# Bullying and ART Nonadherence Among South African ALHIV: Effects, Risks, and Protective Factors

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**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 nonadherence among adolescents living with HIV (ALHIV). However, no known studies assess effects of bullying on adolescent nonadherence or risk and protective factors that could moderate this relationship.

**Setting:** This study investigates (1) the direct longitudinal relationship between bullying exposure and ART nonadherence, and the indirect relationship via psychological distress, and (2) potential risk and modifiable protective factors moderating these pathways, among vertically and horizontally infected ALHIV who initiated treatment across 53 public health care facilities in a South African health district.

**Methods:** Survey data were collected at 2 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 nonadherence, operating indirectly through psychological distress [B = 0.07; 95% confidence interval (CI): (0.03 to 0.13)]. Moderation analyses indicated that older adolescents exposed to bullying are more at risk of nonadherence [B = 0.52; 95% CI: (0.07 to 0.97) P < 0.05], and parental monitoring is a potential protective factor buffering indirect effects of bullying on nonadherence [B = -0.22; 95% CI: (-0.42 to -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.

**Key Words:** bullying victimization, ART nonadherence, adolescents, mental health, parental monitoring

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#### **INTRODUCTION**

Adolescents and youth represent a growing proportion of people living with HIV worldwide. 1,2 They are also a highrisk population for HIV treatment nonadherence and AIDS-related mortality. 3-5 This is of particular public health concern in low-income 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 antiretroviral therapy (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 nonadherence. 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<sup>15,16</sup> and may be at elevated risk of mental health disorders compared with the general population and other high-risk groups.<sup>17–20</sup> Research with ALHIV in Southern Africa, eg, has shown bullying victimization to be associated with worse mental health.<sup>14,21,22</sup> Second, poor mental health has been associated with ART nonadherence among ALHIV.<sup>23–25</sup> However, there are no known studies assessing direct or indirect effects of bullying on adolescent ART nonadherence. Moreover, there is no evidence of risk or protective factors that could moderate these effects.

This study seeks to address the following 3 research questions: (1) are ALHIV who experience bullying more likely to be nonadherent to ARV treatment over time and is this relationship mediated by greater psychological distress? (2) Is the risk of worse adherence greater for specific subgroups of ALHIV who experience bullying? (3) 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 nonadherence?

To address the question of particularly vulnerable subgroups of adolescents (2), 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.<sup>22,26</sup> To address the question of potentially modifiable protective factors (3) 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.<sup>27</sup>

# Family-Level, Clinic-Level, 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, <sup>28–31</sup> although not specifically with ALHIV. Parental monitoring has also been found to buffer effects of bullying on suicidal behavior<sup>32</sup> and antisocial behavior.<sup>28,33</sup> Supportive parenting styles have been linked to better treatment adherence, <sup>34,35</sup> whereas a lack of parental monitoring has been associated with worse treatment adherence<sup>36,37</sup> 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-affected and HIVaffected youth.<sup>22,38</sup> 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.39-42 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. Most 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

Finally, 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. 46–48

#### **METHODS**

### **Data Collection**

The longitudinal Mzantsi Wakho ("Our South Africa") 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 Oxford and University of Cape Town, 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 Oxford University (SSD/CUREC2/12-21), the University of Cape Town (CSSR

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2013/4, 2019/11), and provincial South African Departments of Health, Basic Education and Social Development.

Adolescents were interviewed at 2 time points between 2014 and 2017, approximately 12–18 months apart. This paper analyses data pertaining to the 1046 ALHIV, who had initiated ARV treatment at one of the district's public health care 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, prepiloted, 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: Nonadherence at Follow-up

Self-reported ART adherence over the past week was measured at baseline and follow-up through 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 were available, controlling for key sociodemographic factors and health status (see Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B574). In this analysis, a binary variable was used to denote full past-week self-reported adherence (0) or nonadherence (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 Africa $^{52}$  ( $\alpha = 0.78$  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" (ie, 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 Form,  $^{53}$  whereas anxiety was measured using an abbreviated version of the Revised Children's Manifest Anxiety Scale,  $^{54}$  previously validated in South Africa with AIDS-affected children.  $^{55}$  Internal consistency was good ( $\alpha=0.8$ ) for the combined scale in this sample.

