Author's response to reviews

Title: The impact of home-based HIV counseling and testing on care-seeking and incidence of common infectious disease syndromes in rural western Kenya

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Author's response to reviews: see over
Dear Editor,

RE: MS: 1256639581201910 – THE IMPACT OF HOME BASED HIV COUNSELLING AND TESTING ON HEALTH CARE SEEKING AND INFECTIOUS DISEASE INCIDENCE IN RURAL WESTERN KENYA

We thank you for your quick review of our manuscript. We received valuable comments from the reviewers and we have now completed revisions of the manuscript. Attached to this letter are point by point responses to the comments raised by the two reviewers. In several of our responses, we have included new text which is in **bold font and underlined**, which we have now added to the body of the manuscript. We have also described several sections of the manuscript where changes have been made. Attached also are two versions of the manuscript, one with tracked changes and a second clean version.

Thank you for your willingness to consider our revised manuscript for publication.

Sincerely

Godfrey Bigogo.
Reviewer 1

Reviewer's report:

Overall, the authors have done a good job of revising this manuscript, addressing the reviewers’ comments, and illustrating the primary purpose of this study. However, there are still a few areas which could use some further clarification.

Response: Thank you for this complement. We have provided some explanation and made several changes following the review. All new text added in the manuscript is underlined and in bold font in our responses listed here.

Major compulsory revisions:

1) Abstract. Conclusion. Your conclusion should more clearly match your hypothesis and methods. There’s too much of a jump here as it is not the HBCT that necessarily led to decreased incidence of infectious diseases. It is the high uptake of HBCT which led to raised awareness of status, plus the critical act of seeking care, and receiving appropriate care. The HBCT is just a platform for getting people to know their status, but is not the causal factor in and of itself. I would suggest rephrasing so that you are not going too broad with this conclusion.

Response: Thank you for this comment. We have added text to the conclusion statement to make it more focused. The conclusion now reads as follows. “Large scale HBCT enabled a large number of newly diagnosed HIV-infected persons to know their HIV status, leading to a change in care seeking behavior and ultimately a decrease in incidence of common infectious disease syndromes through receiving appropriate treatment and care”.

2) Introduction. Second paragraph. It seems there is too much description about HBCT here, considering that the HBCT aspect shouldn’t really be your main focus. You can mention it as your platform for testing and raising awareness but don’t need to use this section to make the case for HBCT per se.

I would suggest that you rather use the space here to make the case for why linkage to care is so important (as it relates to your main infectious disease outcomes) so that you set the stage for why you are measuring this and why your results matter. For example, how prevalent are these infectious diseases in this community? And in other communities in sub-Saharan Africa? Among HIV-infected clients? What are their impacts on morbidity and mortality? What is the impact of early versus late treatment? I’m sure these issues are obvious to you, but you need to remind the reader why your study is so important.

Response: We have modified text in paragraph 2 of page 5 as follows. “While it has been shown that HBCT can increase HIV testing and the number of people who know their HIV status, it is not clear whether knowledge of HIV status influences care seeking which in turn impacts incidence of common infectious illnesses such as acute
respiratory illness, febrile illness and diarrhea whose burden is high in several parts of Africa [reference added].

3) Generally, there is a need to be more consistent about the way you state your conclusions throughout the paper. In some places, you mention “a likely causal sequence” whereas in other places you imply a more direct link to your outcomes.

Response: Thank you for this comment. We have reviewed the manuscript and made appropriate adjustments as highlighted in the version with tracked changes.

Minor essential revisions:

4) Introduction. You mention HIV testing rates from 2007. Is this the most recent data available? It may be, but just a note to double check and update if possible.

Response: We have more recent data from the Kenya AIDS Indicator Survey of 2012 (KAIS 2012). The first reference in this manuscript comes from KAIS 2012 data. We have updated the third sentence of the first paragraph of the introduction section to include KAIS 2012 data. The sentence now reads as follows. “Two national AIDS indicator surveys have been done in Kenya. In the first survey of HIV prevalence in Kenya in 2007, only 34% of adults nationwide had been tested before, and among those found to be HIV-infected, only 16% correctly reported their HIV status. These proportions increased to 72% and 47% respectively in the second survey in 2012 [KAIS 2012 ref. added].”

5) Results. Can you make it more clear what the differences were in rates of all of the infectious diseases of interest at baseline between all of the comparison groups? If this is what you show in Table 2, reference the table and add some description in the text.

