6):649-54. *Not relevant to key questions*

4340. Teplan V, Schuck O, Knotek A, et al. Enhanced metabolic effect of erythropoietin and keto acids in CRF patients on low-protein diet: Czech multicenter study. American Journal of Kidney Diseases 2003; 41(3 Suppl 1):S26-30. *Not early CKD*

4341. Teplan V, Schuck O, Knotek A, et al. Effects of low-protein diet supplemented with ketoacids and erythropoietin in chronic renal failure: a long-term metabolic study. Annals of Transplantation 2001; 6(1):47-53. *Not relevant to key questions*

4342. Teplan V, Schuck O, Racek J, et al. Reduction of plasma asymmetric dimethylarginine in obese patients with chronic kidney disease after three years of a low-protein diet supplemented with keto-amino acids: a randomized controlled trial. Wiener Klinische Wochenschrift 2008; 120(15-16):478-85. *Not CKD treatment*

4343. Teplan V, Schuck O, Votruba M, et al. Metabolic effects of keto acid--amino acid supplementation in patients with chronic renal insufficiency receiving a low-protein diet and recombinant human erythropoietin--a randomized controlled trial. Wiener Klinische Wochenschrift 2001; 113(17-18):661-9. *Sample size less than 50 patients*

4344. Ter Maaten JC, Voorburg A, Heine RJ, et al. Renal handling of urate and sodium during acute physiological hyperinsulinaemia in healthy subjects. Clinical Science 1997; 92(1):51-8. *Sample size less than 50 patients*

4345. ter Wee PM, Donker AJ. Clinical strategies for arresting progression of renal disease. Kidney International - Supplement 1992; 38:S114-20. *Not relevant to key questions*

4346. Terrell KM, Perkins AJ, Hui SL, et al. Computerized decision support for medication dosing in renal insufficiency: a randomized, controlled trial. Annals of Emergency Medicine 2010 Dec; 56(6):623-9. *Not CKD treatment*

4347. Tershakovec AM, Keane WF, Zhang Z, et al. Effect of LDL cholesterol and treatment with losartan on end-stage renal disease in the RENAAL study. Diabetes Care 2008; 31(3):445-7. *Not RCT or controlled trial*

4348. Teschan PE, Beck GJ, Dwyer JT, et al. Effect of a ketoacid-aminoacid-supplemented very low protein diet on the progression of advanced renal disease: a reanalysis of the MDRD feasibility study. Clinical Nephrology 1998; 50(5):273-83. *Not early CKD*

4349. Testani JM, Chen J, McCauley BD, et al. Potential effects of aggressive decongestion during the treatment of decompensated heart failure on renal function and survival. Circulation 2010 Jul 20; 122(3):265-72. *Not CKD treatment*

4350. Thakur V, Cook ME, Wallin JD. Antihypertensive effect of the combination of fosinopril and HCTZ is resistant to interference by nonsteroidal antiinflammatory drugs. American Journal of Hypertension 1999; 12(9 Pt 1):925-8. *Sample size less than 50 patients*

4351. Thall PF, Wooten LH, Tannir NM. Monitoring event times in early phase clinical trials: some practical issues. Clinical Trials 2005; 2(6):467-78. *Follow-up less than 6 months*

4352. Thiele H, Hildebrand L, Schirdewahn C, et al. Impact of high-dose N-acetylcysteine versus placebo on contrast-induced nephropathy and myocardial reperfusion injury in unselected patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. The LIPSIA-N-ACC (Prospective, Single-Blind, Placebo-Controlled, Randomized Leipzig Immediate PercutaneouS Coronary Intervention Acute Myocardial Infarction N-ACC) Trial. Journal of the American College of Cardiology 2010 May 18; 55(20):2201-9. *Not CKD treatment*

4353. Thiesson HC, Jensen BL, Jespersen B, et al. Inhibition of cGMP-specific phosphodiesterase type 5 reduces sodium excretion and arterial blood pressure in patients with NaCl retention and ascites. American Journal of Physiology - Renal Physiology 2005; 288(5):F1044-52. *Sample size less than 50 patients*

4354. Thijs A, Nanayakkara PWB, Ter Wee PM, et al. Mild-to-moderate renal impairment is associated with platelet activation: a cross-sectional study. Clinical Nephrology 2008; 70(4):325-31. *Not CKD treatment*

4355. Thomas G, Rojas MC, Epstein SK, et al. Insulin therapy and acute kidney injury in critically ill patients a systematic review. Nephrology Dialysis Transplantation 2007; 22(10):2849-55. *Not relevant to key questions*

4356. Thomas MC. Anemia in diabetes: marker or mediator of microvascular disease? Nature Clinical Practice Nephrology 2007; 3(1):20-30. *Not RCT or controlled trial*

4357. Thomas MC. The assessment and management of albuminuria in primary care. Diabetes Research & Clinical Practice 2008; 80(1):83-8. *Not RCT or controlled trial*

4358. Thomas MC, Cooper ME, Rossing K, et al. Anaemia in diabetes: Is there a rationale to TREAT? Diabetologia 2006; 49(6):1151-7. *Follow-up less than 6 months*

4359. Thomas MC, Jerums G, Tsalamandris C, et al. Increased tubular organic ion clearance following chronic ACE inhibition in patients with type 1 diabetes. Kidney International 2005; 67(6):2494-9. *Not RCT or controlled trial*

4360. Thomas MC, Weekes AJ, Broadley OJ, et al. The burden of chronic kidney disease in Australian patients with type 2 diabetes (the NEFRON study).[Erratum appears in Med J Aust. 2006 Oct 2;185(7):408]. Medical Journal of Australia 2006; 185(3):140-4. *Not RCT or controlled trial*

4361. Thomas ME, Harris KP, Ramaswamy C, et al. Simvastatin therapy for hypercholesterolemic patients with nephrotic syndrome or significant proteinuria. Kidney International 1993; 44(5):1124-9. *Sample size less than 50 patients*

4362. Thompson JF, Pike JM, Chumas PD, et al. Rectal diclofenac compared with pethidine injection in acute renal colic. BMJ 1989; 299(6708):1140-1. *Not early CKD*

4363. Thomsen HS. Contrast-medium-induced nephrotoxicity: are all answers in for acetylcysteine? European Radiology 2001; 11(12):2351-3. *Not early CKD*

4364. Thomsen HS, Morcos SK. Risk of contrast-medium-induced nephropathy in high-risk patients undergoing MDCT--a pooled analysis of two randomized trials. European Radiology 2009 Apr; 19(4):891-7. *Not CKD treatment*

4365. Thomsen HS, Morcos SK, Barrett BJ. Contrast-induced nephropathy: the wheel has turned 360 degrees. Acta Radiologica 2008; 49(6):646-57. *Not CKD treatment*

4366. Thomsen HS, Sos TA, Nielsen SL. Renovascular hypertension. Diagnosis and intervention. Acta Radiologica 1989; 30(2):113-20. *Not relevant to key questions*

4367. Thomsen OO, Danielsen H, Sorensen SS, et al. Effect of captopril on renal haemodynamics and the renin-angiotensin-aldosterone and osmoregulatory systems in essential hypertension. European Journal of Clinical Pharmacology 1986; 30(1):1-6. *Sample size less than 50 patients*

4368. Thornalley PJ, Rabbani N. Therapy: Vitamin B6, B9 and B12 in diabetic nephropathy--beware. Nature Reviews Endocrinology 2010 Sep; 6(9):477-8. *Not RCT or controlled trial*

4369. Thornley-Brown D, Wang X, Wright JT, Jr., et al. Differing effects of antihypertensive drugs on the incidence of diabetes mellitus among patients with hypertensive kidney disease. Archives of Internal Medicine 2006; 166(7):797-805. *Not relevant to key questions*

4370. Thyrum PT, Wong YW, Yeh C. Single-dose pharmacokinetics of quetiapine in subjects with renal or hepatic impairment. Progress in Neuro-Psychopharmacology & Biological Psychiatry 2000; 24(4):521-33. *Not early CKD*

4371. Tillman J. Heparin versus citrate for anticoagulation in critically ill patients treated with continuous renal replacement therapy. Nursing in Critical Care 2009; 14(4):191-9. *Not RCT or controlled trial*

4372. Tincani E, Mannucci C, Casolari B, et al. Safety of dalteparin for the prophylaxis of venous thromboembolism in elderly medical patients with renal insufficiency: a pilot study. Haematologica 2006; 91(7):976-9. *Not CKD treatment*

4373. Tisdale JE, Rudis MI, Padhi ID, et al. Inhibition of N-acetylation of procainamide and renal clearance of N-acetylprocainamide by para-aminobenzoic acid in humans. Journal of Clinical Pharmacology 1995; 35(9):902-10. *Not CKD treatment*

4374. Tiseo M, Martelli O, Mancuso A, et al. Short hydration regimen and nephrotoxicity of intermediate to high-dose cisplatin-based chemotherapy for outpatient treatment in lung cancer and mesothelioma. Tumori 2007; 93(2):138-44. *Not relevant to key questions*

4375. Tleyjeh IM, Kashour T, Hakim FA, et al. Statins for the prevention and treatment of infections: a systematic review and meta-analysis. Archives of Internal Medicine 2009; 169(18):1658-67. *Not RCT or controlled trial*

4376. Tobe S, Epstein M. The use of calcium antagonists in the treatment of hypertensive persons with kidney disease. Current Hypertension Reports 2002; 4(3):191-4. *Not RCT or controlled trial*

4377. Toblli JE, Lombrana A, Duarte P, et al. Intravenous iron reduces NT-pro-brain natriuretic peptide in anemic patients with chronic heart failure and renal insufficiency. Journal of the American College of Cardiology 2007; 50(17):1657-65. *Not RCT or controlled trial*

4378. Tod M, Minozzi C, Beaucaire G, et al. Isepamicin in intensive care unit patients with nosocomial pneumonia: population pharmacokinetic-pharmacodynamic study. Journal of Antimicrobial Chemotherapy 1999; 44(1):99-108. *Not RCT or controlled trial*

4379. Todd PA, Goa KL. Enalapril. A reappraisal of its pharmacology and therapeutic use in hypertension. Drugs 1992; 43(3):346-81. *Not relevant to key questions*

4380. Toivonen J, Kaukinen S, Oikkonen M, et al. Effects of deliberate hypotension induced by labetalol on renal function. European Journal of Anaesthesiology 1991; 8(1):13-20. *Sample size less than 50 patients*

4381. Tokmakova MP, Skali H, Kenchaiah S, et al. Chronic kidney disease, cardiovascular risk, and response to angiotensin-converting enzyme inhibition after myocardial infarction: the Survival And Ventricular Enlargement (SAVE) study. Circulation 2004; 110(24):3667-73. *Not RCT or controlled trial*

4382. Tolman C, Richardson D, Bartlett C, et al. Structured conversion from thrice weekly to weekly erythropoietic regimens using a computerized decision-support system: a randomized clinical study. Journal of the American Society of Nephrology 2005; 16(5):1463-70. *Not RCT or controlled trial*

4383. Tomai F, Petrolini A, De Luca L, et al. Rationale and design of the Randomized comparison of XiEnce V and Multilink VisioN coronary stents in the sAme muLtivessel patient with chronic kiDnEy disease (RENAL-DES) study. Journal of Cardiovascular Medicine 2010 Apr; 11(4):310-7. *Not CKD treatment*

4384. Tombach B, Bremer C, Reimer P, et al. Renal tolerance of a neutral gadolinium chelate (gadobutrol) in patients with chronic renal failure: results of a randomized study. Radiology 2001; 218(3):651-7. *Sample size less than 50 patients*

4385. Tominaga Y, Kohara S, Namii Y, et al. Clonal analysis of nodular parathyroid hyperplasia in renal hyperparathyroidism. World Journal of Surgery 1996; 20(7):744-50; discussion 50-2. *Not RCT or controlled trial*

4386. Tomita K, Marumo F. Effect of long-term carvedilol therapy on renal function in essential hypertension. Journal of Cardiovascular Pharmacology 1992; 19 Suppl 1:S97-101. *Sample size less than 50 patients*

4387. Tomiyama H, Nishikawa E, Watanabe G, et al. Hormonal and cardiorenal responses to acute saline loading in mild congestive heart failure--the effect of angiotensin converting enzyme inhibition. Japanese Circulation Journal 1998; 62(1):29-35. *Sample size less than 50 patients*

4388. Tomiyama H, Watanabe G, Abe M, et al. Systemic and renal effects of atrial natriuretic peptide in patients with heart failure treated with angiotensin-converting enzyme inhibitor or in acute saline solution loading. American Heart Journal 2001; 141(3):422-7. *Not early CKD*

4389. Tomoda F, Takata M, Oh-Hashi S, et al. Altered renal response to enhanced endogenous 5-hydroxytryptamine after tryptophan administration in essential hypertension. Clinical Science 1992; 82(5):551-7. *Sample size less than 50 patients*

4390. Tomson CRV, Foley RN, Li Q, et al. Race and end-stage renal disease in the United States Medicare population: the disparity persists. Nephrology 2008; 13(7):651-6. *Not RCT or controlled trial*

4391. Tonelli M. The effect of statins on preservation of kidney function in patients with coronary artery disease. Current Opinion in Cardiology 2006; 21(6):608-12. *Not relevant to key questions*

4392. Tonelli M, Collins D, Robins S, et al. Effect of gemfibrozil on change in renal function in men with moderate chronic renal insufficiency and coronary disease. American Journal of Kidney Diseases 2004; 44(5):832-9. *Sample size less than 50 patients*

4393. Tonelli M, Collins D, Robins S, et al. Gemfibrozil for secondary prevention of cardiovascular events in mild to moderate chronic renal insufficiency. Kidney International 2004; 66(3):1123-30. *Not CKD treatment*

4394. Tonelli M, Gill J, Pandeya S, et al. Barriers to blood pressure control and angiotensin enzyme inhibitor use in Canadian patients with chronic renal insufficiency. Nephrology Dialysis Transplantation 2002; 17(8):1426-33. *Not relevant to key questions*

4395. Tonelli M, Isles C, Craven T, et al. Effect of pravastatin on rate of kidney function loss in people with or at risk for coronary disease. Circulation 2005; 112(2):171-8. *Sample size less than 50 patients*

4396. Tonelli M, Jose P, Curhan G, et al. Proteinuria, impaired kidney function, and adverse outcomes in people with coronary disease: analysis of a previously conducted randomised trial. BMJ 2006; 332(7555):1426. *Follow-up less than 6 months*

4397. Tonelli M, Keech A, Shepherd J, et al. Effect of pravastatin in people with diabetes and chronic kidney disease. Journal of the American Society of Nephrology 2005; 16(12):3748-54. *Not RCT or controlled trial*

4398. Tonelli M, Manns B, Feller-Kopman D. Acute renal failure in the intensive care unit: a systematic review of the impact of dialytic modality on mortality and renal recovery. American Journal of Kidney Diseases 2002; 40(5):875-85. *Not CKD treatment*

4399. Tonelli M, Moye L, Sacks FM, et al. Effect of pravastatin on loss of renal function in people with moderate chronic renal insufficiency and cardiovascular disease. Journal of the American Society of Nephrology 2003; 14(6):1605-13. *Not relevant to key questions*

4400. Tonelli M, Sacks F, Pfeffer M, et al. Biomarkers of inflammation and progression of chronic kidney disease. Kidney International 2005; 68(1):237-45. *Not RCT or controlled trial*

4401. Tonelli M, Wiebe N, Culleton B, et al. Chronic kidney disease and mortality risk: a systematic review. Journal of the American Society of Nephrology 2006; 17(7):2034-47. *Not CKD treatment*

4402. Tong G-D, Zhou D-Q, He J-S, et al. Clinical research on navel application of Shehuang Paste combined with Chinese herbal colon dialysis in treatment of refractory cirrhotic ascites complicated with azotemia. World Journal of Gastroenterology 2006; 12(48):7798-804. *Not relevant to key questions*

4403. Tong PCY, Ko GTC, Chan WB, et al. The efficacy and tolerability of fosinopril in Chinese type 2 diabetic patients with moderate renal insufficiency. Diabetes, Obesity & Metabolism 2006; 8(3):342-7. *Not relevant to key questions*

4404. Tonolo G, Ciccarese M, Brizzi P, et al. Reduction of albumin excretion rate in normotensive microalbuminuric type 2 diabetic patients during long-term simvastatin treatment. Diabetes Care 1997; 20(12):1891-5. *Sample size less than 50 patients*

4405. Toppozada M, Darwish EA, Osman YF, et al. Low dose acetyl salicylic acid in severe preeclampsia. International Journal of Gynaecology & Obstetrics 1991; 35(4):311-7. *Not CKD treatment*

4406. Torner A, Odar-Cederlof I, Kallner A, et al. Renal function in community-dwelling frail elderly. Comparison between measured and predicted glomerular filtration rate in the elderly and proposal for a new cystatin C-based prediction equation. Aging-Clinical & Experimental Research 2008; 20(3):216-25. *Not RCT or controlled trial*

4407. Toso A, Maioli M, Leoncini M, et al. Usefulness of atorvastatin (80 mg) in prevention of contrast-induced nephropathy in patients with chronic renal disease. American Journal of Cardiology 2010; 105(3):288-92. *Not CKD treatment*

4408. Toto R, Shultz P, Raij L, et al. Efficacy and tolerability of losartan in hypertensive patients with renal impairment. Collaborative Group. Hypertension 1998; 31(2):684-91. *Follow-up less than 6 months*

4409. Toto RD. Management of hypertensive chronic kidney disease: role of calcium channel blockers. Journal of Clinical Hypertension 2005; 7(4 Suppl 1):15-20. *Not early CKD*

4410. Toto RD. Lessons from the African-American Study of Kidney Disease and Hypertension: an update. Current Hypertension Reports 2006; 8(5):409-12. *Not RCT or controlled trial*

4411. Toto RD, Adams-Huet B, Fenves AZ, et al. Effect of ramipril on blood pressure and protein excretion rate in normotensive nondiabetic patients with proteinuria. American Journal of Kidney Diseases 1996; 28(6):832-40. *Sample size less than 50 patients*

4412. Toto RD, Anderson SA, Brown-Cartwright D, et al. Effects of acute and chronic dosing of NSAIDs in patients with renal insufficiency. Kidney International 1986; 30(5):760-8. *Not relevant to key questions*

4413. Toto RD, Greene T, Hebert LA, et al. Relationship between body mass index and proteinuria in hypertensive nephrosclerosis: results from the African American Study of Kidney Disease and Hypertension (AASK) cohort. American Journal of Kidney Diseases 2010 Nov; 56(5):896-906. *Not relevant to key questions*

4414. Toto RD, Grundy SM, Vega GL. Pravastatin treatment of very low density, intermediate density and low density lipoproteins in hypercholesterolemia and combined hyperlipidemia secondary to the nephrotic syndrome. American Journal of Nephrology 2000; 20(1):12-7. *Sample size less than 50 patients*

4415. Toto RD, Mitchell HC, Lee HC, et al. Reversible renal insufficiency due to angiotensin converting enzyme inhibitors in hypertensive nephrosclerosis. Annals of Internal Medicine 1991; 115(7):513-9. *Not relevant to key questions*

4416. Toto RD, Mitchell HC, Pettinger WA. Treatment of hypertension in nondiabetic renal disease. Current Opinion in Nephrology & Hypertension 1994; 3(3):279-85. *Not RCT or controlled trial*

4417. Toto RD, Tian M, Fakouhi K, et al. Effects of calcium channel blockers on proteinuria in patients with diabetic nephropathy. Journal of Clinical Hypertension 2008; 10(10):761-9. *Sample size less than 50 patients*

4418. Toussaint ND, Lau KK, Strauss BJ, et al. Using vertebral bone densitometry to determine aortic calcification in patients with chronic kidney disease. Nephrology 2010 Aug; 15(5):575-83. *Not CKD treatment*

4419. Toussaint ND, Lau KK, Strauss BJ, et al. Effect of alendronate on vascular calcification in CKD stages 3 and 4: a pilot randomized controlled trial. American Journal of Kidney Diseases 2010 Jul; 56(1):57-68. *Not CKD treatment*

4420. Townend JN, Doran J, Lote CJ, et al. Peripheral haemodynamic effects of inhibition of prostaglandin synthesis in congestive heart failure and interactions with captopril. British Heart Journal 1995; 73(5):434-41. *Not CKD treatment*

4421. Townsend RR, Cohen DL, Katholi R, et al. Safety of intravenous gadolinium (Gd-BOPTA) infusion in patients with renal insufficiency. American Journal of Kidney Diseases 2000; 36(6):1207-12. *Sample size less than 50 patients*

4422. Tozija L, Antova Z, Cakalaroski K, et al. Infection as a risk factor in the outcome of patients with acute renal failure assessed by SOFA score. Makedonska Akademija na Naukite i Umetnostite Oddelenie Za Bioloshki i Meditsinski Nauki Prilozi 2006; 27(1):17-27. *Not relevant to key questions*

4423. Tozun N, Berkman K, Tankurt E, et al. Effect of diltiazem on renal function in patients with liver cirrhosis. International Journal of Clinical Pharmacology, Therapy, & Toxicology 1991; 29(5):198-203. *Sample size less than 50 patients*

4424. Tramer MR, Williams JE, Carroll D, et al. Comparing analgesic efficacy of non-steroidal anti-inflammatory drugs given by different routes in acute and chronic pain: a qualitative systematic review. Acta Anaesthesiologica Scandinavica 1998; 42(1):71-9. *Not RCT or controlled trial*

4425. Tramonti G, Donadio C, Silvestri L, et al. Renal effects of prolonged antihypertensive treatment with diltiazem. Kidney International - Supplement 1996; 55:S78-80. *Sample size less than 50 patients*

4426. Trenkwalder C, Stiasny K, Pollmacher T, et al. L-dopa therapy of uremic and idiopathic restless legs syndrome: a double-blind, crossover trial. Sleep 1995; 18(8):681-8. *Sample size less than 50 patients*

4427. Trewhella M, Dawson P, Forsling M, et al. Vasopressin release in response to intravenously injected contrast media. British Journal of Radiology 1990; 63(746):97-100. *Not CKD treatment*

4428. Triposkiadis F, Parissis JT, Starling RC, et al. Current drugs and medical treatment algorithms in the management of acute decompensated heart failure. Expert Opinion on Investigational Drugs 2009; 18(6):695-707. *Not CKD treatment*

4429. Tritrakarn T, Lertakyamanee J, Koompong P, et al. Both EMLA and placebo cream reduced pain during extracorporeal piezoelectric shock wave lithotripsy with the Piezolith 2300. Anesthesiology 2000; 92(4):1049-54. *Not early CKD*

4430. Trivedi H, Daram S, Szabo A, et al. High-dose N-acetylcysteine for the prevention of contrast-induced nephropathy. American Journal of Medicine 2009; 122(9):874.e9-15. *Not CKD treatment*

4431. Trivedi H, Lu N, Andresen BT, et al. Slower decline of renal function after initiation of rosiglitazone in diabetics -- a pilot study. Clinical Nephrology 2009; 72(3):181-5. *Not CKD treatment*

4432. Trivedi HS, Moore H, Nasr S, et al. A randomized prospective trial to assess the role of saline hydration on the development of contrast nephrotoxicity. Nephron 2003; 93(1):C29-34. *Not CKD treatment*

4433. Trocha AK, Schmidtke C, Didjurgeit U, et al. Effects of intensified antihypertensive treatment in diabetic nephropathy: mortality and morbidity results of a prospective controlled 10-year study. Journal of Hypertension 1999; 17(10):1497-503. *Not RCT or controlled trial*

4434. Troiano M, Corsa P, Raguso A, et al. Radiation therapy in urinary cancer: state of the art and perspective. Radiologia Medica 2009; 114(1):70-82. *Not CKD treatment*

4435. Trollfors B, Norrby R, Bergmark J, et al. Comparative toxicity of gentamicin and cefotetan. Scandinavian Journal of Infectious Diseases 1986; 18(2):139-46. *Follow-up less than 6 months*

4436. Tsai C-F, Wang S-J, Fuh J-L. Moderate chronic kidney disease is associated with reduced cognitive performance in midlife women. Kidney International 2010 Sep; 78(6):605-10. *Not CKD treatment*

4437. Tsai J-C, Chen S-C, Hwang S-J, et al. Prevalence and risk factors for CKD in spouses and relatives of hemodialysis patients. American Journal of Kidney Diseases 2010 May; 55(5):856-66. *Not CKD treatment*

4438. Tsai JJ, Yeun JY, Kumar VA, et al. Comparison and interpretation of urinalysis performed by a nephrologist versus a hospital-based clinical laboratory. American Journal of Kidney Diseases 2005; 46(5):820-9. *Not relevant to key questions*

4439. Tsai S-Y, Tseng H-F, Tan H-F, et al. End-stage renal disease in Taiwan: a case-control study. Journal of Epidemiology 2009; 19(4):169-76. *Not RCT or controlled trial*

4440. Tsai YT, Lin HC, Lee FY, et al. Effects of captopril on renal functions, renal and portal hemodynamics in patients with cirrhosis. Proceedings of the National Science Council, Republic of China - Part B, Life Sciences 1996; 20(2):44-50. *Not CKD treatment*

4441. Tsang GM, Allen S, Pagano D, et al. Pentoxifylline preloading reduces endothelial injury and permeability in cardiopulmonary bypass. ASAIO Journal 1996; 42(5):M429-34. *Not CKD treatment*

4442. Tsao C, Greene P, Odlind B, et al. Pharmacokinetics of recombinant human superoxide dismutase in healthy volunteers. Clinical Pharmacology & Therapeutics 1991; 50(6):713-20. *Not CKD treatment*

4443. Tschuppert Y, Buclin T, Rothuizen LE, et al. Effect of dronedarone on renal function in healthy subjects. British Journal of Clinical Pharmacology 2007; 64(6):785-91. *Not RCT or controlled trial*

4444. Tsuboi M, Shiraki M, Hamada M, et al. Effects of phosphorus-containing calcium preparation (bone meal powder) and calcium carbonate on serum calcium and phosphorus in young and old healthy volunteers: a double-blinded crossover study. Journal of Bone & Mineral Metabolism 2000; 18(6):321-7. *Not early CKD*

4445. Tsunoda K, Abe K, Omata K, et al. Effects of cicletanine on the urinary excretion of prostanoids and kallikrein, and on renal function in man. Cardiovascular Drugs & Therapy 1993; 7(2):253-6. *Sample size less than 50 patients*

4446. Tsuruoka K, Yasuda T, Koitabashi K, et al. Evaluation of renal microcirculation by contrast-enhanced ultrasound with Sonazoid as a contrast agent. International Heart Journal 2010 May; 51(3):176-82. *Not CKD treatment*

4447. Tsuruoka S, Ioka T, Wakaumi M, et al. Severe arrhythmia as a result of the interaction of cetirizine and pilsicainide in a patient with renal insufficiency: first case presentation showing competition for excretion via renal multidrug resistance protein 1 and organic cation transporter 2.[Erratum appears in Clin Pharmacol Ther. 2006 Dec;80(6):645]. Clinical Pharmacology & Therapeutics 2006; 79(4):389-96. *Sample size less than 50 patients*

4448. Tugwell P, Ludwin D, Gent M, et al. Interaction between cyclosporin A and nonsteroidal antiinflammatory drugs. Journal of Rheumatology 1997; 24(6):1122-5. *Not CKD treatment*

4449. Tumlin JA, Wang A, Murray PT, et al. Fenoldopam mesylate blocks reductions in renal plasma flow after radiocontrast dye infusion: a pilot trial in the prevention of contrast nephropathy. American Heart Journal 2002; 143(5):894-903. *Not early CKD*

4450. Tuominen JA, Ebeling P, Koivisto VA. Long-term lisinopril therapy reduces exercise-induced albuminuria in normoalbuminuric normotensive IDDM patients. Diabetes Care 1998; 21(8):1345-8. *Sample size less than 50 patients*

4451. Turakhia MP, Varosy PD, Lee K, et al. Impact of renal function on survival in patients with implantable cardioverter-defibrillators. Pacing & Clinical Electrophysiology 2007; 30(3):377-84. *Not RCT or controlled trial*

4452. Turk S, Yeksan M, Tamer N, et al. Effect of 1,25 (OH)2D3 treatment on glucose intolerance in uraemia. Nephrology Dialysis Transplantation 1992; 7(12):1207-12. *Not early CKD*

4453. Turker H, Donmez A, Zeyneloglu P, et al. Effects of enalaprilat infusion on hemodynamics and renal function in patients undergoing cardiac surgery. Anadolu Kardiyoloji Dergisi 2004; 4(4):296-300. *Follow-up less than 6 months*

4454. Turnbull DA, Wilkinson C, Griffith EC, et al. The psychosocial outcomes of antenatal day care for three medical complications of pregnancy: a randomised controlled trial of 395 women. Australian & New Zealand Journal of Obstetrics & Gynaecology 2006; 46(6):510-6. *Not RCT or controlled trial*

4455. Turner R. Hepatic and renal tolerability of long-term naproxen treatment in patients with rheumatoid arthritis. Seminars in Arthritis & Rheumatism 1988; 17(3 Suppl 2):29-35. *Not RCT or controlled trial*

4456. Turner S, Derham C, Orsi NM, et al. Randomized clinical trial of the effects of methylprednisolone on renal function after major vascular surgery. British Journal of Surgery 2008; 95(1):50-6. *Not CKD treatment*

4457. Turner S, Dhamarajah S, Bosomworth M, et al. Effect of perioperative steroids on renal function after liver transplantation. Anaesthesia 2006; 61(3):253-9. *Not early CKD*

4458. Tuttle KR. Albuminuria reduction: the holy grail for kidney protection. Kidney International 2007; 72(7):785-6. *Not CKD treatment*

4459. Tuttle KR, Bakris GL, Toto RD, et al. The effect of ruboxistaurin on nephropathy in type 2 diabetes. Diabetes Care 2005; 28(11):2686-90. *Not RCT or controlled trial*

4460. Tuttle KR, McGill JB, Haney DJ, et al. Kidney outcomes in long-term studies of ruboxistaurin for diabetic eye disease. Clinical Journal of The American Society of Nephrology: CJASN 2007; 2(4):631-6. *Not CKD treatment*

4461. Tuttle KR, Puhlman ME, Cooney SK, et al. Effects of amino acids and glucagon on renal hemodynamics in type 1 diabetes. American Journal of Physiology - Renal Physiology 2002; 282(1):F103-12. *Sample size less than 50 patients*

4462. Tutuncu NB, Gurlek A, Gedik O. Efficacy of ACE inhibitors and ATII receptor blockers in patients with microalbuminuria: a prospective study. Acta Diabetologica 2001; 38(4):157-61. *Sample size less than 50 patients*

4463. Twigg SM, Cao Z, McLennan SV, et al. Renal connective tissue growth factor induction in experimental diabetes is prevented by aminoguanidine. Endocrinology 2002; 143(12):4907-15. *Not human studies*

4464. Tylicki L, Renke M, Rutkowski P, et al. Dual blockade of the renin-angiotensin-aldosterone system with high-dose angiotensin-converting enzyme inhibitor for nephroprotection: an open, controlled, randomized study. Scandinavian Journal of Urology & Nephrology 2008; 42(4):381-8. *Not RCT or controlled trial*

4465. Tylicki L, Renke M, Rutkowski P, et al. Effects of N-acetylcysteine on angiotensin-converting enzyme plasma activity in patients with chronic kidney diseases. Blood Purification 2008; 26(4):354. *Not RCT or controlled trial*

4466. Tylicki L, Rutkowski P, Renke M, et al. Triple pharmacological blockade of the renin-angiotensin-aldosterone system in nondiabetic CKD: an open-label crossover randomized controlled trial. American Journal of Kidney Diseases 2008; 52(3):486-93. *Not CKD treatment*

4467. Tzakis AG, Tryphonopoulos P, Kato T, et al. Preliminary experience with alemtuzumab (Campath-1H) and low-dose tacrolimus immunosuppression in adult liver transplantation.[Erratum appears in Transplantation. 2004 Aug 15;78(3):489]. Transplantation 2004; 77(8):1209-14. *Not relevant to key questions*

4468. Uchino S, Doig GS, Bellomo R, et al. Diuretics and mortality in acute renal failure. Critical Care Medicine 2004; 32(8):1669-77. *Not CKD treatment*

4469. Udelson JE, Smith WB, Hendrix GH, et al. Acute hemodynamic effects of conivaptan, a dual V(1A) and V(2) vasopressin receptor antagonist, in patients with advanced heart failure. Circulation 2001; 104(20):2417-23. *Not early CKD*

4470. Ueda S. New approaches to blockade of the renin-angiotensin-aldosterone system: evidence from randomized controlled trials (RCTs) of angiotensin-converting enzyme inhibitors and angiotensin II-receptor blockers--questions remain unsolved. Journal of Pharmacological Sciences 2010; 113(4):292-5. *Not relevant to key questions*

4471. Uehlinger DE, Gotch FA, Sheiner LB. A pharmacodynamic model of erythropoietin therapy for uremic anemia. Clinical Pharmacology & Therapeutics 1992; 51(1):76-89. *Not early CKD*

4472. Uehlinger DE, Weidmann P, Gnaedinger MP. Cardiovascular regulation and lipoprotein profile during administration of co-dergocrine in essential hypertension. European Journal of Clinical Pharmacology 1989; 36(2):119-25. *Not CKD treatment*

4473. Uhlig K, Wang S-R, Beck GJ, et al. Factors associated with lipoprotein(a) in chronic kidney disease. American Journal of Kidney Diseases 2005; 45(1):28-38. *Not relevant to key questions*

4474. Ujhelyi MR, Bottorff MB, Schur M, et al. Aging effects on the organic base transporter and stereoselective renal clearance. Clinical Pharmacology & Therapeutics 1997; 62(2):117-28. *Sample size less than 50 patients*

4475. Umeki S, Tsukiyama K, Okimoto N, et al. Urinastatin (Kunitz-type proteinase inhibitor) reducing cisplatin nephrotoxicity. American Journal of the Medical Sciences 1989; 298(4):221-6. *Not CKD treatment*

4476. Umscheid CA, Kohl BA, Williams K. Antifibrinolytic use in adult cardiac surgery. Current Opinion in Hematology 2007; 14(5):455-67. *Follow-up less than 6 months*

4477. Ungar A, Fumagalli S, Marini M, et al. Renal, but not systemic, hemodynamic effects of dopamine are influenced by the severity of congestive heart failure. Critical Care Medicine 2004; 32(5):1125-9. *Sample size less than 50 patients*

4478. Uozumi J, Koikawa Y, Yasumasu T, et al. The protective effect of methylprednisolone against cisplatin-induced nephrotoxicity in patients with urothelial tumors. International Journal of Urology 1996; 3(5):343-7. *Not CKD treatment*

4479. Upadhyay L, Tripathi K, Kulkarni KS. A study of prostane in the treatment of benign prostatic hyperplasia. Phytotherapy Research 2001; 15(5):411-5. *Not early CKD*

4480. Upton A, McCune JS, Kirby KA, et al. Fluconazole coadministration concurrent with cyclophosphamide conditioning may reduce regimen-related toxicity postmyeloablative hematopoietic cell transplantation. Biology of Blood & Marrow Transplantation 2007; 13(7):760-4. *Follow-up less than 6 months*

4481. Usui I, Fujisaka S, Yamazaki K, et al. Telmisartan reduced blood pressure and HOMA-IR with increasing plasma leptin level in hypertensive and type 2 diabetic patients. Diabetes Research & Clinical Practice 2007; 77(2):210-4. *Not RCT or controlled trial*

4482. Utsunomiya Y, Hara Y, Ito H, et al. Effects of probenecid on the pharmacokinetics of mizoribine and co-administration of the two drugs in patients with nephrotic syndrome. International Journal of Clinical Pharmacology & Therapeutics 2010 Nov; 48(11):751-5. *Sample size less than 50 patients*

4483. Uzan S, Beaufils M, Breart G, et al. Prevention of fetal growth retardation with low-dose aspirin: findings of the EPREDA trial. Lancet 1991; 337(8755):1427-31. *Not adult population*

4484. Uzu T, Fujii T, Nishimura M, et al. Determinants of circadian blood pressure rhythm in essential hypertension. American Journal of Hypertension 1999; 12(1 Pt 1):35-9. *Not CKD treatment*

4485. Vahabi S, Heidari M, Kazemi AH, et al. Assessment of clonidine effect as premedicative drug on kidney function. JPMA - Journal of the Pakistan Medical Association 2010 Jul; 60(7):570-2. *Not CKD treatment*

4486. Vaitkus PT, Brar C. N-acetylcysteine in the prevention of contrast-induced nephropathy: publication bias perpetuated by meta-analyses. American Heart Journal 2007; 153(2):275-80. *Not early CKD*

4487. Valantine H, Keogh A, McIntosh N, et al. Cost containment: coadministration of diltiazem with cyclosporine after heart transplantation. Journal of Heart & Lung Transplantation 1992; 11(1 Pt 1):1-7; discussion -8. *Not CKD treatment*

4488. Valeri A, Gelfand J, Blum C, et al. Treatment of the hyperlipidemia of the nephrotic syndrome: a controlled trial. American Journal of Kidney Diseases 1986; 8(6):388-96. *Sample size less than 50 patients*

4489. Valvo E, Casagrande P, Bedogna V, et al. Systemic and renal effects of a new angiotensin converting enzyme inhibitor, benazepril, in essential hypertension. Journal of Hypertension 1990; 8(11):991-5. *Sample size less than 50 patients*

4490. van Acker BA, Prummel MF, Weber JA, et al. Effect of prednisone on renal function in man. Nephron 1993; 65(2):254-9. *Follow-up less than 6 months*

4491. van Berge-Landry H, James GD. Serum electrolyte, serum protein, serum fat and renal responses to a dietary sodium challenge: allostasis and allostatic load. Annals of Human Biology 2004; 31(4):477-87. *Not CKD treatment*

4492. Van Biesen W, De Bacquer D, Verbeke F, et al. The glomerular filtration rate in an apparently healthy population and its relation with cardiovascular mortality during 10 years. European Heart Journal 2007; 28(4):478-83. *Not relevant to key questions*

4493. Van Buren D, Payne J, Geevarghese S, et al. Renal function in primary liver transplant recipients receiving neoral (cyclosporine) versus prograf (tacrolimus). Transplantation Proceedings 1998; 30(4):1401-2. *Not CKD treatment*

4494. van de Wal RMA, Gansevoort RT, van der Harst P, et al. Predictors of angiotensin-converting enzyme inhibitor-induced reduction of urinary albumin excretion in nondiabetic patients. Hypertension 2006; 48(5):870-6. *Not relevant to key questions*

4495. van de Wal RMA, van der Harst P, Gerritsen WBM, et al. Plasma matrix metalloproteinase-9 and ACE-inhibitor-induced improvement of urinary albumin excretion in non-diabetic, microalbuminuric subjects. Journal of the Renin-Angiotensin-Aldosterone System 2007; 8(4):177-80. *Not CKD treatment*

4496. van den Bergh JP, Kaufmann BG, van Riet GJ, et al. Comparison of three formulations of calcium acetate tablets to evaluate tolerance and control of hyperphosphatemia in patients with chronic renal failure. Nephron 1994; 68(4):505-6. *Sample size less than 50 patients*

4497. Van den Berghe G, Wilmer A, Hermans G, et al. Intensive insulin therapy in the medical ICU. New England Journal of Medicine 2006; 354(5):449-61. *Not RCT or controlled trial*

4498. van den Meiracker AH, van der Linde NAJ, Broere A, et al. Effects of L-arginine and L-NAME on the renal function in hypertensive and normotensive subjects. Nephron 2002; 91(3):444-51. *Not CKD treatment*

4499. van der Jagt RH, Pari G, McDiarmid SA, et al. Effect of pentoxifylline on regimen related toxicity in patients undergoing allogeneic or autologous bone marrow transplantation. Bone Marrow Transplantation 1994; 13(2):203-7. *Not RCT or controlled trial*

4500. van der Kleij FGH, de Jong PE, Henning RH, et al. Enhanced responses of blood pressure, renal function, and aldosterone to angiotensin I in the DD genotype are blunted by low sodium intake. Journal of the American Society of Nephrology 2002; 13(4):1025-33. *Not early CKD*

4501. van der Linde NA, Boomsma F, van den Meiracker AH. Potentiation of L-NAME-induced systemic and renal vasoconstrictor responses by alpha1-adrenoceptor antagonism. Journal of Hypertension 2005; 23(5):1017-24. *Not relevant to key questions*

4502. van der Linde NA, van den Meiracker AH, Boomsma F. Role of angiotensin II in L-NAME-induced systemic and renal hemodynamic effects in hydrochlorothiazide-pretreated hypertensive subjects. Journal of Hypertension 2003; 21(2):345-51. *Sample size less than 50 patients*

4503. van der Meulen J, Reijn E, Heidendal GA, et al. Comparison of the effects of penbutolol and propranolol on glomerular filtration rate in hypertensive patients with impaired renal function. British Journal of Clinical Pharmacology 1986; 22(4):469-74. *Sample size less than 50 patients*

4504. van der Pijl JW, Lemkes HH, Frolich M, et al. Effect of danaparoid sodium on proteinuria, von Willebrand factor, and hard exudates in patients with diabetes mellitus type 2. Journal of the American Society of Nephrology 1999; 10(6):1331-6. *Sample size less than 50 patients*

4505. van der Pijl JW, van der Woude FJ, Geelhoed-Duijvestijn PH, et al. Danaparoid sodium lowers proteinuria in diabetic nephropathy. Journal of the American Society of Nephrology 1997; 8(3):456-62. *Follow-up less than 6 months*

4506. van der Putten K, Jie KE, van den Broek D, et al. Hepcidin-25 is a marker of the response rather than resistance to exogenous erythropoietin in chronic kidney disease/chronic heart failure patients. European Journal of Heart Failure 2010 Sep; 12(9):943-50. *Sample size less than 50 patients*

4507. van der Zander K, Houben AJHM, Webb DJ, et al. Selective endothelin B receptor blockade does not influence BNP-induced natriuresis in man. Kidney International 2006; 69(5):864-8. *Follow-up less than 6 months*

4508. van der Zee S, Baber U, Elmariah S, et al. Cardiovascular risk factors in patients with chronic kidney disease. Nature Reviews Cardiology 2009; 6(9):580-9. *Not RCT or controlled trial*

4509. van Essen GG, Rensma PL, de Zeeuw D, et al. Association between angiotensin-converting-enzyme gene polymorphism and failure of renoprotective therapy. Lancet 1996; 347(8994):94-5. *Not RCT or controlled trial*

4510. van Hamersvelt HW, Sluiter HE, Wetzels JF, et al. Is natriuresis on felodipine due to reversal of the renal effects of angiotensin II? Kidney International - Supplement 1992; 36:S73-7. *Not CKD treatment*

4511. Van Hamersvelt HW, Wetzels JF, Kloke HJ, et al. Exogenous aldosterone antagonizes distal tubular effects of calcium entry blocker felodipine. American Journal of Physiology 1994; 266(6 Pt 2):F843-9. *Sample size less than 50 patients*

4512. van Hamersvelt HW, Wetzels JF, Koene RA, et al. Metoclopramide stimulates kaliuresis during felodipine without affecting its natriuresis. Hypertension 1994; 24(5):633-9. *Not CKD treatment*

4513. van Paassen P, de Zeeuw D, de Jong PE. Renal and systemic effects of the renin inhibitor remikiren in patients with essential hypertension. Journal of Cardiovascular Pharmacology 1995; 26(1):39-45. *Sample size less than 50 patients*

4514. van Paassen P, Navis GJ, De Jong PE, et al. Pretreatment renal vascular tone predicts the effect of specific renin inhibition on natriuresis in essential hypertension. European Journal of Clinical Investigation 1999; 29(12):1019-26. *Sample size less than 50 patients*

4515. Van Praet JT, De Vriese AS. Prevention of contrast-induced nephropathy: a critical review. Current Opinion in Nephrology & Hypertension 2007; 16(4):336-47. *Not RCT or controlled trial*

4516. van Rijthoven AW, Dijkmans BA, Goei The HS, et al. Longterm cyclosporine therapy in rheumatoid arthritis. Journal of Rheumatology 1991; 18(1):19-23. *Not CKD treatment*

4517. van Rossum LK, Mathot RAA, Cransberg K, et al. Optimal sampling strategies to assess inulin clearance in children by the inulin single-injection method. Clinical Chemistry 2003; 49(7):1170-9. *Not CKD treatment*

4518. van Stralen KJ, Jager KJ, Zoccali C, et al. Agreement between methods. Kidney International 2008; 74(9):1116-20. *Not CKD treatment*

4519. Van Tilborg KA, Rabelink TJ, Koomans HA. Naloxone inhibits renal hemodynamic effect of head-out water immersion in humans. Kidney International 1995; 48(3):860-5. *Sample size less than 50 patients*

4520. Van Wyck DB, Roppolo M, Martinez CO, et al. A randomized, controlled trial comparing IV iron sucrose to oral iron in anemic patients with nondialysis-dependent CKD. Kidney International 2005; 68(6):2846-56. *Sample size less than 50 patients*

4521. Van Zuilen AD, Wetzels JFM, Blankestijn PJ, et al. Rationale and design of the MASTERPLAN study: Multifactorial approach and superior treatment efficacy in renal patients with the aid of nurse practitioners. Journal of Nephrology 2005; 18(1):30-4. *Not RCT or controlled trial*

4522. Van Zuilen AD, Wetzels JFM, Bots ML, et al. MASTERPLAN: study of the role of nurse practitioners in a multifactorial intervention to reduce cardiovascular risk in chronic kidney disease patients. Journal of Nephrology 2008; 21(3):261-7. *Not CKD treatment*

4523. van Zyl A, Jennings AA, Byrne MJ, et al. Effects of therapy on renal impairment in essential hypertension. South African Medical Journal 1992; Suid-Afrikaanse Tydskrif Vir Geneeskunde. 82(6):407-10. *Sample size less than 50 patients*

4524. Vanholder R, Lameire N. Does biocompatibility of dialysis membranes affect recovery of renal function and survival? Lancet 1999; 354(9187):1316-8. *Not RCT or controlled trial*

4525. Vanholder R, Lameire N. Does biocompatibility of dialysis membranes affect recovery of renal function and survival? Lancet 1999; 354(9187):1316-8. *Not RCT or controlled trial*

4526. Vanholder R, Lamiere N, Ringoir S. Therapeutic effect and complication profile of clonidine-beta-blocker combinations. Kidney International - Supplement 1988; 25:S181-3. *Not early CKD*

4527. Vanni S, Polidori G, Cecioni I, et al. ET(B) receptor in renal medulla is enhanced by local sodium during low salt intake. Hypertension 2002; 40(2):179-85. *Sample size less than 50 patients*

4528. Varghese SA, Powell TB, Janech MG, et al. Identification of diagnostic urinary biomarkers for acute kidney injury. Journal of Investigative Medicine 2010 Apr; 58(4):612-20. *Not CKD treatment*

4529. Vargo DL, Brater DC, Rudy DW, et al. Dopamine does not enhance furosemide-induced natriuresis in patients with congestive heart failure. Journal of the American Society of Nephrology 1996; 7(7):1032-7. *Sample size less than 50 patients*

4530. Varriale P, Mossavi A. The benefit of low-dose dopamine during vigorous diuresis for congestive heart failure associated with renal insufficiency: does it protect renal function? Clinical Cardiology 1997; 20(7):627-30. *Not CKD treatment*

4531. Vasavada N, Agarwal R. Role of excess volume in the pathophysiology of hypertension in chronic kidney disease. Kidney International 2003; 64(5):1772-9. *Follow-up less than 6 months*

4532. Vasavada N, Saha C, Agarwal R. A double-blind randomized crossover trial of two loop diuretics in chronic kidney disease. Kidney International 2003; 64(2):632-40. *Sample size less than 50 patients*

4533. Vase H, Lauridsen TG, Bech JN, et al. Eprosartan modulates the reflex activation of the sympathetic nervous system in sodium restricted healthy humans. British Journal of Clinical Pharmacology 2008; 65(6):822-32. *Not CKD treatment*

4534. Vase H, Lauridsen TG, Bech JN, et al. Effects of dihydralazine on renal water and aquaporin-2 excretion in humans. Scandinavian Journal of Clinical & Laboratory Investigation 2009; 69(1):45-51. *Not RCT or controlled trial*

4535. Vasheghani-Farahani A, Sadigh G, Kassaian SE, et al. Sodium bicarbonate in preventing contrast nephropathy in patients at risk for volume overload: a randomized controlled trial. Journal of Nephrology 2010 Mar-Apr; 23(2):216-23. *Not CKD treatment*

4536. Vasheghani-Farahani A, Sadigh G, Kassaian SE, et al. Sodium bicarbonate plus isotonic saline versus saline for prevention of contrast-induced nephropathy in patients undergoing coronary angiography: a randomized controlled trial. American Journal of Kidney Diseases 2009; 54(4):610-8. *Not CKD treatment*

4537. Vaur L, Gueret P, Lievre M, et al. Development of congestive heart failure in type 2 diabetic patients with microalbuminuria or proteinuria: observations from the DIABHYCAR (type 2 DIABetes, Hypertension, CArdiovascular Events and Ramipril) study.[Erratum appears in Diabetes Care. 2003 Aug;26(8):2489]. Diabetes Care 2003; 26(3):855-60. *Not relevant to key questions*

4538. Vecchio M, Navaneethan SD, Johnson DW, et al. Treatment options for sexual dysfunction in patients with chronic kidney disease: a systematic review of randomized controlled trials. Clinical Journal of The American Society of Nephrology: CJASN 2010 Jun; 5(6):985-95. *Not CKD treatment*

4539. Vedder AC, Linthorst GE, Houge G, et al. Treatment of Fabry disease: outcome of a comparative trial with agalsidase alfa or beta at a dose of 0.2 mg/kg. PLoS ONE [Electronic Resource] 2007; 2(7):e598. *Sample size less than 50 patients*

4540. Vedovato M, Lepore G, Coracina A, et al. Effect of sodium intake on blood pressure and albuminuria in Type 2 diabetic patients: the role of insulin resistance. Diabetologia 2004; 47(2):300-3. *Not relevant to key questions*

4541. Veelken R, Delles C, Hilgers KF, et al. Outcome survey in unselected hypertensive patients with type 2 diabetes mellitus: effects of ACE inhibition. American Journal of Hypertension 2001; 14(7 Pt 1):672-8. *Not RCT or controlled trial*

4542. Velussi M, Brocco E, Frigato F, et al. Effects of cilazapril and amlodipine on kidney function in hypertensive NIDDM patients. Diabetes 1996; 45(2):216-22. *Sample size less than 50 patients*

4543. Venkateswaran RV, Charman SC, Goddard M, et al. Lethal mesenteric ischaemia after cardiopulmonary bypass: a common complication? European Journal of Cardio-Thoracic Surgery 2002; 22(4):534-8. *Not CKD treatment*

4544. Ventura P, Panini R, Verlato C, et al. Hyperhomocysteinemia and related factors in 600 hospitalized elderly subjects. Metabolism: Clinical & Experimental 2001; 50(12):1466-71. *Not CKD treatment*

4545. Venugopal V, Laing CM, Ludman A, et al. Effect of remote ischemic preconditioning on acute kidney injury in nondiabetic patients undergoing coronary artery bypass graft surgery: a secondary analysis of 2 small randomized trials. American Journal of Kidney Diseases 2010 Dec; 56(6):1043-9. *Not CKD treatment*

4546. Vercauteren SB, Bosmans JL, Elseviers MM, et al. A meta-analysis and morphological review of cyclosporine-induced nephrotoxicity in auto-immune diseases. Kidney International 1998; 54(2):536-45. *Not CKD treatment*

4547. Verho M, Malerczyk V, Grotsch H, et al. Absence of crystalluria and estimation of renal parameters after oral and intravenous ofloxacin as compared to placebo in healthy volunteers. Drugs Under Experimental & Clinical Research 1988; 14(8):539-45. *Sample size less than 50 patients*

4548. Verma A, Anavekar NS, Meris A, et al. The relationship between renal function and cardiac structure, function, and prognosis after myocardial infarction: the VALIANT Echo Study. Journal of the American College of Cardiology 2007; 50(13):1238-45. *Follow-up less than 6 months*

4549. Verma A, Ranganna KM, Reddy RS, et al. Effect of rosuvastatin on C-reactive protein and renal function in patients with chronic kidney disease. American Journal of Cardiology 2005; 96(9):1290-2. *Follow-up less than 6 months*

4550. Vessal G, Sagheb MM, Shilian S, et al. Effect of oral cromolyn sodium on CKD-associated pruritus and serum tryptase level: a double-blind placebo-controlled study. Nephrology Dialysis Transplantation 2010 May; 25(5):1541-7. *Follow-up less than 6 months*

4551. Vestbo E, Damsgaard EM, Froland A, et al. Urinary albumin excretion in a population based cohort. Diabetic Medicine 1995; 12(6):488-93. *Follow-up less than 6 months*

4552. Vexler AM, Mou X, Gabizon AA, et al. Reduction of the systemic toxicity of cisplatin by intra-arterial hepatic route administration for liver malignancies. International Journal of Cancer 1995; 60(5):611-5. *Sample size less than 50 patients*

4553. Veyrat-Follet C, Vivier N, Trellu M, et al. The pharmacokinetics of idraparinux, a long-acting indirect factor Xa inhibitor: population pharmacokinetic analysis from Phase III clinical trials. Journal of Thrombosis & Haemostasis 2009; 7(4):559-65. *Not CKD treatment*

4554. Vezyroglou G, Mitropoulos A, Antoniadis C. A metabolic syndrome in diffuse idiopathic skeletal hyperostosis. A controlled study.[Erratum appears in J Rheumatol 1997 Aug;24(8):1665]. Journal of Rheumatology 1996; 23(4):672-6. *Not CKD treatment*

4555. Viallet NR, Blakley BW, Begleiter A, et al. Effect of sodium thiosulphate and cis-diamminedichloroplatinum on FADU tumour cells in nude mice. Journal of Otolaryngology 2005; 34(6):371-3. *Not RCT or controlled trial*

4556. Viberti G. Regression of albuminuria: latest evidence for a new approach. Journal of Hypertension - Supplement 2003; 21(3):S24-8. *Not RCT or controlled trial*

4557. Viberti G, Mogensen CE, Groop LC, et al. Effect of captopril on progression to clinical proteinuria in patients with insulin-dependent diabetes mellitus and microalbuminuria. European Microalbuminuria Captopril Study Group. JAMA 1994; 271(4):275-9. *Not relevant to key questions*

4558. Viberti G, Slama G, Pozza G, et al. Early closure of European Pimagedine trial. Steering Committee. Safety Committee. Lancet 1997; 350(9072):214-5. *Not RCT or controlled trial*

4559. Viberti G, Wheeldon NM, MicroAlbuminuria Reduction With VSI. Microalbuminuria reduction with valsartan in patients with type 2 diabetes mellitus: a blood pressure-independent effect. Circulation 2002; 106(6):672-8. *Follow-up less than 6 months*

4560. Vidt DG. Clinical trials report. The effect of Ramipril versus Amlodipine on renal outcomes in hypertension nephrosclerosis. Current Hypertension Reports 2001; 3(5):379-80. *Not RCT or controlled trial*

4561. Vidt DG, Cressman MD, Harris S, et al. Rosuvastatin-induced arrest in progression of renal disease. Cardiology 2004; 102(1):52-60. *Not RCT or controlled trial*

4562. Vidt DG, Harris S, McTaggart F, et al. Effect of short-term rosuvastatin treatment on estimated glomerular filtration rate. American Journal of Cardiology 2006; 97(11):1602-6. *Not relevant to key questions*

4563. Viele MK, Weiskopf RB, Fisher D. Recombinant human hemoglobin does not affect renal function in humans: analysis of safety and pharmacokinetics. Anesthesiology 1997; 86(4):848-58. *Sample size less than 50 patients*

4564. Vigano G, Benigni A, Mendogni D, et al. Recombinant human erythropoietin to correct uremic bleeding. American Journal of Kidney Diseases 1991; 18(1):44-9. *Sample size less than 50 patients*

4565. Vigano GL, Mannucci PM, Lattuada A, et al. Subcutaneous desmopressin (DDAVP) shortens the bleeding time in uremia. American Journal of Hematology 1989; 31(1):32-5. *Not CKD treatment*

4566. Vigneau C, Ardiet C, Bret M, et al. Intermediate-dose (25mg/m2) IV melphalan for multiple myeloma with renal failure. Journal of Nephrology 2002; 15(6):684-9. *Not CKD treatment*

4567. Vijan S, Stevens DL, Herman WH, et al. Screening, prevention, counseling, and treatment for the complications of type II diabetes mellitus. Putting evidence into practice. Journal of General Internal Medicine 1997; 12(9):567-80. *Not RCT or controlled trial*

4568. Vijay SK, Mishra M, Kumar H, et al. Effect of pioglitazone and rosiglitazone on mediators of endothelial dysfunction, markers of angiogenesis and inflammatory cytokines in type-2 diabetes. Acta Diabetologica 2009; 46(1):27-33. *Not CKD treatment*

4569. Vijayan A, Franklin SC, Behrend T, et al. Insulin-like growth factor I improves renal function in patients with end-stage chronic renal failure. American Journal of Physiology 1999; 276(4 Pt 2):R929-34. *Follow-up less than 6 months*

4570. Vilarrasa N, Soler J, Montanya E. Regression of microalbuminuria in type 1 diabetic patients: results of a sequential intervention with improved metabolic control and ACE inhibitors. Acta Diabetologica 2005; 42(2):87-94. *Follow-up less than 6 months*

4571. Vilayur E, Harris DCH. Emerging therapies for chronic kidney disease: what is their role? Nature Reviews Nephrology 2009; 5(7):375-83. *Not RCT or controlled trial*

4572. Vimalachandra D, Craig JC, Cowell CT, et al. Growth hormone treatment in children with chronic renal failure: a meta-analysis of randomized controlled trials. Journal of Pediatrics 2001; 139(4):560-7. *Not adult population*

4573. Vincent J-L. Evidence-based medicine in the ICU: important advances and limitations. Chest 2004; 126(2):592-600. *Not relevant to key questions*

4574. Vincent JL. Do we need a dopaminergic agent in the management of the critically ill? Journal of Autonomic Pharmacology 1990; 10 Suppl 1:s123-7. *Not CKD treatment*

4575. Vincent JL, Biston P, Devriendt J, et al. Dopamine versus norepinephrine: is one better? Minerva Anestesiologica 2009; 75(5):333-7. *Not early CKD*

4576. Vinik AI, Bril V, Kempler P, et al. Treatment of symptomatic diabetic peripheral neuropathy with the protein kinase C beta-inhibitor ruboxistaurin mesylate during a 1-year, randomized, placebo-controlled, double-blind clinical trial. Clinical Therapeutics 2005; 27(8):1164-80. *Not CKD treatment*

4577. Virani SA. Management of acute decompensated heart failure: renal implications. Blood Purification 2008; 26(1):18-22. *Not CKD treatment*

4578. Virani SA, Khosla A, Levin A. Chronic kidney disease, heart failure and anemia. Canadian Journal of Cardiology 2008; 24 Suppl B:22B-4B. *Not RCT or controlled trial*

4579. Virani SA, Khosla A, Levin A. Chronic kidney disease, heart failure and anemia. Canadian Journal of Cardiology 2008; 24 Suppl B:22B-4B. *Not CKD treatment*

4580. Visser FW, Boonstra AH, Titia Lely A, et al. Renal response to angiotensin II is blunted in sodium-sensitive normotensive men. American Journal of Hypertension 2008; 21(3):323-8. *Not RCT or controlled trial*

4581. Vita E, Schroeder DJ. Intralipid in prophylaxis of amphotericin B nephrotoxicity. Annals of Pharmacotherapy 1994; 28(10):1182-3. *Not CKD treatment*

4582. Vivian EM, Rubinstein GB. Pharmacologic management of diabetic nephropathy. Clinical Therapeutics 2002; 24(11):1741-56; discussion 19. *Not relevant to key questions*

4583. Vlachogiannakos J, Tang AK, Patch D, et al. Angiotensin converting enzyme inhibitors and angiotensin II antagonists as therapy in chronic liver disease. Gut 2001; 49(2):303-8. *Not RCT or controlled trial*

4584. Vlagopoulos PT, Sarnak MJ. Traditional and nontraditional cardiovascular risk factors in chronic kidney disease. Medical Clinics of North America 2005; 89(3):587-611. *Not RCT or controlled trial*

4585. Voelker JR, Cartwright-Brown D, Anderson S, et al. Comparison of loop diuretics in patients with chronic renal insufficiency. Kidney International 1987; 32(4):572-8. *Not relevant to key questions*

4586. Vogt L, Chiurchiu C, Chadha-Boreham H, et al. Effect of the urotensin receptor antagonist palosuran in hypertensive patients with type 2 diabetic nephropathy. Hypertension 2010 May; 55(5):1206-9. *Follow-up less than 6 months*

4587. Vogt L, de Zeeuw D, Woittiez AJJ, et al. Selective cyclooxygenase-2 (COX-2) inhibition reduces proteinuria in renal patients. Nephrology Dialysis Transplantation 2009; 24(4):1182-9. *Not RCT or controlled trial*

4588. Vogt L, Kocks MJA, Laverman GD, et al. Renoprotection by blockade of the renin-angiotensin-aldosterone system in diabetic and non-diabetic chronic kidney disease. Specific involvement of intra-renal angiotensin-converting enzyme activity in therapy resistance? Minerva Medica 2004; 95(5):395-409. *Sample size less than 50 patients*

4589. Vogt L, Navis G, Koster J, et al. The angiotensin II receptor antagonist telmisartan reduces urinary albumin excretion in patients with isolated systolic hypertension: results of a randomized, double-blind, placebo-controlled trial. Journal of Hypertension 2005; 23(11):2055-61. *Follow-up less than 6 months*

4590. Vogt L, Waanders F, Boomsma F, et al. Effects of dietary sodium and hydrochlorothiazide on the antiproteinuric efficacy of losartan. Journal of the American Society of Nephrology 2008; 19(5):999-1007. *Not CKD treatment*

4591. von Baeyer H. Plasmapheresis in thrombotic microangiopathy-associated syndromes: review of outcome data derived from clinical trials and open studies. Therapeutic Apheresis 2002; 6(4):320-8. *Not CKD treatment*

4592. Vonend O, Marsalek P, Russ H, et al. Moxonidine treatment of hypertensive patients with advanced renal failure. Journal of Hypertension 2003; 21(9):1709-17. *Not early CKD*

4593. Vonesh EF, Greene T, Schluchter MD. Shared parameter models for the joint analysis of longitudinal data and event times. Statistics in Medicine 2006; 25(1):143-63. *Not relevant to key questions*

4594. Vongterapak S, Dahlan W, Nakasatien S, et al. Impediment of the progressions of microalbuminuria and hyperlipidemia in normotensive type 2 diabetes by low-dose ramipril. Journal of the Medical Association of Thailand 1998; 81(9):671-81. *Sample size less than 50 patients*

4595. Vora JP, Hendre TJ, Atiea J, et al. Renal haemodynamics during short-term angiotensin converting enzyme inhibition in normotensive normoalbuminuric insulin dependent diabetics. Diabetes Research 1989; 11(1):9-12. *Sample size less than 50 patients*

4596. Vora JP, Leese GP, Peters JR, et al. Longitudinal evaluation of renal function in non-insulin-dependent diabetic patients with early nephropathy: effects of angiotensin-converting enzyme inhibition. Journal of Diabetes & its Complications 1996; 10(2):88-93. *Not RCT or controlled trial*

4597. Vora JP, Owens DR, Ryder R, et al. Effect of somatostatin on renal function. British Medical Journal Clinical Research Ed. 1986; 292(6537):1701-2. *Sample size less than 50 patients*

4598. Vorobioff J, Picabea E, Gamen M, et al. Propranolol compared with propranolol plus isosorbide dinitrate in portal-hypertensive patients: long-term hemodynamic and renal effects. Hepatology 1993; 18(3):477-84. *Sample size less than 50 patients*

4599. Voyaki SM, Staessen JA, Thijs L, et al. Follow-up of renal function in treated and untreated older patients with isolated systolic hypertension. Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Journal of Hypertension 2001; 19(3):511-9. *Not early CKD*

4600. Vriesendorp R, Donker AJ, de Zeeuw D, et al. Antiproteinuric effect of naproxen and indomethacin. A double-blind crossover study. American Journal of Nephrology 1985; 5(4):236-42. *Sample size less than 50 patients*

4601. Vuong AD, Annis LG. Ramipril for the prevention and treatment of cardiovascular disease. Annals of Pharmacotherapy 2003; 37(3):412-9. *Not RCT or controlled trial*

4602. Vuurmans JLT, Boer P, Koomans HA. Effects of endothelin-1 and endothelin-1-receptor blockade on renal function in humans. Nephrology Dialysis Transplantation 2004; 19(11):2742-6. *Not CKD treatment*

4603. Waanders F, Vaidya VS, van Goor H, et al. Effect of renin-angiotensin-aldosterone system inhibition, dietary sodium restriction, and/or diuretics on urinary kidney injury molecule 1 excretion in nondiabetic proteinuric kidney disease: a post hoc analysis of a randomized controlled trial. American Journal of Kidney Diseases 2009; 53(1):16-25. *Not CKD treatment*

4604. Wada L, Don BR, Schambelan M. Hormonal mediators of amino acid-induced glomerular hyperfiltration in humans. American Journal of Physiology 1991; 260(6 Pt 2):F787-92. *Not CKD treatment*

4605. Wade VL, Gleason BL. Dual blockade of the renin-angiotensin system in diabetic nephropathy. Annals of Pharmacotherapy 2004; 38(7-8):1278-82. *Not CKD treatment*

4606. Waeber B, Burnier M, Nussberger J, et al. Experience with angiotensin II antagonists in hypertensive patients. Clinical & Experimental Pharmacology & Physiology - Supplement 1996; 3:S142-6. *Not RCT or controlled trial*

4607. Waeber B, de la Sierra A, Ruilope LM. The ADVANCE trial: clarifying the role of perindopril/indapamide fixed-dose combination in the reduction of cardiovascular and renal events in patients with diabetes mellitus. American Journal of Cardiovascular Drugs 2009; 9(5):283-91. *Not RCT or controlled trial*

4608. Wagner EA, Falciglia GA, Amlal H, et al. Short-term exposure to a high-protein diet differentially affects glomerular filtration rate but not Acid-base balance in older compared to younger adults. Journal of the American Dietetic Association 2007; 107(8):1404-8. *Sample size less than 50 patients*

4609. Wagner F, Yeter R, Bisson S, et al. Beneficial hemodynamic and renal effects of intravenous enalaprilat following coronary artery bypass surgery complicated by left ventricular dysfunction. Critical Care Medicine 2003; 31(5):1421-8. *Sample size less than 50 patients*

4610. Wahbah AM, el-Hefny MO, Wafa EM, et al. Perioperative renal protection in patients with obstructive jaundice using drug combinations. Hepato-Gastroenterology 2000; 47(36):1691-4. *Sample size less than 50 patients*

4611. Wahbha MM, Wilson J, Hainsworth R. Cardiovascular responses to upright tilting in hypertensive patients, with and without renal impairment and before and following nisoldipine treatment. British Journal of Clinical Pharmacology 1990; 29(6):733-9. *Not relevant to key questions*

4612. Wahlers T, Kotzerke B, Wagenbreth I, et al. Preventive treatment of renal impairment and graft rejection in cardiac transplantation using cyclosporine with an oral prostaglandin analog. Transplantation Proceedings 1994; 26(5):2743-4. *Sample size less than 50 patients*

4613. Wake N, Hisashige A, Katayama T, et al. Cost-effectiveness of intensive insulin therapy for type 2 diabetes: a 10-year follow-up of the Kumamoto study. Diabetes Research & Clinical Practice 2000; 48(3):201-10. *Not CKD treatment*

4614. Walker BJ, Evans PA, Forsling ML, et al. Somatostatin and water excretion in man: an intrarenal action. Clinical Endocrinology 1985; 23(2):169-74. *Sample size less than 50 patients*

4615. Walker BR, Connacher AA, Webb DJ, et al. Glucocorticoids and blood pressure: a role for the cortisol/cortisone shuttle in the control of vascular tone in man. Clinical Science 1992; 83(2):171-8. *Not CKD treatment*

4616. Walker PD, Brokering KL, Theobald JC. Fenoldopam and N-acetylcysteine for the prevention of radiographic contrast material-induced nephropathy: a review. Pharmacotherapy 2003; 23(12):1617-26. *Sample size less than 50 patients*

4617. Walker RG, Strippoli GFM. A pegylated epoetin in anaemia of renal disease: non-inferiority for an unvalidated surrogate. Lancet 2007; 370(9596):1395-6. *Follow-up less than 6 months*

4618. Walker SL, Fine A, Kryger MH. L-DOPA/carbidopa for nocturnal movement disorders in uremia. Sleep 1996; 19(3):214-8. *Not CKD treatment*

4619. Walker WG, Neaton JD, Cutler JA, et al. Renal function change in hypertensive members of the Multiple Risk Factor Intervention Trial. Racial and treatment effects. The MRFIT Research Group. JAMA 1992; 268(21):3085-91. *Not CKD treatment*

4620. Wall BM, Hardison RM, Molitch ME, et al. High prevalence and diversity of kidney dysfunction in patients with type 2 diabetes mellitus and coronary artery disease: the BARI 2D baseline data. American Journal of the Medical Sciences 2010 May; 339(5):401-10. *Not RCT or controlled trial*

4621. Waller DG, Ramsay B, Fleming JS, et al. Longitudinal assessment of glomerular filtration rate by gamma camera and portable external detector. European Journal of Nuclear Medicine 1987; 13(8):402-3. *Sample size less than 50 patients*

4622. Wallin JD, Frishman WH. Dilevalol: a selective beta-2 adrenergic agonist vasodilator with beta adrenergic blocking activity. Journal of Clinical Pharmacology 1989; 29(12):1057-68. *Not relevant to key questions*

4623. Wallis PJ, Lodwick R, Sinha SK, et al. Effect of naproxen on renal haemodynamics in elderly patients with arthritis. Age & Ageing 1989; 18(1):26-30. *Sample size less than 50 patients*

4624. Walrand S, Short KR, Bigelow ML, et al. Functional impact of high protein intake on healthy elderly people. American Journal of Physiology - Endocrinology & Metabolism 2008; 295(4):E921-8. *Not CKD treatment*

4625. Walser M, Hill SB, Ward L, et al. A crossover comparison of progression of chronic renal failure: ketoacids versus amino acids. Kidney International 1993; 43(4):933-9. *Follow-up less than 6 months*

4626. Walsh SR, Boyle JR, Tang TY, et al. Remote ischemic preconditioning for renal and cardiac protection during endovascular aneurysm repair: a randomized controlled trial. Journal of Endovascular Therapy: Official Journal of the International Society of Endovascular Specialists 2009; 16(6):680-9. *Sample size less than 50 patients*

4627. Walsh TJ, Finberg RW, Arndt C, et al. Liposomal amphotericin B for empirical therapy in patients with persistent fever and neutropenia. National Institute of Allergy and Infectious Diseases Mycoses Study Group. New England Journal of Medicine 1999; 340(10):764-71. *Not CKD treatment*

4628. Walters MR, Bolster A, Dyker AG, et al. Effect of perindopril on cerebral and renal perfusion in stroke patients with carotid disease. Stroke 2001; 32(2):473-8. *Not CKD treatment*

4629. Wang A, Holcslaw T, Bashore TM, et al. Exacerbation of radiocontrast nephrotoxicity by endothelin receptor antagonism. Kidney International 2000; 57(4):1675-80. *Not early CKD*

4630. Wang DJ, Dowling TC, Meadows D, et al. Nesiritide does not improve renal function in patients with chronic heart failure and worsening serum creatinine. Circulation 2004; 110(12):1620-5. *Not CKD treatment*

4631. Wang F, Lu F, Xu L. Effects of Houttuynia cordata thumb on expression of BMP-7 and TGF-beta1 in the renal tissues of diabetic rats. Journal of Traditional Chinese Medicine 2007; 27(3):220-5. *Not RCT or controlled trial*

4632. Wang G, Lai FM-M, Lai K-B, et al. Urinary messenger RNA expression of podocyte-associated molecules in patients with diabetic nephropathy treated by angiotensin-converting enzyme inhibitor and angiotensin receptor blocker. European Journal of Endocrinology 2008; 158(3):317-22. *Not RCT or controlled trial*

4633. Wang H, Deng JL, Yue J, et al. Prostaglandin E1 for preventing the progression of diabetic kidney disease. Cochrane Database of Systematic Reviews 2010; (5):CD006872. *Not CKD treatment*

4634. Wang J-G, Li Y, Franklin SS, et al. Prevention of stroke and myocardial infarction by amlodipine and Angiotensin receptor blockers: a quantitative overview. Hypertension 2007; 50(1):181-8. *Not adult population*

4635. Wang PH, Lau J, Chalmers TC. Metaanalysis of the effects of intensive glycemic control on late complications of type I diabetes mellitus. Online Journal of Current Clinical Trials 1993; Doc No 60:[5023 words; 37 paragraphs]. *Not CKD treatment*

4636. Wang Q-L, Yuan J-L, Tao Y-Y, et al. Fuzheng Huayu recipe and vitamin E reverse renal interstitial fibrosis through counteracting TGF-beta1-induced epithelial-to-mesenchymal transition. Journal of Ethnopharmacology 2010 Feb 17; 127(3):631-40. *Not human studies*

4637. Wang SL, Head J, Stevens L, et al. Excess mortality and its relation to hypertension and proteinuria in diabetic patients. The world health organization multinational study of vascular disease in diabetes. Diabetes Care 1996; 19(4):305-12. *Not RCT or controlled trial*

4638. Wang X, Lewis J, Appel L, et al. Validation of creatinine-based estimates of GFR when evaluating risk factors in longitudinal studies of kidney disease. Journal of the American Society of Nephrology 2006; 17(10):2900-9. *Not relevant to key questions*

4639. Wang X, Xie Z. A clinical study on the effect of reinforcement of kidney on senile brain functions. Journal of Traditional Chinese Medicine 1997; 17(2):92-5. *Not RCT or controlled trial*

4640. Wanner C. Prevention of cardiovascular disease in chronic kidney disease patients. Seminars in Nephrology 2009; 29(1):24-9. *Not RCT or controlled trial*

4641. Ward RA, Buscaroli A, Schmidt B, et al. A comparison of dialysers with low-flux membranes: significant differences in spite of many similarities. Nephrology Dialysis Transplantation 1997; 12(5):965-72. *Not CKD treatment*

4642. Wardle EN. Soyprotein diet therapy in renal disease. Nephron 1998; 78(3):328-31. *Not RCT or controlled trial*

4643. Warrell RP, Jr., Skelos A, Alcock NW, et al. Gallium nitrate for acute treatment of cancer-related hypercalcemia: clinicopharmacological and dose response analysis. Cancer Research 1986; 46(8):4208-12. *Follow-up less than 6 months*

4644. Warren MM, Boyce WH, Evans JW, et al. A double-blind comparison of dezocine and morphine in patients with acute renal and ureteral colic. Journal of Urology 1985; 134(3):457-9. *Not RCT or controlled trial*

4645. Warrington SJ, Lewis Y, Dawnay A, et al. Renal and gastrointestinal tolerability of lornoxicam, and effects on haemostasis and hepatic microsomal oxidation. Postgraduate Medical Journal 1990; 66 Suppl 4:S35-40. *Not CKD treatment*

4646. Warrington SJ, Ravic M, Dawnay A. Renal and general tolerability of repeated doses of nimesulide in normal subjects. Drugs 1993; 46 Suppl 1:263-9. *Sample size less than 50 patients*

4647. Waser M, Maggiorini M, Binswanger U, et al. Irreversibility of cyclosporine-induced renal function impairment in heart transplant recipients. Journal of Heart & Lung Transplantation 1993; 12(5):846-50. *Sample size less than 50 patients*

4648. Waslen TA, McCauley FA, Wilson TW. Sulindac does not spare renal prostaglandins. Clinical & Investigative Medicine - Medecine Clinique et Experimentale 1989; 12(2):77-81. *Sample size less than 50 patients*

4649. Watanabe G, Tomiyama H, Doba N. Effects of oral administration of L-arginine on renal function in patients with heart failure. Journal of Hypertension 2000; 18(2):229-34. *Sample size less than 50 patients*

4650. Waters DD. Clinical insights from the Treating to New Targets trial. Progress in Cardiovascular Diseases 2009; 51(6):487-502. *Not CKD treatment*

4651. Watson AJ, Gimenez LF, Cotton S, et al. Treatment of the anemia of chronic renal failure with subcutaneous recombinant human erythropoietin. American Journal of Medicine 1990; 89(4):432-5. *Sample size less than 50 patients*

4652. Watson CJE, Gimson AES, Alexander GJ, et al. A randomized controlled trial of late conversion from calcineurin inhibitor (CNI)-based to sirolimus-based immunosuppression in liver transplant recipients with impaired renal function. Liver Transplantation 2007; 13(12):1694-702. *Not RCT or controlled trial*

4653. Watson WA, Freer JP, Katz RS, et al. Kidney function during naproxen therapy in patients at risk for renal insufficiency. Seminars in Arthritis & Rheumatism 1988; 17(3 Suppl 2):12-6. *Sample size less than 50 patients*

4654. Watson WJ. Screening for glycosuria during pregnancy. Southern Medical Journal 1990; 83(2):156-8. *Not CKD treatment*

4655. Waugh NR, Robertson AM. Protein restriction for diabetic renal disease. Cochrane Database of Systematic Reviews 2000; (2):CD002181. *Not relevant to key questions*

4656. Weathers LW, Ziada KM. Drug-eluting stents in patients with end-stage renal disease. Minerva Cardioangiologica 2008; 56(1):117-25. *Not early CKD*

4657. Webb JG, Pate GE, Humphries KH, et al. A randomized controlled trial of intravenous N-acetylcysteine for the prevention of contrast-induced nephropathy after cardiac catheterization: lack of effect. American Heart Journal 2004; 148(3):422-9. *Not CKD treatment*

4658. Weber M. Clinical safety and tolerability of losartan. Clinical Therapeutics 1997; 19(4):604-16; discussion 3. *Not relevant to key questions*

4659. Weber MA. Clinical implications of aldosterone blockade. American Heart Journal 2002; 144(5 Suppl):S12-8. *Not relevant to key questions*

4660. Weber MA. New opportunities in cardiovascular patient management: a survey of clinical data on the combination of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. American Journal of Cardiology 2007; 100(3A):45J-52J. *Follow-up less than 6 months*

4661. Weekers L, Bouhanick B, Hadjadj S, et al. Modulation of the renal response to ACE inhibition by ACE insertion/deletion polymorphism during hyperglycemia in normotensive, normoalbuminuric type 1 diabetic patients. Diabetes 2005; 54(10):2961-7. *Not CKD treatment*

4662. Weidmann P. Metabolic profile of indapamide sustained-release in patients with hypertension: data from three randomised double-blind studies. Drug Safety 2001; 24(15):1155-65. *Not RCT or controlled trial*

4663. Weidmann P, Gnadinger MP, Schohn D, et al. Antihypertensive and hypouricaemic effects of nitrendipine in chronic renal failure. European Journal of Clinical Pharmacology 1989; 36(3):223-7. *Sample size less than 50 patients*

4664. Weidmann P, Schohn D, Gnadinger MP, et al. Hypertensive dysregulation and its modification by calcium channel blockade in nonoliguric renal failure. American Journal of Nephrology 1989; 9(4):269-78. *Sample size less than 50 patients*

4665. Weinberg JM, Appel LJ, Bakris G, et al. Risk of hyperkalemia in nondiabetic patients with chronic kidney disease receiving antihypertensive therapy. Archives of Internal Medicine 2009; 169(17):1587-94. *Not CKD treatment*

4666. Weinblatt ME, Germain BF, Kremer JM, et al. Lack of a renal-protective effect of misoprostol in rheumatoid arthritis patients receiving cyclosporin A. Results of a randomized, placebo-controlled trial. Arthritis & Rheumatism 1994; 37(9):1321-5. *Not CKD treatment*

4667. Weiner DE, Rifkin DE. Kidney function and the risk of cardiovascular disease. BMJ 2009; 338:b1307. *Not RCT or controlled trial*

4668. Weiner DE, Sarnak MJ. Managing dyslipidemia in chronic kidney disease. Journal of General Internal Medicine 2004; 19(10):1045-52. *Not RCT or controlled trial*

4669. Weinhandl H, Pachler C, Mader JK, et al. Physiological hyperinsulinemia has no detectable effect on access of macromolecules to insulin-sensitive tissues in healthy humans. Diabetes 2007; 56(9):2213-7. *Not RCT or controlled trial*

4670. Weinrauch LA, Burger AJ, Aepfelbacher F, et al. A pilot study to test the effect of pulsatile insulin infusion on cardiovascular mechanisms that might contribute to attenuation of renal compromise in type 1 diabetes mellitus patients with proteinuria. Metabolism: Clinical & Experimental 2007; 56(11):1453-7. *Follow-up less than 6 months*

4671. Weinrauch LA, Kennedy FJ, Burger A, et al. Prospective evaluation of autonomic dysfunction in aggressive management of diabetic microangiopathy. American Journal of Hypertension 1999; 12(11 Pt 1):1135-9. *Sample size less than 50 patients*

4672. Weinrauch LA, Sun J, Gleason RE, et al. Pulsatile intermittent intravenous insulin therapy for attenuation of retinopathy and nephropathy in type 1 diabetes mellitus. Metabolism: Clinical & Experimental 2010 Oct; 59(10):1429-34. *Not relevant to key questions*

4673. Weinstein JM, Heyman S, Brezis M. Potential deleterious effect of furosemide in radiocontrast nephropathy. Nephron 1992; 62(4):413-5. *Sample size less than 50 patients*

4674. Weir MR. The role of combination antihypertensive therapy in the prevention and treatment of chronic kidney disease. American Journal of Hypertension 2005; 18(4 Pt 2):100S-5S. *Sample size less than 50 patients*

4675. Weir MR. Effects of renin-angiotensin system inhibition on end-organ protection: can we do better? Clinical Therapeutics 2007; 29(9):1803-24. *Not relevant to key questions*

4676. Weir MR. The renoprotective effects of RAS inhibition: focus on prevention and treatment of chronic kidney disease. Postgraduate Medicine 2009; 121(1):96-103. *Not CKD treatment*

4677. Weir MR, Dengel DR, Behrens MT, et al. Salt-induced increases in systolic blood pressure affect renal hemodynamics and proteinuria. Hypertension 1995; 25(6):1339-44. *Sample size less than 50 patients*

4678. Weir MR, Hollenberg NK, Zappe DH, et al. Antihypertensive effects of double the maximum dose of valsartan in African-American patients with type 2 diabetes mellitus and albuminuria. Journal of Hypertension 2010; 28(1):186-93. *Not CKD treatment*

4679. Weir MR, Klassen DK, Hall PS, et al. Minimization of indomethacin-induced reduction in renal function by misoprostol. Journal of Clinical Pharmacology 1991; 31(8):729-35. *Sample size less than 50 patients*

4680. Weisberg LS, Kurnik PB, Kurnik BR. Dopamine and renal blood flow in radiocontrast-induced nephropathy in humans. Renal Failure 1993; 15(1):61-8. *Not CKD treatment*

4681. Weisberg LS, Kurnik PB, Kurnik BR. Risk of radiocontrast nephropathy in patients with and without diabetes mellitus. Kidney International 1994; 45(1):259-65. *Not CKD treatment*

4682. Weisbord SD, Bruns FJ, Saul MI, et al. Provider use of preventive strategies for radiocontrast nephropathy in high-risk patients. Nephron 2004; 96(2):c56-62. *Not relevant to key questions*

4683. Weisbord SD, Palevsky PM. Radiocontrast-induced acute renal failure. Journal of Intensive Care Medicine 2005; 20(2):63-75. *Not RCT or controlled trial*

4684. Weiss JW, Johnson ES, Petrik A, et al. Systolic blood pressure and mortality among older community-dwelling adults with CKD. American Journal of Kidney Diseases 2010 Dec; 56(6):1062-71. *Not CKD treatment*

4685. Weiss MF, Rodby RA, Justice AC, et al. Free pentosidine and neopterin as markers of progression rate in diabetic nephropathy. Collaborative Study Group. Kidney International 1998; 54(1):193-202. *Not RCT or controlled trial*

4686. Welch M, Newstead CG, Smyth JV, et al. Evaluation of dopexamine hydrochloride as a renoprotective agent during aortic surgery. Annals of Vascular Surgery 1995; 9(5):488-92. *Not CKD treatment*

4687. Wellenius GA, Mukamal KJ, Winkelmayer WC, et al. Renal dysfunction increases the risk of saphenous vein graft occlusion: results from the Post-CABG trial. Atherosclerosis 2007; 193(2):414-20. *Not early CKD*

4688. Wellington K, Goa KL. Zoledronic acid: a review of its use in the management of bone metastases and hypercalcaemia of malignancy. Drugs 2003; 63(4):417-37. *Not CKD treatment*

4689. Welz S, Hehr T, Kollmannsberger C, et al. Renal toxicity of adjuvant chemoradiotherapy with cisplatin in gastric cancer. International Journal of Radiation Oncology, Biology, Physics 2007; 69(5):1429-35. *Not RCT or controlled trial*

4690. Wenger NK. Lipid metabolism, physical activity, and postmenopausal hormone therapy. American Journal of Kidney Diseases 1998; 32(5 Suppl 3):S80-8. *Not RCT or controlled trial*

4691. Wennberg A, Hyltander A, Sjoberg A, et al. Prevalence of carnitine depletion in critically ill patients with undernutrition. Metabolism: Clinical & Experimental 1992; 41(2):165-71. *Not CKD treatment*

4692. Wenzel RR. Renal protection in hypertensive patients: selection of antihypertensive therapy. Drugs 2005; 65 Suppl 2:29-39. *Not RCT or controlled trial*

4693. Wenzel RR, Littke T, Kuranoff S, et al. Avosentan reduces albumin excretion in diabetics with macroalbuminuria. Journal of the American Society of Nephrology 2009; 20(3):655-64. *Follow-up less than 6 months*

4694. West SL, Swan VJD, Jamal SA. Effects of calcium on cardiovascular events in patients with kidney disease and in a healthy population. Clinical Journal of The American Society of Nephrology: CJASN 2010 Jan; 5 Suppl 1:S41-7. *Not RCT or controlled trial*

4695. Westberg G, Tarkowski A. Effect of MaxEPA in patients with SLE. A double-blind, crossover study. Scandinavian Journal of Rheumatology 1990; 19(2):137-43. *Not CKD treatment*

4696. Westermann D, Savvatis K, Schultheiss HP, et al. Rational of the use of aliskiren in hypertension and beyond. Minerva Cardioangiologica 2009 Dec; 57(6):761-72. *Not RCT or controlled trial*

4697. Westhuyzen J, Endre ZH, Reece G, et al. Measurement of tubular enzymuria facilitates early detection of acute renal impairment in the intensive care unit. Nephrology Dialysis Transplantation 2003; 18(3):543-51. *Not CKD treatment*

4698. Wetzels JF, van Bergeijk JD, Hoitsma AJ, et al. Triamterene increases lithium excretion in healthy subjects: evidence for lithium transport in the cortical collecting tubule. Nephrology Dialysis Transplantation 1989; 4(11):939-42. *Not CKD treatment*

4699. Wetzels JFM. Letter by Wetzels regarding article, "Renal Insufficiency Following Contrast Media Administration Trial (REMEDIAL): a randomized comparison of 3 preventive strategies". Circulation 2007; 116(8):e310; author reply e1. *Sample size less than 50 patients*

4700. Wetzels JFM, Kiemeney LALM, Swinkels DW, et al. Age- and gender-specific reference values of estimated GFR in Caucasians: the Nijmegen Biomedical Study. Kidney International 2007; 72(5):632-7. *Not relevant to key questions*

4701. Wexler D, Silverberg D, Blum M, et al. Anaemia as a contributor to morbidity and mortality in congestive heart failure. Nephrology Dialysis Transplantation 2005; 20 Suppl 7:vii11-5. *Not RCT or controlled trial*

4702. Wheeler ML, Fineberg SE, Fineberg NS, et al. Animal versus plant protein meals in individuals with type 2 diabetes and microalbuminuria: effects on renal, glycemic, and lipid parameters. Diabetes Care 2002; 25(8):1277-82. *Sample size less than 50 patients*

4703. Whelton A, Fort JG, Puma JA, et al. Cyclooxygenase-2--specific inhibitors and cardiorenal function: a randomized, controlled trial of celecoxib and rofecoxib in older hypertensive osteoarthritis patients.[Erratum appears in Am J Ther 2001 May-Jun;8(3):220]. American Journal of Therapeutics 2001; 8(2):85-95. *Not early CKD*

4704. Whelton A, Lefkowith JL, West CR, et al. Cardiorenal effects of celecoxib as compared with the nonsteroidal anti-inflammatory drugs diclofenac and ibuprofen. Kidney International 2006; 70(8):1495-502. *Not RCT or controlled trial*

4705. Whelton A, Maurath CJ, Verburg KM, et al. Renal safety and tolerability of celecoxib, a novel cyclooxygenase-2 inhibitor. American Journal of Therapeutics 2000; 7(3):159-75. *Not CKD treatment*

4706. Whelton A, Schulman G, Wallemark C, et al. Effects of celecoxib and naproxen on renal function in the elderly. Archives of Internal Medicine 2000; 160(10):1465-70. *Not early CKD*

4707. Whelton A, Stout RL, Spilman PS, et al. Renal effects of ibuprofen, piroxicam, and sulindac in patients with asymptomatic renal failure. A prospective, randomized, crossover comparison. Annals of Internal Medicine 1990; 112(8):568-76. *Sample size less than 50 patients*

4708. Whelton PK, Klag MJ. Hypertension as a risk factor for renal disease. Review of clinical and epidemiological evidence. Hypertension 1989; 13(5 Suppl):I19-27. *Not relevant to key questions*

4709. Whelton PK, Lee JY, Kusek JW, et al. Recruitment experience in the African American Study of Kidney Disease and Hypertension (AASK) Pilot Study. Controlled Clinical Trials 1996; 17(4 Suppl):17S-33S. *Not RCT or controlled trial*

4710. Whitcup SM, Salvo EC, Jr., Nussenblatt RB. Combined cyclosporine and corticosteroid therapy for sight-threatening uveitis in Behcet's disease. American Journal of Ophthalmology 1994; 118(1):39-45. *Not CKD treatment*

4711. White CM. Pharmacologic, pharmacokinetic, and therapeutic differences among ACE inhibitors. Pharmacotherapy 1998; 18(3):588-99. *Not RCT or controlled trial*

4712. White CT, Macpherson CF, Hurley RM, et al. Antiproteinuric effects of enalapril and losartan: a pilot study. Pediatric Nephrology 2003; 18(10):1038-43. *Sample size less than 50 patients*

4713. White HD, Gallo R, Cohen M, et al. The use of intravenous enoxaparin in elective percutaneous coronary intervention in patients with renal impairment: results from the SafeTy and Efficacy of Enoxaparin in PCI patients, an internationaL randomized Evaluation (STEEPLE) trial. American Heart Journal 2009; 157(1):125-31. *Not CKD treatment*

4714. White IR, Royston P. Imputing missing covariate values for the Cox model. Statistics in Medicine 2009; 28(15):1982-98. *Not RCT or controlled trial*

4715. White KE, Bilous RW, Marshall SM, et al. Podocyte number in normotensive type 1 diabetic patients with albuminuria. Diabetes 2002; 51(10):3083-9. *Not CKD treatment*

4716. White KE, Pinel N, Cordonnier DJ, et al. Does ACE inhibition slow progression of glomerulopathy in patients with Type 2 diabetes mellitus? Diabetic Medicine 2001; 18(11):933-6. *Sample size less than 50 patients*

4717. White SL, Polkinghorne KR, Atkins RC, et al. Comparison of the prevalence and mortality risk of CKD in Australia using the CKD Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) Study GFR estimating equations: the AusDiab (Australian Diabetes, Obesity and Lifestyle) Study. American Journal of Kidney Diseases 2010 Apr; 55(4):660-70. *Not relevant to key questions*

4718. White WB, Halley SE. Comparative renal effects of intravenous administration of fenoldopam mesylate and sodium nitroprusside in patients with severe hypertension. Archives of Internal Medicine 1989; 149(4):870-4. *Sample size less than 50 patients*

4719. Whitworth JA, Gordon D, Harpley R, et al. Acute hormonal and renal effects of oral dilevalol in normal men. Clinical & Experimental Pharmacology & Physiology 1989; 16(1):59-63. *Not CKD treatment*

4720. Whitworth JA, Ihle BU, Becker GJ, et al. Preservation of renal function in chronic renal failure. Tohoku Journal of Experimental Medicine 1992; 166(1):165-83. *Not RCT or controlled trial*

4721. Whitworth JA, Williamson PM, Brown MA, et al. Haemodynamic and metabolic effects of carbenoxolone in normal subjects and patients with renal impairment. Clinical & Experimental Hypertension 1994; 16(4):431-50. *Sample size less than 50 patients*

4722. Wiecek A. Anemia: To TREAT or not to TREAT--that is the question. Nature Reviews Nephrology 2010 May; 6(5):254-5. *Not RCT or controlled trial*

4723. Wiecek A, Covic A, Locatelli F, et al. Renal anemia: comparing current Eastern and Western European management practice (ORAMA). Renal Failure 2008; 30(3):267-76. *Sample size less than 50 patients*

4724. Wiecek A, Fliser D, Nowicki M, et al. Effect of moxonidine on urinary electrolyte excretion and renal haemodynamics in man. European Journal of Clinical Pharmacology 1995; 48(3-4):203-8. *Follow-up less than 6 months*

4725. Wiedermann CJ. Hydroxyethyl starch--can the safety problems be ignored? Wiener Klinische Wochenschrift 2004; 116(17-18):583-94. *Not relevant to key questions*

4726. Wiegmann TB, Herron KG, Chonko AM, et al. Effect of angiotensin-converting enzyme inhibition on renal function and albuminuria in normotensive type I diabetic patients. Diabetes 1992; 41(1):62-7. *Sample size less than 50 patients*

4727. Wiersbitzky M, Landgraf R, Gruska S, et al. Hormonal and renal responses to arterial chemoreceptor stimulation by almitrine in healthy and normotensive men. Biomedica Biochimica Acta 1990; 49(11):1155-63. *Not CKD treatment*

4728. Wijeysundera DN, Beattie WS, Djaiani G, et al. Off-pump coronary artery surgery for reducing mortality and morbidity: meta-analysis of randomized and observational studies. Journal of the American College of Cardiology 2005; 46(5):872-82. *Not RCT or controlled trial*

4729. Wijeysundera DN, Beattie WS, Rao V, et al. N-acetylcysteine for preventing acute kidney injury in cardiac surgery patients with pre-existing moderate renal insufficiency. Canadian Journal of Anaesthesia 2007; 54(11):872-81. *Follow-up less than 6 months*

4730. Wijnen MHWA, Vader HL, Van Den Wall Bake AWL, et al. Can renal dysfunction after infra-renal aortic aneurysm repair be modified by multi-antioxidant supplementation? Journal of Cardiovascular Surgery 2002; 43(4):483-8. *Not CKD treatment*

4731. Wiland P, Szechcinski J. Proximal tubule damage in patients treated with gentamicin or amikacin. Polish Journal of Pharmacology 2003; 55(4):631-7. *Follow-up less than 6 months*

4732. Wiland P, Szechinski J. N-acetyl-beta-D-glucosaminidase urinary excretion as an early indicator of kidney damage in rheumatoid arthritis patients starting on parenteral gold and Depo-Medrone/placebo injections. Clinical Rheumatology 1999; 18(2):106-13. *Not CKD treatment*

4733. Wilkins MR, Lewis HM, West MJ, et al. Captopril reduces the renal response to intravenous atrial natriuretic peptide in normotensives. Journal of Human Hypertension 1987; 1(1):47-51. *Sample size less than 50 patients*

4734. Willemsen JM, Rabelink TJ, Boer P, et al. Disparate systemic and renal blocking properties of angiotensin II antagonists during exogenous angiotensin II administration: implications for treatment. Journal of Human Hypertension 2004; 18(12):857-63. *Follow-up less than 6 months*

4735. William J, Saad N, Salib M, et al. The acute effect of intravenously administered recombinant human erythropoietin on the immune response of uremic patients maintained on regular hemodialysis. Artificial Organs 1998; 22(3):192-6. *Sample size less than 50 patients*

4736. Williams AF, Manias E, Walker RG. The devil is in the detail - a multifactorial intervention to reduce blood pressure in co-existing diabetes and chronic kidney disease: a single blind, randomized controlled trial. BMC Family Practice 2010; 11:3. *Not RCT or controlled trial*

4737. Williams CD, Linch DC. Interferon alfa-2a. British Journal of Hospital Medicine 1997; 57(9):436-9. *Not CKD treatment*

4738. Williams GH, Burgess E, Kolloch RE, et al. Efficacy of eplerenone versus enalapril as monotherapy in systemic hypertension. American Journal of Cardiology 2004; 93(8):990-6. *Not CKD treatment*

4739. Williams ME, Bolton WK, Khalifah RG, et al. Effects of pyridoxamine in combined phase 2 studies of patients with type 1 and type 2 diabetes and overt nephropathy. American Journal of Nephrology 2007; 27(6):605-14. *Not human studies*

4740. Williams R. Intensive insulin treatment after acute myocardial infarction in diabetes mellitus. Evidence exists from study of non-insulin dependent diabetes in Japan. BMJ 1997; 315(7107):544. *Not RCT or controlled trial*

4741. Williams RM, Yuen K, White D, et al. Short-term suppression of elevated growth hormone concentrations following insulin-like growth factor 1 administration in young adults with type 1 diabetes does not alter glomerular filtration or albumin excretion rates. Clinical Endocrinology 2006; 65(4):439-45. *Not RCT or controlled trial*

4742. Willox JC, McAllister EJ, Sangster G, et al. Effects of magnesium supplementation in testicular cancer patients receiving cis-platin: a randomised trial. British Journal of Cancer 1986; 54(1):19-23. *Not CKD treatment*

4743. Wilmer WA, Hebert LA, Lewis EJ, et al. Remission of nephrotic syndrome in type 1 diabetes: long-term follow-up of patients in the Captopril Study. American Journal of Kidney Diseases 1999; 34(2):308-14. *Sample size less than 50 patients*

4744. Wilmer WA, Rovin BH, Hebert CJ, et al. Management of glomerular proteinuria: a commentary. Journal of the American Society of Nephrology 2003; 14(12):3217-32. *Follow-up less than 6 months*

4745. Wilson DM, Bergert JH, Larson TS, et al. GFR determined by nonradiolabeled iothalamate using capillary electrophoresis. American Journal of Kidney Diseases 1997; 30(5):646-52. *Not RCT or controlled trial*

