Appendix A. Exact Search Strings

PubMed® search strategy (December 16, 2011)

KQ1: In patients with nonvalvular atrial fibrillation, what are the comparative diagnostic accuracy and impact on clinical decisionmaking (diagnostic thinking, therapeutic, and patient outcome efficacy) of available clinical and imaging tools for predicting thromboembolic risk?

#1	"Atrial Fibrillation"[Mesh] OR "atrial fibrillation"[tiab] OR (atrial[tiab] AND fibrillation[tiab]) OR afib[tiab] OR "atrial flutter"[MeSH Terms] OR "atrial flutter"[tiab]
#2	chads2[tw] OR chads2-vasc[tw] OR "Magnetic Resonance Imaging"[Mesh] OR MRI[tw] OR "Cardiac Imaging Techniques"[Mesh] OR "Tomography, X-Ray Computed"[Mesh] OR "Echocardiography"[Mesh] OR ((transthoracic[tw] OR transesophageal[tw]) AND echo[tw]) OR TTE[tw] OR TEE[tw] OR CT-scan[tw]
#3	"Stroke"[Mesh] OR stroke[tw] OR thromboembolism[tw] OR "Thromboembolism"[Mesh] OR thromboembolic[tw] OR "brain ischemia"[MeSH Terms] OR (brain[tw] AND ischemia[tw]) OR (brain[tw] AND ischaemia[tw]) OR (transient[tw] AND (ischemic[tw] OR ischaemic[tw] OR ischaemia[tw] OR ischemia[tw]) AND attack[tw]) OR TIA[tw]
#4	#1 AND #2 AND #3
#5	(("diagnosis"[Subheading] OR "diagnosis"[tiab] OR "diagnosis"[MeSH Terms]) OR "treatment outcome"[MeSH Terms] OR outcome[tiab] OR outcomes[tiab]) OR (reliability[tw] OR accuracy[tw] OR accurate[tw] OR Sensitivity[tw] OR specificity[tw] OR "Sensitivity and Specificity"[Mesh] OR valid[tw] OR validity[tw] OR validation[tw] OR decision[tw] OR decisions[tw] OR "decision making"[MeSH Terms] OR assessment[tw])
#6	#5 AND #4
#7	#6 NOT (animals[mh] NOT humans[mh]), Limits: English, Publication Date from 2000 to present

KQ2: In patients with nonvalvular atrial fibrillation, what are the comparative diagnostic accuracy and impact on clinical decisionmaking (diagnostic thinking, therapeutic, and patient outcome efficacy) of clinical tools and associated risk factors for predicting bleeding events?

#1	"Atrial Fibrillation"[Mesh] OR "atrial fibrillation"[tiab] OR (atrial[tiab] AND fibrillation[tiab]) OR afib[tiab] OR "atrial flutter"[MeSH Terms] OR "atrial flutter"[tiab]
#2	"Age Factors"[Mesh] OR "Dementia"[Mesh] OR "Accidental Falls"[Mesh] OR "International Normalized Ratio"[Mesh] OR age[tiab] OR dementia[tiab] OR INR[tiab] OR fall[tiab] OR falls[tiab] OR "international normalized ratio"[tiab] OR paroxysmal[tiab] OR persistent[tiab] OR permanent[tiab] OR stratification[tiab] OR classification[tiab] OR schema[tiab] OR has-bled[tiab] OR (cognitive[tw] AND impairment[tw]) OR cognition[tw] OR ((prior[tiab] OR previous[tiab] OR first[tiab])

	AND stroke[tiab])
#3	"Intracranial Hemorrhages"[Mesh] OR "Hemorrhage"[Mesh:noexp] OR hemorrhage[tw] OR hemorrhaging[tw] OR bleeding[tw] OR bleed[tw] OR hemorrhagic[tw] OR haemorrhage[tw] OR haemorrhaging[tw] OR haemorrhagic[tw]
#4	#1 AND #2 And #3
#5	(("diagnosis"[Subheading] OR "diagnosis"[tiab] OR "diagnosis"[MeSH Terms]) OR "treatment outcome"[MeSH Terms] OR outcome[tiab] OR outcomes[tiab]) OR (reliability[tw] OR accuracy[tw] OR accurate[tw] OR Sensitivity[tw] OR specificity[tw] OR "Sensitivity and Specificity"[Mesh] OR valid[tw] OR validity[tw] OR validation[tw] OR decision[tw] OR decisions[tw] OR "decision making"[MeSH Terms] OR assessment[tw])
#6	#5 AND #4
#7	#6 NOT (animals[mh] NOT humans[mh]), Limits: English, Publication Date from 2000 to present

KQ3: What are the comparative safety and effectiveness of specific anticoagulation therapies, antiplatelet therapies, and procedural interventions for preventing thromboembolic events:

(a) In patients with nonvalvular atrial fibrillation?

(b) In specific subpopulations of patients with nonvalvular atrial fibrillation?

KQ3: What are the comparative safety and effectiveness of specific anticoagulation therapies, antiplatelet therapies, and procedural interventions for preventing thromboembolic events: (a) In patients with nonvalvular atrial fibrillation? (b) In specific subpopulations of patients with nonvalvular atrial fibrillation?	
#1	"Atrial Fibrillation"[Mesh] OR "atrial fibrillation"[tiab] OR (atrial[tiab] AND fibrillation[tiab]) OR afib[tiab] OR "atrial flutter"[MeSH Terms] OR "atrial flutter"[tiab]
#2	"Anticoagulants"[Mesh] OR "Anticoagulants"[Pharmacological Action] OR warfarin[tw] OR "Warfarin"[Mesh] OR coumadin[tw] OR "Vitamin K/antagonists and inhibitors"[Mesh] OR vitamin k[tw] OR "Heparin"[Mesh] OR "Enoxaparin"[Mesh] OR enoxaparin[tw] OR lovenox[tw] OR "rivaroxaban" [Supplementary Concept] OR rivaroxaban[tw] OR xarelto[tw] OR "dabigatran etexilate" [Supplementary Concept] OR dabigatran[tw] OR pradaxa[tw] OR heparin[tw] OR "apixaban" [Supplementary Concept] OR apixaban[tw] OR eliquis[tw] OR "edoxaban" [Supplementary Concept] OR edoxaban[tw] OR lixiana[tw]
#3	"Platelet Aggregation Inhibitors"[Mesh] OR "Platelet Aggregation Inhibitors"[Pharmacological Action] OR "clopidogrel" [Supplementary Concept]OR clopidogrel[tw] OR plavix[tw] OR "Aspirin"[Mesh] OR aspirin[tw] OR "Dipyridamole"[Mesh] OR dipyridamole[tw] OR aggrenox[tw] OR persantine[tw] OR antiplatelet[tw] OR anti-platelet[tw] OR antiplatelets[tw] OR anti-platelets[tw]
#4	Atrial Appendage/surgery[mesh] OR atrial appendage[tw] OR LAA[tw] OR occluder[tw] OR AMPLATZER[tw] OR AtriClip[tw] OR PLAATO[tw] OR Watchman[tw] OR (atrial[tw] AND modification[tw]) OR “atriacure isolator”[tw]
#5	"Stroke"[Mesh] OR stroke[tw] OR thromboembolism[tw] OR

	"Thromboembolism"[Mesh] OR thromboembolic[tw] OR "brain ischemia"[MeSH Terms] OR (brain[tw] AND ischemia[tw]) OR (brain[tw] AND ischaemia[tw]) OR (transient[tw] AND (ischemic[tw] OR ischaemic[tw] OR ischaemia[tw] OR ischemia[tw]) AND attack[tw]) OR TIA[tw]
#6	#1 AND (#2 OR #3 OR #4) AND #5
#7	"evaluation studies"[Publication Type] OR "evaluation studies as topic"[MeSH Terms] OR "evaluation study"[tw] OR evaluation studies[tw] OR "intervention studies"[MeSH Terms] OR "intervention study"[tw] OR "intervention studies"[tw] OR "case-control studies"[MeSH Terms] OR "case-control"[tw] OR "cohort studies"[MeSH Terms] OR cohort[tw] OR "longitudinal studies"[MeSH Terms] OR "longitudinal"[tw] OR longitudinally[tw] OR "prospective"[tw] OR prospectively[tw] OR "retrospective studies"[MeSH Terms] OR "retrospective"[tw] OR "follow up"[tw] OR "comparative study"[Publication Type] OR "comparative study"[tw] OR systematic[subset] OR "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[tw] OR "meta-analyses"[tw] OR randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR "drug therapy"[Subheading] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Clinical trial[pt] OR "clinical trial"[tw] OR "clinical trials"[tw] NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp])
#8	#7 AND #6
#9	#8 NOT (animals[mh] NOT humans[mh]), Limits: English, Publication Date from 2000 to present

KQ4: What are the comparative safety and effectiveness of available strategies for anticoagulation in patients with nonvalvular atrial fibrillation who are undergoing invasive procedures?

KQ4: What are the comparative safety and effectiveness of available strategies for anticoagulation in patients with nonvalvular atrial fibrillation who are undergoing invasive procedures?	
#1	"Atrial Fibrillation"[Mesh] OR "atrial fibrillation"[tiab] OR (atrial[tiab] AND fibrillation[tiab]) OR afib[tiab] OR "atrial flutter"[MeSH Terms] OR "atrial flutter"[tiab]
#2	"Anticoagulants"[Mesh] OR "Anticoagulants"[Pharmacological Action] OR warfarin[tw] OR "Warfarin"[Mesh] OR coumadin[tw] OR "Vitamin K/antagonists and inhibitors"[Mesh] OR vitamin k[tw] OR "Heparin"[Mesh] OR "Enoxaparin"[Mesh] OR enoxaparin[tw] OR lovenox[tw] OR "rivaroxaban" [Supplementary Concept] OR rivaroxaban[tw] OR xarelto[tw] OR "dabigatran etexilate" [Supplementary Concept] OR dabigatran[tw] OR pradaxa[tw] OR heparin[tw] OR "apixaban" [Supplementary Concept] OR apixaban[tw] OR eliquis[tw] OR "edoxaban" [Supplementary Concept] OR edoxaban[tw] OR lixiana[tw]
#3	"Surgical Procedures, Operative"[Mesh] OR /surgery[mesh] OR ((surgical[tw] OR invasive[tw]) AND (procedure[tw] OR procedures[tw])) OR "dental care"[MeSH Terms] OR (dental[tw] AND (procedure[tw] OR procedures[tw])) OR surgery[tw] OR

	procedures[tiab] OR procedure[tiab]
#4	#1 AND #2 AND #3
#5	"evaluation studies"[Publication Type] OR "evaluation studies as topic"[MeSH Terms] OR "evaluation study"[tw] OR evaluation studies[tw] OR "intervention studies"[MeSH Terms] OR "intervention study"[tw] OR "intervention studies"[tw] OR "case-control studies"[MeSH Terms] OR "case-control"[tw] OR "cohort studies"[MeSH Terms] OR cohort[tw] OR "longitudinal studies"[MeSH Terms] OR "longitudinal"[tw] OR longitudinally[tw] OR "prospective"[tw] OR prospectively[tw] OR "retrospective studies"[MeSH Terms] OR "retrospective"[tw] OR "follow up"[tw] OR "comparative study"[Publication Type] OR "comparative study"[tw] OR systematic[subset] OR "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[tw] OR "meta-analyses"[tw] OR randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR "drug therapy"[Subheading] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Clinical trial[pt] OR "clinical trial"[tw] OR "clinical trials"[tw] NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp])
#6	#5 AND #4
#7	#7 NOT (animals[mh] NOT humans[mh]), Limits: English, Publication Date from 1990 to present

KQ5: What are the comparative safety and effectiveness of available strategies for switching between warfarin and other novel oral anticoagulants, in patients with nonvalvular atrial fibrillation?

KQ5: What are the comparative safety and effectiveness of available strategies for switching between warfarin and other novel oral anticoagulants, in patients with nonvalvular atrial fibrillation?	
#1	"Atrial Fibrillation"[Mesh] OR "atrial fibrillation"[tiab] OR (atrial[tiab] AND fibrillation[tiab]) OR afib[tiab] OR "atrial flutter"[MeSH Terms] OR "atrial flutter"[tiab]
#2	"warfarin"[MeSH Terms] OR warfarin[tw] OR coumadin[tw]
#3	"antithrombins"[MeSH Terms] OR "antithrombins"[tiab] OR ("direct"[tiab] AND "thrombin"[tiab] AND "inhibitors"[tiab]) OR "direct thrombin inhibitors"[tiab] OR "antithrombins"[Pharmacological Action]
#4	"Anticoagulants"[Mesh] OR "Anticoagulants" [Pharmacological Action] OR anticoagulant[tiab] OR anticoagulants[tiab]
#5	"evaluation studies"[Publication Type] OR "evaluation studies as topic"[MeSH Terms] OR "evaluation study"[tw] OR evaluation studies[tw] OR "intervention studies"[MeSH Terms] OR "intervention study"[tw] OR "intervention studies"[tw] OR "case-control studies"[MeSH Terms] OR "case-control"[tw] OR "cohort studies"[MeSH Terms] OR cohort[tw] OR "longitudinal studies"[MeSH Terms] OR "longitudinal"[tw] OR longitudinally[tw] OR "prospective"[tw] OR prospectively[tw] OR "retrospective studies"[MeSH Terms] OR "retrospective"[tw] OR "follow up"[tw] OR "comparative study"[Publication Type] OR "comparative study"[tw] OR systematic[subset] OR "meta-analysis"[Publication Type] OR "meta-analysis as

	topic"[MeSH Terms] OR "meta-analysis"[tw] OR "meta-analyses"[tw] OR randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR "drug therapy"[Subheading] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Clinical trial[pt] OR "clinical trial"[tw] OR "clinical trials"[tw] NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp])
#6	#1 AND #2 AND (#3 OR #4)
#7	#6 NOT (animals[mh] NOT humans[mh]), Limits: English, Publication Date from 1990 to present

KQ6: What are the comparative safety and effectiveness of available strategies for resuming anticoagulation therapy or performing a procedural intervention as a stroke prevention strategy following a hemorrhagic event (stroke, major bleed, or minor bleed) in patients with nonvalvular atrial fibrillation?

KQ6: What are the comparative safety and effectiveness of available strategies for resuming anticoagulation therapy or performing a procedural intervention as a stroke prevention strategy following a hemorrhagic event (stroke, major bleed, or minor bleed) in patients with nonvalvular atrial fibrillation?	
#1	"Atrial Fibrillation"[Mesh] OR "atrial fibrillation"[tiab] OR (atrial[tiab] AND fibrillation[tiab]) OR afib[tiab] OR "atrial flutter"[MeSH Terms] OR "atrial flutter"[tiab]
#2	"Anticoagulants"[Mesh] OR "Anticoagulants"[Pharmacological Action] OR warfarin[tw] OR "Warfarin"[Mesh] OR coumadin[tw] OR "Vitamin K/antagonists and inhibitors"[Mesh] OR vitamin k[tw] OR "Heparin"[Mesh] OR "Enoxaparin"[Mesh] OR enoxaparin[tw] OR lovenox[tw] OR "rivaroxaban" [Supplementary Concept] OR rivaroxaban[tw] OR xarelto[tw] OR "dabigatran etexilate" [Supplementary Concept] OR dabigatran[tw] OR pradaxa[tw] OR heparin[tw] OR "apixaban" [Supplementary Concept] OR apixaban[tw] OR eliquis[tw] OR "edoxaban" [Supplementary Concept] OR edoxaban[tw] OR lixiana[tw]
#3	"Intracranial Hemorrhages"[Mesh] OR "Hemorrhage"[Mesh:noexp] OR hemorrhage[tw] OR hemorrhaging[tw] OR bleeding[tw] OR bleed[tw] OR hemorrhagic[tw] OR haemorrhage[tw] OR haemorrhaging[tw] OR haemorrhagic[tw]
#4	Resume[tiab] OR resumed[tiab] OR restart[tiab] OR restarted[tiab] OR restarting[tiab] OR re-initiate[tiab] OR reinitiate[tiab] OR continue[tiab] OR continued[tiab] OR start[tiab] OR "time factors"[MeSH Terms] OR resumption[tiab] OR reinitiating[tiab] OR resuming[tiab] OR continuing[tiab]
#5	#1 AND #2 AND #3 AND #4
#6	"evaluation studies"[Publication Type] OR "evaluation studies as topic"[MeSH Terms] OR "evaluation study"[tw] OR evaluation studies[tw] OR "intervention studies"[MeSH Terms] OR "intervention study"[tw] OR "intervention studies"[tw] OR "case-control studies"[MeSH Terms] OR "case-control"[tw] OR "cohort studies"[MeSH Terms] OR cohort[tw] OR "longitudinal studies"[MeSH Terms] OR "longitudinal"[tw] OR longitudinally[tw] OR "prospective"[tw] OR prospectively[tw] OR "retrospective studies"[MeSH Terms] OR "retrospective"[tw] OR "follow up"[tw] OR "comparative study"[Publication Type] OR "comparative study"[tw] OR

	systematic[subset] OR "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[tw] OR "meta-analyses"[tw] OR randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR "drug therapy"[Subheading] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Clinical trial[pt] OR "clinical trial"[tw] OR "clinical trials"[tw] NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp])
#7	#5 AND #6
#8	#7 NOT (animals[mh] NOT humans[mh]), Limits: English, Publication Date from 1990 to present

Embase® search strategy (December 16, 2011)

Platform: Embase.com

KQ1: In patients with nonvalvular atrial fibrillation, what are the comparative diagnostic accuracy and impact on clinical decisionmaking (diagnostic thinking, therapeutic, and patient outcome efficacy) of available clinical and imaging tools for predicting thromboembolic risk?

