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THE RELATIONSHIP BETWEEN ADVERSE CHILDHOOD EXPERIENCES AND HIV PREVALENCE AMONG ADOLESCENT GIRLS AND YOUNG WOMEN IN MPUMALANGA: AN HPTN068 ANALYSIS; 2017

By

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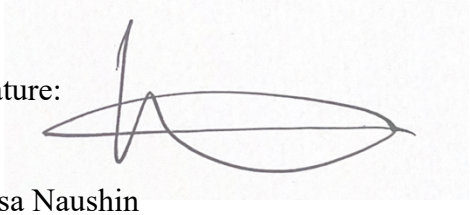
DECLARATION

I, Lamisa Naushin, declare that this Research Report is my unaided work. It is being submitted for the Degree of Master of Science in Infectious Disease Epidemiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

Signature:  Date: 13 Jan 2025

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DEDICATION

To my parents and sister, your unwavering support has been the foundation of my academic journey.

To my partner, Daniel Sher, your kindness, patience, and encouragement sustained me through every challenge.

ABSTRACT

Introduction: Adverse childhood experiences (ACEs) encompass various forms of childhood adversity, including neglect, sexual and physical abuse, and household dysfunction. In Sub-Saharan Africa, adolescent girls and young women (AGYW) face a high prevalence of both HIV infection and ACEs. These experiences have been linked to a range of negative health outcomes, including an elevated risk of HIV infection. Prior research has predominantly focused on the influence of ACEs on HIV related risk behaviours and often overlooks the broader spectrum of ACEs such as exposure to household and community violence. This study aimed to examine the relationship between ACEs and HIV prevalence among AGYW in rural South Africa, with a focus on both cumulative ACEs and individual categories of ACEs and their relationship with HIV infection.

Methods: This cross-sectional study utilised existing data from HIV Prevention Trials Network (HPTN) 068 randomised controlled trial. HPTN 068 investigated the effectiveness of a monthly cash transfer intervention in reducing HIV incidence among AGYW. In this study, individual ACE categories were dichotomised and included physical abuse, emotional abuse, witnessing verbal violence at home, witnessing physical violence at home and witnessing community violence during childhood. Age of sexual debut of less than 14 years was used as a proxy for childhood sexual abuse. A cumulative ACEs score was created, ranging from 0 to 4 or more ACEs. Descriptive analysis was conducted to estimate the prevalence of ACEs and their association with HIV status. The study then used logistic regression models to examine the relationship between cumulative ACEs and HIV prevalence as well as individual ACE categories and HIV prevalence. In addition, mediation analysis was conducted to assess the potential mediating effects of various variables between childhood physical abuse and HIV status. Lastly, a sensitivity analysis was conducted to exclude AGYW living with HIV at enrolment of the primary study, as these individuals were likely to have been perinatally infected with HIV.

Results: HIV prevalence was estimated at 11.48%. While 38% of participants reported no ACEs, 62% experienced at least one ACE. There was no significant association between cumulative ACEs and HIV prevalence. However, individual ACEs such as childhood physical abuse (aOR: 1.57, 95% CI: 1.03–2.41, p=0.038) and witnessing physical violence at home during childhood (aOR: 1.63, 95% CI: 1.07–2.49, p=0.022) were associated with higher odds of HIV infection. Witnessing community violence during childhood was associated with lower

odds of HIV infection (aOR: 0.69, 95% CI: 0.49–0.98, p=0.037). Early sexual debut (aOR: 0.68, 95% CI: 0.20–2.35, p=0.542), childhood emotional abuse (aOR: 1.44, 95% CI: 0.94–2.22, p=0.096), and witnessing verbal violence during childhood (aOR: 0.65, 95% CI: 0.41–1.05, p=0.077) were not significantly associated with HIV prevalence. Mediation analysis suggested that none of the examined mediators demonstrated statistically significant mediation between childhood physical abuse and HIV prevalence. Lastly, the sensitivity analysis suggested that findings remained fairly consistent between HIV prevalence and an approximation of HIV incidence over the course of the study, after removing AGYW with prevalence HIV at enrolment.

Conclusion: Individual ACEs, particularly childhood physical abuse and witnessing physical violence at home, are significant factors associated with greater odds of HIV infection among AGYW in rural South Africa. These results underscore the need for targeted, trauma-related interventions, such as trauma informed care, community-based education programmes, counselling services, and the development of safe spaces for children, adolescents and women.

ACKNOWLEDGEMENTS

I am profoundly grateful to my supervisors, Prof Sumaya Mall and Dr Marie Stoner, whose guidance, expertise, and support have been extremely important throughout the course of my research. Their invaluable insights, constructive feedback, and encouragement have shaped this thesis. I am truly privileged to have had the opportunity to work with them both.

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LIST OF ACRONYMS

ACASI	Audio Computer-Assisted Self-Interview
ACE	Adverse Childhood Experience
ACE-IQ	Adverse Childhood Experiences International Questionnaire
AGYW	Adolescent Girls and Young Women
AIDS	Acquired Immunodeficiency Syndrome
ARV	Antiretroviral
aOR	Adjusted Odds Ratio
BRFSS	Behavioural Risk Factor Surveillance Survey
CI	Confidence Interval
CDE	Controlled Direct Effect
CSA	Childhood Sexual Abuse
DAG	Directed Acyclic Graph
HDSS	Health and Demographic Surveillance Site
HIV	Human Immunodeficiency Virus
HPTN	HIV Prevention Trials Network
HREC	Human Research Ethics Committee
HSV-2	Herpes Simplex Virus Type 2
IRR	Incidence Rate Ratio
NDE	Natural Direct Effect
NIE	Natural Indirect Effect
OR	Odds Ratio
PTSD	Post-Traumatic Stress Disorder
RCT	Randomised Controlled Trial
SES	Socioeconomic Status
SSA	Sub-Saharan Africa
STI	Sexually Transmitted Infection
TE	Traumatic Event
TE	Total Effect
USA	United States of America
VACS	Violence Against Children and Youth Survey
WHO	World Health Organization

CHAPTER 1: INTRODUCTION

1.1 Background

Adverse Childhood Experiences

The relationship between early life events and health and development in adolescence and adulthood is widely acknowledged, and critical to illness over life trajectories (1–3). Positive childhood experiences, marked by nurturing, caregiving, and supportive environments, are linked to lifelong well-being, productivity, and health (1,4,5). On the contrary, adverse childhood experiences (ACEs) have been consistently associated with various negative outcomes including, behavioural outcomes such as alcohol and drug use, tobacco use, and medical outcomes such as respiratory disorders, obesity and cardiovascular disorders (1–3,6).

The Centers for Disease Control and Prevention define ACEs as a range of potentially traumatic events (TE) and environmental factors that occur between the ages of 0 and 17. These include being a victim of abuse, violence or neglect, as well as observing violence within the home or community (7). Abuse can occur in various forms, such as, physical, emotional or sexual, while neglect can be either physical or emotional (3). Physical abuse involves a parent or guardian hitting, punching, or kicking a child, or using objects such as sticks, knives, or whips to inflict harm (8). Emotional abuse involves a parent or guardian yelling, screaming, insulting, or humiliating a child, or threatening to abandon, or actually abandoning the child. Sexual abuse can involve someone, not necessarily a household member, touching or fondling a child in a sexual manner, or attempting or having oral, vaginal, or anal intercourse against the child's will (8). Emotional neglect involves parents or guardians ignoring the child's emotional well-being and failing to address the child's worries. Physical neglect includes not sending a child to school, failing to provide adequate food or shelter, or not ensuring appropriate medical care when needed (8). ACEs also include elements of the child's broader environment which have a negative effect on their sense of safety, for example being raised in a household affected by drug use, mental illness, parental separation or imprisonment of household members (7). It is common for children to experience more than one form of violence (9–11). The term ACE is synonymous with childhood trauma or childhood maltreatment (3).

The History of Adverse Childhood Experiences Research

In 1998, Dr. Vincent Felitti and his colleagues published their seminal paper "Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults: The Adverse Childhood Experiences (ACE) Study", popularly referred to as the ACEs study (6). The landscape of ACEs research has been significantly shaped by this groundbreaking work, which laid the foundation for understanding the profound and long-lasting impact of ACEs on adult health outcomes. As a result of this study, the term ACEs has become widely utilised in the health and social services sectors (1).

Felitti was a physician focusing on obesity treatment, who discovered a compelling correlation between obesity and childhood experiences of sexual abuse. Felitti observed that for these individuals, eating functioned as a coping mechanism to deal with anxiety and depression, while obesity served as a protective shield against unwanted attention (1).

Building upon these observations, the ACEs study delved into the complex relationship between disease in adulthood and experience of physical, sexual, or emotional abuse, and household dysfunction during childhood (6). The study found that exposure to individual ACEs rarely occurred in isolation. When a person reported experiencing a single category of ACE, the probability of experiencing at least one additional ACE ranged from 65% to 93% (6). This suggests that individuals who experience one ACE are at an increased likelihood of experiencing multiple ACEs.

Notably, the ACEs study also identified a dose-response relationship, illustrating the cumulative nature of ACEs (6). This pivotal finding led to the creation and utilisation of a total score of ACEs, representing the cumulative effect of ACEs on adult health outcomes (1). The ACEs study found that individuals who had experienced four or more ACE categories, in comparison to those who experienced none, exhibited a 4-12-fold increase in health risks for conditions such as drug use, alcoholism, and mental health issues (6). Additionally, they displayed a 2-4-fold rise in poor self-rated health, smoking, having more than fifty sexual partners, and contracting sexually transmitted infections (STIs) (6).

The initial ACEs study included seven experiences, namely physical, emotional, and sexual abuse, household substance abuse, violence against a mother, a mentally ill household member,

and an incarcerated household member (6). Over time, ACEs research evolved with the inclusion of additional adversities (12). This expanded framework facilitated a more comprehensive understanding of the adversities which individuals may experience during their formative years.

Since the original ACEs study, ACEs research has consistently documented associations between early life adversity and a plethora of mental and physical health outcomes in adulthood (1–3,13). As the field of ACEs expands, there is a shift in research focus towards more detailed outcomes, broader levels of analysis, and well-defined sub-populations (1). This approach aims to deepen the understanding of the influence of ACEs on health and well-being.

Adverse Childhood Experiences and Health Outcomes

Adverse childhood experiences have been extensively studied and are known to significantly affect mental and physical health as well as health-related behaviour (14). Early-life exposure to chronic stress affects the development of the nervous, immune, and endocrine systems, potentially leading to reduced social, cognitive, and emotional capabilities (15). These physiological changes, combined with engagement in detrimental health behaviours, increase the susceptibility of individuals with ACEs to various health conditions (2,15).

ACEs have a substantial impact on brain development. This impact involves overstimulation of the autonomic nervous system (16) and dysregulation of the hypothalamic–pituitary–adrenal axis (17) (See Figure 1), leading to short-term physical and behavioural changes in response to stressors (18). However, persistent and excessive stimulation of these systems can result in stress-related disorders, implicated in the development of physical and psychiatric diseases as individuals age. This indicates the cumulative strain on the body's regulatory systems caused by prolonged exposure to traumatic stressors (18).

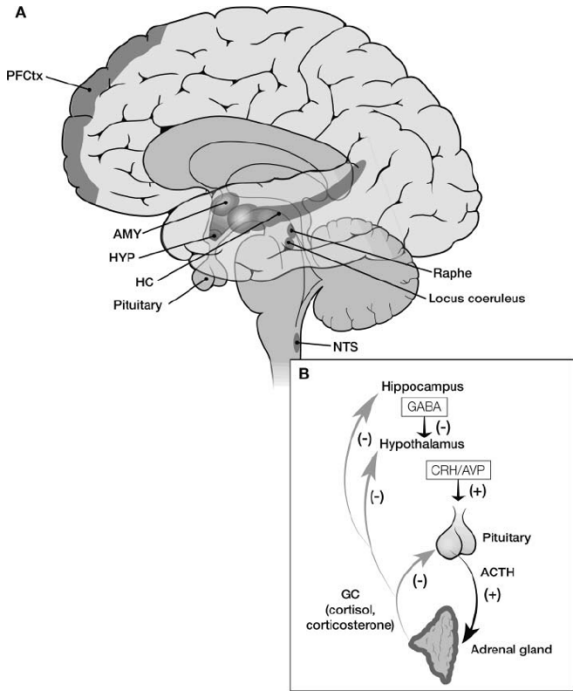

Figure 1. Illustration depicting the anatomy of the hypothalamic–pituitary–adrenal system (19)

Furthermore, evidence suggests that chronic stress response activation due to ACEs, without adequate support, influences dysregulation of the immune and neuroendocrine systems (18). This dysregulation, influenced by social, biological and genetic factors, alters brain architecture and other organ systems, particularly during sensitive developmental periods. The negative health outcomes in adulthood resulting from ACEs encompass a spectrum of physiological, epigenetic, and cognitive consequences (13).

Prevalence of Adverse Childhood Experiences

Globally, over 50% of children aged 2 to 17 years have encountered some form of violence (20). Previous research has identified a significant burden of ACEs among adolescents in South Africa. Richter et al. (10) found that nearly all children (99%) in the Birth to Twenty-Plus cohort in Soweto, an urban region of South Africa, reported exposure to or direct experience of violence within their home, school, and/or community. These experiences ranged from witnessing or hearing violent episodes, exposure to peer violence, and personal experiences of violence, including sexual violence (10). Similarly, a nationally representative survey, including both urban and rural settings, conducted in 2015 reaffirmed the pervasiveness of child abuse in South Africa, albeit at a lower prevalence compared to the specific urban setting of Soweto (21). The survey targeted young people aged 15 to 17 years and revealed the

following statistics: 20% of respondents reported experiencing sexual abuse in their lifetime, 30% reported being subjected to physical abuse by an adult caregiver, 16% reported emotional abuse, and 20% reported feeling neglected by their parents (21).

