

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Symptoms of common mental disorders and adherence to antiretroviral therapy among adults living with HIV in rural Zimbabwe: a cross-sectional study
<b>AUTHORS</b>	Haas, Andreas D; Kunzekwenyika, Cordelia; Hossmann, Stefanie; Manzero, Josphat; van Dijk, Janneke; Manhibi, Ronald; Verhey, Ruth; Limacher, Andreas; von Groote, Per M; Manda, Ethel; Hobbins, Michael; Chibanda, D; Egger, Matthias

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Daniels, Joseph Charles R Drew University of Medicine and Science
<b>REVIEW RETURNED</b>	10-Mar-2021

<b>GENERAL COMMENTS</b>	<p>This manuscript outlines the results of a cross-sectional survey to assess common mental disorders (CMD) among those living with HIV in Zimbabwe. The study was conducted to determine eligibility for an intervention. The manuscript is written well and outlines interesting results of CMD impacting HIV treatment adherence behaviors. Although not the central focus of the manuscript, a brief summary of the friendship bench intervention may be useful in the Methods, and how the outcomes of this study informed intervention recruitment may be needed in the Discussion. The Discussion and Conclusion need additional editing. I would suggest re-organizing the paragraphs such that the current paragraphs 1, 4, 5 are together followed by the current paragraphs 2 and 3. Further, paragraphs 2 and 3 need more elaboration as these read more interpretative based on changes in HIV treatment policy and previous studies in the past. Such elaboration would strengthen the paper because right now it reads more like a report. Also, I would review the Conclusion sentence as it doesn't read quite right, and you may want to outline any needs for mental health services in urban settings too and how these might be different from rural settings, if at all.</p>
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<b>REVIEWER</b>	Pokhrel, Khem Tropical Health and Education Trust
<b>REVIEW RETURNED</b>	04-May-2021

<b>GENERAL COMMENTS</b>	Feedback  General
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	<p>The authors have done an excellent work to contribute scientific community with the Objectives: To examine the proportion of people living with HIV (PLHIV) screening positive for common mental disorders (CMD) and associations between positive CMD screening tests and self-reported adherence to antiretroviral therapy (ART). The description of the study is quite interesting and covered large proportion of HIV positive people. However, the author could improve the manuscript providing the detail of the scale they used and its reliability in their data such as Cronbach's alfa. Also, the data analysis is not sufficient to justify the association, which may not give the liberty to authors to meet the conclusion about the association between common mental health disorders and ART non-adherence.</p> <p>Specific:</p> <p>Abstract</p> <p>Title: Suggested PLHIV who have common mental disorders ( not screening positive for..)</p> <p>Participants: Why non-pregnant only, consider justifying in the latter section</p> <p>Outcome measures: I was not clear why the author did not mention about the association between CMDs and ART adherence. This should be an important outcome measure. Other should be the results only.</p> <p>Please consider revising the results:</p> <p>Those who are positive CMD screening were 1.5 times more likely to have sub-optimal adherence. Use of word higher prevalence is inappropriate.</p> <p>Conclusion: Just focus on screening of CMD rather than integrate as you are not evaluating integration of services and talk about ART as well.</p>
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	<p>Background</p> <p>It is worthwhile to talk about the gender differences in CMDs in the context</p> <p>Justify your study as there is already the evidence cited in ref. 12 and 13.</p> <p>Methods</p> <p>Clearly describe inclusion and exclusion criteria</p> <ul style="list-style-type: none"><li>-pregnant women</li><li>-HIV-positive with severe mental disorders</li></ul> <p>SSQ-14. How the authors define the cutoff point, and provide reliability value (Cronbach's alfa) in your population</p> <p>Provide the reference for use of non-adherence measurement</p> <p>In data analysis, describe the model which is outcome, I think it should be non-adherence</p> <p>Results:</p> <p>Justify the larger sample size of the women in method section. Major portion of the first paragraph of results section comes under methods section. Consider revising.</p> <p>There is no analysis of association between CMD and non-adherence. How the author can provide conclusion of association, is not clear</p> <p>Suboptimal adherence was more common in individuals screening positive for CMD (21.3%, 95% CI 16.8-26.6; aPR 1.53 95% CI 1.37-1.70) than in those screening negative (15.3% 95% CI 12.0-19.3).</p>
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	<p>There should logistic regression controlling the factors</p> <p>Discussion:</p> <p>Please do not repeat methods and results section here</p> <p>Describe the context or programs if there is evidence to contribute to low CMD</p> <p>Table</p> <p>: There is only one table, provide information of sex and age. There should be other characteristics related to such as socioeconomic, education...</p> <p>No table for regression to show association.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Joseph Daniels, Charles R Drew University of Medicine and Science