#1	'heart atrium fibrillation'/exp OR 'heart atrium flutter'/exp OR "atrial fibrillation":ab,ti OR (atrial:ab,ti AND fibrillation:ab,ti) OR afib:ab,ti OR "atrial flutter":ab,ti
#2	'nuclear magnetic resonance imaging'/exp OR 'cardiac imaging'/exp OR 'computer assisted tomography'/exp OR 'echocardiography'/exp OR chads2:ab,ti OR 'chads2 vasc':ab,ti OR (transthoracic:ab,ti AND echo:ab,ti) OR (transesophageal:ab,ti AND echo:ab,ti) OR tte:ab,ti OR tee:ab,ti OR 'ct scan':ab,ti
#3	'stroke'/exp OR 'thromboembolism'/exp OR 'brain ischemia'/exp OR stroke:ab,ti OR thromboembolism:ab,ti OR thromboembolic:ab,ti OR (brain:ab,ti AND ischemia:ab,ti) OR (brain:ab,ti AND ischaemia:ab,ti) OR (transient:ab,ti AND (ischemic:ab,ti OR ischaemic:ab,ti OR ischaemia:ab,ti OR ischemia:ab,ti) AND attack:ab,ti) OR TIA:ab,ti
#4	#1 AND #2 AND #3
#5	'diagnosis'/exp OR 'treatment outcome'/exp OR 'sensitivity and specificity'/exp OR 'clinical decision making'/exp OR 'decision making'/exp OR diagnosis:ab,ti OR outcome:ab,ti OR outcomes:ab,ti OR reliability:ab,ti OR accuracy:ab,ti OR accurate:ab,ti OR Sensitivity:ab,ti OR specificity:ab,ti OR valid:ab,ti OR validity:ab,ti OR validation:ab,ti OR decision:ab,ti OR decisions:ab,ti OR assessment:ab,ti
#6	#5 AND #4
#7	#6 Limits: Humans, English, 2000 - present
#8	#7 AND [embase]/lim NOT [medline]/lim

KQ2: In patients with nonvalvular atrial fibrillation, what are the comparative diagnostic accuracy and impact on clinical decisionmaking (diagnostic thinking, therapeutic, and patient outcome efficacy) of clinical tools and associated risk factors for predicting bleeding events?

#1	'heart atrium fibrillation'/exp OR 'heart atrium flutter'/exp OR "atrial fibrillation":ab,ti OR (atrial:ab,ti AND fibrillation:ab,ti) OR afib:ab,ti OR "atrial flutter":ab,ti
#2	'age'/exp OR 'dementia'/exp OR 'falling'/exp OR 'international normalized ratio'/exp OR "age factors":ab,ti OR "age factor":ab,ti OR age:ab,ti OR dementia:ab,ti OR INR:ab,ti OR fall:ab,ti OR falls:ab,ti OR "international normalized ratio":ab,ti OR paroxysmal:ab,ti OR persistent:ab,ti OR permanent:ab,ti OR stratification:ab,ti OR classification:ab,ti OR schema:ab,ti OR has-bled:ab,ti OR (cognitive:ab,ti AND impairment:ab,ti) OR cognition:ab,ti OR ((prior:ab,ti OR previous:ab,ti OR first:ab,ti) AND stroke:ab,ti)
#3	'brain hemorrhage'/exp OR 'bleeding'/exp OR hemorrhage:ab,ti OR hemorrhaging:ab,ti OR bleeding:ab,ti OR bleed:ab,ti OR hemorrhagic:ab,ti OR haemorrhage:ab,ti OR haemorrhaging:ab,ti OR haemorrhagic:ab,ti
#4	#1 AND #2 And #3
#5	'diagnosis'/exp OR 'treatment outcome'/exp OR 'sensitivity and specificity'/exp OR 'clinical decision making'/exp OR 'decision making'/exp OR diagnosis:ab,ti OR outcome:ab,ti OR outcomes:ab,ti OR reliability:ab,ti OR accuracy:ab,ti OR accurate:ab,ti OR Sensitivity:ab,ti OR specificity:ab,ti OR valid:ab,ti OR validity:ab,ti OR validation:ab,ti OR decision:ab,ti OR decisions:ab,ti OR assessment:ab,ti
#6	#5 AND #4
#7	#6 Limits: Humans, English, 2000 - present
#8	#7 AND [embase]/lim NOT [medline]/lim

KQ3: What are the comparative safety and effectiveness of specific anticoagulation therapies, antiplatelet therapies, and procedural interventions for preventing thromboembolic events:

(a) In patients with nonvalvular atrial fibrillation?
(b) In specific subpopulations of patients with nonvalvular atrial fibrillation?

#1	'heart atrium fibrillation'/exp OR 'heart atrium flutter'/exp OR "atrial fibrillation":ab,ti OR (atrial:ab,ti AND fibrillation:ab,ti) OR afib:ab,ti OR "atrial flutter":ab,ti
#2	'anticoagulant agent'/exp OR 'warfarin'/exp OR 'vitamin K group'/exp OR 'heparin'/exp OR 'enoxaparin'/exp OR 'rivaroxaban'/exp OR 'dabigatran etexilate'/exp OR 'apixaban'/exp OR 'edoxaban'/exp
#3	warfarin:ab,ti OR coumadin:ab,ti OR vitamin k:ab,ti OR enoxaparin:ab,ti OR lovenox:ab,ti OR rivaroxaban:ab,ti OR xarelto:ab,ti OR dabigatran:ab,ti OR pradaxa:ab,ti OR heparin:ab,ti OR apixaban:ab,ti OR eliquis:ab,ti OR edoxaban:ab,ti OR lixiana:ab,ti
#4	#2 OR #3
#5	'antithrombocytic agent'/exp OR 'clopidogrel'/exp OR 'acetylsalicylic acid'/exp OR 'dipyridamole'/exp OR clopidogrel:ab,ti OR plavix:ab,ti OR aspirin:ab,ti OR dipyridamole:ab,ti OR aggrenox:ab,ti OR persantine:ab,ti OR antiplatelet:ab,ti OR

	anti-platelet:ab,ti OR antiplatelets:ab,ti OR anti-platelets:ab,ti
#6	'heart atrium appendage'/exp OR atrial appendage:ab,ti OR LAA:ab,ti OR occluder:ab,ti OR AMPLATZER:ab,ti OR AtriClip:ab,ti OR PLAATO:ab,ti OR Watchman:ab,ti OR (atrial:ab,ti AND modification:ab,ti) OR “atriacure isolator”:ab,ti
#7	'stroke'/exp OR 'thromboembolism'/exp OR 'brain ischemia'/exp OR stroke:ab,ti OR thromboembolism:ab,ti OR thromboembolic:ab,ti OR (brain:ab,ti AND ischemia:ab,ti) OR (brain:ab,ti AND ischaemia:ab,ti) OR (transient:ab,ti AND (ischemic:ab,ti OR ischaemic:ab,ti OR ischaemia:ab,ti OR ischemia:ab,ti) AND attack:ab,ti) OR TIA:ab,ti
#8	#1 AND (#4 OR #5 OR #6) AND #7
#9	('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR (cross NEAR/1 over*):ab,ti OR placebo*:ab,ti OR (doubl* NEAR/1 blind*):ab,ti OR (singl* NEAR/1 blind*):ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR 'clinical study'/exp OR “clinical trial”:ti,ab OR “clinical trials”:ti,ab OR 'controlled study'/exp OR 'evaluation'/exp OR “evaluation study”:ab,ti OR “evaluation studies”:ab,ti OR “intervention study”:ab,ti OR “intervention studies”:ab,ti OR “case control”:ab,ti OR 'cohort analysis'/exp OR cohort:ab,ti OR longitudinal*:ab,ti OR prospective:ab,ti OR prospectively:ab,ti OR retrospective:ab,ti OR 'follow up'/exp OR “follow up”:ab,ti OR 'comparative effectiveness'/exp OR 'comparative study'/exp OR “comparative study”:ab,ti OR “comparative studies”:ab,ti OR 'evidence based medicine'/exp OR “systematic review”:ab,ti OR “meta-analysis”:ab,ti OR “meta-analyses”:ab,ti) NOT ('editorial'/exp OR 'letter'/exp OR 'case report'/exp)
#10	#8 AND #9
#11	#10 Limits: Humans, English, 2000 - present
#12	#11 AND [embase]/lim NOT [medline]/lim

KQ4: What are the comparative safety and effectiveness of available strategies for anticoagulation in patients with nonvalvular atrial fibrillation who are undergoing invasive procedures?

#1	'heart atrium fibrillation'/exp OR 'heart atrium flutter'/exp OR “atrial fibrillation”:ab,ti OR (atrial:ab,ti AND fibrillation:ab,ti) OR afib:ab,ti OR “atrial flutter”:ab,ti
#2	'anticoagulant agent'/exp OR 'warfarin'/exp OR 'vitamin K group'/exp OR 'heparin'/exp OR 'enoxaparin'/exp OR 'rivaroxaban'/exp OR 'dabigatran etexilate'/exp OR 'apixaban'/exp OR 'edoxaban'/exp
#3	warfarin:ab,ti OR coumadin:ab,ti OR vitamin k:ab,ti OR enoxaparin:ab,ti OR lovenox:ab,ti OR rivaroxaban:ab,ti OR xarelto:ab,ti OR dabigatran:ab,ti OR pradaxa:ab,ti OR heparin:ab,ti OR apixaban:ab,ti OR eliquis:ab,ti OR edoxaban:ab,ti OR lixiana:ab,ti
#4	#2 OR #3
#5	'surgery'/exp OR 'dental care'/exp OR ((surgical:ab,ti OR invasive:ab,ti) AND (procedure:ab,ti OR procedures:ab,ti)) OR (dental:ab,ti AND (procedure:ab,ti OR procedures:ab,ti)) OR surgery:ab,ti OR procedures:ab,ti OR procedure:ab,ti

#6	#1 AND #4 AND #5
#7	('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR (cross NEAR/1 over*):ab,ti OR placebo*:ab,ti OR (doubl* NEAR/1 blind*):ab,ti OR (singl* NEAR/1 blind*):ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR 'clinical study'/exp OR “clinical trial”:ti,ab OR “clinical trials”:ti,ab OR 'controlled study'/exp OR 'evaluation'/exp OR “evaluation study”:ab,ti OR “evaluation studies”:ab,ti OR “intervention study”:ab,ti OR “intervention studies”:ab,ti OR “case control”:ab,ti OR 'cohort analysis'/exp OR cohort:ab,ti OR longitudinal*:ab,ti OR prospective:ab,ti OR prospectively:ab,ti OR retrospective:ab,ti OR 'follow up'/exp OR “follow up”:ab,ti OR 'comparative effectiveness'/exp OR 'comparative study'/exp OR “comparative study”:ab,ti OR “comparative studies”:ab,ti OR 'evidence based medicine'/exp OR “systematic review”:ab,ti OR “meta-analysis”:ab,ti OR “meta-analyses”:ab,ti) NOT ('editorial'/exp OR 'letter'/exp OR 'case report'/exp)
#8	#6 AND #7
#9	#8 Limits: Humans, English, 2000 - present
#10	#9 AND [embase]/lim NOT [medline]/lim

KQ5: What are the comparative safety and effectiveness of available strategies for switching between warfarin and other novel oral anticoagulants, in patients with nonvalvular atrial fibrillation?

#1	'heart atrium fibrillation'/exp OR 'heart atrium flutter'/exp OR “atrial fibrillation”:ab,ti OR (atrial:ab,ti AND fibrillation:ab,ti) OR afib:ab,ti OR “atrial flutter”:ab,ti
#2	'warfarin'/exp OR warfarin:ab,ti OR coumadin:ab,ti
#3	antithrombins:ab,ti OR (direct:ab,ti AND thrombin:ab,ti AND inhibitors:ab,ti) OR (direct:ab,ti AND thrombin:ab,ti AND inhibitor:ab,ti) OR "direct thrombin inhibitors":ab,ti OR “Antithrombin III":ab,ti OR “Antithrombin Proteins":ab,ti OR argatroban:ab,ti OR bivalirudin:ab,ti OR “Heparin Cofactor II":ab,ti OR Hirudins:ab,ti OR inogatran:ab,ti OR lepirudin:ab,ti OR melagatran:ab,ti OR “SDZ MTH 958":ab,ti OR ximelagatran:ab,ti
#4	'anticoagulant agent'/exp OR anticoagulant:ab,ti OR anticoagulants:ab,ti
#5	('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR (cross NEAR/1 over*):ab,ti OR placebo*:ab,ti OR (doubl* NEAR/1 blind*):ab,ti OR (singl* NEAR/1 blind*):ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR 'clinical study'/exp OR “clinical trial”:ti,ab OR “clinical trials”:ti,ab OR 'controlled study'/exp OR 'evaluation'/exp OR “evaluation study”:ab,ti OR “evaluation studies”:ab,ti OR “intervention study”:ab,ti OR “intervention studies”:ab,ti OR “case control”:ab,ti OR 'cohort analysis'/exp OR cohort:ab,ti OR longitudinal*:ab,ti OR prospective:ab,ti OR prospectively:ab,ti OR retrospective:ab,ti OR 'follow up'/exp OR “follow up”:ab,ti OR 'comparative effectiveness'/exp OR 'comparative study'/exp OR “comparative study”:ab,ti OR “comparative studies”:ab,ti OR 'evidence based medicine'/exp OR “systematic

	review”:ab,ti OR “meta-analysis”:ab,ti OR “meta-analyses”:ab,ti) NOT ('editorial'/exp OR 'letter'/exp OR 'case report'/exp)
#6	#1 AND #2 AND (#3 OR #4)
#7	#6 Limits: Humans, English, 2000 - present
#8	#7 AND [embase]/lim NOT [medline]/lim

KQ6: What are the comparative safety and effectiveness of available strategies for resuming anticoagulation therapy or performing a procedural intervention as a stroke prevention strategy following a hemorrhagic event (stroke, major bleed, or minor bleed) in patients with nonvalvular atrial fibrillation?