The Relationship between Adverse Childhood Experiences and HIV

Adverse childhood experiences play a crucial role in determining vulnerability to human immunodeficiency virus (HIV) infection (22). ACEs are increasingly acknowledged as clinically significant predictors of HIV risk and HIV-related disease burden (22–25). ACEs are common among people living with HIV and are linked to health risk behaviours that elevate the transmission of HIV. These behaviours include illicit drug use, alcohol abuse, engaging in risky sexual behaviours and intimate partner violence (22,26–28). Additionally, ACEs have been linked to poorer HIV prognosis by reducing adherence to antiretrovirals (ARVs), thus leading to higher viral loads (25).

HIV infection remains a significant global health challenge, with estimates indicating 1.3 million incident cases and 630,000 deaths related to acquired immunodeficiency syndrome (AIDS) in 2022 (29). Women and girls accounted for 46% of incident HIV infections worldwide. In sub-Saharan Africa (SSA), this burden falls disproportionately on adolescent girls and young women (AGYW), who make up 77% of all new infections. Notably, AGYW in SSA are three times as likely to acquire HIV compared to men of the same age (29). In South Africa, particularly in KwaZulu-Natal, HIV incidence rates were found to be greatest among adolescent girls aged 15–19 years (7.79 per 100 person-years) and women aged 20–24 years (8.63 per 100 person-years) (30). While biological factors, such as the larger mucosal surface area in females exposed to HIV during intercourse, contribute to this disparity, it is imperative to recognise the equally significant role played by sociocultural, power, and economic inequalities. These factors intersect to create a complex web of challenges, influencing access to healthcare, educational opportunities, and the ability to negotiate safe sexual practices (31)

The intersection of ACEs and HIV is complex, as ACEs can influence health-related behaviours and exposure to risk factors associated with HIV transmission. What makes this population of AGYW particularly unique is that they face a double burden of both HIV and traumatic experiences, including ACEs (10,29,32). Investigating the relationship between

ACEs and HIV prevalence in this population can provide valuable insights into the factors contributing to the elevated HIV burden among AGYW in this region.

1.2 Literature Review

This section synthesises literature that explores different themes related to ACEs and HIV. It includes discussions on sections 1.2.1 ACEs and health outcomes, 1.2.2 ACEs and sexual risk-taking behaviour, 1.2.3 cumulative ACEs versus individual ACEs, and lastly, 1.2.3 the relationship between ACEs and HIV.

1.2.1 Adverse Childhood Experiences and Health Outcomes

Since the work of Felitti (6), research into the impact of ACEs on health reveals a consistent pattern of associations between ACEs and negative physical and mental health outcomes (2,3,13). A systematic review and meta-analysis by Petruccelli et al. (3) examined and synthesised 96 articles on ACEs and associated health outcomes. They found evidence of a dose-response relationship between the number of ACEs experienced and negative health outcomes, meaning the greater the number of ACEs experienced the greater the odds ratio (OR) associated with that negative health outcome. This was observed for almost all of the behavioural outcomes studied, including smoking, alcohol use disorder, depression, unsafe sexual behaviours, illicit drug use, suicidal thought, poor diet and anxiety. For example, individuals with four or more ACEs had more than double the odds (OR: 2.55, 95% CI: 2.39-2.71) of engaging in unsafe sexual behaviours compared to those who experienced no ACEs (3). The same dose-response relationship was found for poor medical outcomes, including respiratory disorders, sleep disturbances, cardiovascular disease, gastrointestinal disease, somatic pain, and memory deficits. For instance, individuals who had experienced four or more ACEs had double the odds (OR: 2.28, 95% CI: 1.95-2.68) of developing respiratory disease compared to those who experienced no ACEs (3).

A similar meta-analysis and systematic review conducted by Hughes et al. (2) examined and synthesised 37 articles about the relationship between multiple ACEs and health outcomes. The observed relationships lacked significance for lack of physical activity, obesity, and diabetes in relation to exposure to ACEs. A moderate strength for tobacco use, alcohol use disorder, cancer, respiratory disease, and cardiovascular disease, with ORs ranging from two to three,

was observed. The relationships were strong for unsafe sexual behaviours, mental health issues, and alcohol use disorder, with ORs ranging from three to six. The strongest associations were identified for illicit drug use as well as self-directed and interpersonal violence, with ORs of greater than seven. Individuals who had experienced a minimum of four ACEs faced an elevated risk across all health outcomes compared to those with no ACEs (2).

ACEs not only impact adult health outcomes but also exhibit a more immediate influence on child health. ACEs have the potential to disrupt the development of the brain and other body systems, with physiological manifestations detectable during childhood (13). Oh et al. (13) conducted a systematic review, consisting of 35 studies, which aimed to comprehensively understand the paediatric health outcomes associated with ACEs. The reviewed studies revealed that exposure to ACEs was significantly associated with various health challenges in children, including delays in cognitive development, asthma, increased susceptibility to infections, somatic complaints, and disruptions in sleep patterns. For instance, the studies reviewed showed a moderately strong relationship between asthma and childhood adversity, with ORs ranging from one to two. One particularly noteworthy finding was that exposure to ACEs was correlated with alterations in immune and inflammatory responses, suggesting a profound impact on the physiological mechanisms governing the body's defence and regulatory systems (13).

The impact of ACEs extends beyond the individual experiencing them and can affect the well-being and health of subsequent generations (33). A systematic review revealed that offspring of parents exposed to ACEs face a greater risk of various negative health, well-being, and developmental outcomes. For example, a reviewed study showed that each additional maternal ACE was associated with an 18% rise (RR: 1.18, 95% CI: 1.08-1.29) in the risk of developmental delays in communication, motor skills, and problem-solving by age of two (33,34). Notably, this relationship demonstrated a dose-response pattern, indicating that the more ACEs experienced by the parents, the greater the risk for adverse outcomes in their offspring (33).

The systematic reviews cited above drew upon studies predominantly conducted in North America and Europe, with limited contributions from other regions including the Philippines, New Zealand, China, Saudi Arabia and Sri Lanka. None came from the African continent (2,3,13). Despite these geographical gaps, these systematic reviews highlight that ACEs are

ubiquitous and further emphasise the cumulative impact of multiple adversities on health. The variety of these outcomes illustrates the wide-ranging effects ACEs may have on people who experience them. The intergenerational transmission of the consequences of early-life adversity highlights the far-reaching and complex implications of ACEs on the health.

1.2.2 Adverse Childhood Experiences and Sexual Risk-Taking Behaviour

The World Health Organization (WHO) provides a definition of behaviours and conditions that increase the risk of contracting HIV. This encompasses a range of sexual risk-taking behaviours, including but not limited to condomless intercourse, having an STI, and engaging in harmful use of drugs and alcohol within the context of sexual behaviour (35). Research focusing on ACEs and high-risk sexual behaviours, that have been linked to HIV, have revealed compelling association between the two, as discussed below.

Extensive research has consistently demonstrated a robust relationship between childhood sexual abuse (CSA) and subsequent sexual risk behaviours in adulthood however (26,36,37). However, these studies have notable limitations. For example, a nationally representative longitudinal study conducted in the United States of America (USA) followed participants from adolescence into adulthood, revealing a strong association between CSA and engagement in transactional sex during adulthood (OR: 2.17, 95% CI: 1.43-2.49) (26). The study was limited, however, in that it relied on self-reported data and was unable to establish the temporal relationship between CSA and sexual risk-taking outcomes, as these were measured as lifetime values (26). Similarly, a cross-sectional study among men who have sex with men in the USA revealed that individuals who were victims of CSA were more likely to engage in unprotected sex ($\chi 2$ (1, N= 542) = 10.91, p <.001) and transactional sex ($\chi 2$ (1, N= 608) = 16.65, p <.001) in adulthood (36). In a nationally representative Violence Against Children Survey (VACS) across Haiti, Cambodia, and Kenya, CSA was linked to increased odds of transactional sex and STI incidence (37). For instance, in Haiti, individuals who were victims of CSA had triple the odds (OR: 3.3, 95% CI: 1.5-7.6) of engaging in transactional sex compared to those who were not victims of CSA. However, limitations included potential recall bias and reluctance of participants to disclose due to the sensitive nature of the subject matter, as well as the inability to determine temporal relationships (37).

A review and critique of 82 studies by Menard and MacIntosh (38) summarised recent literature on the connection between CSA and adult sexual risk-taking behaviours. They found associations between CSA and having multiple sexual partners, as well as having intercourse under the influence of alcohol or drugs. However, inconsistent findings were reported in studies investigating the links between CSA and STI incidence or unprotected sex. Some of the reviewed studies indicate a link between a history of CSA and both recent and lifetime diagnoses of STIs, in heterosexual women. This relationship was mediated by factors such as mental illness, intimate partner sexual coercion and substance use. However, other reviewed studies did not find such a significant association (38). Similarly, Senn et al. (39) conducted a review and methodological critique, revealing a consistent link between CSA and higher rates of sexual risk behaviours, including multiple sexual partners, transactional sex, and early sexual debut. However, there were limitations, including inconsistent definitions of CSA, lack of investigation into gender as a moderator, and potential confounding of CSA with variables related to sexual risk-taking behaviours. Additionally, while an association between CSA and later sexual risk-taking behaviours exists, causality was not established (39).

Beyond CSA, other ACEs, such as physical abuse, physical and emotional neglect, exposure to household and/or community violence, parental substance abuse, and parental incarceration, have also been linked to various sexual risk-taking behaviours. The nationally representative longitudinal study conducted in the USA, mentioned earlier, found associations between cumulative ACEs scores and sexual risk outcomes, such as having multiple sexual partners, transactional sex, and STI incidence (Chlamydia, Gonorrhoea or Trichomoniasis), which were strongest during adolescence (26). They also discovered that experiences of violence, such as witnessing violence and being a victim of violence, were significant independent factors associated with adolescent sexual risk-taking behaviours (26).

Similarly, a cohort study in the USA among adolescent girls found that self-reports of recent STIs (Chlamydia, Gonorrhoea or Trichomoniasis) were positively associated with sexual abuse (OR:1.77, 95% CI:1.03–3.04), physical abuse (OR:1.73, 95% CI:1.16–2.58) and physical neglect (OR:2.11, 95% CI:1.23–3.62) (27). Another study used data from the National Longitudinal Study of Adolescent Health and found that childhood sexual and physical abuse predicted earlier age of sexual debut and multiple sexual partners (40). A study conducted by Wilson and Widom (28) revealed that experiencing any form of child abuse (sexual or physical) or neglect significantly increased the likelihood of sexual risk-taking behaviours (OR: 2.84,

95% CI: 1.74–4.64), such as transactional sex, inconsistent condom use, and having multiple sexual partners (28,41).

In a cross-sectional study among women in Louisiana, USA, a history of CSA, physical abuse, emotional abuse and physical neglect in childhood increased the adjusted odds of adolescent pregnancy (41). However, the study was limited by differences between included and excluded participants in terms of education, race, gravidity, and depressive symptoms, potentially introducing bias (41). Additionally, Thomas et al. (42) found that females who had experienced ACEs were less likely to use contraception. This was particularly notable among postpartum women in the year following delivery (OR: 0.57, 95% CI: 0.38–0.86).

These studies share a number of limitations, including reliance on retrospective self-reporting of maltreatment histories, potential reluctance of respondents to disclose maltreatment histories accurately, and lack of investigations in an African context. Despite these limitations, the existing body of research underscores the complex interplay between early-life adversity and subsequent sexual health outcomes, emphasising the need for further exploration and nuanced understanding

To my knowledge, research on the relationship between ACEs and sexual risk-taking behaviour is relatively limited in the African context, but recent studies do provide some insights (9,11,43). In a cross-sectional study conducted in Malawi, young adults exposed to ACEs showed a positive, dose-response association with engaging in sexual risk-taking behaviour (9). Specifically, having multiple sexual partners and infrequent condom use were identified as behaviours influenced by ACEs. For example, individuals who experienced three or more ACEs had almost six times the odds (OR: 5.9, 95% CI: 2.1–17.0) of infrequent condom use compared to those who experienced no ACEs (9). Contradictory findings emerged from cross-sectional studies that utilised data from the VACS conducted in Mozambique, Lesotho, Kenya and Cote d'Ivoire. One study, conducted by Miedema et al., (43) found no significant associations between ACEs and sexual behaviours for both males and females. However, another study by Kanagasabai et al. (11) reported contrasting results. They found that women exposed to three or more ACEs were almost four times (OR: 3.75, 95% CI: 2.3–6.2) more likely to engage in transactional sex compared to those with no ACEs. They also found that men exposed to three or more ACEs were more than two times (OR: 2.2, 95% CI: 1.3–3.4) more likely to engage in early sexual debut compared to those with no ACEs (11). A study

closer to home, conducted among young people living in urban informal settlements in Durban, South Africa, found that all forms of childhood trauma, including physical, emotional, and sexual abuse, were associated with various HIV risk behaviours such as engaging in transactional sex, having multiple sexual partners, and inconsistent condom use (44). These studies suggest a complex relationship between ACEs and sexual risk-taking behaviours, with variations observed in different settings and populations. The inconsistent findings indicate that more extensive and context-specific research is needed.

Age-disparate sexual partnerships are prevalent in Southern Africa, raising concerns as these relationships may expose women to an elevated risk of HIV and STI infection. Research by McCloskey, Eloff and Doran (45) indicated that adolescent girls aged 15–19 involved in relationships with partners from different generations face the highest odds of HIV infection (OR: 8.55, 95% CI: 2.1–35.3) compared to other age groups. Similarly, a study utilising HPTN 068 data found that HIV risk was higher among AGYW engaged in age-disparate relationships, with a 5.5-year age gap having a 12.6% (95% CI: 1.9–23.3) higher risk compared to no age gap. (46). Age-disparate sexual relationships can be considered a form of sexual risk-taking behaviour, as they encompass power imbalances and the potential for transactional sex. Moreover, it is important to note that older men have a greater chance of having and transmitting HIV compared to their younger counterparts (45).

