Author's response to reviews

Title: Lessons learned from the conduct of a multisite cluster-randomized practical trial of decision aids in rural and suburban primary cares practices

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Author's response to reviews: see over
Editors, *Trials*
RE: Manuscript No. 6230479818946773

Dear colleagues,

Thank you for the opportunity to respond to the reviewers’ comments.

The first two reviewers raise serious concerns about the ethics of our study, including concerns about possible coercion of participants. They also raise concerns about our use of the terms opt-in and opt-out, and argue that a study of this nature would not have been allowed with careful ethical oversight. Indeed, reviewer #2 considers that our recommended approach for conducting this kind of studies should be banned.

As the editors can imagine we are dismayed by these views. In re-reading the manuscript we can see, however, why these two reviewers decided to assume the worse interpretation of the ambiguous language we chose to describe what happened in our study. Thus we have re-written the description of our procedures to specify clearly why, when, and how we were able to scan records to identify patients and to invite clinicians and patients to participate in the study. Furthermore, these procedures were approved not just by one but by five independent ethics committees:

1. Mayo Clinic Institutional Review Board
2. Olmsted Medical Center Institutional Review Board
3. Albert Lea Medical Center (Mayo Health System) Institutional Review Board
4. Austin Medical Center (Mayo Health System) Institutional Review Board
5. Mayo Clinic Health System in Mankato Institutional Review Board

We now provide itemized responses to each of the reviewers’ comments.

**Reviewer #1**

1. **Title is misspelled** – this problem is limited to the submission, as the manuscript file had the correct title. This is corrected.
2. **The terms ‘opt in’ and ‘opt out’ are unnecessary and even appear to be used inappropriately** – We agree. We have re-written the sections in which we describe the methods of recruitment distinguishing what we thought initially to be the ideal method with the one we tried next which we now describe as in-clinic.
3. **The reviewer believes Lesson 1 is well known; Lesson 2 and 3 are misguided as the in-clinic approach should have been avoided and is**
unethical. We have recast the description of the new approach to avoid the impression this reviewer might have formed that our approach led to limited or coercive discussions. We have thought it redundant and have not included in this description that the study coordinators are all certified research coordinators (not research students or other available personnel) operating under strict rules of institutional review boards in the United States. As indicated above, these boards approved study procedures. Furthermore, the practices also approved the study procedures and facilitated the use of in-clinic offices for study coordinators and patients to carefully discuss the study in a face-to-face manner. Perhaps reviewers are considering other kinds of trials in which participants can take their time to review and consult about their participation and return at any other time to participate in study procedures. Since the study procedures took place during the encounter, the next possible encounter in which they could take place was usually 6 months to 1 year away, thus limiting options. The crux of the argument against what we did is that the in-clinic approach would be coercive. Since we were inviting patients to participate in a study about two ways of receiving information from their doctor and the study procedures comprised of post visit surveys, the informed consent document was not particularly arduous to review or complex to understand. Furthermore, the participation rate compared to the pre-visit phone based approach was only 10% better with 1 in 4 patients declining to participate at the clinic. By clearly discussing the trade-offs of these two approaches, readers can form an opinion about them, the purpose of this study. Lesson 4 is stated backwards: it is not, in our opinion, we have re-written its formulation to improve its clarity: Lesson #4: Procedures that involve working closely with the practice may improve recruitment and may also affect the quality of the implementation of the interventions.

The reviewer finds these lessons are well known in the literature. There are not many randomized trials of shared decision making in the literature in which the interventions occurred within the clinical practice and in rural practices. This was the reason the NIDDK funded this R34 project, seeking to figure out the feasibility of such trials in rural clinics. Not reporting our findings, even as we acknowledge with citations that some of these are known in the literature, would contribute to fail to achieve the goals of the study.

4. There is no figure 1. There is a figure 1 and a link was provided to it. We have now changed this to provide a link only embedded in the text (page 6): “Additional criteria were required according to each of the arms, and a flowchart was developed to facilitate the process of identification of eligible patients (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3468357/figure/F2/).” Figure 2 is now Figure 1 and references to figures have been renumbered.
5. **Strange use of English** – we have now rewritten the offending phrase to say (page 6): “Clinicians were offered to participate in the study and signed written informed consent documents during this meeting. Clinicians who chose not to participate or were absent from this meeting were not approached again.”

6. **Researchers could have learned from engaging the participants and conducting a pilot** – we could not agree more. This paper in fact reports on the results of our pilot and the lessons learned here were learned as the result of conducting this pilot. All of our work is conducted in conjunction with a Patient Advisory Group with whom we meet every third Monday from 5:30-7:00 pm to review our work. Clinicians from the sites were part of our steering committee and many are acknowledged or are authors in this paper.

