Childhood trauma exposure and Adherence to antiretroviral therapy (ART) among patients attending a public Neuropsychiatry health facility

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Contents

Declaration

I, Prinesh Miseer declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Master of Medicine in the branch of Psychiatry at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

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(Signature of candidate)

…18th……day of
……October…….2020…….in……Johannesburg……

Dedication

This research project is dedicated to all people with mental illness and mental health workers, who continue to strive for a better life and continue to advocate for a better future.

Abstract

***Background*:** Despite the latest efforts and guidelines to ensure access to Anti-retroviral (ART) treatment for HIV, South Africa still faces public health concerns with regards to the spread of HIV and adherence to treatment. Due to many factors, South Africans have been exposed to multiple traumas throughout their lives, especially childhood trauma. The study tried to determine the possible association between childhood trauma and adherence to Anti-retroviral treatment.

Methods: Data was collected from Luthando clinic, a public neuropsychiatric facility in Johannesburg, specialising in the treatment of patients with HIV and mental illness. Patients attending the clinic between: June 2017 to December 2017, on ARTs for 2 years and older than 18 years of age were included in the study. Their files were retrospectively reviewed for a history of childhood trauma, number of traumatic events and age of first childhood trauma, demographics collected, psychiatric diagnosis noted, ART regimen and CD4 count and viral load parameters recorded. Two consecutive viral loads were used to determine adherence to HIV treatment. The Chi square test, Fisher's exact test was used to determine the relationship between categorical study variables and a history of childhood trauma, with the strength of associations measured by Cramer's V and phi co – efficient respectively. The relationship between continuous study variables and childhood trauma was assessed by the independent samples t – test and Wilcoxon rank sum test, and associations measured with the Cohen's d (parametric tests) and r – value (non – parametric tests).

Results: A sample of 150 subjects was included in the statistical analysis. 31.3% (n = 47) of subjects experienced childhood trauma. Non – adherence to ARTs and childhood trauma exposure revealed no significant association. Significant associations that were found included a greater proportion of females exposed to childhood trauma compared to females who hadn't experienced childhood trauma (p – value = 0.0096) and a significantly higher ratio of females to males who had experienced childhood trauma. Another significant finding was lower adherence in subjects using 2nd line ART regimen compared to 1st line ART regimen (p – value = 0.0042).

Conclusions: Childhood trauma remains a concern in public health in South Africa. Female childhood trauma exposure remains high and warrants further research in order to find solutions to decrease this problem. Whilst no significant association was found between childhood trauma exposure and non – adherence to ART, further research would be required to establish other variables that could affect non- adherence to ART. Clinics such as Luthando may be used as a model to increase adherence to ART in other clinics.

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Nomenclature

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
CD4	Cluster of differentiation
HIV	Human Immunodeficiency Virus
PLWH	People living with HIV
PTSD	Post traumatic stress disorder
TB	Tuberculosis
RNA	Ribonucleic acid

Study definitions

Childhood trauma is defined as a form of abuse before 17 years of age. Physical abuse includes acts such as hitting, beating or shaking. Sexual abuse is regarded as sexual contact or exposure to sexual acts or materials. Emotional or psychological abuse includes threatening, insulting, ridiculing or confining. A failure to provide education, medical care, shelter or other essentials for a child's healthy development, despite the means, is considered neglect.

CHAPTER 1

1.1 Introduction and Background

HIV continues to be a burden to South Africa's public health system despite initiatives to provide greater access to medication and health services, and new guidelines to provide treatment to all South Africans living with HIV.

In 2016, South Africa had 270 000 (240 000 – 290 000) new HIV infections and 110 000 (88000 – 140000) AIDS-related deaths. There were 7 100 000 (6 400 000 - 7 800 000) people living with HIV in 2016, among whom 56% (50% - 61%) were accessing antiretroviral therapy. Among people living with HIV, approximately 45% (41% - 50%) had a suppressed viral load.[1]

Unsuppressed viral loads are already an indicator that maintaining adherence amongst the population is a public health concern.[1] In addition; South Africa also has a high rate of lifetime trauma exposure.

South Africa also has a high rate of childhood trauma exposure. A South African study, which interviewed high school learners, showed that 83% of the sample size (1140) self-reported childhood trauma exposure.[2]

The association between childhood trauma exposure and its effect on pathogenesis of HIV has been explored, but much less literature exists exploring the relationship between a history of childhood trauma exposure and its effect on adherence to HIV treatment and HIV positive mental health care users.

A study assessing quality of life and how it is affected by HIV and childhood trauma in South African women concluded that both HIV infection and a previous childhood trauma history are significant predictors of a decreased quality of life when compared to testing HIV negative and experiencing no childhood trauma exposure.[3]

These poorer outcomes may have an effect on adherence to HIV treatment or could be a direct effect of poor adherence to treatment.

In a two part series studying developmental traumatology and its effects on biological stress systems and brain development it was shown through use of biological measures and imaging techniques that children exposed to childhood trauma and subsequent development of PTSD, had lower global assessment of functioning scores, greater co – morbidity of depressive illness and adverse brain development shown by magnetic resonance imaging.[4]

The biological consequences of childhood trauma could lead to poor adherence to HIV treatment, as many of the above outcomes can indirectly and directly affect adherence and clinical progression of the HIV illness.

The relationship between childhood trauma and ART adherence needs to be investigated as South Africa is currently burdened by the biggest HIV epidemic in the world. The country has 19% of all people living with HIV (PLWH) globally[1] and high rates of childhood trauma exposure.

The complex interplay of trauma exposure and HIV disease development and progression, especially childhood trauma exposure and its sequelae, such as adverse mental health outcomes, may have an understated role when it comes to explaining the HIV epidemic in South Africa.

1.2 Literature review

1.2.1 HIV/AIDS

South Africa globally accounts for most people living with HIV.[1] South Africa has the biggest HIV treatment rollout in the world and accounts for 19% of people living with HIV globally.[1]

Despite new HIV infections decreasing by 49% and AIDS-related deaths decreasing by 29% since 2010[1], the HIV epidemic still remains a public health dilemma and optimal adherence to ARTs remains vital in maintaining these trends.

1.2.2 ART treatment, adherence and adherence barriers

ART treatment is recommended in all people living with HIV. ART ensures healthier and longer lives and reduces HIV transmission.[5]

In South Africa, ARTs are available and international standards have been adopted with regards to initiation of treatment and treatment guidelines. According to 2016 UNAIDS statistics, amongst people living in South Africa, 6.1 million people living with HIV, are aware of their HIV status.[1]

In this group, 56% are using ART. The number of people living with HIV in South Africa who are virally suppressed is 45%.[1]

Viral suppression is achieved by using ARTs. Current guidelines suggest tenofovir with emtricitabine or lamivudine and efavirenz, dolutegravir or rilpivirine as first line treatment options in a South African context.

There are special populations that need to be considered due to side effects of these drugs, and further second line ART treatments that need to be considered if there is virological failure. These protocols are outlined in the guideline.[6]

As per WHO recommendations for developing countries such as South Africa, routine HIV viral load monitoring can be done at 6 months, then 12 months and then every 12 months thereafter.

These guidelines also further define HIV virological failure/virological suppression in developing countries as persistently demonstrable viral loads exceeding 1000 RNA copies/ml (that is, two consecutive viral load measurements within a 3 month interval, with adherence counselling between measurements) after at least 6 months of starting a new ART regimen.[7]

In order to achieve viral suppression through the use of ART and prevent clinical progression of the illness, more than 95% of treatment adherence to ART must exist all the time.[8,9]
The link between adherence to ART and viral load, and use of viral load as a measure of adherence has been demonstrated. In a prospective study evaluating adherence to ART with use of viral load measurement, analysis showed the relationship between >95% treatment adherence and the final viral load of less than 1000 RNA copies/ml was closer than that between >90% treatment adherence and viral load of less than 1000 RNA copies/ml. The study, done in Mozambique, used electronic pill counts and viral load measurements in order to examine the relationship between adherence and viral load measurements.[10]

The National Department of Health Guidelines regarding integrated ART adherence include seven steps that have been identified as key moments, whereby adherence and continuity of care could be compromised. It has also identified the minimum interventions needed in order to facilitate adherence and retention in practice such as: standardised psycho-education sessions and counselling for initiation on treatment and unstable patients, patient tracing systems, repeat prescriptions for stable patients in order to ensure less waiting times and an integrated model for co – infected patients with non - communicable diseases such as mental

illness, HIV and TB to rationalise frequency of clinic consults and medication pick up.[11]

Luthando clinic, the site of our study, has managed to meet all the minimum requirements for the proposed model to ensure ART adherence at clinic level. Luthando clinic is a specialist clinic that manages and treats mental illness users diagnosed with co – morbid HIV. Its role in our study will be discussed further on.

Adherence to ARTs and the possible barriers to adherence are public health concerns that require further investigation.

The literature, both international and local, further defines these barriers.

Co – morbid substance use and mental illness in HIV positive patients is a major determinant to non - adherence to ART. It was demonstrated in a multisite cohort study in the United States. Increased psychological distress was found to be significantly associated with non – adherence to ART, independent of substance use. Thus the combination of substance use is a further exacerbating factor to non – adherence to ART.[12]

Barriers to adherence to ART were also investigated in a cross sectional design study in South India. It found that financial restrictions, forgetfulness related to taking of medication, absence of family care, alcohol use, depression, social stigma, and ART side effects were associated with low adherence.[13] The socio – economic circumstances in India are shared by South Africa and are of interest when comparing barriers to adherence to ART.

A cross sectional, non - interventional study found that the major factors leading to sub – optimal adherence; were poor social support, a poor understanding of ART, other costs such as transportation and surplus food requirements and the presence of treatment side effects. A Kenyan study further reported that the majority of HIV patients receiving ART are not achieving optimum adherence.[14] Despite this study being in done in Kenya, these challenges are also experienced by South African patients living with HIV.

South African literature regarding adherence to ARTs, also shares similar findings found in the above studies.

A South African study investigating ART refusal, was conducted among newly diagnosed HIV positive patients. The groups were divided into those who accepted ART and those who refused. The study found that 'feeling healthy' was one of the main reasons for ART refusal when eligible for initiation of ART. Almost 20% of the participants refused to be initiated on ART. Other factors to refuse initiation included 'unable to disclose', 'side – effects', 'cultural beliefs' and 'unable to adhere'.[15]

In a prospective South African study which examined reasons for not continuing follow up at a specialized neuropsychiatric clinic, it was determined that 24.8% of patients did not follow - up as per clinic protocol. Costs involving transportation and distance, school schedules and conflict at work, and confusion regarding a return date to the clinic, were the most commonly cited reasons for stopping follow up. These patients were traced and interviewed.[16]

HIV status non – disclosure is also considered to be a barrier to ART adherence. It appears to influence whether a discharged psychiatric inpatient, would attend an outpatient clinic for follow – up. A South African retrospective review found that there was a significant increase in the quantity of non – attendees to an outpatient clinic, who did not disclose their HIV status to their treatment supporter.[17]

Mental illness alone has been found to be a predictor of adherence to ART. A review of the literature by Nel was conducted to determine the influence of mental illness on ART adherence. HIV, AIDS,ARV, ART, antiretroviral, therapy, treatment, barriers, symptoms, depression, anxiety, PTSD, post-traumatic stress disorder, alcohol abuse, substance abuse, mental disorders, mental health, and social support were the key words used to identify literature.

