Reviewer's report

Title: Conducting systematic reviews of adverse effects: didactic guidelines

Version: 2 Date: 7 August 2006

Reviewer: Barnaby Reeves

Reviewer's report:

General

1. I should state at the outset that I applaud the authors for taking on this subject. It is a very important area.

2. However, I don't think it provides guidance but rather structures the problem. I give more detailed comments for this opinion below. I think that badging the paper as guidance may frustrate and mislead readers.

3. Conceptually, I think that the structure of the paper has not been thought through as clearly as it might have been which makes the task of the reader much more difficult and limits the usefulness of the paper because the existing structure is difficult to assimilate with other guidance on systematic reviews. With a bit more work, I feel the paper could be much better.

4. I think it would help if the structure/headings more clearly followed the steps that are already familiar to reviewers: e.g. setting the question, searching for potentially eligible studies, defining inclusion/exclusion criteria, assessing susceptibility to bias (new recommended Cochrane term, rather than quality assessment), synthesising the data, interpreting the findings, etc.

5. It might also be helpful to set the problem of reviewing adverse effects in the context of other frameworks, e.g. for applying evidence. For example, it is widely assumed that the relative effects of treatment generalise to populations at varying risk of the (primary) outcome. Is the problem with studying adverse effects in RCTs primarily because: (a) this assumption does not hold true; (b) it is difficult to quantify the relative risk of relevant outcomes precisely in RCTs?

6. For me, the central difficulty is the trade-off problem. I feel that this is given relatively emphasis. I can see the value of doing the leg work without reaching a clear conclusion but am not sure that reviewers will.

7. It is brave of the authors to set out such a wide range of examples in Table 1. I agree with the three main areas identified in which systematic reviews of adverse effects are justified but am concerned that some of the examples aren't ideal (see below).

8. There is general, not serious problem with inconsistent use of terms / language which is likely to make the paper more difficult to understand for the reader than it need be.

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

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

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions
Level of interest: An article whose findings are important to those with closely related research interests

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

Statistical review: No

Declaration of competing interests:

I should declare a potential conflict of interest with respect to this paper:
- I am a co-convenor of the Cochrane Non-Randomised Studies Methods group, so view the world very much from the perspective of the Cochrane Collaboration
- I know the work of the authors quite well, and have previously discussed with Andrew Herxheimer many of the issues raised in the paper.