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Appendix A. Verbatim Quotes from Guidance Documents

This appendix contains verbatim quotations from the source documents that were reviewed. These quotations were selected for the degree of relevance to EPCs performing evidence synthesis using network meta-analysis methods. The following are not intended to be an exhaustive representation of the content of the source documents.

When to Conduct Network Meta-Analyses

Definitions/Terminology

"Terminology for indirect treatment comparisons, mixed treatment comparisons, and network meta-analysis varies in the literature."[2,3]

"Methods are available for analysing, simultaneously, three or more different interventions in one meta-analysis. These are usually referred to as 'multiple-treatments meta-analysis' ('MTM'), 'network meta-analysis', or 'mixed treatment comparisons' ('MTC') meta-analysis."[16]

"Also called mixed treatments comparison or multiple treatments comparison meta-analysis, network metaanalysis expands the scope of a conventional pair-wise meta-analysis by analyzing simultaneously both direct comparisons of interventions within randomized controlled trials (RCTs) and indirect comparisons across trials based on a common comparator (e.g., placebo or some standard treatment)."[9]

"Indirect and mixed treatment comparisons (MTC), also known as network meta-analysis, represent a recent development in evidence synthesis, particularly in decision making contexts. Rather than pooling information on trials comparing treatments A and B, network meta-analysis combines data from randomised comparisons, A vs B, A vs C, A vs D, B vs D, and so on, to deliver an internally consistent set of estimates while respecting the randomisation in the evidence."[13]

"Network analysis will be used to describe *a single synthesised analysis in which more than one common reference is used to indirectly compare the proposed drug and its main comparator*."[11]

"Multiple-treatments meta-analysis (MTM) is an extension to indirect comparisons that allows the combination of direct with indirect comparisons, and also the simultaneous analysis of the comparative effects of many interventions"[16]

"Mixed treatment comparisons, a special case of network meta-analysis, combine direct evidence and indirect evidence for particular pairwise comparisons, thereby synthesizing a greater share of the available evidence than traditional meta-analysis."[2,3]

"Mixed treatment comparisons (MTC), or network meta-analyses, are used to analyse studies with multiple intervention groups and to synthesise evidence across a series of studies in which different interventions were compared...They build a network of evidence that includes both

direct evidence from head to head studies and indirect comparisons whereby interventions that have not been compared directly are linked through common comparators."[6]

According to the HIQA, a multiple treatment comparison combines direct and indirect evidence to compare a technology to two or more other treatments; a network meta-analysis is appropriate for analysing a combination of direct and indirect evidence where there is at least one closed loop of evidence connecting the two technologies of interest, and a Bayesian mixed treatment comparison is appropriate for comparing multiple treatments using both direct and indirect evidence."[1]

Justification

"In the absence of randomized, controlled trials involving a direct comparison of all treatments of interest, indirect treatment comparisons and network meta-analysis provide useful evidence for judiciously selecting the best choice(s) of treatment."[2,3]

"In the absence of sufficient direct head-to-head evidence and presence of sufficient indirect evidence, indirect comparisons can be considered as an additional analytic tool."[4]

"Direct comparisons are preferred over indirect comparisons; similarly, effectiveness and long-term or serious adverse event outcomes are preferred to efficacy and short-term tolerability outcomes."[5]

"Where relevant direct randomised trials (as defined in Part II, Subsection B.2) comparing the proposed drug directly with the main comparator are available, their analysis and presentation are preferred as the basis of the clinical evaluation (see Part II, Section B). However, in the absence of any such direct randomised trials, the second step in the hierarchy is to determine whether it is possible to present an indirect comparison based on two or more sets of randomised trials involving one or more common reference."[10]

"In situations when both direct and indirect comparisons are available in a review, then unless there are design flaws in the head-to-head trials, the two approaches should be considered separately and the direct comparisons should take precedence as a basis for forming conclusions."[16]

"Although it is often argued that indirect comparisons are needed when direct comparisons are not available, it is important to realize that both direct and indirect evidence contributes to the total body of evidence. The results from indirect evidence combined with the direct evidence may strengthen the assessment between treatments directly evaluated. Even when the results of the direct evidence are conclusive, combining them with the results of indirect estimates in a mixed treatment comparison (MTC) may yield a more refined and precise estimate of the interventions directly compared and broaden inference to the population sampled because it links and maximizes existing information within the network of treatment comparisons"[2,3]

"Data from head-to-head RCTs should be presented in the reference-case analysis, if available. When head-to-head RCTs exist, evidence from mixed treatment comparison analyses may be presented if it is considered to add information that is not available from the head-to-head

comparison. This mixed treatment comparison must be fully described and presented as additional to the reference-case analysis (a 'mixed treatment comparison' includes trials that compare the interventions head-to-head and indirectly). When multiple technologies are being appraised that have not been compared within a single RCT, data from a series of pairwise head-to-head RCTs should be presented. Consideration should also be given to presenting a combined analysis using a mixed treatment comparison framework if it is considered to add information that is not available from the head-to-head comparison. If data from head-to-head RCTs are not available, indirect treatment comparison methods should be used (an 'indirect comparison' is a synthesis of data from a network of trials). The principles of good practice for standard meta-analyses should also be followed in mixed and indirect treatment comparisons."[12]

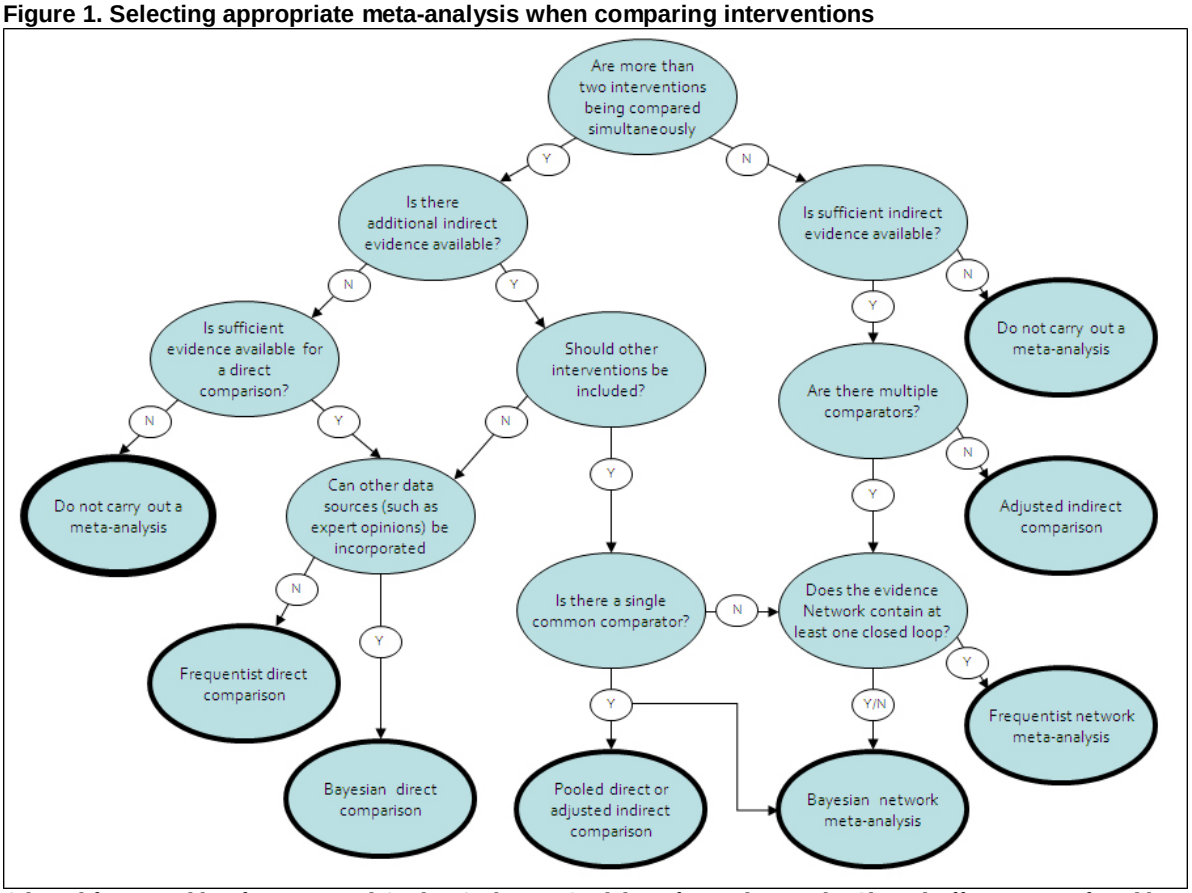
"Pursuit of qualitative or quantitative indirect comparison is never required and decisions to do so must depend on consideration of clinical, methodological, and statistical heterogeneity levels across the individual studies."[5]

"CRGs should be encouraged to identify existing IRs that compare multiple interventions and consider the feasibility of indirect comparisons and MTM."[17]

"The large majority of [intervention reviews] that involve many interventions present meta-analyses of a series of pair-wise comparisons without a specific plan to integrate the various pieces of evidence. Statistical synthesis using MTM could be performed in many cases, provided that the assumptions of this approach are fulfilled."[17]

Flow chart (Figure 1) to select proper meta-analysis when comparing interventions, from the Health Information and Quality Authority.

Figure 1. Selecting appropriate meta-analysis when comparing interventions



Adapted from: Health Information and Quality Authority. Guidelines for Evaluating the Clinical Effectiveness of Health Technologies in Ireland. Dublin: Health Information and Quality Authority; 2011. Available at: http://www.hiqa.ie (Last accessed on December 28, 2011)

Assumptions

"Many assumptions behind network meta-analysis methods appear to be similar to those made in standard pair-wise meta-analysis."[9]

"The validity of an indirect comparison relies on the different subgroups of trials being similar, on average, in all other factors that may affect outcome."[16]

"Indirect comparisons are often performed on the assumption of a constant relative treatment effect across varying baseline risks (with 'adjustment' for the event rate in the common reference group assumed to control for differences in baseline risk). This assumption however is also usually unverifiable unless there are large numbers of trials across the indirect comparison. It also inadequately incorporates all aspects that affect the exchangeability assumption."[11]

"For network meta-analysis, covariates that act as relative treatment effect modifiers must be similar across trials (or adjusted for using meta-regression). And, when it combines indirect evidence with direct evidence, network meta-analysis adds the assumption of consistency: The indirect evidence must be consistent with the direct evidence."[2,3]

"The major assumption of indirect and mixed treatment comparisons is that the direct and the indirect evidence are consistent. That is, the treatment effect dBC estimated by the BC trials, would be the same as the treatment effect estimated by the AC and AB trials if they had included B and C arms. If this is not the case the evidence is inconsistent. Factors such as (relative) treatment effects varying with disease severity may cause inconsistency (e.g. if the BC trials are done in patient populations with higher/lower baseline risks than the AB and AC trials and the treatments interact with baseline risk, the evidence will be inconsistent)."[15]

"MTC analysis requires a connected network; that is, for each treatment, there is a chain of pair-wise comparisons that connects it to every other treatment."[15]

How to Conduct Network Meta-Analyses

Planning/Design

"Objectives of network meta-analysis may include considering all relevant evidence, answering research questions in the absence of direct evidence, improving the precision of estimates by combining direct and indirect evidence, ranking treatments, and assessing the impact of certain components of the evidence network.[2,3]"

"When a new [intervention reviews] seeks to compare multiple interventions (i.e. to determine a preferential ordering of three or more competing interventions for a particular outcome), this should be made explicit in the protocol, and appropriate methods should be planned and implemented."[17]

"The principles of good practice for systematic reviews and meta-analyses should be carefully followed when conducting mixed and indirect treatment comparisons."[12]

"To minimize error and ensure validity of findings from meta-analyses, the systematic review, whether it involves a standard, pair-wise meta-analysis or a network meta-analysis, must be designed rigorously and conducted carefully.[9]

"The literature search for a network meta-analysis builds the network, applying the same basic standards as for a meta-analysis leading to a direct comparison" [ispor]

"It may be difficult to identify all relevant comparators for the treatments of interest, and any search involves costs and tradeoffs. It may be efficient to proceed in stages, using one of the strategies developed by Hawkins et al."[2,3]

"The more interventions that are included in a MTM, the greater the potential gain in precision and the greater the ability to establish whether various sources of evidence 'agree' with each other. Therefore, it may sometimes be useful to include interventions that are not current candidates for clinical practice, such as placebo or no treatment, or interventions that are no longer recommended or available ('legacy treatments')."[17]

"Different specification of eligibility criteria may result in differences in the structure or extent of a network, leading to discrepant findings for network meta-analyses on the same topic. This is

because different combinations of direct and indirect evidence, some independent and some overlapping, contribute to the comparisons and estimates of treatment effect. Certain interventions, for example, interventions that are no longer in use, or placebos, may not be of primary interest but may be included in the network meta-analysis if they provide information concerning the interventions of interest through indirect comparisons."[15]

"To ensure that all relevant studies are identified, the network meta-analyst could search de novo for all relevant studies, but this would waste valuable resources if good systematic reviews with comprehensive searches already exist. To conserve valuable resources, one might consider using data identified through existing high quality systematic reviews of relevant pair-wise treatment comparisons provided the searches in the existing reviews are up-to-date."[15]

"After demonstrating that no relevant direct randomised trials exist, broaden the literature search criteria to identify all randomised trials relevant for an indirect comparison of the proposed drug and the main comparator." [PBAC]

"The network can be restricted to include the minimum number of comparisons required to enable an indirect comparison between the technologies of interest. Alternatively it can be expanded to include as many relevant comparators as possible."[1]

"Extending mixed treatment comparisons networks to include trial comparisons not of direct interest can reduce uncertainty in the comparisons of interest."[15]

Analysis framework

"Network meta-analysis can be performed within a Frequentist or Bayesian framework."[2,3]

"The MTC method can be used to obtain measures of effect for each of the indicated patterns. The network meta-analysis method proposed by Lumley can compare treatments in a network geometry that contains at least one closed loop."[7,8]

"For syntheses where all trials are two-arm, there is no reason why frequentist methods should not be used, as long as statistically sound estimators are used and appropriate steps are taken to propagate parameter uncertainty, including correlations, through the decision model."

