# Assessment of treatment outcomes of adolescents on antiretroviral therapy at selected public primary healthcare clinics in the Cape Metropole, South Africa.

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# ABSTRACT

## Introduction

HIV/AIDS is the leading cause of death among adolescents in sub-Saharan Africa. In 2020, approximately 2.8 million adolescents (aged 10–19 years) were living with HIV/AIDS worldwide, with 85% residing in sub-Saharan Africa. About 50% of adolescents living with HIV globally live in Nigeria, India, Kenya, Mozambique, Tanzania, and South Africa. Adolescents living with HIV (ALHIV) have worse treatment outcomes compared to children and adults. In 2021, an overall 74% viral load suppression (VLS) rate was reported in South Africa among adolescents registered in the antiretroviral therapy (ART) programme. It is essential to assess the performance of adolescents registered on ART in public health care settings because they have been identified as a key population in turning the tide against the HIV pandemic and achieving UNAIDS' 95-95-95 targets.

## Aim

The current study assessed treatment outcomes (viral load suppression (VLS) and retention in care (RiC)) and their associated factors for adolescents on ART at eight selected urban primary healthcare clinics in the Western Cape Province of South Africa.

## Methodology

A retrospective cross-sectional analysis of adolescents (N = 569) aged 12 to 19 years on ART from selected primary health care clinics in Mitchells Plain, Cape Town from January 2016 to December 2020 was undertaken. Baseline socio-demographic, clinical, and treatment outcomes data was extracted from the Patient Record and Health Management Information System and transferred to an Excel spreadsheet. Data was imported to SPSS version 28 for bivariate and multivariate analysis.

## Results

The prevalence of VLS (<1000 copies/ml) among adolescents on ART was 73.6% and retention in care was 34%. In the bivariate analysis, duration on ART ($p$ = 0.004) and ART regimen ($p$ = 0.039) were statistically significantly associated with VLS. Further, current age was statistically significantly associated with retention in care ($p$ = 0.001).

## Conclusion

VLS at selected primary health care facilities in Mitchells Plain is well below the World Health Organisation (WHO) target of 95%. We recommend tailored interventions to improve adherence and retention in care so that VLS among adolescents on ART may improve.



**Keywords:** Adolescents, Antiretroviral therapy, Clinical Outcomes, HIV/AIDS Adherence, Lost to follow-up, Retention in care, Socio-demographic factors, Primary Health Care, Viral Suppression.

# DECLARATION

I declare that the "*Assessment of treatment outcomes for adolescents on antiretroviral therapy at selected public primary healthcare clinics in Cape Metropole, South Africa"* is my work and has not been submitted for any degree or examination. I have in-text referenced all the sources I used and have listed them in the reference section.

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To God be the glory!

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# ABBREVATIONS AND ACRONYMS

A3E ..... Abacavir, Lamivudine and Efavirenz

ABC..... Abacavir

AIDS ..... Acquired Immune Deficiency Syndrome

ALHIV ..... Adolescents Living with Human Immune- deficiency Virus

ART..... Antiretroviral Therapy

ARV ..... Antiretroviral drugs

ATV..... Atazanavir

AYALHIV..... Adolescents and Young Adults Living with HIV

AZT ..... Zidovudine

CD4 ..... Cluster of Differentiation 4

D4T ..... Stavudine

DDI..... Didanosine

DRV ..... Darunavir

DTG..... Dolutegravir

ETR ..... Etravirine

FTC ..... Emtricitabine

HIV..... Human Immune deficiency Virus

LPV ..... Lopinavir

LPV/r..... Lopinavir/Ritonavir

LTFU ..... Lost to follow-up

MVC ..... Maraviroc

NHLS ..... National Health Laboratory Services

NRTI ..... Nucleoside Reverse Transcriptase Inhibitor

NVP ..... Nevirapine

PIs ..... Protease Inhibitors

PLHIV ..... People Living Human Immune deficiency Virus.

PMTCT ..... Prevention of Mother to Child Transmission of HIV.

PREHMIS ..... Patient Record and Electronic Health Management Information System

RiC ..... Retention in Care

RPV ..... Rilpivirine

SSA ..... sub-Saharan Africa

TDF ..... Tenofovir

UNAIDS ..... Joint United Nations Programme on HIV and AIDS

UNICEF ..... United Nations International Children's Emergency Fund

VL ..... Viral Load

VLS ..... Viral Load Suppression

WHO ..... World Health Organisation

# CHAPTER 1: INTRODUCTION

## 1.1 BACKGROUND

According to the 2020 Joint United Nations Programme on HIV/AIDS (UNAIDS, 2020a) report, 37.6 million people were living with HIV globally. Of the 37.6 million people, an estimated 2.78 million were children and adolescents, aged 0–19 years (UNICEF, 2021b). Globally, 1.7 million adolescents (10–19 years old) were living with HIV in 2020 (Silva et al., 2021). Furthermore, over 310 000 children and adolescents in the world were newly infected with HIV in 2020 (UNICEF, 2021).

Sub-Saharan Africa is disproportionately affected by the HIV/AIDS epidemic, with seven out of ten people residing in this region living with HIV (Shanaube *et al.*, 2021). It is reported that 75% of all HIV/AIDS-related deaths and 65% of new HIV infections in 2017 occurred in sub-Saharan Africa (SSA), and this percentage has continued to increase over the years (Nyasulu et al., 2021). Further, it is reported that in 2021, adolescent girls and young women accounted for 63% of all new HIV infections in SSA (Murewanhema et al., 2022). To reduce these HIV-related deaths and infections, early detection strictly needs to be adhered to. However, reports have shown that SSA has low coverage of HIV testing among adolescents. For instance, according to a UNICEF report in 2021, only 25% and 17% of adolescent girls and boys aged 15–19 years in sub-Saharan Africa, respectively, have been tested for HIV in the past 12 months and received the result of their test (UNICEF, 2021). The Southern Africa region is home to nearly 40% of the estimated 1.6 million adolescents aged 10–19 years living with HIV globally (UNAIDS 2021). Further, UNAIDS (2019a) estimates the number of children (0–14 years) living with HIV in South Africa in 2019 at 340 000 (260 000–420 000). Moreover, HIV prevalence among adolescents aged 10–19 years increased from 3% in 2012 to 3.7% in 2017 (Simbayi et al., 2019). Improvements in the provision of antiretroviral therapy (ART) in South Africa (as well as globally) have contributed to the growth in the number of perinatally infected children and behaviourally infected adolescents surviving into adolescence and adult stages, respectively.

Globally, it is observed that HIV/AIDS-related mortality is on the decline among the adult population, which demonstrates the effectiveness of ART in suppressing HIV and improving the quality of life of people living human immune virus (PLHIV) (National Institute of Health, 2010; Slogrove et al., 2017; UNICEF, 2021b). Evidence from a longitudinal

population analysis of HIV/AIDS data in seven African sites, including South Africa, demonstrated a 58% decline in HIV/AIDS-related mortality post-expansion of ART (Fokam et al., 2021). Overall mortality among PLHIV has declined from a peak of 1.7 million in 2004 to 770 000 in 2018 (UNAIDS, 2019b). However, current reports indicate that HIV/AIDS mortality among adolescents living with HIV (ALHIV) remains alarmingly high despite the widespread availability of ART in most countries (Willis et al., 2019; Desmonde et al., 2021). Older adolescents (15–19 years) are the only age group in which HIV/AIDS-related deaths are not declining (Vreeman et al., 2021). An estimated 120 000 children and adolescents died of HIV/AIDS-related causes in 2020 (UNICEF, 2021a).

Contrary to HIV/AIDS mortality trends observed in children and adults, adolescents are the only population group that continues to experience an increase in HIV/AIDS-related deaths (UNAIDS, 2014). Studies have reported that HIV-related deaths have tripled over the last two decades among adolescents (UNAIDS-UNICEF, 2016). Globally, HIV/AIDS is the second leading cause of mortality among adolescents, while in the African region it is the leading cause of death among adolescents (Webb et al., 2018; Willis et al., 2019; Armstrong- Mensah & Tetteh, 2021). Most recent data suggest that an estimated 41 000 adolescents aged 10–19 years lost their lives due to HIV/AIDS-related illnesses (Shanaube et al., 2021). Older adolescents (15–19 years), in particular, are the driving force behind this increase in mortality, as it is estimated that between 2005 and 2015, HIV/AIDS-related deaths increased by 45% in this population group (UNAIDS, 2016).



