Reviewer's report

Title: Can we rely on the best trial? A comparison of individual trials and systematic reviews

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Reviewer: Sally Hopewell

Reviewer's report:

Thank you for asking me to review this manuscript which aims to evaluate how often, and under what circumstances, using trials with the greatest statistical weight arrives at similar conclusions to the full meta-analysis in a random sample of Cochrane reviews. This study is clear and well written, making an important contribution to knowledge in this area, as such my comments are minor:

Page 6; para 1: The single largest trial was selected from the meta-analysis reporting the primary outcome in each Cochrane review. Was there ever a situation where there were two trials with very similar weight but with very different effect estimates, and if so, what did you do?

Page 6; para 4: You mention that it was not possible to tell which trial had the greatest weight in the meta-analysis for four of the 200 randomly selected Cochrane reviews. Is it possible to give an explanation for why this was not possible.

Page 7; para 2: The average number of trials included in the meta-analyses was 7.3 with the largest trials contributing on average 51% of the statistical weight to the summary estimate from the whole meta-analysis. There was agreement between the single largest trial and overall meta-analysis 81% of the time. If would be interesting to know how this percentage agreement varied depending on the number trials included in a meta-analysis. For example, if a meta-analysis contained only a small number of trials compared to one containing a large number of trials (where the largest trial would in theory have less weight).

Page 9; para 3: One of the limitations of this study is how to find the largest single trial to answer a specific clinical questions without doing a comprehensive search of the literature. The authors knowledge that this is a problem and beyond the scope of this study. However, is it possible to draw on guidance from other areas to help guide clinicians who might be wanting to apply this approach to their own clinical setting.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a
statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'