Author's response to reviews

Title: Reconsidering low dose aspirin therapy for cardiovascular disease: a study protocol for physician and patient behavioral change

Authors:

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Author's response to reviews: see over
Dear Mr. Wilson and the Implementation Science Editorial Team,

We thank the reviewers for their helpful comments, and have revised our paper accordingly. Below we present the comments and our specific responses to them.

Reviewer 1:

1. Include a 4th control arm with no academic detailing, decision support, or patient activation.

This is a small project running in one health care system. The clinical leaders of the system reviewed the primary data on ASA for primary prevention and came to the conclusion that there was no evidence of substantial benefit and there were identified risks of therapy. Thus, the system elected to stop recommending ASA for primary prevention. Our IRB indicated we could not ethically withhold the academic detailing to any practice that wished to receive this information. Thus, we could not add a randomized control arm. Thus, the primary question is a comparative effectiveness trial as opposed to a more classic RCT. In comparative effectiveness trials different approaches to therapy or delivery of care are compared head to head instead of against a placebo or usual care arm. One practice in the system did decline the academic detailing presentation. We have added this practice as a “non-randomized temporal control” as a secondary analysis. We have adjusted the paper to indicate that this is a comparative effectiveness trial and the use of the “temporal control arm.”

2.a. Add a provider survey.

This trial is not focused on the various reasons providers elect to continue to use unproven therapies. While this is an interesting area it is best understood through traditional point-of-care practice-based research card studies in which decision processes at the individual patient level are explored (see Westfall, et al, Annals of Family Medicine, Jan 2011; 9:63-68). This information was not the focus of our intervention. Our study was focused on whether provider and patient behavior could be changed, and if one of three change approaches was more effective. As part of an educational experience this project also was intended to demonstrate the concept of a focused and answerable research question. Expanding to this second level of information gathering using very disparate methods (i.e., a provider survey) is not in keeping with the educational focus of this project.

3a. Providers may be confused by conflicts between local and national guidelines.

National guidelines were relaxed by the AHA and ADA around the time of this study. Thus, this study is more in keeping with current guidelines than older guidelines. The point of the academic detailing was to be sure all providers understood the rationale behind our hospital system’s decision. Providers may decide not to change their practice despite the evidence against its effectiveness, which is, in fact, the point of the study: to determine if any of the approaches will result in a clinically meaningful change in use of ASA for primary prevention. Providers were offered unlimited access to the study team if they wished to discuss
or clarify the change in recommendations. Several providers had brief email
discussions with the research group. Providers may have been confused as to why
the local and national guidelines had changed, but they were provided
opportunities to help resolve this confusion if they wished.

3b. There may be disagreement between clinicians and guideline administrators and
this may be a factor in noncompliance.

The individuals who developed the new recommendations for the health system in
question were all clinicians and represented each of the 5 primary care practices in
the study. There were no “guideline administrators” involved. We fully expect that a
failure to change one’s practice pattern has to do with a reluctance to believe in the
data as provided. Clinicians continually believe in and use therapies that have been
shown to be ineffective or even harmful, based on their belief that they can
“predict” who will benefit at the individual patient level. For ASA therapy, there has
not been a single study that indicates ANY “high risk” group without known CAD
benefits from primary prevention with ASA. The point of the academic detailing was
to highlight for the clinicians that while it seems that a clinician can “predict” who
will benefit at the patient level, the evidence says otherwise. Furthermore, there are
clear cut risks associated with the use of ASA for primary prevention that are real
and measurable in all studies that have collected this data. While clinicians may
decide that the use of ASA is warranted, it would not be from any disagreement
between administrators and clinicians, but an independent decision by that
clinician.

3c. A form given to the patient before the provider visit asking them to “check with their
provider concerning the use of ASA for primary prevention” poses more questions: e.g.
What will provider’s reaction be to this?

Most research creates more questions than it answers. This form was developed
with input from the clinicians in the practices. The only difference in the form
between practices was whether the ASA patient message was included or not. The
practices in the study asked for a form of this type prior to the ASA study and the
study simply added an additional message. The ASA message was reviewed by
clinicians at all sites and it was acceptable to all sites involved in the intervention,
even though only one actually received the messages. The study was not designed
to explore the clinician-patient interactions that were created by the form - though
anecdotal information from clinicians is that overall they liked the form. Practices
and clinicians were free to ask to have the forms not printed during the study and
none did so. We have noted this in the paper.

