Author's response to reviews

**Title:** Food insecurity is a barrier to prevention of mother-to-child HIV transmission services in Zimbabwe: A cross-sectional study

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**Version:** 2  
**Date:** 2 April 2015

**Author's response to reviews:** see over
Dear Dr. Natalie Pafitis,

Thank you for the careful review of our BMC Public Health submission. We appreciate the constructive feedback and have incorporated it into the revised manuscript, which has been significantly strengthened.

This manuscript has not been submitted for publication nor has it been published in whole or in part elsewhere. We attest to the fact that all authors listed on the title page have read the manuscript, attest to the validity and legitimacy of the data and its interpretation, and agree to its resubmission to BMC Public Health.

Itemized responses to reviewers are in the following pages. In summary, we hope you will find this revised version of our work appropriate and valuable for the readership of BMC Public Health.

Best Regards,

2023329862147313 Authors
Reviewer 1

1. Assessment of HIV Status—Please indicate whether and how the HIV results were returned to mothers and what was done for those who tested HIV-positive, e.g. referral to clinic?

We have made the suggested addition (Page 7). We have added the following text: “Women were able to receive their HIV test results at the local health facility up to 3 months after the survey using a card with a barcode of their unique identification number.”

2. The most puzzling aspect of these results is the direction of effect for certain outcomes for the moderately food insecure group among the HIV-infected. For example, this group was the least likely to have ever exclusively breastfed and least likely to have an HIV-infected infant. They were also the most likely to have received all key maternal health services among the HIV-infected women (not statistically significant but the direction of effect is opposite of what one might expect). Thus, the “dose-response” one would anticipate is not present for key outcomes. On page 9, line 25, I think the % for the moderate group should also be reported here or in the following sentence. You may need to be more specific in the discussion about severe food insecurity rather than just using the term food insecurity. Relatedly, some of the statements may need to be attenuated in light of this puzzling finding, e.g. p10, line 21, while the severe food insecure group might be providing “supporting” data, doesn’t the moderate food insecure group provide the opposite? Perhaps the food secure population has certain habits due their higher SES which may have paradoxically resulted in more negative outcomes compared to moderately food insecure? Perhaps this indicates some limitations in the food insecurity scale used?

We agree that in some cases there is not a strong dose-response relationship between food insecurity and service utilization. We have therefore: 1) avoided all language suggesting causal relationships; 2) acknowledged the limitations of the food security scale in a full paragraph in the Discussion (Page 13); and 3) cautioned readers against over interpretation of small numbers in the Discussion (new text on Page 10).

We have made several changes in response to the Reviewer’s comments:

- On page 10 we edited the following sentence to acknowledge uncertainty in our conclusions and emphasize that the relationships are strongest among women who are from severely food insecure households: “Although the effect sizes are modest and absolute differences are small, these findings suggest that among a subgroup of pregnant women, severe food insecurity is an important barrier to some maternal health services.”

- On page 11 we added a sentence about the seemingly paradoxical findings among women who are moderately food insecure: “We must nevertheless interpret these findings with caution because a strong ‘dose-response’ relationship between food insecurity and MTCT was not observed, as women in moderately food insecure households unexpectedly had the lowest proportions of exclusive breastfeeding and MTCT.”

- We added new text to Page 12 about the breastfeeding finding: “This study was unable to explore more complex patterns of breastfeeding (such as duration of exclusive breastfeeding) to
support or refute this hypothesis, and our simple measure of exclusive breastfeeding (ever) found that nearly all women exclusively breastfed at some point.”

- We removed the word “supportive” from Page 12 (line 23).

Although HIV-infected women who were moderately food insecure were the most likely to receive all maternal health services, the numbers are very small (107 women) and not statistically different. Thus we have chosen not to highlight this particular finding in the manuscript. (Also, please see our response to Question #3, below).

Lastly, the Reviewer may have missed it, but page 9 line 25 already includes the proportion for moderately food insecure women: “However, women living in severely food insecure households were the most likely to have ever exclusively breastfed their infant (98%, vs. 96% of women in food secure and 92% of women in moderately food insecure households, p<0.01).”

3. “There was no association between food insecurity and completion of the cascade when the analysis was restricted to HIV-infected women.” This finding deserves more recognition and discussion. In Table 3, one might consider adding a middle column on HIV-infected women and completion of PMTCT services. What is the public health/research import if the key group that needs to complete the cascade has no negative association with food insecurity? Why is there a difference compared with the HIV-uninfected women?