It is reported that 90% of the total HIV/AIDS-related deaths (34 000) that occurred in 2019 among adolescents (10–19 years) were in sub-Saharan Africa (UNAIDS, 2019b). At least one study attributed high HIV/AIDS mortality among adolescents in sub-Saharan Africa to attrition from the HIV continuum of care (Shanaube et al., 2021).

To accelerate progress towards ending the HIV/AIDS epidemic in 2025, UNAIDS has set new fast-track targets called 95 95 95 (UNAIDS, 2020b). These targets state that by 2025, 95% of people living with HIV will know their HIV status, 95% of PLHIV be initiated on ART, and 95% of those initiated on ART must achieve viral load suppression (VLS) (Ehrenkranz et al., 2021). The South African progress on the UNAIDS' 95 95 95 targets is 92-75-92 (92% of all South Africans living with HIV know their HIV status, achieving 75% on ART and 92% are virally suppressed among those on ART) (Archary et al., 2021). ALHIV are worse off compared to all other age groups concerning the attainment of the

UNAIDS' third 95% goal, viral suppression. A cross-sectional study in Mpumalanga, South Africa, reported that only 74% of adolescents (10–19 years) who have been on ART for a minimum of six months achieved VLS (Okonji et al., 2021).

South Africa has the world's largest ART programme, which led to improvements in the quality of life of PLHIV and increased life expectancy (Mathews et al., 2021). In 2017, South Africa adopted the WHO guidelines on a universal test, treatment and same-day ART initiation, which led to an expansion of ART coverage among PLHIV. An estimated 72% of PLHIV in South Africa are receiving ART (George et al., 2021). However, in 2014, only 14% of HIV-infected 15–24-year-old South Africans were on ART (Rencken et al., 2021). In 2019, roughly 63% of children and young adolescents (0–15) living with HIV were reported to be on ART in South Africa (Nyasulu et al., 2021).

Despite South Africa's commendable ART rollout programme, poor retention in care and low viral load suppression rates, particularly among young people aged 15–24 years, present a new challenge for the National Health Department (Clouse et al., 2013). Remaining in ART care and adhering to medication is necessary to achieve good treatment outcomes, including neurocognitive and growth outcomes (Azia et al., 2016; Enane et al., 2018). The goal of ART is to suppress viral replication so that VL is lower than detectable levels (Zhou et al., 2010; Ahonkhai et al., 2021). A suppressed viral load is associated with improved clinical outcomes and a better quality of life for PLHIV.



According to the National HIV Seroprevalence, Incidence, Behaviour, and Communication Survey undertaken in South Africa in 2017, VLS rates among adolescents were poor compared to adults (47.7% vs 73%) (Nabukeera et al., 2021). This is partly because adolescents find it difficult to comply with the required high levels of adherence to treatment and remain in care for a sustained period (Rencken et al., 2021). In one study in a low-income setting, it was found that prenatally HIV-infected adolescents exhibit poor retention to care rates when they transition to adult ART care (Shewade et al., 2016). Researchers in a public healthcare clinic in KwaZulu-Natal observed a VLS rate of 56% at 12 months post-ART initiation for HIV-positive children and adolescents under 20 years. As a growing number of adolescents enter adult-oriented ART care services, there are no guidelines or criteria in place to assist healthcare providers in providing adolescent-friendly healthcare services that respond to their needs (Evans et al., 2013). A multi-country survey (447 countries) of adolescents enrolled in ART found that the chief barrier to access to healthcare services was

the unavailability of youth-friendly services. Moreover, 40% of respondents expressed their displeasure at the lack of preparatory discussion regarding the transition to adult care (Fox et al., 2013). This lack of adolescent-specific interventions contributes to high levels of unconfirmed loss to follow-up (Bengura, 2021) and unsuppressed VL among adolescents (Merrill et al., 2021).

## 1.2 PROBLEM STATEMENT

Despite improvements in the provision of ART over the past 15 years to PLHIV, poor treatment outcomes and low retention in care (RiC) rates among ALHIV persist in urban and rural South Africa (Crowley et al., 2020). This poor performance of adolescents enrolled in ART programmes has resulted in virological failure and high HIV mortality. Studies report that South African ALHIV do poorly on treatment compared to adults and children (Okonji et al., 2021). This poor performance of ALHIV has a direct impact on South Africa's ability to attain the UNAIDS' 95-95-95 targets. Considering that adolescents are a growing population in the country that serve future economic workforce benefits, there needs to be more protection and research on managing diseases such as HIV among adolescents. Further, studies have shown that adolescents' transition to adult-orientated services is not well managed in developing countries, as this period has been identified as a grey area that is not covered by the current ART guidelines.

It is critical for PLHIV to consistently remain on treatment and adhere to it as prescribed to achieve viral load suppression and positive clinical outcomes (Cluver et al., 2018). Given the dynamic nature of the adolescence stage and the challenges that come with it (Ferrand et al., 2016), it is even more important for them to remain in care to attain viral suppression. An analysis of routine HIV VL data by the National Health Laboratory Service (NHLS) suggests that children and adolescents in South Africa are not on track to attain UNAIDS's third 95 goal (Mazanderani and Sherman, 2020). NHLS reported a 49.7% VLS among all children and adolescents that had a VL test in the period from July 2019 to June 2020.

The scarcity of adolescent-specific ART programmes means that monitoring of treatment outcomes and retention in care rates for adolescents on ART is limited to research studies. Routine health reporting does not provide data on adolescent treatment outcomes and RiC rates, which means that healthcare providers in public facilities do not have a full picture of how this vulnerable population is performing on ART. This lack of understanding renders the

health system incapable of providing interventions that are specific to adolescents accessing ART in primary healthcare settings. Therefore, there is an urgent need to assess Remaining in Care (RiC) and Viral Load Suppression (VLS) among adolescents on ART in public primary healthcare clinics and to identify factors associated with poor treatment outcomes (Huerga et al., 2018; Mathews et al., 2021).

## 1.3 AIM AND OBJECTIVES

The current study aimed to assess the treatment outcomes (VLS and RiC) and the risk factors of adolescents (12–19 years) on ART in selected primary healthcare clinics in the Mitchells Plain sub-district, Cape Town between the periods of January 2016 to December 2020.

The objectives of this study were:

- To describe the sociodemographic and clinical profile of adolescents enrolled in ART at selected primary healthcare clinics.
- To determine VLS rates for adolescents on ART in selected primary healthcare clinics.
- To describe the RiC of adolescents in selected primary healthcare clinics.
- To determine risk factors for VLS for adolescents on ART in selected primary healthcare clinics.
- To determine risk factors for RiC for adolescents on ART in selected primary healthcare clinics.



## 1.4 OUTLINE OF THESIS

This mini-thesis is comprised of six chapters.

Chapter 1 provided the background to the study and orientated the reader to the magnitude of ART coverage and treatment outcomes in a global, African, and South African context. Further, it clarified the problem the study attempted to solve while also providing information about the aim and objectives of the study.

Chapter 2 describes the literature concerning VLS and RiC rates for adolescents globally and in sub-Saharan Africa. Further, factors that influence VLS and RiC rates among adolescents on ART are explored in other parts of the world, including South Africa.

Chapter 3 describes various components of the study methodology, namely: study design, study population, sampling procedure, data collection, management and analysis. The chapter further discusses the reliability and validity of the study and ethical considerations.

Chapter 4 presents the results of the study.

Chapter 5 discusses the study results in detail, relating them to other studies on similar topics.

Chapter 6 provides recommendations based on the results and concludes the study.

# CHAPTER 2. LITERATURE REVIEW

## 2.1 OVERVIEW OF CHAPTER

This literature review aims to provide the best available evidence on rates of VLS and factors that influence VLS among adolescents. Further, the concept of RiC is described and its associated factors are discussed from the available literature.

## 2.2 DEFINITION AND MEASUREMENT OF VIRAL SUPPRESSION

HIV viral load refers to the number of HIV copies in a millilitre (c/ml) of blood (Lecher et al., 2021). WHO (2021) has revised its threshold for VLS from 1000 c/ml (2016) to 50 c/ml in its 2021 HIV treatment guidelines. The latest South African ART guidelines (2019) stipulate that a VL of less than 50 HIV c/ml of blood is suppressed and is indicative that ART is working as intended. Therefore, a VL outcome of more than 50 c/ml is considered unsuppressed in South Africa and indicates either treatment failure or poor adherence to ART (South African National Department of Health, 2019). Two consecutive VL measurements of greater than 1000 c/ml three months apart with adherence support from the first VL are considered a virological failure (Getawa et al., 2021).