# Moderators: Family-Related, Clinic-Related, and School-Related

Both positive parenting and parental monitoring or supervision were measured using the short form of the Alabama Parenting Questionnaire.<sup>56</sup> 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 rulesetting ( $\alpha = 0.93$  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 analyses, 17 having a treatment buddy and being enrolled in a school.

# Sociodemographic and HIV-Related Moderators and Covariates

All analyses conducted in this paper controlled for 6 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 10–14 and older adolescents aged 15–19), (2) male or female gender, (3) rural versus urban residential location, (4) vertical versus horizontal HIV transmission, assessed after a literature-informed algorithm used for existing sub-Saharan African pediatric HIV cohorts<sup>57</sup>; (5) length of time on ART, measured through self-report and clinic records to indicate more versus less than one year on treatment; and (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 macro.<sup>58</sup> 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 nonadherent at follow-up, and/or an indirect relationship mediated by greater psychological distress, controlling for baseline nonadherence. PROCESS models use bootstrapping, a nonparametric sampling procedure, to

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simultaneously test for direct and indirect effects of the mediator<sup>59</sup>; 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 a greater risk of bullying leading to poor adherence. It tested for moderation of the direct and indirect pathways between bullying and nonadherence, by running a moderated mediation model in PROCESS (model 59) for each of 4 potential sociodemographic 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 5 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 nonadherence; baseline values of the moderator variables were tested for the bullied—psychological distress association and the (direct) bullied—nonadherence association, whereas follow-up values of the moderator variables were tested for the psychological distress—nonadherence 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 illustrated<sup>60</sup> to further explore moderation effects.

### **RESULTS**

Table 1 shows descriptive statistics and frequencies for the sample. At baseline, most 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 nonadherence were 34.2% at baseline and 35.5% at follow-up. Although 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, whereas 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 Supplemental Digital Content (see Table 2, Supplemental Digital Content, http://links.lww.com/QAI/B574).

# Results of Mediation Analysis: Effects of Bullying on ART Nonadherence

As indicated in Table 2 and illustrated in Figure 1, Supplemental Digital Content, http://links.lww.com/QAI/B574, mediation analysis showed no direct association

**TABLE 1.** Descriptive Statistics and Frequencies for the Sample (n = 979)

	N (% Sample)	
Variables	Baseline	Follow-Up
Sociodemographic covariates		
Age		
10–14 years	617 (63%)	
15–19 yrs	362 (37%)	
Gender	` ′	
Female	539 (55.1%)	
Male	440 (44.9%)	
Location	, ,	
Rural	261 (26.7%)	
Urban	716 (73.1%)	
Missing	2 (0.2%)	
Housing (SES status)	2 (0.270)	
Informal housing	183 (18.7%)	
Formal housing	795 (81.2%)	
Missing	1 (0.1%)	
HIV-related covariates	1 (0.170)	
Mode of transmission		
Horizontal	202 (20 70/)	
Vertical	203 (20.7%)	
	769 (78.5%)	
Missing	7 (0.7%)	
Time on treatment	909 (92 50/)	
More than a year	808 (82.5%)	
Less than a year	171 (17.5%)	
Independent variable		
Bullying victimization	500 (50 50)	
Experienced bullying	580 (59.2%)	
Did not experience bullying	399 (40.8%)	
Dependent variable		
Past week nonadherence		
Nonadherent	335 (34.2%)	
Adherent	644 (65.8%)	631 (64.5%)
Mediator variable		
Depression and anxiety symptoms scale (mean, SD)		1.85 (3.17)
Potential moderating variables		
Clinic support group attendance		
Yes	142 (14.5%)	113 (11.5%)
No	837 (85.5%)	866 (88.5%)
Treatment buddy		
Yes	702 (71.2%)	565 (57.7%)
No	277 (28.3%)	414 (42.3%)
School enrolment		
Yes	922 (94.2%)	867 (88.6%)
No	57 (5.8%)	112 (11.4%)
Positive parenting		
High	495 (50.6%)	469 (47.9%)
Low	484 (49.4%)	510 (52.1%)
Parental monitoring	, ,	` ' '
High	405 (41.4%)	433 (44.2%)

between being bullied at baseline and nonadherence at follow-up. However, findings indicated an indirect effect mediated through greater psychological distress [B=0.07; 95% confidence interval (CI): (0.03 to 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 to 0.59) P<0.001], and the association between more psychological distress and higher odds of nonadherence at follow-up [B=0.20;95% CI: (0.11 to 0.28) P<0.001] were significant.

