Author's response to reviews

**Title:** Cost-Effectiveness of a Mailed Educational Reminder to Increase Colorectal Cancer Screening

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**Author's response to reviews:** see over
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Melissa Norton MD, Editor In Chief
BMC Gastroenterology

Dear Dr. Norton,

We would like to re-submit our manuscript entitled “Cost-Effectiveness of a Mailed Educational Reminder to Increase Colorectal Cancer Screening” for consideration for publication in the journal BMC Gastroenterology. We have carefully addressed all the reviewer’s major and minor comments in the “Response to Reviewers” below. We thank you for allowing us to re-submit our revised version of our manuscript; and apologize that it is late as per your request, but due to the recent holiday season several of our co-authors were unavailable. Please let us know if you have any questions or concerns regarding the revisions or reformatting issues.

Sincerely,

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Lee et al. RESPONSE TO REVIEWERS

Reviewer 1: Catherine Lejeune
Minor essentials revisions
1-Abstract page 2:
  a-In the Methods paragraph: it is not clear what the “usual care group” consists of. The authors should describe this option very shortly.
  We have addressed this concern by adding a short description in the abstract (highlighted in red).

  b-in the Conclusions paragraph: it is not clear what the authors mean by “compared to other patient-directed interventions for CRC screening”.
  We have clarified this sentence by adding a short description in our conclusion section of the
abstract (highlighted in red).

2-Introduction page 3
a-Is the reference 6 really relevant to justify CRC incidence reduction?
We agree reference 6 is not necessary to justify CRC incidence reduction, because it is well known and documented that FOBT reduces CRC incidence and mortality. We have deleted this reference.

b-the authors should indicate what “VA” means before using the abbreviation.
We have spelled out VA (Veteran Affairs) in our final draft (highlighted in red).

3-page 6, in the Intervention paragraph:
a-I am sorry, but I was not able to find the appendix 1.
We have attached appendix 1 to this email and cover letter.

b-what does IRB mean? Please indicate what it is before using the abbreviation.
We have spelled out IRB (institutional review board) in our final draft (highlighted in red).

4-page 6: in the Cost Analysis paragraph:
a-I do not understand why the reference 23 has been introduced here to justify the point of view of the payer. This reference is related to the cost of a physical activity. Please find a more appropriate reference, if introducing a reference appears relevant to justify the study’s perspective.
We agree that reference 23 was not necessary to justify the point of view of the payer; therefore, we have deleted this reference (highlighted in red).

b-the sentences “Thus, data collection for research purposes was not included in the analysis……mail reminder study” needs to be clarified. I do not understand the link (expressed by “thus”) between the choice of the point of view and the fact that economic data have not been collected. I also do not understand what the authors mean with “mailed reminder study”. This needs to be clarified.
We have deleted the sentence “Thus, data collection for research purposes was not included in the analysis,” because there is no connection between the prior sentences. In regards to the “mailed reminder study,” we mistakenly inserted “study” to the sentence. The sentence should read as “Intervention costs were based on the actual personnel time and materials used in the mailed reminder and are detailed in the next section.” (highlighted in red)

c-to my opinion, the paragraph “overhead costs…..cost analysis” should be found in the paragraph entitled “costs of the intervention”. More globally, the description of economic parameters needs to be more consistent for the reader.
We have moved this paragraph to the next paragraph, titled “Costs of the Intervention.” (highlighted in red)

5-page 7: What does GI mean? Please indicate what it is before using the abbreviation
We have spelled out GI (gastroenterology) in our final draft (highlighted in red).

6-page 8: The sentence “in addition to calculating…..promotion interventions” should be found in the Discussion section.
We agree that sentence could be moved to the discussion section, but it can also remain in the methods section.
The authors indicate that costs and ICR were markedly lower. I agree, but comparisons were also quite difficult due to different target population and different promotion modalities. Please be careful in your conclusion and perhaps moderate it. We agree that our study was different than other studies mentioned in our manuscript (different intervention, different population, different regions of the country). We have modified the conclusion to state that our intervention “could be recommended for implementation at this time in practices with similar organizational and patient characteristics”.

Given the fact that all details are given in the text concerning other promotions programs, I am not sure that the table 3 is required. We believe Table 3 might be helpful to other readers, because it compiles all recent studies of patient-directed interventions for CRC screening and organizes them in a simple table. Therefore, we will leave Table 3 in our final draft.

**Reviewer 2: Sujha Subramanian**

**Major Compulsory Revisions:**

1) Sensitivity analysis was based on a 10% variation in point estimates. Better explanation is needed as to why this approach was selected

All the referenced patient-directed intervention studies for CRC screening reported a sensitivity analysis based on a 10% variation for costs. Currently, there is no standard % variation in physician salaries, paper, envelopes, stamps, and other materials used for our reminder. Therefore, we used this arbitrary % variation for consistency with other similar studies mentioned in our manuscript.