Early sexual debut (under 14 years of age) does not strictly fall into a category of ACEs, however, it may be considered as an ACE, given that it is associated with many negative health outcomes, similar to other ACEs. Early sexual debut is intricate and multifaceted as it involves societal norms, legal frameworks and individual agency. It may be either coercive or consensual in nature. In South Africa, the legal landscape is clear: individuals under 16 cannot legally consent to or be involved in any sexual act (47). However, consensual sex between adolescents under 16 and partners within a two-year age range is permitted under Act 32 of 2007 (47). Early sexual debut has been linked to risky sexual behaviour, increased incidence of STIs, mental health illness such as depression, and negative health behaviours, including smoking, drug and alcohol use (48–50). Hence, it is important to investigate early sexual debut as an element of early adversity. To my knowledge, literature has not explicitly cited early sexual debut as a proxy for CSA. However, it is important to recognise that early sexual debut is often an indicator of CSA (51). Children who have been victims of CSA frequently exhibit premature sexual development and sexual behaviours that are unexpected or developmentally

inappropriate (51,52). Proxy measures for CSA used in the literature typically include parental proxy reports of CSA (53).

In summary, the research examining the association between ACEs and sexual risk-taking behaviour highlights a significant correlation. This correlation has profound implications for HIV transmission.

1.2.3 Cumulative versus Individual Adverse Childhood Experiences

The concept of cumulative ACEs involves tallying the occurrences of various types of childhood adversity, encompassing a broad range of adversities that individuals may have encountered. This tallying process yields a cumulative risk score, which is widely utilised in numerous studies (3,9,54,55). Typically, these studies show a consistent pattern: individuals who experience a greater number of ACEs tend to be at increased risk of negative health outcomes (2,3,6,54). However, a critical analysis suggests that this cumulative score lacks consideration for crucial factors such as the type, timing, severity, and chronicity of these experiences (54). Therefore, it is imperative to take into account the specific characteristics of each event, in addition to the cumulative risks, to obtain a more comprehensive understanding of their impact.

Several studies have noted the association between individual ACEs and negative health outcomes, including sexual risk-taking behaviour (11,25,56,57). For example, a cross-sectional study of college students in Zambia found that physical abuse and witnessing parental domestic violence were both associated with an increased risk for risky sexual behaviours (56). Similarly, research using the Behavioural Risk Factor Surveillance Survey (BRFSS) revealed that in females, physical and sexual abuse, parental separation, household incarceration and household substance abuse were each significantly associated with decreased HIV testing, particularly among participants with HIV risk behaviours, with ORs ranging from 0.564 to 0.787 (57). Furthermore, a study conducted among mothers living with HIV in Cape Town discovered that physical and emotional abuse and neglect, and exposure to collective violence, were significantly associated with HIV-related outcomes, such as poor adherence to ARVs and high viral load among people living with HIV (25). Additionally, research done across 5 SSA countries found that women who experienced childhood physical abuse had higher odds of

engaging in risky sexual behaviour such as having unprotected sexual intercourse (OR: 1.45, 95% CI: 1.07–1.97) (11).

In the context of ACEs and HIV, examining both cumulative and individual ACEs provides a comprehensive perspective on how ACEs relate to HIV and highlights specific ACEs that warrant targeted interventions.

1.2.4 Adverse Childhood Experiences and HIV

Each week, there are 4000 incident cases of HIV among AGYW aged 15–24 globally, with 3100 of these infections taking place in SSA (29). These statistics reveal a significant public health challenge, particularly in this region where the majority of new HIV infections are concentrated. Additionally, young girls are more susceptible to STIs due to their immature immune systems and sensitive mucosal membranes. Individuals who experience mucosal or hymenal tearing are at increased risk of transmitting bacteria and viruses, including HIV (58). ACEs are common among individuals living with HIV (22). The current body of research regarding ACEs and HIV predominantly focuses on how ACEs influence behaviours associated with HIV risk. Comparatively, few studies focus on the relationship between ACEs and HIV infection.

Reisner, Falb, and Mimiaga (23) conducted a cross-sectional study utilising data from a sample of 13 274 men, revealing that each additional early-life violent event was linked to heightened odds of HIV infection (OR: 1.32, 95% CI: 1.16–1.50). The study suggested that post-traumatic stress disorder (PTSD) played a partial mediating role in the association between ACEs and HIV. Although this study shows a compelling association between ACEs and HIV, certain limitations should be considered. The study focused on men from the USA, limiting its generalisability to AGYW in SSA. Additionally, participants self-reported HIV diagnoses, without the use of biological markers, which introduces the potential for misclassification bias (23).

In a study closer to home, involving rural South African youth, comprising 1367 men and 1415 women, findings indicated that new HIV infections were significantly higher among women who had experienced early-life physical punishment (Incidence Rate Ratio (IRR): 2.13, 95% CI: 1.25–3.06), emotional abuse (IRR: 1.96, 95% CI: 1.25 – 3.06), and sexual abuse (IRR:

1.66, 95% CI: 1.04–2.63) (24). This study highlights the significance of incorporating child abuse prevention into the HIV prevention strategy in sub-Saharan Africa. However, it's crucial to note that this study utilised a volunteer sample, necessitating caution in generalising the results (24).

Not all studies align on this matter. A cross-sectional study done on 1974 Kenyan women found that childhood experiences of emotional neglect (OR: 0.7 95% CI: 0.51–0.97) and sexual abuse (OR: 0.58, 95% CI: 0.41–0.80) were associated with a lower likelihood of reporting an HIV positive status (59). Additionally, a longitudinal Malawian study done on 1878 adolescents found too few new HIV infections at follow-up to allow for further analysis (60).

The divergent findings across these studies reinforce the need for further investigation of this relationship. Notably, the study conducted in South Africa showed significant associations between ACEs and HIV. However, the specific link between ACEs and HIV prevalence, among AGYW remains unexplored, emphasising the importance of research into this area.

1.3 Problem statement

The burden of ACEs is widely recognised for its profound impact on health and development, shaping life trajectories. ACEs have consistently been associated with a range of negative outcomes (1–3). Particularly concerning is the substantial prevalence of ACEs among adolescents in South Africa, as evidenced by the Birth to Twenty-Plus cohort in Soweto, where nearly all children reported experiencing some form of violence (10). This pressing concern is further exacerbated by the disproportionate burden of HIV infection among AGYW in SSA. Despite significant efforts in HIV control and prevention, AGYW continue to face elevated risks of acquiring HIV compared to men of the same age (29).

As the landscape of HIV epidemiology continually evolves, it becomes increasingly evident that ACEs may play an important role in influencing HIV prevalence. ACEs are recognised as clinically significant predictors of HIV risk and disease burden, and contribute to health risk behaviours, including but not limited to, alcohol abuse, drug use, intimate partner violence, and risky sexual behaviours (22). Existing studies, while shedding light on associations between ACEs and HIV, present some divergent findings. Understanding the relationship between ACEs and HIV prevalence is crucial for developing targeted interventions for at-risk

individuals, informing public health strategies, addressing challenges faced by AGYW, and mitigating the disproportionate burden of HIV infection.

1.4 Justification

This study aims to address the limited research on the relationship between ACEs and HIV prevalence, specifically among AGYW in rural South Africa. There is a gap in the existing literature regarding the relationship between ACEs and HIV infection among AGYW in South Africa, as prior research has predominantly centred on the influence of ACEs on HIV risk related behaviours. Additionally, prior research often overlooks the broader spectrum of adverse events such as exposure to community and household violence. Moreover, the study aims to fill a crucial gap in literature by focusing on a rural setting. Research on ACEs and HIV infection has often overlooked rural populations, despite their unique socio-economic and cultural contexts. This focus will allow for examination of ACEs within the specific context of rural communities, which may have distinct patterns of adversity compared to urban areas. Given the ongoing need to develop evidence-based interventions and strategies for HIV prevention and control in this vulnerable population, better understanding the relationship between ACEs and HIV prevalence is essential. This understanding can inform the development of trauma-related interventions and policies tailored to alleviate the HIV incidence among AGYW in rural South Africa.

1.5 Research question

Are AGYW who have experienced any ACEs, or a greater number of ACEs are more likely to be infected with HIV compared to those who did not experience ACEs in Bushbuckridge, Mpumalanga, South Africa?

1.6 Aim

To investigate the relationship between ACEs and HIV prevalence among AGYW in Bushbuckridge Mpumalanga, South Africa.

1.7 Objectives

1. To describe the prevalence of HIV by cumulative number of ACEs and sociodemographic variables among AGYW in Bushbuckridge Mpumalanga, South Africa.
2. To investigate the relationship between cumulative ACEs and HIV infection among AGYW in Bushbuckridge Mpumalanga, South Africa.
3. To identify individual ACE categories that may be associated with prevalence of HIV infection among AGYW in Bushbuckridge Mpumalanga, South Africa.

1.8 Hypothesis

Null Hypothesis: AGYW who have experienced any ACEs, or a greater number of ACEs are not more likely to be infected with HIV compared to those who did not experience ACEs in Bushbuckridge, Mpumalanga, South Africa

Alternate Hypothesis: AGYW who have experienced any ACEs, or a greater number of ACEs are more likely to be infected with HIV compared to those who did not experience ACEs in Bushbuckridge, Mpumalanga, South Africa

CHAPTER 2: METHODS

2.1 Description of Primary Study

The primary study, HIV Prevention Trials Network (HPTN) 068, was a randomised controlled trial (RCT) (61). The RCT investigated the effectiveness of a monthly cash transfer intervention in reducing HIV incidence among AGYW. Participants were randomly assigned to receive a monthly cash transfer contingent on attending school regularly. The study enrolled AGYW between the ages of 13 and 20 who met specific criteria, including being enrolled in school grades 8-11, not pregnant, unmarried, literate, and having the requisite documents to open a bank account. Participants were required to intend to stay in the study area until conclusion of the study. A total of 2533 participants were enrolled. Notably, to prevent unintentional disclosure of HIV status, participants who tested HIV positive at baseline were included in the study. However, they were subsequently excluded from the main analysis. The main HPTN 068 trial occurred from 2011-2015 and participants were followed for 4 more years post-intervention (61).

Participants underwent annual visits during which they completed an Audio Computer-Assisted Self-Interview (ACASI). They provided self-reported information on school attendance, mental health, finances, family dynamics, social circumstances, and sexual behaviours at each visit. Additionally, HIV pre- and post-test counselling, as well as testing for HIV and herpes simplex virus type 2 (HSV-2), were conducted. HIV and HSV-2 testing was conducted at each visit for participants who had tested negative in previous visits (61).

2.1.1. Primary Study Setting

HPTN 086 was conducted in the Agincourt sub district of the Bushbuckridge municipality, situated in the Mpumalanga province of South Africa (See Figure 2) (61). This area is located near the border to Mozambique, approximately 500 km northeast of Johannesburg (62).

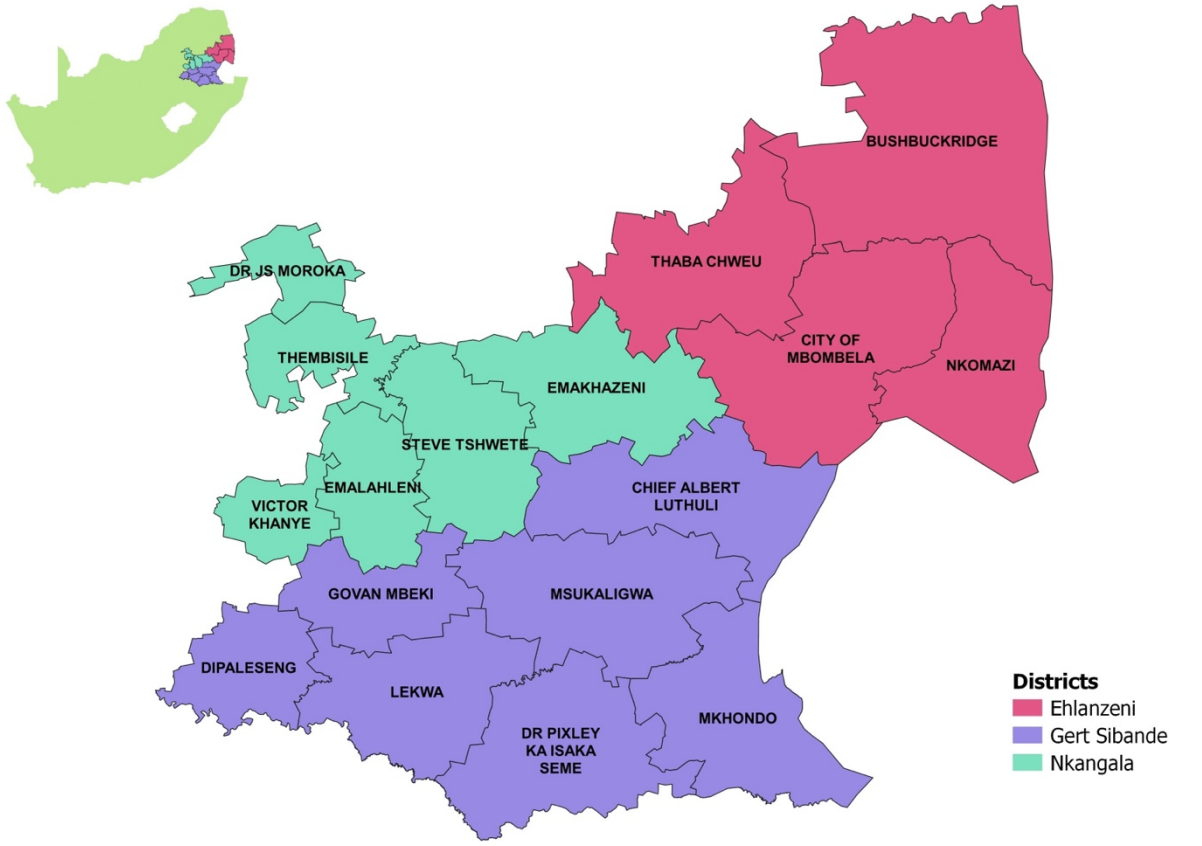

Figure 2. A map of Mpumalanga Province divided into the three districts (Ehlanzeni, Gert Sibande and Nkangala), showing Bushbuckridge municipality, 2016 (63).