"Various approaches for indirect treatment comparisons have been reviewed. The mixed treatment comparison approaches by Lu and Ades are elegant, but require information that may not be available. The challenge of Lumley's network meta-analysis is that it needs a data-based assessment of trial consistency; therefore, it requires information from a large number of different treatment comparisons."[7,8]

"The common Generalised Linear Model (GLM) framework can, of course, be applied in either frequentist or Bayesian contexts. However, Bayesian Markov Chain Monte Carlo (MCMC) has for many years been the mainstay of "comprehensive decision analysis", because simulation from a Bayesian posterior distribution supplies both statistical estimation and inference, and a platform for probabilistic decision making under uncertainty"[13]

"A major advantage of the Bayesian approach is that the method naturally leads to a decision framework that supports decision making"[2,3]

"A particular advantage of using a Bayesian framework is that all interventions in the analysis can be ranked, using probabilistic, rather than crude, methods."[16]

"For a network meta-analysis, a specific advantage is that the posterior probability distribution allows calculating the probability of which of the competing interventions is best and other probability statements. This aspect of a Bayesian analysis is providing information that is directly relevant to health-care decision makers (e.g., policymakers and health-care professionals/clinicians). Other advantages of a Bayesian meta-analysis include the straightforward way to make predictions and the possibility to incorporate different sources of uncertainty."[2,3]

"Because Binomial and Poisson likelihoods with zero cells are allowed, special precautions do not usually need to be taken in the case of the occasional trial with a zero cell count. This is a major strength of the Bayesian MCMC approach, because some popular Frequentist approaches for log odds ratios or log relative risks have to add an arbitrary constant, usually 0.5, to cells in order to obtain non-infinite estimates of treatment effects and non-infinite variance, but in so doing they generate biased estimates of effect size."[13]

Statistical modeling

"When evidence is combined using indirect or mixed treatment comparison frameworks, trial randomisation must be preserved. A comparison of the results from single treatment arms from different randomised trials is not acceptable unless the data are treated as observational and appropriate steps taken to adjust for possible bias and increased uncertainty."[12]

"Extending network metaanalysis models with treatment-by-covariate interactions attempts to explain heterogeneity in relative treatment effects and estimates relative treatment effects for different levels of the covariate... Unfortunately, the number of studies in a network is often limited, and in such cases, adjustment by incorporating study-level covariates with meta-regression models may sometimes be questionable. In addition, aggregate-level covariate adjustment might produce ecological bias, limiting the interpretation of estimated results for subgroups."[2,3]

"If confounders are present in an indirect comparison, it is only possible to adjust for them via meta-regression. However, this would be an unusual situation because at least 10 trials per adjustment variable are required in order to achieve stability in the meta-regression results"[11]

"Network meta-analysis can be performed with fixed- or random-effects models...If there is heterogeneity, however—variation in true (or underlying) relative treatment effects for a particular pairwise comparison—random-effects models must be used. A random-effects approach typically assumes that true relative effects across studies are considered exchangeable (i.e., the prior position of expecting underlying effects to be similar but not identical) and can be described as a sample from a normal distribution whose mean is the pooled relative effect and whose SD reflects the heterogeneity."[2,3]

“Because the standard error obtained from a fixed effect analysis will be too small if there is heterogeneity between trials (beyond random variation), and recognising that there may be additional heterogeneity in an indirect comparison compared to a direct comparison, the Working Group supports the conclusion in the 2005 Glenny AM, et al paper that a random effects method is preferred to a fixed effect method.”[11]

“Choices of prior distributions are, to some extent, arbitrary...”[2,3]

“We recommend vague or flat priors, such as N(0, 1002), throughout for μiand d1k.”[13]

“It has become standard practice to also set vague priors for the between-trial variances. For binomial with logit links models the usual practice is to place a Uniform prior on the standard deviation, for example σ ~ Uniform(0,2)....An alternative approach, which was once popular but has since fallen out of favour, is to set a vague Gamma prior on the precision, for example 1/ σ2 ~ Gamma(.001,.001).”[13]

“The parameters in the distributions of random effects have vague prior distributions: N(0, 106) for the dAk (independently) and Uniform(0, 2) for σ. These priors are common choices in such models.”[2,3]

“Two further alternatives may be found useful when there is insufficient data to adequately estimate the between-trials variation. The first is the use of external data. If there is insufficient data in the metaanalysis, it may be reasonable to use an estimate for σ from a larger meta-analysis on the same trial outcome involving a similar treatment for the same condition. If there is no data on similar treatments and outcomes that can be used, an informative prior can be elicited from a clinician who knows the field.”[13]

“Particular care must be taken in checking convergence, and we suggest that at least three chains are run, starting from widely different (yet sensible) initial values...Posteriors should be examined visually for spikes and unwanted peculiarities, and both the initial “burn-in” and the posterior samples should be conservatively large and the number of iterations for both must be reported in the analysis.”[13]

“While the likelihood is not altered by a change in which treatment is taken to be “Treatment 1 [referent], the choice of the reference treatment can affect the posterior estimates because priors cannot be totally non-informative...Choice should therefore be based on ease of interpretation, with placebo or standard treatment usually taken as Treatment 1.”[13]

“It is incorrect to analyze the pairwise effects in a multiarm trial as if they came from separate studies.”[2,3]

“If the network appropriately includes a multiarm trial, omitting it from the analysis may introduce bias. The analysis, then, must take into account the correlation among the effect estimates for the pairs of arms;”[2,3]

"Shared parameter models allow the user to generate a single coherent synthesis when trials report results in different formats. For example some trials may report binomial data for each arm, while others report only the estimated log odds ratios and their variances; or some may report numbers of events and time at risk, while others give binomial data at given follow-up times.[13]

"The consistency of the comparative treatment effect across trials (and sets of trials) also depends upon whether the appropriate measure of effect is used.... If an appropriate measure of comparative treatment effect is used to minimise variation in comparative treatment effect within each and all sets of included randomised trials, the exchangeability assumption is more likely to be maintained."[11]

"...relative measures of comparative treatment effect are often a robust way of summarising the overall result of the evidence available in order to apply it to any subgroup with a particular baseline risk."[11]

"Whatever the method of analysis, the pooling of individual study results and indirect comparisons should be based on relative effect measures (e.g., OR, difference in change from baseline, hazards ratio) to preserve randomization."[2,3]

One advantage of the OR is that, because it is symmetrical around 1.0 (unlike the RR), the OR for harm is equal to the inverse of OR for benefit, and hence is consistently estimated regardless of how the research question is framed (eg in a study that is to measure survival, the researchers could use a null hypothesis of no difference in survival, or a null hypothesis of no difference in mortality)."[11]

"If the underlying baseline risk is the same across the two sets of trials and the PBS population, then there it may be considered appropriate to use the directly synthesised RD as an absolute measure of comparative treatment effect... If the baseline risk is different, then the primary issue for the indirect comparison is whether the trials are similar in terms of potential confounders... If it is decided to proceed with the indirect comparison, then a ratio measure (OR or RR) is usually preferred to the RD, because as outlined above, it is considered that relative measures of comparative treatment effect have more often been observed to be constant across different baseline risks than absolute measures of comparative treatment effect."[11]

Assessment for and handling of potential bias/inconsistency

"When direct evidence and indirect evidence are combined for a particular pairwise comparison, it is important that the indirect estimate is not biased and there is no discrepancy between the direct and indirect comparisons. Therefore, consistency between these direct and indirect comparisons should be accounted for." [2,3]

"Heterogeneity, inconsistency, and bias may propagate through a network of trials, and may affect the estimates differentially across regions of the network."[9]

"The indirect comparison across trials does not have a randomisation step to allow the characteristics of the patients to differ only due to the play of chance."[10]

"The indirect comparisons involved are not randomized comparisons, and may suffer the biases of observational studies, for example due to confounding".[16]

"...it is important to remember that in a network meta-analysis of RCTs, the value of randomization does not hold across trials.... Hence, an ITC or network meta-analysis of RCTs is a form of observational evidence, but arguably less prone to confounding bias than is a cohort study(or any other observational design)."[2,3]

"the mechanisms that potentially could create "bias" in indirect comparisons appear be to identical to those that cause heterogeneity in pair-wise metaanalysis."[14]

"Inconsistency can be thought of as a conflict between "direct" evidence on a comparison between treatments B and C, and "indirect" evidence gained from AC and AB trials. Like heterogeneity, inconsistency is caused by effect-modifiers, and specifically by an imbalance in the distribution of effect modifiers in the direct and indirect evidence."[14]

"Factors such as the total number of trials in a network, number of trials with more than two comparison arms, heterogeneity (i.e., clinical, methodological, and statistical variability within direct and indirect comparisons), inconsistency (i.e., discrepancy between direct and indirect comparisons), and bias may influence effect estimates obtained from network meta-analyses."[9]

"In principle, the validity of indirect comparison relies on the invariance of treatment effects across study populations. However, in practice, trials can vary in numerous ways including population characteristics, interventions and cointerventions, length of followup, loss to followup, study quality, etc. Given the limited information in many publications and the inclusion of multiple treatments, the validity of indirect comparisons is often unverifiable. Moreover, indirect comparisons, like all other meta-analyses, essentially constitute an observational study, and residual confounding can always be present. Systematic differences in characteristics among trials in a network can bias indirect comparison results. In addition, all other considerations for meta-analyses, such as choice of effect measures or heterogeneity, also apply to indirect comparisons."[4]

The ICWG report quotes Glenny et al.'s definition of inconsistency (they call it exchangeability), "… the two sets of trials should be exchangeable, in the sense that there is no reason to suppose that the results as a whole would be different had the various trialists kept the same protocol and patients, but chosen to study a different treatment comparison."[11]

"Most agencies to which the results of a network meta-analysis could be submitted currently require that direct estimates and indirect estimates be calculated separately and shown to be consistent before direct evidence and indirect evidence are combined."[2,3]

"...network meta-analysis relies on the randomization in the RCTs that compared the treatments directly. It also involves a similarity assumption: "Combining studies should only be considered if they are clinically and methodologically similar". Nevertheless, "no commonly accepted standard [defines] which studies are 'similar enough."[2,3]

"In a multiple treatment comparison involving both direct and indirect evidence, the evidence network can become very complex with many comparisons based on only one or two studies. With increasing complexity and greater numbers of treatments, the prospect of inconsistency increases. There is also a power trade-off between the number of pair-wise comparisons and the number of studies included in the analysis – too many comparisons with too few studies and the analysis may be underpowered to detect true differences."[1]

The ICWG report[11] provides an example framework for assessing the exchangeability assumption of a network meta-analysis. Assuming a indirect comparisons of treatments A and B through a common comparator C is being considered, ICWG first recommends for the AvC and BvC direct randomized trials:

- Assessment of the available trials for factors that may cause heterogeneity of the AvC and BvC comparative treatment effect
- Assessment of the event rates in the drug C populations
- Assessment of whether the measure of the comparative treatment effect for AvC and BvC is appropriate
- Assessment of evidence of the statistical homogeneity of the AvC and BvC comparative treatment effect across the available trials

Then for the BvA <u>indirect comparison</u>:

- Assessment across the sets of trials (i.e. the AvC and the BvC trials) for factors that may cause heterogeneity of the BvA comparative treatment effect
- Assessment of the event rates in the drug C populations across the sets of trials
- Assessment of whether the measure of the comparative treatment effect for BvA is appropriate
- Assessment of evidence of statistical homogeneity of the synthesized comparative treatment effect BvA across the sets of trials (only possible if BvA has been compared via multiple common references)

According to the CADTH, "Whether an indirect treatment comparison provides a valid estimate of the relative efficacy for an intervention of interest significantly depends on the fulfillment of this primary assumption. To determine whether or not this assumption is met, trials included in the indirect comparison can be assessed according to three criteria":

- comparability of the linking treatment;
- comparability of patients/heterogeneity;
- methodological comparability of included trials

"...whichever [indirect comparison/network meta-analysis] method the investigators choose, they should assess the invariance of treatment effects across studies and appropriateness of the chosen method on a case-by-case basis, paying special attention to comparability across different sets of trials."[4]

