Author’s response to reviews

Title: Depression among HIV positive pregnant women in Zimbabwe: a primary health care based cross-sectional study

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Author’s response to reviews:

The Editor

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RE: Revision-Depression among HIV positive pregnant women in Zimbabwe

Thank you for the positive feedback on our manuscript. The comments from the three reviewers are extremely helpful and will help to strengthen the manuscript. We have addressed all the comments and suggestions as follows:

Reviewer 1:

Major

- Abstract

There are several instances where you make a statement without providing the appropriate context, such as in sentence one (lines 5-7) in the introduction and sentence one and two of the conclusion (lines 40-44). This results in a broad overgeneralization.

We thank the reviewer for this observation. The sentence (5-7) has been changed to read as follows:
Depression is a common psychiatric disorder that is two to three times more prevalent among people living with HIV (PLWH) with women being at higher risk. Depression is particularly marked among HIV positive women and may negatively affect birth outcomes.

The reference supporting this sentences is included in the opening paragraph. (Bernard, 2018)

Line (40-44) has been changed to read as follows: Despite these limitations our study reflects findings similar to those from the region and beyond suggesting that depression in the antenatal period among HIV infected women is common [15, 25, 42]. It also highlights the need to focus on IPV which is a growing global problem.

- Introduction

In the second to last paragraph (lines 33-35), your first sentence claims that evidence-based interventions for PLWH affected by depression are known to improve disease outcomes and then only cite one source. If something is known, I would expect there to be more than one source backing this up. You could, for instance include the sources cited in the next sentence (lines 35-37) if they apply. Two of them refer to Zimbabwe and one to Uganda, which does not seem to be representative of all of Sub-Saharan Africa.

Thank you for the observation.

The single reference mentioned (16) is a systematic review which actually highlights a number of interventions that address depression. 16. Chibanda D, Cowan FM, Healy JL, Abas M, Lund C: Psychological interventions for Common Mental Disorders for People Living With HIV in Low- and Middle-Income Countries: systematic review. Trop Med Int Health 2015, 20(7):830-839.

More references have been included though.

In your discussion, you return to this point, stating that the health authorities have been too slow to integrate depression care into antenatal and postnatal care due to lack of evidence, which seemingly contradicts your earlier statement.

Thank you for this observation which has been clarified as follows: Furthermore, despite earlier studies showing effectiveness of group PST for women during the postnatal period [17], the health authorities have been slow to integrate such evidence based care packages in antenatal care services due to lack of specific evidence related to the antenatal period.
Methods

- Please elaborate on how your sample is random by describing your process for randomization.

Thank you for this important observation which has been rectified as follows: Each day during this period participants were approached based on computer generated random number allocation by a trained research assistant and informed about the study.

- Please clarify what associations were identified as associations of interest a priori. For example, in the introduction, IPV is not mentioned and by the discussion it is a key take home point. If you added it later, please justify why you added it in the methods.

We thank the reviewer for this insight and we have added the following in the last sentence of the last paragraph in the introduction.: Our earlier work had highlighted intimate partner violence (IPV) as a factor associated with depression among non-pregnant women and those using postnatal services, however, it was known if these factors were similar in antenatal women[12, 18].

- Results

- Table 2 makes it difficult to distinguish what the p-values and OR are referring to. For example, is the absence IPV associated with current depression? It doesn't sound like it from the text, but it looks like it in the table.

We thank the reviewer for this observation and the Table has been corrected to reflect what is highlighted in the text. (Table 2)

- Discussion

- In your limitations, please note that the EPDS has been validated in the prenatal period: Murray D, Cox JL. Screening for depression during pregnancy with the Edinburgh Depression Scale (EPDS). J Reprod Infant Psychol 1990;8:99-107. Thank you for this insight, the reference has been included. Although the EPDS is recommended for antenatal screening[44] it has not been validated in the antenatal period in Zimbabwe, however, it has good psychometric properties for post-natal depression detection [23].
Minor Revisions:

- All

  o This paper could benefit from the editing for syntax and grammar. I believe that this would help clarify some of the ambiguous sentences and reduce the instances of overgeneralization.

- Abstract

  o none

- Introduction

  o none

- Methods

  o Please move the cut-off you used from the results to the methods and provide an explanation for why you chose your particular cut-off (> 12), given that other studies have used 9-13.

    The chosen cut-off is based on local validation of the tool and the reference is provided.

  o Please elaborate on how the pilot period changed your survey questions/data collection

    The Pilot period did not influence the survey or design.

- Results

  o none

- Discussion

  o Paragraph one, you state "there have been no other studies…", please change this to "we are not aware of any other studies…” in case they exist. Thank you, this has been done.
Angela Lupattelli (Reviewer 2): This is a cross-sectional study investigating the prevalence of depressive symptoms in HIV-positive women in Zimbabwe. The study is relevant, given the scarcity of data in Zimbabwe on the topic. However, I do have some concerns that should be addressed by the authors.