## Results of Moderated Mediation Analyses: Testing for Risk and Protective Factors

Each of the 3 associations constituting the direct and indirect relationship between bullying and nonadherence<sup>61</sup> were evaluated for moderation by sociodemographic 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  $\times$  bullied (B = 0.57, P < 0.05) and female  $\times$  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 1 year later. Instead the nonsignificant 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 nonadherence.

Moderated mediation models were then run to test both the direct and indirect pathways for moderation of each of the clinic-related, school-related, 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 nonadherence among these adolescents.

Based on the results of the first 3 stages of this analysis, described above, a final moderated mediation model was developed and tested, using PROCESS model 23. The 3 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; and (3) high parental monitoring at follow-up for the association between higher psychological distress and nonadherence 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 nonadherent at follow-up, as expected. When all 3 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 to 0.97) P = 0.024] and high parental monitoring [B = -0.22; 95% CI: (-0.42 to -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 nonadherence. Specifically, older adolescents and adolescents with low parental monitoring seem to be more at risk of not adhering to treatment if they experience bullying. Interaction plots support these moderation findings (see Figs. 2-3, Supplemental Digital Content, http://links.lww.com/QAI/B574). There was no significant direct association between high parental monitoring and nonadherence.

**TABLE 2.** Results of PROCESS Model 4 Regressions, Respectively, Predicting Psychological Distress and ART Treatment Nonadherence at Follow-up (n = 969\*)

	Dependent Variable: Psychological Distress		Dependent Variable: ART Nonadherence	
	B (Unstandardized)	95% CIs	B (Unstandardized)	95% CIs
Sociodemographic and HIV-related covariates				
Age (older)	0.447***	0.204 to 0.690	-0.309	-0.628 to $0.010$
Female	0.202	-0.016 to $0.419$	-0.224	-0.503 to $0.056$
Rural location	-0.137	-0.381 to $0.107$	-0.286	-0.604 to $0.033$
Informal housing	-0.076	-0.352 to $0.199$	0.122	-0.229 to $0.473$
Horizontal infection	0.112	-0.202 to $0.426$	0.525**	0.130 to 0.920
Time on treatment $> 1$ yr	-0.108	-0.415 to $0.199$	-0.100	-0.487 to $0.287$
Nonadherence at baseline	0.143	-0.085 to $0.371$	0.449**	0.161 to 0.737
Independent variable				
Bullied (baseline)	0.374***	0.158 to 0.589	0.009	-0.270 to $0.288$
Mediator				
Psychological distress (follow-up)	_	_	0.198***	0.113,0.283
	Model summary: $R = 0.210$ ; $R$ - $sq$ . = 0.044; $F = 5.553$ ; $P < 0.001$		Model summary: Nagelkrk = $0.067$ ; CoxSnell = $0.049$ ; $P < 0.001$	

<sup>\*\*\*</sup>P < 0.001; \*\* P < 0.01; \* P < 0.05.

<sup>\*10</sup> cases had a missing value for one or more variables and were excluded from the regression analyses.

**TABLE 3.** Results of Final PROCESS Model 23 Moderated Mediation Regressions, Respectively, Predicting Higher Psychological Distress and ART Nonadherence at Follow-up (n = 969)