"Where direct and indirect evidence are combined, inconsistencies between the direct and indirect evidence must be assessed and reported."[1]

"Decision makers making use of results of network meta-analyses will need to assess whether the differences between treatments are most likely true or whether they can be explained by bias in the analysis. The internal validity of the analyses is contingent on three factors: 1) the appropriate identification of the studies that make up the evidence network, 2) the quality of the individual RCTs, and 3) the extent of confounding bias due to similarity and consistency violations."[2,3]

"Factors such as the total number of trials in a network, number of trials with more than two comparison arms, heterogeneity (i.e., clinical, methodological, and statistical variability within direct and indirect comparisons), inconsistency (i.e., discrepancy between direct and indirect comparisons), and bias may influence effect estimates obtained from network meta-analyses."[9]

"Evaluation of homogeneity and consistency (if the network supports both direct and indirect comparisons) should be specified as components of the analysis and should reflect the risks and benefits of combining data for the particular research question"[2,3]

"While it is essential to carry out tests for inconsistency, the issue should not be considered in an overly mechanical way... We emphasise that while tests for inconsistency must be carried out, they are inherently underpowered, and will often fail to detect it. Investigators must therefore also ask whether, if inconsistency is not detected, conclusions from combining direct and indirect evidence can be relied upon."[14]

"...tests for statistical heterogeneity have low power, and therefore, even if statistical heterogeneity is not demonstrated, doubts will remain about its presence, particularly in the presence of obvious clinical differences across the AvC and BvC trials by a factor that is known to influence drugs B and/or A."[11]

"When analyzing a network of comparisons, the inconsistency of the network needs to be considered, as well as between-trial heterogeneity and sampling error. Large inconsistencies rule out a meta-analysis, small inconsistencies should add uncertainty to the results." [cadth]

"A departure from consistency arises when the direct and indirect estimates of an effect differ...Researchers must evaluate departures from consistency and determine how to interpret them."[2]

"The assumption of constant efficacy requires all trials included in the analysis to be equivalent and attempting to measure the same treatment effect – that is, the results of one set of trials (A vs. B) should be generalisable to the other set of trials (A vs. C). Determining whether the assumption of generalisability holds is a subjective assessment based on a detailed review of the included studies in both comparisons."[1]

"Disagreement between direct and indirect evidence must be fully investigated and it may preclude pooling data if the disagreement cannot be adequately explained." [Ireland]
"When information on heterogeneity within the direct comparisons is available, consideration of it can form a preliminary step in a network meta-analysis, but one should first examine potential effect modifiers, because disparities among studies may preclude analysis of the network."[2,3]

"Consistency or coherence describes the situation that direct and indirect evidence agrees with each other, and when the evidence of a network of interventions is consistent, investigators could combine direct and indirect evidence using MTM models. Conversely, they should refrain from combining multiple sources of evidence from an incoherent network where there are substantial differences between direct and indirect evidence."[4]

"Decisions should be based on coherent models that fit the data. Careful examination of different sources of evidence may reveal that some estimates are "corroborated" and others not. If inconsistency is detected, the entire network of evidence should be reconsidered from a clinical epidemiology viewpoint with respect to the presence of potential effect modifiers."[14]

"Any adjustment in response to inconsistency is *post hoc*, which emphasizes the importance of identifying potential causes of heterogeneity of effect at the scoping stage, and potential internal biases in advance of synthesis"[14]

"Measures of inconsistency variance or incoherence variance are not recommended as indicators of inconsistency."[14]

"Within a Bayesian framework a consistency model can be compared to an "inconsistency" model. Analyses of residual deviance can provide an "omnibus" test of global inconsistency, and can also help locate it."[14]

"Node splitting24 is another effective method for comparing direct evidence to indirect evidence in complex networks."[14]

Assessment of model fit

"In frequentist analyses, measures of model fit are similar to those for direct evidence and depend on the particular outcome measure. Bayesian analyses customarily use deviance (a likelihood-based measure)—the lower the residual deviance, the better the fit. For comparing models, the deviance information criterion (DIC) adds a penalty term, equal to the effective number of parameters in the model. If a model fits poorly, graphical techniques can aid more-detailed examination."[2,3]

"The goodness-of-fit can be estimated by calculating the difference between the deviance for the fitted model and the deviance for the saturated model (which fits the data perfectly). For example, the Akaike information criterion, which uses the likelihood function, the Bayesian information criterion, or deviance information criterion can all be used for model selection"[2,3]

"...competing models should be compared in terms of their goodness-of-fit to the data, and residual deviance calculations may be provided to justify the study's choice of the base case model."[2,3]

"In this document we suggest that global DIC statistics and res D are consulted both to compare fixed and random effect models, and to ensure that overall fit is adequate."[13]

"The choice of a fixed- or random-effects meta-analysis model, with or without covariate interactions, can be made by comparing different competing models regarding their goodness-of-fit to the data."[2,3]

Use of sensitivity analysis

"Investigators should conduct sensitivity analysis to check the assumptions of the indirect comparison. If the results are not robust to the assumptions, findings from indirect comparisons should be considered as inconclusive."[4]

"Sensitivity analyses should focus on the areas of greatest uncertainty. Potential effect modifiers can be explored by stratifying on variations in study design or population. Comparisons between random-effects and fixed-effects analyses may be appropriate. Bayesian analyses should also explore the influence of choosing different prior distributions."[2,3]

"Choices of prior distributions are, to some extent, arbitrary, so they are often subjected to sensitivity analysis, which may be especially important for priors on heterogeneity in random-effects models."[2,3]

How to Interpret and Report Network Meta-Analyses

Interpretation

"Probability statements could be made about the effectiveness of each treatment [24]. For example, for each treatment, one can calculate the probability that the treatment is the best, second best, or third best among all treatments. Such probability statements should be interpreted carefully since the difference between treatments might be small and not clinically meaningful."[9]

"Investigators should explicitly state assumptions underlying indirect comparisons and conduct sensitivity analysis to check those assumptions. If the results are not robust, findings from indirect comparisons should be considered inconclusive. Interpretation of findings should explicitly address these limitations."[4]

In respect to Bayesian network meta-analysis, "Probability statements could be made about the effectiveness of each treatment."[9]

"The external validity of the network meta-analysis will naturally be limited by the external validity of the RCTs included in the evidence network, and health-care decision makers will need to review whether results can be extrapolated to the population of interest."[2,3]

"Furthermore identification of the "best" or most appropriate treatment cannot be made on the basis of efficacy end points alone. To inform health-care decision making for clinical treatment guidelines and reimbursement policies, the efficacy findings of a network meta-analysis must be interpreted in light of other available (observational) evidence and other characteristics of the competing interventions, such as safety and convenience".[2,3]

"The network of available evidence should be described and used to guide the selection of the method of meta-analysis. The selection of direct and indirect evidence must be clearly defined. The exclusion of relevant evidence, either direct or indirect, should be highlighted and justified. Where direct and indirect evidence are combined, inconsistencies between the direct and indirect evidence must be assessed and reported."[1]

Reporting

"In addition to the estimates of treatment effects, uncertainty, clinical and methodological characteristics, and potential biases within included trials must be conveyed."[9]

"If the analyses were performed within a Bayesian framework, the choice of prior distributions for the model parameters should be defined."[2,3]

"Indicate software package used in the analysis and provide code (at least in an online appendix)"

"Evidence from a mixed treatment comparison may be presented in a variety of ways. The network of evidence may be presented in tabular form. It may also be presented diagrammatically as long as the direct and indirect treatment comparisons are clearly identified and the number of trials in each comparison is stated."[12]

"In order to appreciate the value of a network meta-analysis, it is recommended that results of all (relevant) pairwise comparisons (as a reflection of the functional parameters) are presented as well."[2,3]

"It is critical to report all pairwise effect estimates together with the associated confidence or credible intervals, depending on the statistical model used (i.e., frequentist or Bayesian model)."[9]

"Investigators should make efforts to explain the differences between direct and indirect evidence based upon study characteristics."[4]

"The heterogeneity between results of pairwise comparisons and inconsistencies between the direct and indirect evidence on the technologies should be reported."[12]

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Appendix B. Literature Search Used in Part Two

1. Randomized Controlled Trial/
2. Clinical Trial/
3. randomi$ control$ trial$.tw.
4. controlled clinical trial.sh.
5. clinical trial$.tw.
6. trial$.tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. review literature/
9. meta-analysis.sh.
10. meta-analy$.tw.
11. metaanaly$.tw.
12. (meta adj analy$).tw.
13. 8 or 9 or 10 or 11 or 12
14. (indirect adj2 comparison$).tw.
15. (indirect adj2 evaluat$).tw.
16. (indirectly adj2 compare$).tw.
17. bayesian.tw.
18. (mixed treatment adj compar$).tw.
19. MTC.tw.
20. 14 or 15 or 16 or 17 or 18 or 19
21. 7 and 13
22. 20 and 21
23. limit 22 to english language
24. limit 23 to yr="2006 -Current"
25. remove duplicates from 24

Appendix C. Data Extraction Tool for Part Two

Study identification

Unique ID		**First author last name, year**	
# authors		**In there a methodologist listed as an author?**	☐ Yes ☐ No
Journal Name		**Journal impact factor**	
Is the journal classified as a methods journal? ☐ Yes ☐ No		**Does journal allow online supplement/ appendix?** ☐ Yes ☐ No	
Was there a published appendix or online supplement? ☐ Yes ☐ No		**Does the journal impose a word/table/figure limit?** Word: ☐ Yes ☐ No Table/figure: ☐ Yes ☐ No If yes, what is the limit:	
Geographic location of conduction?		**# printed pages in main document**	
Funding Source: ☐ Industry ☐ Government/Foundation ☐ Academia ☐ Other ☐Unknown			
Publication type: ☐ Full text journal article ☐Report (government, etc) ☐ Other			
Work affiliated with an agency? (ex. AHRQ, NICE, Cochrane, etc.) ☐ Yes ☐ No If yes, which agency:			
What terms were used to describe the indirect comparison? ☐ Network meta-analysis ☐ Mixed treatment comparison ☐Multiple treatment comparison ☐ Other (i.e., simply by reference(s) used; exact terms):			

Study characteristics

Study objective:	Was it clear how the research question pertains to a network meta-analysis? ☐ Yes ☐ No
Disease state evaluated	☐ Endocrinology ☐ Behavioral health ☐ Cardiology ☐ Oncology ☐ Pain ☐ Substance abuse ☐ Respiratory ☐ Infectious disease ☐Rheumatology ☐ Gastroenterology ☐ Neurology ☐ Other:
Methodological inclusion criteria?	
What network pattern was present? ☐ simple star ☐ star ☐ ladder ☐closed loop ☐network with at least one closed loop **Was a diagram displayed to show the network?** ☐ Yes ☐ No	
#and type of interventions compared? (e.g device, procedure, pharmacologic, behavioral, other)	

# of trials / # patients included in analysis:	

Methods Characteristics

Method/model applied: ☐ Bayesian ☐ Frequentist
Was traditional pair-wise meta-analysis also conducted? ☐ Yes ☐ No

For Bayesian networks

Model (all that apply): ☐ Fixed-effects ☐ Random-effects ☐ Adjustment of model for studies with ≥3 treatments? ☐Evaluation on the dependence of treatment effect on a co-variate (adjustment) performed?
Software used (including wrappers): **Was the code published in the main manuscript?** ☐ Yes ☐ No If no, was the code made available to the reader? ☐ Yes ☐ No If it was made available to the reader, in what format? ☐ online supplement ☐ referral to another website/source ☐email author ☐ other: If email author, were we able to obtain the code for this project? ☐ Yes ☐ No **Was the raw data published in the main manuscript?** ☐ Yes ☐ No If no, was the raw data made available to the reader? ☐ Yes ☐ No If it was made available to the reader, in what format? ☐ online supplement ☐ referral to another website/source ☐email author ☐ other: If email author, were we able to obtain the raw data for this project? ☐ Yes ☐ No
Was Markov-chain Monte Carlo modeling used? ☐ Yes ☐ No If no, what sampling method was used? Were the starting value(s) reported (this can be obtained from provided code)? ☐ Yes ☐ No Number of chains: Number of iterations per chain: Number of iterations used for final results (after excluding burn-in): Were convergence statistics evaluated? ☐ Yes ☐ No
Were prior distributions specified anywhere in the paper? (this can be obtained from provided code) ☐ Yes ☐ No If yes, what distribution was used for "D" and "σ" [often $N(0, 10^6)$ for D and Uniform(0, 2) for σ] (this can be obtained from provided code)? **Were prior distributions justified in the paper?** ☐ Yes ☐ No ☐ NA if not specified **Was sensitivity analysis performed based on prior distribution chosen?** ☐ Yes ☐ No If yes, what was the distribution changed to?
Was a graphical representation of the posterior distribution provided?

