Reviewer’s report

Title: Pragmatic Clinical Trials Embedded in Healthcare Systems: Generalizable Lessons from the NIH Collaboratory

Version: 0 Date: 07 Jul 2017

Reviewer: Vance Berger

Reviewer's report:

I found it a bit odd that while this is hailed as an NIH collaborative, and though there is no shortage of authors, not a single one lists the NIH as an affiliation. Is the NIH actually involved in this collaborative?

The conclusions do not follow from the report. In fact, one might even question whether what appear as conclusions are actually conclusions at all. It seems more of an objective to conduct these trials in such a way that they provide the right kind of evidence. What, then, are the conclusions of the study? For that matter, do we actually have a study here? This is not a criticism of the effort, but what is gained by having it published, above and beyond what is gained by disseminating just the trials that grow out of this effort?

Unfortunately, your focus on cluster randomization undermines your effort at providing reliable and unbiased evidence. I certainly understand that it is much easier, logistically, but this is more than offset by the fact that there is then confounding between the interventions and the center effects. And while we can all pretend that these effects can be separated with suitable covariate adjustment, in fact they cannot, and, in this context, "suitable covariate adjustment" is a misnomer, since there will always be center attributes that are not measured. I did see that one trial that made it to the table had individual randomization, so clearly this does fall within the realm of possibility. Why not just do it right all the time?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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