It was found that depression, anxiety and post – traumatic stress disorder were highly prevalent in people living with HIV. Multiple studies confirmed that the effects of mental illness were major determinants of non – adherence to ART.[18]

The studies above illustrate concerns with regards to adherence and access to ART in South Africa. Despite recent guidelines that have allowed use of ART for all HIV infected patients, these barriers to adherence continue to exist.

1.2.3 Trauma, PTSD and Childhood trauma as a Public health concern

South Africa has a high level of trauma exposure, which remains a public health concern. In 2015, 14.1 % of all non – natural deaths in South Africa were attributed to assault.[19]

Due to multiple factors, including *apartheid*, a period of racial oppression, segregation and discrimination, South Africa has a relatively increased level of trauma exposure in the general population. This trauma rate has remained despite the development of a new non – racial democracy post 1994. This unique political and social climate may be contributing to the unique trauma types and socio – demographic factors seen in South Africa compared to other countries.[20]

Direct trauma exposure outside and inside the South African home remains a concern. A complex relationship between direct links such as age of sexual assault, and indirect links such as high – risk attitudes after GBV have been postulated to cause HIV. There were significant prevalence rates of physical abuse by an intimate partner found in three South African provinces.[21]

An analysis of the literature exploring the relationship between gender – based violence

(GBV) and HIV causation in Southern African countries found evidence for indirect and direct links to GBV and HIV causation.[22]

This evidence was further supported by a longitudinal study which showed more than 20% of South African women suffered at least one experience of sexual, psychological or physical intimate partner violence throughout their pregnancy.[23]

PTSD also remains a significant public health concern as indicated in a study examining risk of PTSD associated with interpersonal violence in South Africa. Participants were interviewed and over one – third of South Africans were found to be exposed to some form of violence during their lifetime. This study also went on further to highlight a strong association between the development of PTSD in males and exposure to detention and torture, a common form of trauma exposure during the *apartheid* era in South Africa. In females, rape has the strongest association to development of PTSD, followed by intimate partner abuse, which are also highly prevalent in South African society.[24]

Maltreatment of children, defined as, physical abuse, neglect, emotional maltreatment and sexual abuse (that includes verbally threatening the child, ridiculing, confining and witness to domestic violence) is another public health concern.

WHO statistics show prevalence rates for maltreatment of children is significant. Worldwide rates range from 16% for physical neglect and 36% for emotional abuse in 2017.[25]

With regards to childhood trauma, international studies suggest that one out of every three girls is sexually abused by age 18 in the United States [26], and that elevated prevalence rates of physical (51.1%), emotional (51.9%), and sexual (41.6%) abuse have been documented in individuals who are HIV - positive.[27]

1.2.4 Childhood trauma and its future trajectory towards mental illness

Maltreatment in childhood is both a cause and a risk factor for PTSD. This was demonstrated in an Australian study, whereby a correlate was found between PTSD and three or more kinds of severe child maltreatment. Questionnaires were used as a tool for determining PTSD amongst young offenders in a juvenile detention centre.[28]

In a systematic review on childhood maltreatment and mental health outcomes in people with HIV, an assortment of mixed mental health outcomes were reported. The types of studies included were intervention studies and surveys. Subjects used in these studies were screened for mental illness with various tools, and were not following up as mental health care users. Most of the studies were North American, with the majority of studies from the USA. The most frequently reported psychiatric disorders amongst HIV-positive individuals with a history of childhood maltreatment comprised of: major depressive disorder, substance abuse and post -traumatic stress disorder.[29]

A 2001 prospective study analysed the influence of childhood neglect and abuse on mental health in adulthood. It followed up individuals with documented court cases of previous childhood abuse or neglect after 20 years, and compared them to controls. The childhood trauma group had considerably higher levels of antisocial personality disorder and dysthymia in males compared to the control group. Higher rates of antisocial personality disorder, dysthymia and alcohol use in females affected by childhood trauma were also found compared to the control group. Both childhood trauma exposed males and females experienced more lifetime stressors compared to the control group, which ultimately predisposes an individual to increased risk of developing mental illness. This study differed from previous studies examining childhood trauma that relied on self - reporting of retrospective events rather than official documentation of childhood abuse.[30]

Personal mastery and childhood trauma was examined in a study trying to determine if a history of childhood trauma predicted more negative daily events and to determine emotional

reactions to these events. A history of childhood trauma was associated with decreased overall levels and greater variability of well - being. The study also found a modest association concerning a history of childhood trauma and lower levels of personal mastery. These findings further support the major consequences of childhood trauma in adulthood and how it impacts on resilience and personal agency which modifies health seeking behaviour.[31]

Neuropsychiatric changes due to childhood trauma were found in research. The Minnesota Multiphasic Personality Inventory Scale (MMPI) was used as a means of identifying adults who survived childhood abuse. American inpatients seeking treatment were the subjects that were interviewed as part of the admission process. It was unclear as to which type of patients these were. The results of the MMPI showed that childhood trauma was related to changes in regulating affective arousal such as; behavioural disinhibition, hypervigilance, hyperarousal and depression. It also showed alterations in attention and consciousness, whereby participants were found to have high levels of apathy. There was also a lack of motivation, somatisation and dissociation. The above are all prominent features of PTSD.[32]

These neuropsychiatric manifestations have also been replicated in biological studies. A review of the literature with regards to childhood trauma exposure and neurobiological consequences showed that the major gross anatomical consequences of early stress include: decreased size of the mid-portions of the corpus callosum and reduced development of the left neocortex, amygdala and hippocampus. Major functional consequences include elevated irritability in limbic structures and decreased functional activity of the cerebellar vermis. These deficits have been proposed to lead to impaired episodic memory retrieval and dissociative states. These play significant roles in development of mental illnesses which are severe, such as schizophrenia, major depressive disorder and generalised anxiety disorder.[33]

Childhood trauma and its subsequent neuro - endocrine changes, due to early life stressors, can predispose an individual to the risk of developing depression. This United States study involved interviewing multiple inpatients, including depressed patients with a history of childhood trauma and patients without any childhood trauma or mental illness. Their plasma adrenocorticotropin and cortisol levels were taken after activities that induced mild stress

such as; public speaking and mental arithmetic tasks performed in front of an audience. The study suggested that childhood trauma is associated with persistent sensitisation of the stress responses and altered function of the HPA axis. This would in turn relate to symptoms of depression. It is noteworthy that this study also excluded subjects with severe mental and medical illnesses.[34]

There is a large body of literature regarding childhood trauma and its association with future mental illness. There appears to be less though, when discussing childhood trauma and future links to neuropsychiatric illnesses, especially within a South African context.

1.2.5 Childhood trauma and HIV and its effect on ART adherence

Childhood trauma and HIV have a complex association.

This association was found to be significantly stronger in women. A meta - analysis which included 46 studies, examining risk behaviour amongst women, demonstrated that childhood trauma may intensify HIV risk indirectly by elevating high-risk behaviours such as unprotected sexual intercourse and sex trading. The studies included subjects mostly from community samples, cross sectional design and subjects were interviewed in the majority of studies.[35]

In a cross sectional study which examined childhood violence exposure and its role in development of sexual risk taking behaviour, African American girls were interviewed. They came from a low income, urbanized environment and attended the local mental health clinics in Chicago. It was found that childhood violence exposure is significantly associated with inconsistent condom use and increased numbers of partners. These high risk behaviours are associated with an increased chance of contracting HIV.[36]

A large American randomised control study, examining shame experienced by people living

with HIV and childhood sexual abuse; showed significant poorer quality of life outcomes within this subset of subjects. Patients were recruited from medical clinics and community based organisations within New York City. 'Impaired mental status' was part of the exclusion criteria. The poorer quality of life outcomes in people living with HIV and previous childhood trauma exposure warrant the need for further investigations. Do factors such as adherence to ART influence these initial problems or are they a direct cause of poorer quality of life? Behavioural interventions were recommended in this study as part of the treatment plan.[37]

In the literature there is research that has found an association between childhood trauma exposure and HIV treatment adherence.

A cross sectional research paper in the United States showed that rates of antiretroviral non - adherence increased for each added category of lifetime trauma experienced. It was a cross sectional analysis of a large cohort study, which analysed data from the enrollment interview and medical records of study subjects. Subjects that reported 5 or more lifetime traumatic events, reported ART non – adherence of up to 34%. These subjects were attending infectious diseases clinics and had no formal psychiatric screening.[38]

In a longitudinal study examining women with HIV who are non – adherent, the multivariate analysis showed that documented childhood sexual abuse decreased the likelihood of HIV adherence. The study involved women from infectious diseases clinics throughout the United States. The women were divided into 3 categories: those who had experienced lifetime domestic violence, those with recent domestic violence exposure and those with childhood sexual abuse exposure.[39]

The association between childhood sexual abuse and non – adherence to ARTs was also found in a study that examined gender differences in health care and status among minority HIV – positive drug users, whereby use of medications was adversely related to childhood abuse. The participants were recruited from street outreach programs in New York City and had significant heroin or crack cocaine use.[40]

In a study done in Tanzania, incomplete ART adherence was considerably more likely to be reported amongst participants who suffered a larger number of childhood traumatic events. These events included; sexual abuse before puberty and the death in childhood of an immediate family member not from suicide or homicide. These events were significantly more likely in the non-adherent group and other negative childhood events trended toward being more likely in the non – adherent group. This study also demonstrated that subjects who were not completely adherent had increased post-traumatic stress and depressive symptomatology scores and less social support than the other subjects who reported complete adherence. The longitudinal study involved subjects who had no known mental illness, and were patients following up at hospital based HIV clinics. These subjects were then screened for depression and PTSD.[41]

HIV positive adolescents that have experienced or witnessed trauma are associated with increased rates of non – adherence to ART. This increases with different types of violence exposure. This South African cross sectional study; showed that physical abuse by caregivers, witnessing domestic violence at home, violence from a teacher at school, and verbal victimization from a clinic staff member were more considerably associated with non – adherence to ART. Primary care and community clinics which provided ART to HIV positive adolescents were sampled.[42]

Childhood trauma exposure and its relationship to HIV and adherence to ARTs, has been examined in the studies above.

The literature has very few studies where subjects have confirmed mental illness diagnoses. Most of the studies in the literature involve subjects following up at infectious diseases clinics.

This paucity of research includes patients with severe mental illnesses and patients with neuropsychiatric manifestations of HIV.

Adherence to ARTs in the above studies has also been measured mostly by self - report and not objectively measured by using tools such as a serum HIV viral load.

1.2.6 HIV and Mental illness

A multifaceted association exists between HIV and mental illness. HIV is a predisposing risk factor for the development of mental illnesses. The virus also causes secondary neuropsychiatric complications.
This bi – directional relationship is discussed in the literature.

The inflammatory process caused by HIV is believed to predispose individuals to certain mental illnesses such as depression and PTSD. A review of literature presented the multiple neurobiological circuits involved in HIV and its effects on mental illness. Deranged neuro - immunology and reduced brain-derived neurotrophic factor were postulated as causes of the development of mental illness in HIV patients. The disruption by HIV of dopaminergic receptors and the hypothalamic – pituitary axis has been documented in these studies. It gives further evidence to the interaction between HIV's biological and psychosocial consequences and subsequent mental illness.[43,44]

A review paper found that the most common neurological expressions are; motor disorders, minor cognitive impairment and HIV-associated dementia (HAD). The most common psychiatric manifestations are depressive illnesses. The effect of these syndromes on seropositive patients is e, and suitable interventions are required. The review suggests optimal treatment as early diagnosis and aggressive treatment.[45]

A longitudinal study and a review explored the correlation between the role of stress, depression and trauma and HIV/AIDS. It provided support for the hypothesis that a

psychosocial factor, such as; previous lifetime trauma, can affect immunological and clinical progression of HIV/AIDS. The review of English articles, showed increased viral loads and decreased CD4 counts associated with trauma, depression and stressful events.

