Author's response to reviews

Title: Systematic review of methods for individual patient data meta analysis with binary outcomes

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Manuscript title: Systematic review of methods for individual patient data meta analysis with binary outcomes

Authors: Doneal Thomas, Sanyath Radji and Andrea Benedetti

Dear Editor,

Thank you for your response dated May 27, 2014. We have read your comments and those of the two reviewers and have revised the manuscript based on their comments. Based on the instructions provided in your email we uploaded the file of the revised manuscript on the journal’s website.

As you will notice, we have revised the manuscript by modifying the Introduction, Methods, Results and Discussion sections, based on the comments made by the reviewers. Accordingly, we have uploaded a revised copy of the manuscript with all the changes made during the revision process.

Appended to this letter is our point-by-point response to the comments raised by the two reviewers. We agreed with all, except one of the comments raised by the reviewers. We would like to take this opportunity to express our sincere thanks to the reviewers who identified areas of our manuscript that needed corrections or modification. We would like also to thank you for allowing us to resubmit a revised copy of the manuscript.

I hope that the revised manuscript is accepted for publication in BMC Medical Research and Methodology.

Sincerely Yours,

Doneal Thomas
PhD Candidate
Department of Epidemiology, Biostatistics &Occupational Health, McGill University, Montreal, Canada
Reviewer: David Fisher

Reviewer's report:

Minor essential revisions:

- Methods section: PUBMUD should be PUBMED

  Correction was made to the text

- Penalized quasi-likelihood is referred to in the Discussion as PQL, therefore this abbreviation should be introduced in the Statistical Methods subsection of Results. (I might also suggest adding suitable references for PQL and/or Gaussian quadrature as a discretionary revision)

  Corrections were made to the text and references added.

Discretionary revision:

- In the light of the paper of Kontopantelis et al (PLoS ONE 2013; 8(7): e69930) concerning unobserved/undetected heterogeneity in Cochrane MAs, it might be interesting to present the number of MAs reporting zero heterogeneity and compare this with the results in the PLoS ONE paper.

  While we agree that this is an interesting point, we have opted not to implement it. We believe that this information would not be stated very explicitly in the reviewed papers. Some evidence of the number of MAs reporting zero or low heterogeneity can be inferred from Table 3. This Table depicts the number of MAs that used fixed and/or random treatment effect models. Most authors should have used fixed effects models if they had quantifiable evidence of low heterogeneity between studies.

Reviewer: Joahnnes Reitsma

Reviewer's report:

Minor essential revisions

+ I think projects like these are also known as meta-epidemiological research. Perhaps mention this term in the manuscript.

  We have added this term to the introduction.

+ Introduction, 4th paragraph. DerSimonian and Laird in itself is not a two-step random effects approach. Please rephrase along the following lines: “The well-known random effects approach of Der Simonian and Laird is frequently used in the second step of a two-step IPD approach.”

  Corrections were made to the text.
+ I would replace “trials” with “primary studies” or “studies” in the manuscript as you include both intervention, diagnostic and prognostic studies, and trials have the connotation of studying an intervention.

_We do agree with this suggestion, and made the necessary corrections to the manuscript._

+ Results, 4th paragraph. The sentence ‘while the other IPD-MA also included observational studies’ is still unclear. I suspect that IPD meta-analyses either included only randomized studies or only observational studies (like a diagnostic review), but if you identified IPD meta-analyses including a mix of randomized and observational studies then this is should be specifically mentioned.

_This is a typographical error, and correction was made to the text._

+ Statistical methods, 4th sentence. ‘... to pool the overall treatment effect. Because you include diagnostic and prognostic meta-analysis, it is more appropriate to use “to pool the overall effect”.

_Correction was made to the text._

+ Table 4 Measures of heterogeneity. I would be interested to stratify the results in this table whether 1-stage or 2-stage approach was used. I assume that several 1-stage meta-analyses use the 2-stage approach to calculate measures of heterogeneity.

_We totally agree with this suggestion and made changes to Table 4 accordingly._

+ Figure 2 and 3. “Number of IPD meta-analysis” might be a more direct label for the y-axis.

_Corrections made to Figures._