



Research Paper

Childhood trauma, major depressive disorder, suicidality, and the modifying role of social support among adolescents living with HIV in rural Uganda



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ABSTRACT

Background: Childhood trauma is associated with mental health problems among adolescents living with HIV (ALHIV) in sub-Saharan Africa, but little is known about potential moderating factors.

Methods: We enrolled 224 ALHIV aged 13–17 years and collected information on childhood trauma, major depressive disorder, and suicidality. We used modified multivariable Poisson regression to estimate the association between the mental health outcome variables and childhood trauma, and to assess for effect modification by social support.

Results: Major depressive disorder had a statistically significant association with emotional abuse (adjusted relative risk [ARR] 2.57; 95% CI 1.31–5.04; $P = 0.006$) and physical abuse (ARR 2.16; 95% CI 1.19–3.89; $P = 0.01$). The estimated association between any abuse and major depressive disorder was statistically significant among those with a low level of social support (ARR 4.30; 95% CI 1.64–11.25; $P = 0.003$) but not among those with a high level of social support (ARR 1.30; 95% CI 0.57–2.98; $P = 0.52$). Suicidality also had a statistically significant association with emotional abuse (ARR 2.03; 95% CI 1.05–3.920; $P = 0.03$) and physical abuse (ARR 3.17; 95% CI 1.60–6.25.; $P = 0.001$), but no differences by social support were noted.

Limitations: Corporal punishment is used widely in schools and homes as a form of discipline in Uganda; this cultural practice could have biased reporting about physical abuse.

Conclusions: Childhood trauma is associated with poor mental health among ALHIV, but its effects may be moderated by social support. More research is needed to develop social support interventions for ALHIV with adverse childhood experiences for improved mental health outcomes.

1. Introduction

In 2016, there were 2.1 million adolescents living with HIV (ALHIV) worldwide, 73,000 of whom were living in Uganda constituting 4% of the worldwide population of ALHIV (Slogrove et al., 2017; UNAIDS, 2018). Additionally, there were 1.4 million people living with HIV in Uganda in 2016, and 160,000 of these were young people aged 15–24 years (UNAIDS, 2018). Although availability of antiretroviral

therapy (ART) has enabled children perinatally infected with HIV to grow into adolescence and young adulthood (Brady et al., 2010), ALHIV in sub-Saharan Africa face myriad HIV-related challenges including orphanhood, HIV stigma, and discrimination that affect their ability to engage in care, which in turn affects their physical and mental health outcomes (Ashaba et al., 2018, 2019a, 2019b; Kahana et al., 2015; Mellins and Malee, 2013; Tsai et al., 2010a). These HIV related challenges are often complicated by structural challenges of poverty, food and water insecurity, and violence, which are common in many regions of sub-Saharan Africa, including Uganda (Dewing et al., 2013; Kang et al., 2011; Lund et al., 2010; Mushavi et al., 2020; Tsai et al., 2012, 2016c, 2010b). Violence against children is also common in this

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setting (Hillis et al., 2016). Estimates from the World Health Organization show that over 40 million children aged 15 years and below experience various forms of violence each year, and that the affected children suffer various forms of trauma depending on the severity of the violence (World Health Organization, 2001). Children in sub-Saharan Africa are frequently exposed to adversities including family violence, orphanhood, child labor, and physical punishment, all of which can affect their mental health (Brown et al., 2009; Hillis et al., 2016; Kumar et al., 2017; Lansford et al., 2014; Naker, 2005; Norman et al., 2012).

The risk of exposure to violence increases in adolescence due to increased and increasingly independent interaction with peers (Ward et al., 2018), particularly in environments characterized by widespread poverty (Foster and Brooks-Gunn, 2009). The prevalence of adverse childhood experiences is reportedly higher among adults and children living with HIV compared with people in the general population primarily in sub-Saharan Africa (Abubakar et al., 2017; Bekele et al., 2018; Brezing et al., 2015; Cluver et al., 2012; Lowenthal et al., 2014; Nyamukapa et al., 2010; Yakubovich et al., 2016). The increased risk of adversities among children from HIV-affected families is generally attributed to stress among parents/caregivers with HIV and associated lack of adequate supervision (Cluver et al., 2013). In addition, HIV is associated with other factors that increase the risk of child abuse including intimate partner violence, substance abuse, depression, and HIV stigma (Boyes and Cluver, 2013; Jewkes et al., 2010b; Nakimuli-Mpungu et al., 2011). Moreover, children orphaned by HIV who live in child-headed households or who live with relatives are often maltreated and exploited (Morantz et al., 2013). Common forms of abuse among ALHIV include both physical and emotional abuse, with the majority of affected ALHIV reporting experiencing multiple forms of abuse (Kidman et al., 2018; Radcliffe et al., 2007).

Childhood trauma has been associated with multiple mental health problems (Kidman et al., 2018). Studies among ALHIV with a history of child abuse have shown high rates of depression, suicidality, anxiety, low self-esteem, and post-traumatic stress disorder (Jewkes et al., 2010a; Lewis et al., 2015; Martinez et al., 2009). ALHIV also experience HIV stigma, discrimination, and lack of support, all of which are also associated with abuse (Ashaba et al., 2018; Onuoha et al., 2009), leading to further worsening of mental health outcomes (Ashaba et al., 2018, 2019a, 2019b; Cluver et al., 2010; Meinck et al., 2015). Although population-based studies are lacking, the prevalence of depression among ALHIV generally exceeds that among HIV-unaffected controls by a factor of two to three (Bankole et al., 2017; Ng et al., 2015). Depression in particular has been associated with reduced treatment adherence, poorer HIV-related outcomes, and increased mortality (Burack et al., 1993; Kacanek et al., 2010; Lyketos et al., 1993). Conversely, treatment of depression in combination with adherence counseling has been linked to reduced depression symptom severity, improved treatment adherence, and increased viral suppression (Pence et al., 2015; Safren et al., 2016; Tsai et al., 2013a, 2010b).

Among ALHIV, social support has been reported to be protective against the effects of trauma, including depression and suicidal ideation (Casale et al., 2019, 2015a, 2015b; Newman et al., 2007; Peirce et al., 2000). The protective nature of social support against adverse mental health problems is attributed to the fact that social support acts as a buffer against stressful events (Cheng et al., 2014; Hussong, 2000; Newman et al., 2007) and enables people to cope positively with stressful situations or life circumstances (Humphreys et al., 1999; Thoits, 2011). The relationship between childhood trauma and depression among ALHIV has not been explored in rural Uganda, and few studies have explored the potential for modifiable moderating influences in sub-Saharan Africa (Casale et al., 2015b). To address this gap in the literature, this analysis aimed to estimate the association between childhood trauma, major depressive disorder, and suicidality and to investigate the potential modifying role of social support among ALHIV in rural Uganda.

2. Methods

2.1. Study setting and participants

Study participants were enrolled from the HIV clinic attached to the Mbarara Regional Referral Hospital and Mbarara University of Science and Technology within Mbarara Town. The town is approximately 270 km from Kampala, the capital of Uganda, and has a population of 195,013 (Uganda Bureau of Statistics, 2014). Most of the adolescents attending the adolescent HIV clinic live in rural areas outside of Mbarara Town, where many families earn a living through subsistence agriculture, animal husbandry, and local trading, and where challenges of food and water insecurity are common (Mushavi et al., 2020; Tsai et al., 2011, 2016a). The prevalence of HIV in southwestern Uganda is slightly elevated at 7.7% compared with the national prevalence of 6.2% (Ministry of Health of Uganda, 2019). Among adolescents and young adults, the prevalence of HIV is estimated at 1.1% among those aged 15–19 years and 3.3% among those aged 20–24 years (Uganda AIDS Commission, 2018). The adolescent HIV care clinic within Mbarara Hospital is closely linked to the pediatric HIV care clinic caring for the 0–9 year olds and the young people's HIV care clinic caring for the 20–25-year-olds. The clinic provides care following the National HIV Prevention and Care and Treatment guidelines (Ministry of Health of Uganda, 2020), which were adopted from the WHO guidelines/recommendations for management of adolescents living with HIV. Our total sample included 224 ALHIV aged 13–17 years who we enrolled consecutively. We excluded adolescents who could not complete the interview due to physical ailments and those whose HIV status had not been fully disclosed to them despite being on ART. After screening by a certified Ugandan psychiatrist, adolescents who exhibited cognitive impairments that would impact their ability to comprehend the consent form and contents of the questionnaire were also excluded.

