Author's response to reviews

Title: Factors Associated with Depression among Adolescents Living with HIV in Malawi

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Title: Factors Associated with Depression among Adolescents Living with HIV in Malawi

Maria H Kim, Alick C Mazenga, Xiaoying Yu, Akash Devandra, Chi Nguyen, Saeed Ahmed, Peter N. Kazembe and Carla Sharp

We are grateful for the thoughtful and helpful reviews. Please find below our responses to the requested revisions. Corresponding edits have been made to the manuscript and are highlighted in yellow. In addition, a copy editor has edited the manuscript (track changes in the manuscript). She is now credited in the acknowledgments section. Finally we obtained written assents/consents from all those who participated in the study. We hope that the editorial board will be pleased with our revisions.

Thank you,
Maria Kim

Reviewer’s report

Title: Factors Associated with Depression among Adolescents Living with HIV in Malawi

Version: 1

Date: 28 July 2015

Reviewer: Carryl P Navalta

Major Compulsory Revisions

1. The introduction lacks a review of research on adolescents with depression (but without HIV/AIDS) in general (including risk factors) as well as specific to sub-Saharan Africa and/or Malawi. Such a review should include the epidemiological evidence that depression is the number one cause of illness and disability worldwide (World Health Organization, 2014).

We have now included a more comprehensive review of the research on adolescents with depression in general (including those with/without HIV/AIDS) in addition to the data from sub-Saharan Africa. We have also included the epidemiological evidence that depression is the number one cause of illness and disability worldwide.

Lines 91-103:

“Globally, depression is a major contributor to the burden of disease worldwide and the number one cause of illness and disability amongst adolescents; with suicide ranking as the third most common cause of death [3]. The burden of disease is higher in low and middle-income countries [4]. Risk factors for depression in adolescents in the west
include exposure to psychosocial stressors [4], bullying victimization [5-8], traumatic events, abuse [9, 10], and gender [4]. High-risk behaviours, such as earlier debut of sexual activity, substance misuse, and increased number of sexual partners, have also been associated with depression in youth [8, 11, 12]. In sub-Saharan Africa, evidence on factors potentially associated with depression amongst adolescents such as bullying [16], and substance abuse [16, 17] have just begun to emerge. Correlates, which might be particularly relevant in the African setting including orphanhood [13, 14], exposure to violence [15], poverty, and food insecurity, peer social support, and death in the family, and have been insufficiently described.”

Lines 135-142

“Furthermore, there is little to no evidence regarding depression amongst HIV-infected adolescents in Malawi. Given the paucity of research we performed exploratory testing and included variables, based on prior research on adolescent depression, that were hypothesized to potentially contribute to or be protective of depression in HIV-infected adolescents in Malawi. We evaluated a wide range of factors: socio-demographic, past traumatic events/stressors (including bullying, self-image and school performance), behavioural factors/social support (including HIV disclosure), and bio-clinical parameters.”

2. Because the above-mentioned review is missing, whether the investigators tested a specific hypothesis or model is unclear. The fact that they examined ">70 variables" speaks to this lack of clarity. Rather, the authors should articulate a specific research question, then choose appropriate statistical analyses or, at the very least, confer their reasoning for doing such exploratory testing in their discussion.

We hope that the edits (indicated above) serve to better articulate the reasoning for exploratory testing.

3. Relatedly, the authors’ analytical strategy was difficult to understand, especially given that no specific hypothesis nor model was delineated. Although many analyses were reportedly conducted (i.e., two-sample t-test, analysis of variance, Pearson correlation, Chi-square), several of the corresponding values are missing from the manuscript (e.g., we could not find T, F, nor r values anywhere in the tables). In addition, some of the statistical decisions made are questionable and no citations were provided to support such decisions (e.g., collapsing categories for some variables "with sparse cells or with similar outcome values", combining variables or selecting "the most important variable" when such factors were correlated). In all, the authors did not explain these decisions in any part of their manuscript, which leaves the reader confused about what analyses were utilized or omitted, what data was “important”, and what might be missing.

To clarify the process we have included additional information on the background
We performed initial explorative analysis for variables thought potentially to be associated with depression (based on previously published research included in the background literature review) using two-sample t-test, analysis of variance, Pearson correlation and Chi-square test. The initial univariate analysis identified 28 variables thought to be possibly associated with depression (p-value less than 0.25 or associations postulated based on previously published research). These were reassessed using univariate linear regression (alternative to two-sample t-test, analysis of variance, Pearson correlation for continuous outcome BDI-II score) and univariate logistic regression (alternative to two-sample t-test, Chi-square for binary outcome depression status classified by CDRS score). Then we performed a second round of screening by adjusting for age and sex in the model. We reported the results with and without adjusting age and sex in table 1 and 2. We did not include the initial findings in the results due to the enormous output. Instead, we reported the results using regressions to facilitate comparison between adjusted (for age and sex) versus unadjusted results, and multivariate regressions. To clarify the analytic strategy- we have edited the methods section as follows:

Lines 207-245:

