**Reviewer’s report**

**Title:** Multiple Score Comparison: A network meta-analysis approach to comparison and external validation of prognostic scores

**Version:** 0  **Date:** 31 Aug 2017

**Reviewer:** Adriani Nikolakopoulou

**Reviewer’s report:**

This is a paper regarding the application of network meta-analysis methodology to compare and external validate prognostic scores. I find the idea innovative and interesting and I believe that the paper has the potential to fill a gap in the literature. My main suggestion for improvement would be to place more focus on describing the methodology in the main paper rather than in the supplementary material. I would also suggest placing emphasis on how methods are applied in the context of prognostic scores rather than explaining the concepts of network meta-analysis of treatments. Introducing a fictional small network of three or four scores to illustrate each step of the process in the methods section could be a possible way to exemplify the methodology. Moreover, I think that providing the R code used for implementing the models would be an important step in making the suggested methods accessible. Please see below some specific comments and recommendations.

**Background**

Lines 117 and 135: 3CIA is mentioned first in line 116 but authors explain what it is in line 135.

**Methods**

Lines 159-161: I think here authors need to say that they define a reference score within a cohort (and thus, they need k-1 estimates.).

Lines 170 - 175: I suggest replacing "a two stage process" with "a two stage meta-regression model". Authors state the model "permits direct inclusion of the covariance estimates from multi-arm trials". This is correct but there are other methods as well that do allow for that, so I would avoid defending the method's choice based on this argument.

Lines 193 - 198: It is not common to 'test' transitivity like this using a statistical test. Can authors provide a reference for their approach of testing for homogenous groups using ANOVA? If not, I feel that more explanation is needed. Moreover, I would be interested to read a conceptual explanation of when transitivity is likely to hold in the setting of NMA of prognostic scores. In which cases authors would be suspicious over the plausibility of the transitivity assumption?

Line 198: I suggest rendering it clearer that heterogeneity is going to be discussed afterwards by changing paragraph.
Lines 202 - 203: The reference for the node-splitting approach is given below


Lines 211 - 220: In these lines, authors discuss comparison of direct and indirect evidence. Why this text is not merged with the discussion on inconsistency in lines 202 - 210?

Results

Lines 243 - 248: Table 2 is nice and informative but I think that the network plot would be more suited here rather than in the supplementary material.

Lines 303 - 306: As in methods, I do not understand the distinction between 'inconsistency' and 'comparing direct and indirect evidence'.

Discussion

Lines 365 - 369: Does that mean that authors calculated P-scores and chose not to report them in the paper?

Does the argument that 'the results were essentially the same as those of the network meta-analysis itself' refer to the treatment hierarchy? Even if the suggested hierarchy is the same, I do not believe that results are the same as NMA estimates and P-scores are not estimates for the same question so their interpretation differs.

Conclusions

Lines 371 - 372: the term 'multiple treatment comparison network meta-analysis' is not used. In general, I would suggest choosing a term and use it throughout; network meta-analysis is the most frequently used (47% of networks according to Zarin et al.) so I would suggest picking this one.


References

There is a second list of references starting in page 34/49, which seems to be incorrect.

Supplementary material

There are some typos throughout the supplementary material, for example:

Page 4/43, line 3: $\tau^2/2$ is missing
Page 6/43, line 5: "Due" should not start with a capital letter

Page 8/43, lines 4-5: I could not find an outline of the R implementation (apart from the code for drawing the network plot)

Page 8/43, last two lines: Where is Appendix C? I found up to Appendix B in the main paper.

As in the main paper, there are two lists of references

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Unable to assess

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