#1	'heart atrium fibrillation'/exp OR 'heart atrium flutter'/exp OR “atrial fibrillation”:ab,ti OR (atrial:ab,ti AND fibrillation:ab,ti) OR afib:ab,ti OR “atrial flutter”:ab,ti
#2	'anticoagulant agent'/exp OR 'warfarin'/exp OR 'vitamin K group'/exp OR 'heparin'/exp OR 'enoxaparin'/exp OR 'rivaroxaban'/exp OR 'dabigatran etexilate'/exp OR 'apixaban'/exp OR 'edoxaban'/exp
#3	warfarin:ab,ti OR coumadin:ab,ti OR vitamin k:ab,ti OR enoxaparin:ab,ti OR lovenox:ab,ti OR rivaroxaban:ab,ti OR xarelto:ab,ti OR dabigatran:ab,ti OR pradaxa:ab,ti OR heparin:ab,ti OR apixaban:ab,ti OR eliquis:ab,ti OR edoxaban:ab,ti OR lixiana:ab,ti
#4	#2 OR #3
#5	'brain hemorrhage'/exp OR 'bleeding'/exp OR hemorrhage:ab,ti OR hemorrhaging:ab,ti OR bleeding:ab,ti OR bleed:ab,ti OR hemorrhagic:ab,ti OR haemorrhage:ab,ti OR haemorrhaging:ab,ti OR haemorrhagic:ab,ti
#6	'time'/exp OR resume:ab,ti OR resumed:ab,ti OR restart:ab,ti OR restarted:ab,ti OR restarting:ab,ti OR re-initiate:ab,ti OR reinitiate:ab,ti OR continue:ab,ti OR continued:ab,ti OR start:ab,ti OR resumption:ab,ti OR reinitiating:ab,ti OR resuming:ab,ti OR continuing:ab,ti
#7	#1 AND #4 AND #5 AND #6
#8	('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR (cross NEAR/1 over*):ab,ti OR placebo*:ab,ti OR (doubl* NEAR/1 blind*):ab,ti OR (singl* NEAR/1 blind*):ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR 'clinical study'/exp OR “clinical trial”:ti,ab OR “clinical trials”:ti,ab OR 'controlled study'/exp OR 'evaluation'/exp OR “evaluation study”:ab,ti OR “evaluation studies”:ab,ti OR “intervention study”:ab,ti OR “intervention studies”:ab,ti OR “case control”:ab,ti OR 'cohort analysis'/exp OR cohort:ab,ti OR longitudinal*:ab,ti OR prospective:ab,ti OR prospectively:ab,ti OR retrospective:ab,ti OR 'follow up'/exp OR “follow up”:ab,ti OR 'comparative effectiveness'/exp OR 'comparative study'/exp OR “comparative study”:ab,ti OR “comparative studies”:ab,ti OR 'evidence based medicine'/exp OR “systematic review”:ab,ti OR “meta-analysis”:ab,ti OR “meta-analyses”:ab,ti) NOT ('editorial'/exp OR 'letter'/exp OR 'case report'/exp)
#9	#7 AND #8

#10	#9 Limits: Humans, English, 2000 - present
#11	#10 AND [embase]/lim NOT [medline]/lim

Cochrane search strategy (December 19, 2011)

Platform: Wiley
Database searched: Cochrane Database of Systematic Reviews

KQ1: In patients with nonvalvular atrial fibrillation, what are the comparative diagnostic accuracy and impact on clinical decisionmaking (diagnostic thinking, therapeutic, and patient outcome efficacy) of available clinical and imaging tools for predicting thromboembolic risk?

#1	(atrial fibrillation OR atrial flutter):ti,ab,kw
#2	Magnetic Resonance Imaging explode all trees OR MeSH descriptor Cardiac Imaging Techniques explode all trees OR MeSH descriptor Tomography, X-Ray Computed explode all trees OR MeSH descriptor Echocardiography explode all trees OR (chads2 OR chads2-vasc OR TEE OR TTE OR ct-scan OR transthoracic echo OR transesophageal echo):ti,ab,kw
#3	MeSH descriptor Stroke explode all trees OR MeSH descriptor Thromboembolism explode all trees OR MeSH descriptor Brain Ischemia explode all trees OR (thromboembolism OR thromboembolic OR brain ischemia OR brain ischaemia OR tia):ti,ab,kw OR (transient ischemic attack):ti,ab,kw or (transient ischaemic attack):ti,ab,kw or (transient ischemia attack):ti,ab,kw or (transient ischaemic attack):ti,ab,kw
#4	#1 AND #2 AND #3
#5	#4, Limits: Cochrane Reviews, 2000 to 2011

KQ2: In patients with nonvalvular atrial fibrillation, what are the comparative diagnostic accuracy and impact on clinical decisionmaking (diagnostic thinking, therapeutic, and patient outcome efficacy) of clinical tools and associated risk factors for predicting bleeding events?

#1	(atrial fibrillation OR atrial flutter):ti,ab,kw
#2	MeSH descriptor Age Factors explode all trees OR MeSH descriptor Dementia explode all trees OR MeSH descriptor Accidental Falls explode all trees OR MeSH descriptor International Normalized Ratio explode all trees OR age:ti,ab,kw OR dementia:ti,ab,kw OR INR:ti,ab,kw OR fall:ti,ab,kw OR falls:ti,ab,kw OR "international normalized ratio":ti,ab,kw OR paroxysmal:ti,ab,kw OR persistent:ti,ab,kw OR permanent:ti,ab,kw OR stratification:ti,ab,kw OR classification:ti,ab,kw OR schema:ti,ab,kw OR has-bled:ti,ab,kw OR cognitive impairment:ti,ab,kw OR cognition:ti,ab,kw OR ((prior:ti,ab,kw OR previous:ti,ab,kw OR first:ti,ab,kw) AND stroke:ti,ab,kw)
#3	MeSH descriptor Intracranial Hemorrhages explode all trees OR MeSH descriptor Hemorrhage explode all trees OR hemorrhage:ti,ab,kw OR hemorrhaging:ti,ab,kw OR bleeding:ti,ab,kw OR bleed:ti,ab,kw OR hemorrhagic:ti,ab,kw OR haemorrhage:ti,ab,kw OR haemorrhaging:ti,ab,kw OR haemorrhagic:ti,ab,kw
#4	#1 AND #2 And #3

#5	MeSH descriptor Diagnosis explode all trees OR MeSH descriptor Treatment Outcome explode all trees OR MeSH descriptor Sensitivity and Specificity explode all trees OR MeSH descriptor Decision Making explode all trees OR diagnosis:ti,ab,kw OR outcome:ti,ab,kw OR outcomes:ti,ab,kw OR reliability:ti,ab,kw OR accuracy:ti,ab,kw OR accurate:ti,ab,kw OR Sensitivity:ti,ab,kw OR specificity:ti,ab,kw OR valid:ti,ab,kw OR validity:ti,ab,kw OR validation:ti,ab,kw OR decision:ti,ab,kw OR decisions:ti,ab,kw OR assessment:ti,ab,kw
#6	#4 AND #5
#7	#6, Limits: Cochrane Reviews, 2000 to 2011

KQ3: What are the comparative safety and effectiveness of specific anticoagulation therapies, antiplatelet therapies, and procedural interventions for preventing thromboembolic events:

(a) In patients with nonvalvular atrial fibrillation?

(b) In specific subpopulations of patients with nonvalvular atrial fibrillation?

#1	(atrial fibrillation OR atrial flutter):ti,ab,kw
#2	MeSH descriptor Anticoagulants explode all trees OR warfarin:ti,ab,kw OR coumadin:ti,ab,kw OR vitamin k:ti,ab,kw OR enoxaparin:ti,ab,kw OR lovenox:ti,ab,kw OR rivaroxaban:ti,ab,kw OR xarelto:ti,ab,kw OR dabigatran:ti,ab,kw OR pradaxa:ti,ab,kw OR heparin:ti,ab,kw OR apixaban:ti,ab,kw OR eliquis:ti,ab,kw OR edoxaban:ti,ab,kw OR lixiana:ti,ab,kw OR anticoagulants:ti,ab,kw OR OR anticoagulant:ti,ab,kw
#3	MeSH descriptor Platelet Aggregation Inhibitors explode all trees OR clopidogrel:ti,ab,kw OR plavix:ti,ab,kw OR aspirin:ti,ab,kw OR dipyridamole:ti,ab,kw OR aggrenox:ti,ab,kw OR persantine:ti,ab,kw OR antiplatelet:ti,ab,kw OR anti-platelet:ti,ab,kw OR antiplatelets:ti,ab,kw OR anti-platelets:ti,ab,kw
#4	MeSH descriptor Atrial Appendage explode all trees OR atrial appendage:ti,ab,kw OR LAA:ti,ab,kw OR occluder:ti,ab,kw OR AMPLATZER:ti,ab,kw OR AtriClip:ti,ab,kw OR PLAATO:ti,ab,kw OR Watchman:ti,ab,kw OR (atrial:ti,ab,kw AND modification:ti,ab,kw) OR "atriacure isolator":ti,ab,kw
#5	MeSH descriptor Stroke explode all trees OR MeSH descriptor Thromboembolism explode all trees OR MeSH descriptor Brain Ischemia explode all trees OR (thromboembolism OR thromboembolic OR brain ischemia OR brain ischaemia OR tia):ti,ab,kw OR (transient ischemic attack):ti,ab,kw or (transient ischaemic attack):ti,ab,kw or (transient ischemia attack):ti,ab,kw or (transient ischaemic attack):ti,ab,kw
#6	#1 AND (#2 OR #3 OR #4) AND #5
#7	#6, Limits: Cochrane Reviews, 2000 to 2011

KQ4: What are the comparative safety and effectiveness of available strategies for anticoagulation in patients with nonvalvular atrial fibrillation who are undergoing invasive procedures?

#1	(atrial fibrillation OR atrial flutter):ti,ab,kw
#2	MeSH descriptor Anticoagulants explode all trees OR warfarin:ti,ab,kw OR

	coumadin:ti,ab,kw OR vitamin k:ti,ab,kw OR enoxaparin:ti,ab,kw OR lovenox:ti,ab,kw OR rivaroxaban:ti,ab,kw OR xarelto:ti,ab,kw OR dabigatran:ti,ab,kw OR pradaxa:ti,ab,kw OR heparin:ti,ab,kw OR apixaban:ti,ab,kw OR eliquis:ti,ab,kw OR edoxaban:ti,ab,kw OR lixiana:ti,ab,kw OR anticoagulants:ti,ab,kw OR OR anticoagulant:ti,ab,kw
#3	MeSH descriptor Surgical Procedures, Operative explode all trees OR MeSH descriptor Dental Care explode all trees OR surgical:ti,ab,kw OR invasive:ti,ab,kw OR procedures:ti,ab,kw OR surgery:ti,ab,kw OR procedure:ti,ab,kw
#4	#1 AND #2 AND #3
#5	#4, Limits: Cochrane Reviews, 2000 to 2011

KQ5: What are the comparative safety and effectiveness of available strategies for switching between warfarin and other novel oral anticoagulants, in patients with nonvalvular atrial fibrillation?

#1	(atrial fibrillation OR atrial flutter):ti,ab,kw
#2	warfarin:ti,ab,kw OR coumadin:ti,ab,kw
#3	MeSH descriptor Antithrombins explode all trees OR antithrombins:ti,ab,kw OR (direct:ti,ab,kw AND thrombin:ti,ab,kw AND inhibitors:ti,ab,kw) OR "direct thrombin inhibitors":ti,ab,kw OR "direct thrombin inhibitor":ti,ab,kw
#4	MeSH descriptor Anticoagulants explode all trees OR anticoagulant:ti,ab,kw OR anticoagulants:ti,ab,kw OR vitamin k:ti,ab,kw OR enoxaparin:ti,ab,kw OR lovenox:ti,ab,kw OR rivaroxaban:ti,ab,kw OR xarelto:ti,ab,kw OR dabigatran:ti,ab,kw OR pradaxa:ti,ab,kw OR heparin:ti,ab,kw OR apixaban:ti,ab,kw OR eliquis:ti,ab,kw OR edoxaban:ti,ab,kw OR lixiana:ti,ab,kw
#5	#1 AND #2 AND (#3 OR #4)
#6	#5, Limits: Cochrane Reviews, 2000 to 2011

KQ6: What are the comparative safety and effectiveness of available strategies for resuming anticoagulation therapy or performing a procedural intervention as a stroke prevention strategy following a hemorrhagic event (stroke, major bleed, or minor bleed) in patients with nonvalvular atrial fibrillation?

#1	(atrial fibrillation OR atrial flutter):ti,ab,kw
#2	MeSH descriptor Anticoagulants explode all trees OR warfarin:ti,ab,kw OR coumadin:ti,ab,kw OR vitamin k:ti,ab,kw OR enoxaparin:ti,ab,kw OR lovenox:ti,ab,kw OR rivaroxaban:ti,ab,kw OR xarelto:ti,ab,kw OR dabigatran:ti,ab,kw OR pradaxa:ti,ab,kw OR heparin:ti,ab,kw OR apixaban:ti,ab,kw OR eliquis:ti,ab,kw OR edoxaban:ti,ab,kw OR lixiana:ti,ab,kw OR anticoagulant:ti,ab,kw OR anticoagulants:ti,ab,kw
#3	MeSH descriptor Intracranial Hemorrhages explode all trees OR MeSH descriptor Hemorrhage explode all trees OR hemorrhage:ti,ab,kw OR hemorrhaging:ti,ab,kw OR bleeding:ti,ab,kw OR bleed:ti,ab,kw OR hemorrhagic:ti,ab,kw OR haemorrhage:ti,ab,kw OR haemorrhaging:ti,ab,kw OR haemorrhagic:ti,ab,kw
#4	MeSH descriptor Time Factors explode all trees OR Resume:ti,ab,kw OR

	resumed:ti,ab,kw OR restart:ti,ab,kw OR restarted:ti,ab,kw OR restarting:ti,ab,kw OR re-initiate:ti,ab,kw OR reinitiate:ti,ab,kw OR continue:ti,ab,kw OR continued:ti,ab,kw OR start:ti,ab,kw OR resumption:ti,ab,kw OR reinitiating:ti,ab,kw OR resuming:ti,ab,kw OR continuing:ti,ab,kw
#5	#1 AND #2 AND #3 AND #4
#6	#5, Limits: Cochrane Reviews, 2000 to 2011

Grey Literature Searches

ClinicalTrials.gov (March 9, 2012)

KQ1, KQ2, KQ3, KQ6	
Condition	atrial fibrillation OR afib OR atrial flutter
Outcome	stroke OR thromboembolism OR thromboembolic OR "brain ischemia" OR “brain ischaemia” OR (transient AND ischemic AND attack) OR TIA OR hemorrhage OR hemorrhaging OR bleeding OR bleed OR hemorrhagic OR haemorrhage OR haemorrhaging OR haemorrhagic

KQ4	
Condition	atrial fibrillation OR afib OR atrial flutter
Intervention	Anticoagulants OR anticoagulation OR warfarin OR coumadin OR vitamin k OR Heparin OR enoxaparin OR lovenox OR rivaroxaban OR xarelto OR dabigatran OR pradaxa OR apixaban OR eliquis OR edoxaban OR lixiana
Search Terms	Surgery OR procedures OR procedure

KQ5	
Condition	atrial fibrillation OR afib OR atrial flutter
Intervention	(warfarin OR Coumadin) AND (Antithrombins OR antithrombin OR (direct AND thrombin AND (inhibitors OR inhibitor)) OR anticoagulant OR anticoagulants)

Total number of results: 170

WHO: International Clinical Trials Registry Platform Search Portal (March 19, 2012)

KQs 1-6	
Condition	atrial fibrillation OR afib OR atrial flutter
Recruiting status	ALL

Total number of results: 765

ProQuest COS Conference Papers Index (March 9, 2012)

KQ1, KQ2, KQ3, KQ6	
#1	All (atrial fibrillation OR afib OR atrial flutter)
#3	All (stroke OR thromboembolism OR thromboembolic OR "brain ischemia" OR “brain ischaemia” OR (transient AND (ischemic OR ischaemic) AND attack) OR TIA OR hemorrhage OR hemorrhaging OR bleeding OR bleed OR hemorrhagic OR haemorrhage OR haemorrhaging OR haemorrhagic)
#4	#1 AND #2 AND #3

KQ4	
#1	All (atrial fibrillation OR afib OR atrial flutter)
#2	All (Anticoagulants OR anticoagulation OR warfarin OR coumadin OR vitamin k OR Heparin OR enoxaparin OR lovenox OR rivaroxaban OR xarelto OR dabigatran OR pradaxa OR apixaban OR eliquis OR edoxaban OR lixiana)
#3	All (Surgery OR procedures OR procedure)
#4	#1 AND #2 AND #3

KQ5	
#1	All (atrial fibrillation OR afib OR atrial flutter)
#2	All (warfarin OR Coumadin)
#3	All (Antithrombins OR antithrombin OR (direct AND thrombin AND (inhibitors OR inhibitor)) OR anticoagulant OR anticoagulants)
#6	#1 AND #2 AND #3

Total number of results: 352

Appendix B. Data Abstraction Elements

Study Characteristics

- Study Identifiers
  - Study Name or Acronym
  - Last name of first author
  - Publication Year
- Additional Articles Used in This Abstraction
- Study Objective(s)
- Study Dates
  - Enrollment start (Mon and YYYY)
  - Enrollment end (Mon and YYYY)
  - Follow-up end (Mon and YYYY)
- Study Sites
  - Single center, Multicenter, Unclear/Not reported
  - Number of sites
- Geographic Location (Select all that apply)
  - US, Canada, UK, Europe, S. America, C. America, Asia, Africa, Australia/NZ, Unclear/Not reported, Other (specify)
- Study Design
  - Prospective RCT
  - Prospective Cohort
  - Retrospective Cohort
  - Case-control
  - Cross-sectional
  - Other (specify)
- Funding Source (Select all that apply)
  - Government, Industry, Non-government/non-industry, Unclear/Not reported, Other (specify)
- Setting (Select all that apply)
  - In-patient, Out-patient, Emergency Room, Unclear/Not reported, Other (specify)
- Enrollment Approach (Select all that apply)
  - Consecutive patients, Convenience sample, Unclear/Not reported, Other (specify)
- Study Inclusion and Exclusion Criteria
  - Copy/paste inclusion and exclusion criteria as reported
  - Is the study entirely composed of patients with any of the following characteristics/conditions?
    - Paroxysmal Atrial Fibrillation (AF)
    - Persistent AF
    - Permanent AF
    - Women
    - Pregnant women
    - Patients in the therapeutic range
    - Patients with prior bleed
    - Patients with prior stroke
    - Patients with comorbid conditions such as dementia, renal failure, or hepatic failure