3. Sample size

The study was powered on the basis of estimating the proportion of ALHIV with comorbid major depressive disorder. Using the 17.8% prevalence rate estimated in a previous study of children and ALHIV in Kenya (Kamau et al., 2012), and assuming a two-sided confidence interval width of 10%, we estimated a required sample size of 244 ALHIV (Fleiss et al., 2013; Newcombe, 1998).

3.1. Study measures

All measures were combined into a single questionnaire that was translated into the local language (Runyankore). The questionnaire included questions on self-reported sociodemographic characteristics including age, sex, level of schooling, duration on ART, caregiver/family structure (living with both parents, one parent, grandparents, or siblings), whether the participant was bereaved by the loss of one or both parents, and whether the participant attended a day or boarding school. Additionally, the questionnaire included the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID, version 6) (Sheehan et al., 1998a), the Childhood Trauma Questionnaire (CTQ) (Bernstein and Fink, 1998b), the Social Support Questionnaire-Short Form (SSQ6) (Sarason et al., 1987), the Internalized AIDS-Related Stigma Scale (IARSS) (Kalichman et al., 2009), and the Social and Health Assessment Peer Victimization Scale (Ruchkin et al., 2004).

The MINI-KID is a short, structured diagnostic interview that is used to obtain valid diagnoses of mental disorders in children and adolescents that are consistent with the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) and the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (Sheehan et al., 1998b, 2010). The MINI-KID module on depression consists of two screening questions, seven additional questions

related to depression symptoms, and one question related to functional impairment, all with a recall window of the past month. Similarly, the suicidality module elicits information about suicidal ideation, planning, and attempts over the past month. We applied the recommended algorithm to the MINI-KID suicidality scores and categorized study participants as being at low, moderate, or high risk for suicide. Those who scored 17 and above were classified as high risk suicidality. The MINI-KID has been adapted for use in the Ugandan context (Idro et al., 2016; Kinyanda et al., 2013; Nalugya-Sserunjogi et al., 2016; Okello et al., 2007). The MINI-KID modules (major depressive disorder and suicidality) were administered by a psychiatric clinical officer with diploma level training in diagnosing and managing psychiatric disorders.

The CTQ is a self-report screening tool that measures abuse and neglect. It is comprised of 28 items and 6 subscales. Five of these subscales, each containing 5 items, measure 5 types of maltreatment: emotional, physical, and sexual abuse; and emotional and physical neglect. Items 10, 16, and 22 comprise the denial subscale. Each item is measured on a five-point Likert scale ranging from "Never true" to "Very often true" (Bernstein et al., 2003). A score of one or greater on the denial subscale suggests underreporting (Bernstein and Fink, 1998b). CTQ items are elicited in the context of "when I was growing up" and do not distinguish between past and current experiences of abuse. Sample items include: "When I was growing up I got hit so hard by someone in my family that I had to see a doctor or go to the hospital"; and, "When I was growing up, people in my family said hurtful or insulting things to me." The cutoff scores used in this study for presence (vs. absence) of abuse were identical to those established during the scale development studies (Bernstein and Fink, 1998a, 1998b). The cutoff scores are: sexual abuse, ≥6; physical abuse, ≥8; emotional abuse, ≥9; physical neglect, ≥8; and emotional neglect, ≥10. For the purposes of this analysis, we dichotomized the subscale scores at the indicated cutoffs so that participants who scored above the cutoff were classified as having experienced abuse or neglect while those who scored below the cutoff were classified as having not experienced abuse or neglect. The CTQ scale has been used in South Africa with good reliability (Cronbach's alpha=0.74) (Meinck et al., 2016) and has been validated for use among adults and adolescents in other regions of sub-Saharan Africa (Charak et al., 2017; Kounou et al., 2013). In our sample, the CTQ had a Cronbach's alpha of 0.86.

We measured social support using the SSQ6 (Sarason et al., 1987), a 6-item questionnaire in which participants are asked to list all the people that they can rely on for support when in need. Each item is a question that solicits a two-part answer where part 1 asks participants to list all the people that fit the description of the question, and part 2 asks participants to indicate how satisfied they are with the people listed. Some of the questions in the SSQ6 include "Whom can you really count on to be dependable when you need help?" "Whom can you really count on to care about you, regardless of what is happening to you?" The SSQ6 has high internal reliability and correlates highly with the original SSQ (Sarason et al., 1987). The SSQ6 Number Score is obtained by adding the total number of people identified in each of the items, with a maximum of 9 people per item (score range 0–54). The SSQ6 has been used among people with HIV with good reliability (Cronbach's alpha range between 0.67 and 0.89) (Hart and Heimberg, 2005; Prado et al., 2004; Robbins et al., 2003; Wallace et al., 2019). It has also been used in southwestern Uganda among women of reproductive age (Lubinga et al., 2013).

We measured HIV stigma using the IARSS. The IARSS scale is a six-item scale that was developed for use among a sample of people living with HIV from the United States, South Africa and Swaziland (Kalichman et al., 2009). It is one of the most widely used HIV stigma scales (Pantelic et al., 2015), and it has been validated for use in the Ugandan context (Tsai et al., 2013b). The 6 items in the IARSS focus on self-blame and concealment of HIV status, and each item has two response options (agree/disagree). The total scale score is computed as the sum of the items. Higher scores indicate greater internalized stigma.

We defined high internalized stigma as having a total score greater than or equal to the 75th percentile (≥ 4).

We measured bullying victimization using the nine-item Social and Health Assessment Peer Victimization Scale, which elicits experiences of bullying in the past year (Ruchkin et al., 2004). The items are scored on a four-point Likert-type scale (Never, Once, 2–3 times, ≥ 4 times). Bullying is defined as having 2 or more bullying events in the past year. The scale was adapted from the Multidimensional Peer Victimization Scale in a study conducted among adolescents in the United Kingdom (Mynard and Joseph, 2000) which showed excellent reliability (Cronbach's alpha = 0.82). Subsequent studies conducted among black South African children and adolescents also showed good reliability (Cronbach's alpha = 0.81) (Boyes and Cluver, 2015; Cluver et al., 2010). In this study, the scale also showed good reliability with a Cronbach's alpha of 0.81.

3.2. Ethical considerations

Participants provided consent prior to enrolling in the study. Adolescents below the age of consent provided assent, after their parent/guardian provided written informed consent. Emancipated minors (i.e., those below 18 years but living independently), and "empowered" adolescents (i.e., those who were responsible for their HIV care per report of their HIV care provider) (Uganda National Council for Science and Technology, 2007), provided written informed consent without involvement of their parent/guardian. Participants were given consent forms to read under the guidance of the research assistants and asked clarification questions where information was not clear. The study was approved by the Research Ethics Committee of the Mbarara University of Science and Technology (# 11/04–14) and the Massachusetts General Hospital/Partners Human Research Committee (2016P000482/MGH). The study was also cleared by Uganda National Council for Science and Technology (SS4023) and by the Research Secretariat in the Office of the President in line with Ugandan national guidelines for research. Participants were given 10,000 Ugandan shillings (≈ 3 USD at the time of data collection) for transport reimbursement. Participants who developed acute distress during the interview and/or those who were at a high risk of suicide, as determined by the assessing psychiatric clinical officer, were referred to the psychiatric ward in the hospital to receive appropriate care.

3.3. Data analysis

We used modified multivariable Poisson regression (Zou, 2004) to estimate the association between the mental health outcome variables, childhood trauma, and social support, after adjusting for other potentially confounding variables: sociodemographic characteristics (age, sex, being an orphan, boarding school or day school, serostatus of the caregiver), bullying, and internalized HIV stigma. As described by Zou (2004), the exponentiated regression coefficients can be straightforwardly interpreted as relative risk ratios. In these regression models, we first included physical, sexual, and emotional abuse separately (adjusting for the covariates described above) and then included physical, sexual, and emotional abuse together in a single regression model (adjusting for the covariates described above). The overwhelming majority of our study participants reported both physical and emotional neglect; these variables were dropped from the regression models due to multicollinearity. We fitted separate regression models for major depressive disorder and any suicidality, or 8 regression models total.