WHO regards routinely checking HIV VL as the gold standard for monitoring the effectiveness of ART treatment (World Health Organization, 2021). Timely VL monitoring is critical in assisting healthcare providers and patients to evaluate treatment outcomes, treatment failure, drug resistance and possible non-compliance with treatment so that clinical decisions regarding the need for adherence support and possible treatment regimen change can be made in good time (Cherutich et al., 2016). WHO recommends that the first VL be taken six months post-ART initiation, followed by the second VL at 12 months, and thereafter annually, provided the first two viral loads are suppressed (Boeke et al., 2021). The South African government adopted its VL monitoring guidelines from the World Health Organization.

## 2.3 RATES OF VIRAL LOAD SUPPRESSION AMONG ADOLESCENTS

Attainment of acceptable VLS rates by adolescents enrolled in ART programmes is a worldwide challenge, as the literature continues to report poor clinical outcomes among the adolescent population (Jobanputra et al., 2015a). Globally, UNAIDS' first two 90s targets were narrowly missed at 84–87, while the third 90 was attained. This section covers the

progress countries have made in attaining the new-fast-tracked UNAIDS' 95-95-95 targets, with special attention to the third 95.

In sub-Saharan Africa, despite the commendable expansion of HIV services and ART treatment rollout to all PLHIV, studies have found sub-optimal VLS rates amongst adolescents (Shanaube et al., 2021). Therefore, rapid expansion in access to ART has not shown a concomitant increase in VLS in this region (Wang et al., 2016). Literature has exposed huge variations in VLS among adolescents in this region, with some countries faring better than others, although none have managed to attain the UNAIDS' third 95%. For example, a VLS of 73% was reported from cross-sectional studies conducted in Kenya and Uganda among adolescents and young people registered in ART programmes in 2020 (Njuguna et al., 2020; Brown, Malagala, & Bajunirwe, 2021). Further, Kenyan adolescents enrolled in clinics with high HIV prevalence demonstrated a VLS of 80% and above. This is likely because these clinics are better resourced and have more experience managing adolescents and young adults on ART. Other African regions have recorded even poorer VLS among ALHIV. Fokam and colleagues (2021) recently discovered that 65% and 48% of adolescents enrolled in ART programmes in urban and rural Cameroon were VLS, respectively. This poor VLS rate is not confined to one nation in the western African region. Even in Nigeria, one of the wealthiest countries on the African continent, literature revealed a VLS of 56.4% among adolescents (Oyefabi et al., 2019). Adolescent-specific interventions are needed across the SSA region to meet UNAIDS's target of only 5% VL non-suppression in 2025.

There is consensus that ALHIV in South Africa are doing poorly on ART (Zanoni et al., 2016). This threatens the country's ability to attain the UNAIDS' 95 95 95 targets in three years, as adolescents have been identified as the key population group to change the trend against the HIV/AIDS epidemic in South Africa. There are key differences in the performances of ALHIV enrolled on ART across the nine South African provinces. For example, an NHLS VLS report by Mazanderani and Sherman (2020) recorded a VLS rate of 55% for adolescents in KZN, followed by 50% in Gauteng, and the lowest in the Western Cape at just 41.8%. These marked variations in VLS among adolescents might be due to differences in strategies that each province has employed in addressing ALHIV's unique needs. Low rates of VLS (51%) were also reported for adolescent patients enrolled on ART in a tertiary hospital in Cape Town (Sherr et al., 2020). However, a marginally superior VLS

of 65.1% was recorded among adolescents aged 13–18 years from 11 healthcare facilities in the Western Cape (Crowley et al., 2020). These VL outcomes are well below the UNAIDS' third 95 targets. It seems like the Western Cape healthcare system has no tailor-made interventions to meet the needs of ALHIV. Designing a support structure for ALHIV will go a long way in improving the self-efficacy and self-competence of ALHIV to adhere to their ART medication.

Poor progression of adolescents to the final 95 of the UNAIDS' 95-95-95 targets was also reported in an Eastern Cape district with a VLS rate of 47.5% among ART-initiated adolescents (Haghighat et al., 2021). In one research study undertaken in the Mpumalanga Province, the proportion of ALHIV with viral suppression after six months of ART initiation was relatively high at 74.3% (Okonji et al., 2021) compared to another study (67.6%) (Filiatreau et al., 2021) conducted in the same province, but still falls short of the global target of 95%. These studies employed different VL non-suppression cut-off points (> 400 vs >1000 copies/ml), which might explain the differences in VLS. The results of these studies are almost similar to findings reported by Huerga et al. (2017) of a 67.7% VLS rate among adolescents (10–19 years) on ART living in the Eshowe district in KZN.

## 2.4 FACTORS ASSOCIATED WITH VIRAL SUPPRESSION

In sub-Saharan Africa, where 88% of all ALHIV reside (Nyakato et al., 2022), literature has attributed this poor performance of adolescents to demographics (i.e., age and gender), clinical (i.e. WHO staging and CD4 count level), and behavioural factors (Desta et al., 2020; Njuguna et al., 2020).



### 2.4.1 Demographic factors

Studies have shown associations between individual factors (such as current age, age at ART initiation, and gender) and VLS among adolescents (Rodriguez et al., 2020).

#### *Age*

Literature has demonstrated that current age significantly impacts VL outcomes among ALHIV (Sher et al., 2020; Zungu et al., 2020; Inbarani et al., 2022). Numerous cross- sectional studies conducted on ALHIV in Kenya, Uganda and Swaziland suggest that adolescents are more vulnerable to attaining detectable VL compared to adult patients (Jobanputra et al., 2015a; Mujugira et al., 2016; Bulage et al., 2017). This poor performance is concerning, considering

that adolescents need long-term ART treatment services to maintain a healthy lifestyle (Shanaube et al., 2021). Further, some investigators have observed that among adolescents, the age difference does not influence VL outcome. Mwangi and Van Wyk (2021) and Okonji et al. (2021) observed that VL outcomes of younger and older adolescents (10–14 vs 15–19 years) were not different in Kenya and South Africa, respectively. This discovery mirrors the results of a retrospective cohort study done in another eastern African country (Uganda) among PLHIV, where authors found no association between age and VL outcomes across all participants (Patsis et al., 2020). In South Africa, many sources agree that age does influence VL outcomes among ALHIV. In Cape Town, investigators discovered that younger adolescents (10-14 years) were more likely to attain VLS than older adolescents (15-19 years) older (Van Wyk et al., 2020). Esher et al. (2020) corroborated this finding in a cross-sectional analysis of ALHIV enrolled in ART at Groote Schuur hospital, where it was also reported that older adolescents failed to attain VLS.

***Age at ART initiation***

Sub-Saharan African studies on ALHIV revealed conflicting conclusions regarding the relationship between viral outcomes and the age of ART initiation. Although Mwangi and van Wyk (2021) found that age at ART initiation was not significantly associated with VLS, Elashi and van Wyk (2022) demonstrated that the odds of being virally suppressed declined with increasing age at ART initiation. Researchers in Tanzania and Zimbabwe discovered that there was an association between a younger age at ART initiation and virological failure (Makadzange et al., 2015; Muri et al., 2017). Sub-therapeutic drug levels in young adolescents because of dose-prescribing errors could be one of many reasons for this poor treatment outcome among young adolescents (Chappell et al., 2019).

***Gender***

The association between gender and VL outcome has been a subject of discussion in the literature in recent years. Evidence suggests that male adolescents are more likely not to achieve VLS than females. Njuguna et al. (2020), Desta et al. (2020), Penot et al. (2014), and Jobanputra et al. (2015b) found an association between male adolescents and VL non-suppression in Kenya, Ethiopia, Burkina Faso and Swaziland, respectively. However, these findings contradict Muri et al.'s (2017) observation in Tanzania, where the female gender was associated with poor VLS. In South Africa, studies have pointed out that male adolescents are more prone to viral non-suppression than females. Suboptimal VL suppression among male adolescents was reported in South Africa by Van Wyk et al. (2020) and Nyakato et al. (2022). The

researchers reported that the poor performance of male adolescents on ART is associated with late health-seeking behaviours and the fact that they often engage in risky behaviours, such as having multiple sex partners, alcohol abuse and unprotected sex.

### 2.4.2 Clinical Factors

Literature has demonstrated that clinical parameters such as baseline WHO stage, baseline CD4 count, and current ART regimen are associated with VLS (Araújo Cardoso et al., 2012; Muri et al., 2017; Ssemwanga et al., 2020).

