

Bullying and ART non-adherence among South African adolescents living with HIV: effects, risk and protective factors

Running head: Bullying and non-adherence among ALHIV

Abstract (240 words)

Background: Identifying risk and protective factors for adolescent antiretroviral therapy (ART) adherence is a public health priority, given high HIV-related mortality in this population. An area that merits further investigation is the relationship between bullying victimization, mental health problems, and ART non-adherence among adolescents living with HIV (ALHIV). However, no known studies assess effects of bullying on adolescent non-adherence, or risk and protective factors that could moderate this relationship.

Setting: This study investigates a) the direct longitudinal relationship between bullying exposure and ART non-adherence, and the indirect relationship via psychological distress, and b) potential risk and modifiable protective factors moderating these pathways, among vertically and horizontally infected ALHIV who initiated treatment across 53 public healthcare facilities in a South African health district.

Methods: Survey data was collected at two-time points, between 2014 and 2017, with 1046 ALHIV (94% retention). Various mediation and moderated mediation models were run as part of a staged analysis approach.

Results: A significant longitudinal relationship was found between bullying victimization and non-adherence, operating indirectly via psychological distress ($B=0.07$; 95%CI: [0.03, 0.13]). Moderation analyses indicated that older adolescents exposed to bullying are more at risk of non-adherence ($B=0.52$; 95%CI: [0.07, 0.97] $p<0.05$), and parental monitoring is a potential protective factor buffering indirect effects of bullying on non-adherence ($B=-0.22$; 95%CI: [-0.42, -0.02] $p<0.05$).

Conclusions: These findings underscore the importance of interventions that address bullying and psychological distress, and strengthen parental monitoring, particularly among older ALHIV.

Keywords: bullying victimization, ART non-adherence, adolescents, mental health, parental monitoring

INTRODUCTION

Adolescents and youth represent a growing proportion of people living with HIV worldwide ¹⁻². They are also a high-risk population for HIV treatment non-adherence and AIDS-related mortality ³⁻⁵. This is of particular public health concern in low- and middle- income countries (LMICs) facing high HIV prevalence rates among youth and challenges in the provision of adequate health care services. Identifying risk and protective factors for adolescent ART adherence is key to developing more effective interventions and reaching the most vulnerable adolescents ⁶.

An area that merits further investigation is the relationship between bullying victimization, mental health problems, and ART non-adherence. Bullying remains a widespread phenomenon among adolescents worldwide, estimated to affect over 30% of school-going youth globally, and around 50% in Eastern and Southern Africa ^{7,8}. It has been associated with various negative health outcomes that can manifest during adolescence and extend into adulthood. These include sleep disorders, psychosomatic complaints, poor self-reported physical health, and more difficult social relations ⁹⁻¹¹. However, evidence of causal effects of bullying victimization is strongest for mental health problems, such as depression, anxiety, and suicidal ideation ¹²⁻¹⁴.

Understanding the adverse effects of bullying, and how to prevent or mitigate these, may be particularly salient for adolescents living with HIV (ALHIV). First, these adolescents are already at risk of exposure to HIV-related stigma ^{15,16} and may be at elevated risk of mental health disorders compared to the general population and other

high-risk groups ¹⁷⁻²⁰. Research with ALHIV in Southern Africa, for example, has shown bullying victimization to be associated with worse mental health ^{14,21,22}. Second, poor mental health has been associated with ART non-adherence among ALHIV ²³⁻²⁵. However, there are no known studies assessing direct or indirect effects of bullying on adolescent ART non-adherence. Moreover, there is no evidence of risk or protective factors that could moderate these effects.

This study seeks to address the following three research questions: i) Are ALHIV who experience bullying more likely to be non-adherent to ARV treatment over time and is this relationship mediated by greater psychological distress? ii) Is the risk of worse adherence greater for specific subgroups of ALHIV who experience bullying? iii) Are there modifiable protective factors at the clinic, school, or family level that can buffer the potential effects of being bullied on worse mental health or ART non-adherence?

In order to address the question of particularly vulnerable subgroups of adolescents (ii), age, gender, mode of HIV transmission and urban versus rural location are tested as moderators; previous analyses with South African ALHIV have shown (older) age, (female) gender, living in an urban versus rural location, and horizontal infection to be associated with worse mental health ^{22,26}. To address the question of potentially modifiable protective factors (iii) we assess moderation of factors within adolescents' family, clinic, and school environments, which have been shown to play a protective role for better adolescent mental health or treatment outcomes more broadly. These environments are key structures within adolescents' microsystems and can shape their beliefs and health behaviors ²⁷.