Comments to the Author:

This manuscript outlines the results of a cross-sectional survey to assess common mental disorders (CMD) among those living with HIV in Zimbabwe. The study was conducted to determine eligibility for an intervention. The manuscript is written well and outlines interesting results of CMD impacting HIV treatment adherence behaviors.

Thank you for reviewing our paper.

Although not the central focus of the manuscript, a brief summary of the friendship bench intervention may be useful in the Methods, and how the outcomes of this study informed intervention recruitment may be needed in the Discussion.

We have added a brief summary of the Friendship Bench intervention in the Background.

Background (last paragraph):

"The Friendship Bench intervention is a culturally adapted evidence-based psychological intervention developed to close the treatment gap for CMD in Zimbabwe [21]. The Friendship Bench team trains community health workers to identify people with CMD symptoms and deliver a brief intervention consisting of six sessions of problem-solving therapy and optional group support [21]."

Positive CMD screening (SSQ-14  $\geq 9$ ) was an inclusion criterion of our trial. Individuals who screened positive for CMD and provided written informed consent were included in the trial. We have now clarified this in the 5<sup>th</sup> paragraph of the Methods section.

"Individuals who screened positive for CMD and provided written informed consent were included in the trial and were offered CMD treatment as part of the FB-ART trial."

The Discussion and Conclusion need additional editing. I would suggest re-organizing the paragraphs such that the current paragraphs 1, 4, 5 are together followed by the current paragraphs 2 and 3. Further, paragraphs 2 and 3 need more elaboration as these read more interpretative based on changes in HIV treatment policy and previous studies in the past. Such elaboration would strengthen the paper because right now it reads more like a report. Also, I would review the Conclusion sentence as it doesn't read quite right, and you may want to outline any needs for mental health services in urban settings too and how these might be different from rural settings, if at all.

We have revised and restructured the Discussion. Please see our response to the Editor's comment about our Discussion.

Reviewer: 2

Dr. Khem Pokhrel, Tropical Health and Education Trust

#### General

The authors have done an excellent work to contribute scientific community with the Objectives: To examine the proportion of people living with HIV (PLHIV) screening positive for common mental disorders (CMD) and associations between positive CMD screening tests and self-reported adherence to antiretroviral therapy (ART). The description of the study is quite interesting and covered large proportion of HIV positive people. However, the author could improve the manuscript providing the detail of the scale they used and its reliability in their data such as Cronbach's alfa.

Thank you

Also, the data analysis is not sufficient to justify the association, which may not give the liberty to authors to meet the conclusion about the association between common mental health disorders and ART non-adherence.

We estimated adjusted prevalence ratios for associations between positive CMD screening tests and suboptimal adherence using mixed-effects Poisson regression models. Positive CMD screening was associated with a 53% (95% CI 37%-70%) increase in the prevalence of suboptimal adherence (adjusted prevalence ratio [aPR] 1.53, 95% CI 1.37-1.70). We now show this result more prominently in Table 2.

Specific:

Abstract

Title: Suggested PLHIV who have common mental disorders (not screening positive for..)

The title of the manuscript is "Symptoms of mental disorders and adherence to antiretroviral therapy among adults living with HIV in rural Zimbabwe: a cross-sectional study."

Referring to individuals who screened positive for CMD based on a brief symptoms screen as having CMD is not appropriate. The SSQ-14 is not a diagnostic instrument, and not all individuals who are screening positive for CMD meet diagnostic criteria for CMD.

Participants: Why non-pregnant only, consider justifying in the latter section

The SSSQ-14 has not been validated for pregnant women.