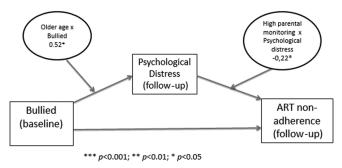
	Dependent Variable: Psychological Distress		Dependent Variable: ART Nonadherence	
	B (Unstandardized)	95% CIs	B (Unstandardized)	95% CIs
Sociodemographic and HIV-related covariates				
Age (older)	0.143	-0.217 to $0.503$	_	_
Female	-0.008	-0.345 to $0.329$	_	_
Rural location	-0.155	-0.398 to $0.088$	-0.307	-0.628 to $0.013$
Informal housing	-0.069	-0.344 to $0.206$	0.141	-0.208 to $0.491$
Horizontal infection	0.126	-0.187 to $0.439$	0.352	-0.011 to $0.714$
Time on treatment $> 1$ yr	-0.102	-0.408 to $0.204$	-0.065	-0.451 to $0.322$
Nonadherence at baseline	0.147	-0.081 to $0.374$	0.383**	0.095 to 0.672
Independent variable				
Bullied (baseline)	-0.017	-0.362 to $0.329$	0.005	-0.274 to $0.283$
Mediator				
Psychological distress (follow-up)	_	_	0.249***	0.142 to 0.356
Moderators				
Older age × bullied	0.517*	0.068 to 0.966		
Female × bullied	0.362	-0.073 to $0.797$	_	_
Better parental monitoring x psychological distress	_	_	-0.220*	-0.418 to $-0.023$
	Model summary: $R = 0.231$ ; $R$ - $sq = 0.531$ ; $F = 5.888$ ; $P < 0.001$		Model summary: Nagelkrk = $0.065$ ; CoxSnell = $0.047$ ; $P < 0.001$	

\*\*\*P < 0.001; \*\* P < 0.01; \*P < 0.05.

Table 4 below indicates whether the indirect relationship between being bullied at baseline and nonadherent at follow-up holds at different combinations of the 3 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 nonadherence 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 to 0.28) and for older females: effect = 0.22; 95% CI: (0.1 to 0.39)].

### DISCUSSION

Results of this analysis indicate that ALHIV who experience bullying victimization are at greater risk of nonadherence to HIV treatment 1 year later and that this relationship operates indirectly through psychological dis-



**FIGURE 1.** Results of the final moderated mediation analysis (PROCESS Model 23; n = 969).  $\frac{\text{full color}}{\text{on Line}}$ 

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tress. 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 nonadherence. 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) ALHIV.<sup>4</sup>

Evaluations of school-based antibullying interventions in high-income countries suggest that complex multicomponent 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.<sup>62,63</sup> 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.<sup>63</sup> Despite promising findings of recent school-based behavioral interventions focusing on teachers and peers,<sup>64,65</sup> to date evaluations of antibullying interventions in LMICs have been scarce and the evidence not overall conclusive.<sup>66</sup> 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 nonadherence 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

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Age (10–14 Vs 15–19)	Gender	Parental Monitoring	Effect	95% CIs	Bullying—Nonadherence Relationship Significant
Younger	Male	Low	-0.004	-0.080 to $0.070$	No
Younger	Male	High	-0.001	-0.037 to $0.023$	No
Younger	Female	Low	0.086	0.011 to 0.185	Yes
Younger	Female	High	0.010	-0.047 to $0.099$	No
Older	Male	Low	0.125	0.016 to 0.279	Yes
Older	Male	High	0.014	-0.063 to $0.143$	No
Older	Female	Low	0.215	0.095 to 0.385	Yes
Older	Female	High	0.025	-0.118 to $0.204$	No

**TABLE 4.** Conditional Indirect effect(s) of Bullying at Baseline on Nonadherence at Follow-up, at Different Values of the moderator(s)

settings<sup>22,39,67,68</sup> 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.<sup>69–71</sup> 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.<sup>62,63</sup>

Moreover, there is recent evidence of the acceptability and efficacy of certain family-based 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 distress. 75–77

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 nonadherence was chosen to minimize recall bias and tested against viral load indicators for the subsample for which clinic data were 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 nonadherence could affect psychological distress, or that the relationship between bullying victimization

and psychological distress could be bidirectional.<sup>13</sup> Testing for mediation would ideally require data at 3 time-points. We note the limitations and bias related to conducting mediation analysis with 2 waves of data, where the mediator variable (psychological distress), and the outcome variable (nonadherence) 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 data set; for example, we were not able to test peer support<sup>8</sup> or strong school performance.<sup>78</sup> 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 nonadherence 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.<sup>79</sup>