Response: Thank you for pointing this out. As you have correctly stated, the baseline rates are shown in Table 2. The last column with rate ratios shows what the differences were in the two groups. The table is already referenced in text in the Results section in the second paragraph of page 12. No change is made here.

6) It seems that your time frame of measurement is one month after testing, and you also mention that this is a limitation, which is fine. But then in the results you also report enrollment in care at 3 months, 1 year, and 24 months. So this seems inconsistent and makes it a bit confusing. How is it that you have this data but weren’t able to use it for the analysis? Please clarify.

Response: Indeed we did have data from the 1-month post-HIV test home follow up visits for all HIV-infected participants to see how many had enrolled for HIV care. However – as described in the methods – we also had additional data from household surveillance for infectious disease syndromes and also data abstracted from HIV registers at several clinics within the study area to see who had enrolled for HIV care. Our key assumption is that because of low annual HIV incidence (1.5%), individuals HIV status likely remained the same in the year before, and after HBCT. To minimize the risk of misclassification, we limit the period to which we consider ones HIV status as to have
remained the same as 1 year pre-test and 1 year post test, and therefore also limit the syndromes’ data to only these periods. We do have more follow-up time for most individuals and we could include these extended follow-up times but, this might lead to greater misclassification of individuals’ HIV status. This is also well explained in the first paragraph of page 17 under the Discussion section. Hope this clarifies the query.

Discretionary revisions:

7) Page 3. Abstract. Consider rephrasing this sentence in the background: However, there is little data on whether knowing one’s HIV-positive status through HBCT will lead to a substantial increase in the number of HIV-infected persons in HIV care, resulting in a reduction in the morbidity of common infectious disease syndromes.

To make your point more clear, consider rephrasing to something along these lines: However, there is little data on whether knowing one’s HIV-positive status necessarily leads to uptake of HIV care, which could in turn, lead to a reduction in the prevalence of common infectious disease syndromes.

Response: Thank you for this. Your suggestion brings clarity and we have accepted this modification in the background section of the abstract.

8) Page 9. Add a comma to this sentence: We calculated the incidence of four syndromes, 
(comma added here) namely acute respiratory illness (ARI)……

Response: Added the comma.

9) In the discussion section, it doesn’t seem necessary to have so much explanation about why so many people went to Lwak hospital rather than other facilities. You could potentially include the important reasons briefly in the methods section instead.

Response: This was raised by earlier reviews and we sought to explain it. We think it is important for readers who may want to know why there was so much higher visitation to Lwak than other facilities. No change made here.

10) Page 14. This sentence in the second paragraph: The Lwak area is a malaria holoendemic area, where even adults suffer from several clinical malaria episodes per year.

Consider rephrasing to something like: The Lwak area is a malaria holoendemic area, where both children and adults suffer from several clinical malaria episodes every year.

Response: Thank you. We have accepted this change and modified the sentence in the second paragraph of page 14 as suggested.

Reviewer 2

Summary: This is an interesting manuscript that seeks to identify whether a large scale HBCT
program in western Kenya leads to increase in the number of patients who enroll in care as well as if there is reduction in the incidence of infectious disease syndromes. The analyses are sound although more detail is needed on recruitment/eligibility criteria. The discussion reads well but there are several areas where clarifications are needed. Importantly, the manuscript requires a proper edit.

Response: Thank you for this comment. We have now described how people were recruited into HBCT in the first paragraph of the sub-section titled Home-based counseling and testing on page 7. To clarify on eligibility, we have added the following sentence in the first paragraph. “To participate in HBCT, one needed to be a resident in the PBIDS area and also provide consent for participation.”

Be consistent on use of acronyms

Response: We have checked for consistency of the use of acronyms

Be consistent with spelling of healthcare and the use of healthcare-seeking (vs. healthcare seeking).

Response: Thank you for this comment. We have reviewed and edited as recommended.

MANDATORY CHANGES

ABSTRACT

1. State specific location and program name in Abstract

Response: We have added the program name as the Kenya Medical Research Institute (KEMRI) in collaboration with the Centers for Disease control and Prevention (CDC) and the study site location as, “Lwak” in the first sentence of the Methods section in the abstract.

2. Specify that you analyzed ‘healthcare-seeking BEHAVIORS’

Response: Accepted. We have added the word behaviors in the third sentence of Methods section of the abstract.