To determine the robustness of the estimated associations, we performed an E-value analysis using methods proposed by VanderWeele and Ding (2017). The E-value describes the minimum strength of association on the risk ratio scale (between a putative confounder and the exposure, and between the putative confounder and the outcome) that would be needed to explain away the observed association between the exposure and the outcome. A large E-value would

Table 1
Characteristics of the sample ($N = 224$).

	Mean /%	SD	Freq.
Age (years)	14.87	1.42	
Duration on ART (years)	8.43	4.37	
<u>Sex</u>			
Female	58		131
Male	42		93
<u>Type of school</u>			
Day	67		150
Boarding	33		74
<u>Orphan</u>			
Yes	22		49
No	78		175
<u>Education level</u>			
Some primary	17		38
Completed primary	52		117
More than primary	31		69
<u>Caregiver</u>			
Both Parents	27		60
Mother	35		79
Father	10		22
Other (sibling, relative)	13		28
Grandparent	16		35
<u>Caregiver HIV status</u>			
Negative	13		28
Positive	65		145
Unknown	23		51
<u>Bullying (2 or more bullying events/year)</u>			
Yes	43		97
No	57		127
<u>High level internalized HIV stigma (score≥4)</u>			
Yes	41		91
No	59		133
<u>Major Depressive Disorder</u>			
Yes	17		37
No	83		187
<u>Suicidality (any)</u>			
Low risk suicidality	4		9
Moderate risk suicidality	6		13
High risk suicidality	4		9
<u>Childhood trauma</u>			
Physical abuse	16		36
Emotional abuse	22		49
Sexual abuse	14		32
Emotional neglect	216		96
Physical neglect	215		96
<u>Social support</u>			
High level social support (SSQ6 Number Score > median)	42		94
Low level social support (SSQ6 Number Score ≤ median)	58		130

suggest that potential confounding would need to be very strong in order to serve as a sufficient explanation for the observed associations (Blum et al., 2020).

We also sought to determine whether social support modified the association between childhood trauma and the mental health outcomes. This investigation was motivated by previously published conceptual and empirical work from sub-Saharan Africa showing that social support modifies the association between mental health and adversities (food insecurity) among adults (Tsai et al., 2012, 2016b). For these analyses, we created a single trauma exposure variable representing any exposure to physical abuse, emotional abuse, or sexual abuse. We dichotomized the SSQ6 Number Score at the median. Effect modification was assessed by including a main effect for high social support (SSQ6 Number Score greater than median), a main effect for exposure to any abuse, and a product term to test for the interaction between any abuse and high social support. These multivariable regression models also adjusted for the covariates listed above. We fitted separate regression models for major depressive disorder and any suicidality, or 2 regression models total. Stratified estimates (high vs. low social support) were also examined to

aid in exposition of the product terms. All analyses were conducted in Stata version 13 (StataCorp LP, College Station, Texas).

4. Results

We interviewed 224 ALHIV, the majority of whom (131[59%]) were girls. The mean age was 14.8 years (standard deviation [SD] 1.4). Thirty-seven participants (17%) had major depressive disorder and 31 (14%) had suicidality (low, moderate and high risk), of whom 9 (4%) were classified as having a high-risk suicidality on the MINI-KID. Forty-nine participants (22%) reported emotional abuse, 36 (16%) reported physical abuse, 32 (14%) reported sexual abuse, 216 (96%) reported emotional neglect, and 215 (96%) reported physical neglect (Table 1).

We estimated statistically significant associations between major depressive disorder and both emotional abuse (adjusted relative risk [ARR] 2.57; 95% CI 1.31–5.04; $P = 0.006$) and physical abuse (ARR 2.16; 95% CI 1.19–3.89; $P = 0.01$) (Table 2). When the different types of abuse were mutually adjusted for each other, emotional abuse was the most important correlate of major depressive disorder (ARR 2.08; 95% CI

Table 2

Associations between childhood trauma and major depressive disorder, by type of abuse.

Childhood trauma, by type	Separately, adjusted for covariates*		Mutually adjusted for each other†	
	Adjusted risk ratio (95% CI)	P-value	Adjusted risk ratio (95% CI)	P-value
Physical abuse	2.16 (1.19–3.89)	0.01	1.37 (0.71–2.67)	0.34
Sexual abuse	1.58 (0.90–2.79)	0.17	1.17 (0.62–2.22)	0.63
Emotional abuse	2.57 (1.31–5.04)	0.006	2.08 (0.99–4.39)	0.05

* Each cell represents the output of a single multivariable Poisson regression model fitted to the data, specifying major depressive disorder as the dependent variable and the row header as the primary explanatory variable of interest, adjusting for age, orphanhood, type of school (boarding versus day), bullying, HIV stigma, and social support.

† The column represents the output of a single multivariable Poisson regression model fitted to the data, specifying major depressive disorder as the dependent variable and the three types of childhood trauma as explanatory variables, mutually adjusted for each other and for the other covariates listed above.

Table 3

Associations between childhood trauma and suicidality, by type of abuse.

Childhood trauma, by type	Separately, adjusted for covariates*		Mutually adjusted for each other†	
	Adjusted risk ratio (95% CI)	P-value	Adjusted risk ratio (95% CI)	P-value
Physical abuse	3.17 (1.60–6.25)	0.001	3.13 (1.45–6.76)	0.004
Sexual abuse	1.00 (0.40–2.46)	0.99	0.62 (0.24–1.58)	0.32
Emotional abuse	2.03 (1.05–3.92)	0.03	1.27 (0.57–2.72)	0.52

* Each cell represents the output of a single multivariable Poisson regression model fitted to the data, specifying any suicidality as the dependent variable and the row header as the primary explanatory variable of interest, adjusting for age, orphanhood, type of school (boarding versus day), bullying, HIV stigma, and social support.

† The column represents the output of a single multivariable Poisson regression model fitted to the data, specifying any suicidality as the dependent variable and the three types of childhood trauma as explanatory variables, mutually adjusted for each other and for the other covariates listed above.

0.99–4.39; $P = 0.052$) although the association was not statistically significant. There was also a statistically significant association between suicidality and physical abuse (ARR 3.17; 95% CI 1.60–6.25; $P = 0.001$) and emotional abuse (ARR 2.03; 95% CI 1.05–3.92; $P = 0.03$) (Table 3). When the different types of abuse were mutually adjusted for each other, physical abuse was the most important correlate of any suicidality (ARR 3.13; 95% CI 1.45–6.76; $P = 0.004$) (Table 3).

The E-value analyses suggested that the estimated associations were robust to potential confounding by unmeasured variables. For the estimated association between emotional abuse and major depressive disorder (RR 2.57), the E-value was 4.58. For the estimated association between physical abuse and suicidality, the E-value was 5.79. Thus, an unmeasured confounder would need to have a strength of association, on the risk ratio scale, with both abuse and mental health, between 5 and 6 in order to explain away the reported estimates.

When a main effect for social support was included in the regression model for major depressive disorder, along with product terms to test for an interaction between social support and any abuse, social support moderated the effect of any abuse on major depressive disorder, but the coefficient on the product term was not statistically significant ($P = 0.076$ for interaction). Among study participants with a low level of social support, the estimated association between any abuse and major depressive disorder was statistically significant (ARR 4.30; 95% CI 1.64–11.25; $P = 0.003$). Among study participants with a high level of social support, the estimated association between any abuse and major depressive disorder was not statistically significant (ARR 1.30; 95% CI 0.57–2.98; $P = 0.52$). The estimated association between any abuse and suicidality did not appear to be modified by social support ($P = 0.87$ for interaction).

5. Discussion

In this clinic-based study of 224 ALHIV in rural Uganda, we show that major depressive disorder and suicidality were associated with dif-

ferent aspects of childhood trauma. The estimated associations were statistically significant, large in magnitude and clinically significant, and robust to potential confounding. These findings add to existing literature showing an association between childhood trauma and various mental health problems among youth living with HIV in sub-Saharan Africa (Gardner et al., 2019; Jewkes et al., 2010a; Kidman et al., 2018; Woollett et al., 2017).

The association between emotional abuse and major depressive disorder estimated in our study is similar to what has been documented in studies in Nigeria and the U.S. (Adeyemo et al., 2020; Murphy et al., 2000). Emotional abuse often leads to low self-esteem, feelings of worthlessness, and inability to cope with stress, which may cause depressive disorder (Murphy et al., 2000). We also estimated a statistically significant association between suicidality and physical abuse, which echoes findings of a previously conducted study in South Africa (Jewkes et al., 2010a). The high suicide risk associated with physical abuse among AL-HIV may similarly result from feelings of worthlessness and hopelessness that are further compounded by HIV stigma and discrimination experiences (Kelly et al., 1998).

