

Associations of Adverse Childhood Experiences With Key Health Outcomes and Viral
Suppression Maintenance Among Tanzanian Youth Living With HIV

by

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Thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Science in the Duke Global Health Institute
in the Graduate School
of Duke University

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ABSTRACT

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Abstract

Background: Despite improved access to HIV testing and medication, AIDS remains a leading cause of death among youth living with HIV (YLWH) in Tanzania. YLWH are prone to worse HIV outcomes than other age groups, which may be caused or mediated by mental health, social determinants of health (SDH), and adverse childhood experiences (ACEs). In this study, the investigators sought to determine if ACEs were correlated with key health variables in hopes of better understanding the factors associated with negative HIV and mental health outcomes among Tanzanian youth. Additionally, the investigators aimed to observe longitudinal trends in virologic suppression to understand the extent to which undetectable = untransmittable or “U=U” messaging applies to the more volatile youth demographic. Finally, the investigators sought to identify patterns and predictors that could aid in understanding risk of virologic failure in this population. **Methods:** The investigators incorporated and merged secondary data from participants who were enrolled in both of two distinct studies to create a longitudinal database spanning from 2013 to 2020. Participant ACE scores were derived from trauma exposure questionnaires and were compared with data about mental health, stigma, SDH, sexual experiences, self-reported adherence and HIV RNA (viral load). Associations of ACEs and other key variables were performed using linear regression. **Results:** ACEs were common among YLWH, especially loss of a parent and physical abuse. ACEs were also correlated with both mental health outcomes and virologic failure. Of the 48 participants who were virologically suppressed at the beginning of the study, one third had subsequent virologic failure, which was often

associated with changes in ACEs, medication regimen, and SDH. **Conclusion:**

Understanding common ACEs in this vulnerable population has direct relevance for the design of targeted interventions to prevent and treat repercussions of childhood trauma and improve mental health and HIV outcomes. ACEs, experiences with suicide risk, and low social support are important correlates of virologic failure and should be an alert when considering repeat HIV RNA testing and eligibility for supportive services.

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List of Abbreviations

Abbreviation	Meaning
ACE	Adverse childhood experience
AIDS	Acquired immune deficiency syndrome
ALWH	Adolescents living with HIV
ART	Antiretroviral therapy
CD4 count	Measure of immune system health
EMH	Evaluating mental health
HIV	Human immunodeficiency virus
HIV RNA	Virus level in sample of blood
HVL	HIV viral load
KCMC	Kilimanjaro Christian Medical Centre
MRRH	Mawenzi Regional Referral Hospital
NIMR	National Institute of Medical Research
PHQ-9	Patient Health Questionnaire (9 question)
SDH	Social determinants of health
SDQ	Strengths and Difficulties Questionnaire
SYV	Sauti Ya Vijana
U=U	Undetectable=Untransmittable
WHO	World Health Organization
YLWH	Youth living with HIV
YPLWH	Young people living with HIV

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1. Introduction

In 2020, there were 400,000 young people (age 10-24 years) newly infected with HIV, and 88% of adolescents (10-19 years) living with HIV globally reside in Sub-Saharan Africa (UNICEF, 2021). In Tanzania, HIV/AIDS is a leading cause of mortality, as well as the leading cause of death amongst young people in Africa (UNAIDS, 2015, 2020a). Many youth living with HIV (YLWH) face mental health challenges along with social and environmental barriers that hinder their ability to effectively manage their HIV treatment (Heestermans et al., 2016). Specifically, barriers such as mental illness, social determinants of health, and childhood trauma can negatively impact adherence to antiretroviral therapy (ART) medications (Heestermans et al., 2016; Hillis et al., 2001; Nestadt et al., 2018; VanderEnde et al., 2018; WHO, 2021). This reduced ART adherence can have drastic effects on an individual's ability to have sustained health, as it leads to reduced virologic suppression and increased likelihood of viral resistance (Kozal et al., 2007). Without viral suppression, individuals can transmit HIV to others and are more prone to having negative outcomes such as HIV progression to AIDS and death (Cohen et al., 2011; Kozal et al., 2007). To minimize these health consequences, it is essential to understand the trends in viral suppression that are observed in YPLWH in Tanzania and to have a comprehensive understanding of the factors that most affect these outcomes.

1.1 Why Young People Are at Risk

Young people are at an increased risk of acquiring HIV and experiencing HIV/AIDS related complications, as they are more likely to engage in risky sexual behavior than older age groups and are less likely to engage with the healthcare system for HIV testing (Hervish, 2012; Nestadt et al., 2018; UNAIDS, 2021). This risk taking behavior can in part be explained by neurodevelopmental conditions at this stage of development (Johnson et al., 2009). Additionally, sex-related behaviors and practices instilled at this age can affect behavior patterns throughout their life, which can affect both their long-term health and the likelihood of HIV transmission (Nestadt et al., 2018; Vranda & Mothi, 2013). Though other age groups have had improvements in AIDS related deaths for the past two decades, adolescents are the only age group that has not seen this shift (Slogrove & Sohn, 2018; UNAIDS, 2016, 2021). Therefore, it is crucial to understand the factors that influence HIV-related behaviors and outcomes in this population.

Additionally, youth are at a heightened risk of experiencing mental health challenges during this stage of life due to both biological and environmental shifts that occur during this stage of life. The adolescent developmental stage is defined by major transitions such as puberty, increased responsibilities in school, entering the workforce, and increasingly complex social lives, which create a unique set of social, environmental, and biological stressors for this age group (Pfeifer & Allen, 2021; Yurgelun-Todd, 2007). Living conditions and stigma faced at this age can also influence mental health and the

availability and likelihood of seeking treatment (Cluver & Orkin, 2009; Vranda & Mothi, 2013).

1.2 Role of Mental Health in HIV

Mental health and HIV challenges are exacerbated bidirectionally and are increasingly prevalent in adolescents (UNICEF, 2016; WHO, 2021). Mental illness and mental health challenges can increase the risk of HIV acquisition and transmission by influencing one's ability to consistently take medication and engage in safe sex practices (Nestadt et al., 2018; Vreeman et al., 2017; WHO, 2021). Living with HIV also increases the risk of experiencing mental health challenges, as having an HIV diagnosis can contribute to increased feelings of hopelessness and increased depressive symptoms (Govender & Schlebusch, 2012). Through understanding these connections, current research has led to programs such as Sauti ya Vijana (SYV), a mental health treatment program that has demonstrated positive effects on mental health and HIV-related outcomes in adolescent populations in Moshi, Tanzania (Dow et al., 2020).

1.3 Effects of Social Determinants of Health in HIV

circumstances that can affect how one lives and is treated in their environment. SDHs largely out of the control of an individual, but their effects on health outcomes can be drastic. Previous research has found that social determinants such as gender and social support are associated with ART non-adherence (Heestermans et al., 2016). Economic

burdens also contribute to treatment non-adherence, primarily as a result of treatment costs and hunger (Hardon et al., 2007). SDHs can also influence mental health outcomes, as they are associated with increased stress, stigma and overall burdens for individuals and communities (Cluver & Orkin, 2009; McDowell & Serovich, 2007; Nurius et al., 2020)

1.4 Effects of ACEs on HIV Health Outcomes

Adverse Childhood Experiences (ACEs) are specific social-environmental stressors, experienced before the age of 18, that often have drastic effects on long-term health outcomes (Felitti et al., 1998). ACEs include various traumas faced during childhood and adolescence that are sources of unrelenting toxic stress exposure (WHO, 2020b). ACEs have been shown to contribute to biological and behavioral changes that can alter one's ability to sustain health (Felitti et al., 1998; Kerker et al., 2015).