7. **How did you recruit patients from clinicians who did not give consent** - We only looked for eligible patients in the panels of clinicians who gave consent to participate in the study in the original approach. In the in-clinic approach, we did not limit our scanning to the patients of clinicians who had agreed to participate in the initial practice presentation. We also scanned the panels of clinicians with unknown interest in the study. If a potentially eligible participant were identified, then the study coordinator contacts the clinician. The clinician then consents (or not) to participate. If the clinician does not consent they could limit that decision to this patient or may request not to be contacted again. In the latter case, we did not scan this clinician’s panel for eligible patients again. Only when the clinician consents to participate did the study coordinator approach the patient in the clinic to invite the patient to participate. We have clarified this in page 11 as follows: “Four new suburban practices were approached using a different method. Clinicians were offered the opportunity to give written informed consent at the initial meeting with the study team, as in the original recruitment policy. In scanning registries and records for potentially eligible patients, study coordinators, however, considered all practice patients with diabetes with upcoming appointments, only avoiding patients from clinicians who had declined participation at the initial visit. If an eligible patient was identified within the panel of a clinician who had not yet given consent for participation, the study coordinators approached the clinician at their next encounter. These clinicians were offered the options of consenting to participation, delaying their participation in the study if the timing was not appropriate (study coordinator could approach them again for future eligible patients), or declining participation definitively. In these practices, we discontinued phone interviews with candidate patients, instead approaching them immediately as they appeared for their scheduled appointment at the clinic. During the interview in the clinic exam room – unhurried, quiet, private, and face-to-face – study coordinators reviewed details of the study and obtained written informed consent.”

8. **The recruitment figures are unclear in the text and the table.** We have completed revamped this presentation. We now offer Figure 1 which shows the two approaches side-by-side using a flow diagram as suggested by the
reviewer with minimal repetition in the text. The figure includes number of sites, duration of recruitment, number of participating clinicians and patients, and reasons why eligible patients were not enrolled. We think this is a major improvement in the clarity of this paper and we thank the reviewer for this suggestion.

9. The researchers offer nothing new except that they should have conducted a thorough review of the literature to learn about optimal recruitment strategies. We think that improvements in the clarity of our report thanks to this reviewer’s suggestions, will yield clearer insights to readers and perhaps a more generous appraisal of what this paper can contribute. This reviewer’s comment remains, however, particularly challenging for our team given that it includes practice-based trialists with experience designing and recruiting patients for practice-based intervention trials. Because of the nature of this trial, we judged it would be best to conduct a pilot trial securing an R34 grant from the NIH for this purpose. Grant reviewers, reviewers of our published protocol paper, and ethics committee members concluded that our approach to recruitment was appropriate. We learned some lessons in conducting this trial that we think can enrich the extant literature on this subject. These are offered, as reviewer 3 can appreciate, in the spirit of improving the practice of trials embedded in the messy world of nonacademic clinical practices. We thank the reviewer for her generous review and suggestions, which have contributed to improve the likelihood we can achieve the goal of this paper.

Reviewer #2
The reviewer is clear in expressing the challenge our original language caused in producing a faithful understanding of what we did in our study. In response to Reviewer #1, language related to describing the approaches as “opt-in” and “opt-out” has been removed and changed for an unlabeled description of the our original approach and a description of the revised approach as “in clinic”.

The reviewer is surprised we could scan records without authorization. In Minnesota, patients are able to provide blanket authorization to review records for research purposes for studies receiving IRB approval, like this trial. These procedures were reviewed and approved by 5 IRBs and conducted by professional study coordinators.

Our speculation that more presence in the clinic led to better recruitment and conduct of the trial is indeed a speculative insight which is the reason we have placed this in the discussion section. We note clearly that since this is not a trial of two recruitment strategies inferences derived from these observations are less than robust.

The reviewer is worried about the ethical implications of our study. I suspect this again refers to the confusing language used in the original version of this report, as no ethical concerns were at issue in the conduct of this study. The main ethical
quandary for these investigators was to ensure that the effort of clinicians and patients becomes justified by the gains in information from this trial, including the insights reported in this paper. Otherwise the risks of participation in the trial could not be ethically justified. All the participating IRBs agreed that the main risks of this trial referred to loss of privacy associated with the video recording of visits (the reason why clinicians needed to give written informed consent for participation) and the review of medical and pharmacy records. All participants provided written informed consent for us to conduct these simple procedures.

The interventions were two forms of medical information provision during the clinical encounter, hardly a dangerous affair. To better clarify this, we now provide electronic links to the decision aids we have used in the trial, something this reviewer correctly requests.

The reviewer also requests that we clarify what we meant by “inadequate glucose control”. We have now expanded that phrase to point out that this was assessed by the clinician as a level of control of diabetes justifying a discussion about antihyperglycaemic medications. The new paragraph now reads: “English speaking patients (≥18 years old) were considered eligible if they had type 2 diabetes, were considered by their clinician to have inadequate glucose control and be at the top of the dose of medication related to the management of their cholesterol or diabetes, and had no major barriers to providing written informed consent. In other words, we sought patients in whom it was necessary and possible to have a discussion about medications.”

The reviewer is referred to our protocol paper in which issues of sample size estimation and a discussion about the study design are offered. We prefer not to add this detail here as we think it will detract from the focus of this manuscript. Furthermore, the protocol paper is available in open access, which means that this information is available to any reader, anywhere.

We greatly appreciate the reviewer’s concerns and suggestions and we hope to have addressed those fully and that as a result the paper has gained in clarity and usefulness.

Reviewer #3
We appreciate the reviewer’s positive appraisal of our report as originally submitted. We can only hope that the extensive changes produced in response to the other reviewers only enhanced what this reviewer considered a “timely and important” article.

The reviewer offers three discretionary revisions, with which we agree and have modified as suggested.

Again, with gratitude and on behalf of my co-authors.
Victor M. Montori, MD, MSc
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