☐ Yes ☐ No
Do the authors rank order the efficacy and/or safety of different interventions compared? ☐ Yes ☐ No
Was model fit tested (i.e., sum deviation, residual deviation, DIC)? ☐ Yes ☐ No If so, which was used?
Was a description of how possible heterogeneity was evaluated (either qualitative or quantitative, e.g., I^2, Cochrane Q, etc.) provided? ☐ Yes ☐ No If yes, how? ☐ traditional meta-analysis, how: ☐ network meta-analysis, how:
Was a description of how possible inconsistency was evaluated (either qualitative or quantitative, e.g., comparison of direct evidence with the indirect evidence) provided? ☐ Yes ☐ No
Does the analysis try to make a claim of: **Equivalence** ☐ Yes ☐ No **Non-inferiority?**☐ Yes ☐ No
Was there an *a priori* decision rule/minimally important difference described? ☐ Yes ☐ No

For Frequentist networks

Model (all that apply): ☐ Fixed-effects ☐ Random-effects ☐Evaluation on the dependence of treatment effect on a co-variate (adjustment) performed?
Software used: **Was the raw data published in the main manuscript?**☐ Yes ☐ No If no, was the raw data made available to the reader? ☐ Yes ☐ No If it was made available to the reader, in what format? ☐ online supplement ☐ referral to another website/source ☐email author ☐ other: If email author, were we able to obtain the raw data for this project? ☐ Yes ☐ No
Was a Linear Mixed Model Used?☐ Yes ☐ No If no, how was the model fit? How were studies weighted (inverse variance, inverse sample size etc?):
Was a description of how possible heterogeneity was evaluated (either qualitative or quantitative, e.g., I^2, Cochrane Q, etc.) provided? ☐ Yes ☐ No If yes, how? ☐ traditional meta-analysis, how: ☐ network meta-analysis, how:
Was a description of how possible inconsistency was evaluated (either qualitative or quantitative, e.g., comparison of direct evidence with the indirect evidence) provided? ☐ Yes ☐ No

Does the analysis try to make a claim of: **Equivalence** ☐ Yes ☐ No **Non-inferiority?** ☐ Yes ☐ No
Was there an *a priori* decision rule/minimally important difference described? ☐ Yes ☐ No

Posterior Distribution

Outcome 1: ☐ Binary ☐ Continuous ☐ Categorical non binary Is this outcome effect measure reported as mean or median data? ☐ Mean ☐ Median ☐ NR Format presented: ☐ Text ☐ Table ☐ Figure
Effect size measured: ☐ Relative risk ☐ Odds ratio ☐ Risk difference ☐ Weighted-mean difference ☐ Other:
Measure of variance: ☐ Credible interval, if yes ☐99% ☐95% ☐SD ☐ Other:
Outcome 2: ☐ Binary ☐ Continuous ☐ Categorical non binary Is this outcome effect measure reported as mean or median data? ☐ Mean ☐ Median ☐ NR Format presented: ☐ Text ☐ Table ☐ Figure
Effect size measured: ☐ Relative risk ☐ Odds ratio ☐ Risk difference ☐ Weighted-mean difference ☐ Other:
Measure of variance: ☐ Credible interval, if yes ☐99% ☐95% ☐SD ☐ Other:
Outcome 3: ☐ Binary ☐ Continuous ☐ Categorical non binary Is this outcome effect measure reported as mean or median data? ☐ Mean ☐ Median ☐ NR Format presented: ☐ Text ☐ Table ☐ Figure
Effect size measured: ☐ Relative risk ☐ Odds ratio ☐ Risk difference ☐ Weighted-mean difference ☐ Other:
Measure of variance: ☐ Credible interval, if yes ☐99% ☐95% ☐SD ☐ Other:
Outcome 4: ☐ Binary ☐ Continuous ☐ Categorical non binary Is this outcome effect measure reported as mean or median data? ☐ Mean ☐ Median ☐ NR Format presented: ☐ Text ☐ Table ☐ Figure
Effect size measured: ☐ Relative risk ☐ Odds ratio ☐ Risk difference ☐ Weighted-mean difference ☐ Other:
Measure of variance: ☐ Credible interval, if yes ☐99% ☐95% ☐SD ☐ Other:

Appendix D. Focus Group Questions

AHRQ Network Meta-analysis methods Project

Insight into Meta-analyses of Networks of Studies

Background: Several methodologies exist to indirectly compare interventions, as do modes to implement such methodologies. These include anchored indirect comparisons as described by Bucher et al., Lumley's Frequentist network meta-analysis (of networks with at least one closed loop) and Bayesian network meta-analysis (commonly referred to as mixed treatment comparison (MTC)). In the simplest form, interventions that are compared in separate trials to a common comparator can be compared indirectly in the anchored indirect treatment comparison. However, as a generalization of indirect comparisons, when more than two treatments are being compared indirectly, and at least one pair of treatments is being compared both directly and indirectly (a closed loop is present), both direct and indirect types of data can be used to estimate effects in a network meta-analysis. Although Lumley's Frequentist network meta-analysis and Bayesian MTC have been used to synthesize networks of studies with at least one closed loop, best practices for their use are unclear.

Invitation to Participate: You have been chosen to participate in this focus group given your involvement as a producer of a Lumley's Frequentist network meta-analysis or a Bayesian MTC in the past few years.

This research is funded by the Agency of Healthcare Research and Quality (AHRQ) and is being undertaken by the University of Connecticut/Hartford Hospital Evidence-based Practice Center (UC/HH EPC). The Lead Investigator of this study is Dr. Craig I. Coleman, Co-Director and Methods-Chief of the UC/HH EPC, based at the University of Connecticut School of Pharmacy (UCSoP).

Instructions: As a participant, we are asking that you thoroughly and conscientiously complete the following questionnaire. We anticipated this should take you about 10-15 minutes. All participants will be acknowledged in the resulting published AHRQ report.

When asked to answer questions regarding your specific network meta-analysis, please note that we are referring to the published work defined in the email message sent to you.

If you have any questions related to this survey, please contact:
Craig I. Coleman
Co-Director and Methods-Chief
University of Connecticut/Hartford Hospital Evidence Based Practice Center
Hartford, Connecticut, USA
Email: ccolema@harthosp.org
Tel: 860-545-2096
Fax: 860-545-2277

On behalf of the UC/HH EPC, thank you in advance for your time.

Please review the following before starting.

Please Note: For the purposes of this questionnaire, we will use the following specific definitions:

- **Network meta-analysis** = Simultaneous synthesis of evidence of all pairwise comparisons across >2 interventions.
- **Closed loop network of evidence** = A network of evidence where >2 interventions are being compared indirectly, and at least one pair of interventions is being compared both directly and indirectly.
- **Mixed treatment comparison (MTC)** = The Bayesian approach as described by Lu and Ades whereby both direct and indirect evidence for particular pair-wise comparisons can be combined, and interventions that have not been compared directly are linked through common comparators.
- **Lumley's Frequentist network meta-analysis** = The Frequentist approach originally described by Lumley whereby both direct and indirect evidence are combined when there is at least one closed loop of evidence connecting two interventions of interest (not Bucher's method of anchored/adjusted indirect comparison).

Demographic Information

1. Work setting
    a. Academic
    b. Nonacademic

2. Are you affiliated with an organization involved in conducting evidence synthesis/systematic review/meta-analysis (i.e., AHRQ, Cochrane, NICE)?
    a. Yes
    b. No

    If yes, which_____(list all that apply)

3. Do you consider yourself to personally have the expertise needed to implement a network meta-analysis on your own?
    a. Yes
    b. No

    If yes, which of the following methods (check all that apply)?
        i. Bayesian mixed treatment comparison
        ii. Frequentist network meta-analysis

4. Prior to conducting your network meta-analysis identified at the beginning of this survey, how would you describe your experience with the methodology?
    a. Knew about network meta-analysis and had used it before
    b. Knew about network meta-analysis but had not used it before
    c. Never heard of it

5. Have you had any formal or informal training in network meta-analysis methods?
    a. Yes
    b. No
    c. If yes, please describe:_____

6. How many network meta-analyses have you been involved in conducting?
    a. Just this one
    b. 2-4
    c. 5 or more

7. What was your role on the network meta-analysis identified at the beginning of this questionnaire (check all that apply)?
    a. Clinical advice/clinical interpretation/policy development
    b. Protocol development
    c. Developed search strategy
    d. Data extraction
    e. Statistical advice/methodologist

f. Writing or critical revision of manuscript/report
g. Obtaining of funding
h. Other (explain):_____

Using the 5-point Likert scale, please respond to the following statements in regard to network meta-analysis in general.

1= strongly disagree; 2=disagree; 3=neutral; 4=agree; 5=strongly agree

8. The terms "network meta-analysis" is used unambiguously and consistently in the medical literature.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

    If strongly disagree or disagree, please explain:

9. The terms "mixed treatment comparison" is used unambiguously and consistently in the medical literature.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

    If strongly disagree or disagree, please explain:

10. The terms "Frequentist network meta-analysis" is used unambiguously and consistently in the medical literature.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

    If strongly disagree or disagree, please explain:

11. Synthesizing direct evidence only from sufficient head-to-head or randomized controlled trials takes precedence over analysis containing indirect evidence.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

12. The combination of indirect and direct evidence adds valuable information that is not available from head-to-head comparisons.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

13. The combination of indirect and direct evidence yields a more refined and precise estimate of the interventions directly compared.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

14. The combination of indirect and direct evidence broadens the external validity of the analysis.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

15. Where analysis of both direct and indirect comparisons is undertaken, each approach should be considered and reported separately.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

16. When conducting a network meta-analysis, an investigator should consider restricting a search to the minimum number of interventions of interest.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

17. When conducting a network meta-analysis, an investigator should consider including comparisons not of direct interest (e.g., placebo controls and therapies no longer used in current practice).
    a. Strongly disagree
    b. Disagree

c. Neutral
d. Agree
e. Strongly agree

18. The more interventions that are included in a network meta-analysis, the greater uncertainty is reduced, precision is increased, and the ability to establish whether various sources of evidence agree with each other is enhanced.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

19. Network meta-analyses should prove a graphical depiction of the evidence network.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

20. The specific statistical code used should be available either as part of the manuscript, appendix/supplemental material, or available on an external website for the reader to freely access.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

21. Current guidance on how to conduct and report a network meta-analysis is sufficient.
    a. Strongly disagree
    b. Disagree
    c. Neutral
    d. Agree
    e. Strongly agree

    If strongly disagree or disagree, please explain:

22. How much did the following play into your decision to conduct a Bayesian mixed treatment comparison meta-analysis?

The method allows for the ranking of Interventions according to the probability they are best.	Not at all	A little	Moderately	Quite a bit	Extremely
The method allows investigators to check and compare the fit of a model(s).	Not at all	A little	Moderately	Quite a bit	Extremely

The methods ability to handle multi·arm studies (those with more than 2 treatment groups).	Not at all	A little	Moderately	Quite a bit	Extremely
Frequency of use in previously published network meta·analyses.	Not at all	A little	Moderately	Quite a bit	Extremely
Ease of software implementation.	Not at all	A little	Moderately	Quite a bit	Extremely
The amount of methodological research supporting this method.	Not at all	A little	Moderately	Quite a bit	Extremely
The method's ability to combine trials reporting result in different formats, for example binomial data and summary log odds with variance (multi· or shared parameter models).	Not at all	A little	Moderately	Quite a bit	Extremely
Access to pre·bullt models.	Not at all	A little	Moderately	Quite a bit	Extremely
Requirement to specify priors which are often arbitrary.	Not at all	A little	Moderately	Quite a bit	Extremely
Collaborator(s) or your prior experience and/or expertise.	Not at all	A little	Moderately	Quite a bit	Extremely

23. We involved a researcher/collaborator in your project, solely due to their methodological expertise in Bayesian mixed treatment comparison meta-analysis?
    a. True
    b. False

24. Formal guidance was used to guide the conduction of your Bayesian mixed treatment comparison meta-analysis.
    a. True
    b. False

    If true, please specify the guidance used and provide a complete reference if possible:

25. What are the three most significant barriers to conducting a Bayesian mixed treatment comparison meta-analysis?
    a.
    b.
    c.

26. What are the three most significant strengths of conducting a Bayesian mixed treatment comparison meta-analysis?
    a.
    b.
    c.

27. How was the code used in your analysis derived (e.g., built from scratch; used/adapted previously published/publically available code; used a wrapper such as BugsXLA or other to generate code, other source)?