The long-term effect of ACEs was first investigated in 1998 among 14,000 patients in the United States. The results quantified the striking long-term effects on both communicable and noncommunicable diseases (Felitti et al., 1998). ACEs were mapped by category with a scale of 0 to 10 and had a direct relationship: the more ACEs, the worse the long-term health outcomes. . Studies have reported that individuals living with HIV have an increased risk of unsuppressed viral load (elevated HIV RNA) and are more likely to engage in high-risk behaviors such as poor medication adherence, increased number of sexual partners, and lower rates of condom use during sexual encounters as

their ACE score increases (Hillis et al., 2001; Kidman et al., 2018; VanderEnde et al., 2018). As for mental health, studies have found that increased ACE scores are associated with greater levels of depression and suicidal behavior (Chang et al., 2019; Felitti et al., 1998). ACEs have also been found to be associated with social determinants of health. Increased ACEs and their associated effects on health have been correlated with poor education and job outcomes, lower socioeconomic status, and worse social support (Folayan et al., 2020; Hardcastle et al., 2018; Manyema & Richter, 2019).

1.5 U=U

Individuals who live with HIV and reach viral suppression, or undetectable levels of HIV in their blood, through excellent antiretroviral therapy adherence do not transmit HIV to sexual partners (Cohen et al., 2011). Therefore, adherence in taking ART medication can improve the longevity of an individual's health and well-being while also preventing HIV transmission to others. This discovery is known in the public domain as "Undetectable=Untransmittable" or "U=U." This finding has created an opportunity to have tremendous changes in the stigma associated with HIV. For instance, at least 92 countries legally criminalize individuals that do not disclose their HIV status to sexual partners, which creates a great amount of stigma and discrimination surrounding those living with HIV (UNAIDS, 2020b). However, with the discovery of U=U, many countries have begun to change these laws, as transmission is no longer a risk so long as the individual has achieved and maintains suppression.

Adolescents have worse ART adherence compared to children or adults (Nachega et al., 2009). Knowing the numerous challenges YPLWH face as they transition through adolescence, and the erratic adherence behaviors that follow, it is unknown how likely young people in this population are to maintain an unsuppressed and untransmittable viral load status over time. In Tanzania, HIV RNA (viral load) testing is only performed once per year if viral load is maintained at <1000 copies/mL, so it is essential to understand the risk of virologic failure between these tests (MoHCDGEC, 2019). Therefore, using these data to understand factors that are associated with maintenance of virologic suppression, continuing to have virologic failure, or vacillating between the two categories is essential for risk stratification of YPLWH between standard of care viral load testing.

1.6 Goal of Study

Given the emotional, physical, and social transitions that define the important developmental period of adolescence, it is essential to have a comprehensive understanding of the factors that exacerbate the health barriers that YPLWH face. This analysis had three primary aims. The first was to determine common ACE's experienced by YPLWH in this setting. The second was to evaluate the correlation between ACEs and key variables including mental health, stigma, sex practices, social determinants of health, adherence, and viral load. The third aim was to describe longitudinal suppression trends in this population and determine possible risk and protective factors that were associated with virologic status.

2. Methods

2.1 Setting

Tanzania is located in East Africa and has a population of 59.7 million people (WorldBank, 2021). About 63% of the population is younger than 25 years (CIA, 2020), and Tanzania's population accounts for 5.8% of the adolescent population living with HIV globally (UNICEF, 2020). HIV/AIDS has continued to be one of the top three leading causes of death in Tanzania for the past ten years (IHME, 2019), and in 2019, the prevalence of HIV in Tanzania was 4.8% (UNICEF, 2020). The data used in this study were collected from participants in Moshi, Tanzania, which is in the Kilimanjaro region. Moshi is the tenth largest city in Tanzania, with a population of 157,000 (Worldometer, 2022). The participants were all recruited from Kilimanjaro Christian Medical Centre (KCMC) or Mawenzi Regional Referral Hospital (MRRH), two regional hospitals in the area that host an adolescent HIV clinic.

2.2 Previous Studies

This study is a secondary data analysis of quantitative data that were previously collected in two separate studies. The first of these studies aimed to evaluate mental health needs (EMH) in the population (Dow et al., 2016), and the other aimed to determine if the mental health treatment program, SYV, improved mental health

outcomes, thereby improving HIV outcomes, in YPLWH. The two studies will be referred to as EMH and SYV, respectively.

The EMH study (2013-2015) was a cross sectional analysis that sought to determine the prevalence and severity of mental health challenges in this population. The study also aimed to determine how these mental health challenges were associated with ART adherence, CD4 count (a measure of immune system health), and stigma. Overall, the findings of this study indicated that significant mental health challenges were present in this population and that mental health symptom severity was negatively correlated with ART adherence and positively correlated with stigma. These findings validated the need to have an intervention focused on improving mental health in YPLWH and led to the creation of Sauti ya Vijana (SYV).

SYV is a group-based mental health intervention aimed to improve HIV outcomes through mediators such as coping strategies, resilience, and familial support (Dow et al., 2020). In the SYV study (2016-2020), participants were randomized to the SYV treatment group or standard of care treatment. Those in the SYV treatment group attended 10 group therapy sessions as well as two individual sessions. Fifteen participants who were initially randomized to the control arm of SYV received the SYV intervention at a later point in the study as part of the stepped-wedge cross-over design. Mental health, stigma, and HIV-related data (among others) were collected for each participant. The results of this study suggested that those receiving SYV demonstrated improved ART adherence and increased virologic suppression as well as improved mental health symptom severity compared to standard of care (Dow, BMC PH 2020).

For this analysis, data from these two studies were combined to allow for a more comprehensive understanding of virologic trends over a greater span time. Data were collected through structured surveys at up to ten different time points spanning up to 7 years. Surveys were administered in Kiswahili, the official language of Tanzania with congruent measures across both studies that allowed for cross-study comparison, and a blood sample (~5mL) was collected to determine the viral load (HIV RNA). Both studies were approved by the Duke University Medical Center Institutional Review Board, the KCMC Research Ethics Committee, and the Tanzanian National Institute Medical Research.

2.3 Participants

There were 128 participants with records from the SYV dataset, and 73 of these participants had previously enrolled in the EMH study and are therefore included in this analysis (Dow et al., 2020; Dow et al., 2016). Participants 18 years or older gave written informed consent at the initial time of enrollment, and those under 18 provided assent along with written consent from a guardian. Participants were recruited from the two regional hospitals (KCMC or MRRH) in Moshi, Tanzania in both studies. All participants were recruited from the adolescent HIV clinics at either KCMC or MRRH.

Participants were 12 to 24 years of age at the time of enrollment, reflecting the age of inclusion in the adolescent HIV clinics. Receiving antiretroviral therapy (ART) was not a requirement in the EMH study, as not all people living with HIV qualified to receive ART in 2013-2015. For SYV, all participants were receiving ART. Knowledge

and awareness of their HIV status was a requirement to participate in either study.

Exclusion criteria included cognitive impairment or psychosis precluding the ability for the participant to give consent/assent or actively engage in either study. The current analysis included only those that enrolled in both the EMH and the SYV study.

2.4 Procedures

Data analysis first required combining the data from the two separate studies (EMH and SYV) into one longitudinal database. Additional IRB approval was received from Duke, KCMC, and the Tanzanian National Institute of Medical Research (NIMR) to combine the datasets from the two studies into this longitudinal database. This was done through REDCap software (version 11). SYV data were previously entered into REDCap and were copied to a new database where the additional time point from the EMH study was added.

Questions were then reviewed for congruency. Questions regarding mental health, stigma, and demographics were consistent between the EMH and SYV study, while questions regarding adherence were different. Data labels were made uniform between studies for survey questions that were present in both studies, and new unique variable names were created for discordant questions. Measurement adjustments made between inconsistent survey questions are detailed in “Measures” below.