3. Specify what type of analyses were used in the Methods

Response: We have modified accordingly. The third sentence now reads as follows. “We analyzed changes in healthcare seeking behaviors using proportions, and incidence (expressed as episodes per person-year) of acute respiratory illness (ARI), severe acute respiratory illness (SARI), acute febrile illness (AFI) and diarrhea among first-time HIV testers in the year before and after HBCT, stratified by their test result and if HIV-positive, whether they sought care at HIV Patient Support Centers (PSCs).”

4. Define RR and CI’s at first use RESULTS

Response: These are now defined as rate ratio (RR) and confidence interval (CI).

MANUSCRIPT
1. What was the response rate for HBCT? How many testers vs. number of tests offered?

**Response:** Acceptance was 79%. This is already given on page 8, the first sentence under the subsection titled “Home-based counseling and testing.”

2. Were there statistically significant differences between men and women?

**Response:** More women than men were tested at HBCT. However in terms of enrollment for care by gender, we did not see any differences in those who were HIV-infected and enrolled for HIV care versus those HIV-infected not enrolled for HIV care. A summary table of this is shown below.

<table>
<thead>
<tr>
<th>Enrollment of HIV-infected persons into care by gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Males</td>
</tr>
<tr>
<td>Females</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

3. Was time to enrollment in PSC measured? It would be useful to know the median time to enrollment (and be able to compare in pre-vs. post-HBCT period).

**Response:** Yes, time to enrollment was measured in months as already shown in Figure 2. Enrollment in PSC could only happen in the post-HBCT period as this study focused only on first time testers at HBCT. The median time to enrollment was 12 months.

4. Report p-values and CI’s and/or state if differences were significant between groups (HIV-infected and enrolled vs. HIV infected and not enrolled vs. HIV-negative)

**Response:** In table 4, the last column titled Ratio of rate ratio shows comparisons between the various groups. All rate ratios already have CI’s around them and hence p-values are not necessary. The differences between the groups are also described in the Results section in the second paragraph on page 13. No change is made here.

5. Significant findings including ORs and 95% CIs should be reported in text.

**Response:** We agree and have now included these in several places in the Results section as shown in the revised version.

**SUGGESTED:**

**INTRODUCTION**

6. Helpful to know what proportion of people do not know their HIV status

**Response:** This is already provided in the third sentence of the first paragraph of the
Introduction. No change is made here.

7. In the 2nd paragraph, first sentence: specify why having more people on treatment is important...i.e., reduce viral load, reduce forward transmission etc.

   **Response:** Thank you for this suggestion. However, we think the text already provided here is sufficient for the focus of this paper.

8. In what ways does HBCT overcome barriers of stigma and cost....describe HBCT further to address this and provide a rationale for the study. Furthermore, this also would help to provide further plausibility of the findings.

   **Response:** HBCT can overcome costs associated with travel such as transport fees, time and distances to testing centers. Traditionally, HIV testing centers such as voluntary counseling and testing centers have been located in unique open places in many health facilities – some even at the entrance to facility premises. Any would-be tester would be scared of being seen walking into this premises. HBCT overcomes such a barrier because it is done in private in one’s home. We have modified the second sentence in the subsection under home based counseling and testing to read as follows. “A team of trained non-resident HIV counselors provided HIV testing and counseling at home to residents ≥13 years of age who gave consent.”

9. It may be worthwhile to emphasize that there are multiple different avenues for testing including provider initiated, HBCT, community-based, ANC etc. Different venues may have different impacts.

   **Response:** Thank you. We agree that there are multiple avenues for testing – which may have different impacts. The focus for this paper was only HBCT and its impact. Because of our desire to be concise, we restricted our discussions to HBCT only.

10. It is great to see hypothesis but specific objectives of analyses in addition to describe the program in general. i.e., we describe the impact of a large scale program to.... METHODS

   **Response:** It is not clear what the question above is, but the specific objective of analysis is explained in the following new text that has been added in the fourth sentence of the second paragraph of the Introduction. This now reads as follows. “While it has been shown that HBCT can increase HIV testing and the number of people who know their HIV status, it is not clear whether knowledge of HIV status influences care seeking which in turn impacts incidence of common infectious illnesses such as acute respiratory illness, febrile illness and diarrhea whose burden is high in several parts of Africa.”