4746. Wilson J, Orchard MA, Spencer AA, et al. Anti-hypertensive drugs non-specifically reduce "spontaneous" activation of blood platelets. Thrombosis & Haemostasis 1989; 62(2):776-80. *Sample size less than 50 patients*

4747. Wilson J, Wahbha MM, Martin PG, et al. The effect of nisoldipine on renal function in the long-term treatment of hypertension in patients with and without renal impairment. European Journal of Clinical Pharmacology 1989; 37(5):437-41. *Not relevant to key questions*

4748. Wilson R, Godwin M, Seguin R, et al. End-stage renal disease: factors affecting referral decisions by family physicians in Canada, the United States, and Britain. American Journal of Kidney Diseases 2001; 38(1):42-8. *Not early CKD*

4749. Wilson RA, Norman DJ, Barry JM, et al. Noninvasive cardiac testing in the end-stage renal disease patient. Blood Purification 1994; 12(1):78-83. *Not RCT or controlled trial*

4750. Wilson TW. The antihypertensive action of hydrochlorothiazide and renal prostacyclin. Clinical Pharmacology & Therapeutics 1986; 39(1):94-101. *Sample size less than 50 patients*

4751. Wimmer A, Stanek B, Kubecova L, et al. Effects of prostaglandin E1, dobutamine and placebo on hemodynamic, renal and neurohumoral variables in patients with advanced heart failure. Japanese Heart Journal 1999; 40(3):321-34. *Sample size less than 50 patients*

4752. Wing AJ. The social responsibility of physicians as agents of public health services. Renal Failure 1996; 18(3):425-31. *Not RCT or controlled trial*

4753. Winkelmayer WC, Glynn RJ, Levin R, et al. Hydroxyethyl starch and change in renal function in patients undergoing coronary artery bypass graft surgery. Kidney International 2003; 64(3):1046-9. *Not CKD treatment*

4754. Winkelmayer WC, Zhang Z, Shahinfar S, et al. Efficacy and safety of angiotensin II receptor blockade in elderly patients with diabetes. Diabetes Care 2006; 29(10):2210-7. *Not CKD treatment*

4755. Winkle RA, Smith NA, Ruder MA, et al. Pharmacodynamics of enoximone during intravenous infusion. International Journal of Cardiology 1990; 28 Suppl 1:S1-2. *Not CKD treatment*

4756. Wintermeyer SM, Nahata MC. Rimantadine: a clinical perspective. Annals of Pharmacotherapy 1995; 29(3):299-310. *Not RCT or controlled trial*

4757. Wirta OR, Pasternack AI, Mustonen JT, et al. Urinary albumin excretion rate and its determinants after 6 years in non-insulin-dependent diabetic patients. Nephrology Dialysis Transplantation 1996; 11(3):449-56. *Not RCT or controlled trial*

4758. Wirta OR, Pasternack AI, Mustonen JT, et al. Urinary albumin excretion rate is independently related to autonomic neuropathy in type 2 diabetes mellitus. Journal of Internal Medicine 1999; 245(4):329-35. *Not RCT or controlled trial*

4759. Wiseman MJ, Saunders AJ, Keen H, et al. Effect of blood glucose control on increased glomerular filtration rate and kidney size in insulin-dependent diabetes. New England Journal of Medicine 1985; 312(10):617-21. *Sample size less than 50 patients*

4760. Witasp A, Nordfors L, Lindholm B, et al. Use of single-nucleotide polymorphisms in the search for genetic modifiers of the uremic phenotype. Journal of Renal Nutrition 2007; 17(1):17-22. *Sample size less than 50 patients*

4761. Witteles RM, Kao D, Christopherson D, et al. Impact of nesiritide on renal function in patients with acute decompensated heart failure and pre-existing renal dysfunction a randomized, double-blind, placebo-controlled clinical trial. Journal of the American College of Cardiology 2007; 50(19):1835-40. *Not CKD treatment*

4762. Wittenberg C, Erman A, Shohat J, et al. Concomitant administration of isradipine and spirapril prevents reduction of renal function induced by acute administration of spirapril in patients with reduced renal function. Blood Pressure Supplement 1994; 1:48-9. *Not CKD treatment*

4763. Wittenberg C, Rosenfeld JB. Acute antihypertensive and renal effects of isradipine in hypertensive patients with normal and reduced renal function. American Journal of Hypertension 1991; 4(2 Pt 2):191S-3S. *Sample size less than 50 patients*

4764. Witting M, Kuo D. Screening with blood urea nitrogen before intravenous contrast. American Journal of Emergency Medicine 2003; 21(6):494-6. *Not CKD treatment*

4765. Wittstock A, Burkert M, Zidek W, et al. N-acetylcysteine improves arterial vascular reactivity in patients with chronic kidney disease. Nephron 2009; 112(3):c184-9. *Not early CKD*

4766. Woittiez AJ, Huysmans FT, Bailey R, et al. A comparison of the safety and efficacy of mibefradil and nifedipine SR in patients with renal disease and hypertension. Clinical Nephrology 1998; 49(3):160-6. *Follow-up less than 6 months*

4767. Wolf DL, Jungbluth GL, Metzler CM, et al. Acute effects of increasing doses of nicorandil on renal function in man. International Journal of Clinical Pharmacology & Therapeutics 1994; 32(5):246-53. *Sample size less than 50 patients*

4768. Wolf DL, Rodriguez CA, Mucci M, et al. Pharmacokinetics and renal effects of cidofovir with a reduced dose of probenecid in HIV-infected patients with cytomegalovirus retinitis. Journal of Clinical Pharmacology 2003; 43(1):43-51. *Not CKD treatment*

4769. Wolf G. Zenon's paradox or how much to lower blood pressure for optimal renoprotection. Nephrology Dialysis Transplantation 2005; 20(11):2304-7. *Not CKD treatment*

4770. Wolfe RA. The United States Renal Data System: a source of national norms for ESRD patient outcome and process of care. Advances in Renal Replacement Therapy 1995; 2(2):95-100. *Not RCT or controlled trial*

4771. Woll PJ, Pettengell R. Interferons in oncology.[Erratum appears in Br J Clin Pract 1997 Apr-May;51(3):146]. British Journal of Clinical Practice 1997; 51(2):111-5. *Not RCT or controlled trial*

4772. Wolpert C, Schimpf R, Giustetto C, et al. Further insights into the effect of quinidine in short QT syndrome caused by a mutation in HERG. Journal of Cardiovascular Electrophysiology 2005; 16(1):54-8. *Not relevant to key questions*

4773. Wong F, Massie D, Hsu P, et al. The dose-dependent effect of misoprostol on indomethacin-induced renal dysfunction in well compensated cirrhosis. American Journal of Gastroenterology 1995; 90(9):1465-70. *Sample size less than 50 patients*

4774. Wong JA, Goodman SG, Yan RT, et al. Temporal management patterns and outcomes of non-ST elevation acute coronary syndromes in patients with kidney dysfunction. European Heart Journal 2009; 30(5):549-57. *Not CKD treatment*

4775. Wong SL, Awni WM, Cavanaugh JH, et al. The pharmacokinetics of single oral doses of zileuton 200 to 800mg, its enantiomers, and its metabolites, in normal healthy volunteers. Clinical Pharmacokinetics 1995; 29 Suppl 2:9-21. *Sample size less than 50 patients*

4776. Wong T, Foote EF, Lefavour GS, et al. Physician knowledge and practice patterns relating to diabetic nephropathy. Journal of the American Pharmaceutical Association 1999; 39(6):785-90. *Not RCT or controlled trial*

4777. Woo EBC, Tang ATM, el-Gamel A, et al. Dopamine therapy for patients at risk of renal dysfunction following cardiac surgery: science or fiction? European Journal of Cardio-Thoracic Surgery 2002; 22(1):106-11. *Not CKD treatment*

4778. Woo KT, Lau YK, Chan CM, et al. ATRA therapy restores normal renal function and renal reserve and prevents renal failure. Annals of the Academy of Medicine, Singapore 2005; 34(1):52-9. *Not RCT or controlled trial*

4779. Woo KT, Lau YK, Wong KS, et al. ACE inhibitor use and the long-term risk of renal failure in diabetics. Kidney International 2006; 70(7):1376-7; author reply 8. *Not RCT or controlled trial*

4780. Wood PJ, Ioannides-Demos LL, Li SC, et al. Minimisation of aminoglycoside toxicity in patients with cystic fibrosis. Thorax 1996; 51(4):369-73. *Not CKD treatment*

4781. Woodman RJ, Mori TA, Burke V, et al. Docosahexaenoic acid but not eicosapentaenoic acid increases LDL particle size in treated hypertensive type 2 diabetic patients. Diabetes Care 2003; 26(1):253. *Not CKD treatment*

4782. Woolf AS, Mansell MA, Hoffbrand BI, et al. The effects of low dose intravenous 99-126 atrial natriuretic factor infusion in patients with chronic renal failure. Postgraduate Medical Journal 1989; 65(764):362-6. *Not early CKD*

4783. Woolfrey SG, Hegbrant J, Thysell H, et al. Dose regimen adjustment for milrinone in congestive heart failure patients with moderate and severe renal failure. Journal of Pharmacy & Pharmacology 1995; 47(8):651-5. *Not CKD treatment*

4784. Woolfson RG, Neild GH. Cyclosporin nephrotoxicity following cardiac transplantation. Nephrology Dialysis Transplantation 1997; 12(10):2054-6. *Not CKD treatment*

4785. Worth DP, Harvey JN, Brown J, et al. gamma-L-Glutamyl-L-dopa is a dopamine pro-drug, relatively specific for the kidney in normal subjects. Clinical Science 1985; 69(2):207-14. *Sample size less than 50 patients*

4786. Wotherspoon F, Laight DW, Turner C, et al. The effect of oral folic acid upon plasma homocysteine, endothelial function and oxidative stress in patients with type 1 diabetes and microalbuminuria. International Journal of Clinical Practice 2008; 62(4):569-74. *Sample size less than 50 patients*

4787. Wright JG, Boddy AV, Highley M, et al. Estimation of glomerular filtration rate in cancer patients. British Journal of Cancer 2001; 84(4):452-9. *Not early CKD*

4788. Wright JT, Jr., Agodoa L, Contreras G, et al. Successful blood pressure control in the African American Study of Kidney Disease and Hypertension. Archives of Internal Medicine 2002; 162(14):1636-43. *Not CKD treatment*

4789. Wright JT, Jr., Probstfield JL, Cushman WC, et al. ALLHAT findings revisited in the context of subsequent analyses, other trials, and meta-analyses. Archives of Internal Medicine 2009; 169(9):832-42. *Not relevant to key questions*

4790. Wright JT, Jr., Probstfield JL, Cushman WC, et al. ALLHAT findings revisited in the context of subsequent analyses, other trials, and meta-analyses. Archives of Internal Medicine 2009; 169(9):832-42. *Not RCT or controlled trial*

4791. Wright S, Bogan A, Chokshi A. DaVita program advocates self-management of CKD. Nephrology News & Issues 2009; 23(13):28-9. *Not RCT or controlled trial*

4792. Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research G. Effect of intensive therapy on the microvascular complications of type 1 diabetes mellitus. JAMA 2002; 287(19):2563-9. *Not CKD treatment*

4793. Wrobel W, Sinkiewicz W, Gordon M, et al. Oral versus intravenous hydration and renal function in diabetic patients undergoing percutaneous coronary interventions. Kardiologia Polska 2010 Sep; 68(9):1015-20. *Not CKD treatment*

4794. Wrone EM, Hornberger JM, Zehnder JL, et al. Randomized trial of folic acid for prevention of cardiovascular events in end-stage renal disease. Journal of the American Society of Nephrology 2004; 15(2):420-6. *Not relevant to key questions*

4795. Wu AYT, Low LP. Managing vascular risk in hypertension with a focus on microalbuminuria: attitude and practices. Singapore Medical Journal 2009; 50(10):976-81. *Not RCT or controlled trial*

4796. Wu S, Han Y, Li J. Treatment of incipient diabetic nephropathy by clearing away the stomach-heat, purging the heart fire, strengthening the spleen and tonifying the kidney. Journal of Traditional Chinese Medicine 2000; 20(3):172-5. *Sample size less than 50 patients*

4797. Wu S-W, Chang H-R, Lian J-D. The effect of low-dose cidofovir on the long-term outcome of polyomavirus-associated nephropathy in renal transplant recipients. Nephrology Dialysis Transplantation 2009; 24(3):1034-8. *Not CKD treatment*

4798. Wuerzner G, Burnier M. Effects of selective angiotensin II and beta1-receptor blockade on renal haemodynamics and sodium handling during orthostatic stress in healthy individuals. Journal of Hypertension - Supplement 2006; 24(1):S89-93. *Not relevant to key questions*

4799. Wuerzner G, Chiolero A, Maillard M, et al. Angiotensin II receptor blockade prevents acute renal sodium retention induced by low levels of orthostatic stress.[Erratum appears in Kidney Int. 2004 Mar;65(3):1131 Note: Chiclero, Arnaud [corrected to Chiolero, Arnaud]]. Kidney International 2004; 65(1):238-44. *Not CKD treatment*

4800. Wuerzner G, Chiolero A, Maillard M, et al. Metoprolol prevents sodium retention induced by lower body negative pressure in healthy men. Kidney International 2005; 68(2):688-94. *Not relevant to key questions*

4801. Wuhl E, Schaefer F. Effects of growth hormone in patients with chronic renal failure: experience in children and adults. Hormone Research 2002; 58 Suppl 3:35-8. *Not CKD treatment*

4802. Wu-Wong JR. Endothelial dysfunction and chronic kidney disease: treatment options. Current Opinion in Investigational Drugs 2008; 9(9):970-82. *Not CKD treatment*

4803. Wyllie BF, Garg AX, Macnab J, et al. Thrombotic thrombocytopenic purpura/haemolytic uraemic syndrome: a new index predicting response to plasma exchange. British Journal of Haematology 2006; 132(2):204-9. *Sample size less than 50 patients*

4804. Wysocki M, Andersson OK, Persson B, et al. Vasoconstriction during acute hypervolemic hemodilution in hypertensive patients is not prevented by calcium blockade. Angiology 1998; 49(1):41-8. *Sample size less than 50 patients*

4805. Xiao HW. An approach to the appropriate dosage of essential amino acids in the treatment of chronic renal failure. Journal of Tongji Medical University 1991; 11(4):240-3. *Not CKD treatment*

4806. Xinwei J, Xianghua F, Jing Z, et al. Comparison of usefulness of simvastatin 20 mg versus 80 mg in preventing contrast-induced nephropathy in patients with acute coronary syndrome undergoing percutaneous coronary intervention. American Journal of Cardiology 2009; 104(4):519-24. *Not CKD treatment*

4807. Xu G, Tu W, Jiang D, et al. Tripterygium wilfordii Hook F treatment for idiopathic refractory nephrotic syndrome in adults: a meta-analysis. Nephron 2009; 111(4):c223-8. *Not CKD treatment*

4808. Xu L, Shao J. Estimation in longitudinal or panel data models with random-effect-based missing responses. Biometrics 2009; 65(4):1175-83. *Not CKD treatment*

4809. Xu X, Ling Q, Gao F, et al. Hepatoprotective effects of marine and kuhuang in liver transplant recipients. American Journal of Chinese Medicine 2009; 37(1):27-34. *Not CKD treatment*

4810. Yallop KG, Sheppard SV, Smith DC. The effect of mannitol on renal function following cardio-pulmonary bypass in patients with normal pre-operative creatinine. Anaesthesia 2008; 63(6):576-82. *Not CKD treatment*

4811. Yamagishi S-i, Fukami K, Ueda S, et al. Molecular mechanisms of diabetic nephropathy and its therapeutic intervention. Current Drug Targets 2007; 8(8):952-9. *Sample size less than 50 patients*

4812. Yamamoto T, Moriwaki Y, Takahashi S, et al. Effects of pyrazinamide, probenecid, and benzbromarone on renal excretion of oxypurinol. Annals of the Rheumatic Diseases 1991; 50(9):631-3. *Not CKD treatment*

4813. Yamazaki M, Ito S, Usami A, et al. Urinary excretion rate of ceruloplasmin in non-insulin-dependent diabetic patients with different stages of nephropathy. European Journal of Endocrinology 1995; 132(6):681-7. *Follow-up less than 6 months*

4814. Yanagawa T, Araki A, Sasamoto K, et al. Effect of antidiabetic medications on microalbuminuria in patients with type 2 diabetes. Metabolism: Clinical & Experimental 2004; 53(3):353-7. *Not CKD treatment*

4815. Yancy CW, Singh A. Potential applications of outpatient nesiritide infusions in patients with advanced heart failure and concomitant renal insufficiency (from the Follow-Up Serial Infusions of Nesiritide [FUSION I] trial). American Journal of Cardiology 2006; 98(2):226-9. *Sample size less than 50 patients*

4816. Yang Q-W, Mou L, Lv F-L, et al. Novel TLR4-antagonizing peptides inhibit LPS-induced release of inflammatory mediators by monocytes. Biochemical & Biophysical Research Communications 2005; 329(3):846-54. *Not CKD treatment*

4817. Yang W, Israni RK, Brunelli SM, et al. Hemoglobin variability and mortality in ESRD. Journal of the American Society of Nephrology 2007; 18(12):3164-70. *Not CKD treatment*

4818. Yang X, So W-Y, Kong APS, et al. Development and validation of a total coronary heart disease risk score in type 2 diabetes mellitus. American Journal of Cardiology 2008; 101(5):596-601. *Not CKD treatment*

4819. Yang XL, So WY, Kong APS, et al. End-stage renal disease risk equations for Hong Kong Chinese patients with type 2 diabetes: Hong Kong Diabetes Registry. Diabetologia 2006; 49(10):2299-308. *Not RCT or controlled trial*

4820. Yanik B, Bavbek N, Yanik T, et al. The effect of alendronate, risedronate, and raloxifene on renal functions, based on the Cockcroft and Gault method, in postmenopausal women. Renal Failure 2007; 29(4):471-6. *Sample size less than 50 patients*

4821. Yano Y, Hoshide S, Ishikawa J, et al. The differential effects of angiotensin II type 1 receptor blockers on microalbuminuria in relation to low-grade inflammation in metabolic hypertensive patients. American Journal of Hypertension 2007; 20(5):565-72. *Not RCT or controlled trial*

4822. Yaqoob MM. Acidosis and progression of chronic kidney disease. Current Opinion in Nephrology & Hypertension 2010 Sep; 19(5):489-92. *Not CKD treatment*

4823. Yasuda G, Ando D, Hirawa N, et al. Effects of atorvastatin versus probucol on low-density lipoprotein subtype distribution and renal function in hyperlipidemic patients with nondiabetic nephropathy. Renal Failure 2010 Jul; 32(6):680-6. *Follow-up less than 6 months*

4824. Yasuda G, Umemura S, Ishii M. Characterization of bunazosin-sensitive alpha1-adrenoceptors in human renal medulla. Journal of Cardiovascular Pharmacology 1997; 30(2):163-8. *Sample size less than 50 patients*

4825. Yasue H, Yoshimura M. Natriuretic peptides in the treatment of heart failure. Journal of Cardiac Failure 1996; 2(4 Suppl):S277-85. *Not CKD treatment*

4826. Yavuz S, Ayabakan N, Dilek K, et al. Renal dose dopamine in open heart surgery. Does it protect renal tubular function? Journal of Cardiovascular Surgery 2002; 43(1):25-30. *Not early CKD*

4827. Yavuz S, Ayabakan N, Goncu MT, et al. Effect of combined dopamine and diltiazem on renal function after cardiac surgery. Medical Science Monitor 2002; 8(5):PI45-50. *Not early CKD*

4828. Ye DQ, Yang SG, Li XP, et al. Polymorphisms in the promoter region of RANTES in Han Chinese and their relationship with systemic lupus erythematosus. Archives of Dermatological Research 2005; 297(3):108-13. *Not relevant to key questions*

4829. Ye S, Zheng M, Hu Y, et al. Hydrochloride pioglitazone decreases urinary monocyte chemoattractant protein-1 excretion in type 2 diabetics. Diabetes Research & Clinical Practice 2010 Jun; 88(3):247-51. *Not CKD treatment*

4830. Yildiz A, Hursit M, Celik AV, et al. Doxazosin, but not amlodipine decreases insulin resistance in patients with chronic renal failure: a prospective, randomized-controlled study. Clinical Nephrology 2002; 58(6):405-10. *Sample size less than 50 patients*

4831. Yilmaz E. Re: Takmaz SA, et al. Analgesic effect of 8- and 16-mg lornoxicam administered before shock wave lithotripsy: a randomized, double-blind, controlled study (Urology 2008;72:282-285). Urology 2009; 73(1):211-2. *Not CKD treatment*

4832. Yilmaz E, Batislam E, Deniz T, et al. Histamine 1 receptor antagonist in symptomatic treatment of renal colic accompanied by nausea: two birds with one stone? Urology 2009; 73(1):32-6. *Not CKD treatment*

4833. Yilmaz MB, Yalta K, Yontar C, et al. Levosimendan improves renal function in patients with acute decompensated heart failure: comparison with dobutamine. Cardiovascular Drugs & Therapy 2007; 21(6):431-5. *Not human studies*

4834. Yilmaz MI, Axelsson J, Sonmez A, et al. Effect of renin angiotensin system blockade on pentraxin 3 levels in type-2 diabetic patients with proteinuria. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(3):535-41. *Sample size less than 50 patients*

4835. Yilmaz MI, Carrero JJ, Martin-Ventura JL, et al. Combined therapy with renin-angiotensin system and calcium channel blockers in type 2 diabetic hypertensive patients with proteinuria: effects on soluble TWEAK, PTX3, and flow-mediated dilation. Clinical Journal of The American Society of Nephrology: CJASN 2010 Jul; 5(7):1174-81. *Follow-up less than 6 months*

4836. Yilmaz MI, Saglam M, Sonmez A, et al. Improving proteinuria, endothelial functions and asymmetric dimethylarginine levels in chronic kidney disease: ramipril versus valsartan. Blood Purification 2007; 25(4):327-35. *Follow-up less than 6 months*

4837. Yilmaz MI, Sonmez A, Caglar K, et al. Peroxisome proliferator-activated receptor gamma (PPAR-gamma) agonist increases plasma adiponectin levels in type 2 diabetic patients with proteinuria. Endocrine 2004; 25(3):207-14. *Sample size less than 50 patients*

4838. Ylitalo P, Pitkajarvi T, Pyykonen ML, et al. Inhibition of prostaglandin synthesis by indomethacin interacts with the antihypertensive effect of atenolol. Clinical Pharmacology & Therapeutics 1985; 38(4):443-9. *Sample size less than 50 patients*

4839. Yokoyama H, Kannno S, Ishimura I, et al. Miglitol increases the adiponectin level and decreases urinary albumin excretion in patients with type 2 diabetes mellitus. Metabolism: Clinical & Experimental 2007; 56(11):1458-63. *Sample size less than 50 patients*

4840. Yokoyama M, Torita M, Yoshizawa M, et al. Indication of vitamin E on microalbuminuria in patients with incipient diabetic nephropathy. Diabetes & Metabolism 2001; 27(5 Pt 1):611-2. *Not CKD treatment*

4841. Yorioka N, Kiribayashi K, Naito T, et al. An oral adsorbent, AST-120, combined with a low-protein diet and RAS blocker, for chronic kidney disease. Journal of Nephrology 2008; 21(2):213-20. *Sample size less than 50 patients*

4842. Yosefy C, Magen E, Kiselevich A, et al. Rosiglitazone improves, while Glibenclamide worsens blood pressure control in treated hypertensive diabetic and dyslipidemic subjects via modulation of insulin resistance and sympathetic activity. Journal of Cardiovascular Pharmacology 2004; 44(2):215-22. *Not relevant to key questions*

4843. Yoshida EM, Marotta PJ, Greig PD, et al. Evaluation of renal function in liver transplant recipients receiving daclizumab (Zenapax), mycophenolate mofetil, and a delayed, low-dose tacrolimus regimen vs. a standard-dose tacrolimus and mycophenolate mofetil regimen: a multicenter randomized clinical trial. Liver Transplantation 2005; 11(9):1064-72. *Not RCT or controlled trial*

4844. Yoshida K, Kohzuki M, Xu HL, et al. Effects of troglitazone and temocapril in spontaneously hypertensive rats with chronic renal failure. Journal of Hypertension 2001; 19(3):503-10. *Not human studies*

4845. Yoshikawa K, Davies A. Safety of ProHance in special populations. European Radiology 1997; 7 Suppl 5:246-50. *Not RCT or controlled trial*

4846. Yoshioka K, Imanishi M, Konishi Y, et al. Glomerular charge and size selectivity assessed by changes in salt intake in type 2 diabetic patients. Diabetes Care 1998; 21(4):482-6. *Sample size less than 50 patients*

4847. Yoshioka K, Ohashi Y, Sakai T, et al. A multicenter trial of mizoribine compared with placebo in children with frequently relapsing nephrotic syndrome. Kidney International 2000; 58(1):317-24. *Not adult population*

4848. Younes H, Egret N, Hadj-Abdelkader M, et al. Fermentable carbohydrate supplementation alters nitrogen excretion in chronic renal failure. Journal of Renal Nutrition 2006; 16(1):67-74. *Not RCT or controlled trial*

4849. Young EW, Ellis CN, Messana JM, et al. A prospective study of renal structure and function in psoriasis patients treated with cyclosporin. Kidney International 1994; 46(4):1216-22. *Sample size less than 50 patients*

4850. Young J, Anwar A. Strong diabetes. British Journal of Sports Medicine 2007; 41(5):335-6; discussion 6. *Not relevant to key questions*

4851. Young JM, Terrin N, Wang X, et al. Asymmetric dimethylarginine and mortality in stages 3 to 4 chronic kidney disease. Clinical Journal of The American Society of Nephrology: CJASN 2009; 4(6):1115-20. *Not CKD treatment*

4852. Yuan W, Wang J, Wu T. Chinese herbal medicine Huangqi type formulations for nephrotic syndrome. Cochrane Database of Systematic Reviews 2008; (2):CD006335. *Not CKD treatment*

4853. Yukawa S, Mune M, Yamada Y, et al. Ongoing clinical trials of lipid reduction therapy in patients with renal disease. Kidney International - Supplement 1999; 71:S141-3. *Not RCT or controlled trial*

4854. Yusuf S. Preventing vascular events due to elevated blood pressure. Circulation 2006; 113(18):2166-8. *Follow-up less than 6 months*

4855. Yusuf S, Lonn E, Bosch J, et al. Summary of randomized trials of angiotensin converting enzyme inhibitors. Clinical & Experimental Hypertension 1999; 21(5-6):835-45. *Not RCT or controlled trial*

4856. Yusuff KB, Balogun OB. Pattern of drug utilization among hypertensives in a Nigerian teaching hospital. Pharmacoepidemiology & Drug Safety 2005; 14(1):69-74. *Follow-up less than 6 months*

4857. Yuyun MF, Khaw KT, Luben R, et al. Microalbuminuria and stroke in a British population: the European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) population study. Journal of Internal Medicine 2004; 255(2):247-56. *Not early CKD*

4858. Yuyun MF, Khaw K-T, Luben R, et al. Microalbuminuria independently predicts all-cause and cardiovascular mortality in a British population: The European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) population study. International Journal of Epidemiology 2004; 33(1):189-98. *Not relevant to key questions*

4859. Zachariae H, Abrams B, Bleehen SS, et al. Conversion of psoriasis patients from the conventional formulation of cyclosporin A to a new microemulsion formulation: a randomized, open, multicentre assessment of safety and tolerability. Dermatology 1998; 196(2):231-6. *Sample size less than 50 patients*

4860. Zacharias M, Conlon NP, Herbison GP, et al. Interventions for protecting renal function in the perioperative period. Cochrane Database of Systematic Reviews 2008; (4):CD003590. *Not CKD treatment*

4861. Zacharias M, Gilmore ICS, Herbison GP, et al. Interventions for protecting renal function in the perioperative period. Cochrane Database of Systematic Reviews 2005; (3):CD003590. *Not CKD treatment*

4862. Zager P, Nikolic J, Raj DS, et al. Hypertension in end-stage renal disease patients. Current Opinion in Nephrology & Hypertension 2000; 9(3):279-83. *Not RCT or controlled trial*

4863. Zagler A, Azadpour M, Mercado C, et al. N-acetylcysteine and contrast-induced nephropathy: a meta-analysis of 13 randomized trials. American Heart Journal 2006; 151(1):140-5. *Not RCT or controlled trial*

4864. Zaleski L, Abello D, Gold MI. Desflurane versus isoflurane in patients with chronic hepatic and renal disease. Anesthesia & Analgesia 1993; 76(2):353-6. *Not RCT or controlled trial*

4865. Zaltzman JS. A comparison of short-term exposure of once-daily extended release tacrolimus and twice-daily cyclosporine on renal function in healthy volunteers. Transplantation 2010 Dec 15; 90(11):1185-91. *Not CKD treatment*

4866. Zalunardo N, Levin A. Anemia and the heart in chronic kidney disease. Seminars in Nephrology 2006; 26(4):290-5. *Not RCT or controlled trial*

4867. Zambraski EJ, Dodelson R, Guidotti SM, et al. Renal prostaglandin E2 and F2 alpha synthesis during exercise: effects of indomethacin and sulindac. Medicine & Science in Sports & Exercise 1986; 18(6):678-84. *Sample size less than 50 patients*

4868. Zanardo G, Michielon P, Rosi P, et al. Effects of a continuous diltiazem infusion on renal function during cardiac surgery. Journal of Cardiothoracic & Vascular Anesthesia 1993; 7(6):711-6. *Sample size less than 50 patients*

4869. Zanchetti A, Hansson L, Leonetti G, et al. Low-dose aspirin does not interfere with the blood pressure-lowering effects of antihypertensive therapy. Journal of Hypertension 2002; 20(5):1015-22. *Not CKD treatment*

4870. Zandbergen AAM, Baggen MGA, Lamberts SWJ, et al. Effect of losartan on microalbuminuria in normotensive patients with type 2 diabetes mellitus. A randomized clinical trial. Annals of Internal Medicine 2003; 139(2):90-6. *Follow-up less than 6 months*

4871. Zandbergen AAM, Lamberts SWJ, Baggen MGA, et al. The IGF-I system and the renal and haemodynamic effects of losartan in normotensive patients with type 2 diabetes mellitus: a randomized clinical trial. Clinical Endocrinology 2006; 64(2):203-8. *Sample size less than 50 patients*

4872. Zannikos PN, Rohatagi S, Jensen BK, et al. Pharmacokinetics, pharmacodynamics, and safety of a platelet GPIIb/IIIa antagonist, RGD891, following intravenous administration in healthy male volunteers. Journal of Clinical Pharmacology 2000; 40(11):1245-56. *Not early CKD*

4873. Zarazaga A, Garcia-De-Lorenzo L, Garcia-Luna PP, et al. Nutritional support in chronic renal failure: systematic review. Clinical Nutrition 2001; 20(4):291-9. *Not relevant to key questions*

4874. Zawada ET, Jr. Renal hemodynamic changes after beta-blocker-diuretic combination therapy in azotemic hypertensive patients. International Journal of Artificial Organs 1986; 9(6):405-12. *Sample size less than 50 patients*

4875. Zawada ET, Jr., Williams L, McClung DE, et al. Renal-metabolic consequences of antihypertensive therapy with diltiazem versus hydrochlorothiazide. Mineral & Electrolyte Metabolism 1987; 13(2):72-7. *Sample size less than 50 patients*

4876. Zeller A, Sigle J-P, Battegay E, et al. Value of a standard urinary dipstick test for detecting microalbuminuria in patients with newly diagnosed hypertension. Swiss Medical Weekly 2005; 135(3-4):57-61. *Not RCT or controlled trial*

4877. Zeller K, Whittaker E, Sullivan L, et al. Effect of restricting dietary protein on the progression of renal failure in patients with insulin-dependent diabetes mellitus. New England Journal of Medicine 1991; 324(2):78-84. *Sample size less than 50 patients*

4878. Zelmanovitz T, Gross JL, Oliveira J, et al. Proteinuria is still useful for the screening and diagnosis of overt diabetic nephropathy. Diabetes Care 1998; 21(7):1076-9. *Not RCT or controlled trial*

4879. Zelmanovitz T, Gross JL, Oliveira JR, et al. The receiver operating characteristics curve in the evaluation of a random urine specimen as a screening test for diabetic nephropathy. Diabetes Care 1997; 20(4):516-9. *Not RCT or controlled trial*

4880. Zeman M, Zak A, Vecka M, et al. N-3 fatty acid supplementation decreases plasma homocysteine in diabetic dyslipidemia treated with statin-fibrate combination. Journal of Nutritional Biochemistry 2006; 17(6):379-84. *Not RCT or controlled trial*

4881. Zemmel MH. The role of COX-2 inhibitors in the perioperative setting: efficacy and safety--a systematic review. AANA Journal 2006; 74(1):49-60. *Not relevant to key questions*

4882. Zerem E, Imamovic G, Omerovic S. Symptomatic simple renal cyst: comparison of continuous negative-pressure catheter drainage and single-session alcohol sclerotherapy. AJR 2008; American Journal of Roentgenology. 190(5):1193-7. *Not CKD treatment*

4883. Zhang J, Fu X, Jia X, et al. B-type natriuretic peptide for prevention of contrast-induced nephropathy in patients with heart failure undergoing primary percutaneous coronary intervention. Acta Radiologica 2010 Jul; 51(6):641-8. *Not CKD treatment*

4884. Zhang JH, Li LS, Zhang M. Clinical effects of rheum and captopril on preventing progression of chronic renal failure. Chinese Medical Journal 1990; 103(10):788-93. *Sample size less than 50 patients*

4885. Zhang M, Zhang D, Zhang W, et al. Treatment of chronic renal failure by supplementing the kidney and invigorating blood flow. Journal of Traditional Chinese Medicine 2004; 24(4):247-51. *Not CKD treatment*

4886. Zhang Z, Shahinfar S, Keane WF, et al. Importance of baseline distribution of proteinuria in renal outcomes trials: lessons from the reduction of endpoints in NIDDM with the angiotensin II antagonist losartan (RENAAL) study. Journal of the American Society of Nephrology 2005; 16(6):1775-80. *Follow-up less than 6 months*

4887. Zhao Q, Wu T-G, Lin Y, et al. Low-dose nesiritide improves renal function in heart failure patients following acute myocardial infarction. Heart & Vessels 2010 Mar; 25(2):97-103. *Not CKD treatment*

4888. Zhou X, Liu J-X, Shi R, et al. Compound ion salt, a novel low-sodium salt substitute: from animal study to community-based population trial. American Journal of Hypertension 2009; 22(9):934-42. *Follow-up less than 6 months*

4889. Zhou XJ, Vaziri ND. Defective calcium signalling in uraemic platelets and its amelioration with long-term erythropoietin therapy. Nephrology Dialysis Transplantation 2002; 17(6):992-7. *Not human studies*

4890. Zhu S, Liu Y, Wang L, et al. Transforming growth factor-beta1 is associated with kidney damage in patients with essential hypertension: renoprotective effect of ACE inhibitor and/or angiotensin II receptor blocker. Nephrology Dialysis Transplantation 2008; 23(9):2841-6. *Not CKD treatment*

4891. Zhu X, Stergiopoulos K, Wu S. Risk of hypertension and renal dysfunction with an angiogenesis inhibitor sunitinib: systematic review and meta-analysis. Acta Oncologica 2009; 48(1):9-17. *Not CKD treatment*

4892. Ziakka S, Ursu M, Poulikakos D, et al. Predictive factors and therapeutic approach of renovascular disease: four years' follow-up. Renal Failure 2008; 30(10):965-70. *Not CKD treatment*

4893. Zierer A, Voeller RK, Melby SJ, et al. Potential renal protective benefits of intra-operative BNP infusion during cardiac transplantation. Transplantation Proceedings 2006; 38(10):3680-4. *Not relevant to key questions*

4894. Zietse R, Derkx FH, Weimar W, et al. Effect of atrial natriuretic peptide on renal and vascular permeability in diabetes mellitus. Journal of the American Society of Nephrology 1995; 5(12):2057-66. *Sample size less than 50 patients*

4895. Zietse R, Schalekamp MA. Effect of synthetic human atrial natriuretic peptide (102-126) in nephrotic syndrome. Kidney International 1988; 34(5):717-24. *Sample size less than 50 patients*

4896. Zijlstra JG, Tulleken JE, Ligtenberg JJM, et al. p38-MAPK inhibition and endotoxin induced tubular dysfunction in men. Journal of Endotoxin Research 2004; 10(6):402-5. *Sample size less than 50 patients*

4897. Zimmerman TW, Schenker S. A comparative evaluation of cimetidine and ranitidine. Rational Drug Therapy 1985; 19(4):1-7. *Not CKD treatment*

4898. Zipser RD. Effects of selective inhibition of thromboxane synthesis on renal function in humans. American Journal of Physiology 1985; 248(6 Pt 2):F753-6. *Sample size less than 50 patients*

4899. Zitta S, Stoschitzky K, Zweiker R, et al. Dynamic renal function testing by compartmental analysis: assessment of renal functional reserve in essential hypertension. Nephrology Dialysis Transplantation 2000; 15(8):1162-9. *Not early CKD*

4900. Zoccali C, Ciccarelli M, Mallamaci F, et al. Effect of naloxone on the defective autonomic control of heart rate in uraemic patients. Clinical Science 1985; 69(1):81-6. *Sample size less than 50 patients*

4901. Zoccali C, Leonardis D, Enia G, et al. The MAURO study: multiple intervention and audit in renal diseases to optimize care. Journal of Nephrology 2008; 21(1):20-2. *Not CKD treatment*

4902. Zoccali C, Mallamaci F. Salt intake and hyperfiltration. Hypertension 1996; 28(6):1100-2. *Not CKD treatment*

4903. Zoungas S, Branley P, Kerr PG, et al. Atherosclerosis and folic acid supplementation trial in chronic renal failure: baseline results. Nephrology 2004; 9(3):130-41. *Not relevant to key questions*

4904. Zoungas S, Cameron JD, Kerr PG, et al. Association of carotid intima-medial thickness and indices of arterial stiffness with cardiovascular disease outcomes in CKD. American Journal of Kidney Diseases 2007; 50(4):622-30. *Follow-up less than 6 months*

4905. Zoungas S, McGrath BP, Branley P, et al. Cardiovascular morbidity and mortality in the Atherosclerosis and Folic Acid Supplementation Trial (ASFAST) in chronic renal failure: a multicenter, randomized, controlled trial. Journal of the American College of Cardiology 2006; 47(6):1108-16. *Follow-up less than 6 months*

4906. Zucchelli P, Ponticelli C, Cagnoli L, et al. Prognostic value of T lymphocyte subset ratio in idiopathic membranous nephropathy. American Journal of Nephrology 1988; 8(1):15-20. *Sample size less than 50 patients*

4907. Zucchelli P, Zuccala A. Blood pressure control effects on the progression of chronic renal failure. Renal Failure 1993; 15(3):339-42. *Not RCT or controlled trial*

4908. Zucchelli P, Zuccala A. Pharmacological treatment of renal parenchymal hypertension. Contributions to Nephrology 1994; 106:198-201. *Not RCT or controlled trial*

4909. Zucchelli P, Zuccala A, Borghi M, et al. Comparison of calcium channel blocker and ACE inhibitor therapy on the progression of renal insufficiency. Contributions to Nephrology 1990; 81:255-63. *Not CKD treatment*

4910. Zucchelli P, Zuccala A, Sturani A. Glomerular dysfunction in diabetic nephropathy. Postgraduate Medical Journal 1988; 64 Suppl 3:22-30; discussion 48-9. *Follow-up less than 6 months*

4911. Zuckermann A, Birsan T, Thaghavi S, et al. Benefit of mycophenolate mofetil in patients with cyclosporine A-induced nephropathy after lung transplantation. Transplantation Proceedings 1999; 31(1-2):1160-1. *Not RCT or controlled trial*

4912. Zuliani E, Zwahlen H, Gilliet F, et al. Vancomycin-induced hypersensitivity reaction with acute renal failure: resolution following cyclosporine treatment. Clinical Nephrology 2005; 64(2):155-8. *Sample size less than 50 patients*

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Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ACE inhibitor monotherapy versus placebo/no treatment trials (n=17 trials)				
Perkovic, 2007[1] PROGRESS Multinational (Europe, Asia, Australia) Funding Source: Industry and other	Inclusion Criteria: history of cerebrovascular disease (ischemic stroke, hemorrhagic stroke, or transient ischemic attack but not subarachnoid hemorrhage) within the previous 5 years and no clear indication for or contraindication to treatment with an ACE inhibitor. Exclusion Criteria: not described.	N=1757 patients with CKD (Baseline GFR <60 ml/min/ 1.73m^2) of 6105 randomized. Age (yr): 70 Gender (Male %): 55 Race/Ethnicity (%): Asian 37 BMI: 24 Systolic BP (mm Hg): 149 Diastolic BP (mm Hg): 84 Serum creatinine (mg/dL): 1.2 (median) Creatinine clearance (ml/min/1.73m^2) (median): 50 Estimated GFR (ml/min/1.73m^2): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 11 History of HTN (%): NR (study reported 53% on HTN medication but did not report prevalence of untreated HTN) History of CHD (%): 20 History of CHF (%): NR History of MI (%): NR History of Stroke (ischemic) (%): 71 History of Stroke (hemorrhagic) (%): 10 History of transient ischemic attack (%): 22 Peripheral arterial disease (%): NR Current smoker (%): 16	Perindopril 4 mg/d (n=895) Placebo (n=862) Followup period: mean 4 years Study withdrawals (%): NR	Allocation Concealment: adequate (central) Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: NA, post hoc analysis

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Asselbergs, 2004[2] PREVEND IT The Netherlands Funding Source: Industry and other	Inclusion Criteria: persistent microalbuminuria (urinary albumin concentration >10 mg/L in 1 early morning spot urine sample and a concentration of 15 to 300 mg/24 hours in 2 24-hour urine samples at least once); BP <160/100 mm Hg and no use of antihypertensive medication; total cholesterol level <8.0 mmol/L, or <5.0 mmol/L in case of previous MI, and no use of lipid-lowering medication. Exclusion Criteria: creatinine clearance <60% of the normal age adjusted value; use of ACE inhibitors or ARB antagonists.	N=864 Age (yr): 51 Gender (Male %): 65 Race/Ethnicity (%): white 96 BMI: 26 Systolic BP (mm Hg): 130 Diastolic BP (mm Hg): 76 Albuminuria (mg/24 h): 23 Serum creatinine (mg/dL): 1 Estimated GFR (ml/min/1.73m^2): NR Total cholesterol (mg/dL): 222 LDL cholesterol (mg/dL): 157 Diabetes (%): 2.5 History of HTN (%): 0 (exclusion criterion) History of CVD (%): NR History of CHF (%): 0 History of MI (%): 0.5 History of Stroke (%): 0.8 Peripheral arterial disease (%): 0.6 Current/ever smoker (%): 73	Fosinopril 20 mg/d (n=431) Placebo (n=433) Followup period: mean 3.8 years Study withdrawals (%): 28 Note: 2 x 2 factorial design with pravastatin	Allocation Concealment: unclear Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes
Marre, 2004[3] DIABHYCAR Multinational (Europe and North Africa) Funding Source: Industry and other	Inclusion Criteria: persistent micro-albuminuria or proteinuria (urinary albumin excretion ≥20 mg/L, in two successive random urine samples); <50 years of age; and type 2 diabetes (defined on the basis of receiving current treatment with at least one oral antidiabetic agent). Exclusion Criteria: serum creatinine concentration >150 mmol/L; treatment with insulin, an ACE inhibitor, or ARB blocker; documented CHF; MI during the past three months; urinary tract infection; previous intolerance to an ACE inhibitor.	N=4,912 Age (yr): 65 Gender (Male %): 70 Race/Ethnicity (%): NR BMI: 29 Systolic BP (mm Hg): 145 Diastolic BP (mm Hg): 82 Microalbuminuria (%): 74 Proteinuria (%): 26 Serum creatinine (mg/dL): 1.0 Estimated GFR (ml/min/1.73m^2): NR HbA_{1c}(%): 7.8 Diabetes (%): 100 History of HTN (%): 56 History of CVD (%): 24 History of CHF (%): 0 History of MI (%): 6 History of Stroke (%): 4 Peripheral arterial disease (%): 10 Current smoker (%): 15	Ramipril 1.25 mg/d (n=2443) Placebo (n=2469) Followup period: median 4 years Study withdrawals (%): 17	Allocation Concealment: adequate Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Katayama, 2002[4] JAPAN-IDDM Sarafidis review Japan Funding Source: Other	Inclusion Criteria: UAE >30 mg/24 h at the time of screening in two consecutive sterile urine samples collected overnight; onset of type 1 diabetes before 20 years; and aged between 20 and 50 years of age. Exclusion Criteria: none stated.	N=53 (imdapril arm excluded) Age (yr): 33 Gender (Male %): 35 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 127 Diastolic BP (mm Hg): 78 Albumin excretion rate (mg/day): 711 Serum creatinine (mg/dL): 0.76 Creatinine clearance (ml/min): 98.4 Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 8.8 Diabetes (%): 100 History of HTN (%): 18 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Captopril 37.5 mg (n=26) Placebo (n=27) Followup period: mean 1.5 years Study withdrawals (%): 30 (excluding subjects reaching endpoint)	Allocation Concealment: adequate Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes
Bojestig, 2001[5] Sarafidis review Sweden Funding Source: Industry	Inclusion Criteria: microalbuminuria (AER of 20–200 µg/min in two of three collections); type 1 diabetes; and normotensive (clinic diastolic <90 mmHg). Exclusion Criteria: Patients treated with any form of hypertensive medication.	N=55 Age (yr): 40 Gender (Male %): 75 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 126 (clinic) Diastolic BP (mm Hg): NR Albumin excretion rate (µg/min): median 69-103 Estimated GFR (ml/min/1.73m^2): median 100-108 HbA_{1c} (%): 7.4 Diabetes (%): 100 History of HTN (%): 0 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Ramipril 1.25 mg/d (n=19) Ramipril 15 mg/d (n=18) Placebo (n=18) Followup period: 2 years Study withdrawals (%): 7	Allocation Concealment: unclear Blinding: double Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Gerstein HOPE Trial, 2001[6] Multinational (North and South America and in Europe) Funding Source: Industry and other	Inclusion Criteria: ≥55 years of age; history of CV disease (either CAD, stroke, or PVD) or with a history of DM; plus at least one other CV risk factor (total cholesterol >200 mg/dL, high-density lipoprotein cholesterol ≤35mg/dL, HTN, known microalbuminaria, or current smoker. Microalbuminuria was defined as an ACR of ≥2mg/mmol for both men and women; dipstick-positive (ie, ≥1+) proteinuria Exclusion Criteria: heart failure; intolerance of ACE inhibitors or vitamin E; serum creatinine concentration >200 mmol/L (2.3 mg/dL), or dipstick-positive proteinuria (>+1)	N=1,140 patients with diabetes and microalbuminuria (urinary albumin-creatinine ratio >2mg/mmol, but not dipstick positive [≥1+] proteinuria) from 1963 with microalbuminuria and 9297 randomized overall in the larger HOPE trial. Patient characteristics not described for microalbuminuric subjects	Ramipril 10 mg/d (n=553) Placebo (n=587) Followup period: median 4.5 years Study withdrawals (%): NR Note: 2 x 2 factorial design with vitamin E.	Allocation Concealment: adequate (from background paper Can J Cardiol) Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: NA, post hoc analysis

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
O'Hare, 2000[7] ATLANTIS UK and Ireland Funding Source: Industry	Inclusion Criteria: microalbuminuria, defined as overnight AER on screening of 20–200 µg/min in two of three collections; type 1 diabetes; and untreated blood pressure <150/90 mmHg for patients <50 years of age and <165/90 mmHg for patients 50–65 years of age. Exclusion Criteria: those pregnant or lactating; were women of child-bearing potential not using adequate contraception; were on concomitant therapy for HTN; were on one or more nonsteroidal anti-inflammatory drugs; history of drug or alcohol abuse; had other known renal diseases or raised creatinine levels (>120 µmol/L) or liver function twice that of normal on repeat testing; or had iodine sensitivity, making them unable to partake in GFR measurements.	N=140 Age (yr): 40 Gender (Male %): 71 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 132 Diastolic BP (mm Hg): 76 Albumin excretion rate (µg/min): 53 Estimated GFR (ml/min/1.73m^2): 104 HbA_{1c} (%): 11.4 Diabetes (%): 100 History of HTN (%): 0 (HTN was exclusion criterion) History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Ramipril 1.25 mg/d (n=47) Ramipril 5 mg/d (n=45) Placebo (n=48) Followup period: 2 years Study withdrawals (%): 30	Allocation Concealment: adequate Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Muirhead, 1999[8] Kunz review Canada Funding Source: Industry	Inclusion Criteria: incipient diabetic nephropathy, defined as AER between 20 to 300 µg/min and a GFR 60 ≥ ml/min/1.73m^2 at visit 1; aged ≥18 years; type 2 DM Exclusion Criteria: "brittle" diabetes (increased risk of hypoglycemia) or patients with a history of noncompliance with medical regimens.	N=60 (excluding valsartan arms) Age (yr): 56 Gender (Male %): 82 Race/Ethnicity (%): white 87, black 2, Asian 5 BMI: NR Systolic BP (mm Hg): 136 Diastolic BP (mm Hg): 84 Serum creatinine (mg/dL): NR Albumin excretion rate (µg/min): 53.4 Estimated GFR (ml/min/1.73m^2): 87 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR HbA_{1c} (%): NR Diabetes (%): 100 History of HTN (%):47% on HTN medication History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Captopril 75 mg/d (n=29) Placebo (n=31) Follow-p period: 1 year Study withdrawals (%): 18	Allocation Concealment: unclear Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Ruggenenti, 1999[9] REIN, proteinuria stratum 1: ≥1 g to <3g/24 h Italy Funding Source: Industry	Inclusion Criteria: chronic nephropathy; persistent proteinuria (≥1 g to <3 g); aged 18 to 70 years; has not received ACEI for 2 months, corticosteroids, NSAIDS, immunosuppressive drugs for 6 months. Exclusion Criteria: treatment with corticosteroids, nonsteroidal anti-inflammatory drugs, or immunosuppressive drugs; acute MI or cerebrovascular accident in the previous 6 months; severe uncontrolled hypertension (diastolic BP ≥115 and/or systolic BP ≥220 mm Hg); evidence or suspicion of renovascular disease, obstructive uropathy, insulin-dependent diabetes mellitus, collagen disease, cancer, higher serum aminotransferase concentrations, or chronic cough; drug or alcohol abuse; pregnancy; breast feeding; and ineffective contraception.	N=186 Age (yr): 50 Gender (Male %): 75 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 143 Diastolic BP (mm Hg): 89 Urinary protein excretion (g/day): 1.7 Serum creatinine (mg/dL): 2.0 Creatinine clearance (ml/min/1.73m^2): 52 Estimated GFR (ml/min/1.73m^2): 46 Total cholesterol (mg/dL): 229 Diabetes (%): NR History of HTN (%): 82 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Ramipril 1.25 mg/d (n=99) Placebo (n=87) Followup period: median 2.6 years Study withdrawals (%): 22 (excluding subjects reaching endpoint)	Allocation Concealment: adequate (*based on GISEN report*) Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Crepaldi, 1998[10] Sarafidis review Italy Funding Source: None stated	Inclusion Criteria: overt albuminuria - median AER value between 20 and 200 µg/min from 3 timed overnight urine collections; GFR ≥80 ml/min/1.73m^2 at randomization; aged 18 to 70 years; onset of insulin-dependent DM before age 35 and insulin treatment within 3 years of diagnosis; clinical stability of DM during past 12 months; standing systolic BP ≥115 and ≤145 mmHg (without HTN therapy) and diastolic BP ≥75 and ≤90 mmHg. Exclusion Criteria: impaired renal function (defined as serum creatinine >10% above the upper limit of normal (125 µmol/L) and median AER >200 µg/min at entry and visit 3 after randomization); nondiabetic renal disease; hematuria; evidence of clinically significant liver or hematological disease; evidence of aortic or mitral valve obstruction; arrhythmias; unstable angina; history of MI within previous 3 months; systemic malignancy; hyperkalemia, serum trigylcerides >3.4mmol/L, or total cholesterol >6.5 mmol/L.	N=96 (66 included in the baseline characteristics and nifedipine arm excluded) Age (yr): 37 Gender (Male %): 67 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 128 Diastolic BP (mm Hg): 83 Albumin excretion rate (µg/min): 71.5 Serum creatinine (mg/dL): 0.98 Creatinine clearance (ml/min/1.73m^2): 114 Estimated GFR (ml/min/1.73m^2): 114 HbA_{1c} (%): 8.6 Diabetes (%): 100 History of HTN (%): 0 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 58	Lisinoprol 2.5-20 mg/d (n=47) Placebo (n=49) Followup period: 3 years Study withdrawals (%): 32 (includes 21 patients excluded for not having AER values between 20 and 200 µg/min)	Allocation Concealment: unclear Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
The GISEN Group, 1997[11] REIN, proteinuria stratum 2: ≥3 g/ 24 h Italy Funding Source: Industry	Inclusion Criteria: chronic nephropathy; persistent proteinuria (≥3 g); aged 18 to 70 years; has not received ACEI for 2 months, corticosteroids, NSAIDS, immunosuppressive drugs for 6 months. Exclusion Criteria: treatment with corticosteroids, nonsteroidal anti-inflammatory drugs, or immunosuppressive drugs; acute MI or cerebrovascular accident in the previous 6 months; severe uncontrolled hypertension (diastolic blood pressure ≥115 and/or systolic blood pressure ≥220 mm Hg); evidence or suspicion of renovascular disease, obstructive uropathy, insulin-dependent diabetes mellitus, collagen disease, cancer, higher serum aminotransferase concentrations, or chronic cough; drug or alcohol abuse; pregnancy; breast feeding; and ineffective contraception.	N=166 Age (yr): 49 Gender (Male %): 78 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 149 Diastolic BP (mm Hg): 92 Urinary protein excretion (g/day): 5.3 Serum creatinine (mg/dL): 2.4 Creatinine clearance (ml/min/1.73m^2): 45 Estimated GFR (ml/min/1.73m^2): 39 Diabetes (%): NR History of HTN (%): 87 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Ramipril 1.25 mg/d (n=78) Placebo (n=88) Followup period: mean 1.3 years Study withdrawals (%): 21 (excluding subjects reaching endpoint) Note: combined endpoint stratified by baseline AER	Allocation Concealment: adequate Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Maschio, 1996[12] Europe Funding Source: Industry	Inclusion Criteria: chronic renal insufficiency caused by various diseases (glomerular disease (in 192 patients), interstitial nephritis (in 105), nephrosclerosis (in 97), polycystic kidney disease (in 64), diabetic nephropathy (in 21) unknown (in 104)); aged 18 to 70 years; serum creatinine concentration of 1.5 to 4.0 mg/dL and a 24-hour estimated creatinine clearance of 30 to 60 ml/min, with variations of <30 percent in at least three measurements of creatinine clearance during a three-month screening period and <15 percent during a subsequent two-week, single-blind placebo period. Exclusion Criteria: therapy-resistant edema; treatment with corticosteroids, nonsteroidal antiinflammatory drugs, or immunosuppressive drugs; a value for urinary protein excretion over 10 g/24 h and a value for serum albumin under 25 g/L (each measured at least three times, and twice during the screening period); renovascular hypertension; malignant HTN or a MI or CVA in the six months preceding the study; congestive heart failure (New York Heart Association class III or IV); insulin-dependent DM; elevated serum amino-transferase concentrations; collagen disease; obstructive uropathy; cancer; chronic cough; history of allergy to ACEI; drug or alcohol abuse; and pregnancy.	N=583 Age (yr): 51 Gender (Male %): 72 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 143 Diastolic BP (mm Hg): 87 Urinary protein excretion (g/day): 1.8 Serum creatinine (mg/dL): 2.1 Creatinine clearance (ml/min): 43 Estimated GFR (ml/min/1.73m^2): NR Diabetes (%): 4 (n=21) have diabetic nephropathy History of HTN (%): 82 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR Severity of renal dysfunction: Creatinine clearance 46 to 60 ml/min) (%): 39 Creatinine clearance 30 to 45 ml/min) (%): 61	Benazepril 10 mg/d (n=300) Placebo (n=283) Followup period: median 3 years Study withdrawals (%): 23 (excluding subjects reaching endpoint)	Allocation Concealment: unclear Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Trevisan, 1995[13] Italy Funding Source: Industry	Inclusion Criteria: persistent microalbuminuria (AER 20-200 µg/min at screening and in at least two of three consecutive sterile urine samples collected overnight); aged 18 to 65 years; had non-insulin-dependent DM (diagnosed according to World Health Organization criteria) of at least 6 months duration; had stable metabolic control with a glycated hemoglobin concentration <10%. Exclusion Criteria: systolic blood pressure was ≥180 mm Hg or diastolic blood pressure ≥105 mm Hg; unstable angina, heart failure; serum creatinine >1.5 mg/dL; history of poor compliance; high serum potassium levels (>5.5 mEq/L); or liver, gastrointestinal, and connective tissue diseases.	N=122 Age (yr): 57 Gender (Male %): 77 Race/Ethnicity: NR BMI: 29 Systolic BP (mm Hg): 149 Diastolic BP (mm Hg): 91 Albumin excretion rate (µg/min): 67 Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 7.1 Diabetes (%): 100 History of HTN (%): NR (among 108 who completed study, 43 (39.8%) had baseline BP ≥160/95 mm Hg) History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 22	Ramipril 1.25 mg/d (n=60) Placebo (n=62) Followup period: 6 months Study withdrawals (%): 11	Allocation Concealment: unclear Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Laffel, 1995[14] North American Micro-albuminuria Study Sarafidis review USA and Canada Funding Source: Industry	Inclusion Criteria: microalbuminaria - overnight AER 20–200 µg/min; aged 14 to 57 years with at least 4 years documented insulin-dependent DM before age 45; normotensive Exclusion Criteria: HbA_{1c} ≥11.5%; body weight outside of 75% to 125% of ideal; serum creatinine and potassium levels beyond normal ranges; white blood cell count <3500/mm^3; BP ≥140/90 mm Hg; antihypertensive therapy; pregnancy/lactation; histories of renal, cardiac, hepatic, gastrointestinal, or autoimmune diseases. No use of CCB, beta-blockers, and non-steroidal agents.	N=143 Age (yr): 33 Gender (Male %): 50 Race/Ethnicity (%): white 92 BMI: NR Systolic BP (mm Hg): 140 Diastolic BP (mm Hg): 90 Albumin excretion rate (µg/min): 62 Serum creatinine (mg/dL): 1.1 Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (ml/min/1.73m^2): 80 HbA_{1c} (%): 7.8 Diabetes (%): 100 History of HTN (%): 0 History of CAD (%): 0 History of CHF (%): 0 History of MI (%): 0 History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 29	Captopril 100 mg (n=70) Placebo (n=73) Followup period: 2 years Study withdrawals (%): 30	Allocation Concealment: unclear Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes
Sano 1994[15] Sarafidis review Japan Funding Source: None stated	Inclusion Criteria: noninsulin dependent diabetes mellitus; persistent microalbuminuria (AER 20-300 mg/24 h on 3-4 separate occasions over a 3 month period; aged 50 to 76 years; serum creatinine <1.2 mg/dL; systolic BP <150 mmHg and diastolic <90 mmHg over a long period; HbA_{1c} <10%; no history of nondiabetic renal disease; no medications other than oral hypoglycemic agents. Exclusion Criteria: none stated.	N=52 (48 included in the baseline characteristics) Age (yr): 64 Gender (Male %): NR Race/Ethnicity (%): NR BMI: 24 Systolic BP (mm Hg): 136 Diastolic BP (mm Hg): 74 Albumin excretion rate (mg/day): 72 Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (ml/min): 90 HbA_{1c} (%): 8.2 Diabetes (%): 100 History of HTN (%): 0 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Enalapril (n=26) No enalapril (n=26) Followup period: 2 years Study withdrawals (%): 8	Allocation Concealment: unclear Blinding: no Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Lewis, 1993[16] USA Funding Source: Industry and other	Inclusion Criteria: urinary protein excretion of ≥ 500 mg/24 h, and a serum creatinine concentration of ≤ 2.5 mg/dL; aged 18 to 49 years; insulin-dependent DM for ≥7 years, with an onset before the age of 30 years, and had diabetic retinopathy; Patients satisfying these criteria during a single examination were eligible for the study, regardless of previous BP status or a previous need for antihypertensive medication. Patients who were receiving ACE inhibitors or CCBs were eligible provided their BP could be maintained within the BP goals required by the trial without these drugs Exclusion Criteria: pregnancy; dietary evaluation that indicated marked departure from standard dietary recommendations; white-cell count <2500 per cubic millimeter; CHF (New York Heart Association class III or worse); and serum potassium concentration of ≥6 mmol/L.	N=409 Age (yr): 35 Gender (Male %): 53 Race/Ethnicity (%): white 89; black 7 BMI: NR Systolic BP (mm Hg): 138 Diastolic BP (mm Hg): 85 Urinary protein excretion (g/day): 2.7 Serum creatinine (mg/dL): 1.3 Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (ml/min): 82 HbA_{1c} (%): 11.7 Diabetes (%): 100 History of HTN (%): 76 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Captopril 75 mg (n=207) Placebo (n=202) Followup period: median 3 years Study withdrawals (%): 26	Allocation Concealment: unclear Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Ravid, 1993[17] Sarafidis review Israel Funding Source: Other	Inclusion Criteria: microabluminuria (urinary protein excretion 30 to 300 mg/24h on two consecutive visits without evidence of a urinary tract infection; type 1 diabetes <10 years with no evidence of systemic, renal, cardiac, or hepatic disease; age <50 years; BMI <27; normal BP on two consecutive examinations (systolic ≤140 mm Hg; diastolic ≤90 mm Hg; Exclusion Criteria: none stated.	N=108 (94 included in the baseline characteristics) Age (yr): 44 Gender (Male %): 45 Race/Ethnicity (%): NR BMI: 24 Mean BP (mm Hg): 98 Proteinuria (mg/day): 133 Serum creatinine (mg/dL): 1.2 Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 10.4 Diabetes (%): 100 History of HTN (%): 0 History of CAD (%):NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Enalapril 10 mg (n=56) Placebo (n=52) Followup period: 5 years Study withdrawals (%): 13	Allocation Concealment: unclear Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes
ACE inhibitor monotherapy versus ARB trials (n=6 trials)				
Mann, 2008[18] ONTARGET Multinational Funding Source: Industry	Inclusion Criteria: aged 55 years or older with established atherosclerotic vascular disease or with diabetes with endorgan damage. Exclusion Criteria: major renal artery stenosis, uncorrected volume or sodium depletion, a serum creatinine concentration above 265 µmol/L, and uncontrolled hypertension (>160 mm Hg systolic or >100 mm Hg diastolic), symptomatic congestive heart failure..	N=4,046 for patients with a baseline GFR <60 ml/min/ 1.73m^2 (of a total of 17,118 randomized to ramipril vs. telmisartan, and not including 8502 subjects randomized to combination ramipril + telmisartan). 2673 patients had micro or macroalbuminuria. Patient characteristics not described for CKD subjects	Ramipril 10 mg/day (n NR for CKD patients) Telmisartan 80 mg/day (n NR for CKD patients) Followup period: median 4.7 years Study withdrawals (%): NR	Allocation Concealment: adequate Blinding: double Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Menne, 2008[19] VALERIA Germany and Hungary Funding Source: Industry	Inclusion Criteria: microalbuminuria (urine albumin creatinine ratio for women ≥3.5 mg/ mmol/L and ≤35.0 mg/mmol and men ≥2.5 mg/ mmol/L and ≤25.0 mg/ mmoL); aged 18 to 75 years; essential hypertension [defined as mean sitting diastolic BP ≥85 mmHg and <110 mm Hg]. To fulfill the criteria of microalbuminuria, two of three first morning void urines needed to be positive during the screening phase. Exclusion Criteria: primary kidney disease, renal impairment (creatinine clearance <30ml/min using the Cockroft and Gault formula; serum potassium values >5.5mmol/L; heart failure, significant arrhythmias or bradycardia; relevant valvular disease, type I DM, uncontrolled type II DM with HbA_{1c} >8.0%; history of MI; percutaneous transluminal coronary angioplasty, bypass surgery or stroke within the last 12 months prior to study inclusion; unstable angina pectoris; renal transplantation; severe hepatic disease or hepatic failure; malignant concomitant diseases or history of malignant diseases within the last 5 years; systemic inflammatory diseases; pregnancy or breast feeding; psychiatric disease; either history of alcohol or drug abuse or both.	N=90 (133 total with combination arm) Age (yr): 58 Gender (Male %): 69 Race/Ethnicity (%): NR BMI: 32 Systolic BP (mm Hg): 153 Diastolic BP (mm Hg): 91 Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (mg/min): 112 Urine albumin creatinine ratio (mg/ mmol): 9.4 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR HbA_{1c} (%): NR Diabetes (%): 74 History of HTN (%): 100 History of CAD “Cardiac disorders”(%): 19 History of CHF (%): 0 (exclusion criterion) History of MI (%): 0 (exclusion criterion) History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Lisinopril 40 mg/d (n=47) Valsartan 320 mg/d (n=43) *Lisinopril + Valsartan (n=43)* Followup period: 2.5 years Study withdrawals (%): 14	Allocation Concealment: adequate Blinding: double plus outcome assessors and data analysts Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Sengul, 2006[20] Turkey Funding Source: none stated	Inclusion Criteria: Type 2 diabetes, microalbuminuria (AER rate 30 to 300 mg/24 h for a minimum of three consecutive occasions); aged 40 to 65 years; previously diagnosed hypertension (systolic BP ≥ 140 mm Hg or diastolic BP ≥90 mm Hg), despite receiving ACE inhibitor monotherapy for ≥6 months. Exclusion Criteria: type 1 DM; BMI ≥ 40; secondary diabetes; alcoholism; thyroid disease; systolic BP >200 mm Hg, any non-diabetic cause of secondary HTN (including bilateral renal artery stenosis); urinary tract infection; persistent hematuria; chronic liver disease; overt carcinoma; any cardiovascular event in the previous 6 months; serum creatinine ≥ 150 mmol/L; serum potassium ≥ 5.5 mmol/L; or pregnancy.	N=219 Age (yr): 57 Gender (Male %): 37 Race/Ethnicity (%): NR BMI: 30 Systolic BP (mm Hg): 151 Diastolic BP (mm Hg): 89 Urinary AER (mg/24 h): 260 Serum creatinine (mg/dL): 1 Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (mg/min): 97 Total cholesterol (mg/dL): 211 LDL cholesterol (mg/dL): 135 HbA_{1c} (%): 7.9 Diabetes (%): 100 History of HTN (%): 100 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 37	Lisinopril 20 mg/d (n=110) Telmisartan 80 mg/d (n=109) After 24 weeks, half of the patients receiving lisinopril were randomized to receive telmisartan in addition. Similarly, half the patients initially treated with telmisartan received a combination of lisinopril plus telmisartan. The remaining patients continued to be treated with monotherapy. Followup period: 1 year Study withdrawals (%): 12	Allocation Concealment: unclear Blinding: open-label Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Barnett, 2004[21] DETAIL Europe Funding Source: Industry	Inclusion Criteria: urinary albumin excretion rate (mean of three consecutive overnight values) between 11 and 999 µg per minute, with two values > 10 µg per minute; aged 35 to 80 years; type 2 DM treated by diet, diet plus oral hypoglycemic drugs (for at least one year), or insulin preceded by treatment with oral agents (also for at least one year). Among those treated with insulin, onset of diabetes had to have occurred after the age of 40 years with a BMI >25 at the time of diagnosis; mild-to-moderate HTN, with a resting BP of less than 180/95 mm Hg after ≥3 months of ACE-inhibitor therapy before entry into the study; normal renal morphology; glycosylated hemoglobin value <12 %; serum creatinine <1.6 mg/dL; GFR >70 ml/min/1.73m^2. Exclusion Criteria: any condition (other than cardiovascular disease) that could restrict long-term survival and known allergy to study drugs or iohexol.	N=250 Age (yr): 61 Gender (Male %): 73 Race/Ethnicity (%): white 98 BMI: 31 Systolic BP (mm Hg): 152 Diastolic BP (mm Hg): 86 Microabluminuria (%): 82 Macroabluminuria (%): 18 Urinary AER (µg/min): median 46 to 60 Serum creatinine (mg/dL): 1 Estimated GFR (ml/min/1.73m^2): 93 Total cholesterol (mg/dL): 223 LDL cholesterol (mg/dL): 137 HbA_{1c} (%): 8.3 Diabetes (%): 100 History of HTN (%): 100 History of CVD (%): 49 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 25	Enalapril 20 mg/d (n=130) Telmisartan 80 mg/d (n=120) Followup period: 5 years Study withdrawals (%): 33	Allocation Concealment: adequate Blinding: double Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Lacourcière, 2000[22] Canada Funding Source: Industry	Inclusion Criteria: early nephropathy characterized by a UAE rate 20 to 350 µg/min without evidence of urinary tract infection; type 2 diabetes diagnosed at 30 years of age or later; mild to moderate essential HTN (sitting diastolic BP 90 to 115 mm Hg); Exclusion Criteria: evidence or suspicion of renovascular disease; history of malignant hypertension; systolic BP > 210 mm Hg; cerebrovascular accident in the previous 12 months or current transient ischemic attacks; myocardial infarction within the previous 12 months; clinically significant arteriovenous (AV) conduction disturbances and/or arrhythmias; unstable angina; history of heart failure, serum creatinine ≥ 200 mmol/L; serum potassium ≥ 5.5 mmol/L or ≤ 3.5 mmol/L; treatment with oral corticosteroids; concomitant use of agents that may affect BP except β-blockers and nitrates used in the treatment of stable angina; drug or alcohol abuse; pregnancy, breast feeding, and ineffective contraception.	N=103 Age (yr): 59 Gender (Male %): 81 Race/Ethnicity (%): white 96; Asian 3; black 1 BMI: NR Systolic BP (mm Hg): 160 Diastolic BP (mm Hg): 96 Urinary AER (µg/min): 69 Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): 96 HbA_{1c} (%): NR Diabetes (%): 100 History of HTN (%): 100 History of CAD (%): NR History of CHF (%): 0 (exclusion criterion) History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Enalapril 5 mg/d (n=51) Losartan 50 mg/d (n=52) Followup period: 1 year Study withdrawals (%): 11	Allocation Concealment: unclear Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Muirhead, 1999[8] Kunz review Canada Funding Source: Industry	Inclusion Criteria: incipient diabetic nephropathy, defined as AER between 20 to 300 µg/min and a GFR 60 ≥ ml/min/1.73m^2 at visit 1; aged ≥ 18 years; type 2 DM Exclusion Criteria: "brittle" diabetes (increased risk of hypoglycemia) or patients with a history of non compliance with medical regimens.	N=91 (excluding placebo arm) Age (yr): 56 Gender (Male %): 67 Race/Ethnicity (%): white 90, black 1, Asian 4 BMI: NR Systolic BP (mm Hg): 136 Diastolic BP (mm Hg): 83 Urinary AER (µg/min): 54 Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): 91 HbA_{1c} (%): NR Diabetes (%): 100 History of HTN (%): 33% on HTN medication History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Captopril 75 mg/d (n=29) Valsartsan 80 mg/d (n=31) Valsartsan 160 mg/d (n=31) Followup period: 1 year Study withdrawals (%): 13	Allocation Concealment: unclear Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ACE inhibitor monotherapy versus Calcium channel blocker trials (n=6 trials)				
Rahman, 2005[23] ALLHAT USA and Canada Funding Source: Industry and other	Inclusion Criteria: aged 55 years or older who had stage 1 or stage 2 hypertension; at least 1 additional risk factor for CHD events (previous (> 6 months) MI or stroke, left ventricular hypertrophy demonstrated by electrocardiography or echocardiography, history of type 2 DM, current cigarette smoking, high-density lipoprotein cholesterol level < 35 mg/dL, or documentation of other atherosclerotic cardiovascular disease). Exclusion Criteria: history of symptomatic heart failure and/or a known left ventricular ejection fraction <35%; serum creatinine level > 2 mg/dL as reported by the investigator.	N=3049 for patients with a baseline GFR <60 ml/min/ 1.73m^2 (of a total of 17,118 randomized and minus the chlorthalidone arm) Age (yr): 70 Gender (Male %): 48 Race/Ethnicity (%): white 58; black 25; Hispanic 13 BMI: 29 Systolic BP (mm Hg): 147 Diastolic BP (mm Hg): 83 Albuminuria: NR Serum creatinine (mmol/L): NR Estimated GFR (ml/min/1.73m^2): 50 HbA_{1c} (%): NR Diabetes (%): 33 History of HTN (%): 100 History of CAD (%): 29 History of CHF (%): NR History of MI or stroke (%): 27 Peripheral arterial disease (%): NR Current smoker (%): 18	Lisinopril up to 40 mg/d (n=1533) Amlodipine up to 10 mg/d (n=1516) *Chlorthalidone arm* 3 x 2 factorial design, Followup period: mean 4.9 years Study withdrawals (%):Not reported for CKD subgroup	Allocation Concealment: adequate (from background paper) Blinding: double Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: Not reported for CKD subgroup

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Fogari, 2002[24] Italy Funding Source: none stated	Inclusion Criteria: microalbuminuria; essential HTN and type 2 DM and noted by sitting diastolic BP values >90 mm Hg and <110 mm Hg; type 2 DM well controlled by diet or by metformin alone or metformin plus a sulfanylurea; UAE ≥30 and ≤300 mg/24 h in two distinct 24-h urine collections during 7 days before enrollment; BMI < 30 kg/m^2; serum creatinine <1.5 mg/dL. Exclusion Criteria: history of previous CHD, stroke, CHF, cancer; smoking habits; electrocardiogram showing left ventricular hypertrophy; total cholesterol values >240 mg/dL; use of diuretics or b-blockers.	N=205 (minus combination arm) Age (yr): 63 Gender (Male %): 58 Race/Ethnicity (%): NR BMI: 28 Systolic BP (mm Hg): 160 Diastolic BP (mm Hg): 99 Urinary AER (µg/min): 97 Serum creatinine (mmol/L): 1 Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (mg/min): 90 HbA_{1c} (%): 7 Diabetes (%): 100 History of HTN (%): 100 History of CAD (%): 0 History of CHF (%): 0 History of MI (%): 0 History of Stroke (%): 0 Peripheral arterial disease (%): NR Current smoker (%): NR	Fosinopril 10-30 mg/d (n=102) Amlodipine up to 10 mg/d (n=103) *Combination arm* Followup period: 4 years Study withdrawals (%): 32% of all subjects (including combination arm) in titration period, 26% during study period.	Allocation Concealment: adequate Blinding: open-label Intention to Treat Analysis: no, 453 were randomized to a 3-month titration period but 144 were removed due to non response or adverse events Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Agodoa, 2002[25] Wright, 2002[26] Norris, 2006[27] (AASK) USA Funding Source: Industry and other	Inclusion Criteria: self-identified African Americans with HTN; aged 18 to 70 years; GFR between 20 and 65 mL/min/1.73 m2 and no other identified causes of renal insufficiency. Exclusion Criteria: diastolic BP of <95 mm Hg; known history of DM (fasting glucose ≥140 mg/dL or random glucose >200 mg/dL); urinary protein to creatinine ratio >2.5; accelerated or malignant HTN within 6 months; secondary HTN; evidence of non–BP-related causes of chronic kidney disease; serious systemic disease; clinical CHF; or specific indication for or contraindication to a study drug or study procedure.	N=653 (minus metoprolol arm of 1,094 randomized) Age (yr): 54 Gender (Male %): 61 Race/Ethnicity (%): African American 100 BMI: NR Systolic BP (mm Hg): 151 Diastolic BP (mm Hg): 96 Proteinuria (g/24 h): 0.5 (pooled men and women) Serum creatinine (mg/dL): 2.21 men; 1.76 women Estimated GFR (ml/min/1.73m^2): 46.3 Diabetes (%): 0 History of HTN (%): 100 History of CAD (%): 52 History of CHF (%): 0 History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Ramipril 2.5-10 mg/d (n=436) Amlodipine 5-10 mg/d (n=217) *Metoprolol arm* 3 x 2 factorial design with lower and usual blood pressure goal arms Followup period: mean 4 years (Norris 2006) Study withdrawals (%): 0 (not counting death or dialysis, or no GFR assessment)	Allocation Concealment: adequate (from background paper) Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Marin, 2001[28] ESPIRAL Spain Funding Source: None stated	Inclusion Criteria: aged 18 to 75 years; serum creatinine values between 1.5 and 5 mg/dl; hypertension (BP >140/90 mmHg, or by the use of antihypertensive agent(s); proven progression of chronic renal failure in the previous 2 years (increase by more than 25% or > 0.5 mg/dl in serum creatinine). Exclusion Criteria: DM; recent history of cardiovascular disease (stroke, myocardial infarction, or heart failure); taking concomitant medications that could interfere with study results (steroids, immuno-suppressant drugs, or NSAIDS); presenting intolerance to fosinopril or nifedipine.	N=241 Age (yr): 56 Gender (Male %): 59 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 156 Diastolic BP (mm Hg): 96 Albuminuria (g/dL): 4.3 Proteinuria (g/24 h): 1.7 Serum creatinine (mg/dL): 2.8 Creatinine clearance (ml/min/1.73m^2): 36 Estimated GFR (ml/min/1.73m^2): NR Diabetes (%): 0 History of HTN (%): 100 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Fosinopril 10-30 mg/d (n=129) Nifedepine 30-60 mg/d (n=112) Followup period: minimum 3 years Study withdrawals (%): 34 (excluding death)	Allocation Concealment: unclear Blinding: open-label Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Crepaldi, 1998[10] Sarafidis review Italy Funding Source: None stated	Inclusion Criteria: age 18 to 70 years; onset of insulin-dependent DM before age 35 and insulin treatment within 3 years of diagnosis; clinical stability of DM during past 12 months; median AER value between 20 and 200 µg/min from 3 timed overnight urine collections; GFR ≥80 ml/min/1.73m^2 at randomization; standing systolic BP ≥115 and ≤145 mmHg (without HTN therapy) and diastolic BP ≥75 and ≤90 mmHg. Exclusion Criteria: impaired renal function (defined as serum creatinine >10% above the upper limit of normal (125 µmol/L) and median AER >200 µg/min at entry and visit 3 after randomization); nondiabetic renal disease; hematuria; evidence of clinically significant liver or hematological disease; evidence of aortic or mitral valve obstruction; arrhythmias; unstable angina; history of MI within previous 3 months; systemic malignancy; hyperkalemia, serum trigylcerides >3.4mmol/L, or total cholesterol >6.5 mmol/L.	N=88 (58 included in the baseline characteristics and nifedipine arm excluded) Age (yr): 37 Gender (Male %): 69 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 128 Diastolic BP (mm Hg): 83 Albumin excretion rate (µg/min): 61.2 Albumin (g/dL): 4.4 Serum creatinine (mg/dL): 0.96 Creatinine clearance (ml/min/1.73m^2): 109 Estimated GFR (ml/min/1.73m^2): 120 HbA_{1c} (%): 8.1 Diabetes (%): 100 (type 1) History of HTN (%): 0 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 57	Lisinoprol 2.5-20 mg/d (n=48) Nifedepine 10-20 mg/d (n=41) Followup period: 3 years Study withdrawals (%): 37 (includes 27 patients excluded for not having AER values between 20 and 200 µg/min)	Allocation Concealment: unclear Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Zucchelli, 1995/1992[29,30] Italy Funding Source: None stated	Inclusion Criteria: aged 18 to 70 years of age; established chronic renal failure (serum creatinine ranging between 1.8 to 5 mg/dL); variation in plasma creatinine < 50% during 3 month observation period; HTN - baseline diastolic BP ≥ 95 mmHg; good general health. Exclusion Criteria: DM; potentially reversible renal disease; systemic diseases; severe cardiac or hepatic dysfunction; peripheral edema; proteinuria >5 g/24 h.	N=121 Age (yr): 55 Gender (Male %): 58 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 165 Diastolic BP (mm Hg): 100 Proteinuria (g/24 h): 1.8 Serum creatinine (mg/dL): 3.0 Estimated GFR (ml/min/1.73m^2): NR Diabetes (%): 0 History of HTN (%): 100 History of CAD (%): NR (none with severe disease) History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Captopril 25-100 mg/d (n=60) Nifedepine 20-40 mg/d (n=61) Followup period: 3 years Study withdrawals (%): 26	Allocation Concealment: unclear Blinding: none stated Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ACE inhibitor monotherapy versus beta-blocker trials (n=3 trials)				
Wright, 2002[26] Norris, 2006[27] (AASK) USA Funding Source: Industry and other	Inclusion Criteria: self-identified African Americans with HTN; aged 18 to 70 years; GFR between 20 and 65 mL/min/1.73 m2 and no other identified causes of renal insufficiency. Exclusion Criteria: diastolic BP of less <95 mm Hg; known history of DM (fasting glucose ≥140 mg/dL or random glucose >200 mg/dL); urinary protein to creatinine ratio >2.5; accelerated or malignant HTN within 6 months; secondary HTN; evidence of non–BP-related causes of chronic kidney disease; serious systemic disease; clinical CHF; or specific indication for or contraindication to a study drug or study procedure.	n=877 (minus amlodipine arm of 1,094 randomized) Age (yr): 55 Gender (Male %): 61.5 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 150.5 Diastolic BP (mm Hg): 95.5 Albuminuria: NR Serum creatinine (mg/dL): 2.15 Estimated GFR (ml/min/1.73m^2): 45.6 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 0 History of HTN (%): 100 History of CAD (%): NR History of “heart disease” (%): 51 History of CHF (%): 0 History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Ramipril 2.5-10.0 mg/d (n=436) Metoprolol 50-200 mg/d (n=441) 3 x 2 factorial design with lower and usual blood pressure goal arms Followup period: 4 years Study withdrawals (%):0 (not counting death or dialysis, or no GFR)	Allocation Concealment: adequate (from background paper) Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
van Essen, 1997[31] The Netherlands Funding Source: Industry	Inclusion Criteria: modest chronic renal insufficiency defined as a creatinine clearance of 30-90 mL/min; aged 18 to 65 years old; no need for immunosuppressive agents or non-steroidal anti-inflammatory drugs; no proven renal artery stenosis, or other conditions for which beta blocking drugs or ACEI are contraindicated. Both patients with and without proteinuria could be included. Exclusion Criteria: NR	N=103 (89 with baseline characteristics and evaluated) Age (yr): 50 Gender (Male %): 64 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 152 Diastolic BP (mm Hg): 90 Proteinuria (g/24h): median 3.3 Serum creatinine (mg/dL): 1.8 Creatinine clearance (ml/min/1.73m^2): 55 Estimated GFR (ml/min/1.73m^2): 53 Diabetes (%): 0 History of HTN (%): 53% were reported to have untreated diastolic BP < 90 mm Hg History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Enalapril 10 mg/d (n=52) Atenolol 50 mg/d (n=51) Followup period: median 3.9 years Study withdrawals (%): 14	Allocation Concealment: unclear Blinding: double Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Hannedouche, 1994[32] France Funding Sources: Industry	Inclusion Criteria: aged 18 to 70 years; chronic renal failure as defined by a serum creatinine concentration of 200-400 µmol/L Exclusion Criteria: patients with the nephrotic syndrome (serum albumin concentration <30 g/L); systemic diseases including diabetes, malignant hypertension, renovascular hypertension, evolving obstructive nephropathy, and serious extrarenal disorders including malignancy, heart failure, and coronary artery disease; also excluded were women who were breast feeding, pregnant, or intending to become pregnant and patients who had taken converting enzyme inhibitors in the three months before inclusion; had contraindications to converting enzyme inhibitors or (B blockers; were unlikely to comply; or were unwilling to give consent	N=100 Age (yr): 51 Gender (Male %): 53 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 167 Diastolic BP (mm Hg): 102 Proteinuria (g/24h): 2.2 Serum creatinine (mg/dL): 3.0 Estimated GFR (ml/min/1.73m^2): NR Diabetes (%): 0 History of HTN (%): 100 History of CAD (%): 0 History of CHF (%): NR History of MI (%): 0 History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Enalapril 5-10 mg/d (n=52) Acebutolol 400 mg/d or Atenolol 100 mg/d (n=48) Followup period: 3 years Study withdrawals (%): 23	Allocation Concealment: adequate Blinding: open-label Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ACE inhibitor monotherapy versus diuretic trials (n= 2 trials)				
Rahman, 2005[23] ALLHAT USA and Canada Funding Source: Industry and other	Inclusion Criteria: aged 55 years or older who had stage 1 or stage 2 hypertension; at least 1 additional risk factor for CHD events (previous (> 6 months) MI or stroke, left ventricular hypertrophy demonstrated by electrocardiography or echocardiography, history of type 2 DM, current cigarette smoking, high-density lipoprotein cholesterol level <35 mg/dL, or documentation of other atherosclerotic cardiovascular disease). Exclusion Criteria: history of symptomatic heart failure and/or a known left ventricular ejection fraction <35%; serum creatinine level > 2 mg/dL as reported by the investigator.	N=4,146 for patients with a baseline GFR <60 ml/min/ 1.73m^2 (of a total of 17,118 randomized and minus the amlodipine arm) Age (yr): 71 Gender (Male %): 49 Race/Ethnicity (%): white 57; black 26; Hispanic 12 BMI: 29 Systolic BP (mm Hg): 147 Diastolic BP (mm Hg): 83 Albuminuria: NR Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): 50 Diabetes (%): 33 (type 2) History of HTN (%): 100 History of CAD (%): 31 History of CVD (%): 61 History of CHF (%): 0 (by exclusion criteria) History of MI or stroke (%): 29 Peripheral arterial disease (%): NR Current smoker (%): 18	Lisinopril up to 40 mg/d (n=1533) Chlorthalidone up to 25 mg/d (n=2613) 3 x 2 factorial design, Followup period: mean 4.9 years Study withdrawals (%): Not reported for CKD subgroup	Allocation Concealment: adequate (from background paper) Blinding: double Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: Not reported for CKD subgroup

Appendix Evidence Table C1. Overview of ACEI monotherapy versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Marre, 2004[33] NESTOR France Funding Sources: Industry	Inclusion Criteria: aged between 35 and 80 years; type 2 DM; persistent micro-albuminuria (AER between 20 and 200 µg/min on at least two of three overnight urine collections); essential HTN. Diabetes was required to be controlled by diet with or without one or more oral antidiabetic treatment, unchanged for at least 3 months. For selection, microalbuminuria had to be documented within the previous year. Exclusion Criteria: severe HTN; BMI > 40 kg/m^2; ventricular rhythm disorders on ECG; urinary tract infection, haematuria or leucocyturia; plasma creatinine > 150 µmol/l; kalaemia < 3.5 mmol/l or > 5.5 mmol/l; uric acid > 536 µmol/l; treatment with potassium supplement or insulin and poor placebo compliance during the run-in period. Previously known intolerance to ACEI or diuretics was also a criterion for exclusion.	N=570 Age (yr): 60 Gender (Male %): 65 Race/Ethnicity (%): white 86; black 4; Asian 2 BMI: 30 Systolic BP (mm Hg): 161 Diastolic BP (mm Hg): 94 Albumin excretion rate (µg/min): 58 Urinary albumin: creatinine ratio: 6.2 Serum creatinine (mg/dL): NR Creatinine clearance (ml/min/1.73m^2): 92 Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 7.6 Diabetes (%): 100 History of HTN (%): 100 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 14	Enalapril 10 mg/d (n=286) Indapamide 1.5 mg/d (n=284) Followup period: 1 year Study withdrawals (%): 11.4	Allocation Concealment: Unclear Blinding: double Intention to Treat Analysis: no (one subject excluded) Withdrawals/Dropouts adequately described: yes

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C2. Summary of study baseline characteristics for ACEI monotherapy versus control treatment trials

Characteristic	Mean (Range) *Unless Otherwise Noted*	Number of Trials Reporting
ACEI versus placebo		**17**
Total number of patients evaluated	11,661 (52-4,912)	17
Age of subjects, years	60 (33-70)	16
Gender, male (%)	66 (35-82)	15
Race/ethnicity, white (%)	77 (63-96)	5
Body Mass Index	28 (24-29)	5
Patients with diabetes (%)	65 (0-100)	17
Patients with diabetic nephropathy‡, n	6,193 (21-4,912)	13
% HbA_{1c} in patients with diabetes	8.2 (7.1-11.0)	10
Estimated GFR ml/min/1.73m^2	68.5 (39-114)	5
Serum creatinine, mg/dL	1.0 (0.8-2.4)	10
Creatinine clearance, ml/min/1.73m^2	64.1 (43-114)	8
Albumin excretion rate, µg/min	61.0 (53-71.5)	5
Albuminuria, mg/24 h	63.2 (72-711)	3
Proteinuria, g/24 h	2.34 (0.13-5.3)	5
Systolic blood pressure, mm Hg	144 (126-149)	15
Diastolic blood pressure, mm Hg	83 (74-92)	14
Patients with hypertension, %	50 (0-100)	16
Patients with cardiovascular disease, %	38 (0-100)	5
Patients randomized to Ramipril versus placebo, n	7,537 (65%) (55-4,912)	7
Patients randomized to Captopril versus placebo, n	665 (6%) (81-409)	4
Patients randomized to Perindopril versus placebo, n	1,757	1
Patients randomized to Fosinopril versus placebo, n	864	1
Patients randomized to Benazepril versus placebo, n	583	1
Patients randomized to Enalapril versus placebo, n	108	1
Patients randomized to Lisinopril versus placebo, n	97	1
Patients randomized to Enalopril versus no treatment, n	52	1
ACEI versus ARB		**6**
Total number of patients evaluated, n	4,799 (90-4,046)	6
Age of subjects, years	59 (56-61)	5
Gender, male, %	62 (37-81)	5
Race/ethnicity, white, %	96 (91-98)	3
Body Mass Index	31 (30-32)	3
Patients with diabetes, %	97 (76-100)	5
Patients with diabetic nephropathy‡, n	730 (67-250)	5
% HbA_{1c} %in patients with diabetes	8.1 (7.9-8.3)	2
Estimated GFR, ml/min/1.73m^2	92 (91-96)	3
Serum creatinine, mg/dL	1.0 (1.0-1.0)	2
Creatinine clearance, ml/min/1.73m^2	101 (97-112)	2
Albumin excretion rate, µg/min	62 (53-69)	2
Systolic blood pressure, mm Hg	151 (136-160)	5
Diastolic blood pressure, mm Hg	87 (83-91)	5
Patients with hypertension, %	94 (33-100)	5
Patients with cardiovascular disease, %	99 (19-100)	3
Patients randomized to Ramipril versus ARB, n	4046	1
Patients randomized to Enalapril versus ARB, n	353 (103-250)	2
Patients randomized to Lisinopril versus ARB, n	309 (90-219)	2
Patients randomized to Captopril versus ARB, n	91	1
Patients randomized to Telmisartan versus ACEI, n	4,515 (219-4,046)	3
Patients randomized to Valsartan versus ACEI, n	181 (90-91)	2
Patients randomized to Losartan versus ACEI, n	103	1

Appendix Table C2. Summary of study baseline characteristics for ACEI monotherapy versus control treatment trials (continued)

Characteristic	Mean (Range) *Unless Otherwise Noted*	Number of Trials Reporting
ACEI versus CCB		**6**
Total number of patients evaluated, n	4,357 (88-3,049)	6
Age of subjects, years	66 (37-71)	6
Gender, male, %	51 (48-69)	6
Race/ethnicity, white, %	48 (0-58)	2
Body Mass Index	29 (28 to 29)	2
Patients with diabetes, %	30 (0-100)	6
Patients with diabetic nephropathy‡, n	293 (88-205)	2
Patients with	1,015 (121-653)	3
% HbA_{1c} in patients with diabetes	7.2 (7.0-8.1)	2
Estimated GFR, ml/min/1.73m^2	50 (46-120)	3
Serum creatinine, mg/dL	2.0 (1.0-3.0)	5
Proteinuria, g/24 h	0.9 (0.5-1.8)	3
Systolic blood pressure, mm Hg	149 (128-165)	6
Diastolic blood pressure, mm Hg	87 (83-100)	6
Patients with hypertension, %	99 (0-100)	6
Patients with cardiovascular disease, %	29 (0-52)	5
Patients randomized to Lisinopril versus CCB, n	3,137 (88-3,049)	2
Patients randomized to Ramipril versus CCB, n	653	1
Patients randomized to Fosinopril versus CCB, n	446 (205-241)	2
Patients randomized to Captopril versus CCB, n	121	1
Patients randomized to Amlodipine versus ACEI, n	3,907 (205-3,049)	3
Patients randomized to Nifedipine versus ACEI, n	450 (88-241)	3
ACEI versus BB		**3**
Total number of patients evaluated, n	1,080 [100-877]	3
Age of subjects, years	54 [50-55]	3
Gender, male, %	61 (53-64)	3
Race/ethnicity, white, %	0*	1
Patients with diabetes, %	0	3
Estimated GFR, ml/min/1.73m^2	47 [46-53]	2
Serum creatinine, mg/dL	2.0 [1.8-3.0]	3
Proteinuria, g/24 h	0.7 [0.5-2.2]	2
Systolic blood pressure, mm Hg	152 (150-167)	3
Diastolic blood pressure, mm Hg	95 (90-102)	3
Patients with hypertension, %	96 (47-100)	3
Patients randomized to Ramipril versus BB, n	877	1
Patients randomized to Enalapril versus BB, n	203 (100-103)	2
Patients randomized to Metropolol versus ACEI, n	877	1
Patients randomized to Atenolol or Acebutelol versus ACEI, n†	203 (100-103)	2
ACEI versus Diuretics		**2**
Total number of patients evaluated, n	4,716 [570-4,146]	2
Age of subjects, years	70 [60-71]	2
Gender, male, %	51 [49-65]	2
Race/ethnicity, white, %	61 [57-85]	2
Patients with diabetes, %	41 [33-100]	2
Estimated GFR, ml/min/1.73m^2	50	1
Creatinine clearance, ml/min/1.73m^2	92	1
Albumin excretion rate, µg/min	58	1
Systolic blood pressure, mm Hg	149 (147-161)	2
Diastolic blood pressure, mm Hg	84 (83-94)	2
Patients with hypertension, %	100	2
Patients randomized to Lisinopril versus Diuretic, n	4,146	1

Appendix Table C2. Summary of study baseline characteristics for ACEI monotherapy versus control treatment trials (continued)

Characteristic	Mean (Range) *Unless Otherwise Noted*	Number of Trials Reporting
Patients randomized to Enalapril versus Diuretic, n	570	1
Patients randomized to Chlorthalidone versus ACEI, n	4,146	1
Patients randomized to Indapimide versusACEI, n	570	1

ACEI = angiotension converting enzyme inhibitor; HbA_{1c} = hemoglobin A_{1c}; GFR = glomerular filtration rate; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; BB = beta blocker

* Only one trial reported ethnicity, the AASK study which limited enrollment to self-identified African Americians.

†In one trial, all participants assigned BB were assigned atenolol while in the other trial, all participants assigned BB were assigned to either atenolol or acebutolol.

‡Diabetic nephropathy defined as present in patients with diabetes and albuminuria or proteinuria.