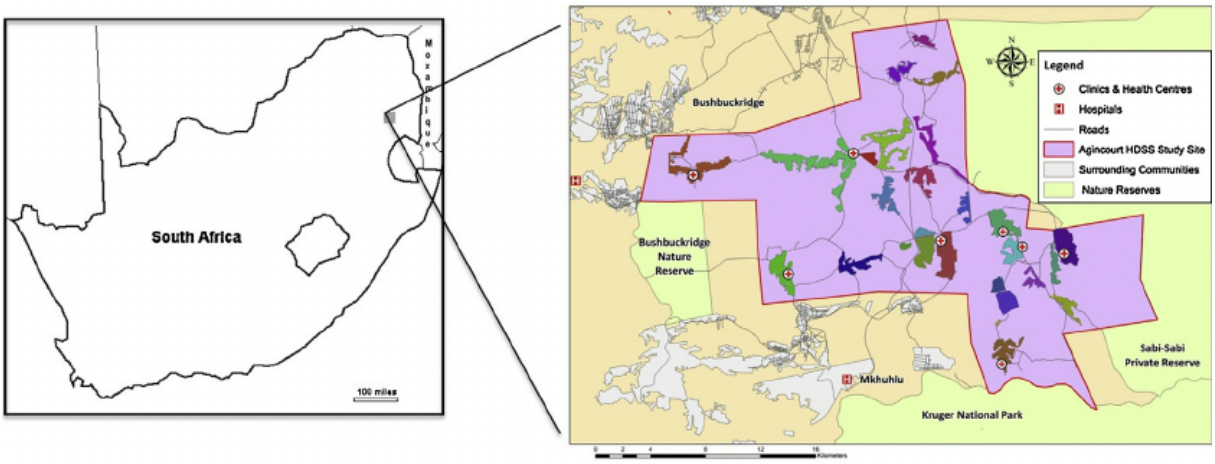

Figure 3. Map of South Africa, Bushbuckridge Municipality, and the Agincourt Health and Demographic Surveillance System Study Site, 2008 (64)**.**

The study was located in the region of the Agincourt Health and Demographic Surveillance Site (HDSS) (See Figure 3). The Agincourt HDSS is a research initiative affiliated with the

University of the Witwatersrand, housed within the Medical Research Council/ Wits Rural Public Health and Health Transitions Research Unit, School of Public Health. This system aimed to generate population-based data, facilitating the informed allocation of resources and funding for health programmes in the area (65).

The Agincourt sub district is an underdeveloped area which is known for its socio-economic marginalisation (62). This site is situated in a remote, rural area that was formerly designated as a "homeland" during the Apartheid period (65). Poverty levels are high and economic opportunities are scarce, forcing most people to seek employment elsewhere (62). The total population of the Agincourt sub district is approximately 70 000, residing in 11 700 households, with a population density of 174 persons/km^2 (65,66). The primary ethnic group is Shangaan, while Mozambicans, initially refugees, constitute nearly one-third of the total population. The region is predominantly Xitsonga speaking (65). There are approximately 21 to 22 secondary schools in this area (62). HIV prevalence is notably elevated in this area among adults, reaching approximately 42% based on cross-sectional estimates (67).

2.2 Secondary Study

2.2.1 Study Design

This secondary study is a cross-sectional study, which utilised existing data from HPTN 068. This study design allowed for the assessment of the association between ACEs and HIV prevalence among AGYW at a time point (2017).

This study defined HIV prevalence as the outcome rather than HIV incidence, despite the primary study measuring incidence. This was because ACEs were retrospectively assessed in 2017 during a follow-up survey after completion of the study. In this case, exposure was measured after the outcome, making prevalence more suitable than incidence. Further, young women were ages 13-20 when enrolled in the primary study so timing of HIV infection after ACEs (before age 18) is not possible to determine for all young women.

2.2.2 Study Population

The study population consisted of participants who were enrolled in the HPTN 068 trial and participated in the ACEs follow up survey in 2017. Among the original 2533 participants, a total of 1891 successfully completed the ACEs questionnaire and had an HIV result at this visit. The 2017 survey was conducted after the intervention ended in 2015; therefore, it was unrelated to the intervention. Consequently, the study population for analysis was limited to AGYW who had participated in and completed the ACEs questionnaire.

2.2.3 Power

The study sample consisted of the 1891 participants who completed the ACEs questionnaire in 2017. Power was calculated using the sample size of 1891 participants. The outcome variable selected was HIV status and the exposure variable selected was childhood physical abuse. Based on a study conducted amongst men who have sex with men in the USA, 16.1% of participants who experienced physical abuse in childhood were HIV positive; and 2.9% of participants who experienced childhood physical abuse were HIV negative (23). Despite the reference study not being specific to this region, it stands out as one of the few studies directly investigating the association between ACEs and HIV, making it a relevant choice for measuring power in the study. Power was calculated with STATA18 using proportions, which generated a power of 100%. This indicated that a sample size of 1891 participants will yield 100% statistical power to detect a difference of 13.2% (at an $\propto = 0.05$) in childhood abuse experiences between individuals who are HIV positive and those who are HIV negative. Therefore, there was less power to detect a smaller difference.

2.2.4 Data Collection

This study conducted secondary analysis of the existing HPTN 068 data and will not collect any primary data. The measurement of variables will be discussed in section 2.2.5.1.

2.2.5 Data Management

The data analysis was conducted using STATA version 18 software. The software was used for data cleaning, the construction of variables and for statistical analysis.

2.2.5.1 Measurement of Variables

The outcome of interest: *HIV Status*

HIV status is a binary variable, coded as 0 for negative and 1 for positive. This classification is applicable at any point during the study, up to and including the 2017 visit.

During the HIV screening process in the HPTN 068 study, participants underwent simultaneous administration of two HIV rapid tests: the Determine HIV-1/2 test and the Uni-gold Recombigen HIV test (61). If both tests produced negative results, no further testing was conducted during that visit. However, if one or both tests produced positive results, confirmatory testing was performed using the western blot assay. If the western blot test showed a positive or indeterminate result, a new blood sample was collected within two weeks for repeat testing. Participants confirmed to be HIV-infected did not undergo further HIV testing during the study. To protect participant confidentiality regarding HIV status, individuals who tested positive at baseline were enrolled in the study but excluded from the primary analysis (61).

The exposure of interest: *Adverse Childhood Experiences*

Category	Question (regarding the first 18 years of life)
Physical Abuse	Did a parent, guardian or other household member spank, slap, kick, punch or beat you up?
	Did a parent, guardian or other household member hit or cut you with an object, such as a stick (or cane), bottle, club, knife, whip etc?
Emotional Abuse	Did a parent, guardian or other household member yell, scream or swear at you, insult or humiliate you?
	Did a parent, guardian or other household member threaten to, or actually, abandon you or throw you out of the house?
Sexual Abuse	'Sexual Debut < 14 years (proxy)'
Witnessed verbal violence at home	Did you see or hear a parent or household member in your home being yelled at, screamed at, sworn at, insulted or humiliated?
Witnessed physical violence at home	Did you see or hear a parent or household member in your home being slapped, kicked, punched or beaten up?
	Did you see or hear a parent or household member in your home being hit or cut with an object, such as a stick (or cane), bottle, club, knife, whip etc.?
Witnessed community violence	Did you see or hear someone being beaten up in real life?
	Did you see or hear someone being stabbed or shot in real life?
	Did you see or hear someone being threatened with a knife or gun in real life?

Figure 4. Table presenting the questions that composed each individual ACE (8)

An attenuated version of the World Health Organization's Adverse Childhood Experiences International Questionnaire (ACE-IQ) was used by HPTN 068 to measure ACEs (8). Participants were asked a series of questions regarding the ACEs they had experienced before the age of 18. The ACEs assessed in this study, included the following experiences: 1) physical abuse, 2) sexual abuse, 3) emotional abuse 4) witnessing verbal violence in the home 5) witnessing physical violence in the home 6) witnessing violence in the community. For the analysis, individual ACE categories were dichotomised. Each ACE was coded as 0 to indicate its absence and 1 to indicate its presence. The process of dichotomising the variables was guided by the WHO's manual for analysing the ACE-IQ (8).

Variables related to direct child abuse included physical, emotional, and sexual abuse. A variable indicating any childhood experience of physical abuse was created using weapon-related violence and physical violence variables and was defined as ever having had any experiences of weapon related or physical violence before the age of 18. To account for the lack of a sexual abuse variable in the dataset, age of sexual debut less than 14 years was used as a proxy for sexual abuse. A variable indicating any childhood experience of emotional abuse

was created using verbal abuse and abandonment variables and was defined as ever having had any experience of verbal abuse, threats of abandonment or experiences of abandonment before the age of 18.

Variables related to witnessed violence in the home included witnessed physical abuse and witnessed verbal abuse. A variable indicating any childhood experiences of witnessing physical abuse in the home was created using witnessed weapon related violence and witnessed physical violence variables and was defined as ever having had any experience of witnessing weapon related violence or physical violence in the home, before the age of 18. A variable indicating the experience of witnessing verbal abuse in the home before the age of 18 already exists in the dataset; hence, there was no need to create a new one.

A variable indicating any childhood experiences of witnessing violence in the community was created using witnessing physical assault, witnessing threats with weapons, and witnessing violent attacks in the community variables. This variable was defined as ever having had any experience of witnessing physical assault, witnessing threats with weapons, or witnessing violent attacks in the community, before the age of 18.

In order to assess the cumulative impact of ACEs, each category of ACEs was used to create a categorical variable consisting of five levels. The dataset contained a limited number of individuals with more than four ACEs. The scoring was as follows: 0 represented no ACEs reported, 1 indicated one ACE reported, 2 signified two ACEs reported, 3 signified three ACES reported, and 4+ represented four or more ACEs (55). As early sexual debut was not part of the standard ACE questionnaire but could be considered an ACE, a cumulative ACEs score was created with and without this variable, for two separate analyses to be conducted.

Demographics and Covariates (Potential Confounders): A range of confounding variables were considered. Variables measured at the baseline visit included grade at enrolment (categorical: grade 8, grade 9, grade 10, grade 11), maternal level of education (categorical: no school, some primary, completed primary, some high school, completed high school, university or technikon[1]), paternal level of education (categorical: no school, some primary, completed primary, some high school, completed high school, university or technikon), randomisation to

[1] A technikon is a higher education institution in South Africa that specialises in vocational training

cash transfer (binary: yes, no) and country of birth (categorical: South Africa, Zimbabwe, Mozambique, Swaziland). Variables measured at the follow-up visit in 2017 included age (continuous), marital status (never married, married, widowed, divorced/separated) and orphan status (single orphan, double orphan, both parents alive). (61).

Potential Mediators: The following variables were considered potential mediators and were all measured at the follow up visit in 2017: experienced sexual violence in the past 12 months (binary: yes, no), transactional sex in the past 12 months (binary: yes, no), age difference with a partner (binary: ≥ 5 years older, < 5 years older), number of lifetime sexual partners (binary: <2, ≥ 2) , ever drank alcohol (binary: yes, no), ever used drugs (binary: yes, no) and ever had condomless sexual intercourse (binary: yes, no) (61).

2.2.5.2 Potential Confounders

To justify the selection of potential confounders in the study, existing literature was considered, highlighting the significance of various variables in the analysis of ACEs and their impacts. Research indicated that country of birth, age, orphan status, marital status, grade, maternal and paternal level of education, and randomisation arm could be potential confounders due to their influence on both ACEs and health outcomes. Notably, these variables are not mediators in the path between ACEs and negative health outcomes.

Studies have noted that ACEs are linked to broad harms in life prospects, such as education, employment, and poverty, which in turn have been linked to health outcomes (2,3). This makes the inclusion of variables like orphan status, grade, and parental education level important, as they are related to educational outcomes and SES, which can confound the relationship between ACEs and health outcomes (3,26,40,68). Marital status was also supported by the literature, as it could influence home stability and SES, thereby associating with exposure to ACEs and negative health outcomes (40,41).

Additionally, studies have consistently highlighted the importance of age as a confounding variable in ACE research. For instance, London et al. (26) included age in their adjusted models, noting that it was important to account for age when examining the long-term effects of childhood maltreatment on sexual risk behaviours and STI outcomes. Similarly, Ryan et al.

(40) controlled for a wide range of variables, including age and family-level socio-economic characteristics, to mitigate potential biases in associations between childhood maltreatment and sexual behaviour outcomes. Grade at school often acts as a proxy for age and should also be considered an important potential confounder.

Country of birth was considered a potential confounder due to its association with variations in SES, cultural norms, and access to resources, all of which can influence exposure to ACEs and negative health outcomes. Studies have shown that ACE prevalence can vary between countries and socio-economic groups (2).
Lastly, controlling for the randomisation arm in the study design ensured that any differences in intervention exposure were accounted for, which was vital for isolating the effect of ACEs on HIV outcomes.

2.2.5.3 Directed Acyclic Graph (DAG)

A DAG was constructed to depict the association between ACEs and HIV. The DAG presents potential confounders, effect modifiers and main variables. This DAG played a valuable role in shaping the ultimate statistical models used in the study. The DAG is appropriate for epidemiological investigations and specifies conceptual relationships between available variables (69).

