Author’s response to reviews

Title: Assessments of attrition bias in Cochrane systematic reviews are highly inconsistent and thus hindering trial comparability

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Author’s response to reviews:

Dirk Krüger

BMC Medical Research Methodology

Re: Revision of the manuscript BMRM-D-17-00482

Dear Dr. Krüger,

Thank you and your reviewers for providing feedback about our manuscript titled Assessments of attrition bias in intervention Cochrane systematic reviews are highly inconsistent and thus
hindering trial comparability (BMRM-D-17-00482). We did our best to address the comments we received, and we provided a point-by-point response. We highlighted all the changes made in the manuscript using track changes.

Technical Comments:

No co-authors email address and list of abbreviations

Response: We added co-authors email addresses and list of abbreviations.

Reviewer reports:

Thomas Rotter, Ph.D. (Reviewer 1):

1. The investigators may have not used a rigorous approach to assess attrition bias in Cochrane reviews. I am a Cochrane author myself and I do not really understand the data extraction process (page 6 manuscript) The authors report, that only 10% of the data extraction was done independently by two. Thus, 90% of the CSRs has been extracted by one? It is not clear for me if this section describes the pilot or the whole data extraction. Also, I miss the search strategy the authors have used to search the Cochrane Library.

Response: This manuscript was submitted in November 2017, and by the time it was submitted our methodology was as described in the manuscript: data extractors manually extracted information from the Risk of Bias (RoB) tables from Cochrane reviews and pasted them into Excel table. We considered that our methodology was adequate (namely: one person doing extraction, has a piloting period on the first batch of extractions, and subsequently another author verifies random 10% of extracted data) because RoB tables in Cochrane reviews are very straightforward, and the data extractors do not have to spend a lot of time in a review, making personal judgments about which data is relevant and what exactly they should extract. Cochrane RoB tables are easy to find in a review, and all domains are clearly specified. So all the extractors followed the same procedure, and had to extract easily findable information.

However, with our evolving ideas on this topic, we ultimately faced a major problem with this type of data extractions, and that was that this is very, very time consuming. For the purpose of this manuscript only we extracted more than 30,000 data items from more then 700 reviews and more than 10,000 trials included in those reviews. These data items were name and detail of a review, number of included studies for each review, and then name of a trial, RoB judgment for attrition bias and comment for the risk of bias for each of more then 10,000 trials. This requires very large human effort to complete manual extraction. For this reason, we enlisted help of a
physician who is also information specialist, and in the beginning of this year he created a software working as a parsing tool, which extracts specific data from Cochrane reviews if they are clearly delimited, and RoB tables are such type of data.

Therefore, in 2018, using this data parsing tool, we extracted many clearly delimited data from Cochrane reviews, including data from the attrition bias domain, and we were able to compare data extracted manually by study authors and data extracted via software. We found only 34 data extraction errors in the entire sample, and these were all for the judgment, not for the comment.

2. On page 10, the authors explain that they have only used the top-five categories. I cannot find a justification for this decision.

Response: We initially presented top five categories for the statistical comments because our manuscript has many information and we were concerned about the length of the table. Encouraged with this comment, we have now revised previous Table 4, which is now Table 5, and listed all categories of statistical comments that we found.

3. The authors could have used a kappa statistic to assess the agreement between reviewers.

Response: We compared data extracted by our seven authors with software-extracted data and found very few discrepancies in the data. RoB tables are very clearly labelled in any Cochrane review, which is itself highly structured. Every RoB table has clearly specified name of the RoB domains presented in the table. Therefore, despite the fact that we initially did not do double independent extraction, we consider that this anyway would not present major methodological weakness, because this type of data is very specific and clearly labelled. As a published and ongoing Cochrane author myself, I know all about difficulties in finding and extracting data from manuscript when it comes to numbers related to efficacy and safety, with data sometimes presented in the text, sometimes in a table, sometimes in a figure (sometimes in multiple places, and sometimes data being discrepant within the same manuscript), problems of missing data, problems with obtaining data or clarifications from original study authors. The data that we used in this manuscript, are completely different – presented in a table that is obligatory part of a Cochrane review, highly structured, uniformly presented in each Cochrane review, always in the same place within a review, with each row in Cochrane RoB table clearly labeled.

Matt Vassar (Reviewer 2):

1. Babic et al. examined risk of attrition bias judgments made by systematic reviewers of Cochrane systematic reviews. I appreciate the opportunity to review this paper. The authors have investigated an important research question, and I offer the following comments to improve the manuscript.
Response: We are grateful to the reviewer for the kind words about our manuscript. We did our best to revise the manuscript and to respond to the suggestions we received.

2. The authors should frame this study within the context of the development of Cochrane's RoB 2.0, which is scheduled for release at the 2018 Cochrane Colloquium. The updated tool addresses limitations of the current one, including updated instructions for authors, renaming the bias categories, bias judgments at the outcome (rather than trial) level, among others. It would seem that this update should be discussed in the current manuscript, especially if the updated version addresses the limitation cited by the authors as the impetus for conducting this study.

Response: As Cochrane authors ourselves, we are aware of the planned Cochrane RoB tool 2.0. We started this study before the Cochrane RoB tool 2.0 was announced, but we believe that the study is still relevant. Last year at the Cochrane Colloquium, the talk was that the application of the tool is not expected in the upcoming two years, to allow for further considerations and author training. We have now addressed the issue of RoB tool 2.0 in Discussion in a very elaborate way. We do not think that Cochrane RoB tool 2.0 is any better than the current version in terms of the domain for assessing attrition bias, and we provided our rationale for this consideration.

