Reviewer’s report

Title: Is network meta-analysis as valid as standard pairwise meta-analysis? It all depends on the distribution of effect-modifiers

Version: 1 Date: 26 March 2013

Reviewer: John Thompson

Reviewer’s report:

Discretionary Revisions

I have been struck recently by the growth in network meta-analysis and by the lack of appreciation by the researchers of the assumptions that they make. I think that this paper will help to address this. Because of my background I chose to check the authors account by writing down the equations for the average treatment effect in a randomised study and then the average across studies in a meta-analysis and finally for the difference between two treatment effects from separate meta-analyses. By writing down the equations it is immediately obvious that unless either the treatment effect is independent of individual and study level factors or the distributions of these factors are the same, then network meta-analysis will be affected. The authors say the same thing but use words rather than equations. I can see that this will be more useful to some people but it does mean that a simple argument appears much more complex and takes many pages to explain. Adding the equations for those who can appreciate them would strengthen the paper.

Given that the paper is aimed at a non-mathematical, perhaps more application oriented reader it is a pity that more attention was not given to making practical recommendations. To say that there might be a bias avoids many difficult issues such as, will the bias be large enough to make a difference and how can I tell if the bias is large?

Minor essential revisions

Otherwise my only concern is with the lack of reference to other papers that have discussed this issue. To give just a couple of examples, there was a network meta-analysis working group that published its findings in BMC Medicine (2011, 9:79 doi:10.1186/1741-7015-9-79 and an Editorial in the BMJ (19 September 2012).

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
nothing to declare