2) Intervention costs in the results sections -- it is not clear exactly what costs are reported here. It is confusing to have time spent on various activities reported in this section. There is no mention of how time spent on activities were calculated in the methods section. Was a time-and-motion analysis used? Better explanation is required in the methods section to better inform the reader.

We added the following statements to our methods section to clarify how we determined the total costs of our intervention. “The labor costs were calculated by multiplying the time spent of performing the task (creating the letter content, editing and approving the content, generating, personalizing, and mailing the reminder) by the employee’s wage per hour. We determined the costs of all materials used for the mailed reminder by multiplying the costs of each material by the number of patients receiving the mailed reminder.” (highlighted in red)

3) No details are provided on the timing as to when the FOBT kits were returned in the intervention and control groups. The reminder mailing was sent out 10 days after the kit and yet the return rate of FOBTs was calculated over a 6-month period. It would be good to know the when the FOBTs kits were returned (to understand the pattern of returns) in the intervention and control groups

The timing of the return of FOBT kits was previously published, and the data indicated that 39% and 49% of patients returned kits by 30 days in the usual care and intervention control arms, respectively; and this increased to 47% and 62% by 90 days. This is now indicated and referenced in the text in the results section.

**Minor Essential Revisions**

1) The 40% compliance rate with CRC screening recommendations referenced in the introduction is outdated. Need to update this reference with new data.

We have corrected this reference to 50% from the most recent study of CRC screening compliance in the United States from the Centers of Disease Control, published in 2008.
2) "In addition, the improvement in screening rats (should be rates) was about one half of what we observed in our study, and as a result, the ICER was much higher than what we report."
We have corrected the spelling to “rates.” (highlighted in red)

Reviewer 3: Guy Launoy
No comments about major or minor revisions

Reviewer 4: Kelvin Tsoi
Major comments:
1. In the original randomized controlled trial, some predictors that affects the FOBT compliance were presented, including prior FOBT returned groups, current or recent illicit drug use, different age groups, percentage of Veteran Affairs appt. kept, mood disorder, and current tobacco use. Subgroup analyses should be performed on these predictors and also the general subgroups, such as gender and race groups. All of these information will provide important reference for the decision makers.
These subgroup analyses were addressed in part in our previous manuscript published in the Journal of General Internal Medicine. We are unclear how these results would affect our current cost analysis, and therefore did not include further subgroup analyses in this paper.

2. The ranges for sensitivity analysis for physicians are arbitrary. Some variables can be over 10% variation. For instance, the physicians’ salary and time spending on the letter drafting should be wider ranges. As the author made an assumption on +/-10% on the time for drafting the letter, the sensitivity analysis is only based on the range from 13.5 to 16.5 minutes. Moreover, sensitivity analysis can be presented as a graph to clearly demonstrate the change of a wide ranged variable.
We agree that our sensitivity analysis based on a 10% variation was arbitrary. All the referenced patient-directed intervention studies for CRC screening reported a sensitivity analysis based on a 10% variation for costs. Currently, there is no standard % variation in physician salaries, paper, envelopes, stamps, and other materials used for our reminder. We used this arbitrary % variation for consistency and comparison purposes with other studies mentioned in our manuscript.

Minor comments:
1. I’m not quite sure the meaning of “First-copy” costs mentioned in P.7. Is it the set-up costs for the intervention? Authors had already presented the startup costs for the reminding letter drafting by the physicians. Detailed items should be listed out. Although there is no universally agreement on handling this cost, assumption can be made for the sensitivity analysis.
First-copy costs, defined as costs incurred in establishing an intervention, are considered quasi-fixed costs independent of the number of units produced once production is started [Gold MR (1st ed). Cost-Effectiveness in Health and Medicine, Oxford University Press Oxford, 1996]. In general, first-copy costs are excluded when they involve situations where much of the intervention is already in existence and only modification is needed to adapt it for implementation [Saywell et al, reference 14]. This is assuming that the final product can be made available to other health care organizations through public access [Saywell et al, reference 14]. Furthermore, it is expected that managed care organizations or community clinics would not develop their own mailed reminder but would rely on public access or licensing arrangements.
2. Any enquiries were raised from the participants? Administrative cost should be included for replying e-mails and phone calls. There were no phone calls or emails documented in the study from any of the participants regarding the use of the FOBT kits, although it is possible that these may have occurred. These potential administrative costs could be considered within the 10% variation in the sensitivity analysis, and this possibility was noted in the results section.

3. The paragraph of statistical analysis in P.8 is not applicable to this cost-effectiveness study. I can’t see any t-test, chi square test, Wilcoxon rank sum test were applied in the results. I think this paragraph is copied from the previous publications, which is irrelevant and can be eliminated. We have deleted this paragraph.