28. How were your prior distributions chosen and why were these distributions chosen over others?

Appendix E. Excluded Studies

Table 1. Excluded studies at the full text level

Not a systematic review published in the English language from January 1, 2006 to July 30, 2011 (n=9)
Basu A, Meltzer HY, Dukic V. Estimating transitions between symptom severity states over time in schizophrenia: a Bayesian meta-analytic approach. Stat Med 2006 Sep 15;25(17):2886-2910.
Biondi-Zoccai GG, Lotrionte M, Abbate A, Valgimigli M, Testa L, Burzotta F, et al. Direct and indirect comparison meta-analysis demonstrates the superiority of sirolimus- versus paclitaxel-eluting stents across 5854 patients. Int J Cardiol 2007 Jan 2;114(1):104-105.
Biondi-Zoccai G, Lotrionte M, Moretti C, Agostoni P, Sillano D, Laudito A, et al. Percutaneous coronary intervention with everolimus-eluting stents (Xience V): systematic review and direct-indirect comparison meta-analyses with paclitaxel-eluting stents (Taxus) and sirolimus-eluting stents (Cypher). Minerva Cardioangiol 2008 Feb;56(1):55-65.
Buti J, Glenny AM, Worthington HV, Nieri M, Baccini M. Network meta-analysis of randomised controlled trials: direct and indirect treatment comparisons. Eur j oral implantol 2011;4(1):55-62.
Moayyedi P, Shelly S, Deeks JJ, Delaney B, Innes M, Forman D. Pharmacological interventions for non-ulcer dyspepsia. Cochrane Database of Systematic Reviews 2011;2.
Singh JA, Christensen R, Wells GA, Suarez-Almazor ME, Buchbinder R, Lopez-Olivo MA, et al. A network meta-analysis of randomized controlled trials of biologics for rheumatoid arthritis: a Cochrane overview. CMAJ 2009 Nov 24;181(11):787-796.
Trkulja V, Kolundzic R. Rivaroxaban vs dabigatran for thromboprophylaxis after joint-replacement surgery: exploratory indirect comparison based on meta-analysis of pivotal clinical trials. Croat Med J 2010 Apr 15;51(2):113-123.
Virgili G, Novielli N, Menchini F, Murro V, Giacomelli G. Pharmacological treatments for neovascular age-related macular degeneration: can mixed treatment comparison meta-analysis be useful? Curr Drug Targets 2011 Feb;12(2):212-220.
Wong MC, Clarkson J, Glenny AM, Lo EC, Marinho VC, Tsang BW, et al. Cochrane reviews on the benefits/risks of fluoride toothpastes. J Dent Res 2011 May;90(5):573-579.
Did not conduct meta-analysis of clinical effectiveness using randomized controlled trials (n=8)
Jefferson T, Di Pietrantonj C, AlAnsary LA, Ferroni E, Thorning S, Thomas RE. Vaccines for preventing influenza in the elderly. Cochrane Database of Systematic Reviews 2010;6.
Jefferson T, Rivetti A, Harnden A, Di Pietrantonj C, Demicheli V. Vaccines for preventing influenza in healthy children. Cochrane Database of Systematic Reviews 2009;1.
Medical Advisory Secretariat. Ontario Ministry of Health and Long-Term Care (MAS). Artificial disc replacement for lumbar and cervical degenerative disc disease- update: an evidence-based analysis (Structured abstract). Health Technology Assessment Database 2011 Issue 3, John Wiley & Sons, Ltd. Chichester:UK. Dson: ST.
Miller, J. Chan, BKS. Nelson,H. Hormone replacement therapy and risk of venous thromboembolism (Structured abstract). Health Technology Assessment Database 2011 Issue 3, John Wiley & Sons, Ltd. Chichester:UK. Dson: ST.
Paravastu SCV, Mendonca D, Da Silva A. Beta blockers for peripheral arterial disease. Cochrane Database of Systematic Reviews 2010;3.
Richy FF, Banerjee S, Brabant Y, Helmers S. Levetiracetam extended release and levetiracetam immediate release as adjunctive treatment for partial-onset seizures: an indirect comparison of treatment-emergent adverse events using meta-analytic techniques. Epilepsy Behav 2009 Oct;16(2):240-245.
Takeda AL, Colquitt J, Clegg AJ, Jones J. Pegaptanib and ranibizumab for neovascular age-related macular degeneration: a systematic review. Br J Ophthalmol 2007 Sep;91(9):1177-1182.
van Till JO, van Ruler O, Lamme B, Weber RJ, Reitsma JB, Boermeester MA. Single-drug therapy or selective decontamination of the digestive tract as antifungal prophylaxis in critically ill patients: a systematic review. Crit Care 2007;11(6):R126.
Did not conduct an indirect comparison of more than two arms (n=113)
Abba K, Ramaratnam S, Ranganathan NL. Anthelmintics for people with neurocysticercosis. Cochrane Database of Systematic Reviews 2010;6.
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Appendix F. Evidence Tables

Table 2. Journal level characteristics

Journal	Included studies	Impact factor*	Supplement or appendix; format	Word count limit	Table limit	Figure limit
Alimentary Pharmacology & Therapeutics	Edwards, 2009a	3.861	Y, online	N	N	N
Annals of Clinical Microbiology & Antimicrobials	Mills, 2009	1.71*	Y, not specified	N	N	N
Annals of Internal Medicine	Gross, 2011	16.792	Y, not specified	3,500-4,000	4 tables or figures	4 tables or figures
Archives of Internal Medicine	Sciarretta, 2011; Cooper, 2006	10.639	Y, online	3,500	6 to 8 tables or figures	6 to 8 tables or figures
BMC Neurology	Quilici, 2009	2.797	Y, online	N	N	N
British Medical Journal	Baldwin, 2011; Hartling, 2011l Jalota, 2011; Trelle, 2011; Wandel, 2010; Stettler, 2008; Lam, 2007	13.471	Y, online	N	N	N
British Journal of Anaesthesia	Maund, 2011†	4.224	Y, online	5,000	N	N
British Journal of Cancer	Coon, 2009	4.831	Y, online	5,000-5,500	1 table reduces word limit by 200	1 figure reduces word limit by 200
British Journal of Ophthalmology	Van den Bruel, 2011	2.934	Y, online	3,000	5 tables or figures	5 tables or figures
Cancer Treatment Reviews	Golfinopoulus, 2009	6.811	N	N	N	N
Clinical Therapeutics	Edwards, 2009b	2.551	Y, online	5,500-6,000	N	N
Cochrane Database of Systematic Reviews	Singh, 2011; Walsh, 2010	6.186	N	N	N	N
Current Medical Research and Opinion	van de Kerkhof, 2011; Orme, 2010; Uthman, 2010; Vissers, 2010; Edwards, 2009c; Jansen, 2009; Jansen, 2006	2.609*	Y, online	11,200	N	N
Dermatology	Bansback, 2009	2.714	Y, not specified	13 pages for text, tables, figures	Included in page count	Included in page count

Journal	Included studies	Impact factor*	Supplement or appendix; format	Word count limit	Table limit	Figure limit
Drug and Alcohol Dependence	Meader, 2009	3.365	Y, online	6,000	N	N
Europace	Freemantle, 2011	1.842	Y, not specified	5,000	5	5
Gastroenterology	Woo, 2010	12.023	Y, online	6,000	Minimum of 4 to 6 figures or illustrations	Minimum of 4 to 6 figures or illustrations
Health technology assessment (Winchester, England)	Maund, 2011†	4.197	N	N	N	N
International Clinical Psychopharmacology	Hansen, 2008	2.762	Y, online	7,500	N	N
The Journal of the American medical Association	Anothaisintawee, 2011; Phung, 2010	30	Y, online	3,500	4 tables or figures	4 tables or figures
Journal of Antimicrobial Chemotherapy	Freemantle, 2011	4.659	Y, online	N	N	N
Journal of Hospital Infection	Wang, 2010	3.078	N	5,000	N	N
Journal of Hypertension	Coleman, 2008	3.98	Y, online	N	N	N
Journal of the American College of Cardiology	Mills, 2008	14.293	N	4,500	N	N
Journal of the National Cancer Institute	Mauri, 2008; Kyrgiou, 2006	14.697	Y, online	6,000	8 table or figures	8 tables or figures
Lancet	Trikalinos, 2009; Elliot, 2007; Cipriani, 2009l Stettler, 2007	33.633	Y, online	4,500	“Should include about 5 illustrations”	“Should include about 5 illustrations”
Lancet Infectious Disease	Manzoli, 2009	16.144	Y, online	3,000-5,000	“Should include about 5 illustrations”	“Should include about 5 illustrations”
Lancet Neurology	Bangalore, 2011	21.659	Y, online	3,000-4,500	“Should include about 5 illustrations”	“Should include about 5 illustrations”
Lancet Oncology	Golfinopoulos, 2007	17.764	Y, online	3,000-5,000	“Should include about 5-6 illustrations”	“Should include about 5-6 illustrations”
Pharmacotherapy	Baker, 2009	2.631	N	7,000	N	N
QJM	Mills, 2011	2.146*	N	N	N	N

Journal	Included studies	Impact factor*	Supplement or appendix; format	Word count limit	Table limit	Figure limit
Rheumatology	Nixon, 2007	4.171	Y, online	3,500	6 figures or tables	6 figures or tables
Seminars in Arthritis and Rheumatism	Jansen, 2011; Bergman, 2010	4.744*	N	N	N	N
Sleep Medicine	Quilici, 2008	3.43	Y, online	N	N	N
Value in Health	Dakin, 2010	2.342	Y, online	N	N	N

Abbreviations: Y: yes; N: no

*: The impact factor was obtained from Web of Science, except when the symbol appears for that journal the impact factor was not available in Web of Science and was taken from the journal's website.
†: Published as a manuscript and health technology assessment report, but counted as one unique publication

Table 3. General characteristics of Bayesian mixed treatment comparisons

Author, year (N authors)	Method-ologist*	Country	Funding	# printed pages	Affiliation	Supplement or appendix	Disease state evaluated	N and type of interventions compared	N trials, N patients	Network pattern
Baldwin, 2011 (4)†	Yes	UK	Industry	11	No	Yes	Behavioral Health (GAD)	10, Rx	27 3,989	Network with ≥1 closed loop
Bangalore, 2011 (10)	No	USA	Unfunded	18	No	Yes	Cardiology (anti-hypertensives)	8, Rx	70 324,168	Network with ≥1 closed loop
Freemantle, 2011 (3)	No	UK	Industry, other	11	No	No	Infectious disease (invasive mold disease)	7, Rx	10 4,094	Ladder
Gross, 2011 (9)	No	Brazil	Government /foundation	8	No	Yes	Endocrinology (T2DM)	6, Rx	18 4,535	Network with ≥1 closed loop
Hartling, 2011 (8)	Yes	Canada, Portugal	Government /foundation	10	No	Yes	Respiratory (acute bronchiolitis)	7, Rx	48 4897	Network with ≥1 closed loop
Jansen, 2011 (4)	No	USA	Industry	10	No	Yes	Endocrinology (osteoporosis)	6, Rx	8 20,902	Star
Maund, 2011 (6)	No	UK	Government /foundation	6‡	HTA	Yes	Pain (major surgery)	4, Rx	60 5,236	Network with ≥1 closed loop

Author, year (N authors)	Method-ologist*	Country	Funding	# printed pages	Affiliation	Supplement or appendix	Disease state evaluated	N and type of interventions compared	N trials, N patients	Network pattern
Mills, 2011 (10)	Yes	Canada	NR	16	No	No	Cardiology (statin in any population)	7, Rx	76 170,255	Star
Sciarretta, 2011 (5)	Yes	Italy	NR	11	No	No	Cardiology (HTN and heart failure)	8, Rx	26 223,313	Network with ≥1 closed loop
Trelle, 2011 (8)	Yes	Switzerland	Government /foundation	11	No	Yes	Pain (NSAIDs)	8, Rx	31 116,429	Network with ≥1 closed loop
van de Kerkhof, 2011 (4)	No	UK	Industry	13	No	Yes	Dermatology (psoriasis)	17, Rx	19 9,134	Network with ≥1 closed loop
van den Bruel, 2011 (6)	No	Belgium	Unfunded	6	No	No	Opthamology (cataract surgery)	6, Devices	21 1,769	Network with ≥1 closed loop
Bergman, 2010 (6)	Yes	USA	Industry	9	No	Yes	Rheumatology (RA)	5, Rx	18 10,419	Star[§]
Dakin, 2010 (3)	Yes	UK	Industry	12	No	Yes	Gastroenterology (chronic hepatitis B)	8, Rx	23 3,702	Network with ≥1 closed loop
Orme, 2010 (5)	No	UK	Industry	18	No	Yes	Opthamology (glaucoma)	10, Rx[‖] 19, Rx	93 16,898	Network with ≥1 closed loop
Phung, 2010 (4)	No	USA	Government /foundation	9	No	Yes	Endocrinology (T2DM)	7, Rx	27 11,198	Network with ≥1 closed loop
Uthman, 2010 (2)	Yes	UK	NR	7	No	No	Behavioral Health (anxiety)	6, Rx	16 IC	Network with ≥1 closed loop
Vissers, 2010 (5)	No	Netherlands	Industry	9	No	No	Pain (cancer)	5, Rx	6 594	Network with ≥1 closed loop[§]
Walsh, 2010 (6)	No	UK	Government /foundation	221[¶]	Cochrane	No	Dental	7, Rx	75 105,969	Network with ≥1 closed loop

