Reviewer's report

Title: Randomised placebo-controlled trials of individualised homeopathic treatment: systematic review and meta-analysis

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Reviewer: Wayne Jonas

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Review of Mathie, RT. Randomized placebo-controlled trials of individualized homeopathic treatment: systematic review and meta-analysis

To the authors:

1. First, it is not true (as has been stated in the abstract and article) that this is the first individual homeopathic treatment meta-analysis. At least two and possibly three previous meta-analyses have looked at individualized homeopathic subgroups.

2. The statement on page 3, line 95 that the other reviews have combined all forms of homeopathy is also not true. Several of the other meta-analyses did subgroup analysis that did distinguish between the different types of homeopathy.

3. Page 4, line 102 needs explanation. The authors say that previous meta-analyses were lacking but do not describe what those lacking areas were. It does not appear that they've used anything different in this meta-analysis.

4. Page 4, line 121. Many experts in meta-analysis say that combining multiple clinical outcomes into a single measure is not appropriate. And yet that's what these authors have done. They need to more fully justify doing that given the heterogeneity of the studies.

5. Page 5, line 133. There is some concern over the search strategy implemented in PubMed. NOT(animals[mh] NOT humans[mh]) I am not quite clear why this was done as well as some of the other terms. The authors should have chosen limiters rather than putting those terms into their search like random, etc. Also, homeopathy is a MeSH term and that should have also been chosen rather than the * terms for a more comprehensive search. The author should ensure all literature relevant was captured.

6. I was surprised to see that the Davidson et al. homeopathy systematic review on psychiatric disorders was not cited in this paper.

7. Page 5, line 137. How did the authors know that the patients did not get a combined or mixed approach homeopathy - which is commonly done in practice?

8. Page 5, line 139. The fact that the practitioners were not blinded to the
assigned intervention when selecting the studies for the meta-analysis opens itself to bias in the selection of studies. Homeopathic practitioners should not have been the ones allowed to select the studies.

9. Page 5, lines 144 to 147. While the Linde approach to selecting the main outcome measures is reasonable, the World Health Organization approach does not seem to have been validated. The authors need to justify its use here. Who did the selection of the outcomes and was it conducted in duplicate with a third reviewer confirming agreement? This needs to be detailed in the methodology.

10. Page 6. The authors do not demonstrate that their selection and quality assessment approach is reliable. What was the Kappa between the two reviewers who are involved in this judgment? What was the percent disagreement needing third party resolution? How was that resolution obtained?

11. There is concern in the fact that the studies either rated as uncertain risk of bias or high risk of bias. I would think this be a red flag not to proceed with meta-analysis techniques and more so examine the gaps in the research methods to date to improve the research field. Those studies with uncertain or high ROB should not be trusted as much as the studies with low ROB. I appreciate the sensitivity analysis of the uncertain ROB to the high ROB but this does not demonstrate much, what you want to see is that those studies do not differ from the low ROB studies, which you found none meeting that criteria.

12. Page 6. It's not clear how the research sponsorship was taken into account for the sensitivity analysis.

13. Page 10, line 251. How did the authors determine whether a study was a pilot or not?

14. Page 16, lines 407-408. This is very awkwardly worded and was also repeated in the abstract; what does it mean that these meta-analysis results "do not necessarily contradict" previous meta-analyses. That's a use of a double negative and should be changed. The sentence is very ambiguous. This is also conveyed in the abstract as well and is quite confusing to the reader as the author is stating (1) that this is the first of its kind and then (2) that this one is not necessarily contradicting previous meta-analysis of its kind. This needs attention.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare no competing interests