***WHO stage***

In the absence of ART, HIV gradually destroys the immune system while advancing in WHO stages (i.e., stages I, II, III, and IV), which eventually results in AIDS-defining illnesses (Aregay et al., 2020). The WHO has developed a standardised clinical staging and immunological classification of HIV in HIV-infected adults and children who are 15 years and older (Schwartz et al., 2010). The WHO staging is particularly important in resource- limited nations, where viral load and CD4 count monitoring are not efficiently executed; it aids clinicians to determine the severity of a patient's condition, risk of mortality, urgency, and timing of ART initiation, and whether or not there is a need for cotrimoxazole prophylaxis (Vanhamelel at., 2019).

According to the WHO, HIV-infected people who are asymptomatic or experience generalised lymphadenopathy are classified as being in HIV clinical stage I (WHO, 2007b). PLHIV in WHO clinical stage II are usually mildly symptomatic and may present with moderate unexplained weight loss (< 10% of body weight), herpes zoster, angular cheilitis, recurrent oral ulceration, popular eruptions and recurrent upper respiratory conditions such as bronchitis, sinusitis and ear infection. (South African Department of Health, 2010). PLHIV who present with unexplained chronic diarrhoea for longer than one month, unexplained severe weight loss (> 10% of presumed or measured body weight), unexplained persistent fever (≥ 37.5 degrees Celsius) for more than one month, persistent oral candidiasis, pulmonary tuberculosis, severe bacterial infections (i.e., pneumonia, meningitis, bone infection, etc.) and gingivitis are considered to be on the WHO clinical stage III (moderately symptomatic stage) (World Health Organization, 2007a; Araújo Cardoso et al., 2012). The WHO clinical stage IV is characterised by the presence of HIV wasting syndrome, pneumocystis pneumonia, recurrent severe bacterial pneumonia, chronic herpes simplex infection, Kaposi sarcoma, HIV encephalopathy, and extra-

pulmonary Cryptococcus (Centre for Disease Control and Prevention, 2015).

Advanced WHO clinical stage IV was associated with virological failure in a cross-sectional study conducted between December 2018 and May 2019 among a cohort of adolescents (10–19 years) in various ART centres in Cameroon (Fokam et al., 2021). Comparable findings were made by a study that routinely analysed collected data in Swaziland, which suggests that there is an association between WHO stage III/IV and detectable VL (Jobanputra et al., 2015b). In contrast, findings from a retrospective analysis of adolescents (10–19) and children (0–9) in Lagos, Nigeria, found that patients in WHO clinical stage IV had eight times greater odds of attaining a suppressed VL compared to those on WHO clinical stage I (Egbonrelu, 2021). Maena et al. (2021) observed a correlation between WHO stage II and VL non-suppression among adolescents on ART in eastern Uganda. This shows that adolescents' risk of developing detectable VL is present even in WHO clinical stages that are considered less severe. In South Africa, a retrospective cohort study conducted in an ART-offering clinic in Johannesburg, among children and adolescents aged 0–18 years, found that patients classified as WHO stage III/IV were less likely to have unsuppressed VL than those at WHO stage I/II (Hendrickson et al., 2019).

***Baseline CD4 count***

A retrospective cross-sectional analysis of routinely collected data in Nigeria found that older adolescents who initiated ART with a CD4 count <200 cells/µl had a higher probability of failing to attain viral suppression than those who entered care with a CD4 count greater than 200 cells/µl (Ndembi et al., 2020). In line with the above findings, results of a cross-sectional study conducted in Tanzania among adolescents (10–18 years) and children (0–9 years) suggest that having a baseline CD4 count of >500 cells/µ is significantly associated with viral suppression (Martelli et al., 2019). Further, a cross-sectional study conducted among adolescents (10–19) on ART in 11 clinics in Cambodia observed that adolescents with a

recent CD4 count of >672 cells/µl were more likely to attain unsuppressed VL (Chhim et al., 2018). Moreover, a study that assessed factors associated with VL non-suppression in adolescents and adults on ART in Swaziland suggests that a CD4 count of <350 cells/µl was associated with VL non-suppression (Jobanputra et al., 2015a). A recent analysis of adolescents enrolled in multi-cohorts in six South African provinces found that with increasing CD4 (>200 cells/µl), the incidence of viral non-suppression decreased among all adolescents (Nyakato et al., 2022).

***ART regimen***

Once patients are enrolled in an ART regimen that is potent enough to stop ongoing viral replication and prevent the occurrence of drug resistance, the immune system usually recovers, and AIDS-defining clinical diseases become rare (Margolis et al., 2017). Rapid and early initiation of ART remains the only weapon in the absence of a cure to control the endemic and optimise the health of PLHIV (Boyd et al., 2019). Dolutegravir (DTG) in combination with two nucleoside reverse transcriptase inhibitors (e.g., Tenofovir and Lamivudine) is recommended by the WHO as the preferred first-line regimen for people living with HIV starting ART (World Health Organization, 2021). Drugs in the first-line regimen work by inhibiting the enzyme responsible for incorporating viral DNA into the host genome (Cotrellet et al., 2014). A randomised, double-blinded study of the safety and efficacy of dolutegravir 50MG daily dose, found that subjects on DTG rapidly achieved viral suppression compared to those initiated on raltegravir (Cotrellet al., 2014). The second-line regimen recommended by WHO consists of boosted protease inhibitors in combination with an optimised nucleoside reverse transcriptase inhibitor (NRTI) (World Health Organization, 2019). HIV drugs such as Tenofovir (TDF), Lamivudine (3TC), Emtricitabine (FTC), Abacavir (ABC), Zidovudine (AZT), Stavudine (d4T), Didanosine (ddI), Efavirenz (EFV), Nevirapine (NVP), Rilpivirine (RPV), Etravirine (ETR), Atazanavir (ATV), Lopinavir/Ritonavir (LPV/r), Darunavir (DRV), and Maraviroc (MVC) are available in most countries in this region (Meintjes et al., 2017).

The South African National Department of Health recommends the initiation of adolescents (> 10 years and weighing > 35 kg) and adults on Tenofovir (TDF) 300mg, Lamivudine (3TC) 300mg, and Dultigravir (DTG) 50mg (South African National Department of Health, 2019). Further, for children younger than 10 years, the department recommends that such patients be

initiated on a different ART regimen containing: Abacavir (ABC), Lamivudine (3TC) and Lopinavir (LPV) (South African National Department of Health, 2019).

In Uganda, Kibalama et al. (2021) discovered that children and adolescents who had no previous exposure to NVP had high odds of attaining VL suppression compared to those who were previously exposed to NVP. This is because prior exposure to NVP increases the risk of developing NVP resistance, leading to virological failure. A cohort study that followed adolescents (10–19 years) registered on ART in a tertiary hospital in Zimbabwe found that VLS appear higher in those treated with an EFV-based regimen (73%) compared to those treated with an NVP-based regimen (61%) (Mapangisana et al., 2021). Comparable findings were made by Desta et al. (2020) in Ethiopia, where they discovered that adolescent patients on AZT-3TC-NVP were 1.3 times more likely to develop a high viral load when compared to those on AZT-3TC-EFV.

Protease inhibitors have long been viewed as the most effective class of drugs for suppressing HIV and stopping further replication; however, the literature reports contradictory arguments. In Kenya, it was found that adolescents on protease inhibitors (PIs) were less likely to have viral suppression compared to those on non-nucleoside reverse transcriptase inhibitors (NNRTIs) (Njuguna et al., 2020). In contrast, Sherr et al. (2020) discovered that adolescents on PIs managed to attain VLS compared to those enrolled on NNRTIs.

Prior exposure to prevention of mother to child transmission (PMTCT) was protective against viral non-suppression, according to the results of a study conducted in five South African districts among PLHIV, including adolescents (Joseph Davey et al., 2018). Being switched to an ART second-line ART regimen was associated with VL non-suppression, according to the outcomes of a retrospective cohort analysis of adolescents enrolled in ART in Ehlanzeni District, Mpumalanga (Okonji et al., 2021).

### 2.4.3 Behavioural Factors

Many behavioural factors have been suggested to be associated with poor treatment outcomes in ALHIV on ART, such as alcohol consumption, disclosure and adherence (Miti et al., 2020; Tanner et al., 2021; Zanoni et al., 2021).

***Alcohol consumption***

Studies conducted in two southern African nations, namely, South Africa and Zimbabwe, revealed a correlation between viral non-suppression and alcohol consumption among adolescents enrolled in ART (Wyk, Kriel and Mukumbang, 2020b; Sithole et al., 2021). The association between alcohol consumption and virological failure in the aforementioned study is not surprising because alcohol use among ALHIV has been associated with poor adherence and failed viral suppression (Boeke et al., 2018).

