Reviewer's report

Title: When Should Observational Studies Be Afforded More Weight in Evidence Reviews? Case Examples

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Reviewer: Susan L Norris

Reviewer's report:

Major compulsory comments

1. The focus appears to be on the effectiveness and harms of health care interventions, but this is not explicit in the abstract. For example, the first sentence of the abstract states that SRs most often focus on RCTs. However, SRs of prevalence or diagnostic tests do not. On page 5 the subtitle is “when to include OS in SRs”. I think you need to specify why type(s) of SRs.

2. The requirement that observational studies can only be upgraded if there is no reason to downgrade them is not made clear in this paper (there is some discussion that downgrading for directness may be exempt). On page 10 the three domains that can lead to upgrading are discussed, but this important caveat is totally missing. This important omission perpetuates the upgrading of OS when they are poorly performed (is high risk of bias) and have a large effect size: clearly inappropriate upgrading.

3. Although the examples are interesting, this paper lacks an underlying structure or framework upon which to “pin” each of the examples. The debate on best evidence is referenced, but the paper doesn’t inform this debate. The purpose of systematic reviews is most often to inform decision-making, yet this paper seems to look at systematic reviews as an end product. Perhaps the authors can tie their examples to user’s potential needs, and to the anticipated validity of observational data within the context of the question. Simply seeking OS when RCT data are lacking is not a good use of resources. (The example on page 8 when RCT data are limited, is rather weak. Could you find an example where RCT data were limited on a key outcome and search for observational data added significantly to the value of the information to the user?)

4. It is unclear why on page 16 two examples of primary studies are provided in this manuscript on systematic reviews.

5. Page 18, conclusions: “OS should be included in SRs and be afforded greater weight in the review conclusions”. Greater weight than what? The paragraph goes on to suggest that the authors advocate for a best evidence approach, which is actually not clear from the manuscript (see above). “studies met criteria for causation” does not make sense. Studies do not meet these criteria, rather specific outcomes and effect estimates are assessed on these criteria.

Minor compulsory comments
1. The title refers to “evidence reviews”, yet the text uses “systematic reviews”. What is the difference?

2. The manuscript would benefit from some copy editing and review by a technical writer.

3. Page 4, Methods section: “several chapters of the Methods Guide…”. Please specify which guide you are referring to.

4. Page 7: “the review team found that some trials were using doses that were well above… doses found to be …. least likely to result in adverse events…”. This doesn’t make sense.

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

Declaration of competing interests:

I have no financial competing interests.

I have worked directly with several of the authors of this paper within the last 3 years.