11. Study site and surveillance population

   -include a figure to show study site, area in Kenya

   **Response:** We have now added Figure 1

   -define HOLOENDEMIC as it is not commonly used
Response: Thank you. We have added the text “infecting almost everyone” in parentheses

1. Move Home-Based Counseling and Testing section before Household Surveillance

   Response: Actually we think the current flow is better as the HBCT exercise was done on the household surveillance platform. So we think a description of the household surveillance platform should come prior to describing the HBCT exercise. No change is made here.

2. Household Surveillance:

   - State the eligibility criteria for households to be included

   Response: We have added the following sentence on page 7 in the paragraph under the sub-section titled “household surveillance” for clarity. “The catchment population included people living within a 5km radius of Lwak hospital, the project’s referral facility.”

   - do all household members have to participate?

   Response: No. Participation was voluntary. We have provided some references about the study site and population.

   - it should be clarified was ‘disabled’ means in this setting. I’m assuming it is only those who are cognitively impaired.

   Response: Thank you for this comment. What we meant are cognitively impaired persons. We have corrected this in this paragraph.

   - add ‘recording’ after auxiliary temperature in the last sentence of the paragraph

   Response: We have added this.

13. Clinical Care -2nd paragraph, please clarify what is meant by ‘providing free HIV care and treatment services once a week’. Does this mean HIV care is only provided free of charge once a week but is offered daily or does this mean that HIV care was only offered once per week.

Response: We agree this needs clarification. We have added text in the second paragraph under the subsection titled ‘Clinical care’ on page 8. The paragraph has been modified as follows. “In 2007 Lwak Hospital, through support from the President’s Emergency Plan for HIV/AIDS Relief (PEPFAR), began providing free HIV care and treatment services. At the start in 2007, the clinic was only operational once a week on Mondays, and later increasing operations to five days a week in 2008 with an expanded team of nurses, clinical officers and counselors.”

14. Data Collection and Analysis

   - How outcomes were defined and measured should be stated explicitly: i.e., binary, categorical, continuous etc...

Response: We have added the following sentence in the “Data collection and analysis” sub-section of the Methods. Each of these syndromes was measured at a binary level
as being either present or absent.

-Clarify what is meant by: we assumed an individual’s HIV status at HBCT would likely be the same in pre-and post-HBCT. Do you mean that individuals found to be positive in post-HBCT were already positive in the pre-HBCT period or do you mean the overall proportion of individuals infected would be similar in the pre-vs. post-HBCT period?

**Response:** Preliminary data from HIV transmission studies from areas adjacent to our study site show transmission at 1.5% per year. Given this we assumed that an individual’s HIV result at HBCT would likely have been the same in the year before (which is the pre-HBCT period). The same analogy applies for the post-HBCT period.

-Why did you adjust for age and sex? The rationale for this is unclear.

**Response:** We needed to control for potential confounding. HIV prevalence does vary by age and sex and analyses might be biased unless these are adjusted for.

-Time to enrollment, Time to ART initiation would also be worthwhile to explore in order to determine if HBCT speeds up linkage to care. A simple survival or time to event analyses may be useful here.

**Response:** This indeed is an important aspect and thank you for this comment. We however felt that this is way beyond the scope of this paper. Different authors here are currently examining linkages to care and timing of ART initiation as parts of other ongoing analyses.

15. Ethical Review

-please state if consent was verbal or written. What about consenting for proxies?

**Response:** Signed participant consent was obtained prior to participation in the study. In the second sentence under the sub-section titled “Ethical review” on page 11 we have modified the sentence to read as follows. “Signed participant consent was obtained for linking of HIV data to individuals’ morbidity and demographic data.” Proxy interviews could be conducted if the absent members were already consented and enrolled in the study.

DISCUSSION

20. 1st paragraph:

-“HIV testing and counseling is considered the entry point into HIV care”. The location of testing and counseling matters for entry into care as specified by the objective of this manuscript so a less general statement may be more appropriate.

**Response:** Thank you for the comment. It really is more of the awareness of one’s HIV status than testing location that drives people into care. For this manuscript, HBCT is one strategy for getting many people to be aware of their HIV status, and therefore opening the opportunity to get into care.

-Sentence: ‘For the persons who did access a PSC, the majority received appropriate treatment’. Appropriate treatment for what? HIV? Please specify.
Response: Yes, appropriate treatment for HIV. We have clarified this in the third sentence of the first paragraph of the discussion which now reads as follows. “For those persons who did access a PSC, the majority received appropriate treatment for HIV.”