“Descriptive statistics, such as, mean, standard deviation (SD) for continuous variables, and frequency and proportion for categorical variables, were calculated among all subjects and by groups. For the BDI-II score, we performed explorative analysis using two-sample t-test, analysis of variance (ANOVA) or Pearson correlation. For CDRS-R score, we defined depression by having a score equal to or higher than 55 [26]. Chi-square test or two-sample t-test was used to explore the association between potential factors and depression. We collapsed categories for some variables with sparse cells or with similar outcome values. For example, we collapsed ‘not in school’ (n=3) with ‘Junior primary school’, ‘tertiary’ (n=4) with ‘junior/senior secondary school’ in meaningful way; we also combined the categories of ‘mother alone’ and ‘father alone’ for caregiver since the results demonstrated a similar degree of depression for two separate categories (19% and 18% in depression by CDRS respectively). For correlated variables which measured similar features, we either combined the variables or selected the most important variable for further analysis. For example, we combined three variables related to violence (forced sex, physical abuse and witness physical violence in the home) into one variable with yes indicating experience on any of three; similarly we had two variables that referred to the caregiver, ‘who currently cares for this teenager’ and ‘who do you live with’. We chose to use the former since it is more relevant/meaningful to the provision of supportive HIV care. Malnutrition was categorized according to the National Center for Health Statistics reference standards. Z-scores for BMI and height-for-age were calculated using WHO growth standards.”
“All of the variables thought to be potentially correlated with depression based on previously published research were assessed. The initial univariate analysis identified 28 variables thought to be possibly associated with depression (p-value less than 0.25 or p-value less than 0.25 or associations postulated based on previously published research). We reassessed these variables by univariate linear/logistic regression, and then we performed a second round of screening by adjusting for age and sex using linear/logistic regression (Table 1 and 2). Eighteen candidates with p-values <0.1 from either model were entered into the multivariate regressions. For both the linear and logistic regressions, we included age and sex in the models, regardless of the statistical significance, and performed backwards selection on other variables with significance ≤ 0.05. Two-way interactions were checked. Only biologically meaningful and significant interactions (such as age*satisfaction with appearance, and age*height) were retained. We rescaled age (age minus 12) so the main effect term of age could be meaningfully interpreted in the model that included interactions with age. Final models were checked by model diagnostic techniques such as residual analysis and influence statistics.”

4. The authors engaged in little discussion regarding how and why they believe the risk factors they identified as increasing the odds for depression in adolescents living with HIV in Malawi are different than those that might increase the risk for a similar population not living with HIV. One way in which this possible discrepancy might be remedied would be to include information on non-HIV sub-Saharan adolescents in the introduction, and discuss the potential differences in their discussion section, or suggest ways in which this differential might lead to a follow-up study.

As described above, information on non-HIV-infected adolescents have been included in the introduction. Potential differences noted in the present study are now further highlighted in the discussion section as below:

“As compared to prior studies in the west or sub-Saharan Africa amongst non-HIV infected adolescents, several HIV-related potential risk factors for depression were highlighted in the present study. Specifically, stunting, immunosuppression, dissatisfaction with one’s physical appearance, and fewer years of or failing school - all possibly the result of HIV infection, were found to be significantly associated with depression. Earlier identification of HIV infection in children with prompt initiation of ART could improve growth potential, immunity, physical appearance, and intellectual capacity and could therefore prevent many of these potential risk factors for depression amongst HIV-infected adolescents.”

Reviewer’s report □ Title: Factors Associated with Depression among Adolescents Living with HIV in Malawi
Version: 1

Date: 11 August 2015

Reviewer: Tsuyoshi Sasaki

Reviewer's report:

Discretionary Revisions

Although, I have a few suggestions that should be addressed by the authors.

#1: In the sample description, the authors should provide probable information about which co-morbidities (especially anxiety disorders) existed except depression.

Excellent point. Unfortunately, we did not collect information on co-morbidities such as anxiety disorders or intellectual disability. We have now included this limitation in our discussion as follows:

“We also did not assess potential co-morbidities such as anxiety or intellectual disability.”

#2: In the sample description, is there data of intellectual disability co-morbidity?

As above.

#3: Would you tell us the rater who had a diagnosis? (A psychiatrist, a pediatrician, or a child psychiatrist?)

In Malawi there is only one practicing psychiatrist in the whole country. Clinical officers with specialized mental health training provide the majority of psychiatric care. To help ensure optimal administration, only clinicians with mental health training and over two years of experience in adolescent HIV care, were selected to undergo one week training in the administration of the CDRS-R. Interviewers received on-going supervision by a qualified mental health professional with expertise in adolescent depression (Clinical officer with a Bachelor of Science in Clinical Medicine specializing in Mental Health and a diploma in Psychiatry).

The following has been added to the methods section as follows:

“Clinician interviewers, with mental health training and over two years of experience in adolescent HIV care, were trained in the administration of the CDRS-R by a mental health clinical officer.”
In summary, the work is of good quality and the results convincing, and thus of high value to the community.

**Level of interest:** An article of importance in its field