Family-, clinic- and school- level potential protective factors

At the family level, we test for moderating effects of positive parenting and parental monitoring. Both have respectively been associated with a lower likelihood of mental health problems among children and adolescents ²⁸⁻³¹, although not specifically with ALHIV. Parental monitoring has also been found to buffer effects of bullying on suicidal behavior ³² and antisocial behavior ^{28,33}. Supportive parenting styles have been linked to better treatment adherence ^{34,35}, while a lack of parental monitoring has been associated with worse treatment adherence ^{36,37} among youth living with (other) chronic illness.

At the clinic level, we test for moderating effects of support groups and treatment buddies. Support group interventions have been found to improve mental health and psychosocial functioning in ALHIV and HIV-affected youth ^{38,22}. Evaluation research from Southern Africa indicates that HIV support groups, within or linked to public health facilities, may have a positive impact on adherence and virological outcomes among children, adolescents, and adults ^{39,40, 41,42}. Treatment buddies are individuals in the patient's network who provide support with ART adherence; support may include transport to health facilities, observing ingestion of medication, assisting with management of adverse effects, reminding participants of drug pickup, and providing encouragement. The majority of studies conducted in Southern Africa show treatment buddies to be positively associated with patient outcomes such as increased ART adherence, better clinic attendance ^{43,44}, better medium-term survival rates, and virological and immunological responses ^{40,45}.

Lastly, at the school level, we test for moderating effects of school enrolment. Although there is limited evidence on the role of school-level variables as protective factors for mental health and treatment adherence in LMICs, associations have been found between school absenteeism or dropout and poor mental health in Lebanon, North America, Europe, and Asia ^{46,47,48}.

METHODS

Data collection

The longitudinal *[identifying information omitted]* study was conducted with 1046 ALHIV (10-19) in one of South Africa's highest HIV-prevalence health districts in the Eastern Cape Province. The province is characterized by high morbidity, low human development and poor infrastructure. Led by the University of *[identifying information omitted]* and University of *[identifying information omitted]*, this study was a collaboration with the South African Departments of Health and Basic Education, UNICEF, PEPFAR-USAID, and regional and local NGOs. Ethical clearance was obtained from *[identifying information of universities omitted]*, and provincial South African Departments of Health, Basic Education and Social Development.

Adolescents were interviewed at two-time points between 2014 and 2017, approximately 12-18 months apart. This paper analyses data pertaining to the 1046 adolescents living with HIV, who had initiated ARV treatment at one of the district's

public healthcare facilities (n=53) at baseline. Both vertically and horizontally infected adolescents were included in this sample. Eligible ALHIV were identified through clinic patient records and traced back to their communities, to ensure inclusion of adolescents no longer engaged in care. Voluntary informed consent was obtained from all adolescents and their primary caregivers at both time points. Questionnaires were developed with input from adolescent advisory groups, pre-piloted and administered in the adolescents' language of choice, including Xhosa and English. The tablet-assisted 60–90-minute individual interviews were conducted in clinics or communities by researchers trained in working with vulnerable adolescents. Confidentiality was maintained, except where participants disclosed serious risk of harm to themselves or others, in which case safeguarding procedures were followed, in conjunction with the relevant government services. The rate of baseline uptake was 90% (1046) and 94% of these adolescents (979) were retained at follow up (with 2.4% mortality).

Outcome variable: non-adherence at follow up

Self-reported ART adherence over the past week was measured at baseline and follow-up via items adapted from the standardized Patient Medication Adherence Questionnaire ⁴⁹, combined with measures developed in Botswana ⁵⁰. This adherence measure was validated against undetectable viral load (<50 copies/ml) for adolescent subsamples for which patient file data was available, controlling for key socio-demographic factors and health status (see Table S1). In this analysis a binary variable was used to denote full past-week self-reported adherence (0) or non-adherence (1).

Independent variable: Exposure to bullying at baseline

Bullying victimization was measured using the 9-item ‘Social and Health Assessment Peer Victimization Scale’⁵¹ previously used in research with vulnerable children in South Africa⁵² ($\alpha = 0.78$ for this sample). Items include: being called names, being hit or threatened, and having possessions broken or stolen. Response options range from 1/ ‘not at all’ to 4/ ‘4 or more times.’ For this analysis, the scale variable was dichotomized so that any reported experience of bullying was recorded as ‘1’, and no experience of bullying as ‘0’ (i.e. when the adolescent answered 1/ ‘not at all’ to all items).

