



Writing network meta-analysis 3

Reporting on inconsistency and appraising the findings

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Network meta-analysis

A project-based course using R

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Evaluate consistency (1)

Report on methods for:

- Assessment of **statistical inconsistency locally**
 - identify pairwise comparisons or loops of evidence that might be important sources of inconsistency
 - e.g. the loop-specific or node-splitting approach
- Assessment of **statistical inconsistency globally**
 - evaluate the presence of inconsistency in the entire network
 - Q test for inconsistency
 - Compare consistency vs inconsistency models
- Use I^2 for **heterogeneity/inconsistency/both**

Evaluate consistency (2)

- Describe **how conclusions will be drawn** based on the results of each approach
 - e.g. based on the magnitude and the confidence intervals of the estimated inconsistency factors, using p-values
 - Be careful - tests for inconsistency have low power
- Explain what you will do **if important inconsistency is identified**
 - Explore sources of inconsistency?
 - Fit inconsistency models?
 - Split the network into smaller, consistent networks?
 - Do NOT exclude studies

Example

Safety of anti-epileptic drugs

“We will ensure the following factors are present prior to conducting network meta-analysis: [...] ii) consistency between direct and indirect data, which will be examined locally (i.e., in certain paths of the network) using the loop-specific method and the node-splitting method, and globally (i.e., evaluating the network as a whole), using the design-by-treatment interaction model; and iii) we will quantify the amount of variability attributed to heterogeneity and inconsistency rather than sampling error, by calculating the I^2 . [...] We will compare the magnitude of heterogeneity between consistency and inconsistency models to determine how much heterogeneity will be explained by inconsistency. We will first use the design-by-treatment model for the evaluation of inconsistency in a network as a whole and then, if inconsistency is detected, we will employ the loop-specific and node-splitting methods to identify which piece of evidence is responsible for inconsistency”

Investigating heterogeneity & inconsistency (1)

Heterogeneity & inconsistency → caused by differences in populations and study characteristics **within** and **across** comparisons

- Specify the **additional analyses** that will be performed to explain heterogeneity and inconsistency
 - e.g. **subgroup analyses, network meta-regression** (if sufficient data are available)
- **Pre-specify the variables** that will be considered as possible sources of heterogeneity and inconsistency
 - choose a subset of the potential effect modifiers listed earlier (see also Data Extraction section)

Investigating heterogeneity & inconsistency (2)

- The use of network **meta-regression** requires further details
 - e.g. *assumptions regarding the regression coefficients* and the directionality of the effect of covariates
 - if it is fitted in a Bayesian framework, prior distributions for the coefficients (in an appendix)

Example

Efficacy and acceptability of psychological interventions for bipolar disorder

“If we find important heterogeneity and/or inconsistency, we will explore the possible sources. If sufficient studies are available, we will perform meta-regression or subgroup analyses by using the following effect modifiers as possible sources of inconsistency and/or heterogeneity: (i) year of publication; (ii) study precision; (iii) baseline severity and (iv) blinding”

Reporting bias

- It is as much of a threat as in pairwise meta-analysis
- Not to be confused with small study effects
- Use **contour-enhanced funnel plots** (per comparison)
Peters J et al. J Clin Epidemiol. 2008 Oct;61(10):991-6
- Use **comparison-adjusted funnel plots** (for the entire network) Chaimani A, Salanti G: *ResSynthMeth* 2012, 3:161–176.
 - Requires assumption about direction of potential small study effects
- Use **selection models** in the case of serious reporting bias
Mavridis D et al. Stat Med. 2014 Dec 30;33(30):5399-412.
 - Example: antidepressants and placebo network

In the manuscript...

Assessment of inconsistency

- Methods
 - Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment networks studied
 - Describe efforts taken to address its presence when found.
- Results
 - Describe results from investigations of inconsistency.
 - Comparison between consistency and inconsistency models,
 - P values from statistical tests
 - Summary of inconsistency estimates from different parts of the treatment network.

Exploration of inconsistency/heterogeneity

- Methods
 - Describe methods of additional analyses if done, indicating which were pre-specified
 - Sensitivity or subgroup analyses
 - Meta-regression analyses
 - Alternative formulations of the treatment network
- Results
 - Give results of additional analyses, if done, at least in an appendix

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Discussion

- Summary of evidence
 - Summarize the main findings
 - Strength/confidence of evidence for each main outcome
 - Relevance to end-users (e.g., health care providers, researchers, and policymakers).
- Limitations
 - Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias)
 - Comment on the validity of the assumptions, such as transitivity and consistency
 - Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons)

Conclusions

- Provide a general interpretation of the results in the context of other evidence, and implications for future research
- Give potential explanations of any disagreements with previews reviews