#### **REFERENCES**

- UNICEF. For Every Child, End AIDS: Seventh Stocktaking Report. New York, NY: UNICEF; 2016.
- UNICEF. Turning the Tide against AIDS Will Require More Concentrated Focus on Adolescents and Young People. 2018. Available at: https://data.unicef.org/topic/adolescents/hiv-aids/. Accessed August 5, 2018
- Adejumo O, Malee K, Ryscavage P, et al. Contemporary issues on the epidemiology and antiretroviral adherence of HIV-infected adolescents in sub-Saharan Africa: a narrative review. J Int AIDS Soc. 2015;18:20049.
- Slogrove AL, Sohn AH. The global epidemiology of adolescents living with HIV: time for more granular data to improve adolescent health outcomes. Curr Opin HIV AIDS. 2018;13:170–178.
- Kim MH, Mazenga AC, Yu X, et al. High self-reported non-adherence to antiretroviral therapy amongst adolescents living with HIV in Malawi: barriers and associated factors. *JIAS*. 2017;20:21437.
- Casale M, Carlqvist A, Cluver L. Recent interventions to improve retention in HIV care and adherence to antiretroviral treatment among adolescents and youth: A systematic review. AIDS Patient Care STDs. 2019;33.
- Richardson D, Fen Hiu C. Developing a Global Indicator on Bullying of School-Aged Children. Italy, Europe: UNICEF; 2018.

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- Biswas T, Scott J, Munir K, et al. Global variation in the prevalence of bullying victimisation amongst adolescents:Role of peer and parental supports. E Clin Med. 2020;20:100276.
- Takizawa R, Maughan B, Arseneault L. Adult health outcomes of childhood bullying victimization: evidence from a five-decade longitudinal British birth cohort. Am J Psychiat. 2014;17:777–784.
- Hansson E, Garmy P, Vilhjálmsson R, et al. Bullying, health complaints, and self-rated health among school-aged children and adolescents. J Int Med Res. 2020;48:0300060519895355.
- Richter M, Bowles D, Melzer W, et al. Bullying, psychosocial health and risk behaviour in adolescence. *Gesundheitswesen*. 2007;69:475–482.
- Arseneault L, Bowes L, Shakoor S. Bullying victimization in youths and mental health problems: much ado about nothing? *Psychol Med.* 2010; 40:717–729.
- Boyes M, Bowes L, Cluver L, et al. Bullying victimisation, internalising symptoms, and conduct problems in South African children and adolescents: a longitudinal investigation. *J Abnormal Child Psychol*. 2014;42:1313–1324.
- Moore S, Norman R, Suetani S, et al. Consequences of bullying victimization in childhood and adolescence: a systematic review and meta-analysis. World J Psychiatry. 2017;7:60–76.
- Human Sciences Research Council. The People Living with HIV Stigma Index: South Africa. Pretoria, South Africa: Human Sciences Research Council; 2014.
- Pantelic M, Boyes M, Cluver L, et al. HIV, violence, blame and shame: pathways of risk to internalized HIV stigma among South African adolescents living with HIV. J Int AIDS Soc. 2017;20:21771.
- Casale M, Boyes M, Pantelic M, Toska E, Cluver L. Suicidal thoughts and behaviour among South African adolescents living with HIV: can social support buffer the impact of stigma? *J Affective Disord*. 2019;245: 82–90
- Hoare J, Phillips N, Brittain K, et al. Mental health and functional competence in the Cape Town adolescent antiretroviral cohort. *J Acquir Immune Defic Syndr*. 2019;81:e109–e116.
- Buckley J, Otwombe K, Joyce C, et al. Mental health of adolescents in the era of antiretroviral therapy: is there a difference between HIVinfected and uninfected youth in South Africa? *J Adolesc Health*. 2020; S1054–139X(20)30037-9 [epub ahead of print].
- Mellins C, Malee K. Understanding the mental health of youth living with perinatal HIV infection: lessons learned and current challenges. *J Int* AIDS Soc. 2013;16:18593.
- Ashaba S, Cooper-Vince C, Maling S, et al. Internalized HIV stigma, bullying, major depressive disorder, and high-risk suicidality among HIVpositive adolescents in rural Uganda. Glob Ment Health. 2018;5:e22.
- Boyes M, Cluver L, Meinck F, Casale M, Newnham E. Mental health in South African adolescents living with HIV: correlates of internalising and externalising symptoms. AIDS Care. 2018;31:95–104.
- Dow DE, Turner EL, Shayo AM, et al. Evaluating mental health difficulties and associated outcomes among HIV-positive adolescents in Tanzania. AIDS Care. 2016;28:825–833.
- Mutumba M, Musiime V, Lepkwoski JM, et al. Examining the relationship between psychological distress and adherence to anti-retroviral therapy among Ugandan adolescents living with HIV. AIDS Care. 2016; 28:807–815.
- Smith Fawzi MC, Ng L, Kanyanganzi F, et al. Mental health and antiretroviral adherence among youth living with HIV in Rwanda. *Pediatrics*. 2016;138:e20153235.
- Sherr L, Cluver LD, Toska E, et al. Differing psychological vulnerabilities among behaviourally and perinatally HIV infected adolescents in South Africa implications for targeted health service provision. AIDS Care. 2018:1–10.
- Bronfenbrenner U. The Ecology of Human Development. Cambridge, MA: Harvard University Press; 1979.
- Bacchini D, Concetta Miranda M, Affuso G. Effects of parental monitoring and exposure to community violence on antisocial behavior and anxiety/depression among adolescents. *J Interpersonal Violence*. 2011;26:269–292.
- Nguyen H, Nakamura K, Seino K, et al. Impact of parent-adolescent bonding on school bullying and mental health in Vietnamese cultural setting: evidence from the global school-based health survey. BMC Psychol. 2019;7:16.