Mediator: psychological distress at follow up

A composite psychological distress variable was computed, by adding the standardized scores of the respective depression and anxiety scales at follow up. Depression was measured with the Child Depression Inventory – Short Form⁵³ while anxiety was measured using an abbreviated version of the Revised Children’s Manifest Anxiety Scale⁵⁴, previously validated in South Africa with AIDS-affected children⁵⁵. Internal consistency was good ($\alpha = 0.8$) for the combined scale in this sample.

Moderators: family-, clinic- and school-related

Both positive parenting and parental monitoring or supervision were measured using the short form of the Alabama Parenting Questionnaire⁵⁶. Positive parenting included

7 items on praise, positive reinforcement, and support from the caregiver ($\alpha = 0.9$ at baseline and 0.92 at follow up). Good parental supervision included 10 items focused on monitoring of adolescent social activities and home rule-setting ($\alpha = 0.93$ at baseline and 0.89 at follow up). Response options were on a 5-point scale ranging from 0/ 'never' to 4/ 'always', based on the child-report of frequency of parental behaviors. For greater consistency with the other moderators tested and ease of interpretation, these scale variables were dichotomized into 'high' (1) and low (0) levels of positive parenting and parental monitoring respectively. A code of '1' was allocated if adolescents answered 'always' or 'often' to all positive parenting or good parental monitoring items for the respective scales. Binary variables were also used to denote clinic support group attendance, as in previous analyses¹⁷, having a treatment buddy and being enrolled in a school.

Socio-demographic and HIV-related moderators and covariates

All analyses conducted in this paper controlled for six binary covariates measured at baseline, where these were not included as moderators. These were recorded using adolescent self-report, in some cases combined with clinical records: (1) age (dichotomized to denote younger adolescents aged 10 to 14 and older adolescents aged 15 to 19); (2) male or female gender; (3) rural versus urban residential location; (4) vertical versus horizontal HIV transmission, assessed following a literature-informed algorithm used for existing Sub-Saharan African pediatric HIV cohorts⁵⁷; (5) length of time on ART, measured via self-report and clinic records to indicate more versus less than one year on treatment; (6) informal (versus formal) housing, as a proxy measure of socio-economic-status.

Statistical Analysis

Statistical analyses were conducted using SPSS 25 and the PROCESS macro⁵⁸. Descriptive statistics and frequencies were run for all variables used in the analysis, to provide an overview of participant characteristics for the sample. The main analysis was conducted in 4 sequential stages. First, PROCESS model 4 was run to test for a direct relationship between being bullied at baseline and non-adherent at follow up, and/or an indirect relationship mediated by greater psychological distress, controlling for baseline non-adherence. PROCESS models use bootstrapping, a non-parametric sampling procedure, to simultaneously test for direct and indirect effects of the mediator⁵⁹; for 5000 bootstrap samples, results are statistically significant where 95% confidence intervals do not overlap zero.

The second stage of the analysis aimed to address the question of whether specific subgroups of adolescents were at greater risk of bullying leading to poor adherence. It tested for moderation of the direct and indirect pathways between bullying and non-adherence, by running a moderated mediation model in PROCESS (model 59) for each of four potential socio-demographic or HIV-related moderators of interest: age, gender, mode of HIV transmission and urban versus rural location.

The third stage consisted of testing for moderation of the five clinic, school, and parenting-related potential protective factors, to determine whether any of these could buffer direct or indirect effects of bullying on adherence. Each potential moderator was tested in a separate moderated mediation model, controlling for baseline non-

adherence; baseline values of the moderator variables were tested for the bullied - psychological distress association and the (direct) bullied - non-adherence association, while follow-up values of the moderator variables were tested for the psychological distress - non-adherence association, using PROCESS model 22.

The fourth stage of the analysis consisted of combining all previously tested moderating variables with interaction terms significant at the $p < 0.05$ level into one final moderated mediation model. In the final model, moderators were tested for the specific association(s) for which they had shown significance during stages 2 and 3 of the analysis. Significant interactions were then probed and illustrated⁶⁰ to further explore moderation effects.