Data points were then linked to participants through patient identification numbers. Prior de-identified study documentation was first used to determine which participants had participated in both SYV and EMH (N=73) and to correlate participants’

identification numbers between studies. Participants' birthdays and gender were then compared across studies to confirm that the identification number matching was accurate. The identification numbers were then matched with the REDCap study ID for each participant so that the new EMH data entry would be correctly aligned with each participant's SYV data. From this, measures of interest were identified so that the data could be analyzed for each participant across all EMH and SYV time points.

2.5 Measures

Measures that were used in analysis included general demographics, ACEs, mental health, stigma, sex practices, social determinants of health, adherence, and viral load. The baseline and follow-up data were collected through surveys that identified these characteristics, but several measures had to be created or made uniform between the studies for the current analysis.

2.5.1 Measure 1: ACE

We calculated an ACE score using items assessing the incidence of common traumas experienced in this setting and informed by prior literature. As identified by the WHO and literature, an ACE score is composed from a number of traumas youth face that expose them to toxic stress, a stress response created by severe or sustained adversity (Felitti et al., 1998; WHO, 2020b). Traumas that were used to calculate the ACE score in this study were identified through the WHO ACE questionnaire and other literature

(Hughes et al., 2017; WHO, 2020b). The WHO is in the pilot stage of developing an ACE questionnaire, which currently identifies 13 key traumas through a series of 43 questions (WHO, 2020b, 2020c). Several studies have identified additional traumas to be significant sources of prolonged toxic stress that are not included in the WHO questionnaire, such as living with a serious childhood illness (Hughes et al., 2017). Of the most common traumas considered for the ACE score, eight traumas were accounted for in the study questionnaire. The official ACE questionnaire was not used in these studies, but many of the traumas included in the official questionnaire and in literature were asked in the UCLA Trauma Exposure Screener, the SDQ and in demographics regarding death of a parent. ACEs identified and used in this study included 1) living with a severe childhood illness, 2) loss of a parent, 3) bullying, 4) collective violence, 5) community violence, 6) physical abuse, 7) sexual abuse, and 8) witnessing the violent treatment of a household member. For details about each ACE and how these were quantified, please see Appendix A.

2.5.2 Measure 2: Mental Health

Mental health measures were harmonized across the EMH and SYV. Depression symptoms were measured with the Patient Health Questionnaire (PHQ-9). The response range of this measure is 0-27, with a higher score indicating greater symptoms of depression, and the raw score was used as a continuous variable for analysis. A score greater than 10 was an indicator of moderate to severe depression. This cutoff has been

validated in numerous studies and the tool has been validated in African settings (Cholera et al., 2014; Gelaye et al., 2013). Participant suicidality was measured using question nine from the PHQ-9 questionnaire, which asked about the frequency of suicidal thoughts in participants. For this study, the variable was considered on a continuous scale ranging from “none” to “nearly every day,” which was consistent with the questionnaire.

The Strengths and Difficulties Questionnaire (SDQ) measured emotional and behavioral symptoms with a score ranging from 0-40. The SDQ was analyzed as both a continuous and dichotomous score, where a score of 17 or more was considered suggestive of emotional/behavioral challenges. This questionnaire has been previously used in studies across sub-Saharan Africa, but its validity across settings has been variable (Hoosen et al., 2018; Sharp et al., 2014).

The UCLA PTSD Reaction Index was used to evaluate post-traumatic stress symptoms with a scale ranging from 0-51, with higher scores indicating greater symptoms (Dow et al., 2016). A dichotomous measure of the score indicated moderate of severe levels of traumatic symptoms if the participant had a score 18 or more. This measure was previously translated and validated for use in children and youth across several countries in sub-Saharan Africa (Harder et al., 2012; Murray et al., 2011).

2.5.3 Measure 3: Stigma

An adapted Berger HIV Stigma Scale (Berger et al., 2001) was used to measure stigma, which used 10 relevant questions from the scale to quantify internalized (4

questions) and externalized (6 questions) stigma. The combined scale ranged from 10-40, with a higher score indicating more stigma. Continuous measures of overall, internalized, and externalized stigma were each compared to the continuous ACE score of participants at the EMH time point.

2.5.4 Measure 4: Sex Practices

Measurements of sex practices were determined from a series of questions that asked about sex-related behaviors and characteristics in both studies. Dichotomous variables used for this analysis identified if participants had ever engaged in sexual intercourse, whether participants disclosed their HIV status to their sexual partner, and whether the participant used a condom during their most recent sexual encounter. Continuous variables used for this analysis identified participant age of sexual debut and number of sexual partners.

2.5.5 Measure 5: Social Determinants of Health

Dichotomous measurements for social determinants of health were determined from survey questions that related to participants' gender, presence of a support system, and engagement in work or school. Continuous variables included an additional living condition: the number of people living in a participant's home. Variables related to living conditions were used as a proxy to be indicative of socioeconomic status.

2.5.6 Measure 6: Adherence

Self-reported adherence to antiretroviral medication was measured differently across the two studies. The EMH survey asked about adherence through two questions, one of which identified adherence dichotomously through days of missed medication, and one that identified frequency of adherence categorically. SYV used a validated tool with 3 questions that assessed number of days of missed medication in the past month, frequency of medication adherence, and rate of medication adherence (Wilson et al., 2016). Thus, adherence is presented as a dichotomous variable that indicates if participants ever missed taking their medication, and a continuous variable that quantified how often medication was missed. Further detail is available in Appendix B.

2.5.7 Measure 7: Viral Load

HIV RNA obtained from blood samples were analyzed in a quality assured biotechnology lab. Virologic suppression was defined as HIV RNA < 400 copies/mL and presented as log(10) transformed when presented continuously to limit data skewness.

2.6 Analysis

Analyses were performed using Stata 16 software. Descriptive statistics were presented as N and percentage, mean and standard deviation, or median and interquartile

range. To understand correlations between ACEs and the outcome variables of interest, ACEs were the predictor using the continuous scale (0-8) at the EMH time point only. Linear regression was used to describe the mean difference (β coefficient) with continuous outcome variables and the risk ratio (RR) was reported for binary outcome variables. Each of the statistical tests described used an alpha probability of 0.05 to determine significance.

HIV RNA was analyzed across all time points to determine trends over time. Participants viral status was classified as (i) achieved viral suppression and remained suppressed, (ii) began with virologic failure (HIV RNA > 400 copies/mL), but eventually achieved viral suppression; or (iii) vacillated between suppression and failure. Characteristics of each of these groups were then identified to determine if any key variables of interest were associated with long term viral outcomes to inform clinical predictions of when a YPLWH may be prone to changing virologic status.

3. Results

Participants were 15.8 years old on average at the time of the EMH study, and 66% (n=48) of the participants were female. The overall distribution of demographics and predictors can be seen in Table 1.