Our findings highlight a need to develop interventions aimed at protecting children and adolescents affected and infected with HIV against trauma so that associated poor mental health outcomes can be prevented (Cluver et al., 2018; Jewkes et al., 2010a; Nakimuli-Mpungu et al., 2014). The need to address childhood trauma is paramount since existing literature shows that exposure to violence is a major risk for mental health problems among children and adolescents in sub-Saharan Africa (Skeen et al., 2016; Woollett et al., 2017) and that adolescents are at greater risk of exposure to violence than adults and young children (Devries, 2016; Kang et al., 2011; Norman et al., 2012). Moreover, AL-HIV are at greater risk of violence and trauma compared with adolescents in the general population (Abubakar et al., 2017; Brezing et al., 2015; Lowenthal et al., 2014; Yakubovich et al., 2016) due to lack of supervision by parents/caregivers who may be struggling to manage their own HIV-related stressors (Cluver et al., 2013). Furthermore, HIV is of

ten syndemic (Tsai et al., 2017) with other factors that increase the risk of childhood trauma, including intimate partner violence, depression and HIV stigma (Boyes and Cluver, 2013; Jewkes et al., 2010a). Many ALHIV come from HIV-affected families, where their living environments are characterized by social discrimination and lack of support with heightened risk of abuse (Cluver et al., 2011; Onuoha et al., 2009), while many others are orphans, further increasing their risk of exposure to violence through bullying by peers (Cluver et al., 2010, 2012).

Other findings from our study indicated that social support had a potentially moderating effect on the effect of any abuse (emotional, physical, or sexual) on major depressive disorder. While any abuse had a strong association with major depressive disorder among ALHIV who had low levels of social support, the estimated association was not statistically significant among ALHIV who had high levels of social support. However, the estimated coefficient on the product term was not statistically significant. This potentially moderating effect of social support is in line with previous research indicating the role of social support on mental health outcomes among adolescents in the context of HIV (Petersen et al., 2010; Skeen et al., 2016). Social support has been documented to be protective against adverse mental health outcomes, with reports indicating that perceived support from peers and caring adults has positive effects on the mental wellbeing of adolescents despite exposure to stressful life events (Casale et al., 2015b; Cheng et al., 2014). Social support has also been documented to be protective against depression among adolescents and adults living with HIV (Ashaba et al., 2018; Matsumoto et al., 2017; Nanni et al., 2015). This is further reinforced by reports indicating that peer support groups within HIV clinics in Zimbabwe were associated with improved mental health outcomes among ALHIV (Mupambireyi et al., 2014).

5.1. Limitations

Our findings should be interpreted bearing in mind certain limitations. First the study was conducted among ALHIV attending a single HIV clinic in southwestern Uganda, which may limit generalizability of our findings only to ALHIV elsewhere in Uganda and sub-Saharan Africa. Second, our sample consisted of adolescents in a limited age range (13–17 years), which would have limited our ability to assess trauma experiences among older adolescents in this setting. Third, corporal punishment is used widely in schools and homes as a form of discipline in Uganda (Boydell et al., 2017; Devries et al., 2015; Kaltenbach et al., 2018). This cultural practice could have biased reporting about physical abuse, but the direction of bias is unpredictable: some participants could have perceived corporal punishment as an acceptable practice, which would have caused us to estimate lower rates of physical abuse; but other participants who do not believe it to be acceptable may have had corporal punishment in mind when reporting physical abuse, which would have caused us to estimate higher rates of physical abuse. Fourth, the study was cross sectional in nature. We could not estimate the causal effect of childhood abuse on mental health.

A final limitation is that confounding by unmeasured covariates could have biased our estimates. An example of a potentially important unmeasured variable is parental incarceration, which could be associated with both childhood trauma and child mental health. Such confounding could induce a spurious correlation between childhood trauma and child mental health. However, our E-value analysis indicates that only strong confounding by parental incarceration could explain away our findings. Using data from the U.S. Fragile Families and Child Wellbeing Study, Turney (2014) showed that, among children of parents who lived together prior to confinement, paternal incarceration was associated with increased maternal use of harsh parenting and physical aggression, but the estimated effect size was small in magnitude. There is also robust evidence to suggest that parental incarceration is associated with poor mental health among children, with odds ratios ranging from 1.2–1.6 in numerous community samples (Lee et al., 2013; Murray et al., 2012). Thus, estimates from this literature suggest that parental incar-

ceration is unlikely to be a strong enough confounder to explain away the observed associations. Other potential confounders might exist, but given the E-values estimated in our study, such a confounder would need to exceed typical legal standards of causation (Carruth and Goldstein, 2001; Mengersen et al., 2007) as well as commonly accepted thresholds exceeding “weak associations” (Doll, 1985; Wynder, 1987).

6. Conclusions

Our findings show that traumatic experiences – in the form of emotional, physical and sexual abuse – are common among ALHIV in rural Uganda, and that emotional and physical abuse were associated with major depressive disorder and suicidality. The findings also show that social support potentially moderates the effect of trauma on major depressive disorder among ALHIV. These findings highlight a major public health problem in relation to HIV care among ALHIV since both childhood trauma and depression have been associated with sub-optimal adherence to HIV medication, with concomitant worsened health outcomes (Fawzi et al., 2016; Kim et al., 2017; Tsai et al., 2010b; Willis et al., 2018) and involvement in HIV transmission risk behavior (Adejumo et al., 2015; Cluver et al., 2018; Kidman et al., 2018). There is a need to incorporate screening for childhood trauma in clinics for ALHIV and to develop social support interventions aimed at addressing trauma-related challenges and prevention of trauma among ALHIV. Such interventions will contribute toward improved mental health and adherence to ART and overall improved health among ALHIV in Uganda.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

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Author contributions

SA conceived the idea, supervised data collection, analyzed data and wrote the first draft of the manuscript. ACT supervised data collection, guided data analysis and interpretation, and read and edited all drafts of the manuscript. CEC, SM, ENS, CB, DA, DN, and FB contributed to reviewing and editing the manuscript. All authors read and approved the final version of the manuscript.

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References

- Abubakar, A., Van de Vijver, F.J.R., Hassan, A.S., Fischer, R., Nyongesa, M.K., Kabunda, B., Berkley, J.A., Stein, A., Newton, C.R., 2017. Cumulative psychosocial risk is a salient predictor of depressive symptoms among vertically HIV-infected and HIV-affected adolescents at the Kenyan Coast. *Ann. Glob. Health* 83 (5–6), 743–752.
- Adejumo, O.A., Malee, K.M., Ryscavage, P., Hunter, S.J., Taiwo, B.O., 2015. Contemporary issues on the epidemiology and antiretroviral adherence of HIV-infected adolescents in sub-Saharan Africa: a narrative review. *J. Int. AIDS Soc.* 18 (1), 20049.
- Adeyemo, S., Adeosun, I.I., Ogun, O.C., Adewuya, A., David, A.N., Adegbohun, A.A., Adejumo, O., Ogunlowo, O.A., Adeyemo, O.O., 2020. Depression and suicidality among adolescents living with human immunodeficiency virus in Lagos, Nigeria. *Child Adolesc. Psychiatry Ment. Health* 14 (1), 1–10.