Appendix Table C3. Clinical outcomes (outcomes part A), ACEI monotherapy versus control treatment trials

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Nonfatal n/N (%)		Stroke or CVA, Any n/N (%)	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
ACEI versus placebo/no treatment trials (n=17)												
Perkovic, 2007[1] (PROGRESS)	153/895* (17.1)	138/862* (16.0)	85/895* (9.5)	86/862* (10.0)							112/895* (12.5)	152/862* (17.6)
Asselbergs, 2004[2] (PREVD)	5/431 (1.2)	4/433 (0.9)	5/431 (1.2)	3/433 (0.7)					12/431 (2.8)	11/433 (2.5)	1/431 (0.2)*	10/433 (2.3)
Marre, 2004[3] (DIAB)	334/2443 (13.7)	324/2469 (13.1)	179/2443 (7.3)	175/2469 (7.1)	61/2443 (2.5)	78/2469 (3.2)			52/2443 (2.1)	59/2469 (2.4)	118/2443 (4.8)	116/2469 (4.7)
Katayama, 2002[4]	0/52	0/27										
Bojestig, 2001[5]	0/37	0/18										
Gerstein, 2001[6] (MICROHOPE)	90/553 (16.3)	122/587 (20.8)										
O'Hare, 2000[7] (ATLANTIS)	5/92 (5.4)	0/48							3/92 (3.3)	1/48 (2.1)		
Muirhead, 1999[8]												
REIN, 1999[9] stratum 1	1/99 (1.0)	0/87									1/99 (1.0)	0/87
Crepaldi, 1998[10]	0/32	0/34			0/32	1/34 (2.9)			0/32	1/34 (2.9)		
REIN, 1997[11] stratum 2	2/78 (2.6)	1/88 (1.1)					1/78 (1.3)	0/88	1/78 (1.3)	1/88 (1.1)		
Maschio, 1996[12]	8/300 (2.7)	1/283 (0.4)					3/300 (1.0)	0/283	2/300 (0.7)	2/283 (0.7)		
Trevisan, 1995[13]					1/60 (1.7)	1/62 (1.6)			1/60 (1.7)	1/62 (1.6)		
Laffel, 1995[14]	1/70 (1.4)	0/73										
Sano, 1994[15]	1/31 (3.2)	0/31										
Lewis, 1993[16]	8/207 (3.9)	14/202 (6.9)										
Ravid, 1993[17]	0/49	0/45										

Appendix Table C3. Clinical outcomes (outcomes part A), ACEI monotherapy versus control treatment trials (continued)

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Nonfatal n/N (%)		Stroke or CVA, Any n/N (%)	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
ACEI versus ARB trials (n=6)												
Perkovic, 2007[1] (PROGRESS)	153/895* (17.1)	138/862* (16.0)	85/895* (9.5)	86/862* (10.0)							112/895* (12.5)	152/862* (17.6)
Asselbergs, 2004[2] (PREVD)	5/431 (1.2)	4/433 (0.9)	5/431 (1.2)	3/433 (0.7)					12/431 (2.8)	11/433 (2.5)	1/431 (0.2)*	10/433 (2.3)
Marre, 2004[3] (DIAB)	334/2443 (13.7)	324/2469 (13.1)	179/2443 (7.3)	175/2469 (7.1)	61/2443 (2.5)	78/2469 (3.2)			52/2443 (2.1)	59/2469 (2.4)	118/2443 (4.8)	116/2469 (4.7)
Katayama, 2002[4]	0/52	0/27										
Bojestig, 2001[5]	0/37	0/18										
Gerstein, 2001[6] (HOPE)	149/952† (15.7)	204/1004† (20.3)										
O'Hare, 2000[7] (ATLANTIS)	5/92 (5.4)	0/48							3/92 (3.3)	1/48 (2.1)		
Muirhead, 1999[8]												
REIN, 1999[9] stratum 1	1/99 (1.0)	0/87									1/99 (1.0)	0/87
Crepaldi, 1998[10]	0/32	0/34			0/32	1/34 (2.9)			0/32	1/34 (2.9)		
REIN, 1997[11] stratum 2	2/78 (2.6)	1/88 (1.1)					1/78 (1.3)	0/88	1/78 (1.3)	1/88 (1.1)		
Maschio, 1996[12]	8/300 (2.7)	1/283 (0.4)					3/300 (1.0)	0/283	2/300 (0.7)	2/283 (0.7)		
Trevisan, 1995[13]					1/60 (1.7)	1/62 (1.6)			1/60 (1.7)	1/62 (1.6)		
Laffel, 1995[14]	1/70 (1.4)	0/73										
Sano, 1994[15]	1/31 (3.2)	0/31										
Lewis, 1993[16]	8/207 (3.9)	14/202 (6.9)										
Ravid, 1993[17]	0/49	0/45										

Appendix Table C3. Clinical outcomes (outcomes part A), ACEI monotherapy versus control treatment trials (continued)

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Nonfatal n/N (%)		Stroke or CVA, Any n/N (%)	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
ACEI versus CCB trials (n=6)												
Rahman, 2006[34] ALLHAT											99/1533 (6.5)	100/1516 (6.6)
Rahman, 2006[34] ALLHAT, DM patients*											33/501 (6.6)	42/506 (8.3)
Fogari, 2002[24]	3/102 (2.9)	4/103 (3.9)										
Norris, 2006[27] Agodoa 2001[25] (AASK)	34/436 (7.8)	22/217 (10.1)	12/436 (2.8)	7/217 (3.2)							23/436 (5.3)	9/217 (4.1)
Marin, 2001[28] ESPIRAL	4/129 (3.1)	6/112 (5.4)	3/129 (2.3)	6/112 (5.4)							1/129 (0.8)	2/112 (1.8)
Crepaldi, 1998[10]	0/48	1/41 (2.4)			0/32	0/26			0/32	0/26		
Zucchelli, 1995[29]	1/60 (1.7)	0/61	1/60 (1.7)	0/61								
ACEI versus BB trials (n=3)												
Norris, 2006[27] (AASK)	34/436 (7.8)	49/441 (11.1)	12/436 (2.8)	12/441 (2.7)							23/436 (5.3)	23/441 (5.2)
van Essen, 1997[31]	2/43 (4.7)	1/46 (2.2)	2/43 (4.7)	1/46 (2.2)			2/43 (4.7)	1/46 (2.2)				
Hannedouche, 1994[32]	1/52 (1.9)	2/48 (4.2)										

Appendix Table C3. Clinical outcomes (outcomes part A), ACEI monotherapy versus control treatment trials (continued)

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Nonfatal n/N (%)		Stroke or CVA, Any n/N (%)	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
ACEI versus diuretics trials (n=2)												
Rahman, 2006[34] ALLHAT											99/1533 (6.5)	157/2613 (6.0)
Rahman, 2006[34] ALLHAT, DM patients**											33/501 (6.6)	63/881 (7.2)
Marre, 2004[33] NESTOR	1/286 (0.3)	2/284 (0.7)	1/286 (0.3)	2/284 (0.7)			0/286	1/284 (0.3)				

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor II blocker; CCB = calcium channel blocker; BB = beta blocker ; CVA = cerebrovascular accident (i.e., stroke); DM = diabetes mellitus

*Patients with CKD, defined as creatinine clearance <60 ml/min

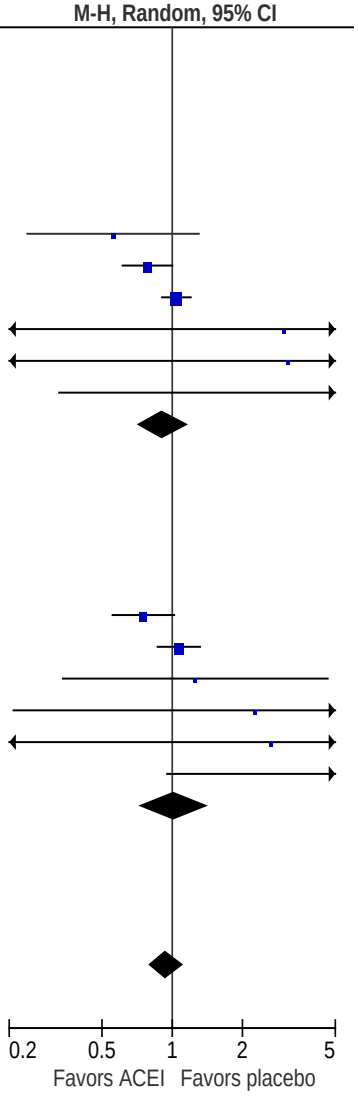
†Patients with CKD, defined as presence of microalbuminuria

**Rahman 2006 ALLHAT DM patients is a report on the subgroup of diabetic patients from the overall ALLHAT study

Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials
ACEI VERSUS PLACEBO

All-cause mortality

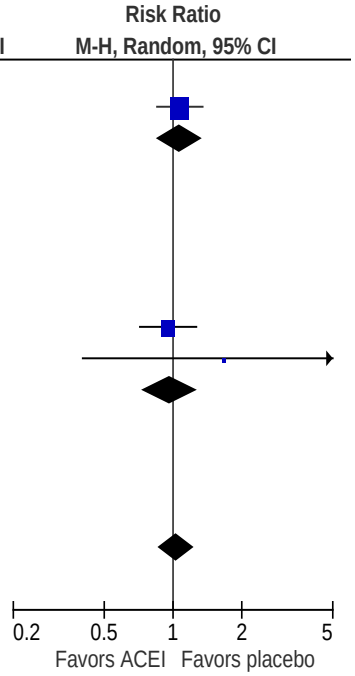
Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Diabetic nephropathy						
Muirhead 1999	0	29	0	31		Not estimable
Katayama 2002	0	26	0	27		Not estimable
Ravid 1993	0	49	0	45		Not estimable
Bojestig 2001	0	37	0	18		Not estimable
Crepaldi 1998	0	47	0	49		Not estimable
Lewis 1993	8	207	14	202	3.7%	0.56 [0.24, 1.30]
Gerstein (HOPE) 2001	90	553	122	587	21.2%	0.78 [0.61, 1.00]
Marre (DIABHYCAR) 2004	334	2443	324	2469	30.0%	1.04 [0.90, 1.20]
Sano 1994	1	31	0	31	0.3%	3.00 [0.13, 70.92]
Laffel 1995	1	70	0	73	0.3%	3.13 [0.13, 75.49]
O'Hare (ATLANTIS) 2000	5	92	0	48	0.3%	5.80 [0.33, 102.66]
Subtotal (95% CI)		**3584**		**3580**	**55.8%**	**0.91 [0.70, 1.18]**
Total events	439		460			
Heterogeneity: Tau² = 0.03; Chi² = 8.01, df = 5 (P = 0.16); I² = 38%						
Test for overall effect: Z = 0.70 (P = 0.48)						
1.1.2 Non-diabetic or mixed nephropathy						
Gerstein (HOPE) 2001	59	399	82	417	17.1%	0.75 [0.55, 1.02]
Perkovic (PROGRESS) 2007	153	895	138	862	24.1%	1.07 [0.87, 1.32]
Asselbergs (PREVEND) 2004	5	431	4	433	1.6%	1.26 [0.34, 4.64]
REIN Stratum-2 1997	2	78	1	88	0.5%	2.26 [0.21, 24.41]
REIN Stratum-1 1999	1	99	0	87	0.3%	2.64 [0.11, 63.98]
Maschio 1996	8	300	1	283	0.7%	7.55 [0.95, 59.96]
Subtotal (95% CI)		**2202**		**2170**	**44.2%**	**1.01 [0.72, 1.43]**
Total events	228		226			
Heterogeneity: Tau² = 0.05; Chi² = 8.29, df = 5 (P = 0.14); I² = 40%						
Test for overall effect: Z = 0.07 (P = 0.94)						
Total (95% CI)		**5786**		**5750**	**100.0%**	**0.94 [0.80, 1.12]**
Total events	667		686			
Heterogeneity: Tau² = 0.02; Chi² = 16.30, df = 11 (P = 0.13); I² = 33%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Test for subgroup differences: Chi² = 0.23, df = 1 (P = 0.63), I² = 0%						



Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

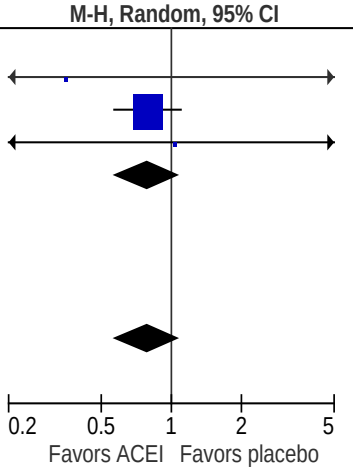
Cardiovascular mortality

Study or Subgroup	ACE Inhibitor Events	ACE Inhibitor Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 Diabetic nephropathy						
Marre (DIABHYCAR) 2004	141	2443	133	2469	59.5%	1.07 [0.85, 1.35]
Subtotal (95% CI)		**2443**		**2469**	**59.5%**	**1.07 [0.85, 1.35]**
Total events	141		133			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						
1.2.2 Non-diabetic or mixed nephropathy						
Perkovic (PROGRESS) 2007	85	895	86	862	38.9%	0.95 [0.72, 1.27]
Asselbergs (PREVEND) 2004	5	431	3	433	1.6%	1.67 [0.40, 6.96]
Subtotal (95% CI)		**1326**		**1295**	**40.5%**	**0.97 [0.74, 1.29]**
Total events	90		89			
Heterogeneity: Tau² = 0.00; Chi² = 0.58, df = 1 (P = 0.45); I² = 0%						
Test for overall effect: Z = 0.19 (P = 0.85)						
Total (95% CI)		**3769**		**3764**	**100.0%**	**1.03 [0.86, 1.23]**
Total events	231		222			
Heterogeneity: Tau² = 0.00; Chi² = 0.85, df = 2 (P = 0.65); I² = 0%						
Test for overall effect: Z = 0.33 (P = 0.74)						



Myocardial infarction (any)

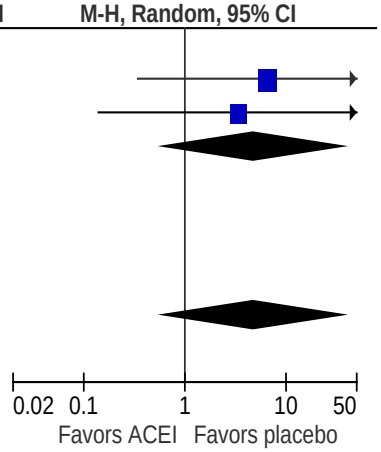
Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 Diabetic nephropathy						
Crepaldi 1998	0	32	1	34	1.1%	0.35 [0.01, 8.38]
Marre (DIABHYCAR) 2004	61	2443	78	2469	97.5%	0.79 [0.57, 1.10]
Trevisan 1995	1	60	1	62	1.4%	1.03 [0.07, 16.15]
Subtotal (95% CI)		**2535**		**2565**	**100.0%**	**0.79 [0.57, 1.09]**
Total events	62		80			
Heterogeneity: Tau² = 0.00; Chi² = 0.28, df = 2 (P = 0.87); I² = 0%						
Test for overall effect: Z = 1.44 (P = 0.15)						
Total (95% CI)		**2535**		**2565**	**100.0%**	**0.79 [0.57, 1.09]**
Total events	62		80			
Heterogeneity: Tau² = 0.00; Chi² = 0.28, df = 2 (P = 0.87); I² = 0%						
Test for overall effect: Z = 1.44 (P = 0.15)						
Test for subgroup differences: Not applicable						



Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

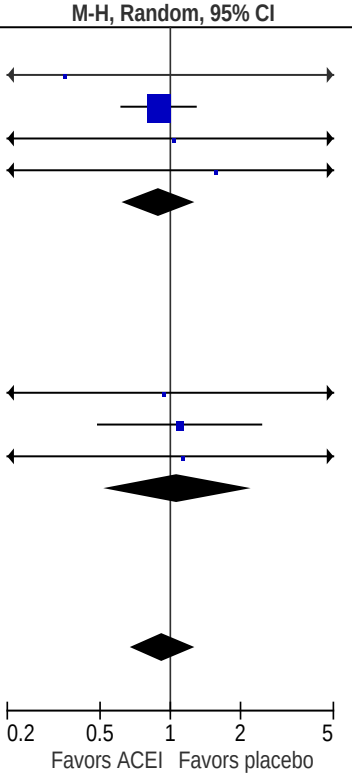
Myocardial infarction (fatal)

Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 Non-diabetic or mixed nephropathy						
Maschio 1996	3	300	0	283	53.7%	6.60 [0.34, 127.30]
REIN Stratum-2 1997	1	78	0	88	46.3%	3.38 [0.14, 81.78]
Subtotal (95% CI)		**378**		**371**	**100.0%**	**4.84 [0.55, 42.34]**
Total events	4		0			
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.76); I² = 0%						
Test for overall effect: Z = 1.43 (P = 0.15)						
Total (95% CI)		**378**		**371**	**100.0%**	**4.84 [0.55, 42.34]**
Total events	4		0			
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.76); I² = 0%						
Test for overall effect: Z = 1.43 (P = 0.15)						
Test for subgroup differences: Not applicable						



Myocardial infarction (nonfatal)

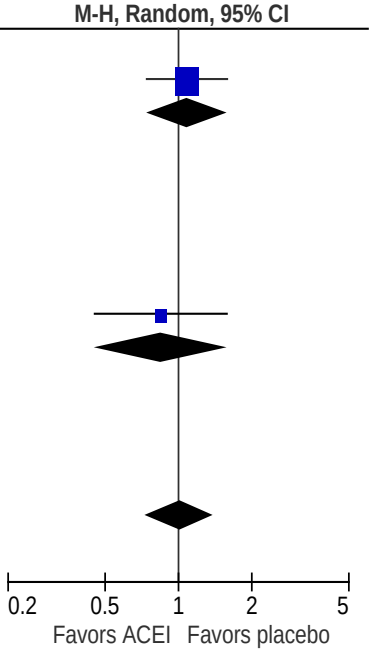
Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 Diabetic nephropathy						
Crepaldi 1998	0	32	1	34	1.0%	0.35 [0.01, 8.38]
Marre (DIABHYCAR) 2004	52	2443	59	2469	75.7%	0.89 [0.62, 1.29]
Trevisan 1995	1	60	1	62	1.4%	1.03 [0.07, 16.15]
O'Hare (ATLANTIS) 2000	3	92	1	48	2.1%	1.57 [0.17, 14.65]
Subtotal (95% CI)		**2627**		**2613**	**80.2%**	**0.90 [0.63, 1.28]**
Total events	56		62			
Heterogeneity: Tau² = 0.00; Chi² = 0.58, df = 3 (P = 0.90); I² = 0%						
Test for overall effect: Z = 0.60 (P = 0.55)						
1.5.2 Non-diabetic or mixed nephropathy						
Maschio 1996	2	300	2	283	2.7%	0.94 [0.13, 6.65]
Asselbergs (PREVEND) 2004	12	431	11	433	15.8%	1.10 [0.49, 2.46]
REIN Stratum-2 1997	1	78	1	88	1.4%	1.13 [0.07, 17.74]
Subtotal (95% CI)		**809**		**804**	**19.8%**	**1.08 [0.52, 2.21]**
Total events	15		14			
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 2 (P = 0.99); I² = 0%						
Test for overall effect: Z = 0.20 (P = 0.84)						
Total (95% CI)		**3436**		**3417**	**100.0%**	**0.93 [0.67, 1.28]**
Total events	71		76			
Heterogeneity: Tau² = 0.00; Chi² = 0.80, df = 6 (P = 0.99); I² = 0%						
Test for overall effect: Z = 0.45 (P = 0.65)						
Test for subgroup differences: Chi² = 0.20, df = 1 (P = 0.65), I² = 0%						



Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

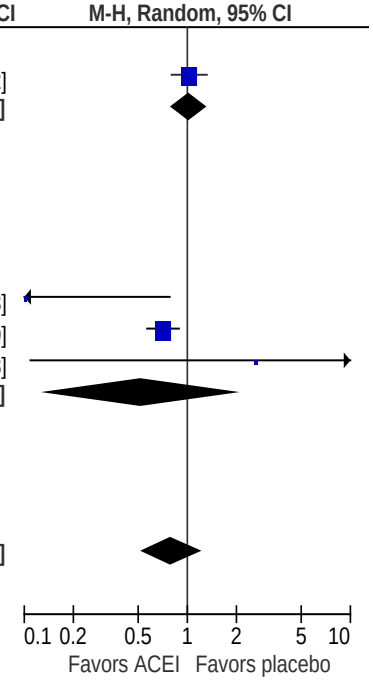
Congestive heart failure hospitalization

Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.18.1 Patients with DM						
Gerstein (HOPE) 2001	49	553	48	587	72.9%	1.08 [0.74, 1.59]
Subtotal (95% CI)		**553**		**587**	**72.9%**	**1.08 [0.74, 1.59]**
Total events	49		48			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.41 (P = 0.68)						
1.18.2 Patients without DM						
Gerstein (HOPE) 2001	17	399	21	417	27.1%	0.85 [0.45, 1.58]
Subtotal (95% CI)		**399**		**417**	**27.1%**	**0.85 [0.45, 1.58]**
Total events	17		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.52 (P = 0.60)						
Total (95% CI)		**952**		**1004**	**100.0%**	**1.01 [0.73, 1.40]**
Total events	66		69			
Heterogeneity: Tau² = 0.00; Chi² = 0.44, df = 1 (P = 0.51); I² = 0%						
Test for overall effect: Z = 0.08 (P = 0.94)						
Test for subgroup differences: Chi² = 0.44, df = 1 (P = 0.51), I² = 0%						



Stroke

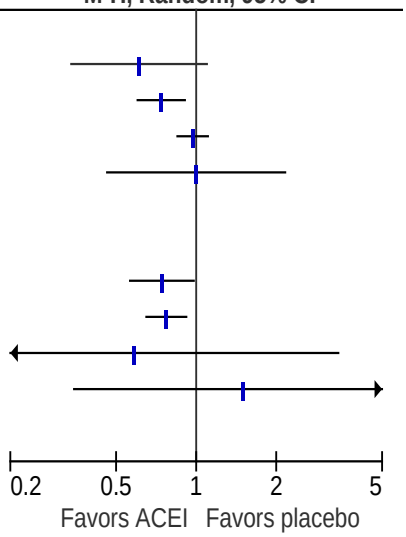
Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 Diabetic nephropathy						
Marre (DIABHYCAR) 2004	118	2443	116	2469	46.3%	1.03 [0.80, 1.32]
Subtotal (95% CI)		**2443**		**2469**	**46.3%**	**1.03 [0.80, 1.32]**
Total events	118		116			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.22 (P = 0.83)						
1.6.2 Non-diabetic or mixed nephropathy						
Asselbergs (PREVEND) 2004	1	431	10	433	4.1%	0.10 [0.01, 0.78]
Perkovic (PROGRESS) 2007	112	895	152	862	47.7%	0.71 [0.57, 0.89]
REIN Stratum-1 1999	1	99	0	87	1.8%	2.64 [0.11, 63.98]
Subtotal (95% CI)		**1425**		**1382**	**53.7%**	**0.51 [0.13, 2.09]**
Total events	114		162			
Heterogeneity: Tau² = 0.85; Chi² = 4.18, df = 2 (P = 0.12); I² = 52%						
Test for overall effect: Z = 0.93 (P = 0.35)						
Total (95% CI)		**3868**		**3851**	**100.0%**	**0.80 [0.52, 1.23]**
Total events	232		278			
Heterogeneity: Tau² = 0.09; Chi² = 9.25, df = 3 (P = 0.03); I² = 68%						
Test for overall effect: Z = 1.03 (P = 0.30)						
Test for subgroup differences: Chi² = 0.91, df = 1 (P = 0.34), I² = 0%						



Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

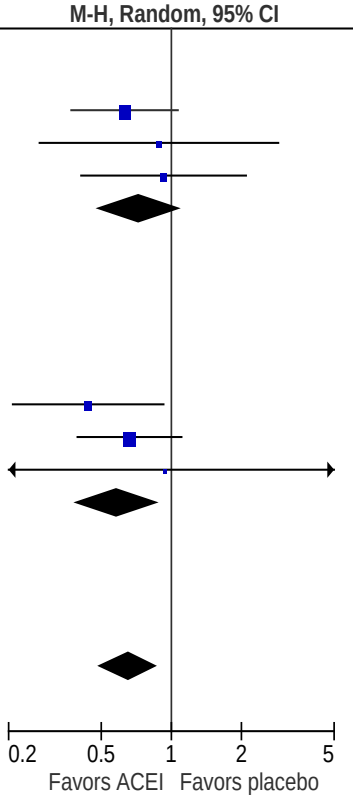
Composite vascular outcome (see Table C5 for definitions)

Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Risk Ratio M-H, Random, 95% CI
1.8.1 Diabetic nephropathy					
Asselbergs (PREVEND) 2004	17	431	28	433	0.61 [0.34, 1.10]
Gerstein (HOPE) 2001	117	553	168	587	0.74 [0.60, 0.91]
Marre (DIABHYCAR) 2004	362	2443	377	2469	0.97 [0.85, 1.11]
O'Hare (ATLANTIS) 2000	16	92	8	46	1.00 [0.46, 2.16]
1.8.2 Non-diabetic or mixed nephropathy					
Gerstein (HOPE) 2001	69	399	97	417	0.74 [0.56, 0.98]
Perkovic (PROGRESS) 2007	178	895	222	862	0.77 [0.65, 0.92]
REIN Stratum-1 1999	2	99	3	87	0.59 [0.10, 3.43]
REIN Stratum-2 1997	4	78	3	88	1.50 [0.35, 6.51]



End-stage renal disease

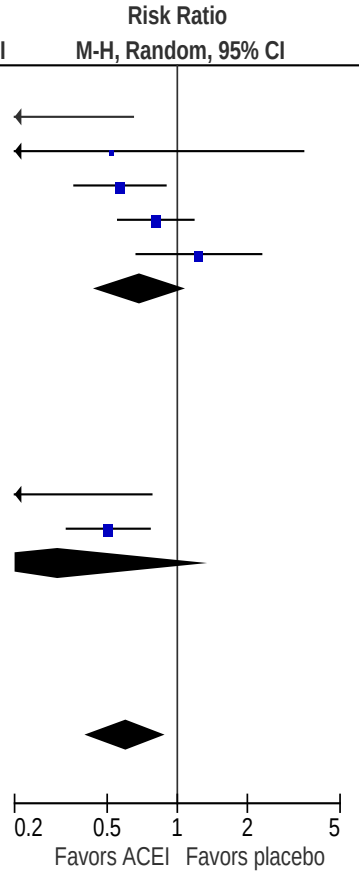
Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.9.1 Diabetic nephropathy						
Ravid 1993	0	49	0	45		Not estimable
Lewis 1993	20	207	31	202	31.2%	0.63 [0.37, 1.07]
Micro-HOPE 2001	5	553	6	587	6.2%	0.88 [0.27, 2.88]
Marre (DIABHYCAR) 2004	11	2443	12	2469	13.1%	0.93 [0.41, 2.10]
Subtotal (95% CI)		**3252**		**3303**	**50.5%**	**0.73 [0.48, 1.10]**
Total events	36		49			
Heterogeneity: Tau² = 0.00; Chi² = 0.73, df = 2 (P = 0.69); I² = 0%						
Test for overall effect: Z = 1.52 (P = 0.13)						
1.9.2 Non-diabetic or mixed nephropathy						
REIN Stratum-1 1999	9	99	18	87	15.6%	0.44 [0.21, 0.93]
REIN Stratum-2 1997	17	78	29	88	32.7%	0.66 [0.40, 1.11]
Maschio 1996	1	300	1	283	1.1%	0.94 [0.06, 15.01]
Subtotal (95% CI)		**477**		**458**	**49.5%**	**0.59 [0.39, 0.89]**
Total events	27		48			
Heterogeneity: Tau² = 0.00; Chi² = 0.90, df = 2 (P = 0.64); I² = 0%						
Test for overall effect: Z = 2.50 (P = 0.01)						
Total (95% CI)		**3729**		**3761**	**100.0%**	**0.65 [0.49, 0.88]**
Total events	63		97			
Heterogeneity: Tau² = 0.00; Chi² = 2.13, df = 5 (P = 0.83); I² = 0%						
Test for overall effect: Z = 2.83 (P = 0.005)						
Test for subgroup differences: Chi² = 0.50, df = 1 (P = 0.48), I² = 0%						



Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

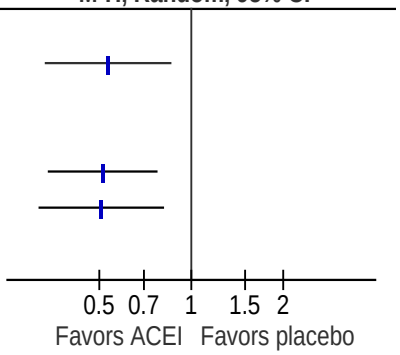
Doubling of serum creatinine

Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.10.1 Diabetic nephropathy						
Ravid 1993	2	49	12	45	6.1%	0.15 [0.04, 0.65]
Katayama 2002	2	52	2	27	3.9%	0.52 [0.08, 3.49]
Lewis 1993	25	207	43	202	21.9%	0.57 [0.36, 0.89]
Marre (DIABHYCAR) 2004	48	2443	60	2469	24.0%	0.81 [0.56, 1.18]
Micro-HOPE 2001	21	553	18	587	17.6%	1.24 [0.67, 2.30]
Subtotal (95% CI)		**3304**		**3330**	**73.5%**	**0.69 [0.44, 1.09]**
Total events	98		135			
Heterogeneity: Tau² = 0.13; Chi² = 8.93, df = 4 (P = 0.06); I² = 55%						
Test for overall effect: Z = 1.61 (P = 0.11)						
1.10.2 Non-diabetic or mixed nephropathy						
REIN Stratum-2 1997	1	78	11	88	3.5%	0.10 [0.01, 0.78]
Maschio 1996	30	300	56	283	23.0%	0.51 [0.33, 0.76]
Subtotal (95% CI)		**378**		**371**	**26.5%**	**0.31 [0.07, 1.35]**
Total events	31		67			
Heterogeneity: Tau² = 0.77; Chi² = 2.39, df = 1 (P = 0.12); I² = 58%						
Test for overall effect: Z = 1.56 (P = 0.12)						
Total (95% CI)		**3682**		**3701**	**100.0%**	**0.60 [0.40, 0.89]**
Total events	129		202			
Heterogeneity: Tau² = 0.14; Chi² = 14.42, df = 6 (P = 0.03); I² = 58%						
Test for overall effect: Z = 2.52 (P = 0.01)						
Test for subgroup differences: Chi² = 1.03, df = 1 (P = 0.31), I² = 2.8%						



Composite renal outcome (see Table C7 for defintions)

Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Risk Ratio M-H, Random, 95% CI
1.11.1 Diabetic nephropathy					
Lewis 1993	23	207	42	202	0.53 [0.33, 0.86]
1.11.2 Non-diabetic or mixed nephropathy					
Maschio 1996	31	300	57	283	0.51 [0.34, 0.77]
REIN Stratum-2 1997	18	78	40	88	0.51 [0.32, 0.81]

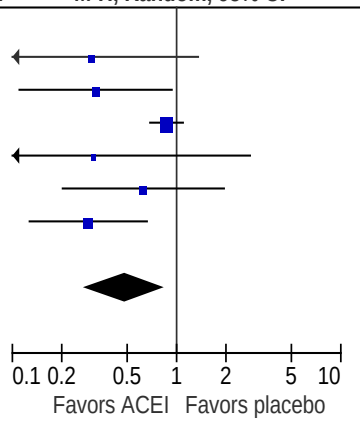


Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

Progression from microalbuminuria to macroalbuminuria

Study or Subgroup	ACEI Events	ACEI Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Bojestig 2001	0	37	0	18		Not estimable
Crepaldi 1998	2	32	7	34	10.3%	0.30 [0.07, 1.35]
Laffel 1995	4	67	13	70	15.8%	0.32 [0.11, 0.94]
Micro-HOPE 2001	104	553	127	587	33.2%	0.87 [0.69, 1.10]
Muirhead 1999	1	29	3	27	5.7%	0.31 [0.03, 2.81]
O'Hare (ATLANTIS) 2000	6	88	5	46	14.8%	0.63 [0.20, 1.95]
Ravid 1993	6	49	19	45	20.3%	0.29 [0.13, 0.66]
Total (95% CI)		**855**		**827**	**100.0%**	**0.48 [0.27, 0.85]**
Total events	123		174			

Heterogeneity: Tau² = 0.24; Chi² = 11.30, df = 5 (P = 0.05); I² = 56%
Test for overall effect: Z = 2.52 (P = 0.01)

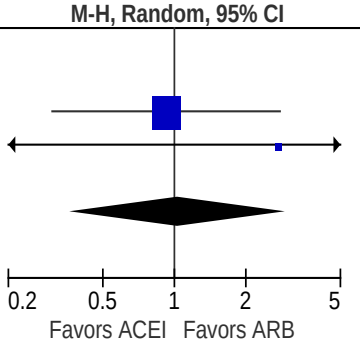


ACEI VERSUS ARB

All-cause mortality

Study or Subgroup	ACEI Events	ACEI Total	ARB Events	ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
Lacourcière 2000	0	51	0	52		Not estimable
Muirhead 1999	0	29	0	62		Not estimable
Barnett (DETAIL) 2004	6	130	6	120	89.2%	0.92 [0.31, 2.78]
Menne (VALERIA) 2008	1	47	0	43	10.8%	2.75 [0.12, 65.76]
Total (95% CI)		**257**		**277**	**100.0%**	**1.04 [0.37, 2.95]**
Total events	7		6			

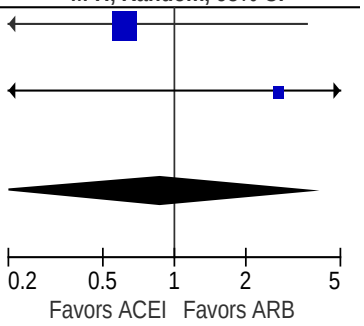
Heterogeneity: Tau² = 0.00; Chi² = 0.41, df = 1 (P = 0.52); I² = 0%
Test for overall effect: Z = 0.07 (P = 0.94)



Cardiovascular mortality

Study or Subgroup	ACEI Events	ACEI Total	ARB Events	ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
Barnett (DETAIL) 2004	2	130	3	120	76.2%	0.62 [0.10, 3.62]
Lacourcière 2000	0	51	0	52		Not estimable
Menne (VALERIA) 2008	1	47	0	43	23.8%	2.75 [0.12, 65.76]
Muirhead 1999	0	29	0	62		Not estimable
Total (95% CI)		**257**		**277**	**100.0%**	**0.88 [0.19, 4.13]**
Total events	3		3			

Heterogeneity: Tau² = 0.00; Chi² = 0.66, df = 1 (P = 0.42); I² = 0%
Test for overall effect: Z = 0.16 (P = 0.87)



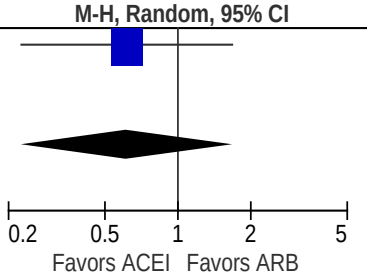
Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

Myocardial infarction (nonfatal)

Study or Subgroup	ACEI Events	ACEI Total	ARB Events	ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
Barnett (DETAIL) 2004	6	130	9	120	100.0%	0.62 [0.23, 1.68]
Lacourcière 2000	0	51	0	52		Not estimable
Total (95% CI)		**181**		**172**	**100.0%**	**0.62 [0.23, 1.68]**
Total events	6		9			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.95 (P = 0.34)

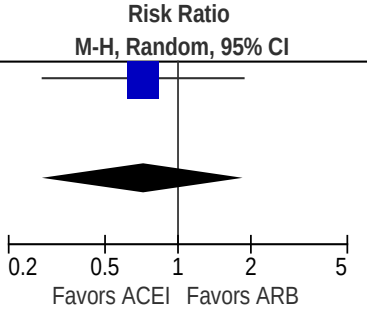


Congestive heart failure

Study or Subgroup	ACEI Events	ACEI Total	ARB Events	ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
Barnett (DETAIL) 2004	7	130	9	120	100.0%	0.72 [0.28, 1.87]
Lacourcière 2000	0	51	0	52		Not estimable
Total (95% CI)		**181**		**172**	**100.0%**	**0.72 [0.28, 1.87]**
Total events	7		9			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.68 (P = 0.50)

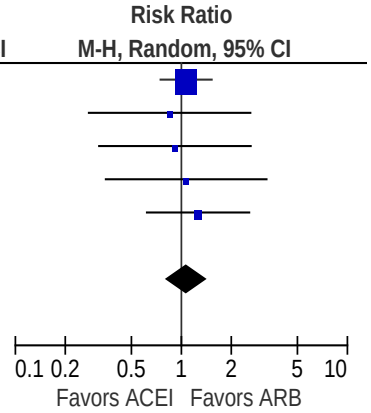


Any study withdrawal

Study or Subgroup	ACEI Events	ACEI Total	ARB Events	ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
Barnett (DETAIL) 2004	44	130	38	120	63.8%	1.07 [0.75, 1.53]
Lacourcière 2000	5	51	6	52	6.4%	0.85 [0.28, 2.61]
Menne (VALERIA) 2008	6	47	6	43	7.3%	0.91 [0.32, 2.62]
Muirhead 1999	4	29	8	62	6.5%	1.07 [0.35, 3.26]
Sengul 2006	15	109	12	110	16.0%	1.26 [0.62, 2.57]
Total (95% CI)		**366**		**387**	**100.0%**	**1.07 [0.80, 1.42]**
Total events	74		70			

Heterogeneity: Tau² = 0.00; Chi² = 0.45, df = 4 (P = 0.98); I² = 0%

Test for overall effect: Z = 0.46 (P = 0.64)



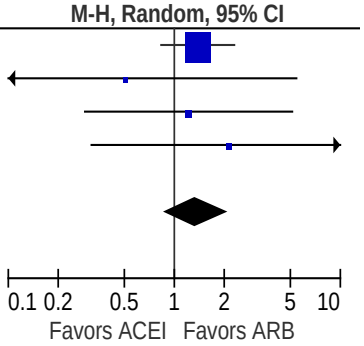
Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

Study withdrawal due to AE

Study or Subgroup	ACEI Events	ACEI Total	ARB Events	ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
Barnett (DETAIL) 2004	30	130	20	120	80.5%	1.38 [0.83, 2.30]
Lacourcière 2000	1	51	2	52	3.7%	0.51 [0.05, 5.45]
Menne (VALERIA) 2008	4	47	3	43	10.1%	1.22 [0.29, 5.14]
Muirhead 1999	2	29	2	62	5.7%	2.14 [0.32, 14.43]
Total (95% CI)		**257**		**277**	**100.0%**	**1.35 [0.86, 2.13]**
Total events	37		27			

Heterogeneity: Tau² = 0.00; Chi² = 0.90, df = 3 (P = 0.82); I² = 0%

Test for overall effect: Z = 1.29 (P = 0.20)

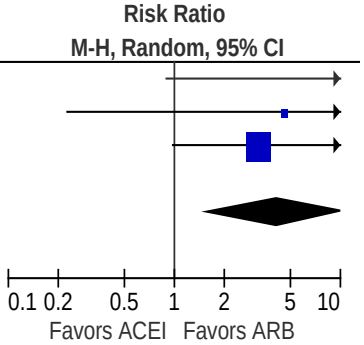


Cough

Study or Subgroup	ACEI Events	ACEI Total	ARB Events	ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
Lacourcière 2000	7	51	0	52	13.1%	15.29 [0.90, 260.90]
Menne (VALERIA) 2008	2	47	0	43	11.7%	4.58 [0.23, 92.86]
Muirhead 1999	6	29	4	62	75.2%	3.21 [0.98, 10.50]
Total (95% CI)		**127**		**157**	**100.0%**	**4.10 [1.47, 11.48]**
Total events	15		4			

Heterogeneity: Tau² = 0.00; Chi² = 1.16, df = 2 (P = 0.56); I² = 0%

Test for overall effect: Z = 2.69 (P = 0.007)



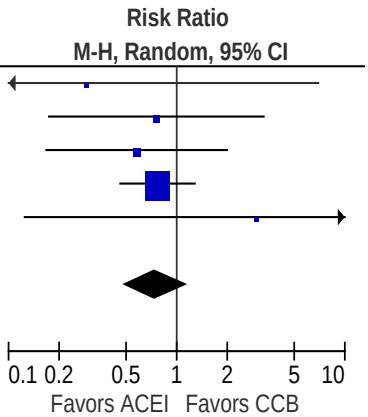
ACEI VERSUS CCB

All-cause mortality

Study or Subgroup	ACE-I Events	ACE-I Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Crepaldi 1998	0	47	1	41	1.9%	0.29 [0.01, 6.97]
Fogari 2002	3	102	4	103	9.0%	0.76 [0.17, 3.30]
Marin (ESPIRAL) 2001	4	129	6	112	12.7%	0.58 [0.17, 2.00]
Norris (AASK) 2006	34	436	22	217	74.5%	0.77 [0.46, 1.28]
Zucchelli 1992	1	60	0	60	1.9%	3.00 [0.12, 72.20]
Total (95% CI)		**774**		**533**	**100.0%**	**0.75 [0.48, 1.16]**
Total events	42		33			

Heterogeneity: Tau² = 0.00; Chi² = 1.25, df = 4 (P = 0.87); I² = 0%

Test for overall effect: Z = 1.30 (P = 0.19)

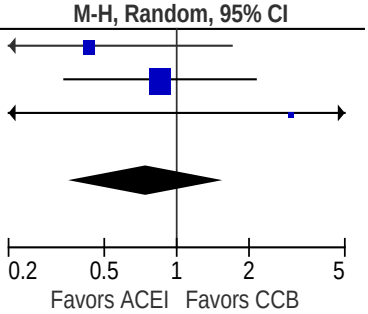


Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

Cardiovascular mortality

Study or Subgroup	ACEI Events	ACEI Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Marin (ESPIRAL) 2001	3	129	6	112	29.5%	0.43 [0.11, 1.70]
Norris (AASK) 2006	12	436	7	217	65.1%	0.85 [0.34, 2.14]
Zucchelli 1992	1	60	0	60	5.4%	3.00 [0.12, 72.20]
Total (95% CI)		**625**		**389**	**100.0%**	**0.75 [0.36, 1.57]**
Total events	16		13			

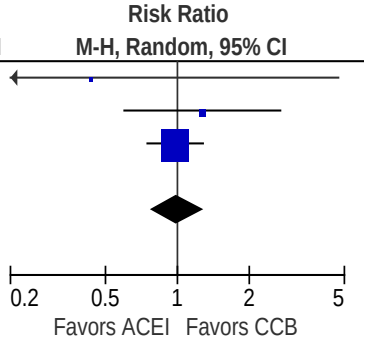
Heterogeneity: Tau² = 0.00; Chi² = 1.42, df = 2 (P = 0.49); I² = 0%
Test for overall effect: Z = 0.77 (P = 0.44)



Stroke

Study or Subgroup	ACEI Events	ACEI Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Marin (ESPIRAL) 2001	1	129	2	112	1.1%	0.43 [0.04, 4.72]
Norris (AASK) 2006	23	436	9	217	11.2%	1.27 [0.60, 2.70]
Rahman (ALLHAT) 2006	99	1533	100	1516	87.7%	0.98 [0.75, 1.28]
Total (95% CI)		**2098**		**1845**	**100.0%**	**1.00 [0.78, 1.28]**
Total events	123		111			

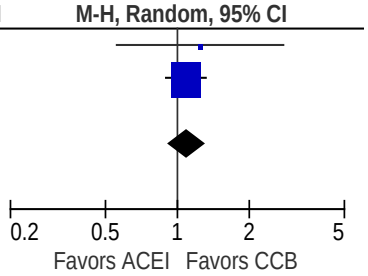
Heterogeneity: Tau² = 0.00; Chi² = 0.89, df = 2 (P = 0.64); I² = 0%
Test for overall effect: Z = 0.01 (P = 0.99)



Congestive heart failure

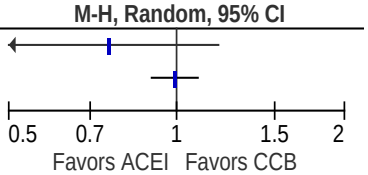
Study or Subgroup	ACEI Events	ACEI Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	20	436	8	217	5.4%	1.24 [0.56, 2.78]
Rahman (ALLHAT) 2006	191	1533	174	1516	94.6%	1.09 [0.90, 1.32]
Total (95% CI)		**1969**		**1733**	**100.0%**	**1.09 [0.91, 1.32]**
Total events	211		182			

Heterogeneity: Tau² = 0.00; Chi² = 0.10, df = 1 (P = 0.75); I² = 0%
Test for overall effect: Z = 0.94 (P = 0.35)



Composite vascular outcome (1)* (see Table C5 for definitions)

Study or Subgroup	ACEI Events	ACEI Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	23	217	61	436		0.76 [0.48, 1.19]
Rahman (ALLHAT) 2006	537	1516	547	1533		0.99 [0.90, 1.09]

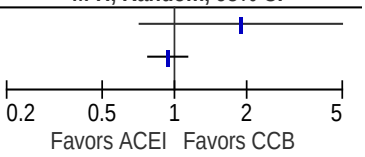


*First outcome identified for each study

Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

Composite vascular outcome (2)* (see Table C5 for defintions)

Study or Subgroup	ACEI Events	ACEI Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	19	436	5	217		1.89 [0.72, 5.00]
Rahman (ALLHAT) 2006	184	1533	194	1516		0.94 [0.78, 1.13]



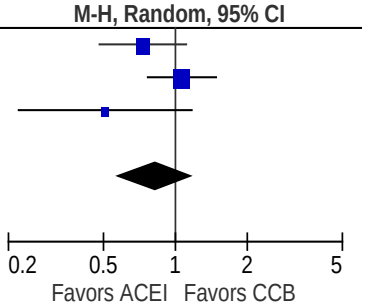
*Second outcome identified for each study

End stage renal disease

Study or Subgroup	ACEI Events	ACEI Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	47	436	32	217	38.0%	0.73 [0.48, 1.11]
Rahman (ALLHAT) 2006	70	1533	65	1516	46.4%	1.06 [0.77, 1.48]
Zucchelli 1992	7	60	14	61	15.6%	0.51 [0.22, 1.17]
Total (95% CI)		**2029**		**1794**	**100.0%**	**0.82 [0.57, 1.19]**
Total events	124		111			

Heterogeneity: Tau² = 0.05; Chi² = 3.71, df = 2 (P = 0.16); I² = 46%

Test for overall effect: Z = 1.03 (P = 0.30)

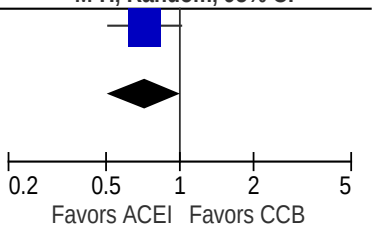


Composite renal outcome (see Table C7 for definition)

Study or Subgroup	ACEI Events	ACEI Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	65	436	45	217	100.0%	0.72 [0.51, 1.01]
Total (95% CI)		**436**		**217**	**100.0%**	**0.72 [0.51, 1.01]**
Total events	65		45			

Heterogeneity: Not applicable

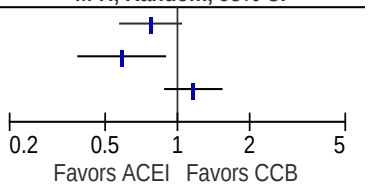
Test for overall effect: Z = 1.88 (P = 0.06)



Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

Composite renal outcome (see Table C7 for defintions)

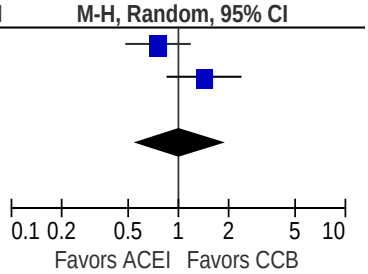
Study or Subgroup	ACEI Events	ACEI Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Agodoa (AASK) 2001	87	436	56	217		0.77 [0.58, 1.04]
Marin (ESPIRAL) 2001	27	129	40	112		0.59 [0.39, 0.89]
Rahman (ALLHAT) 2006	106	1533	90	1516		1.16 [0.89, 1.53]



Halving of GFR

Study or Subgroup	ACEI Events	ACEI Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	44	436	29	217	52.0%	0.76 [0.49, 1.17]
Rahman (ALLHAT) 2006	36	1533	25	1516	48.0%	1.42 [0.86, 2.36]
Total (95% CI)		**1969**		**1733**	**100.0%**	**1.02 [0.55, 1.91]**
Total events	80		54			

Heterogeneity: Tau² = 0.14; Chi² = 3.47, df = 1 (P = 0.06); I² = 71%
Test for overall effect: Z = 0.07 (P = 0.94)

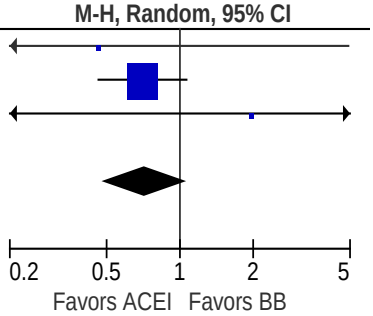


ACEI VS. BB

All-cause mortality

Study or Subgroup	ACEI Events	ACEI Total	Beta blocker Events	Beta blocker Total	Weight	Risk Ratio M-H, Random, 95% CI
Hannedouche 1994	1	52	2	48	2.9%	0.46 [0.04, 4.93]
Norris (AASK) 2006	34	436	49	441	94.2%	0.70 [0.46, 1.06]
van Essen 1997	2	52	1	51	2.9%	1.96 [0.18, 20.97]
Total (95% CI)		**540**		**540**	**100.0%**	**0.71 [0.48, 1.07]**
Total events	37		52			

Heterogeneity: Tau² = 0.00; Chi² = 0.84, df = 2 (P = 0.66); I² = 0%
Test for overall effect: Z = 1.63 (P = 0.10)



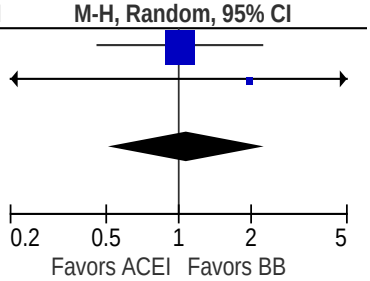
Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

Cardiovascular mortality

Study or Subgroup	ACEI Events	ACEI Total	Beta blocker Events	Beta blocker Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	12	436	12	441	90.0%	1.01 [0.46, 2.23]
van Essen 1997	2	52	1	51	10.0%	1.96 [0.18, 20.97]
Total (95% CI)		**488**		**492**	**100.0%**	**1.08 [0.51, 2.28]**
Total events	14		13			

Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 1 (P = 0.60); I² = 0%

Test for overall effect: Z = 0.20 (P = 0.84)

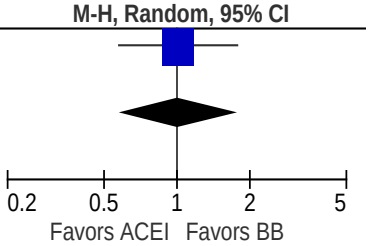


Stroke

Study or Subgroup	ACEI Events	ACEI Total	Beta blocker Events	Beta blocker Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	23	436	23	441	100.0%	1.01 [0.58, 1.78]
Total (95% CI)		**436**		**441**	**100.0%**	**1.01 [0.58, 1.78]**
Total events	23		23			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.04 (P = 0.97)

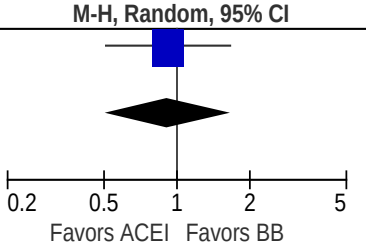


Congestive heart failure

Study or Subgroup	ACEI Events	ACEI Total	Beta blocker Events	Beta blocker Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	20	436	22	441	100.0%	0.92 [0.51, 1.66]
Total (95% CI)		**436**		**441**	**100.0%**	**0.92 [0.51, 1.66]**
Total events	20		22			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.28 (P = 0.78)

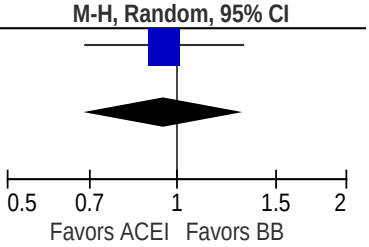


Composite vascular outcome (A) (See Table C5 for definition)

Study or Subgroup	ACEI Events	ACEI Total	Beta blocker Events	Beta blocker Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	61	436	65	441	100.0%	0.95 [0.69, 1.31]
Total (95% CI)		**436**		**441**	**100.0%**	**0.95 [0.69, 1.31]**
Total events	61		65			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.32 (P = 0.75)

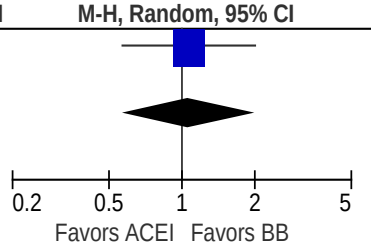


Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

Composite vascular outcome (B) (see Table C5 for definition)

Study or Subgroup	ACEI Events	ACEI Total	Beta blocker Events	Beta blocker Total	Weight	Risk Ratio M-H, Random, 95% CI
Norris (AASK) 2006	19	436	18	441	100.0%	1.07 [0.57, 2.01]
Total (95% CI)		**436**		**441**	**100.0%**	**1.07 [0.57, 2.01]**
Total events	19		18			

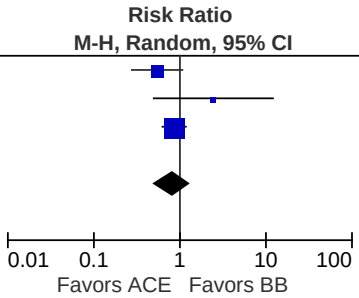
Heterogeneity: Not applicable
Test for overall effect: Z = 0.20 (P = 0.84)



End stage renal disease

Study or Subgroup	ACE Events	ACE Total	BB Events	BB Total	Weight	Risk Ratio M-H, Random, 95% CI
Hannedouche 1994	10	52	17	48	31.8%	0.54 [0.28, 1.07]
van Essen 1997	5	52	2	51	8.6%	2.45 [0.50, 12.07]
Wright 2002	62	436	73	441	59.6%	0.86 [0.63, 1.17]
Total (95% CI)		**540**		**540**	**100.0%**	**0.81 [0.50, 1.33]**
Total events	77		92			

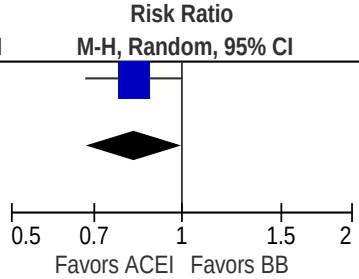
Heterogeneity: Tau² = 0.08; Chi² = 3.34, df = 2 (P = 0.19); I² = 40%
Test for overall effect: Z = 0.82 (P = 0.41)



Composite renal outcome (see Table C7 for definition)

Study or Subgroup	ACEI Events	ACEI Total	Beta blocker Events	Beta blocker Total	Weight	Risk Ratio M-H, Random, 95% CI
Wright (AASK) 2002	126	436	155	441	100.0%	0.82 [0.68, 1.00]
Total (95% CI)		**436**		**441**	**100.0%**	**0.82 [0.68, 1.00]**
Total events	126		155			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.97 (P = 0.05)

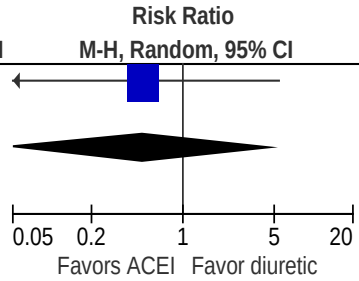


ACEI VERSUS DIURETICS

All-cause mortality

Study or Subgroup	ACEI Events	ACEI Total	Diuretic Events	Diuretic Total	Weight	Risk Ratio M-H, Random, 95% CI
Marre (NESTOR) 2004	1	286	2	284	100.0%	0.50 [0.05, 5.44]
Total (95% CI)		**286**		**284**	**100.0%**	**0.50 [0.05, 5.44]**
Total events	1		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.57 (P = 0.57)

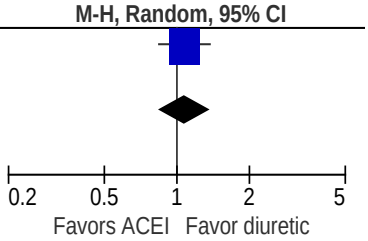


Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

Stroke

Study or Subgroup	ACEI Events	ACEI Total	Diuretic Events	Diuretic Total	Weight	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) 2006	99	1533	157	2613	100.0%	1.07 [0.84, 1.37]
Total (95% CI)		**1533**		**2613**	**100.0%**	**1.07 [0.84, 1.37]**
Total events	99		157			

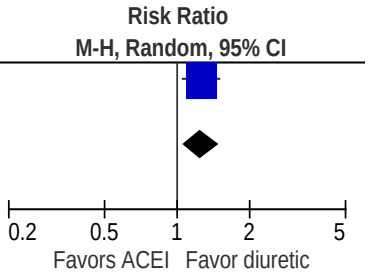
Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)



Congestive heart failure

Study or Subgroup	ACEI Events	ACEI Total	Diuretic Events	Diuretic Total	Weight	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) 2006	191	1533	259	2613	100.0%	1.26 [1.05, 1.50]
Total (95% CI)		**1533**		**2613**	**100.0%**	**1.26 [1.05, 1.50]**
Total events	191		259			

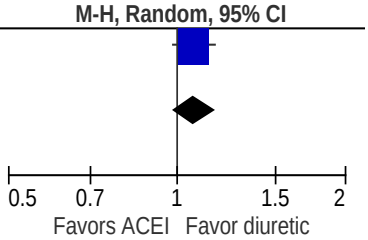
Heterogeneity: Not applicable
Test for overall effect: Z = 2.55 (P = 0.01)



Composite vascular outcome (1) (see Table C5 for definition)

Study or Subgroup	ACEI Events	ACEI Total	Diuretic Events	Diuretic Total	Weight	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) 2006	547	1533	870	2613	100.0%	1.07 [0.98, 1.17]
Total (95% CI)		**1533**		**2613**	**100.0%**	**1.07 [0.98, 1.17]**
Total events	547		870			

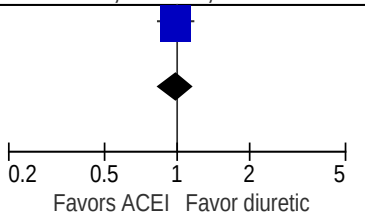
Heterogeneity: Not applicable
Test for overall effect: Z = 1.57 (P = 0.12)



Composite vascular outcome (2) (see Table C5 for definition)

Study or Subgroup	ACEI Events	ACEI Total	Diuretic Events	Diuretic Total	Weight	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) 2006	184	1533	318	2613	100.0%	0.99 [0.83, 1.17]
Total (95% CI)		**1533**		**2613**	**100.0%**	**0.99 [0.83, 1.17]**
Total events	184		318			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.16 (P = 0.87)



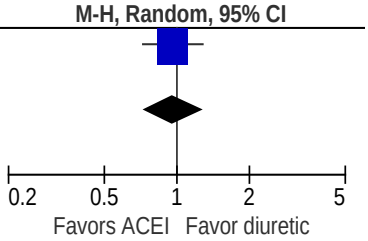
Appendix Figure C1. Forest plots for ACEI monotherapy versus control treatment trials (continued)

End-stage renal disease

Study or Subgroup	ACEI Events	ACEI Total	Diuretic Events	Diuretic Total	Weight	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) 2006	70	1533	124	2613	100.0%	0.96 [0.72, 1.28]
Total (95% CI)		**1533**		**2613**	**100.0%**	**0.96 [0.72, 1.28]**
Total events	70		124			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.26 (P = 0.79)

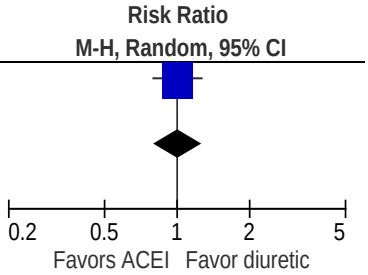


Composite renal outcome (see Table C7 for definition)

Study or Subgroup	ACEI Events	ACEI Total	Diuretic Events	Diuretic Total	Weight	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) 2006	106	1533	180	2613	100.0%	1.00 [0.80, 1.27]
Total (95% CI)		**1533**		**2613**	**100.0%**	**1.00 [0.80, 1.27]**
Total events	106		180			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.03 (P = 0.97)



Appendix Table C4. Clinical outcomes (outcomes part B), ACEI monotherapy versus control treatment trials

Study	Stroke or CVA, Nonfatal n/N (%)		Stroke or CVA, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) or Any (C) n/N (%)		Composite Vascular Outcome n/N (%)*	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
ACEI versus placebo/no treatment trials (n=17)										
Perkovic, 2007[1] (PROGRESS)									(1) 178/895 (19.9) (2) 46/895 (5.1)	(1) 222/862 (25.8) (2) 52/862 (6.0)
Asselbergs, 2004[2] (PREVD)					0/431	2/433 (0.5)			17/431 (3.9)	28/433 (6.5)
Marre, 2004[3] (DIAB)	89/2443 (3.6)	84/2469 (3.4)			76/2443 (3.1)	91/2469 (3.7)	85/2443 (3.5) (C)	102/2469 (4.1) (C)	362/2443 (14.8)	377/2469 (15.3)
Katayama, 2002[4]										
Bojestig, 2001[5]										
Gerstein, 2001[6] (HOPE)							66/952 (6.9) (A)	69/1004 (6.9) (A)	186/952 (19.5)	265/1004 (26.4)
O'Hare, 2000[7] (ATLANTIS)									16/92 (17.4)	8/46 (17)
Muirhead, 1999[8]										
REIN, 1999[9] stratum 1					0/99	2/87 (2.3)			2/99 (2.0)	3/87 (3.4)
Crepaldi, 1998[10]										
REIN, 1997[11] stratum 2									4/78 (5.1)	3/88 (3.4)
Maschio, 1996[12]	2/300 (0.7)	3/283 (1.1)								
Trevisan, 1995[13]										
Laffel,1995[14]										
Sano, 1994[15]										
Lewis, 1993[16]										
Ravid, 1993[17]										
(ACEI) versus ARB trials (n=6)										
Mann, 2008[18] ONTARGET										
Menne, 2008[19] VALERIA										
Sengul, 2006[20]										

Appendix Table C4. Clinical outcomes (outcomes part B), ACEI monotherapy versus control treatment trials (continued)

Study	Stroke or CVA, Nonfatal n/N (%)		Stroke or CVA, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) or Any (C) n/N (%)		Composite Vascular Outcome n/N (%)*	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
Barnett, 2004[21] DETAIL					7/130 (5.4)	9/120 (7.5)				
Lacourcière, 2000[22]	0/51	0/52	0/51	0/52	0/51	0/52	0/51 (C)	0/52 (C)		
Muirhead, 1999[8]										
ACEI versus CCB trials (n=5)										
Rahman, 2005/2006[23,34] ALLHAT					191/1533 (12.5)	174/1516 (11.5)			(1) 547/1533 (35.7); (2) 184/1533 (12.0)	(1) 537/1516 (35.4); (2) 194/1516 (12.8)
Rahman, 2006[34] ALLHAT, DM patients					81/501 (16.2)	87/506 (17.2)			(1) 193/501 (38.5); (2) 76/501 (15.2)	(1) 224/506 (44.3); (2) 83/506 (16.4)
Fogari, 2002[24]										
Norris, 2006[27] Agodoa 2001[25] (AASK)					20/436 (4.6)	8/217 (3.7)			(1) 61/436 (14.0); (2) 19/436 (4.4)	(1) 23/217 (10.6); (2) 5/217 (2.3)
Marin, 2001[28] ESPIRAL										
Crepaldi, 1998[10]										
Zucchelli, 1995[29]										
ACEI versus BB trials (n=3)										
Norris, 2006[27] Agodoa 2001[25] (AASK)					20/436 (4.6)	22/441 (5.0)			(2) 19/436 (4.4)	(2) 18/441 (4.1)
van Essen, 1997[31]										
Hannedouche 1994[32]										
ACEI versus diuretics (n=2)										
Rahman, 2006[34] ALLHAT					191/1533 (12.5)	259/2613 (9.9)			(1) 547/1533 (35.7); (2) 184/1533 (12.0)	(1) 870/2613 (33.3); (2) 318/2613 (12.2)
Rahman, 2006[34] ALLHAT, DM patients					81/501 (16.2)	104/881 (11.8)			(1) 193/501 (38.5); (2) 76/501 (15.2)	(1) 326/881 (37.0); (2) 132/881 (15.0)

Appendix Table C4. Clinical outcomes (outcomes part B), ACEI monotherapy versus control treatment trials (continued)

Study	Stroke or CVA, Nonfatal n/N (%)		Stroke or CVA, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) or Any (C) n/N (%)		Composite Vascular Outcome n/N (%)*	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
Marre, 2004[33] NESTOR										

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor II blocker; CCB = calcium channel blocker; BB = beta blocker; CVA = cerebrovascular accident (or stroke); CHF = congestive heart failure; DM = diabetes mellitus; CAD = coronary artery disease.
*See Composite vascular outcome definitions table.

Appendix Table C5. Composite vascular outcome definitions for ACEI monotherapy versus control treatment trials

Study	Definition
ACEI versus placebo/no treatment trials	
Perkovic, 2007[1] PROGRESS	(1) "Major cardiovascular events," defined as any of the following: nonfatal stroke, nonfatal MI, or cardiovascular death; and (2) Major "Coronary heart disease event," defined as nonfatal myocardial infarction or death ascribed to coronary heart disease.
Asselbergs, 2004[2] PREVEND IT	Cardiovascular death or hospitalization for cardiovascular morbidity (latter defined as hospitalization for either nonfatal MI or myocardial ischemia, heart failure, peripheral vascular disease, and/or cerebrovascular accident).
Marre, 2004[3] DIABHYCAR	Cardiovascular death (including sudden death), nonfatal acute MI, stroke, heart failure requiring admission to hospital, or end stage renal failure (defined as dialysis or kidney transplant)
Gerstein, 2001[6] Micro-HOPE	Cardiovascular death, MI, or stroke
O'Hare, 2000[7] ATLANTIS	Incident "cardiovascular adverse events" reported but not defined. Incidence of death, MI and angina/chest pain separately provided.
REIN, 1999[9] stratum 1	Incident "nonfatal cardiovascular events" reported but not defined.
REIN, 1997[11] stratum 2	Nonfatal cardiovascular events included any of the following: MI, aortic aneurysm, or uncontrolled hypertension.
Maschio, 1996[12]	Nonfatal cardiovascular events included any of the following: MI, stroke, transient ischemic attack, hypertensive crisis, angina, hypotension or dizziness.
ACEI versus CCB trials	
Rahman, 2006[34] ALLHAT	Defined two composite vascular endpoints, as follows: (1) Death from coronary heart disease, nonfatal MI, stroke, coronary revascularization procedures, hospitalized or treated angina, treated or hospitalized heart failure, and peripheral arterial disease requiring hospitalization or outpatient revascularization; and (2) "Coronary heart disease event" defined as nonfatal MI or fatal coronary heart disease death
Norris, 2006[27] Wright, 2002[26] AASK	Defined two composite vascular endpoints, as follows: (1) Cardiovascular mortality or first cardiovascular hospitalization and (2) "Coronary heart disease event" defined as CAD hospitalization (probable MI) and/or fatal coronary heart disease death.
ACEI versus BB trial	
Norris, 2006 AASK[27]	(A) Cardiovascular mortality or first cardiovascular hospitalization (B) Coronary heart disease event" defined as CAD hospitalization (probable MI) and/or fatal coronary heart disease death.
ACEI versus diuretic trials	
Rahman, 2006[34] ALLHAT	Defined two composite vascular endpoints, as follows: (1) Death from coronary heart disease, nonfatal MI, stroke, coronary revascularization procedures, hospitalized or treated angina, treated or hospitalized heart failure, and peripheral arterial disease requiring hospitalization or outpatient revascularization and (2) "Coronary heart disease event" defined as nonfatal MI or fatal coronary heart disease death

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor II blocker; CCB = calcium channel blocker; BB = beta blocker; MI = myocardial infarction; CAD = coronary artery disease

Appendix Table C6. Clinical renal outcomes (outcomes part C), ACEI monotherapy versus control treatment trials

Study	End-Stage Renal Disease n/N (%)		Doubling of Serum Creatinine n/N (%)		Halving of GFR n/N (%)		Progression from Micro- to Macroalbuminuria n/N (%)		Composite Renal Outcome n/N (%)*	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
ACEI versus placebo trials (n=17)										
Perkovic, 2007[1] (PROGRESS)										
Asselbergs, 2004[2] (PREVD)										
Marre, 2004[3] (DIAB)	11/2443 (0.5)	12/2469 (0.5)	48/2443 (2.0)	60/2469 (2.4)						
Katayama, 2002[4]			2/52 (3.8)	2/27 (7.4)						
Bojestig, 2001[5]							0/37	0/18		
Gerstein, 2001[6] (MICROHOPE)†	5/553 (0.9)	6/587 (1.0)	21/553 (3.8)*	18/587 (3.1)			104/553 (18.8)	127/587 (21.6)		
O'Hare, 2000[7] (ATLANTIS)							6/88 (6.8)	5/46 (10.9)		
Muirhead, 1999[8]							1/29 (3.4)	3/27 (11.1)		
REIN, 1999[9] stratum 1	9/99 (9.1)	18/87 (20.7)								
Crepaldi, 1998[10]							2/32 (6.3)	7/34 (20.6)		
REIN, 1997[11] stratum 2	17/78 (21.8)	29/88 (33.0)	1/78 (1.3)	11/88 (12.5)					18/78 (23.1)	40/88 (45.5)
Maschio, 1996[12]	1/300* (0.3)	1/283 (0.4)	30/300 (10)*	56/283 (19.8)					31/300 (10.3)	57/283 (20.1)
Trevisan, 1995[13]										
Laffel, 1995[14]							4/67 (6.0)	13/70 (18.6)		
Sano, 1994[15]										
Lewis, 1993[16]	20/207 (9.7)	31/202 (15.3)	25/207 (12.1)	43/202 (21.3)					23/207 (11.1)	42/202 (20.8)
Ravid, 1993†[17]	0/49*	0/45	2/49 (4.1)*	12/45 (26.7)			2/49 (4.1)	22/45 (48.9)		
ACEI versus ARB trials (n=6)										
Mann, 2008[18] ONTARGET							§	§	*Numbers not provided for CKD subgroup*	
Menne, 2008[18] VALERIA										
Sengul, 2006[20]							0/110	0/109		
Barnett, 2004[21] DETAIL										
Lacourcière, 2000[22]							NR‡	NR‡		

Appendix Table C6. Clinical renal outcomes (outcomes part C), ACEI monotherapy versus control treatment trials (continued)

Study	End-Stage Renal Disease n/N (%)		Doubling of Serum Creatinine n/N (%)		Halving of GFR n/N (%)		Progression from Micro- to Macroalbuminuria n/N (%)		Composite Renal Outcome n/N (%)*	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
Muirhead, 1999[8]							1/29 (3.4)	1/62 (1.6)		
ACEI versus CCB trials (n=6)										
Rahman, 2005[23] ALLHAT	70/1533 (4.6)	65/1516 (4.3)					36/1533 (2.3)	25/1516 (1.6)	106/1533 (6.9)	90/1516 (5.9)
Rahman, 2005[23] ALLHAT, DM patients††									61/501 (12.2)	56/506 (11.1)
Fogari, 2002[24]										
Agodoa, 2001 (AASK)	47/436 (10.8)	32/217 (14.7)					44/436 (10.1)	29/217 (13.4)	(1) 70/436 (16.1); (2) 87/436 (20.0)	(1) 43/217 (19.8); (2) 56/217 (25.8)
Marin, 2001[28] ESPIRAL									27/129 (20.9)	40/112 (35.7)
Crepaldi, 1998[10]										
Zucchelli, 1995[29]	7/60 (11.7)	14/61 (23.0)								
ACEI versus BB trials (n=3)										
Wright, 2002[26]	62/436 (14.2)	73/441 (16.6)							126/436 (28.9)	155/441 (35.1)
van Essen, 1997[31]	5/52 (9.6)	2/51 (3.9)								
Hannedouche, 1994[32]	10/52 (19.2)	17/48 (35.4)								
ACEI versus diuretic trials (n=3)										
Rahman, 2006[34] ALLHAT	70/1533 (4.6)	124/2613 (4.7)							106/1533 (6.9)	180/2613 (6.9)
Rahman, 2006[34] ALLHAT, DM patients	41/501 (8.2)	68/881 (7.7)							61/501 (12.1)	96/881 (10.9)
Marre, 2004[33] NESTOR							18/286 (6.3)	26/283 (9.2)		

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor II blocker; CCB = calcium channel blocker; BB = beta blocker; GFR = glomerular filtration rate
*See Composite renal outcome definitions table
† Data obtained from Ksirsagar Am J Kidney Dis 2000;35(4):695-707) or Stroppoli BMJ/Cochrane review 2004.
‡Study reported that 3/103 participants converted from micro- to microalbuminuria, but did not report results by treatment group.
§Study reported in text that progression from microalbuminuria to microalbuminuria occurred in 166 (2.12%) of ramipril subjects, 138 (1.8%) of telmisartan subjects, but this is not possible given that in figure study reports that 2673 subjects had either microalbuminuria or macroalbuminuria at baseline.
††Rahman 2006 ALLHAT DM patients is a report on the subgroup of diabetic patients from the overall ALLHAT study.

Appendix Table C7. Composite renal outcome definitions for ACEI versus control treatment trials

Study	Definition
ACEI versus placebo/no treatment trials	
REIN, 1997[11] stratum 2	Doubling of baseline serum creatinine concentration or end stage renal disease.
Maschio, 1996[12]	Doubling of baseline serum creatinine concentration or the need for dialysis.
Lewis, 1993[16]	Death, dialysis, or renal transplantation.
ACEI versus ARB trials	
Mann, 2008[18] ONTARGET	Dialysis, renal transplantation, doubling of serum creatinine, or death.
ACEI versus CCB trials	
Rahman, 2005[23] ALLHAT	End stage renal disease (death due to kidney disease, dialysis, or renal transplantation) or reduction in GFR by 50% or by 25 mL/min/1.73 m^2 from the mean of the two baseline GFRs.
Agodoa, 2001[25] AASK	End stage renal disease (need for renal replacement therapy), reduction in GFR by 50% or by 25 mL/min/1.73 m^2 from the mean of the two baseline GFRs, or death.
Marin. 2001[28] ESPIRAL	Doubling of baseline serum creatinine concentration or the need for dialysis.
ACEI versus BB trials	
Wright, 2002[26] (AASK)	End stage renal disease (need for renal replacement therapy), reduction in GFR by 50% or by 25 mL/min/1.73 m^2 from the mean of the two baseline GFRs, or death.
ACEI versus diuretic trials	
Rahman, 2005[23] ALLHAT	End stage renal disease (death due to kidney disease, dialysis, or renal transplantation) or reduction in GFR by 50% or by 25 mL/min/1.73 m^2 from the mean of the two baseline GFRs.

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor II blocker; CCB = calcium channel blocker; BB = beta blocker; GFR = glomerular filtration rate

Appendix Table C8. Study withdrawals and adverse events (outcomes Part D), ACEI monotherapy versus control treatment trials

Study	Any Study Withdrawals		Any or Serious Adverse Events Leading to Study Withdrawal		Adverse Event: Cough		Adverse Event: Hyperkalemia		Renal Adverse Events Leading to Withdrawal*		Renal Adverse Events	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
ACEI versus placebo/no treatment trials (n=17)												
Perkovic, 2007[1] (PRGRESS)												
Asselbergs, 2004[2] (PREVD)	103/431 (24)	110/433 (25.4)										
Marre, 2004[3] (DIAB)	334/2443 (13.7)**	324/2469 (13.1)**	609/2443 (24.9)	554/2469 (22.4)	80/2443 (3.3)	21/2469 (0.9)						
Katayama, 2002[4]	12/52 (23.1)	10/27 (37)	2/52 (3.8)	1/27 (3.7)								
Bojestig, 2001[5]	4/37 (10.8)	0/18	3/37 (8.1)	0/18	1/37 (2.7)	0/18						
Gerstein, 2001[6] (MICROHOPE)												
O'Hare, 2000[7] (ATLANTIS)	31/92 (33.7)	11/48 (22.9)	15/92 (16.3)	5/48 (10.4)								
Muirhead, 1999[8]	4/29 (13.8)	7/31 (22.6)	2/29 (6.9)	0/31	6/29 (20.7)	1/31 (3.2)						
REIN, 1999[9 11] Stratum 1	20/99 (20.2)†	20/87 (23)†	11/99 (11.1)	6/87 (6.9)	1/99 (1.0)	0/87	0/99	1/87 (1.1)	1/99 (1.0)	0/87	Worsening renal insufficiency	
Crepaldi, 1998[10]	2/32 (6.3)	6/34 (17.6)	1/32 (3.1)	6/34 (17.6)					0/32	1/34 (2.9)	Diabetic nephropathy	
REIN, 1997[11] Stratum 2	14/78 (17.9) †	21/88 (23.9) †	9/78 (11.5)	11/88 (12.5)			1/78 (1.3)	1/88 (1.1)	0/78	2/88 (2.3)	Worsening renal insufficiency	
Maschio, 1996[12]	68/300 (22.7)	61/283 (21.6)	52/300 (17.3)	41/283 (14.5)	25/300 (8.3)	10/283 (3.5)	5/300 (1.7)	3/283 (1.1)	3/300 (1.0)	6/283 (2.1)	Worsening renal insufficiency	
Trevisan, 1995[13]	6/60 (10)	8/62 (12.9)	4/60 (6.7)	7/62 (11.3)	1/60 (1.7)	1/62 (1.6)						
Laffel, 1995[14]	22/70 (31.4)	21/73 (28.8)	4/70 (5.7)	5/73 (6.8)	15/70 (21.4)	16/73 (21.9)	0/70	0/73				
Sano, 1994[15]			0/26	0/26	0/26	0/26	0/26	0/26				
Lewis, 1993[16]			46/207 (22.2)	58/202 (28.7)			3/207 (1.4)	0/202				

Appendix Table C8. Study withdrawals and adverse events (outcomes Part D), ACEI monotherapy versus control treatment trials (continued)

Study	Any Study Withdrawals		Any or Serious Adverse Events Leading to Study Withdrawal		Adverse Event: Cough		Adverse Event: Hyperkalemia		Renal Adverse Events Leading to Withdrawal*		Renal Adverse Events	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
Ravid, 1993[17]	3/56 (5.3)	3/52 (5.8)	4/56 (7.1)	3/52 (5.8)	4/56 (7.1)	2/52 (3.8)						
ACEI versus ARB trials (n=6)												
Mann, 2008[18] ONTARGET												
Menne, 2008[19] VALERIA	6/47 (12.8)	6/43 (14.0)	4/47 (8.5)	3/43 (7)	2/47 (4.3)	0/43	1/47 (2.1)	1/43 (2.3)				
Sengul, 2006[20]	15/109 (13.8)	12/110 (10.9)										
Barnett, 2004[21] DETAIL	44/130 (33.8)	38/120 (31.7)	30/130 (23.1)	20/120 (16.7)					2/130 (1.5)	2/120 (1.7)	Elevated serum creatinine	
Lacourcière, 2000[22]	5/51 (9.8)	6/52 (11.5)	1/51 (2)	2/52 (3.8)	7/51 (13.7)	0/52						
Muirhead, 1999[8]	4/29 (13.8)	8/62 (12.9)	2/29 (6.9)	2/62 (3.2)	6/29 (20.7)	4/62 (6.5)			0/29 0	1/62 (1.6)	Decreased GFR and creatinine clearance	
ACEI versus CCB trials (n=5)												
Rahman, 2006[34] ALLHAT												
Fogari, 2002[24]	26/102 (25.5)	27/103 (26.2)	3/102 (2.9)	4/103 (3.9)	2/102 (2.0)	0/103			2/102 (2.0)	2/103 (1.9)	Worsening kidney function	
Wright, 2002[26] (AASK)	0/436	0/217	0/436	0/217	54.9*	46.3*	3/436 (0.7)	0/217				
Wright, 2002[26] (AASK)	Other adverse events that were significantly different between groups (p<0.5): angioedema ACE 6.4* vs. 2.3* for CCB; Syncope ACE 6.7* vs. 2.3* for CCB; Edema ACE 46* vs. 59.8* for CCB											
Marin, 2001[28] ESPIRAL	45/129 (34.9)	38/112 (33.9)	15/129 (11.6)	12/112 (10.7)	3/129 (2.63)	0/112			4/129 (3.1)	1/112 (0.9)	Impaired kidney function	
Crepaldi, 1998[10]	17/47 (36.2)	17/41 (41.2)	1/32 (3.1)	0/26					0/32	0/26		
Zucchelli, 1995[29]	15/60 (25)	16/61 (26)	5/60 (8.3)	7/61 (11.5)	2/60 (3.3)	0/61						
ACEI versus BB trials (n=3)												
Wright, 2002[26] (AASK)	0/436	0/441	0/436	0/441	54.9*	41.5*	3/436 (0.7)	1/441 (0.2)				
van Essen, 1997[31]	9/52 (17.3)	5/51 (9.8)	9/52 (17.3)	5/51 (9.8)			1/52 (1.9)	0/51				

Appendix Table C8. Study withdrawals and adverse events (outcomes Part D), ACEI monotherapy versus control treatment trials (continued)

Study	Any Study Withdrawals		Any or Serious Adverse Events Leading to Study Withdrawal		Adverse Event: Cough		Adverse Event: Hyperkalemia		Renal Adverse Events Leading to Withdrawal*		Renal Adverse Events	
	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control	ACEI	Control
Hannedouche, 1994[32]	11/52 (21.2)	12/48 (25.0)	3/52 (5.8)	3/48 (6.3)			2/52 (3.8)	0/48				
ACEI versus diuretics (n=2)												
Rahman, 2006[34] ALLHAT												
Marre, 2004[33] NESTOR	30/286 (10.5)	35/284 (12.3)	15/286 (5.2)	14/284 (4.9)								

* Results reported as percent of patients experiencing adverse event per patient year of followup (patients were followed up for 3 to 6.4 years)
ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor II blocker; CCB = calcium channel blocker; BB = beta blocker

Appendix Evidence Table C9. Overview of ARB monotherapy trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ARB versus placebo/no treatment trials (n= 5 trials)				
Tobe, 2011[35] TRANSCEND Location Multinational (40 countries) Funding Source Industry	Inclusion Criteria: patients intolerant to ACE inhibitors were enrolled if they had established coronary artery, peripheral vascular or CVD, or diabetes with end-organ damage. Intolerance to ACE inhibitors was defined as previous discontinuation by a physician because of intolerance, with a specific documented cause. Exclusion Criteria: heart failure, significant primary valvular or cardiac outflow tract obstruction, constrictive pericarditis, complex congenital heart disease, unexplained syncope, planned cardiac surgery or cardiac revascularization within the previous 3 months, systolic BP >160 mm Hg, heart transplantation, subarachnoid hemorrhage, significant renal artery stenosis, creatinine levels >265 µmol/L, proteinuria, or hepatic dysfunction.	5926 total were randomized, 1480 had a GFR <60 ml/min/1.73m^2 and an additional 511 had micro or macroalbuminuria with a GFR ≥60 ml/min/ 1.73m^2 (n=1991). *Demographic data for the 1991 unless noted*. N=1991 Age (yr): 68.7 Gender (Male %): 51 Race/Ethnicity (%): European 59, Asian 23 BMI: 28 Systolic BP (mm Hg): 143 Diastolic BP (mm Hg): 82 Albuminuria-to-creatinine ratio (ACR): 6.8 (4.4 GFR <60; 6.8 with micro and GFR ≥60; 52.1 with macro and GFR ≥60) Serum creatinine (mg/dL): 1.2 (1.3 GFR <60; 0.95 with micro and GFR ≥60; 0.98 with macro and GFR ≥60) Estimated GFR (ml/min/1.73m^2): 57.7 (50.1 GFR <60; 79.7 with micro and GFR ≥60; 78.8 with macro and GFR ≥60) Total cholesterol (mg/dL): 201 LDL cholesterol (mg/dL): 120 Diabetes (%): 41 History of HTN (%): 81 History of CAD (%): 73 History of CHF (%): 0 (see exclusion criteria) History of MI (%): 45 History of Stroke (%): 22 Peripheral arterial disease (%): 12 Current smoker (%): 8	Telmisartan 80mg/day (n=729 plus 226 with micro and GFR ≥60 and 37 with macro and GFR ≥60) Placebo (n=751 plus 208 with micro and GFR ≥60 and 40 with macro and GFR ≥60) Study duration: median 4.7 years (all subjects) Study withdrawals (%):	Allocation Concealment : adequate (main publication)* Blinding: double, endpoints adjudication committee Intention to Treat Analysis (ITT): yes (for all subjects) Withdrawals/Dropouts adequately described: yes (for all subjects) * TRANSCEND, Lancet 2008;372:1174-83.[36] Note: Post-hoc analysis

Appendix Evidence Table C9. Overview of ARB monotherapy trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Makino, 2007[37] Location Japan Funding Source NR	Inclusion Criteria: Age 30 to 74, type 2 DM and urinary albumin-to-creatinine ratio 100-300 mg/g, serum creatinine <1.5 mg/dl (men) and <1.3 mg/dl (women). Exclusion Criteria: DM type 1, age of diabetes onset <30 years, seated systolic blood pressure (SBP)/diastolic blood pressure (DBP) >180/100 mmHg, and definable chronic kidney disease other than diabetic nephropathy	N=527 Age (yr): 61.7 Gender (Male %): NR Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 137 Diastolic BP (mm Hg): 77 Albuminuria: NR, see Inc. criteria Serum creatinine (mg/dL): NR, see Inc. criteria Estimated GFR (ml/min/1.73m2): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): NR History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	n= 168 to Telmisartan 80mg/day n= 172 to Telmisartan 40mg/day n= 174 to placebo period: median 1.3 +/- 0.5 years Study withdrawals (%): 2.4 % excluded from primary analysis due to suspected type 1 DM or for missing UACR measurements	Allocation Concealment Unclear Blinding: Double blinded Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes

Appendix Evidence Table C9. Overview of ARB monotherapy trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Brenner, 2001[38] RENAAL Location Multinational Funding Source Industry	Inclusion Criteria: Age 31 to 70 years with type 2 DM and nephropathy defined as 2 occasions of urinary albumin/creatinine ratio ≥300 mg/g (or urinary protein excretion ≥0.5 g/day) and serum creatinine 1.3 – 3.0 mg/dL with lower limit of 1.5 mg/dL for male patients weighing >60kg. Exclusion Criteria: Type 1 DM or nondiabetic renal disease including renal-artery stenosis. MI or CABG within the previous month, PCI within the previous six months, CVA or TIA within the previous year. History of CHF. Patients on ACEI or ARB prior to study had these medications stopped.	N=1513 Age (yr): 60 Gender (Male %): 63.2 Race/Ethnicity (%): Asian: 16.7, Black: 15.2, White: 48.6, Hispanic: 18.2, Other: 1.3 BMI: 29 Systolic BP (mm Hg): 153 Diastolic BP (mm Hg): 82 Albuminuria: Median Urine Alb/Cr: 1250 mg/g Serum creatinine (mg/dL): 1.9 Estimated GFR (ml/min/1.73m2): NR Total cholesterol (mg/dL): 228 LDL cholesterol (mg/dL): 142 Diabetes (%): 100 History of HTN (%): 93.5 History of CAD (%): 0.1 (not all CAD as only refers to history of coronary revascularization procedure) History of CHF (%): 0 History of MI (%): 11.2 History of Stroke (%): 0.1 Peripheral arterial disease (%): NR Current smoker (%): 18.3	n= 751 for 50-100mg/day Losartan (71% reached 100 mg/day) n= 762 Placebo All patients also given “standard antihypertensive therapy” (CCB, Diuretics, Alpha blockers, Beta-blockers and centrally acting agents) to maintain BP<140/90. Followup period: median 3.4 years Study withdrawals (%): 7.8 46.5 Losartan	Allocation Concealment Adequate Blinding: Double blind Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Appendix Evidence Table C9. Overview of ARB monotherapy trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Parving, 2001[39] IRMA-2 Location: 96 centers worldwide Funding Source Industry	Inclusion Criteria: HTN, age 30 to 70, type 2 DM, persistent microalbuminuria (UAER 20 to 200 µg/min in 2 of 3 consecutive, sterile, overnight samples), serum creatinine ≤1.5 mg/dl for men and ≤1.1 mg/dl for women. Exclusion Criteria: Nondiabetic kidney disease, cancer, life-threatening disease with death expected to occur within two years, and an indication for ACEI or ARBs.	N=590 Age (yr): 58 Gender (Male %): 68.5 Race/Ethnicity (%): White: 97.3, Non-White: 2.7 BMI: 30 Systolic BP (mm Hg): 153 Diastolic BP (mm Hg): 90 Albuminuria: 55.5 µg/min Serum creatinine (mg/dL): 1.18 Estimated GFR (ml/min/1.73m2):NR Total cholesterol (mg/dL): 224 LDL cholesterol (mg/dL): 140 Diabetes (%): 100 History of HTN (%): 100 History of CAD (%): 4.5 History of CHF (%): NR History of MI (%): 3.0 History of Stroke (%): 3.1 Peripheral arterial disease (%): 5.2 Current smoker (%): 18.6	n= 201 placebo n= 195 Irbesartan 150mg n= 194 Irbesartan 300mg Followup period: median 2 years Study withdrawals (%): 13	Allocation Concealment: Not defined Blinding: Double blind Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Appendix Evidence Table C9. Overview of ARB monotherapy trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Lewis, 2001[40] IDNT Location USA Funding Source: Industry	Inclusion Criteria: Age 30 - 70, documented diagnosis of type 2 DM, HTN (SBP>135 mm Hg, DBP>85 mm Hg, or documented treatment with antihypertensive agents), proteinuria (urinary protein excretion ≥ 900 mg per 24 hours), serum creatinine 1.0 - 3.0 mg/dL in women and 1.2 - 3.0 mg/dL in men Exclusion Criteria: NR	N=1,148 Age (yr): 59 Gender (Male %): 68 Race/Ethnicity (%): White 74.3 Hispanic 4.7 Black 12.3 Asian 4.4 Other 4.3 BMI: 30.7 Systolic BP (mm Hg): 159 Diastolic BP (mm Hg): 87 Albuminuria: NR Median Urine Protein Excretion 2.9 g/24hr Median Urine Albumin Excretion 1.9 g/24hr Serum creatinine (mg/dL): 1.68 Estimated GFR (ml/min/1.73m2): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100% History of HTN (%): 100% History of CAD (%): 28.0 with history of "cardiovascular disease" History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	n= 579 Irbesartan 300 n= 569 Placebo Additional antihypertensives (excluding ACEI, ARB or CCB) allowed to maintain SBP <135mmHg (or 10mmHg less than baseline if SBP >145) and DBP <85. Followup period: median 2.6 years Study withdrawals (%): 0.8	Allocation Concealment : Adequate Blinding: Patients, investigators, and assessors Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: yes

Appendix Evidence Table C9. Overview of ARB monotherapy trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ARB versus CCB trials (n=4 trials)				
Saruta, 2009[41] CASE-J Location Japan Funding Source Industry and Government	Inclusion Criteria: For main study, inclusion criteria were: SBP >180mmHg or DBP >110mmHg, type II diabetes, history of stroke or transient ischemic attack, left-ventricular hypertrophy, angina pectoris or a history of myocardial infarction, proteinuria or a serum creatinine ≥1.3mg/dL, or arteriosclerotic peripheral artery obstruction. For this post-hoc analysis, CKD defined as proteinuria (positive urine dipstick) and/or decreased GFR (<60ml/min/1.73m2). Exclusion Criteria: SBP ≥200 mmHg or DBP ≥120 mmHg, Type I DM, MI or CVA ≤6 months before screening, PTCA or CABG ≤6 months before screening or currently scheduled, current treatment for CHF (New York Heart Association functional class II-IV) or ejection fraction <40%, CAD requiring beta blocker or calcium channel blocker, atrial fibrillation or atrial flutter, serum creatinine ≥3 mg/dL, AST and/or ALT ≥100 IU/L, malignancy ≤5 years before enrollment, suspected contraindication for candesartan or amlodipine, pregnancy, possible pregnancy, or plan to conceive a child within 5 years of enrollment, not suited to the clinical trial as judged by a collaborating physician, inability to give informed consent.	N= 2720 (subset with GFR <60ml/min/1.73m2 from among larger study cohort of 4728) Age (yr): 65 Gender (Male %): 51.8 Race/Ethnicity (%): NR BMI: 24.5 Systolic BP (mm Hg): 163 Diastolic BP (mm Hg): 91 Albuminuria: NR Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL):NR Diabetes (%): 42.4 History of HTN (%): 100 History of CAD (%): NR History of CHF (%): NR History of MI (%): 4.8 History of Stroke (%): 11.8 Peripheral arterial disease (%): 1.2 Current smoker (%): NR	n=1376 Candesartan 4 to 12mg daily titrated to target BP n=1344 Amlodipine 2.5 to 10mg daily titrated to target BP Doses titrated to goal BP <130/85 for ages <60 years <140/90 for ages 60-69 <150/90 for ages 70-79 <160/90 for ages >80 Followup period: Total 36 months Study withdrawals (%):No data were reported	Allocation Concealment: Not defined Blinding: Assessor Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Inadequate

Appendix Evidence Table C9. Overview of ARB monotherapy trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Ogawa, 2007[42] Location Japan Funding Source NR	Inclusion/Exclusion Criteria: Type 2 DM outpatients who previously had untreated moderate hypertension (130/80 – 200/110 mmHg); microalbuminuria with repeat x 3 urinary albumin-to-creatinine ratio (ACR) of 100-300 mg/g; glycated hemoglobin Alc (HbAlc)<8.0%; no changes in medications or hospitalization during past 3 years; body mass index (BMI)<30 kg/m2; serum creatinine < 1.2 mg/dl; no other renal diseases; no severe cerebral or cardiovascular diseases or liver dysfunction; and no active retinopathy.	N=58 Age (yr): 62.7 Gender (Male %): 46.6 Race/Ethnicity (%): NR BMI: 23.6 Systolic BP (mm Hg): 152 Diastolic BP (mm Hg): 90 Albuminuria: 100% Mean urine Alb/Cr ratio: 237 Serum creatinine (mg/dL): 0.74 Estimated GFR (ml/min/1.73m^2): NR Total cholesterol (mg/dL): 199.6 LDL cholesterol (mg/dL): NR Diabetes (%): 100% History of HTN (%): 100% Peripheral arterial disease (%): NR Current smoker (%): NR History of CHF (%): NR History of CAD (%): NR History of MI (%): NR History of Stroke (%): NR	n=40 Candesartan 4 - 8mg/d n=18 Nifedipine 20 - 40mg/d Followup period: median 56 weeks Study withdrawals (%): 2/58 (3.4) Candesartan and Nifedipine doses were 4 mg and 20mg daily, respectively, for first 48 weeks, then doses increased to 8mg and 40 mg daily, respectively.	Allocation Concealment: Not defined Blinding: Patient only Intention to Treat Analysis (ITT): Unclear Withdrawals/Dropouts adequately described: Yes

Appendix Evidence Table C9. Overview of ARB monotherapy trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Viberti, 2002[43] MARVAL Location 31 centers in the United Kingdom Funding Source Industry	Inclusion Criteria: 35 to 75 years of age, type 2 diabetes mellitus, persistent microalbuminuria (median UAER of 3 nonconsecutive timed overnight urine collections 20 to 200 g/min during 5 week period before entry), normal serum creatinine, BP <180/105 mm Hg. Exclusion Criteria: Type 1 DM (onset at <35 years of age and requiring insulin within the first year), use of ACEIs, alpha 2 blockers, or CCB ≤5 weeks before random assignment; child-bearing potential for women; heart failure within preceding 6 months requiring ACE inhibitor therapy; MI, PTCA or CVA within the preceding 3 months; severe diabetic neuropathy; history of hypertensive or hepatic encephalopathy; hepatic disease.	N=332 Age (yr): 58 Gender (Male %): 79.8 Race/Ethnicity (%): White: 86.5 Asian: 10 BMI: 30.8 Systolic BP (mm Hg): 148 Diastolic BP (mm Hg): 86 Albuminuria: 100% Baseline UAER: 56.7 μg/min Serum creatinine (mg/dL): 1.08 Estimated GFR (ml/min/1.73m^2): NR Total cholesterol (mg/dL): 198.5 LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 65 History of CAD (%): NR History of CHF (%): NR History of MI (%): 0 History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	n= 169 valsartan initiated at 80 mg/d, could be titrated to 160 mg/d to reach target BP 135/85 mm Hg n= 163 amlodipine initiated at 5 mg/d, could be titrated to 10 mg/d to reach target BP 135/85 mm Hg Mean daily doses at end of study were 122 mg valsartan and 8 mg amlodipine. If BP target not reached with maximum study drug dose, 2.5 mg/d bendrofluazide could be added. Followup period: median 12 weeks, total 24 weeks Study withdrawals (%): 12.3	Allocation Concealment: Yes Blinding: Patients, investigators Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Appendix Evidence Table C9. Overview of ARB monotherapy trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Lewis, 2001[40] IDNT Location USA Funding Source Industry	Inclusion Criteria: Age 30 – 70 yrs, type 2 DM, HTN (SBP >135 or DBP >85 mm Hg or treatment with antihypertensive agents), and proteinuria, with urinary protein excretion of at least 900 mg per 24 hours, serum Cr 1.0 - 3.0 mg per deciliter (88 and 265 µmol per liter) in women and 1.2 - 3.0 mg per deciliter (106 and 265 µmol per liter) in men Exclusion Criteria: NR Exclusion Criteria: NR ** Other antihypertensives (besides Ace, Arb or CCB) where permitted to maintain target BP (SBP<135mmHg, or 10mmHg lower than SBP at screening if SBP>145, and DBP<85), including diuretics, BB, a1 blockers and a2 agonists. Plac□bo required av□ 3.3 nonstudy drugs, 3.0 for patients of ARB and CCB groups	N=1,146 Age (yr): 59 Gender (Male %): 64.3 Race/Ethnicity (%): White 72.1 Hispanic 5.0 Black 13.0 Asian 5.1 Other 4.7 BMI: 30.2 Systolic BP (mm Hg): 160 Diastolic BP (mm Hg): 87 Albuminuria: NR Median Urine Protein Excretion: 2.9 g/24hr Median Urine Albumin Excretion: 1.9 g/24hr Serum creatinine (mg/dL): 1.66 Estimated GFR (ml/min/1.73m2): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100% History of HTN (%): 100% History of CAD (%): 29.7 with history of "cardiovascular disease" History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	N=1148 Age (yr): 59 Gender (Male %): 68 Race/Ethnicity (%): White 74.3 Hispanic 4.7 Black 12.3 Asian 4.4 Other 4.3 BMI: 30.7 Systolic BP (mm Hg): 159 Diastolic BP (mm Hg): 87 Albuminuria: Median Urine Protein Excretion: 2.9 g/24hr Median Urine Albumin Excretion 1.9 g/24hr Serum creatinine (mg/dL): 1.68 Estimated GFR (ml/min/1.73m2): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100% History of HTN (%): 100% History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR History of Cardiovascular Disease": 28.0	n=579 Irbesartan 300 mg daily n=567 Amlodipine 10mg daily Additional antihypertensives (excluding ACEI, ARB or CCB) allowed to maintain SBP <135mmHg (or 10mmHg less than baseline if SBP >145) and DBP <85. Followup period: 2.6 years Study withdrawals (%): 0.6	n= 579 Irbesartan 300 mg n= 569 Placebo Follow-up period: median 2.6 years Study withdrawals (%): 23.7	Allocation Concealment : Yes Blinding: Patients, investigators, assessors Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Adequate

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ALT = alanine aminotransferase; ARB = angiotensin II receptor blocker; AST = aspartate aminotransferase; BB = bete blocker; BMI = body mass index; BP = blood pressure; DBP=diastolic blood pressure; CABG= coronary artery bypass grafting; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP=diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PTCA= percutaneous transluminal coronary angioplasty; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP=systolic blood pressure; TIA = transient ischemic attack; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin

Appendix Table C10. Summary of study baseline characteristics for ARB monotherapy trials

Characteristic	Mean (Range) *(unless otherwise noted)*	Number of Trials Reporting
ARB versus placebo trials		*5*
Patients randomized, n	5769 (527-1513)	5
Age of subjects, years	62.7 (58-68.7)	5
Male gender, %	60 (51-69)	4
White race/ethnicity, %	64 (49-97)	4
Body Mass Index	29 (28-31)	4
Patients with diabetic nephropathy, n	3,778 (527-1,513)	4
Serum creatinine, mg/dL	1.5 (1.2-1.9)	4
Estimated GFR, TRANSCEND, GFR <60 ml/min/1.73m^2	50.1	1
Estimated GFR, TRANSCEND, GFR ≥60 and microalbuminuria	79.7	
Estimated GFR, TRANSCEND, GFR ≥60 and macroalbuminuria	78.8	
ACR, TRANSCEND, GFR <60 ml/min/1.73m^2	4.4	
ACR, TRANSCEND, GFR ≥60 and microalbuminuria	6.8	
ACR, TRANSCEND, GFR ≥60 and macroalbuminuria	52.1	
Albuminuria, μg/min	55.5	*1
Systolic blood pressure, mm Hg	149 (137-159)	5
Diastolic blood pressure, mm Hg	83 (77-90)	5
History of Hypertension, %	91 (81-100)	4
History of Diabetes, %	80 (41-100)	5
History of Cardiovascular disease, %	28	1
History of CAD, %	57 (5-73)	2
History of MI, %	26 (3-45)	3
Patients randomized to Irbesartan versus placebo, n	1,738 (590-1,148)	2
Patients randomized to Losartan versus placebo, n	1,513	1
Patients randomized to Telmisartan versus placebo, n	2526 (527-1991)	2
ARB versus CCB trials		3
Patients randomized, n	3,924 (58-2,720)	3
Age of subjects, years	63.2 (59 - 65)	3
Male gender, %	55.4 (46.6-64.3)	3
Race/ethnicity, white, %	72.1	1
Body Mass Index	26.4 (23.6-30.9)	3
Patients with diabetic nephropathy, n	†1,204 (58-1,146)	2
Serum creatinine, mg/dL	1.6 (0.74-1.66)	2
Estimated GFR, ml/min/1.73m^2	Not reported	0
Systolic blood pressure, mm Hg	162 (152-163)	3
Diastolic blood pressure, mm Hg	90 (87-91)	3
History of HTN, %	100 (100-100)	3
History of Cardiovascular disease, %	28.7	1
History of CAD, %	Not reported	0
Patients with history of MI, %	4.8	1
Patients randomized to Candesartan versus CCB, n	2,778 (58-2,720)	2
Patients randomized to Irbesartan versus CCB, n	1146	1
Patients randomized to Amlodipine versus ARB, n	3,866 (1,146-2,720)	2
Patients randomized to Nifedipine versus ARB, n	58	1

ACR = urinary albumin-to-creatinine ratio, ARB = angiotensin receptor blocker, GFR = glomerular filtration rate, CAD = coronary artery disease, MI = myocardial infarction, CCB = calcium channel blocker

*All 4 trials that compared ARB versus placebo required that participants have albuminuria or proteinuria at baseline for entry, but all reported this measure differently, as albumin-to-creatinine ratio100-300 mg/g (no baseline mean or median reported), urinary albumin/creatinine ratio (UACR) ≥300 mg/g or urinary protein excretion ≥0.5 g/day (median UACR 1250 mg/g), urinary albumin excretion rate (UAER) 20 to 200 μg/min (mean UAER 55.5 μg/min), and urinary protein excretion ≥900 mg per 24 hours (median urinary albumin excretion 1.9gm/24 hrs), respectively.