        - Patients with multiple coexisting conditions (e.g. combinations of hypertension, diabetes, CHF, CAD, and high cholesterol)
        - Patients non-compliant with treatment
        - None of the above
- Study Enrollment/Study Completion
    - N assessed for eligibility
    - N eligible
    - N enrolled/included
    - N completed follow-up (most distal timepoint of the primary outcome)
    - N analyzed
- Key Question Applicability (Select all that apply)
    - KQ1, KQ2, KQ3, KQ4, KQ5, KQ6
- Comments

Baseline Characteristics – Record the following elements for Total Population, Arm 1, Arm 2, Arm 3, and Arm 4 (as applicable)

- Number of Patients, Age, Ethnicity, and Race
    - Number of Patients
        - Total
        - Female
        - Male
    - Percentage
        - Female
        - Male
    - Age
        - Mean
        - Standard Deviation
        - Standard Error
        - Median
        - IQR
        - Min
        - Max
        - NR
    - Ethnicity
        - Hispanic or Latino
        - Not Hispanic or Latino
        - NR
    - Race
        - Black/African American
        - American Indian or Alaska Native
        - Asian
        - Native Hawaiian or other Pacific Islander
        - White
        - Multiracial
        - Other (specify)
        - NR
- Baseline Characteristics
    - Diabetes
        - N
        - %

- Heart failure (NYHA Class), N and % for the following:
  - Class I
  - Class II
  - Class III
  - Class IV
  - All classes
- Sleep apnea
  - N
  - %
- Hyperlipidemia
  - N
  - %
- Hypertension
  - N
  - %
- Kidney disease
  - N
  - %
- Congestive Heart Failure (CHF)
  - N
  - %
- Coronary Artery Disease (CAD)
  - N
  - %
- Prior Myocardial Infarction (MI)
  - N
  - %
- Prior Percutaneous Coronary Intervention (PCI)
  - N
  - %
- Prior CABG
  - N
  - %
- Left Ventricular Ejection Fraction (LVEF), Mean or median
  - Mean or median
  - SD, SE, or IQR
- LVEF, Number of patients (<35% or other [define])
  - N
  - %
- Evidence of Left Atrial Appendage (LAA) thrombus
  - N
  - %
- Any Left Ventricular (LV) dysfunction
  - N
  - %
- Prior stroke or Transient Ischemic Attack (TIA), N and % for the following types:
  - Ischemic
  - Hemorrhagic
  - TIA
  - All types

- Tobacco use
  - N
  - %
- Obesity (define)
  - N
  - %
- Patients non-compliant with treatment
  - N
  - %
- Prior vascular disease
  - N
  - %
- Prior bleed
  - N
  - %
- $CHADS_2$ score
  - Mean or median
  - SD, SE, or IQR
- $CHADS_2$, N and % of patients with the following scores:
  - 0
  - 1
  - 2+
- CHA_2DS_2-VASc score
  - Mean or median
  - SD, SE, or IQR
- CHA_2DS_2-VASc, N and % of patients with the following scores:
  - 0
  - 1
  - 2+
- HAS-BLED score
  - Mean or median
  - SD, SE, or IQR
- HAS-BLED, N and % of patients with the following scores:
  - <3
  - 3+
- Duration of AF
  - Mean or median
  - SD, SE, or IQR
- Paroxysmal AF
  - N
  - %
- Persistent AF
  - N
  - %
- Permanent AF
  - N
  - %

- Comments

Intervention Characteristics – Record the following elements for Total Population, Arm 1, Arm 2, Arm 3, and Arm 4 (as applicable)

- Interventions (Check all that apply)
    - Placebo or control; Clinical & imaging tools for thromboembolic risk; Clinical tools & individual factors for bleeding risk; Anticoagulation therapy (all oral anticoagulants); Procedural interventions; Antiplatelet therapy; Anticoagulation bridging therapies
        - If 'Placebo or control' selected:
            - Placebo/control
                - Placebo, Usual care/Optimal medical therapy (OMT), Other (specify)
        - If 'Clinical & imagine tools for thromboembolic risk' selected:
            - Thromboembolic risk tools
                - $CHADS_2$ score, CHA_2DS_2-VASc score, Transthoracic echo (TTE), Transesophageal echo (TEE), CT scan, Cardiac MRI, Framingham Score
        - If 'Clinical tools & individual factors for bleeding risk' selected:
            - Intracerebral bleeding risk tools/factors
                - Patient age, Prior stroke, Type of AF (paroxysmal, persistent, permanent), International normalized ratio (INR), Dementia/cognitive impairment, Falls risk, $CHADS_2$ score, CHA_2DS_2-VASc score, $HEMORR_2HAGES$, HAS-BLED, ATRIA, Bleeding Risk Index, Framingham
        - If 'Anticoagulation therapy (all oral anticoagulants)' selected:
            - Anticoagulation therapy
                - Vitamin K antagonists, Dabigatran (Pradaxa), Rivaroxaban (Xarelto), Apixaban (Eliquis), Edoxaban (DU-176b)
                - If 'Vitamin K antagonists' selected:
                - Warfarin (Coumadin), Other
        - If 'Procedural interventions' selected:
            - Procedural interventions
                - Surgical LAA resection, Surgical LAA ligation, Surgical – other (specify), Minimally invasive – Atriclip, Minimally invasive – other (specify), Transcatheter – WATCHMAN, Transcatheter – AMPLATZER, Transcatheter – PLAATO, Transcatheter – Other (specify)
        - If 'Antiplatelet therapy' selected:
            - Antiplatelet therapy
                - Clopidogrel (Plavix), Aspirin (ASA), ASA + dipyridamole (Aggrenox), Dipyridamole (Persantine), Other (specify)
        - If 'Anticoagulation bridging therapies' selected:
            - Anticoagulation bridging
                - Unfractionated Heparin, Low Molecular Weight Heparin (LMWH), Factor IIa Inhibitors, Factor Xa Inhibitors, Other (specify)
                - If 'Unfractionated Heparin' selected:
                - IV Heparin, Other
                - If 'LMWH' selected:

            - Bemiparin, Certoparin, Dalteparin, Enoxaparin, Nadroparin, Parnaparin, Reviparin, Tinzaparin, Other
        - If 'Factor IIa Inhibitors' selected:
            - Dabigatran, Other
        - If 'Factor Xa Inhibitors' selected:
            - Apixaban, Edoxaban, Rivaroxaban, Other
- Intervention Descriptors
    - Describe the intervention received by each patient group. If the intervention includes medication(s), include pertinent details such as dose, frequency, and potential for adjustment.
- Duration of Follow-up: Record the following elements for Arm 1, Arm 2, Arm 3, and Arm 4 (as applicable)
    - Mean or median (include units)
    - SD, SE, or IQR
    - NR

Clinical/ Patient-Centered Outcomes

- Select the outcome reported on this form:
    - Cerebrovascular infarction
    - Transient ischemic attack (TIA)
    - Systemic embolism (excludes pulmonary embolism and deep vein thrombosis)
    - CV infarction/stroke
    - Ischemic stroke
    - Intercerebral hemorrhage
    - Subdural hematoma
    - Major bleed
    - Minor bleed
    - Myocardial infarction
    - All-cause mortality
    - CV mortality
    - Health-related QOL/Functional capacity
    - Healthcare utilization – Hospital admissions
    - Healthcare utilization – Other measures
    - Long-term adherence to therapy
    - Time in therapeutic range
    - Composite outcome
    - No clinical or patient-centered outcomes of interest reported
- Define/specify the following for the outcome, if applicable
    - Major bleed type and location
    - Minor bleed type and location
    - Health-related QOL/Functional capacity measure/scale
    - Other Healthcare utilization measure/scale
    - Components of composite outcomes:
        - Cerebrovascualr infarction; Transient ischemic attach (TIA); Systemic embolism (excludes pulmonary embolism and deep vein thrombosis); CV infarction/stroke; Intercerebral hemorrhage; Subdural hematoma; Major bleed; Minor bleed; Myocardial infarction; All-cause mortality; CV mortality; Infection; Heart block; Esophageal fistula; Tamponade; Dyspepsia; Health-

related QOL/Functional capacity; Healthcare utilization – Hospital admissions; Healthcare utilization – Other measures; Long-term adherence to therapy; Time in therapeutic range; Ischemic stroke

- Record additional details to describe outcome measure, as needed
- Timepoints to be abstracted (Check all that apply)
    - Close to 1 month
    - Close to 3 months
    - Close to 6 months
    - Close to 1 yr
    - Most distal timepoint after one year
    - Untimed measure (e.g., time to event)
- For each timepoint, record the following elements as applicable:
    - Specify actual timing of outcome (in months)
    - Group: Arm 1, Arm 2, Arm 3, Arm 4
    - N Analyzed (enter UNK if unknown)
    - Unadjusted Result
        - Mean
        - Median
        - Mean within group change
        - Mean between group change
        - Number of patients with outcome
        - % of patients with outcome
        - Events/denominator
        - Odds ratio
        - Hazard ratio
        - Relative risk
        - Other (specify)
    - Unadjusted Result Variability
        - Standard Error (SE)
        - Standard Deviation (SD)
        - IQR
        - 95% CI
        - Other % CI (specify)
        - Other (specify)
    - Unadjusted Result, p-value between groups
    - Unadjusted Result, Reference group (for comparison between groups)
    - Adjusted Result
        - Mean
        - Median
        - Mean within group change
        - Mean between group change
        - Number of patients with outcome
        - % of patients with outcome
        - Events/denominator
        - Odds ratio
        - Hazard ratio
        - Relative risk
        - Other (specify)
    - Adjusted Result Variability
        - Standard Error (SE)

        - Standard Deviation (SD)
        - IQR
        - 95% CI
        - Other % CI (specify)
        - Other (specify)
    - Adjusted Result, p-value between groups
    - Adjusted Result, Reference group (for comparison between groups)
    - If adjusted data is recorded, indicate the adjustments applied
- Does the study report any subgroup analyses for this outcome? (Yes/No)
    - If Yes, describe the subgroup analyses and summarize results
- Comments

Adverse Events

- Are adverse events reported? (Yes/No)
- Record the Number of patients, % of patients, and exact p-value for the Total Population, Arm 1, Arm 2, Arm 3, and Arm 4 (as applicable) for the following:
    - Infection
    - Heart block
    - Esophageal fistula
    - Tamponade
    - Dyspepsia
- Does the study report any AE subgroup analyses? (Yes/No)
    - If Yes, describe the subgroup analyses and summarize results
- Comments

KQ1/2 Diagnostic Efficacy

- Type of risk being evaluated
    - Thromboembolic risk
    - Intracerebral hemorrhage bleeding risk
- Tool of individual risk factor being tested
    - $CHADS_2$ score
    - CHA_2DS_2-VASc score
    - Transthoracic echo (TTE)
    - Transesophageal echo (TEE)
    - CT scan
    - Cardiac MRI
    - $HEMORR_2HAGES$
    - HAS-BLED
    - ATRIA
    - Framingham score
    - Bleeding Risk Index
    - Patient age
    - Prior stroke
    - Type of AF (paroxysmal, persistent, permanent)
    - International normalized ratio (INR)
    - Dementia/cognitive impairment
    - Falls risk
- Additional details describing risk being evaluated

- Outcomes reported on this form for this tool or risk factor (Select all that apply): Diagnostic Accuracy; Diagnostic Thinking/Therapeutic Efficacy; Patient Outcome Efficacy
    - If Diagnostic Accuracy:
        - Timing of the outcome data reported
        - Total Population, Group 1, Group 2, Group 3, Group 4, Group 5, Group 6
            - N and %
            - C statistic
            - C statistic CI (Lower – Upper bound)
                - 95% CI
                - Other % (specify)
            - Hazard Ratio
            - Hazard Ratio (Lower – Upper bound)
                - 95% CI
                - Other % (specify)
            - Event rate (define)
            - Event rate (Lower – Upper bound)
                - 95% CI
                - Other % (specify)
            - True positive (# patients)
            - True negative (# patients)
            - False positive (# patients)
            - False negative (# patients)
            - Indeterminate/inadequate results (# patients)
            - Sensitivity (%)
            - Sensitivity (SD)
            - Sensitivity CI (Lower – Upper bound)
                - 95% CI
                - Other % (specify)
            - Specificity (%)
            - Specificity (SD)
            - Specificity CI (Lower – Upper bound)
                - 95% CI
                - Other % (specify)
            - Positive predictive value (%)
            - Positive predictive value (Std dev)
            - Positive predictive value (Lower – Upper bound)
                - 95% CI
                - Other % (specify)
            - Negative predictive value (%)
            - Negative predictive value (SD)
            - Negative predictive value (Lower – Upper bound)
                - 95% CI
                - Other % (specify)
            - Positive likelihood ratio
            - Negative likelihood ratio
            - Other (specify)
    - If Diagnostic Thinking/Therapeutic Efficacy: Describe
    - If Patient Outcome Efficacy: Describe

- Does the study report any subgroup analyses for this tool/ outcome? (Yes/No)
    - If Yes, describe the subgroup analyses and summarize results
- QUADAS 2 Tool for Quality Assessment of Study of Diagnostic Accuracy. Indicate Yes, No, or Unclear for the following:
    - Signaling questions
        - Patient Selection
            - Was a consecutive or random sample of patients enrolled?
            - Was a case-control design avoided?
            - Did the study avoid inappropriate exclusions?
        - Index Test
            - Were the index test results interpreted without knowledge of the results of the reference standard?
            - If a threshold was used, was it pre-specified?
        - Reference Standard
            - Is the reference standard likely to correctly classify the target condition?
            - Were the reference standard results interpreted without knowledge of the results of the index test?
        - Flow & Timing
            - Was there an appropriate interval between index test(s) and reference standard?
            - Did all patients receive a reference standard?
            - Did all patients receive the same reference standard?
            - Were all patients included in the analysis?
    - Risk of bias
        - Patient Selection
            - Could the selection of patients have introduced bias?
        - Index Test
            - Could the conduct or interpretation of the index test have introduced bias?
        - Reference Standard
            - Could the reference standard, its conduct or its interpretation have introduced bias?
        - Flow & Timing
            - Could the patient flow have introduced bias?
    - Concerns regarding applicability
        - Patient Selection
            - Are there concerns that the included patients do not match the review question?
        - Index Test
            - Are there concerns that the index test, its conduct, or interpretation differ from the review question?
        - Reference Standard
            - Are there concerns that the target condition as defined by the reference standard does not match the review question?
- Overall study rating
    - High risk of bias/ Low risk of bias/ Unclear
- Comments

Quality

- Study Type (select one): RCT, Cohort, Case-control, Cross-sectional
- If RCT, select Yes/No/Unclear for each of the following questions:
    - Selection Bias
        - Was the allocation sequence generated adequately (e.g., random number table, computer-generated randomization)?
        - Was the allocation of treatment adequately concealed (e.g., pharmacy-controlled randomization or use of sequentially numbered sealed envelopes)?
        - Were participants analyzed within the groups they were originally assigned to?
        - Does the design or analysis control account for important confounding and modifying variables through matching, stratification, multivariable analysis, or other approaches?
    - Performance Bias
        - Did researchers rule out any impact from a concurrent intervention or an unintended exposure that might bias results?
        - Did the study maintain fidelity to the intervention protocol?
    - Attrition Bias
        - If attrition (overall or differential nonresponse, dropout, loss to follow-up, or exclusion of participants) was a concern, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?
    - Detection Bias
        - In prospective studies, was the length of follow-up different between the groups, or in case-control studies, was the time period between the intervention/exposure and outcome different for cases and controls?
        - Were the outcome assessors blinded to the intervention or exposure status of participants?
        - Were interventions/exposures assessed/defined using valid and reliable measures, implemented consistently across all study participants?
        - Were outcomes assessed/defined using valid and reliable measures, implemented consistently across all study participants?
    - Reporting Bias
        - Were the potential outcomes prespecified by the researchers? Are all prespecified outcomes reported?
- If Cohort, select Yes/No/Unclear for each of the following questions:
    - Selection Bias
        - Were participants analyzed within the groups they were originally assigned to?
        - Did the study apply inclusion/exclusion criteria uniformly to all comparison groups?
        - Did the strategy for recruiting participants into the study differ across study groups?
        - Does the design or analysis control account for important confounding and modifying variables through matching, stratification, multivariable analysis, or other approaches?
    - Performance Bias
        - Did researchers rule out any impact from a concurrent intervention or an unintended exposure that might bias results?
        - Did the study maintain fidelity to the intervention protocol?