- Washington T, Rose T, Coard S, et al. Family-level factors, depression, and anxiety among african American children: a systematic review. *Child Youth Care Forum*. 2017;46:137–156.
- Paterson J, Tautolo E-S, Lusitini L, et al. Cultural, individual, and familial risk and protective factors associated with depressive symptoms in Pacific youth living in New Zealand. Soc Work Ment Health. 2018;16:728–745.
- 32. Jantzer V, Haffner J, Parzer P, et al. Does parental monitoring moderate the relationship between bullying and adolescent nonsuicidal self-injury and suicidal behavior? A community-based self-report study of adolescents in Germany. *BMC Public Health*. 2015;15:1–8.
- Vassallo S, Edwards B, Renda J, et al. Bullying in early adolescence and antisocial behavior and depression six years later: what are the protective factors?. J Sch Violence. 2014;13:100–124.
- Murphy C, Miller V. Concurrent and longitudinal associations among parenting style, responsibility, and adherence in youth with cystic fibrosis. *Children's Health Care*. 2020;49:153–167.
- Manne S, Jacobsen P, Gorfinkle K, et al. Treatment adherence difficulties among children with cancer: the role of parenting style. *J Pediatr Psychol.* 1993;18:47–62.
- Al-Kloub M, Abed M, Al khawaldeh O, et al. Predictors of nonadherence to follow-up visits and deferasirox chelation therapy among Jordanian adolescents with thalassemia major. *Pediatr Hematol Oncol.* 2014;31:624–637.
- Robinson E, Weaver P, Rusan C, et al. A model of parental distress and factors that mediate its link with parental monitoring of youth diabetes care, adherence, and glycemic control. *Health Psychol.* 2016;35: 1373–1382.
- Smith Fawzi M, Eustache E, Oswald C, et al. Psychosocial support intervention for HIV-affected families in Haiti: implications for programs and policies for orphans and vulnerable children. Soc Sci Med. 2012;74: 1494–1503.
- Sithole Z, Mbizvo E, Chonzi P, et al. Virological failure among adolescents on ART, Harare City, 2017- a case-control study. BMC Infect Dis. 2018;18:469.
- Wouters E, Van Dammeb W, Van Loona F, et al. Public-sector ART in the free state province, South Africa: community support as an important determinant of outcome. Soc Sci Med. 2009;69:1177–1185.
- Willis N, Napei T, Armstrong A, et al. Zvandiri—Bringing a differentiated service delivery program to scale for children, adolescents, and young people in Zimbabwe. *J Acquir Immune Def Synd*. 2018;78(2018 supplement):S115–S123.
- Vu L, Burnett-Zieman B, Banura C, et al. Increasing uptake of HIV, sexually transmitted infection, and family planning services, and reducing HIV-related risk behaviors among youth living with HIV in Uganda. J Adolesc Health. 2017;60:S22–S28.
- Kibaara C, Blat C, Lewis-Kulzer J, et al. Treatment Buddies Improve Clinic Attendance Among Women but Not Men on Antiretroviral Therapy in the Nyanza Region of Kenya. AIDS Res Treat. 2016:1–9; Article ID 9124541.
- Kunutsor S, Walley J, Katabira E, et al. Clinic Attendance for Medication Refills and Medication Adherence Amongst an Antiretroviral Treatment Cohort in Uganda: A Prospective Study. AIDS ResTreat. 2010; Article ID 872396.
- Nachega J, Chaisson RE, Goliath R, et al. Randomized controlled trial of trained patient-nominated treatment supporters providing partial directly observed antiretroviral therapy. AIDS. 2010;24:1273–1280.
- 46. Finning K, Ukoumunne O, Ford T, et al. The association between child and adolescent depression and poor attendance at school: a systematic review and meta-analysis. *J Affect Disord*. 2019;245:928–938.
- Hjorth C, Bilgrav L, Frandsen L, et al. Mental health and school dropout across educational levels and genders: a 4.8-year follow-up study. BMC Public Health. 2016;16:1–12.
- Maalouf F, Ghandour L, Halabi F, et al. Psychiatric disorders among adolescents from Lebanon: prevalence, correlates, and treatment gap. Soc Psychiat Psychiatr Epidemiol. 2016;51:1105–1116.
- Duong M, Piroth L, Grappin M, et al. Evaluation of the Patient Medication Adherence Questionnaire as a tool for self-reported adherence assessment in HIV-infected patients on antiretroviral regimens. HIV Clin trials. 2001;2:128–135.
- Lowenthal ED, Jibril HB, Sechele ML, et al. Disclosure of HIV status to HIV-infected children in a large African treatment center: lessons learned in Botswana. *Child youth Serv Rev.* 2014;45:143–149.