Author, year (N authors)	Method-ologist*	Country	Funding	# printed pages	Affiliation	Supplement or appendix	Disease state evaluated	N and type of interventions compared	N trials, N patients	Network pattern
Wandel, 2010 (8)	Yes	Switzerland	Government /foundation	9	No	No	Rhuematology (OA)	4, Rx	10 3,803	Network with ≥1 closed loop
Wang, 2010 (9)	No	China	Government /foundation	11	No	No	Infectious Disease (CVCs for infections)	10, Device	48 11,525	Network with ≥1 closed loop
Woo, 2010 (10)	No	Canada	Industry	12	No	Yes	Gastroenterology (chronic hepatitis B)	10, Rx	20 8,624	Network with ≥1 closed loop§
Baker, 2009 (3)	No	USA	NR	15	No	No	Pulmonology (COPD)	5, Rx	43 31,020	Network with ≥1 closed loop§
Bansback, 2009 (6)	Yes	Canada	Industry	10	No	No	Dermatology (psoriasis)	8, Rx	22 9,917	Network with ≥1 closed loop§
Cipriani, 2009 (12)	Yes	Italy	Unfunded	13	No	No	Behavioral Health (depression)	12, Rx	117 25,928	Network with ≥1 closed loop
Edwards, 2009a (4)	No	UK	Industry	10	No	No	Gastroenterology (erosive esophagitis)	5, Rx	12 5,181	Network with ≥1 closed loop
Edwards, 2009b (2)	No	UK	Industry	14	No	Yes	Behavioral Health (bipolar and schizophrenia)	5, Rx	48 NR	Network with ≥1 closed loop
Edwards, 2009c (4)	Yes	UK	Industry	11	No	No	Infectious disease (inpatient infection)	5, Rx	34 NR	Star
Golfinopoulos , 2009 (6)	Yes	Greece	NR	4	No	Yes	Oncology (unknown primary site)	5, Rx	10 683	Network with ≥1 closed loop§
Jansen, 2009 (4)	No	USA	Industry	8	No	No	Endocrinology (osteoporosis)	5, Rx	7 21,848	Star§

Author, year (N authors)	Method-ologist*	Country	Funding	# printed pages	Affiliation	Supplement or appendix	Disease state evaluated	N and type of interventions compared	N trials, N patients	Network pattern
Manzoli, 2009 (6)	Yes	Italy	NR	11	No	Yes	Infectious disease (avian flu vaccine)	13, Other	13 8,382	Network with ≥1 closed loop
Meader, 2009 (1)	No	UK	Unknown	5	No	Yes	Substance Absuse (opiod detoxification)	4, Rx	20 2,112	Network with ≥1 closed loop§
Mills, 2009 (7)	Yes	Canada	Industry	11	No	Yes	Infectious Disease (fungal infection)	8, Rx	11 965	Ladder
Quilici, 2009 (8)	No	UK	Industry	14	No	No	Neuology (DM peripheral neuropathy)	4, Rx	11 2,709	Star§
Thompson Coon, 2009 (8)	No	UK	Government /foundation	6	HTA	No	Oncology (RCC)	3, Rx	3 2,131	Simple star§
Coleman, 2008 (4)	No	USA	NR	8	No	No	Cardiology (anti-hypertensives)	6, Rx	27 126,137	Network with ≥1 closed loop
Mauri, 2008 (5)	Yes	Greece	Unfunded	12	No	Yes	Oncology (breast cancer)	22, Rx	128 26,031	Network with ≥1 closed loop
Mills, 2008 (6)	Yes	Canada	NR	13	No	No	Cardiology (primary prevention, statin)	5, Rx	20 65,261	Star
Quilici, 2008 (7)	No	UK	Industry	12	No	Yes	Neurology (RLS)	3, Rx	5 1,620	Simple star§
Stettler, 2008 (29)	Yes	Switzerland	Government /foundation	11	No	Yes	Cardiology (stents)	3, Device	35 14,799	Closed loop§
Golfinopoulos , 2007 (4)	Yes	Greece	Unfunded	14	No	Yes	Oncology (colorectal cancer)	12, Rx	40 15,802	Network with ≥1 closed loop
Lam, 2007 (2)	No	China	Unfunded	10	No	No	Cardiology (left ventricular dysfunction)	5, Device and Rx	12 8,307	Network with ≥1 closed loop

Author, year (N authors)	Method-ologist*	Country	Funding	# printed pages	Affiliation	Supplement or appendix	Disease state evaluated	N and type of interventions compared	N trials, N patients	Network pattern
Nixon, 2007 (3)	Yes	UK	Other	8	No	No	Rheumatology (RA)	9, Rx	13 6,694	Network with ≥1 closed loop§
Stettler, 2007 (29)	Yes	Switzerland	Government /foundation	12	No	Yes	Cardiology (stents)	3, Device	38 18,023	Simple star§
Cooper, 2006 (4)	No	England	Government /foundation	7	No	Yes	Cardiology (stroke prevention)	8, Rx	19 17,833	Network with ≥1 closed loop
Jansen, 2006 (1)	No	Netherlands	Industry	11	No	No	Endocrinology (DM)	4, Other	12 1,930	Star§
Kyrgiou, 2006 (5)	Yes	Greece	NR	9	No	Yes	Oncology (ovarian cancer)	8, Rx	60 16,478	Network with ≥1 closed loop§

Abbreviations: CODP: chronic obstructive pulmonary disease; CVC: central venous catheter; DM: diabetes mellitus; HTA: Health Technology Assessment; HTN: hypertension; NSAID: non-steroidal anti-inflammatory drugs; RA: rheumatoid arthritis; RCC: renal cell carcinoma; RLS: restless leg syndrome; Rx: pharmacologic; T2DM: type 2 diabetes mellitus;

*: A methodologist was considered an individual with affiliation to a department of statistics, biostatistics, epidemiology, clinical epidemiology, or public health services, as determined by author information and affiliations listed in the publication.
†: Includes both a Bayesian and Frequentist model, therefore appears in both Bayesian and Frequentist tables.
‡: Published as a manuscript and report, with the manuscript serving as the primary data source.
§: Diagram was not provided, pattern determined from study characteristics reported
||: Two models reported
¶: Cochrane report

Table 4. Methodologcal characteristics of Bayesian mixed treatment comparisons

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Baldwin, 2011*	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? Yes Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: 21,000 iterations; 1,000 burn-in Convergence statistics evaluated: Yes, considering kernel density plots Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: No; “Vague prior parameters were chosen” Was a sensitivity analysis conducted based on priors? NR	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Compared consistency of results from mixed treatment meta-analysis and the direct comparative meta-analysis Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Bangalore, 2011	Was traditional meta-analysis run? Yes Model(s): Fixed and random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4.3	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: Yes; vague priors were used for comparisons of treatments so the findings were close to those obtained with frequentist models Was a sensitivity analysis conducted based on priors? NR	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Used various statistical modeling (traditional MA, network MA, and trial sequential analyses) to assess for consistency in the magnitude and direction of effect size Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: “Our meta-analysis refutes a 5.0% to 10.0% relative risk increase in either cancer or cancer related death with most antihypertensive drug classes.” “10% relative risk increase because this small increase in cancer risk is likely to be clinically meaningful”

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Freemantle, 2011	Was traditional meta-analysis run? None for same outcomes analyzed in MTC Model(s): Fixed and random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, DIC Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague priors or not Was a sensitivity analysis conducted based on priors? NR	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: “There is no agent that appears significantly better or worse out of those examined in empirical therapy” Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Gross, 2011	Was traditional meta-analysis run? Yes Model(s): NR Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4.3	Was the code available? Option to email author although no reply Was the raw data available? Yes, in manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? NR	Heterogeneity assessment in traditional meta-analysis: Cochrane Q-statistic, I^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Compare findings with prior meta-analysis and between traditional and network meta-analyses Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Hartling, 2011	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: 220,000 iterations; burn-in 20,000 Convergence statistics evaluated: NR Prior distribution of d: Normal, 0 to 10,000 Prior distribution for σ: Uniform, 0 to 2 (admissions) or 0 to 10 (length of stay) Were priors justified: NR, consider these non-informative priors Was a sensitivity analysis conducted based on priors? Yes	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Cross validation of all contrasts that had direct evidence Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Jansen, 2011	Was traditional meta-analysis run? No Model(s): Fixed effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? Yes, in manscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: Normal(0,1000) Prior distribution for σ: NA Were priors justified: Yes, To not influence the observed results by the prior distribution, a non-informative (i.e. “flat”) normal distribution was used for the treatment effect. Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: Qualitative evaluation of the overlap of confidence intervals Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Maund, 2011	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: Yes Adjustment for covariates: Yes, baseline morphine consumption Model fit tested: Yes, residual deviation and DIC Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? Yes, referral to another website/source Was the raw data available? Yes, in the full report published as a HTA Starting values: NR Number of chains: NR Number of iterations and burn-in: 105,000 iterations; Burn-in 5,000 Convergence statistics evaluated: Yes, NR Prior distribution of d: dnorm(0,0.0001) Prior distribution for σ: dunif(0,2) Were priors justified: Yes, used uninformative priors Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: Consideration of PICO, visualization of results, Chi^2, I^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Compared with direct evidence synthesis within this report and with prior reports. Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Mills, 2011	Was traditional meta-analysis run? Yes Model(s): NR Adjustment for multiple arms: NR Adjustment for covariates: Yes, low-density lipoprotein Model fit tested: Yes, DIC Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: 40,000 Iterations; 20,000 burn-in Convergence statistics evaluated: Yes, trace and time series plots; Gelman Rubin statistic for burn-in Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR, and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: I^2, heterogeneity p-values Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Sciarretta, 2011	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS	Was the code available? No Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: 2 Number of iterations and burn-in: 105,000 Iterations; 5,000 burn-in Convergence statistics evaluated: Yes, Gelman Rubin statistics to determine burn in Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR; We also used noninformative priors that represented complete lack of credible prior information. Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: Chi-squared Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Inconsistency was calculated as suggested by Lu and Ades, σ^2_w Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Trelle, 2011	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: Yes Adjustment for covariates: NR Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? Yes Did authors rank order interventions? No Software used: WinBUGS	Was the code available? Yes, in the online supplement Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: 100,000 iterations; 50,000 burn-in Convergence statistics evaluated: Yes, Gelman Rubin statistic Prior distribution of d: dnorm(0, 0.001) Prior distribution for σ: dunif(0,2) Were priors justified: NR, used minimally informative priors Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in Bayesian meta-analysis: Tau^2 Evaluation of inconsistency: Inconsistency factors, defined as the difference in log rate ratios derived from direct and indirect comparisons Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: Pre-specified rate ratio of 1.3 as the primary threshold for outcomes evaluated

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
van de Kerkhof, 2011	Was traditional meta-analysis run? No Model(s): Fixed and random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, but method NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: Yes, In order not to influence the estimates by the choice of the prior distribution, a non-informative (i.e., 'flat') distribution was used for the parameters of the model. With such a prior distribution, results as reflected with the posterior distribution are solely driven by the data. Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Compare results with previously conducted meta-analyses Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Van den Bruel, 2011	Was traditional meta-analysis run? Yes Model(s): Fixed and random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, DIC Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not report if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Consistency of evidence sources was assessed by calculating the posterior mean residual deviance for each individual treatment arm Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: A difference of more than 100 cells/mm^3 was clinically relevant difference, further justified in text

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Bergman, 2010	Was traditional meta-analysis run? No Model(s): Fixed and random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: Yes, “Analysis was conducted without prior assumptions about coefficient sizes… this is known as noninformative priors. Under these conditions, the results of Bayesian analysis are equivalent to results obtained through the traditional statistical perspective…” Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: “This meta-analysis suggests the efficacy of toclizumab is as least as good as that of other biologics and may be even better” Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Dakin, 2010	Was traditional meta-analysis run? Yes Model(s): Fixed and random effects Adjustment for multiple arms: Yes Adjustment for covariates: NR Model fit tested: Yes, DIC and residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4	Was the code available? Yes, in the online supplement Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: 2 Number of iterations and burn-in: 520,000 to 945,000 Iterations; 500,000 to 925,000 burn-in Convergence statistics evaluated: Yes, NR Prior distribution of d: dnorm(0, 0.001) Prior distribution for σ: dnorm(0,K)I(0,) or unif(0,10) Were priors justified: Yes, “Sensitivity analyses suggested that the posterior estimates of the uncertainty around treatment effects (but not the posterior means) were sensitive to the priors used. Informative half-normal priors were therefore used for the between-studies SD in order to allow this external data to help inform the between-studies SD; these distributions were based on a meta-analysis of interferon trials identified in a published systematic review.” Was a sensitivity analysis conducted based on priors? Yes, alternate priors NR	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in Bayesian meta-analysis: Between study SD Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Orme, 2010	Was traditional meta-analysis run? No Model(s): Random effects Adjustment for multiple arms: Yes Adjustment for covariates: Not in main model but sensitivity analysis conducted to adjust for baseline intra-ocular pressure Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: 2 Number of iterations and burn-in: 120,000 Iterations; 100,000 burn-in Convergence statistics evaluated: Yes, visual plot inspection Prior distribution of d: Normal Prior distribution for σ: Uniform(0,10) Were priors justified: No, “Uninformative normal priors were used for all model parameters except for the between-studies SD for which an uninformative uniform prior.” Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: Between study SD Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Phung, 2010	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not report if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Qualitative comparison of results from traditional and network analyses Equivalence claims: NR Non-inferiority claims: Drugs investigated produce similar glucose lowering when applying minimally important difference Minimally important difference defined: 0.4% non-inferioirity margin used by the Food and Drug Administration

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Uthman, 2010	Was traditional meta-analysis run? No Model(s): NR Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? No Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not report if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Vissers, 2010	Was traditional meta-analysis run? No Model(s): Fixed effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, method NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Walsh, 2010	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: Yes Adjustment for covariates: NR Model fit tested: Yes, median sum deviation Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS	Was the code available? Yes, external website Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: dnorm(0,0.001) Prior distribution for σ: dunif(0,2) Were priors justified: NR, code says “vague priors” Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: Chi^2 and I^2 Heterogeneity assessment in Bayesian meta-analysis: Tau Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Wandel, 2010	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: No Adjustment for covariates: Yes, time, allocation concealment, intention-to-treat, quality, glucosamine type, quality control of preparation, joint type Model fit tested: Yes, Q-Q plots Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: 150,000 iterations; 50,000 burn-in Convergence statistics evaluated: Yes, Gelman Rubin statistic Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: No, model used minimally informative prior distributions Was a sensitivity analysis conducted based on priors? Yes	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in Bayesian meta-analysis: Tau^2, calculated p-value for heterogeneity Evaluation of inconsistency: Inconsistency factors Equivalence claims: “None of the pooled estimates crossed the pre-specified boundary of a minimal clinically important difference of -0.9 cm on a 10cm visual analogue scale.” Non-inferiority claims: “The lower end of the credible intervals did not cross the pre-specified boundaries.” Minimally important difference defined: Minimal clinically important difference of 0.37 SD units corresponding to 0.9cm on a 10cm visual analogue scale. Based on recent studies in patients with OA.