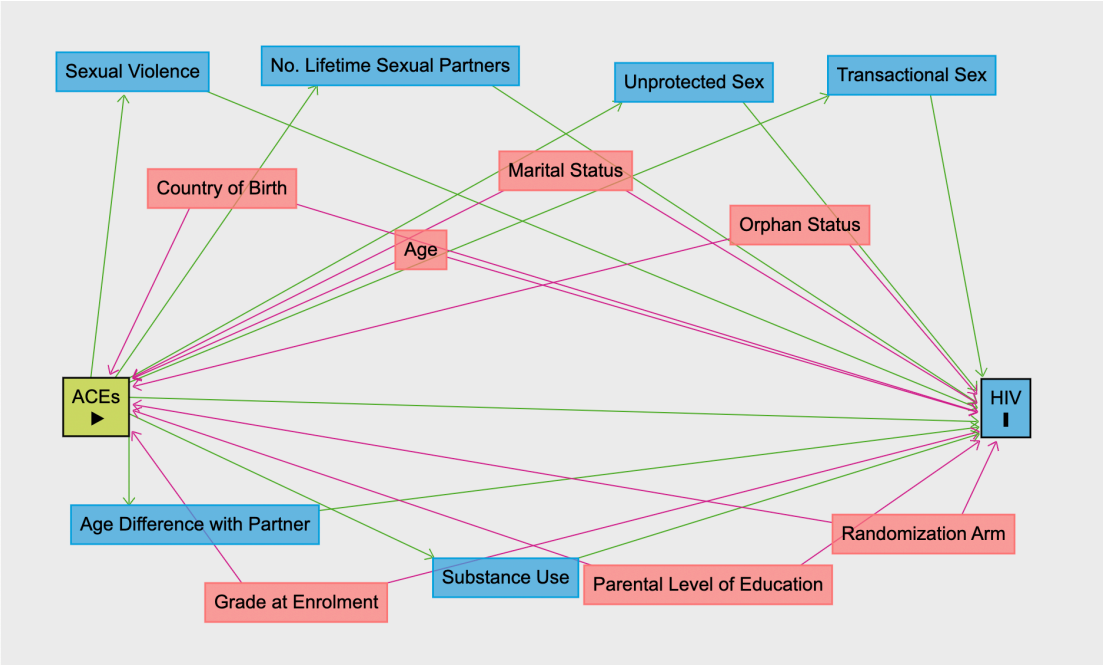

Figure 5. DAG showing the association between ACEs and HIV (2,3,26,38–41,68,70–72)

The choice of confounders was based on their potential to influence both ACEs and HIV outcomes, ensuring that the observed relationship was not distorted. Mediators were chosen due to their capacity to alter the strength of the relationship between ACEs and HIV. The potential of these factors to influence the relationship between ACEs and HIV was recognised in the literature (2,3,26,38–41,68,70–72).

As indicated in Figure 4, potential mediators (illustrated by the pink tiles) were sexual violence, transactional sex, age difference with a partner, number of lifetime sexual partners, unprotected sex and substance use.

Potential confounders (illustrated by the blue tiles) in the relationship between ACEs and HIV included age, parental level of education, school grade at enrolment, country of birth, marital status, orphan status and randomisation to the cash transfer intervention. Data on socioeconomic status (SES) were missing for a substantial number of observations; therefore, maternal and paternal level of education was used as a proxy for household SES (73). The minimally sufficient adjusted set for this relationship included age, parental level of education, school grade at enrolment, country of birth, marital status, orphan status and randomisation to the cash transfer intervention.

2.2.6 Data Analysis

Descriptive analysis was conducted to examine the prevalence of all variables among the study population. This analysis also involved exploring cumulative ACEs, individual ACEs, sociodemographic variables, potential confounders, and potential mediators in relation to HIV status. Categorical variables were summarised using frequencies and proportions. Age, being the only continuous variable, was summarised using mean and standard deviations, as it had a normal distribution. Bivariate analysis was performed to assess the association between all the variables and HIV status using Pearson’s chi-square test and independent t-test, as appropriate.

Bivariate analysis was also conducted to investigate the associations between individual ACE variables and HIV status. The Pearson's chi-square test was applied for emotional abuse, physical abuse, witnessed verbal violence at home, witnessed physical violence at home and witnessed community violence variables to establish whether there was a statistically

significant relationship at a p-value of 0.05. The Fishers Exact test was used for the sexual abuse variable, due to one of the expected values in a cell being less than 5.

Multivariable logistic regression was conducted to investigate the relationship between binary HIV status and cumulative ACEs. In this case, the outcome was relatively rare, therefore the odds ratio could approximate a risk ratio. The analysis involved two iterations, one including early sexual debut as a component of cumulative ACEs and the other excluding it, because early sexual debut as a proxy for CSA has not typically been included in prior literature. Early sexual debut does not strictly fall into a category of ACEs; however, it can be considered one due to its association with numerous negative health outcomes similar to those caused by ACEs. The nature of early sexual debut is complex and can involve coercion, therefore it was chosen as a proxy measure. For cumulative ACEs including early sexual debut, a stepwise selection process was employed, utilising both forward and backward selection techniques. Both forward and backward selection procedures yielded identical outcomes. Fractional polynomials of the first degree were used to determine the best way to include cumulative ACEs and age in the model. Likelihood ratio tests were conducted to compare the fit of the full model with that obtained through stepwise regression, with the latter being determined as the better fit. Goodness-of-fit tests were also performed to assess the adequacy of the final model. The *margins* command was used to ascertain the predicted means for cumulative ACEs, adjusted for other variables in the model. As the mean of a categorical variable represents its prevalence, the predicted means were referred to as "predicted prevalence". An unadjusted model was fitted for cumulative ACEs to evaluate the unmitigated association with HIV status. This process was repeated for cumulative ACEs excluding early sexual debut, maintaining the same methodology to ascertain the association between cumulative ACEs and HIV status while excluding sexual abuse as a variable.

Multivariable logistic regression was also utilised to investigate the association between the binary HIV status and each of the individual ACEs, both in unadjusted and adjusted models. Each type of ACE was analysed separately, including physical abuse, early sexual debut (proxy for sexual abuse), emotional abuse, witnessed verbal violence, witnessed physical violence and witnessed community violence. For each individual ACEs, a stepwise selection process was utilised. This process aimed to identify the most relevant variables for inclusion in the model. In cases where both forward and backward selection models did not yield identical results, a likelihood ratio test was used to determine the best model between the two. First-degree

fractional polynomials were used to determine the best way to include age in the model. Likelihood ratio tests compared the full model with the stepwise model, and goodness-of-fit tests were performed to ensure the adequacy of the final model. In addition to the adjusted models, unadjusted models were fitted for each ACE category.

Mediation analysis was conducted to examine the potential mediating effects of various variables between physical abuse and HIV status. The *paramed* package was used in STATA which is based on the potential outcomes framework used in causal mediation (74). For each mediator variable, logistic regression models were fitted to assess mediating effects in the association between HIV status (outcome) and childhood physical abuse (exposure). Potential mediators include sexual violence, transactional sex, lifetime sexual partners, alcohol use, drug use, unprotected sex and age difference with partner. Control variables, such as randomisation arm, age, grade at enrolment, orphan status and witnessed community violence in childhood, were included in both the outcome and mediator regression models to account for potential confounding effects.

Lastly, a sensitivity analysis was conducted to determine if there were any differences between including all participants living with HIV (including those who were HIV positive at enrolment) and considering only those who became positive during the primary study and follow-up. This analysis aimed to compare HIV prevalence and an approximation of HIV incidence within a cross-sectional study design. This was done by excluding HIV cases that were more likely to be perinatally transmitted (those at enrolment) and including only new cases over the course of the primary study that were through sexual transmission during adolescence and young adulthood. A multivariable logistic regression was conducted to investigate the relationship between an approximation to HIV incidence and cumulative ACEs a (including and excluding early sexual debut), as well as individual ACE categories. The processes described above for multivariable logistic regression were repeated for this analysis.

Although multiple comparisons increase the risk of both Type I and Type II errors, there is still sufficient power to detect meaningful effects.

2.3 Ethical Considerations

Ethical clearance for HPTN 068 was previously obtained from the Human Research Ethics Committee (HREC) of the University of Witwatersrand (Ethics Clearance Certificate Number: 101012). In addition, ethical clearance for the current secondary data analysis was obtained (Ethics Clearance Certificate Number: M240218) from HREC (Medical) (See Appendix 3).

CHAPTER 3: RESULTS

3.1 Descriptive and Bivariate Analysis

Table 1 presents the prevalence estimate of each factor in the study population. When considering cumulative ACEs, including early sexual debut, the distribution among participants is as follows: 37.95% have no ACEs, 25.01% have 1 ACE, 13.90% have 2 ACEs, 10.74% have 3 ACEs, and 12.40% have 4 or more ACEs. Excluding early sexual debut from the cumulative ACEs score, 38.64% have no ACEs, 24.48% have 1 ACE, 14.06% have 2 ACEs, 10.48% have 3 ACEs, and 12.35% have 4 or more ACEs. The majority of participants, 62.05% when including early sexual debut and 61.37% when excluding early sexual debut, have indicated experiencing at least one ACE in their lifetime.

The distribution of individual ACEs is as follows: 16.55% of participants have experienced physical abuse, 1.69% of participants have had an early sexual debut, 27.67% of participants have experienced emotional abuse, 27.67% witnessed verbal violence at home, 16.08% witnessed physical violence at home and lastly, 51.99% of participants witnessed community violence. These statistics show a very high prevalence of ACEs among this study population.

Table 1. Prevalence of cumulative and individual ACEs in the study population

Factor	Level	Total	Column Percentages of Total (%)
Cumulative ACEs (incl. sexual abuse)	0	710	37.95%
	1	468	25.01%
	2	260	13.90%
	3	201	10.74%
	4+	232	12.40%
Cumulative ACEs (excl. sexual abuse)	0	723	38.64%
	1	458	24.48%
	2	263	14.06%
	3	196	10.48%
	4+	231	12.35%
Physical Abuse	No	1568	83.45%
	Yes	311	16.55%
Early sexual debut (proxy for sexual abuse)	No	1859	98.31%
	Yes	32	1.69%
Emotional Abuse	No	1359	72.33%
	Yes	520	27.67%
Witnessed verbal violence at home	No	1362	72.33%
	Yes	521	27.67%
Witnessed physical violence at home	No	1576	83.92%
	Yes	302	16.08%
Witnessed Community Violence	No	904	48.01%
	Yes	979	51.99%

Table 2 summarises the prevalence of HIV among AGYW in this population, indicating an overall prevalence of 11.48%.

The prevalence of HIV does not exhibit a linear increase with an increasing cumulative ACEs score. Notably, individuals with no ACEs have a relatively high HIV prevalence of 12.54% when early sexual debut is included in the score and 12.45% when early sexual debut is excluded. However, those with a cumulative ACEs score of 3 or more, regardless of including or excluding early sexual debut, demonstrate a slightly higher prevalence of HIV compared to those with less than 3 ACEs.

The mean age is slightly higher for participants who are HIV positive (20.66 years) compared to those who are HIV negative (20.05 years). In terms of nationality, the vast majority of participants are South African (97.88%) while smaller proportions represent Mozambique (1.90%), Zimbabwe (0.16%), and Swaziland (0.05%) (See Appendix 4). Notably, the prevalence of HIV is higher in Mozambicans (13.89%) compared to South Africans (11.45%). Additionally, the grade at enrolment into the primary study shows variation, with high HIV prevalence among participants who enrolled in grade 11 (13.51%) compared to those who enrolled in grade 8, 9, or 10.

Most of the participants in the study (97.09%) (See Appendix 4) have never been married with a lower HIV prevalence among this group (11.38%) compared to those who have been married (14.81%). Although not statistically significant, the educational attainment of participants' parents emerges as an important factor in HIV prevalence within the study population. Participants whose mothers achieved the highest educational level of either university or technikon exhibit the lowest HIV prevalence (3.64%). Conversely, those whose mothers had no formal education (12.05%), attained some primary schooling (12.54%), completed primary school (12.64%), achieved some high school education (12.88%), or completed high school (10.27%) demonstrate higher HIV prevalence. Similarly, participants with fathers who attained the highest education level of either university or technikon also show the lowest HIV prevalence (6.06%). Conversely, those whose fathers had no formal education (14.33%), attained some primary schooling (12.68%), completed primary school (13.33%), achieved some high school education (9.87%), or completed high school (10.09%) exhibit higher HIV prevalence.

Finally, parental status plays a statistically significant role ($p = 0.001$), with participants who have lost both parents showing a substantially higher HIV prevalence (21.05%) compared to those who have only lost one parent (12.25%) or have both parents alive (10.10%).

