Reviewer's report

Title: Meta-analysis of randomised Phase II trials to inform subsequent Phase III decisions

Version: 1 Date: 29 May 2014

Reviewer: David Jones

Reviewer's report:

This paper describes and illustrates (in the context of the earlier Eikelboom analyses cited) use of a Bayesian random effects logistic regression model for meta-analysis of Phase II trial results to underpin subsequent Phase III study design. There is little if any novel methodology involved, but the collation of existing approaches which it comprises may well nonetheless be very useful to practitioners. Improvement on the fixed effect model adopted by Eikelboom is demonstrated, but other examples of the use of meta-analytical methods in summarising Phase II study results are not mentioned or critically reviewed. Since the Eikelboom analysis is a rather old one, demonstration that fixed effect analyses are still performed in this context, and that the approach advocated in the paper out-performs other methods in recent use would strengthen the paper.

Major Compulsory Revisions

1. Must perform and summarise results of a (critical) literature review of methods of meta-analysis available for and used in the context of synthesizing Phase II study results. This literature is not particularly extensive, but if necessary the emphasis could be on Bayesian random effects models. One example likely to be included is the study by Assifi et al in Surgery 2011:150;466.

Discretionary Revisions

2. Some tendency to repeat material about the sequence of issues to be addressed in 2.2 in following results and Discussion sections could be reduced.

3. Model 2 (p8, section 2.2.1): Since this section is mostly presented at a tutorial level, the provenance and interpretation of the suggested priors, and the reason for the use of I(0,) should perhaps be set out explicitly.

4. Sections 2.2.3 and (especially) 2.2.4 are long, if reasonably clear. The paper would read better if the more technical details of implementation were moved to appendices/supplementary materials, leaving relatively brief outlines of approaches in the main text.

5. Section 3.2.2: The possibility indicated here is of course worth mentioning, but more specific indications of how to proceed are needed to make it practically useful, and potential dangers of use of strong priors not based on evidence of plausibility should perhaps be noted. Fig 6 could go in supplementary materials.
6. Conclusions: Although these currently reflect the comparison with Eikelboom’s approach/results, this is rather limited. Could brief conclusions/recommendations for good practice in meta-analysis of Phase II trials not be added?

7. Abstract – Results l2: ‘.. encompass the subsequent Phase III trial results’?
8. Abstract – Results l4: 0.82 or 0.83 (as in 3.1.3)?
9. p9 l-4: I dislike the ‘...will likely be..’ expression used here and elsewhere. [However, I concede that the it may be regarded as quite acceptable my many other readers!]
10. p12 l10: ‘...typical number (<10) of studies..’?
11. p18 l-11: ‘.. actually entirely plausible..’ This seems a little over-emphatic, even if technically correct.
12. P20 l-1: ‘..such as in the example by..’

Minor Essential Revisions

13. P21 l12: ‘including’, not ‘included’

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.