    - Attrition Bias
        - If attrition (overall or differential nonresponse, dropout, loss to follow-up, or exclusion of participants) was a concern, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?
    - Detection Bias
        - In prospective studies, was the length of follow-up different between the groups, or in case-control studies, was the time period between the intervention/exposure and outcome different for cases and controls?
        - Were the outcome assessors blinded to the intervention or exposure status of participants?
        - Were interventions/exposures assessed/defined using valid and reliable measures, implemented consistently across all study participants?
        - Were outcomes assessed/defined using valid and reliable measures, implemented consistently across all study participants?
        - Were confounding variables assessed using valid and reliable measures, implemented consistently across all study participants?
    - Reporting Bias
        - Were the potential outcomes prespecified by the researchers? Are all prespecified outcomes reported?
- If Case-Control, select Yes/No/Unclear for each of the following questions:
    - Selection Bias
        - Were cases and controls selected appropriately (e.g., appropriate diagnostic criteria or definitions, equal application of exclusion criteria to case and controls, sampling not influenced by exposure status) (Yes/No/Unclear)
        - Does the design or analysis control account for important confounding and modifying variables through matching, stratification, multivariable analysis, or other approaches?
    - Performance Bias
        - Did researchers rule out any impact from a concurrent intervention or an unintended exposure that might bias results?
        - Did the study maintain fidelity to the intervention protocol?
    - Attrition Bias
        - If attrition (overall or differential nonresponse, dropout, loss to follow-up, or exclusion of participants) was a concern, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?
    - Detection Bias
        - In prospective studies, was the length of follow-up different between the groups, or in case-control studies, was the time period between the intervention/exposure and outcome different for cases and controls?
        - Were the outcome assessors blinded to the intervention or exposure status of participants?
        - Were interventions/exposures assessed/defined using valid and reliable measures, implemented consistently across all study participants?
        - Were outcomes assessed/defined using valid and reliable measures, implemented consistently across all study participants?
        - Were confounding variables assessed using valid and reliable measures, implemented consistently across all study participants?
    - Reporting Bias
        - Were the potential outcomes prespecified by the researchers? Are all prespecified outcomes reported?

- If Cross-sectional, select Yes/No/Unclear for each of the following questions:
    - Selection Bias
        - Did the study apply inclusion/exclusion criteria uniformly to all comparison groups?
        - Does the design or analysis control account for important confounding and modifying variables through matching, stratification, multivariable analysis, or other approaches?
    - Performance Bias
        - Did researchers rule out any impact from a concurrent intervention or an unintended exposure that might bias results?
    - Attrition Bias
        - If attrition (overall or differential nonresponse, dropout, loss to follow-up, or exclusion of participants) was a concern, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?
    - Detection Bias
        - Were the outcome assessors blinded to the intervention or exposure status of participants?
        - Were interventions/exposures assessed/defined using valid and reliable measures, implemented consistently across all study participants?
        - Were outcomes assessed/defined using valid and reliable measures, implemented consistently across all study participants?
        - Were confounding variables assessed using valid and reliable measures, implemented consistently across all study participants?
    - Reporting Bias
        - Were the potential outcomes prespecified by the researchers? Are all prespecified outcomes reported?
- Other Bias
    - If applicable, describe any other concerns that may impact risk of bias
- Overall Study Rating (Good/Fair/Poor)
    - **Good** (low risk of bias). These studies have the least bias, and the results are considered valid. These studies adhere to the commonly held concepts of high quality, including the following: a clear description of the population, setting, approaches, and comparison groups; appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; a low dropout rate; and clear reporting of dropouts.
    - **Fair**. These studies are susceptible to some bias, but not enough to invalidate the results. They do not meet all the criteria required for a rating of good quality because they have some deficiencies, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.
    - **Poor** (high risk of bias). These studies have significant flaws that may have invalidated the results. They have serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.
    - **If the study is rated as "Fair" or "Poor," provide rationale.**

Applicability – Use the PICOS format to identify specific issues, if any, that may limit the applicability of the study to this review.

- Population (P)
    - Narrow eligibility criteria and exclusion of those with comorbidities

    - Large differences between demographics of study population and community patients
    - Narrow or unrepresentative severity, stage of illness, or comorbidities
    - Run-in period with high-exclusion rate for nonadherence or side effects
    - Event rates much higher or lower than observed in population-based studies
- Intervention (I)
    - Doses or schedules not reflected in current practice
    - Monitoring practices or visit frequency not used in typical practice
    - Older versions of an intervention no longer in common use
    - Cointerventions that are likely to modify effectiveness of therapy
    - Highly selected intervention team or level of training/proficiency not widely available
- Comparator (C)
    - Inadequate comparison therapy
    - Use of substandard alternative therapy
- Outcomes (O)
    - Composite outcomes that mix outcomes of different significance
    - Short-term or surrogate outcomes
- Setting (S)
    - Standards of care differ markedly from setting of interest
    - Specialty population or level of care differs from that seen in community
- Comments

Appendix C. List of Included Studies

Ad N, Henry L, Schlauch K, et al. The CHADS score role in managing anticoagulation after surgical ablation for atrial fibrillation. Ann Thorac Surg. 2010;90(4):1257-62. PMID: 20868824.

Aspinall SL, DeSanzo BE, Trilli LE, et al. Bleeding Risk Index in an anticoagulation clinic. Assessment by indication and implications for care. J Gen Intern Med. 2005;20(11):1008-13. PMID: 16307625.

Baruch L, Gage BF, Horrow J, et al. Can patients at elevated risk of stroke treated with anticoagulants be further risk stratified?. Stroke. 2007;38(9):2459-63. PMID: 17673721.

Beinart R, Heist EK, Newell JB, et al. Left atrial appendage dimensions predict the risk of stroke/TIA in patients with atrial fibrillation. J Cardiovasc Electrophysiol. 2011;22(1):10-5. PMID: 20662984.

Berge E, Abdelnoor M, Nakstad PH, et al. Low molecular-weight heparin versus aspirin in patients with acute ischaemic stroke and atrial fibrillation: a double-blind randomised study. HAEST Study Group. Heparin in Acute Embolic Stroke Trial. Lancet. 2000;355(9211):1205-10. PMID: 10770301.

Bousser MG, Bouthier J, Buller HR, et al. Comparison of idraparinux with vitamin K antagonists for prevention of thromboembolism in patients with atrial fibrillation: a randomised, open-label, non-inferiority trial. Lancet. 2008;371(9609):315-21. PMID: 18294998.

Bunch TJ, Crandall BG, Weiss JP, et al. Warfarin is not needed in low-risk patients following atrial fibrillation ablation procedures. J Cardiovasc Electrophysiol. 2009;20(9):988-93. PMID: 19473299.

Burton C, Isles C, Norrie J, et al. The safety and adequacy of antithrombotic therapy for atrial fibrillation: a regional cohort study. Br J Gen Pract. 2006;56(530):697-702. PMID: 16954003.

Connolly S, Pogue J, Hart R, et al. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. Lancet. 2006;367(9526):1903-12. PMID: 16765759.

Connolly SJ, Eikelboom J, Joyner C, et al. Apixaban in patients with atrial fibrillation. N Engl J Med. 2011;364(9):806-17. PMID: 21309657.

Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361(12):1139-51. PMID: 19717844.

Connolly SJ, Pogue J, Hart RG, et al. Effect of clopidogrel added to aspirin in patients with atrial fibrillation. N Engl J Med. 2009;360(20):2066-78. PMID: 19336502.

Crandall MA, Horne BD, Day JD, et al. Atrial fibrillation significantly increases total mortality and stroke risk beyond that conveyed by the CHADS2 risk factors. Pacing Clin Electrophysiol. 2009;32(8):981-6. PMID: 19659615.

Diener HC, Connolly SJ, Ezekowitz MD, et al. Dabigatran compared with warfarin in patients with atrial fibrillation and previous transient ischaemic attack or stroke: a subgroup analysis of the RE-LY trial. Lancet Neurol. 2010;9(12):1157-63. PMID: 21059484.

Doucet J, Greboval-Furstenfeld E, Tavildari A, et al. Which parameters differ in very old patients with chronic atrial fibrillation treated by anticoagulant or aspirin? Antithrombotic treatment of atrial fibrillation in the elderly. Fundam Clin Pharmacol. 2008;22(5):569-74. PMID: 18844728.

Easton JD, Lopes RD, Bahit MC, et al. Apixaban compared with warfarin in patients with atrial fibrillation and previous stroke or transient ischaemic attack: a subgroup analysis of the ARISTOTLE trial. Lancet Neurol. 2012;11(6):503-11. PMID: 22572202.

Eikelboom J, Synhorst D, Wright R, et al. Efficacy and safety of apixaban compared with aspirin in patients with atrial fibrillation who previously used and discontinued warfarin therapy: A secondary analysis of the AVERROES trial. Eur Heart J. 2011;32:465.

Eikelboom JW, Wallentin L, Connolly SJ, et al. Risk of bleeding with 2 doses of dabigatran compared with warfarin in older and younger patients with atrial fibrillation: an analysis of the randomized evaluation of long-term anticoagulant therapy (RE-LY) trial.

Circulation. 2011;123(21):2363-72. PMID: 21576658.

Ezekowitz MD, Reilly PA, Nehmiz G, et al. Dabigatran with or without concomitant aspirin compared with warfarin alone in patients with nonvalvular atrial fibrillation (PETRO Study). Am J Cardiol. 2007;100(9):1419-26. PMID: 17950801.

Fang MC, Go AS, Chang Y, et al. A new risk scheme to predict warfarin-associated hemorrhage: The ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) Study. J Am Coll Cardiol. 2011;58(4):395-401. PMID: 21757117.

Fang MC, Go AS, Chang Y, et al. Comparison of risk stratification schemes to predict thromboembolism in people with nonvalvular atrial fibrillation. J Am Coll Cardiol. 2008;51(8):810-5. PMID: 18294564.

Fox KA, Piccini JP, Wojdyla D, et al. Prevention of stroke and systemic embolism with rivaroxaban compared with warfarin in patients with non-valvular atrial fibrillation and moderate renal impairment. Eur Heart J. 2011;32(19):2387-94. PMID: 21873708.

Frost L, Johnsen SP, Pedersen L, et al. Atrial fibrillation or flutter and stroke: a Danish population-based study of the effectiveness of oral anticoagulation in clinical practice. J Intern Med. 2002;252(1):64-9. PMID: 12074740.

Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA. 2001;285(22):2864-70. PMID: 11401607.

Gage BF, Yan Y, Milligan PE, et al. Clinical classification schemes for predicting hemorrhage: results from the National Registry of Atrial Fibrillation (NRAF). Am Heart J. 2006;151(3):713-9. PMID: 16504638.

Gao F, Zhou YJ, Wang ZJ, et al. Comparison of different antithrombotic regimens for patients with atrial fibrillation undergoing drug-eluting stent implantation. Circ J. 2010;74(4):701-8. PMID: 20208381.

Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365(11):981-92. PMID: 21870978.

Hammerstingl C, Schmitz A, Fimmers R, et al. Bridging of chronic oral anticoagulation with enoxaparin in patients with atrial fibrillation: results from the prospective BRAVE registry. Cardiovasc Ther. 2009;27(4):230-8. PMID: 19903186.

Hankey GJ, Patel MR, Stevens SR, et al. Rivaroxaban compared with warfarin in patients with atrial fibrillation and previous stroke or transient ischaemic attack: a subgroup analysis of ROCKET AF. Lancet Neurol. 2012;11(4):315-322. PMID: 22402056.

Hansen ML, Sorensen R, Clausen MT, et al. Risk of bleeding with single, dual, or triple therapy with warfarin, aspirin, and clopidogrel in patients with atrial fibrillation. Arch Intern Med. 2010;170(16):1433-41. PMID: 20837828.

Hart RG, Bhatt DL, Hacke W, et al. Clopidogrel and aspirin versus aspirin alone for the prevention of stroke in patients with a history of atrial fibrillation: subgroup analysis of the CHARISMA randomized trial. Cerebrovasc Dis. 2008;25(4):344-7. PMID: 18303254.

Healey JS, Hart RG, Pogue J, et al. Risks and benefits of oral anticoagulation compared with clopidogrel plus aspirin in patients with atrial fibrillation according to stroke risk: the atrial fibrillation clopidogrel trial with irbesartan for prevention of vascular events (ACTIVE-W). Stroke. 2008;39(5):1482-6. PMID: 18323500.

Hobbs FD, Roalfe AK, Lip GY, et al. Performance of stroke risk scores in older people with atrial fibrillation not taking warfarin: comparative cohort study from BAFTA trial. BMJ. 2011;342:d3653. PMID: 21700651.

Hohnloser SH, Oldgren J, Yang S, et al. Myocardial ischemic events in patients with atrial fibrillation treated with dabigatran or warfarin in the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) trial. Circulation. 2012;125(5):669-76. PMID: 22215856.

Hohnloser SH, Pajitnev D, Pogue J, et al. Incidence of stroke in paroxysmal versus sustained atrial fibrillation in patients taking oral anticoagulation or combined antiplatelet therapy: an ACTIVE W Substudy. J Am Coll Cardiol. 2007;50(22):2156-61. PMID: 18036454.

Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the left atrial appendage versus warfarin

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Jacobs LG, Billett HH, Freeman K, et al. Anticoagulation for stroke prevention in elderly patients with atrial fibrillation, including those with falls and/or early-stage dementia: a single-center, retrospective, observational study. Am J Geriatr Pharmacother. 2009;7(3):159-66. PMID: 19616184.

Komatsu T, Tachibana H, Sato Y, et al. Relationship between CHADS2 score and ischemic stroke during rhythm control therapy for paroxysmal atrial fibrillation. Int Heart J. 2010;51(1):24-29. PMID: 20145347.

Kwak JJ, Pak HN, Jang JK, et al. Safety and convenience of continuous warfarin strategy during the periprocedural period in patients who underwent catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol. 2010;21(6):620-5. PMID: 20039992.

Lane DA, Kamphuisen PW, Minini P, et al. Bleeding risk in patients with atrial fibrillation: the AMADEUS study. Chest. 2011;140(1):146-55. PMID: 21415134.

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Lind M, Fahlen M, Kosiborod M, et al. Variability of INR and its relationship with mortality, stroke, bleeding and hospitalisations in patients with atrial fibrillation. Thromb Res. 2012;129(1):32-5. PMID: 21851969.

Lip GY, Frison L, Halperin JL, et al. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. J Am Coll Cardiol. 2011;57(2):173-80. PMID: 21111555.

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Lip GY, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest. 2010;137(2):263-72. PMID: 19762550.

Lorenzoni R, Lazzerini G, Cocci F, et al. Short-term prevention of thromboembolic complications in patients with atrial fibrillation with aspirin plus clopidogrel: the Clopidogrel-Aspirin Atrial Fibrillation (CLAAF) pilot study. Am Heart J. 2004;148(1):e6. PMID: 15215815.

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Mant J, Hobbs FD, Fletcher K, et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. Lancet. 2007;370(9586):493-503. PMID: 17693178.

Manzano-Fernandez S, Pastor FJ, Marin F, et al. Increased major bleeding complications related to triple antithrombotic therapy usage in patients with atrial fibrillation undergoing percutaneous coronary artery stenting. Chest. 2008;134(3):559-67. PMID: 18641090.

Masaki N, Suzuki M, Iwatsuka R, et al. Effectiveness of risk stratification according to CHADS2 score in Japanese patients with nonvalvular atrial fibrillation. Int Heart J. 2009;50(3):323-9. PMID: 19506336.

Miyazaki S, Ito T, Suwa M, et al. Role of transesophageal echocardiography in the prediction of thromboembolism in patients with chronic nonvalvular atrial fibrillation. Jpn Circ J. 2001;65(10):874-8. PMID: 11665791.

Morgan CL, McEwan P, Tukiendorf A, et al. Warfarin treatment in patients with atrial fibrillation: observing outcomes associated with varying levels of INR control. Thromb Res. 2009;124(1):37-41. PMID: 19062079.

