Reviewer’s report

Title: Individual patient data meta-analysis in surgery. A systematic review.

Version: 2 Date: 28 December 2012

Reviewer: Doug Altman

Reviewer’s report:

Given the paper’s title I had assumed this would be a wide-ranging literature review but rather the clear intended focus is on subgroup analyses. This emphasis should be reflected in the paper’s title. Rather than reviewing the use of IPDMA in surgery the paper is really about subgroup analyses within IPDMA in surgery, and also the extent to which published subgroups analyses are incorporated into clinical practice guidelines.

Because of its narrow focus I didn’t find the paper especially interesting. It seems to fall between a literature review and an educational article, doing neither thoroughly. The two Boxes briefly describe two interesting examples of IPDMA but there is no real discussion of these nor the lessons learnt.

Major Compulsory Revisions
None

Minor Essential Revisions

Methods
1. IPDMAs have multiple advantages over MAs based in (published) summary data. The authors give 5 reasons, of which the first, third and fifth relate to subgroup analyses. The ordering here could be improved. But there are other important advantages which are not mentioned (see Riley et al 2012 for 14 reasons ) perhaps because of the clear focus here on subgroups.

2. Why does this review focus only on surgery? In fact the emphasis is on surgical interventions rather than surgical studies more widely; this should be stated clearly in the title and introduction.

3. The flow diagram is misleading and needs to be improved in several ways. I presume all 2433 records were screened, not just 583, of which 1850 were excluded. Then of the 583 retained full text was obtained for 42, of which 20 were excluded. At this point the PRISMA flow diagrams asks for reasons to be stated – the phrase “with reasons” has just been copied here from the template, where what is wanted is the actual reasons for excluding those 20. But there is no indication of who or why the sample fell from 583 to 42. I suspect that 1850 were excluded for one reason and 541 for another (presumably they weren’t related to surgical interventions) but this isn't clear. Lastly, there was no quantitative synthesis so the last box in the flow diagram is misleading. Having written that based on the appendix I then saw that a different flow diagram is in the main file,
which is much more informative. It would be good to combine the most useful aspects of both.

4. There should be an explicit statement about eligibility criteria. Eligibility criteria are mixed up with the section process. It isn't until part way down p4 that there is a mention of the need for the primary studies to be randomised trials. This is never stated explicitly.

5. Quality of reporting was assessed using 7 of Riley’s 18 criteria and not explicitly in relation to the 27 items of PRISMA, which those 18 items were intended to supplement. The rationale should be given for choosing just the specific 7 items.

6. It is surprising, in a critical review of what others have done, that the present study lacks key information about methods, despite the authors having provided a completed PRISMA checklist. So, for example, they don’t state whether they had a protocol, and indeed say (wrongly) in the PRISMA form that this question is not applicable. As noted already there is only implicit mention of eligibility criteria and rather poor signposting of the key requirements that the IPDMAs were of RCTs only. It is not stated who selected eligible studies and extracted data nor whether these steps were done in duplicate independently. Of course not all PRISMA is relevant as this study is a review of reviews, but the presentation needs to be much more explicit and informative.

Results

7. It would be good to learn more about the published IPDMAs. To take just one example, we are told how often it was specified whether a one- or two-step analysis was done but not how many did each type of analysis.

8. The authors should distinguish more carefully between what was reported and what may have been done. They say “The median number of subgroups studied in these IPDMA was 3.5” but this is what was reported – it is possible and indeed likely that additional analyses went unreported (see p9).

9. It is implied but never stated that the IPDMAs only included RCTs. Please be explicit.

10. The main discussion of the subgroup analyses in the IPDMAs is based on very small numbers and fails adequately to take account of the fact that there were multiple subgroup analyses for a single IPDMA, although this idea is noted on p9. There is no mention here of whether any of the reported analyses was clearly prespecified.

11. On P8 it is reported that “More than half of the IPDMA failed to report whether or not there was a protocol for the IPDMA project available” but Fig 3 shows that for 12/22 studies there was no protocol, thus disagreeing both numerically and textually with the text.

12. One key problem when conducting an IPDMA is obtaining data from all eligible studies. I had expected some mention in the review of whether this was an issue in the IPDMAs reviewed, but there is no mention although it is implicit in fig 3. Similarly, often one cannot include all trials in a subgroup analysis as the data weren’t available in all cases. Again this issue isn’t mentioned.
Discussion

13. Near the start of Discussion it is noted that 44% (8 out of 18) of the significant subgroups were implemented in clinical guidelines, but this information should be in Results. That said, I don’t believe that this is especially useful or interpretable information. Given that the data of IPDMAs could be as recent as April 2012 there is little chance for the more recent studies to have been influential. The data of searching for clinical guidelines should be given. Again this point is mentioned later, on p10.

14. The authors might note that single factor subgroup analyses, whether for single trials or a collection of trials, are problematic and a multivariable approach may be preferred (Kent et al, Trials 2010;11:85.). In fact, the example in Box 2 uses this approach, although based on a model derived from the same data rather than a pre-existing risk prediction model.

Abstract

15. There are 8 sentences of which one reports the number of IPDMAs and 6 relate to subgroup analyses. This is seriously unbalanced in relation to the planned and indeed actual content of the review as a whole.

Discretionary Revisions

16. I feel it is correct to use IPDMA for one meta-analysis and IPDMAs for the plural form (cf RCTs on p4).

17. The search strategy might be accompanied by a brief explanation of the rationale.

18. The 2 case studies are useful. it would be good to include references for the clinical guidelines where relevant.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare that I have no competing interests