†One additional study included 2,720 participants with diabetes and CKD, defined by either impaired GFR or proteinuria, but did not specify how many participants had proteinuria. These study subjects were not counted toward the total number of patients with diabetic nephropathy.

Appendix Table C11. Clinical outcomes (outcomes part A), ARB monotherapy trials

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any, n/N (%)		Myocardial Infarction, Fatal, n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke or CVA, Any, n/N (%)	
	ARB	Control	ARB	Control	ARB	Control	ARB	Control	ARB	Control	ARB	Control
ARB versus placebo trials (n=5)												
Tobe, 2011[35] TRANSCEND	184/992* (18.5)	166/999* (16.6)	114/992* (11.5)	112/999* (11.2)								
Makino, 2007[37]												
Brenner, 2001[38] RENAAL	158/751 (21.0)	155/762 (20.3)			50/751 (6.7)	68/762 (8.9)						
Parving, 2001[39] IRMA-2	IRB 150mg 0/195 IRB 300mg 3/194 (1.5)	1/201 (0.5)										
Lewis, 2001[40] IDNT	87/579 (15.0)	93/569 (16.3)										
ARB versus CCB trials (n=3)												
Saruta, 2009[41] CASE-J	**NR	**NR	*NR	*NR			*NR	*NR			44/1376 (3.1)	40/1344 (3.0)
Ogawa, 2007[42]	0/40	0/18	0/40	0/18			0/40	0/18				
Lewis, 2001[40] IDNT	87/579 (15.0)	83/567 (14.6)										

ARB = angiotensin receptor blocker; IRB = irbesartan; CCB = calcium channel blocker

*Includes all subjects with a GFR <60 ml/min/1.73m^2 *and* subjects with a GFR ≥60 ml/min/1.73m^2 and micro or macroalbuminuria. **Study did not report results for all cause mortality, but reported incidence of "sudden deaths" as 8/1376 (0.6%) in candesartan (ARB) group vs. 12/1344 (0.9%) in amlodipine (CCB) group, p=0.34.

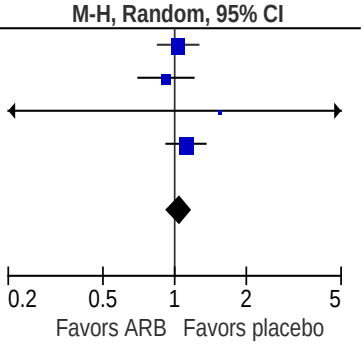
Appendix Figure C2. Forest plots for ARB monotherapy trials

ARB VERSUS PLACEBO

All-cause mortality

Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Brenner (RENAAL) 2001	158	751	155	762	38.2%	1.03 [0.85, 1.26]
Lewis (IDNT) 2001	87	579	93	569	20.6%	0.92 [0.70, 1.20]
Parving (IRMA-2) 2001	3	389	1	201	0.3%	1.55 [0.16, 14.81]
TRANSCEND 2011	184	992	166	999	40.9%	1.12 [0.92, 1.35]
Total (95% CI)		**2711**		**2531**	**100.0%**	**1.04 [0.92, 1.18]**
Total events	432		415			

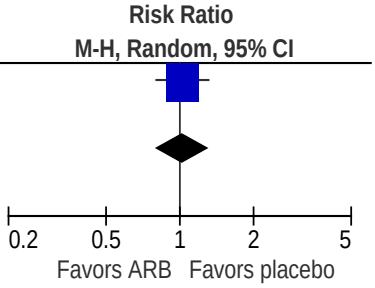
Heterogeneity: Tau² = 0.00; Chi² = 1.46, df = 3 (P = 0.69); I² = 0%
Test for overall effect: Z = 0.67 (P = 0.50)



Cardiovascular mortality

Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
TRANSCEND 2011	114	992	112	999	100.0%	1.03 [0.80, 1.31]
Total (95% CI)		**992**		**999**	**100.0%**	**1.03 [0.80, 1.31]**
Total events	114		112			

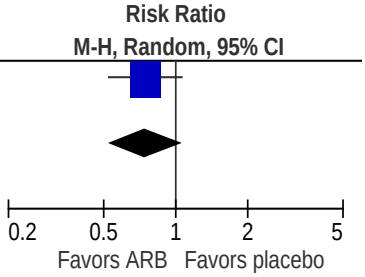
Heterogeneity: Not applicable
Test for overall effect: Z = 0.20 (P = 0.84)



MI, any

Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Brenner (RENAAL) 2001	50	751	68	762	100.0%	0.75 [0.53, 1.06]
Total (95% CI)		**751**		**762**	**100.0%**	**0.75 [0.53, 1.06]**
Total events	50		68			

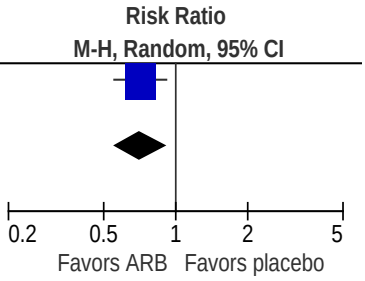
Heterogeneity: Not applicable
Test for overall effect: Z = 1.64 (P = 0.10)



Congestive heart failure hospitalization

Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Brenner (RENAAL) 2001	89	751	127	762	100.0%	0.71 [0.55, 0.91]
Total (95% CI)		**751**		**762**	**100.0%**	**0.71 [0.55, 0.91]**
Total events	89		127			

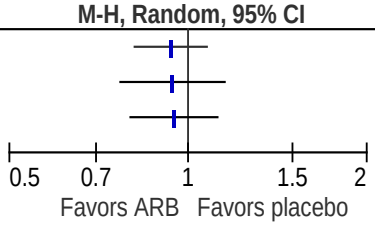
Heterogeneity: Not applicable
Test for overall effect: Z = 2.66 (P = 0.008)



Appendix Figure C2. Forest plots for ARB monotherapy trials (continued)

Composite vascular outcome (see Table C13 for definition)

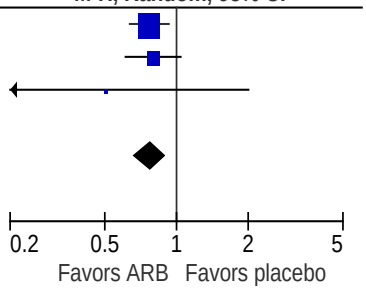
Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Risk Ratio M-H, Random, 95% CI
Brenner (RENAAL) 2001	247	751	268	762	0.94 [0.81, 1.08]
Lewis (IDNT) 2001	138	579	144	569	0.94 [0.77, 1.15]
TRANSCEND 2011	205	992	218	999	0.95 [0.80, 1.12]



End-stage renal disease

Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Brenner (RENAAL) 2001	147	751	194	762	65.8%	0.77 [0.64, 0.93]
Lewis (IDNT) 2001	82	579	101	569	32.9%	0.80 [0.61, 1.04]
TRANSCEND 2011	3	992	6	999	1.2%	0.50 [0.13, 2.01]
Total (95% CI)		**2322**		**2330**	**100.0%**	**0.77 [0.66, 0.90]**
Total events	232		301			

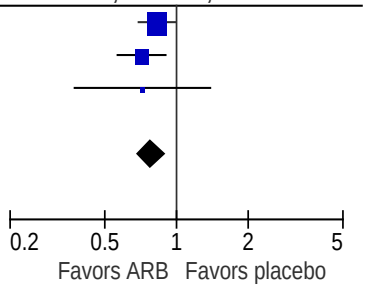
Heterogeneity: Tau² = 0.00; Chi² = 0.43, df = 2 (P = 0.81); I² = 0%
Test for overall effect: Z = 3.27 (P = 0.001)



Doubling of serum creatinine

Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Brenner (RENAAL) 2001	162	751	198	762	59.4%	0.83 [0.69, 1.00]
Lewis (IDNT) 2001	98	579	135	569	36.1%	0.71 [0.57, 0.90]
TRANSCEND 2011	15	992	21	999	4.5%	0.72 [0.37, 1.39]
Total (95% CI)		**2322**		**2330**	**100.0%**	**0.78 [0.68, 0.90]**
Total events	275		354			

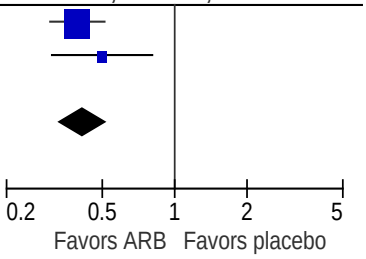
Heterogeneity: Tau² = 0.00; Chi² = 1.08, df = 2 (P = 0.58); I² = 0%
Test for overall effect: Z = 3.46 (P = 0.0005)



Progression from microalbuminuria to macroalbuminuria

Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Makino 2007	67	340	87	174	77.3%	0.39 [0.30, 0.51]
Parving (IRMA-2) 2001	29	389	30	201	22.7%	0.50 [0.31, 0.81]
Total (95% CI)		**729**		**375**	**100.0%**	**0.42 [0.33, 0.52]**
Total events	96		117			

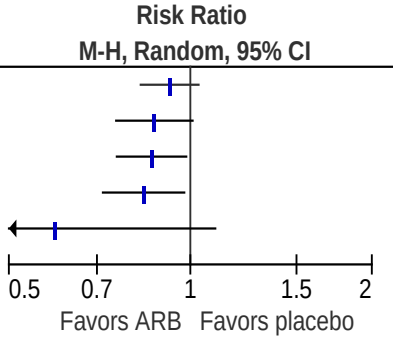
Heterogeneity: Tau² = 0.00; Chi² = 0.73, df = 1 (P = 0.39); I² = 0%
Test for overall effect: Z = 7.49 (P < 0.00001)



Appendix Figure C2. Forest plots for ARB monotherapy trials (continued)

Composite renal outcome (see Table C15 for definitions)

Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Risk Ratio M-H, Random, 95% CI
Brenner (RENAAL) A	327	751	359	762	0.92 [0.83, 1.03]
Brenner (RENAAL) B	226	751	263	762	0.87 [0.75, 1.01]
Brenner (RENAAL) C	255	751	300	762	0.86 [0.75, 0.99]
Lewis (IDNT) 2001	189	579	222	569	0.84 [0.72, 0.98]
TRANSCEND 2011	16	992	27	999	0.60 [0.32, 1.10]

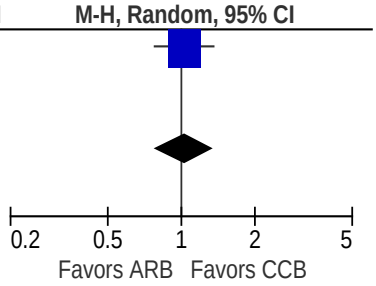


ARB VERSUS CCB

All-cause mortality

Study or Subgroup	ARB Events	ARB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) 2001	87	579	83	567	100.0%	1.03 [0.78, 1.35]
Ogawa 2007	0	40	0	18		Not estimable
Total (95% CI)		**619**		**585**	**100.0%**	**1.03 [0.78, 1.35]**
Total events	87		83			

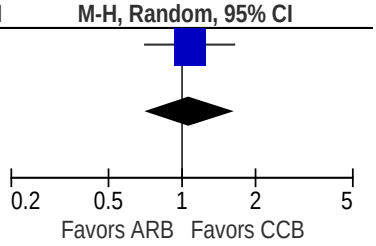
Heterogeneity: Not applicable
Test for overall effect: Z = 0.18 (P = 0.85)



Stroke

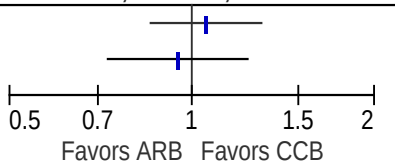
Study or Subgroup	ARB Events	ARB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Saruta (CASE-J) 2009	44	1376	40	1344	100.0%	1.07 [0.70, 1.64]
Total (95% CI)		**1376**		**1344**	**100.0%**	**1.07 [0.70, 1.64]**
Total events	44		40			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)



Composite vascular outcome (see Table C13 for definitions)

Study or Subgroup	ARB Events	ARB Total	CCB Events	CCB Total	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) 2001	138	579	128	567	1.06 [0.86, 1.30]
Saruta (CASE-J) 2009	99	1376	102	1344	0.95 [0.73, 1.24]



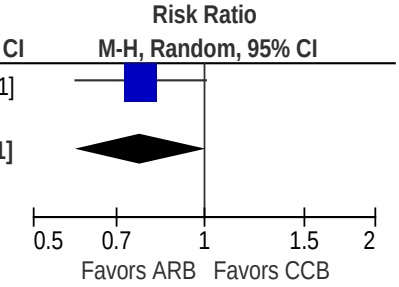
Appendix Figure C2. Forest plots for ARB monotherapy trials (continued)

End-stage renal disease

Study or Subgroup	ARB Events	ARB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) 2001	82	579	104	567	100.0%	0.77 [0.59, 1.01]
Total (95% CI)		**579**		**567**	**100.0%**	**0.77 [0.59, 1.01]**
Total events	82		104			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.91 (P = 0.06)

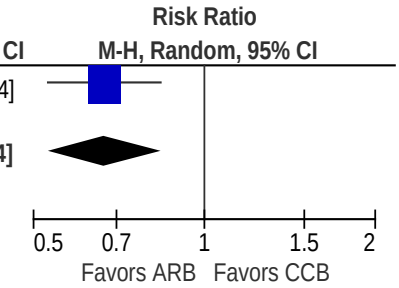


Doubling of serum creatinine

Study or Subgroup	ARB Events	ARB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) 2001	98	579	144	567	100.0%	0.67 [0.53, 0.84]
Total (95% CI)		**579**		**567**	**100.0%**	**0.67 [0.53, 0.84]**
Total events	98		144			

Heterogeneity: Not applicable

Test for overall effect: Z = 3.47 (P = 0.0005)

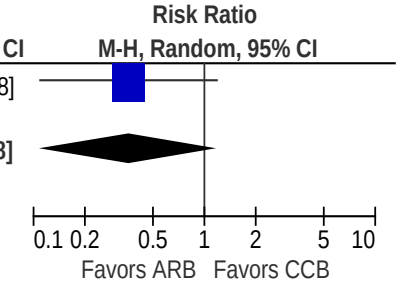


Progression from microalbuminuria to macroalbuminuria

Study or Subgroup	ARB Events	ARB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Ogawa 2007	4	40	5	18	100.0%	0.36 [0.11, 1.18]
Total (95% CI)		**40**		**18**	**100.0%**	**0.36 [0.11, 1.18]**
Total events	4		5			

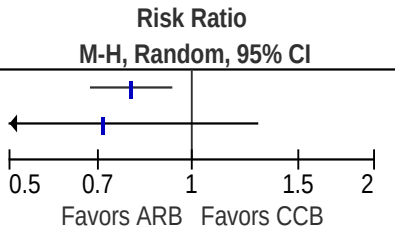
Heterogeneity: Not applicable

Test for overall effect: Z = 1.68 (P = 0.09)



Composite renal outcome (see Table C15 for definition)

Study or Subgroup	ARB Events	ARB Total	Placebo Events	Placebo Total	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) 2001	189	579	233	567	0.79 [0.68, 0.93]
Saruta (CASE-J) 2009	19	1376	26	1344	0.71 [0.40, 1.28]



Appendix Table C12. Clinical outcomes (outcomes part B), ARB monotherapy trials

Study	Stroke or CVA, Nonfatal n/N (%)		Stroke or CVA, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B), n/N (%)		Composite Vascular Outcome n/N (%)**	
	ARB	Control	ARB	Control	ARB	Control	ARB	Control	ARB	Control
ARB versus placebo trials (n=5)										
Tobe, 2011[35] TRANSCEND									205/992 (20.7)	218/999 (21.8)
Makino, 2007[37]										
Brenner, 2001[38] RENAAL							(A): 89/751 (11.9)*	(A): 127/762 (16.7)	247/751 (32.9)	268/762 (35.2)
Parving, 2001[39] IRMA-2									#	#
Lewis, 2001[40] IDNT							§(A): NR	§(A): NR	138/579 (23.8)	144/569 (25.3)
ARB versus CCB trials (n=3)										
Saruta, 2009[41] CASE-J									†99/1376 (7.2)	†102/1344 (7.6)
Ogawa, 2007[42]			0/40	0/18			(B): 0/40	(B): 0/18		
Lewis, 2001[40] IDNT									138/579 (23.8)	128/567 (22.6)

ARB = angiotensin receptor blocker; CCB = calcium channel blocker; NR = not reported

* P < 0.05 versus control

**See Composite vascular outcome definitions table

† In addition to defined composite cardiovascular events presented in this table, study also reported results for undefined, but apparently composite "cerebrovascular events" and "cardiac events." "Cerebrovascular events" occurred in 44/1376 (3.1%) in candesartan (ARB) group vs. 40/1344 (3.0%) in amlodipine (CCB) group, p=0.73, while "cardiac events" occurred in 30/1376 (2.2%) in candesartan (ARB) group vs. 32/1344 (2.4%) in amlodipine (CCB) group, p=0.71.

§ Study did not report proportion of participants with hospitalization due to CHF, but stated that "patients assigned to receive irbesartan (ARB) had a rate of congestive heart failure necessitating hospitalization that was 23 percent lower than that among the patients assigned to receive placebo."

Study reported that nonfatal cardiovascular events (undefined) occurred in 8.7% of patients in the placebo group vs. 4.5% of those in the irbesartan (ARB) 300 mg/daily group, p=0.11, but the proportion of subjects in each group with these events was not reported and was not possible to calculate.

Appendix Table C13. Composite vascular outcome definitions for ARB monotherapy trials

Study	Definition
ARB versus placebo/no treatment trials	
Tobe, 2011[35] TRANSCEND	Cardiovascular death, MI, fatal or nonfatal stroke, or hospitalization for heart failure.
Brenner, 2001[38] RENAAL	MI, stroke, first hospitalization from heart failure or unstable angina, coronary or peripheral revascularization, or death from cardiovascular causes.
Lewis, 2001[40] IDNT	Death from cardiovascular causes, nonfatal MI, heart failure resulting in hospitalization, stroke resulting in permanent neurological defect, lower limb AKA.
ARB versus CCB trials	
Saruta, 2009[41] CASE-J	First cardiovascular event defined as any of the following: sudden death (unexpected death within 24 h without external cause); cerebrovascular event (stroke or transient ischemic attack); cardiac event (heart failure, angina pectoris, or acute myocardial infarction); renal event (included serum creatinine concentration of 4.0 mg/dl or higher, doubling of serum creatinine concentration, or end-stage renal disease); and/or vascular event (dissecting aortic aneurysm or arteriosclerotic occlusion of a peripheral artery).
Lewis, 2001[40] IDNT	Death from cardiovascular causes, nonfatal MI, heart failure resulting in hospitalization, stroke resulting in permanent neurological defect, or lower limb AKA

Abbreviations: ARB = angiotensin receptor blocker; MI = myocardial infarction; AKA = above the knee amputation

Appendix Table C14. Clinical renal outcomes (outcomes part C), ARB monotherapy trials

Study	End Stage Renal Disease, n/N (%)		Doubling of Serum Creatinine n/N (%)		Halving of GFR n/N (%)		Progression from Micro- to Macroalbuminuria n/N (%)		Composite Renal Outcome n/N (%)**	
	ARB	Control	ARB	Control	ARB	Control	ARB	Control	ARB	Control
ARB versus placebo trials (n=5)										
Tobe, 2011[35] TRANSCEND	3/992 (0.3) *Chronic dialysis*	6/999 (0.6) *Chronic dialysis*	15/992 (1.5)	21/999 (2.1)					16/992 (1.6)	27/999 (2.7)
Makino, 2007[37]							<u>TEL 80 mg</u> 28/168 (16.7)* <u>TEL 40 mg</u> 39/172 (22.6)*	87/174 (49.9)		
Brenner, 2001[38] RENAAL	147/751 (19.6)*	194/762 (25.5)	162/751 (21.6)*	198/762 (26.0)					(1)327/751 (43.5)*; (2)226/751 (30.1)*; (3)255/751 (34.0)*	(1)359/762 (47.1); (2)263/762 (34.5); (3)300/762 (39.4)
Parving, 2001[39] IRMA-2							<u>IRB 150 mg</u> 19/195 (9.7) <u>IRB 300 mg</u> 10/194 (5.2)*	30/201 (14.9)		
Lewis, 2001[40] IDNT	82/579 (14.2)	101/569 (17.8)	98/579 (16.9)*	135/569 (23.7)					189/579 (32.6)*	222/569 (39.0)
ARB versus CCB trials (n=4)										
Saruta, 2009[41] CASE-J									‡19/1376 (1.4)	‡26/1244 (1.9)
Ogawa, 2007[42]							4/40 (10.0)	5/18 (27.8)		
Lewis, 2001[40] IDNT	82/579 (14.2)	104/567 (18.3)	98/579 (16.9)*	144/567 (25.4)					189/579 (32.6)*	233/567 (41.1)

ARB = angiotensin receptor blocker; TEL = telmisartan; IRB = irbesartan; CCB = calcium channel blocker; GFR = glomerular filtration rate.
*P < 0.05 versus control
**See Composite renal outcome definitions table
‡ Composite renal events reported overall, as above, and stratified by baseline CKD stage: Stage 1+2 = 2/152 (1.2%) candesartan group vs. 3/158 (1.9%) amlodipine group (p=0.58); Stage 3 = 14/1140 (1.2%) candesartan group vs. 9/1125 (0.8%) amlodipine group (p=0.32), and Stage 4 = 3/64 (4.7%) candesartan group vs. 14/61 (23.0%) amlodipine group (p=0.008).

Appendix Table C15. Composite renal outcome definitions for ARB monotherapy trials

Study	Definition
ARB versus placebo/no treatment trials	
Tobe, 2011[35] TRANSCEND	Doubling of baseline serum creatinine or chronic dialysis.
Brenner, 2001[38] RENAAL	Study defined multiple composite renal endpoints, including: (1) doubling of the serum creatinine concentration, end-stage renal disease, or death; (2) doubling of serum creatinine concentration or end-stage renal disease; and (3) end-stage renal disease or death.
Parving, 2001[39] IRMA-2	Time to first detection of overt nephropathy (overnight urinary albumin excretion rate greater than 200 µg per minute and at least 30 percent higher than baseline rate on at least two consecutive visits).
Lewis, 2001[40] IDNT	Doubling of baseline serum creatinine, incident ESRD (hemodialysis, renal transplant, serum creatinine concentration at least 6.0mg/dl), or death from any cause.
ARB versus CCB trials	
Saruta 2009[41] CASE-J	Serum creatinine concentration of 4.0 mg/dl or higher, doubling of the serum creatinine concentration or end-stage renal disease.
Lewis 2001[40] IDNT	Doubling of baseline serum creatinine, incident ESRD (hemodialysis, renal transplant, serum creatinine concentration at least 6.0mg/dl, or death from any cause.

ARB = angiotensin receptor blocker; ESRD = end stage renal disease; CCB = calcium channel blocker

Appendix Table C16. Study withdrawals and adverse events (outcomes part D), ARB monotherapy trials

Study	Study Withdrawals: Any		Serious Adverse Event: Any		Serious Adverse Event: Any Leading to Withdrawal		Adverse Event: Any		Adverse Event: Cough		Adverse Event: Hyperkalemia		Renal Adverse Events*	
	ARB	Control	ARB	Control	ARB	Control	ARB	Control	ARB	Control	ARB	Control	ARB	Control
ARB versus placebo/no treatment trials														
Tobe, 2011[35] TRANSCEND	236/992 (23.8)	249/999 (24.9)							5/992 (0.5)	1/999 (0.1)	*>5.5 mmol/L* 56/992 (5.6)	*>5.5 mmol/L* 25/999 (2.5)	*Acute dialysis* 1/992 (0.1)	*Acute dialysis* 3/999 (0.3)
Makino, 2007[37]	#NR	#NR					NR*	NR*						
Brenner, 2001[38] RENAAL	59/751 (7.9)	59/762 (7.8)									8/751 (1.1)	4/762 (0.5)	11/751 (1.5)	9/762 (1.2)
Parving, 2001[39] IRMA-2	IRB 150mg 27/195 (13.8) IRB 300mg 20/194 (10.3)	30/201 (14.9)	§ 60/389 (15.4)	46/201 (22.9)	IRB 150mg 18/195 (9.2) IRB 300mg 8/194 (4.1)	17/201 (8.5)								
Lewis, 2001[40] IDNT	5/579 (0.9)	4/569 (0.7)	NR‡	NR‡			NR**	NR**			11/579 (1.9)†	2/569 (0.4)	NR††	NR††
ARB versus CCB trials														
Saruta, 2009[41] CASE-J														
Ogawa, 2007[42]	0/40	2/18 (11.1)			0/40	0/18								
Lewis, 2001[40] IDNT	5/579 (0.9)	2/567 (0.4)	NR‡	NR‡			NR**	NR**			11/579 (1.9)†	3/567 (0.5)	NR††	NR††

ARB = angiotensin receptor blocker; CCB = calcium channel blocker; NR = not reported

* Study reported that "one or more adverse event was recorded in >90% of patients in each treatment group;" no additional adverse events information was provided, including on specific types of adverse events.

† $p < 0.05$

‡ 61% of overall cohort had serious adverse event; results were not provided by treatment group, but were reported to not differ significantly between treatment groups.

§ Study reported serious adverse events for the two ARB treatment dose groups combined only.

#Study reported that 13 of 527 (2.4%) randomized participants were excluded from analyses** Results were not reported for the proportion of study participants with any adverse event, either overall or within groups; subjects in the irbesartan group had a significantly lower rate of adverse events per 1000 days of treatment than those in the placebo and amlodipine groups (P=0.002).

†† Study reported one episode of an early increase in serum creatinine concentration suggestive of renal artery stenosis that necessitated stopping the study medication, but did not indicate in which treatment group this adverse event occurred.

Appendix Table C17. Overview of ACEI plus ARB versus ACEI or ARB trials (n=6 trials)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ONTARGET A *Dual vs monotherapy (ACEI or ARB)*Tobe 2011[35] Multinational Funding Source: Industry	Inclusion Criteria: aged 55 years or older with established atherosclerotic vascular disease or with diabetes with end-organ damage. Exclusion Criteria: major renal artery stenosis, uncorrected volume or sodium depletion, a serum creatinine concentration above 265 µmol/L, and uncontrolled hypertension (>160 mm Hg systolic or >100 mm Hg diastolic).	23,422 total were randomized, 5623 had a GFR <60 ml/min/1.73m^2 and an additional 3310 had micro (2631) or macroalbuminuria (679) with a GFR ≥60 ml/min/ 1.73m^2 (n=8933). *Demographic data for the 8933 unless noted*. N=8933 Age (yr): 68.2 Gender (Male %): 68 Race/Ethnicity (%): European 70, Asian 16 BMI: 28 Systolic BP (mm Hg): 144 Diastolic BP (mm Hg): 82 Albuminuria-to-creatinine ratio (ACR): 14.6 (12.2 with GFR <60; 6.7 with micro and GFR ≥60; 65.5 with macro and GFR ≥60) Serum creatinine (mg/dL): 1.2 (1.4 GFR <60; 0.96 with micro and GFR ≥60; 0.98 with macro and GFR ≥60) Estimated GFR (ml/min/1.73m^2): 61.8 (50.2 with a GFR <60; 81.7 with micro and GFR ≥60; 81.3 with macro and GFR ≥60) Total cholesterol (mg/dL): 192 LDL cholesterol (mg/dL): 115 Diabetes (%): 49 History of HTN (%): 77 History of CAD (%): 70 History of CHF (%): NR History of MI (%): 45 History of Stroke (%): 20 Peripheral arterial disease (%): 17 Current smoker (%): 12	Ramipril 10 mg/d + telmisartan 80 mg/d (n=2943) Ramipril 10 mg/d or telmisartan 80 mg/d (n=5990) Followup period: median 4.7 years (followup is for the entire cohort) Study withdrawals (%): 29 (2591/8933)	Allocation Concealment: adequate Blinding: double, endpoints adjudication committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes Note: Post-hoc analysis

Appendix Table C17. Overview of ACEI plus ARB versus ACEI or ARB trials (n=6 trials) (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ONTARGET B *Dual vs ACEI* Mann, 2008[18] ONTARGET Multinational Funding Source: Industry	Inclusion Criteria: aged 55 years or older with established atherosclerotic vascular disease or with diabetes with end-organ damage. Exclusion Criteria: major renal artery stenosis, uncorrected volume or sodium depletion, a serum creatinine concentration above 265 µmol/L, and uncontrolled hypertension (>160 mm Hg systolic or >100 mm Hg diastolic).	This was a 3-arm trial of 25,620 subjects; number with CKD is not specified Estimated GFR (ml/min/1.73m2) 51.0* Urine albumin creatinine ratio (mg/mmol): 0.81* *Patient characteristics not described for the different arms or for CKD subgroup	Ramipril 10 mg/d + telmisartan 80 mg/d (n=8502 overall) Ramipril 10 mg/d (n=8576 overall) Followup period: median 4.7 years (Followup is for the entire cohort) Study withdrawals (%): NR	Allocation Concealment: adequate Blinding: double Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes
Sengul, 2006[20] Turkey Funding Source: none stated	Inclusion Criteria: microalbuminuria (AER rate 30 to 300 mg/24 hours for a minimum of three consecutive occasions); aged 40 to 65 years; previously diagnosed hypertension (systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg), despite receiving ACEI monotherapy for ≥6 months. Exclusion Criteria: type 1 DM; BMI ≥ 40; secondary diabetes; alcoholism; thyroid disease; systolic BP >200 mm Hg, any nondiabetic cause of secondary HTN (including bilateral renal artery stenosis); urinary tract infection; persistent hematuria; chronic liver disease; overt carcinoma; any cardiovascular event in the previous 6 months; serum creatinine ≥150 mmol/L; serum potassium ≥5.5 mmol/L; or pregnancy.	N=219 Age (yr): 57 Gender (Male %): 37 Race/Ethnicity (%): NR BMI: 30 Systolic BP (mm Hg): 151 Diastolic BP (mm Hg): 89 Urinary AER (mg/24 h): 260 Serum creatinine (mg/dL): 1 Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (mg/min): 97 Total cholesterol (mg/dL): 211 LDL cholesterol (mg/dL): 135 HbA_{1c} (%): 7.9 Diabetes (%): 100 History of HTN (%): 100 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 37	Lisinopril 20 mg/d (n=110) Telmisartan 80 mg/d (n=109) After 24 weeks, half of the patients receiving lisinopril were randomized to receive telmisartan in addition. Similarly, half the patients initially treated with telmisartan received a combination of lisinopril plus telmisartan. Follow up for the combination period was 28 weeks. The remaining patients continued to be treated with monotherapy Followup period: 1 year Study withdrawals (%): 12	Allocation Concealment: unclear Blinding: open-label Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Table C17. Overview of ACEI plus ARB versus ACEI or ARB trials (n=6 trials) (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Menne, 2008[19] VALERIA Germany and Hungary Funding Source: Industry	Inclusion Criteria: microalbuminuria (urine albumin creatinine ratio for women ≥3.5 mg/ mmol/L and ≤35.0 mg/mmol and men ≥2.5 mg/ mmol/L and ≤25.0 mg/mmoL); aged 18 to 75 years; essential hypertension [defined as mean sitting diastolic BP ≥85 mmHg and <110 mm Hg]. To fulfill the criteria of microalbuminuria, two of three first morning void urines needed to be positive during the screening phase. Exclusion Criteria: primary kidney disease, renal impairment (creatinine clearance <30ml/min using the Cockroft and Gault formula; serum potassium values >5.5mmol/L; heart failure, significant arrhythmias or bradycardia; relevant valvular disease, type I DM, uncontrolled type II DM with HbA_{1c} >8.0%; history of MI; percutaneous transluminal coronary angioplasty, bypass surgery or stroke within the last 12 months prior to study inclusion; unstable angina pectoris; renal transplantation; severe hepatic disease or hepatic failure; malignant concomitant diseases or history of malignant diseases within the last 5 years; systemic inflammatory diseases; pregnancy or breast feeding; psychiatric disease; either history of alcohol or drug abuse or both.	N=90 (in addition, there was 3rd trial arm of ARB monotherapy with n=43) Age (yr): 58 Gender (Male %): 69 Race/Ethnicity (%): NR BMI: 32 Systolic BP (mm Hg): 153 Diastolic BP (mm Hg): 91 Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (mg/min): 112 Urine albumin creatinine ratio (mg/ mmol): 9.4 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR HbA_{1c} (%): NR Diabetes (%): 74 History of HTN (%): 100 History of CAD “Cardiac disorders”(%): 19 History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Lisinopril 40 mg/d + Valsartan 320 mg/d (n=43) Lisinopril 40 mg/d (n=47) Followup period: 30 weeks Study withdrawals (%): 14	Allocation Concealment: adequate Blinding: double plus outcome assessors and data analysts Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Table C17. Overview of ACEI plus ARB versus ACEI or ARB trials (n=6 trials) (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Kanno, 2006[44] Japan Funding Source: none stated	Inclusion Criteria: serum creatinine concentration of between 1.2 and 5.0 mg/dl; systolic BP (SBP) of >130 and <180 mmHg; diastolic BP (DBP) >80 and <120mmHg; and a daily urinary protein excretion of >1.0g Exclusion Criteria: secondary hypertension, including patients who were on dialysis therapy or receiving renal transplantation; patients who had chronic renal diseases and were receiving corticosteroid hormone; patients with myocardial infarction or stroke within the previous 6 months or angina pectoris that required treatment with B blockers or calcium channel blocker; and patients with heart failure or left ventricular ejection fraction of 40% or less or with a disorder that in the treating physician's opinion for other types of ARB	N=90 Age (yr): 60.1 Gender (Male %): 40 Race/Ethnicity (%): 100 Japanese BMI: NR Total BP (mm Hg): 137.5 Urinary protein excretion (g/24 h): 1.7 Serum creatinine (mg/dL): 3.01 Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (mg/min): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR HbA_{1c} (%): NR Diabetes (%): NR History of HTN (%): 100 History of CAD (%): NR History of CHF (%): NR History of MI (%): 0 History of Stroke (%): 0 Peripheral arterial disease (%): NR Current smoker (%): NR	ACEI + candesartan 2-12 mg/d (n=45) ACEI (n=45) The main ACEI used were benazepril 2.5-10 mg/d or trandolapril 2-4 mg/d Followup period: 3.1 years Study withdrawals (%): 5.6	Allocation Concealment: unclear Blinding: not blinded Intention to Treat Analysis: no Withdrawals/ Dropouts adequately described: yes

Appendix Table C17. Overview of ACEI plus ARB versus ACEI or ARB trials (n=6 trials) (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Mehdi, 2009[45] United States, single-site Funding Source: Government	Inclusion Criteria: Age 20 to 65; type 1 or 2 DM; seated systolic BP<130mmHg; proteinuria (2-24-h UACR≥300 mg/g despite treatment with ACEI or ARB for at least 3 months* Exclusion Criteria: BMI>45kg/m^2; serum creatinine>3.0mg/dl (females) or >4.0 mg/dl (males); known nonddiabetic kidney disease; serum potassium >5.5 mEq/L; hemoglobin A1c>11%; stroke or myocardial infarction within preceding 12 mo; heart failure; known adverse reaction to losartan or spironolactone; anticipated need for dialysis within 12 months *Effort was made to recruit younger patients with type 2 DM as recommended by study sponsor	Baseline characteristics based on 26 in losartan group (excluded 1 patient who withdrew prior to first dose) N=53 Age (yr): 50.8 Gender (Male %): 47 Race/Ethnicity (%): 45% Hispanic, 34% black, 19% non-Hispanic white, 2% Native American Weight (kg): NR BMI: 31.3 Clinic Systolic BP (mm Hg): 134.0 Clinic Diastolic BP (mm Hg): 73.0 CKD stage: NR Serum creatinine (mg/d/l): 1.6 Creatinine clearance (mL/min): 64.5 Albuminuria (µg/min): NR Proteinuria (g/day): NR Albumin/creatinine ratio (mg/g): 907.2 GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 7.9 Total cholesterol (mg/dl): 193.4 LDL cholesterol (mg/dl): 97.5 Diabetes (%): 100 History of HTN (%): NR Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of MI, CABG, PCTA (%): 9.4 History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	Losartan 50 mg/day for 1 week then 100mg/day (n=27)# Placebo (n=27)# Followup period: 48 weeks Study withdrawals (%): 24.1 #All patients were taking lisinopril 80 mg/day	Allocation Concealment: Unclear Blinding: Double blinded Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes

Appendix Table C17. Overview of ACEI plus ARB versus ACEI or ARB trials (n=6 trials) (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Anand, 2009[46] United States, Multi-site Funding Source: Industry	Inclusion Criteria: Ages 18 and older; stable symptomatic heart failure (HF); receiving recommended HF therapy; left ventricular ejection fraction <40%; left ventricular internal diameters in diastole adjusted for body surface area ≥2.9 cm/m^2 Exclusion Criteria: Persistent mean standing SBP <90 mm Hg or serum creatinine >2.5 mg/dL NOTE: results presented are from subgroup analysis of patients with CKD	N=2916 Age (yr): 65.9 Gender (Male %): 88 Race/Ethnicity (%): 91% white Weight (kg): NR BMI: 27 Systolic BP (mm Hg):123.8 Diastolic BP (mm Hg): 74.5 CKD stage: NR Serum creatinine (mg/d/l): NR Serum albumin (g/dL): 4.2 Creatinine clearance (mL/min): NR Albuminuria (µg/min): NR Proteinuria (g/day): NR Dipstick Proteinuria Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): 47.8 HbA_{1c} (%): NR Total cholesterol (mg/dl): NR LDL cholesterol (mg/dl): NR Diabetes (%): 29.1 History of HTN (%): 6.9 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): 100 Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	Valsartan 40 mg twice per day; dose doubled every 2 weeks to reach target of 160 mg twice per day (n= 1477 with CKD)*# to Placebo (n= 1439 with CKD)# Followup period: 23 months (mean) Study withdrawals (%): 10% discontinued treatment (other withdrawals not reported for subgroup) *provided SBP ≥90 mmHg; no signs or symptoms of hypotension; serum creatinine not >150% of baseline #91% of patients in CKD subgroup were taking an ACEI at randomization	Allocation Concealment: Adequate Blinding: Double blind Intention to Treat Analysis (ITT): Yes for the outcomes we are recording Withdrawals/Dropouts adequately described: Yes

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C18. Summary of study baseline characteristics for ACEI plus ARB versus ACEI or ARB trials

Characteristic	Mean (Range Unless Otherwise Noted)	Number of Trials Reporting
ACEI plus ARB versus ACEI (n=6)		
Total number of patients evaluated	18962 (53 to 15594*)	6
Age of subjects, years	64.7 (51 to 66)	5
Gender, male (%)	83.4 (37 to 88)	5
Race/ethnicity, white (%)	89.7 (19 to 91)	2
Race/ethnicity, black (%)	34	1
Race/ethnicity, Asian/Pacific Islander (%)	100% (Japanese)	1
Body Mass Index	27.4 (27 to 32)	4
Weight (kg)		
SBP (mmHg)	126.6 (123.8 to 153)	4
DBP (mmHg)	75.9 (73 to 91)	4
Proteinuria or AER (g/day)	0.68 (0.26 to 1.7) #	5
Serum creatinine (mg/dL)	1.46 (1 to 3)	3
Creatinine Clearance (ml/min/1.73m2)	96.0 (64.5 to 112)	3
Estimated GFR (ml/min/1.73m^2)	49.8 (47.8 to 50.7)	2
Total cholesterol (mg/dl)	207.6 (193.4 to 211.0)	2
LDL Cholesterol (mg/dl)	127.7 (97.7 to 135.0)	2
DM (%)	36.2 (29.1 to 100)	4
HbA_{1c} (%)	7.9 (both 7.9)	2
HTN (%)	18.5 (6.9 to 100)	4
CAD (%) *	19	1
CHF (%) *	100	1
MI (%) *	3.5 (0 to 9.4)	2
Stroke **(%) ***	0	1
AKI **(%)**		
PAD **(%)**		
Current Smoker **(%)**	37	1
ACEI plus ARB versus ARB (n=3)		
Total number of patients evaluated	16143 (90 to 15834*)	3
Age of subjects, years	57.3 (57 to 58)	2
Gender, male (%)	46.3 (37 to 69)	2
Race/ethnicity, white (%)		
Race/ethnicity, black (%)		
Body Mass Index	30.6 (30 to 32)	2
Weight (kg)		
SBP (mmHg)	151.6 (151 to 153)	2
DBP (mmHg)	89.6 (89-91)	2
MAP (mmHg)		
Proteinuria or AER (g/day)	0.26 #	2
Serum creatinine (mg/dL)	1	1
Creatinine Clearance (ml/min/1.73m2)	101.4 (97 to 112)	2
Estimated GFR (ml/min/1.73m^2)	50	1
Total cholesterol (mg/dl)	211	1
LDL Cholesterol (mg/dl)	135	1
DM (%)	92.4 (74 to 100)	2
HbA_{1c} (%)	7.9	1
HTN (%)	100 (100 to 100)	2
CAD (%) *		
CHF (%) *		
MI (%) *		
Stroke **(%) ***		
AKI **(%)**		
PAD **(%)**		
Current Smoker **(%)**	37	1

Appendix Table C18. Summary of study baseline characteristics for ACEI plus ARB versus ACEI or ARB trials (continued)

Characteristic	Mean (Range Unless Otherwise Noted)	Number of Trials Reporting
ACEI plus ARB versus ACE or ARB [ONTARGET 2011] (n=1)		
Total number of patients evaluated	8933	1
Age of subjects, years	68.2	1
Gender, male (%)	68	1
Race/ethnicity, white (%)	70	1
Race/ethnicity, Asian (%)	16	1
Body Mass Index	28	1
SBP (mmHg)	144	1
DBP (mmHg)	82	1
Proteinuria or AER (g/day)		
ACR, GFR <60 ml/min/1.73m^2	12.2	1
ACR, GFR ≥60 and microalbuminuria	6.7	1
ACR, GFR ≥60 and macroalbuminuria	65.5	1
Serum creatinine (mg/dL)	1.2	1
Creatinine Clearance (ml/min/1.73m2)		
Estimated GFR, GFR <60 ml/min/1.73m^2	50.2	1
Estimated GFR, GFR ≥60 and microalbuminuria	81.7	1
Estimated GFR, GFR ≥60 and macroalbuminuria	81.3	1
Total cholesterol (mg/dl)	192	1
LDL Cholesterol (mg/dl)	115	1
DM (%)	49	1
HTN (%)	77	1
CAD (%) *	70	1
CHF (%) *		
MI (%) *	45	1
Stroke **(%) ***	20	1
PAD **(%)**	17	1
Current Smoker **(%)**	12	1

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; SBP = systolic blood pressure; DBP = diastolic blood pressure, AER = albumin excretion rate; ACR = urinary albumin-to-creatinine ratio; GFR = glomerular filtration rate; LDL = low density lipoprotein; DM = diabetes mellitus, HTN = hypertension, CAD = coronary artery disease; CHF = congestive heart failure; MI = myocardial infarction; PAD = peripheral arterial disease

*N for Mann 2008 ONTARGET study based on back calculation of reported progression to macroalbuminuria; # data from one trial not included in calculations as value in mg/mmo

Appendix Table C19. Clinical outcomes (outcomes part A), ACEI plus ARB versus ACEI or ARB trials

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Non-fatal n/N (%)		Stroke or CVA, Any n/N (%)	
ACEI plus ARB versus ACEI trials (n=5)												
	ACEI+ARB	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**
Sengul, 2006[20]												
Menne, 2008[19] VALERIA	0/43 (0)	1/47 (2.1)										
Mann ,2008[18] ON-TARGET												
Kanno, 2006[44]												
Mehdi, 2009[45]	1/26 (3.8)	0/27 (0.0)										
Anand, 2009[46]	362/1477 (24.5)	341/1439 (23.7)										
ACEI plus ARB versus ARB trials (n=3)												
	ACEI+ARB	**ARB**	**ACEI+ARB**	**ARB**	**ACEI+ARB**	**ARB**	**ACEI+ARB**	**ARB**	**ACEI+ARB**	**ARB**	**ACEI+ARB**	**ARB**
Sengul, 2006[20]												
Menne, 2008[19] VALERIA	0/43 (0)	0/43 (0)										
Mann, 2008 [18]ON-TARGET												
ACEI plus ARB versus ACEI or ARB (monotherapy) trials (n=1)												
	ACEI+ARB	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**
Tobe 2011[35] Mann, 2008 [18]ON-TARGET	520/2943 (17.7)	1033/5990 (17.2)	317/2943 (10.8)	654/5990 (11.0)								

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; CVA = cerebrovascular accident
*reported for the overall participants but not for the CKD subgroup

Appendix Table C20. Clinical outcomes (outcomespart B), ACEI plus ARB versus ACEI or ARB* trials

Study	Stroke or CVA, Nonfatal n/N (%)		Stroke or CVA, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) n/N (%)		Composite Vascular Outcome n/N (%)**	
ACEI plus ARB versus ACEI trials (n=6)										
	ACEI+ARB	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**
Sengul, 2006[20]										
Menne, 2008[19] VALERIA										
Mann, 2008[18] ON TARGET										
Kanno, 2006[44]										
Mehdi, 2009[45]	1/26 (3.8)	1/27 (3.7)			2/26 (7.7)	0/27 (0.0)				
Anand, 2009[46]									499/1477 (33.8)	549/1439 (38.1)
ACEI plus ARB versus ACEI or ARB (monotherapy) trials (n=1)										
	ACEI+ARB	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**
Tobe 2011[35]									653/2943 (22.2)	1372/5990 (22.9)
Mann, 2008[18] ON-TARGET										

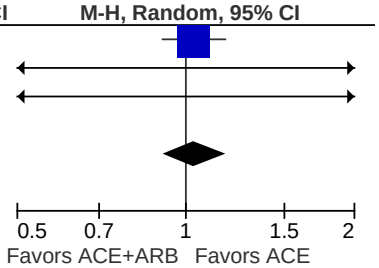
ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker
*No ACE+ARB versus ARB studies reported these outcomes
**See Composite vascular outcome definitions table

Appendix Figure C3. Forest plots for ACEI plus ARB versus ACEI trials

All-cause mortality

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Anand 2009	362	1477	341	1439	99.7%	1.03 [0.91, 1.18]
Mehdi 2009	1	26	0	27	0.2%	3.11 [0.13, 73.09]
Menne 2008	0	43	1	47	0.2%	0.36 [0.02, 8.70]
Total (95% CI)		**1546**		**1513**	**100.0%**	**1.03 [0.91, 1.18]**
Total events	363		342			

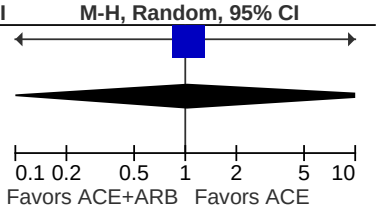
Heterogeneity: Tau² = 0.00; Chi² = 0.88, df = 2 (P = 0.64); I² = 0%
Test for overall effect: Z = 0.52 (P = 0.61)



Stroke, nonfatal

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Mehdi 2009	1	26	1	27	100.0%	1.04 [0.07, 15.75]
Total (95% CI)		**26**		**27**	**100.0%**	**1.04 [0.07, 15.75]**
Total events	1		1			

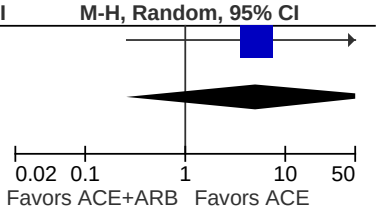
Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.98)



Congestive heart failure, any

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Mehdi 2009	2	26	0	27	100.0%	5.19 [0.26, 103.11]
Total (95% CI)		**26**		**27**	**100.0%**	**5.19 [0.26, 103.11]**
Total events	2		0			

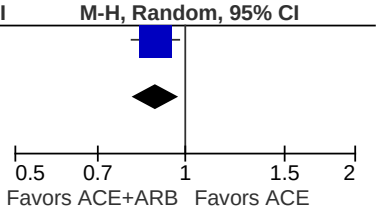
Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)



Composite vascular outcome (See Table C21 for definitions)

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Anand 2009	499	1477	549	1439	100.0%	0.89 [0.80, 0.98]
Total (95% CI)		**1477**		**1439**	**100.0%**	**0.89 [0.80, 0.98]**
Total events	499		549			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.45 (P = 0.01)

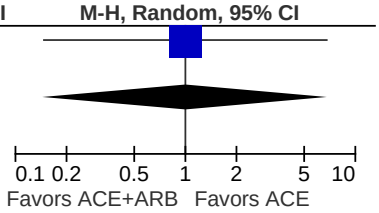


Appendix Figure C3. Forest plots for ACEI plus ARB versus ACEI trials (continued)

End-stage renal disease

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Kanno 2006	2	45	2	45	100.0%	1.00 [0.15, 6.79]
Total (95% CI)		**45**		**45**	**100.0%**	**1.00 [0.15, 6.79]**
Total events	2		2			

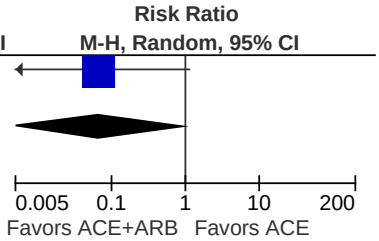
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



Doubling of serum creatinine

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Kanno 2006	0	45	7	45	100.0%	0.07 [0.00, 1.13]
Total (95% CI)		**45**		**45**	**100.0%**	**0.07 [0.00, 1.13]**
Total events	0		7			

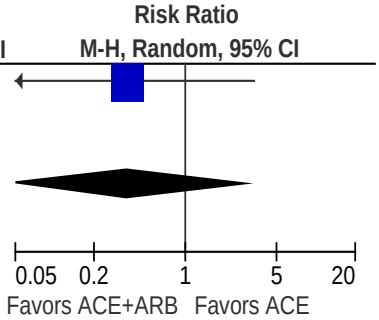
Heterogeneity: Not applicable
Test for overall effect: Z = 1.87 (P = 0.06)



Progression from microalbuminuria to macroalbuminuria

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Menne 2008	1	43	3	47	100.0%	0.36 [0.04, 3.37]
Sengul 2005	0	96	0	48		Not estimable
Total (95% CI)		**139**		**95**	**100.0%**	**0.36 [0.04, 3.37]**
Total events	1		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.89 (P = 0.37)



Appendix Table C21. Composite vascular outcome definitions for ACEI plus ARB versus ACEI or ARB trials

Study	Definition
Tobe 2011[35] ON-TARGET	Cardiovascular death, MI, fatal or nonfatal stroke, or hospitalization for heart failure.
Anand, 2009[46]	Death, sudden death with resuscitation, hospitalization for heart failure, or administration of intravenous inotropic or vasolilator drugs for 4 hours or more without hospitalization

ACEI = angiotensin converting enzyme; ARB = angiotensin receptor blocker

Appendix Table C22. Clinical renal outcomes (outcomes part C), ACEI plus ARB versus ACEI or ARB trials

Study	End-stage Renal Disease n/N (%)		Doubling of Serum Creatinine n/N (%)		Halving of GFR n/N (%)		Progression from Micro- to Macroalbuminuria n/N (%)		Composite Renal Outcome n/N (%)#	
ACEI plus ARB versus ACEI trials (n=5)										
	ACEI+ARB	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**
Sengul, 2006[20]							0/96 (0)	0/48 (0)		
Menne, 2008[19] VALERIA							1/43 (2.5)	3/47 (6.4)		
Kanno, 2006[44]	2/45 (4.4)	2/45 (4.4)	0/45 (0)	7/45 (15.6)						
Mehdi, 2009[45]			**NR	**NR						
Anand, 2009[46]										
ACEI plus ARB versus ARB trials (n=3)										
			ACEI+ARB	**ARB**			**ACEI+ARB**	**ARB**	**ACEI+ARB**	**ARB**
Sengul, 2006[20]							0/96 (0)	0/48 (0)		
Menne, 2008[19]							1/43 (2.5)	3/43 (7.1)		
ACEI plus ARB versusACEI or ARB trials (monotherapy) (n=1)										
	ACEI+ARB	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**
Tobe 2011[35] Mann, 2008[18] ON-TARGET	*Chronic dialysis* 31/2943 (1.1)	*Chronic dialysis* 53/5990 (0.9)	86/2943 (2.9)	140/5990 (2.3)					104/2943 (3.5)	173/5990 (2.9)

ACEI = angiotensin convertng enzyme; ARB = angiotensin receptor blocker; GFR = glomerular filtration rate
#See composite renal outcome definitions table
*Reported for the overall participants but not for the CKD subgroup
**Reported 50% increase in serum creatinine in 13/26 (50%) of ACEI+ARB group and 10/27 (37%) of ACEI group
†Had microalbuminuria at baseline; N based on back calculation using percentage with progression

Appendix Table C23. Composite renal outcome definitions for ACEI plus ARB versus ACEI or ARB trials

Study	Definition
Tobe 2011[35] ON-TARGET	Chronic dialysis or doubling of serum creatinine

ACEI = angiotensin converting enzyme; ARB = angiotensin receptor blocker

Appendix Table C24. Study withdrawals and adverse events (outcomes part D), ACEI plus ARB versus ACEI or ARB trials

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Event: Any, n/N (%)		Serious Adverse Event: Any Leading to Withdrawal, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event: Any Specific, n/N (%)		Renal Adverse Event: Any, n/N (%)	
ACEI plus ARB versus ACEI trials (n=6)												
	ACEI+ARB	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**	**ACEI+ARB**	**ACEI**
Sengul, 2006[20]	*NR	*NR					**NR	**NR	***NR	***NR		
Menne, 2008[19] VALERIA	6/43 (14.0)	5/47 (10.6)	4/43 (9.3)	5/47 (10.6)	3/43 (7.0)	4/47 (8.5)	31/43 (72.1)	29/47 (69.7)	Hypotension: 5/43 (11.6); Hyperkalemia: 1/43 (2.3); Cough: 2/47 (4.3)§	Hypotension: 1/47 (2.1); Hyperkalemia: 1/47 (2.1); Cough: 1/43 (2.3)§		
Mann, 2008[18] ON-TARGET	#NR	#NR										
Kanno, 2006[44]	2/45 (4.4)	3/45 (6.7)	†NR	†NR	†NR	†NR	†NR	†NR				
Mehdi, 2009[45]	8/27 (29.6)	6/27 (22.2)					2/27 (7.4)	1/27 (3.7)	Heart failure: 2/27 (7.4)	Stroke: 1/27 (3.7)		
Anand, 2009[46]									Hyperkalemia: 126/1477 (8.5)	Hyperkalemia 65/1439 (4.5)		
ACEI plus ARB versus ARB trials (n=3)												
	ACEI+ARB	**ARB**	**ACEI+ARB**	**ARB**	**ACEI+ARB**	**ARB**	**ACEI+ARB**	**ARB**	**ACEI+ARB**	**ARB**	**ACEI+ARB**	**ARB**
Sengul, 2006[20]	*NR	*NR					**NR	**NR	***NR	***NR		
Menne, 2008[19] VALERIA	6/43 (14.0)	6/43 (14.0)	4/43 (9.3)	1/43 (2.3)	3/43 (7.0)	3/43 (7.0)	31/43 (72.1)	27/ 43 (62.8)	Hypotension: 5/43 (11.6); Hyperkalemia: 1/43 (2.3); Cough: 2/47 (4.3)§ §	Hypotension: 4/43 (9.3); Hyperkalemia: 1/43 (2.3); Cough: 0/43 (0)§ §		
Mann, 2008[18] ON-TARGET	#NR	#NR										

Appendix Table C24. Study withdrawals and adverse events (outcomes part D), ACEI plus ARB versus ACEI or ARB trials (continued)

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Event: Any, n/N (%)		Serious Adverse Event: Any Leading to Withdrawal, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event: Any Specific, n/N (%)		Renal Adverse Event: Any, n/N (%)	
ACEI plus ARB versus ACEI or ARB (monotherapy) trials (n=1)												
	ACEI+ARB	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**	**ACEI+ARB**	**Mono**
Sengul, 2006[20]	947/2943 (32.2)	1644/5990 (27.4)							Hypotension: 110/2943 (3.7); Cough: 114/2943 (3.9); Syncope: 6/2943 (0.2);	Hypotension: 135/5990 (2.3); Cough: 135/5990 (2.3); Syncope: 5/5990 (0.08);		

ACEI = angiotensin converting enzyme; ARB = angiotensin receptor blocker
*Reported withdrawals for original randomization groups (ACEI: 15/110 [13.6%], ARB: 12/109 [11.0%])
**Adverse events not distinguished from withdrawals
***Reported most frequent adverse events were cough (only in patients receiving lisinopril) and headache, experienced by <10% of patients; other noted side effects were nausea, stomach upset, respiratory infection, dizziness, feeling weak, gastrointestinal problems
§Other reported adverse events: vertigo (2.3% ACEI+ARB, 4.3% ACEI), dizziness (2.3% ACEI+ARB, 2.1% ACEI), headache (0% ACEI+ARB, 2.1% ACEI)
§§Other reported adverse events: vertigo (2.3% ARB), dizziness (2.3% ARB), headache (2.3% ARB)
#Reported follow-up of all but 43/25,620 (0.2%)
^Reported as “renal abnormalities”
†Reported “few” discontinuations as a result of AE and discontinuations as a result of drug-related AE
~reported for the overall participants but not for the CKD subgroup

Appendix Table C25. Overview of ACEI plus ARB versus ARB trials (n=3 trials)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Sengul, 2006[20] Turkey Funding Source: none stated	Inclusion Criteria: microalbuminuria (AER rate 30 to 300 mg/24 hour for a minimum of three consecutive occasions); aged 40 to 65 years; previously diagnosed hypertension (systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg), despite receiving ACEI monotherapy for ≥6 months. Exclusion Criteria: type 1 DM; BMI ≥40; secondary diabetes; alcoholism; thyroid disease; systolic BP >200 mm Hg, any nondiabetic cause of secondary HTN (including bilateral renal artery stenosis); urinary tract infection; persistent hematuria; chronic liver disease; overt carcinoma; any cardiovascular event in the previous 6 months; serum creatinine ≥ 150 mmol/L; serum potassium ≥ 5.5 mmol/L; or pregnancy.	N=219 Age (yr): 57 Gender (Male %): 37 Race/Ethnicity (%): NR BMI: 30 Systolic BP (mm Hg): 151 Diastolic BP (mm Hg): 89 Urinary AER (mg/24 h): 260 Serum creatinine (mg/dL): 1 Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (mg/min): 97 Total cholesterol (mg/dL): 211 LDL cholesterol (mg/dL): 135 HbA_{1c} (%): 7.9 Diabetes (%): 100 History of HTN (%): 100 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 37	Lisinopril 20 mg/d (n=110) Telmisartan 80 mg/d (n=109) After 24 weeks, half of the patients receiving lisinopril were randomized to receive telmisartan in addition. Similarly, half the patients initially treated with telmisartan received a combination of lisinopril plus telmisartan. The remaining patients continued to be treated with monotherapy Followup period: 1 year Study withdrawals (%): 12	Allocation Concealment: unclear Blinding: open-label Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Table C25. Overview of ACEI plus ARB versus ARB trials (n=3 trials) (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Menne, 2008[19] VALERIA Germany and Hungary Funding Source: Industry	Inclusion Criteria: microalbuminuria (urine albumin creatinine ratio for women ≥3.5 mg/ mmol/L and ≤35.0 mg/mmol and men ≥2.5 mg/ mmol/L and ≤25.0 mg/mmoL); aged 18 to 75 years; essential hypertension [defined as mean sitting diastolic BP ≥85 mmHg and <110 mm Hg]. To fulfill the criteria of microalbuminuria, two of three first morning void urines needed to be positive during the screening phase. Exclusion Criteria: primary kidney disease, renal impairment (creatinine clearance <30ml/min using the Cockroft and Gault formula; serum potassium values >5.5mmol/L; heart failure, significant arrhythmias or bradycardia; relevant valvular disease, type I DM, uncontrolled type II DM with HbA_{1c} >8.0%; history of MI; percutaneous transluminal coronary angioplasty, bypass surgery or stroke within the last 12 months prior to study inclusion; unstable angina pectoris; renal transplantation; severe hepatic disease or hepatic failure; malignant concomitant diseases or history of malignant diseases within the	N=90 (133 total with combination arm) Age (yr): 58 Gender (Male %): 69 Race/Ethnicity (%): NR BMI: 32 Systolic BP (mm Hg): 153 Diastolic BP (mm Hg): 91 Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): NR Creatinine clearance (mg/min): 112 Urine albumin creatinine ratio (mg/ mmol): 9.4 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR HbA_{1c} (%): NR Diabetes (%): 74 History of HTN (%): 100 History of CAD “Cardiac disorders”(%): 19 History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Lisinopril 40 mg/d + valsartan 320 mg/d (n=43) Valsartan 320 mg/d (n=43) Followup period: 30 weeks Study withdrawals (%): 14	Allocation Concealment: adequate Blinding: double plus outcome assessors and data analysts Intention to Treat Analysis: no Withdrawals/Dropouts adequately described: yes

Appendix Table C25. Overview of ACEI plus ARB versus ARB trials (n=3 trials) (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	last 5 years; systemic inflammatory diseases; pregnancy or breast feeding; psychiatric disease; either history of alcohol or drug abuse or both.			
Mann, 2008[18] ONTARGET Multinational Funding Source: Industry	Inclusion Criteria: aged 55 years or older with established atherosclerotic vascular disease or with diabetes with end-organ damage. Exclusion Criteria: major renal artery stenosis, uncorrected volume or sodium depletion, a serum creatinine concentration above 265 µmol/L, and uncontrolled hypertension (>160 mm Hg systolic or >100 mm Hg diastolic).	This was a 3-arm trial of 25,620 subjects; number with CKD is not specified Estimated GFR (ml/min/1.73m^2): 51.0* Urine albumin creatinine ratio (mg/mmol): 0.81* *Patient characteristics not described for the different arms or for CKD subgroup	Ramipril 10 mg/d + telmisartan 80 mg/d (n= 8502 overall) Telmisartan 80 mg/d (n= 8542 overall) Followup period: median 4.7 years (followup is for the entire cohort) Study withdrawals (%): NR	Allocation Concealment: adequate Blinding: double Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes

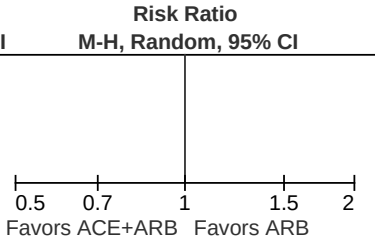
ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Figure C4. Forest plots ACEI plus ARB versus ARB trials

All-cause mortality

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ARB Events	ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
Menne 2008	0	43	0	43		Not estimable
Total (95% CI)		**43**		**43**		**Not estimable**
Total events	0		0			

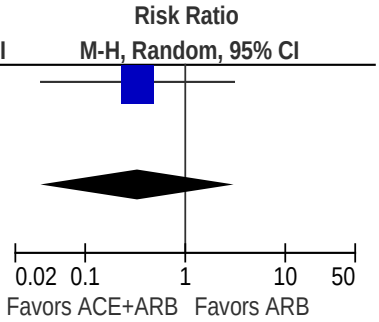
Heterogeneity: Not applicable
Test for overall effect: Not applicable



Progression from microalbuminuria to macroalbuminuria

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ARB Events	ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
Menne 2008	1	43	3	43	100.0%	0.33 [0.04, 3.08]
Sengul 2005	0	96	0	48		Not estimable
Total (95% CI)		**139**		**91**	**100.0%**	**0.33 [0.04, 3.08]**
Total events	1		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.97 (P = 0.33)



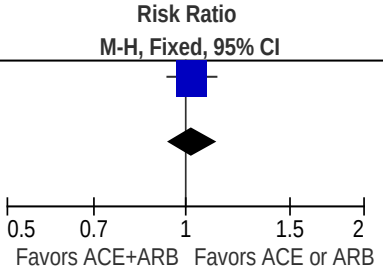
Appendix Figure C5. Forest plots ACEI plus ARB versus ACEI or ARB trial

All-cause mortality

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE or ARB Events	ACE or ARB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tobe (ONTARGET) 2011	520	2943	1033	5990	100.0%	1.02 [0.93, 1.13]
Total (95% CI)		**2943**		**5990**	**100.0%**	**1.02 [0.93, 1.13]**
Total events	520		1033			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.50 (P = 0.62)

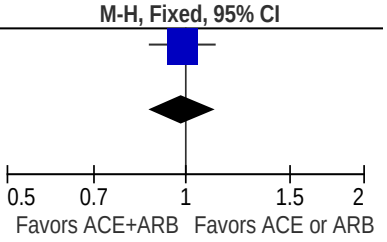


Cardiovascular mortality

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE or ARB Events	ACE or ARB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tobe (ONTARGET) 2011	317	2943	654	5990	100.0%	0.99 [0.87, 1.12]
Total (95% CI)		**2943**		**5990**	**100.0%**	**0.99 [0.87, 1.12]**
Total events	317		654			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.21 (P = 0.83)

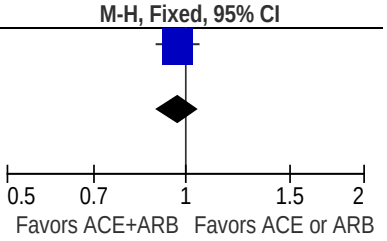


Composite vascular outcome (See Table C21 for definition)

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE or ARB Events	ACE or ARB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tobe (ONTARGET) 2011	653	2943	1372	5990	100.0%	0.97 [0.89, 1.05]
Total (95% CI)		**2943**		**5990**	**100.0%**	**0.97 [0.89, 1.05]**
Total events	653		1372			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.76 (P = 0.45)

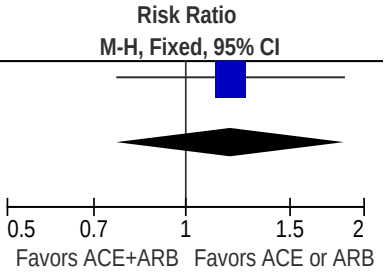


End-stage renal disease (chronic dialysis)

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE or ARB Events	ACE or ARB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tobe (ONTARGET) 2011	31	2943	53	5990	100.0%	1.19 [0.77, 1.85]
Total (95% CI)		**2943**		**5990**	**100.0%**	**1.19 [0.77, 1.85]**
Total events	31		53			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.77 (P = 0.44)



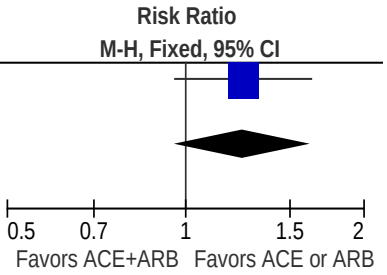
Appendix Figure C5. Forest plots ACEI plus ARB versus ACEI or ARB trial (continued)

Doubling of serum creatinine

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE or ARB Events	ACE or ARB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tobe (ONTARGET) 2011	86	2943	140	5990	100.0%	1.25 [0.96, 1.63]
Total (95% CI)		**2943**		**5990**	**100.0%**	**1.25 [0.96, 1.63]**
Total events	86		140			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.65 (P = 0.10)

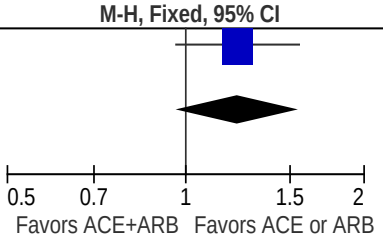


Composite renal outcome (See Table C23 for definition)

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE or ARB Events	ACE or ARB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tobe (ONTARGET) 2011	104	2943	173	5990	100.0%	1.22 [0.96, 1.55]
Total (95% CI)		**2943**		**5990**	**100.0%**	**1.22 [0.96, 1.55]**
Total events	104		173			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.65 (P = 0.10)



Appendix Evidence Table C26. Overview of ACEI plus ARB versus ACEI plus aldosterone antagonist trial

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Mehdi, 2009[45] Location United States, single-site Funding Source Government	Inclusion Criteria: Age 20 to 65; type 1 or 2 DM; seated systolic BP >130mmHg; proteinuria (24-h UACR≥300 mg/g despite treatment with ACEI or ARB for at least 3 months* Exclusion Criteria: BMI >45kg/m^2; serum creatinine >3.0mg/dl (females) or >4.0 mg/dl (males); known nonddiabetic kidney disease; serum potassium >5.5 mEq/L; hemoglobin A1c >11%; stroke or myocardial infarction within preceding 12 months; heart failure; known adverse reaction to losartan or spironolactone; anticipated need for dialysis within 12 months *Effort was made to recruit younger patients with type 2 DM as recommended by study sponsor	Baseline characteristics based on 26 in Losartan group (excluded 1 patient who withdrew prior to first dose) and 27 in spironolactone group N=53 Age (yr): 52 Gender (Male %): 49 Race/Ethnicity (%): 55% Hispanic, 28% black, 15% non-Hispanic white, 2% Native American Weight (kg): NR BMI: 32.0 Clinic Systolic BP (mm Hg): 134.0 Clinic Diastolic BP (mm Hg): 72.5 CKD stage: NR Serum creatinine (mg/dl): 1.75 Creatinine clearance (ml/min): 58.0 Albuminuria (µg/min): NR Proteinuria (g/day): NR Albumin/creatinine ratio (mg/g): 997.4 GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 7.5 Total cholesterol (mg/dl): 186.8 LDL cholesterol (mg/dl): 87.3 Diabetes (%): 100 History of HTN (%): NR Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%):0 Peripheral arterial disease (%): NR History of MI (%): 0 in past 12 months History of MI, CABG, or PCTA (%): 7.5 History of Stroke (%): 0 in past 12 months Current smoker (%): NR History of AKI (%): NR	n= 27 to Losartan 100mg/day# n= 27 to Spironolactone 25mg/day# Followup period: 48 weeks Study withdrawals (%): 35.2 #All patients were taking Lisinopril 80 mg/day	Allocation Concealment: Unclear Blinding: Double blinded Intention to Treat Analysis (ITT): No (excluded 1 subject who withdrew prior to first losartan dose from analyses) Withdrawals/Dropouts adequately described: Yes

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CABG= coronary artery bypass grafting; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PTCA= Percutaneous transluminal coronary angioplasty; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; TIA = transient ischemic attack; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C27. Clinical outcomes (outcomes part A), ACEI plus ARB versus ACEI plus aldosterone antagonist trial

Study	All-Cause Mortality, n/N (%)		Cardiovascular Mortality, n/N (%)		Myocardial Infarction, Any, n/N (%)		Myocardial Infarction, Fatal, n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke, Any, n/N (%)	
	ACEI+ ARB	ACEI+ Aldo Antag	ACEI+ ARB	ACEI+ Diuretic	ACEI+ ARB	ACEI+ Diuretic	ACEI+ ARB	ACEI+ Diuretic	ACEI+ ARB	ACEI+ Diuretic	ACEI+ ARB	ACEI+ Diuretic
Mehdi, 2009[45]	1/26 (3.8)	0/27			0/26 (0.0)	1/27 (3.7)					NR*	NR*

ACEI = angiotensin converting enzyme; ARB = angiotensin receptor blocker; Aldo Antag = aldosterone antagonist

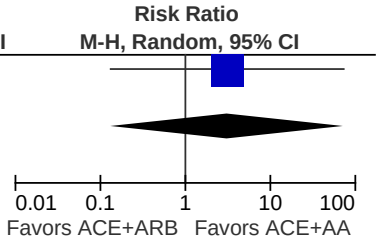
* The study reports both that hospitalizations for stroke occurred in no subjects assigned to ACEI plus ARB and two subjects assigned to ACEI plus diuretic, and that withdrawals for stroke occurred in one subject assigned to ACEI plus ARB and two subjects assigned to ACEI plus diuretic. It is unclear whether one of the reports is in error or whether there is nonoverlap between the strokes leading to hospitalization and those leading to withdrawal.

Appendix Figure C6. Forest plots for ACEI plus ARB versus ACEI plus aldosterone antagonist trial

All-cause mortality

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE+AA Events	ACE+AA Total	Weight	Risk Ratio M-H, Random, 95% CI
Mehdi 2009	1	26	0	27	100.0%	3.11 [0.13, 73.09]
Total (95% CI)		**26**		**27**	**100.0%**	**3.11 [0.13, 73.09]**
Total events	1		0			

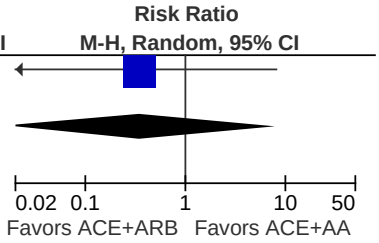
Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.48)



Myocardial infarction, any

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE+AA Events	ACE+AA Total	Weight	Risk Ratio M-H, Random, 95% CI
Mehdi 2009	0	26	1	27	100.0%	0.35 [0.01, 8.12]
Total (95% CI)		**26**		**27**	**100.0%**	**0.35 [0.01, 8.12]**
Total events	0		1			

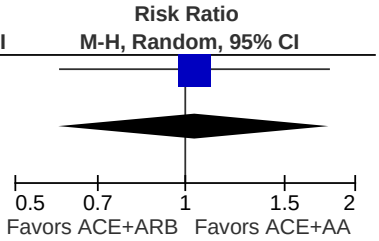
Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)



Doubling of serum creatinine

Study or Subgroup	ACE+ARB Events	ACE+ARB Total	ACE+AA Events	ACE+AA Total	Weight	Risk Ratio M-H, Random, 95% CI
Mehdi 2009	13	26	13	27	100.0%	1.04 [0.60, 1.80]
Total (95% CI)		**26**		**27**	**100.0%**	**1.04 [0.60, 1.80]**
Total events	13		13			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.13 (P = 0.89)



Appendix Table C28. Clinical renal outcomes (outcomes part C), ACEI plus ARB versus ACEI plus aldosterone antagonist trial

Study	End-Stage Renal Disease, n/N (%)		Doubling of Serum Creatinine, n/N (%)		Halving of GFR, n/N (%)		Progression from Micro- to Macroalbuminuria, n/N (%)		Composite Renal Outcome, n/N (%)	
	ACEI+ ARB	ACEI+ AA	ACEI+ ARB	ACEI+ AA	ACEI+ ARB	ACEI+ AA	ACEI+ ARB	ACEI+ AA	ACEI+ ARB	ACEI+ AA
Mehdi, 2009[45]			13/26 (50.0)	13/27 (48.0)						

GFR = glomerular filtration rate; ACEI = angiotension converting enzyme; ARB = angiotensin receptor blocker: AA = aldosterone antagonist

Appendix Table C29. Study withdrawals and adverse events (outcomes part D), ACEI plus ARB versus ACEI plus aldosterone antagonist trial

Study	Study Withdrawals, Any, n/N (%)		Serious Adverse Events, Any, n/N (%)		Withdrawals Due to Adverse Events, Any, n/N (%)		Adverse Events, Any, n/N (%)		Adverse Events, Specific, n/N (%)		Renal Adverse Events, Any, n/N (%)	
	ACEI+ ARB	ACEI+ AA	ACEI+ ARB	ACEI+ AA	ACEI+ ARB	ACEI+ AA	ACEI+ ARB	ACEI+ AA	ACEI+ ARB	ACEI+ AA	ACEI+ ARB	ACEI+ AA
Mehdi, 2009[45]	9/27 (33.3)	10/27 (37.0)			2/26 (7.7)	7/27 (25.9)			0/26 (0.0)	1/27 (3.7)	Recurrent hyperkalemia: 0/26; Withdrawn due to increased SCr: 0/27	Recurrent hyperkalemia: 2/27 (7.4); Withdrawn due to increased SCr: 1/27

ACEI = angiotensin converting enzyme inhibitor; ARB = antiogensin receptor blocker; AA = aldosterone antagonist ; SCr = serum creatinine

Appendix Evidence Table C30. Overview of ACEI plus CCB versus ACEI monotherapy or CCB monotherapy trial

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Fogari, 2002[24] Italy Multisite Funding Source: none stated	Inclusion: microalbuminuria (UAE ≥30 and ≤300 mg/24 h in two distinct 24-hour urine collections during 7 days before enrollment); essential hypertension (sitting diastolic BP values >90 mmHg and <110 mmHg); type 2 diabetes well controlled by diet or by metformin alone or metformin plus a sulfanylurea; BMI <30 kg/m^2; serum creatinine <1.5 mg/dL. Exclusion Criteria: history of previous coronary heart disease, stroke, CHF, cancer; smoking habits; electrocardiogram showing left ventricular hypertrophy; total cholesterol values >240mg/dL; use of diuretics or beta-blockers.	N=453 randomized Baseline characteristics reported only for N=309 who were judged responders on completion of dose titration phase and did not complain of side effects. N=206 ACE+CCB vs. ACE Age (yr): 62.5 Gender (Male %): 57 Race/Ethnicity (%): NR Weight (kg): NR BMI: 27.6 Systolic BP (mm Hg): 160.3 Diastolic BP (mm Hg): 99.3 CKD stage: NR Serum creatinine (mg/dL): 1.0 Creatinine clearance (mg/min): 89.9 Albuminuria (µg/min): 97.9 Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 7.1 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 100 History of CAD (%): 0 History of CHF (%): 0 Peripheral arterial disease (%): NR History of MI (%): 0 History of Stroke (%): 0 Peripheral arterial disease (%): NR Current smoker (%): NR (excluded for "smoking habits" – not defined) History of AKI (%): NR N=207 ACE+CCB vs. CCB Age (yr): 62.2 Gender (Male %): 55 Race/Ethnicity (%): NR	n= 102 Fosinopril 10-30 mg/day* n=103 Amlodipine 5-15 mg/day* n=104 Amlodipine 5 to 15 mg/day + Fosinopril 10 to 30 mg/day * Followup period: 4 years Study withdrawals (%): 47% (215/453), including 144/453 (32%) in titration period and 71/309 (23%) during study period. *N=453 randomized to 3 month dose titration period with goal of DBP <90 mmHg for monotherapy groups and <85 mmHg for combined therapy group.	Allocation Concealment: Adequate Blinding: Open-label Intention to Treat Analysis: No Withdrawals/Dropouts adequately described: No

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
		Weight (kg): NR BMI: 27.8 Systolic BP (mm Hg): 160.8 Diastolic BP (mm Hg): 99.4 CKD stage: NR Serum creatinine (mmol/L): 1.0 Creatinine clearance (mg/min): 89.3 Albuminuria (µg/min): 96.6 Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 7.0 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 100 History of CAD (%): 0 History of CHF (%): 0 Peripheral arterial disease (%): NR History of MI (%): 0 History of Stroke (%): 0 Peripheral arterial disease (%): NR Current smoker (%): NR (excluded for "smoking habits" – not defined) History of AKI (%): NR		

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C31. Clinical outcomes (outcomes part A), ACEI plus CCB versus ACEI monotherapy or CCB monotherapy trial

Study	All-Cause Mortality, n/N (%)			Cardiovascular Mortality, n/N (%)			Myocardial Infarction, Any, n/N (%)			Myocardial Infarction, Fatal, n/N (%)			Myocardial Infarction, Nonfatal, n/N (%)			Stroke, Any, n/N (%)		
	ACEI+ CCB	ACEI	CCB	ACEI+ CCB	ACEI	CCB	ACEI+ CCB	ACEI	CCB	ACEI+ CCB	ACEI	CCB	ACEI+ CCB	ACEI	CCB	ACEI+ CCB	ACEI	CCB
Fogari, 2002[24]	2/104 (1.9)	3/102 (2.9)	4/103 (3.9)	1/104 (1.0)	2/102 (1.9)	2/103 (1.9)	1/104 (1.0)	3/102 (2.9)	4/103 (3.9)	0/104	1/102 (1.0)	2/103 (1.9)	1/104 (1.0)	2/102 (1.9)	2/103 (1.9)	1/104 (1.0)	3/102 (2.9)	2/103 (1.9)

ACEI = angiotensin converting enzyme inhibitor; CCB = calcium channel blocker

Appendix Table C32. Clinical outcomes (outcomespart B), ACEI plus CCB versus ACEI monotherapy or CCB monotherapy trial

Study	Stroke, Nonfatal, n/N (%)			Stroke, Fatal, n/N (%)			CHF, Any, n/N (%)			CHF Hospitalization (A) or Death (B), n/N (%)			Composite Vascular Outcome, n/N (%)		
	ACEI+ CCB	ACEI	CCB	ACEI+ CCB	ACEI	CCB	ACEI+ CCB	ACEI	CCB	ACEI+ CCB	ACEI	CCB	ACEI+ CCB	ACEI	CCB
Fogari, 2002[24]	1/104 (1.0)	2/102 (1.9)	2/103 (1.9)	0/104	1/102 (1.0)	0/103									

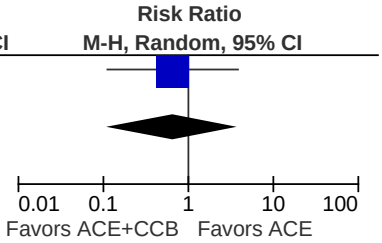
ACEI = angiotensin converting enzyme; CCB = calcium channel blocker; CHF = congestive heart failure
*Other no-fatal cardiovascular events (not defined): ACEI+CCB: 1/104 (1.0%), ACEI: 1/102 (1.0%), CCB: 2/103 (1.9%)

Appendix Figure C7. Forest plots for ACEI plus CCB versus ACE monotherapy trial

All-cause mortality

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	2	104	3	102	100.0%	0.65 [0.11, 3.83]
Total (95% CI)		**104**		**102**	**100.0%**	**0.65 [0.11, 3.83]**
Total events	2		3			

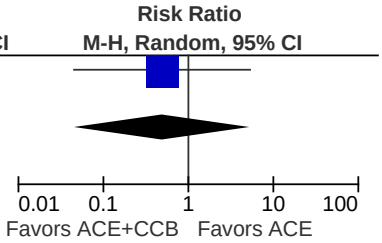
Heterogeneity: Not applicable
Test for overall effect: Z = 0.47 (P = 0.64)



Cardiovascular mortality

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	1	104	2	102	100.0%	0.49 [0.05, 5.32]
Total (95% CI)		**104**		**102**	**100.0%**	**0.49 [0.05, 5.32]**
Total events	1		2			

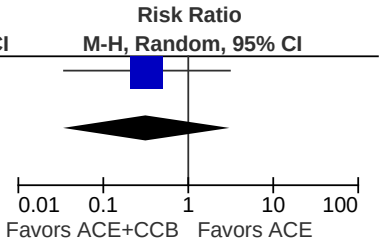
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)



Myocardial infarction, any

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	1	104	3	102	100.0%	0.33 [0.03, 3.09]
Total (95% CI)		**104**		**102**	**100.0%**	**0.33 [0.03, 3.09]**
Total events	1		3			

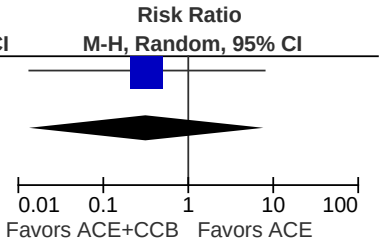
Heterogeneity: Not applicable
Test for overall effect: Z = 0.98 (P = 0.33)



Myocardial infarction, fatal

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	0	104	1	102	100.0%	0.33 [0.01, 7.93]
Total (95% CI)		**104**		**102**	**100.0%**	**0.33 [0.01, 7.93]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)

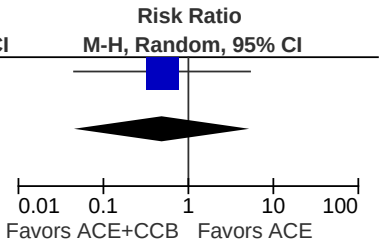


Appendix Figure C7. Forest plots for ACEI plus CCB versus ACE monotherapy trial (continued)

Myocardial infarction, nonfatal

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	1	104	2	102	100.0%	0.49 [0.05, 5.32]
Total (95% CI)		**104**		**102**	**100.0%**	**0.49 [0.05, 5.32]**
Total events	1		2			

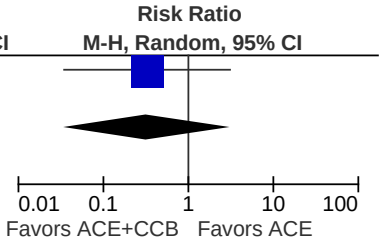
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)



Stroke, any

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	1	104	3	102	100.0%	0.33 [0.03, 3.09]
Total (95% CI)		**104**		**102**	**100.0%**	**0.33 [0.03, 3.09]**
Total events	1		3			

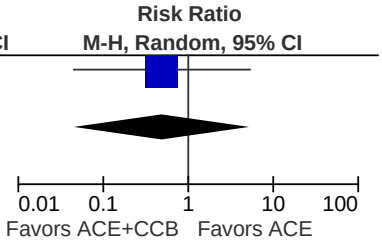
Heterogeneity: Not applicable
Test for overall effect: Z = 0.98 (P = 0.33)



Stroke, nonfatal

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	1	104	2	102	100.0%	0.49 [0.05, 5.32]
Total (95% CI)		**104**		**102**	**100.0%**	**0.49 [0.05, 5.32]**
Total events	1		2			

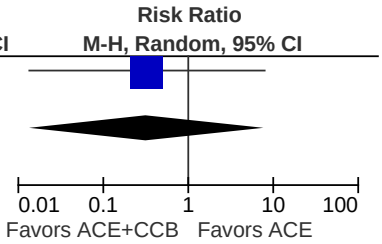
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)



Stroke, fatal

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	ACE Events	ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	0	104	1	102	100.0%	0.33 [0.01, 7.93]
Total (95% CI)		**104**		**102**	**100.0%**	**0.33 [0.01, 7.93]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)

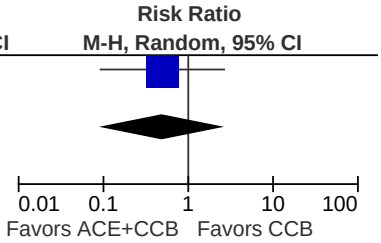


Appendix Figure C8. Forest plots for ACEI plus CCB versus CCB monotherapy trial

All-cause mortality

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	2	104	4	103	100.0%	0.50 [0.09, 2.64]
Total (95% CI)		**104**		**103**	**100.0%**	**0.50 [0.09, 2.64]**
Total events	2		4			

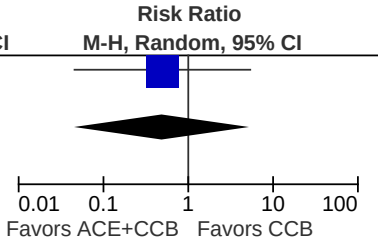
Heterogeneity: Not applicable
Test for overall effect: Z = 0.82 (P = 0.41)



Cardiovascular mortality

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	1	104	2	103	100.0%	0.50 [0.05, 5.38]
Total (95% CI)		**104**		**103**	**100.0%**	**0.50 [0.05, 5.38]**
Total events	1		2			

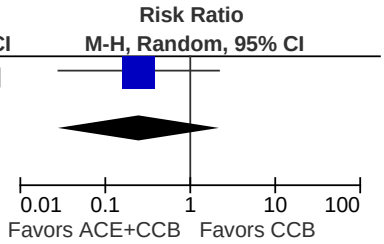
Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)



Myocardial infarction, any

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	1	104	4	103	100.0%	0.25 [0.03, 2.18]
Total (95% CI)		**104**		**103**	**100.0%**	**0.25 [0.03, 2.18]**
Total events	1		4			

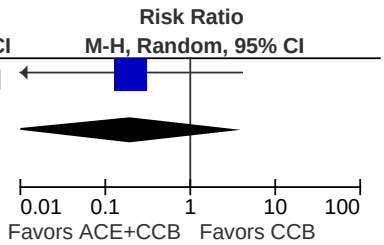
Heterogeneity: Not applicable
Test for overall effect: Z = 1.26 (P = 0.21)



Myocardial infarction, fatal

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	0	104	2	103	100.0%	0.20 [0.01, 4.08]
Total (95% CI)		**104**		**103**	**100.0%**	**0.20 [0.01, 4.08]**
Total events	0		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.05 (P = 0.29)

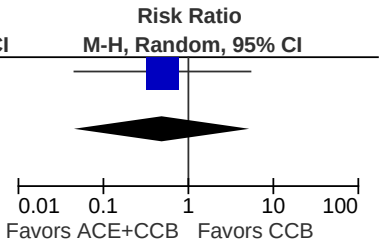


Appendix Figure C8. Forest plots for ACEI plus CCB versus CCB monotherapy trial (continued)

Myocardial infarction, nonfatal

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	1	104	2	103	100.0%	0.50 [0.05, 5.38]
Total (95% CI)		**104**		**103**	**100.0%**	**0.50 [0.05, 5.38]**
Total events	1		2			

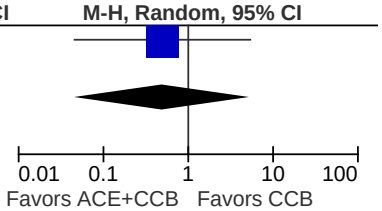
Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)



Stroke, any

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	1	104	2	103	100.0%	0.50 [0.05, 5.38]
Total (95% CI)		**104**		**103**	**100.0%**	**0.50 [0.05, 5.38]**
Total events	1		2			

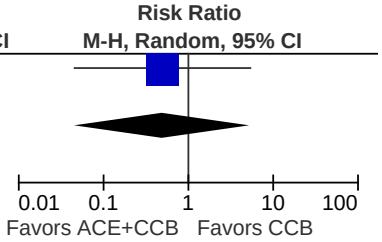
Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)



Stroke, nonfatal

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	1	104	2	103	100.0%	0.50 [0.05, 5.38]
Total (95% CI)		**104**		**103**	**100.0%**	**0.50 [0.05, 5.38]**
Total events	1		2			

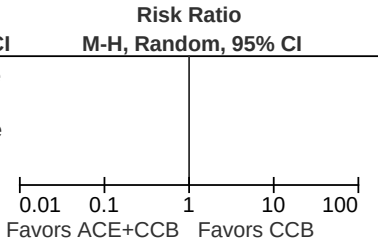
Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)



Stroke, fatal

Study or Subgroup	ACE+CCB Events	ACE+CCB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Fogari 2002	0	104	0	103		Not estimable
Total (95% CI)		**104**		**103**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable



Appendix Table C33. Study withdrawals and adverse events (outcomes part D), ACEI plus CCB versus ACEI monotherapy or CCB monotherapy trial

Study	Any Study Withdrawals, n/N (%)			Withdrawals Due to Serious Adverse Events, n/N (%)			Serious Adverse Events, n/N (%)			Adverse Events, Any, n/N (%)			Adverse Events, Specific, n/N (%)			‡Renal Adverse Events, n/N (%)		
	ACEI + CCB	ACEI	CCB	ACEI + CCB	ACEI	CCB	ACEI + CCB	ACEI	CCB	ACEI + CCB	ACEI	CCB	ACEI + CCB	ACEI	CCB	ACEI + CCB	ACEI	CCB
Fogari, 2002[24]	*NR	*NR	*NR	†NR	†NR	†NR							Cough: 1/104 (1.0); Edema 0/104	Cough: 2/102 (1.9) Edema 0/102	Cough: 0/103 Edema 2/103	1/104 (1.0)	2/102 (1.9)	2/103 (1.9)

ACEI = angiotensin converting enzyme inhibitor; CCB = calcium channel blocker

*Study reported that after randomization, during dose titration phase, 144/453 subjects discontinued due to their being nonresponders or because of side effects, but their treatment group was not reported. Following dose titration, another 71/309 subjects dropped out of the study (18/104 [17.3%] ACEI+CCB, 26/102 [25.4%] ACEI, and 27/103 [26.2%] CCB).

†Study reported that of 309 completing dose titration phase, 4/103 CCB subjects, 3/102 ACEI subjects, and 2/104 ACEI+CCB subjects withdrew due to adverse events, though no data were reported on withdrawals due to serious adverse events.

‡Study reported renal adverse event of discontinuing study medication due to worsening kidney function.

Appendix Table C34. Overview of ACEI plus diuretic versus ACEI plus CCB trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Bakris, 2008[47] (GUARD) Location United States Multisite Funding Industry	Inclusion Criteria: age 21 to 85 years; type 2 diabetes; albuminuria (repeated UACR 20-500 mg/g); hypertension (mean SBP≥130 mmHg and <180 mmHg, mean DBP≥80 mmHg and <110 mmHg) Exclusion Criteria: kidney disease not caused by diabetes and/or hypertension; confirmed or suspected renal artery stenosis; cardiovascular disease event (MI, stroke, TIA, CABG, PTCA) within previous 6 months; evidence of heart failure or documented left ventricular ejection fraction <40%; type 1 diabetes or uncontrolled type 2 diabetes (hgb A1C >9.5%, serum creatinine >1.5 mg/100ml (men) or >1.3 mg/100ml (women)	N=332 Age (yr): 57.7 Gender (Male %): 65.4 Race/Ethnicity (%): 60.2% white, 26.2% black, 1.5% Asian, 12.0% other Weight: NR BMI: 35 Systolic BP (mm Hg): 150.5 Diastolic BP (mm Hg): 87.8 CKD stage: NR HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): 0 Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR Following baseline characteristics available only from n=304 subjects who completed followup (n=151 (B+HCTZ) and n=153 (B+A)): Serum creatinine (µmol/L): NR Creatinine clearance (mL/min): NR Albuminuria (g/100ml)*: 4.2 (median) Albumin/creatinine ratio (mg/g): 60.5 (median) Estimated GFR (ml/min/1.73m^2): 90.6 (median)	n=166 (ACEI/Diuretic) benazepril/HCTZ (B+HCTZ) initiated at 20/12.5 mg/day; titrated to 40/12.5 mg/day at 4 weeks if not at <130/80 mm Hg target; titrated to 40/25 mg/day at 8 weeks if not at target <130/80 mm Hg* n=166 (ACEI/CCB) benazepril/amlodipine (B+A) initiated at 20/5 mg/day; titrated to 40/5 mg at 4 weeks if not at <130/80 mm Hg target; titrated to 40/10 mg/day at 8 weeks if not at target <130/80 mm Hg* All other antihypertensive medications were discontinued during pre-randomization wash-out phase. Followup period: 12 months Study withdrawals (%): 18.7% *At 12 weeks and all subsequent visits, patients titrated to next dose if not at target BP; if at max dose (40/25 mg B+HCTZ or 40/10 mg B+A), other anti-hypertensives added (alpha blockers, beta blockers, etc.); no added ACEi, ARB, or aldosterone receptor blocker	Allocation Concealment: Adequate Blinding: Double blind Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes

Appendix Table C34. Overview of ACEI plus diuretic versus ACEI plus CCB trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Bakris, 2010[48] Jamerson 2004[49] (ACCOMPLISH) Location Multinational, US and Europe Funding Industry	Inclusion Criteria: men and women, age ≥60 years, systolic blood pressure ≥160 mmHg or currently on antihypertensive therapy, evidence of prior MI, hospitalization for unstable angina, coronary revascularization, stroke, PAD, diabetes, left ventricular hypertrophy, renal disease (SCr >1.5 mg/dL (women) or >1.7 mg/dL (men) (NOTE: ages 55-59 years old eligible if ≥2 cardiovascular disease or target organ damage markers) Exclusion Criteria: current (within 3 months) evidence for angina pectoris; hisotry of symptomatic heart failure or evidence of LVEF<40%; myocardial infarction, acute coronary syndromes, or coronary revascularization within prior month; stroke or ischemic cerebrovascular episodes in prior 3 months; hypertension that is excessively severe, known to be refractory to treatment or known to have a secondary cause; any other condition that could interfere with effective conduct of the study	N=1,093 with CKD Age (yr): 70.9 Gender (Male %): 67.2 Race/Ethnicity (%): 77.2% white, 19.9% black, 2.8% other Weight: NR BMI: 31.3 Systolic BP (mm Hg): 145 Diastolic BP (mm Hg): 78.4 CKD stage: NR Serum creatinine (μmol/L): 139.7 Creatinine clearance (mL/min): NR Albuminuria (g/100ml): NR Albumin/creatinine ratio (mg/mmol): 28.8 Estimated GFR (ml/min/1.73m^2): 45.1 HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 58.9 History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	n=561 combination pill - benazepril (20 mg) plus amlodipine (5 mg) daily n=532 combination pill - benazepril (20 mg) plus hydrochlorothiazide (12.5 mg) At one month, benazepril in both groups force titrated to 40 mg; at 2 months, doses of either drug could be titrated to maximum, if needed, to reach blood pressure <140/90 mmHg (or <130/80 mmHg for patients with diabetes or chronic kidney disease); at 3 months, add-on antihypertensives (beta-blockers, alpha-blockers, clonidine, and spironolactone) were allowed; once-daily loop diuretics allowed for volume management No wash-out of previous medications Followup period: 2.9 years (terminated early because of superior efficacy of ACEI + CCB Study withdrawals (%): NA	Allocation Concealment: Adequate Blinding: Double blind Intention to Treat Analysis (ITT): Subgroup analysis Withdrawals/Dropouts adequately described: Subgroup analysis

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C35. Clinical outcomes (outcomes part A), ACEI plus diuretic versus ACEI plus CCB trials

Study	All-cause Mortality, n/N (%)		Cardiovascular Mortality, n/N (%)		Myocardial Infarction, Any, n/N (%)		Myocardial Infarction, Fatal, n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke, Any, n/N (%)	
	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB
Bakris, 2008[47]	2/166 (1.2)	1/166 (0.6)										
Bakris, 2010[48]												

ACEI = angiotensin converting enzyme; CCB = calcium channel blocker

Appendix Table C36. Clinical outcomes (outcomes part B), ACEI plus diuretic versus ACEI plus CCB trials

Study	Stroke, Nonfatal, n/N (%)		Stroke, Fatal, n/N (%)		CHF, Any, n/N (%)		CHF Hospitalization (A) or Death (B), n/N (%)		Composite Vascular Outcome, n/N (%)	
	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB
Bakris, 2008[47]									*NR	*NR
Bakris, 2010[48]										

ACEI = angiotensin converting enzyme inhibitor; CCB = calcium channel blocker; CHF = congestive heart failure

*Study reported discontinuation due to “cardiac disorders” in 3/166 ACEI + Diuretic subjects and in 2/166 ACEI + CCB subjects as well as due to “vascular disorders” in 2/166 ACEI + Diuretic subjects.