The longitudinal study in the southern United States examined HIV positive clinic users and followed up adverse HIV related events. [46,47]

Depression is known to affect immunological function in people living with HIV and result in changes in health status and quality of life. A review article examined the prevalence of depression in HIV and highlighted some of the evidence showing the impact of depression on immunological function. The review included multiple longitudinal studies related to these relationships.[48]

In a US study comparing 93 HIV-seropositive women and 62 HIV-seronegative women, it was found that the prevalence of major depressive disorders was as much as 4 times higher among HIV-positive women than among HIV-negative controls. Subjects were recruited via various methods and a modified Structured Clinical Interview for DSM-IV, Hamilton Depression Rating Scale and the Hamilton Anxiety Rating Scale were used as diagnostic and screening tools. These subjects had no confirmed previous mental illness diagnosis.[49]

Another United States study showed increased prevalence in HIV and its association with mania. The study reviewed 162 patients that had HIV and were referred for psychiatric evaluation by primary medical caregivers. HIV disease development and associated mania are observed in up to 8% of HIV seropositive patients. This increase in manic presentations was associated with increasing clinical severity of HIV associated neurocognitive disorders.[50]

A meta – analysis tried to determine HIV prevalence and other viruses which are blood borne in severe mental illness. It managed to show that in the United States and Europe, HIV prevalence in people with severe mental illness is much greater than the general population. The prevalence was as much as ten times higher in the United States. Yet this study also

showed that in some African countries (4 studies were included from South Africa in the analysis), the prevalence of HIV in people with severe mental illness is on par with the prevalence of HIV in the general population. The hypothesis given for this discrepancy is that in the developing countries studied, severe mental illness may not be the only factor increasing HIV prevalence, but also variables such as substance misuse, socio – economic status, ethnic origin and gender.[51]

Common mental disorders were found to have a prevalence of 19% in HIV – infected primary health care users, with the most common diagnoses being depression, PTSD or alcohol use disorder. A Cape Town study assessed the prevalence of common mental illnesses and HIV – infected individuals in community clinics. Subjects were diagnosed and screened using the Mini-International Neuropsychiatric Interview (MINI) administered by trained research nurses. All participants were screened for depression, posttraumatic stress disorder (PTSD) and alcohol dependence/abuse. [52]

South African studies trying to determine HIV prevalence amongst those diagnosed with severe mental illness have been limited to mostly inpatient psychiatric patients. These studies have been unable to specify clear figures; regarding HIV prevalence in patients with severe mental illness, due to ethical issues with consent testing in the severely mentally ill.

There is also a paucity of research with regards to literature on outpatient clinics that specialise in dual diagnosis (HIV and severe mental illness). These clinics are ideally set up to examine both HIV and mental illness, and other variables that may influence the clinical outlook of the two disorders.

The studies presented in the literature review details the public health concerns that are faced due to the effects of HIV, childhood trauma and the subsequent trajectory towards the development of mental illness. The complex interaction of all these factors can directly and indirectly affect health behaviours such as ART adherence and further add to the burden of disease. A specialised clinic such as Luthando clinic, has given us the opportunity to examine all these factors together and to determine if there are any associations between these

variables. Due to the paucity of research, with regards to HIV adherence and Childhood trauma, it was a clear motivation for these variables and their association to be examined.

1.3 Study Aim and Objectives

The aim and objectives of this study were to:

- To obtain a socio – demographic profile of a sample of stable individuals with HIV, who have been on ART for at least 2 years, attending the Luthando Neuropsychiatric clinic. Stable subjects are defined as: patients who are clinically well, with no overt social and occupational dysfunction.

- To determine the occurrence of exposure to childhood trauma in outpatients attending a specialised Neuropsychiatric clinic.

- To determine the relationship between exposure to childhood trauma and adherence to ART.

- To investigate the relationship between childhood trauma and other demographic and clinical variables. These relationships may impact on adherence to ART.

- To examine the relationship between the number of childhood traumatic events and adherence to ART and the relationship between age of first traumatic event and adherence to ART.

- To determine the relationship between ART regimen and adherence.

CHAPTER 2

2.Methodology

2.1 Research Question

Does a previous history of childhood trauma have any significant association with adherence to ART in a specialised neuropsychiatric clinic?

2.2 Methodology and Research Design

A retrospective review of the records at Luthando clinic was conducted.

There was an examination of each subject's records, and it was determined whether a history of childhood trauma exposure was documented in previous clinical interactions.

Luthando is a specialised clinic and for the purposes of this study, patients attending the clinic on Friday were used.

2.3 Subjects, Measures and Methods

The Luthando Neuropsychiatric clinic, at Chris Hani Baragwanath Hospital, accommodates adult patients who are HIV positive and have a mental illness (Dual diagnosis patients).

Most of the patients are referred as inpatients from the acute psychiatric wards within the hospital itself. The clinic runs from Monday to Friday, with Fridays being reserved for stable patients. The service includes vitals monitoring, adherence counseling, urinalysis, group

events, review by a psychiatry registrar or consultant and blood monitoring of CD4 counts and viral load levels. Other concerns such as side effects to treatment or other medical concerns are also addressed.

Adherence is measured by self – report but also by viral load monitoring. Routine viral load monitoring is done every 6 – 12 months in the clinic.

If a patient is found to have a high viral load (more than 1000 RNA copies/ml), adherence counseling is performed. The patient is then usually reviewed within one month, and an HIV viral load test is done again. This is done to determine if there is re – established adherence or virological failure.

Patients that are reserved for the Friday clinic are given follow up dates, after each review, ranging from 1 month to 6 months.

This date is determined by nature of their problems (such as side effects; non adherence; treatment of co- morbid illnesses; follow up of blood results etc.), or they could be admitted or down referred to their local clinic if unstable/stable.

Patients with; severe neurocognitive problems due to HIV or any other cause, severely intellectually disabled patients, patients who are non – adherent to ART, or any patient that has a deteriorating clinical picture are reserved for other clinic days.

Their problems can be reviewed more extensively, due to the Friday clinic being the busiest day of the clinic.

The study focused on the Friday clinic patients, as it was determined that these patients would have been able to have given a more accurate history and clinical interview at some

point in their interaction with the clinic. Thus allowing their account of whether there was childhood trauma, to be used in the retrospective review of their file.

For the study; all patients who attended the clinic every Friday, between June and December 2017 were included. Their files were reviewed and accessed through the Luthando database and histories obtained from their files found in the general psychiatry outpatient department.

Their files were accessed and relevant clinical and demographic data was entered onto a data collection sheet (Appendix 1). Study participants were 18 years and older, HIV positive, had a mental illness and attended the Friday clinic.

The patients were not interviewed at any point throughout the study. Patients with more than one attendance day in the 6 month study period were only captured once in the analysis, so as not to confound study results.

Demographic and clinical characteristics were captured by means of a record review. This included age, gender, and relationship status, highest level of education and source of income.

Due to certain demographic details associated with increased risk of childhood trauma it was necessary to include specific variables in the data sheet.

The inclusion of these demographic details, allowed the primary investigator to identify specific groups of participants that may have an associated increased risk of non-adherence to ARTs and childhood trauma. This may have potential benefits for future research.

The Childhood Trauma Questionnaire Short Form (Appendix 2) was used as a reference tool when checking for histories of previous childhood trauma in patient files.[53]

Its use as a screening tool provided value when capturing the patient file data, as it provided brief, yet informative insights into childhood trauma.

On the Childhood Trauma Questionnaire Short Form there are five types of maltreatment: physical, emotional and sexual abuse and physical and emotional neglect.

The age of the first childhood traumatic event was recorded and the number of traumatic events included throughout childhood.

In some histories, the age of the first childhood traumatic event was not clear, and was omitted from the data sheet.

Adherence was interpreted from analysing the last two consecutive HIV viral loads from the patient's blood results chart.

When there was no viral load done within the study dates, viral load results from outside the study date were used, and were consecutive results. This has proven to be an indicator of adherence to ARTs, and this finding has been replicated in a study examining virological failure and its relationship to adherence to ARTs. Any patient, whose 2nd HIV viral load was more than a 1000 copies/ml, was deemed non – adherent, as in keeping with the literature.[54]

The Luthando clinic team was immediately notified of any patients that were discovered to be non – adherent to ARTs or not virally suppressed during the course of the study.

A baseline and most recent CD4- lymphocyte count was obtained from the recorded blood sample results to assess for clinical disease progression and to determine any correlates between CD4 lymphocyte count and other variables. As childhood trauma has an effect on immunological disease progression, these variables were considered to determine if there was a relationship between CD4 count and childhood trauma.

Psychiatric diagnoses were also noted, as specific psychiatric diagnoses are associated with childhood trauma.[28, 29, 30, 32, 33, 34] Confirmed psychiatric diagnoses in a specialised neuropsychiatric facility such as Luthando, were of interest, as most of the samples studied in the literature focused on patients attending infectious disease clinics.

ART regimen (1st or 2nd line) was also included as part of the data collection and analysis. It was of interest to determine if more subjects who had experienced childhood trauma, were more likely to be on 2nd line ART regimens. This may have indicated whether these patients are more vulnerable to HIV disease progression after childhood trauma exposure. Additionally it may have indicated if this subset of patients were more likely to be non – adherent and required 2nd line regimens after developing resistance.

2.4 Ethics

The research Protocol was submitted to the Human Research Ethics Committee (HREC) for ethical consideration and was granted (Appendix 3) – certificate number M170385.

Any subject who was identified as non – adherent/ or virally not suppressed while the record review was done, had their details given to the Luthando clinical team.

The primary investigator assigned a unique identification study number to each subject, only known to the primary investigator, in order to ensure that clinical data remained non – identifiable to each subject.

2.5 Sample

A convenient sampling method was used for the purposes of the study. The entire sample size included all patients who attended the Friday Luthando clinic between June and December 2017.

The total number of patients seen every Friday for the above period was 975.

The sample size was reduced due to exclusions such as patients who had already re – attended the clinic in the study period, patients not on ARTs for at least 2 years, patients with no laboratory results and subjects where no clinical record file could be found.

After examining patient files, subjects who were eligible for the study, had to have had a clinical interview after which a diagnosis according to DSM IV was made. A clear recording of a previous history of childhood trauma exposure or not, had to be documented.

All subjects were HIV positive, aged 18 and over with a mental illness on ARTs for at least 2 years.

