Reviewer's report

**Title:** Systematic review of methods used in meta-analyses where a primary outcome is an adverse or unintended event

**Version:** 1  **Date:** 18 July 2011

**Reviewer:** Sheena Derry

**Reviewer's report:**

This is a useful review of methods used to review adverse events in published systematic reviews. I found the text quite hard going, with lists of numbers of studies doing one thing or another – the tables are much easier to follow. I welcome the suggestion on P13 that it may be more appropriate to restrict focus to simpler methods of analyses coupled with appropriate caveats, than to embark on complex statistical methods. There is a risk that complex statistical analysis may confer a false validity.

**Major compulsory revisions**

1. P8, Heterogeneity. Where does the denominator of 128 come from? Should it be 128, not 124 that performed a quantitative assessment?

2. Discussion. No limitations are mentioned. It is important to remember that the included reviews differ in intervention, outcomes, type of study etc, for which different approaches may be entirely reasonable. It would be useful to have some consideration of this in the Discussion, and any guidelines will need to take account of this.

**Minor essential revisions**

1. The search was limited to the English language, and while I do not think this in any way invalidates the work, I think the authors should acknowledge that the findings might not extrapolate to non-English language reviews.

2. The title clearly refers to ‘adverse or unintended events’, which is how data are usually reported, and does not assume causality. On P3, final paragraph, the authors talk of ‘unintended or adverse reactions to non-interventional activities’. For consistency, I think this should be changed to ‘adverse events associated with ….’ or similar.

3. The sentence in brackets on P4, paragraph 3, referring to determination of sponsorship should really go into Methods.

4. Statistical methodology aspects. I suggest this section would be easier to follow if it were broken down with subheadings (Outcome measures, Method of meta-analysis, Type of primary study).

5. The first sentence on P5 is disjointed and back-to-front. Suggest: ‘Table 3 sets out the number of included reviews including assessment of heterogeneity, quality, and dissemination bias, by year of publication, to examine any changes
over time.’

6. P6, 1st and 3rd paragraph. Are the three studies with insufficient detail the same studies in both paragraphs? If so, how can there be insufficient detail to determine the type of analysis in paragraph 1, but in paragraph 3 they can be classified as fixed effect? In paragraph 5, you say the method was unclear in only one review.

Discretionary revisions

1. I am unsure about calling the included studies ‘meta-analysis references’. It is not wrong, and I understand the difficulties of language when carrying out a systematic review of systematic reviews but this term does not read well for me. Can you call them ‘included reviews’?

2. There are a number of minor typos, including two sets of referencing in places.

**Level of interest:** An article of importance in its field

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

**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