4. Add a control group to account for the time it takes for behavioral extinction.

As mentioned before it would not be ethical to add a true control group within this
environment. We have added a “non-randomized temporal control” to the study.

5. Add a qualitative investigation.

While we perform many mixed methods studies, this project was designed to be a
quantitative evaluation at the patient level of actual change in use of a commonly
recommended medication that has never been demonstrated to be effective. We
will consider a follow up qualitative investigation once the results of the quantitative study are revealed. The qualitative investigation would logically include both patients and clinicians, be conducted in conjunction with a “card study” as discussed above and to be fully implemented would be a considerable undertaking. We concur that a qualitative investigation would add to the results of this trial, particularly if the results are negative (as is highly likely). But we also feel there is worthwhile information to be gained from the quantitative information and that a qualitative investigation should be considered as an add on project.

6. Include the patient activation form.

We have added this as a figure.

Reviewer 2:

Major compulsory revisions

1. Title: The title of the manuscript should better specify the aim of the study: it is not clear that the trial is focused on a physicians’ behavior change interventions; furthermore, terms like “study protocol” should be included.

Though the first reviewer felt the title was appropriate, we had adjusted the title with these recommendations in mind.

2. Design and Methods, Design, description of intervention arms: details about academic detailing should be provided. What type of documentation will be given to participating physicians?

Greater details related to the academic detailing have been provided along with a link to a website where the entire presentation is available to the public. A link/reference to this information has been added to the manuscript. All providers also received a one-page “synopsis” of the data and the system-wide decision to stop recommending ASA for primary prevention. This has been noted as well in the paper. We have also placed this one page information sheet on a public web site and provided the link.

3. Design and Methods, Data Analysis Approach: the Authors reported the description of the statistical analyses that will be performed; however more details about “patient clinical covariates” that will be taken into account in the logistic regression analyses are needed. Furthermore, will physicians’ characteristics (age, gender, specialty) be collected?

We have provided greater detail of the patient covariates we will be including in the analysis. Only two medical specialties are involved, family medicine and general internal medicine. Physician characteristics are available. The study was designed as a practice-level evaluation. A hierarchical analysis at the physician level was considered, but the sites in each arm of the study include primarily part-time clinicians (both faculty and residents); thus, the typical patient is likely to see several clinicians during the study, making linking of a patient to a clinician not particularly reliable. For this reason, as well as the similar characteristics of practices, our bio-statistician has recommended against a hierarchical analysis at the physician level.
Minor essential revisions

1. Abstract, Methods paragraph: the first sentence of the paragraph should be moved to the end of the Background paragraph to explain the aim of the study. The three interventional strategies should be specified as well as the duration of the trial.
   These changes have been made.

2. Design and Methods, Design, first paragraph: randomization procedure is not adequately described. Will the practices or eligible patients be randomized to one of the three arms? This aspect is perhaps inferable from the figure, but a brief description could be more informative.
   The randomization schema has been further described.

3. Design and Methods, Participants: more details about inclusion and exclusion criteria should be reported (i.e. age limit, ASA dosage,…).
   All individuals on ASA therapy (not combination drugs) that was once a day only were included in the cohorts.
   Cohorts were then divided into those with known disease for which ASA therapy is clearly indicated, and those without known disease. The known disease group includes individuals with a diagnosis of coronary artery disease, diagnosis of thrombotic cerebral vascular accidents or transient ischemic attacks. The primary prevention cohort included individuals on ASA without these diagnoses. As a secondary analysis we will explore whether there was any differential stoppage of ASA in patients with diagnoses previously considered CVD equivalents versus patients on ASA for other reasons. This has been further clarified in the manuscript.

4. Design and Methods, Participants, last paragraph: The sample size description should be completed with the statistical power with which the study could detect a 7% difference between two groups.
   This has been done.
5. Design and Methods, Design: the duration of the trial should be reported after the description of the outcome of the study.
   This has been added.

6. Design and Methods, Data Analysis Approach: information on secondary analyses on diabetes subgroup should be mentioned.
   This has been added.

7. Design and Methods, Human Subject Protection: Use of waiver of consent for all eligible patients should be reported in the manuscript.
   This has been added.

We appreciate the reviewers’ comments and look forward to your decision regarding our manuscript.

Sincerely,

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