Appendix Table C37. Clinical renal outcomes (outcomes part C), ACEI plus diuretic versus ACEI plus CCB trials

Study	End-Stage Renal Disease, n/N (%)		Doubling of Serum Creatinine, n/N (%)		Halving of GFR, n/N (%)		Progression from Micro- to Macroalbuminuria, n/N (%)		Composite Renal Outcome, n/N (%)*	
	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB
Bakris, 2008[47]							6/153 (4.0)	7/150 (4.6)		
Bakris, 2010[48]									A. 17/309** (5.5) B. 30/309 (9.7)	A. 16/335** (4.8) B. 28/335 (8.4)

ACEI = angiotensin converting enzyme inhibitor; CCB = calcium channel blocker; GFR = glomerular filtration rate
*See Composite renal outcome definitions table
**Composite renal outcome data reported only for patients with chronic kidney disease and diabetic nephropathy

Appendix Table 38. Composite renal outcome definition, ACEI plus diuretic versus ACEI plus CCB trials

Study	Definition
Bakris 2010[48]	A. Doubling of serum creatinine concentration or end-stage renal disease (eGFR<15 mL/min/1.73m^2 or need for chronic dialysis B. Doubling of serum creatinine concentration or end-stage renal disease (eGFR<15 mL/min/1.73m^2 or need for chronic dialysis plus cardiovascular mortality

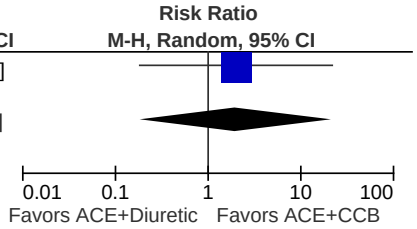
ACEI = angiotensin converting enzyme inhibitor; CCB = calcium channel blocker; GFR = glomerular filtration rate

Appendix Figure C9. Forest plots forACEI plus diuretic versus ACEI plus CCB trials

All-cause mortality

Study or Subgroup	ACE+Diuretic Events	ACE+Diuretic Total	ACE+CCB Events	ACE+CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Bakris 2008	2	166	1	166	100.0%	2.00 [0.18, 21.84]
Total (95% CI)		**166**		**166**	**100.0%**	**2.00 [0.18, 21.84]**
Total events	2		1			

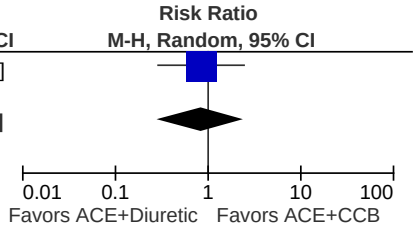
Heterogeneity: Not applicable
Test for overall effect: Z = 0.57 (P = 0.57)



Progression from microalbuminuria to macroalbuminuria

Study or Subgroup	ACE+Diuretic Events	ACE+Diuretic Total	ACE+CCB Events	ACE+CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Bakris 2008	6	153	7	150	100.0%	0.84 [0.29, 2.44]
Total (95% CI)		**153**		**150**	**100.0%**	**0.84 [0.29, 2.44]**
Total events	6		7			

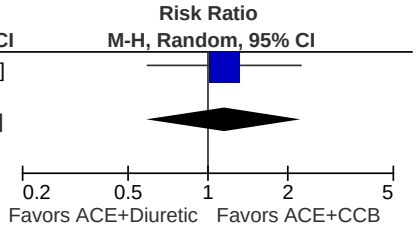
Heterogeneity: Not applicable
Test for overall effect: Z = 0.32 (P = 0.75)



Composite renal outcome A (See Table C38 for definition)

Study or Subgroup	ACE+Diuretic Events	ACE+Diuretic Total	ACE+CCB Events	ACE+CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Bakris 2010	17	309	16	335	100.0%	1.15 [0.59, 2.24]
Total (95% CI)		**309**		**335**	**100.0%**	**1.15 [0.59, 2.24]**
Total events	17		16			

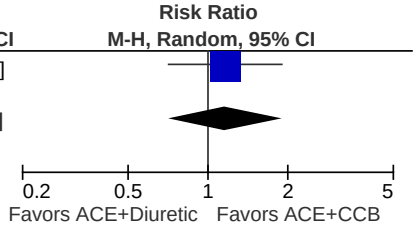
Heterogeneity: Not applicable
Test for overall effect: Z = 0.42 (P = 0.68)



Composite renal outcome B (See Table C38 for definition)

Study or Subgroup	ACE+Diuretic Events	ACE+Diuretic Total	ACE+CCB Events	ACE+CCB Total	Weight	Risk Ratio M-H, Random, 95% CI
Bakris 2010	30	309	28	335	100.0%	1.16 [0.71, 1.90]
Total (95% CI)		**309**		**335**	**100.0%**	**1.16 [0.71, 1.90]**
Total events	30		28			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)



Appendix Table C39. Study withdrawals and adverse events (outcomes part D), ACEI plus diuretic versus ACEI plus CCB trials

Study	Any Study Withdrawals, n/N (%)		Withdrawals Due to Serious Adverse Events, n/N (%)		Serious Adverse Events, n/N (%)		Adverse Events, Any, n/N (%)		‡Adverse Events, Specific, n/N (%)		Renal Adverse Events, n/N (%)	
	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB	ACEI + Diuretic	ACEI + CCB
Bakris, 2008[47]	*NR	*NR	†NR	†NR					Edema: 12/166 (7.2); Cough: 17/166 (10.2); Dizzy: 11/166 (6.6)	Edema: 29/166 (17.5); Cough: 23/166 (13.9); Dizzy: 15/166 (9.0)		
Bakris, 2010[48]									Edema: 85/532 (16.0) Dizzy: 129/532 (24.2 Cough: 93/532 (17.5) Hypotension: 29/532 (5.5) Hyperk: 1/532 (0.2)	Edema: 189/561 (33.7) Dizzy: 141/561 (25.1)) Cough: 120/561 (21.4) Hypotension: 24/561 (4.3) Hyperk: 0/561 (0.0)		

ACEI = angiotensin converting enzyme inhibitor; CCB = calcium channel blocker

*Study reported 215/453 (47%) withdrawals after randomization overall, including 144/453 (32%) during dose titration period who were considered to be either nonresponders to treatment or had complained of side effects (treatment group not reported) and 71/309 (23%) during study period (36/166 [21.7%] in ACEI + Diuretic group and 26/166 [15.7%] in ACEI + CCB group).

†Study reported adverse event reasons for study medication discontinuations due to adverse events (18/166 [10.8%] for ACEI + Diuretic group and 9/166 [5.4%] for ACEI + CCB group), but did not report serious adverse events or discontinuations due to serious adverse events.

‡Study reported additional side effects by treatment group, including: fatigue (13/166 [7.8%] in each treatment group); headache (16/166 [9.6%] in ACEI + Diuretic group and 14/166 [8.4%] in ACEI + CCB group).

Appendix Table C40. Overview of ACEI plus diuretic versus ACEI monotherapy trial

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (Expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Mogensen, 2003[50] Country Multinational Funding Source: Industry	Inclusion: ages 40 to 75 years; type 2 diabetes; hypertension (SBP ≥140 mmHg but < 180 mmHg; DBP <110 mmHg); urinary albumin excretion rate ≥20 µg/min but <500 µg/min in at least 2 of 3 assays Exclusion: HbA1c ≥9% within 3 months before study; presumed nondiabetic kidney disease; serum creatinine ≥140 µmol/L (=1.58 mg/dL); known contraindication to ACEI or indapamide; other severe disease.	N=481 (baseline results reported for n=457 [n=233 perindopril/indapamide; n=224 enalapril] with albuminuria at baseline, who took at least one dose of treatment, and had albuminuria measured at least once under treatment) Age (yr): 58.9 Gender (Male %): 61.3 Race/Ethnicity (%): 91.0 white, 4.4 black, 0.7 Asian, 3.7 other Weight: 82.5 kg BMI: 30 Systolic BP (mm Hg): 158.4 Diastolic BP (mm Hg): 93.3 CKD stage: NR Serum creatinine (µmol/L): NR Creatinine clearance (mL/min): NR Albuminuria (µg/min): 82.1 Albumin/Creatinine ratio (mg/mmol): 8.5 HbA_{1c} (%): 7.2 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	n=244 Initiated with combination of 2 mg perindopril/0.625 mg indapamide once daily, titrated to maximum of 8 mg perindopril/2.5 mg indapamide for BP target.* n= 237 Initiated with 10 mg enalapril, titrated to maximum of 40 mg enalapril for BP target* Nonstudy antihypertensive drugs were not allowed. Diabetic management left to discretion of investigator. Followup period: mean 10.7 months Study withdrawals (%): Text says 20% did not complete the study, but list of reasons for early withdrawal add to 50/244 (20.5%) for perindopril and 60/237 (25.3%) for enalapril (110/481=22.9% overall) *Dose adjustment (doubling) allowed at weeks 12, 24, or 36 if SBP ≥140 mm Hg or DBP ≥90 mm Hg based on BP permitted after week 12 (doubling of ddosage in 2 steps at 12 week intervals if SBP ≥ 140 mmHg or DBP ≥90 mmHg	Allocation Concealment: Unclear Blinding: Double Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: No

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C41. Clinical outcomes (outcomes part B), ACEI plus diuretic versus ACEI monotherapy trial

Study	Stroke, Nonfatal n/N (%)		Stroke, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) n/N (%)		Composite Vascular Outcome n/N (%)*	
	ACEI + Diuretic	ACEI	ACEI + Diuretic	ACEI	ACEI + Diuretic	ACEI	ACEI + Diuretic	ACEI	ACEI + Diuretic	ACEI
Mogensen, 2003[50]									6/244 (2.5)	15/237 (6.3)

ACEI = angiotensin converting enzyme inhibitor; CHF = congestive heart failure
*See Composite vascular outcome definitions table

Appendix Table C42. Composite vascular outcome definitions, ACEI plus diuretic versus ACEI monotherapy trial

Study	Definition
Mogensen, 2003[50]	"Serious cardiovascular events," with serious defined as "fatal or requiring prolonged hospitalization" and cardiovascular events defined according to ICD9-1975 revision, codes 7981 (sudden death) and 390-448 (rheumatic fever with or without acute or chronic heart involvement, diseases of cardiac valves, essential hypertension, hypertensive heart or renal disease, MI, angina, chronic ischemic heart disease, cardiac aneurysm, pulmonary artery disease, pericarditis, endocarditis, myocarditis, cardiomyopathy, heart conduction disorders/dysrhythmias, heart failure, stroke, atherosclerosis, aortic aneurysm disease, peripheral arterial disease, arterial embolism/thrombosis, other disorders or the arteries/arterioles/capillaries)

ACEI = angiotensin converting enzyme; MI = myocardial infarction

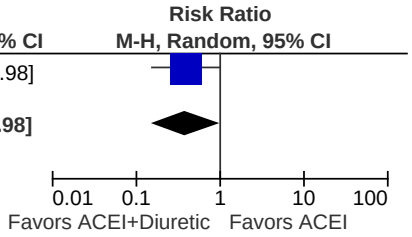
Appendix Figure C10. Forest plot for ACEI plus diuretic versus ACEI monotherapy trial

Composite vascular outcome (see Table C42 for definition)

Study or Subgroup	ACEI+Diuretic Events	ACEI+Diuretic Total	ACEI Events	ACEI Total	Weight	Risk Ratio M-H, Random, 95% CI
Mogensen 2003	6	244	15	237	100.0%	0.39 [0.15, 0.98]
Total (95% CI)		**244**		**237**	**100.0%**	**0.39 [0.15, 0.98]**
Total events	6		15			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.99 (P = 0.05)



Appendix Table C43. Study withdrawals and adverse events (outcomes part D), ACEI plus diuretic versus ACEI monotherapy trial

Study	Any Study Withdrawals, n/N (%)		Withdrawals Due to Serious Adverse Event, n/N (%)		Serious Adverse Event: Any, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event, Specific, n/N (%)		Renal Adverse Event, n/N (%)	
	ACEI + Diuretic	ACEI	ACEI + Diuretic	ACEI	ACEI + Diuretic	ACEI	ACEI + Diuretic	ACEI	ACEI + Diuretic	ACEI	ACEI + Diuretic	ACEI
Mogensen, 2003[50]	*50/244 (20.5)	*60/237 (25.3%)	†NR	†NR			‡NR	‡NR	HyperK: 8/244 (3.3); Cough: 9/244 (3.7)	HyperK: 13/237 (5.5); Cough: 5/237 (2.1)		

ACEI = angiotensin converting enzyme inhibitor; HyperK = hyperkalemia

* Study also reported that one patient was lost to follow-up, but didn't indicate the patient's treatment group assignment.

† Study reported withdrawal due to adverse events by treatment group, 19/244 (7.8%) for ACEI + diuretic group and 21/237 (8.8%) for ACEI group, but did not report serious adverse events or withdrawals due to serious adverse events.

‡ Study did not report adverse events overall or by treatment group, but only reported results for participants with adverse events related to drug treatment: ACEI + diuretic group 34/244 (13.9%) and ACEI group 35/237 (14.8%).

Appendix Evidence Table C44. Overview of ACEI plus diuretic versus placebo trial

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (Expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Lambers Heerspink 2010[51] ADVANCE Management Committee 2001[52] Country Multinational Funding Source: Industry and Government	Inclusion: age 55 years or older, diagnosed with type 2 diabetes at age 30 or older, evidence of elevated risk of cardiovascular disease (age 65 or older, diabetes diagnosed ≥ 10 years prior to entry, history of stroke or MI, hospital admission for TIA or unstable angina, coronary or peripheral revascularization, amputation secondary to vascular disease, macroalbuminuria, proliferative retinopathy or retinal photocoagulation therapy, macular edema, blindness in one eye related to diabetes, other major risk factor [current smoking, total cholesterosl >6.0 mmol/l, HDL <1.0 mmol/l, or microalbuminuria]) Exclusion: definite indication for long-term insulin therapy	N=10,640 (baseline results below are for n=2,482 with CKD stage 1 or 2 and 2,044 with CKD stage 3) Age (yr): 66.59 Gender (Male %): 52.6 Race/Ethnicity (%): NR Weight: NR BMI: 28.4 Systolic BP (mm Hg): 147.6 Diastolic BP (mm Hg): 81.0 CKD stage: subgroup analysis for CKD stages 1-3 Serum creatinine (μmol/L): NR Creatinine clearance (mL/min): NR eGFR (mL/min): 70.7 Albuminuria (μg/min): NR Albumin/Creatinine ratio (μg/mg, median): 48.1 HbA_{1c} (%): 7.7 Total cholesterol (mg/dL): NR LDL cholesterol (mmol/L): 3.2 Diabetes (%): 100 History of HTN (%): 74.6 (currently treated) Dyslipidemia (%): NR History of CAD (%): 34.7 (major macrovascular disease) History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): 12.8 History of Stroke (%): 10.8 Current smoker (%): NR History of AKI (%): NR	All subjects – 6 week run-in with 2 mg perindopril and 0.625 mg indapamide Those who were tolerant randomized to same dose or placebo; doses doubled after 3 months to 4 mg perindopril and 1.25 mg indapamide Comcomitant treatment at descretion of provider except that open-label perindopril to max of 4 mg/day was only ACEI allowed and thiazide (-like) diuretics were not permitted Followup period: mean 4.3 years Study withdrawals (%): NA	Allocation Concealment: Adequate Blinding: Double Intention to Treat Analysis (ITT): NA-subgroup analysis Withdrawals/Dropouts adequately described: NA-subgroup analysis

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HDL=high density lipoprotein cholesterol; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; TIA=transient ischemic attack; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C45. Clinical outcomes (outcomes part A), ACEI plus diuretic versus placebo trial

Study	All-Cause Mortality, n/N (%)		Cardiovascular Mortality, n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Nonfatal n/N (%)		Stroke, Any, n/N (%)	
	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo
Lambers Heerspink, 2010[51]	CKD 1,2 9.2% CKD ≥3 11.6%	CKD 1,2 10.1% CKD ≥3 13.2%	CKD 1,2 4.9% CKD ≥3 6.5%	CKD 1,2 6.4% CKD ≥3 8.0%	CKD 1,2 5.6% CKD ≥3 7.3%	CKD 1,2 6.2% CKD ≥3 8.4%					CKD 1,2 4.5% CKD ≥3 5.0%	CKD 1,2 5.1% CKD ≥3 5.9%

Appendix Table C46. Clinical outcomes (outcomes part B), ACEI plus diuretic versus placebo trial

Study	Stroke, Nonfatal n/N (%)		Stroke, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) n/N (%)		Composite Vascular Outcome n/N (%)*	
	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo
Lambers Heerspink, 2010[51]									CKD 1,2 10.3% CKD ≥3 12.4	CKD 1,2 11.4 CKD ≥3 14.0

ACEI = angiotensin converting enzyme inhibitor; CHF = congestive heart failure
*See Composite vascular outcome definitions table

Appendix Table C47. Composite vascular outcome definition, ACEI plus diuretic versus placebo trial

Study	Definition
Lambers Heerspink 2010[51]	Cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke

ACEI = angiotensin converting enzyme inhibitor

Appendix Table C48. Clinical outcomes (outcomes part C), ACEI plus diuretic versus placebo trial

Study	End-Stage Renal Disease, n/N (%)		Doubling of Serum Creatinine, n/N (%)		Halving of GFR, n/N (%)		Progression from Micro- to Macroalbuminuria, n/N (%)		Composite Renal Outcome, n/N (%)*	
	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo
Lambers Heerspink, 2010[51]									CKD 1,2 6.1% CKD ≥3 6.3%	CKD 1,2 8.5% CKD ≥3 6.7%

ACEI = angiotensin converting enzyme inhibitor; CHF = congestive heart failure
*See Composite renal outcome definitions table

Appendix Table C49. Composite renal outcome definitions, ACEI plus diuretic versus placebo trial

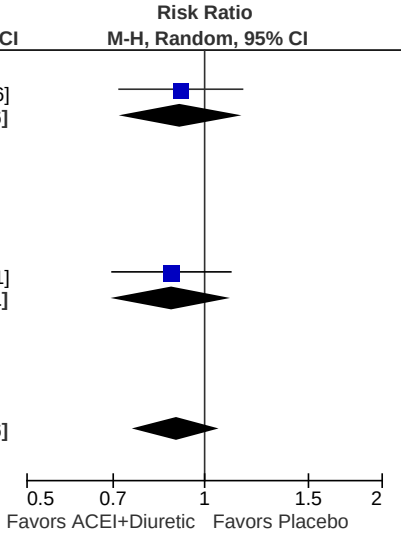
Study	Definition
Lambers Heerspink 2010[51]	Development of macroalbuminuria, doubling of serum creatinine to a level of at least 2.26 mg/dL (200 μmol/L), need for renal replacement therapy, or death due to renal illness

ACEI = angiotensin converting enzyme inhibitor

Appendix Figure C11. Forest plots for ACEI plus diuretic versus placebo trial

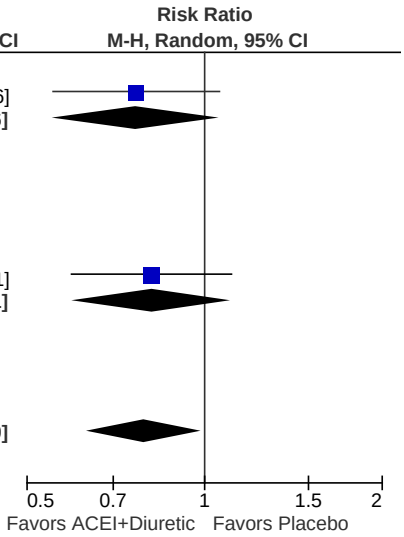
All-cause mortality

Study or Subgroup	ACEI+Diuretic Events	ACEI+Diuretic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.9.1 CKD 1 or 2						
Lambers Heerspink 2010	114	1239	126	1248	48.1%	0.91 [0.72, 1.16]
Subtotal (95% CI)		**1239**		**1248**	**48.1%**	**0.91 [0.72, 1.16]**
Total events	114		126			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.76 (P = 0.45)						
1.9.2 CKD 3+						
Lambers Heerspink 2010	117	1009	135	1023	51.9%	0.88 [0.70, 1.11]
Subtotal (95% CI)		**1009**		**1023**	**51.9%**	**0.88 [0.70, 1.11]**
Total events	117		135			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.09 (P = 0.27)						
Total (95% CI)		**2248**		**2271**	**100.0%**	**0.89 [0.76, 1.06]**
Total events	231		261			
Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = 0.83); I² = 0%						
Test for overall effect: Z = 1.31 (P = 0.19)						
Test for subgroup differences: Not applicable						



Cardiovascular mortality

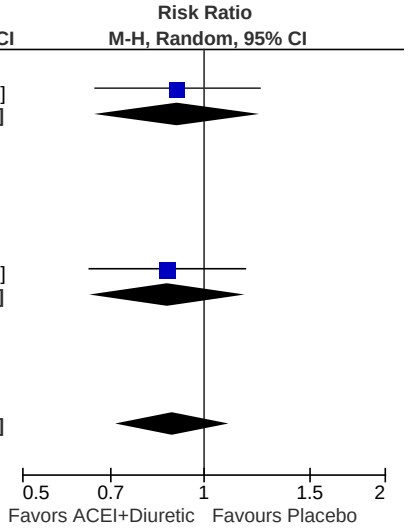
Study or Subgroup	ACEI+Diuretic Events	ACEI+Diuretic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.8.1 CKD 1 or 2						
Lambers Heerspink 2010	61	1244	79	1234	48.1%	0.77 [0.55, 1.06]
Subtotal (95% CI)		**1244**		**1234**	**48.1%**	**0.77 [0.55, 1.06]**
Total events	61		79			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.61 (P = 0.11)						
1.8.2 CKD 3+						
Lambers Heerspink 2010	66	1015	82	1025	51.9%	0.81 [0.59, 1.11]
Subtotal (95% CI)		**1015**		**1025**	**51.9%**	**0.81 [0.59, 1.11]**
Total events	66		82			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						
Total (95% CI)		**2259**		**2259**	**100.0%**	**0.79 [0.63, 0.99]**
Total events	127		161			
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 1 (P = 0.80); I² = 0%						
Test for overall effect: Z = 2.05 (P = 0.04)						
Test for subgroup differences: Not applicable						



Appendix Figure C11. Forest plots for ACEI plus diuretic versus placebo trial (continued)

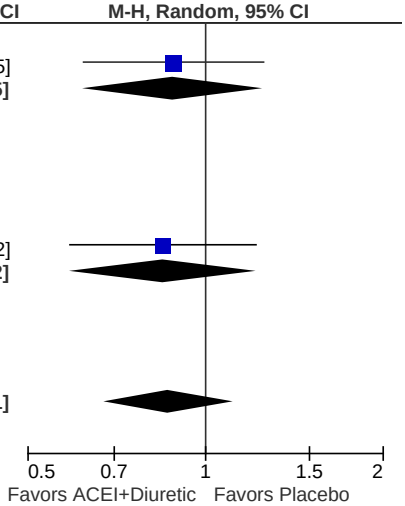
Myocardial infarction

Study or Subgroup	ACEI+Diuretic Events	ACEI+Diuretic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.10.1 CKD 1 or 2						
Lambers Heerspink 2010	69	1232	77	1242	47.3%	0.90 [0.66, 1.24]
Subtotal (95% CI)		**1232**		**1242**	**47.3%**	**0.90 [0.66, 1.24]**
Total events	69		77			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						
1.10.2 CKD 3+						
Lambers Heerspink 2010	74	1014	86	1024	52.7%	0.87 [0.64, 1.17]
Subtotal (95% CI)		**1014**		**1024**	**52.7%**	**0.87 [0.64, 1.17]**
Total events	74		86			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.92 (P = 0.36)						
Total (95% CI)		**2246**		**2266**	**100.0%**	**0.89 [0.71, 1.10]**
Total events	143		163			
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.86); I² = 0%						
Test for overall effect: Z = 1.10 (P = 0.27)						
Test for subgroup differences: Not applicable						



Stroke

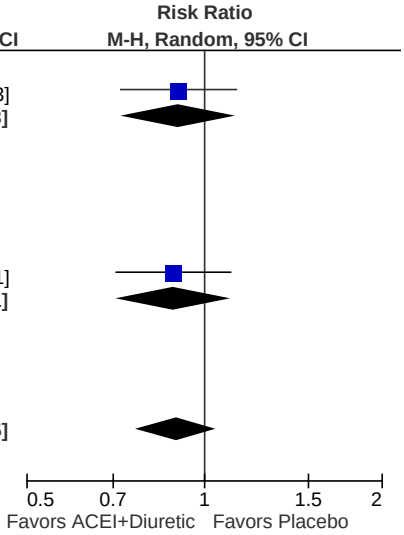
Study or Subgroup	ACEI+Diuretic Events	ACEI+Diuretic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.11.1 CKD 1 or 2						
Lambers Heerspink 2010	56	1244	63	1235	51.7%	0.88 [0.62, 1.25]
Subtotal (95% CI)		**1244**		**1235**	**51.7%**	**0.88 [0.62, 1.25]**
Total events	56		63			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.70 (P = 0.49)						
1.11.2 CKD 3+						
Lambers Heerspink 2010	51	1021	60	1017	48.3%	0.85 [0.59, 1.22]
Subtotal (95% CI)		**1021**		**1017**	**48.3%**	**0.85 [0.59, 1.22]**
Total events	51		60			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.90 (P = 0.37)						
Total (95% CI)		**2265**		**2252**	**100.0%**	**0.86 [0.67, 1.11]**
Total events	107		123			
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%						
Test for overall effect: Z = 1.13 (P = 0.26)						
Test for subgroup differences: Not applicable						



Appendix Figure C11. Forest plots for ACEI plus diuretic versus placebo trial (continued)

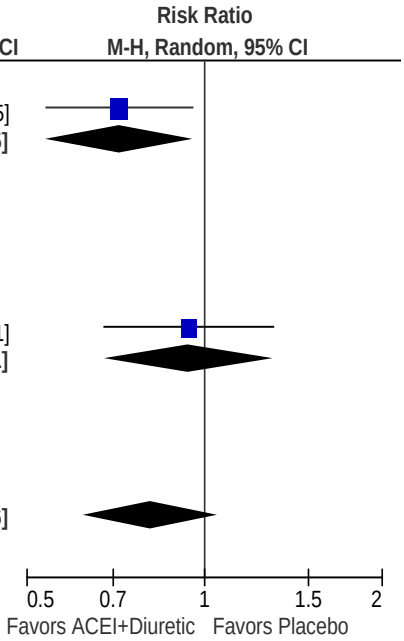
Composite vascular outcome (see Table C47 for definition)

Study or Subgroup	ACEI+Diuretic Events	ACEI+Diuretic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 CKD 1 or 2						
Lambers Heerspink 2010	128	1243	142	1246	49.5%	0.90 [0.72, 1.13]
Subtotal (95% CI)		**1243**		**1246**	**49.5%**	**0.90 [0.72, 1.13]**
Total events	128		142			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.88 (P = 0.38)						
1.7.2 CKD 3+						
Lambers Heerspink 2010	126	1016	143	1021	50.5%	0.89 [0.71, 1.11]
Subtotal (95% CI)		**1016**		**1021**	**50.5%**	**0.89 [0.71, 1.11]**
Total events	126		143			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.07 (P = 0.29)						
Total (95% CI)		**2259**		**2267**	**100.0%**	**0.89 [0.76, 1.05]**
Total events	254		285			
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0%						
Test for overall effect: Z = 1.38 (P = 0.17)						
Test for subgroup differences: Not applicable						



Composite renal outcome (see Table C49 for definition)

Study or Subgroup	ACEI+Diuretic Events	ACEI+Diuretic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.12.1 CKD 1 or 2						
Lambers Heerspink 2010	75	1230	105	1235	54.9%	0.72 [0.54, 0.95]
Subtotal (95% CI)		**1230**		**1235**	**54.9%**	**0.72 [0.54, 0.95]**
Total events	75		105			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.28 (P = 0.02)						
1.12.2 CKD 3+						
Lambers Heerspink 2010	64	1016	68	1015	45.1%	0.94 [0.68, 1.31]
Subtotal (95% CI)		**1016**		**1015**	**45.1%**	**0.94 [0.68, 1.31]**
Total events	64		68			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.37 (P = 0.71)						
Total (95% CI)		**2246**		**2250**	**100.0%**	**0.81 [0.62, 1.06]**
Total events	139		173			
Heterogeneity: Tau² = 0.01; Chi² = 1.48, df = 1 (P = 0.22); I² = 32%						
Test for overall effect: Z = 1.56 (P = 0.12)						
Test for subgroup differences: Chi² = 1.48, df = 1 (P = 0.22), I² = 32.4%						



Appendix Table C50. Study withdrawals and adverse events (outcomes part D), ACEI plus diuretic versus placebo trial

Study	Any Study Withdrawals, n/N (%)		Withdrawals Due to Serious Adverse Event, n/N (%)		Serious Adverse Event: Any, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event, Specific, n/N (%)		Renal Adverse Event, n/N (%)	
	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo	ACEI + Diuretic	Placebo
Lambers Heerspink, 2010[51]					CKD 1,2 1.4% CKD ≥3 2.2%	CKD 1,2 1.6% CKD ≥3 1.9%			Cough CKD 1,2 3.1% CKD ≥3 3.9% Hypo/Dizz CKD 1,2 0.7% CKD ≥3 1.4%	Cough CKD 1,2 1.4% CKD ≥3 1.8% Hypo/Diz z CKD 1,2 0.5% CKD ≥3 0.3%		

ACEI = angiotensin converting enzyme inhibitor, Hypo/Dizz=hypotension/dizziness; CKD = chronic kidney disease

Appendix Table C51. Overview of ARB versus ARB trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ARB versus different ARB trials				
Bakris, 2008[53] (AMADEO) Multinational (Argentina, Australia, Brazil, Canada, Mexico, New Zealand, South Korea, Taiwan, Thailand, United States) Funding Source: Industry	Inclusion: ages 21-80 years; history of type 2 diabetes mellitus; total HbA_{1c} ≤10%; serum creatinine ≤3 mg/dl (women) or ≤3.2 mg/dl (men); first-morning spot urine protein/creatinine ratio ≥700 mg/g; mean BP ≥130/80 but less than 160/110 mmHg or receiving antihypertensive(s) for hypertension Exclusion: women who were nursing, pregnant, or surgically sterile and not using effective contraception; >35% increase in serum creatinine during washout period or serum potassium level >5 mEq/l; nondiabetic renal disease; clinically significant heart disease, stroke, renal artery stenosis, hepatic dysfunction, or electrolyte imbalance; known hypersensitivity to any component of study medications; requiring chronic immunosuppressive therapy; hematuria.	N=860 Age (yr): 60.3 Gender (Male %): 62.2 Race/Ethnicity (%): 47% Caucasian, 12% black, 41% Asian, 0.1% missing Weight (kg): NR BMI: 30.0* Systolic BP (mm Hg): 143.4 Diastolic BP (mm Hg): 79.7 CKD stage: NR Serum creatinine (mg/dl): 1.55 Creatinine clearance (mL/min): NR Albuminuria (µg/min): NR Proteinuria (mg/day): NR Urine protein/creatinine ratio (m/g): 1991.2 Urine albumin/creatinine ratio (mg/g): 1393.7* Estimated GFR (ml/min/1.73m^2): 49.6 HbA_{1c} (%): 7.9* Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): 0 (clinically significant excluded) History of CHF (%): 0 (clinically significant excluded) Peripheral arterial disease (%): NR History of MI (%): 0 (clinically significant excluded) History of Stroke (%): 0 (clinically significant excluded) Current smoker (%): 15.6 History of AKI (%): NR *sample size <860 for these characteristics	n= 419 Telmisartan 40 mg/day for 2 weeks then 80 mg/day for 50 weeks* n= 441 Losartan 50 mg/day for 2 weeks then 100 mg/day for 50 weeks* Follow-up period: mean of 324.25 days (i.e. 10.7 months) Study withdrawals (%): 18.4 *Additional antihypertensive medications (except other ARBs, ACEIs, or direct vasodilators) allowed after forced titration period to reach BP target <130/80 mmHg	Allocation Concealment: Unclear Blinding: Double blind Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: No

Appendix Table C51. Overview of ARB versus ARB trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Galle, 2008[54] Multinational (11 countries in Europe, 3 countries in Asia, South Africa) Funding Source: Industry	Inclusion: ages 30-80 years; history of type 2 diabetes mellitus; overt nephropathy (serum creatinine ≤3.0 mg/dl and proteinuria ≥900 mg/24h); hypertensive (mean BP > 130/80 mm Hg or receiving antihypertensive therapy at enrollment) Exclusion: HgbA1c >10%; premenopausal women not surgically sterile or using acceptable contraception or who were pregnant or breast feeding; recent acute cardiovascular event; congestive heart failure; receipt of metformin in patients with elevated serum creatinine levels; nondiabetic renal disease; >30% increase in serum creatinine during run-in; secondary hypertension; hepatic dysfunction; biliary obstructive disorders; renal arterial stenosis; chronic immunosuppressive therapy; history of drug or alcohol dependency; SBP >180 mmHg and/or DBP >110 mmHg on two consecutive visits during run-in	N=885 Age (yr): 61.2 Gender (Male %): 64.1 Race/Ethnicity (%): 79% white, 2% black, 19% Asian Weight: NR BMI: 30.2 Systolic BP (mm Hg): 148.1 Diastolic BP (mm Hg): 82.0 CKD stage: NR Serum creatinine (mg/dl): NR Creatinine clearance (mL/min): NR Albuminuria (µg/min): NR Proteinuria (g/24h): 2.78 Albumin/Creatinine ratio (mg/mmol): NR Estimated GFR (ml/min/1.73m^2): 56.6 HbA_{1c} (%): 7.8 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): 0 Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): 18.2 History of AKI (%): NR	n= 443 Telmisartan 40 mg/day for 2 weeks then 80 mg/day for 50 weeks* n= 442 Valsartan 80 mg/day for 2 weeks then 160 mg/day for 50 weeks* Followup period: mean of 363.5 days (1 yr) Study withdrawals (%): 19.1 *Additional antihypertensive medications (except other ARBs or ACEIs) allowed if SBP/DBP >130/80	Allocation Concealment: Unclear Blinding: Double blind Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Appendix Table C51. Overview of ARB versus ARB trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ARB (higher dose) versus ARB (lower dose) trial				
Burgess, 2009[55] Canada, Multisite Funding Source: Industry	Inclusion: ages 18 to 80 years; primary glomerular disease not currently treated with any disease-specific treatment; diabetic nephropathy or hypertensive nephrosclerosis; urine protein ≥1g/d on at least 2 occasions in previous 6 months; not taking immunosuppressant drugs, corticosteroids, or nonsteroidal anti-inflammatory medications; stable hypertension (no new antihypertensive medications within 6 weeks of visit 1); if taking ACE or ARB use stable for at least 3 months before visit 1; SBP <170 and DBP <100 mm Hg with use of antihypertensive medications Exclusion: presence of known or suspected secondary hypertension including bilateral renal artery stenosis or unilateral renal artery stenosis to a solitary kidney; pregnancy; serum creatinine >300 µmol/L (=3.4 mg/dl) or eGFR <30 ml/min/1.73m^2; presence of polycystic kidney disease, systemic lupus erythematosus; polyarteritis nodosa, amyloidosis or myeloma, or serum potassium ≥ 5.5 mmol/L at baseline or on >1 occasion in 6 months before visit 1.	N=269 Age (yr): 55.3 Gender (Male %): 79.6 Race/Ethnicity (%): 83.2% white, 3.7% black, 9.3% Asian, 3.7% other Weight (kg): 91.9 BMI: 31.8 Systolic BP (mm Hg): 132.5 Diastolic BP (mm Hg): 77.4 CKD stage: NR Serum creatinine (µmol/L): 127.0 (=1.44 mg/dl) Creatinine clearance (mL/min): NR Albuminuria: NR Proteinuria (g/day): 2.83 Degree of Proteinuria: 57.3% with 1-3 g/day, 42.7% with >3 g/day Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): 52.0 HbA_{1c} (%): NR Total cholesterol: NR LDL cholesterol: NR Diabetes (%): NR History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	n= 90 Candesartan 16 mg/day* n= 90 Candesartan 64 mg/day# n= 89 Candesartan 128 mg/day## Followup period: 30 weeks Study withdrawals (%): 14 *16 mg/day was highest approved antihypertensive dosage of candesartan in Canada at the time the study was initiated #dose titrated from 16 mg/day over 4 weeks ##dose titrated from 16 mg/day over 6 weeks	Allocation Concealment: Adequate Blinding: Double blind Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Appendix Table C51. Overview of ARB versus ARB trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Makino, 2007[37] Location Japan Funding Source NR	Inclusion Criteria: Age 30 to 74, type 2 DM and urinary albumin-to-creatinine ratio 100-300 mg/g, serum creatinine <1.5 mg/dl (men) and <1.3 mg/dl (women). Exclusion Criteria: DM type 1, age of diabetes onset <30 years, seated systolic blood pressure (SBP)/diastolic blood pressure (DBP) >180/100 mmHg, and definable chronic kidney disease other than diabetic nephropathy	N=527 Age (yr): 61.7 Gender (Male %): NR Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 137 Diastolic BP (mm Hg): 77 Albuminuria: NR, see Inc. criteria Serum creatinine (mg/dL): NR, see Inc. criteria Estimated GFR (ml/min/1.73m2): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): NR History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	n= 172 to Telmisartan 40mg/day n= 168 to Telmisartan 80mg/day (plus n= 174 to placebo) period: median 1.3 +/- 0.5 years Study withdrawals (%): 2.4 % excluded from primary analysis due to suspected type 1 DM or for missing UACR measurements	Allocation Concealment Unclear Blinding: Double blinded Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes

Appendix Table C51. Overview of ARB versus ARB trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Parving, 2001[39] IRMA-2 Location: 96 centers worldwide Funding Source Industry	Inclusion Criteria: HTN, age 30 to 70, type 2 DM, persistent microalbuminuria (UAER 20 to 200 µg/min in 2 of 3 consecutive, sterile, overnight samples), serum creatinine ≤1.5 mg/dl for men and ≤1.1 mg/dl for women. Exclusion Criteria: Nondiabetic kidney disease, cancer, life-threatening disease with death expected to occur within two years, and an indication for ACEI or ARBs.	N=590 Age (yr): 58 Gender (Male %): 68.5 Race/Ethnicity (%): White: 97.3, Non-White: 2.7 BMI: 30 Systolic BP (mm Hg): 153 Diastolic BP (mm Hg): 90 Albuminuria: 55.5 µg/min Serum creatinine (mg/dL): 1.18 Estimated GFR (ml/min/1.73m2):NR Total cholesterol (mg/dL): 224 LDL cholesterol (mg/dL): 140 Diabetes (%): 100 History of HTN (%): 100 History of CAD (%): 4.5 History of CHF (%): NR History of MI (%): 3.0 History of Stroke (%): 3.1 Peripheral arterial disease (%): 5.2 Current smoker (%): 18.6	n= 194 Irbesartan 300mg n= 195 Irbesartan 150mg (plus n= 201 placebo) Followup period: median 2 years Study withdrawals (%): 13	Allocation Concealment: Not defined Blinding: Double blind Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C52. Summary of study baseline characteristics for ARB versus ARB studies

Characteristic	Mean (range unless otherwise noted)	Number of Trials Reporting
ARB versus Different ARB (n=2)		
Total number of patients evaluated	1745 (860-885)	2
Age of subjects, years	60.8 (60.3-61.2)	2
Gender, male, %	63.2 (62.2-64.1)	2
Race/ethnicity, white, %	63.2 (47-79)	2
Race/ethnicity, black, %	6.9 (2-12)	2
Body Mass Index, kg/m^2	30.1 (30.0-30.2)	2
SBP, mmHg	145.8 (143.4-148.1)	2
DBP, mmHg	80.9 (79.7-82.0)	2
Proteinuria, g/day	2.78	1
Albuminuria, mg/day or µg/min	NR	0
Serum creatinine, mg/dL	1.55	1
Creatinine clearance, $ml/min/1.73m^2$	NR	0
Estimated GFR, $ml/min/1.73m^2$	53.2 (49.6 to 56.6)	2
History of diabetes mellitus, %	100 (both 100)	2
HbA_{1c}, %	7.85 (7.8 to 7.9)	2
History of hypertension, %	100 (both 100)	2
Coronary artery disease, %	0	1
Congestive heart failure, %	0 (both 0)	2
Myocardial infarction, %	0	1
Stroke, **%**	0	1
Current smoker, **%**	16.9 (15.6 to 18.2)	2

ARB = angiotensin receptor blocker, SBP = systolic blood pressure; DBP = diastolic blood pressure; GFR = glomerular filtration rate

Appendix Table C53. Clinical outcomes (outcomes part A), ARB versus ARB trials

Study	All-Cause Mortality, n/N (%)		Cardiovascular Mortality, n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Nonfatal n/N (%)		Stroke, Any, n/N (%)	
	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control
Bakris, 2008[53]	TEL: 2/419 (0.5)*	LOS: 13/441 (2.9)										
Galle, 2008[54]	TEL: 15/428 (3.5)	VAL: 8/429 (1.9)	TEL: 8/428 (1.9)	VAL: 6/429 (1.4)	TEL: 4/428 (0.9)	VAL: 11/429 (2.6)					TEL: 11/428 (2.6)	VAL: 5/429 (1.2)
Burgess, 2009[55]	CAN 64mg/d: 0/90; CAN 128mg/d: 0/89	CAN 16mg/d: 0/90	CAN 64mg/d: 0/90; CAN 128mg/d: 0/89	CAN 16mg/d: 0/90			CAN 64mg/d: 0/90; CAN 128mg/d: 0/89	CAN 16mg/d: 0/90				
Makino, 2007[37]												
Parving, 2001[39] IRMA-2	IRB 300mg 3/194 (1.5)	IRB 150mg 0/195										

ARB = angiotensin receptor blocker; TEL = telmisartan; LOS = losartan; VAL = valsartan; CAN = candesartan; IRB = irbesartan

Appendix Table C54. Clinical outcomes (outcomes part B), ARB versus ARB trials

Study	Stroke, Nonfatal, n/N (%)		Stroke, Fatal, n/N (%)		CHF, Any, n/N (%)		CHF Hospitalization (A) or Death (B), n/N (%)		Composite Vascular Outcome, n/N (%)*	
	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control
Bakris, 2008[53]									TEL: 21/419 (5.0)	LOS: 37/441 (8.4)
Galle, 2008[54]							(A)7/428 (1.6)	(A)6/442 (1.4)	TEL: 31/428 (7.2)	VAL: 33/429 (7.7)
Burgess 2009[55]			CAN 64mg/d: 0/90; CAN 128mg/d: 0/89	CAN 16mg/d: 0/90			(B) CAN 64mg/d: 0/90; CAN 128mg/d: 0/89	(B) CAN 16mg/d: 0/90		
Makino, 2007[37]										
Parving, 2001[39] IRMA-2										

ARB = angiotensin receptor blocker; CHF = congestive heart failure; TEL = telmisartan; LOS = losartan; VAL = valsartan
*See Composite vascular outcome definitions table

Appendix Table C55. Composite vascular outcome definitions, ARB versus ARB trials

Study	Definition
Bakris, 2008[47] Ref #49	Cardiovascular morbidity (not defined) or mortality
Galle, 2008[54]	Myocardial infarction, stroke, or hospitalization for heart failure or unstable angina, coronary or peripheral revascularization

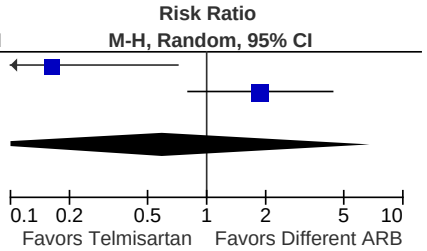
ARB = angiotensin receptor blocker

Appendix Figure C12. Forest plots for ARB versus different ARB trials

All cause mortality

Study or Subgroup	Telmisartan Events	Telmisartan Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Bakris 2008 Amadeo	2	419	13	441	46.9%	0.16 [0.04, 0.71]
Galle 2008	15	428	8	429	53.1%	1.88 [0.81, 4.39]
Total (95% CI)		**847**		**870**	**100.0%**	**0.59 [0.05, 6.88]**
Total events	17		21			

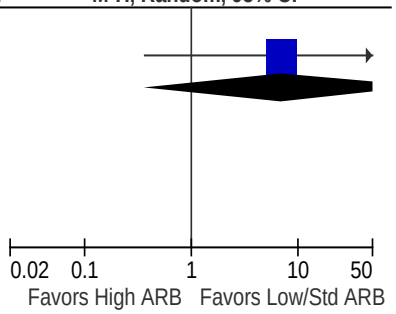
Heterogeneity: Tau² = 2.75; Chi² = 8.25, df = 1 (P = 0.004); I² = 88%
Test for overall effect: Z = 0.42 (P = 0.68)



All cause mortality (high dose versus low or standard dose)

Study or Subgroup	High ARB Events	High ARB Total	Low/Std ARB Events	Low/Std ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
27.2.1 Irbesartan 300 mg versus irbesartan 150 mg						
Parving (IRMA-2) 2001	3	194	0	195	100.0%	7.04 [0.37, 135.31]
Subtotal (95% CI)		**194**		**195**	**100.0%**	**7.04 [0.37, 135.31]**
Total events	3		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.29 (P = 0.20)

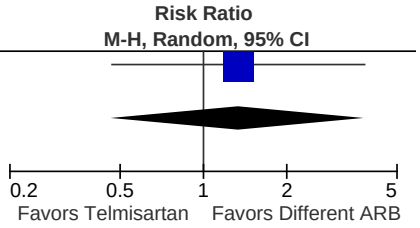


Test for subgroup differences: Not applicable

Cardiovascular mortality

Study or Subgroup	Telmisartan Events	Telmisartan Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Galle 2008	8	428	6	429	100.0%	1.34 [0.47, 3.82]
Total (95% CI)		**428**		**429**	**100.0%**	**1.34 [0.47, 3.82]**
Total events	8		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)

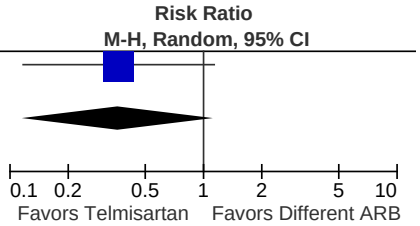


Appendix Figure C12. Forest plots for ARB versus different ARB trials (continued)

Myocardial infarction

Study or Subgroup	Telmisartan Events	Telmisartan Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Galle 2008	4	428	11	429	100.0%	0.36 [0.12, 1.14]
Total (95% CI)		**428**		**429**	**100.0%**	**0.36 [0.12, 1.14]**
Total events	4		11			

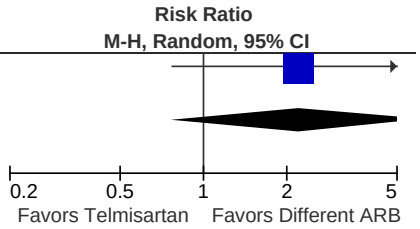
Heterogeneity: Not applicable
Test for overall effect: Z = 1.74 (P = 0.08)



Stroke

Study or Subgroup	Telmisartan Events	Telmisartan Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Galle 2008	11	428	5	429	100.0%	2.21 [0.77, 6.29]
Total (95% CI)		**428**		**429**	**100.0%**	**2.21 [0.77, 6.29]**
Total events	11		5			

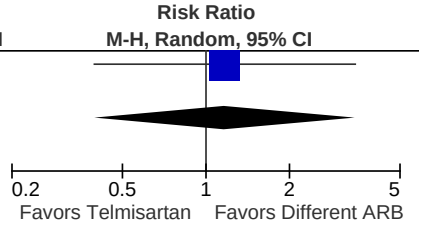
Heterogeneity: Not applicable
Test for overall effect: Z = 1.48 (P = 0.14)



Congestive heart failure, hospitalization

Study or Subgroup	Telmisartan Events	Telmisartan Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Galle 2008	7	428	6	429	100.0%	1.17 [0.40, 3.45]
Total (95% CI)		**428**		**429**	**100.0%**	**1.17 [0.40, 3.45]**
Total events	7		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.28 (P = 0.78)

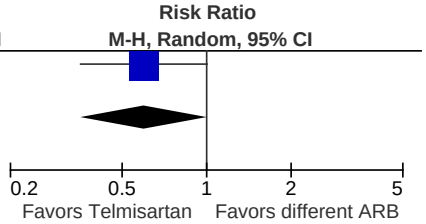


Appendix Figure C12. Forest plots for ARB versus different ARB trials (continued)

Composite vascular (outcome (see Table C55 for definition)

Study or Subgroup	Telmisartan Events	Telmisartan Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Bakris 2008 Amadeo	21	419	37	441	100.0%	0.60 [0.36, 1.00]
Total (95% CI)		**419**		**441**	**100.0%**	**0.60 [0.36, 1.00]**
Total events	21		37			

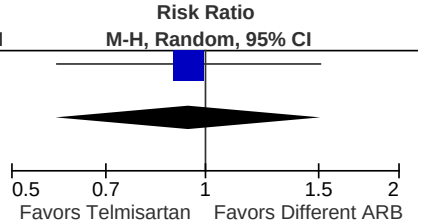
Heterogeneity: Not applicable
Test for overall effect: Z = 1.95 (P = 0.05)



Composite vascular outcome (see Table C55 for definition)

Study or Subgroup	Telmisartan Events	Telmisartan Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Galle 2008	31	428	33	429	100.0%	0.94 [0.59, 1.51]
Total (95% CI)		**428**		**429**	**100.0%**	**0.94 [0.59, 1.51]**
Total events	31		33			

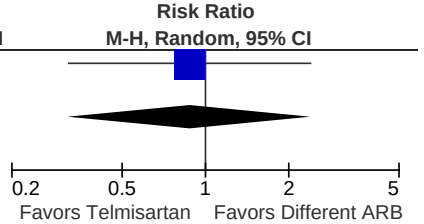
Heterogeneity: Not applicable
Test for overall effect: Z = 0.25 (P = 0.80)



End-stage renal disease

Study or Subgroup	Telmisartan Events	Telmisartan Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Galle 2008	7	428	8	429	100.0%	0.88 [0.32, 2.40]
Total (95% CI)		**428**		**429**	**100.0%**	**0.88 [0.32, 2.40]**
Total events	7		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.26 (P = 0.80)



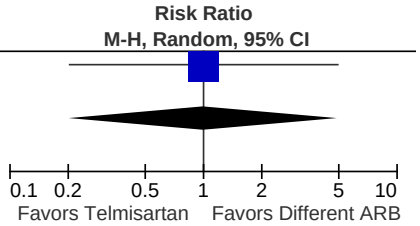
Appendix Figure C12. Forest plots for ARB versus different ARB trials (continued)

Doubling of serum creatinine

Study or Subgroup	Telmisartan Events	Telmisartan Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Galle 2008	3	428	3	429	100.0%	1.00 [0.20, 4.94]
Total (95% CI)		**428**		**429**	**100.0%**	**1.00 [0.20, 4.94]**
Total events	3		3			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)



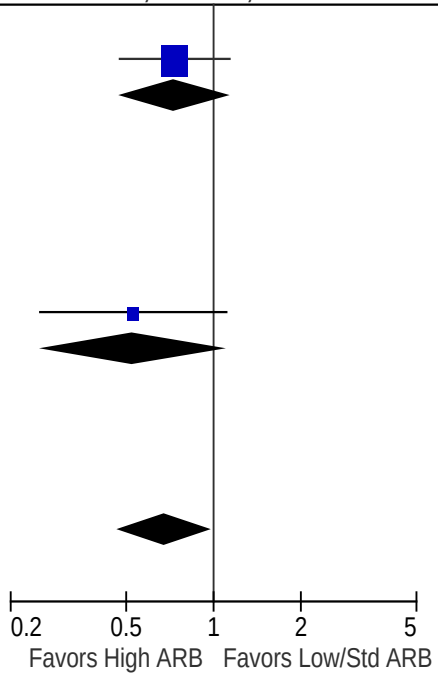
Progression from microalbuminuria to macroalbuminuria

Study or Subgroup	High ARB Events	High ARB Total	Low/Std ARB Events	Low/Std ARB Total	Weight	Risk Ratio M-H, Random, 95% CI
27.1.1 Telmisartan 80 mg versus telmisartan 40 mg						
Makino 2007	28	168	39	172	74.2%	0.74 [0.48, 1.14]
Subtotal (95% CI)		**168**		**172**	**74.2%**	**0.74 [0.48, 1.14]**
Total events	28		39			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.38 (P = 0.17)						
27.1.2 Irbesartan 300 mg versus irbesartan 150 mg						
Parving (IRMA-2) 2001	10	194	19	195	25.8%	0.53 [0.25, 1.11]
Subtotal (95% CI)		**194**		**195**	**25.8%**	**0.53 [0.25, 1.11]**
Total events	10		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.69 (P = 0.09)						
Total (95% CI)		**362**		**367**	**100.0%**	**0.68 [0.46, 0.98]**
Total events	38		58			

Heterogeneity: Tau² = 0.00; Chi² = 0.57, df = 1 (P = 0.45); I² = 0%

Test for overall effect: Z = 2.05 (P = 0.04)

Test for subgroup differences: Chi² = 0.56, df = 1 (P = 0.45), I² = 0%



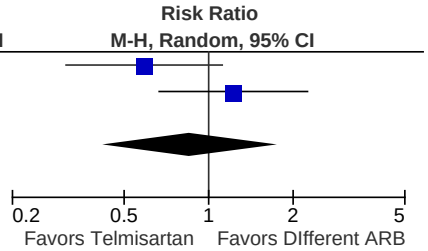
Appendix Figure C12. Forest plots for ARB versus different ARB trials (continued)

Composite renal outcome (see Table C57 for definition)

Study or Subgroup	Telmisartan Events	Telmisartan Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Bakris 2008 Amadeo	14	419	25	441	49.0%	0.59 [0.31, 1.12]
Galle 2008	22	428	18	429	51.0%	1.23 [0.67, 2.25]
Total (95% CI)		**847**		**870**	**100.0%**	**0.86 [0.42, 1.75]**
Total events	36		43			

Heterogeneity: Tau² = 0.17; Chi² = 2.64, df = 1 (P = 0.10); I² = 62%

Test for overall effect: Z = 0.43 (P = 0.67)



Appendix Table C56. Clinical renal outcomes (outcomes part C), ARB versus ARB trials

Study	End-Stage Renal Disease, n/N (%)		Doubling of Serum Creatinine, n/N (%)		Halving of GFR, n/N (%)		Progression from Micro- to Macroalbuminuria, n/N (%)		Composite Renal Outcome, n/N (%)*	
	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control
Bakris, 2008[53]									TEL: 14/419 (3.3)	LOS: 25/441 (5.7)
Galle, 2008[54]	TEL: 7/428 (1.6)	VAL: 8/429 (1.9)	TEL: 3/428 (0.7)	VAL: 3/429 (0.7)					TEL: 22/428 (5.1)	VAL: 18/429 (4.2)
Burgess, 2009[55]										
Makino, 2007[37]							TEL 80 mg 28/168 (16.7)*	TEL 40 mg 39/172 (22.6)*		
Parving, 2001[39] IRMA-2							IRB 300mg 10/194 (5.2)*	IRB 150mg 19/195 (9.7)		

ARB = angiotensin receptor blocker; GFR = glomerular filtration rate; TEL = telmisartan; LOS = losartan; VAL = valsartan; CAN = candesartan; IRB = irbesartan
*See Composite renal outcome definitions table

Appendix Table C57. Composite renal outcome definitions, ARB versus ARB trials

Study	Definition
Bakris, 2008[53]	Doubling of serum creatinine concentration, end-stage renal disease (need for long-term dialysis, renal transplantation, or serum creatinine ≥6 mg/dl), or death.
Galle, 2008[54]	Doubling of serum creatinine, end-stage renal disease (need for long-term dialysis, renal transplantation, or serum creatinine ≥6 mg/dl), and all-cause death

ARB = angiotensin receptor blocker

Appendix Table C58. Study withdrawals and adverse events (outcomes part D), ARB versus ARB trials

Study	Any Study Withdrawals, n/N (%)		Serious Adverse Events, Any, n/N (%)		Withdrawals Due to Serious Adverse Events, n/N (%)		Adverse Event, Any, n/N (%)		Adverse Event, Specific, n/N (%)		Renal AE	
	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control	Interven-tion	Control
Bakris, 2008[53]	TEL: 74/419 (17.7)	LOS: 99/441 (22.4)	TEL: 65/419 (15.5)	LOS: 99/441 (22.4)	TEL: 6/419 (1.4)	LOS: 6/441 (1.4)	TEL: 352/419 (84.0)	LOS: 362/441 (82.1)	*NR	*NR		
Galle, 2008[54]	TEL: 81/443 (18.3)	VAL: 88/442 (19.9)	TEL: 116/443 (26.2)	VAL: 104/442 (23.5)	TEL: 14/443 (3.2)	VAL: 9/442 (2.0)	TEL: 320/443 (72.3)	VAL: 316/442 (71.6)	TEL: HyperK: 10/443 (2.2)	VAL: HyperK: 12/429 (2.9)	TEL: "Renal & urinary disorders": 18/443 (4.0)	VAL: "Renal & urinary disorders": 17/442 (3.8)
Burgess, 2009[55]	C64: 6/90 (6.7); C128: 14/89 (15.7);	C16: 18/90 (20.0)	†NR	†NR	C64: 5/90 (5.5); C128: 8/89 (9.0)	C16: 11/90 (12.2)			C64: HyperK: 4/90 (4.4); C128: HyperK: 3/89 (3.3)	C16: HyperK: 4/90 (4.4)	Withdrawn for high SCr: C64: 0/90 C128: 2/89; Withdrawn for ARF: C64: 0/90 C128: 0/89	‡Withdrawn for high SCr: C16: 1/90 Withdrawn for ARF: C16: 1/90
Makino, 2007[37]	#NR	#NR					NR**	NR**				
Parving, 2001[39] IRMA-2	IRB 300mg 20/194 (10.3)	IRB 150mg 27/195 (13.8)	§ 60/389 (15.4)		IRB 300mg 8/194 (4.1)	IRB 150mg 18/195 (9.2)						

ARB = angiotensin receptor blocker; TEL = telmisartan; LOS = losartan; VAL = valsartan; IRB = irbesartan; C16 = candesartan 16mg/day; C64 = candesartan 64mg/day; C128 = candesartan 128mg/day; ARF = acute renal failure; SCr = serum creatinine; HyperK = hyperkalemia

*Study reported that 1.8% of entire cohort had hyperkalemia, but didn't report results by treatment group.

** Study reported that "one or more adverse event was recorded in >90% of patients in each treatment group;" no additional adverse events information was provided, including on specific types of adverse events.

†Study reported that 24 patients (8.9%) had one or more serious adverse event but didn't report this result by treatment group.

‡Study also reported that 1/90 patients in C16 treatment group was withdrawn after developing crescentic glomerulonephritis superimposed on pre-existing IgA nephropathy.

§ Study reported serious adverse events for the two ARB treatment dose groups combined only.

Appendix Evidence Table C59. Overview of ACEI plus aldosterone antagonist versus ACEI trial

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Mehdi, 2009[45] Location United States, Single-site Funding Source Government	Inclusion Criteria: Age 20 to 65; type 1 or 2 DM; seated systolic BP >130mmHg; proteinuria (24-h UACR≥300 mg/g despite treatment with ACEI or ARB for at least 3 months* Exclusion Criteria: BMI>45kg/m^2; serum creatinine >3.0mg/dl (females) or >4.0 mg/dl (males); known nondiabetic kidney disease; serum potassium >5.5 mEq/L; hemoglobin A1c >11%; stroke or myocardial infarction within preceding 12 months; heart failure; known adverse reaction to losartan or spironolactone; anticipated need for dialysis within 12 months *Effort was made to recruit younger patients with type 2 DM as recommended by study sponsor	N=54 Age (yr): 50.5 Gender (Male %): 46.3 Race/Ethnicity (%): 31.5% black, 53.7% Hispanic, 11.1% non-Hispanic white, 3.7% Native American Weight: NR BMI: 33 Systolic BP (mm Hg): 132 Diastolic BP (mm Hg): 73.5 CKD stage: NR Serum creatinine (mg/dL): 1.6 Creatinine clearance (mL/min): 62.2 Albuminuria: NR Urine albumin/creatinine ratio (mg/g): 1005.5 Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 7.8 Total cholesterol: 182.5 LDL cholesterol: 85 Diabetes (%): 100 History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): 0 Peripheral arterial disease (%): NR History of MI (%): NR History of MI/CABG/PTCA(%): 9.3 History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	n= 27 to Spironolactone 12.5 mg/day for 1 week then 25mg/day† n= 27 to placebo †All patients were taking Lisinopril 80 mg/day at baseline and throughout treatment Followup period: 11.1 months Study withdrawals (%): 29.6	Allocation Concealment: Unclear Blinding: Double blinded Intention to Treat Analysis (ITT): No While the overall study analysis was not by intention-to-treat, this pertains to exclusion from analyses of a single subject randomized into the ACE plus ARB treatment group that is not the focus of this section of the report. Withdrawals/ Dropouts adequately described: No

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C60. Clinical outcomes (outcomes part A), ACEI plus aldosterone antagonist versus ACEI plus placebo trial

Study	All-Cause Mortality, n/N (%)		Cardiovascular Mortality, n/N (%)		Myocardial Infarction, Any, n/N (%)		Myocardial Infarction, Fatal, n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke, Any, n/N (%)	
	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo
Mehdi, 2009[45]	0/27	0/27	0/27	0/27	1/27 (3.7)	0/27	0/27	0/27	1/27 (3.7)	0/27	2/27 (7.4)	1/27 (3.7)

ACEI = angiotensin converting enzyme inhibitor; Aldo Antag = aldosterone antagonist

Appendix Table C61. Clinical outcomes (outcome part B), ACEI plus aldosterone antagonist versus ACEI plus placebo trial

Study	Stroke, Nonfatal, n/N (%)		Stroke, Fatal, n/N (%)		CHF, Any, n/N (%)		CHF Hospitalization (A) or Death (B), n/N (%)		Composite Vascular Outcome, n/N (%)	
	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo
Mehdi, 2009[45]	2/27 (7.4)	1/27 (3.7)					(A)2/27 (7.4)	(A)0/27		

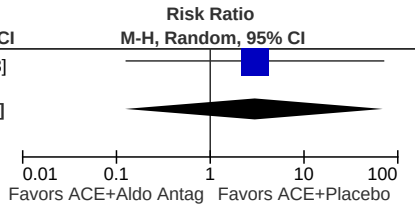
ACEI = angiotensin converting enzyme inhibitor; CHF = congestive heart failure; Aldo Antog = aldosterone antagonist

Appendix Figure C13. Forest plots for ACEI plus aldosterone antagonist versus ACEI plus placebo trial

Myocardial infarction, any

Study or Subgroup	ACE+Aldo Antag vs ACE Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Mehdi 2009	1	27	0	27	100.0%	3.00 [0.13, 70.53]
Total (95% CI)		**27**		**27**	**100.0%**	**3.00 [0.13, 70.53]**
Total events	1		0			

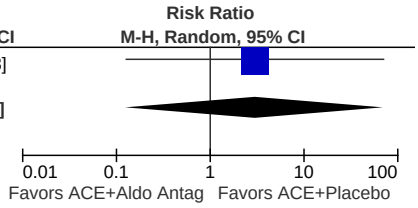
Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)



Myocardial infarction, nonfatal

Study or Subgroup	ACE+Aldo Antag vs ACE Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Mehdi 2009	1	27	0	27	100.0%	3.00 [0.13, 70.53]
Total (95% CI)		**27**		**27**	**100.0%**	**3.00 [0.13, 70.53]**
Total events	1		0			

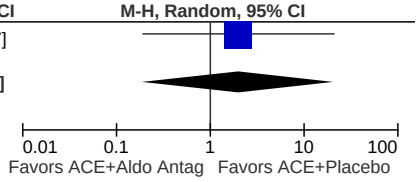
Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)



Stroke, any

Study or Subgroup	ACE+Aldo Antag vs ACE Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Mehdi 2009	2	27	1	27	100.0%	2.00 [0.19, 20.77]
Total (95% CI)		**27**		**27**	**100.0%**	**2.00 [0.19, 20.77]**
Total events	2		1			

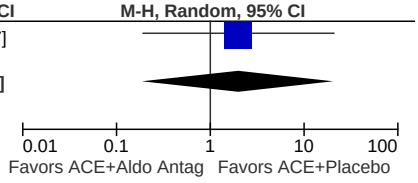
Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)



Stroke, nonfatal

Study or Subgroup	ACE+Aldo Antag vs ACE Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Mehdi 2009	2	27	1	27	100.0%	2.00 [0.19, 20.77]
Total (95% CI)		**27**		**27**	**100.0%**	**2.00 [0.19, 20.77]**
Total events	2		1			

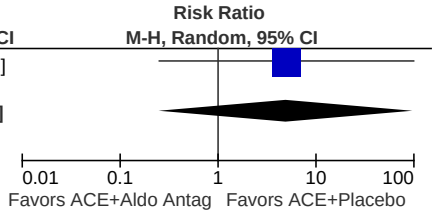
Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)



Congestive heart failure, hospitalization

Study or Subgroup	ACE+Aldo Antag Events	Total	ACE+Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Mehdi 2009	2	27	0	27	100.0%	5.00 [0.25, 99.51]
Total (95% CI)		**27**		**27**	**100.0%**	**5.00 [0.25, 99.51]**
Total events	2		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.05 (P = 0.29)



Appendix Table C62. Study withdrawals and adverse events (outcomes part D), ACEI plus aldosterone antagonist versus. ACEI plus placebo trials

Study	Any Study Withdrawals, n/N (%)		Withdrawals Due to Serious Adverse Event, n/N (%)		Serious Adverse Event: Any, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event, Specific, n/N (%)		Renal Adverse Event, n/N (%)	
	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo	ACEi + Aldo Antag	ACEI + Placebo	ACEI + Aldo Antag	ACEI + Placebo
Mehdi, 2009[45]	10/27 (37.0)	6/27 (22.2)	*NR	*NR					HyperK: 2/27 (7.4)	HyperK: 0/27		

ACEI = angiotensin converting enzyme inhibitor; HyperK = hyperkalemia; Aldo Antag = aldosterone antagonist

*Study reported withdrawals due to adverse events, but not specifically due to serious adverse events: ACEI + Aldo Antag (2 hyperkalemia, 2 stroke, 1 hypotension, 1 increased serum creatinine, 1 gynecomastia) and ACEI + placebo (1 stroke, 1 increased serum creatinine).

Appendix Evidence Table C63. Overview of ACE/ARB plus aldosterone antagonist versus ACE/ARB plus placebo trial

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
van den Meiracker, 2006[56] Location Netherlands, multiple clinic sites Funding Source None reported	Inclusion Criteria: Patients with type 2 diabetes and macroalbuminuria (24-hour urinary albumin excretion >300 mg or urinary albumin to creatinine ratio >20 mg/mmol) despite use of an ACEI inhibitor or ARB in recommended dosages for at least 1 year; ages 20 to 80 years Exclusion Criteria: Serum creatinine >265 µmol/l (i.e. >3.0 mg/dl); serum potassium >5.0 mmol/l; renal disease other than diabetic nephropathy; underlying malignant, hepatic, or gastrointestinal disease; myocardial infarction or stroke within the past 3 months; unstable angina pectoris; alcohol or drug abuse; psychological illness	N=59 Age (yr): 52.2 Gender (Male %): 66 Race/Ethnicity (%): NR Weight (kg): NR BMI: 31.0 Systolic BP (mm Hg): 147.6 Diastolic BP (mm Hg): 80.7 CKD stage: NR Serum creatinine (µmol/l): 98.2 (=1.11 mg/dl) Creatinine clearance (mL/min): NR Albuminuria (µg/min): NR Proteinuria (g/day): NR Urine Albumin/creatinine ratio (mg/mmol): 81.0 Urine Protein/creatinine ratio (mg/mmol): 128.5 estimated GFR (ml/min/1.73m^2): 70.5 (MDRD formula) HbA_{1c} (%): 8.1 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): NR Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%) NR Current smoker (%): NR History of AKI (%): NR	n=29 Spironolactone 50 mg/day* n=30 Placebo, matched tablets* Study medication added to antihypertensive medication already used by patients (71% of spironolactone group and 86% of placebo group taking an ACE inhibitor, with remainder taking an ARB) *Medication halved if potassium >5.5 mmol/l when checked 2 weeks after start; patients withdrawn if potassium >5.5 mmol/l after 2 weeks on half dose Antihypertensive medications kept constant throughout study Followup period: 1 year Study withdrawals (%): 11.9	Allocation Concealment: Adequate Blinding: Double Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C64. Clinical outcomes (outcomes part A), ACEI/ARB plus aldosterone antagonist versus ACEI/ARB plus placebo trial

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal, n/N (%)		Myocardial infarction, Nonfatal, n/N (%)		Stroke, Any n/N (%)	
	ACEI/ARB+ AA	ACEI/ ARB + PBO	ACEI/ARB + AA	ACEI/ ARB + PBO	ACEI/ARB + AA	ACEI/ARB + PBO	ACEI/ARB + AA	ACEI/ARB + PBO	ACEI/ARB + AA	ACEI/ARB + PBO	ACEI/ARB + AA	ACEI/ARB + PBO
van der Meiracker, 2006[56]	0/29	2/30 (6.7%)					0/29	2/30 (6.7%)				

ACEI/ARB = angiotensin converting enzyme inhibitor or angiotensin receptor blocker; AA = aldosterone antagonist; PBO = placebo

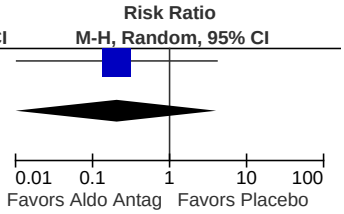
Appendix Figure C14. Forest plot for ACEI/ARB plus aldosterone antagonist versus ACEI/ARB plus placebo trial

All-cause mortality

Study or Subgroup	Aldosterone Antagonist Events	Aldosterone Antagonist Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
van der Meiracker 2006	0	29	2	30	100.0%	0.21 [0.01, 4.13]
Total (95% CI)		**29**		**30**	**100.0%**	**0.21 [0.01, 4.13]**
Total events	0		2			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.03 (P = 0.30)



Appendix Table C65. Study withdrawals and adverse events (outcomes part D), ACEI/ARB plus aldosterone antagonist versus ACEI/ARB plus placebo trial

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Event: Any, n/N (%)		Study Withdrawals Due to Serious Adverse Event: Any, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event: Specific, n/N (%)		Renal Adverse Events, n/N (%)	
	ACEI/ARB + AA	ACEI/ARB + PBO	ACEI/ARB + AA	ACEI/ARB + PBO	ACEI/ARB + AA	ACEI/ARB + PBO	ACEI/ARB + AA	ACEI/ARB + PBO	ACEI/ARB + AA	ACEI/ARB + PBO	ACEI/ARB + AA	ACEI/ARB + PBO
van der Meiracker, 2006[56]	5/29 (17.2)	2/30 (6.7)							HyperK: 5/29 (17.2)	HyperK: 1/30 (3.3)		

ACEI/ARB = angiotensin converting enzyme inhibitor or angiotensin receptor blocker; AA = aldosterone antagonist; PBO = placebo

Appendix Evidence Table C66. Overview of BB versus placebo trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Cohen-Solal, 2009[57] Flather, 2005[58] SENIORS Country Europe (11 countries) Funding Source: Private Industry	Inclusion: Men and women, age ≥70 years, clinical history of chronic heart failure with at least one of the following: a) documented hospital admission in past 12 months with discharge diagnosis of CHF or b) documented LVEF ≤35% in past 6 months Exclusion: New drug therapy for CHF in the 6 weeks prior to randomization, any change in cardiovascular drug therapy in the 2 weeks prior to randomization, heart failure due primarily to uncorrected valvular heart disease, contraindication or previous intolerance to beta-blockers, current use of beta-blockers, significant hepatic or renal dysfunction, cerebrovascular accidents within the previous 3 months, on a waiting list for percutaneous coronary intervention or cardiac surgery or other major medical conditions that may have reduced survival during the period of the study	n=704 (this is subgroup with GFR ≤55.5 ml/min/1.73m2 from larger study of 2,135 patients) Age (yr): 77.4 Gender (Male %): 59.2 Race/Ethnicity (%): NR Weight (kg): NR BMI: 26.6 Systolic BP (mm Hg): 134.0 Diastolic BP (mm Hg): 78.1 CKD stage: NR Serum creatinine (umol/L): 137.8 (=1.56 mg/dL) Creatinine clearance (mL/min): NR Albuminuria (µg/min): NR Proteinuria (mg/day): NR Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): 43.5 HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 29.4 History of HTN (%): NR Dyslipidemia (%): 46.9 (hyperlipidemia) History of CAD (%): NR History of CHF (%): 100 Peripheral arterial disease (%): NR History of MI (%): 46.4 History of Stroke (%): NR Current smoker (%): 5.4 History of AKI (%): NR	n=348 Nebivolol, 1.25 mg once daily increased to 2.5 and 5 mg every 1-2 weeks to target of 10 mg once daily over max of 16 weeks n=356 Placebo Followup period: 21 months Study withdrawals (%): Not reported for eGFR subgroups	Allocation Concealment: adequate Blinding: double blind Intention to Treat Analysis (ITT): no (7 excluded from main analysis; additional 16 excluded from sub-group analysis due to missing basline creatinine) Withdrawals/Dropouts adequately described: unclear

Appendix Evidence Table C66. Overview of BB versus placebo trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Ghal, 2009[59] MERIT-HF Country U.S., Sweden Norway, multi-site Funding Source: NA	Inclusion: Eligible patients were men and women, aged 40-80 years, supine resting heart rate ≥68/min. who had had symptomatic heart failure (New York Heart Association [NYHA] functional class II–IV) for 3 months or more before randomization and who were receiving optimum standard therapy at enrollment (2 weeks before randomization), defined as any combination of diuretics and an ACEI. If an ACEI was not tolerated, hydralazine, long-acting nitrate, or an angiotensin-II-receptor antagonist could be used. Digitalis could also be prescribed. Other inclusion criteria were a stable clinical condition during the 2-week run-in phase between enrollment and randomization, and a left-ventricular ejection fraction of 0.40 or lower within 3 months before enrollment. Patients with ejection fraction 0.36 to 0.40 included only if their maximum walking distance was 450 m or less in a 6 min walk test. Exclusion: acute myocardial infarction or unstable angina within 28 days before randomisation; indication or contraindication for treatment with B-blockade or drugs with B-blocking properties such as amiodarone; B-blockade within 6	n=1,469 (this is subgroup with GFR ≤60 ml/min/1.73m2 from larger MERIT study of 3,991 patients) Age (yr): 68.1 Gender (Male %): 68.3 Race/Ethnicity (%): NR Weight (kg): NR BMI: 26.8 Systolic BP (mm Hg): 130.3 Diastolic BP (mm Hg): 76.7 CKD stage: NR Serum creatinine (umol/L): 134.1 (=1.52 mg/dL) Creatinine clearance (mL/min): NR Albuminuria (µg/min): NR Proteinuria (mg/day): NR Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): 47.7 HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 29.3 History of HTN (%): 49.0 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): 100 Peripheral arterial disease (%): NR History of MI (%): 55.3 History of Stroke (%): NR Current smoker (%): 9.7 History of AKI (%): NR	n= 735 Metoprolol CR/XL, 12.5 mg daily for NYHA III-IV pts and 25.0 mg daily for NYHA II pts, to a targeted 200 mg daily over 8 weeks n=734 Placebo Followup period: 1 year Study withdrawals (%): Not reported for CKD subgroup	Allocation Concealment: adequate Blinding: double blind Intention to Treat Analysis (ITT): yes Withdrawals/Dropouts adequately described: unclear

Appendix Evidence Table C66. Overview of BB versus placebo trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	weeks before enrollment; heart failure secondary to systemic disease or alcohol abuse; scheduled or performed heart transplantation or cardiomyoplasty, or implanted cardioversion defibrillator (expected or performed), or procedures such as coronary-artery bypass grafting or percutaneous transluminal coronary angioplasty planned or performed in the past 4 months; atrioventricular block of the second and third degree, unless the patient had an implanted pacemaker and a spontaneous heart rate of 68 beats per min or more; unstable decompensated heart failure (pulmonary oedema, hypoperfusion) or supine systolic blood pressure lower than 100 mm Hg at enrollment; any other serious disease that might complicate management and followup according to the protocol; use of calcium antagonists such as diltiazem or verapamil; use of amiodarone within 6 months before enrollment; or poor compliance, defined as more than a 25% deviation of the number of observed compared with number of expected consumed placebo tablets during the run-in period.			

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR =

glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C67. Clinical outcomes (outcomes part A), BB versus placebo trials

Study	All-Cause Mortality, n/N (%)		Cardiovascular Mortality, n/N (%)		Myocardial Infarction, Any, n/N (%)		Myocardial Infarction, Fatal, n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke, Any, n/N (%)	
	BB	Placebo	BB	Placebo	BB	Placebo	BB	Placebo	BB	Placebo	BB	Placebo
Cohen-Solal, 2009[57]	71/348 (20.4)	92/356 (25.8)	49/348 (14.1)	67/356 (18.8)								
Ghali, 2009[59]	63/735 (8.6)	105/734 (14.3)										

BB = beta blocker

Appendix Table C68. Clinical outcomes (outcomes part B), BB versus placebo trials

Study	Stroke, Nonfatal, n/N (%)		Stroke, Fatal, n/N (%)		CHF, Any, n/N (%)		CHF Hospitalization (A) or Death (B), n/N (%)		Composite Vascular Outcome, n/N (%)*	
	BB	Placebo	BB	Placebo	BB	Placebo	BB	Placebo	BB	Placebo
Cohen-Solal, 2009[57]									129/348 (37.1)	153/356 (43.0)
Ghali, 2009[59]							(A)90/735 (12.2); (B)15/735 (2.0)	(A)147/734 (20.0); (B)36/734 (4.9)	(A)136/735 (18.5); (B)64/735 (8.7)	(A)214/734 (29.2); (B)107/734 (14.6)

CHF = congestive heart failure; BB = beta blocker
*See Composite vascular outcome definitions table

Appendix Table C69. Composite vascular outcome definitions, BB versus placebo trials

Study	Definition
Cohen-Solal, 2009[57]	All-cause mortality or cardiovascular hospital admission (time to first event)
Ghali. 2009[59]	Study defined multiple composite vascular outcomes, including: (A) all-cause mortality and CHF hospitalization;and (B) cardiac death and nonfatal MI.

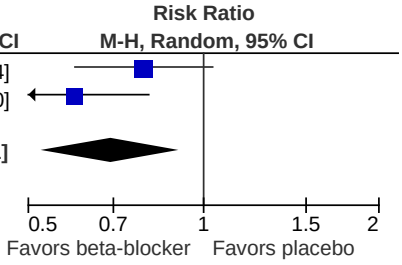
BB = beta blocker; CHF = congestive heart failure; MI = myocardial infarction

Appendix Figure C15. Forest plots for BB versus placebo trials

All-cause mortality

Study or Subgroup	Beta-blocker Events	Beta-blocker Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Cohen-Solal 2009	71	348	92	356	52.2%	0.79 [0.60, 1.04]
Ghali 2009	63	735	105	734	47.8%	0.60 [0.45, 0.80]
Total (95% CI)		**1083**		**1090**	**100.0%**	**0.69 [0.53, 0.91]**
Total events	134		197			

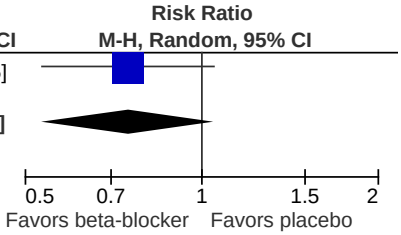
Heterogeneity: Tau² = 0.02; Chi² = 1.83, df = 1 (P = 0.18); I² = 45%
Test for overall effect: Z = 2.66 (P = 0.008)



Cardiovascular mortality

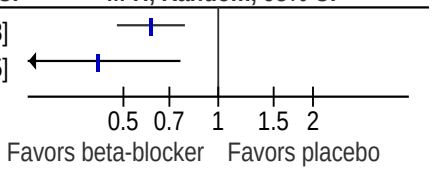
Study or Subgroup	Beta-blocker Events	Beta-blocker Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Cohen-Solal 2009	49	348	67	356	100.0%	0.75 [0.53, 1.05]
Total (95% CI)		**348**		**356**	**100.0%**	**0.75 [0.53, 1.05]**
Total events	49		67			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.68 (P = 0.09)



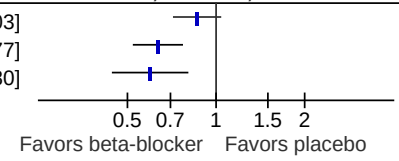
Congestive heart failure hospitalization (A) and death (B)

Study or Subgroup	Beta-blocker Events	Beta-blocker Total	Placebo Events	Placebo Total	Risk Ratio M-H, Random, 95% CI
Ghali (MERIT-HF) A	90	735	147	734	0.61 [0.48, 0.78]
Ghali (MERIT-HF) B	15	735	36	734	0.42 [0.23, 0.75]



Composite vascular outcome (see Table C69 for definitions)

Study or Subgroup	Beta-blocker Events	Beta-blocker Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Cohen-Solal 2009	129	348	153	356		0.86 [0.72, 1.03]
Ghali (MERIT-HF) A	136	735	214	734		0.63 [0.53, 0.77]
Ghali (MERIT-HF) B	64	735	107	734		0.60 [0.45, 0.80]



Appendix Table C70. Study withdrawals and adverse events (outcomes part D), BB versus placebo trials

Study	Study Withdrawals: Any		Serious Adverse Event: Any		Serious Adverse Event: Any Leading to Withdrawal		Adverse Event: Any		Adverse Event: Other Specific		Renal Adverse Events: Any	
	BB	Placebo	BB	Placebo	BB	Placebo	BB	Placebo	BB	Placebo	BB	Placebo
Cohen-Solal, 2009[57]							23/440 (5.2)	11/446 (2.5)	Hypo-tension 2/440 (0.5) Brady-cardia 10/440 (2.3) Heart failure 12/440 (2.7)	Hypo-tension 0/446 (0.0) Brady-cardia 3/446 (0.7) Heart failure 9/446 (2.0)	0/440*	0/446*
Ghali, 2009[59]							NR**	NR**				

BB = beta blocker; NR = not reported

*For safety analysis, cut point was eGFR<60 mL/min/1.73m^2 (efficacy analyis cut point was eGFR<55.5 mL/min/1.73m^2)

**Study reported rates of discontinuation of study medication due to adverse events per 100 person years but did not report data on the number of patients with any withdrawal or adverse event endpoint by treatment group. The most commonly reported adverse events leading to discontinuation of study medication were cardiac failure, fatigue, bradycardia, dizziness, and hypotension, with no data reported by treatment group.

Appendix Evidence Table C71. Overview of CCB versus placebo trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Berl, 2003[60] Lewis, 2001[40] IDNT International (North America, Latin America, Europe, United Kingdom, Israel, Australia, New Zealand, Southeast Asia) Multi-site Funding Source: Industry	Inclusion: ages 30-70; documented diagnosis of type 2 DM; hypertension (sitting SBP >135 mm Hg, sitting DBP >85 mm Hg, or documented treatment with antihypertensive agents); proteinuria (urinary protein excretion >900 mg/24h); serum creatinine between 1.0 and 3.0 mg/dL (women) and 1.2-3.0 mg/dL (men) Exclusion: none stated	N=1,136 Age (yr): 58.7 Gender (Male %): 67 Race/Ethnicity (%): 71.0% white, 14.5% African American, 5.0% Hispanic, 5.5% Asian/Pacific Islander, 4.5% other Weight (kg): NR BMI: 30.7 Systolic BP (mm Hg): 158.5 Diastolic BP (mm Hg): 87.0 CKD stage: NR Serum creatinine (mg/dL): 1.7 Creatinine clearance (mL/min): NR Albuminuria (gday): 1.9 Proteinuria (g/day): 2.9 Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 8.2 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 100 Dyslipidemia (%): NR History of cardiovascular disease (%): 29.5 History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	n= 567 amlodipine (titrated from 2.5 to 10 mg/day)* n= 569 placebo* Followup period: 2.5 years (mean) Study withdrawals (%): 0.5 *Antihypertensives other than ACEIs, ARBs, and CCBs used as needed; target blood pressure was SBP ≤135 mm Hg (or 10 mm Hg lower than screening value if that value was >145 mmHg) and DBP ≤85 mm Hg	Allocation Concealment: Adequate Blinding: Double blind Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Appendix Evidence Table C71. Overview of CCB versus placebo trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Crepaldi, 1998[10] Italy Multi-site Funding Source: None reported	Inclusion: ages 18 to 65 years; onset of insulin-dependent diabetes mellitus before age 35; insulin treatment within 3 years of diagnosis; clinical stability (HbA_{1c} <11% at entry and within 30% of value at entry during past 12 months; standing SBP from 115 to 140 mm Hg (without antihypertensives) and DBP from 75 to 90 mmHg at entry; median albumin excretion rate between 20 and 200 µg/min from 3 timed overnight urine collections within 2 weeks of entry; GFR ≥80 ml/min/1.73m^2 at randomization Exclusion: impaired renal function; serum creatinine >10% above upper limit of normal laboratory range (125 µmol/l) and median (from 3 measures) albumin excretion rate >200 µg/min at entry (after randomization); history of any nondiabetic renal disease; hematuria; evidence of clinically significant liver or hematological disease; evidence of aortic or mitral valve obstruction, arrhythmias, unstable angina, or history of myocardial infarction within the previous 3 months; clinical evidence of autonomic neuropathy; systematic malignancy; hyperkalemia (serum potassium >5.5 mmol/l at pretrial screen or entry; serum triglycerides >3.4 mmol/l or total cholesterol >6.5 mmol/l at routine pretrial check; known familiar lipid disorders; known risk of transmitting AIDS or viral hepatitis; known hypersensitivity or contraindications to ACEIs, nifedipine, or atenolol; women of child-bearing age not using medically acceptable methods of birth control (oral contraceptives were not allowed) or those planning pregnancy	N= 90 (baseline data reported for 60 patients who were not excluded during run-in phase) Age (yr): 36.6 Gender (Male %): 70 Race/Ethnicity (%): NR Weight (kg): 67.4 BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR CKD stage: NR Albumin (g/dl): 4.4 Serum creatinine (µmol/L): 85.8 (=0.97 mg/dL) Creatinine clearance (mL/min): 107.8 Albuminuria (µg/min): 80.2 Albumin/Creatinine ratio (mg/mmol): NR GFR (ml/min/1.73m^2): 111.8 HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 0 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): 58.3 History of AKI (%): NR	n= 41 10 mg nifedipine* n= 49 placebo* Followup period: 3 years Study withdrawals (%): 32.2 *If BP not controlled at 1 month after randomization (reduction of SBP and DBP by <5% of baseline), dose was doubled; if BP not controlled at 3 months (reduction of SBP and DBP by <5% of baseline and standing BP >140/90 mm HG) 50 mg/day atenolol added; if BP not controlled (standing BP >140/90 mm Hg) atenolol doubled; if BP still not adequately controlled (standing BP > 160/90 mmHg) patient withdrawn	Allocation Concealment: Unclear Blinding: Double blind Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes

Appendix Evidence Table C71. Overview of CCB versus placebo trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	during the treatment period; treatment compliance over the 4 wk placebo run in of <85%; on antihypertensive treatment			

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C72. Summary of study baseline characteristics, CCB versus placebo trials

Characteristic	Mean (range unless otherwise noted)	Number of Trials Reporting
Patients randomized, n	1226 (90-1,136)	2
Age of subjects, years	57.6 (36.6-58.7)	2
Gender, male, %	67.2 (67-70)	2
Race/ethnicity, white, %	71	1
Race/ethnicity, black, %	14.5	1
Body Mass Index	30.7	1
Weight (kg)	67.4	1
Systolic blood pressure, mmHg	158.5	1
Diastolic blood pressure, mmHg	87.0	1
Albuminuria, g/day	1.9	1
Albuminuria, µg/min	80.2	1
Proteinuria, g/day	2.9	1
Serum creatinine, mg/dL	1.7 (0.97-1.7)	2
Creatinine clearance, ml/min	107.8	1
GFR, ml/min/1.73m^2	111.8	1
History of diabetes, %	100 (both studies)	2
% HbA_{1c}	8.2	1
History of hypertension (%)	95 (0-100)	2
History of cardiovascular disease, %*	29.5	1
History of CHF, %	NR	0
Current smoker, %	58.3	1

CCB = calcium channel blocker; GFR = glomerular filtration rate, CHF = congestive heart failure

Appendix Table C73. Clinical outcomes (outcomes part A), CCB versus placebo trials

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any, n/N (%)		Myocardial Infarction, Fatal, n/N (%)		Myocardial infarction, Nonfatal n/N (%)		Stroke, Any n/N (%)	
	CCB	Placebo	CCB	Placebo	CCB	Placebo	CCB	Placebo	CCB	Placebo	CCB	Placebo
Berl, 2003[60] Lewis, 2001[40]	83/567 (14.6)	93/569 (16.3)	37/567 (6.5)	46/569 (8.1%)	27/567 (4.8)	46/569 (8.1)					15/567 (2.6)	26/569 (4.6)
Crepaldi, 1998[10]	1/41 (2.4)	0/49	1/41 (2.4)	0/49	0/41	1/49 (2.0)						

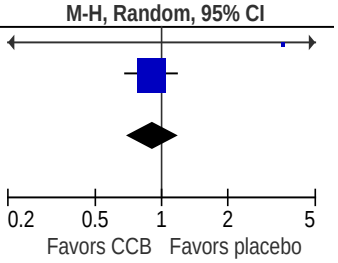
CCB = calcium channel blocker

Appendix Figure C16. Forest plots for CCB versus placebo trials

All-cause mortality

Study or Subgroup	Calcium channel blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Crepaldi 1998	1	41	0	49	0.7%	3.57 [0.15, 85.39]
Lewis (IDNT) 2001	83	567	93	569	99.3%	0.90 [0.68, 1.18]
Total (95% CI)		**608**		**618**	**100.0%**	**0.90 [0.69, 1.19]**
Total events	84		93			

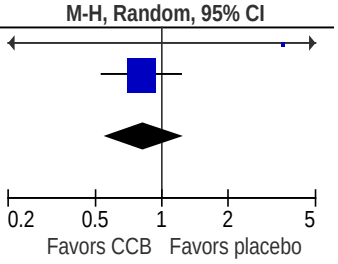
Heterogeneity: Tau² = 0.00; Chi² = 0.73, df = 1 (P = 0.39); I² = 0%
Test for overall effect: Z = 0.72 (P = 0.47)



Cardiovascular mortality

Study or Subgroup	Calcium channel blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Crepaldi 1998	1	41	0	49	1.7%	3.57 [0.15, 85.39]
Lewis (IDNT) 2001	37	567	46	569	98.3%	0.81 [0.53, 1.22]
Total (95% CI)		**608**		**618**	**100.0%**	**0.83 [0.55, 1.25]**
Total events	38		46			

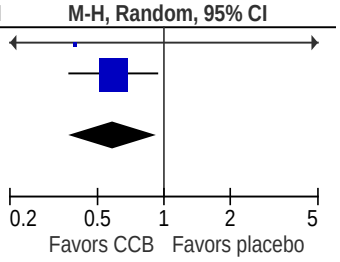
Heterogeneity: Tau² = 0.00; Chi² = 0.83, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 0.90 (P = 0.37)



Myocardial infarction

Study or Subgroup	Calcium channel blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Crepaldi 1998	0	41	1	49	2.1%	0.40 [0.02, 9.49]
Lewis (IDNT) 2001	27	567	46	569	97.9%	0.59 [0.37, 0.93]
Total (95% CI)		**608**		**618**	**100.0%**	**0.58 [0.37, 0.92]**
Total events	27		47			

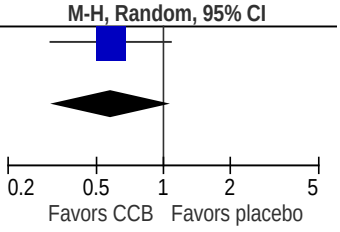
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.81); I² = 0%
Test for overall effect: Z = 2.31 (P = 0.02)



Stroke

Study or Subgroup	Calcium channel blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) 2001	15	567	26	569	100.0%	0.58 [0.31, 1.08]
Total (95% CI)		**567**		**569**	**100.0%**	**0.58 [0.31, 1.08]**
Total events	15		26			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.71 (P = 0.09)



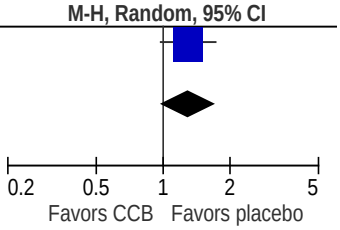
Appendix Figure C16. Forest plots for CCB versus placebo trials (continued)

Congestive heart failure

Study or Subgroup	Calcium channel blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) 2001	93	567	72	569	100.0%	1.30 [0.97, 1.72]
Total (95% CI)		**567**		**569**	**100.0%**	**1.30 [0.97, 1.72]**
Total events	93		72			

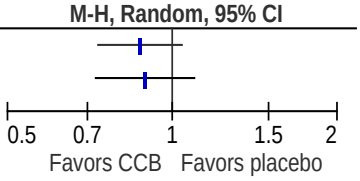
Heterogeneity: Not applicable

Test for overall effect: Z = 1.79 (P = 0.07)



Composite vascular outcome (see Table C75 for definitions)

Study or Subgroup	Calcium channel blocker Events	Total	Placebo Events	Total	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) A	161	567	185	569	0.87 [0.73, 1.04]
Lewis (IDNT) B	128	567	144	569	0.89 [0.72, 1.10]

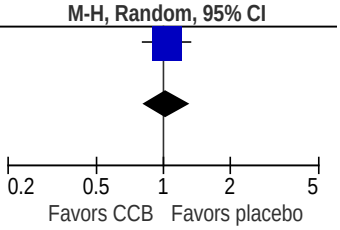


End-stage renal disease

Study or Subgroup	Calcium channel blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) 2001	104	567	101	569	100.0%	1.03 [0.81, 1.32]
Total (95% CI)		**567**		**569**	**100.0%**	**1.03 [0.81, 1.32]**
Total events	104		101			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.26 (P = 0.80)

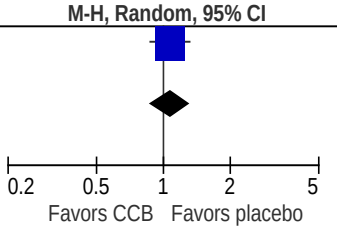


Doubling of serum creatinine

Study or Subgroup	Calcium channel blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) 2001	144	567	135	569	100.0%	1.07 [0.87, 1.31]
Total (95% CI)		**567**		**569**	**100.0%**	**1.07 [0.87, 1.31]**
Total events	144		135			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.65 (P = 0.51)



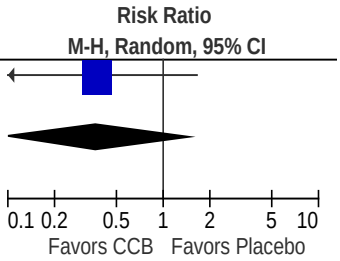
Appendix Figure C16. Forest plots for CCB versus placebo trials (continued)

Progression from microalbuminuria to macroalbuminuria

Study or Subgroup	Calcium channel blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Crepaldi 1998	2	26	7	34	100.0%	0.37 [0.08, 1.65]
Total (95% CI)		**26**		**34**	**100.0%**	**0.37 [0.08, 1.65]**
Total events	2		7			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.30 (P = 0.19)

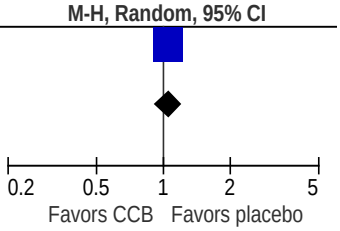


Composite renal outcome (see Table C77 for definitions)

Study or Subgroup	Calcium channel blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Lewis (IDNT) 2001	233	567	222	569	100.0%	1.05 [0.91, 1.21]
Total (95% CI)		**567**		**569**	**100.0%**	**1.05 [0.91, 1.21]**
Total events	233		222			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.71 (P = 0.48)



Appendix Table C74. Clinical outcomes (outcomes part B), CCB versus placebo trials

Study	Stroke, Nonfatal n/N (%)		Stroke, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) n/N (%)		Composite Vascular Outcome n/N (%)*	
	CCB	Placebo	CCB	Placebo	CCB	Placebo	CCB	Placebo	CCB	Placebo
Berl, 2003[60] Lewis, 2001[40]					93/567 (16.4)	72/569 (12.7)			(A)161/567 (28.4) (B)128/567 (22.6)	(A)185/569 (32.5) (B)144/569 (25.3)
Crepaldi, 1998[10]										

CCB = calcium channel blocker; CHF = congestive heart failure
*See Composite vascular outcome definitions table

Appendix Table C75. Composite vascular outcome definitions, CCB versus placebo trials

Study	Definition
Berl, 2003[60] Lewis, 2001[40]	Study defined two composite vascular endpoints as follows: (A) Myocardial infarction, heart failure, permanent neurologic deficit of at least 24-hour duration attributed to stroke, or unplanned (at time of randomization) coronary artery revascularization procedure (all before renal failure, death, or censorship)[60] and (B) Death from cardiovascular causes, nonfatal myocardial infarction, heart failure resulting in hospitalization, permanent neurologic deficit caused by a cerebrovascular event, or lower limb amputation above the ankle.[40]

CCB = calcium channel blocker

Appendix Table C76. Clinical renal outcomes (outcomes part C), CCB versus placebo trials

Study	End-stage Renal Disease n/N (%)		Doubling of Serum Creatinine n/N (%)		Halving of GFR n/N (%)		Progression from Micro- to Macroalbuminuria n/N (%)		Composite Renal Outcome n/N (%)*	
	CCB	Placebo	CCB	Placebo	CCB	Placebo	CCB	Placebo	CCB	Placebo
Berl, 2003[60] Lewis, 2001[40]	104/567 (18.3)	101/569 (17.8)	144/567 (25.4)	135/569 (23.7)					233/567 (41.1)	222/569 (39.0)
Crepaldi, 1998[10]							2/26 (7.7)	7/34 (20.6)		

CCB = calcium channel blocker; GFR = glomerular filtration rate
*See Composite renal outcome definitions table

Appendix Table C77. Composite renal outcome definitions, CCB versus placebo trials

Study	Definition
Berl, 2003[60] Lewis, 2001[40]	Doubling of baseline serum creatinine concentration, onset of end-stage renal disease (initiation of dialysis, renal transplantation, or serum creatinine concentration ≥6.0 mg/dL), or death from any cause

CCB = calcium channel blocker

Appendix Table C78. Study withdrawals and adverse events (outcomes part D), CCB versus placebo trials

Study	Study Withdrawals, Any, n/N (%)		Serious Adverse Event: Any, n/N (%)		Serious Adverse Event: Any Leading to Withdrawal, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event: Any Specific, n/N (%)		Renal Adverse Events: Any, n/N (%)	
	CCB	Placebo	CCB	Placebo	CCB	Placebo	CCB	Placebo	CCB	Placebo	CCB	Placebo
Berl 2003[60] Lewis 2001[40]	2/567 (0.4)	4/569 (0.7)	*NR	*NR	†NR	†NR	†NR	†NR	HyperK: 3/567 (0.5)	HyperK: 2/569 (0.4)	‡NR	‡NR
Crepaldi 1998[10]	15/41 (36.6)	15/49 (30.6)					#NR	#NR	#NR	#NR		

CCB = calcium channel blocker; ARB = angiotensin receptor blocker; HyperK = hyperkalemia

*Study reported that 61% of participants had at least one serious adverse event but didn't report results by treatment group (note that study also included an ARB arm).