Nair CK, Holmberg MJ, Aronow WS, et al. Thromboembolism in patients with atrial fibrillation with and without left atrial thrombus documented by transesophageal echocardiography. Am J Ther. 2009;16(5):385-92. PMID: 19955857.

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Oldgren J, Alings M, Darius H, et al. Risks for Stroke, Bleeding, and Death in Patients With Atrial Fibrillation Receiving Dabigatran or Warfarin in Relation to the CHADS2 Score: A Subgroup Analysis of the RE-LY Trial. Ann Intern Med. 2011;155(10):660-667. PMID: 22084332.

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Olesen JB, Lip GYH, Hansen PR, et al. Bleeding risk in 'real world' patients with atrial fibrillation: Comparison of two established bleeding prediction schemes in a nationwide cohort. Journal of Thrombosis and Haemostasis. 2011;9(8):1460-1467.

Olesen JB, Torp-Pedersen C, Hansen ML, et al. The value of the CHA2DS2-VASc score for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0-1: A nationwide cohort study. Thromb Haemost. 2012;107(6):1172-9. PMID: 22473219.

Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365(10):883-91. PMID: 21830957.

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Appendix D. List of Excluded Studies

All studies listed below were reviewed in their full-text version and excluded for the reasons cited. Reasons for exclusion signify only the usefulness of the articles for this study and are not intended as criticisms of the articles.

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Appendix E. Key to Included Primary and Companion Articles

*Companion articles marked with an asterisk did not individually meet criteria for inclusion but were considered for supplemental information (e.g., methods data pertinent to an included study).

Study Designation	Primary Abstracted Article	Companion Articles*
ACE (Anticoagulation in Cardioversion Using Enoxaparin)	Stellbrink, 2004[1]	Stellbrink, 2002[2]*
ACTIVE-A (The Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events - A)	Connolly, 2009[3]	Connolly, 2006[4]*
ACTIVE-W (The Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events - W)	Connolly, 2006[5]	Healey, 2008[6] Hohnloser, 2007[7] Connolly, 2006[4]*
AMADEUS (Evaluating the Use of SR34006 Compared to Warfarin or Acenocoumarol in Patients With Atrial Fibrillation)	Bousser, 2008[8]	Lane, 2011[9]
ARISTOTLE (Apixaban for reduction in stroke and other ThromboemboLic events in atrial fibrillation)	Granger, 2011[10]	Lopes, 2010[11]* Easton, 2012[12]
ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation)	Fang, 2011[13]	None
	Fang, 2008[14]	None
	Hylek, 2003[15]	Go, 1999[16]*

Study Designation	Primary Abstracted Article	Companion Articles*
AVERROES (Apixaban Versus Acetylsalicylic Acid [ASA] to Prevent Stroke in Atrial Fibrillation Patients Who Have Failed or Are Unsuitable for Vitamin K Antagonist Treatment)	Connolly, 2011[17]	Eikelboom, 2011[18] Diener, 2012[19] Eikelboom, 2010[20]*
BAFTA (Birmingham Atrial Fibrillation Treatment of the Aged Study)	Mant, 2007[21]	Hobbs, 2011[22] Mant, 2003[23]*
BRAVE (Bonn Registry of Alternative Anticoagulation to Prevent Vascular Events)	Hammerstingl, 2009[24]	None
CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance)	Hart, 2008[25]	None
CLAAF (Clopidogrel-Aspirin Atrial Fibrillation)	Lorenzoni, 2004[26]	None
ELAT (Embolism in Left Atrial Thrombi)	Stollberger, 2004[27]	None
Euro Heart Survey for AF	Pisters, 2010[28]	Nieuwlaat, 2008[29]* Nieuwlaat, 2005[30]*
	Lip, 2010[31]	None
HAEST (Heparin in Acute Embolic Stroke Trial)	Berge, 2000[32]	None
Medicare National Stroke Project	Shireman, 2004[33]	None
NRAF (National Registry of Atrial Fibrillation)	Gage, 2006[34]	Gage, 2001[35]

Study Designation	Primary Abstracted Article	Companion Articles*
NRAF (National Registry of Atrial Fibrillation)	Gage, 2001[35]	None
PETRO (Prevention of Embolic and Thrombotic Events in Patients with Persistent AF)	Ezekowitz, 2007[36]	None
POSTEC (Post-cardioversion Transesophageal Echocardiography)	Sorino, 2007[37]	None
PROTECT-AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation)	Holmes, 2009[38]	Viles-Gonzalez, 2012[39] Fountain, 2006[40]*
RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy)	Connolly, 2009[41]	Oldgren, 2011[42] Eikelboom, 2011[43] Diener, 2010[44] Hohnloser, 2012[45] Ezekowitz, 2009[46]* Nagarakanti, 2011[47]
ROCKET-AF (Rivaroxaban Once-daily, oral, direct factor Xa inhibition compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation)	Patel, 2011[48]	Fox, 2011[49] Anonymous, 2010[50]*
	Hankey, 2012[51]	Patel, 2011[48] Fox, 2011[49]
SPORTIF	Baruch, 2007[52]	Lip, 2011[53] Lip, 2010[54] Halperin, 2003[55]* Olsson, 2003[56]*
The Framingham Heart Study	Sam, 2004[57]	None
	Wang, 2003[58]	None

Study Designation	Primary Abstracted Article	Companion Articles*
WASPO (Warfarin Versus Aspirin for Stroke Prevention in Octogenarians with Atrial Fbrillation)	Rash, 2007[59]	None
None	Saad, 2011[60]	None
None	Olesen, 2011[61]	None
None	Poli, 2011[62]	None
None	Olesen, 2011[63]	None
None	Van Staa, 2011[64]	None
None	Sadanaga, 2010[65]	Sadanaga, 2010[66]*
None	Ad, 2010[67]	None
None	Hansen, 2010[68]	Hansen, 2008[69]*
None	Weitz, 2010[70]	None
None	Beinart, 2011[71]	None
None	Poli, 2011[72]	None
None	Gao, 2010[73]	None
None	Ruiz Ortiz, 2010[74]	None
None	Kwak, 2010[75]	None
None	Lee, 2010[76]	None
None	Nair, 2009[77]	None
None	Crandall, 2009[78]	None
None	Jacobs, 2009[79]	None
None	Masaki, 2009[80]	None
None	Bunch, 2009[81]	None
None	Poli, 2009[82]	Poli, 2009[83]
None	Morgan, 2009[84]	None
None	Doucet, 2008[85]	None
None	Maegdefessel, 2008[86]	None
None	Manzano-Fernandez, 2008[87]	None
None	Rietbrock, 2008[88]	Rietbrock, 2009[89]
None	Okuyama, 2008[90]	None
None	Ruiz-Nodar, 2008[91]	None
None	Wazni, 2007[92]	None
None	Poli, 2007[93]	None
None	Shireman, 2006[94]	None
None	Burton, 2006[95]	None
None	Inoue, 2006[96]	Nozawa, 2004[97]*
None	Vemmos, 2006[98]	None
None	Vemmos, 2004[99]	None
None	Tentschert, 2004[100]	None
None	Tsivgoulis, 2005[101]	None
None	Yigit, 2003[102]	None
None	Stoddard, 2003[103]	None
None	Frost, 2002[104]	None

Study Designation	Primary Abstracted Article	Companion Articles*
None	Miyazaki, 2001[105]	None
None	Yamaguchi, 2000[106]	None
None	Aspinall, 2005[107]	None
None	Lind, 2011[108]	None
None	Olesen, 2011[109]	None
None	Ruiz-Nodar, 2011[110]	None
None	Komatsu, 2010[111]	None
None	Ruiz Ortiz, 2008[112]	None
None	Olesen, 2012[113]	None

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Appendix F. Study Characteristics Tables

Appendix Table F-1. Study Characteristics—KQ 1

Study: **Author** **Year** **Acronym**	**Study Design;** **Setting;** **Location;** **Funding Source;** **Quality**	**Tools Assessed**	**Total N**	**Follow up period**	**Mean Age**	**Special Population**
Gage, 2001[1] NRAF	Retrospective cohort; Outpatient; US; Government; Low risk of bias	CHADS 2 score	1733	Total: 1.2	Total: 81	None
Miyazaki, 2001[2]	Prospective cohort; Outpatient; Asia; NR; Low risk of bias	TEE	89	Total: 29 mo Arm 1: 29 mo	Total: 66 (SD 9)	Persistent AF
Hylek, 2003[3] ATRIA	Retrospective cohort; Outpatient; US; Government; Low risk of bias	INR	596	NR	Total: 78	None
Stoddard, 2003[4]	Prospective cohort; Outpatient; US; NR; Low risk of bias	TEE	272	Total: 30.3 mo (SD 20.6) Arm 1: 28.3 mo (SD 23.3) Arm 2: 30.9 mo (SD 20)	Total: 66 (SD 11)	None
Wang, 2003[5] Framingham	Prospective cohort; Outpatient; US; Government, Non-govt, non-industry; Low risk of bias	Framingham score	705	Total: 4.3 yr Arm 1: 4.0 yr	Total: 75 (SD 9)	None
Stollberger, 2004[6] ELAT	Prospective cohort; Outpatient; Europe; NR; Low risk of bias	TTE	409	Total: 101 mo (SD 2)	Total: 62 (IQR 61-64)	None

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Tools Assessed	Total N	Follow up period	Mean Age	Special Population
Baruch, 2007[7]	RCT; Outpatient; NR; Industry; Low risk of bias	HAS-BLED CHADS 2 score CHA2DS2-VASc score	7329	Total: 1.5 years	NR	None
Ruiz Ortiz, 2008[8]	Prospective cohort; Outpatient; Europe; Non-govt, non-industry; Low risk of bias	CHADS 2 score	1137	Total: 21 mo (SD 17) Arm 1: 21 mo (SD 17)	Total: 75 (SD 9)	Permanent AF
Fang, 2008[9] ATRIA	Retrospective cohort; Outpatient; US; Government, Non-govt, non-industry; Low risk of bias	CHADS 2 score Framingham score	10932	Total: Median 6.0 yr (IQR 3.1-6.7)	Total: 72	None
Okuyama, 2008[10]	Retrospective cohort; Inpatient; Asia, Other (specify) : Japan; Government, Other (specify) : partial funding from govt; Low risk of bias	TEE	192	Total: 450 days (SD 120) Arm 1: 450 days (SD 120)	Total: 70 (SD 11)	Patients with prior stroke
Rietbrock, 2008[11]	Retrospective cohort; Outpatient; UK; Industry; Low risk of bias	CHADS 2 score	51807	Total: Median 2.5 yr Arm 1: Median 2.5 yr Arm 2: Median 2.5 yr	Total: 76.01 (SD 10.13)	Persistent AF, Permanent AF
Connolly, 2009[12] RE-LY	RCT; Outpatient; US, Canada, UK, Europe, S. America, C. America, Asia, Africa, Australia/NZ; Industry; Low risk of bias	CHADS 2 score	18113	Total: Median 2.0 yr	Total: 71	None

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Tools Assessed	Total N	Follow up period	Mean Age	Special Population
Crandall, 2009[13]	Retrospective cohort; NR; US; Other (specify) : Deseret Foundation; High risk of bias	CHADS 2 score	343	Arm 1: 9.1 yr (SD 1.8)	NR	None
Masaki, 2009[14]	Prospective cohort; Outpatient; Asia, Other (specify) : Japan; NR; Low risk of bias	CHADS 2 score	293	Total: 703 days (SD 88)	Total: 72 (SD 11)	Paroxysmal AF, Persistent AF, Permanent AF
Morgan, 2009[15]	Retrospective cohort; Inpatient; UK; Industry; High risk of bias	CHADS 2 score	5513	Total: 1025.1 days (SD 714.8) Arm 1: 986.4 days (SD 722)	Total: 69 (SD 10)	Paroxysmal AF, Persistent AF, Permanent AF
Nair, 2009[16]	Prospective cohort; NR; US; NR; Low risk of bias	TTE	226	Arm 1: 13 mo (SD 17) Arm 2: 93 mo (SD 173)	Total: 72	None
Poli, 2009[17]	Prospective cohort; Inpatient, Outpatient; Europe; NR; Low risk of bias	CHADS 2 score	662	Total: Median 3.1 yr	Total: 75	Paroxysmal AF, Persistent AF, Permanent AF
Ad, 2010[18]	Prospective cohort; Outpatient; US; NR; Low risk of bias	CHADS 2 score	385	Total: 32.77 mo (SD 16.33)	Total: 64.6 (+/- 11.6)	None
Komatsu, 2010[19]	Retrospective cohort; Outpatient; Asia; NR; Low risk of bias	CHADS 2 score	344	Total: 60 mo (SD 35)	Total: 68 (SD 12)	Paroxysmal AF

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Tools Assessed	Total N	Follow up period	Mean Age	Special Population
Lip, 2010[20] Euro Heart Survey for AF	Retrospective cohort; Outpatient; UK, Europe; Industry, Non-govt, non-industry; Low risk of bias	CHADS 2 score Framingham score CHA2DS2-VASc score	1084	Total: 1 yr	Total: 66 (SD 14)	None
Ruiz Ortiz, 2010[21]	Prospective cohort; Outpatient; Europe; Other (specify) : This work was supported by a grant from the Spanish Society of Cardiology.; Low risk of bias	CHADS 2 score	796	Total: 2.4 yr (SD 1.9)	Total: 73 (SD 8)	Permanent AF
Sadanaga, 2010[22]	Prospective cohort; Outpatient; Asia; NR; Low risk of bias	CHADS 2 score	245	Total: 753 days (SD 223) Arm 1: 753 days (SD 223) Arm 2: 753 days (SD 223)	Total: 74 (SD 9)	None
Van Staa, 2011[23]	Retrospective cohort; Outpatient; UK; NR; High risk of bias	CHADS 2 score	79844	Total: 4.0 yr	Total: 73.3 (SD 12.5)	None
Beinart, 2011[24]	Retrospective cohort; Inpatient, Outpatient; US; Other (specify) : The study was supported by a grant from the Deane Institute for Integrative Research in Stroke and Atrial Fibrillation at the Massachusetts General Hospital.; High risk of bias	Cardiac MRI	144	NR	Total: 54.5 (SD 9.9)	None

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Tools Assessed	Total N	Follow up period	Mean Age	Special Population
Lind, 2012[25]	Retrospective cohort; Outpatient; Europe; NR; High risk of bias	INR	19180	NR	NR	None
Olesen, 2011[26]	Retrospective cohort; Inpatient; Europe; NR; High risk of bias	CHADS 2 score CHA2DS2-VASc score	132,372	Total: Max 12 yr	NR	Paroxysmal AF, Persistent AF, Permanent AF
Olesen, 2011[27]	Retrospective cohort; Outpatient; Europe; Other (specify) : None; Low risk of bias	CHADS 2 score CHA2DS2-VASc score	73538	NR	NR	None
Poli, 2011[28]	Prospective cohort; NR; Europe; Other (specify) : none; Low risk of bias	CHADS 2 score Bleeding Risk Index	3302	Total: Median 2.3 yr (IQR 0.8-4.4)	Total: Median 74 (IQR 68-80)	Paroxysmal AF, Persistent AF, Permanent AF
Poli, 2011[29]	Prospective cohort; Outpatient; Europe; NR; Low risk of bias	CHA2DS2-VASc score	662	Total: 3.6 yr (SD 2.7) Arm 1: 3.6 yr (SD 2.7) Arm 2: 3.6 yr (SD 2.7)	Total: 74 (SD 7.7)	None
Ruiz-Nodar, 2011[30]	Retrospective cohort; Outpatient; Europe; NR; Low risk of bias	CHADS 2 score	604	Total: 642 days (SD 503) Arm 1: 642 days (SD 503) Arm 2: 642 days (SD 503)	Total: 71.8 (SD 8.4)	None
Olesen, 2012[31]	Retrospective cohort; Outpatient; Europe; NR; Low risk of bias	CHA2DS2-VASc score	47576	Total: 12 yr Arm 1: 12 yr Arm 2: 12 yr	Total: 69.4 (SD 14.7)	None

Abbreviations: [complete list to be provided in final report]: AF = atrial fibrillation; IQR = interquartile range; N = number of patients; NR = not reported; RCT = randomized controlled trial; SD = standard deviation