Table 1. Population Demographics

Demographic or Predictor	Sub-scale (where relevant)	EMH (2013-2015) (N=73)	SYV (2016-2017) (N=73)
Sex	Female	48 (65.8%)	48 (65.8%)
Age		15.8 (2.3)	17.8 (2.3)
Site	KCMC	33 (45.2%)	33 (45.2%)
	Mawenzi	40 (54.8%)	40 (54.8%)
ACE Score (continuous)	1	4 (5.5%)	2 (2.7%)
	2	10 (13.7%)	23 (31.5%)
	3	25 (34.3%)	27 (37.0%)
	4	26 (35.6%)	15 (20.6%)
	5	6 (8.2%)	5 (6.9%)
	6	2 (2.7%)	1 (1.4%)
PHQ-9 score	Average	5.6 (5.0)	6.3 (4.2)
	>=10	17 (23.6%)	15 (20.8%)
Suicide (Q9 in PHQ-9)	No risk	60 (82.2%)	44 (61.1%)
	Minimal risk	11 (15.1%)	23 (31.9%)
	Medium risk	0	4 (5.6%)
	High risk	2 (2.7%)	1 (1.4%)
SDQ score	Average	13.7 (9.0)	8.0 (3.5)
	>=17	24 (34.3%)	0 (0%)
UCLA reaction index	Average	9.7 (7.2)	9.6 (7.7)
	>=18	10 (14.1%)	13 (17.8%)
Stigma	Overall	20.9 (4.9)	22.7 (4.5)
	Internal	7.0 (2.5)	8.2 (1.9)
	External	13.9 (3.6)	14.7 (3.9)
Sexual history	Has had sexual intercourse	10 (14.1%)	29 (40.3%)
	Average age of sexual debut	14.6 (3.4)	16.7 (2.7)
	Number of sexual partners	2 (1.2)	2.1 (3.0)

Demographic or Predictor	Sub-scale (where relevant)	EMH (2013-2015) (N=73)	SYV (2016-2017) (N=73)
Sexual history	Condom use (if having sexual intercourse)	7 (77.8%)	21 (70.0%)
Substance use	Alcohol	4 (5.6%)	7 (9.6%)
	Drugs	1 (1.4%)	0 (0%)
Social Determinants of Health	Is in school or working	64 (87.7%)	58 (79.5%)
	Has social support	61 (83.6%)	58 (79.5%)
	Number living in home	4.7 (1.8)	4.9 (2.3)
Antiretroviral therapy (ART)	Is receiving ART	67 (91.8%)	72 (98.6%)
	1 st line (NVP)	23 (32.4%)	18 (25.0%)
	1 st line (EFV)	30 (42.3%)	43 (59.7%)
	2 nd line (LVP/r)	11 (15.5%)	0 (0%)
	2 nd line (ATZ/r)	3(4.2%)	11 (15.3%)
Adherence* (continuous)	Do not miss	53 (73.6%)	25 (34.3%)
	Miss some	5 (6.9%)	30 (41.1%)
	Miss often	5 (6.9%)	17 (23.3%)
	Miss very often	9 (12.5%)	1 (1.4%)
Adherence* (dichotomous)	Do not miss	56 (76.7%)	41 (56.2%)
	Miss any	17 (23.3%)	32 (43.8%)
HIV RNA *	>400 copies/mL	24 (33.3%)	19 (27.5%)

*Denominator is of those receiving ART

3.1 Adverse Childhood Experiences

Eight ACE categories were identified from the study questionnaires and were then used to calculate the ACE score for each participant. The overall distribution of ACE scores can be seen in Table 1 and the exposure and time point distribution can be seen in Table 2. No participant had an ACE > 6, and the majority (N=51, (70%)) had a score of 3 or 4. Because all participants in the study live with HIV, they all had the experience of living with a severe childhood illness (all diagnosed before 18), and the majority experienced the loss of a parent (N=54, (74%)).

Youth reported lifetime ACE exposures with at least 75% consistency across the two studies in all categories except physical abuse (62%). While some categories of ACEs were always reported consistently between studies (parent status), most ACEs were reported inconsistently across time. For instance, participants who reported being sexually abused or bullied at some point in their lifetime during the EMH study often did not report such abuse at later time points in SYV. As a result, ACE scores differed across time points for some participants.

Table 2. Distribution of ACE Scores

Adverse Experience	EMH	SYV (baseline)	SYV baseline consistent with EMH*
Serious childhood illness	73 (100%)	73 (100%)	73 (100%)
Loss of parent	54 (74.0%)	55 (75.3%)	73 (100%)
Sexual abuse	5 (6.8%)	8 (11.0%)	69 (94.5)
Physical abuse	41 (56.2%)	22 (31.1%)	45(61.64)
Bullied	17 (23.3%)	2 (2.7%)	57 (78.1%)
Collective violence	2 (2.7%)	3 (4.1%)	71 (97.3%)
Community violence	4 (5.5%)	10 (13.7%)	71 (97.3%)
Witness violence in household	49 (67.1%)	37 (50.7%)	55 (75.3)

* Traumas were considered inconsistent if they were reported in the EMH time point but were not reported at the following SYV time point

As seen in Table 3, positive correlations were found between ACE scores and SDQ scores ($\beta=3.6$, 95% CI [1.8, 5.4]), PHQ-9 scores ($\beta=1.5$, 95% CI [0.5, 2.5]), and UCLA reaction index scores ($\beta=2.0$, 95% CI [0.5, 3.5]), each indicating that higher ACE scores were meaningfully correlated with greater mental health difficulties at the initial EMH time point. Similarly, an increased ACE score was also correlated with higher levels of external stigma ($\beta = 0.8$, 95% CI [0.01, 1.5]). Interestingly, internal stigma was

negatively correlated with an increased ACE score ($\beta = -0.4$, 95% CI [-1.0, 0.2]), though this trend had less statistical significance than external stigma. Figure 1 displays the distribution for the total SDQ, PHQ-9, and UCLA Trauma Index, and stigma scores.

Sex was the only variable that was analyzed as a predictor of ACEs instead of an outcome of ACE exposure since participant sex could not change as a result of trauma. Being female did not predict increased risk of ACEs. With every point increase in ACE score, participants were 1.3 times more likely to engage in sexual activity (RR=1.3, 95% CI [0.7, 2.2]). Those with more ACEs were also likely to have more sexual partners (RR=0.5, 95% CI [-0.3, 1.3]) and an older age of sexual debut (RR=2.0, 95% CI [0.4, 3.7]) though all crossed the null in the confidence interval.

For every one-point increase in ACE score, participants were 1.2 times more likely to reported missing doses of medicine for every increase in ACE score (RR=1.2, 95% CI [0.8, 1.6]). However, the opposite relationship was seen with the categorical classification of adherence ($\beta = -0.2$ 95% CI [-0.4, 0.1]), but neither adherence measurement had statistical significance. As for viral load, risk of being unsuppressed was higher in those with a higher ACE score (RR= 2.0, 95% CI [1.2, 3.2]). Additionally, every participant with an ACE score of 1 (N=4) was virally suppressed.

Table 3. Linear Regression for Continuous ACE as a Predictor at EMH Time Point

Outcome Variable	Coefficient	[95% CI] or mean ACE score per category
SDQ (continuous)	3.6 +	[1.8, 5.4]
PHQ -9 (continuous)	1.5 +	[0.5, 2.5]
UCLA (continuous)	2.0 +	[0.5, 3.5]
Suicide	-0.1 +	[-.2, 0.1]
No risk		3.4
Minimal risk		3.4
Medium risk		N/A
High risk		2.5
Stigma		
Overall	0.3 +	[-.8, 1.4]
Internal	-0.4 +	[-1.0, 0.2]
External	0.8 +	[0.01, 1.5]
Has had sex	1.3 *	[0.7, 2.2]
No		3.3
Yes		3.6
Number of partners	0.5 +	[-.3, 1.3]
Debut age	2 +	[0.4, 3.7]
Disclose to partner	0.9 *	[0.8, 1.0]
No		3.2
Yes		3.7
Condom use	1.1 *	[.7, 1.8]
No		3.0
Yes		3.7
Adherence (continuous)	-0.2 +	[-.4, 0.1]
Do not miss		3.4
Miss some		3.6
Miss often		3.0
Miss very often		2.9
Adherence (dichotomous)	1.2 *	[0.8, 1.6]
Do not miss		3.3
Miss often		3.5
Unsuppressed***(>400)	2 *	[1.2, 3.2]
No		4.0
Yes		2.8
Sex**	0.1 *	[-.4, 0.7]

Outcome Variable	Coefficient	[95% CI] or mean ACE score per category
Male		3.4
Female		3.3
Job/School	0.9 *	[0.86, 1.0]
No		3.4
Yes		2.7
Support	1.1 *	[0.97, 1.2]
No		2.9
Yes		3.4
# Living in home	0.2 +	[-.2, 0.6]

+ Coefficient was determined for a continuous outcome and should be interpreted as a mean difference. CI should not cross 0 for significance.