***Disclosure***

Researchers found no significant association between awareness of HIV status and VL failure in the Eastern Cape, South Africa (Haghighat et al., 2021). However, a study conducted in nine districts in Zimbabwe found that non-disclosure of HIV status heightened the risk of virological failure among ALHIV (Simms et al., 2021). Similarly early disclosure of HIV status was protective against treatment failure among ALHIV in Nigeria (Ndembi et al., 2020).

***Adherence***

The optimal adherence level required to attain HIV viral suppression is unclear, though 95% has been seen as a gold standard (Sher *et al*., 2020). Importantly, researchers have demonstrated that it is possible to attain optimal viral suppression at an adherence rate below 95% (Altice *et al.*, 2019). Adherence is usually assessed by a variety of methods, which include self-report, pill counts, pharmacy refills, and VL outcomes (Costa *et al.*, 2018).

Worldwide, huge variations in adherence levels among adolescents and young adults have been reported: 52% in North America to 62% in Europe and South America; 84% in Asia and Africa. Compared to adults, only 20% of ALHIV achieved 100% ART adherence levels, while 40% of adults achieved 100% ART adherence (Villiera *et al.*, 2022).

Studies report conflicting results regarding the impact of adherence on VLS across the sub-Saharan African region. A large longitudinal cohort study undertaken in the Eastern Cape, South Africa, discovered that adolescents who claimed to be adherent to treatment were more likely to be virally suppressed (Cluver et al., 2021). Further, a statistically significant association was observed between self-reported adherence and viral suppression among adolescents and young adults living with HIV in Ghana (Justice et al., 2021). However, intensified adherence counselling yielded no positive results among adolescents enrolled in

ART in Kenya, as 57% of ALHIV were reported to be virally unsuppressed (Kansiime and Gwokyalya, 2020).

## 2.5 RETENTION IN CARE

For people living with HIV, the ability to remain in care plays a vital role in preventing onward HIV transmission and achieving good health. The definition of retention in care tends to differ within and between regions (Bulsara et al., 2021). In the United Kingdom and Australia, PLHIV are considered to have remained in care if they attend one visit in 12 months, with VL outcome being used as a proxy (The Kirby Institute, 2012; Goodman, 2016). Roscoe and Hachey (2021) define retention in care as the patient's regular engagement with medical care at a healthcare facility post-linkage into the HIV care continuum.

According to the Centre for Disease Control and Prevention CDC, retention in HIV care is the recording of at least two CD4 count cell results or VL tests done at least three months apart in the year under review (CDC, 2021). PLHIV need to remain in care to ensure that they attain favourable treatment outcomes (Yang et al., 2015). When one is considered to have remained in ART, this implies that they are engaged with the health care system from enrolment to ART discharge or death (Stricker et al., 2014). However, because of a variety of factors, some PLHIV fail to remain in care for a sustained period; hence, they are lost from the treatment care system. Agbor et al. (2021) reported a mortality rate of 8–16% among patients recorded as lost to follow-up (LTFU) in sub-Saharan Africa. In South Africa, patients are considered LTFU if they have not attended their clinic appointment 90 days after their last clinic attendance (Fox et al., 2010).



In their assessment of the progress to attain the UNAIDS' 95-95-95 targets from data submitted by 170 countries to UNAIDS in 2018, Marsh et al. (2019) found that just 56% of younger adolescents (10–14 years) and children were RiC. Even in high-income countries, which possess the resources to provide comprehensive ART services to PLHIV, keeping adolescents engaged in care is a challenge. In a longitudinal cohort study conducted in 14 ART facilities in the USA, researchers discovered that just under 60% of participants were RiC 12 months after ART initiation (Lally et al., 2018). Contrary to most research findings, an observational study conducted in 10 cities in the United States of America revealed that youth and adolescents attained better RiC rates (62.1%) than their adult counterparts (50.9%) (Hall et al., 2012). However, results elsewhere in Asia revealed a higher RiC rate of 98% among adolescents 3

years after starting treatment (Zhou et al., 2010).

Marked differences in RiC among ALHIV have been observed in sub-Saharan Africa. This is supported by the findings of a literature review of studies undertaken in Zimbabwe, South Africa, Uganda, Rwanda and Ethiopia, where the pooled LTFU rate was 15.21%. Further analysis of these studies revealed that South Africa had the lowest LTFU rate of 1.6%, while Uganda recorded the highest LTFU rate of 32% (Dwyer-Lindgren *et al.*, 2019).

Researchers discovered an alarmingly low RiC rate of 29.3% in an HIV diagnosis, treatment, and care facility in Uganda (Izudi et al., 2018). Nevertheless, a mixed-method research study conducted in 10 Ugandan districts, which were said to be representative of the adolescent ART population, suggests that RiC rates declined over time. This study indicates that Ric was 96% after six months of treatment, 90% at 12 months, 83% at 24 months, 76% at 36 months, and 71% at 48 months (WHO, 2020). Another retrospective analysis of secondary data in Uganda also discovered a low RiC of 69% among adolescents who accessed ART from facilities supported by The AIDS Support Organization (TASO) (Okoboi et al., 2016).

In West Africa, researchers found RiC rates exceeding 90% among a cohort of adolescents who had undergone status disclosure. This underscores the importance of timely disclosure of HIV status, which promotes better adherence and RiC among adolescents (Arrivé et al., 2012). A research study undertaken to determine RiC rates of young adolescents and children younger than 15 years found RiC rates that ranged from 71% in West Africa to 95% in Rwanda (Abuogi, Smith, and McFarland, 2016). Similar findings were made by a retrospective cohort study conducted in Zimbabwe, which observed RiC rates upward of 70– 77% (Shroufi et al., 2013).

A meta-analysis of six research articles conducted among adolescents accessing ART in South Africa found RiC rates of 83% 1–2 years post-ART initiation (Zanoni et al., 2016). Zanoni et al. (2017) observed a RiC of 89% from a retrospective cohort study undertaken in a specialised ART facility in the South African province of KwaZulu-Natal. However, results of a retrospective cohort study conducted in Khayelitsha, Cape Town, found a RiC of 70% (Kaplan et al., 2017). Researchers sought to describe variations in the quality of care as measured by RiC in healthcare facilities in South Africa; the top quintile facilities achieved a RiC rate of 84%, while the bottom quintile could only manage a RiC of 56% six months after

ART treatment (Crowley et al., 2020). A prospective observational study that looked at a cohort of adolescents (10–19 years) who had been transferred to other facilities in South Africa found RiC rates of 84% one year after transfer and 95% three years post-transfer (Davies et al., 2017).

## 2.6 RISK FACTORS FOR RETENTION IN CARE

Literature has demonstrated that risk factors for disengagement from care vary from psychological factors and disclosure of HIV status to gender and stigma. ALHIV in particular has shown vulnerability to mental health, disclosure and stigma (Enane et al., 2018; Haas et al., 2020; Armstrong-Mensah and Tetteh, 2021).

### 2.6.1 Psychological factors

Studies have demonstrated that mental illness is associated with poor RIC rates. These findings were revealed in a literature search conducted among adolescents aged 10–18 years accessing ART in public health facilities in the United States of America, where researchers revealed a high rate of lost to follow up (LTFU) among adolescents with mental health illnesses (Lall et al., 2015). Likewise, Ryscavage et al. (2016) discovered that mental illness predicts low retention in care rates among adolescents on ART.

Okonji et al. (2020) suggest that mental health conditions such as anxiety, depression, and suicidal thoughts contribute to poor RiC rates among ALHIV. Further, a recent cross- sectional survey conducted in Mpumalanga, South Africa, found that the prevalence of LTFU among participants with higher perceived stress was 1.77 (95% CI 1.07–2.91) times the prevalence of LTFU among those with lower perceived stress (Filiatreau *et al.*, 2021). However, this study found no association between heightened depressive symptoms and loss to care (Filiatreau et al., 2021).

### 2.6.2 Disclosure

In West Africa, researchers conducted a retrospective analysis of children (0–9) and adolescents (10–20) enrolled in multicentre cohorts and they discovered that non-disclosure was associated with poor retention in care (Arrivé et al., 2012). Similarly, ill-timed HIV status disclosure was a common risk factor for poor RiC rates among adolescents accessing ART in three healthcare centres in Uganda in 2016 (Inzaule et al., 2016). Adolescents interviewed from five health facilities in Ethiopia described non-disclosure of HIV status to family or friends as a barrier to retention in care (Tunjeet al., 2021). Recently, Zanoni et al. (2021) explored

reasons for poor retention in care in South Africa, among ALHIV and their caregivers and found that non-disclosure of HIV status and poor social support were associated with disengagement from care for ALHIV.