- Ashaba, S., Cooper-Vince, C., Maling, S., Rukundo, G., Akena, D., Tsai, A., 2018. Internalized HIV stigma, bullying, major depressive disorder, and high-risk suicidality among HIV-positive adolescents in rural Uganda. *Global Mental Health* 5 (e22), 1–10.
- Ashaba, S., Cooper-Vince, C., Vořechovská, D., Maling, S., Rukundo, G.Z., Akena, D., Tsai, A.C., 2019a. Development and validation of a 20-item screening scale to detect major depressive disorder among adolescents with HIV in rural Uganda: a mixed-methods study. *SSM-Popul. Health* 7, 100332.
- Ashaba, S., Cooper-Vince, C.E., Vořechovská, D., Rukundo, G.Z., Maling, S., Akena, D., Tsai, A.C., 2019b. Community beliefs, HIV stigma, and depression among adolescents living with HIV in rural Uganda. *Afr. J. AIDS Res.* 18 (3), 169–180.
- Bankole, K.O., Bakare, M.O., Edet, B.E., Igwe, M.N., Ewa, A.U., Bankole, I.A., Olose, E.E., 2017. Psychological complications associated with HIV/AIDS infection among children in South-South Nigeria, sub-Saharan Africa. *Cogent Med.* 4 (1), 1372869.
- Bekele, T., Collins, E., Maunder, R., Gardner, S., Rueda, S., Globerman, J., Le, T., Hunter, J., Benoit, A., Rourke, S., 2018. Childhood adversities and physical and mental health outcomes in adults living with HIV: findings from the Ontario HIV treatment network cohort study. *AIDS Res Treat* 2018, 2187232.
- Bernstein, D., Fink, L., 1998a. Manual for the Childhood Trauma Questionnaire. The Psychological Corporation, New York.
- Bernstein, D.P., Fink, L., 1998b. *Childhood Trauma Questionnaire: A Retrospective Self-Report Manual*. Harcourt Brace & Company.
- Bernstein, D.P., Stein, J.A., Newcomb, M.D., Walker, E., Pogge, D., Ahluvalia, T., Stokes, J., Handelman, L., Medrano, M., Desmond, D., 2003. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse Negl.* 27 (2), 169–190.
- Blum, M.R., Tan, Y.J., Ioannidis, J.P.A., 2020. Use of E-values for addressing confounding in observational studies—An empirical assessment of the literature. *Int. J. Epidemiol.* 49 (5), 1482–1494.
- Boydell, N., Nalukenge, W., Siu, G., Seeley, J., Wight, D., 2017. How mothers in poverty explain their use of corporal punishment: a qualitative study in Kampala, Uganda. *Eur. J. Dev. Res.* 29 (5), 999–1016.
- Boyes, M.E., Cluver, L.D., 2013. Relationships among HIV/AIDS orphanhood, stigma, and symptoms of anxiety and depression in South African youth: a longitudinal investigation using a path analysis framework. *Clin. Psychol. Sci.* 1 (3), 323–330.
- Boyes, M.E., Cluver, L.D., 2015. Relationships between familial HIV/AIDS and symptoms of anxiety and depression: the mediating effect of bullying victimization in a prospective sample of South African children and adolescents. *J. Youth Adolesc.* 44 (4), 847–859.
- Brady, M.T., Oleske, J.M., Williams, P.L., Elgie, C., Mofenson, L.M., Dankner, W.M., Van Dyke, R.B., Pediatric AIDS Clinical Trials Group 219/219C Team, 2010. Declines in mortality rates and changes in causes of death in HIV-1-infected children during the HAART era. *J. Acquir. Immune Defic. Syndr.* 53 (1), 86.
- Brezing, C., Ferrara, M., Freudenreich, O., 2015. The syndemic illness of HIV and trauma: implications for a trauma-informed model of care. *Psychosomatics* 56 (2), 107–118.
- Brown, D.W., Riley, L., Butchart, A., Meddings, D.R., Kann, L., Harvey, A.P., 2009. Exposure to physical and sexual violence and adverse health behaviours in African children: results from the Global School-based Student Health Survey. *Bull. World Health Organ.* 87, 447–455.
- Burack, J.H., Barrett, D.C., Stall, R.D., Chesney, M.A., Ekstrand, M.L., Coates, T.J., 1993. Depressive symptoms and CD4 lymphocyte decline among HIV-infected men. *JAMA* 270 (21), 2568–2573.
- Carruth, R.S., Goldstein, B.D., 2001. Relative risk greater than two in proof of causation in toxic tort litigation. *Jurimetrics* 195–209.
- Casale, M., Boyes, M., Pantelic, M., Toska, E., Cluver, L., 2019. Suicidal thoughts and behaviour among South African adolescents living with HIV: can social support buffer the impact of stigma? *J. Affect. Disord.* 245, 82–90.
- Casale, M., Cluver, L., Crankshaw, T., Kuo, C., Lachman, J.M., Wild, L.G., 2015a. Direct and indirect effects of caregiver social support on adolescent psychological outcomes in two South African AIDS-affected communities. *Am. J. Commun. Psychol.* 55 (3–4), 336–346.
- Casale, M., Wild, L., Cluver, L., Kuo, C., 2015b. Social support as a protective factor for depression among women caring for children in HIV-endemic South Africa. *J. Behav. Med.* 38 (1), 17–27.
- Charak, R., de Jong, J., Berckmoes, L.H., Ndayisaba, H., Reis, R., 2017. Assessing the factor structure of the Childhood Trauma Questionnaire, and cumulative effect of abuse and neglect on mental health among adolescents in conflict-affected Burundi. *Child Abuse Negl.* 72, 383–392.
- Cheng, Y., Li, X., Lou, C., Sonenstein, F.L., Kalamar, A., Jejeebhoy, S., Delany-Moretlwe, S., Brahmbhatt, H., Olumide, A.O., Ojengbede, O., 2014. The association between social support and mental health among vulnerable adolescents in five cities: findings from the study of the well-being of adolescents in vulnerable environments. *J. Adolesc. Health* 55 (6), S31–S38.
- Cluver, L., Bowes, L., Gardner, F., 2010. Risk and protective factors for bullying victimization among AIDS-affected and vulnerable children in South Africa. *Child Abuse Negl.* 34 (10), 793–803.
- Cluver, L., Meinck, F., Toska, E., Orkin, F.M., Hodes, R., Sherr, L., 2018. Multitype violence exposures and adolescent antiretroviral nonadherence in South Africa. *AIDS* 32 (8), 975.
- Cluver, L., Operario, D., Gardner, F., Boyes, M.E., 2011. A family disease: mental health of children orphaned by AIDS and living with HIV+ caregivers. In: *Child psychology and mental health. International perspectives on children and mental health*, Vols. 1 and 2: Development and context, prevention and treatment. In: *International Perspectives on Children and Mental Health [2 Volumes]*, 2. Praeger/ABC-CLIO, pp. 65–87.
- Cluver, L., Orkin, M., Boyes, M.E., Sherr, L., Makasi, D., Nikelo, J., 2013. Pathways from parental AIDS to child psychological, educational and sexual risk: developing an empirically-based interactive theoretical model. *Soc. Sci. Med.* 87, 185–193.
- Cluver, L.D., Orkin, M., Gardner, F., Boyes, M.E., 2012. Persisting mental health problems among AIDS-orphaned children in South Africa. *J. Child Psychol. Psychiatry* 53 (4), 363–370.
- Devries, K., 2016. Violence against children and education. *Int. Health* 8 (1), 1–2.
- Devries, K.M., Knight, L., Child, J.C., Mirembe, A., Nakuti, J., Jones, R., Sturgess, J., Allen, E., Kyegombe, N., Parkes, J., 2015. The good school toolkit for reducing physical violence from school staff to primary school students: a cluster-randomised controlled trial in Uganda. *The Lancet Global Health* 3 (7), e378–e386.
- Dewing, S., Tomlinson, M., le Roux, I.M., Chopra, M., Tsai, A.C., 2013. Food insecurity and its association with co-occurring postnatal depression, hazardous drinking, and suicidality among women in peri-urban South Africa. *J. Affect. Disord.* 150 (2), 460–465. doi:10.1016/j.jad.2013.04.040.
- Doll, R., 1985. Occupational cancer: a hazard for epidemiologists. *Int. J. Epidemiol.* 14 (1), 22–31.
- Fawzi, M.C.S., Ng, L., Kanyanganzani, F., Kirk, C., Bizimana, J., Cyamatatre, F., Mushashi, C., Kim, T., Kayiteshonga, Y., Binagwaho, A., 2016. Mental Health and Antiretroviral Adherence Among Youth Living With HIV in Rwanda. *Pediatrics* 138 (4), e20153235.
- Fleiss, J.L., Levin, B., Paik, M.C., 2013. *Statistical Methods for Rates and Proportions*. John Wiley & Sons, New York.
- Foster, H., Brooks-Gunn, J., 2009. Toward a stress process model of children's exposure to physical family and community violence. *Clin. Child. Fam. Psychol. Rev.* 12 (2), 71–94.
- Gardner, M., Thomas, H., Erskine, H., 2019. The association between five forms of child maltreatment and depressive and anxiety disorders: a systematic review and meta-analysis. *Child Abuse Negl.* 96, 104082.
- Hart, T.A., Heimberg, R.G., 2005. Social anxiety as a risk factor for unprotected intercourse among gay and bisexual male youth. *AIDS Behav.* 9 (4), 505–512.
- Hillis, S., Mercy, J., Amobi, A., Kress, H., 2016. Global prevalence of past-year violence against children: a systematic review and minimum estimates. *Pediatrics* 137 (3), e20154079.
- Humphreys, K., Mankowski, E.S., Moos, R.H., Finney, J.W., 1999. Do enhanced friendship networks and active coping mediate the effect of self-help groups on substance abuse? *Ann. Behav. Med.* 21 (1), 54.
- Hussong, A.M., 2000. Perceived peer context and adolescent adjustment. *J. Res. Adolesc.* 10 (4), 391–415.
- Idro, R., Kakooza-Mwesige, A., Asea, B., Ssebyala, K., Bangirana, P., Opoka, R.O., Lubowa, S.K., Semrud-Clikeman, M., John, C.C., Nalugya, J., 2016. Cerebral malaria is associated with long-term mental health disorders: a cross sectional survey of a long-term cohort. *Malar.* 15 (1), 184.
- Jewkes, R.K., Dunkle, K., Nduna, M., Jama, P.N., Pure, A., 2010a. Associations between childhood adversity and depression, substance abuse and HIV and HSV2 incident infection in rural South African youth. *Child Abuse Negl.* 34 (11), 833–841.
- Jewkes, R.K., Dunkle, K., Nduna, M., Shai, N., 2010b. Intimate partner violence, relationship power inequity, and incidence of HIV infection in young women in South Africa: a cohort study. *The Lancet* 376 (9794), 41–48.
- Kacanek, D., Jacobson, D.L., Spiegelman, D., Wanke, C., Isaac, R., Wilson, I.B., 2010. Incident depression symptoms are associated with poorer HAART adherence: a longitudinal analysis from the Nutrition for Healthy Living (NFHL) study. *J. Acquir. Immune Defic. Syndr.* 53 (2), 266 (1999).
- Kahana, S.Y., Fernandez, M.I., Wilson, P.A., Bauermeister, J.A., Lee, S., Wilson, C.M., High-tow-Weidman, L.B., 2015. Rates and correlates of antiretroviral therapy use and virologic suppression among perinatally and behaviorally infected HIV+ youth linked to care in the United States. *J. Acquir. Immune Defic. Syndr.* 68 (2), 169 (1999).
- Kalichman, S.C., Simbayi, L.C., Cloete, A., Mthembu, P.P., Mkhonta, R.N., Ginindza, T., 2009. Measuring AIDS stigmas in people living with HIV/AIDS: the Internalized AIDS-Related Stigma Scale. *AIDS Care* 21 (1), 87–93.
- Kaltenbach, E., Hermenau, K., Nkuba, M., Goessmann, K., Hecker, T., 2018. Improving interaction competencies with children—A pilot feasibility study to reduce school corporal punishment. *J. Aggress Maltreat. Trauma* 27 (1), 35–53.
- Kamau, J.W., Kuria, W., Mathai, M., Atwoli, L., Kangethe, R., 2012. Psychiatric morbidity among HIV-infected children and adolescents in a resource-poor Kenyan urban community. *AIDS Care* 24 (7), 836–842.
- Kang, E., Mellins, C.A., Dolezal, C., Elkington, K.S., Abrams, E.J., 2011. Disadvantaged neighborhood influences on depression and anxiety in youth with perinatally acquired human immunodeficiency virus: how life stressors matter. *J. Commun. Psychol.* 39 (8), 956–971.
- Kelly, B., Raphael, B., Judd, F., Perdices, M., Kernutt, G., Burnett, P., Dunne, M., Burrows, G., 1998. Suicidal ideation, suicide attempts, and HIV infection. *Psychosomatics* 39 (5), 405–415.
- Kidman, R., Nachman, S., Dietrich, J., Liberty, A., Violari, A., 2018. Childhood adversity increases the risk of onward transmission from perinatal HIV-infected adolescents and youth in South Africa. *Child Abuse Negl.* 79, 98–106.
- Kim, M.H., Mazenga, A.C., Yu, X., Ahmed, S., Paul, M.E., Kazembe, P.N., Abrams, E.J., 2017. High self-reported non-adherence to antiretroviral therapy amongst adolescents living with HIV in Malawi: barriers and associated factors. *J. Int. AIDS Soc.* 20 (1), 21437.
- Kinyanda, E., Kizza, R., Abbo, C., Ndyanabangi, S., Levin, J., 2013. Prevalence and risk factors of depression in childhood and adolescence as seen in 4 districts of north-eastern Uganda. *BMC Int. Health Hum. Rights* 13 (1), 19.
- Kounou, K.B., Bui, E., Dassa, K.S., Hinton, D., Fischer, L., Djasso, G., Birmes, P., Schmitt, L., 2013. Childhood trauma, personality disorders symptoms and current major depressive disorder in Togo. *Soc. Psychiatry Psychiatr. Epidemiol.* 48 (7), 1095–1103.
- Kumar, A.S., Stern, V., Subrahmanian, R., Sherr, L., Burton, P., Guerra, N., Muggah, R., Samms-Vaughan, M., Watts, C., Mehta, S.K., 2017. Ending violence in childhood: a global imperative. *Psychol. Health Med.* 22 (s1), 1–16.