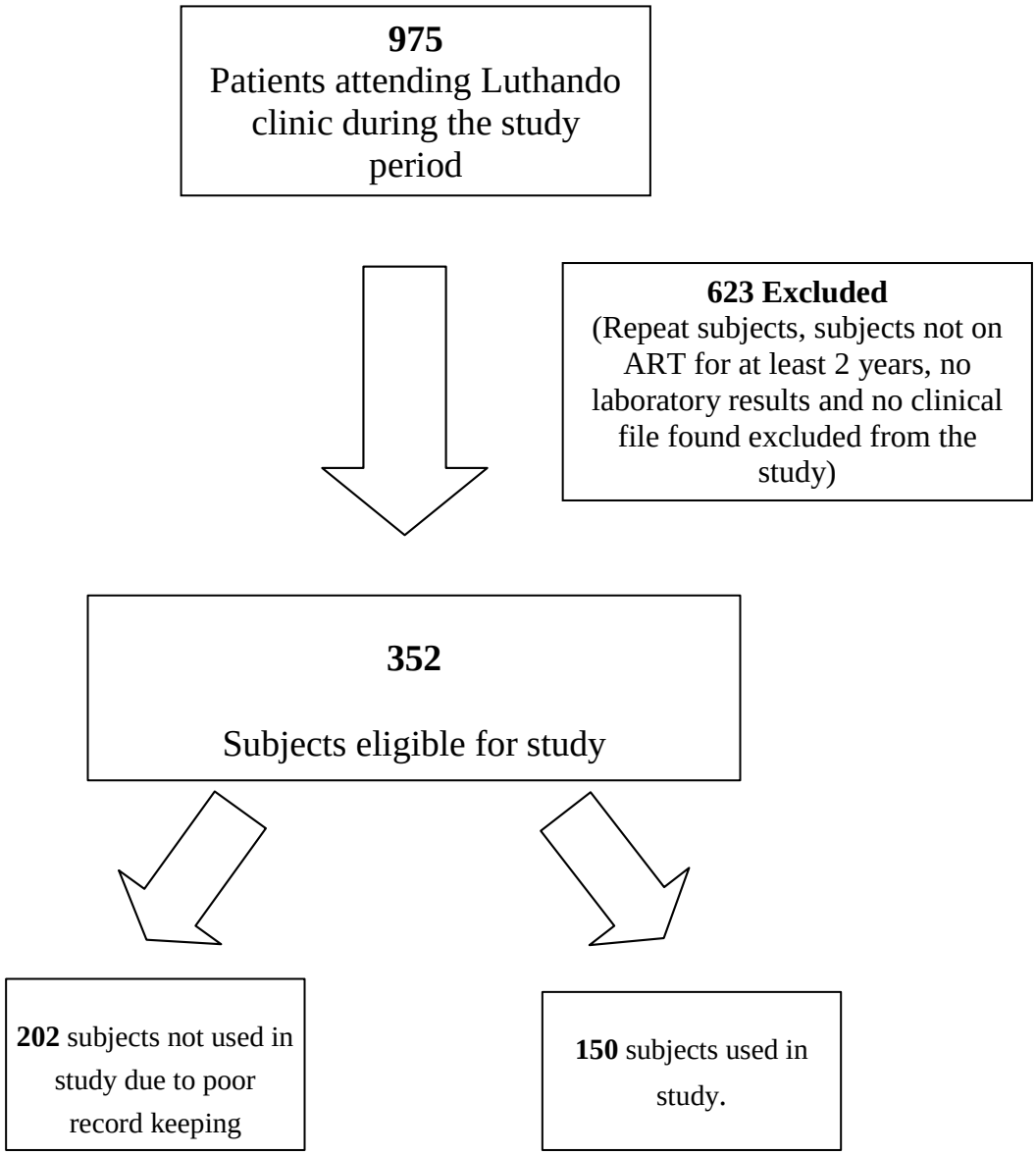

Figure 2 Sample size

2.6 Data Collection

Data collection was done by the primary investigator. Clinical data was collected from the subject's clinical Luthando file and entered into the data sheet. Demographic data and clinical interviews detailing whether a history of childhood trauma existed were obtained from the Psychiatry Outpatient clinic at Chris Hani Baragwanath Academic hospital and entered on the data sheet.

2.7 Data Analysis

The data analysis was carried out using SAS version 9.4 for Windows. Descriptive analysis of the data was carried out. The 5% significance level was used. With the Chi – square test a medium effect sample size of 108 is aimed for and in the eventual study, the sample size of 150 was adequate.[55]

Categorical variables were illustrated using bar charts and summarised by frequency and percentage tabulation.

Continuous variables were summarised by the mean, median and standard deviation, interquartile range and their distribution was illustrated by histograms.

The Chi – square test (X^2 test) was used to answer the research questions, as it involved determining possible relationships between adherence, the various demographic and other clinical variables and whether or not the subject had experienced childhood trauma or not .

Fisher's exact test was used when the Chi – square test requirements could not be met.

The strength of the associations was measured by Cramer's V and the Phi co – efficient.

The scale used for interpretation was:

0.50 and above	high/strong association
0.30 to 0.49	moderate association
0.10 to 0.29	weak association
Below 0.10	little if any association

The relationship between continuous study variables and the exposed childhood trauma group was assessed by independent samples t – test (parametric test) and where data could not be extrapolated using this test, the Wilcoxon rank sum test (non – parametric test) was used.

The above associations were measured using Cohen's d for parametric tests and r – value for non – parametric tests.

The scale used for interpretation was:

0.80 and above	large effect
0.50 to 0.79	moderate effect
0.20 to 0.49	small effect
Below 0.20	near zero effect

CHAPTER 3

3. RESULTS

3.1 Demographic and Clinical Profile

3.1.1. Demographic profile of the study sample

The final subject sample size of 150 was analysed.

The study focused on determining the relationship between childhood trauma and the following demographic variables: gender, age, marital status, highest level of education and main source of income.

The study also focused on determining the relationship between childhood trauma and the following clinical variables: CD4 count, Viral load, ART regimen, psychiatric diagnosis, the age of traumatic event and the number of traumatic events.

The analysis also extended to determine a relationship between adherence and ART regimen.

Demographic details of the patients and the age distribution of the sample size is described below (Table 1). Most of the subjects used in the study were between the ages of 30 and 59 years old, with 38% (n = 57) of subjects aged between 40 – 49 years old.

Most of the subjects were female; 72.7% (n = 109) (Table 1).

Once grouped, 18.2% (n = 27) of patients, were in a relationship (formal marriage or partner) and 81.8% (n = 121) of the sample were single (Table 1).

83.1% (n = 123) of subjects have a highest level of education between Grade 8 and Grade 12 (Table 1).

In the study sample, the main source of income was a social grant, with 28% (n = 42) of subjects receiving this and a further 49.3% (n = 74) of subjects had no formal employment (Table 1). The unemployed category was the largest in the study sample. Many of these individuals had no formal employment. They likely acquired an income in the informal sector or relied on financial assistance from their support system.

Table 1. Demographic characteristics

Variable	Category	Overall	
		n	%
n		150	
Age	20-29y	13	8.7
	30-39y	40	26.7
	40-49y	57	38.0
	50-59y	37	24.7
	60y+	3	2.0
Gender	Male	41	27.3
	Female	109	72.7
Relationship Status	Unknown	2	
	Single	94	63.5
	Married	15	10.1
	Partner	12	8.1
	Separated	7	4.7
	Widowed	11	7.4
	Divorced	9	6.1
Relationship Status (grouped)	Single	121	81.8
	In a relationship	27	18.2
	Unknown	2	
HLOE	Unknown	2	
	None	1	0.7
	< G8	14	9.5
	G8-12	123	83.1
	Diploma	6	4.1
	Degree	4	2.7
HLOE (grouped)	None/Less than G8	15	10.1
	G8-12	123	83.1
	Tertiary	10	6.8
	Missing	2	
Source of income	Unemployed (i.e. none)	74	49.3
	Social grant	42	28.0
	Employment	28	18.7
	Other	5	3.3
	Family	1	0.7

3.1.2 Clinical profile of the study sample

3.1.2.1 HIV characteristics: Viral suppression; CD4 counts; ART regimen and number of years on ART

Overall 91.3% (n = 137) of the study sample were virally suppressed (Table 2). Adherence was determined by using the viral load parameters. The use of viral load suppression as a measure of adherence to ART has been demonstrated in the literature.[54]

If a subject had an initial viral load of >1000 RNA copies/ml and a subsequent viral load of <1000 RNA copies/ml, the subject was deemed adherent to ART. Patients who had an initial viral load of <1000 RNA copies/ml and a subsequent viral load of >1000 RNA copies/ml were deemed non – adherent to ARTs.

If both viral loads were >1000 RNA copies/ml, then the subject was deemed non adherent to ARTs.

The baseline and most recent CD4 serum counts in the clinical file were reviewed.

At baseline visit to the clinic, the median CD4 count was 274 (inter - quartile range of 155 – 435 and range of 3 – 1353) (Figure 3.1).

At most recent clinic visit, the median CD4 count was 540 (inter – quartile range of 376 – 737 and range of 25 – 1384) (Figure 3.2).

The subjects were on 1st line or 2nd line regimens. 74.7% (n = 112) were on the 1st line ART regimen (Table 2).

Table 2. Clinical characteristics

Variable	Category	Overall	
		n	%
Adherence	Not suppressed	13	8.7
	Suppressed	137	91.3
HAART regimen	1st line	112	74.7
	2nd line	38	25.3
Diagnosis	Mood/psychotic disorder due to HIV	51	34.0
	Bipolar I	42	28
	HIV Associated Neurocognitive Disorder	17	11.3
	Psychotic disorder due to HIV	14	9.3
	Schizophrenia	13	8.7
	Major Depressive disorder	12	8.0
	Mood disorder due to HIV	11	7.3
	Temporal lobe epilepsy	3	2.0
	Personality disorder	3	2.0
	Intellectual disability	3	2.0
	Substance-induced psychotic/mood disorder	2	1.3
	Schizoaffective disorder	2	1.3
	PTSD	2	1.3
	Anxiety disorder	1	0.7
	Bipolar II	1	0.7
Number of diagnoses	1	124	82.7
	2	25	16.7
	3	1	0.7
Childhood trauma	No	103	68.7
	Yes	47	31.3