† Results were not reported for the proportion of study participants with any adverse event, or any serious adverse event leading to withdrawal, either overall or within groups. However, study reported that 51/567 (9.0%) of CCB group and 41/569 (7.2%) of placebo group discontinued treatment due to adverse event.

‡ Study reported one episode of an early increase in serum creatinine concentration suggestive of renal artery stenosis that necessitated stopping the study medication, but did not indicate in which treatment group this adverse event occurred.

During run-in period, three adverse events resulted in withdrawal from placebo group (two lower limb edema, one hyperkalemia); during randomized study, six adverse events resulted in withdrawal from placebo group (one each herpes zoster, lunge cancer, flaulence, tuberculosis, severe diabetic neuropathy, and myocardial infarction; also reported that 27% of those on CCB and 20% of those on placebo experienced side effects that did not cause withdrawal from study.

Appendix Evidence Table C79. Overview of diuretic versus placebo trial

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Pahor, 1998[61] Multi-center United States Funding Source: Government	Inclusion: aged 60 and above; BP inclusion criteria were a systolic BP of 160 to 219 mm Hg and a diastolic BP of less than 90 mm Hg assessed as the average of 4 measurements (2 measurements were obtained at each of the 2 baseline visits). Exclusion: a systolic BP of 220 mm Hg or higher, a recent myocardial infarction or stroke, or the presence of a major illness such as cancer, alcoholic liver disease, renal failure, insulin-treated diabetes mellitus, and depression. Participants who were receiving an antihypertensive treatment were considered potentially eligible if they had a systolic BP between 130 and 219 mm Hg and a diastolic BP of less than 85 mmHg and were free of major illnesses.	n=393 (subgroup with baseline serum creatinine above normal level [119.4-212.2 µmol/L or 1.35-2.40 mg/dL from overall cohort of 4,336) Baseline characteristics from n=393 with elevated baseline creatinine: Age (yr): 74.0 Gender (Male %): 81.4 Race/Ethnicity (%): White 76.1 Black 19.8 Asian 2.8 Weight (kg): NA BMI: 27.2 Systolic BP (mm Hg): 172 Diastolic BP (mm Hg): 77 CKD stage: NA Serum creatinine (umol/L): NR Creatinine clearance (mL/min): NR Albuminuria (µg/min): NR Proteinuria (mg/day): NR Albumin/creatinine ratio (mg/g): NA GFR (ml/min/1.73m^2): NA HbA_{1c} (%): NA Total cholesterol (mg/dL): NA LDL cholesterol (mg/dL): NA Diabetes (%): 11.7 History of HTN (%): 100 Dyslipidemia (%): NA History of CAD (%): NA History of CHF (%): NA Peripheral arterial disease (%): NA History of MI (%): 5.4 History of Stroke (%): 3.8 Current smoker (%): NA History of AKI (%): NA	n= 216 Initiated chlorthalidone 12.5mg/day (if goal BP not met, dose may be increased, followed by addition of atenolol, then reserpine) n=177 Placebo Treatment goal was SBP <160 mm Hg or at least 20 mm Hg reduction from baseline. Followup period: 5 years Study withdrawals (%): Not reported for elevated serum creatinine group.	Allocation concealment: adequate Blinding: double blinded (though open-label potassium supplement given to all participants with serum potassium levels <3.5 mmol/L) Intention to Treat Analysis (ITT): yes Withdrawals/Dropouts adequately described: yes (in original RCT)

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR =

glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C80. Clinical outcomes (outcomes part A), diuretic versus placebo trial

Study	All-Cause Mortality, n/N (%)		Cardiovascular Mortality, n/N (%)		Myocardial Infarction, Any, n/N (%)		Myocardial Infarction, Fatal, n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke, Any, n/N (%)	
	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo
Pahor, 1998[61]	37/216 (17.1)	26/177 (14.7)									14/216 (6.5)	22/177 (12.4)

Appendix Table C81. Clinical outcomes (outcomes part B), diuretic versus placebo trial

Study	Stroke, Nonfatal, n/N (%)		Stroke, Fatal, n/N (%)		CHF, Any, n/N (%)		CHF Hospitalization (A) or Death (B), n/N (%)		Composite Vascular Outcome, n/N (%)*	
	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo
Pahor, 1998[61]									(A)36/216 (16.7) (B)16/216 (7.4)	(A)47/177 (26.6); (B)21/177 (11.9)

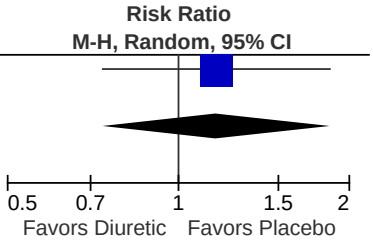
CHF = congestive heart failure
*See Composite vascular outcome definitions table

Appendix Figure C17. Forest plots for diuretic versus placebo trial

All-cause mortality

Study or Subgroup	Diuretic Events	Diuretic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Pahor 1998	37	216	26	177	100.0%	1.17 [0.74, 1.85]
Total (95% CI)		**216**		**177**	**100.0%**	**1.17 [0.74, 1.85]**
Total events	37		26			

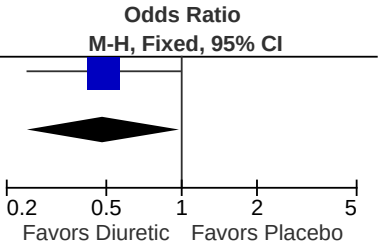
Heterogeneity: Not applicable
Test for overall effect: Z = 0.65 (P = 0.51)



Stroke, any

Study or Subgroup	Diuretic Events	Diuretic Total	Placebo Events	Placebo Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Pahor 1998	14	216	22	177	100.0%	0.49 [0.24, 0.99]
Total (95% CI)		**216**		**177**	**100.0%**	**0.49 [0.24, 0.99]**
Total events	14		22			

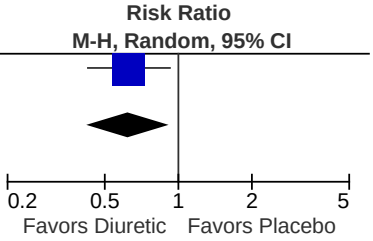
Heterogeneity: Not applicable
Test for overall effect: Z = 2.00 (P = 0.05)



Composite vascular outcome (A) (see Table C82 for definition)

Study or Subgroup	Diuretic Events	Diuretic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Pahor 1998	36	216	47	177	100.0%	0.63 [0.43, 0.92]
Total (95% CI)		**216**		**177**	**100.0%**	**0.63 [0.43, 0.92]**
Total events	36		47			

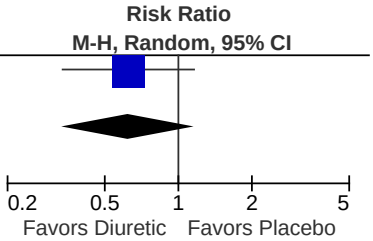
Heterogeneity: Not applicable
Test for overall effect: Z = 2.37 (P = 0.02)



Composite vascular outcome (B) (see Table C82 for definition)

Study or Subgroup	Diuretic Events	Diuretic Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Pahor 1998	16	216	21	177	100.0%	0.62 [0.34, 1.16]
Total (95% CI)		**216**		**177**	**100.0%**	**0.62 [0.34, 1.16]**
Total events	16		21			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.49 (P = 0.14)



Appendix Table C82. Composite vascular outcome definitions, diuretic versus placebo trial

Study	Definition
Pahor, 1998[61]	Study defined multiple composite vascular outcomes, including: (A) "Any cardiovascular event" defined as stroke, TIA, MI, heart failure, CABG, angioplasty, aneurysm, endarterectomy, sudden death, or rapid cardiac death (within 1-24 hours of onset of severe cardiac symptoms unrelated to other known causes); and (B) "Any coronary event" defined as fatal and nonfatal coronary heart disease.

TIA = transient ischemic attack; MI = myocardial infarction; CABG = coronary artery bypass grafting

Appendix Table C83. Study withdrawals and adverse events (outcomes part D), diuretic versus placebo trial

Study	Study Withdrawals: Any		Serious Adverse Event: Any		Serious Adverse Event: Any Leading to Withdrawal		Adverse Event: Any		Adverse Event: Other Specific		Renal Adverse Events: Any	
	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo	Diuretic	Placebo
Pahor, 1998[61]												

Study did not report withdrawals or adverse events overall or by treatment group within the strata of participants with CKD (i.e. baseline serum creatinine 119.4 to 212.2 µmol/L [corresponding to 1.35 to 2.40 mg/dL]).

Appendix Evidence Table C84. Overview of ACEI versus conventional therapy without ACEI trial

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Cinotti, 2001[62] Country Italy, multisite Funding Source: Industry	Inclusion: ages 18-70 years; chronic renal insufficiency due to primary renoparenchymal diseases; no ACEI therapy for at least 3 months; renal insufficiency of at least 12 months with creatinine clearance between 20 and 50 ml/min/1.73m^2 with variation <30% in at least 3 determinations during past 3 months; hypertension (either nontreated DBP ≥95 mmHg or well-documented treatment with antihypertensive drugs*); proteinuria ≤1.0 g/day Exclusion: nephropathy secondary to diabetes or other systemic diseases; malignant hypertension or previous antihypertensive treatment with >2 drugs; cerebrovascular events in the last 6 months or MI in the last 3 months; heart failure, angina, or other major cardiac diseases; significant liver, hemopoietic, or endocrine pathology; concomitant therapy with steroids or immuosuppressive drugs and erythropoietin; pregnancy; lactation; serum potassium <3 mEq/l or >5.8 mEq/l; hypersensitivity or any contraindication to use of ACEI *During 3 month run-in period, patients to follow 0.8 g/kg IBW protein and 3-4 g/day salt diet. Antihypertensive agents (CCB, BB or alpha blocker) continued or added. Patients required to be “compliant” and have stable DBP ≤90 mm Hg with one or two drugs at end of run-in to proceed to randomization.	N=131 Age (yr): 50.8 Gender (Male %): 66 Race/Ethnicity (%): NR Weight (kg): 71.4 BMI: NR Systolic BP (mm Hg): 141.6 Diastolic BP (mm Hg): 85.7 CKD stage: NR Serum creatinine (mg/dL): 2.3 Creatinine clearance (mL/min): 36.3 Albuminuria (µg/min): NR Proteinuria (mg/day): 512 Albumin/creatinine ratio (mg/g): NR measured GFR (ml/min/1.73m^2): 35.8 HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 0 History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): 0 Peripheral arterial disease (%): NR History of MI (%): NR (no recent) History of Stroke (%): NR (no recent) Current smoker (%): NR History of AKI (%): NR	n=66 Lisinopril 5-10 mg/day or Lisinopril 10 mg/day with other antihypertensive drug (L) n=65 Conventional antihypertensive therapy (without ACEI) (C) NSAID use limited to 7 days, ASA allowed at <500 mg/d. Followup period: 22.5 months Study withdrawals (%): No information reported on study withdrawals	Allocation Concealment: Unclear Blinding: Open-label Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: No data reported on withdrawals/dropouts.

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction;

NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C85. Clinical outcomes (outcomes part A), ACEI versus conventional therapy without ACEI trial

Study	All-cause Mortality, n/N (%)		Cardiovascular Mortality, n/N (%)		Myocardial Infarction, Any, n/N (%)		Myocardial Infarction, Fatal, n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke, Any, n/N (%)	
	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI
Cinotti, 2001[62]					0/66	1/65 (1.5)						

ACEI = angiotensin converting enzyme inhibitor

Appendix Table C86. Clinical renal outcomes (outcomes part C), ACEI versus conventional therapy without ACEI trial

Study	End-Stage Renal Disease, n/N (%)		Doubling of Serum Creatinine, n/N (%)		Halving of GFR, n/N (%)		Progression from Micro- to Macroalbuminuria, n/N (%)		Composite Renal Outcome, n/N (%)*	
	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI
Cinotti, 2001[62]	2/66 (3.0)	5/65 (7.7)			3/66 (4.5)	7/65 (10.8)			5/66 (7.8)	12/65 (18.5)

ACEI = angiotensin converting enzyme inhibitor; GFR = glomerular filtration rate
*See Composite renal outcome definitions table

Appendix Table C87. Composite renal outcome definitions, ACEI versus conventional therapy without ACEI trial

Study	Definition
Cinotti, 2001[62]	Halving of GFR or need for dialysis.

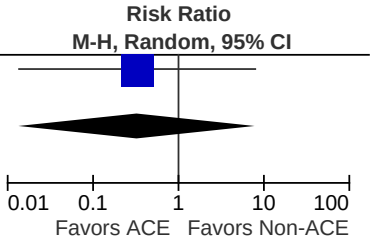
ACEI = angiotensin converting enzyme inhibitor; GFR = glomerular filtration rate

Appendix Figure C18. Forest plots for ACEI versus conventional therapy without ACEI trial

Myocardial infarction

Study or Subgroup	ACE Events	ACE Total	Non-ACE Events	Non-ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Cinotti 2001	0	66	1	65	100.0%	0.33 [0.01, 7.92]
Total (95% CI)		**66**		**65**	**100.0%**	**0.33 [0.01, 7.92]**
Total events	0		1			

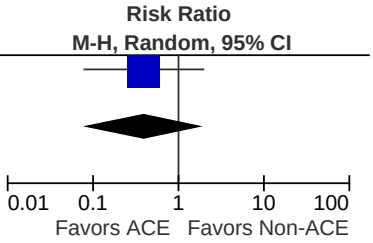
Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)



End-stage renal disease

Study or Subgroup	ACE Events	ACE Total	Non-ACE Events	Non-ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Cinotti 2001	2	66	5	65	100.0%	0.39 [0.08, 1.96]
Total (95% CI)		**66**		**65**	**100.0%**	**0.39 [0.08, 1.96]**
Total events	2		5			

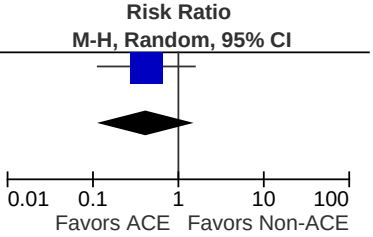
Heterogeneity: Not applicable
Test for overall effect: Z = 1.14 (P = 0.25)



Halving of GFR

Study or Subgroup	ACE Events	ACE Total	Non-ACE Events	Non-ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Cinotti 2001	3	66	7	65	100.0%	0.42 [0.11, 1.56]
Total (95% CI)		**66**		**65**	**100.0%**	**0.42 [0.11, 1.56]**
Total events	3		7			

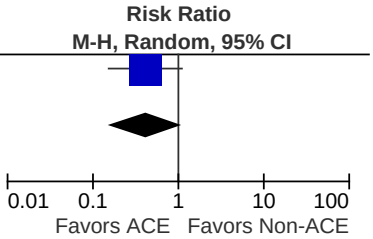
Heterogeneity: Not applicable
Test for overall effect: Z = 1.29 (P = 0.20)



Composite renal outcome (see Table C87 for definition)

Study or Subgroup	ACE Events	ACE Total	Non-ACE Events	Non-ACE Total	Weight	Risk Ratio M-H, Random, 95% CI
Cinotti 2001	5	66	12	65	100.0%	0.41 [0.15, 1.10]
Total (95% CI)		**66**		**65**	**100.0%**	**0.41 [0.15, 1.10]**
Total events	5		12			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.77 (P = 0.08)



Appendix Table C88. Study withdrawals and adverse events (outcomes part D), ACEI versus conventional therapy without ACEI trial

Study	Study Withdrawals, Any, n/N (%)		Study Withdrawals Due to Serious Adverse Events, n/N (%)		Serious Adverse Events, Any, n/N (%)		Adverse Events, Any, n/N (%)		Adverse Events, Specific, n/N (%)		Renal Adverse Events, Any, n/N (%)	
	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI	ACEI	Non-ACEI
Cinotti, 2001[62]	*NR	*NR	*NR	*NR	*NR	*NR			HyperK: 1/66 (1.5%); Uncontrolled hypotension: 1/66 (1.5%)	HyperK: 0/65; Uncontrolled hypotension: 0/65		

ACEI = angiotensin converting enzyme inhibitor
*Study did not report withdrawals, serious adverse events, or withdrawals due to serious adverse events, but did report discontinuation of treatment due to adverse events (4/66 [6.1%] in ACEI group and 3/65 [4.6%] in non-ACEI group).

Appendix Table C89. Overview of CCB versus BB trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Bakris[63] 1996 United States, Single-site Funding Source: Private (Foundation)	Inclusion: non-insulin dependent diabetes for ≥8 years; diabetic retinopathy; proteinuria ≥2.0 g/day; renal insufficiency (creatinine clearance <1.16 ml/sec [i.e. <70ml/min]); hypertension for ≥8 years; age ≥45 years Exclusion: Diastolic blood pressure >125 mm Hg on three consecutive readings during 2 week wash out period with no antihypertensive medications. Heart failure (ejection fraction ≤40%); history of poor diabetes control (blood glucose 11 mmol/l or HbA_{1c} >13%; history of difficult blood pressure control (maximum dose of ≥3 medications or diastolic blood pressure >105 mm Hg with medication); blindness, documented coronary artery disease; severe claudication (peripheral arterial disease); orthostatic hypotension (diabetic neuropathy); required intake of antiarrhythmic medications, calcium channel blockers, or angiotensin converting enzyme inhibitor; documented psychiatric disease; active urine sediment; blood glucose control by insulin therapy alone.	N=34 (CCB and BB groups) Age (yr): 62.1 Gender (Male %): 44.4 Race/Ethnicity (%): 56% black, 44% white Weight (kg): 105.6 BMI: 32.6 (calculated from given height & weight) Systolic BP (mm Hg): 158.4 Diastolic BP (mm Hg): 97.9 CKD stage: NR Serum creatinine (mmol/l): 163.8 (=1.85 mg/dL) Creatinine clearance (ml/s/1.73m^2): 1.01 (=60.6 ml/min/1.73m^2) Albuminuria (gday): NR Proteinuria (g/day): 4.36 Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 10.5 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 100 Dyslipidemia (%): NR History of cardiovascular disease (%): NR History of CAD (%): 0 History of CHF (%): 0 Peripheral arterial disease (%): NR (severe claudication is excluded) History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	n= 18 to either verapamil SR (n=8) or diltiazem SR (n=10)* n= 16 atenolol* Study including additional treatment arm of lisinopril (n=16) Followup period: 64 months (median) Study withdrawals (%): 11.5 *initial dose not reported; dosages titrated over two week period and then periodically throughout study to ensure similar arterial pressure control among groups; if additional blood pressure reduction needed, furosemide added (100% received furosemide by year 4); other antihypertensives (including alpha blockers and/or vasodilators) added if further blood pressure reduction needed. All patients also instructed in 90 meq/day Na and 0.8 g/kg protein and 6300 kJ ADA diet.	Allocation concealment: Unclear Blinding: Not reported Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Appendix Table C89. Overview of CCB versus BB trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Wright, 2002[26] Wright, 1996[64] AASK United States Multi-site Funding Source: Government, Industry	Inclusion: self-identified African Americans; hypertension; ages 18 to 70; GFR between 20 and 65 mL/min/1.73m^2; no other identified causes of renal insufficiency Exclusion: diastolic BP <95 mm Hg; known history of diabetes mellitus (fasting glucose ≥149 mg/dL or random glucose >200 mg/dL); urinary protein to creatinine ratio >2.5; accelerated or malignant hypertension within 6 months; secondary hypertension; evidence of non-BP-related causes of chronic kidney disease; clinical congestive heart failure; specific indications for or contraindication to a study drug or study procedure.	N= 658 Age (yr): 54.8 Gender (Male %): 61.1 Race/Ethnicity (%): NR Weight (kg): NR BMI: NR Systolic BP (mm Hg): 150.0 Diastolic BP (mm Hg): 95.3 CKD stage: NR Albumin (g/dl): NR Serum creatinine (mg/dL): 2.03 Creatinine clearance (mL/min): NR Albuminuria (µg/min): NR Proteinuria (g/24h): 0.54 Protein/Creatinine ratio: 0.33 Urine protein/creatine ratio ≥0.22 (%): 32 GFR (ml/min/1.73m^2): 45.8 HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 0 History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): 0 Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	n= 217 amlodipine (5 to 10 mg/day)* n= 441 metropolol (50 to 200 mg/day)* Followup period: 3 years (median, for GFR outcome)** Study withdrawals (%): 0 *if BP goal could not be achieved by randomized drug, additional open-labeled antihypertensives were added sequentially (furosemide, doxazosin, clonidine, and hydralazine or minoxidil) **amlodipine arm stopped early on recommendation of the data and safety monitoring board; patients in this arm were switched to open-label medication.	Allocation Concealment: Adequate Blinding: Participants and investigators masked to randomized drug but not BP goal; cardiovascular events classified by blinded end points committee Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes
Dahlof, 2005[65] ASCOT-BPLA Europe multi-site Funding Source: Industry	Inclusion: aged 40-79 years; untreated hypertension, SBP ≥160 mm Hg, DBP ≥100 mm Hg or both, treated hypertension with SBP ≥140 mm Hg or DBP 90 mm Hg or both; and at least 3 of the following risk factors (left ventricle hypertrophy, abnormalities on electrocardiogram, type II diabetes, PAD, previous stroke or TIA, male sex, age ≥55,	N=12,074 with "renal dysfunction" (undefined) in subgroup analysis out of 19,342 randomized overall Baseline data not presented for subgroup with renal dysfunction, though by entry criteria, the following characteristics could be determined: History of HTN (%): 100 History of MI (%): 0	n=5,893 amlodipine 5-10 mg, adding perindopril 4-8 mg as required n=6181 atenolol 50-100 mg, adding bendroflumethiazide 1.25-2.5 mg and potassium as required Followup period: 5.5 years	Allocation Concealment: adequate Blinding: Open with blinded end-point classification Intention to Treat Analysis (ITT): yes

Appendix Table C89. Overview of CCB versus BB trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	microalbuminuria or proteinuria, smoking, ratio of plasma total cholesterol to HDL ≥6, family history of premature CHD) Exclusion: previous MI; currently treated angina; a cerebrovascular event within previous 3 months; fasting triglycerides >4.5 mmol/L; heart failure; uncontrolled arrhythmias; any clinical important hematological or biochemical abnormality on routine screening	History of CHF (%): 0	(median) (trial was stopped prematurely) Study withdrawals (%): 0.6 overall, but not reported for "renal dysfunction" subgroup	Withdrawals/Dropouts adequately described: yes

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PAD = peripheral arterial disease; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C90. Summary of study baseline characteristics, CCB versus BB trials

Characteristic	Mean (range unless otherwise noted)	Number of Trials Reporting
Patients randomized, n	12,766 (34-12,074)	3
Age of subjects, years	55.2 (54.8-62.1)	2
Gender, male, %	60.3 (44.4-61.1)	2
Race/ethnicity, white, %	2 (0-44)	2
Race/ethnicity, black, %	98 (56-100)	2
Body Mass Index	32.6	1
Systolic blood pressure, mmHg	150.4 (150.0-158.4)	2
Diastolic blood pressure, mmHg	95.4 (95.3-97.9)	2
Proteinuria, g/day	0.70 (0.54-4.36)	2
Serum creatinine, mg/dL	2.02 (1.85-2.03)	2
Creatinine clearance, ml/min/1.73m^2	60.6	1
GFR, ml/min/1.73m^2	45.8	1
Total cholesterol, mg/dl	NR	
LDL cholesterol, mg/dl	NR	
History of diabetes, %	4.9 (0 to 100)	2
% HbA_{1c}	10.5	1
History of hypertension (%)	100	3
History of cardiovascular disease, %*	NR	
History of CHF, %	0	3
Current smoker, %	NR	

CCB = calcium channel blocker; BB = beta blocker; GFR = glomerular filtration rate; LDL = low density lipoprotein; CHF = congestive heart failure; NR = not reported

*One study (n=34) excluded patients with history of heart failure or coronary artery disease; one study (n=12,074) excluded patients with history of MI

Appendix Table C91. Clinical outcomes (outcomes part A), CCB versus BB trials

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial infarction, Fatal, n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke, Any n/N (%)	
	CCB	BB	CCB	BB	CCB	BB	CCB	BB	CCB	BB	CCB	BB
Bakris, 1996[63]	1/18 (5.6)	4/16 (25.0)	*NR	*NR			*NR	*NR				
Wright, 2002[26]; Norris 2006[27]	13/217 (6.0)	38/441 (8.6)	†NR	†NR								
Dahlof, 2005[65]												

CCB = calcium channel blocker; BB = beta blocker

* Study reported 5 (9.6%) cardiovascular deaths, 4 (7.7%) fatal myocardial infarctions, and 1 (1.9%) fatal stroke, but didn't indicate to which treatment group these patients had been assigned.

† Study did not report the number of participants with cardiovascular death, but instead the percentage of patients with cardiovascular death per patient year of followup: CCB 0.9%, BB 0.8%.

Appendix Table C92. Clinical outcomes (outcomes part B), CCB versus BB trials

Study	Stroke, Nonfatal n/N (%)		Stroke, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) n/N (%)		Composite Vascular Outcome n/N (%)*	
	CCB	BB	CCB	BB	CCB	BB	CCB	BB	CCB	BB
Bakris, 1996[63]			**NR	**NR						
Wright, 2002[26]									†NR	†NR
Dahlof, 2005									825/5893 (14.0)	989/6181 (16.0)

CCB = calcium channel blocker; BB = beta blocker; CHF = congestive heart failure; NR = not reported

*See Composite vascular outcome definitions table

**Study reported 1 fatal stroke (1.9%), but didn't indicate participant treatment group.

†Study did not report number of patients with composite vascular endpoint, "cardiovascular event," overall or by treatment group, but reported results as percent of patients with event per patient-year of follow-up: cardiovascular event CCB 1.7%, BB 2.9%.

Appendix Table C93. Composite vascular outcome definitions, CCB versus BB trials

Study	Definition
Wright, 2002[26]	Cardiovascular event, defined as cardiovascular mortality or first cardiovascular hospitalization.
Dahlof, 2005[65]	Study defined six composite vascular endpoints, but reported results within the subgroup of participants with “renal dysfunction” only in one of the secondary composite vascular endpoints, as follows: (A) Cardiovascular mortality, nonfatal MI (symptomatic and silent), unstable angina, chronic stable angina, life threatening arrhythmias, silent nonfatal heart failure, nonfatal stroke, peripheral arterial disease, revascularization procedures, and retinal vascular thromboses.

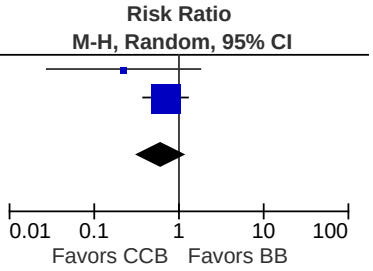
CCB = calcium channel blocker; BB = beta blocker

Appendix Figure C19. Forest plots for CCB versus BB trials

All-cause mortality

Study or Subgroup	CCB Events	CCB Total	BB Events	BB Total	Weight	Risk Ratio M-H, Random, 95% CI
Bakris 1996	1	18	4	16	10.3%	0.22 [0.03, 1.79]
Wright 2002	13	217	38	441	89.7%	0.70 [0.38, 1.28]
Total (95% CI)		**235**		**457**	**100.0%**	**0.62 [0.31, 1.22]**
Total events	14		42			

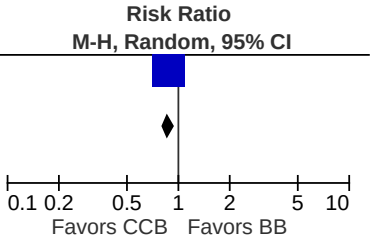
Heterogeneity: Tau² = 0.04; Chi² = 1.06, df = 1 (P = 0.30); I² = 6%
Test for overall effect: Z = 1.39 (P = 0.17)



Composite vascular outcome (see Table C93 for definition)

Study or Subgroup	CCB Events	CCB Total	BB Events	BB Total	Weight	Risk Ratio M-H, Random, 95% CI
Dahlof 2005	825	5893	989	6181	100.0%	0.87 [0.80, 0.95]
Total (95% CI)		**5893**		**6181**	**100.0%**	**0.87 [0.80, 0.95]**
Total events	825		989			

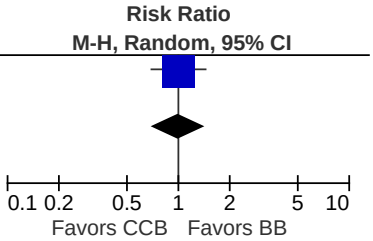
Heterogeneity: Not applicable
Test for overall effect: Z = 3.07 (P = 0.002)



End-stage renal disease

Study or Subgroup	CCB Events	CCB Total	BB Events	BB Total	Weight	Risk Ratio M-H, Random, 95% CI
Wright 2002	36	217	73	441	100.0%	1.00 [0.70, 1.44]
Total (95% CI)		**217**		**441**	**100.0%**	**1.00 [0.70, 1.44]**
Total events	36		73			

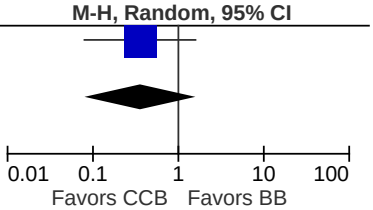
Heterogeneity: Not applicable
Test for overall effect: Z = 0.01 (P = 0.99)



Doubling of serum creatinine

Study or Subgroup	CCB Events	CCB Total	BB Events	BB Total	Weight	Risk Ratio M-H, Random, 95% CI
Bakris 1996	2	18	5	16	100.0%	0.36 [0.08, 1.59]
Total (95% CI)		**18**		**16**	**100.0%**	**0.36 [0.08, 1.59]**
Total events	2		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.36 (P = 0.18)



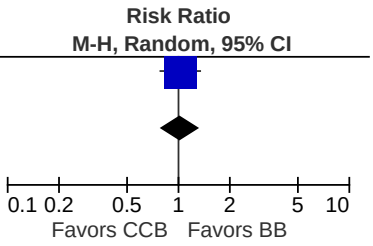
Appendix Figure C19. Forest plots for CCB versus BB trials (continued)

Composite renal outcome A (see Table C95 for definition)

Study or Subgroup	CCB Events	CCB Total	BB Events	BB Total	Weight	Risk Ratio M-H, Random, 95% CI
Wright 2002	59	217	117	441	100.0%	1.02 [0.78, 1.34]
Total (95% CI)		**217**		**441**	**100.0%**	**1.02 [0.78, 1.34]**
Total events	59		117			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.18 (P = 0.86)

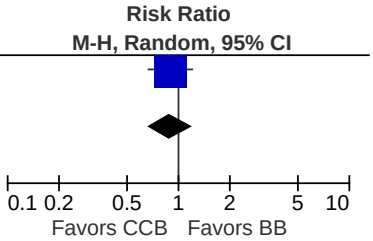


Composite renal outcome C (see Table C95 for definition)

Study or Subgroup	CCB Events	CCB Total	BB Events	BB Total	Weight	Risk Ratio M-H, Random, 95% CI
Wright 2002	49	217	111	441	100.0%	0.90 [0.67, 1.20]
Total (95% CI)		**217**		**441**	**100.0%**	**0.90 [0.67, 1.20]**
Total events	49		111			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.72 (P = 0.47)



Appendix Table C94. Clinical renal outcomes (outcomes part C), CCB versus BB trials

Study	End-stage Renal Disease n/N (%)		Doubling of Serum Creatinine n/N (%)		Halving of GFR n/N (%)		Progression from Micro- to Macroalbuminuria n/N (%)		Composite Renal Outcome, n/N (%)*	
	CCB	BB	CCB	BB	CCB	BB	CCB	BB	CCB	BB
Bakris 1996[63]	**NR	**NR	2/18 (11.1)	5/16 (31.3)						
Wright 2002[26]	36/217 (16.6)	73/441 (16.6)							†(A)59/217 (27.2); (C)49/217 (22.5)	†(A)117/441 (26.5); (C)111/441 (25.2)
Dahlof 2005[65]										

CCB = calcium channel blocker; BB = beta blocker; GFR = glomerular filtration rate; NR = not reported
*See Composite renal outcome definitions table
**Study reported that 5/52 (9.6%) patients (includes the 18 in a separate ACEI group) started dialysis during trial, but didn't report results by treatment group.
†Study did not report number of participants with other composite renal outcomes reported, but instead reported multivariate adjusted relative risk (BB versus CCB) of these composite renal outcome events: (B) ESRD or death (RR 0.58; 95%CI, 0.40 to 0.83); and (C) ESRD or ≥50% decline in GFR (RR 0.76; 95%CI, 0.53 to 1.09).

Appendix Table C95. Composite renal outcome definitions, CCB versus BB trials

Study	Definition
Wright 2002[26]	(A) GFR event (reduction in GFR by 50% or by 25 ml/min/1.73m^2 from baseline mean) (C) ESRD or ≥50% decline in GFR

BB = beta blocker; CCB = calcium channel blocker; GFR = glomerular filtration rate; ESRD = end-stage renal disease

Appendix Table C96. Study withdrawals and adverse events (outcomes part D), CCB versus BB trials

Study	Study Withdrawals, Any, n/N (%)		Serious Adverse Event: Any, n/N (%)		Serious Adverse Event: Any Leading to Withdrawal, n/N (%)		Adverse event: Any, n/N (%)		Adverse Event: Any Specific, n/N (%)		Renal Adverse Events: Any, n/N (%)	
	CCB	BB	CCB	BB	CCB	BB	CCB	BB	CCB	BB	CCB	BB
Bakris, 1996[63]	*NR	*NR			0/18	0/16			†Pedal edema: 2/18 (11.1) Constipation: 10/18 (55.6) Impotence: 3/18 (16.7) Insomnia: 1/18 (5.6) Lethargy: 0/18	†Pedal edema: 2/16 (12.5) Constipation: 7/16 (43.8) Impotence: 9/16 (56.3) Insomnia: 6/16 (37.5) Lethargy: 13/16 (81.3)		
Wright, 2002[26]	‡0/217	‡0/441					†NR	†NR	†NR	†NR		
Dahlof, 2005[65]												

CCB = calcium channel blocker; BB = beta blocker

* 6 withdrawals, treatment group not specified

† Study reported additional participants with specific adverse events as follows: hyperkalemia (CCB 0/18, BB 1/16), dizziness (CCB 2/18, BB 3/16); headache (CCB 2/18, BB 1/16); exercise intolerance (CCB 0, BB 7); dry mouth (CCB 1, BB 13)

‡ Study reported no withdrawals in either treatment group, but also indicated that excluding deaths and dialysis, 23/217 randomized to CCB and 30/441 assigned to BB were no longer active study participants at its end.

† Study did not report the number and percentage of participants overall or by treatment group with any or specific adverse events, but instead reported as percentage of patients experiencing the adverse event per patient year of follow-up (%/pt-yr): hyperkalemia CCB 0, BB 0.2; angioedema CCB 2.3, BB 2.7; shortness of breath CCB 44.4, BB 45.8; syncope CCB 2.3, BB 6.3; dizziness CCB 46.7, BB 47.8; lightheadedness CCB 48.1, BB 47.8; edema CCB 59.8, BB 51.0; cough CCB 46.3, BB 41.5; sexual dysfunction CCB 25.7, BB 25.2.

Appendix Table C97. Overview of CCB versus diuretic trial

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Rahman 2005/2006[23,34] U.S., Canada, Puerto Rico, U.S. Virgin Islands, multi-site Funding Source: government	Inclusion: men and women 55 years or older who had stage 1 or stage 2 hypertension with at least 1 additional risk factor for coronary heart disease events. The risk factors included previous (>6 months) myocardial infarction or stroke, left ventricular hypertrophy demonstrated by electrocardiography or echocardi-ography, history of type 2 diabetes mellitus, current cigarette smoking, high-density lipoprotein cholesterol level of <5 mg/dL (<0.91 mmol/L), or documentation of other atherosclerotic cardiovascular disease. Exclusion: Individuals with a history of symptomatic heart failure and/or a known left ventricular ejection fraction of <35% were excluded. Participants with a serum creatinine level >2 mg/dL (176.8 µmol/L) as reported by the investigator were excluded. However, if the serum creatinine level measured at the time of randomization was found to exceed 2 mg/dL (176.8 µmol/L), these participants were maintained in the trial and followed up according to the study protocol.	n= 4,129 (Post hoc subgroup analysis within participants with GFR <60 ml/min/1.73m2 from overall study population for these treatment groups of 23,261) Age (yr): 70.8 Gender (Male %): 46.8 Race/Ethnicity (%): White non-Hispanic: 57.4 Black non-Hispanic: 25.3 White Hispanic: 11.6 Black Hispanic: 1.1 Othe:r 4.6 Weight (kg): NA BMI: 29.1 Systolic BP (mm Hg): 146.7 Diastolic BP (mm Hg): 82.5 CKD stage: NA Serum creatinine (umol/L): NA Creatinine clearance (mL/min): NA Albuminuria (µg/min): NA Proteinuria (mg/day): NA Albumin/creatinine ratio (mg/g): NA GFR (ml/min/1.73m^2): 50.3 HbA_{1c} (%): NA Total cholesterol (mmol/L): NA LDL cholesterol (mmol/L): NA Diabetes (%): 33.6 History of HTN (%): 100 Dyslipidemia (%): NA History of CAD (%): 30.2 History of CVD (%): 59.7 History of CHF (%): 0 Peripheral arterial disease (%): NA History of MI or stroke (%): 28.0 Current smoker (%): 17.6 History of AKI (%): NA	n=1,516 amlodipine 2.5, 5 and 10 mg/d n= 2,613 chlorthalidone 12.5, 12.5 (sham titration), and 25 mg/d Followup period: 4.9 yr Study withdrawals (%): Not reported for low GFR by treatment groups	Allocation Concealment:Unclear Blinding: double blind Intention-to-Treat Analysis (ITT): yes Withdrawals/Dropouts adequately described: Yes for study overall, but not specified by treatment groups

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF =

congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C98. Summary of study baseline characteristics, CCB versus diuretic trial

Characteristic	Mean (range unless otherwise noted)	Number of Trials Reporting
Patients randomized, n	4,129	1
Age of subjects, years	70.8	1
Gender, male, %	46.8	1
Race/ethnicity, white, %	69.0	1
Race/ethnicity, black, %	26.4	1
Body Mass Index	29.1	1
Systolic blood pressure, mmHg	146.7	1
Diastolic blood pressure, mmHg	82.5	1
Proteinuria, g/day	NR	
Serum creatinine, mg/dL	NR	
Creatinine clearance, ml/min/1.73m^2	NR	
GFR, ml/min/1.73m^2	50.3	1
Total cholesterol, mg/dl	NR	
LDL cholesterol, mg/dl	NR	
History of diabetes, %	33.6	1
% HbA_{1c}	NR	
History of hypertension (%)	100	1
History of cardiovascular disease, %	59.7	1
History of CHF, %	0	1
Current smoker, %	17.6	1

CCB = calcium channel blocker; NR = not reported; GFR = glomerular filtration rate; LDL = low density lipoprotein; CHF = congestive heart failure

Appendix Table C99. Clinical outcomes (outcomes part A), CCB versus diuretic trial

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any, n/N (%)		Myocardial Infarction, Fatal, n/N (%)		Myocardial infarction, Nonfatal, n/N (%)		Stroke, Any n/N (%)	
	CCB	Diuretic	CCB	Diuretic	CCB	Diuretic	CCB	Diuretic	CCB	Diuretic	CCB	Diuretic
Rahman, 2006[34]											100/1516 (6.6)	157/2613 (6.0)

CCB = calcium channel blocker

Appendix Table C100. Clinical outcomes (outcomes part B), CCB versus diuretic trial

Study	Stroke, Nonfatal n/N (%)		Stroke, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) n/N (%)		Composite Vascular Outcome n/N (%)*	
	CCB	Diuretic	CCB	Diuretic	CCB	Diuretic	CCB	Diuretic	CCB	Diuretic
Rahman, 2006[34]					174/1516 (11.5)	259/2613 (9.9)			(A)194/1516 (12.8) (B)537/1516 (35.4)	(A)318/2613 (12.2) (B)870/2613 (33.3)

CCB = calcium channel blocker; CHF = congestive heart failure
*See Composite vascular outcome definitions table

Appendix Table C101. Composite vascular outcome definitions, CCB versus diuretic trial

Study	Definition
Rahman, 2005[23]	(A) CHD, defined as nonfatal MI and fatal CHD (B) Combined CVD, defined as CHD death, nonfatal MI, coronary revascularization, hospitalized or treated angina, stroke, treated or hospitalized heart failure, and peripheral arterial disease (hospitalized or outpatient revascularization).

CCB = calcium channel blocker; CHD = coronary heart diease; CVD = cardiovascular disease; MI = myocardial infarction

Appendix Table C102. Clinical renal outcomes (outcomes part C), CCB versus diuretic trial

Study	End-stage Renal Disease n/N (%)		Doubling of Serum Creatinine n/N (%)		Halving of GFR n/N (%)		Progression from Micro- to Macroalbuminuria n/N (%)		Composite Renal Outcome n/N (%)*	
	CCB	Diuretic	CCB	Diuretic	CCB	Diuretic	CCB	Diuretic	CCB	Diuretic
Rahman, 2005[23]	Overall: 65/1516 (4.3) Diabetics: 44/506 (8.7)	Overall: 124/2613 (4.7) Diabetics: 68/881 (7.7)							**Overall: 90/1516 (5.9) Diabetics: 56/506 (11.1)	**Overall: 180/2613 (6.9)** Diabetics: 96/881 (10.9)

CCB = calcium channel blocker; GFR = glomerular filtration rate; ESRD = end-stage renal disease
*See Composite renal outcome definitions table
** Study also reported no difference in risk (RR 1.02 [95% CI, 0.90-1.15]) between treatment groups for another composite renal outcome (≥50% decline in GFR, ESRD or death), but didn't report the number of participants reaching this event overall or by treatment group.

Appendix Table C103. Composite renal outcome definitions, CCB versus diuretic trial

Study	Definition
Rahman, 2005[23]	50% or greater decline in GFR or incident end-stage renal disease (death due to kidney disease, kidney transplantation, or start of long-term renal dialysis)

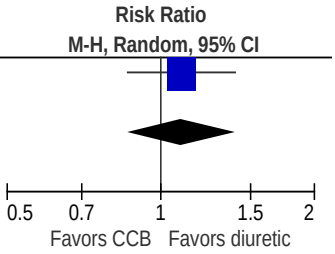
CCB = calcium channel blocker; GFR = glomerular filtration rate

Appendix Figure C20. Forest plots for CCB versus diuretic trial

Stroke

Study or Subgroup	Calcium channel blocker Events	Total	Diuretic Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) 2006	100	1516	157	2613	100.0%	1.10 [0.86, 1.40]
Total (95% CI)		**1516**		**2613**	**100.0%**	**1.10 [0.86, 1.40]**
Total events	100		157			

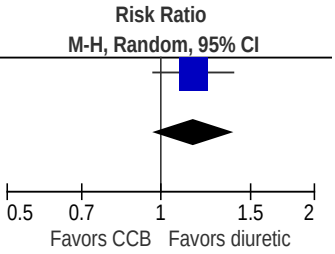
Heterogeneity: Not applicable
Test for overall effect: Z = 0.75 (P = 0.45)



Heart failure

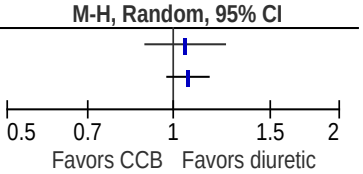
Study or Subgroup	Calcium channel blocker Events	Total	Diuretic Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) 2006	174	1516	259	2613	100.0%	1.16 [0.97, 1.39]
Total (95% CI)		**1516**		**2613**	**100.0%**	**1.16 [0.97, 1.39]**
Total events	174		259			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.58 (P = 0.11)



Composite vascular outcome (see Table C101 for definition)

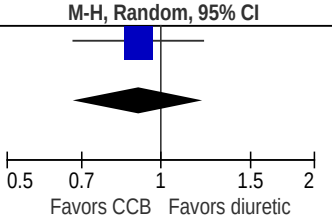
Study or Subgroup	Calcium channel blocker Events	Total	Diuretic Events	Total	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) A	194	1516	318	2613	1.05 [0.89, 1.24]
Rahman (ALLHAT) B	537	1516	870	2613	1.06 [0.98, 1.16]



End-stage renal disease

Study or Subgroup	Calcium channel blocker Events	Total	Diuretic Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) 2006	65	1516	124	2613	100.0%	0.90 [0.67, 1.21]
Total (95% CI)		**1516**		**2613**	**100.0%**	**0.90 [0.67, 1.21]**
Total events	65		124			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)



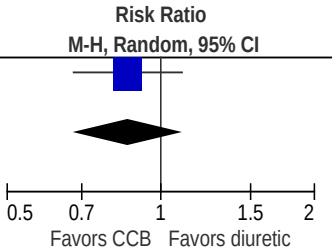
Appendix Figure C20. Forest plots for CCB versus diuretic trial (continued)

Composite renal outcome (see Table C103 for definition)

Study or Subgroup	Calcium channel blocker Events	Total	Diuretic Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Rahman (ALLHAT) 2006	90	1516	180	2613	100.0%	0.86 [0.67, 1.10]
Total (95% CI)		**1516**		**2613**	**100.0%**	**0.86 [0.67, 1.10]**
Total events	90		180			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.19 (P = 0.23)



Appendix Table C104. Overview of strict versus standard blood pressure control trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Blood pressure target comparison trials (n= 6)				
Ruggenenti, 2005[66] REIN-2 Multi-center Italy Industry and other (nonprofit research institute)	Inclusion Criteria: Age 18–70 years, who had nondiabetic nephropathy and persistent proteinuria (urinary protein excretion ≥1 g/24 hr for at least 3 months without evidence of urinary-tract infection or overt heart failure) and who had not received ACEI therapy for at least 6 weeks. Patients with proteinuria of 1–3 g /24 hr were included if their creatinine clearance was less than 45 mL/min per 1·73m^2; those with a proteinuria ≥3 g /24 h were included if their creatinine clearance was less than 70 mL/min per 1·73 m^2. Exclusion Criteria: Urinary tract infection, NYHA class III or IV heart failure, treatment with corticosteroids, non-steroidal anti-inflammatory drugs, or immunosuppressive drugs; acute myocardial infarction or cerebrovascular accident in the previous 6 months, severe uncontrolled hypertension, evidence or suspicion of renovascular disease, obstructive uropathy, type 1 diabetes mellitus, collagen disease, cancer, "higher" serum aminotransferase concentrations, or chronic cough, history of allergy, or poor tolerance to ACEI or dihydropyridine calcium-channel blockers; drug or alcohol abuse; pregnancy; breastfeeding; and ineffective contraception.	N= 338 (baseline characteristics reported on 335, excluding 3 subjects who never took study drugs) Age (yr): 53.8 Gender (Male %): 74.9 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 136.7 Diastolic BP (mm Hg): 84.1 MAP (mm Hg): 101.6 Proteinuria (g/day): 2.85 Serum creatinine (mg/dL): 2.7 Creatinine Clearance (ml/min/1.73m^2): 38.8 Measured GFR (ml/min/1.73m^2): 35.0 Total cholesterol (mg/dL): 217.5 LDL cholesterol (mg/dL): NR Diabetes (%): NR HgbA1C (%): NR History of HTN (%): NR History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR History of AKI (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Conventional BP control (n= 169), with target DBP <90 mm Hg, irrespective of SBP Intensified BP control (n=169), with target <130/80 mm Hg, using felodipine, initially at 5 mg/day then titrated up as needed to 10 mg/day. During pre-randomization run-in, all participants started on ramipril and uptitrated as tolerated to 5 mg/day while concomitant blood pressure medications tapered down as tolerated to keep SBP <90 mm Hg. After randomization, adjustment of concomitant BP meds (excluding ACEI, ARB, or dihydropiridine CCB other than felodipine) allowed to meet BP target/avoid hypotension. Followup period (median): 19 months Study withdrawals (%): 15.4 (52/338)	Allocation Concealment Adequate. Centrally administered randomization process. Blinding: No. Investigators and patients aware of allocation. Intention to Treat Analysis (ITT): No. Three subjects not included in analysis after randomization. Withdrawals/Dropouts adequately described: Yes

Appendix Table C104. Overview of strict versus standard blood pressure control trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Wright, 2002[26] AASK Multi-center USA Funding Source: Industry and Government	Inclusion Criteria: Self-identified African Americans with hypertension (n=1094), aged 18 to 70 yr, GFR 20 to 65 mL/min per 1.73 m^2, and no other identified causes of renal insufficiency. Exclusion Criteria: DBP 95 mm Hg, known history of diabetes mellitus (fasting glucose, ≥140 mg/dL or random glucose >200 mg/dL), urinary protein to creatinine ratio >2.5, accelerated or malignant hypertension within 6 months, secondary hypertension, evidence of non–BP-related causes of chronic kidney disease, serious systemic disease, clinical CHF, or specific indication for or contraindication to a study drug or study procedure.	N= 1094 Age (yr): 54.6 Gender (Male %): 61.2 Race/Ethnicity (%): African American 100 BMI: 30.6 Weight: 89.5 Systolic BP (mm Hg): 150.5 Diastolic BP (mm Hg): 95.5 MAP (mm Hg): 114 Proteinuria (g/24h): 0.53 Urine protein/creatinine ratio: 0.33 Serum creatinine (mg/dL): 2.0 Creatinine Clearance (ml/min/1.73m^2): NR Measured GFR (ml/min/1.73m^2): 45.6 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 0 HgbA1C (%): NR History of HTN (%): 100 History of CAD (%): NR History of CHF (%): 0 History of MI (%): NR Current smoker (%): NR	Target MAP 102-107 mm Hg (n=554) Target MAP ≤92 mm Hg (n=540) Study was 3x2 factorial design, including 2 target BP groups and 3 BP drug groups (amlodipine, metoprolol or ramipril). If BP target couldn't be achieved by randomized drug, additional open-label BP meds could be added. Followup period: median 3.8 yrs (median 4.1 yr in ramipril and metoprolol groups, and 3.0 yr in amlodipine group) Study withdrawals (%): Study reported 0 withdrawals, but stated that 8.1% with no GFR in their final year of followup were not "active participants" at study end.	Allocation Concealment Unclear Blinding: No, not for BP target groups Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes
Estacio 2000[67] - Study B; Schrier 2002[68] - Study A ABCD USA Industry and other	Inclusion Criteria: Study A enrolled normotensive subjects (mean DBP between 80-89 mmHg) with type 2 diabetes aged between 40 and 74 years; Study B enrolled hypertensive (DBP ≥ 90 mmHg) subjects with type 2 diabetes aged between 40 and 74 years. Subjects were to be off antihypertensive medication at the randomization visit. Exclusion Criteria: Known allergy to dihydropyridines or ACE-I, MI or CVA	Study B: N=232 of which 150 (32%) had microalbuminuria and 82 (17%) had overt albuminuria of a total study population of 470. No further baseline details provided. Study A: N=162 of which 111 (23%) had microalbuminuria and 51 (11%) had overt albuminuria of a total study population of 480. No further	Intensive blood pressure control: Study A target DBP goal 10 mmHg below baseline DBP; Study B target DBP goal of 75 mmHg Moderate blood pressure control: target DBP goal between 80-89 mmHg. Initial medications included	Allocation Concealment : unclear Blinding: Estacio described as "blinded," unclear if double-blinded; blinded end point commitee Intention to Treat Analysis (ITT): unclear Withdrawals/Dropouts

Appendix Table C104. Overview of strict versus standard blood pressure control trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	within previous six months, coronary artery bypass surgery within previous three months, unstable angina pectoris within previous six months, Class III or IV New York Heart Association classification of CHF, demonstrated absolute need for ACE-I or calcium channel blockers, were receiving hemo- or peritoneal dialysis and/or had a serum creatinine >3mg/dL.	baseline details provided.	nisoldipine or enalapril. If single study medication did not achieve target BP, open-lable antihypertensives were added. Followup period: mean 5.3 years Study withdrawals (%): No details provided for CKD subgroups.	adequately described: yes (overall) for Study B.
Lewis, 1999[69] Multi-center USA Industry	Inclusion Criteria: Previously participated in the Study of ACEI in Diabetic Nephropathy, which had randomized 409 subjects who met inclusion criteria to captopril vs. placebo as follows: age 18-40 yr, type 1 diabetes mellitus ≥7 years with onset before age 30 yr, presence of diabetic retinopathy, urinary protein excretion ≥500 mg/24 h, serum creatinine ≤2.5 mg/dL. Current study participants further had to have been receiving coded medication from the earlier study when it terminated, and current serum creatinine level had to be <4 mg/dL. Patients were not required to have a history of hypertension Exclusion Criteria: Serum creatinine >4.0 mg/dL, serum potassium ≥6.0 mEq/L, white blood cell count <2,500/muL, or a medical or psychiatric problem that precluded the patient following the protocol or taking study medication. Documented acute myocardial infarction or overt coronary artery disease. Not enrolled if investigators at their site declined to participate in the study.	N= 129 Age (yr): 37 Gender (Male %): 47.3 Race/Ethnicity (%): White 94.6 BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR MAP (mm Hg): 96.0 Proteinuria (g/24h): 1.1 Serum creatinine (mg/dL): 1.3 Creatinine Clearance (ml/min/1.73m^2): NR Measured GFR (ml/min/1.73m^2): 63.0 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 HgbA1C (%): 10.8 History of HTN (%): 77 History of CAD (%): 0 History of CHF (%): NR History of MI (%): 0 History of Stroke (%): NR History of AKI (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Target MAP ≤92 mm Hg (n=63) Target MAP 100 -107 mm Hg (n=66) Ramipril used as primary antihypertensive agent to achieve target BP goals. If needed, other BP drugs could later be used, except other ACEI or ARB. All patients to restrict dietary protein to <1 gm/kg/day, and diabetes managed “in accord with the historical treatment schedule.” Followup period: Neither mean nor median duration reported. Study reported that all subjects were followed a minimum of 2 yr, but also reported that 26% (n=33) did not complete 2 yr followup. Study withdrawals (%): 16.3	Allocation Concealment Unclear Blinding: Unclear Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: No, n=5 not accounted for.

Appendix Table C104. Overview of strict versus standard blood pressure control trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Toto, 1995[70] Multi-center USA Funding Source Government and Industry	Inclusion Criteria: Age 25 to 73 yr, with hypertensive nephrosclerosis, DBP ≥95 mm Hg, serum creatinine >1.6 mg/dl, GFR of ≤70 ml/min/1.73 m^2, long-standing hypertension, an inactive urine sediment, a urinary protein excretion rate ≤2 g/day, and no physical or biochemical evidence for a humoral-mediated cause for hypertension. Among 87 eligible patients, only those 77 "responders" whose DBP was able to be lowered to ≤80 mm Hg during 3-6 month run-in were eligible for randomization. Exclusion Criteria: Patients with diabetes mellitus, a recent history (<4 months) of malignant hypertension, stroke or myocardial infarction, acute renal failure of any cause, analgesic abuse, polycystic kidney disease, systemic lupus erythematosus, scleroderma, rapidly progressive glomerulonephritis, evidence of significant hepatic impairment (AST and ALT greater than 2.5 x normal or serum total bilirubin >1.5 mg/dl), mental incapacity, pregnancy or lactation, primary aldosteronism, renovascular hypertension, pheochromocytoma, or a serum creatinine >7.0 mg/dl	N= 77 Age (yr): 55.7 Gender (Male %): 62.3 Race/Ethnicity (%): Black 75.3, Nonblack 24.7 BMI: 28.7 Systolic BP (mm Hg): 123 Diastolic BP (mm Hg): 76 MAP (mm Hg) 92 Proteinuria (mg/day): 359 Serum creatinine (mg/dL): 2.3 Creatinine Clearance (ml/min/1.73m^2): NR Measured GFR (ml/min/1.73m^2): 37.8 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 0 HgbA1C (%): NR History of HTN (%): 100 History of cardiovascular disease (any of angina, MI, CHF or stroke) (%): 36.4 History of AKI (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR	Conventional target DBP 85-95 mm Hg (n=35) Strict target DBP 65-80 mm Hg (n=42) Stepped use of BP drugs during run-in to achieve DBP <80 mm Hg (diuretic; BB; hydralazine or minoxidil; clonidine, alpha-methyldopa or alpha blocker). 2x2 factorial design to strict vs. conventional BP target and to enalapril vs. placebo. Followup period (Mean): 3.4 years Study withdrawals (%): No information reported	Allocation Concealment Unclear Blinding: Double Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Unclear
Peterson, 1995[71] Klahr, 1994[72] Greene, 1993[73] MDRD (Study A) Multicenter USA Government	Inclusion Criteria: Age of 18 to 70 years; serum creatinine level of 1.2 to 7.0 mg/dL for women and 1.4 to 7.0 mg/dL for men or a creatinine clearance less than 70 mL/min • 1.73 m^2; and mean arterial pressure of 125 mm Hg or less (Study A+B). Study A had patients with GFR of 25-55 mL/min • 1.73 m^2 Dietary protein intake ≥0.9 g/kg body	N= 585 (Reported baseline characteristics differed slightly between different study reports. For characteristics reported by multiple studies, results from the most recent report were used.) Age (yr): 52 Gender (Male %): 61.0	Low target MAP (≤92 mm Hg for patients ≤60 yr old, and ≤98 mm Hg for patients ≥61 yr old) Usual target MAP (≤107 mm Hg for patients ≤60 yr old, and ≤113 mm Hg for patients ≥61 yr old)	Allocation Concealment Unclear Blinding: Unclear Intention to Treat Analysis (ITT): Unclear Withdrawals/Dropouts adequately described: Yes

Appendix Table C104. Overview of strict versus standard blood pressure control trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	weight/day. Exclusion Criteria: Diabetes requiring insulin, proteinuria of 10 g/d or more, or body weight less than 80% or more than 160% of standard body weight, Pregnancy, history of renal transplant, chronic medical conditions or doubts about compliance	Race/Ethnicity (%): White 84.6, Black 9.1, Other 6.3 BMI: 27.6 Systolic BP (mm Hg): 131 Diastolic BP (mm Hg): 81 MAP (mm Hg): 98 Proteinuria (g/day): 0.9 Serum creatinine (mg/dL): 1.9 Creatinine Clearance (ml/min/1.73m^2): 50.4 Measured GFR (ml/min/1.73m^2): 38.6 Total cholesterol (mg/dL): 221 LDL cholesterol (mg/dL): 150 Diabetes (%): NR HgbA1C (%): NR History of HTN (%): 85.3 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR History of AKI (%): NR Peripheral arterial disease (%): NR Current smoker (%): 80	Followup period: Mean 2.2 yrs Study withdrawals (%): 1.9	
Shulman, 1989[74] HDFP Location United States Funding Source: Government	Inclusion Criteria: From general population subgroups of the United States. Recruited through 2 stage community based, screening program for high blood pressure in 14 U.S. communities. Adults, 30 to 69 years of age with an average home screening DBP of 95 mm Hg or above and a confirmed followup average diastolic pressure of 90 mm Hg or above. Exclusion Criteria: Only terminally ill and institutionalized persons were excluded. Treated hypertensives with	N=297 (subgroup analysis of subjects with baseline serum creatinine ≥1.7 mg/dl from overall study of N=10, 940) Age (yr): NR Gender (Male %): 68.4 Race/Ethnicity (%): White 40.4, Black 59.6 Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR MAP (mm Hg): NR CKD stage: NR	Stepped care (n= 5,485; of which n=159 had creatinine ≥1.7 mg/dl). Target goal DBP ≤90 mm Hg for those entering trial on BP drug treatment or with baseline DBP ≥100 mm Hg, or goal 10mm Hg DBP decrease if baseline DBP 90-99 mm Hg. Referred care (n=5,455; of which n=138 had creatinine ≥1.7 mg/dl)	Allocation Concealment Adequate Blinding: No (participants and clinic staff aware) Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: No

Appendix Table C104. Overview of strict versus standard blood pressure control trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	DBP below 95 were excluded.	Serum creatinine (mg/dL): NR Creatinine clearance (mL/min): NR Albuminuria: NR Proteinuria (1+ proteinuria, %): 35.0 (Measured in 89.6% of patients with creatinine ≥1.7 mg/dl and 91.2% in overall study. Among HDFP subjects with creatinine <1.7 mg/dl, an additional 597/9556 = 6.2% had at least 1+ proteinuria.) Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 15.8 History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	Followup period: 5 yrs Study withdrawals (%): Not reported	

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C105. Summary of study baseline characteristics, strict versus standard blood pressure control trials

Characteristic	Mean (Range) (unless otherwise noted)	Number of Trials Reporting
Patients randomized, n	2,914 (77-1094)	7
Age of subjects, years	52.8 (37-55.7)	5
Gender, male, %	63.2 (47.3-74.9)	6
Race/ethnicity, white, %	35.0 (0-94.6)	4
Race/ethnicity, black, %	67.3 (9.1-100)	4
Body Mass Index	29.5 (27.6-30.6)	3
Systolic blood pressure, mmHg	141.8 (123-150.5)	4
Diastolic blood pressure, mmHg	88.9 (76-95.5)	4
Mean arterial blood pressure, mmHg	106.1 (92-114)	5
Proteinuria, g/day	1.0 (0.36-2.85)	5
Serum creatinine, mg/dL	2.0 (1.3-2.7)	5
Creatinine clearance, ml/min/1.73m^2	46.2 (38.8-50.4)	2
GFR, ml/min/1.73m^2	42.9 (35.0-63.0)	5
Total cholesterol, mg/dl	219.7 (217.5-221)	2
LDL cholesterol, mg/dl	150	1
History of diabetes, %	11.0 (0-100)	4
% HbA_{1c}	10.8	1
History of hypertension (%)	94.7 (77-100)	5
History of cardiovascular Disease, %*	36.4	1
History of CHF, %	0	1
Current smoker, %	80	1

GFR = glomerular filtration rate; LDL = low density lipoprotein; CHF = congestive heart failure

*No study reported separate prevalence of coronary artery disease, myocardial infarction or stroke. However, one study (n=77) reported that 36.4% of participants had a history of either angina, myocardial infarction, congestive heart failure, or stroke.

Appendix Table C106. Clinical outcomes (outcomes part A), strict versus standard blood pressure control trials

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial infarction, Nonfatal n/N (%)		Stroke, Any n/N (%)	
	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP
Ruggenenti, 2005[66] REIN-2	2/169 (1.2)	3/169 (1.8)	1/169 (0.6)	2/169 (1.2)			1/169 (0.6)	1/169 (0.6)				
Wright, 2002[26] AASK	37/540 (6.9)	43/554 (7.8)										
Schrier 2002[68] - Study A, Estacio 2000[67] - Study B ABCD												
Lewis, 1999[69]												
Toto, 1995[70]	1/42 (2.4)	0/35										
Peterson, 1995[71] Klahr, 1994[72] MDRD, Study A	†NR	†NR	†NR	†NR								
Shulman, 1989[74] HDFP	56/159 (35.2)	57/138 (41.3)	32/159 (20.1)	33/138 (23.9)								

BP = blood pressure

*Study did not report the proportion of patients with all-cause mortality or cardiovascular mortality, but instead reported only the percentage of patients experiencing these outcomes per patient year of followup (1.6 vs. 1.9% for all-cause mortality and 0.6 vs. 0.7% for cardiovascular mortality events per patient year for the strict target BP vs. control target BP groups, respectively).

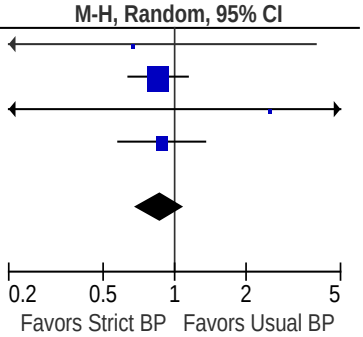
†Overall, study reported 30 deaths, including 18 cardiovascular deaths. It did not report the number of these events separately for each treatment group, though it stated that there were no significant differences in the number or causes of deaths between the two treatment groups.

Appendix Figure C21. Forest plots for strict versus standard blood pressure control trials

All-cause mortality

Study or Subgroup	Strict BP Events	Strict BP Total	Usual BP Events	Usual BP Total	Weight	Risk Ratio M-H, Random, 95% CI
Ruggenenti (REIN-2) 2005	2	169	3	169	1.8%	0.67 [0.11, 3.94]
Shulman (HDFP) 1989	56	159	57	138	66.5%	0.85 [0.64, 1.14]
Toto 1995	1	42	0	35	0.6%	2.51 [0.11, 59.79]
Wright (AASK) 2002	37	540	43	554	31.2%	0.88 [0.58, 1.35]
Total (95% CI)		**910**		**896**	**100.0%**	**0.86 [0.68, 1.09]**
Total events	96		103			

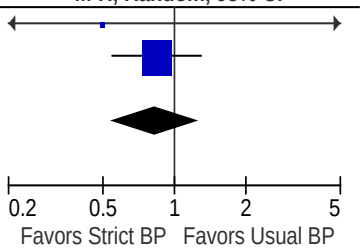
Heterogeneity: Tau² = 0.00; Chi² = 0.54, df = 3 (P = 0.91); I² = 0%
Test for overall effect: Z = 1.22 (P = 0.22)



Cardiovascular mortality

Study or Subgroup	Strict BP Events	Strict BP Total	Usual BP Events	Usual BP Total	Weight	Risk Ratio M-H, Random, 95% CI
Ruggenenti (REIN-2) 2005	1	169	2	169	3.1%	0.50 [0.05, 5.46]
Shulman (HDFP) 1989	32	159	33	138	96.9%	0.84 [0.55, 1.29]
Total (95% CI)		**328**		**307**	**100.0%**	**0.83 [0.54, 1.26]**
Total events	33		35			

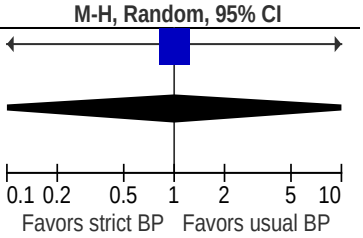
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 1 (P = 0.67); I² = 0%
Test for overall effect: Z = 0.87 (P = 0.38)



Myocardial infarction, fatal

Study or Subgroup	Strict BP Events	Strict BP Total	Usual BP Events	Usual BP Total	Weight	Risk Ratio M-H, Random, 95% CI
Ruggenenti (REIN-2) 2005	1	169	1	169	100.0%	1.00 [0.06, 15.86]
Total (95% CI)		**169**		**169**	**100.0%**	**1.00 [0.06, 15.86]**
Total events	1		1			

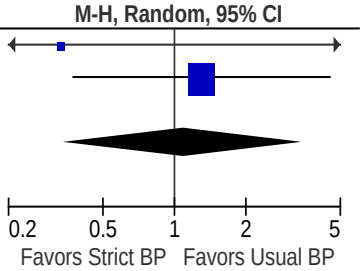
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



Stroke or CVA, fatal

Study or Subgroup	Strict BP Events	Strict BP Total	Usual BP Events	Usual BP Total	Weight	Risk Ratio M-H, Random, 95% CI
Ruggenenti (REIN-2) 2005	0	169	1	169	13.2%	0.33 [0.01, 8.12]
Shulman (HDFP) 1989	6	159	4	138	86.8%	1.30 [0.38, 4.52]
Total (95% CI)		**328**		**307**	**100.0%**	**1.09 [0.34, 3.47]**
Total events	6		5			

Heterogeneity: Tau² = 0.00; Chi² = 0.61, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 0.14 (P = 0.89)



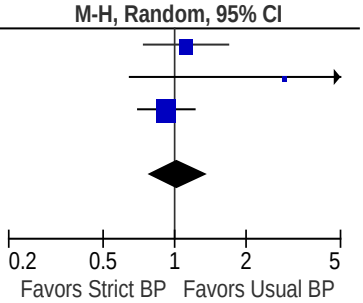
Appendix Figure C21. Forest plots for strict versus standard blood pressure control trials (continued)

End-stage renal disease

Study or Subgroup	Strict BP Events	Strict BP Total	Usual BP Events	Usual BP Total	Weight	Risk Ratio M-H, Random, 95% CI
Ruggenenti (REIN-2) 2005	38	169	34	169	36.1%	1.12 [0.74, 1.69]
Toto 1995	7	42	2	35	3.6%	2.92 [0.65, 13.15]
Wright (AASK) 2002	81	540	90	554	60.3%	0.92 [0.70, 1.22]
Total (95% CI)		**751**		**758**	**100.0%**	**1.03 [0.77, 1.38]**
Total events	126		126			

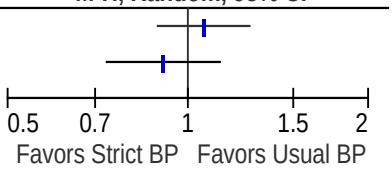
Heterogeneity: Tau² = 0.02; Chi² = 2.55, df = 2 (P = 0.28); I² = 21%

Test for overall effect: Z = 0.21 (P = 0.84)



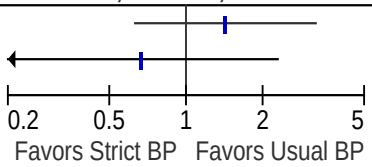
Composite renal outcome (see Table 110 for definitions)

Study or Subgroup	Strict BP Events	Strict BP Total	Usual BP Events	Usual BP Total	Risk Ratio M-H, Random, 95% CI
Wright AASK 2002 A	173	540	167	554	1.06 [0.89, 1.27]
Wright AASK 2002 B	118	540	133	554	0.91 [0.73, 1.13]



Composite renal outcome (see Table 110 for definitions)

Study or Subgroup	Strict BP Events	Strict BP Total	Usual BP Events	Usual BP Total	Risk Ratio M-H, Random, 95% CI
Toto 1995 A	12	42	7	35	1.43 [0.63, 3.23]
Toto 1995 B	4	42	5	35	0.67 [0.19, 2.29]



Appendix Table C107. Clinical outcomes (outcomes part B), strict versus standard blood pressure control trials

Study	Stroke, Nonfatal n/N (%)		Stroke, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) n/N (%)		Composite Vascular Outcome n/N (%)*	
	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP
Ruggenenti, 2005[66] REIN-2			0/169	1/169 (0.6)			(A) NR; (B) 0/169	(A) NR; (B) 0/169		
Wright, 2002[26] AASK									**NR	**NR
Schrier 2002[68] - Study A, Estacio 2000[67] - Study B ABCD										
Lewis, 1999[69]										
Toto, 1995[70]										
Peterson, 1995[71] Klahr, 1994[72] MDRD, Study A										
Shulman, 1989[74] HDFP			6/159 (3.8)	4/138 (2.9)						

CHF = congestive heart failure; BP = blood pressure; NR = not reported

*See Composite vascular outcome definitions table

**Study did not report the proportion of patients with a composite vascular event (defined as cardiovascular mortality or first cardiovascular hospitalization), but instead reported only the percentage of patients experiencing a composite vascular outcome per patient year of followup (2.3 versus 2.7% per patient year for the strict versus control target blood prssure treatment groups).

Appendix Table C108. Composite vascular outcome definitions, strict versus standard blood pressure control trial

Study	Definition
Wright, 2002[26] AASK	"Cardiovascular event" defined as cardiovascular mortality or first cardiovascular hospitalization.

Appendix Table C109. Clinical renal outcomes (outcomes part C), strict versus standard blood pressure control trials

Study	End Stage Renal Disease n/N (%)		Doubling of Serum Creatinine n/N (%)		Halving of GFR n/N (%)		Progression from Micro- to Macroalbuminuria n/N (%)		Composite Renal Outcome n/N (%)*	
	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP
Ruggenenti, 2005[66] REIN-2	38/169 (22.5)	34/169 (20.1)								
Wright, 2002[26] AASK	81/540 (15.0)	90/554 (16.2)							**(A)173/540 (32.0) (B) 118/540 (21.9) (C) NR	**(A)167/554 (30.1) (B) 133/554 (24.0) (C) NR
Estacio 2000[67] - Study B ABCD††							12/73 (16.4)	18/77 (23.4)		
Lewis, 1999[69]	†NR	†NR								
Toto, 1995[70]	7/42 (16.7)	2/35 (5.7)							(A)12/42 (28.6) (B) 4/42 (9.5)	(A) 7/35 (20.0) (B) 5/35 (14.3)
Peterson, 1995[71] Klahr, 1994[72] MDRD, StudyA	§NR	§NR			#NR	#NR				
Shulman, 1989[74] HDFP study			***NR	***NR						

GFR = glomerular filtration rate; BP = blood pressure; NR = not reported; ESRD = end stage renal disease

*See Composite renal outcome definitions table

**Study reported that 263 participants experienced the composite endpoint of (C) halving of GFR or ESRD, but did not report results for this endpoint separately for the two treatment groups.

†Study reported that 12 patients reached ESRD, but didn't report this result separately for the two treatment groups.

§Study also reported that 12 participants developed end stage renal disease, but like the Lewis study did not report this result separately for the two treatment groups.

#Study reported that 60 patients overall reached a study stopping point due to "rapidly declining glomerular filtration rate." Though study did not report this result separately for the two treatment groups, it did state that there was no significant difference between the results for the two groups.

***In 59.6% of participants with baseline creatinine $\geq$1.7 mg/dl, study reported outcome of end of follow-up serum creatinine $\geq$2.0 mg/dl and at least 25% above the baseline level (29/106 = 27.4% for strict BP group, and 19/71 = 26.8% for control target BP group).

††Schrier 2002 - Study A reported that a significantly lower percentage of patients with microalbuminuria at baseline in the intensive therapy group progressed to overt albuminuria in comparison to the moderate therapy group (p=0.028).

Appendix Table C110. Composite renal outcome definitions, strict versus standard blood pressure control trials

Study	Definition
Wright, 2002[26] AASK	Study defined three composite renal endpoints, including: (A) 50% or 25 mL/min reduction in GFR, ESRD (dialysis or transplantation), or death; (B) ESRD or death; and (C) 50% or 25 mL reduction in GFR, or ESRD
Toto, 1995[70]	Study defined two composite renal endpoints, including: (A) 50% decline in GFR, doubled serum creatinine, ESRD, or death; and (B) 50% decline in GFR or doubled serum creatinine.

GFR = glomerular filtration rate; ESRD = end stage renal disease

Appendix Table C111. Study withdrawals and adverse events (outcomes part D), strict versus standard blood pressure control trials

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Event: Any n/N (%)		Serious Adverse Event: Any Leading to Withdrawal n/N (%)		Adverse Event: Any n/N (%)		Adverse Event: Any Specific n/N (%)		Renal Adverse Events: Any, n/N (%)	
	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP
Ruggenenti, 2005[66] REIN-2	22/169 (13.0)	30/169 (17.8)	37/169 (21.9)	25/169 (14.8)	6/169 (3.6)	3/169 (1.8)			Hyperkalemia 0/169	Hyperkalemia 0/169		
Wright, 2002[26] AASK	0/540†	0/554†							‡Hyperkalemia: 0/540 Cough: 295/540 (54.6)*	‡Hyperkalemia: 4/554 (0.7) Cough: 260/554 (47.0)		
Schrier 2002[68] - Study A, Estacio 2000[67] - Study B ABCD												
Lewis, 1999[69]	§NR	§NR			§NR	§NR			Postural hypotension: 11/63 (17.5)* Edema: 4/63 (6.3)* Bronchitis: 2/63 (3.2)* Sinusitis: 3/63 (4.8)*	Postural hypotension: 4/66 (6.1) Edema: 10/66 (15.2) Bronchitis: 7/66 (10.6)* Sinusitis: 13/66 (19.7)*		
Toto, 1995[70]												
Peterson, 1995[71] MDRD, StudyA	#NR	#NR										

Appendix Table C111. Study withdrawals and adverse events (outcomes part D), strict versus standard blood pressure control trials (continued)

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Event: Any n/N (%)		Serious Adverse Event: Any Leading to Withdrawal n/N (%)		Adverse Event: Any n/N (%)		Adverse Event: Any Specific n/N (%)		Renal Adverse Events: Any, n/N (%)	
	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP	Strict Target BP	Control Target BP
Shulman, 1989[74] HDFP											**Death due to renal disease: 9/159 (5.7)	**Death due to renal disease: 12/138 (8.7)

BP = blood pressure; NR = not reported; GFR = glomerular filtration rate
*p< 0.05
†Study reported no withdrawals, but described 8.1% of subjects with no GFR measurement in the final year of follow-up (n=42/540 and 47/554 from the strict and control target treatment groups, respectively) as not active participants at study end.
‡Study reported additional specific adverse events, all of which were not statistically different in incidence between strict and control target blood pressure treatment groups, including: angioedema (3.5 vs. 5.4%), shortness of breath (48.4 vs. 45.8%), syncope (6.3 vs. 5.2%), dizziness (53.4 vs. 49.0%), lightheadedness (51.2 vs. 49.2%), edema (55.1 vs. 54.2%), and sexual dysfunction (29.6 vs. 27.1%).
§Study reported 21/129 (16.3%) withdrawals overall, including 3 withdrawals for adverse events, but didn't specify either of these outcomes by treatment group.
#Study reported 11/585 (1.9%) participants lost to followup overall, but did not report results by treatment group.
**Deaths attributed to renal disease were those with ICD codes 580-599, which includes: acute or chronic glomerulonephritis, nephrotic syndrome, acute or chronic renal failure, hydronephrosis, urolithiasis, urethritis, urethral stricture, urinary tract infection, and other disorders of the kidneys and urinary tract.

Appendix Table C112. Overview of low protein diet versus usual protein diet and other dietary intervention trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Koya, 2009[75] (Low-Protein Diet Study Group) Japan Funding Source: Government	Inclusion Criteria: Japanese type 2 diabetics (at least 5 years duration); treated by diet or diet plus oral hypoglycemics or insulin injection; ages 30 to 70; urinary protein excretion >1g/day but <10g/day; urinary albumin excretion rate >200µg/min at least twice in 1 yr period; serum creatinine <176µmol/l; at least simple diabetic retinopathy; on normal-protein diet (1.2 g/kg/day) Exclusion Criteria: Type 1 diabetes; other renal diseases, body weight <80% of ideal; clinically significant illness such as CHF, hepatic disease, recent MI and stroke, urinary tract infection; current treatment with low protein diet (0.8 g/kg/day) and/or ACEI or ARB	N=112 Age (yr): 56.9 Gender (Male %): 58.9 Race/Ethnicity (%): NR Weight (kg): 63.4 BMI: 24.6 Systolic BP (mm Hg): 137.5 Diastolic BP (mm Hg): 77.0 CKD stage: NR Serum creatinine (mg/dL): 1.1 Creatinine clearance (mL/min): NR Albuminuria (µg/min): 507.5 Proteinuria (g/day): 1.15 Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): 62.3 (MDRD formula) HbA_{1c} (%): 7.65 Total cholesterol (mg/dL): 222.4 LDL cholesterol (mg/dL): NR Diabetes (%): 100% (by inclusion criteria) History of HTN (%): 65.8 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): 0 Peripheral arterial disease (%): NR History of MI (%): NR (no recent) History of Stroke (%): NR (no recent) Current smoker (%): NR History of AKI (%): NR	Low-protein diet (0.8 g/kg/day); n=56 Normal-protein diet (1.2 g/kg/day); n=56 All participants met with dietician every 3 months, at which time their diet was modified as necessary to achieve assigned treatment group protein intake target. Followup period: 1 to 5 years (approximately 3.5 years) Study withdrawals (%): 21.4	Allocation Concealment: Adequate (central location) Blinding: Participants and investigators were not blinded; unclear if central laboratory outcomes assessors blinded Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes

Appendix Table C112. Overview of low protein diet versus usual protein diet and other dietary intervention trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Dussol, 2005[76] France Funding Source: Government	Inclusion Criteria: Recruited from Endocrinology Unit of 3 hospitals; ages 18 to 75 years; type 1 or 2 diabetes; either pathologic or clinical evidence of diabetic nephropathy (diabetes duration >10 yrs, diabetic retinopathy, no evidence of other kidney or urinary tract disease); at least two microalbuminuria levels >30 mg/day (incipient nephropathy) or macroalbuminuria levels >300 mg/day (overt nephropathy)* Exclusion Criteria: absence of nephropathy; ESRD (GFR<15 mL/min); pregnancy; cachexy, body mass index >33 *Note: 87% microalbuminuria	N=63 (baseline data presented for 47 completers only) Age (yr): 57.9 Gender (Male %): 83.0 Race/Ethnicity (%): NR Weight: 79.5 kg BMI: 27.5 Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Mean BP (mm Hg): 98.9 CKD stage: NR Serum creatinine (mg/dL): 1.1 Creatinine clearance (mL/min): NR Albuminuria (mg/d): 366 (320 for n=41 with microalbuminuria; 680 for n=6 with microalbuminuria) Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): 85.7 HbA_{1c} (%): 8.1 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): NR Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): 14.9 History of AKI (%): NR	Low protein diet (0.8 g/kg/day, isocaloric). Received dietician telephone call every 6 weeks to counsel and reinforce dietary instructions; n=30 Usual protein diet (no higher than 1.2 g/kg/day); n=33 All participants in both groups received either ACEI or ARB treatment at study onset and throughout diet treatment course. Followup period: 2 years Study withdrawals (%): 25.4	Allocation Concealment: Unclear Blinding: None Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes
Kopple, 1997[77] Peterson, 1995[71] Klahr, 1994[72] Greene, 1993[73] Modification of Diet in Renal Disease (MDRD) Study A only	Inclusion Criteria: age 18-70 years; serum creatinine 1.4-7.0 mg/dl (men) or 1.2-7.0 mg/dl (women) or other objective evidence of kidney disease; mean arterial pressure (MAP) ≤125 mmHg; GFR 25-55 ml/min/1.73m^2; urinary protein excretion <10g/day; protein intake >0.90g/kg/day	N=585 (end of baseline values reported where available) Age (yr): 52.6 Gender (Male %): 61.0 Race/Ethnicity (%): 84.6 white, 9.1 black, 4.3 Hispanic, 2.1 other Weight: 81.0 kg BMI: 27.6 Systolic BP (mm Hg): 131	Low protein diet (0.58g/kg/day); n=291 (140 to usual MAP, 151 to low MAP) Usual diet (1.3 g/kg/day); n=294 (145 to usual MAP, 149 to low MAP)	Allocation Concealment: Adequate Blinding: Double (for followup GFRs) Intention to Treat Analysis (ITT): Unclear

Appendix Table C112. Overview of low protein diet versus usual protein diet and other dietary intervention trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
(GFR 25 to 55 ml/min/1.73m^2) United States Funding Source: Government	Exclusion Criteria: insulin-dependent diabetes or fasting serum glucose >200 mg/dl; dialysis; kidney transplant recipient; lactating or pregnant woman or planning to become pregnant in time frame of study; doubtful compliance; body weight <80% or >160% of standard weight; serum albumin <3.0g/dl; selected renal disorders (UTI, renal artery stenosis, branched or staghorn calculi); serious medical conditions (NYHA class 3 or 4 HF, lung disease, liver disease, GI disease, chronic systemic infection, collagen vascular disease, frequent hospitalization or disability); immunosuppressive agents (including corticosteroids in excess of replacement dosage for ≥2 months/yr); gold or penicillamine in past month; >20 tablets salicylates per week; other NSAIDS >3 times/week in past 2 months; investigational drugs; allergy to iothalamate or iodine; inability or unwilling to give consent	Diastolic BP (mm Hg): 81 Mean arterial pressure (mm Hg): 98 CKD Stage: NR Serum creatinine (mg/dL): 1.9 Creatinine clearance (ml/min/1.73m^2): 50.4 Albuminuria: NR Proteinuria (g/day/1.73m^2): 0.18 (Females), 0.35 (Males) Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): 38.6 HbA_{1c} (%): NR Total cholesterol (mg/dL): 218.2 LDL cholesterol (mg/dL): 148.4 Diabetes (%): NR Diabetic nephropathy (%): 2.9 History of HTN (%): 85.3 History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): 13.7 History of AKI (%): NR	Followup period: mean 2.2 years Study withdrawals (%): 1.9% lost to followup; 14.3% reached stop point including 10% with rapidly declining GFR, 2% with renal failure and 2% with other serious medical condition NOTE: 2 x 2 factorial design with usual (MAP=107 mmHg) or low (MAP=92mmHg) goal	Withdrawals/Dropouts adequately described: Yes
D'Amico, 1994[78] Italy Funding Source: Government	Inclusion Criteria: Consecutive patients with chronic renal insufficiency attending outpatient clinic; age >18; creatinine clearance between 70 and 15 ml/min stable or moderate decline over past 3 months; no evidence of potentially reversible diseases; not affected by systemic illness (including diabetes); no nephrotic syndrome (proteinuria >3g/24h and serum albumin <2.5 g/dl); no drugs in past 6 months that	N=134 (baseline data reported for 128 completers only) Age (yr): 54 Gender (Male %): 61 Race/Ethnicity (%): NR Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Mean BP (mmHg): 115 CKD stage: NR Serum creatinine (mg/dL): NR	Low protein diet (0.6 g/kg lean body weight/day) plus energy supplement of 35 kcal/kg daily; phosphate restricted to 0.26 mmol/kg; n=63 (analyzed) Control (1.0 g/kg lean body weight/day) plus 30 kcal/kg/day; phosphate restricted to 0.42 mmol/kg); n=65 (analyzed)	Allocation Concealment Unclear Blinding: None Intention to Treat Analysis (ITT): No Withdrawals/ Dropouts adequately described: No

Appendix Table C112. Overview of low protein diet versus usual protein diet and other dietary intervention trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	might alter natural history of disease; informed consent given Exclusion Criteria: none stated	Creatinine clearance (mL/min): 33 Albuminuria: NR Proteinuria (g/24 hr): 1.5 Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 0 (by inclusion criteria) History of HTN (%): NR Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	Followup period: mean of 2.3 years Study withdrawals (%): 4.5% (6 withdrew at beginning of trial – group not specified)	
Locatelli, 1991[79] Northern Italy Cooperative Study Group Italy Funding Source: Not reported	Inclusion Criteria: ages 18 to 65 years; outpatients; plasma creatinine from 1.5 (men) or 1.35 (women) to 7.0 mg/dl, GFR <60ml/min (Cockroft formula); written consent Exclusion Criteria: nephrotic syndrome (serum albumin <2.5 g/dl, proteinuria >3 g/l); ideal body weight <45 kg or >90 kg; diabetes; recent MI; acute renal failure; acute obstruction and infection of urinary tract; systemic diseases; previous gastrointestinal resection surgery; doubling of plasma creatinine during 3 month preliminary observation period	N=456 Age (yr): 48.5 Gender (Male %): 54.2 Race/Ethnicity (%): NR Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR CKD stage: NR Serum creatinine (mg/dL): NR Creatinine clearance (mL/min): NR Albuminuria: NR Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 0 (by exclusion criteria) History of HTN (%): NR Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR	Low protein diet (0.6 g/kg ideal body weight) with energy supplement of 35 kcal/kg daily; phosphate restricted to 0.26 mmol/kg; n=230 Control (1.0 g/kg/ideal body weight) with energy supplement of 30 kcal/kg daily; phosphate restricted to 0.42 mmol/kg; n=226 Followup period: 2 years or until endpoint reached Study withdrawals (%): 15.6	Allocation Concealment Adequate Blinding: Not reported Intention to Treat Analysis (ITT): No Withdrawals/ Dropouts adequately described: Yes

Appendix Table C112. Overview of low protein diet versus usual protein diet and other dietary intervention trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
		Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): 0 (by exclusion criteria)		
Rosman, 1989/1984[80,81] United Kingdom Funding Source: Foundation	Inclusion Criteria: nephrology outpatients who visited clinic between 1/1/82 and 4/1/84; creatinine clearance between 10 and 60 ml/min/1.73m^2 or less; no lethal disease Exclusion Criteria: lupus erythematosus, active vasculitis and Wegener's disease	N=136 in 1984 publication (reported on subjects who entered study before 1/1/1984); N=151 in 1989 publication (reported on subjects who entered study before 4/1/1984). Inclusion here only of subgroup with creatinine clearance >30 and ≤60 ml/min/1.73m^2. Baseline data reported only for a subset of participants with 18 month followup data in 1984 paper, with sample size not stated: Weight: 72 kg (low protein); 70 kg (usual) Systolic BP (mm Hg): 140 (both groups) Diastolic BP (mm Hg): 90 (both groups) Serum albumin (g/l): 42 (both groups) Creatinine excretion (mmol/l in 24 hr): 10.4 (low protein), 11.0 (usual)	Low protein diet (0.6g/kg/day); n=74 Usual diet; n=77 NOTE: all patients received a vitamin and trace element preparation Followup period: minimum of 1.5 years for 1984 publication; minimum of 3 years for 1989 publication Study withdrawals (%): 4% for n=153 with 3 years followup (1989 publication)	Allocation Concealment: Unclear Blinding: None reported Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: No
Facchini, 2003[82] United States Funding Source: Not reported	Inclusion Criteria: Type 2 diabetes referred to nephrology clinics for renal failure (GFR 15-75 ml/min) and otherwise unexplained proteinuria (350-12,000 mg/day) Exclusion Criteria: None stated	N=191 Age (yr): 59.5 Gender (Male %): 53.0 Race/Ethnicity (%): NR Weight: 78 kg reported for CR-LIPE group, 79 kg for Control (for subset of completers, number per group not reported) BMI: 28 Systolic BP (mm Hg): 156 Diastolic BP (mm Hg): 88 CKD stage: NR Serum creatinine (mg/dL): 1.84 Creatinine clearance (mL/min): NR Albuminuria: NR Proteinuria: 2,469 mg/day Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): 63.0 HbA_{1c} (%): 7.6	50% carbohydrate restricted, low-iron-available, polyphenol-enriched diet (CR-LIPE)† (suggested macronutrient composition: 35% CHO, 30% fat, 25-30% protein, 5-10% ethanol); n=100 Control (protein restricted (0.8g/kg/day) (suggested macronutrient composition: 65% CHO, 25% fat, 10% protein, 0% ethanol); n=91 Followup period: mean of 3.9 years	Allocation Concealment: Unclear ("concealed" but no details) Blinding: Study personnel blinded to aim of study; outcomes unclear Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes

Appendix Table C112. Overview of low protein diet versus usual protein diet and other dietary intervention trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
		Total cholesterol: 5.6 mmol/l for subset of completers with fasting lipids LDL cholesterol: 3.6 mmol/l for subset of completers with fasting lipids Diabetes (%): 100 History of HTN (%): NR Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	Study withdrawals (%): 11 †Intended to complement angiotensin system inhibition and pharmacotherapy for glycemic and blood pressure control	
Williams, 1991[83] United Kingdom Funding Source: Foundation	Inclusion Criteria: adults <70 yrs attending 1 of 2 hospital clinics; chronic renal failure (plasma creatinine >150 µmol/l for males, >150 µmol/l for women) with evidence of deteriorating renal function on serial plasma creatinine or creatinine clearance estimations; plasma creatinine <900 µmol/l and plasma phosphate < 2 µmol/l Exclusion Criteria: patients receiving active therapy for their primary disease; proven malignancy; psychologically unstable or noncompliant; dietary protein <0.8 g/kg/day; obese patients on a reducing diet	N=98 Age (yr): 45.0 Gender (Male %): 66.3 Race/Ethnicity (%): NR Weight: 71.3 kg BMI: NR Systolic BP (mm Hg): 151 Diastolic BP (mm Hg): 90 CKD stage: NR Plasma creatinine (µmol/l): 398.1 Creatinine clearance (mL/min/1.73m^2): 26.8 Albuminuria: NR Proteinuria (g/24h): 3.15 Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): NR History of HTN (%): NR Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR	Dietary protein (0.6g/kg/day) and phosphate (800 mg/day) restriction; n=33 Phosphate restriction (1000 mg/day plus phosphate binders with each meal); n=30 Unrestricted (at least 0.8 g/kg/day protein); n=32 Followup period: mean 1.6 years Study withdrawals (%): 5.3 within 3 months	Allocation Concealment: Adequate Blinding: None Intention to Treat Analysis (ITT): No Withdrawals/ Dropouts adequately described: No

Appendix Table C112. Overview of low protein diet versus usual protein diet and other dietary intervention trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
		Current smoker (%): NR History of AKI (%): NR		
Samuelsson, 1997[84] Sweden Funding Source: Government, Foundation	Inclusion Criteria: nondiabetic primary renal disease; moderately advanced renal insufficiency (GFR 10 to 70 ml/min/1.73m^2) Exclusion Criteria: none stated	N=57 Age (yr): 51.3 Gender (Male %): 75 Race/Ethnicity (%): NR Weight (kg): 81.4 BMI: 26.2 Systolic BP (mm Hg): 136.5 Diastolic BP (mm Hg): 84.0 CKD stage: NR Serum creatinine (mg/dL): 2.4 Creatinine clearance (mL/min): NR Albuminuria: 0.95g/24 hr Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): 35.5 HbA_{1c} (%): NR Total cholesterol (mg/dL): 243.6 LDL cholesterol (mg/dL): 170.2 Diabetes (%): 0 (by inclusion criteria) History of HTN (%): NR Dyslipidemia (%): unclear History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	Triglyceride lowering diet (with dietary counseling), n=29 Gemfibrozil - 300mg/day increased to 300 mg twice/day after 1 month with further titration up to 450 mg twice/day at 3 months if triglyceride levels was above 1.7 mmol/l (no dietary counseling); n=28 Followup period: 1 year Study withdrawals (%): 15.8	Allocation Concealment Unclear Blinding: None Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C113. Summary of study baseline characteristics for low protein diet versus usual protein diet and other dietary intervention trials

Characteristic	Mean (Range) (unless otherwise noted)	Number of Trials Reporting
Low protein versus usual protein diet trials (n=6)		
Total number of patients evaluated	1480 (63-585)	6
Age of patients, years	51.9 (48.5-57.9)	5
Gender, male, %	59.3 (54.2-83.0)	5
Race/ethnicity, white, %	85.0	1
Body Mass Index	27.1 (24.6-27.6)	3
Patients with diabetes, %	21.4 (0-100)	4
Diabetic nephropathy trials, number of patients	159 (47-112)	2
% HbA_{1c} in patients with diabetes	7.8 (7.65-8.1)	2
Estimated or measured GFR, ml/min/1.73m^2	45.1 (38.6-85.7)	3
Serum creatinine, mg/dL	1.8 (1.1-1.9)	2
Creatinine clearance, ml/min/1.73m^2	47.3 (33-50.4)	2
Albumin excretion rate, µg/min	507.5	1
Albuminuria, mg/24 h	366.0	1
Systolic blood pressure, mm Hg	133.3 (131.0-140.0)	3
Diastolic blood pressure, mm Hg	81.9 (77.0-90.0)	3
Patients with hypertension, %	82.2 (66.1-85.3)	2
Patients with cardiovascular disease, %	NR	NR
Low protein diet versus other diets (n=2)		
Total number of patients evaluated	289 (98-191)	2
Age of patients, years	54.6 (45-59.5)	2
Gender, male, %	56.7 (52.9-64.3)	2
Race/ethnicity, white, %	NR	NR
Body Mass Index	28	1
Patients with diabetes, %	100	1
Diabetic nephropathy trials, number of patients	191	1
% HbA_{1c} in patients with diabetes	7.6	1
Estimated or measured GFR, ml/min/1.73m^2	63	1
Serum creatinine, mg/dL	1.84	1
Creatinine clearance, ml/min/1.73m^2	NR	NR
Albumin excretion rate, µg/min	NR	NR
Albuminuria, mg/24 h	NR	NR
Systolic blood pressure, mm Hg	154.3 (151-156)	2
Diastolic blood pressure, mm Hg	88.7 (88-90)	2
Patients with hypertension, %	NR	NR
Patients with cardiovascular disease, %	NR	NR
Low triglyceride diet versus gemfibrozil (n=1)		
Total number of patients evaluated	57	1
Age of patients, years	51.3	1
Gender, male (%)	75.4	1
Race/ethnicity, white (%)	NR	NR
Body Mass Index	26.2	1
Patients with diabetes (%)	0	1
Estimated or measured GFR (ml/min/1.73m^2)	35.5	1
Serum creatinine (mg/dL)	2.4	1
Creatinine clearance (ml/min/1.73m^2)	NR	NR
Albumin excretion rate (µg/min)	NR	NR
Albuminuria (mg/24 h)	950.0	1
Systolic blood pressure (mm Hg)	136.5	1
Diastolic blood pressure (mm Hg)	84	1
Patients with hypertension (%)	NR	NR
Patients with cardiovascular disease, %	NR	NR

*NR=Not reported; GFR = glomerular filtration rate

Appendix Table C114. Clinical outcomes (outcomes part A), low protein diet versus usual protein diet and other dietary intervention trials

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke, Any n/N (%)	
Low protein diet versus usual protein diet trials (n=6)												
	Low Protein	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**
Koya, 2009[75]	1/47 (2.1)	1/41 (2.4)					0/47	1/41 (2.4)				
Dussol, 2005[76]												
Kopple, 1997[77]	5/291 (1.7)	10/294 (3.4)	4/291 (1.4)	5/294 (1.7)								
Peterson, 1995[71]												
Klahr, 1994[72]												
Greene, 1993[73]												
MDRD												
D'Amico, 1994[78]												
Locatelli, 1991[79]	2/230 (0.9)	3/226 (1.3)										
Rosman, 1989/1984[80,81]	4/74 (5.4)	7/77 (9.1)										
Low protein diet versus other diet trials (n=2)												
	Low Protein	**Other Diet**	**Low Protein**	**Other Diet**	**Low Protein**	**Other Diet**	**Low Protein**	**Other Diet**	**Low Protein**	**Other Diet**	**Low Protein**	**Other Diet**
Facchini, 2003[82]	14/79 (17.7)	8/91 (8.8)										
Williams**, 1991[83]	†1/31 (3.0)	†Lo-Phos: 4/29 (13.3); †Control: 1/29 (3.1)										
Low triglyceride diet versus gemfibrozil (GF) trials (n=1)												
	Low TG Diet	**GF**	**Low TG Diet**	**GF**	**Low TG Diet**	**GF**	**Low TG Diet**	**GF**	**Low TG Diet**	**GF**	**Low TG Diet**	**GF**
Samuelsson, 1997[84]												

GF = gemfibrozil; TG = triglyceride

* $p < 0.05$ versus control

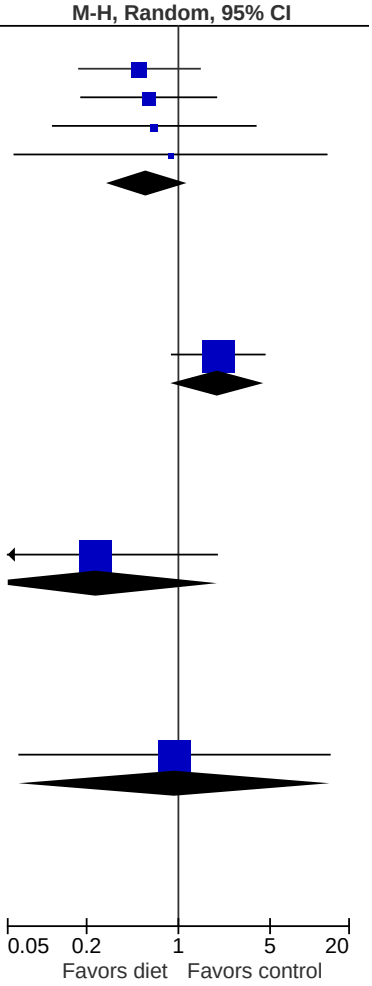
†Study also reported one death that occurred during the first 3 months of post-randomization followup, that they excluded from outcomes analyses, and for which they didn't report original treatment group assignment.

