Reviewer's report

Title: The interpretation of meta-analyses: an objective or subjective process?

Version: 2 Date: 14 February 2008

Reviewer: Tom A Trikalinos

Reviewer's report:

I read the revised paper with great interest. This is a much improved version. I have the following comments. I made these comments quite specific this time, as some are comments from the first round that have not been addressed/have been avoided.

General:
1. To enhance clarity, please to adhere to unambiguous terminology. For operational purposes, define in the Methods:
   a. Meta-analysis as the process of quantitative synthesis.
   b. Quantitative systematic review, a SR that has meta-analysis (Systematic reviews may be quantitative or not)
2. Persuant to 1 change the term "meta-analysis" to "quantitative synthesis" whenever you refer to summarizing quantitative data, including the title.
3. Mention in the results section the apparent tendency for people who probably know the topic very well (such as the 2 cardiologists-specialists and the non-practicing physician - epidemiologist with years of experience??) to be conservative and unconvinced and contrast to the other reviewers who were convinced (as if they were following a "stick with random effects" heuristic rule).
4. Clarify in the text whether the reviewers were given information on the standard of care at each time period. The "placebo" arms received no Mg, but a bunch of other treatments, and there probably is the explanation of the discrepancy with ISIS-4. Another explanation from the other side of the river is null bias in ISIS-4.
5. Please, comment on the limitation of the choice of the topic in the Discussion.

Abstract:

1. The opening sentence is still strong. The corresponding phrase in the text is much better. I think that even if you quote Jadad et al verbatim, this is an obviously incorrect statement, i.e., Jadad et al should had been more careful in their writing, or the sentence is out of context.
   Please, rephrase to "Discrepancies between the conclusions of different meta-analyses are often ascribed to methodological differences."
2. The 2nd package contained a quantitative synthesis of the package's RCT data.

3. Results: Please, rephrase to The discrepancies increased when the heterogeneity of the quantitative syntheses increased.

4. Conclusions: Please, rephrase to something along the lines of to discordant conclusions even when the methodology used to provide quantitative summaries is the same.

Background:
1. p4 Line 5: Along the same lines, consider revising to A quantitative systematic review (a systematic review including a meta-analysis is often considered)

2. p4, lines 6 from bottom to 3 from bottom: I cannot understand what you mean here.

Methods
1. You state that the reviewers were given all pertinent reviews up to the corresponding times per package. How were these identified? Based on the publication type in the corresponding MEDLINE field? How many were there? It seems daunting to go through all reviews that have been written on this topic!!!

2. Please, state how long did it take the reviewers to do this? Minutes, hours, days or weeks?

Results
1. See my General comment #3.

2. Please, provide 2 graphs (forest plots), one with fixed and one with random effects models. The layout should summarize the information succinctly:
   a. Group studies per package and provide an overall updated (cumulative) summary diamond right after each package. The final diamond after the final package corresponds to the overall summary OR.
   b. Name the studies so that ISIS

3. Summarize in 3-4 lines the thoughts/comments of the various reviewers on the discrepancies between ISIS-4 and the smaller RCTs. I understand that there was room for such comments in the forms the reviewers filled in. If none of the reviewers commented on this, this is very interesting to know and please state it.

4. Relevant to my general comment #4, please indicate if any of the reviewers commented on the differences in the standard of care over time periods. If none did, please state so in the text (you may note that this may be because they are aware of such differences and they were all too well known).

Discussion:
1. Page 10, last three lines: The Jadad scale is at best indicative, and scores
reporting quality to a large extent.

2. Page 11, 1st paragraph: Comment here on the problems stemming from the choice of this particular example.

3. Please drop the 2nd paragraph in page 11, to shorten the discussion. The comments in this paragraph are not essential to this project. Moreover, if you were to open this can of worms you also have to explicitly refer to decision analysis and decisions under uncertainty.

4. Page 12, in the study limitations, you do not really discuss the study limitations.
   a. I suggested to discuss the limitation of the topic choice earlier on and you can briefly remind this here.
   b. There was only one topic analyzed but there were objective constraints
   c. One cannot really tell someone to forget what he/she knows about the topic but again there is no other way around this problem short of picking an unknown topic
   d. There was no qualitative analysis of the reviewers' written comments, as done in qualitative research designs

That being said,

I want to thank you and the journal for the opportunity to review this work. I apologize to you and the journal for the tardiness of my second review. This is an empirical demonstration of something we all believe that is true to some extent or other. Some shortcomings in the design and implementation (many of them unavoidable and due to objective reasons) mandate that the paper be strictly discussed.

Best regards,

Tom Trikalinos

What next?: Accept after minor essential revisions

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