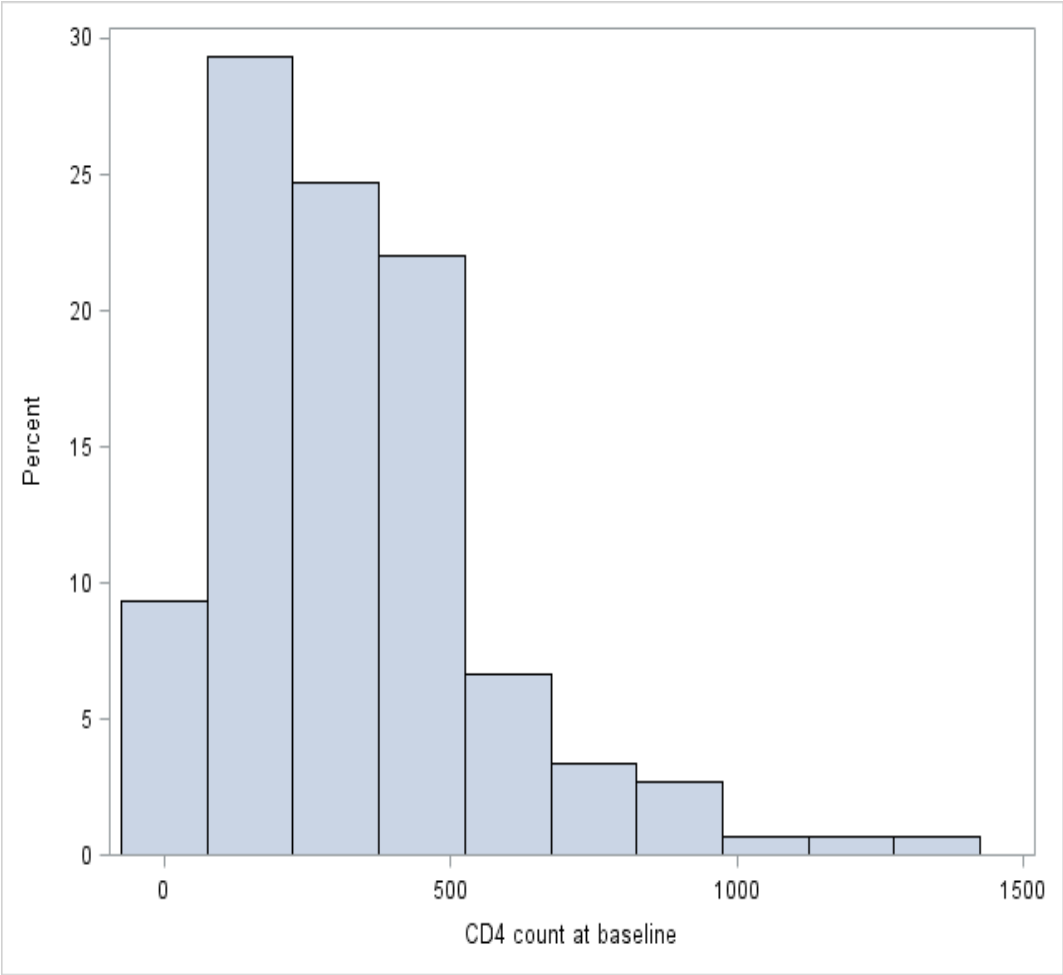

Figure 3.1 CD 4 count at baseline visit

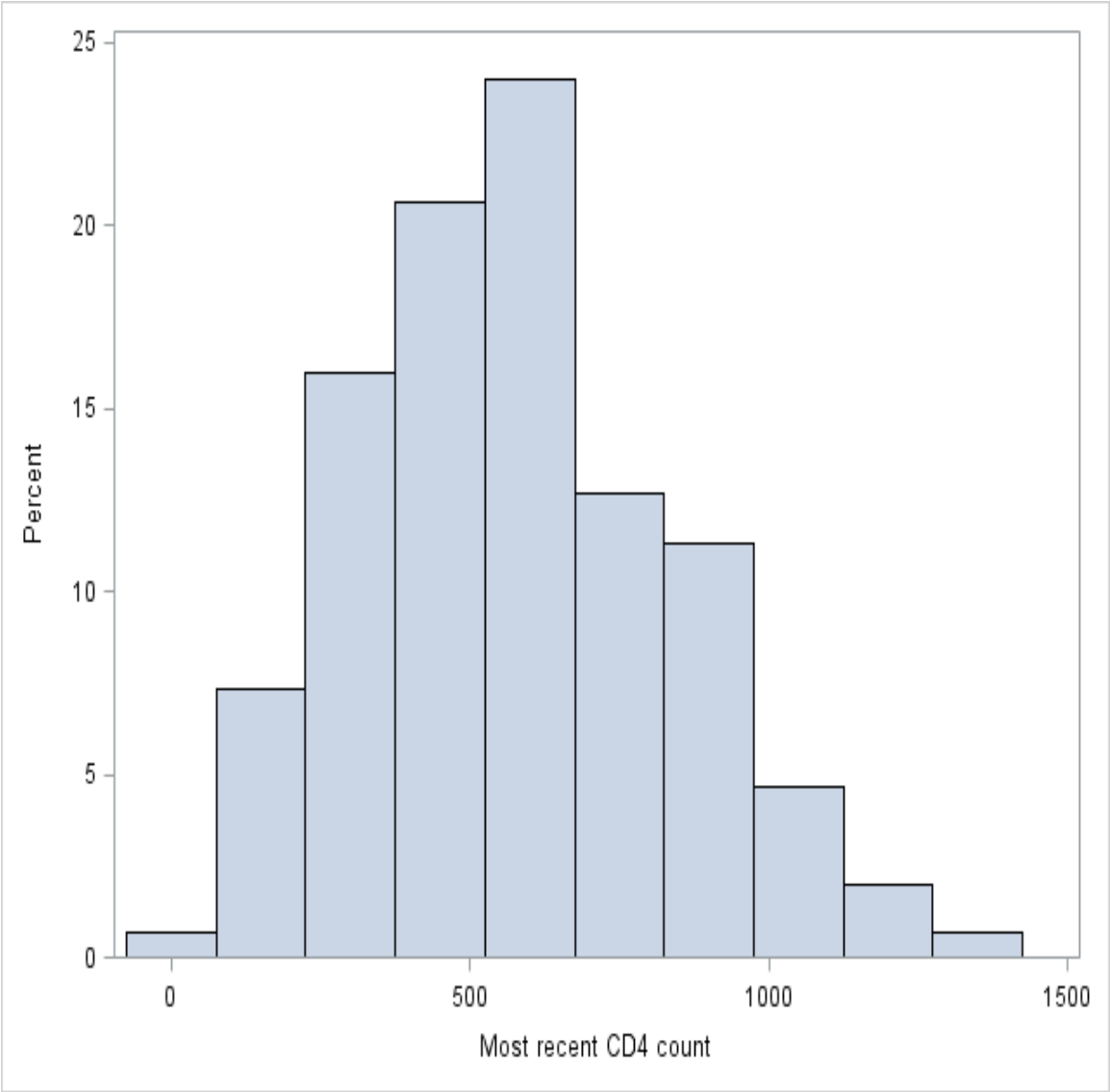

Figure 3.2 CD4 count at most recent visit

In terms of viral load suppression and ART regimen, 95.5% (n = 107) of subjects on 1st line ART regimen were suppressed compared to 78.9% (n = 30) of subjects virally suppressed on the 2nd line ART regimen.

The median duration of subjects on ARTs was 6 years (Inter – quartile range 3 – 8 years and range of 2 – 21 years) (Figure 3.3).

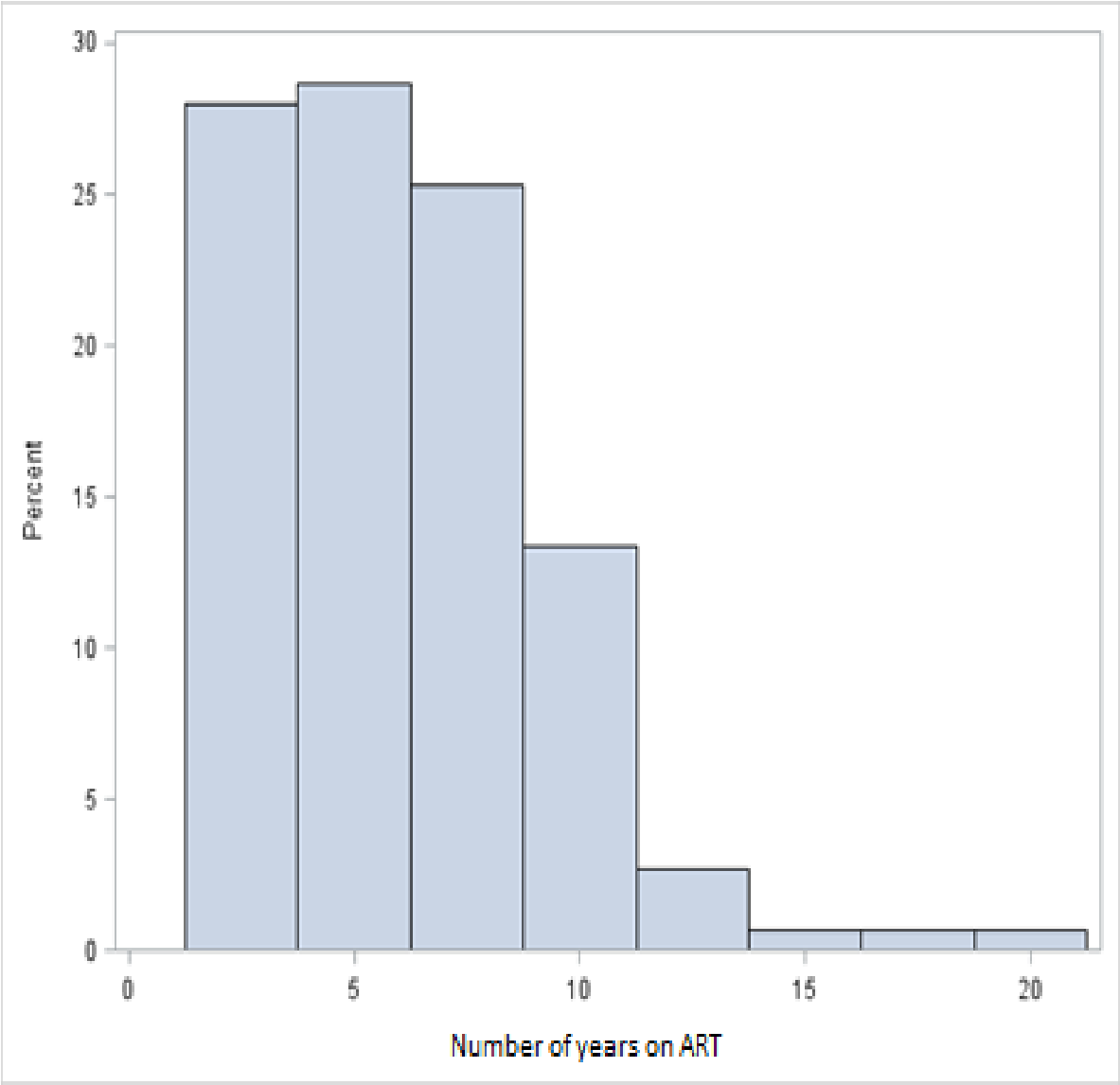

Figure 3.3 Number of years on ART

3.1.2.2 Psychiatric Diagnosis

The most common clinical diagnosis in the sample was Mood/Psychotic disorder due to HIV. 34% (n = 51) of subjects had this diagnosis made as part of their clinical evaluation (Table 2). This is also represented in Figure 3.4.

82.7% (n = 124) of subjects had one diagnosis made on clinical evaluation (Table 2). A history of childhood trauma was found in 31.3% (n = 47) of the sample (Table 2).

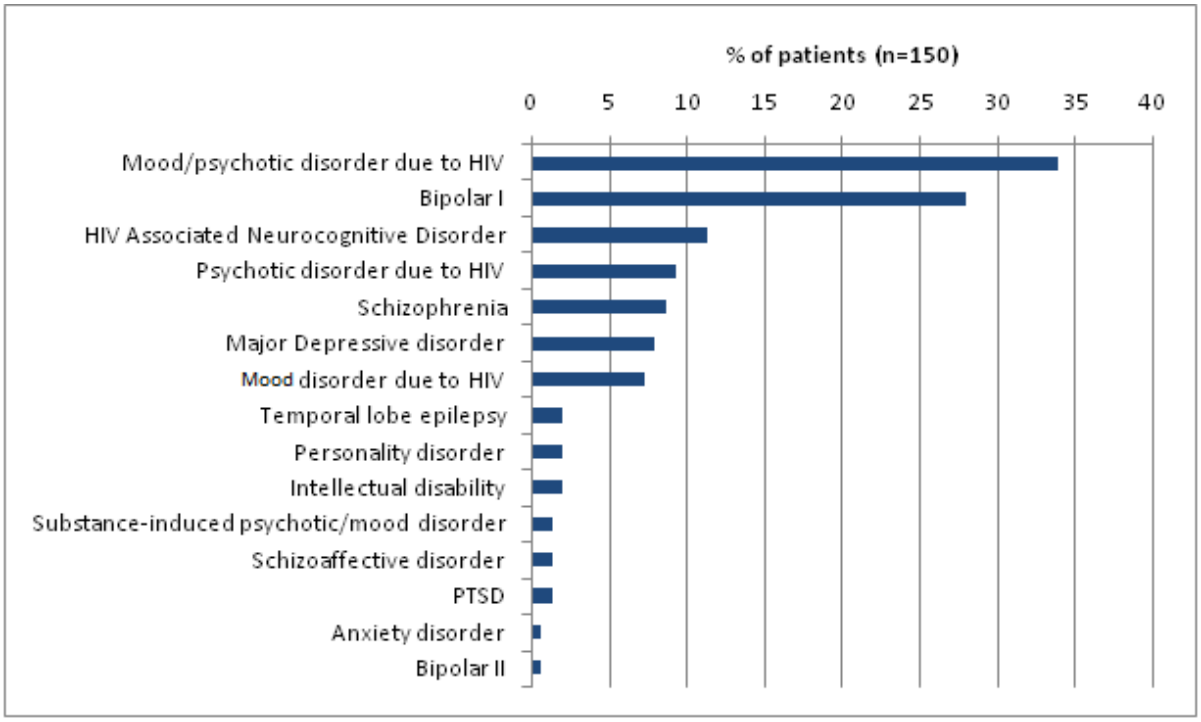

Figure 3.4 Psychiatric diagnoses of subjects

3.1.2.3 Exposure to childhood trauma

The number of childhood traumatic events experienced by each subject was also included in the study, and 55.3% (n = 26) of subjects experienced one traumatic childhood event, while 21.3% (n = 10) had experienced 6 or more events (Figure 3.5).

