Reviewer’s report

Title: Progression Criteria in trials with an internal pilot: an audit of publically funded randomised controlled trials

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Reviewer: Stephanie MacNeill

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This was an interesting paper describing an audit of NIHR HTA funded RCTs where the focus was on the recruitment-related progression criteria in their internal pilots. The research team provided useful exemplars of "good practice" in terms of setting progression criteria as well as detailed characteristics of those studies using internal pilots.

Major comments:

1. Please confirm the statistics quoted in lines 147 and 148 as they are not those presented in table 3

Minor comments:

1. The key thing that this study is missing is an assessment of whether or not the internal pilots used lead to more successful trials in the long run. Did the recruitment-based progression criteria minimise the risk of studies failing in the long term? Did these studies require costed (or un-costed) extensions to meet their recruitment target in the end? I expect that many of the studies included in this audit are still recruiting so publicly available data to answer this question is not yet available. It would, however, make for an interesting follow-up paper in due course. In light of this, it might be worth defining what is meant by "good criteria" (see line 180).

2. Another question raised by this work is what are the progression criteria in cluster randomised trials with internal pilots. Again, this would make for an interesting follow-up paper.

3. Some of the text was not entirely clear. For example, "HTA funded trials were also chosen because of the level of quality planning required for funding approval with a principle for internal pilots" (lines 66-68); "Overall a reasonable number of studies were audited from each year of funding decisions" (line 110).

4. Could "risky trials" be clarified in line 45?
5. I appreciate that this research is focusing on recruitment-related progression criteria, but the reality is that other factors could potentially be used in the progression estimates. This could be clarified in the Background section.

6. In line 49 the researchers mention that "for the purpose of this research the focus is on internal pilots as a means to test or monitor study recruitment". Can you clarify what is meant by test?

7. In table 1 it would be useful to have a footnote that would explain what the "other" categories comprise of

8. Table 2 should be clarified that it relates to all years and would benefit from being presented as a 2x2 table (type of criteria used vs number/rate used)

9. The authors refer to a "typical study" having a sample size of 520 and given that the median sample size was 510 I was curious why 520 was chosen.

10. On line 152 the researchers state that "We are not looking here at within-site lag to recruitment (ie a slow start caused by staff familiarising themselves with the protocol) but rather a lag caused by the process of setting up multiple centres whilst recruitment is ongoing.". The researchers have shown in table 3 that the internal pilot stage invariably uses fewer sites than required for the full trial, but the authors cannot exclude the possibility that the recruitment target for the internal pilot might allow for both a lag in opening sites as well as a slow start within each site once opened.

11. Please clarify how the categories were defined in figure 6

12. Throughout the paper the authors have used the expression "stop-go criteria", but on line 213 refer to "Go/No-go criteria". It would be good to be consistent.

13. On line 216 the authors state that "red equates to definitely stop", but this was not the case in the Prepare For Kidney Care Trial used as one of the exemplars. There it was "predominantly red targets would probably illustrate that the trial would not be feasible". A single "red" would not be sufficient to close the study in that case.

14. The Discussion section should incorporate mention of the limitations of this study.

15. Figure 3 requires some clarification of what each of the categories mean.

16. Figures 4 and 5 might benefit from having proportions on the y-axis rather than frequencies.

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I am on the research team for the Prepare for Kidney Care Trial which was used as an exemplar in this paper.
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