The introduction could be amended with prevalence estimates of antenatal depression in HIV-positive women in African countries other than Zimbabwe - if these are available in the literature. This could be informative.

Prevalence rates for antenatal depression have been included to read as follows: During pregnancy rates ranging from 12% to 30% have been reported through a number of systematic reviews[11-13] including regional studies[9, 14-17]

Because the study is also exploring factors associated with antenatal depression in HIV-positive women, the authors should consider adding one-two sentences about the factors most strongly associated with this outcome as found in prior studies. This has been done

Methods, Participants: please rephrase the word "handicapped". The authors could use the wording "intellectual disability".

Thank you for this important observation. We have changed this to read as “intellectual disability”

Please indicate at what gestational week women were enrolled in the study. This information should also be presented in Table 1, since symptom severity prevalence can vary across the stages of pregnancy.

Thank you, this information is available in the paragraph headed “participants” and reads as follows, “All pregnant HIV positive women in the first trimester booked at Chitungwiza city council antenatal clinics were eligible for inclusion in the study.

Has the EPDS been validated only in postpartum women in Zimbabwe? Please clarify.

The EPDS has been validated in the postpartum period in Zimbabwe. This is mentioned in the paragraph headed, “screening tools”. And reads, “The EPDS was used to screen for antenatal depression in all 4 clinics by trained research assistants. The EPDS has been validated in Zimbabwe in the postnatal period and found to have good psychometric properties with
sensitivity and specificity of 88% and 87% respectively with a Chronbach’s alpha of 0.87 at cut-off of 11/12 [30].

Furthermore in the discussion this is mentioned and highlighted as a possible limitation as there has been no validation in the antenatal period.

Please specify whether the cut-off of 12 on the total EPDS score has been validated in the population in Zimbabwe. If not, this is an important point (limitation) to address since it is well established that the validity of EPDS cut-off values differ across populations/cultures.

Thank you for this request. We have indicated above that the EPDS has been validated in Zimbabwe and the cut off score of 12 is based on this validation.

The authors performed univariate analysis using chi-square test; however, in some instances, it seems that an exact test is necessary given the low number of expected counts per cell. Could the author address this issue?

When expected number of counts per cell are low SPSS will automatically calculate the Fishers’ exact tests, and this was considered.

Also, the method part on the binary logistic regression is insufficiently described; there is no information on steps in model building, model robustness, presence of potential interaction, criteria as to how variables were excluded from the model. Please amend this section as appropriate; the work done by Prof Hosmer may be of help for this.

It would be relevant to provide the 95% CI of the prevalence estimate for antenatal depression.

The 95%CI has been included in the results section to read as follows: A total of 78 (39.4%), 95%CI 32.5-46.3 met depression criteria according to the EPDS.

A logistic regression analysis was conducted to predict depression among HIV positive mothers of 198 participants using the variables in the table. A test of the full model against a constant only model was carried out to determine significance and to indicate that the predictors as a set reliably distinguished between those who were depressed and non-depressed. Nagelkerke’s R² was measured to determine strengthen of relationship. Prediction success overall was 69.5% (81.7% non-depressed and 50.6% depressed).
As shown in Table 1 and 2, there are many variables with zero cells. This could be an issue in the multivariate analysis. How did the author handle the zero cells problem? Please clarify.

It was marital status only with zero cells as described above and the necessary test was carried out as a result.

Please indicate how missing values on one or more of the EPDS items were handled, and so missing values on sociodemographic variables.

Since there was no pattern in the missing data on any variables, missing responses were omitted. Noteworthy for Table 1 zero cells were noted on Marital status.

One important limitation is that the EPDS was administered only one time. So, these results could in fact be an overestimation of the true antenatal depression prevalence. We thank the reviewer for this observation and indeed this could be an overestimation of the results and this is a limitation which we have included in the discussion.

Thandi van Heyningen, M.A. (Reviewer 3): This is a very important contribution to the literature on common mental disorders amongst HIV positive pregnant women in Sub-Saharan Africa. It is well-written and interesting to read.

I have only a few minor comments:

1. Perhaps more can be included in the background on the effect of maternal depression on maternal functioning and outcomes for child health and development and also on maternal self-care wrt to ART adherence and uptake of antenatal health care.

Thank you for this suggestion and we have included this information based on a similar request from reviewer 1.

2. There could be more detail included about the interface between IPV, HIV and mental health during the perinatal period, especially for women living in adverse circumstances. This link has been highlighted in the discussion.
3. References needed for the validation studies of EPDS and cut-offs (in the paragraph on screening - line 53. References have been added including a review study.

4. I think the methods used in data analysis was multivariable analysis rather than multivariate analysis. Although the terms are often used interchangeably, multivariate regression refers to analysis where there is more than one outcome variable with different independent variables. While in Multivariable analysis there is only one dependent/outcome variable with many independent variables - as is the case with this study.

The study methods have been elaborated according to reviewer 1 and 2 suggestions above.

We hope that these responses meet the reviewers’ satisfaction.

Thank you

Dr. D. Chibanda