RESULTS

At baseline, the majority of ALHIV were between 10 and 14 years of age (63%), female (55%), and based in an urban area (73%). 78.5% were vertically infected with HIV and 82.5% had been on treatment for a year or more. The rates of non-adherence were 34.2% at baseline and 35.5% at follow-up. While more than half the sample reported having a treatment buddy at both data collection points, less than 15% were attending a clinic support group, and the large majority were enrolled in school (89% at follow up). Approximately half the sample reported high positive parenting at both time points, while just over 40% reported high parental monitoring. Additional descriptive statistics for this sample, disaggregated by mode of HIV transmission and gender respectively, are also provided in the supplementary material (see Table S2).

[Table 1: Approx. here]

Results of mediation analysis: effects of bullying on ART non-adherence

As indicated in Table 2 and illustrated in Figure S1, mediation analysis showed no direct association between being bullied at baseline and non-adherence at follow up. However, findings indicated an indirect effect mediated through greater psychological distress ($B = 0.07$; 95%CI: [0.03, 0.13]). Both the association between having experienced bullying at baseline and more psychological distress at follow up ($B = 0.37$, 95%CI: [0.16, 0.59] $p < 0.001$), and the association between more psychological distress and higher odds of non-adherence at follow up ($B = 0.20$; 95%CI: [0.11, 0.28] $p < 0.001$) were significant.

[Table 2: Approx. here]

Results of moderated mediation analyses: testing for risk and protective factors

Each of the three associations constituting the direct and indirect relationship between bullying and non-adherence⁶¹ were evaluated for moderation by socio-demographic or HIV-related factors (age, gender, mode of transmission, and rural versus urban location). Two interaction terms were significant for the psychological distress outcome: older age x bullied ($B = 0.57$, $p < 0.05$) and female x bullied ($B = 0.43$, $p < 0.05$). The direction of the interaction term coefficients suggested that older (15-19) adolescents exposed to bullying victimization were at higher risk than younger

adolescents, and that female adolescents exposed to bullying were more at risk than male adolescents of having greater psychological distress one year later. Instead the non-significant interaction terms for mode of transmission and participant location indicated that these factors were not moderating the direct or indirect relationship between bullying victimization and non-adherence.

Moderated mediation models were then run to test both the direct and indirect pathways for moderation of each of the clinic-, school- and family-related variables. Only the better parental monitoring x psychological distress at follow up ($B=-0.23$, $p<0.05$) interaction term was significant. The negative coefficient indicated that this was in the expected direction, suggesting that parental monitoring could be buffering the risk of high psychological distress leading to non-adherence among these adolescents.

Based on the results of the first three stages of this analysis, described above, a final moderated mediation model was developed and tested, using PROCESS model 23. The three moderators for which interaction terms were significant at the 0.05 level in the individual models were included in this final model: 1) older age for the association between being bullied at baseline and higher psychological distress at follow up; 2) gender (female) for the association between being bullied at baseline and higher psychological distress at follow up; 3) high parental monitoring at follow up for the association between higher psychological distress and non-adherence at follow up.

Results of this final moderated mediation model are illustrated in Table 3 and Figure 1 below. They showed no significant direct effect between being bullied at baseline and non-adherent at follow up, as expected. When all three potential moderators were included in the same model, the interaction for female gender was not significant but the interaction terms for age ($B=0.52$; 95% CI: $[0.07, 0.97]$ $p=0.024$) and high parental monitoring ($B=-0.22$; 95% CI: $[-0.42, -0.02]$ $p=0.029$) maintained significance. These significant interaction terms suggest that age and parental monitoring respectively moderate the indirect relationship between bullying victimization and HIV treatment non-adherence. Specifically, older adolescents and adolescents with low parental monitoring appear to be more at risk of not adhering to treatment if they experience bullying. Interaction plots support these moderation findings (see Figures S2 and S3). There was no significant direct association between high parental monitoring and non-adherence.

[Table 3: Approx. here]

[Figure 1: Approx. here]

Table 4 below indicates whether the indirect relationship between being bullied at baseline and non-adherent at follow up holds at different combinations of the three moderators. For adolescents reporting high parental monitoring at follow up, there is no evidence of a significant indirect relationship between being bullied at baseline and worse non-adherence at follow up (regardless of age or gender). However, for older adolescents who report low parental monitoring this indirect relationship is significant (for older males: Effect = 0.13; 95%CI: $[0.02, 0.28]$ and for older females: Effect= 0.22; 95%CI: $[0.1, 0.39]$).

