Critical Appraisal

Critical Appraisal of a Network Meta-Analysis in Emergency Medicine

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Introduction

Network meta-analysis (NMA) involves indirect treatment comparisons or mixed treatment comparisons, which include both direct and indirect evidence. It provides quantitative information for evidence-based decision making in the absence of randomized controlled trials involving direct comparisons of all the treatments of interest within the studies [1-6].

NMA apply to the setting of interest and is captured by four questions:

1. Is the population relevant?

2. Are there any relevant interventions missing?

3. Are there any relevant outcomes missing?

4. Is the context (settings and circumstances) applicable?

The table 1 shows a summary critical appraisal of evaluating the quality of evidence from a NMA [1-6].

References

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Table 1: Shows a summary critical appraisal of evaluating the quality of evidence from a NMA [1-6].

GRADE domain	Domain assessment in NMA	Description of procedure	Instructions for downgrading
Evaluate the confidence in a specific pairwise effect estimated in NMA			
Study limitations	Study limitations	Determine which direct comparisons contribute to estimation of the NMA treatment effect a and integrate risk of bias assessments from these into a single judgment	Use standard GRADE considerations to inform judgment
Indirectness	Joint consideration of indirectness and intransitivity	Evaluate indirectness of populations, interventions, and outcomes as in standard GRADE. Evaluate transitivity by comparing the distribution of known effect modifiers across comparisons that contribute evidence to estimation of the NMA treatment effect	If a priori assessment makes a transitivity assumption reasonable and suggests that effect modifiers are balanced, then do not downgrade. Otherwise, downgrade (either if a transitivity assumption does not look reasonable or if there is insufficient evidence to judge)
Inconsistency	Joint consideration of statistical heterogeneity and statistical inconsistency	(1) Judge the extent of heterogeneity, considering the comparison-specific heterogeneity variance, the NMA estimate of variance, a prediction interval and/or other relevant metrics such as I^2 (2) Evaluate the extent to which the comparison under evaluation is involved in inconsistent loops of evidence	(1) If important heterogeneity is found, downgrade. If heterogeneity is low, do not downgrade (2) Power to detect inconsistency may be low; downgrade in absence of statistical evidence for inconsistency when direct and indirect estimates imply different clinical decisions
Imprecision	Imprecision	Focus on width of the confidence interval	Assess uncertainty around the pairwise estimate. Downgrade if confidence interval crosses null value or includes values favoring either treatment
Publication bias	Publication bias	Nonstatistical consideration of likelihood of nonpublication of evidence that would inform the pairwise comparison. Plotpairwiseestimatesoncontour-enhancedfunnelplot	Use standard GRADE to inform judgment
Evaluate the confidence in treatment ranking estimated in NMA			
Study limitations	Study limitations	Integrate risk of bias assessments from each direct comparison to formulate a single overall confidence rating for treatment rankings[a]	Use standard GRADE considerations to inform judgment
Indirectness	Joint consideration of indirectness and intransitivity	Evaluate indirectness of populations, interventions, and outcomes as in standard GRADE. Evaluate transitivity across network by comparing the distribution of known effect modifiers across comparison [a]	If a priori assessment of transitivity suggests effect modifiers are balanced across the network, do not downgrade. Otherwise, downgrade (either if a transitivity assumption does not look reasonable or if there is insufficient evidence to judge)

Inconsistency	Joint consideration of statistical heterogeneity and statistical inconsistency	(1) Judge the extent of heterogeneity considering primarily the NMA variance estimate(s) used and other network-wise metrics such as Q for heterogeneity in a network (2) Evaluate inconsistency in network using statistical methods (such as global tests of inconsistency, or global inconsistency parameter)	(1) If important heterogeneity is found, downgrade. If heterogeneity is low do not downgrade. (2) For overall treatment rankings, inconsistency should be given greater emphasis, since ranks are based on mean effects and the uncertainty they are estimated with. Downgrade in absence of statistical evidence for inconsistency when several direct and indirect estimates imply different clinical decisions
Imprecision	Imprecision	Visually examine ranking probabilities (e.g., rank grams) for overlap to assess precision of treatment rankings	If probabilities are similarly distributed across the ranks, downgrade for imprecision
Publication bias	Publication bias	Nonstatistical consideration of likelihood of nonpublication for each pairwise comparison. If appropriate, plot NMA estimates on a comparison adjusted funnel plot and assess asymmetry	As asymmetry does not provide concrete evidence of publication bias, downgrading should only be considered jointly with the nonstatistical assessment

[a]When integrating assessments about direct comparisons into a judgment about an NMA treatment effect or the ranking, more weight should be given to assessments from direct comparisons that contribute more information. We recommend use of the contributions matrix to quantify how much information each direct comparison contributes to the estimation of the NMA treatment effect under evaluation or the ranking.

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