* Coefficient was determined for a binary outcome and should be interpreted as a risk ratio. CI should not cross 1 for significance

** Sex was the only variable that was analyzed as a predictor with ACE score as an outcome.

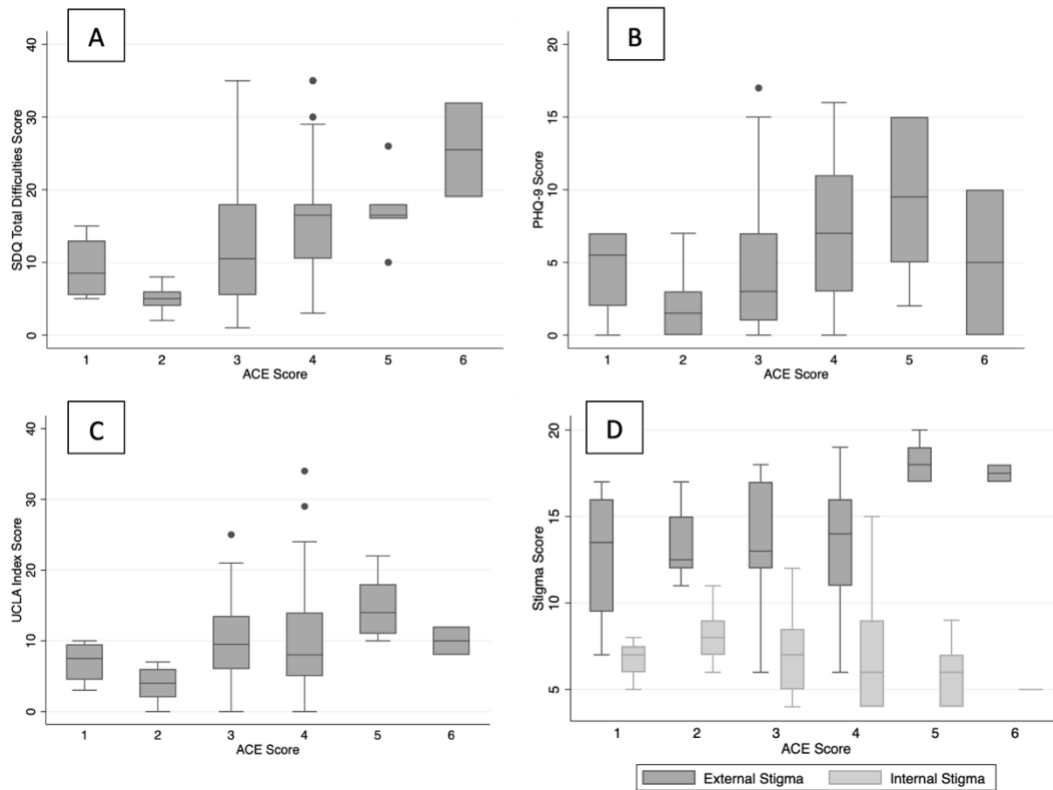


Figure 1: Mental Health and Stigma Scores vs ACE Score

(A) (SDQ score (N=72), (B) PHQ-9 score (N=72), (C) UCLA Reaction Index (N=71), and (D) Stigma; the darker boxes represent external stigma (N=73), and the lighter boxes

represent internal stigma (N=71) The centermost line represents the median score for each ACE value, with the top and bottom of the boxes representing the 75th and 25th percentiles of the score distributions, respectively. The top and bottom “whiskers” indicate the maximum and minimum scores. Points outside of these were greater than 1.5 times the interquartile range and are considered outliers. Participants were not included in several figures (N<73) due to incomplete responses in a given survey.

3.2 Undetectable = Untransmittable

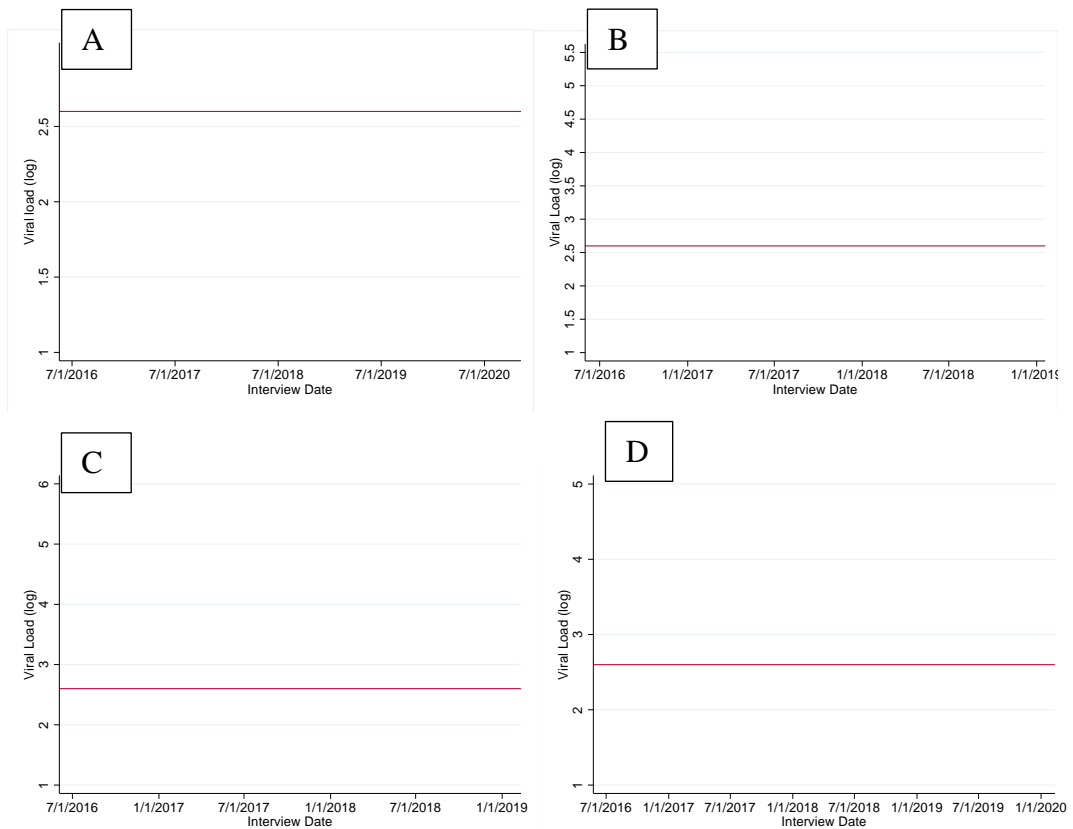
The next step of analysis looked at longitudinal outcomes of viral suppression and potential risk and protective factors that could be used to predict suppression outcomes. Each participant had a minimum of 2 time points from which data were collected (Table 1), but a median of 3 time points were collected overall. The maximum number of time points collected was 10 (N=2), and participants data spanned an average of 4.1 years (SD= 1.3). Analysis was done to determine correlations between predictors and participants’ likelihood of staying suppressed, becoming suppressed, or fluctuating between suppression states. For this, each of the evaluations compared variable status at the participant’s first time point (EMH) with their long-term suppression trends across the longitudinal SYV study. Data were then analyzed to determine if any variables were associated with changes in suppression status. The overall distribution of suppression status can be seen in Table 4 and Figure 2. For this analysis, every time point that a participant had a new HIV RNA (viral load) was included. Though the participant number is small across time points, many trends could be observed.