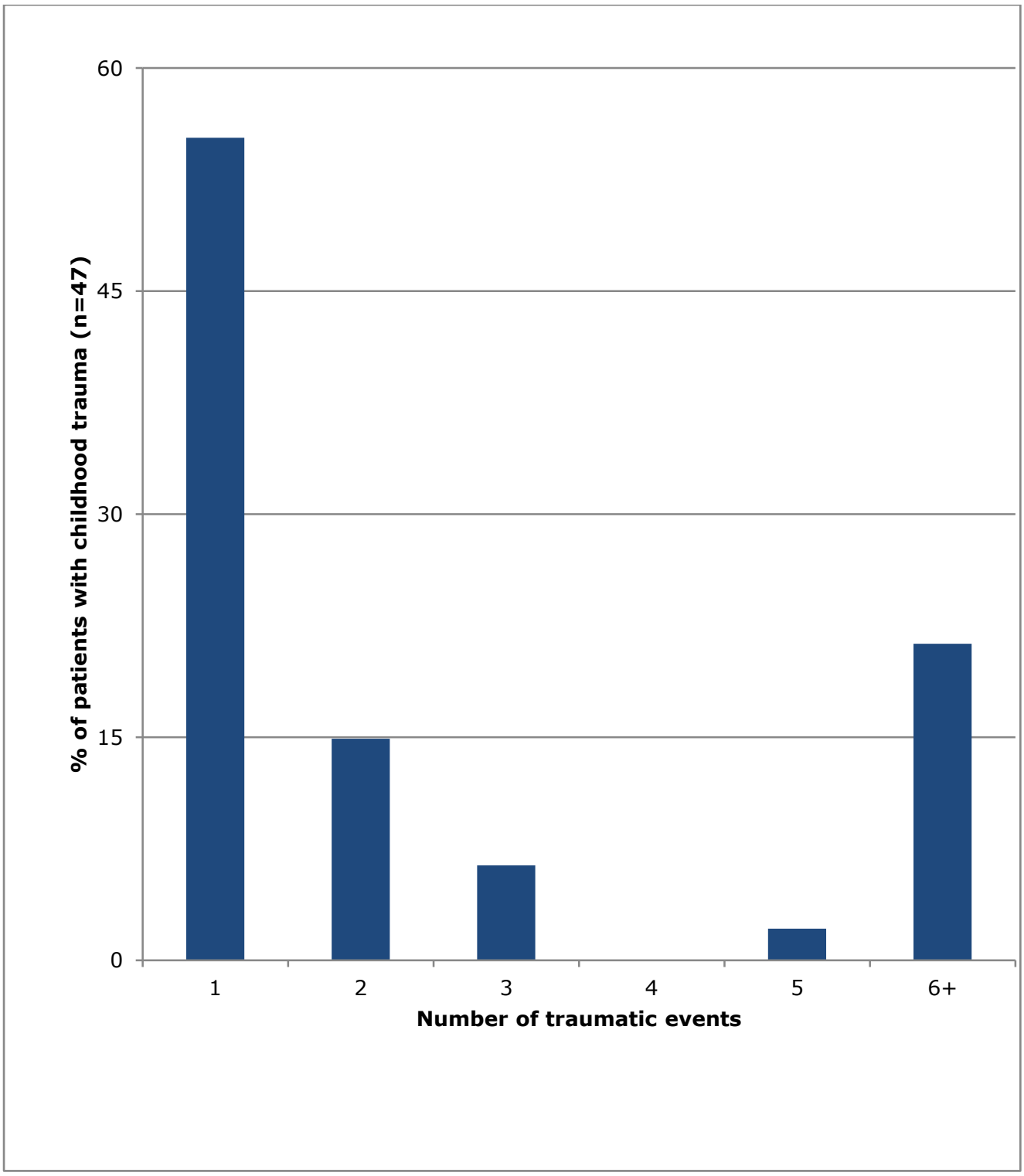

Figure 3.5 Number of childhood traumatic events

The age of first childhood traumatic event, could not be analysed as the missing data was more than 30%, with 32% (n = 15) of subjects not having this information accurately recorded in their clinical files. 68% (n = 32) of the remaining subjects, who did have age of first childhood traumatic event recorded, had a median age of 8 years old (inter – quartile range of 5 – 12 and range of 3 – 17 years).

The subjects that had experienced childhood trauma did have documented different types of childhood maltreatment in their records, but because the subject was not interviewed and a more detailed account of what had occurred in childhood was not possible, this data was deemed insufficient to meaningfully analyse.

3.2 Relationships between variables

3.2.1 Relationships between childhood trauma and variables

No significant association was found within the clinical data pertaining to the main research question.

Non – adherence to ARTs was not found to be associated with a history of childhood trauma (p – value 0.76).

The association between a history of childhood trauma and the demographic data collected; revealed one significant association.

The proportion of females was higher among those who had experienced childhood trauma (87.2%; n = 41) compared to those who had not (66% n = 68) (p – value = 0.0096).

The study determined that; in the non - exposed childhood trauma group, the ratio of females to males is almost 2:1. The childhood trauma exposed group, had a ratio of females to males of 7:1.

This relationship shows the vastly differing childhood trauma exposure between males and females.

No significant association was also found between childhood trauma or no childhood trauma and 1st or 2nd line ART regimen (p – value = 0.55). Specific psychiatric diagnoses were also included in the analysis. Three separate diagnoses were analysed, as the number of subjects with each diagnosis, needed more than 15 subjects for analysis to be valid. No statistical significance was found between no childhood trauma and exposure, and a specific psychiatric diagnosis (p – value = 0.58, 0.70 and >0.99).

The number of psychiatric diagnoses did not show any significant association, to whether a subject experienced no childhood trauma or childhood trauma exposure (p – value = 0.55).

Regarding the association between CD4 counts (baseline and most recent visit), and childhood trauma or no childhood trauma, there was no statistical significance observed (p – values of 0.33 and 0.53 respectively).

The number of years on ARTs was also determined to have no significant relationship, to whether a subject experienced childhood trauma or not (p – value = 0.42).

3.2.2 Relationship between adherence and ART regimen

Within the clinical data only one significant association was found. This was between adherence and the ART regimen variable.

The proportion of subjects who were adherent/virally suppressed were higher among those on first line ART regimens (95.5% n = 107) versus those on second line ART regimens (78.9% n = 30) (p - value = 0.0042).

CHAPTER 4

4. Discussion

4.1 Limitations

The study sample was collected from a specific clinic day (every Friday at Luthando clinic), where generally most of the patients are clinically well. This could infer that they are more likely to be adherent to ARTs and confound our study results.

The small sample size and highly selective sample is a limitation that may have contributed to our results. The sample was decreased from 975 patients to 150 records that were finally reviewed. This sample size may have been insufficient for a significant association between childhood trauma and ART adherence to have been demonstrated.

Our sample is also confounded by the structure of the clinic. The majority of the non – adherent patients attend the clinic on other days of the week. Patients who have co – morbid substance use issues and severe neurocognitive decline are also attended to on other days of the week. These patients were not included in our sample and are more likely to be non – adherent to ARTs. This would be a confounding factor in terms of the results for variables such as ART adherence and psychiatric diagnosis that were determined in our study.

A further limitation was the retrospective nature of the study meant that the reliability of reported childhood trauma hinged on adequate records. Childhood trauma is always more reliably deduced from face to face interviews. In our study the subject was unable to self - report the childhood trauma. A retrospective record review was necessary to determine this data.

There may have been cases histories of childhood trauma that were underreported due to shame, fear and avoidance of the trauma. The reverse is also a possibility. The childhood trauma exposure may have been overstated and misinterpreted by the interviewer as patients may have been ill at the time of interview.

There is a possibility that the account of their childhood trauma may have been affected by their mental state at the time.

The sample size, despite being adequate for data analysis, was also decreased due to poor record keeping of files and notes and omission of details by interviewers.

The study was conducted at a specialised neuropsychiatric clinic (Luthando). Due to the specialised nature of patients attending the clinic, variables such as diagnosis would have impacted on results. The presence of mental illness and its impact on adherence to ART is another confounding factor that was difficult to control for due to the retrospective study design. The relative control for ongoing mental illness, was that patients analysed in the data were considered to be clinically stable due to their attendance on the 'stable patient's day' of the clinic. Future research in this area needs to demonstrate how the presence of mental illness will be controlled for in the statistical analysis, especially prospective study designs.

The use of consecutive viral loads outside of the study time, and sometimes not within 6 monthly periods may have confounded study results. Virological suppression may have been assumed, and not given an accurate prediction of adherence to ART.

4.2. Childhood Trauma and HIV adherence relationship

The association between non – adherence and childhood trauma exposure was determined to be insignificant (p – value 0.76). The majority of the subjects who experienced childhood trauma were adherent.

This finding was not supported by previous studies which examined ART adherence and childhood trauma. The majority of these studies were international.[38, 39, 40, 41, 42]

The differences in results may be supported by South Africa's increased focus on the HIV epidemic. South Africa has the biggest ART programme in the world and invests billions of rands annually to fund its HIV programmes.[1]

It therefore stands to reason that with more resource allocation to and emphasis on HIV programmes that adherence to HIV treatment may be improved. This differs from other countries where research has been performed examining factors that affect adherence. Due to decreased focus on HIV in many other countries, issues such as ART adherence may not be adequately addressed and may explain differing adherence rates between our study and many of the international studies.

The study samples had various differences when compared to our study sample.

In terms of the demographics, the samples studied varied from; the homeless and HIV positive outpatients to HIV positive adolescents. These samples differ from our sample population and may explain the different results determined compared to our study results.

The demographics of the sample in some of the studies can have a significant impact on adherence to ART. Homeless, illicit drugs users were interviewed and an association between childhood abuse and ART adherence was determined.[40]

The use of illicit substances and the hardships of homelessness and may play a larger role in directly and indirectly influencing non - adherence to ARTs than the effects of past childhood trauma.

Our sample, despite socio – economic challenges, is not homeless and co – morbid substance use is not as prevalent as the study sample mentioned above. Thus our study may reflect differing adherence rates to ART due to the controlling of factors such as co – morbid substance use and homelessness.