**Study compared a low protein and low phosphate diet to two different diets, a low phosphate diet, and a usual protein/usual phosphate diet.

Appendix Figure C22. Forest plots for low protein diet versus usual protein diet and other dietary intervention trials

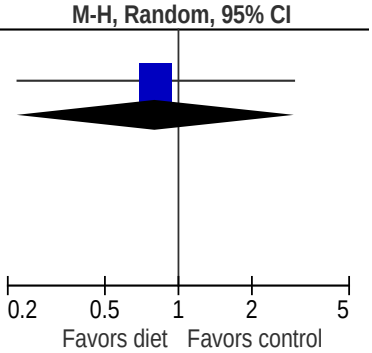
All-cause mortality

Study or Subgroup	Diet Events	Diet Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
9.1.1 Low protein diet versus usual protein diet						
Kopple 1997	5	291	10	294	43.4%	0.51 [0.17, 1.46]
Rosman 1989	4	74	7	77	34.7%	0.59 [0.18, 1.95]
Locatelli 1991	2	230	3	226	15.4%	0.66 [0.11, 3.88]
Koya 2009	1	47	1	41	6.5%	0.87 [0.06, 13.51]
Subtotal (95% CI)		**642**		**638**	**100.0%**	**0.58 [0.29, 1.16]**
Total events	12		21			
Heterogeneity: Tau² = 0.00; Chi² = 0.17, df = 3 (P = 0.98); I² = 0%						
Test for overall effect: Z = 1.54 (P = 0.12)						
9.1.2 Low protein versus other diet						
Facchini 2003	14	79	8	91	100.0%	2.02 [0.89, 4.55]
Subtotal (95% CI)		**79**		**91**	**100.0%**	**2.02 [0.89, 4.55]**
Total events	14		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.69 (P = 0.09)						
9.1.3 Low protein/low phosphate diet versus low phosphate diet						
Williams 1991	1	31	4	29	100.0%	0.23 [0.03, 1.97]
Subtotal (95% CI)		**31**		**29**	**100.0%**	**0.23 [0.03, 1.97]**
Total events	1		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.34 (P = 0.18)						
9.1.4 Low protein/low phosphate versus usual protein diet						
Williams 1991	1	31	1	29	100.0%	0.94 [0.06, 14.27]
Subtotal (95% CI)		**31**		**29**	**100.0%**	**0.94 [0.06, 14.27]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.05 (P = 0.96)						



Cardiovascular mortality

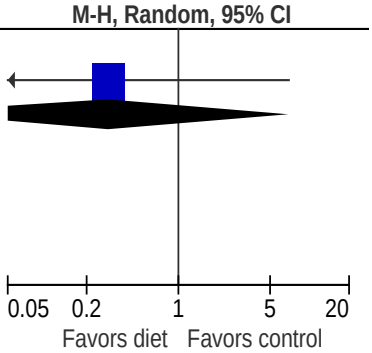
Study or Subgroup	Diet Events	Diet Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
9.2.1 Low protein diet versus usual protein diet						
Kopple 1997	4	291	5	294	100.0%	0.81 [0.22, 2.98]
Subtotal (95% CI)		**291**		**294**	**100.0%**	**0.81 [0.22, 2.98]**
Total events	4		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.32 (P = 0.75)						



Appendix Figure C22. Forest plots for low protein diet versus usual protein diet and other dietary intervention trials (continued)

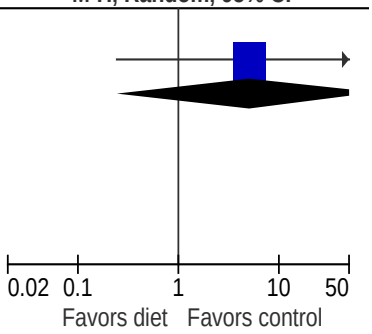
Myocardial infarction, fatal

Study or Subgroup	Diet Events	Diet Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
9.9.1 Low protein diet versus usual protein diet						
Koya 2009	0	47	1	41	100.0%	0.29 [0.01, 6.97]
Subtotal (95% CI)		**47**		**41**	**100.0%**	**0.29 [0.01, 6.97]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.76 (P = 0.45)						



Stroke, nonfatal

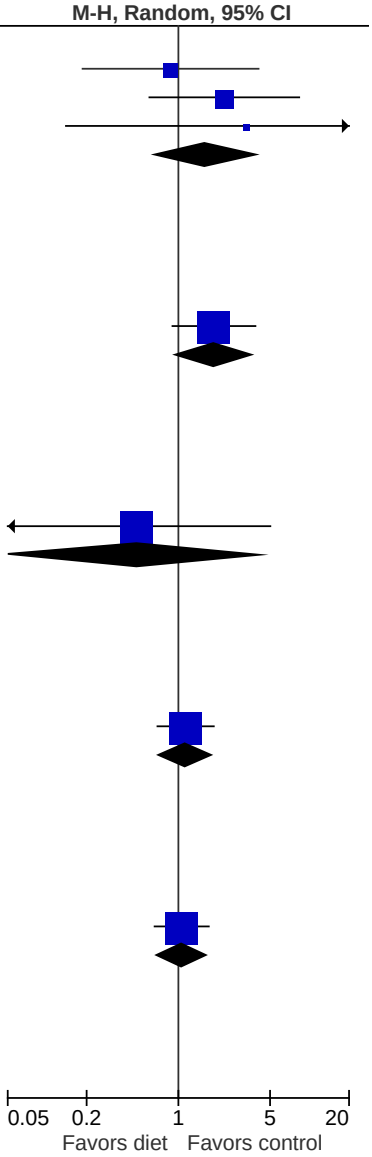
Study or Subgroup	Diet Events	Diet Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
9.4.2 Low protein diet versus usual protein diet						
Kopple 1997	2	291	0	294	100.0%	5.05 [0.24, 104.76]
Subtotal (95% CI)		**291**		**294**	**100.0%**	**5.05 [0.24, 104.76]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.05 (P = 0.30)						



Appendix Figure C22. Forest plots for low protein diet versus usual protein diet and other dietary intervention trials (continued)

End-stage renal disease

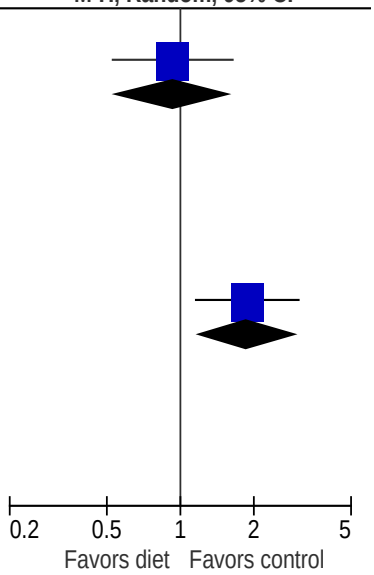
Study or Subgroup	Diet Events	Diet Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
9.5.1 Low protein diet versus usual protein diet						
Koya 2009	3	47	3	41	38.2%	0.87 [0.19, 4.09]
Rosman 1989	7	77	3	74	52.7%	2.24 [0.60, 8.35]
Dussol 2005	1	30	0	33	9.1%	3.29 [0.14, 77.82]
Subtotal (95% CI)		**154**		**148**	**100.0%**	**1.62 [0.62, 4.21]**
Total events	11		6			
Heterogeneity: Tau² = 0.00; Chi² = 1.05, df = 2 (P = 0.59); I² = 0%						
Test for overall effect: Z = 0.99 (P = 0.32)						
9.5.2 Low protein diet versus other diet						
Facchini 2003	17	91	10	100	100.0%	1.87 [0.90, 3.87]
Subtotal (95% CI)		**91**		**100**	**100.0%**	**1.87 [0.90, 3.87]**
Total events	17		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.68 (P = 0.09)						
9.5.3 Low triglyceride diet versus gemfibrozil						
Samuelsson 1997	1	29	2	28	100.0%	0.48 [0.05, 5.03]
Subtotal (95% CI)		**29**		**28**	**100.0%**	**0.48 [0.05, 5.03]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.61 (P = 0.54)						
9.5.4 Low protein/low phosphate diet versus low phosphate diet						
Williams 1991	17	31	14	29	100.0%	1.14 [0.69, 1.86]
Subtotal (95% CI)		**31**		**29**	**100.0%**	**1.14 [0.69, 1.86]**
Total events	17		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.51 (P = 0.61)						
9.5.5 Low protein/low phosphate diet versus usual protein diet						
Williams 1991	17	31	15	29	100.0%	1.06 [0.66, 1.70]
Subtotal (95% CI)		**31**		**29**	**100.0%**	**1.06 [0.66, 1.70]**
Total events	17		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.24 (P = 0.81)						



Appendix Figure C22. Forest plots for low protein diet versus usual protein diet and other dietary intervention trials (continued)

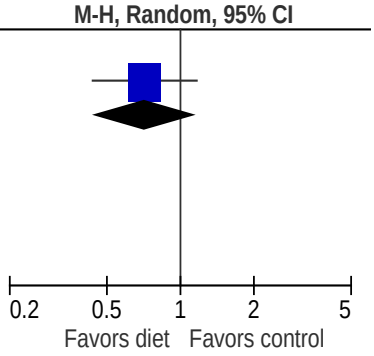
Doubling of serum creatinine

Study or Subgroup	Diet Events	Diet Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
9.6.1 Low protein diet versus usual protein diet						
Koya 2009	16	47	15	41	100.0%	0.93 [0.53, 1.64]
Subtotal (95% CI)		**47**		**41**	**100.0%**	**0.93 [0.53, 1.64]**
Total events	16		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.25 (P = 0.80)						
9.6.2 Low protein diet versus other diet						
Facchini 2003	31	79	19	91	100.0%	1.88 [1.16, 3.05]
Subtotal (95% CI)		**79**		**91**	**100.0%**	**1.88 [1.16, 3.05]**
Total events	31		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.55 (P = 0.01)						



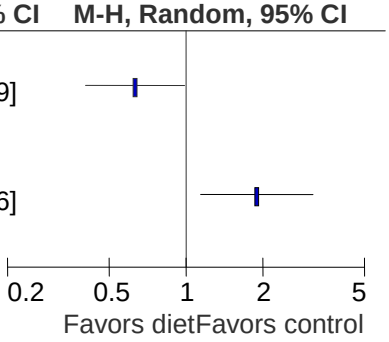
Halving of GFR

Study or Subgroup	Diet Events	Diet Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
9.7.1 Low protein diet versus usual protein diet						
D'Amico 1994	18	63	26	65	100.0%	0.71 [0.44, 1.17]
Subtotal (95% CI)		**63**		**65**	**100.0%**	**0.71 [0.44, 1.17]**
Total events	18		26			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.34 (P = 0.18)						



Composite renal outcome (See Table C117 for definitions

Study or Subgroup	Diet Events	Diet Total	Control Events	Control Total	Risk Ratio M-H, Random, 95% CI
9.8.1 Low protein diet versus usual protein diet					
Locatelli 1991	27	230	42	226	0.63 [0.40, 0.99]
9.8.2 Low protein versus other diet					
Facchini 2003	31	79	18	91	1.98 [1.21, 3.26]



Appendix Table C115. Clinical outcomes (outcomes part B), low protein diet versus usual protein diet and other dietary intervention trials

Study	Stroke, Nonfatal n/N (%)		Stroke, Fatal n/N (%)		CHF, Any n/N (%)		CHF Hospitalization (A) or Death (B) n/N (%)		Composite Vascular Outcome n/N (%)	
Low protein diet versus usual protein diet trials (n=6)										
	Low Protein	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**
Koya, 2009[75]										
Dussol, 2005[76]										
Kopple, 1997[77]	2/291 (0.7)	0/294								
Peterson, 1995[71]										
Klahr, 1994[72]										
Green, 1993[73]										
MDRD										
D'Amico, 1994[78]										
Locatelli, 1991[79]										
Rosman, 1989/1984[80,81]										
Low protein diet versus other diet trials (n=2)										
	Low Protein	**Other Diet**	**Low Protein**	**Other Diet**	**Low Protein**	**Other Diet**	**Low Protein**	**Other Diet**	**Low Protein**	**Other Diet**
Facchini, 2003[82]										
Williams, 1991[83]										
Low triglyceride diet versus GF trials (n=1)										
	Low TG Diet	**GF**	**Low TG Diet**	**GF**	**Low TG Diet**	**GF**	**Low TG Diet**	**GF**	**Low TG Diet**	**GF**
Samuelsson, 1997[84]										

CHF = congestive heart failure; TG = triglyceride; GF = gemfibrozil

Appendix Table C116. Clinical renal outcomes (outcomes part C), low protein diet versus usual protein diet and other dietary intervention trials

Study	End Stage Renal Disease n/N (%)		Doubling of Serum Creatinine n/N (%)		Halving of GFR n/N (%)		Progression from Micro- to Macroalbuminuria n/N (%)		Composite Renal Outcome n/N (%)**	
Low protein diet versus usual protein diet trials (n=6)										
	Low Protein	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**
Koya, 2009[75]	3/47 (6.4)	3/41 (7.3)	16/47 (34.0)	15/41 (36.6)						
Dussol, 2005[76]	1/30 (3.3)	0/33								
Kopple, 1997[77] Peterson, 1995[71] Klahr, 1994[72] Greene, 1993[73] MDRD	†NR	†NR			†NR	†NR				
D'Amico, 1994[78]					‡18/63 (28.6)	‡26/65 (40.0)				
Locatelli, 1991[79]									27/230 (11.7)	42/226 (18.6)
Rosman, 1989/1984[80,81]	7/77 (9.1)	3/74 (4.1)								
Low protein diet versus other diet trials (n=2)										
	Low Protein	**Other Diet**	**Low Protein**	**Other Diet**	**Low Protein**	**Other Diet**	**Low Protein**	**Other Diet**	**Low Protein**	**Other Diet**
Facchini, 2003§[82]	17/79 (21.5)	10/91 (11.0)	31/79 (39.2)	19/91 (20.9)					31/79 (39.2)	18/91 (19.8)
Williams, 1991#[83]	17/31 (54.8)	Lo-Phos: 14/29 (48.3) Control: 15/29 (51.7)								
Low triglyceride diet versus GF trials (n=1)										
	Low TG Diet	**GF**	**Low TG Diet**	**GF**	**Low TG Diet**	**GF**	**Low TG Diet**	**GF**	**Low TG Diet**	**GF**
Samuelsson, 1997[84]	1/29 (3.4)	2/28 (7.1)								

GFR = glomerular filtration rate; NR = not reported; TG = triglyceride; GF = gemfibrozil; Lo-Phos = low phosphate diet
*Not statistically significant versus control
**See Composite renal outcome definitions table
†Study reported that 12 participants developed end stage renal disease but did not report this result separately for the two treatment groups. Study further reported that 60 patients overall reached a study stopping point due to "rapidly declining glomerular filtration rate." Although study did not report this result separately for the two treatment groups, it did state that there was no significant difference between the results for the two groups.
‡Study reported on outcome of halving of creatinine clearance.
§Facchini study compared a low protein diet to a CR-LIPE diet (Carbohydrate Restricted, Low-Iron-available, Polyphenol-Enriched).
#Williams study compared a low protein and low phosphate diet to two different diets, a low phosphate diet, and a usual protein/usual phosphate diet.

Appendix Table C117. Composite renal outcome definitions, low protein diet versus usual protein diet and other dietary intervention trials

Study	Definition
Locatelli, 1991[79]	Dialysis or doubling of plasma creatinine concentration
Facchini, 2003[82]	Renal replacement therapy or death

Appendix Table C118. Study withdrawals and adverse events (outcomes part D), low protein diet versus usual protein diet and other dietary intervention trials

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Event: Any n/N (%)		Study Withdrawals Due to Serious Adverse Event: Any, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event: Specific n/N (%)		Renal Adverse Events n/N (%)	
Low protein diet versus usual protein diet trials (n=6)												
	Low Protein	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**	**Low Protein**	**Usual Protein**
Koya, 2009[75]	9/56 (16.1)	15/56 (26.8)										
Dussol, 2005[76]	5/30 (16.7)	7/33 (21.2)										
Kopple, 1997[77] Peterson, 1995[71] Klahr, 1994[72] Greene, 1993[73] MDRD	†NR	†NR							‡"Stop point due to serious medical condition": 6/291 (2.1); Weight loss 29%; Weight gain 25%; Hyperkalemia 10%	‡" Stop point due to serious medical condition": 6/294 (2.0); Weight loss 18%; Weight gain 40%; Hyperkalemia 17%	ARF: 1/291 (0.3)	ARF: 0/294
D'Amico, 1994[78]	§NR	§NR										
Locatelli, 1991[79]	36/230 (15.7)	35/226 (15.5)										
Rosman, 1989/1984[80,81]	3/77 (3.9)	3/74 (4.1)										
Low protein diet versus other diet trials (n=2)												
	Low Protein	**Other Diet**	**Low Protein**	**CR-LIPE Diet**	**Low Protein**	**CR-LIPE Diet**	**Low Protein**	**CR-LIPE Diet**	**Low Protein**	**CR-LIPE Diet**	**Low Protein**	**CR-LIPE Diet**
Facchini, 2003#[82]	12/91 (13.2)	9/100 (9.0)										
Williams, 1991**[83]	††NR	††NR										

Appendix Table C118. Study withdrawals and adverse events (outcomes part D), low protein diet versus usual protein diet and other dietary intervention trials (continued)

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Event: Any n/N (%)		Study Withdrawals Due to Serious Adverse Event: Any, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event: Specific n/N (%)		Renal Adverse Events n/N (%)	
Low triglyceride diet versus GF trials (n=1)												
	Low TG Diet	GF	Low TG Diet	GF	Low TG Diet	GF	Low TG Diet	GF	Low TG Diet	GF	Low TG Diet	GF
Samuelsson, 1997[84]	0/29	6/28 (21.4)							"Mild GI symptoms": 0/29	"Mild GI symptoms": 6/28 (21.4)		

NR = not reported; ARF = acute renal failure; GF = gemfibrozil; GI = gastrointestinal
*p<0.05 versus control
†Study reported that 11/585 participants overall were lost to followup, but didn't report results by treatment group.
‡Specific causes of stop points due to serious medical condition were as follows, by treatment group: Low protein diet (pregnancy (1), stroke (2), acute renal failure (1), diabetes necessitating insulin (1), and cancer (1); and Usual protein diet (diabetes necessitating insulin (3), cardiomyopathy (1), cancer (1), severe liver disease (1).
§Study reported that 6/134 (4.5%) participants withdrew overall, but didn't report results by treatment group.
#Facchini study compared a low protein diet to a CR-LIPE diet (Carbohydrate Restricted, Low-Iron-available, Polyphenol-Enriched).
**Williams study compared a low protein and low phosphate diet to two different diets, a low phosphate diet, and a usual protein/usual phosphate diet.
††Study reported that 6/95 patients were withdrawn from the trial overall but didn't report results by treatment group.

Appendix Evidence Table C119. Overview of glycemic control trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Duckworth, 2009[85] VADT Multi-center United States Funding Source: Government, Foundation, and Industry	Inclusion: Veterans with type 2 diabetes inadequately controlled on maximal doses of an oral agent or insulin therapy. Exclusion: Glycated hemoglobin <7.5%, cardiovascular event during previous 6 months, advanced congestive heart failure, severe angina, live expectancy <7 years, BMI >40, serum creatinine >1.6 mg/dL, alanine aminotransferase >3 times upper limit of normal	N=491 (subgroup analysis of subjects with baseline microalbuminuria from overall study of N=1,791) Age (yr): NR Gender (Male %): NR Race/Ethnicity (%): NR Weight (kg): NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR CKD stage: NR Serum creatinine (mg/dL): NR Creatinine clearance (mL/min): NR Albuminuria (µg/min): NR Proteinuria (g/day): NR Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): NR HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): NR Dyslipidemia (%): NR History of previous cardiovascular event (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR History of AKI (%): NR	Intensive therapy (n=251): Started on maximal doses of oral therapy*; insulin added if patients did not achieve glycated hemoglobin <6%. Subsequent changes per protocol and local assessment, though not specified. Standard therapy (n=240): Started on ½ of maximal doses of oral therapy*; insulin added if patients did not achieve glycated hemoglobin <9%. Subsequent changes per protocol and local assessment, though not specified. *Initial oral therapy was metformin plus rosiglitazone if BMI ≥27; initial therapy was glimepiride plus rosiglitazone if BMI <27 Followup period: median 5.6 years Study withdrawals (%): Reported for overall study, but not for microalbuminuria subgroup	Allocation Concealment: Adequate Blinding: No Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Appendix Evidence Table C119. Overview of glycemic control trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Microalbuminuria Collaborative Study Group, 1995[86] United Kingdom Funding Source: Government and Foundation	Inclusion Criteria: Insulin dependent diabetic patients attending 9 hospital-based diabetes centers; ages 16-60; onset of diabetes before age 39; sitting BP <160/95 mm Hg; no antihypertensive treatment; no clinical evidence of cardiovascular, peripheral vascular, or renal disease. Subjects must further have had no albuminuria on urine dipstick, but have had morning urine albumin ≥15 mg/L or albumin-creatinine ratio ≥3.5 mg/mmol, followed by overnight urine albumin excretion rate >30µg/min but <200µg/min on at least 1 of 2 samples. Exclusion Criteria: none stated	N=70 Age (yr): 37.0 Gender (Male %): 72.9 Race/Ethnicity (%): NR Weight (kg): NR BMI: 26.0 Systolic BP (mm Hg): 127.5 Diastolic BP (mm Hg): 77.5 CKD stage: NR Serum creatinine (mg/dL): 0.97 Creatinine clearance (mL/min): NR Albuminuria (µg/min): 47.9 Proteinuria (g/day): NR Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): 116.7 HbA_{1c} (%): 10.1 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): NR Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): 47.1 History of AKI (%): NR	Intensive therapy (n=36): Insulin by continuous infusion or multiple daily injections; goals were glycated hemoglobin concentration ≤7.5%, fasting blood glucose 4-6 mmol/l, and 2 hr postprandial blood glucose ≤10 mmol/l. Frequent visits and medication adjustment were made as needed to achieve targets. 24 hr/day consultation available if needed. Conventional therapy (n=34): 2 daily injections of insulin (except for 9 patients who were receiving >2 doses insulin per day at baseline); Conventional education given about diet, exercise and blood glucose monitoring, but no targets set. Insulin dose and regimen was adjusted only if patients became symptomatic. No changes were made to the usual diabetic diet of any patient. BP was assessed every 3 months, and all patients were treated to keep BP <160/95. Followup period: median 5 years	Allocation Concealment: Adequate (central location) Blinding: Unclear Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
			Study withdrawals (%): 11.4	

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C120. Summary of study baseline characteristics for glycemic control trials

Characteristic	Mean (Range) (unless otherwise noted)	Number of Trials Reporting
Patients randomized, n	561 (70-491)	2
Age of subjects, years	37.0	1
Male gender, %	72.9	1
Body Mass Index, kg/m2	26.0	1
Patients with diabetic nephropathy, n	561 (70-491)	2
Serum creatinine, mg/dL	0.97	1
Estimated GFR, ml/min/1.73m^2	116.7	1
Albuminuria, µg/min	47.9	1
Systolic blood pressure, mm Hg	127.5	1
Diastolic blood pressure, mm Hg	77.5	1
History of diabetes, %	100 (100-100)	2
HbA_{1c} (%)	10.1	1
Current smokers, %	47.1	1

GFR = glomerular filtration rate; HbA_{1c} = hemoglobin A_{1c}

Appendix Table C121. Clinical outcomes (outcomes part A), glycemic control trials

Study	All-cause Mortality n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke, Any n/N (%)	
	IT	CT	IT	CT	IT	CT	IT	CT	IT	CT	IT	CT
Duckworth, 2009[85]												
Microalbuminuria Collaborative, 1995[86]	*NR	*NR										

IT = intensive treatment; CT = conventional treatment
*Study reported 1/70 (1.4%) deaths overall, but did not report this result by treatment group. included in withdrawals

Appendix Table C122. Clinical renal outcomes (outcomes part C), glycemic control trials

Study	End Stage Renal Disease, n/N (%)		Doubling of Serum Creatinine, n/N (%)		Halving of GFR n/N (%)		Progression from Micro- to Macroalbuminuria n/N (%)		Composite Renal Outcome, n/N (%)	
	IT	CT	IT	CT	IT	CT	IT	CT	IT	CT
Duckworth, 2009[85]							19/251 (7.6)	29/240 (12.1)		
Microalbuminuria Collaborative, 1995[86]							6/36 (16.7)	6/34 (17.6)		

GFR = glomerular filtration rate; IT = intensive treatment; CT = conventional treatment

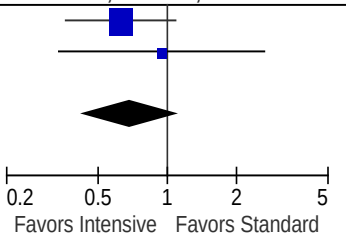
Appendix Figure C23. Forest plot for glycemic control trials

Progression from microalbuminuria to macroalbuminuria

Study or Subgroup	Intensive Tx Events	Intensive Tx Total	Conventional Tx Events	Conventional Tx Total	Weight	Risk Ratio M-H, Random, 95% CI
Duckworth 2009	19	251	29	240	77.8%	0.63 [0.36, 1.09]
Microalbumin Collab 1995	6	36	6	34	22.2%	0.94 [0.34, 2.65]
Total (95% CI)		**287**		**274**	**100.0%**	**0.69 [0.42, 1.12]**
Total events	25		35			

Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 1 (P = 0.49); I² = 0%

Test for overall effect: Z = 1.52 (P = 0.13)



Appendix Table C123. Study withdrawals and adverse events (outcomes part D), glycemic control trials

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Events: Any n/N (%)	Study Withdrawals Due to Serious Adverse Events: Any, n/N (%)		Adverse Event: Any n/N (%)		Adverse Event: Specific, n/N (%)		Renal Adverse Event: Any, n/N (%)	
	IT	CT		IT	CT	IT	CT	IT	CT	IT	CT
Duckworth, 2009[85]								Severe hypoglycemia: 5/36 (13.9); DKA: 3/36 (8.3)	Severe hypoglycemia: 5/34 (14.7); DKA: 2/34 (5.9)		
Microalbuminuria Collaborative, 1995[86]	5/36 (13.9)	3/34 (8.8)		*NR	*NR						

IT = intensive treatment; CT = conventional treatment; DKA = diabetic ketoacidosis

*Study reported 3/70 (4.3%) withdrawals due to serious adverse events overall (1 death, 1 leukemia, 1 acute renal failure), but did not report these outcomes by treatment group.

Appendix Table C124 Overview of anti-lipid trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
HMG-CoA Reductase Inhibitor versus Placebo trials (n=12)				
Kendrick, 2010[87] AFCAPS/TexCAPS United States Funding Source: Industry and other	Inclusion Criteria: Men aged 45-73 years or postmenopausal women aged 55-73 years who met the lipid entrance criteria at both 4 and 2 weeks before randomization with a <15% difference in LDL-C values between visits. Lipid entry criteria included total cholesterol 180-264 mg/dL, LDL-C 130-190 mg/dL, HDL-C ≤ 45 mg/dL for men or ≤ 47 mg/dL for women, and triglycerides ≤ 400 mg/dL. Exclusion Criteria: Clinical evidence atherosclerotic CVD, secondary hyperlipoproteinemia, nephrotic syndrome, uncontrolled HTN, and type 1 or 2 diabetes mellitus.	N=304 (Post hoc analysis in subgroup with baseline GFR < 60 ml/min/ 1.73m^2 from total of 6605 randomized). Age (yr): 62 Gender (Male %): 79 Race/Ethnicity (%): White NR, Mexican American NR, African American 1 BMI: 26 Systolic BP (mm Hg): 142 Diastolic BP (mm Hg): 79 Albuminuria (mg/24 h): NR Serum creatinine (mg/dL): 1.4 Estimated GFR (ml/min/1.73m^2): 53 Total cholesterol (mg/dL): 222 LDL cholesterol (mg/dL): 151 Diabetes (%): 2 History of HTN (%): 35 (p<0.05 between groups) History of CAD (%): 0 History of CHF (%): NR History of MI (%): 0 PTCA (%): 0 CABG (%): 0 History of Stroke (%): NR Peripheral arterial disease (%):NR Current smoker (%): 8	Lovastatin initiated at 20 mg/d, titrated up to 40 mg/d to reach goal LDL ≤110 mg/dL (n=145) Placebo (n=159) Followup period: mean 5.1 years Study withdrawals (%): No information reported for CKD group; stated both that all had complete data and that 24% of original AFCAPS/TexCAPS participants did not have data to calculate yearly change in GFR.	Allocation Concealment: Unclear Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis (ITT): yes Withdrawals/ Dropouts adequately described: Study reported available followup data on all participants

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Ridker, 2010[88] JUPITER United States Funding Source: Industry	Inclusion Criteria: apparently healthy men over age 50 years and women over age 60 years with LDL-C <130 mg/dl at increased vascular risk due to high-sensitivity C-reactive protein (hsCRP) ≥2 mg/l. Exclusion Criteria: treatment within 6 weeks of screening with any lipid lowering therapies, current use of hormone replacement therapy, evidence of hepatic dysfunction, creatinine >2.0 mg/dl, diabetes, uncontrolled hypertension, prior malignancy, uncontrolled hypothyroidism, or a recent history of alcohol, drug abuse, or other medical condition that might compromise safety.	N=3,267 (Post hoc analysis in subgroup with baseline GFR < 60 ml/min/ 1.73m^2 from total of 17,795 randomized). Age (yr): 70 Gender (Male %): 35 Race/Ethnicity (%): White 74, Hispanic 19, African American 3 BMI: 29 Systolic BP (mm Hg): 133 Diastolic BP (mm Hg): 80 Albuminuria (mg/24 h): NR Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): 56 (51 to 58) Total cholesterol (mg/dL): 189 LDL cholesterol (mg/dL): 109 Diabetes (%): 0 History of HTN (%): NR (none with uncontrolled) History of CAD (%): NR History of CHF (%): NR History of MI (%): NR PTCA (%): NR CABG (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 8	Rosuvastatin 20 mg/d (n=1638) Placebo (n=1629) Followup period: median 1.9 years (maximum 5 years) Study withdrawals (%): No information reported for CKD group in this secondary analyses.	Allocation Concealment: adequate Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis (ITT): yes Withdrawals/ Dropouts adequately described: No information reported
Nakamura, 2009[89] MEGA Japan Funding Source: Government and industry	Inclusion Criteria: Men and postmenopausal women aged 40-70 years with total cholesterol 220-270 mg/dL and no history of CHD and/or stroke. Exclusion Criteria: Familial hypercholesterolemia, history of CVD, cancer, serum creatinine ≥1.5 mg/dL, significant liver disease, and secondary hyperlipidemia	N=2,978 (Secondary analysis in subgroup with baseline GFR 30 to 59 ml/min/ 1.73m2 from total of 7,196 patients randomized. Age (yr): 60 Gender (Male %): 24 Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): 133 Diastolic BP (mm Hg): NR Albuminuria (mg/24 h): NR Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m2): 53 Total cholesterol (mg/dL): 244	Pravastatin (low dose) 10-20 mg/d + Step I diet counseling (n=1471) Diet counseling (n=1,507) Followup period 5.3 years Study withdrawals (%): No information reported	Allocation Concealment: Adequate (from main paper) Blinding: open-label Intention to Treat Analysis (ITT): yes Withdrawals/ Dropouts adequately described: No information reported

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
		LDL cholesterol (mg/dL): 155 Diabetes (%): 19 History of HTN (%): 46 History of CAD (%): 0 History of CHF (%): NR History of MI (%): 0 PTCA (%): 0 CABG (%): 0 History of stroke (%): 0 Peripheral arterial disease (%): NR Current smoker (%): 13		
Colhoun, 2009[90] CARDS United Kingdom and Ireland Funding Source: Industry	Inclusion Criteria: Diabetes and at least 1 of the following risk factors: (1) history of HTN, (2) retinopathy (i.e., any retinopathy, maculopathy, or prior photocoagulation), (3) microalbuminuria (urinary albumin/creatinine ratio 22 to 221 mg/g) or microalbuminuria (urinary albumin/creatinine ratio >221 mg/g), or (4) current smoking. Exclusion Criteria: History of MI, angina, coronary vascular surgery, cerebrovascular accident, or severe peripheral vascular disease (defined as warranting surgery); creatinine concentration > 1.7 mg/dL or glycated hemoglobin (hemoglobin A1c) level >12%.	N=970 (Secondary analysis in subgroup with baseline GFR <60 ml/min/ 1.73m^2 from total of 2,838 randomized) Age (yr): 65 Gender (Male %): 48 Race/Ethnicity (%): white 96 BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Albuminuria (% > Micro): 21 Albumin/creatinine ratio: 10 Serum creatinine (mg/dL): 1.3 Estimated GFR (ml/min/1.73m^2): 54 Total cholesterol (mg/dL): 211 LDL cholesterol (mg/dL): 120 Diabetes (%): 100 History of HTN (%): NR History of CAD (%): 0 History of CHF (%): NR History of MI (%): 0 PTCA (%): 0 CABG (%): 0 History of Stroke (%): 0 Peripheral arterial disease (%): NR Current smoker (%): NR	Atorvastatin 10 mg/d (n=482) Placebo (n=488) Followup period: median 3.9 years Study withdrawals (%): No information reported	Allocation Concealment: Adequate (from main paper) Blinding: double, end points adjudicated by blinded committee Intention to Treat Analysis (ITT): yes Withdrawals/ Dropouts adequately described: No information reported
Koren, 2009[91] Isaacsohn, 2000[92]	Inclusion Criteria: Male or female older than 18 years of age with known CHD, defined as prior acute MI, CABG, or unstable angina >3	N= 579 (Secondary analysis in subgroup with baseline GFR <60 ml/min/ 1.73m^2) from total of 2,442 randomized). Age (yr): 65	Atorvastatin, started at 10 mg/day, then titrated up to achieve LDL goal of <80 mg/dL up to maximum of	Allocation Concealment: Adequate Blinding: open-label

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
ALLIANCE United States Funding Source: Industry	months before screening, or PTCA >6 months before screening. LDL-C 110-200 mg/dL for patients on antilipid drugs or 130-250 mg/dL for patients receiving no antilipid drugs. Exclusion Criteria: Patients with chronic stable angina or awaiting revascularization procedures. Breastfeeding or pregnancy; women of childbearing age planning to become pregnant during the study or who did not practice a method of birth control acceptable to the investigator; any significant abnormalities investigator believed may compromise the patient's safety or successful completion of the study; any disease process likely to limit life to less than the duration of the study; all cancers (excluding basal cell and squamous cell skin cancers); New York Heart Association class III or IV congestive heart failure; known hypersensitivities to hydroxymethylglutaryl coenzyme A reductase inhibitors.	Gender (Male %): 77 Race/Ethnicity (%): white 88; African American 9 BMI: 29 Systolic BP (mm Hg): 137 Diastolic BP (mm Hg): 78 Albuminuria (mg/24 h): NR Serum creatinine (mg/dL): 1.5 Estimated GFR (ml/min/1.73m^2): 51 Total cholesterol (mg/dL): 228 LDL cholesterol (mg/dL): 147 Diabetes (%): 28 History of HTN (%): NR History of CAD (%): 100 History of CHF (%): 10 History of MI (%): 62 PTCA (%): 33 CABG (%): 53 History of Stroke (%): 10 Peripheral arterial disease (%): NR Current smoker (%): 15	80 mg/day (n=286) Usual care (n=293) Followup period: median 4.5 years Study withdrawals (%): 19% (n=465/2,442) withdrawals from main study, but data not reported for CKD subgroup.	Intention to Treat Analysis (ITT): yes Withdrawals/Dropouts adequately described: No information reported.
Rahman, 2008[93] ALLHAT-LLT United States, Puerto Rico, U.S. Virgin Islands, and Canada Funding: Government and Industry	Inclusion Criteria: age ≥55 years and stage 1 or 2 hypertension with at least 1 additional CHD risk factor); fasting LDL-C level of 120-189 mg/dL for those with no known CHD, or 100-129 mg/dL for those with known CHD, and fasting triglyceride levels lower than 350 mg/dL. Exclusion Criteria: currently using prescribed lipid-lowering agents or large doses (500 mg/day) of	N=1,557 (Secondary analysis in subgroup with baseline GFR < 60 ml/min/1.73m^2) from total of 10,060 randomized). Age (yr): 71 Gender (Male %): 46 Race/Ethnicity (%): white 51 , black 29, Hispanic 15 BMI: 29 Systolic BP (mm Hg): 146 Diastolic BP (mm Hg): 82 Albuminuria (mg/24 h): NR Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m2): 50	Pravastatin 40 mg/d (n=779) Usual care (n=778) Followup period: mean 4.8 years Study withdrawals (%): No information reported	Allocation Concealment: Unclear Blinding: open-label Intention to Treat Analysis (ITT): yes Withdrawals/Dropouts adequately described: No information reported

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	nonprescription niacin; were known to be intolerant of statins or to have significant liver dysfunction (serum alanine aminotransferase >100 IU/L); had other contraindications for statin therapy; or had a known secondary cause of hyperlipidemia.	Total cholesterol (mg/dL): 225 LDL cholesterol (mg/dL): 146 Diabetes, type 2 (%): 31 History of HTN (%): 100 History of CAD (%): 18 History of CHF (%): NR History of MI or Stroke (reported pooled % only): 22.0 History of coronary revascularization: 9 Peripheral arterial disease (%): NR Current smoker (%): 19		
Chonchol, 2007[94] 4S Trial Huskey, 2009[95] Scandanavia	Inclusion criteria: Men and women aged 35-70 yrs, with history of CHD (MI and/or angina), total cholesterol 212-309 mg/dL, triglycerides <221 mg/dL Exclusion criteria: Secondary hypercholesterolemia, unstable angina, planned CABG or PTCA, recent MI (recent not defined), CHF requiring treatment, hypersensitivity to HMG-CoA reductase inhibitors.	N=505 (Subgroup analysis of patients with eGFR <60 mL/min/1.73m2 performed within a post hoc analysis of patients with eGFR <75 mL/min/1.73m2 from the 4,420 with baseline creatinine measurements) from total of 4,444 participants randomized in 4S Trial. Baseline characteristics not reported for n=505 participants with eGFR <60 mL/min/1.73m2 in Chonchol paper, but are reported for n=409 participants (n=199 simvastatin, n=210 placebo) with eGFR <60 mL/min/1.73m2 in Huskey paper. Age (yr): 62.2 Gender (% male): 54 BMI (kg/m2): 25.9 Systolic BP (mm Hg): 143.1 Diastolic BP (mm Hg): 83.7 Serum creatinine (mg/dL): 1.21 Estimated GFR (mL/min/1.73m2): 54.7 Total cholesterol (mg/dL): 265 LDL cholesterol (mg/dL): 191.5 Diabetes (%): 2.7 History of HTN (%): 37.4 History of CAD (%): 100 History of CHF (%): NR History of MI (%): 77.8 PTCA or CABG (%): 7.1	Simvastatin (n=245), initiated at 20 mg/day, titrated up to 40 mg/day as needed to get total cholesterol to <200 mg/dL Placebo (n=260) Followup duration: median 5.4 years Study withdrawals (%): No data reported for eGFR<60 group	Allocation concealment: Unclear Blinding: Double blind. Outcome assessors blinded to treatment assignment Intention to treat analysis (ITT): No Withdrawals/dropouts adequately described: No data reported

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
		History of Stroke (%): NR Peripheral arterial disease (%):NR Current smoker (%): 16		
Kjekshus, 2007[96] CORONA Multinational, including 19 European countries, Russia, and South Africa Funding Source: Industry	Inclusion Criteria: ≥60 years of age, chronic NYHA class II, III, or IV heart failure of ischemic cause (as reported by investigators) and an ejection fraction of no more than 40% (no more than 35% in patients in NYHA class II); investigator did not think patient needed treatment with a cholesterol-lowering drug. Exclusion Criteria: Previous statin-induced myopathy/hypersensitivity reaction; decompensated heart failure or need for inotropic therapy; MI within past 6 months; unstable angina or stroke within past 3 months; PCTA, CABG, or the implantation of a cardioverter-defibrillator or biventricular pacemaker within past 3 months or planned implantation of such a device; previous or planned heart transplantation; clinically significant, uncorrected primary valvular heart disease or malfunctioning prosthetic valve; hypertrophic cardiomyopathy; acute endomyocarditis or myocarditis, pericardial disease, or systemic disease (e.g. amyloidosis); acute or chronic liver disease; levels of alanine aminotransferase or thyrotropin >2 times the ULN range; a serum creatinine level >2.5 mg/dL; chronic muscle disease or unexplained creatine kinase level >2.5 times the ULN range; previous treatment with cyclosporine; any	N=1,635 patients with CKD (Subgroup analysis within patients with baseline GFR < 51 ml/min/1.73m^2 from among total of 5,011 randomized in CORONA study). Baseline characteristics not reported for CKD subjects only except for those identifiable from entry criteria. Age (yr): NR Gender (Male %): NR Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Albuminuria (mg/24 h): NR Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): NR History of HTN (%): NR History of CAD (%): 100 History of CHF (%): 100 History of MI (%): NR PTCA (%): NR CABG (%): NR History of Stroke (%): NR Peripheral arterial disease (%):NR Current smoker (%): NR	Rosuvastatin 10 mg/day (n=1,418) Placebo (n=1,432) Followup period: Median 2.7 years Study withdrawals (%): No data reported for CKD subgroup	Allocation concealment: Adequate (centralized interactive Web-based response system) Blinding: double, end points adjudicated by blinded committee Intention-to-treat analysis: yes Withdrawals/dropouts adequately described: No data reported for CKD subgroup

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	other condition that would substantially reduce life expectancy or limit compliance with the protocol; or the receipt of <80% of dispensed placebo tablets during the run-in period.			
Lemos, 2005[97] LIPS Multinational Funding Source: Industry	Inclusion Criteria: Successful completion of a first percutaneous coronary intervention (successful defined as residual stenosis <50%, no post-procedural in-hospital myocardial necrosis, repeat vascularization or death); Eligible participants had to meet at least one of the following: (1) total cholesterol level of 135 to 270 mg/dl with a fasting triglyceride level <400 mg/dl, or (2) total cholesterol level <212 mg/dl for patients whose lipids levels were measured 24 hours to 4 weeks after an episode of MI, or (3) total cholesterol level <232 mg/dl for patients who had diabetes. Exclusion Criteria: baseline serum creatinine value >1.8 mg/dl	N=310 (post hoc subgroup analysis limited to patients with creatinine clearance in the lowest quintile or <55.9 ml/min from among 1,558 subjects with complete data for creatinine clearance calculation from among 1,677 randomized participants in the LIPS study) Age (yr): 69 Gender (Male %): 67 Race/Ethnicity (%): NR BMI: 25.0 (calculated from given weight and height) Systolic BP (mm Hg): 132 Diastolic BP (mm Hg): 75 Albuminuria (mg/24 h): NR Serum creatinine (mg/dL): 1.33 Creatinine clearance (ml/min): 47 Estimated GFR (ml/min/1.73m2): NR Total cholesterol (mg/dL): 200 LDL cholesterol (mg/dL): 131 Diabetes (%): 12 History of HTN (%): 51 History of CAD (%): 100 History of CHF (%): NR History of MI (%): 47 PTCA (%): 100 CABG (%): NR History of Stroke (%): 5 Peripheral arterial disease (%): 11 Current smoker (%): 17	Fluvastatin 40 mg twice daily (n=150) Placebo (n=160) Followup period: 3 to 4 years Study withdrawals (%): No data reported, but 100% included in endpoint analysis	Allocation Concealment: Unclear in this report Blinding: double and outcomes assessors Intention to Treat Analysis (ITT): Yes Withdrawals/ Dropouts adequately described: No data reported, but 100% included in endpoint analysis
Asselbergs, 2004[2] PREVEND IT	Inclusion Criteria: Age 28-75 years, urinary albumin concentration >10 mg/L in 1 early morning spot urine sample and urine albumin excretion	N=864 Age (yr): 51.3 Gender (Male %): 65.0 Race/Ethnicity (%): white 96.1	Pravastatin 40 mg/d (n=433) Placebo (n=431)	Allocation Concealment: Yes Blinding: double, end

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Single center Groningen, The Netherlands Funding Source: Industry and other (Foundations)	rate of 15 to 300 mg/24 hours in at least one of two 24-hour urine samples); BP <160/100 mm Hg and no use of antihypertensive medication; total cholesterol level <309 mg/dL, or <193 mg/dL in case of previous MI, and no use of lipid-lowering medication. Exclusion Criteria: creatinine clearance <60% of the normal age adjusted value; use of ACE inhibitors or ARB antagonists.	BMI: 26.4 Systolic BP (mm Hg): 130.5 Diastolic BP (mm Hg): 76.5 Albuminuria (mg/24 h): 22.8 Serum creatinine (mg/dL): 1.0 Estimated GFR (ml/min/1.73m^2): NR Total cholesterol (mg/dL): 224 LDL cholesterol (mg/dL): 156 Diabetes (%): 2.6 History of HTN (%): 0 History of CAD (%): 3.3 History of CHF (%): 0 History of MI (%): 0.5 CABG or PTCA (%): 0.8 History of Stroke (%): 0.8 Peripheral arterial disease (%): 0.6 Current smoker (%): 39.9	Followup period: mean 3.8 years Study withdrawals (%): NR Study reported 199 (23.0%) withdrawals excluding deaths, but included 56 for "other medical reasons," which included but were not entirely comprised of subjects reaching study endpoints. Note: 2 x 2 factorial design with fosinopril 20 mg/day versus placebo	points adjudicated by blinded committee Intention to Treat Analysis: yes Withdrawals/Dropouts adequately described: yes
Tonelli, 2004[98] WOSCOPS/ CARE/ LIPID Multinational Funding Source: Not stated in current report	Entry Criteria: WOSCOPS studied high-risk patients who had not previously experienced an MI. Excluded baseline creatinine >1.7 mg/dL CARE and LIPID were trials of subjects with previous acute coronary syndromes and average cholesterol levels. Excluded baseline creatinine levels of >2.5 mg/dL and >4.5 mg/dL, respectively. Current report restricted to subjects with GFR 30-59.99 ml/min/1.73m2 using Cockroft-Gault formula. No further information on entry criteria provided.	N=4,491 (post hoc subject-level pooling of results in patients with GFR 30-59.99 mL/min per 1.73m2 body surface area from 19,700 subjects in three previously completed RCTs comparing pravastatin 40 mg/day to placebo, i.e. CARE, WOSCOPS and LIPID studies) Age (yr): 65.7 Gender (Male %): 81.7 Race/Ethnicity (%): NR BMI: 25.5 Systolic BP (mm Hg): 135.5 Diastolic BP (mm Hg): 79.5 Albuminuria (mg/24h): NR Serum creatinine (mg/dL): 1.4 Estimated GFR (ml/min/1.73m2, per MDRD): 55.0 Total cholesterol (mg/dL): 221.3 LDL cholesterol (mg/dL): 151.5 Diabetes (%): 9.9 History of HTN (%): 44.8 History of CAD (%): 73.7	Pravastatin 40 mg/d (n=2217) Placebo (n=2,274) Followup period: approximately 5 years Study withdrawals (%): No data reported	Allocation Concealment: Not described in current report Blinding: double and outcomes assessors Intention to Treat Analysis (ITT): unclear Withdrawals/Dropouts adequately described: Not described in current report

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
		History of CHF (%): NR History of MI (%): 67.6 PTCA (%): NR CABG (%): NR History of Stroke (%): 5.3 Peripheral arterial disease (%): NR Current smoker (%): 10.3		
Tonelli, 2003[99] CARE Multicenter Funding Source: Industry	Inclusion Criteria: Men and post-menopausal women, 21-75 years, had acute MI 3-20 months before randomization, total plasma cholesterol <240 mg/dL; LDL 115-174 mg/dL; triglyceride <350 mg/dL; fasting glucose <220 mg/dL, LVEF ≥25%; no symptomatic CHF. All lipid measures collected after 4 weeks treatment with National Cholesterol Education Program Step 1 diet. Exclusion Criteria: ≥2+ proteinuria on dipstick or serum creatinine >1.5 times upper limit of normal	N= 1,711 (post hoc subgroup analysis limited to patients with creatinine clearance ≤75 mL/min from among 4,159 randomized participants in the CARE study) Age (yr): 64.3 Gender (Male %): 78.4 Race/Ethnicity (%): White 91.9, Other 8.1 BMI: NR Systolic BP (mm Hg): 131.0 Diastolic BP (mm Hg): 77.3 Proteinuria (dipstick positive, %): 31 Serum creatinine (mg/dL): 1.26 Creatinine clearance (ml/min): 61 Total cholesterol (mg/dL): 209.0 LDL cholesterol (mg/dL): 138.6 HDL cholesterol (mg/dL): 40.6 Diabetes (%): 13.9 History of HTN (%): 47.2 History of CAD (%): 100 History of CHF (%): 9.6 History of MI (%): 100 PTCA (%): NR CABG (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): 12.3	Pravastatin , 40 mg/d (n=844); Placebo (n=867) Followup Period: 4.9 years Study withdrawals (%): No participants were lost to followup and 100% were included in analyses	Allocation Concealment: Yes Blinding: double Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes
High versus Low Dose HMG-CoA Reductase Inhibitor trials (n=2)				
SEARCH, 2010[100] UK Funding Source:	Inclusion Criteria: Adults aged 18–80 years with a history of previous MI were eligible provided they Fulfilled the following criteria: either current statin use or clear indication for this treatment (and no	N=1,686 patients with CKD (Subgroup analysis within patients with baseline GFR < 60 ml/min/1.73m^2 from among total of 12,064 randomized. Baseline characteristics not reported for	Simvastatin 80 mg/d (n=820) Simvastatin 20 mg/d (n=866)	Allocation concealment: Yes (centralized telephone randomisation system) Blinding: double, end

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Industry and other	clear indication for folic acid); total cholesterol of at least 3·5 mmol/L if already on a statin or 4·5 mmol/L if not; and no clear contraindications to the study treatments. Exclusion Criteria: Predominant medical problems that could reduce compliance with long-term study treatment.	CKD subjects only except for those identifiable from entry criteria. Age (yr): NR Gender (Male %): NR Race/Ethnicity (%): NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Albuminuria (mg/24 h): NR Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): NR History of HTN (%): NR History of CAD (%): 100 History of CHF (%): NR History of MI (%): 100 PTCA (%): NR CABG (%): NR History of Stroke (%): NR Peripheral arterial disease (%):NR Current smoker (%): NR	Followup Period: mean 6.7 years Study withdrawals (%): No data reported for CKD subgroup	points adjudicated by blinded committee Intention-to-treat analysis: yes (overall) Withdrawals/dropouts adequately described: No data reported for CKD subgroup
Shepard, 2008[101] TNT La Rosa, 2005[102] Waters, 2004[103] Multinational Funding Source: Industry	Inclusion Criteria: Men and women aged 35 to 75 years with clinically evident CHD (defined as previous myocardial infarction, previous or current angina with objective evidence of atherosclerotic CHD, or a history of coronary revascularization). LDL 130-250 mg/dL and triglycerides ≤600 mg/dL off anti-lipid drugs, with LDL <130 mg/dL after 8 week open label run-in on atorvastatin 10 mg/d. Exclusion criteria: hypersensitivity to statins; active liver disease or hepatic dysfunction defined as alanine	N=3,107 (Post hoc analysis of subjects with eGFR <60 ml/min/1.73 m^2 from among 10,003 randomized in TNT trial; 3,078 had CKD stage 3 (GFR 30-59) and 29 had CKD stage 4 (GFR 15-29) Age (yr): 65.5 Gender (Male %): 67.7 Race/Ethnicity (%): white 95.2; black 1.6, other 3.2 BMI: 28.5 Systolic BP (mm Hg): 133.0 Diastolic BP (mm Hg): 77.5 Albuminuria (mg/24 h): NR Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): 52.9 Total cholesterol (mg/dL): 175.9	Atorvastatin 10 mg/d (n=1505) Atorvastatin 80 mg/d (n=1602) Followup period: median 5 years Study withdrawals (%): 0.4	Allocation Concealment: unclear Blinding: double-blind, end points adjudicated by blinded committee Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	aminotransferase or aspartate aminotransferase >1.5 times the ULN; women who are pregnant or breastfeeding; nephrotic syndrome; uncontrolled DM; uncontrolled hypothyroidism; uncontrolled HTN (defined by the investigator) at the screening visit; a MI, coronary revascularization procedure or severe/unstable angina within 1 month of screening; any planned surgical procedure for the treatment of atherosclerosis; an ejection fraction <30%; hemodynamically important valvular disease; gastrointestinal disease limiting drug absorption or partial ileal bypass; any nonskin malignancy, malignant melanoma or other survival-limiting disease; unexplained creatine phosphokinase levels >6 times the ULN; concurrent therapy with long-term immunosuppressants; concurrent therapy with lipid-regulating drugs not specified as study treatment in the protocol; history of alcohol abuse; and participation in another clinical trial concurrently or within 30 days before screening.	LDL cholesterol (mg/dL): 96.4 Diabetes (%): 17.6 History of HTN (%): 62.7 History of CAD (%): 100 History of CHF (%): 12.2 History of MI (%): 57.5 PTCA (%): 50.4 CABG (%): 53.7 History of Stroke (%): 7.3 Peripheral arterial disease (%): 16.3 Current smoker (%): 9.0		
HMG-CoA Reductase Inhibitor versus Bile Acid Sequestrant trials (n=1)				
Tonolo, 2006[104] Single Center Funding Source: Other	Inclusion criteria: Type II diabetics with hemoglobin A1c >7% and proliferative or background retinopathy; hypertension (>130/85mm Hg) and microalbuminuria (median albumin/creatinine ratio between 30 and 300 µg/mg in three consecutive urine specimens), treated by angiotensinsin-converting enzyme	N= 86 (Baseline characteristics reported in 82 who completed study) Age (yr): 61.5 Gender (Male %): NR Race/Ethnicity (%): NR BMI: 27.5 Systolic BP (mm Hg): 131 Diastolic BP (mm Hg): 76 Albuminuria (ug/mg): 82.5	Simvastatin, 40 mg/d (n=43) cholestyramine, 30 g/d (n=43) Followup Period: 4 yr Study withdrawals (%): 4 (5%)	Allocation Concealment: Unclear Blinding: double Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
	inhibitors (5 mg ramipril or 20 mg lisinopril/day), 12.5 mg/day thiazides, and 100 mg/day atenolol in the last 3 years, with a glycemic control accomplished by 1,500 mg/day metformin with either three insulin analogs before meals or once daily long-acting insulin injection; a decrease of GFR >1 ml/min/1.73m2/year had to be observed during the 3 years before the recruitment Exclusion Criteria: NR	Serum creatinine (mg/dL): NR Estimated GFR (ml/min/1.73m^2): 90.5 Total cholesterol (mg/dL): 229 LDL cholesterol (mg/dL): 149 Diabetes (%): 100 % Hemoglobin A1C: 7.35 History of HTN (%): 100 History of CAD (%): NR History of CHF (%): NR History of MI (%): NR PTCA (%): NR CABG (%): NR History of Stroke (%): NR Peripheral arterial disease (%): NR Current smoker (%): NR		
Gemfibrozil versus Placebo/Control trials (n=2)				
Tonelli, 2004[98] VA-HIT Multi-center United States Funding source: Government and Industry	Inclusion criteria: Male veterans with coronary artery disease (previous MI, angina corroborated by objective evidence of ischemia, coronary revascularization, or angiographic evidence of stenosis >50% in 1+ major coronary arteries, age <74 yr, HDL ≤40 mg/dL, LDL ≤140 mg/dL, triglyceride ≤300 mg/dL Exclusion criteria: Serum creatinine > 2.0 mg/dL	N=470 (Subgroup analysis of patients with eGFR <60 mL/min/1.73m2 performed within a post hoc analysis of 1046 patients with creatinine clearance <75 mL/min/1.73m2 from the 2,505 with baseline creatinine measurements) from total of 2,531 participants randomized in VA-HIT Trial. Baseline characteristics not reported for n=470 participants with eGFR <60 mL/min/1.73m2 in Tonelli 2004 Kidney International paper, but are reported for n=399 participants (n=199 gemfibrozil, n=200 placebo) with eGFR <60 mL/min/1.73m2 in Tonelli 2004 Am J Kidney Disease paper: Age (yr): 67.4 Gender (% male): 100 Race (%): White 91.0 BMI (kg/m2): NR Systolic BP (mm Hg): 134.0 Diastolic BP (mm Hg): 77.2	Gemfibrozil 600 mg bid (n=242) Placebo (n=228) Followup period: 5.3 yr Study withdrawals (%): No participants were lost to followup	Allocation Concealment: Unclear Blinding: double Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Yes, because no subjects were lost to followup

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
		Serum creatinine (mg/dL): NR Creatinine clearance (mL/min/1.73m2): 59.7 Estimated GFR (mL/min/1.73m2): 52.2 Total cholesterol (mg/dL): 176 LDL cholesterol (mg/dL): 111 Diabetes (%): 30.3 History of HTN (%): 67.2 History of CAD (%): 100 History of CHF (%): 10.0 History of MI (%): NR PTCA or CABG (%): NR History of Stroke (%): NR Peripheral arterial disease (%):NR Current smoker (%): 14.0		
Samuelsson, 1997[84] Single Center Sweden Funding Source Government and Foundations	Inclusion Criteria: Nondiabetic primary renal disease and moderately advanced renal insufficiency (GFR 10-70 ml/min/1.73m2) Exclusion Criteria: NR	N=57 Age (yr): 51.3 Gender (Male %): 75 Race/Ethnicity (%): NR Weight (kg): 81.4 BMI: 26.2 Systolic BP (mm Hg): 136.5 Diastolic BP (mm Hg): 84.0 CKD stage: NR Serum creatinine (mg/dL): 2.4 Creatinine clearance (mL/min): NR Albuminuria: 0.95g/24 hr Albumin/creatinine ratio (mg/g): NR GFR (ml/min/1.73m^2): 35.5 HbA_{1c} (%):NR Total cholesterol (mg/dL): 243.6 LDL cholesterol (mg/dL): 170.2 Diabetes (%): 0 (by inclusion criteria) History of HTN (%): NR Dyslipidemia (%): unclear History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): NR	Gemfibrizol initiated at 300mg/day, and could be titrated up to 450 mg twice daily (n=28) Triglyceride lowering Diet (n=29) Followup Period: 1.0 yr Study withdrawals (%): 10.5	Allocation Concealment: Unclear Blinding: Open label Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes

Appendix Table C124 Overview of anti-lipid trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
		History of AKI (%): NR		

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; NYHA = New York Heart Association; PTCA = percutaneous transluminal coronary angioplasty; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion; ULN = upper limit of the normal

Appendix Table C125. Summary of study baseline characteristics, anti-lipid (AL) monotherapy versus control treatment trials

Characteristic	Mean (range unless otherwise noted)	Number of Trials Reporting
HMG-CoA Reductase Inhibitors versus Placebo trials		12 studies*
Patients randomized, n	17,460 (304-4491)**	12
Age of subjects, years	65 (51-71)	10
Gender, male, %	53 (24-82)	10
Race/ethnicity, white, %	79 (51-96)	6
Body Mass Index	27 (25-29)	8
Systolic blood pressure, mm Hg	136 (131-146)	9
Diastolic blood pressure, mm Hg	80 (75-84)	8
Albuminuria, mg/24	22.8	1
Serum creatinine (mg/dL)	1.3 (1.0-1.5)	9
Estimated GFR, ml/min/1.73m^2	54 (50 to 56)	9
Creatinine Clearance, ml/min/1.73m^2	59 (4-7-61)	2
Total Cholesterol, mg/dL	220 (189-265)	10
Low Density Lipoprotein Cholesterol, mg/dL	142 (109-192)	10
Diabetes, %	17 (0-100)	10
Hypertension, %	49 (0-100)	9
Coronary Artery Disease, %	46 (0-100)	12
Congestive Heart Failure, %	39 (0-100)	4
Myocardial Infarction, %	29 (0-100)	8
Stroke, %	1 (0-10)	7
High versus Low Dose HMG-CoA Reductase Inhibitor trials		2
Patients randomized, n	4,793	2
Age of subjects, years	66	1†
Gender, male, %	68	1
Race/ethnicity, white, %	95	1
Body Mass Index	29	1
Systolic blood pressure, mm Hg	133	1
Diastolic blood pressure, mm Hg	78	1
Albuminuria, mg/24	NR	0
Serum creatinine (mg/dL)	NR	0
Estimated GFR, ml/min/1.73m^2	53	1
Creatinine Clearance, ml/min/1.73m^2	NR	0
Total Cholesterol, mg/dL	176	1
Low Density Lipoprotein Cholesterol, mg/dL	96	1
Diabetes, %	18	1
Hypertension, %	63	1
Coronary Artery Disease, %	100	2
Congestive Heart Failure, %	12	1
Myocardial Infarction, %	58	1
Stroke, %	7	1
HMG-CoA Reductase Inhibitor versus Bile Acid Sequestrant trials		1
Patients randomized, n	86	1
Age of subjects, years	62	1
Gender, male, %	NR	0
Race/ethnicity, white, %	NR	0
Body Mass Index	28	1
Systolic blood pressure, mm Hg	131	1
Diastolic blood pressure, mm Hg	76	1
Albuminuria, µg/mg	83	1
Serum creatinine (mg/dL)	NR	0
Estimated GFR, ml/min/1.73m^2	91	1
Creatinine Clearance, ml/min/1.73m^2	NR	0
Total Cholesterol, mg/dL	229	1

Appendix Table C125. Summary of study baseline characteristics, anti-lipid (AL) monotherapy versus control treatment trials (continued)

Characteristic	Mean (range unless otherwise noted)	Number of Trials Reporting
Low Density Lipoprotein Cholesterol, mg/dL	149	1
Diabetes, %	100	1
Hypertension, %	100	1
Coronary Artery Disease, %	NR	0
Congestive Heart Failure, %	NR	0
Myocardial Infarction, %	NR	0
Stroke, %	NR	0
Gemfibrozil versus Placebo/Control trials		2
Patients randomized, n	527	2
Age of subjects, years	65 (51-67)	2
Gender, male, %	97 (75-100)	2
Race/ethnicity, white, %	91	1
Body Mass Index	26	1
Systolic blood pressure, mm Hg	134 (134-137)	2
Diastolic blood pressure, mm Hg	78 (77- 84)	2
Albuminuria, mg/24 hr	950	1
Serum creatinine (mg/dL)	2.4	1
Estimated GFR, ml/min/1.73m^2	50 (36-52)	2
Creatinine Clearance, ml/min/1.73m^2	60	1
Total Cholesterol, mg/dL	184 (176-244)	2
Low Density Lipoprotein Cholesterol, mg/dL	118 (111-170)	2
Diabetes, %	27 (0-30)	2
Hypertension, %	67	1
Coronary Artery Disease, %	100	1
Congestive Heart Failure, %	10	1
Myocardial Infarction, %	NR	0
Stroke, %	NR	0

AL = anti-lipid; CKD = chronic kidney disease; NR = not recorded; GFR = glomerular filtration rate
*12 studies represent 13 individual RCTs (one study was a pooled analyses of CKD patients from 3 trials - WOSCOP/LIPID/CARE). Two studies included the CARE trial, the pooled analysis and one with only CARE patients. The CARE only study was excluded unless it provided information not available from the pooled analysis such as race/ethnicity.
**4,491 were in the pooled analysis of WOSCOP/LIPID/CARE. Otherwise, the largest single study of CKD patients was 2,978.
† Baseline characteristics for the subgroup of CKD patients were not reported in the SEARCH trial.

Appendix Table C126. Clinical outcomes (outcomes part A), AL monotherapy versus control treatment trials

Study	All-cause Mortality, n/N (%)		Cardiovascular Mortality n/N (%)		Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Nonfatal n/N (%)		Stroke, Any n/N (%)	
	AL	**Control**	**AL**	**Control**	**AL**	**Control**	**AL**	**Control**	**AL**	**Control**	**AL**	**Control**
HMG-CoA reductase inhibitors versus placebo trials (n=12)												
Kendrick, 2010[87] AFCAPS/ TexCAPS			0/145	1/159 (0.6)	2/145 (1.4)	6/159 (3.8)						
Ridker, 2010[88] JUPITER	34/1638 (2.1)*	61/1629 (3.7)							8/1638 (0.5)*	20/1629 (1.2)		
Nakamura, 2009[89] MEGA	16/1471 (2.3)*	34/1507 (4.8)									8/1471 (0.5)*	29/1507 (4.1)
Colhoun, 2009[90] CARDS	27/482 (5.6)	30/488 (6.1)									6/482 (1.2)*	15/488 (3.1)
Koren, 2009[91] ALLIANCE	47/286 (16.4)	59/293 (20.1)	17/286 (5.9)	27/293 (9.2)					17/286 (5.9)	29/293 (9.9)	11/286 (3.8)	12/293 (4.1)
Rahman, 2008[93] ALLHAT-LLT												
Chonchol, 2007[94] 4S	37/245 (15.1)	40/260 (15.4)	§NR	§NR					§NR	§NR	§NR	§NR
Kjekshus, 2007[96] CORONA												
Lemos, 2005[97] LIPS	3/150 (2.0)	3/160 (1.9)	3/150 (2.0)	3/160 (1.9)								
Asselbergs, 2004[2] PREVD	6/433 (1.4)	4/431 (0.9)	4/433 (0.9)	4/431 (0.9)							7/433 (1.6)	4/431 (0.9)
Tonelli, 2004[98] WOSCOPS/ CARE/LIPID	322/2217 (14.5)	383/2274 (16.8)										
Tonelli, 2003[99] CARE	86/844 (10.2)	111/867 (12.8)			65/844 (7.7)	90/867 (10.4)					29/844 (3.4)	46/867 (5.3)
High versus low dose HMG-CoA reductase inhibitor trials (n=2)												
	High Dose	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**
SEARCH, 2010[100]												

Study	All-cause Mortality, n/N (%)		Cardiovascular Mortality n/N (%)	Myocardial Infarction, Any n/N (%)		Myocardial Infarction, Fatal n/N (%)	Myocardial Infarction, Nonfatal n/N (%)	Stroke, Any n/N (%)
Shepherd, 2008[101] TNT	112/1602 (7.0)	113/1505 (7.5)						
HMG-CoA reductase inhibitor versus bile acid sequestrant trials (n=1)								
Tonolo, 2006[104]				‡NR	‡NR			
Gemfibrozil versus placebo/control trials (n=2)								
Tonelli, 2004[98] VA-HIT	20/199 (10.1)	22/200 (11.0)						
Samuelsson, 1997[84]								

* p<0.05 versus control

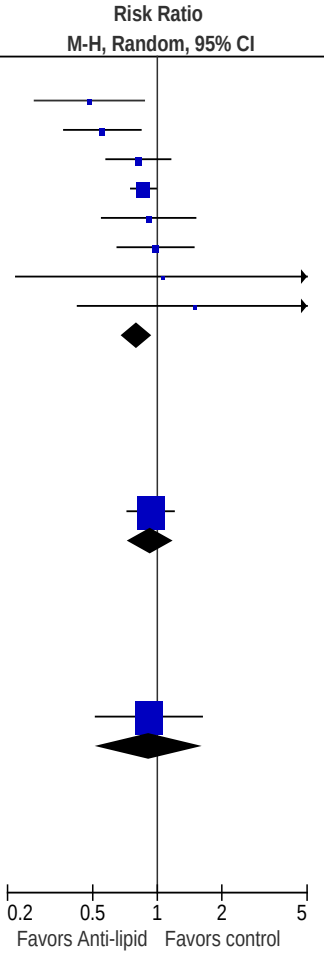
‡Study reported that one participant had a myocardial infarction, but didn't indicate the patient's treatment group.

§Study did not provide the number of patients with and without the following events overall or by treatment group, but stated there was no significant difference in risk for simvastatin vs. placebo, respectively, for the following endpoints: CHD deaths (no data provided), nonfatal MI (HR 0.73, CI 0.51-1.04), and stroke (HR 1.07, CI 0.48-2.39).

Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials

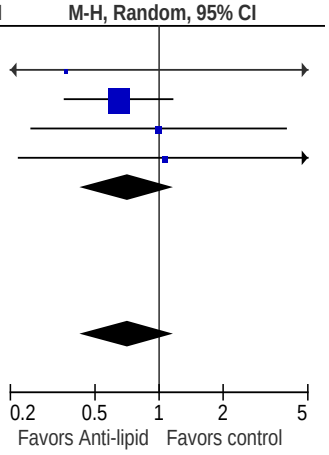
All-cause mortality

Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
6.1.1 HMG-CoA Reductase Inhibitors versus placebo						
Nakamura (MEGA) 2009	16	1471	34	1507	6.7%	0.48 [0.27, 0.87]
Ridker (JUPITER) 2010	34	1638	61	1629	12.1%	0.55 [0.37, 0.84]
Koren (ALLIANCE) 2009	47	286	59	293	15.9%	0.82 [0.58, 1.15]
Tonelli (WOS/C/LIP) 2004	322	2217	383	2274	41.7%	0.86 [0.75, 0.99]
Colhoun (CARDS) 2009	27	482	30	488	8.7%	0.91 [0.55, 1.51]
Chonchol (4S) 2007	37	245	40	260	12.2%	0.98 [0.65, 1.48]
Lemos (LIPS) 2005	3	150	3	160	1.0%	1.07 [0.22, 5.20]
Asselbergs (PREVEND) 2004	6	433	4	431	1.6%	1.49 [0.42, 5.25]
Subtotal (95% CI)		**6922**		**7042**	**100.0%**	**0.80 [0.68, 0.95]**
Total events	492		614			
Heterogeneity: Tau² = 0.01; Chi² = 8.95, df = 7 (P = 0.26); I² = 22%						
Test for overall effect: Z = 2.64 (P = 0.008)						
6.1.2 High versus low dose HMG-CoA Reductase Inhibitors						
Shepard (TNT) 2008	112	1602	113	1505	100.0%	0.93 [0.72, 1.20]
Subtotal (95% CI)		**1602**		**1505**	**100.0%**	**0.93 [0.72, 1.20]**
Total events	112		113			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.56 (P = 0.58)						
6.1.3 Gemfibrozil versus control						
Tonelli (VA-HIT) 2004	20	199	22	200	100.0%	0.91 [0.52, 1.62]
Subtotal (95% CI)		**199**		**200**	**100.0%**	**0.91 [0.52, 1.62]**
Total events	20		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.31 (P = 0.76)						



Cardiovascular mortality

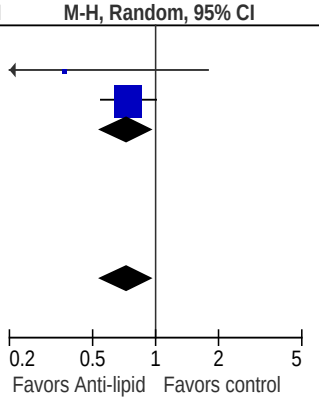
Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
6.2.1 HMG-CoA Reductase Inhibitors versus placebo						
Kendrick (AF/TxCAPS) 2010	0	145	1	159	2.5%	0.37 [0.01, 8.90]
Koren (ALLIANCE) 2009	17	286	27	293	74.1%	0.65 [0.36, 1.16]
Asselbergs (PREVEND) 2004	4	433	4	431	13.3%	1.00 [0.25, 3.95]
Lemos (LIPS) 2005	3	150	3	160	10.1%	1.07 [0.22, 5.20]
Subtotal (95% CI)		**1014**		**1043**	**100.0%**	**0.71 [0.43, 1.17]**
Total events	24		35			
Heterogeneity: Tau² = 0.00; Chi² = 0.75, df = 3 (P = 0.86); I² = 0%						
Test for overall effect: Z = 1.34 (P = 0.18)						
Total (95% CI)		**1014**		**1043**	**100.0%**	**0.71 [0.43, 1.17]**
Total events	24		35			
Heterogeneity: Tau² = 0.00; Chi² = 0.75, df = 3 (P = 0.86); I² = 0%						
Test for overall effect: Z = 1.34 (P = 0.18)						
Test for subgroup differences: Not applicable						



Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

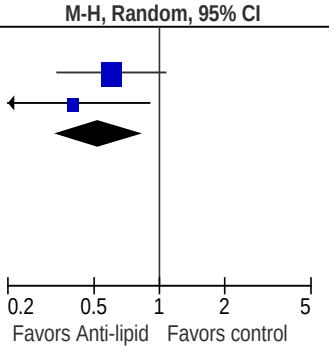
Myocardial infarction, any

Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
6.3.1 HMG-CoA Reductase Inhibitors versus placebo						
Kendrick (AF/TxCAPS) 2010	2	145	6	159	3.6%	0.37 [0.07, 1.78]
Tonelli (CARE) 2003	65	844	90	867	96.4%	0.74 [0.55, 1.01]
Subtotal (95% CI)		**989**		**1026**	**100.0%**	**0.72 [0.54, 0.98]**
Total events	67		96			
Heterogeneity: Tau² = 0.00; Chi² = 0.74, df = 1 (P = 0.39); I² = 0%						
Test for overall effect: Z = 2.12 (P = 0.03)						
Total (95% CI)		**989**		**1026**	**100.0%**	**0.72 [0.54, 0.98]**
Total events	67		96			
Heterogeneity: Tau² = 0.00; Chi² = 0.74, df = 1 (P = 0.39); I² = 0%						
Test for overall effect: Z = 2.12 (P = 0.03)						
Test for subgroup differences: Not applicable						



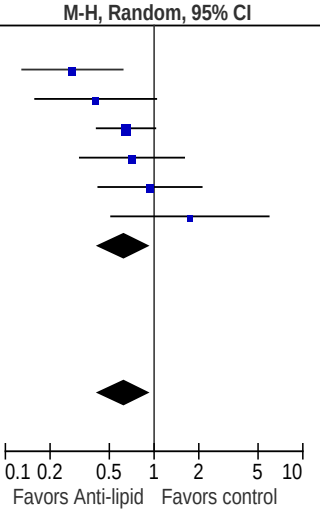
Myocardial infarction, nonfatal

Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
6.4.1 HMG-CoA Reductase Inhibitors versus placebo						
Koren (ALLIANCE) 2009	17	286	29	293	66.8%	0.60 [0.34, 1.07]
Ridker (JUPITER) 2010	8	1638	20	1629	33.2%	0.40 [0.18, 0.90]
Subtotal (95% CI)		**1924**		**1922**	**100.0%**	**0.52 [0.33, 0.84]**
Total events	25		49			
Heterogeneity: Tau² = 0.00; Chi² = 0.65, df = 1 (P = 0.42); I² = 0%						
Test for overall effect: Z = 2.69 (P = 0.007)						



Stroke, any

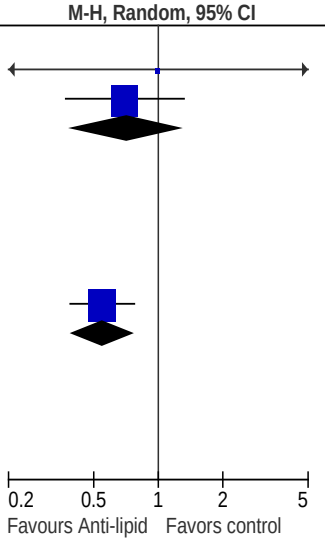
Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
6.5.1 HMG-CoA Reductase Inhibitors versus placebo						
Nakamura (MEGA) 2009	8	1471	29	1507	17.0%	0.28 [0.13, 0.62]
Colhoun (CARDS) 2009	6	482	15	488	13.4%	0.40 [0.16, 1.04]
Tonelli (CARE) 2003	29	844	46	867	27.7%	0.65 [0.41, 1.02]
Ridker (JUPITER) 2010	10	1638	14	1629	16.3%	0.71 [0.32, 1.59]
Koren (ALLIANCE) 2009	11	286	12	293	16.4%	0.94 [0.42, 2.09]
Asselbergs (PREVEND) 2004	7	433	4	431	9.2%	1.74 [0.51, 5.91]
Subtotal (95% CI)		**5154**		**5215**	**100.0%**	**0.62 [0.41, 0.95]**
Total events	71		120			
Heterogeneity: Tau² = 0.11; Chi² = 8.65, df = 5 (P = 0.12); I² = 42%						
Test for overall effect: Z = 2.20 (P = 0.03)						
Total (95% CI)		**5154**		**5215**	**100.0%**	**0.62 [0.41, 0.95]**
Total events	71		120			
Heterogeneity: Tau² = 0.11; Chi² = 8.65, df = 5 (P = 0.12); I² = 42%						
Test for overall effect: Z = 2.20 (P = 0.03)						
Test for subgroup differences: Not applicable						



Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

Congestive heart failure, hospitalization

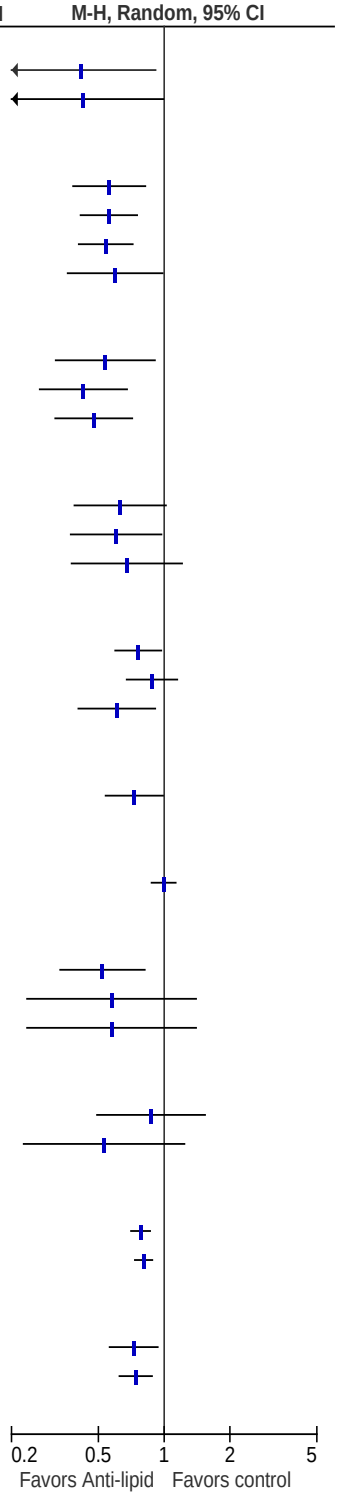
Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
6.6.1 HMG-CoA Reductase Inhibitors versus placebo						
Asselbergs (PREVEND) 2004	1	433	1	431	5.0%	1.00 [0.06, 15.86]
Koren (ALLIANCE) 2009	15	286	22	293	95.0%	0.70 [0.37, 1.32]
Subtotal (95% CI)		**719**		**724**	**100.0%**	**0.71 [0.38, 1.32]**
Total events	16		23			
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.81); I² = 0%						
Test for overall effect: Z = 1.08 (P = 0.28)						
6.6.2 High versus low dose HMG-CoA Reductase Inhibitors						
Shepard (TNT) 2008	49	1602	84	1505	100.0%	0.55 [0.39, 0.77]
Subtotal (95% CI)		**1602**		**1505**	**100.0%**	**0.55 [0.39, 0.77]**
Total events	49		84			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.41 (P = 0.0006)						



Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

Composite vascular outcome: HMG-CoA Reductase Inhibitors versus placebo (see Table C128 for definitions)

Study or Subgroup	Anti-lipid monotherapy Events	Total	Control Events	Total	Risk Ratio M-H, Random, 95% CI
6.7.1 Kendrick (AFCAPS/TexCAPS) 2010					
Kendrick (B)	8	145	21	159	0.42 [0.19, 0.91]
Kendrick (C)	7	145	18	159	0.43 [0.18, 0.99]
6.7.2 Ridker (JUPITER) 2010					
Ridker (JUPITER) A	40	1638	71	1629	0.56 [0.38, 0.82]
Ridker (JUPITER) B	64	1638	114	1629	0.56 [0.41, 0.75]
Ridker (JUPITER) C	69	1638	127	1629	0.54 [0.41, 0.72]
Ridker (JUPITER) D	24	1638	40	1629	0.60 [0.36, 0.99]
6.7.3 Nakamura (MEGA) 2009					
Nakamura (A)	21	1471	40	1507	0.54 [0.32, 0.91]
Nakamura (B)	25	1471	60	1507	0.43 [0.27, 0.68]
Nakamura (C)	33	1471	71	1507	0.48 [0.32, 0.72]
6.7.4 Colhoun (CARDS) 2009					
Colhoun (A -albuminuric)	24	276	38	275	0.63 [0.39, 1.02]
Colhoun (A)	25	482	42	488	0.60 [0.37, 0.97]
Colhoun (B)	18	482	27	488	0.67 [0.38, 1.21]
6.7.5 Koren (ALLIANCE) 2009					
Koren (A)	78	286	105	293	0.76 [0.60, 0.97]
Koren (B)	73	286	85	293	0.88 [0.67, 1.15]
Koren (C)	32	286	54	293	0.61 [0.40, 0.91]
6.7.6 Chonchol (4S) 2007					
Chonchol (A)	53	245	77	260	0.73 [0.54, 0.99]
6.7.7 Kjekshus (CORONA) 2007					
Kjekhus (A)	288	791	309	844	0.99 [0.88, 1.13]
6.7.8 Lemos (LIPS) 2005					
Lemos (A)	23	150	47	160	0.52 [0.33, 0.82]
Lemos (B)	7	150	13	160	0.57 [0.24, 1.40]
Lemos (C)	7	150	13	160	0.57 [0.24, 1.40]
6.7.9 Asselbergs (PREVD) 2004					
Asselbergs (A)	21	433	24	431	0.87 [0.49, 1.54]
Asselbergs (B)	8	433	15	431	0.53 [0.23, 1.24]
6.7.10 Tonelli (WOSCOPS/CARE/LIPID) 2004					
Tonelli (W/C/L) (A)	492	2217	647	2274	0.78 [0.70, 0.86]
Tonelli (W/C/L) (B)	573	2217	730	2274	0.81 [0.73, 0.88]
6.7.11 Tonelli (CARE) 2003					
Tonelli (CARE) (A)	89	844	126	867	0.73 [0.56, 0.94]
Tonelli (CARE) (B)	171	844	237	867	0.74 [0.62, 0.88]

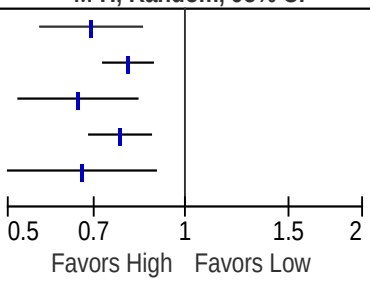


Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

Composite vascular outcome: High versus low-dose HMG-CoA Reductase Inhibitors (see Table C128 for definitions)

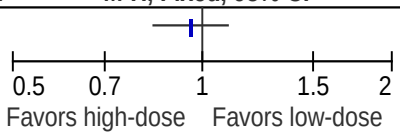
A. Atorvastatin

Study or Subgroup	High-dose Events	High-dose Total	Low-dose Events	Low-dose Total	Risk Ratio M-H, Random, 95% CI
Shepard (TNT) (A)	149	1602	202	1505	0.69 [0.57, 0.85]
Shepard (TNT) (B)	489	1602	574	1505	0.80 [0.73, 0.88]
Shepard (TNT) (C)	110	1602	157	1505	0.66 [0.52, 0.83]
Shepard (TNT) (D)	356	1602	431	1505	0.78 [0.69, 0.88]
Shepard (TNT) (E)	74	1602	104	1505	0.67 [0.50, 0.89]



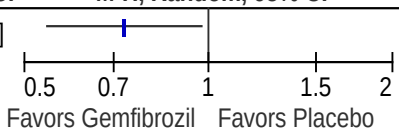
B. Simvastatin

Study or Subgroup	High-dose Events	High-dose Total	Low-dose Events	Low-dose Total	Risk Ratio M-H, Fixed, 95% CI
SEARCH 2010	265	820	292	866	0.96 [0.84, 1.10]



Composite vascular outcome: Gemfibrozil versus placebo (see Table C128 for definition)

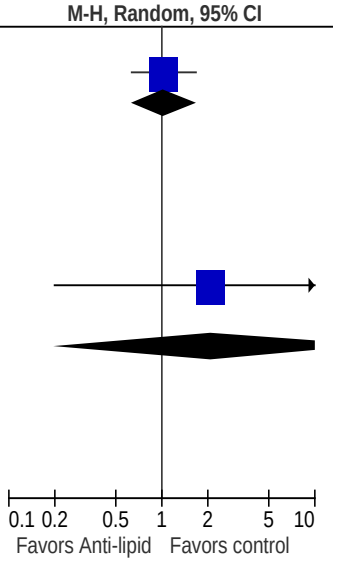
Study or Subgroup	Gemfibrozil Events	Gemfibrozil Total	Placebo Events	Placebo Total	Risk Ratio M-H, Random, 95% CI
Tonelli (VA-HIT) (B)	58	242	75	228	0.73 [0.54, 0.97]



Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

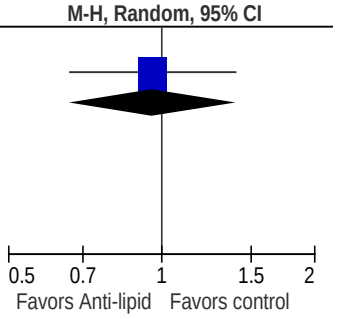
End-stage renal disease

Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
6.11.1 HMG-CoA Reductase Inhibitors versus placebo						
Rahman (ALLHAT) 2008	32	779	31	778	100.0%	1.03 [0.64, 1.67]
Subtotal (95% CI)		**779**		**778**	**100.0%**	**1.03 [0.64, 1.67]**
Total events	32		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.12 (P = 0.90)						
6.11.2 Gemfibrozil versus control						
Samuelsson 1997	2	28	1	29	100.0%	2.07 [0.20, 21.58]
Tonelli (VA-HIT) 2004	0	199	0	200		Not estimable
Subtotal (95% CI)		**227**		**229**	**100.0%**	**2.07 [0.20, 21.58]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.61 (P = 0.54)						



Composite renal outcome (see Table C130 for definition)

Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
6.15.2 HMG-CoA Reductase Inhibitors versus placebo						
Rahman (ALLHAT) 2008	50	779	52	778	100.0%	0.96 [0.66, 1.40]
Subtotal (95% CI)		**779**		**778**	**100.0%**	**0.96 [0.66, 1.40]**
Total events	50		52			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.83)						

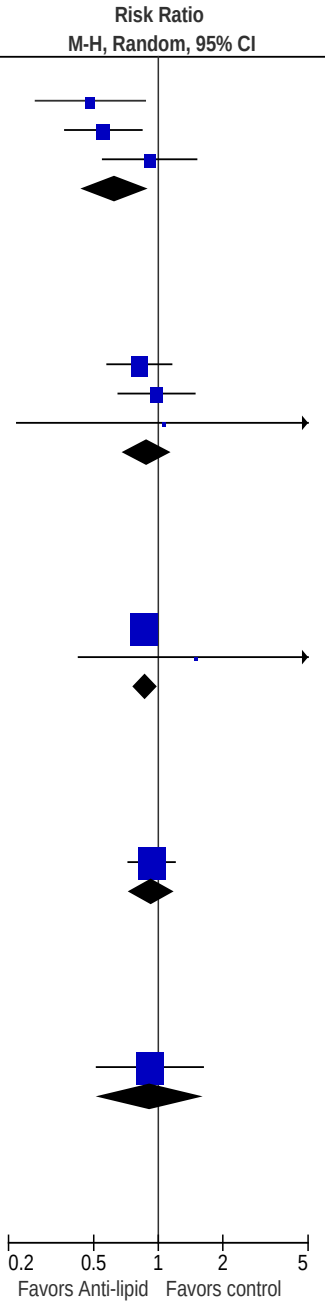


Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

Anti-lipid monotherapy versus control: subgroup analyses

All-cause mortality

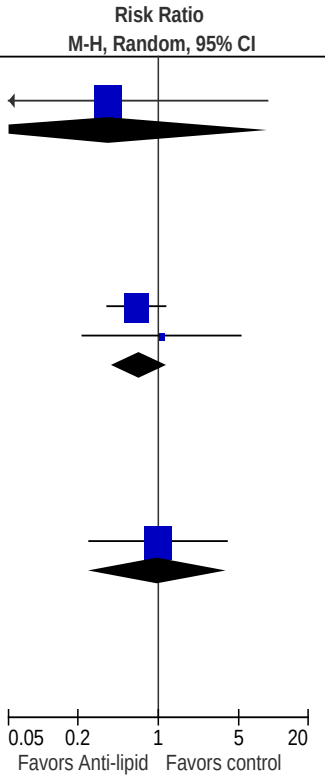
Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
7.1.1 HMG-CoA Reductase Inhibitors versus placebo: non-CAD patient studies						
Nakamura (MEGA) 2009	16	1471	34	1507	26.5%	0.48 [0.27, 0.87]
Ridker (JUPITER) 2010	34	1638	61	1629	41.0%	0.55 [0.37, 0.84]
Colhoun (CARDS) 2009	27	482	30	488	32.6%	0.91 [0.55, 1.51]
Subtotal (95% CI)		**3591**		**3624**	**100.0%**	**0.63 [0.44, 0.90]**
Total events	77		125			
Heterogeneity: Tau² = 0.04; Chi² = 3.22, df = 2 (P = 0.20); I² = 38%						
Test for overall effect: Z = 2.51 (P = 0.01)						
7.1.2 HMG-CoA Reductase Inhibitors versus placebo: CAD patient studies studies						
Koren (ALLIANCE) 2009	47	286	59	293	56.9%	0.82 [0.58, 1.15]
Chonchol (4S) 2007	37	245	40	260	40.4%	0.98 [0.65, 1.48]
Lemos (LIPS) 2005	3	150	3	160	2.7%	1.07 [0.22, 5.20]
Subtotal (95% CI)		**681**		**713**	**100.0%**	**0.89 [0.68, 1.15]**
Total events	87		102			
Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 2 (P = 0.78); I² = 0%						
Test for overall effect: Z = 0.91 (P = 0.36)						
7.1.3 HMG-CoA Reductase Inhibitors versus placebo: Mixed CAD and non-CAD patient studies						
Tonelli (WOS/C/LIP) 2004	322	2217	383	2274	98.8%	0.86 [0.75, 0.99]
Asselbergs (PREVEND) 2004	6	433	4	431	1.2%	1.49 [0.42, 5.25]
Subtotal (95% CI)		**2650**		**2705**	**100.0%**	**0.87 [0.76, 0.99]**
Total events	328		387			
Heterogeneity: Tau² = 0.00; Chi² = 0.72, df = 1 (P = 0.40); I² = 0%						
Test for overall effect: Z = 2.05 (P = 0.04)						
7.1.4 High versus low dose HMG-CoA Reductase Inhibitors: CAD patient studies						
Shepard (TNT) 2008	112	1602	113	1505	100.0%	0.93 [0.72, 1.20]
Subtotal (95% CI)		**1602**		**1505**	**100.0%**	**0.93 [0.72, 1.20]**
Total events	112		113			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.56 (P = 0.58)						
7.1.5 Gemfibrozil versus control: CAD patient studies						
Tonelli (VA-HIT) 2004	20	199	22	200	100.0%	0.91 [0.52, 1.62]
Subtotal (95% CI)		**199**		**200**	**100.0%**	**0.91 [0.52, 1.62]**
Total events	20		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.31 (P = 0.76)						



Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

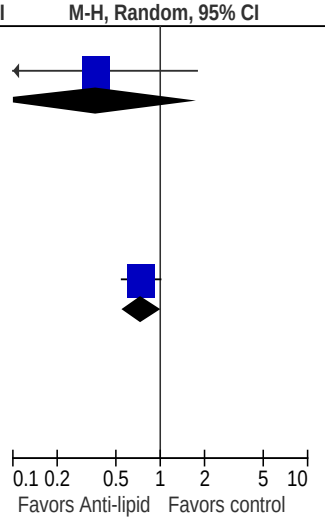
Cardiovascular mortality

Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
7.2.1 HMG-CoA Reductase Inhibitors versus placebo: non-CAD patient studies						
Kendrick (AF/TxCAPS) 2010	0	145	1	159	100.0%	0.37 [0.01, 8.90]
Subtotal (95% CI)		**145**		**159**	**100.0%**	**0.37 [0.01, 8.90]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.62 (P = 0.54)						
7.2.2 HMG-CoA Reductase Inhibitors versus placebo: CAD patient studies						
Koren (ALLIANCE) 2009	17	286	27	293	88.0%	0.65 [0.36, 1.16]
Lemos (LIPS) 2005	3	150	3	160	12.0%	1.07 [0.22, 5.20]
Subtotal (95% CI)		**436**		**453**	**100.0%**	**0.69 [0.40, 1.19]**
Total events	20		30			
Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 1 (P = 0.56); I² = 0%						
Test for overall effect: Z = 1.35 (P = 0.18)						
7.2.3 HMG-CoA Reductase Inhibitors versus placebo: Mixed CAD and non-CAD patient studies						
Asselbergs (PREVEND) 2004	4	433	4	431	100.0%	1.00 [0.25, 3.95]
Subtotal (95% CI)		**433**		**431**	**100.0%**	**1.00 [0.25, 3.95]**
Total events	4		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						



Myocardial infarction, any

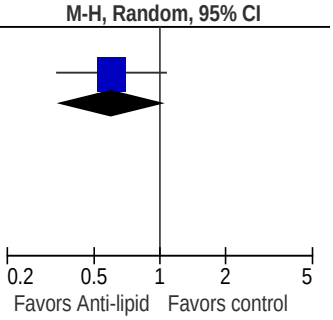
Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
7.3.1 HMG-CoA Reductase Inhibitors versus placebo: non-CAD patient studies						
Kendrick (AF/TxCAPS) 2010	2	145	6	159	100.0%	0.37 [0.07, 1.78]
Subtotal (95% CI)		**145**		**159**	**100.0%**	**0.37 [0.07, 1.78]**
Total events	2		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.25 (P = 0.21)						
7.3.2 HMG-CoA Reductase Inhibitors versus placebo: CAD patient studies						
Tonelli (CARE) 2003	65	844	90	867	100.0%	0.74 [0.55, 1.01]
Subtotal (95% CI)		**844**		**867**	**100.0%**	**0.74 [0.55, 1.01]**
Total events	65		90			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.92 (P = 0.05)						



Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

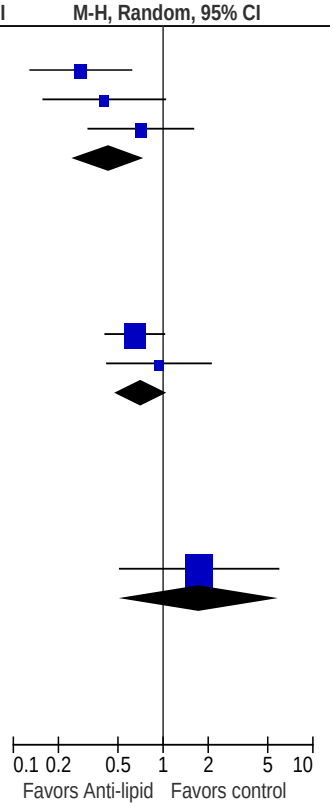
Myocardial infarction, nonfatal

Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
7.4.1 HMG-CoA Reductase Inhibitors versus placebo: CAD patient studies						
Koren (ALLIANCE) 2009	17	286	29	293	100.0%	0.60 [0.34, 1.07]
Subtotal (95% CI)		**286**		**293**	**100.0%**	**0.60 [0.34, 1.07]**
Total events	17		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.73 (P = 0.08)						