Table 4. Distribution of Suppression States

	Suppressed at Baseline (HIV RNA <400 copies/mL)		Not suppressed at Baseline** (HIV RNA <400 copies/mL)	
Baseline EMH* (2013-2015)	N= 48 (66.7%)		N=24 (33.3%)	
Change from baseline	Stayed suppressed at all future time points	Did not stay suppressed	Stayed unsuppressed at all future time points	Eventually became suppressed
	N= 32 (43.8%)	N= 16 (22.2%)	N=9 (12.3%)	N=15 (20.8%)

* One participant did not have a viral load at baseline

** 6 of these participants were not taking medication at the EMH time point



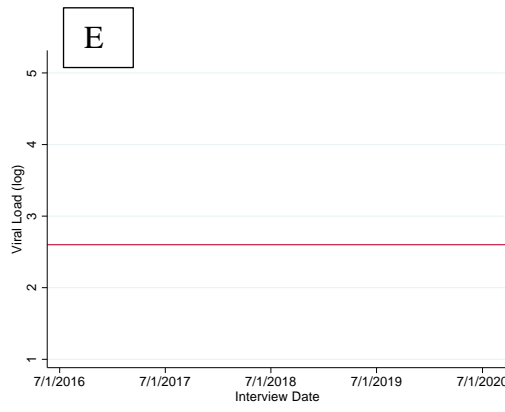


Figure 2: Viral Load (Log) vs Interview Date

(A) Viral load trends for those that were suppressed at the EMH time point and remained suppressed (average of 5.5 timepoints, $N=32$). (B) Viral load trends for those that were unsuppressed at the EMH timepoint and stayed unsuppressed (average of 2.7 time points, $N=9$). (C) Viral load for those that fluctuated between suppression states with 2, 3, or 4 timepoints ($N=7$). (D) Viral load for those that fluctuated between suppression states with 5 or 6 timepoints ($N=13$). (E) Viral load for those that fluctuated between suppression states with 7, 8, 9, or 10 timepoints ($N=11$). The red curve ($VL=2.6$) indicates the cutoff for viral suppression, and darker points and curves indicate increased frequency of occurrence.

Of the participants receiving antiretroviral therapy ($N=67$), 27% ($N=18$) had virologic failure at baseline EMH and 9% ($N=6$) continued to be unsuppressed throughout the study. Of these 33.3% ($N=2$) reported being sexually active, but all sexually active participants with virologic failure that had data ($N=5$) reported using condoms during their most recent sexual encounter at the EMH time point. However, five sexually active participants with virologic failure later reported that they did not use condoms throughout the SYV study. Four participants experience virologic failure at the time of medication change, primarily when switching from 2nd line to 1st line treatment, but each later returned to a suppressed viral load. Nine participants became suppressed at the time of medication change after starting treatment or changing to a similar or more progressed line of treatment. Additionally, 3 of the 4 participants that were sexually

active and virally suppressed at the initial EMH time point ended up fluctuating suppression states throughout the study, and 4 of the 31 participants that became sexually active throughout the study were not suppressed at the time that they started engaging in sexual intercourse.

Most measures of mental health were not meaningfully correlated with long term suppression outcomes. However, participants (N=19) reverted to the unsuppressed status 21 times throughout the study, and 8 of these were associated with a change in suicide severity at the same time point. Though most results lacked statistical significance, certain predictors had consistent harmful or protective trajectories across suppression types. For instance, those that had experienced sexual abuse were less likely to stay suppressed and more likely to fluctuate suppression states, but this was derived from a small sample size (N=5). Those that had experienced sexual abuse were also more likely to revert to an unsuppressed status at the same time point of reporting. Those that had lost a parent were less likely to become suppressed (RR=.7, 95% CI [0.4, 1.3]) or fluctuate suppression states (RR=.7, 95% CI [.2, 1.9]) but were more likely to stay suppressed (RR=1.1, 95% CI [0.7, 1.8]). Internal stigma was not associated with staying or becoming suppressed, but a higher level of internal stigma was correlated with reduced likelihood of fluctuating between suppressions states (RR=0.8, 95% CI [0.6, 1.0]).

As for social determinants of health, several factors had consistent (though statistically non-significant) trends across suppression types. For instance, males were less likely to become suppressed (RR=.75, 95% CI [0.3, 1.8]) and more likely to fluctuate suppression states (RR=2, 95% CI [0.7, 5.7]) than females. Those that reported having

social support at the initial EMH timepoint were more likely to eventually become suppressed (RR=1.7, 95% CI [0.5, 5.3]), and four participants reverted to an unsuppressed viral load at the same time they started having less social support. Additionally, an increased number of people living in the participant's household was correlated with a reduced chance of staying (RR=.9, 95% CI [0.8, 1.0]) or becoming (RR=.7, 95% CI [0.4, 1.3]) suppressed and an increased chance of fluctuating between suppression states (RR=1.1, 95% CI [1.0, 1.3]) relative to those that had the same initial suppression status.

Another factor that had protective, though statistically non-significant, trends was enrollment in the intervention arm of the SYV study. Those that were enrolled in the intervention arm of the SYV program were also less likely to fluctuate (RR=0.9, 95% CI [0.3, 2.6]) between suppression states and were more likely to become (RR=1.4, 95% CI [0.7, 2.8]) and stay (RR=1.2, 95% CI [0.7, 1.9]) suppressed than those that were not enrolled in the intervention arm, which is consistent with findings from previous studies.

4. Discussion

4.1 Common Types of Adverse Childhood Experiences

Though ACEs cannot be erased from one's lived experience, understanding the interconnectedness of ACEs with YPLWH's environments and health outcomes through this descriptive analysis can inform future interventions to prevent ACEs for the next generation and reduce the burden that they impose on young people's lives. No participant reported exposure to all ACEs (max reported was six); however, at least two participants were exposed to each category of ACEs.

The most common ACEs were experience with a serious childhood illness as all participants live with HIV and nearly three-quarters, 74% (N=54), experienced the death of a parent. Of those that knew their mother's (N=18) or father's (N=16) cause of death, 78% reported that their mother passed away from HIV and 57% (N=9) reported that their father passed away from HIV. Losing a parent to HIV/AIDS has been shown to affect many areas of mental health and create worse outcomes than other causes of parental death (Nabunya & Ssewamala, 2014). Thankfully, improvements in HIV testing and treatment have created better outcomes for people living with HIV (UNAIDS, 2021). Along with this, medications to prevent mother to child transmission has dramatically reduced the number of children living with HIV (Buchanan et al., 2014; Mwendu et al., 2014; UNAIDS, 2021). Through test and treat strategies, these interventions will reduce these ACEs for the next generation for HIV exposed newborns to grow up HIV free with healthy parents to raise them.

Experiencing and witnessing abuse were other common ACEs amongst this population. The data did not allow for identification of the exact circumstances of this abuse, but it has been well documented that occurrences of abuse are common both at home and school (UNICEF, 2017). Experiencing physical or sexual abuse during adolescence has been correlated with later risk of engaging in more HIV risk behaviors and of engaging in physical or sexual violence later in life (Richter et al., 2014), and it has been suggested that prevention of child abuse be included in HIV prevention agendas (Jewkes et al., 2010).