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Wang, 2010	Was traditional meta-analysis run? No Model(s): Fixed and random effects Adjustment for multiple arms: NR Adjustment for covariates: In sensitivity analysis only (methodological quality and no central venous catheter per patient) Model fit tested: Yes, DIC and residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS 1.4.3	Was the code available? No Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: Tau^2 Evaluation of inconsistency: Results of head-to-head comparisons from previous conventional meta-analyses were concordant with results from our network meta-analysis, indicating that the network of trials was consistent Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Woo, 2010	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4.3	Was the code available? Yes, in online supplement Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: 3 Number of iterations and burn-in: 25,000 iterations; 5,000 burn-in Convergence statistics evaluated: Yes, Gelman Rubin Brooke statistic Prior distribution of d: dnorm(0, 0.1) Prior distribution for σ: dt(0,1,2)I(0,) Were priors justified: NR and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in Bayesian meta-analysis: Between study SD in log OR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Baker, 2009	Was traditional meta-analysis run? Yes Model(s): NR Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS + BUGSXLA Wrapper	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: Cochrane Q statistic Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NA

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Bansback, 2009	Was traditional meta-analysis run? No Model(s): NR Adjustment for multiple arms: NR Adjustment for covariates: Yes, placebo response rate Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4.1	Was the code available? No Was the raw data available? Yes, in manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: 15,000 iterations; 5,000 burn-in Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR, uninformative prior distributions for each treatment. Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Cipriani, 2009	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? Yes Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? No Was the raw data available? Yes, referred to external website Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague prior used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: I^2 and visual inspection of forest plots Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Calculated ratio of odds ratios for indirect versus direct evidence whenever indirect estimates could be constructed with a single common comparator. Incoherence was defined as the disagreement between direct and indirect evidence with a 95% confidence interval excluding 1 Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Edwards, 2009a	Was traditional meta-analysis run? No Model(s): Fixed and random effects Adjustment for multiple arms: NR Adjustment for covariates: Yes, publication year Model fit tested: Yes, DIC Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4.3	Was the code available? No Was the raw data available? Yes, in manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: SD Evaluation of inconsistency: Posterior mean residual deviance Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Edwards, 2009b	Was traditional meta-analysis run? No Model(s): Random effects Adjustment for multiple arms: Yes Adjustment for covariates: NR Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: Yes, Vague prior distributions were used for comparisons of treatments so that the findings would be close to those obtained with frequentist methods. Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: Pre-specified SD values within pairwise comparisons Evaluation of inconsistency: Estimated by assessing the posterior mean residual deviance Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Edwards, 2009c	Was traditional meta-analysis run? No Model(s): Fixed and random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, residual deviance and DIC Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? No Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not report if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Posterior mean residual deviance Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Golfinopoulos, 2009	Was traditional meta-analysis run? Yes Model(s): NR Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: 3 Number of iterations and burn-in: 70,000 iterations; 20,000 burn-in Convergence statistics evaluated: Yes, ensured after observing mixing of 3 chains Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR, used approximately vague normal priors for all location parameters Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: State “there was no clear evidence for incoherence” although do not report methods used to determine this Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Jansen, 2009	Was traditional meta-analysis run? No Model(s): Fixed and random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? Yes, in manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: Norm (0,1000) Prior distribution for σ: NR Were priors justified: Yes, In order not to influence the observed results by the prior distribution, a non-informative (i.e. 'flat') normal distribution was used for the log odds ratio of each treatment versus placebo. Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Manzoli, 2009	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS 1.4.3	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: 3 Number of iterations and burn-in: 250,000 iterations; 50,000 burn-in Convergence statistics evaluated: Yes, observing mix of 3 chains and Brooks Gelman Rubin diagnostic tool Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR, we used approximately vague normal priors for all location parameters Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Assessed inconsistency between different sources of evidence (direct and indirect) in each closed loop, as previously described Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: Absolute immunogenicity of 70% considered satisfactory based on the Committee for Proprietary Medicinal Products, and used to make superiority claims.

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Meader, 2009	Was traditional meta-analysis run? Yes Model(s): Fixed and random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? Yes, online supplement Was the raw data available? Yes, in manuscript Starting values: NR Number of chains: 2 Number of iterations and burn-in: 100,000 iterations; 20,000 burn-in Convergence statistics evaluated: Yes, Brooks Gelman Rubin diagnostic plot Prior distribution of d: dnorm(0,.001) Prior distribution for σ: sdunif(0,2) Were priors justified: NR and did not specify if vague prior used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: State that direct and mixed treatment comparison were largely consistent for most data although do not report methods to determine consistency Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Mills, 2009	Was traditional meta-analysis run? Yes Model(s): Fixed effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: Multiple Number of iterations and burn-in: 100,000 iterations; 500 burn-in Convergence statistics evaluated: Yes, trace and times series plots Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: “Our study suggests that azoles and echinocandins are equally effective interventions for treating invasive candidiasis and confirms the Infectious Disease Society of America guidelines” Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Quilici, 2009	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: NR	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR, specify non-informative priors used Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: Cochrane Q-test, I^2, and Tau^2 Heterogeneity assessment in Bayesian meta-analysis: Tau^2 Evaluation of inconsistency: NR Equivalence claims: “Using stricter criteria of equivalence, there was no difference in the 24 hour average pain severity scores between duloxetine and each of the comparator drugs, and we conclude duloxetine is equivalent to gabapentin and pregabalin on this outcome.” Non-inferiority claims: “Duloxetine was not inferior to pregabalin in 24 hour average pain severity.” Minimally important difference defined: “A difference of 2 points on the 11 point scale was selected as the non-inferiority margin for the 24 hour average pain severity, based on previous research”

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Thompson Coon, 2009	Was traditional meta-analysis run? No Model(s): Fixed effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS	Was the code available? No Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: 110,000 iterations; 10,000 burn-in Convergence statistics evaluated: NR Prior distribution of d: N(0, 0.001) Prior distribution for σ: NR Were priors justified: NR, Vague earlier distributions were used in the analyses Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: Examined trial populations and comparability of outcomes in the common treatment group facilitating the comparison Evaluation of inconsistency: Compare findings with prior systematic review Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Coleman, 2008	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: Yes Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? NR Software used: WinBUGS	Was the code available? No Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: Cochrane Q statistic Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Compare results of network and traditional meta-analyses Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Mauri, 2008	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? Yes, in the online supplement Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in Bayesian meta-analysis: Tau^2 Evaluation of inconsistency: Estimated incoherence in each closed loop, none found except one loop with modest incoherence Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Mills, 2008	Was traditional meta-analysis run? Yes Model(s): NR Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: Multiple Number of iterations and burn-in: 100,000 iterations; 500 burn-in Convergence statistics evaluated: Yes, trace and time series plots Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify of vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: I^2 and heterogeneity p-value Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Compare results with previously conducted meta-analyses Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Quilici, 2008	Was traditional meta-analysis run? Yes Model(s): Fixed effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: Yes, residual deviance and DIC Was there graphical representation of the posterior distribution? Yes Did authors rank order interventions? Yes Software used: WinBUGS 1.4.1	Was the code available? Yes, in appendix Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: 150,000 iterations; 50,000 burn-in Convergence statistics evaluated: Yes, considering different initial starting values and by varying the lengths of both 'burn-in' and sample size Prior distribution of d: dnorm (0.0, 0.001) Prior distribution for σ: NR Were priors justified: NR, consider vague for D Was a sensitivity analysis conducted based on priors? Yes, on heterogeneity priors	Heterogeneity assessment in traditional meta-analysis: Cochran Q test, I^2, and tau^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Examined by comparing actual data points with those predicted by the model using Bayesian mixed p-values Equivalence claims: NR Non-inferiority claims: NI of pramipexole versus ropinirole tested; Report the probabilities for pramipexole being non-inferioir to ropinirole for International Resteless Leg Study Group Rating Scale and Clinical Global Impression-Improvement Minimally important difference defined: Difference of 2.5 points on International Resteless Leg Study Group Rating Scale score between pramipexole and ropinirole and a 10% change for the number of Clinical Global Impression-Improvement responders were considered non-significant clinical differences and used as non-inferioirity margins

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Stettler, 2008	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: Yes, trial covariates Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS 1.4.1	Was the code available? No Was the raw data available? Yes, referral to online appendix Starting values: NR Number of chains: NR Number of iterations and burn-in: 100,000 iterations; 60,000 burn-in Convergence statistics evaluated: Yes, Gelman Rubin statistic Prior distribution of d: N~(0,1000) Prior distribution for σ: NR Were priors justified: NR Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in Bayesian meta-analysis: Tau^2 Evaluation of inconsistency: Calculated inconsistency factors- the estimated difference between the log hazard ratios from direct comparisons within randomized trials and the log hazard ratios from indirect comparisons between randomized trials in common. Compare results from traditional and network meta-analyses. Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Golfinopoulos, 2007	Was traditional meta-analysis run? Yes Model(s): NR Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS + S-Plus	Was the code available? No Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and do not specify of vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: “No direct evidence was available and evaluation of incoherence was therefore impossible” method Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Lam, 2007	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: Yes Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS 1.4.1	Was the code available? No Was the raw data available? No Starting values: NR Number of chains: 3 Number of iterations and burn-in: 55,000 iterations, 5,000 burn-in Convergence statistics evaluated: NR Prior distribution of d: Normal (0, 10,000) Prior distribution for σ: Uniform (0, 2) Were priors justified: Yes, "To ensure that overall effects were dominated by data from the trials and not influenced by choice of initial distribution we used low information (noninformative) prior distributions." Was a sensitivity analysis conducted based on priors? Yes	Heterogeneity assessment in traditional meta-analysis: Chi^2/Cochran Q test, I^2, L'Abbe plots Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Present results of traditional and network analyses together showing consistency of data Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Nixon, 2007	Was traditional meta-analysis run? No Model(s): Random effects Adjustment for multiple arms: Yes Adjustment for covariates: Yes, model includes average disease duration and average baseline HAQ for each study Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS 1.4.3	Was the code available? No Was the raw data available? Yes, in manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and do not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Stettler, 2007	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: Yes, follow-up time Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: WinBUGS	Was the code available? No Was the raw data available? Yes, online supplement Starting values: NR Number of chains: NR Number of iterations and burn-in: Up to 1000,000 iterations; 80,000 burn-in Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR, used vague priors Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: Tau^2 Heterogeneity assessment in Bayesian meta-analysis: Tau^2 Evaluation of inconsistency: Determined consistency of network with use of inconsistency factors. Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Cooper, 2006	Was traditional meta-analysis run? No Model(s): Random effects Adjustment for multiple arms: Yes Adjustment for covariates: NR Model fit tested: Yes, residual deviance Was there graphical representation of the posterior distribution? No Did authors rank order interventions? No Software used: NR	Was the code available? Yes, in the appendix Was the raw data available? Yes, in the manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: Uniform (-10,10) Prior distribution for σ: Uniform (0,2) Were priors justified: No, all priors were intended to be vague Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Generic comparison to previously conducted meta-analyses Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Jansen, 2006	Was traditional meta-analysis run? No Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: Yes, baseline A1C and variance of trials Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? No Was the raw data available? Yes, in manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: Normal (0, 1000) Prior distribution for σ: NR Were priors justified: Yes In order not to influence the observed results by the prior distribution, non-informative (i.e. 'flat') normal distributions were used for the (relative) treatment effects Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: NA Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: NR Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Author, year	Meta-analysis model	MCMC details and Priors	Heterogeneity, inconsistency, and claims of equivalence or non-inferiority
Kyrgiou, 2006	Was traditional meta-analysis run? Yes Model(s): Random effects Adjustment for multiple arms: NR Adjustment for covariates: NR Model fit tested: NR Was there graphical representation of the posterior distribution? No Did authors rank order interventions? Yes Software used: WinBUGS	Was the code available? No Was the raw data available? Yes, in manuscript Starting values: NR Number of chains: NR Number of iterations and burn-in: NR Convergence statistics evaluated: NR Prior distribution of d: NR Prior distribution for σ: NR Were priors justified: NR and did not specify if vague priors used or not Was a sensitivity analysis conducted based on priors? No	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in Bayesian meta-analysis: NR Evaluation of inconsistency: Calculated incoherence values Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NR

