Reviewer's report

Title: Evidence-based mapping of design heterogeneity prior to meta-analysis: a systematic review and research synthesis

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Reviewer: Barnaby Reeves

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1. I think it is a great concept - although, arguably, we/everyone is moving in this direction already (encouragement to review authors to think about pre-specifying as much as possible in the protocol). But there is some difficulty in thinking exactly when the concept should be applied during a review. Can't be strictly at protocol stage, since studies won't be available then (also some aspects of heterogeneity may be anticipated). I prefer an analogy with the "analysis plan" for a primary study (usually a RCT), which is typically finalised during the course of the study (long after the protocol has been finalised) but before data are unblinded to the analyst and any comparisons carried out. Perhaps there is a need for such a step in a systematic review?

2. I think terminology is badly used (e.g. "evidence-mapping" when referring to design heterogeneity).

3. "Covariable" (used to cover confounders, population characteristics, etc.) is also an awful term. Since they refer to the PICO elements, I think they should very clearly analyse heterogeneity for each element (where relevant) AND confounding (as a new element when dealing with non-RCTs).

4. I think authors need to make a very clear distinction between using observational studies / NRS to address aetiological vs. intervention research QQs. Some of the text implies that they think these are essentially the same kinds of studies. (Increasingly, I would argue not.)

5. I was expecting to see some really interesting graphs, but to no avail. I think the mapping tables really don't work very well (graphically, for extracting useful information). I may well just be inexperienced with the technique - but it all looks very dense. I started thinking about some kind of 'star' plots (one per included study) to show the diversity more clearly - but haven't thought it through properly.

6. I don't think (but need to check carefully) that they do anything about the potential multidimensional nature of the diversity.