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- Ruchkin V, Schwab-Stone M, Vermeiren R. Social and Health Assessment (SAHA). Psychometric Development Summary; 2004. Available at: https://www.scienceopen.com/document?vid=25ea2912-527c-41fc-bfc2-a5d2558694cc. Accessed November 5, 2013.
- Ward CL, Martin E, Theron C, et al. Factors affecting resilience in children exposed to violence. South Afr J Psychol. 2007;37:165–187.
- Kovacs M. Childrens' Depression Inventory. Niagara Falls, NY: Multi-Health Systems; 1992.
- Reynolds CR, Richmond BO. What I think and feel: a revised measure of children's manifest anxiety. J Abnormal Child Psychol. 1978;6:271–280.
- Boyes M, Cluver L. Performance of the Revised Children's Manifest Anxiety Scale in a Sample of Children and Adolescents from Poor Urban Communities in Cape Town European Journal of Psychological Assessment. Eur J Psychol Assess. 2012;29:113–120.
- Elgar FJ, Waschbusch DA, Dadds MR, et al. Development and validation of a short form of the Alabama Parenting Questionnaire. *J Child Fam Stud.* 2007;16:243–259.
- Cluver L, Pantelic M, Orkin M, et al. Sustainable survival for adolescents living with HIV: do SDG-aligned provisions reduce potential mortality risk? *J Int AIDS Soc.* 2018;21(suppl 1):e25056.
- Hayes A. Beyond Baron and Kenny: statistical mediation analysis in the new millennium. *Commun Monogr.* 2009;76:408–420.
- Preacher K, Hayes A. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behav Res Methods*. 2008;40:879–891.
- Dawson JF, Richter AW. Probing three-way interactions in moderated multiple regression: development and application of a slope difference test. *J Appl Psychol.* 2006;91:917–926.
- Andersson U, Cuervo-Cazurra A, Nielsen BB. From the Editors: explaining interaction effects within and across levels of analysis. *J Int Business Stud.* 2014;45:1063–1071.
- Vreeman R, Carroll A. A systematic review of school-based interventions to prevent bullying. Arch Pediatr Adolesc Med. 2007;161:78–88.
- Silva J, Oliveira W, Mello F, et al. Anti-bullying interventions in schools: a systematic literature review. Ciencia Saude Coletiva. 2017;22:2329–2340.
- 64. Devries K, Knight L, Child J, et al. The Good School Toolkit for reducing physical violence from school staff to primary school students: a cluster-randomised controlled trial in Uganda. *Lancet Glob Health*. 2015;385:e378–386.
- Arënliu A, Strohmeier D, Konjufca J, et al. Empowering the peer group to prevent school bullying in Kosovo: effectiveness of a short and ultrashort version of the ViSC social competence program. *Int J Bullying Prev.* 2020;2:65–78.
- Sivaramana B, Nyea E, Bowes L. School-based anti-bullying interventions for adolescents in low- and middle-income countries: a systematic review. Aggression Violent Behav. 2019;45:154–162.