Abbreviations: DIC=deviance informtion criterion; HTA=health technology assessment; MCMC=Markov-chain Monte Carlo; MTC=mixed treatment comparison; NA=not applicable; NR=not reported; OR=odds ratio; SD=standard deviation

*: Includes both a Bayesian MTC and Lumley's network meta-analysis methods therefore appears in both tables

Table 5. Reporting of outcomes in Bayesian mixed treatment comparisons

Author, year (N authors)	Outcome type	Measure of effect	Measure of variance	Mean or median of distribution	Presentation of results
Baldwin, 2011*	Binary	OR	95% CrI	NR	Text and table
Bangalore, 2011	Binary	OR	95% CrI	NR	Table
Freemantle, 2011	Binary	OR	95% CrI	NR	Text and figure
Gross, 2011	Continuous	WMD	95% CrI	NR	Text and table
Hartling, 2011	Binary	OR	95% CrI	NR	Text and figure
	Continuous	WMD	95% CrI	NR	Text and figure
Jansen, 2011	Binary	RR	95% CrI	NR	Text, table, and figure
Maund, 2011	Binary	OR	95% CrI	NR	Text, table, and figure
	Continuous	WMD	95% CrI	NR	Text, table, and figure
Mills, 2011	Binary	OR	95% CrI	Mean	Table
Sciarretta, 2011	Binary	OR	95% CrI	Median	Text, table, and figure
Trelle, 2011	Binary	RR	95% CrI	Median	Text and figure
van de Kerkhof, 2011	Binary	RR	95% CrI	NR	Text and figure
	Continuous	WMD	95% CrI	NR	Text and figure
Van den Bruel, 2011	Continuous	WMD	95% CrI	NR	Table
Bergman, 2010	Binary	RR	95% CrI	NR	Table and figure
Dakin, 2010	Binary	OR	95% CrI	NR	Text, table, and figure
Orme, 2010	Binary	OR	SE	NR	Table
	Continuous	WMD	95% CrI and SE	NR	Text and table
Phung, 2010	Binary	RR	95% CrI	NR	Text, table, and figure
	Continuous	WMD	95% CrI	NR	Text, table, and figure
Uthman, 2010	Binary	RR	95% CrI	NR	Text and figure
Vissers, 2010	Continuous	WMD	95% CrI	NR	Text and figure
Walsh, 2010	Continuous	SMD and prevention fraction	95% CrI	NR	Text, table, and figure
Wandel, 2010	Binary	OR	95% CrI	NR	Text
	Continuous	WMD and SMD	95% CrI	NR	Text and figure
Wang, 2010	Binary	OR	95% CrI	NR	Text, table, and figure
Woo, 2010	Binary	OR	95% CrI	Median	Text and table
Baker, 2009	Binary	OR	95% CrI	NR	Text, table, and figure
Bansback, 2009	Categorical non-binary	RR	95% CrI	NR	Text, table, figure
Cipriani, 2009	Binary	OR	95% CrI	NR	Text, table, figure
Edwards, 2009a	Binary	OR	95% CrI	NR	Text, table, and figure
Edwards, 2009b	Binary	OR	95% CrI	NR	Table
Edwards, 2009c	Binary	OR	95% CrI	NR	Text and table
Golfinopoulos, 2009	Binary	HR	95% CrI	NR	Text and table
Jansen, 2009	Binary	OR and RR	95% CrI	NR	Text, table, and figure
Manzoli, 2009	Binary	OR and RD	95% CrI	NR	Table
Meader, 2009	Binary	OR	95% CrI	NR	Text and table
Mills, 2009	Binary	OR	95% CrI	Mean	Table and figure

Author, year (N authors)	Outcome type	Measure of effect	Measure of variance	Mean or median of distribution	Presentation of results
Quilici, 2009	Binary	Log OR	95% CrI	Mean and median	Text and table
	Continuous	WMD	95% CrI	Mean and median	Text and table
Thompson Coon, 2009	Binary	HR	95% CrI	NR	Table
Coleman, 2008	Binary	OR	95% CrI	NR	Table and figure
Mills, 2008	Binary	OR	95% CrI	Mean	Table and figure
Mauri, 2008	Binary	HR	95% CrI	NR	Text and table
Quilici, 2008	Binary	OR	95% CrI	NR	Text, table, and figure
	Continuous	WMD	95% CrI	NR	Text, table and figure
Stettler, 2008	Binary	HR	95% CrI	Median	Text, table, and figure
Golfinopoulos, 2007	Binary	HR	95% CrI	NR	Text and table
Lam, 2007	Binary	OR	95% CrI	Mean	Text and figure
Nixon, 2007	Binary	OR	95% CrI	NR	Text, table, and figure
Stettler, 2007	Binary	HR	95% CrI	Median	Table
Cooper, 2006	Binary	RR	95% CrI	NR	Text and figure
Jansen, 2006	Continuous	WMD	95% CrI	NR	Text and table
Kyrgiou, 2006	Binary	RR and HR	95% CrI	NR	Text and table

Abbreviations: CrI=credible interval; NR=not reported; OR=odds ratio; RD=risk difference; RR=relative risk

* Includes both a Bayesian MTC and Lumley's network meta-analysis methods therefore appears in both tables.

Table 6. Characteristics of analyses using Lumley's network meta-analysis methods

Author, year (N authors)	Method-ologist*	Country	Funding	# printed pages	Affiliation	Supplement or appendix	Disease state evaluated	N and type of interventions compared	N trials, N patients	Network pattern
Anothais-intawee, 2011 (7)	Yes	Thailand	Government/ foundation	9	No	Yes	Genitourinary (Chronic prostatitis)	9, Rx	23 NR	Network with ≥1 closed loop
Baldwin, 2011 (4)†	Yes	UK	Industry	11	No	Yes	Behavioral Health (GAD)	10, Rx	27 3,989	Network with ≥1 closed loop
Freemantle, 2011 (5)	No	France	Industry	17	No	Yes	Cardiology (AF)	5, Rx	39 174,662	Network with ≥1 closed loop‡
Jalota, 2011 (8)	No	USA	Academia	18	No	Yes	Pain	8, Rx and other	101 NR	Unclear‡
Trikalinos, 2009 (5)	No	USA	Government/ foundation	8	No	Yes	Cardiology (Stents)	4, Procedure, device and Rx	61 25,388	Network with ≥1 closed loop
Hansen, 2008 (6)	Yes	USA	Government/ foundation	10	HTA	Yes	Behavioral Health (Social anxiety disorder)	7, Rx	18 5,172	Network with ≥1 closed loop‡
Elliot, 2007 (2)	No	USA	Government/ foundation	7	No	No	Cardiology (anti-hypertensives)	6, Rx	22 143,513	Network with ≥1 closed loop

Abbreviations: AF=atrial fibrillation; GAD=generalized anxiety disorder; HTA=health technology assessment; NR=not reported; Rx=pharmacologic; UK=United Kingdom

*: A methodologist was considered an individual with affiliation to a department of statistics, biostatistics, epidemiology, clinical epidemiology, or public health services, as determined by author information and affiliations listed in the publication.
†: Includes both a Bayesian MTC and Lumley's network meta-analysis methods therefore appears in both tables
‡: Diagram was not provided, pattern determined from study characteristics reported

Table 7. Methodological characteristics of analyses that used Lumley's network meta-analysis methods

Author, year	Network model characteristics	Measure of heterogeneity, inconsistency and claims of equivalence or non-inferiority
Anothaisin-tawee, 2011	Was traditional meta-analysis run? Yes Model(s): Mixed-effect hierarchical model with a log-link function using the "xtpoisson" command Weighting of studies: Inverse variance Adjustment for covariates: Yes, effects of study were included as covariates Was the raw data available? Yes, in manuscript Software used: Stata 11.0	Heterogeneity assessment in traditional meta-analysis: Cochrane Q-statistic, I^2 Heterogeneity assessment in network meta-analysis: NR Evaluation of inconsistency: Compare results from traditional and network meta-analyses Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NA
Baldwin, 2011*	Was traditional meta-analysis run? Yes Model(s): Frequentist framework using random effects Weighting of studies: NR Adjustment for covariates: NR Was the raw data available? No Software used: Stata 9	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in network meta-analysis: NR Evaluation of inconsistency: Test for consistency between results of the direct meta-analysis and those of the mixed treatment meta-analyses by subtracting the odds ratios and using a t-test to identify differences in effect estimates between the two models Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NA

Author, year	Network model characteristics	Measure of heterogeneity, inconsistency and claims of equivalence or non-inferiority
Freemantle, 2011	Was traditional meta-analysis run? Yes Model(s): Random effects, non-linear mixed model based upon psuedoliklihood Weighting of studies: NR Adjustment for covariates: NR Was the raw data available? Yes, in manuscript Software used: SAS	Heterogeneity assessment in traditional meta-analysis: NR Heterogeneity assessment in network meta-analysis: Covariance statistic and SE Evaluation of inconsistency: Compare results from traditional and network meta-analyses Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NA
Jalota, 2011	Was traditional meta-analysis run? Yes Model(s): Frequentist mixed-effects meta-regression Weighting of studies: NR Adjustment for covariates: NR Was the raw data available? Yes, in online appendix Software used: R code using Metafor package	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in network meta-analysis: Chi^2 test and tau^2 Evaluation of inconsistency: Compare results from network meta-analysis to previously published literature Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NA

Author, year	Network model characteristics	Measure of heterogeneity, inconsistency and claims of equivalence or non-inferiority
Trikalinos, 2009	Was traditional meta-analysis run? Yes Model(s): Two level linear mixed-effects model with heteroscedastic errors Weighting of studies: NR Adjustment for covariates: NR Was the raw data available? Yes, in online appendix Software used: R 2.6.0 nlme package	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in network meta-analysis: NR Evaluation of inconsistency: Measured and reported network incoherence values Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NA
Hansen, 2008	Was traditional meta-analysis run? Yes Model(s): Frequentist mixed-effects meta-regression Weighting of studies: NR Adjustment for covariates: NR Was the raw data available? Yes, in online appendix Software used: R code using Metafor package	Heterogeneity assessment in traditional meta-analysis: I^2 Heterogeneity assessment in network meta-analysis: NR Evaluation of inconsistency: Compare results from network meta-analysis to previously published literature Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NA

Author, year	Network model characteristics	Measure of heterogeneity, inconsistency and claims of equivalence or non-inferiority
Elliot, 2007	Was traditional meta-analysis run? Yes Model(s): “online program published by Lumely” Weighting of studies: NR Adjustment for covariates: NR Was the raw data available? Yes, in manuscript Software used: R 1.14 framework 2.21	Heterogeneity assessment in traditional meta-analysis: Riley-Day test Heterogeneity assessment in network meta-analysis: NR Evaluation of inconsistency: Measured and reported incoherence values Equivalence claims: NR Non-inferiority claims: NR Minimally important difference defined: NA

Abbreviations: NA= not applicable; NR=not reported; SE=standard error

*: Includes both a Bayesian MTC and Lumley’s network meta-analysis methods therefore appears in both tables

Table 8. Reporting of outcomes in analyses that use Lumely's network meta-analysis methods

Author, year (N authors)	Outcome type	Measure of effect	Measure of variance	Presentation of results
Baldwin, 2011*	Binary	OR	95% CI	Text and table
Freemantle, 2011	Binary	OR	95% CI	Text and figure
Anothaisintawee, 2001	Continuous	WMD	95% CI	Text
Jalota, 2011	Binary	RR	95% CI	Text and table
Trikalinos, 2009	Binary	RR	95% CI	Text, table, and figure
Hansen, 2008	Binary	Relative benefit	95% CI	Figure
Elliott, 2007	Binary	OR	95% CI	Text and figure

Abbreviations: CI=confidence interval; NR=not reported; OR=odds ratio; RR=relative risk; WMD=weighted-mean difference

*: Includes both a Bayesian MTC and Lumley's network meta-analysis methods therefore appears in both tables.

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Appendix G. Glossary

Closed loop network of evidence: A network of evidence where greater than two interventions are being compared indirectly, and at least one pair of interventions is being compared both directly and indirectly.

Lumley's network meta-analysis: The Frequentist approach originally described by Lumley whereby both direct and indirect evidence are combined when there is at least one closed loop of evidence connecting two interventions of interest.

Meta-Analysis: The process of extracting and pooling data from several studies investigating a similar topic to synthesize a final outcome

Mixed treatment comparison (MTC): An approach whereby both direct and indirect evidence for particular pair-wise comparisons are combined, and interventions that have not been compared directly are linked through common comparators.

Network meta-analysis or indirect comparison: Meant generically to define the simultaneous synthesis of evidence of all pairwise comparisons across >two interventions.