Reviewer’s report

Title: Network meta-analysis incorporating randomized controlled trials and non-randomized comparative cohort studies for assessing the safety and effectiveness of medical treatments: Challenges and opportunities

Version: 3 Date: 28 August 2015

Reviewer: Shannon Cope

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Major revisions:
1. There is no discussion here regarding meta-regression. If you have access to distributed data networks the more powerful approach would be to perform meta-regression using the individual patient data from observational studies as well as RCTs. This is critical, because even if the estimate from cohort study is unbiased, the population may differ from RCTs.

2. Lines 182-185. The differences in costs of performing NMA with observational evidence are mentioned, but it would be more useful to suggest possible restrictions regarding quality of observational studies, especially with respect to types of analyses that minimize risk of confounding (i.e. propensity score matching etc.).

Minor revisions:
Line 51: It's not clear if including non-randomized trials is desirable, although you could argue it should be 'considered'

Line 105: 'been' should be change to 'be'

Lines 128-140: The authors seem to assume that high quality observational studies will not have differences in treatment effect modifiers, which is not necessarily the case. While it is imperative to assess quality, especially for cohort studies, this paragraph should be revised to avoid confusing these two ideas.

Line 135: How is GRADE specific to NMA context? Please clarify.

Lines 137-138: check capitalization for STROBE when written in full

Line 183: replace 'than' with 'as compared to'

Line 220: grammar is incorrect - needs to be rephrased