Several interventions have been developed throughout Tanzania and East Africa to curb these trends. For instance, a gender-based violence program that is administered through HIV/AIDS programs has been proven to be both feasible and effective in reducing behaviors surrounding violence (Settergren et al., 2018), and several other studies have reduced intimate partner violence and teacher abuse throughout Tanzania and East Africa (Abramsky et al., 2014; Knight et al., 2018; Nkuba et al., 2018). Addressing these forms of violence will ideally reduce both the amount of abuse experienced by YPLWH and prevent such behaviors for the next generation.

4.2 Association of ACEs on Key Health Outcomes

The data provided critical insight into how ACEs influence health outcomes in YPLWH. One important trend observed throughout the study was the correlation between ACEs and mental health. All three mental health measures (SDQ, PHQ-9, UCLA Reaction Index), had direct association with ACE scores (higher ACE scores meant increased mental health symptoms). Several studies have previously evaluated ACEs in

YPLWH in Africa and found that ACEs were meaningfully correlated with mental health outcomes (Kidman et al., 2018; Kidman et al., 2019). A previous study of 546 adolescents found that ACE scores and PHQ-9 scores were positively correlated ($\beta = 1.1$, 95% CI [0.872, 1.373]) (Tsehay et al., 2020), which was similar to the results found in this study ($\beta=1.5$, 95% CI [0.5, 2.5]). Though a validated ACE questionnaire was not used in this study, the congruency found between these trends indicates that the approach used to calculate ACE scores for participants in this study yielded similar and expected results, supporting this method as a proxy for ACE scores.

Another interesting trend was that internal and external stigma seemed to have opposite correlations with ACE scores. In the future, stigma should be further investigated; previous studies in this population also found surprising results regarding stigma, as mental health treatment through SYV was correlated with improved internal stigma but worse external stigma outcomes (Dow et al., 2020). Those with higher ACE scores may have experienced more situations in which they were negatively viewed or mistreated by others, which may have resulted in an increased perception of being negatively viewed by others (external stigma) in relation to their HIV status as well. Those with a higher ACE score may have also had an easier time accepting their HIV diagnosis, which could have resulted in lower levels of internal stigma.

An increased number of ACEs was also associated with a greater number of sexual partners, which has been shown in previous literature (VanderEnde et al., 2018). A greater age of sexual debut was also reported with an increased number of ACEs, which contradicts previous literature (Hillis et al., 2001). It should be noted, however, that all

participants had a sexual debut at 13-18 years (N=9), except one participant that reported a debut age of 6 years (though they did not report sexual abuse), which could have greatly skewed these results. .

Additionally, being employed or enrolled in school was associated with reduced ACE scores. Participants that were not in school nor working (N=8) were 17 years or older (17.6-21.8 years) at the time of the interview. To counteract the potential burdens created by ACEs, providing resources for employment and employment empowerment could provide benefit to the negative burdens associated with ACE scores and would align with the national aims of improving youth employment (MLEYD, 2007). Increased social support was associated with a higher ACE score, which was unexpected, as literature has often found the opposite (Folayan et al., 2020). A majority of those that reported having social support indicated that their parent was the person that they would turn to. Since many of the traumas identified in this study may have affected both the participant and parent, this may have led to increased levels of support in these relationships relative to previous literature.

The expected trends were also observed between ACE scores and adherence and viral outcomes. ACE scores in this study were also meaningfully correlated with suppression status, with higher ACE scores predicting increased risk of virologic failure (HIV RNA >400 copies/mL). The pathway to this correlation may be mediated indirectly through mental health and SDH given ACEs were also correlated with these important variables.

4.3 Viral Suppression Trends

Knowing if participants who achieve viral suppression stay virally suppressed or vacillate between virologic suppression and virologic failure is important for strategic counseling of HIV transmission risk in YPLWH. In Tanzania, adolescents living with HIV are classified under the same HIV viral load (HVL) testing algorithm as adults (MoHCDGEC, 2019). Under these guidelines, adolescents receive HVL testing annually, unless the result is >1000 copies/mL. In that case, enhanced adherence counseling is recommended with a follow-up HVL after three adherence visits (approximately 3 months). These guidelines assume that once viral suppression is reached, it is likely to be maintained and allows for a great amount of time between tests in which adolescents may have virologic failure before it is discovered. This analysis is one of the first studies for this population that identifies whether this assumption holds true.

Of the participants in this study that had achieved viral suppression at the beginning of the study (N=48), one third (N=16) had subsequent virologic failure at some point throughout the study. Of those that achieved suppression at some point after the initial time point (N=15), 20% (N=3) also eventually reverted to virologic failure. Previous research has also found that this trend is less common in adults, as they tend to maintain viral suppression over time more than adolescents (Fokam et al., 2019; Kwarisiima et al., 2017). This fluctuation is a great risk to YPLWH because inadequate suppression can increase the likelihood of having viral mutation, resistance to medication, and disease progression towards AIDS. Additionally, being unsuppressed increases the chances that HIV will be transmitted to sexual partners, which is a primary

concern for this population since several participants with virologic failure reported that they did not use condoms during intercourse throughout the study.

Understanding the various suppression patterns as well as the environmental and health characteristics that are associated with these outcomes may provide insight to helping clinicians predict when virologic failure is likely to occur. For times when testing is not available, this study has identified possible factors that could aid in predicting when a YPLWH is at risk of virologic failure. For instance, reporting worsened social support or a new experience of sexual abuse were both associated with participants reverting to an unsuppressed viral load, though the sample size was small. In association with prior knowledge of the protective factors that social support has on HIV outcomes, it is especially important to ensure that YPLWH have a strong support system (Cheong et al., 2017; Kahamba; et al., 2017). Additionally, reporting suicidal thoughts was also commonly associated with a change in viral suppression, and those with increased prevalence of suicidal thoughts had worse long-term outcomes with viral suppression. Youth should therefore be monitored both for risk of suicide and risk of virologic failure. Notably, several occurrences of virologic failure were associated with participants switching from a 2nd line to 1st line treatment. Though these shifts in medications could be from conditions such as medication shortages, considerable effort should be made to ensure participants are appropriately prescribed medications and supported through changes in regimen.

Being male was associated with worse suppression outcomes, which aligns with previous findings of men having worse ART adherence. Having an increased number of

people living in one's household was also associated with worse suppression outcomes, possibly due to concerns of unintended disclosure and hiding medication. Alternatively, increased household size tends to be correlated with increased levels of poverty in Tanzania (WorldBank, 2015), so this suggests that those in lower income households may have reduced chances of becoming or staying suppressed, which is consistent with previous findings (Kahamba; et al., 2017; Tomori et al., 2014). Again, improving employment empowerment and resources could help offset this burden in those that are old enough to work (MLEYD, 2007).

Based on these findings, it is recommended that mental health, social support, changes in the household should be evaluated at clinic visits and ALWH with reported risk factors have more frequent HVL testing. Guidelines for adolescents should be categorized separately from adults as they are at higher risk of emotional, physical, and social transitions and may be more likely to engage in risky sexual behavior or have poor adherence to ART medication in the face of changing environments. As ALWH have been shown to be at increased risk of virologic failure, increased access to testing would allow a quicker detection of virologic failure and reduced likelihood of HIV progression and transmission (Fokam et al., 2019; Scott Braithwaite et al., 2014). In alignment with this, the SYV program was shown to improve these virologic outcomes, so efforts should be made to promote its reach throughout Tanzania.

4.4 Study Limitations

There are several limitations of this study. The ACE score calculation is derived from other trauma exposure screeners used in the EMH and SYV study and applied to the ACE criteria specified by the literature (Felitti et al., 1998; Hughes et al., 2017; WHO, 2020a). Several traumas outlined in the WHO ACE-IQ were not asked in this survey, and many of the ACEs that were included in this study had a less comprehensive set of questions than found in ACE specific questionnaires. Additionally, ACEs are typically asked of adults about their life up to 18 years. Given the mean age at EMH was 15.8 years, one may continue to accumulate ACEs in their adolescence. Therefore, the ACE data provided here may have an incomplete scope of the actual number of ACEs participants will face.