Stroke, any

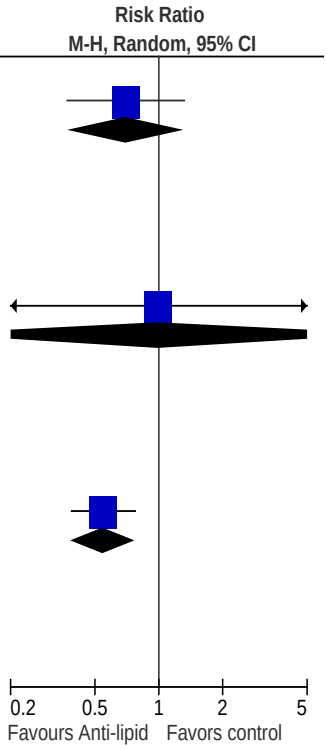
Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
7.5.1 HMG-CoA Reductase Inhibitors versus placebo: non-CAD patient studies						
Nakamura (MEGA) 2009	8	1471	29	1507	37.1%	0.28 [0.13, 0.62]
Colhoun (CARDS) 2009	6	482	15	488	27.9%	0.40 [0.16, 1.04]
Ridker (JUPITER) 2010	10	1638	14	1629	35.1%	0.71 [0.32, 1.59]
Subtotal (95% CI)		**3591**		**3624**	**100.0%**	**0.43 [0.25, 0.75]**
Total events	24		58			
Heterogeneity: Tau² = 0.06; Chi² = 2.62, df = 2 (P = 0.27); I² = 24%						
Test for overall effect: Z = 2.97 (P = 0.003)						
7.5.2 HMG-CoA Reductase Inhibitors versus placebo: CAD patient studies						
Tonelli (CARE) 2003	29	844	46	867	75.6%	0.65 [0.41, 1.02]
Koren (ALLIANCE) 2009	11	286	12	293	24.4%	0.94 [0.42, 2.09]
Subtotal (95% CI)		**1130**		**1160**	**100.0%**	**0.71 [0.48, 1.05]**
Total events	40		58			
Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 1.70 (P = 0.09)						
7.5.3 HMG-CoA Reductase Inhibitors versus placebo: Mixed CAD and non-CAD patient studies						
Asselbergs (PREVEND) 2004	7	433	4	431	100.0%	1.74 [0.51, 5.91]
Subtotal (95% CI)		**433**		**431**	**100.0%**	**1.74 [0.51, 5.91]**
Total events	7		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.89 (P = 0.37)						



Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

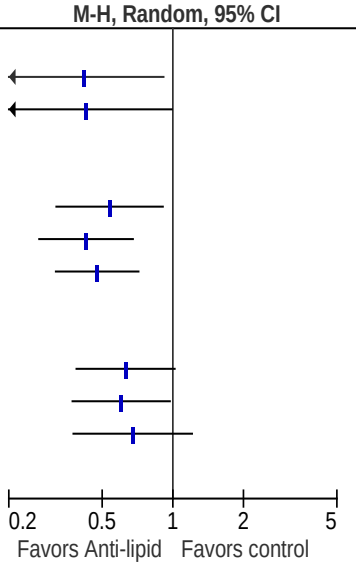
Congestive heart failure, hospitalization

Study or Subgroup	Anti-lipid monotherapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
7.6.1 HMG-CoA Reductase Inhibitors versus placebo: CAD patient studies						
Koren (ALLIANCE) 2009	15	286	22	293	100.0%	0.70 [0.37, 1.32]
Subtotal (95% CI)		**286**		**293**	**100.0%**	**0.70 [0.37, 1.32]**
Total events	15		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.11 (P = 0.27)						
7.6.2 HMG-CoA Reductase Inhibitors versus placebo: Mixed CAD and non-CAD patient studiesstudies						
Asselbergs (PREVEND) 2004	1	433	1	431	100.0%	1.00 [0.06, 15.86]
Subtotal (95% CI)		**433**		**431**	**100.0%**	**1.00 [0.06, 15.86]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
7.6.3 High versus low dose HMG-CoA Reductase Inhibitors: CAD patient studies						
Shepard (TNT) 2008	49	1602	84	1505	100.0%	0.55 [0.39, 0.77]
Subtotal (95% CI)		**1602**		**1505**	**100.0%**	**0.55 [0.39, 0.77]**
Total events	49		84			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.41 (P = 0.0006)						



Composite vascular outcome: HMG-CoA Reductase Inhibitors versus placebo, non-CAD patient studies (see Table C128 for definition)

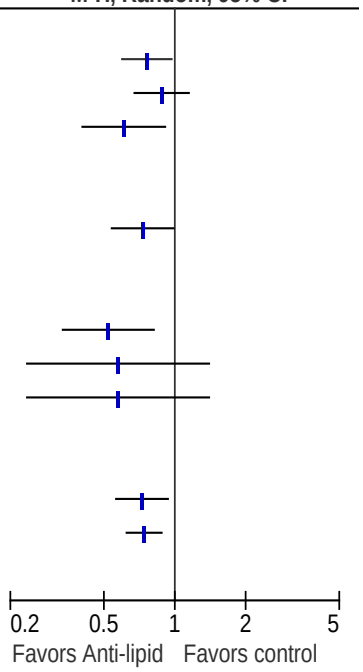
Study or Subgroup	Anti-lipid monotherapy Events	Total	Control Events	Total	Risk Ratio M-H, Random, 95% CI
7.7.1 Kendrick (AFCAPS/TexCAPS) 2010					
Kendrick (B)	8	145	21	159	0.42 [0.19, 0.91]
Kendrick (C)	7	145	18	159	0.43 [0.18, 0.99]
7.7.2 Nakamura (MEGA) 2009					
Nakamura (A)	21	1471	40	1507	0.54 [0.32, 0.91]
Nakamura (B)	25	1471	60	1507	0.43 [0.27, 0.68]
Nakamura (C)	33	1471	71	1507	0.48 [0.32, 0.72]
7.7.3 Colhoun (CARDS) 2009					
Colhoun (A -albuminuric)	24	276	38	275	0.63 [0.39, 1.02]
Colhoun (A)	25	482	42	488	0.60 [0.37, 0.97]
Colhoun (B)	18	482	27	488	0.67 [0.38, 1.21]



Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

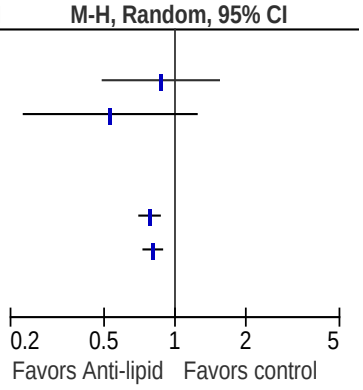
Composite vascular outcome: HMG-CoA Reductase Inhibitors versus placebo, CAD patient studies (see Table C128 for definitions)

	Anti-lipid monotherapy		Control		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% CI
7.8.4 Koren (ALLIANCE) 2009					
Koren (A)	78	286	105	293	0.76 [0.60, 0.97]
Koren (B)	73	286	85	293	0.88 [0.67, 1.15]
Koren (C)	32	286	54	293	0.61 [0.40, 0.91]
7.8.5 Chonchol (4S) 2007					
Chonchol (A)	53	245	77	260	0.73 [0.54, 0.99]
7.8.7 Lemos (LIPS) 2005					
Lemos (A)	23	150	47	160	0.52 [0.33, 0.82]
Lemos (B)	7	150	13	160	0.57 [0.24, 1.40]
Lemos (C)	7	150	13	160	0.57 [0.24, 1.40]
7.8.10 Tonelli (CARE) 2003					
Tonelli (CARE) (A)	89	844	126	867	0.73 [0.56, 0.94]
Tonelli (CARE) (B)	171	844	237	867	0.74 [0.62, 0.88]



Composite vascular outcome: HMG-CoA Reductase Inhibitors versus placebo, mixed CAD and non-CAD patient studies (see Table C128 for definitions)

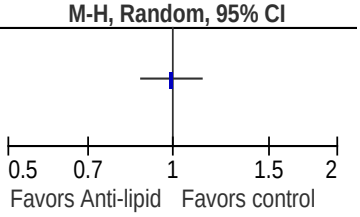
	Anti-lipid monotherapy		Control		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% CI
7.9.8 Asselbergs (PREVD) 2004					
Asselbergs (A)	21	433	24	431	0.87 [0.49, 1.54]
Asselbergs (B)	8	433	15	431	0.53 [0.23, 1.24]
7.9.9 Tonelli (WOSCOPS/CARE/LIPID) 2004					
Tonelli (W/C/L) (A)	492	2217	647	2274	0.78 [0.70, 0.86]
Tonelli (W/C/L) (B)	573	2217	730	2274	0.81 [0.73, 0.88]



Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

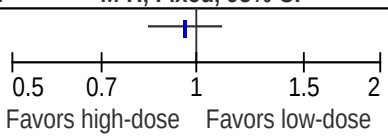
Composite vascular outcome: HMG-CoA Reductase Inhibitors versus placebo, heart failure studies (see Table C128 for definitions)

Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Risk Ratio M-H, Random, 95% CI
7.10.6 Kjekshus (CORONA) 2007					
Kjekhus (A)	288	791	309	844	0.99 [0.88, 1.13]

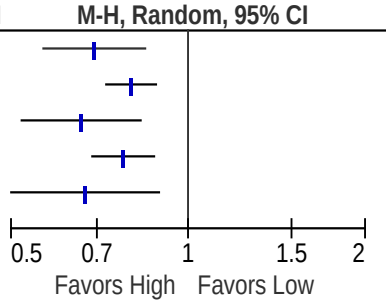


Composite vascular outcome: High versus low-dose HMG-CoA Reductase Inhibitors, CAD patient studies (See Table C128 for definitions)

Study or Subgroup	High-dose Events	High-dose Total	Low-dose Events	Low-dose Total	Risk Ratio M-H, Fixed, 95% CI
SEARCH 2010	265	820	292	866	0.96 [0.84, 1.10]

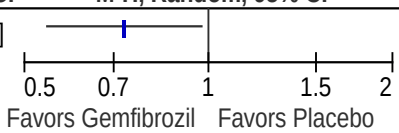


Study or Subgroup	High-dose Events	High-dose Total	Low-dose Events	Low-dose Total	Risk Ratio M-H, Random, 95% CI
Shepard (TNT) (A)	149	1602	202	1505	0.69 [0.57, 0.85]
Shepard (TNT) (B)	489	1602	574	1505	0.80 [0.73, 0.88]
Shepard (TNT) (C)	110	1602	157	1505	0.66 [0.52, 0.83]
Shepard (TNT) (D)	356	1602	431	1505	0.78 [0.69, 0.88]
Shepard (TNT) (E)	74	1602	104	1505	0.67 [0.50, 0.89]



Composite vascular outcome: Gemfibrozil versus placebo, CAD patient studies (see Table C128 for definitions)

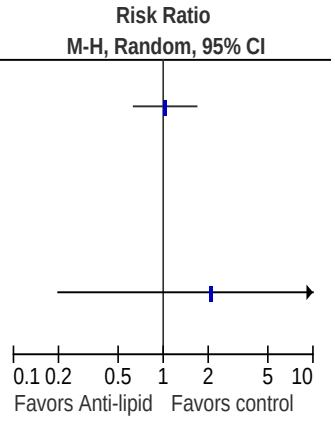
Study or Subgroup	Gemfibrozil Events	Gemfibrozil Total	Placebo Events	Placebo Total	Risk Ratio M-H, Random, 95% CI
Tonelli (VA-HIT) (B)	58	242	75	228	0.73 [0.54, 0.97]



Appendix Figure C24. Forest plots for anti-lipid monotherapy versus control trials (continued)

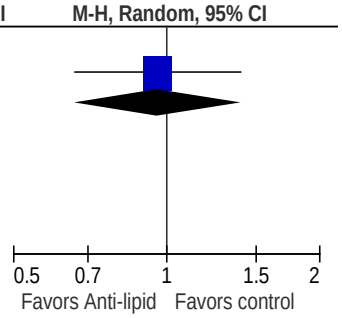
End-stage renal disease

Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Risk Ratio M-H, Random, 95% CI
7.13.1 HMG-CoA Reductase Inhibitors versus placebo: Mixed CAD and non-CAD patient studies					
Rahman (ALLHAT) 2008	32	779	31	778	1.03 [0.64, 1.67]
7.13.2 Gemfibrozil versus control: CAD patient studies					
Tonelli (VA-HIT) 2004	0	199	0	200	Not estimable
7.13.3 Gemfibrozil versus control: Unclear if patients had preexisiting CAD					
Samuelsson 1997	2	28	1	29	2.07 [0.20, 21.58]



Composite renal outcome (see Table C130 for definition)

Study or Subgroup	Anti-lipid monotherapy Events	Anti-lipid monotherapy Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
7.15.2 HMG-CoA Reductase Inhibitors versus placebo: Mixed CAD and non-CAD patient studies						
Rahman (ALLHAT) 2008	50	779	52	778	100.0%	0.96 [0.66, 1.40]
Subtotal (95% CI)		**779**		**778**	**100.0%**	**0.96 [0.66, 1.40]**
Total events	50		52			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.83)						



Appendix Table C127. Clinical outcomes (outcomes part B), AL monotherapy versus control treatment trials

Study	Stroke, Nonfatal n/N (%)		Stroke, Fatal n/N (%)		CHF Hospitalization (A) or CHF Death (B), n/N (%)		Composite Vascular Outcome n/N (%)**	
	AL	Control	AL	Control	AL	Control	AL	Control
HMG-CoA reductase inhibitors versus placebo trials (n=12)								
Kendrick, 2010[87] AFCAPS/ TexCAPS							†(A) NR; (B) 8/145 (5.5)*; (C)7/145 (4.8)*	†(A) NR; (B) 21/159 (13.2); (C) 18/159 (11.3)
Ridker, 2010[88] JUPITER	10/1638 (0.6)	14/1629 (0.9)					(A) 40/1638 (2.4)* (B) 64/1638 (3.9)* (C) 69/1638 (4.2)* (D) 24/1638 (1.5)*	(A) 71/1629 (4.4) (B) 114/1629 (7.0) (C) 127/1629 (7.8) (D) 40/1629 (2.5)
Nakamura, 2009[89] MEGA							(A)21/1471 (1.2)*; (B) 25/1471 (3.7)*; (C)33/1471 (4.9)*	(A)40/1507 (5.7); (B)60/1507 (8.7); (C)71/1507 (10.3)
Colhoun, 2009[90] CARDS							§(A) Low GFR: 25/482 (5.2)*, Albuminuric: 24/276 (8.7)*; (B) Low GFR: 18/482 (3.7)	§(A) Low GFR: 42/488 (8.6)*, Albuminuric: 38/275 (13.8); (B) Low GFR: 27/488 (5.5)
Koren, 2009[91] ALLIANCE					(A): 15/286 (5.2)	(A): 22/293 (7.5)	(A)78/286 (27.3)*; (B)73/286 (25.5); (C) 32/286 (11.2)*	(A)105/293 (35.8); (B) 85/293 (29.0); (C) 54/293 (18.4)
Rahman, 2008[93] ALLHAT-LLT								
Chonchol, 2007[94] 4S							53/245 (21.6)	77/260 (29.6)
Kjekshus, 2007[96] CORONA							288/791 (15.8)	309/844 (16.3)
Lemos, 2005[97] LIPS							(A) 23/150 (15.3)*; (B) 7/150 (4.7); (C) 7/150 (4.7)	(A) 47/160 (29.4); (B) 13/160 (8.1); (C) 13/160 (8.1)
Asselbergs, 2004[2] PREVD					(A)1/433 (0.2)	(A)1/431 (0.2)	(A) 21/433 (4.8); (B) 8/433 (1.8)	(A) 24/431 (5.6); (B) 15/431 (3.5)
Tonelli, 2004[98] WOSCOPS/ CARE/ LIPID							(A)492/2217 (22.2); (B)573/2217 (25.9)	(A)647/2274 (28.5); (B)730/2274 (32.1)
Tonelli, 2003[99] CARE							(A) 89/844 (10.5)*; (B) 171/844 (20.3)*	(A)126/867(14.5); (B) 237/867 (27.0)
High versus low dose HMG-CoA reductase inhibitor trials (n=2)								
	High Dose	Low Dose	High Dose	Low Dose	High Dose	Low Dose	High Dose	Low Dose
SEARCH, 2010[100]							265/820 (32.3)	292/866 (33.7)

Study	Stroke, Nonfatal n/N (%)	Stroke, Fatal n/N (%)	CHF Hospitalization (A) or CHF Death (B), n/N (%)		Composite Vascular Outcome n/N (%)**	
Shepherd, 2008[101] TNT			(A) 49/1602 (3.1)	(A) 84/1505 (5.6)	(A)149/1602 (9.3); (B)489/1602 (30.5); (C)110/1602 (6.9)*; (D)356/1602 (22.2); (E)74/1602 (4.6)	(A)202/1505 (13.4); (B)574/1505 (38.1); (C)157/1505 (10.4); (D)431/1505 (28.6); (E)104/1505 (6.9)
HMG-CoA reductase inhibitor versus bile acid sequestrant trials (n=1)						
Tonolo, 2006[104]						
Gemfibrozil versus placebo/control trials (n=2)						
Tonelli, 2004[98] VA-HIT					58/242 (24.0)	75/228 (32.9)
Samuelsson, 1997[84]						

AL = antilipid; CHF = congestive heart failure; NR = not reported; GFR = glomerular filtration rate; MI = myocardial infarction; CABG = coronary artery bypass grafting; CHD = coronary heart disease; CKD = chronic kidney disease; CVD = cardiovascular disease

*$p < 0.05$

**See Composite vascular outcomes definition table

† Participants treated with lovastatin were reported to have an adjusted RR of 0.32 (95% CI, 0.10-1.11; $P = 0.06$) for the endpoint of "first major cardiac event," though the proportion of participants with this endpoint was not reported for either treatment group.

§ Results for composite endpoint A were reported separately for participants with CKD defined based on GFR (<60 ml/min/ 1.73m^2) and for this outcome only for participants with CKD defined based on albuminuria (urinary albumin/creatinine ratio $\geq$22 mg/g).

Appendix Table C128. Composite vascular outcome definitions, AL monotherapy versus control treatment trials

Study	Definition
HMG-CoA reductase inhibitors versus placebo trials	
Kendrick, 2010[87] AFCAPS/TexCAPS	Defined two composite vascular endpoints, as follows: (A) "First major cardiac event," which included any of unstable angina, fatal or nonfatal MI, and/or sudden cardiac death; (B) "Fatal and nonfatal cardiovascular events;" and (C) "Fatal and nonfatal coronary events."
Ridker, 2010[88] JUPITER	Study defined the primary composite endpoint as: (A) nonfatal myocardial infarction, nonfatal stroke, hospital stay for unstable angina, arterial revascularization, or confirmed cardiovascular death; (B) same as A plus any death; (C) same as A plus any death plus venous thromboembolism; (D) non-fatal myocardial infarction, nonfatal stroke, or confirmed cardiovascular death
Nakamura, 2009[89] MEGA	The primary composite endpoint was defined as: (A) the first occurrence of a CHD event, including fatal and nonfatal MI, angina pectoris, cardiac/sudden death, and coronary revascularization. Additional composite endpoints included (B) first CHD event or ischemic stroke; and (C) total CVD events, which was not defined.
Colhoun, 2009[90] CARDS	The primary composite endpoint was defined as: (A) "Major cardiovascular disease", including acute CHD event (MI, including silent MI, unstable angina, acute CHD death, or resuscitated cardiac arrest), stroke, coronary revascularization, or death. An additional composite endpoint was (B) acute CHD event as defined above.
Koren, 2009[91] ALLIANCE	Defined three composite vascular endpoints, as follows: (A) First primary cardiovascular event, including cardiac death, nonfatal MI, resuscitated cardiac arrest, cardiac revascularization, or unstable angina requiring hospitalization; (B) All-cause mortality, peripheral revascularization, hospitalization for CHF, or stroke; and (C) Nonfatal MI or cardiac death.
Chonchol, 2007[94] 4S	Study defined the primary composite vascular endpoint as: (A) Major coronary event, including coronary death, nonfatal MI, resuscitated cardiac arrest, ECG confirmed silent MI. Additional composite vascular endpoints (results not reported) were: (B) Any coronary event, including coronary death, nonfatal MI, resuscitated cardiac arrest, ECG confirmed silent MI, myocardial revascularization procedure, hospitalization for acute CHD without MI diagnosis; and (C) Death, nonfatal MI, resuscitated cardiac arrest, ECG confirmed silent MI, myocardial revascularization procedure, hospitalization for acute CHD without MI diagnosis, and hospital-verified nonfatal coronary atherosclerotic events.
Kjekshus, 2007[96] CORONA	Study defined the primary composite vascular endpoint as: (A) Cardiovascular death, nonfatal MI, or nonfatal stroke. An additional composite vascular endpoint (results not reported) was: (B) Any coronary event, which included sudden death, fatal or nonfatal MI, coronary revascularization (CABG or PCI), ventricular defibrillation by an implantable cardioverter-defibrillator, resuscitation after cardiac arrest, or hospitalization for unstable angina.
Lemos, 2005[97] LIPS	Study defined the primary composite vascular endpoint as: (A) Adverse coronary atherosclerotic events, which included cardiac death, nonfatal MI, and all surgical or percutaneous coronary interventions not caused by restenosis after an index percutaneous coronary intervention. Additional composite vascular endpoints included: (B) Cardiac death or MI; and (C) All-cause mortality or MI.
Asselbergs, 2004[2] PREVEND IT	Study defined the primary composite endpoint as: (A) Cardiovascular mortality or hospitalization for any of the following: nonfatal MI, myocardial ischemia, CHF, PVD or stroke. An additional composite endpoint was: (B) Hospitalization for nonfatal MI or myocardial ischemia.
Tonelli, 2004[98] WOSCOPS/CARE/LIPID	Study defined the primary composite vascular endpoint as: (A) Fatal CHD, nonfatal MI, or coronary revascularization. An additional composite vascular endpoint was defined as: (B) Fatal CHD, nonfatal MI, coronary revascularization, or stroke.
Tonelli, 2003[99] CARE	Study defined the primary composite vascular endpoint as: (A) Death from coronary disease (including fatal MI, sudden death, death during a coronary intervention, and death from other coronary causes) or a symptomatic nonfatal biochemically confirmed myocardial infarction. An additional composite endpoint was: (B) Major coronary events, defined as fatal coronary disease, nonfatal MI, CABG, or coronary angioplasty.

Appendix Table C128. Composite vascular outcome definitions, AL monotherapy versus control treatment trials (continued)

Study	Definition
High versus low dose HMG-CoA reductase inhibitor trials	
SEARCH, 2010[100]	Study defined the primary composite vascular endpoint as first major vascular event, including coronary death, myocardial infarction, any stroke, or any arterial revascularization.
Shepard, 2008[101] TNT	Study defined the primary composite vascular endpoint as: (A) Major cardiovascular events, which included CHD death, nonfatal nonprocedure-related MI, resuscitation after cardiac arrest, and stroke. Additional composite vascular endpoints included: (B) Any cardiovascular event (defined as CHD death, nonfatal MI, resuscitation from cardiac arrest, revascularization procedure, documented angina, stroke, TIA, CABG, or CHF hospitalization); (C) Major coronary event (defined as CHD death, nonfatal nonprocedure-related MI, or resuscitation from cardiac arrest); (D) Any coronary event (defined as CHD death, nonfatal MI, resuscitation from cardiac arrest, revascularization procedure, or documented angina); and (E) Cerebrovascular event (stroke or TIA).
Gemfibrozil versus placebo/control trials	
Tonelli, 2004[98] VA-HIT	Results reported for outcome (B): Major cardiovascular event, which included fatal CHD, nonfatal MI, and stroke. Additional composite vascular endpoint was: (A) Coronary disease death (included fatal MI, sudden death, death during a coronary intervention, and death from other coronary causes) and nonfatal MI..

AL = anti-lipid; CVA = cerebrovascular accident (i.e. stroke); HTN = hypertension; MI = myocardial infarction; PVD = peripheral vascular disease; CHD = coronary heart disease; CVD = cardiovascular disease; CHF = congestive heart failure; ECG = electrocardiogram; CABG = coronary artery bypass grafting; TIA = transient ischemic attack; PCI = percutaneous coronary intervention.

Appendix Table C129. Clinical renal outcomes (outcomes part C), AL monotherapy versus control treatment trials

Study	End Stage Renal Disease, n/N (%)		Doubling of Serum Creatinine, n/N (%)		Halving of GFR, n/N (%)		Progression from Micro- to Macroalbuminuria, n/N (%)		Composite Renal Outcome, n/N (%)**	
	AL	Control	AL	Control	AL	Control	AL	Control	AL	Control
HMG-CoA reductase inhibitors versus placebo trials (n=11)										
Kendrick, 2010[87] AFCAPS/TexCAPS										
Ridker, 2010[88] JUPITER										
Nakamura, 2009[89] MEGA										
Colhoun, 2009[90] CARDS										
Koren, 2009[91] ALLIANCE										
Rahman, 2008[93] ALLHAT	32/779 (4.1)	31/778 (4.0)							(B)50/779 (6.4)	(B)52/778 (6.7)
Chonchol, 2007[94] 4S										
Kjekshus, 2007[96] CORONA										
Lemos, 2005[97] LIPS										
Asselbergs, 2004[2] PREVD										
Tonelli, 2004[98] WOSCOPS/CARE/ LIPID										
Tonelli, 2003[99] CARE										

Appendix Table C129. Clinical renal outcomes (outcomes part C), AL monotherapy versus control treatment trials (continued)

Study	End Stage Renal Disease, n/N (%)		Doubling of Serum Creatinine, n/N (%)		Halving of GFR, n/N (%)		Progression from Micro- to Macroalbuminuria, n/N (%)		Composite Renal Outcome, n/N (%)**	
High versus low dose HMG-CoA reductase inhibitor trials (n=1)										
	High Dose	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**
SEARCH, 2010[100]										
Shepherd, 2008[101] TNT										
HMG-CoA Reductase Inhibitor versus Bile Acid Sequestrant trials (n=1)										
Tonolo, 2006[104]						*†(4)	†(15)			
Gemfibrozil versus placebo/control trials (n=2)										
Tonelli, 2004[98] VA-HIT	0/199	0/200								
Samuelsson, 1997[84]	2/28 (7.1)	1/29 (3.4)								

AL = antilipid; GFR = glomerular filtration rate;
* $p < 0.05$ versus control
**See Composite renal outcome definitions table
†Study reported that conversion from microalbuminuria to overt proteinuria occurred in 4 vs. 15% in simvastatin vs. cholestyramine subjects, respectively ($p<0.01$). However, from results reported, it was not possible to determine the numerator and denominator used to derive these results for both treatment groups.

Appendix Table C130. Composite renal outcome definitions for AL monotherapy versus control treatment trials

Study	Definition
HMG-CoA Reductase Inhibitors (Statins) versus Placebo/Usual care/No treatment trials	
Rahman, 2008[93] ALLHAT-LLT	Study defined multiple composite renal outcomes, including: (A) ESRD (start of long-term dialysis, death due to kidney disease, or kidney transplantation) or ≥50% decline in GFR; and (B) ESRD or ≥50% decline in GFR.

AL = antilipid; ESRD = end stage renal disease; GFR = glomerular filtration rate

Appendix Table C131. Study withdrawals and adverse events (outcomes part D), AL monotherapy versus control treatment trials

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Event: Any, n/N (%)		Study Withdrawal Due to Serious Adverse Event, Any, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event: Specific, n/N (%)		Renal Adverse Events, n/N (%)	
	AL	Control	AL	Control	AL	Control	AL	Control	AL	Control	AL	Control
HMG-CoA reductase inhibitors versus placebo trials (n=11)												
Kendrick, 2010[87] AFCAPS/ TexCAPS									†Rhabdo: 0/145; CK>10x ULN: 0/159	†Rhabdo: 1/159 (0.6); CK>10x ULN: 1/159 (0.6)		
Ridker, 2010[88] JUPITER												
Nakamura‡ 2009[89] MEGA							166/1471 (11.3)	158/1507 (10.5)	AST >100IU: 18/1471 (1.2); ALT >100IU: 37/1471 (2.5); CK >500IU: 38/1471 (2.6)	AST >100IU: 17/1507 (1.1); ALT >100IU: 41/1507 (2.7); CK >500IU: 39/1507 (2.6)	sCr >4mg/dl: 0.3%	sCr >4mg/dL: 0.2%
Colhoun, 2009[90] CARDS												
Koren, 2009[91] ALLIANCE									Rhabdo 0/286; AST >3x ULN 1/286; ALT >3x ULN 1/286; CK >10xULN: 0/286	Rhabdo 0/293; AST >3x ULN NR; ALT >3x ULN NR; CK >10xULN: NR		
Rahman, 2008[93] ALLHAT-LLT												
Chonchol, 2007[94] 4S												
Kjekshus, 2007[96] CORONA												

Appendix Table C131. Study withdrawals and adverse events (outcomes part D), AL monotherapy versus control treatment trials (continued)

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Event: Any, n/N (%)		Study Withdrawal Due to Serious Adverse Event, Any, n/N (%)		Adverse Event: Any, n/N (%)		Adverse Event: Specific, n/N (%)		Renal Adverse Events, n/N (%)	
	AL	Control	AL	Control	AL	Control	AL	Control	AL	Control	AL	Control
Lemos, 2005[97] LIPS												
Asselbergs, 2004[2] PREVD	§NR	§NR										
Tonelli, 2004[98] WOSCOPS/ CARE/ LIPID												
Tonelli, 2003[99] CARE	0/844	0/867			0/844	0/867			#Rhabdo: 0/844; CK>3x ULN: 6/844 (0.7); Abnormal LFTs: 5/844 (0.6)	#Rhabdo: 3/867 (0.3); CK>3x ULN: 3/867 (0.3); Abnormal LFTs: 5/867 (0.6)		
High versus low dose HMG-CoA reductase inhibitor trials (n=1)												
	High Dose	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**	**High Dose**	**Low Dose**
SEARCH, 2010[100]												
Shepherd, 2008[101] TNT	6/1602 (0.4)	6/1505 (0.4)			68/1602 (4.2)	29/1505 (1.9)	140/1602 (8.7)	78/1505 (5.2)	ALT or AST >3x ULN: 22/1602 (1.4); CK >10xULN: 0/1602	ALT or AST >3x ULN: 1/1505 (0.1); CK >10xULN: 0/1505	Hematuria: 58/1602 (3.6)	Hematuria: 51/1505 (3.4)
HMG-CoA reductase inhibitor versus bile acid sequestrant trials (n=1)												
Tonolo, 2006[104]	1/43 (2.3)	3/43 (7.0)					1/43 (2.3)	3/43 (7.0)	‡NR	‡NR	‡NR	‡NR
Gemfibrozil versus placebo/control trials (n=2)												
Tonelli, 2004[98] VA-HIT	0/199	0/200			0/199	0/200			**Rhabdo: 0/199; CK>3x ULN: 0/199	**Rhabdo: 0/200; CK>3x ULN: 0/200		

Appendix Table C131. Study withdrawals and adverse events (outcomes part D), AL monotherapy versus control treatment trials (continued)

Study	Study Withdrawals: Any, n/N (%)		Serious Adverse Event: Any, n/N (%)	Study Withdrawal Due to Serious Adverse Event, Any, n/N (%)	Adverse Event: Any, n/N (%)	Adverse Event: Specific, n/N (%)		Renal Adverse Events, n/N (%)
Samuelsson, 1997[84]	8/28 (28.6)	1/29 (3.4)				"Mild GI symptoms": 6/28 (21.4)	"Mild GI symptoms": 0/29	

AL = antilipid agent; Rhabdo = rhabdomyolysis; NR = not reported; AST = aspartase aminotransferase; ALT = alanine aminotransferase; LFTs = liver function tests; IU = international units; ULN = upper limit of normal; CK = creatine phosphokinase; GI = gastrointestinal; sCr = serum creatinine

*p < 0.05 versus control

†Study reported that increases >3 times ULN in liver function test results were rare, and incidence was similar in both treatment groups.

‡Study reported that two patients developed renal cancer, and that one patient developed a 3 to 4-fold increase of AST and ALT above baseline levels, but didn't indicate either patient's treatment group.

§Study reported total withdrawals of n = 92/433 (21.2%) and 117/431 (27.1%) in pravastatin and placebo groups, respectively. Among total withdrawals, however, the study reported those for "other medical reasons," which included but were not entirely comprised of subjects reaching study endpoints (i.e. cardiovascular mortality or hospitalization) (n = 23 and 33 for pravastatin and placebo groups, respectively.

#Study also reported the following specific adverse effects in pravastatin vs. placebo participants, respectively: depression (10/844 vs. 14/867), nondermatologic malignancy (133/844 vs. 146/867), and skin cancer (57/844 vs. 41/867, p = 0.08).

**Study also reported the following specific adverse effects in gemfibrozil vs. placebo participants, respectively: depression (4/199 vs. 7/200), nondermatologic malignancy (17/199 vs. 23/200), and skin cancer (0/199 vs. 2/200).

Appendix Evidence Table C132. Overview of intensive multicomponent intervention (INT) versus control treatment trials

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Multicomponent trials (n=4)				
Chan, 2009[105] Location China, Multi-site Funding Source Government	Inclusion Criteria: Type 2 DM and Plasma creatinine level 150-350 µmol/L, age 35-75 yrs Exclusion Criteria: Reversible cause of renal dysfunction (e.g. renal artery stenosis), malignancy or life threatening disease, nondiabetic renal disease, unstable psychiatric illness, and ≥20% difference in two consecutive plasma creatinine values within 3 months before recruitment.	N=205 Age (yr): 65 Gender (Male %): 66 Race/Ethnicity (%): NR Weight: NR BMI: 25.4 Systolic BP (mm Hg): 145 Diastolic BP (mm Hg): 74 CKD stage: NR Serum creatinine (mg/dL): NR Creatinine clearance (mL/min): NR Albuminuria: NR Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 96 Dyslipidemia (%): NR History of CAD (%): 16 History of CHF (%): 7 Peripheral arterial disease (%): 1 History of MI (%):2 History of Stroke (%):15 Current smoker (%): NR History of AKI (%): NR	n=104 structured care (managed by multidisciplinary diabetes care team, including dietician, MD, and nurse educator, with regular lab monitoring, and treatment to target BP <130/80 mm Hg, HbA1c <7%, LDL-C <2.6 mmol/L, triglycerides <2 mmol/L, and treatment with ACEI or ARB unless develop persistent hyperkalemia or increase in baseline creatinine by >30%) n= 101 Usual care/control Followup period: median 2 years Study withdrawals (%): 2.4%	Allocation Concealment Adequate Blinding: None (i.e. open) Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: Adequate

Appendix Evidence Table C132. Overview of intensive multicomponent intervention (INT) versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Joss, 2004[106] Location: Scotland/multi-site Funding Source Other-non industry	Inclusion Criteria: Pts w/ type 2 DM and nephropathy (albuminuria >300 mg/24h, characteristic diabetic retinopathy, kidneys w/near normal morphology on ultrasound), HTN Exclusion Criteria: NR	N= 90 Age (yr): 63 Gender (Male %): 63.3 Race/Ethnicity (%):NR Weight: NR BMI (kg/m2): 30.4 Systolic BP (mm Hg): 165 Diastolic BP (mm Hg): 88 CKD stage: NR Serum creatinine (mg/dL): NR Creatinine clearance (mL/min): 55 mL/min Albuminuria: median 755 mg/24 hrs Albumin/creatinine ratio (mg/g): 78.8 mg/mmol Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): 7.9 Total cholesterol (mg/dL): 212.7 LDL cholesterol (mg/dL): NR Diabetes (%): 100 History of HTN (%): 100 Dyslipidemia (%): NR History of CAD (%): NR History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): NR Current smoker (%): 28 History of AKI (%): NR	n= 47 Intensive therapy/Project team care (Managed by multidisciplinary project care team, including dietician, MD, and nurse, with initial visits as often as every 2-3 weeks.) n= 43 Control treatment (Patients managed in their usual clinic.) Treatment goals were identical for both groups, including SBP <140 mm Hg, DBP <80 mm Hg, HbA1c <8%, sodium intake <120 mmol/day, protein intake 0.7-1 g/kg of ideal body weight per day, cholesterol <4 mmol/L or cholesterol :HDL ratio <4. Exercise was encouraged and advice was given on smoking. For both groups, BP and lab measures were collected for monitoring every 3-6 months to guide management. Followup period: median 2 years Study withdrawals (%): 3.3%	Allocation Concealment Adequate Blinding: None (i.e. open) Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Yes
Gaede, 2003/1999[107,108] STENO-2	Inclusion Criteria: Type 2 DM and microalbuminuria (defined as urinary albumin excretion rate of 30-300 mg/24hr in 4 of 6 urine samples).	N=160 Age (yr): 55.1 yrs Gender (Male %): 74 Race/Ethnicity (%): NR	n=80 Intensive care, with management by multidisciplinary Diabetes Center team, including a	Allocation Concealment Adequate Blinding: No blinding

Appendix Evidence Table C132. Overview of intensive multicomponent intervention (INT) versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Location Denmark, single site Funding Source Industry	Exclusion Criteria: Age older than 65 or younger than 40; a stimulated serum C-peptide concentration less than 600 pmol/L 6 min after IV injection of 1 mg glucagon; pancreatic insufficiency or diabetes secondary to pancreatitis; alcohol abuse; nondiabetic kidney disease; malignancy; or life threatening disease with death probable within 4 years.	Weight: NR BMI (kg/m2): 29.8 Systolic BP (mm Hg): 148 Diastolic BP (mm Hg): 86 CKD stage: NR Serum creatinine (mmol/L): 77 Creatinine clearance (mL/min): NR Albuminuria: 73.5 mg/24 hr Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): 117 HbA_{1c} (%): 8.6 Total cholesterol (mg/dL): 217 LDL cholesterol (mg/dL): 130 Diabetes (%): 100 History of HTN (%): NR Dyslipidemia (%):NR History of CAD (%): 24 (based only on ischemia on resting or stress ECG) History of CHF (%): NR Peripheral arterial disease (%): NR History of MI (%): NR History of Stroke (%): 3 Current smoker (%): 38 History of AKI (%): NR	dietician, MD, and nurse. Targeted treatment goals of SBP <140 mm Hg, DBP <85 mm Hg, HbA1c <6.5%, triglycerides <1.7 mmol/L, total cholesterol <5.0 mmol/L, HDL-cholesterol >1.1 mmol/L, aspirin for patients with known ischemia or peripheral vascular disease, ACEI regardless of blood pressure. n= 80 Standard care, with management by their regular general practitioner, who was to follow Danish diabetes management guidelines, including treatment goals of SBP <160 mm Hg, DBP <95 mm Hg, HbA1c <7.5%, triglycerides <2.2 mmol/L, total cholesterol <6.5 mmol/L, HDL-cholesterol >0.9 mmol/L, aspirin for patients with known ischemia. Followup period: median 7.8 yrs for mortality outcome, median 3.8 yrs for other outcomes Study withdrawals (%): 3.1 for longer followup period, 1.9 for shorter followup period	Intention to Treat Analysis (ITT): No Withdrawals/Dropouts adequately described: Adequate in report with 7.8 yrs followup

Appendix Evidence Table C132. Overview of intensive multicomponent intervention (INT) versus control treatment trials (continued)

Study/Region/ Funding Source	Inclusion/Exclusion Criteria	Patient Characteristics (expressed in means unless otherwise noted)	Intervention/Duration	Study Quality
Harris, 1998[109] Location USA, multi site Funding Source Other (Foundation)	Inclusion Criteria: Primary care in the general medicine practice with ≥1 physician visit in the past year, and two serum creatinine levels at least 6 months apart with estimated creatinine clearances <50 mL/min both times, and most recent serum creatinine concentration before enrollment >1.4 mg/dL. Exclusion Criteria: Living in an institution (NH or prison), inability to communicate with the research assistants, either because of a sensory or neurologic deficit or because could not speak and/or understand English.	N=437 Age (yr): 68.5 Gender (Male %): 34 Race/Ethnicity (%): African American 80.5 Weight: 172.7 lbs BMI: NR Systolic BP (mm Hg): 144 Diastolic BP (mm Hg): 83 CKD stage: NR Serum creatinine (mg/dL): 2.1 Creatinine clearance (mL/min): 34 Albuminuria: NR Albumin/creatinine ratio (mg/g): NR Estimated GFR (ml/min/1.73m^2): NR HbA_{1c} (%): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Diabetes (%): 43.5 History of HTN (%): 98.6 Dyslipidemia (%): NR History of CAD (%): 47.8 History of CHF (%): 40 Peripheral arterial disease (%): NR History of MI (%): 37 History of Stroke (%): 20 Current smoker (%): NR History of AKI (%): NR	n=206 Intensive case management in multidisciplinary renal clinic (nephrologist, renal nurse, renal dietician, social worker) including recommendations to patient's primary care provider to reduce use of nephrotoxic drugs, decrease dietary protein, initiate ACEI use if possible, with focus on improving medication compliance. n= 231 Standard care, with management by their regular general medicine physician. Followup period: median 5 years Study withdrawals (%): 0	Allocation Concealment Not described Blinding: No blinding Intention to Treat Analysis (ITT): Yes Withdrawals/Dropouts adequately described: No withdrawals were reported

ACEI = angiotensin converting enzyme inhibitor; ACR = albumin/creatinine ratio; AER = albumin excretion rate; AKI = acute kidney injury; ARB = angiotensin II receptor blocker; BB = bete blocker; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; CVA = cerebrovascular accident; DBP = diastolic blood pressure; DM = diabetes mellitus; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HTN = hypertension; INT = intensive multi-component intervention; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NSAIDS = non-steroidal anti-inflammatory drug; PVD = peripheral vascular disease; RCT = randomized controlled trial; SBP = systolic blood pressure; UACR = urinary albumin/creatinine ratio; UAE = urinary albumin excretion

Appendix Table C133. Summary of study baseline characteristics for INT versus control treatment trials

Characteristic	Mean (range) *(unless otherwise noted)*	Number of Trials Reporting
INT trials		*4*
Patients randomized, n	892 (90 to 437)	4
Age of subjects, years	64.7 (55.1 to 68.5)	4
Male gender, %	51.5 (34 to 74)	4
African American Race/ethnicity, %	*80.5	1
Body Mass Index, kg/m2	27.9 (25.4 to 30.4)	3
Patients with diabetic nephropathy, n	†250 (90 to 160)	2
Serum creatinine, mg/dL	1.8 (0.9 to 2.1)	2
Estimated GFR, ml/min/1.73m^2	117	1
Creatinine clearance (mL/min)	37.6 (34 to 55)	2
Albuminuria, mg/24 hr	‡	2
Systolic blood pressure, mm Hg	147 (144 to 165)	4
Diastolic blood pressure, mm Hg	82 (74 to 88)	4
History of hypertension, %	98.0 (96 to 100)	3
HbA_{1c} (%)	8.3 (7.9 to 8.6)	2
History of CAD, %	‡34.9 (16 to 47.8)	3
History of MI, %	25.8 (2 to 37)	2
History of CHF,%	29.5 (7 to 40)	2
History of Stroke, %	15.3 (3 to 20)	3
Total cholesterol, mg/dL	215 (213 to 216.5)	2
LDL cholesterol, mg/dL	129.5	1
Current smokers, %	34.4 (28 to 38)	2

INT = Intensive Multi-Component Intervention; GFR = glomerular filtration rate; HbA_{1c} = hemoglobin A_{1c}; CAD = coronary artery disease; MI = myocardial infarction; CHF = congestive heart failure; LDL = low density lipoprotein

*This study reported data only for African American race/ethnicity, but did not report information regarding the race/ethnicity of its remaining participants.

†Two other studies included a total of 395 participants with diabetes and either impaired creatinine clearance or GFR, but did not report information on albuminuria or proteinuria. These study subjects were not counted toward the total number of patients with diabetic nephropathy.

‡Of the two studies reporting baseline albuminuria, one reported a mean of 73.5 mg/24 hours and the other a median of 755 mg/24 hours.

Appendix Table C134. Clinical outcomes (outcomes part A), INT versus control treatment trials

Study	All-Cause Mortality, n/N (%)		Cardiovascular Mortality, n/N (%)		Myocardial Infarction, Any, n/N (%)		Myocardial Infarction, Fatal n/N (%)		Myocardial Infarction, Nonfatal, n/N (%)		Stroke, Any, n/N (%)	
	INT	Control	INT	Control	INT	Control	INT	Control	INT	Control	INT	Control
INT versus control treatment trials (n=4)												
Chan, 2009[105]	8/104 (7.7)	11/101 (11.0)			4/104 (3.8)	4/101 (4.0)					*NR	*NR
Joss, 2004[106]	6/47 (12.8)	3/43 (7.0)	†4/47 (8.5)	†3/43 (7.0)	‡NR	‡NR	2/47 (4.3)	1/43 (2.3)	‡NR	‡NR	‡NR	‡NR
§Gaede, 2003/ 1999[107,108]	12/80 (15.0)	15/80 (18.8)	7/80 (8.8)	7/80 (8.8)					4/80 (5.0)	8/80 (10.0)		
Harris, 1998[109]	59/206 (28.6)	77/231 (33.3)										

INT = Intensive Multi-Component Intervention; NR = not reported

*Study reported results for composite endpoint of stroke or transient ischemic attack (2/104 in INT group vs. 3/101 in control group), but not for stroke outcome only.

†Study didn't define cardiovascular death, but these results derived from sum of participants in each group with sudden death, fatal myocardial infarction, or fatal stroke.

‡Study reported myocardial infarction, nonfatal myocardial infarction, and stroke by number of events per treatment group and not by the proportion of participants in each treatment group with one or more event.

§Study results taken from 2003 report except when data for a specific outcome only was available from the earlier 1999 report.

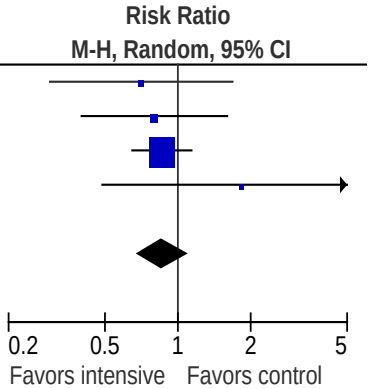
Appendix Figure C25. Forest plots for INT versus control treatment trials

All-cause mortality

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chan 2009	8	104	11	101	8.0%	0.71 [0.30, 1.68]
Gaede 2003	12	80	15	80	12.6%	0.80 [0.40, 1.60]
Harris 1998	59	206	77	231	75.9%	0.86 [0.65, 1.14]
Joss 2004	6	47	3	43	3.5%	1.83 [0.49, 6.87]
Total (95% CI)		**437**		**455**	**100.0%**	**0.86 [0.67, 1.10]**
Total events	85		106			

Heterogeneity: Tau² = 0.00; Chi² = 1.49, df = 3 (P = 0.68); I² = 0%

Test for overall effect: Z = 1.20 (P = 0.23)

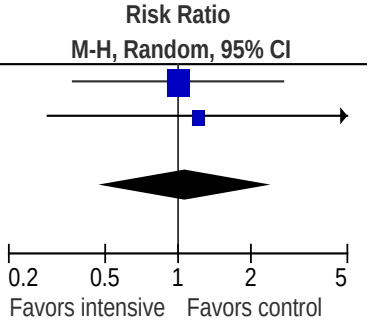


Cardiovascular mortality

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Gaede 2003	7	80	7	80	67.4%	1.00 [0.37, 2.72]
Joss 2004	4	47	3	43	32.6%	1.22 [0.29, 5.14]
Total (95% CI)		**127**		**123**	**100.0%**	**1.07 [0.47, 2.43]**
Total events	11		10			

Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = 0.82); I² = 0%

Test for overall effect: Z = 0.15 (P = 0.88)

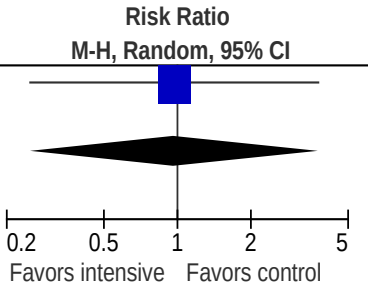


Myocardial infarction, any

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chan 2009	4	104	4	101	100.0%	0.97 [0.25, 3.78]
Total (95% CI)		**104**		**101**	**100.0%**	**0.97 [0.25, 3.78]**
Total events	4		4			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.04 (P = 0.97)



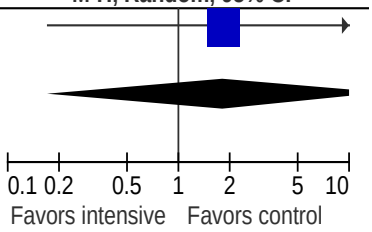
Appendix Figure C25. Forest plots for INT versus control treatment trials (continued)

Myocardial infarction, fatal

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Joss 2004	2	47	1	43	100.0%	1.83 [0.17, 19.47]
Total (95% CI)		**47**		**43**	**100.0%**	**1.83 [0.17, 19.47]**
Total events	2		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.50 (P = 0.62)

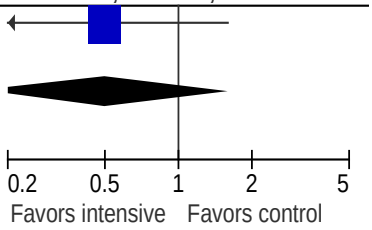


Myocardial infarction, nonfatal

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Gaede 2003	4	80	8	80	100.0%	0.50 [0.16, 1.59]
Total (95% CI)		**80**		**80**	**100.0%**	**0.50 [0.16, 1.59]**
Total events	4		8			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.17 (P = 0.24)

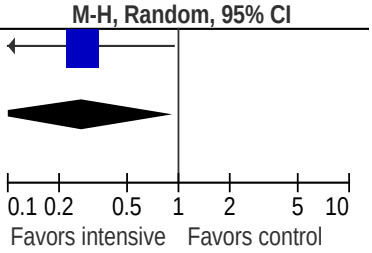


Stroke, nonfatal

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Gaede 2003	3	80	11	80	100.0%	0.27 [0.08, 0.94]
Total (95% CI)		**80**		**80**	**100.0%**	**0.27 [0.08, 0.94]**
Total events	3		11			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.06 (P = 0.04)

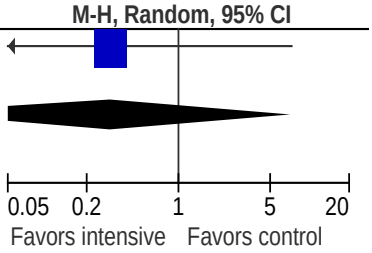


Stroke, fatal

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Joss 2004	0	47	1	43	100.0%	0.31 [0.01, 7.31]
Total (95% CI)		**47**		**43**	**100.0%**	**0.31 [0.01, 7.31]**
Total events	0		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.73 (P = 0.46)



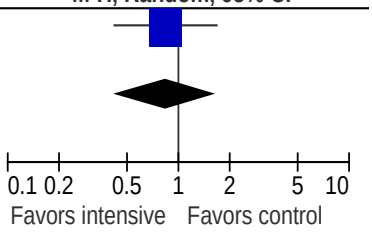
Appendix Figure C25. Forest plots for INT versus control treatment trials (continued)

Congestive heart failure, hospitalization

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chan 2009	13	104	15	101	100.0%	0.84 [0.42, 1.68]
Total (95% CI)		**104**		**101**	**100.0%**	**0.84 [0.42, 1.68]**
Total events	13		15			

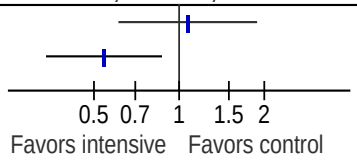
Heterogeneity: Not applicable

Test for overall effect: Z = 0.49 (P = 0.62)



Composite vascular outcome (see Table C136 for definitions)

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chan 2009	21	104	19	101		1.07 [0.62, 1.87]
Gaede 2003	19	80	35	80		0.54 [0.34, 0.86]

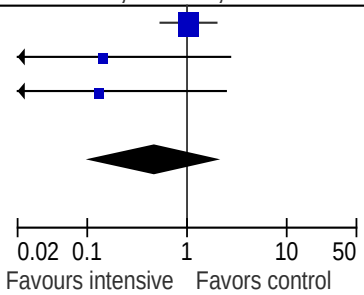


End stage renal disease

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chan 2009	16	104	15	101	60.6%	1.04 [0.54, 1.98]
Gaede 2003	0	80	3	80	19.7%	0.14 [0.01, 2.72]
Joss 2004	0	47	3	43	19.8%	0.13 [0.01, 2.46]
Total (95% CI)		**231**		**224**	**100.0%**	**0.47 [0.10, 2.20]**
Total events	16		21			

Heterogeneity: Tau² = 0.92; Chi² = 3.53, df = 2 (P = 0.17); I² = 43%

Test for overall effect: Z = 0.96 (P = 0.33)

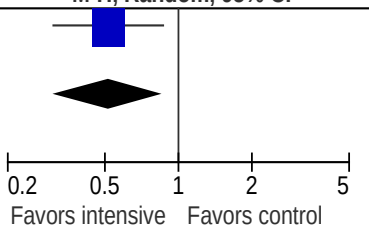


Progression from microalbuminuria to macroalbuminuria

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Gaede 2003	16	80	31	80	100.0%	0.52 [0.31, 0.87]
Total (95% CI)		**80**		**80**	**100.0%**	**0.52 [0.31, 0.87]**
Total events	16		31			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.50 (P = 0.01)



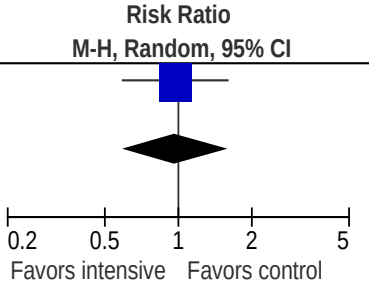
Appendix Figure C25. Forest plots for INT versus control treatment trials (continued)

Composite renal outcome (see Table C138 for definition)

Study or Subgroup	Intensive Events	Intensive Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chan 2009	24	104	24	101	100.0%	0.97 [0.59, 1.59]
Total (95% CI)		**104**		**101**	**100.0%**	**0.97 [0.59, 1.59]**
Total events	24		24			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.12 (P = 0.91)



Appendix Table C135. Clinical outcomes (outcomes part B), INT versus control treatment trials

Study	Stroke, Nonfatal, n/N (%)		Stroke, Fatal, n/N (%)		CHF, Any, n/N (%)		CHF Hospitalization (A) or Death (B), n/N (%)		Composite Vascular Outcome, n/N (%)**	
	INT	Control	INT	Control	INT	Control	INT	Control	INT	Control
INT versus control treatment trials (n=4)										
Chan, 2009[105]							(A)13/104 (12.5) (B) NR	(A)15/101 (14.8) (B) NR	21/104 (20.2)	19/101 (18.8)
Joss, 2004[106]	†NR	†NR	0/47	1/43 (2.3)	†NR	†NR			†NR	†NR
*Gaede, 2003/1999[107,108]	3/80 (3.8)	11/80 (13.8)							(A)19/80 (23.8)	(A)35/80 (43.8)
Harris, 1998[109]										

INT = Intensive Multi-Component Intervention; CHF = congestive heart failure; NR = not reported

*Study results taken from 2003 report except when data for a specific outcome only was available from the earlier 1999 report.

**See Composite vascular outcome definitions table

†Study reported nonfatal stroke, CHF, and composite vascular outcomes by number of events per treatment group and not by the proportion of participants in each treatment group with one or more event.

Appendix Table C136. Composite vascular outcome definitions for INT versus control treatment trials

Study	Definition
INT versus control treatment trials (n=4)	
Chan, 2009[105]	"Composite cardiovascular end point" included any of the following: hospitalization for heart failure, hospitalization for angina, hospitalization for arrhythmia, MI, coronary revascularization (PTCA/CABG), other revascularization, CVA or transient ischemic attack, and lower limb amputation.
Joss, 2004[106]	"Cardiovascular events" included any of the following: sudden death, fatal and nonfatal MI, fatal and nonfatal CVA, CABG, CHF (undefined), amputation (undefined) or interventional vascular surgery.
Gaede, 2003/1999[107,108]	The primary composite endpoint was defined as (A) death from cardiovascular causes, nonfatal MI, CABG, PCI, nonfatal stroke, amputation as a result of ischemia, or surgery for peripheral atherosclerotic artery disease. Additional composite vascular endpoints were defined as: (B) All cause mortality, nonfatal MI, nonfatal CVA, CABG, PTCA, arterial revascularization to the legs, or amputation to the legs for ischemia; (C) cardiovascular mortality, nonfatal MI, nonfatal CVA, CABG, PTCA, arterial revascularization to the legs, or amputation to the legs for ischemia; and (D) nonfatal MI, nonfatal CVA, CABG, PTCA, arterial revascularization to the legs, or amputation to the legs for ischemia.

INT = Intensive Multi-Component Intervention; PTCA = percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass grafting; MI = myocardial infarction; CVA = cerebrovascular accident (i.e. stroke)

Appendix Table C137. Clinical renal outcomes (outcomes part C), INT versus control treatment trials

Study	End Stage Renal Disease, n/N (%)		Doubling of Serum Creatinine, n/N (%)		Halving of GFR, n/N (%)		Progression from Micro to Macroalbuminuria, n/N (%)		Composite Renal Outcome, n/N (%)**	
	INT	Control	INT	Control	INT	Control	INT	Control	INT	Control
Intensive Multi-Component Intervention (INT) versus Control treatment trials (n=4)										
Chan, 2009[105]	16/104 (15.4)	15/101 (14.9)							24/104 (23.1)	24/101 (23.8)
Joss, 2004[106]	0/47	3/43 (7.0)								
*Gaede, 2003/1999[107,108]	0/80	3/80 (3.8)					16/80 (20.0)	31/80 (38.8)		
Harris, 1998[109]										

INT = Intensive Multi-Component Intervention; GFR = glomerular filtration rate
*Study results taken from 2003 report except when data for a specific outcome only was available from the earlier 1999 report.
**See Composite renal outcome definitions table

Appendix Table C138. Composite renal outcome definitions for INT versus control treatment trials

Study	Definition
INT versus control treatment trials (n=4)	
Chan, 2009[105]	ESRD (defined as the need for dialysis, or plasma creatinine level ≥500 µmol/l) or death.

INT = Intensive Multi-Component Intervention; ESRD = end-stage renal disease

Appendix Table C139. Study withdrawals and adverse events (outcomes part D), INT versus control treatment trials

Study	Study Withdrawals: Any		Serious Adverse Event: Any		Serious Adverse Event: Any Leading to Withdrawal		Adverse Event: Any		Renal Adverse Events: Any		Adverse Event: Other Specific	
	INT	Control	INT	Control	INT	Control	INT	Control	INT	Control	INT	Control
INT versus control treatment trials (n=4)												
Chan, 2009[105]	*NR	*NR			0/104	0/101						
Joss, 2004[106]	2/47 (4.2)	1/43 (2.3)										
†Gaede, 1999/2003[107,108]	1/80 (1.3)	2/80 (2.5)	1/80 (1.3)	0/80	0/80	0/80					Hypoglycemia: Minor 42/80 (52.5), Major 5/80 (6.3)	Hypoglycemia: Minor 39/80 (48.8), Major 12/80 (15.0)
Harris, 1998[109]	0/206	0/231										

INT = Intensive Multi-Component Intervention; NR = not reported

*Study reported withdrawals only for combined treatment groups (n=5 [2.4%]), but not for each treatment group by itself.

†Study results taken from 2003 report except when data for a specific outcome only was available from the earlier 1999 report.

Table C140. Assessment of individual study quality for KQ5 and KQ6

Study ID	Allocation Concealment	Blinding	Intention to Treat Analysis	WithdrawalsDescribed	Study Rating
Angiotensin converting enzyme inhibitor (ACEI) versus placebo/no treatment trials (n=17)					
Perkovic, 2007[1] PROGRESS	adequate	double*	yes	yes for overall study population**	Good
Asselbergs, 2004[2]	unclear	double*	yes	yes	Fair
Marre, 2004[3] DIABHYCAR	adequate	double*	yes	yes	Good
Katayama, 2002[4] JAPAN-IDDM	adequate	double*	no	yes	Fair
Bojestig, 2001[5]	unclear	double	yes	yes	Fair
Gerstein HOPE Trial, 2001[6]	adequate**	double*	yes	yes for overall study population**	Good
O'Hare, 2000[7] ATLANTIS	adequate	double	no	yes	Fair
Muirhead, 1999[8]	unclear	double	no	yes	Fair
Ruggenenti, 1999[9] REIN	adequate	double*	yes	yes	Good
Crepaldi, 1998[10]	unclear	double	no	yes	Fair
The GISEN Group, 1997[11]	adequate	double*	yes	yes	Good
Maschio, 1996[12]	unclear	double*	yes	yes	Fair
Trevisan, 1995[13]	unclear	double	no	yes	Fair
Laffel, 1995[14]	unclear	double	no	yes	Fair
Sano 1994[15]	unclear	no	no	yes	Fair
Lewis, 1993[16]	unclear	double*	yes	yes	Fair
Ravid, 1993[17]	unclear	double	no	yes	Fair
Angiotensin converting enzyme inhibitor (ACEI) versus angiotensin II-receptor blocker (ARB) trials (n=6)					
Mann, 2008[18] ONTARGET	adequate	double	yes	yes	Good
Menne, 2008[19] VALERIA	adequate	double*	no	yes	Fair
Sengul, 2006[20]	unclear	no	no	yes	Fair
Barnett, 2004[21] DETAIL	adequate	double	yes	yes	Good
Lacourcière, 2000[22]	unclear	double	no	yes	Fair
Muirhead, 1999[8]	unclear	double	no	yes	Fair
Angiotensin converting enzyme inhibitor (ACEI) versus Calcium channel blocker (CCB) trials (n=6)					
Rahman, 2005[23,110] ALLHAT	adequate**	double*	yes	yes for overall study population**	Good
Fogari, 2002[24]	adequate	no	no	yes	Fair
Agodoa, 2002[25] Wright, 2002[26] Norris, 2006[27] (AASK)	adequate**	double*	yes	yes	Good
Marin, 2001[28] ESPIRAL	unclear	no	yes	yes	Fair
Crepaldi, 1998[10]	unclear	double	no	yes	Fair
Zucchelli, 1995/1992[29,30]	unclear	no	yes	yes	Fair

Table C140. Assessment of individual study quality for KQ5 and KQ6 (continued)

Study ID	Allocation Concealment	Blinding	Intention to Treat Analysis	WithdrawalsDescribed	Study Rating
Angiotensin converting enzyme inhibitor (ACEI) versus beta-blocker trials (n=3)					
Wright, 2002[26] Norris, 2006[27] (AASK)	adequate**	double*	yes	yes	Good
van Essen, 1997[31]	unclear	double	no	yes	Fair
Hannedouche, 1994[32]	adequate	no	yes	yes	Fair
Angiotensin converting enzyme inhibitor (ACEI) versus diuretics trials (n=2)					
Rahman, 2005[23,110] ALLHAT	adequate**	double*	yes	yes for overall study population**	Good
Marre, 2004[33]NESTOR	unclear	double	no (one subject excluded)	yes	Fair
ARB versus placebo trials (n=5)					
Tobe, 2011[35] TRANSCEND	adequate**	double*	yes	yes (for CKD patients)	Good
Makino, 2007[37]	unclear	double	no	yes	Fair
Brenner, 2001[38] RENAAL	adequate	double*	yes	yes	Good
Parving, 2001[39] IRMA-2	unclear	double	yes	yes	Fair
Lewis, 2001[40] IDNT	adequate	double*	yes	yes	Good
ARB versus CCB trials (n=4)					
Saruta, 2009[41] CASE-J	unclear	no	yes	no	Fair
Ogawa, 2007[42]	unclear	single (patient)	unclear	yes	Fair
Viberti, 2002[43] MARVAL	adequate	double	yes	yes	Good
Lewis, 2001[40] IDNT	adequate	double*	yes	yes	Good
ACEI plus ARB versus ACEI or ARB trials (n=1)					
Tobe, 2011[35] ON-TARGET	adequate**	double*	yes	yes (for CKD patients)	Good
ACEI plus ARB versus ACEI trials (n=5)					
Sengul, 2006[20]	unclear	no	no	yes	Fair
Menne, 2008[19] VALERIA	adequate	double*	no	yes	Fair
Kanno, 2006[44]	unclear	no	no	yes	Fair
Mehdi, 2009[45]	unclear	double	no (one subject excluded)	yes	Fair
Anand, 2009[46]	adequate	double	yes	yes	Good
ACEI plus ARB versus ARB trials (n=2)					
Sengul, 2006[20]	unclear	no	no	yes	Fair
Menne, 2008[19] VALERIA	adequate	double*	no	yes	Fair
ACEI plus ARB versus ACEI plus aldosterone antagonist trial					
Mehdi, 2009[45]	unclear	double	no (one subject excluded)	yes	Fair
ACEI plus CCB versus ACEI monotherapy or CCB monotherapy trial					
Fogari 2002	adequate	no	no	yes	Fair

Table C140. Assessment of individual study quality for KQ5 and KQ6 (continued)

Study ID	Allocation Concealment	Blinding	Intention to Treat Analysis	WithdrawalsDescribed	Study Rating
ACEI plus diuretic versus ACEI plus CCB trials (n=2)					
Bakris, 2010[48] (ACCOMPLISH)	adequate**	double*	yes for overall study population	yes for overall study population	Good
Bakris, 2008[47] (GUARD)	adequate	double	no	yes	Fair
ACEI plus diuretic versus ACEI trial					
Mogensen, 2003[50]	unclear	double	no	no	Fair
ACEI plus diuretic versus placebo trial					
Lambers Heerspink 2010[51] ADVANCE	adequate**	double*	yes for overall study population	yes for overall study population	Good
ARB versus different ARB trials (n=2)					
Bakris, 2008[53] (AMADEO)	unclear	double	no	no	Fair
Galle, 2008[54]	unclear	double	yes	yes	Fair
ARB (high dose) versus ARB (standard dose) trials					
Burgess, 2009[55]	adequate	double	yes	yes	Good
Makino, 2007[37]	unclear	double	no	yes	Fair
Parving, 2001[39] IRMA-2	unclear	double	yes	yes	Fair
ACEI plus aldosterone antagonist versus ACEI trial					
Mehdi, 2009[45]	unclear	double	no (one subject excluded)	yes	Fair
ACEI/ARB plus aldosterone antagonist versus ACEI/ARB trial					
van den Meiracker, 2006[56]	adequate	double	no	yes	Fair
Beta blocker versus placebo trials (n=2)					
Cohen-Solal, 2009[57] Flather, 2005[58] SENIORS	adequate**	double*	no	unclear	Fair
Ghal, 2009[59] MERIT-HF	adequate	double	yes	yes	Good
CCB versus placebo trials (n=2)					
Berl, 2003[60] Lewis, 2001[40]	adequate	double	yes	yes	Good
Crepaldi, 1998[10]	unclear	double	no	yes	Fair
Diuretic versus placebo trial					
Pahor, 1998[61]	adequate	double	yes	yes	Good
ACEI versus conventional therapy without ACEI trial					
Cinotti, 2001[62]	unclear	no	yes	no	Fair
CCB versus BB trials (n=3)					
Bakris, 1996[63]	unclear	unclear	yes	yes	Fair
Wright, 2002[26] AASK	adequate**	double*	no	yes	Good
Dahlof, 2005[65]	adequate	open-label*	yes	yes	Good
CCB versus diuretic trial					
Rahman 2006 ALLHAT	adequate**	double*	yes	yes for overall study population**	Good

Table C140. Assessment of individual study quality for KQ5 and KQ6 (continued)

Study ID	Allocation Concealment	Blinding	Intention to Treat Analysis	WithdrawalsDescribed	Study Rating
Strict versus standard blood pressure control trials (n=6)					
Ruggenenti, 2005[66] REIN-2	adequate	no	no, 3 subjects excluded	yes	Fair
Wright, 2002[26] AASK	adequate**	no	yes	yes	Good
Estacio 2000 - Study B ABCD	unclear	"blinded," unclear if double-blinded*	unclear	yes	Fair
Lewis, 1999[69]	unclear	unclear	yes	no	Fair
Toto, 1995[70]	unclear	double	yes	unclear	Fair
Peterson, 1995[71] Klahr, 1994[72] MDRD, Study A	unclear	unclear	yes	yes	Fair
Shulman, 1989[74] HDFP	adequate	no	no	no	Fair
Anti-lipid trials: HMG-CoA reductase inhibitor versus placebo trials (n=12)					
Kendrick, 2010[87] AFCAPS/ TexCAPS	unclear	double*	yes	yes for overall study population**	Fair
Ridker, 2010 JUPITER	adequate**	double*	yes	yes for overall study population**	Good
Nakamura, 2009[89] MEGA	adequate**	open-label	no (382 excluded from analyses)**	yes for overall study population**	Fair
Colhoun, 2009[90] CARDS	adequate**	double*	no (3 randomized patients were excluded - investigators realized they did not meet the entry criteria before they actually took their first dose of study drug)	yes for overall study population**n	Good
Koren, 2009[91] ALLIANCE	adequate	open-label	yes	yes for overall study population**	Good
Rahman, 2008[93] ALLHAT-LLT	adequate**	open-label*	no for CKD subgroups (need valid baseline eGFR); yes for overall study population	yes (for CKD patients)	Good
Chonchol, 2007[94] 4S	adequate**	double*	no (24 excluded, no serum creatinine at baseline)	partially for overall study population**	Fair
Kjekshus, 2007[96] CORONA	adequate**	double*	yes	yes	Good

Table C140. Assessment of individual study quality for KQ5 and KQ6 (continued)

Study ID	Allocation Concealment	Blinding	Intention to Treat Analysis	WithdrawalsDescribed	Study Rating
Lemos, 2005[97] LIPS	unclear	double*	yes	yes for overall study population**	Fair
Asselbergs, 2004[2] PREVD	unclear	double*	yes	yes	Fair
Tonelli, 2004[98] WOSCOPS/ CARE/LIPID	adequate**	double*	yes	yes for overall study populations for CARE, LIPID; no for WOSCOPS**	Good
Tonelli, 2003[99] CARE	adequate	double*	yes	yes for overall study population**	Good
Anti-lipid trials: high versus low dose HMG-CoA reductase inhibitor trial					
SEARCH, 2010[100]	adequate	double*	yes	yes	Good
Shepherd, 2008[101] TNT	unclear	double*	no	yes (for CKD patients)	Fair
Anti-lipid trials: HMG-CoA reductase inhibitor versus bile acid sequestrant trial					
Tonolo, 2006[104]	unclear	double	yes	yes	Fair
Anti-lipid trials: Gemfibrozil versus placebo/control trials (n=2)					
Tonelli, 2004[98] VA-HIT	adequate	double*	yes	yes for overall study population**	Good
Samuelsson, 1997[84]	unclear	open-label	no	yes	Fair
Low protein diet versus usual protein diet and other dietary intervention trials (n=9)					
Koya, 2009[75]	adequate	no	no	yes	Fair
Dussol, 2005[76]	unclear	no	no	yes	Fair
Kopple, 1997[77] Peterson, 1995[71] Klahr, 1994[72] Greene, 1993[73] MDRD	adequate	double for followup GFRs	unclear	yes	Fair
D'Amico, 1994[78]	unclear	no	no	no	Fair
Locatelli, 1991[79]	adequate	unclear	no	yes	Fair
Rosman, 1989/1984[80,81]	unclear	no	no	no	Fair
Facchini, 2003[82]	unclear	study personnel blinded to aim of study	no	yes	Fair
Williams, 1991[83]	adequate	no	no	no	Fair
Samuelsson, 1997[84]	unclear	no	no	yes	Fair
Glycemic control trials (n=2)					
Duckworth, 2009[85]	adequate	open-label*	yes	yes	Good
Microalbuminuria Collaborative, 1995[86]	adequate	open-label	yes	yes	Good
Intensive multi-component intervention trials (n=4)					
Chan, 2009[105]	adequate	open-label	yes	yes	Good
Joss, 2004[106]	adequate	open-label	no	yes	Fair
Gaede, 2003/1999[107,108]	adequate	open-label	no	yes	Fair

Table C140. Assessment of individual study quality for KQ5 and KQ6 (continued)

Study ID	Allocation Concealment	Blinding	Intention to Treat Analysis	WithdrawalsDescribed	Study Rating
Harris, 1998[109]	unclear	open-label	yes	yes	Fair

*In addition, end points/clinical outcomes were adjudicated by blinded committee

** Detailed in baseline/study design or main findings manuscript. Included study was a secondary/post-hoc analysis with subgroup(s) of CKD patients.

References for Appendix C

1. Perkovic V, Ninomiya T, Arima H, et al. Chronic kidney disease, cardiovascular events, and the effects of perindopril-based blood pressure lowering: data from the PROGRESS study. Journal of the American Society of Nephrology 2007 Oct; 18(10):2766-72 17804673.

2. Asselbergs FW, Diercks GFH, Hillege HL, et al. Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. Circulation 2004 Nov 2; 110(18):2809-16 15492322.

3. Marre M, Lievre M, Chatellier G, et al. Effects of low dose ramipril on cardiovascular and renal outcomes in patients with type 2 diabetes and raised excretion of urinary albumin: randomised, double blind, placebo controlled trial (the DIABHYCAR study).[Erratum appears in BMJ. 2004 Mar 20;328(7441):686]. BMJ 2004 Feb 28; 328(7438):495 14960504.

4. Katayama S, Kikkawa R, Isogai S, et al. Effect of captopril or imidapril on the progression of diabetic nephropathy in Japanese with type 1 diabetes mellitus: a randomized controlled study (JAPAN-IDDM).[Erratum appears in Diabetes Res Clin Pract 2002 Jul;57(1):71]. Diabetes Research & Clinical Practice 2002 Feb; 55(2):113-21 11796177.

5. Bojestig M, Karlberg BE, Lindstrom T, et al. Reduction of ACE activity is insufficient to decrease microalbuminuria in normotensive patients with type 1 diabetes. Diabetes Care 2001 May; 24(5):919-24 11347755.

6. Gerstein HC, Mann JF, Yi Q, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA 2001 Jul 25; 286(4):421-6 11466120.

7. O'Hare P, Bilbous R, Mitchell T, et al. Low-dose ramipril reduces microalbuminuria in type 1 diabetic patients without hypertension: results of a randomized controlled trial. Diabetes Care 2000 Dec; 23(12):1823-9 11128360.

8. Muirhead N, Feagan BF, Mahon J, et al. The effects of valsartan and captopril on reducing microalbuminuria in patients with type 2 diabetes mellitus: a placebo-controlled trial. Current Therapeutic Research - Clinical and Experimental 1999 1999 Dec; 60(12):650-60

9. Ruggenenti P, Perna A, Gherardi G, et al. Renoprotective properties of ACE-inhibition in non-diabetic nephropathies with non-nephrotic proteinuria. Lancet 1999 Jul 31; 354(9176):359-64 10437863.

10. Crepaldi G, Carta Q, Deferrari G, et al. Effects of lisinopril and nifedipine on the progression to overt albuminuria in IDDM patients with incipient nephropathy and normal blood pressure. The Italian Microalbuminuria Study Group in IDDM. Diabetes Care 1998 Jan; 21(1):104-10 9538979.

11. Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy. The GISEN Group (Gruppo Italiano di Studi Epidemiologici in Nefrologia). Lancet 1997 Jun 28; 349(9069):1857-63 9217756.

12. Maschio G, Alberti D, Janin G, et al. Effect of the angiotensin-converting-enzyme inhibitor benazepril on the progression of chronic renal insufficiency. The Angiotensin-Converting-Enzyme Inhibition in Progressive Renal Insufficiency Study Group. New England Journal of Medicine 1996 Apr 11; 334(15):939-45 8596594.

13. Trevisan R, Tiengo A. Effect of low-dose ramipril on microalbuminuria in normotensive or mild hypertensive non-insulin-dependent diabetic patients. North-East Italy Microalbuminuria Study Group. American Journal of Hypertension 1995 Sep; 8(9):876-83 8541002.

14. Laffel LM, McGill JB, Gans DJ. The beneficial effect of angiotensin-converting enzyme inhibition with captopril on diabetic nephropathy in normotensive IDDM patients with microalbuminuria. North American Microalbuminuria Study Group. American Journal of Medicine 1995 Nov; 99(5):497-504 7485207.

15. Sano T, Kawamura T, Matsumae H, et al. Effects of long-term enalapril treatment on persistent micro-albuminuria in well-controlled hypertensive and normotensive NIDDM patients. Diabetes Care 1994 May; 17(5):420-4 8062609.

16. Lewis EJ, Hunsicker LG, Bain RP, et al. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. The Collaborative Study Group.[Erratum appears in N Engl J Med 1993 Jan 13;330(2):152]. New England Journal of Medicine 1993 Nov 11; 329(20):1456-62 8413456.

17. Ravid M, Savin H, Jutrin I, et al. Long-term stabilizing effect of angiotensin-converting enzyme inhibition on plasma creatinine and on proteinuria in normotensive type II diabetic patients. Annals of Internal Medicine 1993 Apr 15; 118(8):577-81 8452322.

18. Mann JFE, Schmieder RE, McQueen M, et al. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. Lancet 2008 Aug 16; 372(9638):547-53 18707986.

19. Menne J, Farsang C, Deak L, et al. Valsartan in combination with lisinopril versus the respective high dose monotherapies in hypertensive patients with microalbuminuria: the VALERIA trial. Journal of Hypertension 2008 Sep; 26(9):1860-7 18698222.

20. Sengul AM, Altuntas Y, Kurklu A, et al. Beneficial effect of lisinopril plus telmisartan in patients with type 2 diabetes, microalbuminuria and hypertension. Diabetes Research & Clinical Practice 2006 Feb; 71(2):210-9 16112244.

21. Barnett AH, Bain SC, Bouter P, et al. Angiotensin-receptor blockade versus converting-enzyme inhibition in type 2 diabetes and nephropathy.[Erratum appears in N Engl J Med. 2005 Apr 21;352(16)1731]. New England Journal of Medicine 2004 Nov 4; 351(19):1952-61 15516696.

22. Lacourciere Y, Belanger A, Godin C, et al. Long-term comparison of losartan and enalapril on kidney function in hypertensive type 2 diabetics with early nephropathy. Kidney International 2000 Aug; 58(2):762-9 10916100.

23. Rahman M, Pressel S, Davis BR, et al. Renal outcomes in high-risk hypertensive patients treated with an angiotensin-converting enzyme inhibitor or a calcium channel blocker vs a diuretic: a report from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Archives of Internal Medicine 2005 Apr 25; 165(8):936-46 15851647.

24. Fogari R, Preti P, Zoppi A, et al. Effects of amlodipine fosinopril combination on microalbuminuria in hypertensive type 2 diabetic patients. American Journal of Hypertension 2002 Dec; 15(12):1042-9 12460699.

25. Agodoa LY, Appel L, Bakris GL, et al. Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial. JAMA 2001 Jun 6; 285(21):2719-28 11386927.

26. Wright JT, Jr., Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial.[Erratum appears in JAMA. 2006 Jun 21;295(23):2726]. JAMA 2002 Nov 20; 288(19):2421-31 12435255.

27. Norris K, Bourgoigne J, Gassman J, et al. Cardiovascular outcomes in the African American Study of Kidney Disease and Hypertension (AASK) Trial. American Journal of Kidney Diseases 2006 Nov; 48(5):739-51 17059993.

28. Marin R, Ruilope LM, Aljama P, et al. A random comparison of fosinopril and nifedipine GITS in patients with primary renal disease. Journal of Hypertension 2001 Oct; 19(10):1871-6 11593109.

29. Zucchelli P, Zuccala A, Gaggi R. Comparison of the effects of ACE inhibitors and calcium channel blockers on the progression of renal failure. Nephrology Dialysis Transplantation 1995 Oct; 10 Suppl 9:46-51 8643208.

30. Zucchelli P, Zuccala A, Borghi M, et al. Long-term comparison between captopril and nifedipine in the progression of renal insufficiency. Kidney International 1992 Aug; 42(2):452-8 1405330.

31. van Essen GG, Apperloo AJ, Rensma PL, et al. Are angiotensin converting enzyme inhibitors superior to beta blockers in retarding progressive renal function decline? Kidney International - Supplement 1997 Dec; 63:S58-62 9407423.

32. Hannedouche T, Landais P, Goldfarb B, et al. Randomised controlled trial of enalapril and beta blockers in non-diabetic chronic renal failure. BMJ 1994 Oct 1; 309(6958):833-7 7950612.

33. Marre M, Puig JG, Kokot F, et al. Equivalence of indapamide SR and enalapril on microalbuminuria reduction in hypertensive patients with type 2 diabetes: the NESTOR Study. Journal of Hypertension 2004 Aug; 22(8):1613-22 15257186.

34. Rahman M, Pressel S, Davis BR, et al. Cardiovascular outcomes in high-risk hypertensive patients stratified by baseline glomerular filtration rate.[Summary for patients in Ann Intern Med. 2006 Feb 7;144(3):I33; PMID: 16461958]. Annals of Internal Medicine 2006 Feb 7; 144(3):172-80 16461961.

35. Tobe SW, Clase CM, Gao P, et al. Cardiovascular and renal outcomes with telmisartan, ramipril, or both in people at high renal risk: results from the ONTARGET and TRANSCEND studies. Circulation 2011 Mar 15; 123(10):1098-107 21357827.

36. Yusuf S, Sleight P, Pogue J, et al. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. New England Journal of Medicine 2000 Jan 20; 342(3):145-53 10639539.

37. Makino H, Haneda M, Babazono T, et al. Prevention of transition from incipient to overt nephropathy with telmisartan in patients with type 2 diabetes. Diabetes Care 2007 Jun; 30(6):1577-8 17389334.

38. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. New England Journal of Medicine 2001 Sep 20; 345(12):861-9 11565518.

39. Parving HH, Lehnert H, Brochner-Mortensen J, et al. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. New England Journal of Medicine 2001 Sep 20; 345(12):870-8 11565519.

40. Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. New England Journal of Medicine 2001 Sep 20; 345(12):851-60 11565517.

41. Saruta T, Hayashi K, Ogihara T, et al. Effects of candesartan and amlodipine on cardiovascular events in hypertensive patients with chronic kidney disease: subanalysis of the CASE-J Study. Hypertension Research - Clinical & Experimental 2009 Jun; 32(6):505-12 19390535.

42. Ogawa S, Takeuchi K, Mori T, et al. Effects of monotherapy of temocapril or candesartan with dose increments or combination therapy with both drugs on the suppression of diabetic nephropathy. Hypertension Research - Clinical & Experimental 2007 Apr; 30(4):325-34 17541211.

43. Viberti G, Wheeldon NM, MicroAlbuminuria Reduction With VSI. Microalbuminuria reduction with valsartan in patients with type 2 diabetes mellitus: a blood pressure-independent effect. Circulation 2002 Aug 6; 106(6):672-8 12163426.

44. Kanno Y, Takenaka T, Nakamura T, et al. Add-on angiotensin receptor blocker in patients who have proteinuric chronic kidney diseases and are treated with angiotensin-converting enzyme inhibitors. Clinical Journal of The American Society of Nephrology: CJASN 2006 Jul; 1(4):730-7 17699280.

45. Mehdi UF, Adams-Huet B, Raskin P, et al. Addition of angiotensin receptor blockade or mineralocorticoid antagonism to maximal angiotensin-converting enzyme inhibition in diabetic nephropathy. Journal of the American Society of Nephrology 2009 Dec; 20(12):2641-50 19926893.

46. Anand IS, Bishu K, Rector TS, et al. Proteinuria, chronic kidney disease, and the effect of an angiotensin receptor blocker in addition to an angiotensin-converting enzyme inhibitor in patients with moderate to severe heart failure. Circulation 2009 Oct 20; 120(16):1577-84 19805651.

47. Bakris GL, Toto RD, McCullough PA, et al. Effects of different ACE inhibitor combinations on albuminuria: results of the GUARD study. Kidney International 2008 Jun; 73(11):1303-9 18354383.

48. Bakris GL, Sarafidis PA, Weir MR, et al. Renal outcomes with different fixed-dose combination therapies in patients with hypertension at high risk for cardiovascular events (ACCOMPLISH): a prespecified secondary analysis of a randomised controlled trial. Lancet 2010 Apr 3; 375(9721):1173-81 20170948.

49. Jamerson KA, Bakris GL, Wun CC, et al. Rationale and design of the avoiding cardiovascular events through combination therapy in patients living with systolic hypertension (ACCOMPLISH) trial: the first randomized controlled trial to compare the clinical outcome effects of first-line combination therapies in hypertension. Am J Hypertens 2004 Sep; 17(9):793-801 15363822.

50. Mogensen CE, Viberti G, Halimi S, et al. Effect of low-dose perindopril/indapamide on albuminuria in diabetes: preterax in albuminuria regression: PREMIER. Hypertension 2003 May; 41(5):1063-71 12654706.

51. Lambers Heerspink HJ, Gansevoort RT, Brenner BM, et al. Comparison of different measures of urinary protein excretion for prediction of renal events. J Am Soc Nephrol 2010 Aug; 21(8):1355-60 20634296.

52. Study rationale and design of ADVANCE: action in diabetes and vascular disease--preterax and diamicron MR controlled evaluation. Diabetologia 2001 Sep; 44(9):1118-20 11596665.

53. Bakris G, Burgess E, Weir M, et al. Telmisartan is more effective than losartan in reducing proteinuria in patients with diabetic nephropathy. Kidney International 2008 Aug; 74(3):364-9 18496508.

54. Galle J, Schwedhelm E, Pinnetti S, et al. Antiproteinuric effects of angiotensin receptor blockers: telmisartan versus valsartan in hypertensive patients with type 2 diabetes mellitus and overt nephropathy. Nephrology Dialysis Transplantation 2008 Oct; 23(10):3174-83 18450829.

55. Burgess E, Muirhead N, Rene de Cotret P, et al. Supramaximal dose of candesartan in proteinuric renal disease. Journal of the American Society of Nephrology 2009 Apr; 20(4):893-900 19211712.

56. van den Meiracker AH, Baggen RG, Pauli S, et al. Spironolactone in type 2 diabetic nephropathy: Effects on proteinuria, blood pressure and renal function. Journal of Hypertension 2006 Nov; 24(11):2285-92 17053552.

57. Cohen-Solal A, Kotecha D, van Veldhuisen DJ, et al. Efficacy and safety of nebivolol in elderly heart failure patients with impaired renal function: insights from the SENIORS trial. Eur J Heart Fail 2009 Sep; 11(9):872-80 19648605.

58. Flather MD, Shibata MC, Coats AJ, et al. Randomized trial to determine the effect of nebivolol on mortality and cardiovascular hospital admission in elderly patients with heart failure (SENIORS). Eur Heart J 2005 Feb; 26(3):215-25 15642700.

59. Ghali JK, Wikstrand J, Van Veldhuisen DJ, et al. The influence of renal function on clinical outcome and response to beta-blockade in systolic heart failure: insights from Metoprolol CR/XL Randomized Intervention Trial in Chronic HF (MERIT-HF). Journal of Cardiac Failure 2009 May; 15(4):310-8 19398079.

60. Berl T, Hunsicker LG, Lewis JB, et al. Cardiovascular outcomes in the Irbesartan Diabetic Nephropathy Trial of patients with type 2 diabetes and overt nephropathy.[Summary for patients in Ann Intern Med. 2003 Apr 1;138(7):I43; PMID: 12667050]. Annals of Internal Medicine 2003 Apr 1; 138(7):542-9 12667024.

61. Pahor M, Shorr RI, Somes GW, et al. Diuretic-based treatment and cardiovascular events in patients with mild renal dysfunction enrolled in the systolic hypertension in the elderly program. Archives of Internal Medicine 1998 Jun 22; 158(12):1340-5 9645829.

62. Cinotti GA, Zucchelli PC, Collaborative Study G. Effect of Lisinopril on the progression of renal insufficiency in mild proteinuric non-diabetic nephropathies. Nephrology Dialysis Transplantation 2001 May; 16(5):961-6 11328901.

63. Bakris GL, Copley JB, Vicknair N, et al. Calcium channel blockers versus other antihypertensive therapies on progression of NIDDM associated nephropathy. Kidney International 1996 Nov; 50(5):1641-50 8914031.

64. Wright JT, Jr., Kusek JW, Toto RD, et al. Design and baseline characteristics of participants in the African American Study of Kidney Disease and Hypertension (AASK) Pilot Study. Controlled Clinical Trials 1996 Aug; 17(4 Suppl):3S-16S 8889350.

65. Dahlof B, Sever PS, Poulter NR, et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. Lancet 2005 Sep 10-16; 366(9489):895-906 16154016.

66. Ruggenenti P, Perna A, Loriga G, et al. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicentre, randomised controlled trial. Lancet 2005 Mar 12-18; 365(9463):939-46 15766995.

67. Estacio RO, Jeffers BW, Gifford N, et al. Effect of blood pressure control on diabetic microvascular complications in patients with hypertension and type 2 diabetes. Diabetes Care 2000 Apr; 23 Suppl 2:B54-64 10860192.

68. Schrier RW, Estacio RO, Esler A, et al. Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes. Kidney Int 2002 Mar; 61(3):1086-97 11849464.

69. Lewis JB, Berl T, Bain RP, et al. Effect of intensive blood pressure control on the course of type 1 diabetic nephropathy. Collaborative Study Group. American Journal of Kidney Diseases 1999 Nov; 34(5):809-17 10561135.

70. Toto RD, Mitchell HC, Smith RD, et al. “Strict” blood pressure control and progression of renal disease in hypertensive nephrosclerosis. Kidney International 1995 Sep; 48(3):851-9 7474675.

71. Peterson JC, Adler S, Burkart JM, et al. Blood pressure control, proteinuria, and the progression of renal disease. The Modification of Diet in Renal Disease Study. Annals of Internal Medicine 1995 Nov 15; 123(10):754-62 7574193.

72. Klahr S, Levey AS, Beck GJ, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. New England Journal of Medicine 1994 Mar 31; 330(13):877-84 8114857.

73. Greene T, Bourgoignie JJ, Habwe V, et al. Baseline characteristics in the Modification of Diet in Renal Disease Study.[Republished from J Am Soc Nephrol 1993 May;3(11):1819-34]. Journal of the American Society of Nephrology 1993 Nov; 4(5):1221-36 8305650.

74. Shulman NB, Ford CE, Hall WD, et al. Prognostic value of serum creatinine and effect of treatment of hypertension on renal function. Results from the hypertension detection and follow-up program. The Hypertension Detection and Follow-up Program Cooperative Group. Hypertension 1989 May; 13(5 Suppl):I80-93 2490833.

75. Koya D, Haneda M, Inomata S, et al. Long-term effect of modification of dietary protein intake on the progression of diabetic nephropathy: a randomised controlled trial. Diabetologia 2009 Oct; 52(10):2037-45 19652945.

76. Dussol B, Iovanna C, Raccah D, et al. A randomized trial of low-protein diet in type 1 and in type 2 diabetes mellitus patients with incipient and overt nephropathy. Journal of Renal Nutrition 2005 Oct; 15(4):398-406 16198932.

77. Kopple JD, Levey AS, Greene T, et al. Effect of dietary protein restriction on nutritional status in the Modification of Diet in Renal Disease Study. Kidney International 1997 Sep; 52(3):778-91 9291200.

78. D'Amico G, Gentile MG, Fellin G, et al. Effect of dietary protein restriction on the progression of renal failure: a prospective randomized trial. Nephrology Dialysis Transplantation 1994; 9(11):1590-4 7870348.

79. Locatelli F, Alberti D, Graziani G, et al. Prospective, randomised, multicentre trial of effect of protein restriction on progression of chronic renal insufficiency. Northern Italian Cooperative Study Group. Lancet 1991 Jun 1; 337(8753):1299-304 1674294.

80. Rosman JB, Langer K, Brandl M, et al. Protein-restricted diets in chronic renal failure: a four year follow-up shows limited indications. Kidney International - Supplement 1989 Nov; 27:S96-102 2636680.

81. Rosman JB, ter Wee PM, Meijer S, et al. Prospective randomised trial of early dietary protein restriction in chronic renal failure. Lancet 1984 Dec 8; 2(8415):1291-6 6150320.

82. Facchini FS, Saylor KL. A low-iron-available, polyphenol-enriched, carbohydrate-restricted diet to slow progression of diabetic nephropathy. Diabetes 2003 May; 52(5):1204-9 12716753.

83. Williams PS, Stevens ME, Fass G, et al. Failure of dietary protein and phosphate restriction to retard the rate of progression of chronic renal failure: a prospective, randomized, controlled trial. Quarterly Journal of Medicine 1991 Oct; 81(294):837-55 1801057.

84. Samuelsson O, Attman PO, Knight-Gibson C, et al. Effect of gemfibrozil on lipoprotein abnormalities in chronic renal insufficiency: a controlled study in human chronic renal disease. Nephron 1997; 75(3):286-94 9069450.

85. Duckworth W, Abraira C, Moritz T, et al. Glucose control and vascular complications in veterans with type 2 diabetes. New England Journal of Medicine 2009 Jan 8; 360(2):129-39 19092145.

86. Intensive therapy and progression to clinical albuminuria in patients with insulin dependent diabetes mellitus and microalbuminuria. Microalbuminuria Collaborative Study Group, United Kingdom. BMJ 1995 Oct 14; 311(7011):973-7 7580637.

87. Kendrick J, Shlipak MG, Targher G, et al. Effect of lovastatin on primary prevention of cardiovascular events in mild CKD and kidney function loss: a post hoc analysis of the Air Force/Texas Coronary Atherosclerosis Prevention Study. American Journal of Kidney Diseases 2010 Jan; 55(1):42-9 19932541.

88. Ridker PM, MacFadyen J, Cressman M, et al. Efficacy of rosuvastatin among men and women with moderate chronic kidney disease and elevated high-sensitivity C-reactive protein: a secondary analysis from the JUPITER (Justification for the Use of Statins in Prevention-an Intervention Trial Evaluating Rosuvastatin) trial. J Am Coll Cardiol 2010 Mar 23; 55(12):1266-73 20206456.

89. Nakamura H, Mizuno K, Ohashi Y, et al. Pravastatin and cardiovascular risk in moderate chronic kidney disease. Atherosclerosis 2009 Oct; 206(2):512-7 19423108.

90. Colhoun HM, Betteridge DJ, Durrington PN, et al. Effects of atorvastatin on kidney outcomes and cardiovascular disease in patients with diabetes: an analysis from the Collaborative Atorvastatin Diabetes Study (CARDS). American Journal of Kidney Diseases 2009 Nov; 54(5):810-9 19540640.

91. Koren MJ, Davidson MH, Wilson DJ, et al. Focused atorvastatin therapy in managed-care patients with coronary heart disease and CKD. American Journal of Kidney Diseases 2009 May; 53(5):741-50 19216014.

92. Isaacsohn JL, Davidson MH, Hunninghake D, et al. Aggressive Lipid-Lowering Initiation Abates New Cardiac Events (ALLIANCE)-rationale and design of atorvastatin versus usual care in hypercholesterolemic patients with coronary artery disease. Am J Cardiol 2000 Jul 15; 86(2):250-2 10913499.

93. Rahman M, Baimbridge C, Davis BR, et al. Progression of kidney disease in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin versus usual care: a report from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). American Journal of Kidney Diseases 2008 Sep; 52(3):412-24 18676075.

94. Chonchol M, Cook T, Kjekshus J, et al. Simvastatin for secondary prevention of all-cause mortality and major coronary events in patients with mild chronic renal insufficiency. American Journal of Kidney Diseases 2007 Mar; 49(3):373-82 17336698.

95. Huskey J, Lindenfeld J, Cook T, et al. Effect of simvastatin on kidney function loss in patients with coronary heart disease: findings from the Scandinavian Simvastatin Survival Study (4S). Atherosclerosis 2009 Jul; 205(1):202-6 19124121.

96. Kjekshus J, Apetrei E, Barrios V, et al. Rosuvastatin in older patients with systolic heart failure. New England Journal of Medicine 2007 Nov 29; 357(22):2248-61 17984166.

97. Lemos PA, Serruys PW, de Feyter P, et al. Long-term fluvastatin reduces the hazardous effect of renal impairment on four-year atherosclerotic outcomes (a LIPS substudy). American Journal of Cardiology 2005 Feb 15; 95(4):445-51 15695126.

98. Tonelli M, Isles C, Curhan GC, et al. Effect of pravastatin on cardiovascular events in people with chronic kidney disease. Circulation 2004 Sep 21; 110(12):1557-63 15364796.

99. Tonelli M, Moye L, Sacks FM, et al. Pravastatin for secondary prevention of cardiovascular events in persons with mild chronic renal insufficiency.[Summary for patients in Ann Intern Med. 2003 Jan 21;138(2):I28; PMID: 12529112]. Annals of Internal Medicine 2003 Jan 21; 138(2):98-104 12529091.

100. Armitage J, Bowman L, Wallendszus K, et al. Intensive lowering of LDL cholesterol with 80 mg versus 20 mg simvastatin daily in 12,064 survivors of myocardial infarction: a double-blind randomised trial. Lancet 2010 Nov 13; 376(9753):1658-69 21067805.

101. Shepherd J, Kastelein JJP, Bittner V, et al. Intensive lipid lowering with atorvastatin in patients with coronary heart disease and chronic kidney disease: the TNT (Treating to New Targets) study. Journal of the American College of Cardiology 2008 Apr 15; 51(15):1448-54 18402899.

102. LaRosa JC, Grundy SM, Waters DD, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med 2005 Apr 7; 352(14):1425-35 15755765.

103. Waters DD, Guyton JR, Herrington DM, et al. Treating to New Targets (TNT) Study: does lowering low-density lipoprotein cholesterol levels below currently recommended guidelines yield incremental clinical benefit? Am J Cardiol 2004 Jan 15; 93(2):154-8 14715339.

104. Tonolo G, Velussi M, Brocco E, et al. Simvastatin maintains steady patterns of GFR and improves AER and expression of slit diaphragm proteins in type II diabetes. Kidney International 2006 Jul; 70(1):177-86 16710349.

105. Chan JC, So W-Y, Yeung C-Y, et al. Effects of structured versus usual care on renal endpoint in type 2 diabetes: the SURE study: a randomized multicenter translational study. Diabetes Care 2009 Jun; 32(6):977-82 19460913.

106. Joss N, Ferguson C, Brown C, et al. Intensified treatment of patients with type 2 diabetes mellitus and overt nephropathy. Qjm 2004 Apr; 97(4):219-27 15028852.

107. Gaede P, Vedel P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. New England Journal of Medicine 2003 Jan 30; 348(5):383-93 12556541.

108. Gaede P, Vedel P, Parving HH, et al. Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study. Lancet 1999 Feb 20; 353(9153):617-22 10030326.

109. Harris LE, Luft FC, Rudy DW, et al. Effects of multidisciplinary case management in patients with chronic renal insufficiency. American Journal of Medicine 1998 Dec; 105(6):464-71 9870830.

110. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2002 Dec 18; 288(23):2981-97 12479763.