Table 2. Prevalence of HIV infection presented by cumulative ACEs and sociodemographic factors

		HIV Negative (N=1674)	HIV Positive (N=217)	Total (N=1891)	P-Value
Cumulative ACEs (incl. early sexual debut)	0	621 (87.46%)	89 (12.54%)	710	0.118
	1	423 (90.38%)	45 (9.62%)	468	
	2	239 (91.92%)	21 (8.08%)	260	
	3	173 (86.07%)	28 (13.93%)	201	
	4+	201 (86.64%)	31 (13.36%)	232	
Cumulative ACEs (excl. early sexual debut)	0	633 (87.55%)	90 (12.45%)	723	0.225
	1	414 (90.39%)	44 (9.61%)	458	
	2	240 (91.25%)	23 (8.75%)	263	
	3	170 (86.73%)	26 (13.27%)	196	
	4+	200 (86.58%)	31 (13.42%)	231	
Age (mean ±SD)		20.05 ±1.39	20.66 ±1.51		<0.001
Country of Birth	South Africa	1639 (88.55%)	212 (11.45%)	1851	0.867
	Zimbabwe	3 (100.0%)	0	3	
	Mozambique	31 (86.11%)	5 (13.89%)	36	
	Swaziland	1 (100.0%)	0	1	
Grade at Enrolment	Grade 8	421 (90.15%)	46 (9.85%)	467	0.096
	Grade 9	448 (90.51%)	47 (9.49%)	495	
	Grade 10	485 (86.76%)	74 (13.24%)	559	
	Grade 11	320 (86.49%)	50 (13.51%)	370	
Marital Status	Never Married	1627 (88.62%)	209 (11.38%)	1836	0.692
	Married	46 (85.19%)	8 (14.81%)	54	
	Widow	1 (100.0%)	0	1	
	Divorced/Separated	0	0	0	
Maternal Level of Education	No School	270 (87.95%)	37 (12.05%)	307	0.379
	Some Primary	300 (87.46%)	43 (12.54%)	343	
	Completed Primary	76 (87.36%)	11 (12.64%)	87	
	Some High School	460 (87.12%)	68 (12.88%)	528	
	Completed High School	367 (89.73%)	42 (10.27%)	409	
	University/ Technikon	53 (96.36%)	2 (3.64%)	55	
Paternal Level of Education	No School	281 (85.67%)	47 (14.33%)	328	0.222
	Some Primary	241 (87.32%)	35 (12.68%)	276	
	Completed Primary	65 (86.67%)	10 (13.33%)	75	
	Some High School	338 (90.13%)	37 (9.87%)	375	
	Completed High School	383 (89.91%)	43 (10.09%)	426	
	University/ Technikon	62 (93.94%)	4 (6.06%)	66	
Orphan Status	Both Parents Alive	1068 (89.90%)	120 (10.10%)	1188	0.001
	Single Orphan	480 (87.75%)	67 (12.25%)	547	
	Double Orphan	105 (78.95%)	28 (21.05%)	133	
Randomisation Arm	Control Group	798 (88.08%)	108 (11.92%)	906	0.56
	Conditional Cash Transfer Group	876 (88.93%)	109 (11.07%)	985	

Table 3 provides insights into HIV prevalence in relation to sexual risk factors and substance use factors, which are potential mediators in the relationship between ACEs and HIV. Notably, individuals who experienced sexual violence in the past 12 months exhibit a significantly higher HIV prevalence (20.0%) compared to those who did not experience such violence ($p = 0.018$). Similarly, participants engaged in transactional sex within the past year demonstrate a higher HIV prevalence (17.36%) compared to their counterparts who did not engage in transactional sex ($p = 0.002$). Moreover, participants reporting two or more lifetime sexual partners show a higher HIV prevalence (14.88%) compared to those with fewer than two lifetime sexual partners ($p = 0.027$).

The following potential mediators show no statistically significant association. Individuals who have ever consumed alcohol present a lower HIV prevalence (10.89%) compared to those who have never consumed alcohol (11.63%); however, the difference is minimal. Conversely, participants who have ever used drugs exhibit a higher HIV prevalence (13.33%) compared to those who have never used drugs (11.43%). Additionally, participants reporting sexual intercourse without condoms demonstrate a slightly higher HIV prevalence (13.38%) compared to those who have never engaged in unprotected sexual activity (12.20%). Finally, individuals with an age gap of five years or more with their sexual partners exhibit a higher HIV prevalence (18.29%) compared to those with a smaller age difference (12.05%).

Table 3. Prevalence of HIV infection presented by sexual risk factors and substance use factors that are potential mediators in the relationship between ACEs and HIV

		HIV Negative (N=1674)	HIV Positive (N=217)	Total (N=1891)	P-Value
Experienced Sexual Violence in the past 12 months	No	1603 (88.86%)	201 (11.14%)	1804	0.018
	Yes	60 (80.0%)	15 (20.0%)	75	
Transactional Sex in the past 12 months	No	1229 (89.45%)	145 (10.55%)	1374	0.002
	Yes	200 (82.64%)	42 (17.36%)	242	
Lifetime Sexual Partners	< 2	505 (89.38%)	60 (10.62%)	565	0.027
	≥2	555 (85.12%)	97 (14.88%)	652	
Ever Drank Alcohol	No	1375 (88.37%)	181 (11.63%)	1556	0.670
	Yes	289 (89.20%)	35 (10.80%)	324	
Ever Used Drugs	No	1589 (88.57%)	205 (11.43%)	1794	0.580
	Yes	78 (86.67%)	12 (13.33%)	90	
Ever had condomless sexual intercourse	No	216 (87.80%)	30 (12.20%)	246	0.626
	Yes	803 (86.62%)	124 (13.38%)	927	
Age Difference with Partner	< 5 years older	73 (87.95%)	10 (12.05%)	83	0.169
	≥ 5 years older	344 (81.71%)	77 (18.29%)	421	

Table 4 presents HIV prevalence by individual ACE categories and examines the statistical associations between them.

With regards to HIV prevalence, participants who experienced childhood physical abuse exhibit a higher HIV prevalence (14.47%) compared to those who did not experience such abuse (10.84%). Although this relationship shows marginal statistical significance (p=0.066), it suggests a potential association between childhood physical abuse and HIV prevalence.

In contrast, participants who had an early sexual debut demonstrate a similar HIV prevalence (12.50%) compared to those who did not (11.46%), with no statistically significant association between the two (p=0.78). Similarly, participants reporting childhood emotional abuse show a comparable HIV prevalence (12.31%) to those who did not experience such abuse (11.11%), with a lack of a statistically significant relationship (p=0.47).

Regarding witnessed violence at home during childhood, participants who witnessed verbal violence exhibit a similar HIV prevalence (10.75%) compared to those who did not (11.67%), with no statistically significant association observed (p=0.57). However, participants who witnessed physical violence at home display a higher HIV prevalence (15.23%) compared to

those who did not (10.66%), revealing a statistically significant association (p=0.022). Interestingly, participants who witnessed violence in their community present a slightly lower HIV prevalence (10.52%) compared to those who did not (12.50%). Despite this difference, there is no statistically significant association between witnessing community violence and HIV prevalence (p=0.18).

Table 4. Prevalence of HIV infection by individual ACE categories

		HIV Negative (N=1674)	HIV Positive (N=217)	P-value
Physical Abuse	No	1398 (89.16%)	170 (10.84%)	0.066
	Yes	266 (85.53%)	45 (14.47%)	
Early Sexual Debut < 14 years (proxy for sexual abuse)	No	1646 (88.54%)	213 (11.46%)	0.78
	Yes	28 (87.50%)	4 (12.50%)	
Emotional Abuse	No	1208 (88.89%)	151 (11.11%)	0.47
	Yes	456 (87.69%)	64 (12.31%)	
Witnessed verbal violence at home	No	1203 (88.33%)	159 (11.67%)	0.57
	Yes	465 (89.25%)	56 (10.75%)	
Witnessed physical violence at home	No	1408 (89.34%)	168 (10.66%)	0.022
	Yes	256 (84.77%)	46 (15.23%)	
Witnessed Community Violence	No	791 (87.50%)	113 (12.50%)	0.18
	Yes	876 (89.48%)	103 (10.52%)	

3.2 Multivariable Analysis

Table 5 presents the unadjusted and adjusted ORs with their corresponding 95% CIs for the association between HIV prevalence and cumulative ACEs score, including early sexual debut.

In the unadjusted analysis, the odds of HIV infection among participants with 1 ACE are 0.74 times the odds of HIV infection among those with no ACEs, suggesting a potential protective effect (95% CI: 0.51–1.08). However, this association is not statistically significant (p = 0.123). Similarly, participants with 2 ACEs exhibit lower odds of HIV infection, with an odds ratio of 0.61 (95% CI: 0.37–1.01) compared to those with no ACEs. While this indicates a possible protective effect, the significance level is marginal (p = 0.054) and does not remain after adjusting for other covariates. Conversely, participants with 3 or 4 or more ACEs demonstrate higher odds of HIV infection compared to those with no ACEs, although these associations are not statistically significant.

When adjusting for randomisation arm, age, orphan status, and grade at enrolment, the association between cumulative ACEs score (including early sexual debut) and HIV prevalence remained nonsignificant across all levels. These findings suggest that, after adjusting for potential confounders, there is no significant dose-response relationship between cumulative ACEs score (including early sexual debut) and HIV prevalence among the study participants.

Table 5. Unadjusted and adjusted odds ORs and 95% confidence intervals (CIs) for the association between HIV prevalence and cumulative ACEs score, including early sexual debut

		HIV Prevalence			
		Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Cumulative ACEs (including early sexual debut)	**0**	1		1	
	1	0.74 (0.51 - 1.08)	0.123	0.82 (0.53 - 1.27)	0.372
	2	0.61 (0.37 - 1.01)	0.054	0.76 (0.44 - 1.31)	0.319
	3	1.13 (0.72 - 1.78)	0.602	1.17 (0.68 - 2.00)	0.577
	4+	1.08 (0.69 - 1.67)	0.743	1.09 (0.67 - 1.77)	0.742

*adjusted for randomisation arm, age, orphan status, grade at enrolment

Table 6 presents the predicted prevalence of HIV infection by cumulative ACEs score, including early sexual debut, along with their corresponding 95% CIs. The marginal means reveal that the prevalence of HIV is highest among participants with 3 ACEs. However, it's important to note that the predicted prevalence remains relatively consistent across all levels

of cumulative ACEs, with only slight variations. This suggests that while there may be a trend indicating higher HIV prevalence among those with a certain number of ACEs, the differences in predicted prevalence are not substantial.

Table 6. Predicted prevalence of HIV infection by cumulative ACEs score, including early sexual debut

		Predicted Prevalence	95% CI
Cumulative ACEs (including early sexual debut)	**0**	12.10%	9.42 - 14.78%
	1	10.20%	7.10 - 13.31%
	2	9.53%	5.53 - 13.53%
	3	13.77%	8.37 - 19.17%
	4+	12.97%	8.48 - 17.46%

*adjusted for randomisation arm, age, orphan status, grade at enrolment

Table 7 displays the unadjusted and adjusted ORs along with their respective 95% CIs for the relationship between HIV prevalence and cumulative ACEs score, excluding early sexual debut. Consistent with the findings in Table 5, both the unadjusted and adjusted models indicate that the association between cumulative ACEs score (excluding early sexual debut) and HIV prevalence remains nonsignificant across all levels. This suggests that there is no statistically significant dose-response relationship between cumulative ACEs score (excluding early sexual debut) and HIV prevalence among the study participants.

Table 7. Unadjusted and adjusted ORs and 95% CIs for the association between HIV prevalence and cumulative ACEs score, excluding early sexual debut

		HIV Prevalence			
		Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Cumulative ACEs (excluding early sexual debut)	**0**	1		1	
	1	0.75 (0.51 - 1.09)	0.135	0.84 (0.54 - 1.31)	0.446
	2	0.67 (0.42 - 1.09)	0.108	0.80 (0.47 - 1.36)	0.413
	3	1.07 (0.67 - 1.72)	0.760	1.16 (0.67 - 2.01)	0.592
	4+	1.09 (0.70 - 1.69)	0.699	1.10 (0.68 - 1.79)	0.697

*adjusted for randomisation arm, age, orphan status, grade at enrolment

Table 8 presents the predicted prevalence of HIV infection by cumulative ACEs score, excluding early sexual debut, along with their corresponding 95% CIs. Similar to table 6, the predicted prevalence remains relatively consistent across all levels of cumulative ACEs, with only minor variations. This, again, suggests that while there may be a trend indicating higher

HIV prevalence among those with a certain number of ACEs, the differences in predicted prevalence are not substantial.

Table 8. Predicted prevalence of HIV infection by cumulative ACEs score, excluding early sexual debut

		Predicted Prevalence	95% CI
Cumulative ACEs (excluding early sexual debut)	**0**	11.95%	9.32 - 14.58%
	1	10.32%	7.14 - 13.50%
	2	9.86%	5.83 - 13.89%
	3	13.56%	8.10 - 19.02%
	4+	12.97%	8.48 - 17.46%

*adjusted for randomisation arm, age, orphan status, grade at enrolment

Table 9 presents the unadjusted and adjusted ORs with 95% CIs for the association between HIV prevalence and individual ACE categories. Regarding childhood physical abuse, participants who experienced childhood physical abuse have 1.39 (95% CI: 0.98–1.98, p=0.067) times higher odds of HIV infection compared to those who did not, though this relationship is only marginally statistically significant at an alpha of 0.05. After adjusting for confounders, the relationship becomes statistically significant, with an adjusted OR of 1.57 (95% CI: 1.03–2.41, p=0.038), indicating that those who experienced childhood physical abuse have a 1.57 times higher odds of HIV infection compared to those who did not.

Witnessing physical violence at home during childhood suggests a significant association with HIV prevalence at an alpha of 0.05. The unadjusted OR is 1.51 (95% CI: 1.06–2.14, p=0.023), indicating higher odds of HIV infection among those who witnessed physical violence at home during childhood compared to those who did not. After adjustment, the OR increases to 1.63 (95% CI: 1.07–2.49, p=0.022), showing that those who witnessed physical violence at home during childhood have 1.63 times higher odds of HIV infection compared to those who did not.

Interestingly, witnessing community violence during childhood shows no significant association with HIV prevalence in the unadjusted model (OR: 0.82, 95% CI: 0.62–1.09, p=0.179). However, after adjustment, the OR is 0.69 (95% CI: 0.49–0.98,p = 0.037), indicating lower odds of HIV infection among those who witnessed community violence during childhood compared to those who did not.

For early sexual debut and emotional abuse, both the unadjusted and adjusted ORs suggest no significant association with HIV infection. Notably, the adjusted estimate for early sexual debut of 0.68 (95% CI: 0.20–2.35,p = 0.542) is similar to the adjusted estimate of 0.69 (95% CI: 0.49–0.98,p = 0.037) for witnessed community violence, but less precise. Similarly the adjusted estimate of 1.44 (95% CI: 0.94–2.22, p = 0.096) for emotional abuse is akin to the adjusted estimate of 1.57 (95% CI: 1.03–2.41, p = 0.038) for physical abuse, but less precise. Witnessing verbal violence at home during childhood also shows no significant association with HIV prevalence, as indicated by both unadjusted and adjusted ORs. However, similar to early sexual debut, the adjusted estimate of 0.65 (95% CI: 0.41–1.05, p = 0.077) is akin to the adjusted estimate of 0.69 (95% CI: 0.49–0.98, p = 0.037) for witnessed community violence, but less precise.