In terms of clinical profiles, these studies did not include known mental health care users attending a dual diagnosis clinic. [38, 39, 40, 41, 42]

The association between childhood trauma and its trajectory towards future mental illness has been determined in the literature.[28, 29, 30, 31, 32, 33, 34]

The studies in the literature determining the association between childhood trauma and non - adherence to ARTs did not acknowledge the intimate association between childhood trauma and future development of mental illness.

The confounding factor in these studies could be undiagnosed and untreated mental illness. Mental illness, especially if untreated, is associated with adverse immunological and clinical progression of HIV.[46 ,47]

Undiagnosed and untreated mental illness could be confounding the association between increased non – adherence to ARTs and childhood trauma exposure seen in other studies. [38, 39, 40, 41, 42]

The sample in our study, have a formal mental illness diagnosis and are treated by a multi – disciplinary outpatient team. This factor is controlled for in our study and thus may be reflected in our study results as a positive effect on ART adherence and hence the differing results.

The HIV epidemic and subsequent investments have led to the development of clinics such as Luthando, where apart from the treatment of mental illness, special consideration has had to be made for HIV treatment and its related co – morbidities. These clinics have become highly specialised in their approach to patients with HIV and other illnesses and have created policies that treat both afflictions effectively and simultaneously.

This highly focused approach may be directly and indirectly responsible for increasing ART adherence in our sample. The literature that investigated childhood trauma and ART adherence did not analyse subjects that were following up at a specialised clinic such as Luthando. [38, 39, 40, 41, 42]

Our subjects are intensively followed up and immediately contacted once laboratory results reveal viral loads of >1000copies/ml (non – adherent). This specialised protocol may increase adherence to ARTs and ensure that our subjects are aware of need for treatment at all times.

Luthando clinic offers patients a multi - disciplinary service. It holds weekly supportive psychotherapy groups and has a clinical team that addresses patients who are non – adherent and follows these patients up. The clinic has permanent staff members; which allows continuity of care.

This type of clinic set – up may be a blueprint for other clinics to use where adherence to ARTs is poor and difficult to control. This may be an influencing factor on our study results.

The possible implications of these findings, is that childhood trauma, and its effects on adherence to ARTs could possibly be negated with a clinic system such as Luthando clinic.

The studies focused on known HIV positive subjects and various screening tools were used, either through direct interview or self-report questionnaires.

Adherence to ART was determined by interview and these studies did not use an objective tool to measure adherence. [38, 39, 40, 41, 42]

This could lead to inaccurate measuring of adherence and account for the differing results found in the literature compared to our study. Our study used HIV viral loads as a measurement of adherence and is an objective tool to determine adherence to ART and is considered highly accurate in determining adherence rates.[10, 54]

South Africa has had problems with the initiation of ART rollout in the past. Different policies, throughout its democratic history have determined eligibility for ARTs. ARTs were officially introduced into the public health system in 2005, despite identification of the epidemic in the 1990s, but were reserved for patients with specific clinical parameters. In 2016 ARTs were made available to all people living with HIV.[56]

These policy changes in South Africa in the last 10 years, may have had an effect on influencing adherence to ARTs. Thus by solving these public health problems, it may have led to better adherence to treatment and influenced our study results. All of the studies examining the relationship between childhood trauma and ART adherence were conducted before 2016 and lack of access to ARTs due to government policies may have contributed to ART non adherence. [38, 39, 40, 41, 42]

4.3 Childhood Trauma prevalence and Gender bias

After clinical record reviews, 31.3 % (n = 47) of the subjects had experienced childhood trauma, similar to the prevalence seen in general epidemiological studies. A review of the literature from the United States was performed, which only included studies where personal

accounts of childhood trauma were obtained and a strict screening method was used. Each sample had a large national representation.[57]

The significant association (p – value 0.0096) found in the demographic data, whereby the proportion of females was higher among the subjects who experienced childhood trauma compared to those who did not, is of interest.

This is similar to the literature, specifically in a military study that allowed self - reporting of childhood trauma using the Childhood Trauma Questionnaire.[58]

Our study also determined that females are at greater risk of childhood trauma compared to males as evidenced by a prevalence ratio of 7:1.

This was also determined in a study that reviewed retrospective data obtained in a National comorbidity survey in the United States.[59]

Another possible explanation could be the underreporting of male childhood trauma. This is a worldwide phenomenon that has been examined in the literature, especially with regards to male childhood sexual abuse.[60]

4.4 Childhood Trauma and Socio – economic status

The link between childhood trauma and level of education is important. Despite the study not showing any significant associations between level of education and childhood trauma (p – value 0.38), 2.2% (n = 1) of the subjects who experienced childhood trauma attained a tertiary qualification compared to 6.8% (n = 10) of subjects who did not experience childhood trauma.

In the literature, childhood trauma is associated with lower levels of higher education attainment. An online research study assessed previous childhood trauma amongst internet users and most of the participants had a tertiary qualification. Access to the internet to complete the survey also denoted a more affluent subject compared to our study group where almost half the sample were unemployed. [61]

The possible explanation for our study result is that Luthando clinic serves mainly a previously disadvantaged community and lower socio – economic population.

South Africa's unique political past may have influenced our findings and our sample may be biased. This sample may not have attained higher levels of education due to previous disadvantages.

Past disadvantages such as apartheid based education, political and socio - economic inequality policies have adversely affected the sample's community and the opportunity to achieve a tertiary education.

Childhood physical abuse that is severe in nature has been associated with lower income as an adult in the literature. Analysis of longitudinal data from a child health study in Canada determined that severe childhood abuse is associated with lower income and unemployment in males.[62]

Our study determined no significant relationship between income and childhood trauma. Our study results may be determined by our sample's previous disadvantages due to apartheid policies that increased economic inequality. These disadvantages may have a significant effect, other than the influence of childhood trauma, on our results.

4.5 ART regimen and CD4 serum count

Due to childhood trauma and its association with non – adherence to ARTs in the literature [38, 39, 40, 41, 42], ART regimens were of interest in our study analysis.

The type of ART regimen and association to childhood trauma was analysed. It was determined that there was no significant relationship between childhood trauma and a specific ART regimen.

All patients, withstanding any contraindications or severe side effects, are initiated on first line treatment. This is a single fixed dose combination consisting of three drugs.
Regular 6 monthly HIV viral loads are performed in order to assess whether the drug is effective. When resistance develops to these drugs, due to either non – adherence or

spontaneous mutation of the HIV virus, drug resistance testing must be done. This test result determines if a new regimen of ART needs to be prescribed.

Due to childhood trauma associated with non – adherence to ARTs [38, 39, 40, 41, 42], it could be inferred that subjects with childhood trauma exposure would be more likely to be on 2nd line regimens compared to non – exposed subjects.

There is also a paucity of literature with regards to childhood trauma and its association to a specific ART regimen that can be compared with our study.

The percentage of subjects with childhood trauma, that are on 1st line ART regimens, was comparable to the non - childhood trauma group. It indicates that the majority of these patients have been adherent to ART and have no drug resistance to the HIV virus. There was no significant relationship between childhood trauma exposure and the 2nd line ART regimen.

The highly specialised clinic structure at Luthando may again be influencing the above results found in our study. The continuity of care and consistent tracking of non - adherent patients has possibly had an effect on the childhood trauma exposed subjects. The majority of the childhood trauma exposed group has comparable 1st line ART regimen use compared to the non – childhood trauma exposed group. Our hypothesis, that exposure to childhood trauma should lead to more subjects using the 2nd ART regimen due to childhood trauma and its association with non – adherence to ARTs, was therefore disproved. [38, 39, 40, 41, 42]

The CD4 count at baseline and most recent also shared no significant relationship to childhood trauma. Both these results are of interest, as severe childhood trauma has been shown to have significant associations to HIV disease progression.[35, 36, 37]

A mediation analysis of longitudinal United States data, with clearly documented histories of lifetime trauma in people living with HIV was done. It determined that lifetime trauma is associated with accelerated HIV disease progression and non – adherence to ARTs.[63]

HIV disease progression could have an effect on adherence, especially when patients have neurocognitive illness due to HIV. This would impair cognitive functions such as memory, and could lead to non – adherence.

The possible explanation for the discrepancy in results between our study and the literature may be due to Luthando clinic's specialised structure and support offered by the multi - disciplinary team. Disease progression may be halted by the individualised care of each patient. Frequent monitoring of HIV viral loads and follow- up of patients that are non – adherent could positively impact on disease progression and its related co – morbidities.

4.6 Psychiatric diagnosis

Specific psychiatric diagnoses and its association to childhood trauma were also examined. No significant association was determined. This finding was significant as there are studies in the literature that examine this association.

This association was also considered in our study due to its effects on ART adherence. A specific diagnosis may influence adherence and may be a confounding factor in determining adherence to ART.

Childhood trauma and HIV and its effects with regards to mental health outcomes are well investigated and outlined in a review that showed substance abuse, major depressive disorder, and post -traumatic stress disorder were the most commonly reported psychiatric disorders diagnosed.[29]

Specific psychiatric diagnoses such as depression, anxiety and post – traumatic disorders were determined to influence ART adherence. A review established that the effects of these illnesses could be determinants of non – adherence to ART.[18]

This study is the first to research patients with a history of childhood trauma at a specialised HIV neuro – psychiatric facility. The majority of subjects had a diagnosis of Mood/Psychotic disorder due to HIV. Hence the diagnoses found in this study are in keeping with this subset of patients.

The outcome of patients with Neuropsychiatric disorders due to HIV improves with treatment from ART and psychotropics. The HIV virus is suppressed in the cerebrospinal fluid and the serum due to the ART. Thus the patient will improve clinically and may no longer require psychotropics.

This differs from a patient with established Schizophrenia or Bipolar I disorder and a co – morbid diagnosis of HIV. In these cases the mental illness is permanent. Sometimes, despite adequate control of the HIV, the patient has ongoing clinical deterioration due to the mental illness.

Thus patients with a primary psychiatric illness and HIV may have different ongoing rates of adherence to ART compared to patients with Neuropsychiatric disorders due to HIV.
This may be a reason that explains why ART adherence is not as affected in our study population compared to the literature.

A possible reason that our study did not determine an association between a specific psychiatric diagnosis and childhood trauma could be due to clinical difficulties. These difficulties arise when a clinician is tasked with determining if a psychiatric diagnosis is a direct result of the HIV infection or is primary in nature.
Clinicians unfortunately are sometimes unable to conclusively determine the precise cause of an illness despite multiple reviews and an extensive history and clinical examination. This would occur often in a dual diagnosis clinic such as Luthando.
Another challenge that is faced is when both illnesses occur simultaneously and the presence of a primary psychiatric diagnosis and psychiatric illness due to HIV blur the clinical presentation.

Thus in clinics such as Luthando, separation of diagnoses and the ability to accurately determine a diagnosis can be challenging. This may explain why our study could not identify specific diagnoses associated with childhood trauma exposure compared to the literature.[28, 29, 30, 32, 33, 34]

Patients with co – morbid substance use problems may have not attended the Friday clinic (reserved for clinically stable patients) due to deteriorating clinical condition or attendance on another day. This may also explain why our study has very few subjects that have a substance use disorder.

4.7 Number of traumatic events and age of first traumatic event

The number of traumatic events in childhood and its effect on adherence would have been of great interest in the analysis, but unfortunately could not be analysed due to missing data that exceeded our analytic threshold percentage.