- Bowes L, Maughan B, Caspi A, et al. Families promote emotional and behavioural resilience to bullying: evidence of an environmental effect. J Child Psychol Psychiat. 2010;51:809–817.
- Mellins C, Brackis-Cott E, Dolezal C, et al. The role of psychosocial and family factors in adherence to antiretroviral treatment in human immunodeficiency virus-infected children. *Pediatr Infect Dis J.* 2004;23:1035–1041.
- 69. Cluver L, Meinck F, Steinert J, et al. Parenting for Lifelong Health: a pragmatic cluster randomised controlled trial of a non-commercialised parenting programme for adolescents and their families in South Africa. BMJ Glob Health. 2018;3:e000539.
- Kuo C, Mathews C, Giovenco D, et al. Acceptability, feasibility, and preliminary efficacy of a resilience-oriented family intervention to prevent adolescent HIV and depression: a pilot randomized controlled trial. AIDS Edu Prev. 2020;32:67–81.
- Annan J, Kazembe P, Bundervoet T, et al. A Randomized Impact Evaluation of Village Savings and Loans Associations and Family-Based Interventions in Burundi. Final Evaluation. March 2013. New York, NY: International Rescue Committee; 2013.
- Barry M, Clarke A, Jenkins R, et al. A systematic review of the effectiveness of mental health promotion interventions for young people in low and middle income countries. BMC Public Health. 2013;11:835.
- Davaasambuu S, Hauwadhanasuk T, Matsuo H, et al. Effects of interventions to reduce adolescent depression in low- and middleincome countries: a systematic review and meta-analysis. *J Psychiatr Res.* 2020:123:201–215.
- Rose-Clarke K, Bentley A, Marston C, et al. Peer-facilitated communitybased interventions for adolescent health in low- and middle-income countries: a systematic review. *PLoS One*. 2019;14:e0210468.
- World Health Organization. Global Accelerated Action for the Health of Adolescents (AA-HA!). 2017. Available at: http://apps.who.int/iris/ bitstream/handle/10665/255415/9789241512343eng.pdf; jsessionid=B2626A5AB85675D96B840C78270E4955?sequence=1. Accessed July 4, 2020.
- 76. Akol A, Makumbi F, Babirye J, et al. Does mhGAP training of primary health care providers improve the identification of child-and adolescent mental, neurological or substance use disorders? Results from a randomized controlled trial in Uganda. Glob Ment Health. 2018;5:e29.
- Gaitho D, Kumar M, Wamalwa D, et al. Understanding mental health difficulties and associated psychosocial outcomes in adolescents in the HIV clinic at Kenyatta National Hospital, Kenya. *Ann Gen Psychiatry*. 2018;17:29.
- Ttofi M, Bowes L, Farrington D, et al. Protective factors interrupting the continuity from school bullying to later internalizing and externalizing problems: a systematic review of prospective longitudinal studies. *J Sch Violence*. 2014;3:5–38.
- United Nations. Transforming Our World: The 2030 Agenda for Sustainable Development. 2015.