-final statement re: ART coverage, it would be worthwhile to comment on whether this is low or expected in this context.

Response: This appears low but we suspect this was a transient logistical challenge.

21. 2nd paragraph
-1st sentence: The ultimate goal should also include reductions in HIV incidence.

Response: Agreed. We have modified the first sentence of the second paragraph to read as follows. “Reductions in morbidity, mortality, HIV incidence and transmission reductions are the ultimate goal of large-scale efforts at counseling and testing as people may likely enroll for HIV care if they know they are HIV-infected.

-A strong positive association may have been found but other factors help to determine if the relationship is causal. Again, understanding why HBCT may be effective and improving outcomes should be explored here.

Response: We believe the question here is in reference to reduction of incidence in some syndromes. That is possibly true that other factors may determine the causal relationship. But the absence of a decrease in incidence in the HIV-infected persons not in care – which was a comparison – lends credence to the fact that it is enrollment in care and getting appropriate treatment for HIV that likely led to the impact observed in those with HIV and enrolled in care.

-Sentence: “In addition to contrimoxazole, initiation of ART has been shown...”. It is important to add the impact of ART on HIV infection in addition to diarrheal illness etc.

Response: We agree to modify the sentence which now reads as follows. “Additionally, ART leads to reduction in the incidence of known causes of AFI, such as bacteremia, as well as suppress viral load.”

-Other factors which lead to uptake of care should be discussed including patient-provider relationships, distance to clinic, severity of illness, stigma etc.

Response: Thank you. We agree this is an important point, but these analyses are being conducted independently of this paper.

-How many people had SARI in your sample? Helpful to restate the sample size in relation to your comment on statistical power.

Response: Please see table 3 to see the distribution of episodes of SARI and other syndromes. Denominators are provided for those with HIV and the HIV-uninfected.

-Please reference final statement re: masking impact of ART.

Response: The statement about masking the impact of ART is borne out of the SARI
trends observed in Table 4. The argument is that since there was a general decline of SARI among all groups (although significantly only for the HIV negative), the impact of ART treatment may be unclear for this syndrome.

23. 3rd paragraph: -please revise sentence beginning “As access to free care and hospitalization....” to something along the lines of: Access to free care was available at Lwak Hospital in both the pre-and post-HBCT period. A key difference in motivation may, therefore, have resulted from an increased knowledge of one’s HIV positive status. Indeed, similar increases in attendance were not observed for the HIV-negative group in the pre versus post period.

   **Response:** Thank you for this suggestion. We have accepted it and changed accordingly. The paragraph in part now reads as follows. “Access to free care was available at Lwak Hospital in both the pre-and post-HBCT period. A key difference in motivation may, therefore, have resulted from an increased knowledge of one’s HIV positive status. Indeed, similar increases in attendance were not observed for the HIV-negative group who served as a comparison group to identify secular trends in health-care seeking in the pre versus post HBCT period.”

24. 5th paragraph: -It would be interesting to know the time to enrollment into care (e.g., time to linkage) or time to ART initiation.

   **Response:** Thank you. This is already provided. Please refer to Figure 2.

Please reference statement regarding changes in names and addresses (see literature on losses to follow-up and retention).

   **Response:** We have added a reference to this statement in the second paragraph on page 16.

25. 6th paragraph:
-Which diseases would demonstrate annual variations? Malaria? Please clarify.

   **Response:** One example is acute febrile illness.

   -A limitation related to unmeasured confounders and explored variables should be added. More specifically, the implications of not exploring factors which may be more important in explaining findings. For example, factors such as improved continuity of care, early initiation and diagnosis, positive patient provider relationships etc. These factors may explain why or mediate the relationship between HBCT and improved health.

   **Response:** Thank you. We agree that there might be unmeasured confounders. However, we believe we have listed potential limitations directly linked to the outcomes found in this paper including a mention of temporal factors that we might not have accounted for.

Table 1: were significant difference identified between groups (Males, Females or by age group)?
**Response:** We did not conduct any statistical test for differences as this was simply a descriptive table to show how the study population was distributed. No change made here.

1. **Table 4: add sample size for each group**

   **Response:** They are already provided as 351, 347 and 5668 for the HIV-infected and enrolled in care, HIV-infected and not enrolled in care, and HIV-uninfected group respectively.