- Lansford, J.E., Sharma, C., Malone, P.S., Woodlief, D., Dodge, K.A., Oburu, P., Pastorelli, C., Skinner, A.T., Sorbring, E., Tapanya, S., 2014. Corporal punishment, maternal warmth, and child adjustment: a longitudinal study in eight countries. *J. Clin. Child Adolesc. Psychol.* 43 (4), 670–685.
- Lee, R.D., Fang, X., Luo, F., 2013. The impact of parental incarceration on the physical and mental health of young adults. *Pediatrics* 131 (4), e1188–e1195.
- Lewis, J.V., Abramowitz, S., Koenig, L.J., Chandwani, S., Orban, L., 2015. Negative life events and depression in adolescents with HIV: a stress and coping analysis. *AIDS Care* 27 (10), 1265–1274. doi:10.1080/09540121.2015.1050984.
- Lowenthal, E.D., Bakeera-Kitaka, S., Marukutira, T., Chapman, J., Goldrath, K., Ferland, R.A., 2014. Perinatally acquired HIV infection in adolescents from sub-Saharan Africa: a review of emerging challenges. *Lancet Infect. Dis.* 14 (7), 627–639.
- Lubinga, S.J., Levine, G.A., Jenny, A.M., Ngondi, J., Mukasa-Kivunike, P., Stergachis, A., Babigumira, J.B., 2013. Health-related quality of life and social support among women treated for abortion complications in western Uganda. *Health Qual. Life Outcomes* 11 (1), 118.
- Lund, C., Breen, A., Flisher, A.J., Kakuma, R., Corrigall, J., Joska, J.A., Swartz, L., Patel, V., 2010. Poverty and common mental disorders in low and middle income countries: a systematic review. *Soc. Sci. Med.* 71 (3), 517–528. doi:10.1016/j.socscimed.2010.04.027.
- Lyketsos, C.G., Hoover, D.R., Guccione, M., Senterfitt, W., Dew, M.A., Wesch, J., Van-Raden, M.J., Treisman, G.J., Morgenstern, H., Saah, A., 1993. Depressive symptoms as predictors of medical outcomes in HIV infection. *JAMA* 270 (21), 2563–2567.
- Martinez, J., Hosek, S.G., Carleton, R.A., 2009. Screening and assessing violence and mental health disorders in a cohort of inner city HIV-positive youth between 1998 and 2006. *AIDS Patient Care STDs* 23 (6), 469–475.
- Matsumoto, S., Yamaoka, K., Takahashi, K., Tanuma, J., Mizushima, D., Do, C.D., Nguyen, D.T., Nguyen, H.D.T., Van Nguyen, K., Oka, S., 2017. Social support as a key protective factor against depression in HIV-infected patients: report from large HIV clinics in Hanoi, Vietnam. *Sci. Rep.* 7 (1), 1–12.
- Meinck, F., Cluver, L.D., Boyes, M.E., 2015. Household illness, poverty and physical and emotional child abuse victimisation: findings from South Africa's first prospective cohort study. *BMC Public Health* 15 (1), 444.
- Meinck, F., Cluver, L.D., Boyes, M.E., Loening-Voysey, H., 2016. Physical, emotional and sexual adolescent abuse victimisation in South Africa: prevalence, incidence, perpetrators and locations. *J. Epidemiol. Commun. Health* 70 (9), 910–916.
- Mellins, C.A., Malee, K.M., 2013. Understanding the mental health of youth living with perinatal HIV infection: lessons learned and current challenges. *J. Int. AIDS Soc.* 16 (1), 18593.
- Mengersen, K., Moynihan, S.A., Tweedie, R.L., 2007. Causality and association: the statistical and legal approaches. *Stat. Sci.* 227–254.
- Ministry of Health of Uganda, 2019. *Uganda Population-based HIV Impact Assessment (UP-HIA) 2016-2017: Final Report*. Ministry of Health of Uganda, Kampala.
- Ministry of Health of Uganda, 2020. *Consolidated Guidelines for the Prevention and Treatment of HIV and AIDS in Uganda*. Ministry of Health of Uganda, Kampala.
- Morantz, G., Cole, D., Vreeman, R., Ayaya, S., Ayuku, D., Braitsstein, P., 2013. Child abuse and neglect among orphaned children and youth living in extended families in sub-Saharan Africa: what have we learned from qualitative inquiry? *Vulnerable Child Youth Stud.* 8 (4), 338–352.
- Mupambireyi, Z., Bernays, S., Bwakura-Dangarembizi, M., Cowan, F.M., 2014. I don't feel shy because I will be among others who are just like me...": the role of support groups for children perinatally infected with HIV in Zimbabwe. *Child Youth Serv. Rev.* 45, 106–113.
- Murphy, D.A., Moscicki, A.B., Vermund, S.H., Muenz, L.R., Network, A.M.H.A.R., 2000. Psychological distress among HIV+ adolescents in the REACH study: effects of life stress, social support, and coping. *J. Adolesc. Health* 27 (6), 391–398.
- Murray, J., Farrington, D.P., Sekol, I., 2012. Children's antisocial behavior, mental health, drug use, and educational performance after parental incarceration: a systematic review and meta-analysis. *Psychol. Bull.* 138 (2), 175.
- Mushavi, R.C., Burns, B.F., Kakuhikire, B., Owembabazi, M., Vořechovská, D., McDonough, A.Q., Cooper-Vince, C.E., Baguma, C., Rasmussen, J.D., Bangsberg, D.R., 2020. When you have no water, it means you have no peace": a mixed-methods, whole-population study of water insecurity and depression in rural Uganda. *Soc. Sci. Med.* 245, 112561.
- Mynard, H., Joseph, S., 2000. Development of the multidimensional peer-victimization scale. *Aggress. Behav.* 26 (2), 169–178.
- Naker, D., 2005. *Violence Against Children: The Voices of Ugandan Children and Adults*. Raising Voices, Kampala.
- Nakimuli-Mpungu, E., Musisi, S., Katabira, E., Nachege, J., Bass, J., 2011. Prevalence and factors associated with depressive disorders in an HIV+ rural patient population in southern Uganda. *J. Affect. Disord.* 135 (1–3), 160–167.
- Nakimuli-Mpungu, E., Wamala, K., Okello, J., Alderman, S., Odokonyero, R., Musisi, S., Mojtabai, R., 2014. Developing a culturally sensitive group support intervention for depression among HIV infected and non-infected Ugandan adults: a qualitative study. *J. Affect. Disord.* 163, 10–17.
- Nalugya-Sserunjogi, J., Rukundo, G.Z., Ovuga, E., Kiwuwa, S.M., Musisi, S., Nakimuli-Mpungu, E., 2016. Prevalence and factors associated with depression symptoms among school-going adolescents in Central Uganda. *Child Adolesc. Psychiatry Ment. Health* 10 (1), 39.
- Nanni, M., Caruso, R., Mitchell, A., Meggiolaro, E., Grassi, L., 2015. Depression in HIV infected patients: a review. *Curr. Psychiatry Rep.* 17 (1), 530.
- Newcombe, R.G., 1998. Two-sided confidence intervals for the single proportion: comparison of seven methods. *Stat. Med.* 17 (8), 857–872.
- Newman, B.M., Newman, P.R., Griffen, S., O'Connor, K., Spas, J., 2007. The relationship of social support to depressive symptoms during the transition to high school. *Adolescence* 42 (167), 441.