### 2.6.3 Gender

A study conducted in the US among adolescents and young people enrolled in ART in 20 Adolescent Medicine Trials Network for HIV/AIDS Intervention Units, found that females were less likely to report current ART use than males (Kahana et al., 2016). Moreover, a retrospective analysis of routinely collected data in the US found that the incidence of missed appointments was 74.9% (95% C.I. 1.480–2.045) higher for females than males (Lally et al., 2018). Furthermore, studies undertaken in Ethiopia and Kenya found that female adolescents were at higher risk of LTFU than adolescent males (Jerene et al., 2019). A cohort of adolescents and young people (15–24 years) on ART were followed up in Mozambique to determine remaining in care variations based on gender, and it was established that females were more likely to remain on treatment than their male counterparts (Ahonkhai et al., 2021). In contrast, a retrospective cohort analysis discovered one year after ART initiation that females had higher odds of RiC than males (Ahonkhai et al., 2021). Even so, an analysis of adolescents and children enrolled in multiple cohorts in sub-Saharan Africa showed no significant difference between males and females concerning LTFU (Slogrove, 2018). However, the results of a retrospective cross-sectional study conducted in South Africa revealed that female participants were more likely to be lost to care than male participants (Filiatreau et al., 2021).

### 2.6.4 Stigma

An assessment of RiC rates in adolescents and adults in the United States of America discovered that stigma played a role in participants being disengaged from care (Hall et al., 2012). Likewise, a systematic review conducted in sub-Saharan Africa found stigma to be one of the factors that predicted LTFU among adolescents on ART (Govindasamy et al., 2012). In addition, a facility-based cross-sectional analysis carried out in Nigeria among adolescents (10–20 years) reported that 71% of adolescents excluded themselves from clinical care because of fear of being stigmatised by their peers (Oladunni et al., 2021). In South Africa, stigma was associated with reduced retention in care among adolescents assessing ART care services in 53 government healthcare facilities (Pantelic et al., 2020).

## 2.7 SUMMARY

In conclusion, the reviewed literature on VLS rates among ALHIV in sub-Saharan Africa revealed that no country is on track to attain the UNAIDS' third 95 targets in this region. Moreover, regarding factors associated with VLS, the literature review presented conflicting conclusions. For example, some studies found that demographic factors such as age and gender do not affect VLS, while others found an effect.

Clinical parameters' impact on VLS was also reviewed. Researchers reached contradicting conclusions about the influence of various clinical parameters on VLS. They found that patients with WHO clinical stage IV were more susceptible to developing virological failure. In contrast, other studies have reported that WHO clinical stage IV is associated with VLS. Further, studies showed that ALHIV treated with an EFV-based regimen was more likely to be VLS. Several studies associated a CD4 >500 cells/μ with a high probability of VLS, while others suggested that a CD4 <200 cells/μ is associated with poor VLS outcomes. In the literature review of the baseline treatment regimen, studies differed on whether the protease-inhibitors-based regimen suppressed VL. Some studies reported that they are effective in VLS, while others revealed that they are not.

Furthermore, the literature review focused on retention in care rates and factors that might influence RiC among ALHIV. The reviewed literature revealed huge variations in RiC rates among adolescents in sub-Saharan Africa. For example, a RiC rate of 29.3% was reported in one of Uganda's healthcare facilities, while a RiC of more than 90% was revealed in a study conducted in West Africa. Researchers attributed this impressive RiC rate to timely disclosure of HIV status.

On factors associated with RiC rates, studies correlate psychological conditions such as stress and anxiety with a heightened risk of LTFU. Researchers did not find a consensus regarding the influence of gender on RiC. Some suggested that females were more likely to RiC, while others suggested the opposite. Further, an overwhelming number of studies found that non-disclosure of HIV among ALHIV was a barrier to RiC.

# CHAPTER 3: METHODOLOGY

## 3.1 STUDY DESIGN

The research study of adolescents aged 12–19 years on ART in public primary healthcare facilities located in the Mitchells Plain sub-district in Cape Town, South Africa, was conducted using a descriptive, retrospective cross-sectional study design. This study design allowed for the collection of data elements that had already occurred at a point in time, which assisted with measurements of outcome variables (VLS and RiC) and various exposure variables (Wang and Cheng, 2020). The cross-sectional study design saves time and costs as it measures variables at one given point in time across a pre-defined sample, unlike an observational prospective study design, which follows participants over time (Setia, 2016). Therefore, the use of this type of study was beneficial because existing data on adolescents initiated on ART and the facilities at which they were initiated were identified efficiently, saving time and resources.

## 3.2 STUDY SETTING

This research study took place in the Mitchells Plain sub-district, located in the city of Cape Town Metropole district, Western Cape Province, South Africa. According to the latest population estimates (2021), the Cape Town Metropole district has a population of 4 758 433, and approximately 635 716 (13%) of this population reside in Mitchells Plain sub-district (Western Cape Government, 2021). The ethnic and racial composition of Cape Town is as follows: 42.4% are Coloured, 38.6% are Black African, 15.7% are White, 1.4% are Asian or Indian and 1.9% are other. Mitchells Plain has an unemployment rate of 28.6%, with as many as 16% of individuals having not completed grade 12 (Masquillier et al., 2020).

Mitchells Plain district was created during the apartheid era in the 1970s to accommodate the "coloured" population of the Western Cape Province, who were forcefully removed from the Cape Town City Centre (Graham & Anthony, 2013). This township is located in the Cape Flats suburb and lies about 27.4 km away from the Cape Town City Centre. The Mitchells Plain sub-district is one of the eight sub-districts that are located in the Cape Metropole district (Western Cape Provincial Health Department, 2020). The City of Cape Town has a total of 11 primary healthcare facilities that are located in the Mitchells Plain sub-district.

HIV prevalence in the Cape Town Metropole district was 10% among people aged 15–49 years in 2020 (Western Cape Provincial Health Department, 2020). The total number of registered ART patients in the district was 209 279 in 2021. In addition, Mitchells Plain sub- district had about 28 182 PLHIV on ART in 2020. The proportion of patients that remained in ART care in the Mitchells Plain sub-district as of 2020 was 58.5% (Masquillier et al., 2020). Relative to its headcount and other sub-districts in the Cape Town Metropole, Mitchells Plain sub-district is under-resourced. Anecdotal evidence suggests that one clinician sees an average of 27 clients per day in the Mitchells Plain sub-district, with the majority of these patients being PLHIV.

## 3.3 STUDY POPULATION AND SAMPLING

The study population for this research was HIV-positive adolescents aged 12–19 years who were registered to receive ART in primary healthcare clinics in Mitchells Plain sub-district in the period January 2016–December 2020. The study population formed part of the general population, as well as the cohort of adolescents that were on ART at selected primary healthcare clinics in the period January 2016–December 2020. I have deliberately deviated from the World Health Organization's definition of adolescents (10–19 years) because the ART programme starts at 12 years in this study setting. The selected clinics only start ART from the age of 12 years, they do not have a paediatric ART programme.

### *Inclusion Criteria*

The research study was comprised of adolescents aged 12 to 19 years enrolled on ART in the period January 2016 to December 2020. The time frame was chosen in order to have an adequate sample of records. The ALHIV included must have been on a first and second line ART regimen at the time of the study and have been initiated and taking treatment at the Mitchells Plain sub-district facilities. The participants must have at least one documented VL result to be eligible for inclusion in the study.

### *Exclusion Criteria*

- Clients with that require concurrent intensive treatment (e.g., TB);
- Clients who are hospitalised at any time during the study period.; and
- Clients that transferred out before having their first viral load taken.

The research study made use of a total population sampling method, which was inclusive of all adolescents aged 12–19 years on ART at Mitchells sub-district primary healthcare clinics in the period January 2016–December 2020. Total sampling is a type of non-probability sampling procedure that entails studying the entire population that has predefined characteristics of interest. The total sampling method and research design allowed for effective data collection and analysis (Etikan, 2016).

The number of adolescents on ART at the selected primary health clinics in the period of January 2016–December 2020 was approximately 581. The minimum sample size for the study was worked out to be approximately 399. This value was determined using Yamane's formula with a confidence level set at 95% and a margin of error of 0.05. However, all adolescents on ART during the period under study who met the inclusion criteria were included in the study.

### 3.4 DATA COLLECTION

The City of Cape Town's clinics store patient data electronically on the Patient Record and Electronic Health Management Information System (PREHMIS). PREHMIS is an electronic system designed to capture and store patient demographics, clinical data, and various services rendered to the patient within the facility. Primary health care clinics use PREHMIS in conjunction with paper-based patient files, as not all clinical data can be captured on them. However, it is a valuable resource for data management and the instant generation of automated reports. The clinic clerks capture each clinical visit made by the patient on PREHMS from the patient's paper-based file. On the fifth day of every month, clerical staff, the facility manager, and the sub-district Health Information Officer (HIO) meet to validate the facility data. This is where errors are identified and rectified to ensure accurate and complete data before it is submitted to the Cape Metropole district office. After data validation of all clinics' data in the Mitchells Plain sub-district, the HIO escalates it to the Cape Metropole district's head of health information office.