3. The manuscript would benefit from changes to its structure. I found it difficult to follow in its current form. There are a lot of categories and subcategories in the results sections. That structure could lend itself to clarity or confusion, depending on how well the reader is able follow this structure. Moving or removing the paragraph that starts with "In the first category a third of supporting explanations were unclear (32%)" would increase clarity. Defining terms (e.g., "unclear supporting explanations" and "single judgement") would also increase clarity.

Response: We revised the text regarding these two specific suggestions, to clarify matters that were deemed unclear by the reviewer:

- Specific suggestion to “Moving or removing the paragraph that starts with "In the first category a third of supporting explanations were unclear (32%)"

- Defining terms (e.g., "unclear supporting explanations" and "single judgement") would also increase clarity.
Furthermore, we switched position of Table 1 and Table 2, to mention the new Table 1 (former Table 2) immediately after we mention explanations that were unclear. Additionally, we put a number in the first paragraph in front of each category, so that this paragraph is easier to follow.

4. The introduction could be improved by eliminating the paragraph which discusses all domains included in the Cochrane risk of bias tool. If this information is necessary for readers, it could be placed in a table. I suggest replacing this paragraph with one that provides a robust discussion on attrition bias. Such a discussion would properly motivate the need for this study. In particular, I would suggest discussing what attrition bias is and how it can affect clinical trials, clinical outcomes, and/or systematic reviews. Specific clinical examples are also welcome here.

Response: Introduction was revised as suggested; we focused only on attrition bias and indicated example of influence of attrition on trial results.

5. The authors justify the need for this study by stating that the instructions for this bias domain are unclear; however, the authors do not provide evidence to support this claim. Results from a survey study of Cochrane reviewers or a study showing poor interrater reliability for the attrition bias domain would provide a more credible justification for this assertion. Otherwise, I recommend that the authors more explicitly state the directions for this domain and explain why the instructions are problematic.

Response: Da Costa et al. have published a study in 2017 about training in risk of bias, and showed that “Kappa values between the minimal training group and reference across items of the risk of bias tool ranged from 0.10 (poor agreement) for incomplete outcome data (…)” Therefore, inter-rater agreement in participants with minimal training was worst for the ‘attrition bias’ domain, compared to other domains of Cochrane RoB. Since Cochrane authors rarely have structured training that was tested in the study of da Costa et al., these data could very well provide real-world situation for assessment of attrition bias. We indicated this in our manuscript. Furthermore, we included a Box (currently located on the last page of the manuscript), where we indicate specific problems with instructions to authors given in the Cochrane Handbook on the subject of judging risk of attrition bias, and we indicate why the instructions are problematic.

6. Please include the initials of all authors that screened articles for inclusion or extracted data. This information was included for the author (AB) that extracted data from a random sample of 10% of the included studies and for the author (LP) that resolved discrepancies, but not for the authors that screened studies for inclusion or the author that extracted data from all studies.
Response: We included now initials of authors who did screening, and extraction. In the response to the first comment of the first reviewer we provided elaborate explanation regarding data extraction method and discrepancies.

7. Please address how systematic errors in data extraction were addressed. In the manuscript, the authors mention that one author extracted data from all included studies while a second author extracted data from a random sample of 10% of the included studies. It is unclear what steps were taken if disagreements were found in the 10% of data extracted by both authors. Interrater reliability estimates would provide evidence for the accuracy of the extracted data. In general, I would like to see the authors address the methodological safeguards used to ensure that the extracted data are accurate.

Response: In the response to the first comment of the first reviewer we provided elaborate explanation regarding data extraction method and discrepancies.

8. In the Data Extraction section the authors state that they, "reported only analysis of attrition bias for included CSRs with a single judgment, regardless of the number of supporting explanations that were provided for that judgment". Please provide a definition for "a single judgement" as this phrase is unclear. Does this mean a single judgement for an entire systematic review or a single judgement from each author in a systematic review?

Response: Expressions single judgment and multiple judgments appear first time in the Methods, and indeed, after this comment, we realize that a definition of what is single vs. multiple judgments would be helpful.

We provided now definition of “single judgment” in the manuscript in the brackets, at the first mention of these terms:

- single judgment (i.e. CSRs with only one domain for attrition bias, and one judgment in that one domain)

- characteristics of attrition bias reporting for CSRs that reported multiple judgments of attrition bias for the same trial (i.e. CSRs with multiple assessments of attrition bias for the same RCT, where this RoB domain was split into two or more sub-domains analyzing specific aspects of attrition bias),
As we have reported in the section “Secondary analysis: Studies with multiple judgments of attrition bias for the same study”, some RCTs did not have one attrition bias domain in the RoB table; instead they created multiple “sub-domains” judging different aspects of attrition bias.

9. In the Data Extraction section the authors mention that parts 1, 2, and 3 of the secondary analysis investigated characteristics of risk of bias and attrition bias. I suggest that the authors consider either listing specific characteristics of risk of bias and attrition bias that are being investigated or provide a better explanation of what the word characteristics signifies in this context.

Response: We deleted the words “characteristics of” and left simply information that attrition bias was analyzed. Secondary analysis was devoted to unconventional RoB tables in terms of risk of bias, and “characteristics” in this context simply meant that we analyzed who those SRs addressed attrition bias.

10. I would like to see the authors place the results into a table. For example, along the left side of the table, each row could represent one category (and associated subcategories) and there could be columns for Low, Unclear, and High risk of bias (n/N, %). This would make it easier to view the results in aggregate and allow for more clarity in the interpretation of the results. It would also free up words in the results to discuss more items beyond the description of proportions and percentages.

Response: We created a table, as suggested – new Table 3, and deleted the redundant text from Results accordingly.

We hope that the revised manuscript will be satisfactory.

Sincerely,

Livia Puljak and co-authors