Author’s response to reviews

Title: Protocol publication, transparency, and selective reporting: increasing value and reducing waste in clinical trials

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REVIEWER #1

This commentary paper mainly provides an overview of existing publications in this field. It is clearly written and outlines some key issues currently under discussion in the field. However, I think it is limited in the extent to which it moves the debate on from papers that have gone before it. There are a lot of general statements about the publication of protocols, which I am in full agreement with, but I wonder whether some more in-depth discussion of the practicalities around implementation would strengthen the paper and give it more impact.

Response: Thank you for suggesting additional discussion of implementation issues. We have now added in-depth discussion of practicalities and specific recommendations (summarized in a box) focusing on solutions for each challenge raised in the paper.

For example what do you mean by "publication" of the protocol - do you mean that it is in the public domain or do you mean published in a peer reviewed journal - what are the advantages and disadvantages of the different approaches, does it matter which it is? For example if researchers are to ensure that the protocol is published in a journal before participant enrolment this has actually considerable consequences for several stakeholders e.g. for trials teams there is generally a relatively small window between ethical approval (which may require protocol changes) and recruitment of first participant and this is an extremely busy time for trials teams. Equally the considerable length of time it can take journals to process submissions is another factor that may affect the timeliness of the publication - how might some of these practicalities be tackled?

Response: We have clarified the wording throughout the title and manuscript to refer to public availability of the protocol, which includes uploading to trial registries as well as journal publication. We have added sections about prospective access and the optimal venue for sharing protocols, including their advantages and disadvantages (Lines 221-87).

Do protocol amendments need to be publicised and how should this be done?
Response: Yes, we have proposed that the final protocol version (including a list of amendments) be shared in the trial registry or supplementary journal appendix (Lines 235-37, 264-67, 285-87, Box).

Lines 189-191 need to also give some consideration of the known limitations of peer review and the practicalities of how much a protocol can be changed by the time it gets to a journal having been approved by an ethics committee and often a funder.

Response: Agreed. We have acknowledged this issue on Lines 272-74.

There is suggestion in the paper that publication of protocols will get around the limitations of poor reporting in registries and published papers of results - is there an argument for improving these and using these existing structures more effectively?

Response: We agree that it is important to improve the quality of trial registries and published papers of results, which - despite various initiatives - has not improved sufficiently over the years. However, this is a large topic that is related to but distinct from the issue of protocol sharing, and would warrant its own paper to fully address the issues. We have decided to focus primarily on protocol sharing.

Similarly, with some of the other general statements made it would be useful to have some more 'unpacking' of the issues.

Response: Agreed. We have added substantial content to discuss specific challenges and solutions.

REVIEWER #2

The commentary is well written and clearly presents the current thinking around protocol publication. However, it fails to support some statements and does not go much beyond summarising the current state of play.

Response: We have added specific recommendations (summarized in a Box) to address next steps for each challenge discussed in the paper.

Statements such as ‘most trials do not have accessible protocols’ could be supported by presenting percentages or numbers.

Response: We have added references to support this statement (Line 70).

I feel that the commentary would be enhanced by a more critical consideration of the issues that have hindered accessibility/publication and what might be done to address these in the future. Steps have been taken by some regulators, but these are suggested to be insufficient, what else might be done? Where next? Trials may have led the way, but could more be done?
Response: Agreed. We have substantially revised the paper and added recommendations to address next steps for each challenge.