Thank you for this comment. Sample size is clearly one possible reason that there is no association between food insecurity and completion of the cascade when the analysis was restricted to HIV-infected women. Specifically, the model limited to HIV-infected women is 12% of the full sample so we likely have limited power. A second reason might be because HIV-infected women, even if food insecure, are motivated to receive services to protect their infant’s health (and their own health) once they are diagnosed in ANC. A third reason is because women might receive supportive nutritional services, including food support, during pregnancy and postpartum. These hypotheses are purely speculative but we have added one sentence to the Discussion about this finding (Page 10):

“Among HIV-infected women, we unexpectedly found that there was no association between food insecurity and completion of the cascade. This might be due to the small sample size, women’s motivation to protect their infant from HIV infection, or nutritional support provided during pregnancy and postpartum that partially mitigates household food insecurity.”

Minor Essential Revisions

1. It is not clear what the primary outcome(s) of the study are and if they were conceived a priori. It may be that there were none and the analytic strategy was more exploratory in nature. That is okay, but it would be good to clarify as there may be an issue with multiple comparisons given there are quite a few outcomes listed in Table 2.

We added the primary outcomes for the parent impact evaluation (Page 4, MTCT and HIV-free infant survival). We clarified that the analysis presented in this paper was exploratory on Page 7.
2. Related to #3 above, I think it would help to be clear about what population is being described in 
the abstract, e.g. in the conclusions section, “...in the PMTCT cascade among women with a 
recent birth...

We have made the suggested change in the abstract.

3. Re: abstract. I would suggest framing the results in a more conservative manner, e.g. “In the 
unadjusted analysis, among HIV-exposed infants....”.

We have made the suggested change.

Discretionary Revisions

1. Is the eMTCT acronym really needed as I didn’t see it used much?

We have removed the eMTCT acronym.

2. In general, throughout, I would prefer seeing p values in addition to the 95% CIs. I think this may 
be somewhat up to the style and preference of this journal.

P-values appear in Table 2. P-values are appropriately absent from Table 1, which displays 
sociodemographic characteristics of the study population. We have now added P-values to Table 3.

Reviewer 2

1. While there is reported the sampling strategy, I would like to read also what are the implications 
of this strategy to the inferences made.

We have enhanced our comments on the limitations of the sampling strategy in the discussion (Page 
14). Specifically, we describe:

“Although our data are representative of the communities from which the sample was selected, they 
are not representative of all regions in Zimbabwe, and it is possible that the relationship between food 
insecurity and service utilization are different in other parts of the country. In addition, although our 
strategy to create a sampling frame of 9-18 month old infants in the community was comprehensive, it 
is possible that some mother-infant pairs were missed. Lastly, women’s and infant’s HIV status was 
measured at the time of the survey, 9-18 months postpartum. Although we have assumed that women 
who were HIV-infected at the time of the survey were also HIV-infected during their pregnancy, it is 
possible that a small proportion were infected during pregnancy or postpartum. Likewise, infants who 
were still breastfeeding at the time of the survey remained at risk of MTCT, so we may not have 
captured all possible infant infections.”

2. Do the authors think that socio-economic position may affect access to services through pathway 
such that low status women are not given the quality of services given to those of higher status 
and so subsequently affecting future uptake?
This is theoretically possible and a very interesting hypothesis. However, we do not have any data to support this statement from this study or other studies. Thus, we have not commented on this specific pathway in the manuscript.

Reviewer 3

1. **Not entirely clear the etiology of the Survey, or why some 300+ mother infant pairs were excluded. Can the authors clarify? not to overdue it, just to give some context of where this data came from**

As described on page 4, the survey was conducted as part of the impact evaluation of Zimbabwe’s Accelerated National PMTCT Program. We have added more description of the primary outcomes for the impact evaluation to this paragraph:

“We analyzed data from a 2012 cross-sectional survey of mother/caregiver-infant pairs conducted as part of the impact evaluation of Zimbabwe’s Accelerated National PMTCT Program. The survey targeted women who were ≥16 years old and biological mothers or caregivers of infants (alive or deceased) born 9-18 months earlier in order to capture MTCT during pregnancy, delivery and breastfeeding. The primary outcomes of the impact evaluation were MTCT and HIV-free infant survival.”

At the top of page 5, we describe that we excluded 356 caregiver-infant pairs in order to restrict the sample to biological mothers only. This is because our outcomes were service utilization during pregnancy and mother to child HIV transmission, outcomes that would have been impossible to assess among children who were living with caregivers and not their biological mothers. This excluded 3.9% of the overall sample.