Table 9. Unadjusted and adjusted ORs and 95% CIs for the association between HIV prevalence and individual ACE categories

		HIV Prevalence			
		Unadjusted OR (95% CI)	P-Value	Adjusted OR (95% CI)	P-value
Physical Abuse*	No	1		1	
	Yes	1.39 (0.98 - 1.98)	0.067	1.57 (1.03 - 2.41)	0.038
Early Sexual Debut < 14 years (proxy for sexual abuse)**	No	1		1	
	Yes	1.10 (0.38 - 3.18)	0.855	0.68 (0.20 - 2.35)	0.542
Emotional Abuse ***	No	1		1	
	Yes	1.12 (0.82 - 1.53)	0.466	1.44 (0.94 - 2.22)	0.096
Witnessed verbal violence at home******	No	1		1	
	Yes	0.91 (0.66 - 1.26)	0.572	0.65 (0.41 - 1.05)	0.077
Witnessed physical violence at home*	No	1		1	
	Yes	1.51 (1.06 - 2.14)	0.023	1.63 (1.07 - 2.49)	0.022
Witnessed community violence *******	No	1		1	
	Yes	0.82 (0.62 - 1.09)	0.179	0.69 (0.49 - 0.98)	0.037

*adjusted for randomisation arm, orphan status, age, grade at enrolment and witnessed community violence
** adjusted for randomisation arm, orphan status, age, grade at enrolment, witnessed physical violence at home and witnessed community violence
*** adjusted for randomisation arm, orphan status, age, grade at enrolment, witnessed physical violence at home, witnessed verbal abuse at home and witnessed community violence
****adjusted for randomisation arm, orphan status, age, grade at enrolment, and witnessed physical violence at home
*****adjusted for randomisation arm, orphan status, age, grade at enrolment, maternal level of education, paternal level of education, and witnessed physical violence at home

3.3 Mediation Analysis

Table 10 presents the results of a mediation analysis examining the relationship between physical abuse and HIV prevalence, mediated through various behaviours associated with HIV risk. Notably, transactional sex emerges as the most substantial mediator, indicating that 19.89% of the total impact of childhood physical abuse on HIV prevalence is mediated through transactional sex. However, none of the examined mediators demonstrate statistically significant mediation between childhood physical abuse and HIV. This is evidenced by the 95% confidence interval of the Natural Indirect Effect (NIE) containing the value 1.

Table 10. Mediation effects and 95% CIs for the effect of physical abuse and HIV prevalence through various mediators

	Total Effect (TE)	**Controlled Direct Effect (CDE)**	**Natural Direct Effect (NDE)**	**Natural Indirect Effect (NIE)**	**Proportion Mediated**
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	(%)
Experienced Sexual Violence in the past 12 months	1.49 (1.00 - 2.21)	1.44 (0.96 - 2.16)	1.44 (0.96 - 2.16)	1.03 (0.97 - 1.10)	7.61
Transactional Sex in the past 12 months	1.49 (0.98 - 2.28)	1.38 (0.90 - 2.11)	1.38 (0.90 - 2.11)	1.08 (0.99 - 1.19)	19.89
Number of Lifetime Sexual Partners	1.48 (0.92 - 2.38)	1.46 (0.94 - 2.28)	1.46 (0.94 - 2.28)	1.01 (0.86 - 1.19)	2.92
Ever Drank Alcohol	1.53 (1.03 - 2.28)	1.54 (1.04 - 2.28)	1.54 (1.04 - 2.28)	1.00 (0.94 - 1.05)	1.03
Ever Used Drugs	1.52 (1.03 - 2.25)	1.54 (1.04 - 2.28)	1.54 (1.04 - 2.28)	0.99 (0.94 - 1.04)	2.75
Ever had condomless sexual intercourse	1.45 (0.82 - 2.56)	1.45 (0.92 - 2.28)	1.45 (0.92 - 2.28)	1.00 (0.71 - 1.41)	0.09
Age Difference with Partner	1.22 (0.54 - 2.79)	1.22 (0.66 - 2.25)	1.22 (0.66 - 2.25)	1.00 (0.58 - 1.74)	1.46

*adjusted for randomisation arm, orphan status, age, grade at enrolment and witnessed community violence

3.4 Sensitivity Analysis

Initially, there were 217 participants living with HIV, including participants who were already positive at enrolment for the primary study. After excluding the 48 participants who were HIV positive at enrolment, the number of HIV positive participants was reduced to 169. Consequently, the overall prevalence of HIV among those who became positive during the primary study was found to be 9.17%.

Much like the results found in Tables 5 and 7, when examining cumulative ACEs (both including and excluding early sexual debut) in relation to new sexually transmitted HIV cases over the course of the primary study, the unadjusted and adjusted models indicate that the association remains nonsignificant across all levels. This suggests that there is no statistically significant dose-response relationship between cumulative ACEs (including and excluding early sexual debut) and an approximation of HIV incidence among the study participants. These models were controlled for randomisation arm and age.

Table 11 presents the unadjusted and adjusted ORs with 95% CIs for the association between an approximation to HIV incidence and individual ACE categories. With regards to childhood physical abuse, participants who experienced childhood physical abuse have a 1.20 (95% CI: 0.87–1.94, p=0.209) times higher odds of HIV incidence compared to those who did not. However, this is not statistically significant. After adjusting for confounders, the OR increases to 1.30 (95% CI: 0.83–2.01, p=0.251), however still remains statistically nonsignificant. When comparing this to Table 9, the direction of the ORs are consistent, however, the aOR in Table 9 is statistically significant.

For early sexual debut, emotional abuse and witnessed verbal violence at home, both the unadjusted and adjusted ORs suggest no significant association with HIV incidence. This is consistent with the findings in Table 9.

Witnessing physical violence at home is significantly associated with HIV incidence in the adjusted model. The aOR is 1.90 (95% CI: 1.08–3.36, p=0.026) indicating higher odds of HIV incidence among those who witnessed physical violence at home during childhood compared to those who did not. This is also consistent with findings in Table 9.

Witnessing community violence shows an OR of 0.92 (95% CI: 0.67–1.27, p=0.629) in the unadjusted model and an OR of 0.93 (95% CI: 0.65–1.32, p=0.671) in the adjusted model, indicating a lower odds of HIV incidence among those who witnessed community violence during childhood compared to those who did not. However, this relationship is not statistically significant. When comparing this to Table 9, the direction of the ORs are the same, however, the aOR in Table 9 is statistically significant.

Table 11. Unadjusted and adjusted ORs and 95% CIs for the association between an approximation of HIV incidence and individual ACE categories

		HIV Incidence Approximation			
		Unadjusted OR (95% CI)	P-Value	Adjusted OR (95% CI)	P-value
Physical Abuse*	No	1		1	
	Yes	1.29 (0.87 - 1.94)	0.209	1.30 (0.83 - 2.01)	0.251
Early Sexual Debut < 14 years (proxy for sexual abuse)*	No	1		1	
	Yes	1.06 (0.32 - 3.53)	0.921	0.73 (0.17 - 3.14)	0.669
Emotional Abuse *	No	1		1	
	Yes	1.01 (0.71 - 1.44)	0.969	1.17 (0.79 - 1.73)	0.441
Witnessed verbal violence at home**	No	1		1	
	Yes	0.84 (0.58 - 1.22)	0.360	0.61 (0.36 - 1.04)	0.068
Witnessed physical violence at home***	No	1		1	
	Yes	1.36 (0.91 - 2.04)	0.131	1.90 (1.08 - 3.36)	0.026
Witnessed community violence *	No	1		1	
	Yes	0.92 (0.67 - 1.27)	0.629	0.93 (0.65 - 1.32)	0.671

* adjusted for randomisation arm and age
* *adjusted for randomisation arm, age, and witnessed physical violence at home
***adjusted for randomisation arm, age and witnessed verbal violence at home

CHAPTER 4: DISCUSSION

4.1 Discussion

The study findings offer valuable insights into the relationship between ACEs and HIV prevalence among AGYW. By addressing the question of whether AGYW who have any ACEs, or a greater number of ACEs are more likely to be infected with HIV compared to those who have not, this research contributes to the understanding of the intersection between ACEs and HIV infection. Overall, the study population had an HIV prevalence of 11.48%. While a large percentage of participants did not report experiencing any ACEs, the majority indicated the presence of at least one ACE. Descriptive analysis suggested that parental status plays a role in HIV prevalence, with participants who have lost both parents showing a substantially higher HIV prevalence compared to those who have not. Contrary to initial expectations, the analysis revealed no significant association between increasing cumulative ACEs score and HIV prevalence, regardless of whether early sexual debut was included in the score. Certain individual ACEs had a compelling association with HIV prevalence. Participants who experienced childhood physical abuse have a higher odds of HIV infection compared to those who did not. Participants who witnessed physical violence at home during childhood also have a higher odds of HIV infection compared to those who did not. Interestingly, participants who witnessed community violence during childhood had a lower odds of HIV infection compared to those who did not. Due to physical abuse being the most direct form of abuse that showed a statistically significant association with HIV, mediation analysis was done between these two variables. However, none of the examined mediators demonstrated statistically significant mediation between childhood physical abuse and HIV prevalence, although transactional sex mediation is the largest portion of the effect.

The elevated burden of HIV observed among the study population highlights the urgent need for targeted interventions and research efforts aimed at addressing this pressing public health issue. Comparing the current HIV prevalence rates among AGYW in this study to previous estimates reveals a concerning trend of escalating HIV burden. While 2012 data indicated an HIV prevalence of 5.5% among adolescent girls, the current study found a nearly double burden of HIV within this age group (67). Given the substantial influence of HIV on the well-being and health of AGYW, as well as its broader implications for public health, there is an urgent need for multi-sectoral approaches to HIV prevention and treatment. Moreover, the

elevated burden of HIV observed in this population underscores the importance of continued research into the underlying drivers of HIV transmission and acquisition.

The prevalence of ACEs observed in this study population, aligns with global statistics which indicate that over 50% of individuals have encountered some form of violence during childhood (20). Interestingly, the prevalence of ACEs in this population appears to be lower than in other parts of South Africa, such as Soweto, where nearly all children reported exposure to direct experiences of violence within their home, school, and/or community (10). Several factors may contribute to this discrepancy. Firstly, the ACEs questionnaire used in this study may not have been fully tailored to the cultural and linguistic context of the population, potentially leading to underreporting of ACEs. Although all questionnaires were translated into Xitsonga (62), cultural nuances and differences in language expression may influence how individuals perceive and report traumas (75,76). Thus, the use of standardised assessment tools that are not culturally adapted may underestimate the true prevalence of ACEs in specific populations. Secondly, the rural setting of Bushbuckridge, in contrast to the urban environment of Soweto, may also contribute to differences in the prevalence of ACEs. Rural communities may exhibit different patterns of social dynamics, familial structures, and community norms that influence the occurrence and reporting of ACEs (77). Additionally, socio-economic factors, including poverty, unemployment, and access to education and healthcare, may play a role in shaping childhood experiences and exposure to ACEs (77). Rural areas often face distinct socio-economic challenges compared to urban areas, which may impact the prevalence of ACEs. According to police recorded crime statistics for the first quarter of 2021, Bushbuckridge has a notably high crime rate (78). The police station in Bushbuckridge ranked in the top 4 for robbery cases and in the top 30 for hijacking cases, nationally. Despite this high crime rate, urban areas generally experience even higher crime rates, with the Johannesburg central police station ranking in the top 2 for robberies (78). When it comes to cases of reported child neglect and ill-treatment, Johannesburg central had a substantially larger number of reported cases than Bushbuckridge, with 274 reported cases compared to 8 cases in Bushbuckridge in 2021. However, underreporting of these cases is common (79).

Parental status significantly influenced HIV prevalence, as descriptive analysis revealed that participants who lost both parents had a markedly higher HIV prevalence compared to those who had lost one or no parents. This finding is consistent with existing literature, which associates orphanhood with decreased social support, fewer resources, and poorer mental

health outcomes (80). For instance, a pooled data analysis across 19 countries in sub-Saharan Africa found that orphans who lost their mother or both parents were two to three times more likely to test positive for HIV infection (81). Similarly, a meta-analysis of HIV testing data across 12 SSA countries reported a substantially higher HIV seroprevalence among orphaned youth compared to non-orphaned youth (82). The maternal HIV status and perinatal transmission of HIV are likely explanations for this association, as parental HIV status is often linked to their illness and death (83). Other contributing factors may include altered sexual behaviours and increased vulnerability to abusive situations following the loss of parents.

The absence of an association between increasing cumulative ACEs and HIV prevalence observed in this study diverges from the predominant trend reported in the literature. The majority of existing research indicates a dose-response relationship between ACEs and a range of negative health outcomes, whereby higher levels of adversity are linked with increased risks of negative health outcomes (2,3,13). This foundational concept was first established in the seminal ACEs study (6) and has since been consistently replicated across numerous studies (2,3,13). However, when specifically examining the association between cumulative ACEs and HIV prevalence, the literature presents a more varied landscape. While some studies, such as one conducted on men from the USA, have demonstrated a clear link between increasing ACEs and elevated odds of HIV infection, findings from other studies have been less conclusive (23,59,60). Notably, there is a scarcity of research specifically exploring the relationship between cumulative ACEs and HIV in the South African context, with the available evidence suggesting associations between individual ACEs and HIV incidence among South African youth, rather than cumulative ACEs (24). The divergence in findings may stem from the scope of outcomes examined in previous research, with many studies exploring a wide array of negative health outcomes beyond HIV. By focusing solely on HIV as the primary outcome, this study has limited its ability to capture the full breadth of health consequences related to ACEs. When examining cumulative ACEs and HIV, the divergence in findings may also be due to the composition of study populations, with differences in socio-economic status, cultural backgrounds, and environmental contexts potentially influencing the relationship between ACEs and HIV. For instance, the study on men from the USA may not directly translate to the experiences of AGYW in South Africa (23). Additionally, ACEs are more common in this study's population than in the study conducted on men from the USA, where only 33.5% reported at least one ACE, compared to almost double that in this study's population (23) Another explanation for this discrepancy is that the ACEs questionnaire used in this study may

not have been adapted to the cultural and linguistic context of the population, potentially leading to underreporting of ACEs. This study's findings suggest that the mere accumulation of various types of childhood adversity may not necessarily translate to a heightened odds of HIV infection among AGYW. Moreover, these findings suggest that there is a need for an examination of individual ACEs and their specific associations with HIV prevalence.