Some variables used were discordant between surveys. Examples include adherence, which asked about different time frames number of missed doses between surveys. With this, the dichotomous and continuous measures of self-reported adherence had opposite trends in association with ACEs and minimal to no associations with viral load at the EMH time point. Additionally, virologic failure tended to change with both improved and worsening adherence at the same time point, again showing the discrepancies in the adherence measurements. This indicates that the self-reported adherence measures, especially those used at the EMH time point, may not have been an accurate measure of adherence. Some of this may be explained reporting bias due to participant self-report.

Additionally, measurements of mental health are not always valid across different languages and cultures due to the differences in symptom presentation and the language surrounding it; therefore, the conclusions drawn from them may not be accurate representations of the actual population. Though most of the studies had been previously validated across languages and various countries, the SDQ survey has had variable applicability across settings (Hoosen et al., 2018; Sharp et al., 2014). Since this was not used for diagnosis and only to indicate presence of common emotional and behavioral challenges relative to others in the study cohort, these discrepancies have limited impact on the validity of the results.

The relatively small sample size also limited the number of outcomes that had statistical significance through this study, especially when it came to analyzing differences between subcategories of the population. As the database continues to grow with the addition of more participants being enrolled in SYV, trends and findings will have more statistical weight. With this, participants had a range of timepoints collected (between 2 and 10), so those with fewer timepoints collected had fewer opportunities to switch suppression categories. Ideally, the number of timepoints collected would be consistent across participants to counteract these discrepancies.

This study primarily referenced individual's total ACEs scores, but it would be worthwhile to further investigate the correlations between individual ACEs with health and environmental variables in future studies. With this, the study did not quantify the effects of common emotional abuse and neglect, which are ACEs that have also been shown to have a great amount of impact on HIV and mental health outcomes (Jewkes et

al., 2010). In future iterations of the study, it would be beneficial to include a more standardized ACE questionnaire that accounts for such factors that could be incorporated into the analysis.

5. Conclusion

This analysis provided insight into potential factors that contribute to important health outcomes in YPLWH. Findings showed the prevalence of exposure to adverse childhood experiences and their correlations with various health outcomes. From this, it is clear that addressing and preventing ACEs through interventions such as the SYV mental health and life skills intervention and other related programs could have lasting effects on sustained health. The database created in this study also allowed for a unique analysis of virologic suppression trends over time. Combined, the data highlight the associated factors with virologic failure and potential benefits from evaluating key factors that may predict virologic failure requiring sustained surveillance of this population.

At a national level, the insight gained can aid in continuing Tanzania's progression towards the 95-95-95 goals by improving adherence and continuing risk assessment in the population most at risk of virologic failure. Additionally, these findings would support policy efforts to increase access to HVL testing for youth, as it has been shown that they are at a substantial risk of virologic failure, even when they have previously had viral suppression. Overall, this knowledge aids in upholding the UN's Sustainable Development Goal of ensuring health and well-being (UNICEF, 2020; United Nations, 2015), while providing insight that can have a direct impact on the health of YPLWH in Tanzania.

Appendix A: ACE Score

Each participant was given an ACE score between 1 and 8. For each ACE-identified trauma that a participant had experienced, the participant's ACE score increased by 1. Living without a parent, whether from parental separation or death, is considered to be an ACE (WHO, 2020b). Therefore, participants' ACE scores increased by one if their responses indicated that one or more of their parents had passed away in the EMH study. Experiencing bullying is another ACE. If a participant indicated that they were "sometimes" or "usually" bullied in their SDQ responses, their ACE score was increased by one. Additionally, living with a serious childhood illness has been identified as an ACE and source of toxic stress in literature (Hughes et al., 2017). Since all the participants were living with HIV before they were 18, they were all considered to have an additional ACE score of 1. Though this inclusion increased each participant's ACE score, it did not significantly affect the regression results derived in analysis since it applied to all participants.

The remainder of the ACEs were derived from the UCLA Reaction Index. ACE scores were considered separately from the UCLA index because though traumas are indicated through the UCLA Index, they are not all considered to be sources of prolonged toxic stress. In the UCLA Index, responses were ranked on a Likert scale where trauma frequency could be reported as happening "never," "one time," or "more than one time." If a trauma was reported as having happened at all (one time or more than one time), a participant's ACE score was increased by one. This is in accordance with the binary version of the ACE score as outlined by the WHO ((WHO, 2020c). The traumas

identified from the UCLA Reaction Index were physical abuse, sexual abuse, community violence, collective violence, and witnessing the violent treatment of a family member. Physical abuse was derived from a single question that asked if participants had been beaten to the extent that it created fear, and sexual abuse was derived from two questions that asked if participants had been raped or inappropriately touched without consent. Community violence was derived from two questions that asked if participants had witnessed someone in their town be shot at or killed or witnessed someone be hurt or killed in a conflict, war, or riots. Collective violence was derived from a question that asked if participants were forced to move or run due to war or conflict. Witnessing violence was derived from three questions that asked if participants had seen a household member being treated violently, raped, or killed.

ACE Identification and Characterization

ACE	Source	Included	Question
Physical Abuse	(Hughes et al., 2017; WHO, 2020a)	Yes	UCLA: physical abuse
Emotional Abuse	(Hughes et al., 2017; WHO, 2020a)	No	N/A
Contact Sexual Abuse	(Hughes et al., 2017; WHO, 2020a)	Yes	UCLA: sexual abuse; UCLA: rape
Alcohol and/or drug abuser in the household	(Hughes et al., 2017; WHO, 2020a)	No	N/A
Incarcerated household member	(Hughes et al., 2017; WHO, 2020a)	No	N/A
Someone chronically depressed, mentally ill, institutionalized, or suicidal	(Hughes et al., 2017; WHO, 2020a)	No	N/A
Household member treated violently	(Hughes et al., 2017; WHO, 2020a)	Yes	UCLA: witness family abuse;

			UCLA: witness family member killed; UCLA: witness family member sexual assault
One or no parents, parental separation, or divorce	(Hughes et al., 2017; WHO, 2020a)	Yes	Questionnaire: death of parent
Emotional neglect	(Hughes et al., 2017; WHO, 2020a)	No	N/A
Physical neglect	(Hughes et al., 2017; WHO, 2020a)	No	N/A
Bullying	(Hughes et al., 2017; WHO, 2020a)	Yes	SDQ: Bully
Community violence	(WHO, 2020a)	Yes	UCLA: Witness hurt/killed during war/conflict; UCLA: Witness shot/killed in town
Collective violence	(WHO, 2020a)	Yes	UCLA: forced to leave home from war/conflict
Serious childhood illness or injury	(Hughes et al., 2017)	Yes	HIV diagnosis before 18
Separation from family	(Hughes et al., 2017)	No	N/A
Family conflict or discord	(Hughes et al., 2017)	No	N/A
Family financial problems	(Hughes et al., 2017)	No	N/A

Appendix B: Adherence Recategorization

The dichotomous adherence variable evaluated questions in each survey that indicated if participants had ever missed their medication. Here, the variable responses were standardized to either always taking their medication or periodically missing their medication. The continuous variable used adherence questions from each survey that were related to the frequency with which participants missed their medication. In the EMH survey, this question had four responses asking for the number of missed days in the past week. In the SYV surveys, the questionnaire provided four responses for the number of missed days in the previous 30 days. These were each then recategorized to correspond to be one variable that identified if participants “never miss,” “rarely miss,” “often miss,” and “always miss.”

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