Reviewer's report

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

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Reviewer: Joahnnes Reitsma

Reviewer's report:

General issues
- The decision to limit this review to binary outcomes is regrettable in my view as several issues under investigation equally apply to other types of outcomes (time-to-event, continuous).
- The number of IPD meta-analysis is still rather moderate. A 2-year period would have been more insightful.

Major compulsory revisions
- It appears that the authors focused on intervention reviews, otherwise I expected to see IPD reviews of diagnostic and prognostic reviews as these can also examine binary outcomes. The restriction to intervention reviews is not clear from the in- and exclusion criteria. Please provide further details.
- A crucial question is in this field is to IPD or not. A tabulation of potential reasons why these IPD’s might have generated additional information compared to traditional meta-analysis of aggregate data is informative.
- A major potential benefit of IPD is the greater flexibility, validity, and power when examining variation in treatment effects across patient groups. More detail should be given to this issue, which might include the type and number of patient subgroups examined, if based on a continuous characteristic (e.g. age) how handled in the analysis, how these examinations were reported (p-values, relative or absolute differences etc.), whether the consistency in subgroup effects across studies were examined, etc.
- The observation that 50% of the IPD meta-analyses included data from both randomised and non-randomised studies is an interesting one. Please provide more information about these IPD meta-analyses, like the type of review question(s) they address; the rationale for including non-randomized studies; whether it led to a specific statistical approach.
- Missing data in an IPD setting can be handled in different ways. Please provide data how missing data were handled in the IPD meta-analyses.

Minor essential revisions
- In Abstract the Methods section I would rephrase the sentence “methods to adjust for the effects of covariates” because the issue is also about examining whether the treatment effect is different between subgroups of patients.
- Provide more numbers in the Results section of the Abstract rather than most, some form, most-used etc.
- Table 2: the “Other measures” group is relatively large and interesting. Please list in more detail.
- Table 3. I assume that several IPD meta-analyses examined more than 1 type of covariate. How were these counted because there appears to be no double counting? A table that would start with the total number of covariates examined, the type of covariates they were (patient-level or study-level), and how they were handled in the analyses would be a more informative structure of this table.
- Table 3: it is unclear where “Both” and “Unclear” stands for, especially as it doesn’t match the numbers in Table1. For instance, in table 1 there is only one unclear study and apparently no IPD review having a mixture of analytical approaches. Please clarify and make consistent.

Discretionary revisions
- Results section the paragraph on Heterogeneity: there is a question mark I the 5th sentence that is out of place.
- Figure 1 prints-out very badly
- Figure 1. At the bottom the number of reviews is 55, one layer above it is 57. Please explain. Furthermore, I assume that some IPD review examined different types of outcomes, how are these counted.
- Table 1 in additional files. Please explain difference between Chi squared test and Q statistic.
- Table 1 in additional files. The heterogeneity column has an entry “Not described”. Does it mean “Not examined” or is it examined but the approach how it was done has not been described?

**Level of interest:** An article of limited interest

**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