Outcome measures: I was not clear why the author did not mention about the association between CMDs and ART adherence. This should be an important outcome measure. Other should be the results only.

We now mention adjusted prevalence ratios (aPR) for factors associated with CMD, suicidal ideation, perceptual symptoms, and suboptimal ART adherence as outcome measures.

"Secondary outcomes were the proportion of participants reporting suicidal ideation, perceptual symptoms, and suboptimal ART adherence and adjusted prevalence ratios (aPR) for factors associated with CMD, suicidal ideation, perceptual symptoms, and suboptimal ART adherence."

Please consider revising the results:

Those who are positive CMD screening were 1.5 times more likely to have sub-optimal adherence. Use of word higher prevalence is inappropriate.

We assume that the reviewer is referring to the following sentence:

"Positive CMD screen was associated with a higher prevalence of suboptimal adherence (aPR 1.53; 95% CI 1.37-1.70)."

We have rephrased the sentence. The sentence now reads: "Positive CMD screen was associated with suboptimal adherence (aPR 1.53; 95% CI 1.37-1.70)."

Conclusion: Just focus on screening of CMD rather than integrate as you are not evaluating integration of services and talk about ART as well.

Our study shows that one in five persons living with HIV screened positive for CMD and that positive CMD screens are associated with suboptimal ART adherence. We feel that these results support our conclusion that there is a need to address mental health problems in people living with HIV by integrating mental health services in HIV programs.

Background

It is worthwhile to talk about the gender differences in CMDs in the context.

Thank you. We agree and have added a sentence in the Background and a paragraph in the Discussion to discuss gender differences in CMD prevalence.

Background

" The prevalence of depression and anxiety disorders is higher in women than in men [7,8]."

Discussion (3<sup>rd</sup> paragraph):

"In line with the national [10] and international literature [27,28], we found that CMDs were much more common in women than in men. Biological factors, including sex hormones and sex differences in the neuroendocrine response to stress, psychosocial factors such as gender differences in interpersonal orientation, self-esteem, body shaming, and rumination might contribute to the gender gap in CMD

[7,8]. In addition to these individual-level factors, gender inequity and higher exposure of women and girls to traumatising life events, including gender-based violence or sexual abuse, may further contribute to the gender gap in CMD [7,10,29]. "

Justify your study as there is already the evidence cited in ref. 12 and 13.

In Zimbabwe, the majority of people living with HIV reside in rural areas. To the best of our knowledge, CMD prevalence and associations between CMD and adherence have not been evaluated in rural populations in Zimbabwe.

#### Methods

Clearly describe inclusion and exclusion criteria

- pregnant women
- HIV-positive with severe mental disorders

We clearly state the eligibility criteria for CMD screening in the 2<sup>nd</sup> paragraph of the Methods section:

"HIV-positive non-pregnant adults aged 18 years or older who lived in Bikita district and had received ART for at least six months were eligible."

In the 3<sup>rd</sup> paragraph, we specify the inclusion criteria for the study:

"Individuals who participated in SSQ screening were eligible for this analysis."

- SSQ-14. How the authors define the cutoff point, and provide reliability value (Cronbach's alpha) in your population

The optimal cutoff score of  $\geq 9$  was selected in the validation study [2] to have a good balance of sensitivity and specificity. In our study population, the SSQ-14 showed good internal consistency (Cronbach's  $\alpha=0.82$ ). We have added the following paragraph in the Methods section to provide more detail on the validity and reliability of the SSQ.

"An SSQ-14 score of  $\geq 9$  had a sensitivity of 88% and a specificity of 76% for depression or general anxiety in HIV-positive adults in Harare [9]. The tool had a high internal consistency in the validation study (Cronbach's  $\alpha=0.74$ ) and in our study (Cronbach's  $\alpha=0.82$ )."

- Provide the reference for use of non-adherence measurement

Reference has been added:

"Adherence was assessed based on self-report using the following question: "In the last 30 days, how many days have you missed taking any of your ARV [antiretroviral] pills?" [23]."

