Reviewer’s report

Title: Guidelines for randomized clinical trial protocol content: a systematic review

Version: 2 Date: 11 May 2012

Reviewer: Marian McDonagh

Reviewer’s report:

Overall, I think this review is both an important contribution to the literature and is well done. My main comments relate to how the concepts are contextualized and clarifications in the text.

• Major Compulsory Revisions

None.

• Minor Essential Revisions

See attached text with notations of editing suggestions.

• Discretionary Revisions

1. My recommendation is to consider the proportion of RCTs funded by the various sources identified. Some of the funding sources most likely represent the majority (e.g. industry and government) while others are relatively minor players. I cannot see that this has been taken into account either in the introduction or in the analysis and discussion. I would like to see an evaluation of the results stratified by industry vs government sponsored guidance as these are, in my mind, the most common funders of trials in terms of both numbers of trials and money spent. In the introduction, I found myself thinking about the different motivations behind protocol guidelines depending on the source. Likewise, the accessibility of guidance may vary by source.

2. Because industry typically interacts with the FDA, their decisions on protocol guidance likely overlaps with FDA guidance. This could be evaluated.

3. In Method, subsection ‘Guideline content’. This section is unclear. It is difficult to tell why this was done, what is the purpose based on the text, and how or why the subset was selected. Similarly, the results for this subsection are somewhat opaque.

4. The discussion could go into more detail on the author’s thoughts on the downsides to their findings earlier.

5. In the discussion it is noted that there recently has been recommendations on guideline development reporting. I would think these should be also mentioned in the introduction.

6. In the discussion, paragraph 6, the sentence “Given the evidence or protocol deficiencies...” needs citations to support these statements. I do not know that those statements are true, or what they entail off the top of my head so would like
to be able to refer to the original research.
7. Table 1 should include the % of guidance from each of the types of funders.
8. Table 4 is difficult to read as formatted.

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

**Quality of written English:** Acceptable

**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'