Reviewer’s report

Title: The Methodology for Developing a Prospective Meta-Analysis in the Family Planning Community

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Reviewer: Mike Clarke

Reviewer’s report:

This is a well written description of the rationale for a prospective meta-analysis (PMA) and an outline for an example of this type of research. However, I think it would benefit from more discussion, and from a more detailed description of the methods (including perhaps the statistical analysis plan for this PMA). I presume that this detail is in the published protocol for the Cochrane review but this article feels light because of its absence.

Major revisions

1. I would like to see more within the article about how this review differs from many other PMA. In this example, the idea for the research seems to have come from one group (or person), rather than occurring to several different research groups at about the same time. For example, how many of the sites would have initiated such a randomized trial if they had not been approached to take part in the PMA? You write “After the principal investigator developed a preliminary PMA protocol, he identified potential collaborating investigators at other sites. Investigators at six sites joined the PMA collaborative.” Which seems to indicate that the research project began in one place and then others were asked to initiate studies. Your use of the term “site” rather than “trial” to mean the individual elements in the PMA also suggest that this is closer to a multi-centre trial than a PMA. How does it differ from multi-centre randomized trials of the past that were designed to be flexible enough to allow each centre to modify the overall trial design to meet local circumstances (for example, by using a radiotherapy regimen that was in use locally and comparing this with no radiotherapy). It would also be good to know what influence the other sites had on the design of the PMA. Did they influence the choice of the dose of misoprostol to test, the primary and secondary outcomes, or the eligibility criteria for the trial.

Minor revisions

2. Abstract: It would be good to have more information in the abstract about the research question being answered by the PMA, and how the studies vary across the different sites. This is important to show how this research is different to a multi-centre trial.

3. Introduction: it would be worth discussing the difficulties faced by regular meta-analyses when they try to include all relevant data: selective reporting
biases and unwillingness by researchers to share their data.

4. When discussing why PMA might be more cost efficient than a multi-centre trial, it would be good to have more about the possible cost disadvantages of the PMA. For example, might there be economies of scale in a multi-centre trial, which are not available when separate trials are conducted at each site. This can be important if the placebo has to be made especially or if each site prints its own materials.

5. It would also be helpful to have more discussion of the problems that can arise in a PMA compared to a multi-centre trial. For example, will publication of the PMA need to wait for each site’s study to be completed, analysed and reported? If a site does not report their study, will it still be included in the PMA? If a study fails at one site (for example, because of local recruitment difficulties), what will happen to its data for the PMA? Will there be site specific Data Monitoring Committees? Will they have access to data from the other sites?

6. Are you able to cite something to support the statement “IUDs are an ideal method of contraception as they are effective, have few side effects or contraindications, require only a single act of motivation for many years of use and are highly rated among users”? For example, is there a systematic review that shows this?

7. How will you ensure that future reviewers and others who use the results from the six sites and from the PMA do not re-use the data without realizing it?

Discretionary revisions

8. I disagree that PMA is “new” as a research tool is “new”. It might be better to say “relatively new” since, as you show, there are examples from nearly 20 years ago.

9. Are you able to cite something (a personal communication, if not a published article) to support the statement that your review is the first PMA to be registered with The Cochrane Collaboration?

10. Did you approach any sites that declined to join the PMA?

11. How will you decide if a site meets the requirement: “assuming subjects are properly randomized” for their data to be included?

12. If you identify new trials in the future, will you invite them to join the PMA regardless of where they are being conducted? Do you have any concerns about adding further trials after the publication of the results from any of the existing six sites?

**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 have no competing interests that I am aware of.