[Table 4: Approx. here]

DISCUSSION

Results of this analysis indicate that adolescents living with HIV who experience bullying victimization are at greater risk of non-adherence to HIV treatment one year later, and that this relationship operates indirectly via psychological distress. This highlights the importance of preventing, identifying, and addressing exposure to bullying and psychological distress. Findings also indicate that older adolescents who are bullied are more at risk for psychological distress and treatment non-adherence. Particular attention should be paid to this group of older (15-19) adolescents, also considering that trends in HIV-associated deaths in this group are not following the decline observed among younger (10-14) ALHIV⁴.

Evaluations of school-based anti-bullying interventions in high-income countries suggest that complex multi-component interventions are most successful, particularly where they include families of students, and lead to increased adult supervision in school and community locations where aggression is likely to occur ^{62,63}. These approaches recognize that bullying is a complex phenomenon that involves not only victims, but also other actors in an adolescent's life, including bullies, teachers and caregivers ⁶³. Despite promising findings of recent school-based behavioral interventions focusing on teachers and peers ^{64, 65}, to date evaluations of anti-bullying interventions in LMICs have been scarce and the evidence not overall conclusive ⁶⁶.

There is clearly a need to invest in developing and testing further interventions in LMICS in Southern Africa and beyond.

This study also exposed parental monitoring as a potential protective factor against the effects of bullying and psychological distress on treatment non-adherence among ALHIV. Positive parenting and peer support, through support groups and treatment buddies, instead did not emerge as similarly protective in this study. However, these factors have been found to have direct positive effects on mental health and ART adherence in various populations and settings ^{22,39,67,68} and should be considered as protective resources for health and retention in care more broadly. For this study, caregiver rule-setting and monitoring of adolescents' social activities and treatment were found to be important for treatment adherence among ALHIV already experiencing bullying and psychological distress. This finding reinforces the importance of developing and expanding access to family-based interventions, such as those that work with both adolescents and caregivers to strengthen parenting skills and improve caregiver-adolescent interaction ⁶⁹⁻⁷¹. It also highlights the need to involve caregivers, where possible, in interventions not primarily designed as 'family interventions'; these include school-based initiatives aimed at addressing violence or boosting positive health behaviors ^{62,63}.

Moreover, there is recent evidence of the acceptability and efficacy of certain family- and community- based interventions in improving adolescent mental health in LMICs, particularly those that incorporate cognitive-behavioral approaches ^{70,72-74}. It would be useful to further explore the effectiveness of community-based interventions with ALHIVs that seek to both strengthen caregiver-adolescent interaction and address

adolescent psychological distress. Another key area for intervention is increasing the awareness of bullying and mental health among school and clinic staff, community health workers, and ART treatment supporters. It may be possible to use or adapt existing tools, such as the World Health Organization mhGAP training or the HEADSSS tool, to help these providers better identify and support adolescents experiencing bullying and distress⁷⁵⁻⁷⁷.

This study has a number of limitations. The adherence variable, and other indicators used in this study, are based primarily on self-report data and therefore may reflect some level of bias in perception and recall of events. However, adolescent self-report was considered the most reliable option for non-adherence in this context, given limited availability and reliability of patient medical data in this context of a very overburdened health system. Moreover, a short-term measure of non-adherence was chosen to minimize recall bias and tested against viral load indicators for the subsample for which clinic data was available (as described above). Also, despite the strong empirical and theoretical bases for our hypotheses, causality cannot be inferred; it is possible, for example, that consequences of non-adherence could affect psychological distress, or that the relationship between bullying victimization and psychological distress could be bidirectional¹³. Testing for mediation would ideally require data at 3 time-points. We note the limitations and bias related to conducting mediation analysis with two waves of data, where the mediator variable (psychological distress) and the outcome variable (non-adherence) were measured at the same time point. In addition, our choice of potential protective factors to test as moderators was limited by the variables included in the dataset; for example, we were not able to test peer support⁸ or strong school performance⁷⁸. It was also not possible

to determine the extent to which reported bullying victimization was linked to participants' HIV status.

Despite these limitations, this remains the first longitudinal analysis to investigate the direct and indirect relationship between bullying victimization and non-adherence among ALHIV, and to identify factors potentially moderating these pathways. It supports the case for investing in evaluation research and interventions that can address bullying exposure and poor mental health among ALHIV in low-resourced settings, as well as programs that strengthen parenting and caregiver-adolescent interaction. Improving adolescent HIV treatment adherence should be a key public health priority in Southern Africa and globally if we are to protect adolescent health and move closer to achieving the Sustainable Development Goals' health targets ⁷⁹.

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Figure Legends

Figure 1: Results of the final moderated mediation analysis (PROCESS Model 23; n=969)