Reviewer’s report

Title: Reporting of heterogeneity of treatment effect in cohort studies: a review of the literature.

Version: 0 Date: 19 Jul 2017

Reviewer: Jo Leonardi-Bee

Reviewer's report:

This paper describes how heterogeneity has been assessed within cohort studies assessing the effectiveness of a treatment, using systematic review methodology. This is an important area to focus on as cohort studies are being used more and more frequently to address the association between an exposure or treatment and health outcomes, especially where it is unethical or unfeasible to conduct RCTs.

Overall, this paper is well written; however, I have a major few comments that the authors may wish to address:

1. A systematic review includes all of the eligible studies addressing a single focused question - however, this systematic review included a random sample of journal articles from high impact and lower impact journals. it is not clear whether this would have introduced bias - the selection was stratified by high versus lower impact journals - but this does assume that the instructions to authors for the journals within each strata are exactly the same and have not changed over time. This assumption is likely to be violated as the papers were sampled over the past 15 years - additionally, whilst we can assess the similarity of instruction to authors for the high impact journals, this cannot be done for the lower impact journals due to the sheer number. Additionally, it is gleaned from the methods that the studies were included in a reverse chronological order - therefore it is not clear how this can be a random selection of eligible papers? Finally, as the number of high impact journals is so much smaller than the lower impact journals, you should find that the high impact journals are much more similar in their reporting - the authors need to address all these points, and describe how they could have impacted on the findings of the review.

2. The background only glosses over the potential biases introduced from using cohort studies to look at treatment effects - more recognition and discussion is needed regarding confounding by indication - and how this links to conducting full explorations of heterogeneity

3. How generalisable are the results from this systematic review given that only 119 journals from the Abridged Index Medicus are included in the review, and are very likely to be from specific areas of the world. Discussion regarding this needs to be provided
4. At the bottom of Page 6 - beginning of Page 7 - "High impact journal studies were identified by generating a random list of 75 journal names..." - this is contradictory from the other text which states only 6 high impact journals were included.

5. How did the authors deal with prospective controlled cohort studies which were matched for specific characteristics - for example, age and sex? Did they exclude these studies from the review or just exclude them from the age and sex predictive variables analysis?

6. The fact that such a very high proportion of the included studies were funded by industry is great cause for concern - can the authors provide more information as to whether the industry funders were involved in the design, analysis and interpretation stages of the paper?

Minor comments include:

1. What was the rationale for including 150 cohort studies rather than a different number - it is not fully clear what the precision of a 50% probability means - this needs to be explained in sufficiently more detail.

2. As the outcomes reported are typically quite common, then estimating the association based on an odds ratio is likely to over-estimate the true association.

3. The protocol seems to have been documented before the review was conducted - however, the protocol has not been attached/uploaded with the review, and hasn't been published.

4. The search terms for identifying a prospective controlled cohort study are very brief and it is not clear that this would yield all eligible studies from the particular journals - this is likely to result in selection bias.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No
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I am able to assess the statistics

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