- Ng, L.C., Kirk, C.M., Kanyanganzi, F., Fawzi, M.C.S., Sezibera, V., Shema, E., Bizimana, J.I., Cyamatare, F.R., Betancourt, T.S., 2015. Risk and protective factors for suicidal ideation and behaviour in Rwandan children. *Br. J. Psychiatry* 207 (3), 262–268.
- Norman, R.E., Byambaa, M., De, R., Butchart, A., Scott, J., Vos, T., 2012. The long-term health consequences of child physical abuse, emotional abuse, and neglect: a systematic review and meta-analysis. *PLoS Med.* 9 (11), e1001349.
- Nyamukapa, C., Gregson, S., Wambe, M., Mushore, P., Lopman, B., Mupambireyi, Z., Nhongo, K., Jukes, M., 2010. Causes and consequences of psychological distress among orphans in eastern Zimbabwe. *AIDS Care* 22 (8), 988–996.
- Okello, Onen, Musisi, 2007. Psychiatric disorders among war-abducted and non-abducted adolescents in Gulu district, Uganda: a comparative study. *Afr. J. Psychiatry (Johannesburg)* 10 (4), 225–231.
- Onuoha, F.N., Munakata, T., Serumaga-Zake, P.A., Nyonyintono, R.M., Bogere, S.M., 2009. Negative mental health factors in children orphaned by AIDS: natural mentoring as a palliative care. *AIDS Behav.* 13 (5), 980.
- Pantelic, M., Shenderovich, Y., Cluver, L., Boyes, M., 2015. Predictors of internalised HIV-related stigma: a systematic review of studies in sub-Saharan Africa. *Health Psychol. Rev.* 9 (4), 469–490. doi:10.1080/17437199.2014.996243.
- Peirce, R.S., Frone, M.R., Russell, M., Cooper, M.L., Mudar, P., 2000. A longitudinal model of social contact, social support, depression, and alcohol use. *Health Psychol.* 19 (1), 28.
- Pence, B.W., Gaynes, B.N., Adams, J.L., Thielman, N.M., Heine, A.D., Mugavero, M.J., McGuinness, T., Raper, J.L., Willig, J.H., Shirey, K.G., 2015. The effect of antidepressant treatment on HIV and depression outcomes: the SLAM DUNC randomized trial. *AIDS* 29 (15), 1975.
- Petersen, I., Bhana, A., Myeza, N., Alicea, S., John, S., Holst, H., McKay, M., Mellins, C., 2010. Psychosocial challenges and protective influences for socio-emotional coping of HIV+ adolescents in South Africa: a qualitative investigation. *AIDS Care* 22 (8), 970–978.
- Prado, G., Feaster, D.J., Schwartz, S.J., Pratt, I.A., Smith, L., Szapocznik, J., 2004. Religious involvement, coping, social support, and psychological distress in HIV-seropositive African American mothers. *AIDS Behav.* 8 (3), 221–235.
- Radcliffe, J., Fleisher, C.L., Hawkins, L.A., Tanney, M., Kassam-Adams, N., Ambrose, C., Rudy, B.J., 2007. Posttraumatic stress and trauma history in adolescents and young adults with HIV. *AIDS Patient Care STDs* 21 (7), 501–508.
- Robbins, M., Szapocznik, J., Tejeda, M., Samuels, D., Ironson, G., Antoni, M., 2003. The protective role of the family and social support network in a sample of HIV-positive African American women: results of a pilot study. *J. Black Psychol.* 29 (1), 17–37.
- Ruchkin, V., Schwab-Stone, M., Vermeiren, R., 2004. *Social and Health Assessment (SAHA): Psychometric Development Summary*. Yale University, New Haven.
- Safren, S.A., Bedoya, C.A., O'Clearigh, C., Biello, K.B., Pinkston, M.M., Stein, M.D., Traeger, L., Kojic, E., Robbins, G.K., Lerner, J.A., 2016. Cognitive behavioural therapy for adherence and depression in patients with HIV: a three-arm randomised controlled trial. *The Lancet HIV* 3 (11), e529–e538.
- Sarason, I.G., Sarason, B.R., Shearin, E.N., Pierce, G.R., 1987. A brief measure of social support: practical and theoretical implications. *J. Soc. Pers. Relat.* 4 (4), 497–510.
- Sheehan, D., LeCrubier, Y., Sheehan, K.H., Sheehan, K., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G., 1998a. Diagnostic psychiatric interview for DSM-IV and ICD-10. *J. Clin. Psychiatr.* 59, 22–33.
- Sheehan, D., LeCrubier, Y., Sheehan, K.H., Sheehan, K., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G., 1998b. Diagnostic Psychiatric Interview for DSM-IV and ICD-10. *J. Clin. Psychiatr.* 59, 22–33.
- Sheehan, D., LeCrubier, Y., Sheehan, K.H., Sheehan, K., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G., 1998c. Diagnostic Psychiatric Interview for DSM-IV and ICD-10. *J. Clin. Psychiatr.* 59, 22–33.
- Sheehan, D.V., Sheehan, K.H., Shytle, R.D., Janavs, J., Bannon, Y., Rogers, J.E., Milo, K.M., Stock, S.L., Wilkinson, B., 2010. Reliability and validity of the mini international neuropsychiatric interview for children and adolescents (MINI-KID). *J. Clin. Psychiatr.* 71 (3), 313–326.
- Skeen, S., Macedo, A., Tomlinson, M., Hensels, I., Sherr, L., 2016. Exposure to violence and psychological well-being over time in children affected by HIV/AIDS in South Africa and Malawi. *AIDS Care* 28 (sup1), 16–25.
- Slogrove, A.L., Mahy, M., Armstrong, A., Davies, M.A., 2017. Living and dying to be counted: what we know about the epidemiology of the global adolescent HIV epidemic. *J. Int. AIDS Soc.* 20, 21520.
- Thoits, P.A., 2011. Mechanisms linking social ties and support to physical and mental health. *J. Health Soc. Behav.* 52 (2), 145–161.
- Tsai, A.C., Bangsberg, D.R., Emenyonu, N., Senkungu, J.K., Martin, J.N., Weiser, S.D., 2011. The social context of food insecurity among persons living with HIV/AIDS in rural Uganda. *Soc. Sci. Med.* 73 (12), 1717–1724.
- Tsai, A.C., Bangsberg, D.R., Frongillo, E.A., Hunt, P.W., Muozora, C., Martin, J.N., Weiser, S.D., 2012. Food insecurity, depression and the modifying role of social support among people living with HIV/AIDS in Rural Uganda. *Soc. Sci. Med.* 74 (12), 2012–2019 (1982(12)).
- Tsai, A.C., Kakuhikire, B., Mushavi, R., Vořechovská, D., Perkins, J.M., McDonough, A.Q., Bangsberg, D.R., 2016a. Population-based study of intra-household gender differences in water insecurity: reliability and validity of a survey instrument for use in rural Uganda. *J. Water Health* 14 (2), 280–292.
- Tsai, A.C., Karasic, D.H., Hammer, G.P., Charlebois, E.D., Ragland, K., Moss, A.R., Sorenson, J.L., Dilley, J.W., Bangsberg, D.R., 2013a. Directly observed antidepresant medication treatment and HIV outcomes among homeless and marginally housed HIV-positive adults: a randomized controlled trial. *Am. J. Public Health* 103 (2), 308–315.
- Tsai, Alexander C., Mendenhall, Emily, Trostle, James A., Ichiro, Kawachi, 2017. *Co-occurring epidemics, syndemics, and population health*. *Lancet* 389, 978–982.
- Tsai, A.C., Tomlinson, M., Comulada, W.S., Rotheram-Borus, M.J., 2016b. Food insufficiency, depression, and the modifying role of social support: evidence from a population-based, prospective cohort of pregnant women in peri-urban South Africa. *Soc. Sci. Med.* 151, 69–77.