The data was collected from an electronic database called PREHMIS. A detailed report of all adolescents initiated on ART in selected primary healthcare clinics in Mitchells Plain sub-district, Western Cape, South Africa, during the period January 2016 to December 2020 was drawn. After obtaining the sample of ALHIV in selected primary healthcare clinics in Mitchells Plain sub-district from the electronic database, the principal investigator extracted

the required data and entered it into an abstraction form. Once all relevant data was collected and entered into the abstraction form, it was entered into an Excel spreadsheet and cleaned. After data cleaning and coding were complete, it was then imported into SPSS version 28 and analysed. Below is a description of the data variables that were collected, which included baseline socio-demographic, baseline clinical, behavioural, viral load, and retention in care variables.

### 3.4.1 Baseline socio-demographic variables

Data extracted under this category included the gender, and age of the participants at the time of starting ART. The other variables extracted were disclosure of status to a parent, relative, or friend and history of experiencing stigma.

### 3.4.2 Baseline clinical variables

The clinical variables extracted were baseline WHO staging, baseline CD4 count, current ART regimen, and history of psychological conditions.

### 3.4.3 Behavioural variables

The behavioural variables collected included a history of alcohol consumption and disclosure of status to a significant other (parent, relative, or friend).

### 3.4.4 Viral load suppression

A viral load is used as a biomarker to measure the effectiveness of ART and to assess the adherence of a patient to medication. For this study and in line with the latest Western Cape government ART guidelines, a VL <50 c/mL was considered suppressed and a VL > 50 c/mL was unsuppressed. The study also assessed the proportion of VL done at various time points (4, 12, and 24 months).

### 3.4.5 Retention in Care

Retention in care is an important element that defines the success of an ART programme. This dependent variable is influenced by the death and the loss of follow-up of a patient. When a patient dies or fails to attend a scheduled clinic visit for three months, the patient is considered lost to follow-up. The 90 days are calculated from the date the patient last visited the clinic.

### 3.5 DATA ANALYSIS

Once the data had been collected and transcribed into an Excel spreadsheet, quality control checks were undertaken before data analysis. The dataset was checked for missing data variables, internal consistency, errors, and outliers (i.e., age). Once the data was checked for completeness and accuracy, it was categorised and coded before being imported into SPSS version 28.0. Categorical baseline data for demographic and clinical variables were described using descriptive frequency tables. The proportion of adolescents in various categories was determined using percentages. Continuous variables such as age, CD4 count, and VL outcomes were demonstrated using measures of central tendency such as median and interquartile range. Using bivariate analysis, the significance and strength of associations were determined at various points between independent variables (age and gender) and dependent variables (RiC and VLS) at 6, 12 and 24 months post-ART initiation.

### 3.6 VALIDITY AND RELIABILITY

Validity refers to the extent to which an instrument measures what it intends to measure (Heale and Twycross, 2015). The City of Cape Town's health directorate has put several systems in place for the purpose of developing healthcare providers to maintain high standards of accurate data collection and storage. Over and above undergraduate training and qualification, the City of Cape Town's clinicians attends HIV/AIDS courses: the HIV Management course and the Nurse Initiation and Management of ART (NIMART) course. These pieces of training are the cornerstones, which promote good clinical practices and the recording of accurate information on the patient's file. Further, the City of Cape Town has specialised ART stationery that is prepared specifically for the accurate collection of data. This stationery has explanatory texts and definitions at the back to simplify concepts for a variety of data that clinicians need to collect from the patients.

Moreover, the clerical staff undergoes robust preparatory training that prepares them for capturing data related to HIV/AIDS. There are also systems in place to monitor and evaluate their performance on an ongoing basis; errors are identified and rectified, while *ad hoc* in-service training is organised intermittently. The clinics' managers run reports every Friday to check for errors, and this is repeated at the end of the month before data validation. During data validation, the Health Information Officer (HIO) sits with the clerical staff and facility manager to identify and rectify errors. In essence, it can be said that data on PREHMIS has a high degree of validity because of the high quality of the data that is routinely collected and captured.

### 3.7 ETHICS CONSIDERATIONS

Approval of the study for degree purposes was obtained from the University of the Western Cape's Higher Degrees Committee, and ethics clearance was obtained from the Biomedical Science Research Ethics Committee of the University of the Western Cape (Appendix 1). After obtaining approval from UWC's committees, an online application (http://web1.capetown.gov.za/web1/Mars) to the City of Cape Town's Health Department for permission to conduct research at the City of Cape Town's healthcare facilities was made.

Access to routine health data of adolescents on ART at selected primary healthcare clinics in Mitchells Plain sub-district was obtained from the city health department (Appendix 2).

Consent was not needed as the study made use of routine health data. There was no direct contact with the study participants. In line with the Protection of Personal Information Act (POPIA), personal data was protected through the allocation of unique identifiers. Anonymised data was stored on a password-protected computer for use by the research team only. No personal information related to identity was extracted. The data was stored in a password-protected computer, only authorized individuals had access to the data.

# CHAPTER 4: RESULTS

## 4.1 INTRODUCTION

The results of the study are reported in this chapter. It includes sections outlining the realisation of the study sample, a description of the baseline socio-demographic and clinical characteristics of the study participants, a description of the viral load suppression of adolescents, a bivariate analysis of the viral load suppression and baseline characteristics, and a description of the retention in care of adolescents, as well as a bivariate analysis of retention in care and baseline characteristics.

## 4.2 REALISATION OF THE SAMPLE

Data from 569 adolescent patients (12–19 years) on ART from the city of Cape Town's facilities, located in the Mitchells Plain sub-district, was obtained from the City of Cape Town's data management system, called PREHMIS. Adolescents without VL results were excluded from the study. The realised sample size was 420 from the original 569 patients recruited; 149 patients did not have a VL result. Records without a VL at all 3 time points (6 months, 12 months or 24 months) was excluded, those with VL at any of the time points was included in the study.

Table 4.1 Realisation of Study sample

| **Name of the facility** | **Sample size** |
|---|---|
| Mzamomhle clinic | 160 |
| Weltevreden Valley clinic | 120 |
| Phumlani clinic | 69 |
| Crossroad clinic | 28 |
| Tafelsig clinic | 16 |
| Rockland clinic | 9 |
| Westridge clinic | 10 |
| Eastridge clinic | 8 |
| **TOTAL** | **420** |

## 4.3 CHARACTERISTICS OF THE STUDY PARTICIPANTS

Table 4.2 describes the study participants study characteristics. It provides a description of the baseline demographics and clinical characteristics of the study participants. The median age of adolescents in this study was 15.28 years (interquartile range (IQR)), and the majority (64.8%) of adolescents in this study were 15–19 years old and female (89.3%).

At ART initiation, 53.6% (n = 225) of adolescents had a CD4 count less than 350 cell/$mm^3$ and 46% (n = 193) had a baseline CD4 of more than 350 cell/$mm^3$. Of the adolescents with a recorded WHO stage at ART initiation, 91.2% (n = 383) were classified as WHO stage I, 1.2% (n = 5) were classified as WHO stage II and 7.6% (n = 32) were classified as WHO stage III.

The proportion of adolescents who were on ART for more than 24 months was 60% (n = 252), while 17.1% (n = 72) were on ART for 12 months or less and 22.9% (n = 96) for 12–24 months.

The proportion of adolescents initiated on ART between 2016 and 2018 was 83.3% (n = 350), while 16.7% (n = 87) were initiated in the period 2019–2020.

Most adolescents (91%, n = 382) were initiated on the TFE (Tenofovir + Emitricitabine + Efavirenz) regimen, and 2.9% (n = 12) were on Z3L (Zidovudine + Lamivudine + Lopinavir/ritonavir). For 26 (6.2%) adolescents on ART, the baseline regimen was not recorded. TEE is the 1st line ART regimen that PLHIV are initiated on, while Z3L is the 2nd line ART regimen, which is normally initiated on patients failing the 1st line regimen.