Appendix Table F-2. Study Characteristics—KQ 2

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Tools Assessed	Total N	Follow up period (years)	Mean Age (years)	Special Population
Hylek, 2003[3] ATRIA	Retrospective cohort; Outpatient; US; Government; Low risk of bias	INR	596	NR	NR	Patients with prior stroke
Aspinall, 2005[32]	Retrospective cohort; Outpatient; US; Other (specify) : Unfunded; Low risk of bias	Bleeding Risk Index	1269	Total: 1.03	Total: 67.9 (SD 11.4)	None
Gage, 2006[33] NRAF	Retrospective cohort; Outpatient; US; Government, Non-govt, non-industry; Low risk of bias	HEMORR2HAGES Bleeding Risk Index	3791	Total: 0.82 (3138 pt-yrs/3791 yrs)	Total: 80.2	None
Shireman, 2006[34]	Retrospective cohort; Outpatient; US; Government; Low risk of bias	Bleeding Risk Index	26345	NR	NR	None
Baruch, 2007[7] SPORTIF	RCT; Outpatient; NR; Industry; Low risk of bias	HAS-BLED CHADS 2 score CHA2DS2-VASc score	7329	NR	NR	None
Poli, 2007[35]	Prospective cohort; Outpatient; Europe; NR; Low risk of bias	CHADS 2 score	290	Total: 2.8	Total: Median 82	None

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Tools Assessed	Total N	Follow up period (years)	Mean Age (years)	Special Population
Connolly, 2009[12] RE-LY	RCT; Outpatient; US, Canada, UK, Europe, S. America, C. America, Asia, Africa, Australia/NZ; Industry; Low risk of bias	CHADS 2 score	18113	Total: Median 2.0	NR	None
Ad, 2010[18]	Prospective cohort; Outpatient; US; NR; Low risk of bias	CHADS 2 score	385	Total: 32.77 months (SD 16.33)	NR	None
Ruiz Ortiz, 2010[21]	Prospective cohort; Outpatient; Europe; Other (specify) : This work was supported by a grant from the Spanish Society of Cardiology.; Low risk of bias	CHADS 2 score	796	Total: 2.4 (SD 1.9)	Total: 73 (SD 8)	Permanent AF
Pisters, 2010[36] Euro Heart Survey for AF	Prospective cohort; Inpatient, Outpatient; Europe; Industry; Low risk of bias	HAS-BLED HEMORR2HAGES	3456	Total: ~1	NR	None
Fang, 2011[37] ATRIA	Retrospective cohort; Outpatient; US; Government, Industry, Non-govt, non-industry; Low risk of bias	ATRIA HEMORR2HAGES Bleeding Risk Index	9186	Total: Median 3.5 (IQR 1.2-6.0)	NR	None
Lind, 2011[25]	Retrospective cohort; Outpatient; Europe; NR; High risk of bias	INR	19180	NR	NR	None

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Tools Assessed	Total N	Follow up period (years)	Mean Age (years)	Special Population
Olesen, 2011[26]	Retrospective cohort; Inpatient; Europe; NR; High risk of bias	CHADS 2 score CHA2DS2-VASc score	132,372	Total: Max 12	NR	None
Olesen, 2011[38]	Retrospective cohort; Inpatient; Europe; NR; Low risk of bias	HAS-BLED HEMORR2HAGES	118584	Total: 10	NR	None
Poli, 2011[28]	Prospective cohort; NR; Europe; Other (specify) : none; Low risk of bias	CHADS 2 score Bleeding Risk Index	3302	Total: Median 2.3 (IQR 0.8-4.4)	Total: Median 74 (IQR 68-80	None

Abbreviations: [complete list to be provided in final report]: AF = atrial fibrillation; IQR = interquartile range; N = number of patients; NR = not reported; RCT = randomized controlled trial; SD = standard deviation

Appendix Table F-3. Study Characteristics—KQ 3

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Berge, 2000[39] HAEST	RCT; Inpatient; Europe; Non-govt, non-industry; Good	Arm 1: LMWH: Dalteparin Arm 2: Aspirin	449; Arm 1 (224) Arm 2 (225)	Total: 14 days	Arm 1: Median 80 (IQR 55-96) Arm 2: Median 80 (IQR 44-98)	Patients with prior stroke	Ischemic stroke Intracerebral hemorrhage All-cause mortality
Yamaguchi, 2000[40]	RCT; Outpatient; Asia, Other (specify) : Japan; Government; Poor	Arm 1: Vitamin K antagonists: Warfarin Arm 2: Vitamin K antagonists: Warfarin	115; Arm 1 (55) Arm 2(60)	Total: 658 days (SD 423) Arm 1: 605 days (SD 406) Arm 2: 706 days (SD 455)	Arm 1: 65.7 (SD 6.8) Arm 2: 67.6 (SD 6.1)	None	Ischemic stroke Major bleed Minor bleed
Frost, 2002[41]	Retrospective cohort; Inpatient, Outpatient; Europe; Government, Non-govt, non-industry; Poor	Arm 1: Vitamin K antagonists: Warfarin Arm 2: No oral anticaogulation	5124; Arm 1 (1390) Arm 2 (3734)	Total: 2.31 yr	NR	None	CV infarction/stroke
Hylek, 2003[3] ATRIA	Retrospective cohort; Outpatient; US; Government; Good	Arm 1: No antithrombotic therapy Arm 2: Aspirin Arm 3: Vitamin K antagonists: Warfarin	596; Arm 1 (248) Arm 2 (160) Arm 3 (188)	NR	Arm 1: 79 Arm 2: 80 Arm 3: 76	Patients with prior stroke	All-cause mortality Diagnostic Thinking/ Therapeutic Efficacy

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Yigit, 2003[42]	RCT; Inpatient, Other (specify) : outpatients admitted for study procedures; Other (specify) : Turkey; NR; Fair	Arm 1: TEE; Vitamin K antagonists: Warfarin; LMWH: Dalteparin Arm 2: TEE; Vitamin K antagonists: Warfarin; UFH: IV Heparin	170: Arm 1 (89) Arm 2 (81)	Total: 6 mo Arm 1: 4 wks Arm 2: 4 wks	Total: 62.6 (SD 10.2) Arm 1: 63.4 (SD 9.4) Arm 2: 61.9 (SD 10.2)	Persistent AF	Systemic embolism
Lorenzoni, 2004[43] CLAAF	RCT; Outpatient; Europe; Industry; Fair	Arm 1: Vitamin K antagonists: Warfarin Arm 2: Clopidogrel, Aspirin	30; Arm 1 (14) Arm 2 (16)	Arm 1: 3 mo Arm 2: 3 mo	Arm 1: Median 72 Arm 2: Median 68	None	Composite outcome: Major bleed, minor bleed
Sam, 2004[44] Framingham	Retrospective cohort; Outpatient; US; Government; Fair	Arm 1: no therapy Arm 2: Aspirin Arm 3: Vitamin K antagonists: Warfarin	393; Arm 1 (231) Arm 2 (82) Arm 3 (80)	Arm 1: ~ 5yr Arm 2: ~ 5yr Arm 3: ~ 5yr	Arm 1: 77.3 (SD 10.6) Arm 2: 76.4 (SD 10.6) Arm 3: 70.7 (SD 11.4)	None	Major bleed Minor bleed Intracerebral hemorrhage
Shireman, 2004[45] Medicaid National Stroke Project	Retrospective cohort; Inpatient; US; Non-govt, non-industry; Fair	Arm 1: Vitamin K antagonists: Warfarin Arm 2: Vitamin K antagonists: Warfarin; Clopidogrel, Aspirin	10093; Arm 1 (8131) Arm 2 (1962)	Total: 90 days	Arm 1: 77.4 Arm 2: 76.2	None	Major bleed Composite outcome: Intracerebral hemorrhage, Subdural hematoma

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Stellbrink, 2004[46] ACE: Anticoagulation in Cardioversion Using Enoxaparin	RCT; Inpatient, Outpatient; Europe; Industry; Fair	Arm 1: LMWH: Enoxaparin Arm 2: Vitamin K antagonists: Other; UFH: IV Heparin	496; Arm 1 (248) Arm 2 (248)	Total: 28-49 days	Arm 1: 66 (SD 11) Arm 2: 65 (SD 11)	None	Systemic embolism Cerebrovascular infarction TIA All-cause mortality Major bleed Minor bleed CV mortality Composite outcome: Cerebrovascular infarction, TIA, Systemic embolism, Major bleed, All-cause mortality
Tentschert, 2004[47]	Prospective cohort; Inpatient, Outpatient; Europe; Government, Industry; Good	Arm 1: Clopidogrel, Aspirin, ASA + dipyridamole Arm 2: Vitamin K antagonists: Warfarin Arm 3: LMWH: Other	401; Arm 1 (153) Arm 2 (188) Arm 3 (60)	Total: Median 25 mo (IQR 15-38) Arm 1: Median 24 mo (IQR 13-36) Arm 2: Median 27 mo (IQR 19-40) Arm 3: Median 19 mo (IQR 7-32	Arm 1: 78 (IQR 73-86) Arm 2: 75 (IQR 69-78) Arm 3: 78 (IQR 74-81)	None	Cerebrovascular infarction Intracerebral hemorrhage All-cause mortality CV mortality Major bleed Composite outcome: Cerebrovascular infarction, Intracerebral hemorrhage, CV mortality
Vemmos, 2004[48]	Prospective cohort; Inpatient, Outpatient; Europe; NR; Fair	Arm 1: Vitamin K antagonists: Warfarin Arm 2: Aspirin	191; Arm 1 (67) Arm 2 (124)	Total: 50.4 mo (IQR 12-60)	Arm 1: 74.6 (SD 6.5) Arm 2: 76.2 (SD 6.9)	Patients with prior stroke	All-cause mortality Major bleed Composite outcome: Systemic embolism, Ischemic stroke
Tsivgoulis, 2005[49]	Prospective cohort; Inpatient, Outpatient; Europe; NR; Good	Arm 1: Vitamin K antagonists: Warfarin Arm 2: Aspirin	207; Arm 1 (72) Arm 2 (135)	Total 88.4 mo (IQR 3-120)	Arm 1: 79.9 (SD 2.8) Arm 2: 80.7 (SD 3.1)	Patients with prior stroke	All-cause mortality Composite outcome: Cerebrovascular infarction, Systemic embolism

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Burton, 2006[50]	Retrospective cohort; NR; UK; Government, Non-govt, non-industry; Poor	Arm 1: Usual care/OMT Arm 2: Aspirin Arm 3: Vitamin K antagonists: Warfarin	601; NR	Total: up to 5 yr	Total: 77 Arm 1: 458 patient yrs (SD 21.48) Arm 2: 721 patient yrs (SD 33.82) Arm 3: 953 patient yrs (SD 44.7)	Persistent AF	CV infarction/stroke All-cause mortality Major bleed Composite outcome: Major bleed, Minor bleed
Connolly, 2006[51] ACTIVE-W	RCT; NR; US, Canada, UK, Europe, S. America, Asia, Africa, Australia/NZ; Industry; Good	Arm 1: Clopidogrel, Aspirin Arm 2: Vitamin K antagonists: Warfarin	6706; Arm 1 (3335) Arm 2 (3371)	Total: Median 1.28 yr	Arm 1: 70.2 (SD 9.4) Arm 2: 70.2 (SD 9.5)	None	Systemic embolism Myocardial infarction CV infarction/stroke Ischemic stroke Intracerebral hemorrhage HRQOL/ Functional capacity All-cause mortality CV mortality Major bleed Minor bleed Composite outcome: Systemic embolism, CV infarction/stroke, Myocardial infarction, CV mortality
Inoue, 2006[52]	Prospective cohort; NR; Asia,Other (specify) : Japan; NR; Poor	Arm 1: Usual care/OMT Arm 2: Aspirin, ticlopidine Arm 3: Vitamin K antagonists: Warfarin	509; Arm 1 (83) Arm 2 (163) Arm 3 (263)	Total: 2 yr (SD 0.4)	Arm 1: 63.4 (SD 12) Arm 2: 67.5 (SD 11) Arm 3: 67 (SD 9)	Paroxysmal AF, Persistent AF, Permanent AF	Composite outcome: TIA, Systemic embolism, CV infarction/stroke

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Vemmos, 2006[53]	RCT; Outpatient; Europe, Other (specify) : Greece; NR; Fair	Arm 1: Aspirin Arm 2: Vitamin K antagonists: Warfarin Arm 3: Vitamin K antagonists: Warfarin	45; Arm 1 (15) Arm 2 (14) Arm 3 (16)	Total: 3.7 (IQR 1-6 mo) Arm 1: 3.6 Arm 2: 3.9 Arm 3: 3.7	Arm 1: 79.5 (SD 2.9) Arm 2: 79.9 (SD 1.7) Arm 3: 80.1 (SD 2.5)	Paroxysmal AF, Persistent AF, Permanent AF	Ischemic stroke Systemic embolism All-cause mortality Myocardial infarction Major bleed
Ezekowitz, 2007[54] PETRO	RCT; Inpatient; US, Europe; Industry; Good	Arm 1: Dabigatran Arm 2: Dabigatran Arm 3: Dabigatran Arm 4: Warfarin	502; Arm 1 (105) Arm 2 (166) Arm 3 (161) Arm 4 (70)	Arm 1: 3 mo Arm 2: 3 mo	Arm 1: 70 (SD 8.8) Arm 2: 70 (SD 8.1) Arm 3: 69.5 (SD 8.4) Arm 4: 69 (SD 8.3)	None	Major bleed CV infarction/stroke Composite outcome: Clinically relevant outcome, major bleed
Mant, 2007[55] BAFTA	RCT; Inpatient; UK; Non-govt, non-industry; Good	Arm 1: Vitamin K antagonists: Warfarin Arm 2: Aspirin	973; Arm 1 (488) Arm 2 (485)	Total: 2.7 y (SD 1.2)	Arm 1: 81.5 (SD 4.3) Arm 2: 81.5 (SD 4.2)	None	Ischemic stroke Intracerebral hemorrhage Systemic embolism Major bleed All-cause mortality Composite outcome: Systemic embolism, CV infarction/stroke, Intracerebral hemorrhage Composite outcome: CV infarction/stroke, Myocardial infarction, CV mortality Composite outcome: Systemic embolism, CV infarction/stroke, Intracerebral hemorrhage

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Rash, 2007[56] WASPO	RCT; Outpatient; UK; NR; Good	Arm 1: Vitamin K antagonists: Warfarin Arm 2: Aspirin	75; Arm 1 (36) Arm 2 (39)	Total: 12 mo Arm 1: 12 mo Arm 2: 12 mo	Total: Median (IQR 80-90) Arm 1: Median 83.5 (IQR 80-90) Arm 2: Median 82.6 (IQR 80-90)	Permanent AF	All-cause mortality TIA Composite outcome: TIA, Major bleed, Ischemic stroke
Bousser, 2008[57] AMADEUS	RCT; NR; US, Canada, UK, Europe, Australia/NZ; Industry; Good	Arm 1: Factor Xa Inhibitors: Other Arm 2: Vitamin K antagonists: Warfarin	4576; Arm 1 (2283) Arm 2 (2293)	Arm 1: 311 (SD 161) Arm 2: 339 (SD 165)	Total: 70.1 (SD 9.1) Arm 1: 70.1 (SD 9) Arm 2: 70.2 (SD 9.1)	None	Time in therapeutic range Ischemic stroke Intracerebral hemorrhage Myocardial infarction Systemic embolism Major bleed All-cause mortality Composite outcome: Cerebral infarction, Systemic embolism
Doucet, 2008[58]	Prospective cohort; Inpatient; Europe, Other (specify) : France; NR; Poor	Arm 1: Vitamin K antagonists: Other Arm 2: Aspirin	209; Arm 1 (102) Arm 2 (107)	Total: 3 mo Arm 1: 3 mo Arm 2: 3 mo	Arm 1: 82.9 (SD 7.1) Arm 2: 86.5 (SD 6.5)	Permanent AF	Cerebrovascular infarction All-cause mortality Healthcare utilization - Hospital admissions Composite outcome: Major bleed, Minor bleed

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Hart, 2008[59] CHARISMA	RCT; NR; US; Industry; Good	Arm 1: Clopidogrel, Aspirin Arm 2: Aspirin	NA; Arm 1 (298) Arm 2 (285)	Total: 2.3 yr	Total: 70 Arm 1: 70 Arm 2: 70	None	Ischemic stroke Intracerebral hemorrhage Myocardial infarction CV mortality All-cause mortality Healthcare utilization - Hospital admissions Composite outcome: Intracerebral hemorrhage, Ischemic stroke Composite outcome: Myocardial infarction, CV mortality, Ischemic storke Composite outcome: Cerebrovascular infarction, Intracerebral hemorrhage, Myocardial infarction, CV mortality, Healthcare utilization – Hospital admissions