- Tsai, A.C., Tomlinson, M., Comulada, W.S., Rotheram-Borus, M.J., 2016c. Intimate partner violence and depression symptom severity among South African women during pregnancy and postpartum: population-based prospective cohort study. *PLoS Med.* 13 (1), e1001943. doi:[10.1371/journal.pmed.1001943](https://doi.org/10.1371/journal.pmed.1001943).
- Tsai, A.C., Weiser, S.D., Petersen, M.L., Ragland, K., Kushel, M.B., Bangsberg, D.R., 2010a. A marginal structural model to estimate the causal effect of antidepressant medication treatment on viral suppression among homeless and marginally housed persons with HIV. *Arch. Gen. Psychiatry* 67 (12), 1282–1290. doi:[10.1001/archgenpsychiatry.2010.160](https://doi.org/10.1001/archgenpsychiatry.2010.160).
- Tsai, A.C., Weiser, S.D., Petersen, M.L., Ragland, K., Kushel, M.B., Bangsberg, D.R., 2010b. A marginal structural model to estimate the causal effect of antidepressant medication treatment on viral suppression among homeless and marginally housed persons with HIV. *Arch. Gen. Psychiatry* 67 (12), 1282–1290.
- Tsai, A.C., Weiser, S.D., Steward, W.T., Mukabi, N.F., Kawuma, A., Kembabazi, A., Muzaora, C., Hunt, P.W., Martin, J.N., Bangsberg, D.R., 2013b. Evidence for the reliability and validity of the internalized AIDS-related stigma scale in rural Uganda. *AIDS Behav.* 17 (1), 427–433.
- Turney, K., 2014. The consequences of paternal incarceration for maternal neglect and harsh parenting. *Soc. Forces* 92 (4), 1607–1636.
- Uganda AIDS Commission, 2018. *Uganda HIV and AIDS Country Progress Report, July 2016-June 2017*. Uganda AIDS Commission, Kampala.
- Uganda Bureau of Statistics, 2014. *The population of the regions of the Republic of Uganda and all cities and towns of more than 15,000 inhabitants*. Uganda Bureau of Statistics, Kampala.
- Uganda National Council for Science and Technology, 2007. National Guidelines for Research Involving Humans As Research Participants.
- UNAIDS, 2018. *Global AIDS Update 2018: State of the Epidemic*. UNAIDS, Geneva.
- VanderWeele, T.J., Ding, P., 2017. Sensitivity analysis in observational research: introducing the E-value. *Ann. Intern. Med.* 167 (4), 268–274.
- Wallace, D.D., Pack, A., Castonguay, B.U., Stewart, J., Schalkoff, C., Cherkur, S., Schein, M., Go, M., Devadas, J., Fisher, E.B., 2019. Validity of social support scales utilized among HIV-infected and HIV-affected populations: a systematic review. *AIDS Behav.* 23 (8), 2155–2175.
- Ward, C.L., Artz, L., Leoschut, L., Kassanjee, R., Burton, P., 2018. Sexual violence against children in South Africa: a nationally representative cross-sectional study of prevalence and correlates. *The Lancet Global Health* 6 (4), e460–e468.
- Willis, N., Mavhu, W., Wogrin, C., Mutzinze, A., Kagee, A., 2018. Understanding the experience and manifestation of depression in adolescents living with HIV in Harare, Zimbabwe. *PLoS ONE* 13 (1) e0190423-e0190423.
- Woollett, N., Cluver, L., Bandeira, M., Brahmbhatt, H., 2017. Identifying risks for mental health problems in HIV positive adolescents accessing HIV treatment in Johannesburg. *J. Child Adolesc. Mental Health* 29 (1), 11–26. doi:[10.2989/17280583.2017.1283320](https://doi.org/10.2989/17280583.2017.1283320).
- World Health Organization, Geneva. *Trauma among children who are victims of violence*, 2001.
- Wynder, E.L., 1987. *Workshop on Guidelines to the Epidemiology of Weak Associations: introduction*. *Prev. Med.* 16 (2), 139–141.
- Yakubovich, A.R., Sherr, L., Cluver, L.D., Skeen, S., Hensels, I.S., Macedo, A., Tomlinson, M., 2016. Community-based organizations for vulnerable children in South Africa: reach, psychosocial correlates, and potential mechanisms. *Child Youth Serv. Rev.* 62, 58–64.
- Zou, G., 2004. A modified poisson regression approach to prospective studies with binary data. *Am. J. Epidemiol.* 159 (7), 702–706.