Reviewer's report

Title: Conducting systematic reviews of adverse effects: didactic guidelines

Version: 2 Date: 2 October 2006

Reviewer: Lisa Prof Bero

Reviewer's report:

General

This is a well-written paper with a very limited audience. It has appeal to methodologists.

Another drawback to the paper is that it did not leave me with a clear idea of how to incorporate adverse effects into systematic reviews. I realize that the authors were trying not to be prescriptive, but by laying out so many options for what can be done and difficulties in doing it ... I wasn't sure what I would do to conduct a systematic review of adverse events.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

p. 4 A much more detailed description of the consensus process used to develop this document should be presented.

Table 1 is important to set the context for the paper. However, I found it confusing. For example, in the first section "the margin between benefit and harm is narrow," the 3rd example mentions only benefit and not harm.

p 5-6. In the section "What types of adverse outcomes" why were outcomes categorized by how the information was collected (e.g., diagnosed by physician, self-reported, etc.) I'm not clear how these would help determine the most "relevant" outcomes, although they would help determine which ones are measured most rigorously. Relevance, however, would also be influenced by the severity or reversibility of the outcome.

Page 7 - 9. This section is a bit repetitive as it lays out the same problem -- benefits and harms may be difficult to compare directly -- but doesn't offer any solutions. I'm left with thinking that this comparison should not be made.

Page 12 - 15. This section has a number of problems. All the quality instruments that are referenced are for RCTs whereas the possibility of including studies of other design is acknowledged earlier in the document. There are quality assessment instruments for observational epidemiological studies. If the authors choose to ignore these, they should explain why. I agree that these instruments (as well as many items on RCT instruments) lack an empirical basis, but I was not clear why they were not being discussed. Page 14: It seems like a criteria (similar to one used for efficacy data) is that that data must be extractable from the source document. Page 14. Under general principals, study design itself could be added as a question to establish a hierarchy of design (even without specific quality assessment).

page 16-17. Using withdrawal / dropout rates as an outcome measure is an important issue. I'd like to see more discussion of this .. what's the evidence that low rates are associated with underreporting of adverse events?

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

page 18. What's the evidence for the "rule of 3" - more discussion of reference #21 is required.

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Discretionary Revisions (which the author can choose to ignore)

The middle paragraph on page 7 re different study designs that can be used to assess adverse effects...
seems to fit better with the section on quality assessment (page 12)

page 11. Why was limiting by study design not included in the search strategy? By not doing so, the number of identified studies could be overwhelming. Although, the entire search seems geared towards high sensitivity and low specificity, so this rationale should be explained.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.