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Connolly, 2009[12] RE-LY	RCT; Outpatient; US, Canada, UK, Europe, S. America, C. America, Asia, Africa, Australia/NZ; Industry; Good	Arm 1: Dabigatran Arm 2: Dabigatran Arm 3: Vitamin K antagonists: Warfarin	18113; Arm 1 (6015) Arm 2 (6076) Arm 3 (6022)	Total: Median 2.0 yr	Arm 1: 71.4 (SD 8.6) Arm 2: 71.5 (SD 8.8) Arm 3: 71.6 (SD 8.6)	None	Intracerebral hemorrhage All-cause mortality Myocardial infarction Major bleed Minor bleed Healthcare utilization - Hospital admissions CV mortality Composite outcome: Intracerebral hemorrhage, Subdural hematoma Composite outcome: Systemic embolism, Intracerebral hemorrhage, Subdural hematoma, Ischemic stroke Composite outcome: Systemic embolism, Intracerebral hemorrhage, Subdural hematoma, Major bleed, Myocardial infarction, All-cause mortality, Ischemic stroke Diagnostic Thinking/ Therapeutic Efficacy
Connolly, 2009[60] ACTIVE-A	RCT; Outpatient; Other (specify) : 33 countries; Industry; Good	Arm 1: Clopidogrel, Aspirin Arm 2: Aspirin	7554; Arm 1 (3772) Arm 2 (3782)	Total: 3.6 yr Arm 1: 3.6 yr Arm 2: 3.6 yr	Total: 71 Arm 1: 70.9 (SD 10.2) Arm 2: 71.1 (SD 10.2)	None	CV infarction/stroke Ischemic stroke Intracerebral hemorrhage Myocardial infarction Systemic embolism CV mortality All-cause mortality Major bleed Minor bleed Composite outcome: Systemic embolism, CV infarction/stroke, Myocardial infarction, CV mortality

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Holmes, 2009[61] PROTECT-AF	RCT; Inpatient; US, Europe; Industry; Good	Arm 1: Transcatheter: WATCHMAN Arm 2: Vitamin K antagonists: Warfarin	707; Arm 1 (463) Arm 2 (244)	Arm 1: 18 mo (SD 10) Arm 2: 18 mo (SD 10)	Arm 1: 71.7 (SD 8.8) Arm 2: 72.7 (SD 9.2)	Paroxysmal AF, Persistent AF, Permanent AF	Ischemic stroke CV mortality Intracerebral hemorrhage All-cause mortality Composite outcome: Systemic embolism, CV infarction/stroke, Intracerebral hemorrhage, CV mortaltiy Composite outcome: Major bleed, Minor bleed
Jacobs, 2009[62]	Retrospective cohort; Outpatient; US; Industry; Poor	Arm 1: Vitamin K antagonists: Warfarin Arm 2: Aspirin	106; Arm 1 (90) Arm 2 (16)	Total: 12 mo Arm 1: 12 mo Arm 2: 12 mo	all >=65 see below	Paroxysmal AF, Persistent AF, Permanent AF	All-cause mortality Major bleed CV infarction/stroke
Lee, 2010[63]	Retrospective cohort; NR; Asia; Government, Non-govt, non-industry; Fair	Arm 1: No antiplt agent or anticoagulation Arm 2: Aspirin Arm 3: Clopidogrel, Ticlopidine Arm 4: Vitamin K antagonists: Warfarin	422; Arm 1 (110) Arm 2 (124) Arm 3 (45) Arm 4 (143)	Total: 22.3 mo (SD 17.8) Arm 1: 16.8 mo (SD 17.5) Arm 2: 24.9 mo (SD 17.1) Arm 3: 18.6 mo (SD 18.3) Arm 4: 25.6 (SD 17.4)	Total: 62.9 (SD 10.7) Arm 1: 64.1 (SD 12.6) Arm 2: 63.2 (SD 9.8) Arm 3: 62.8 (SD 11) Arm 4: 61.8 (SD 9.8)	Paroxysmal AF, Persistent AF	Ischemic stroke All-cause mortality Intracerebral hemorrhage Minor bleed Cerebrovascular infarction

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Gao, 2010[64]	Prospective cohort; NR; Asia; NR; Fair	Arm 1: Vitamin K antagonists: Warfarin; Clopidogrel, Aspirin Arm 2: Clopidogrel, Aspirin Arm 3: Vitamin K antagonists: Warfarin; ASA or clopidogrel	622; Arm 1 (142) Arm 2 (355) Arm 3 (125)	NR	Arm 1: 70.97 (SD 5.56) Arm 2: 71.7 (SD 5.4) Arm 3: 72.81 (SD 5.22)	None	All-cause mortality Myocardial infarction Ischemic stroke Major bleed Minor bleed Composite outcome: Myocardial infarction, All-cause mortality, Ischemic stroke Composite outcome: Major bleed, Myocardial infarction, All-cause mortality, Ischemic stroke
Hansen, 2010[65]	Retrospective cohort; Outpatient; Europe; Industry; Good	Arm 1: Vitamin K antagonists: Warfarin Arm 2: Aspirin Arm 3: Clopidogrel Arm 4: Clopidogrel, Aspirin Arm 5: Vitamin K antagonists: Warfarin, Aspirin Arm 6: Vitamin K antagonists: Warfarin, Clopidogrel Arm 7: Vitamin K antagonists: Warfarin; Clopidogrel, Aspirin	118,606; Arm 1 (50919) Arm 2 (47541) Arm 3 (3717) Arm 4 (2859) Arm 5 (18345) Arm 6 (1430) Arm 7 (1261)	Total: 3.3 yr (SD 2.6)	Total: 73.7 (SD 12.3) Arm 1: 70.3 (SD 10.7) Arm 2: 74.7 (SD 11.4) Arm 3: 72.6 (SD 10.2) Arm 4: 72.1 (SD 10.3) Arm 5: 70.8 (SD 10.0) Arm 6: 70.2 (SD 8.9) Arm 7: 69.9 (SD 9.2)	Paroxysmal AF, Persistent AF, Permanent AF	Major bleed

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Ruiz Ortiz, 2010[21]	Prospective cohort; Outpatient; Europe; Other (specify) : This work was supported by a grant from the Spanish Society of Cardiology.; Fair	Arm 1: Vitamin K antagonists: Warfarin, Other Arm 2: Non-OAC	796; Arm 1 (564) Arm 2 (232)	Total: 2.4 yr (SD 1.9)	Total: 73 (SD 8)	Permanent AF	Major bleed All-cause mortality Composite outcome: TIA, Ischemic stroke Diagnostic Accuracy, Diagnostic Thinking/ Therapeutic Efficacy
Weitz, 2010[66]	RCT; Outpatient; NR; Industry; Good	Arm 1: Edoxaban (30mg qd) Arm 2: Edoxaban (30mg bid) Arm 3: Edoxaban (60mg qd) Arm 4: Edoxaban (60mg bid) Arm 5: Vitamin K antagonists: Warfarin	1146; Arm 1 (235) Arm 2 (244) Arm 3 (234) Arm 4 (180) Arm 5 (250)	Total: 12 wks	Arm 1: 65.2 (SD 8.3) Arm 2: 64.8 (SD 8.8) Arm 3: 64.9 (SD 8.8) Arm 4: 64.7 (SD 9) Arm 5: 66.0 (SD 8.5)	Persistent AF	Major bleed Minor bleed Myocardial infarction CV mortality Hospitalization Composite outcome: Intracerebral hemorrhage, Stroke, TIA, and or Systemic Embolism Composite outcome: Cerebrovascular infarction, TIA, Intracerebral hemorrhage, Ischemic stroke

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Connolly, 2011[67] AVERROES	RCT; Outpatient; NR; Industry; Good	Arm 1: Apixaban Arm 2: Aspirin	5599; Arm 1 (2808) Arm 2 (2791)	Total: 1.1 yr Arm 1: 1.1 yr Arm 2: 1.1 yr	Arm 1: 70 (SD 9) Arm 2: 70 (SD 10)	None	Intracerebral hemorrhage Systemic embolism Myocardial infarction CV infarction/stroke Subdural hematoma Minor bleed Major bleed Ischemic stroke All-cause mortality Healthcare utilization - Hospital admissions Composite outcome: Systemic embolism, CV infarction/stroke, All-cause mortality Composite outcome: Systemic embolism, CV infarction/stroke, Myocardial infarction, CV mortality Composite outcome: Systemic embolism, CV infarction/stroke
Granger, 2011[68] ARISTOTLE	RCT; NR; US, Canada, Europe, Asia, Australia/NZ; Industry; Good	Arm 1: Apixaban Arm 2: Vitamin K antagonists: Warfarin	18201; Arm 1 (9120) Arm 2 (9081)	Total: ~2 yr Arm 1: ~2 yr Arm 2: ~2 yr	Arm 1: Median 70 (IQR 63-76) Arm 2: Median 70 (IQR 63-76)	Paroxysmal AF, Persistent AF, Permanent AF	Ischemic stroke CV infarction/stroke Intracerebral hemorrhage Systemic embolism All-cause mortality Myocardial infarction Major bleed Cerebrovascular infarction Intracerebral hemorrhage Major bleed Composite outcome: Systemic embolism, CV infarction/stroke

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Olesen, 2011[26]	Retrospective cohort; Inpatient; Europe; NR; Poor	Arm 1: Placebo Arm 2: Vitamin K antagonists: Warfarin, Other Arm 3: Aspirin Arm 4: Vitamin K antagonists: Warfarin, Other; Aspirin	132372; Arm 1 (58883) Arm 2 (37425) Arm 3 (24984) Arm 4 (11080)	Total: Max 12 yr	Arm 1: 72.8 (SD 14.4) Arm 2: 70.6 (SD 11.1) Arm 3: 78.1 (SD 11.2) Arm 4: 73.1 (SD 9.6)	Paroxysmal AF, Persistent AF, Permanent AF	NA Diagnostic Accuracy
Patel, 2011[69] ROCKET-AF	RCT; Outpatient; US, Canada, UK, Europe, S. America, Asia, Africa, Australia/NZ; Industry; Good	Arm 1: CHADS2 score; Rivaroxaban Arm 2: CHADS2 score; Vitamin K antagonists: Warfarin	14264; Arm 1 (7131) Arm 2 (7133)	Total: Median 707 days	Total: Median 73 Arm 1: Median 73 (IQR 65-78) Arm 2: Median 73 (IQR 65-78)	Paroxysmal AF, Persistent AF	Major bleed Composite outcome: Cerebrovascular infarction, TIA, Systemic embolism, CV infarction/stoke, Intracerebral hemorrhage, CV mortality, Myocardial infarction, Ischemic stroke
Hankey, 2012[70] ROCKET-AF	RCT; Outpatient; US, Canada, UK, S. America, Asia, Africa, Australia/NZ; Industry; Good	Arm 1: CHADS2 Score; Rivaroxaban (no hx of stroke) Arm 2: CHADS2 Score; Vitamin K antagonists: Warfarin (no hx of stroke) Arm 3: CHADS2 Score; Rivaroxaban (hx of stroke) Arm 4: CHADS2 Score; Vitamin K antagonists: Warfarin (hx of stroke)	14264 Arm 1 (3377) Arm 2 (3419) Arm 3 (3754) Arm 4 (3714)	Total: Median 707 days	Total: Median 73 Arm 1: 75 (IQR 68-79) Arm 2: 75 (IQR 67-79) Arm 3: 71 (IQR 64-76) Arm 4: 71 (IQR 64-77)	Paroxysmal AF, Persistent AF	Major bleed Composite outcome #1: Cerebrovascular infarction, Systemic embolism, CV infarction/stroke, Intracerebral hemorrhage, and Ischemic stroke

Abbreviations: [complete list to be provided in final report]: AF = atrial fibrillation; IQR = interquartile range; N = number of patients; NR = not reported; RCT = randomized controlled trial; SD = standard deviation

Appendix Table F-4. Study Characteristics—KQ 4

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
Ablation							
Wazni, 2007[71]	Prospective cohort; NR; US; NR; Good	Arm 1: LMWH: Enoxaparin (1mg/kg BID) Arm 2: LMWH: Enoxaparin (0.5 mg/kg) Arm 3: Vitamin K antagonists: Warfarin	355; Arm 1 (105) Arm 2 (100) Arm 3 (150)	Total: 3-4 mo Arm 1: 3-4 mo Arm 2: 3-4 mo Arm 3: 3-4 mo	Arm 1: 56 (SD 9.6) Arm 2: 55.5 (SD 12) Arm 3: 55.1 (SD 10.6)	Persistent AF	Ischemic stroke Minor bleed Major bleed
Bunch, 2009[72]	Prospective cohort; NR; US; NR; Poor	Arm 1: Aspirin Arm 2: Vitamin K antagonists: Warfarin	630; Arm 1 (123) Arm 2 (507)	Total: 12 mo Arm 1: 12 mo Arm 2: 12 mo	Arm 1: 59.8 (SD 10.7) Arm 2: 66 (SD 10.1)	Paroxysmal AF, Persistent AF, Permanent AF	All-cause mortality CV infarction/stroke TIA
Kwak, 2010[73]	Prospective cohort; Inpatient, Outpatient; Asia; Government; Good	Arm 1: LMWH: Enoxaparin Arm 2: Vitamin K antagonists: Warfarin	104; Arm 1 (55) Arm 2 (49)	NR	Arm 1: 55 (SD 12) Arm 2: 56 (SD 12)	Paroxysmal AF, Persistent AF	Major bleed Minor bleed Ischemic stroke
Saad, 2011[74]	Prospective cohort; Inpatient; S. America; Other (specify) : none; Fair	Arm 1: LMWH: Enoxaparin Arm 2: Vitamin K antagonists: Warfarin	140; Arm 1 (70) Arm 2 (70)	Arm 1: 16 mo (SD 8) Arm 2: 16 mo (SD 8)	Arm 1: 76 (SD 7.4) Arm 2: 73 (SD 5.6)	Persistent AF, Permanent AF	Minor bleed Major bleed CV mortality All-cause mortality Systemic embolism

Study: Author Year Acronym	Study Design; Setting; Location; Funding Source; Quality	Intervention or Tool and Comparators	Total N; Interventions (N)	Follow up period	Mean Age	Special Population	Outcomes Assessed
PCI							
Maegdefessel, 2008[75]	Prospective cohort; Inpatient; Europe; NR; Good	Arm 1: Clopidogrel, Aspirin Arm 2: Clopidogrel, Aspirin; LMWH: Other Arm 3: Vitamin K antagonists: Warfarin	159; Arm 1 (103) Arm 2 (42) Arm 3 (14)	Total: 1.4 mo (IQR 2 mo-5.7 yr)	Arm 1: 69.8 (SD 9.2) Arm 2: 72.1 (SD 8.5) Arm 3: 68.5 (SD 10.6)	None	Major bleed Myocardial infarction Ischemic stroke CV mortality
Manzano-Fernandez, 2008[76]	Retrospective cohort; Inpatient; Europe; NR; Good	Arm 1: Vitamin K antagonists: Warfarin; Clopidogrel, Aspirin Arm 2: Non-triple therapy	104; Arm 1 (51) Arm 2 (53)	Total: 12 mo (IQR 10-12)	Arm 1: 69 (SD 4) Arm 2: 74 (SD 8)	None	Major bleed Composite outcome: Myocardial infarction, CV mortality
Ruiz-Nodar, 2008[77]	Retrospective cohort; Inpatient; Europe; NR; Good	Arm 1: Vitamin K antagonists: Warfarin; Clopidogrel, Aspirin Arm 2: Clopidogrel, Aspirin	426; Arm 1 (242) Arm 2 (184)	Total: Median 595 days (IQR 0-2190)	Arm 1: 71.6 (SD 8.7) Arm 2: 71.2 (SD 8.5)	None	Major bleed Minor bleed All-cause mortality Myocardial infarction Composite outcome: Myocardial infarction, All-cause mortality Composite outcome: CV infarction/stroke, Major bleed, Myocardial infarction, All-cause mortality
Various Operative Procedures							
Hammerstingl, 2009[78] BRAVE	Prospective cohort; Inpatient, Outpatient; Europe; Industry; Fair	Arm 1: LMWH: Enoxaparin (1mg/kg once a day) Arm 2: LMWH: Enoxaparin (1mg/kg twice a day)	703; Arm 1 (358) Arm 2 (345)	Arm 1: 30 days Arm 2: 30 days	Arm 1: 78.6 (SD 73.9) Arm 2: 73.9 (SD 10.8)	None	Major bleed Minor bleed Composite outcome: TIA, Systemic embolism, CV infarction/stroke

Abbreviations: [complete list to be provided in final report]: AF = atrial fibrillation; IQR = interquartile range; N = number of patients; NR = not reported; RCT = randomized controlled trial; SD = standard deviation

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