Reviewer's report

Title: A Systematic Review of Techniques and Interventions for Improving Adherence to Inclusion and Exclusion Criteria During Enrolment into Randomised Controlled Trials

Version: 1 Date: 13 December 2009

Reviewer: Brian Rowe

Reviewer's report:

The purpose of this paper was to systematically identify and review techniques and interventions proven to prevent or avoid inappropriate enrolment of patients into RCTs. The authors conducted a systematic review using standard methods to complete this task. The premise was to examine evidence of interventions to reduce enrollment error.

Was an identifiable question formulated? Unclear

It's not surprising there is a lack of evidence in this field; however, I wonder if the question was the wrong one. Why not start with an indirect comparison of effects. For example, it might have been fruitful to examine a number of trials with specific enrollment error rates reported and determine what “interventions” were applied and compare all similar efforts. For example if 10 studies were identified that reported NO EFFORT to reduce errors and their rate of enrollment error was say a median of 5%, this could be compared to all studies that staggered their enrollment start-date (or some similar such intervention). Indirect comparisons are more complicated to analyze, but would have been more informative.

This manuscript will be evaluated using the Oxman and Guyatt OQAQ tool:

Were the search methods used to find evidence (primary studies) on the primary question(s) stated? Yes.

A complete list of these concept-related terms are presented in Table 1. Databases searched up to 2009, unpublished and non-English language articles were searched for.

Was the search for evidence reasonably comprehensive? Yes.

EMBASE, MEDLINE, Cochrane Database of Systematic Reviews and grey literature searched.

Were the criteria used for deciding which studies to include in the review reported? Yes. Any intervention designed to reduce any form of protocol error or violation were retrieved in full text for detailed review. Very broad inclusion criteria: Any design, any error type and any form of evaluation of effectiveness were accepted.
Was bias in the selection of articles avoided?
Two reviewers for screening and 3 for selection; differences resolved by consensus. No comment on independence and blinding?

Were the criteria used for assessing the validity of the studies that were reviewed reported?
No mention of the quality assessment or scoring system.

Was the validity of all of the studies referred to in the text assessed using appropriate criteria (either in selecting studies for inclusion or in analyzing the studies that are cited)? No.
No mention of the quality assessment or scoring system.

Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported? – No.
No methods for combining were discussed. This would be especially important for indirect comparisons of trials that used a method to reduce enrollment errors and reported error rates; however, no primary publications were found.

Were the findings of the relevant studies combined appropriately relative to the primary question the review addresses? – No.
No primary publications were found.

Were the conclusions made by the author(s) supported by the data and/or analysis reported in the review? - Partially.

Overall, how would you rate the scientific quality of this review?
Moderate.

In the large section in the discussion entitled: "Interventions recommended to reduce enrolment errors, but not evaluated."

How sure can the readers be that this list is comprehensive? It’s not stated where this list came from. Off the top of my head, I would also suggest mock scenarios, simulations scenarios, study check-lists, double (PI)- review, and several other techniques may be useful. A focus group or survey could have helped to inform the research question here.

The discussion seems to focus on large trials, and I would think the effect of enrollment error there may be less than smaller trials. Can you comment?

Strengths and Limitations:
Should discuss the exclusion of indirect comparisons and why.

Overall, its well written but could be shortened.

**Level of interest:** An article of limited interest
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

No COI!