2. **The sampling strategy is described as 2 stage cluster. First stage, purposeful sample of 5 provinces. The second stage is a bit confusing. Rather than take every "nth" mother infant pair that enters a clinic (for example) it seems the authors actually sought out mother infant pairs known to community health workers, I'm not sure if this is correct, but the way it's written suggests that to be the case. In which case it shouldn't be described as a 2 stage cluster design.**

We appreciate the opportunity to clarify our sampling strategy (Page 5) and we have modified the language in the Sampling Strategy paragraph to describe our approach. After we determined the geographic scope of the study (which provinces), the first sampling stage was random selection of 157 of 699 health facilities offering PMTCT services. The second stage was random selection of infants from the sampling frame of all eligible infants. The sampling frame of infants was generated using data pooled from multiple sources: 1) community health workers, 2) immunization registers from both sampled and nearby health facilities, and 3) peer referral. Selection of infants in this second sampling stage was indeed random once the sampling frame was constructed.

3. **The results are interesting but also a testament to the fact that a robust sample size will result in small differences between sub groups being significant. and some of those being a bit counter intuitive. For instance, a 98 v 96 v 92% difference in exclusive breastfeeding, which makes some sense, except moderately FI women have the lowest rate. Other than showing significant results,**
I'm not sure of the utility of highlighting this particular finding. And to be sure, it would make sense that those with severe FI would have the hardest time adhering to PMTCT, the differences in ANC attendance while significant, are small (95 v 94 v 92%). I'm not sure those proportions are particularly useful if we're thinking of what the response might be (I'm actually heartened by such high proportions as you present).

We agree that the exclusive breastfeeding findings are challenging to explain; therefore we have added a sentence on Page 11 about the seemingly paradoxical findings among women who are moderately food insecure: “We must nevertheless interpret these findings with caution because a strong ‘dose-response’ relationship between food insecurity and MTCT was not observed, as women in moderately food insecure households unexpectedly had the lowest proportions of exclusive breastfeeding and MTCT.”

We have also added a new sentence to the Discussion about this particular finding (Page 12, new text is underlined):

“Another possible explanation is more complex: severe food insecurity increases MTCT risk due to cumulative loss of women from the cascade coupled with an increased risk of MTCT associated with undernutrition[26, 27] and the possible increased propensity for mixed feeding.[29] This study was unable to explore more complex patterns of breastfeeding (such as duration of exclusive breastfeeding) to support or refute this hypothesis, and our simple measure of exclusive breastfeeding (ever) found that nearly all women exclusively breastfed at some point.”

On one hand, we might hypothesize that severely food insecure women are the most likely to exclusively breastfeed because of a shortage of food or infant formula in their household. However, this contradicts data from Young 2013 and Levy 2010, references 29-30 in the manuscript, who report that severely food insecure women may be the least likely to exclusively breastfeed and/or exclusively breastfeed for shorter durations. Furthermore, this does not explain why women who are moderately food insecure were the least likely to exclusively breastfeed. This is certainly an area for more research with longitudinal datasets.

We also agree that the differences in ANC attendance are small, and we have included language in the Discussion to caution readers against over-interpreting the results (please see response to #4, below). Also, we agree that we are observing some “ceiling effects” as ANC becomes universal in Zimbabwe (at least one ANC visit) and we approach the upper bound of 100% coverage. However, given the volume of women who become pregnant each year, compounded with the essential “gateway” role of ANC in PMTCT services, we believe that even small differences in ANC uptake could result in meaningful absolute numbers of women annually who are deterred from care if indeed food insecurity is causally related to ANC attendance (although the data used in this analysis are not suitable to infer whether this association is causal). Thus, we believe it is important to report the data and we have exercised caution in our interpretation.

4. SO the discussion should perhaps be attenuated somewhat to acknowledge that the differences are actually smaller than might be expected. The one variable that I recall with more striking differences is that for women completing all steps of PMTCT. Although all groups were well below 50%, which is in line with practical and programmatic experience. but perhaps one way to
think about it is that FI, both moderate and severe, may account for at least some of the difficulties women face in trying to be compliant to PMTCT programming.

We agree that FI may account for some of the challenges women face when accessing maternal and child health services, including PMTCT. Nevertheless, we acknowledge that the differences in some of our comparisons are small. We have added the following language to the discussion (Page 10) to acknowledge the small absolute differences: “Although the effect sizes are modest and absolute differences are small, these findings suggest that among a subgroup of pregnant women, food insecurity is an important barrier to some maternal health services.”