- In data analysis, describe the model which is outcome, I think it should be nonadherence

We calculated unadjusted and adjusted hazard ratios for factors associated with suboptimal adherence using mixed-effects Poisson regression models with robust standard errors. We have extended the description of the used models in the Methods section.

"We estimated adjusted prevalence ratios (aPRs) for factors associated with positive screening for CMD, suicidal ideation, and perceptual symptoms using mixed-effects Poisson regression models with robust standard errors [25]. Models were adjusted for sex, age, and clustering of data at facility-

level using a random intercept for study facilities. We used the same models to calculate unadjusted and aPRs for factors associated with suboptimal adherence.”

Results:

Justify the larger sample size of the women in method section.

We continued screening until the target sample size of our trial was reached. The overrepresentation of women in our sample is likely a result of a higher prevalence of HIV and CMD in women than in men and the gender difference in health care-seeking behavior.

Major portion of the first paragraph of results section comes under methods section. Consider revising.

As per STROBE reporting guidelines [3], we report the numbers of individuals at each stage of study (item 13 a), reasons for non-participation at each stage (item 13 b) and characteristics of study participants in the first paragraph of the Results section.

See STROBE checklist: [https://www.equator-network.org/wp-content/uploads/2015/10/STROBE\\_checklist\\_v4\\_combined.pdf](https://www.equator-network.org/wp-content/uploads/2015/10/STROBE_checklist_v4_combined.pdf)

There is no analysis of association between CMD and non-adherence. How the author can provide conclusion of association, is not clear Suboptimal adherence was more common in individuals screening positive for CMD (21.3%, 95% CI 16.8-26.6; aPR 1.53 95% CI 1.37-1.70) than in those screening negative (15.3% 95% CI 12.0-19.3). There should logistic regression controlling the factors

We calculated an adjusted prevalence ratio (aPR) with 95% confidence interval (CI) to quantify the association between suboptimal adherence and positive CMD screening using mixed-effects Poisson regression models adjusting for age, sex and accounted for clustering of participants in study facilities. Prevalence ratios are valid measures of associations in cross-sectional studies [4]. We chose prevalence ratios over odds ratios for their ease of interpretation. A difference in the odds of a binary outcome is less intuitive than a difference in prevalence. Odds ratios are sometimes misinterpreted as a difference in probability.

Discussion:

Please do not repeat methods and results section here

As recommended by the Editor, the first paragraph of our Discussion is a summary of the results "statement of the principal findings" [1].

Describe the context or programs if there is evidence to contribute to low CMD

We are unclear what the reviewer is referring to here.

Table

There is only one table, provide information of sex and age. There should be other characteristics related to such as socioeconomic, education...

Detailed sociodemographic data were collected for participants who enrolled in the trial (N=516). No further sociodemographic data were collected for the population (N=3,480) included in this analysis of the screened population.

No table for regression to show association.

Table 1 shows adjusted prevalence ratios for associations between positive CMD screening tests and demographic factors from mixed-effect Poisson regression models.

We have added Table 2 to show prevalence ratios for factors associated with suboptimal adherence. In the previous version of the manuscript, associations between suboptimal adherence and positive CMD screening tests were reported in the text.

"Suboptimal adherence was more common in individuals screening positive for CMD (21.3%, 95% CI 16.8-26.6; aPR 1.53 95% CI 1.37-1.70) than in those screening negative (15.3% 95% CI 12.0-19.3)."

#### References:

1. Docherty M, Smith R. The case for structuring the discussion of scientific papers. *BMJ*. 1999 May 8;318(7193):1224–5.
2. Chibanda D, Verhey R, Gibson LJ, Munetsi E, Machando D, Rusakaniko S, et al. Validation of screening tools for depression and anxiety disorders in a primary care population with high HIV prevalence in Zimbabwe. *J Affect Disord*. 2016;198:50–5 PubMed .
3. Vandembroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *PLoS Med*. 2007 Oct 16;4(10):e297.
4. Tamhane AR, Westfall AO, Burkholder GA, Cutter GR. Prevalence odds ratio versus prevalence ratio: choice comes with consequences. *Stat Med*. 2016 Dec 30;35(30):5730–5.

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