With an increasing number of traumatic life events, the literature does support that it does increase non - adherence to ARTs.[30, 32, 35]

The age at first exposure to childhood trauma and its effect on ART adherence could also not be analysed due to missing data. There is a paucity of literature with regards to examining this association and this relationship would have been of interest.

4.8 Adherence and ART regimen

A significant association was determined in our study with regards to type of ART regimen and adherence (p – value = 0.0042). The results determined that subjects who were on the 1st line ART regimen were more likely to be adherent/virally suppressed compared to subjects on the 2nd line ART regimen.

The 1st line ART regimen usually consists of a non – nucleoside reverse transcriptase inhibitor and two nucleoside reverse transcriptase inhibitors. An integrase inhibitor has recently been added to this regimen.

The recommended 2nd line ART regimen consists of the addition of a ritonavir boosted protease inhibitor to two nucleoside reverse transcriptase inhibitors. Based on drug resistance testing, a regimen is adapted for the 2nd line.[64]

The most likely explanation for our study results is that subjects on the 2nd line ART regimen are on this regimen due to problems with non – adherence to the 1st line ART regimen and subsequent virological failure. Thus by conjecture, these subjects are more likely to be non – adherent to ART treatment.

Intolerable side effects to ART regimens and subsequent non – adherence are also another reason why patients are changed to the 2nd line regimen.

The 2nd line ART regimen is also sometimes poorly tolerated by patients due to severe gastrointestinal side effects that are intractable unless medication is stopped. This may also further explain why the 2nd line ART regimen subjects were found to be less adherent/virally suppressed compared to the 1st line ART regimen. Usually the 1st line regimen has more tolerable side effects than the 2nd line ART regimen.

4.9 Recommendations

Future studies in this area should be conducted using a cross – sectional or prospective study design that makes use of the childhood trauma questionnaire.

It is also recommended that a comprehensive interview be done on all patients entering Luthando clinic, which includes an exploration of childhood as well as current trauma experiences. Future reviews would thus benefit from this intervention.

A further recommendation is that future studies examining the relationship between childhood trauma and adherence to ARTs, include subjects from other similar clinical sites, which also specialise in neuropsychiatry.

CHAPTER 5

5.Conclusion

Our study results do confirm a high prevalence of childhood trauma, with prevalence rates of childhood trauma exposure similar to epidemiological studies where childhood trauma was examined.[57]

Our study design supports, despite previous limitations mentioned, that subjects are not re – exposed to the memory of the childhood trauma. Guidelines developed by the Royal College of Psychiatrists and the British Psychological Society, detail trauma and the possibility of reactivation. These guidelines were put together by multiple multi – disciplinary health care professionals, PTSD sufferers and guideline methodologists. Trauma and its unique storage in memory to form 'trauma memories', is well documented, and PTSD can be retriggered when exposure to stimuli activates these memories.[65]

The significantly greater proportion of females to males who experienced childhood trauma, compared to the ratio of females to males with no childhood trauma, highlights the need for attendance to Gender - based violence and calls for political policies to combat this serious problem.

This study is currently the only study in South Africa to investigate ART adherence and its association to childhood trauma in a neuropsychiatric setting. Variables such as ART regimen and its association with childhood trauma have also not been previously examined in the literature.

While this research study did not show an association between childhood trauma and non – adherence to ARTs, it did determine that ART adherence at the clinic studied was above

national norms. The adherence rates to ART determined in the study at Luthando clinic, are almost twice as much the adherence rates in PLWH attending primary health clinics.[1]

Luthando clinic could be utilised as a model for other dual diagnosis and general HIV clinics in South Africa. Previous research in fact showed that on outcome analysis that there was 95% ART adherence amongst the 467 subjects studied at Luthando clinic. Adherence to ARTs was obtained by self – report and pill counts.[66]

Luthando clinic's unique approach to the management of patients could be extrapolated and used as a blueprint for increasing adherence to ARTs in other centres and the treatment of HIV related co - morbidities.

Luthando clinic, despite the additional burden of treating severe mental illness, has still managed to optimise the management of PLWH and achieve adherence rates that are significantly higher than most. Vulnerable patients that have been identified such as the Triple diagnosis patients (HIV, mental illness and co – morbid substance use) and allocation of a specific clinic day for these patients have further enhanced Luthando clinic's ability to optimally manage the most complex patients.

A dedicated outpatient team that includes psychologists and occupational therapists has also allowed Luthando patients to benefit from these forms of therapy and ensure more holistic care and likely increase ART adherence rates and follow up amongst patients.

CHAPTER 6

6. References

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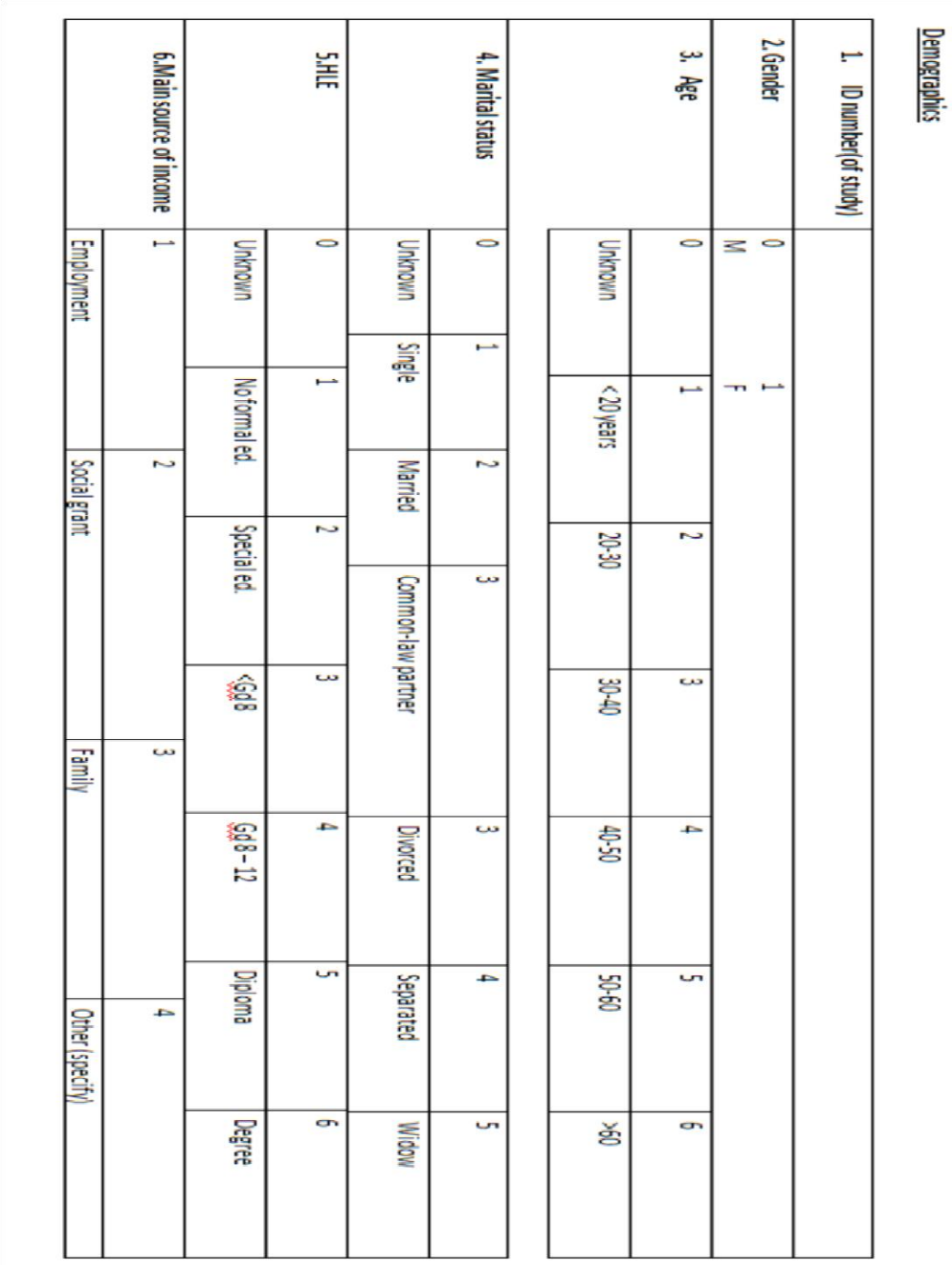
CHAPTER 7

7. Appendices

Appendix 1: Data collection sheet (both sides).



Demographics

1. ID number(of study)						
2.Gender	0 M	1 F				
3. Age	0 Unknown	1 <20 years	2 20-30	3 30-40	4 40-50	5 50-60	6 >60
4. Marital status	0 Unknown	1 Single	2 Married	3 Common-law partner	3 Divorced	4 Separated	5 Widow
5.HLE	0 Unknown	1 No formal ed.	2 Special ed.	3 <Gd 8	4 Gd 8 – 12	5 Diploma	6 Degree
6.Main source of income	1 Employment	2 Social grant	3 Family	4 Other (specify)			

Clinical Characteristics

8. CD4 Baseline Before Most Recent Most Recent	
9. Viral Load Baseline Most Recent	
10. HAART	
11. Date commenced on HAART	
12. Psychiatric Diagnoses	
13. Childhood trauma YES/ NO	
14. If yes for Childhood Trauma: Age of Traumatic Event	
15. If yes for Childhood Trauma: Number of Traumatic Events (1-6)	

Appendix 2: Childhood trauma questionnaire Short Form

Childhood Traumatic Events Scale

For the following questions, answer each item that is relevant. Each question refers to any event that you may have experienced **prior to the age of 17.**

1. Prior to the age of 17, did you experience a death of a very close friend or family member? _____

   If yes, how old were you? _____

   If yes, how traumatic was this? (using a 7-point scale, where 1 = not at all traumatic,

   4 = somewhat traumatic, 7 = extremely traumatic) _____

   If yes, how much did you confide in others about this traumatic experience at the time? (1 = not at all, 7 = a great deal) _____

2. Prior to the age of 17, was there a major upheaval between your parents (such as a divorce, separation)? _____

   If yes, how old were you? _____

   If yes, how traumatic was this? (7 = extremely traumatic) _____

   If yes, how much did you confide in others? (7 = a great deal)_____

3. Prior to the age of 17, did you have a traumatic sexual experience (raped, molested, etc.)? _____

   If yes, how old were you? _____

   If yes, how traumatic was this? (7 = extremely traumatic) _____

   If yes, how much did you confide in others? (7 = a great deal) _____

4. Prior to the age of 17, were you the victim of violence (child abuse, mugged or assaulted – other than sexual)? _____

   If yes, how old were you? _____

   If yes, how traumatic was this? (7 = extremely traumatic) _____

   If yes, how much did you confide in others? (7 = a great deal) _____

5. Prior to the age of 17, were you extremely ill or injured? _____

   If yes, how old were you? _____

   If yes, how traumatic was this? (7 = extremely traumatic) _____

   If yes, how much did you confide in others? (7 = a great deal) _____

Appendix 3: Ethics clearance certificate

R14/49 Dr Prinesh Miseer

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M170385

NAME: (Principal Investigator)	Dr Prinesh Miseer
DEPARTMENT:	Psychiatry Luthando Clinic Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Childhood Trauma Exposure and Adherence to AntiRetroviral Therapy among Patients attending a Public Neuropsychiatry Health Facility
DATE CONSIDERED:	31/03/2017
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	
APPROVED BY:	Prof P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	24/05/2017

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.