This study found that certain individual ACEs had a significant association with HIV prevalence. Particularly, participants who had been exposed to childhood physical abuse and witnessed physical violence at home had a higher odds of HIV infection compared to those who did not. These findings align with current literature, which suggests that individual ACEs are associated with risky sexual behaviour linked to HIV acquisition and other HIV-related outcomes (11,24,25,56). For instance, a study conducted in Zambia found that physical abuse and witnessing domestic violence were both linked to an increased risk of risky sexual behaviour (56). Similarly, research across five Sub-Saharan African countries found that women who experienced childhood physical abuse had higher odds of engaging in risky sexual behaviour, such as unprotected sexual intercourse (11). Furthermore, a study conducted on mothers living with HIV in Cape Town identified emotional and physical abuse and neglect, and exposure to collective violence as primary drivers of HIV-related outcomes, including poor adherence to ARVs and high viral load (25). Additionally, a South African study focusing on HIV incidence found that women who had experienced early-life physical punishment, emotional abuse, and sexual abuse had significantly higher rates of incident HIV infections (24). What sets this study apart is its focus on a population not extensively covered in previous research, highlighting the far-reaching impact of violence against children. This finding underscores the enduring effect of exposure to violence, both directly and indirectly, and emphasises the need for interventions aimed at addressing the root causes of interpersonal violence to mitigate its impact on HIV risk.

While existing evidence consistently supports the association between individual ACEs and HIV-related risks or outcomes (11,24,25,56), this study revealed that certain ACEs, including early sexual debut (proxy for child sexual abuse), emotional abuse, and witnessed verbal abuse during childhood, did not show significant associations with HIV. Several factors may contribute to this discrepancy. Firstly, due to the absence of a specific question on sexual abuse in the ACEs questionnaire, the study employed age of sexual debut below 14 years as a proxy measure for CSA. However, this approach may have limited the accuracy and

comprehensiveness of assessing sexual abuse as an ACE, potentially contributing to the lack of significant association with HIV. Moreover, as previously stated, the ACEs questionnaire used in this study was not tailored to the cultural and linguistic characteristics of the study population. This oversight might have led to underreporting of ACEs, particularly sensitive experiences such as sexual and emotional abuse, thereby impacting the overall findings. While previous research consistently links childhood sexual and emotional abuse to heightened HIV risk (24–26,36,38,39,84), the absence of significant associations in this study suggests that other factors, such as access to HIV prevention services or supportive social networks, could have mitigated the effects of ACEs on HIV risk among this population.

The unexpected finding that participants who reported witnessing community violence during childhood had lower odds of HIV infection compared to those who did not witness such violence presents a notable divergence from conventional expectations. It contradicts the commonly accepted notion that exposure to violence and trauma heightens susceptibility to HIV (85). Literature has established pathways linking exposure to community violence with increased risk of HIV or STIs through alterations in sexual behaviour (86). For instance, a study conducted on African American youth demonstrated links between experiencing community violence and engaging in risky sexual behaviours, as well as early initiation of sexual activity (86). The unexpected inverse association between witnessing community violence and HIV infection emphasises that pathways to HIV are complicated. Several factors may contribute to the discrepancy between this study's findings and anticipated outcomes. Firstly, the study was conducted in Bushbuckridge, a former homeland characterised by high poverty rates and endemic community violence, similar to many other regions in South Africa (65). Over 50% of the study participants witnessed community violence in childhood. In such environments, where community violence is pervasive and individuals adapt to its presence as part of daily life, the relationship between violence exposure and HIV risk may be complex. It's plausible that both community violence and HIV prevalence coexist as prevalent issues within this community, without necessarily directly influencing or protecting each other. Furthermore, individuals who are regularly exposed to chronic community violence may have developed resilience mechanisms to cope with their environment (87,88), potentially reducing the effect the violence has on their susceptibility to HIV. This resilience hypothesis suggests that adaptation to adversity could confer some level of protection against negative health outcomes. Additionally, in such environments with high rates of community violence, parents or guardians may enforce that their children, especially their daughters, stay home rather than

socialising outside of school hours, in an effort to protect them. This would lead to less interaction with peers in an unsupervised environment. Lastly, as mentioned above, the lack of cultural appropriateness in the questionnaire used for data collection may have contributed to under or overreporting of ACEs, including exposure to community violence. This reporting could potentially mask the true extent of the relationship between violence exposure and HIV risk in this population.

Mediation analysis aimed to uncover potential pathways through which physical abuse might influence HIV prevalence. Physical abuse was selected as the primary exposure due to its statistically significant association with HIV prevalence, as well as its distinction as the most direct form of abuse showing any significance. Although, none of the examined mediators demonstrated statistically significant mediation, transactional sex was the most substantial mediator, indicating that 19.89% of the total impact of childhood physical abuse on HIV prevalence is mediated through transactional sex. This finding aligns with existing literature, which consistently links ACEs, particularly childhood physical abuse, with risky sexual behaviour, which in turn is associated with HIV acquisition (26,27,40). Specifically, several studies have linked childhood physical abuse with engagement in transactional sex in adulthood (27,28,41). Although there is a lack of statistically significant mediation, it is important to acknowledge that this study is cross-sectional, and the timing of events cannot be discerned. Without clarity on whether mediation factors preceded or followed the outcome or exposure, the interpretation of results may be constrained.

4.2 Strengths and Limitations

The study has a number of notable strengths that significantly add to the understanding of HIV prevalence among AGYW in Bushbuckridge. Firstly, it addresses a critical gap in research by focusing on a population that has been historically underexamined. By shedding light on the unique challenges faced by AGYW in this specific geographic area, the study provides insights into the factors driving HIV acquisition within this vulnerable population. This provides valuable information to the ongoing need to develop evidence-based interventions and strategies for HIV prevention and control.

Additionally, this study benefits from a relatively large sample size, allowing for robust statistical analysis which potentially enhances the generalisability of the data. Consequently,

policymakers and public health practitioners can have greater confidence in the applicability of the study's results to similar populations and contexts.

Furthermore, the study's comprehensive assessment of ACEs is a significant strength. By examining a wide range of ACEs, including direct forms such as childhood physical and emotional abuse, as well as indirect forms such as community and household violence, the study provides a nuanced understanding of how these experiences relate to HIV prevalence. Moreover, the examination of ACEs both cumulatively and individually allows for a comprehensive perspective, highlighting specific ACEs that warrant targeted interventions. This broad approach enhances our understanding of the complex interplay between ACEs and HIV acquisition among AGYW.

While the study provides valuable insights, it does nonetheless have several limitations. Firstly, this study examined HIV prevalence rather than incidence as the primary outcome. The primary study originally measured HIV incidence, capturing new HIV infections over a specified period. However, ACEs were retrospectively assessed in 2017 during a follow-up survey conducted after the completion of the primary study. As a result, the exposure was measured after the outcome, which can introduce bias. Furthermore, the study population consisted of young women aged 13-20 at enrolment, therefore there would have been challenges in deciphering the timing of ACE exposure and HIV incident infection. The use of HIV prevalence was more appropriate than HIV incidence for analysing the association with ACEs. To mitigate this limitation, a sensitivity analysis was done to compare HIV prevalence and an approximation of HIV incidence within a cross-sectional study design. This analysis showed that findings remained fairly consistent.

Another limitation in the study was that there was a reliance on self-reported data for ACEs. This could introduce potential recall bias and social desirability bias, which could ultimately lead to inaccuracies in the study results. Moreover, the ACEs questionnaire used in the study did not capture the full spectrum of ACEs. It specifically lacked questions pertaining to CSA, necessitating the use of early sexual debut as a proxy measure. However, this proxy measure may not have fully captured the complexities of CSA. Finally, cultural and contextual factors specific to the community of Bushbuckridge were not incorporated into the ACEs questionnaire. potentially resulting in the underestimation or misrepresentation of ACEs.

CHAPTER 5: CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

This study offers a nuanced understanding of the relationship between ACEs and HIV prevalence among AGYW. The findings reveal that individual ACEs are more significant factors in HIV infection and prevalence than cumulative ACEs. Specifically, childhood physical abuse and witnessing physical violence at home were significantly associated with higher odds of HIV infection. Conversely, early sexual debut, emotional abuse, and witnessing verbal violence did not show any statistically significant association with HIV prevalence. This highlights the complex intersection between specific types of childhood adversity and HIV infection. Notably, witnessing community violence was associated with lower odds of HIV infection, underscoring the need for further research to understand the complexity of this finding in the South African context.

This study addresses the limited research on the relationship between ACEs and HIV prevalence specifically among AGYW in rural South Africa. Previous research has predominantly focused on ACEs and HIV risk-related behaviours, whereas this study centres on HIV infection itself as the primary outcome. Additionally, prior research often lacked consideration of the broader spectrum of ACEs, such as exposure to community and household violence, which this study has included. By examining ACEs within the specific context of rural communities, where patterns of adversity differ from those in urban areas, the study provides insights that can inform the development of trauma-related interventions and policies tailored to reduce HIV incidence among AGYW in rural South Africa.

5.2 Recommendations

Given the above insights, several recommendations emerge. Public health strategies should prioritise interventions addressing childhood physical abuse and domestic violence. These interventions could include community-based education programmes, counselling services, and the development of safe spaces for children, adolescents, and women. Additionally, providing comprehensive support services that include mental health support, trauma-related care, and social support networks for AGYW who have experienced ACEs can help mitigate the long-term effects of childhood adversity on health outcomes, including HIV risk.

Future research should adapt ACEs assessment tools to better fit the cultural and linguistic context of the study population. This can improve the accuracy of reporting and provide a fuller understanding of the prevalence and impact of ACEs. Furthermore, conducting longitudinal studies to establish causal relationships between ACEs and HIV incidence can provide a clearer picture of the temporal associations and inform more effective intervention strategies.

Additionally, it would be valuable to explore the profiles of AGYW who did not report any ACEs. Understanding what differentiates this group and identifying protective factors or resilience strategies could provide critical insights for designing future interventions. By implementing these recommendations, policymakers and public health practitioners can better address the dual burden of ACEs and HIV among AGYW, ultimately improving health outcomes and quality of life for this vulnerable population.

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APPENDICES

Appendix 1: Plagiarism Declaration

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Lamisa Naushin (Student number: 680108) am a student registered for the degree of MSc Infectious Disease Epidemiology in the academic year 2024/25

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: _____ Date: 13 Jan 2025

Appendix 2: Turnitin Cover Page

20/06/2024, 09:41 Turnitin - Originality Report - Research Report Submission for TurnItIn.docx

Turnitin Originality Report

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Appendix 3: Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R49 Dr L Naushin

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M240218

NAME: Dr L Naushin **DEGREE:** MSc
Principal and Co-Investigators

DEPARTMENT: School of Public Health
Division of Epidemiology and Biostatistics
Medical School
University

PROJECT TITLE: *The relationship between adverse childhood experiences and HIV prevalence amongst adolescent girls and young women in Mpumalanga: an HPTN068 analysis; 2017*

DATE CONSIDERED: 01 March 2024

DECISION: Approved unconditionally

CONDITIONS: Sub-study under WHC Clearance No. 10/10/12

NOTE: If contact information regarding student study participants is required, please contact the Registrar's office <Nicoleen.Potgieter@wits.ac.za>

SUPERVISOR: Professor S Mall and Dr M Stoner

APPROVED BY:
Professor P Ruff, Chairperson, HREC (Medical)

DATE OF APPROVAL: 18 April 2024 **EXPIRY DATE:** 17 April 2029

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report** in the format available at https://wits.ac.za/research/researcher-support/research-ethics/ethics-committees/. This report is due annually, for the duration of the Clearance Certificate, beginning on the first anniversary of Date of Approval above. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

19 April 2024
Date

Appendix 4: Supplementary Tables

Table 12. Prevalence of socio-demographic factors and potential mediating factors in the study population

Factor	Level	Total	Column Percentages of Total (%)
Country of Birth	South Africa	1851	97.88%
	Zimbabwe	3	0.16%
	Mozambique	36	1.90%
	Swaziland	1	0.05%
Grade at Enrolment	Grade 8	467	24.70%
	Grade 9	495	26.18%
	Grade 10	559	29.56%
	Grade 11	370	19.57%
Marital Status	Never Married	1836	97.09%
	Married	54	2.86%
	Widow	1	0.05%
	Divorced/Seperated	0	0.00%
Maternal Level of Education	No School	307	17.76%
	Some Primary	343	19.84%
	Completed Primary	87	5.03%
	Some High School	528	30.54%
	Completed High School	409	23.66%
	University/ Technikon	55	3.18%
Paternal Level of Education	No School	328	21.22%
	Some Primary	276	17.85%
	Completed Primary	75	4.85%
	Some High School	375	24.26%
	Completed High School	426	27.55%
	University/ Technikon	66	4.27%
Orphan Status	Both Parents Alive	1188	63.60%
	Single Orphan	547	29.28%
	Double Orphan	133	7.12%
Randomization Arm	Control Group	906	47.91%
	Conditional Cash Transfer Group	985	52.09%
Experienced Sexual Violence in the past 12 months	No	1804	96.01%
	Yes	75	3.99%
Transactional Sex in the past 12 months	No	1374	85.02%
	Yes	242	14.98%
Lifetime Sexual Partners	< 2	565	26.43%
	≥ 2	652	53.57%

Ever Drank Alcohol	No	1556	82.77%
	Yes	324	17.23%
Ever Used Drugs	No	1794	95.22%
	Yes	90	4.78%
Ever had condomless sexual intercourse	No	246	20.97%
	Yes	927	79.03%
Age Difference with Partner	< 5 years older	83	16.47%
	≥ 5 years older	421	83.53%