Table 4.2: Demographic and clinical characteristics of adolescent participants on ART at selected PHC facilities in Mitchells Plain sub-district (N = 420)

| | | Frequency (n) | Percent (%) |
|---|---|---|---|
| Gender | Male | 48 | 11.4 |
| | Female | 372 | 88.6 |
| Age (in years) | 0-11 | 35 | 8.3 |
| | 12-14 | 108 | 25.7 |
| | 15-19 | 277 | 66 |
| Baseline CD4 count (in cell/$mm^3$) | <350 | 225 | 53.6 |
| | >350 | 193 | 46.0 |
| | Missing | 2 | 0.5 |
| WHO Clinical Stage | Stage I | 383 | 91.2 |
| | Stage II | 5 | 1.2 |
| | Stage III | 32 | 7.6 |
| | Stage IV | 0 | 0 |
| Duration on ART (in months) | <12 | 72 | 17.1 |
| | 12-24 | 96 | 22.9 |
| | >24 | 252 | 60 |
| ART Regimen | NNRTI | 382 | 91 |
| | PI | 12 | 2.9 |
| | Not recorded | 26 | 6.2 |
| VLS at 6 months (in copies/ml) | Full suppression (<50) | 71 | 16.9 |
| | Suppressed (50-999) | 238 | 56.7 |
| | Not suppressed (>1000) | 51 | 12.7 |
| | Missing | 60 | 14.3 |
| VL at 12 months | Full suppression (<50) | 37 | 8.8 |
| | Suppressed (50-999) | 201 | 47.9 |
| | Not Suppressed (1000) | 48 | 11.4 |
| | Missing | 134 | 31.9 |

| | | | |
|---|---|---|---|
| VL at 24 months | Full Suppression (<50) | 29 | 6.9 |
| | Suppressed (50-999) | 138 | 32.9 |
| | Not Suppressed (>1000) | 30 | 7.1 |
| | Missing | 223 | 53.1 |
| Retention in care | In care | 167 | 39.8 |
| | LTFU | 149 | 35.5 |
| | Unconfirmed Lost to Follow | 12 | 2.9 |
| | Defaulted treatment | 92 | 21.9 |

## 4.4 VIRAL SUPPRESSION OF ADOLESCENTS ON ANTIRETROVIRAL TREATMENT

The median VL for adolescents at six months was 124 c/ml (IQR 91–135.5). Most adolescents were transient suppressed 56.7% (n = 238), while 16.9% (n = 71) were fully suppressed (<50 c/ml) and 12.7% (n = 51) were unsuppressed (>1000 c/ml).

The median VL for participants at 12 months was 124 c/ml (IQR 124–270). Most 47.9% (n = 201) adolescents were transient suppressed (50–1000 c/ml), while 8.8% (n = 37) were fully suppressed (<50c/ml) and 11.4% (n = 48) were unsuppressed (>1000c/ml).

The median VL for participants at 24 months was 124 c/ml (IQR 100–124). The majority, 32.9% (n = 138) of participants were transient suppressed (50–100 c/ml), while 6.9% (n = 29) were fully suppressed (<50 c/ml) and 7.1% (n = 30) were unsuppressed (>1000 c/ml).

## 4.5 FACTORS ASSOCIATED WITH VIRAL SUPPRESSION

Table 4.3 presents the outcomes of a bivariate analysis of demographic and clinical factors associated with viral suppression.

### 4.4.1 Demographic characteristics

Older adolescents (15–19 years) had a significantly higher prevalence of viral suppression compared to younger adolescents (12–14 years) ($p = 0.030$). However, there was no statistically significant association between VLS and gender ($p = 0.203$) or ART start date ($p = 0.456$).



### 4.4.2. Clinical characteristics

Adolescents with CD4 <350 cell/mm $^3$ had a higher viral suppression compared to adolescents with CD4 > 350 cell/mm $^3$ even though the difference between baseline CD4 count and viral suppression was not statistically significant ($p = 0.756$). Adolescents who presented with WHO baseline clinical stages I and II had a higher viral suppression than those who presented with WHO clinical stages III and IV; however, the difference between the baseline WHO clinical stages and viral suppression was not statistically significant ($p = 0.837$).

It was observed that VLS was highest among adolescents on treatment for a duration of less than 12 months compared to adolescents who were on treatment for 12–24 months and >24 months, and the difference between ART duration and viral suppression was statistically significant ($p = 0.004$). Adolescents switched to a protease inhibitor (PI)-based regimen had a slightly higher viral suppression than those initiated on a NNRTI-based regimen, and this difference was found to be statistically significant ($p = 0.039$).

Table 4.3: Viral suppression of adolescent participants on ART in selected primary healthcare facilities by demographic and clinical characteristics (N= 420)

| | | Viral Suppression | | | |
|---|---|---|---|---|---|
| | | **Full Suppressed** (<50 copies/ml) **n (%)** | **Not suppressed** (50-1000 copies/ml) **n (%)** | **Not suppressed** (>1000 copies/ml) **n (%)** | ***p*-value** |
| Current age (in years) | 0-11 | 9 (25.7) | 19 (54.3) | 5 (14.3) | **0.030** |
| | 12-14 | 13 (12) | 54 (50) | 20 (18.5) | |
| | 15-19 | 49 (17.7) | 165 (59.6) | 26 (9.4) | |
| Gender | Male | 9 (18) | 22 (45) | 10 (20.8) | 0.203 |
| | Female | 62 (16.7) | 216 (58.1) | 41 (11) | |
| ART start date | 2016-2018 | 61 (17) | 200 (55.9) | 42 (11.7) | 0.456 |
| | 2019-2020 | 10 (16.1) | 38 (61.3) | 9 (14.5) | |
| Baseline CD4 count (in cell/ $mm^3$) | <350 | 41 (18.2) | 127 (56.4) | 29 (12.9) | 0.756 |
| | >350 | 30 (15.5) | 109 (56.5) | 22 (11.4) | |
| WHO Clinical stage | Stage I | 62 (16.2) | 218 (56.9) | 47 (12.3) | 0.837 |
| | Stage II | 1 (20) | 3 (60) | 0 (0) | |
| | Stage III | 8 (25) | 17 (53.1) | 4 (12.5) | |
| | Stage IV | 0 (0) | 0 (0) | 0 (0) | |
| Duration on ART (in months) | <12 | 10 (13.9) | 51 (70.8) | 11 (15.3) | **0.004** |
| | 12-24 | 19 (19.8) | 53 (55.2) | 12 (12.5) | |
| | >24 | 42 (16.7) | 134 (53.2) | 28 (11.1) | |
| ART Regimen | NNRTI | 63 (16.5) | 221 (57.9) | 45 (11.8) | 0.039 |
| | PI | 1 (8.3) | 7 (58.3) | 4 (33.3) | |
| | Missing | 7 (26.9) | 10 (38.5) | 2 (7.7) | |

## 4.5 RETENTION IN CARE

The current study found an overall RiC rate of 34% over a period of 24 months. Younger women and female adolescents who started treatment in the period 2019–2020 had higher RiC rates. The Lost To Follow Up (LTFU), Unconfirmed Lost To Follow (ULTF) and defaulter rates were found to be 64.5%, 1.5% and 46.5%, respectively.

Table 4.4 presents the results of bivariate analysis of demographic and clinical factors associated with retention in care (RiC) at 24 months.

### 4.5.1 Demographic characteristics

Younger adolescents (12–14 years) had a higher RiC rate compared to older adolescents and the difference was statistically significant ($p$= 0.001). Female adolescents had a higher RiC compared to males even though the difference was not statistically significant ($p$ = 0.880). With regards to ART start date, adolescents that started ART in the period 2019-2020 had a higher RiC compared to those that started treatment in 2016-2018, however there was no statistical significance observed ($p$ = 0.132).

### 4.5.2 Clinical characteristics

Adolescents who presented with WHO clinical stage II at ART initiation had a higher RiC rate than adolescents on WHO clinical stage I and III, although there was no statistical significance ($p$ = 0.435). Adolescents with baseline CD4 of <350 cell/mm$^3$ had a higher RiC rate compared to those with baseline CD4 of >350 cell/mm$^3$ even though statistically there was no significance ($p$ = 0.669). Similarly, adolescents on PI ART regimen had a higher RiC rate compared to those on NNRTI ART regimen; although not statistically significant ($p$ = 0.670).

Table 4.4: Retention in care by demographic and clinical characteristics of adolescents on ART in selected primary healthcare facilities in Mitchells Plain sub-district (N = 420)

| | | RETENTION IN CARE | | |
|---|---|---|---|---|
| | | **In care n (%)** | **LTFU n (%)** | ***p*-value** |
| Current age (in years) | 0-11 | 22 (62.9) | 13 (37.2) | **0.001** |
| | 12-14 | 53 (49.1) | 55 (50.9) | |
| | 15-19 | 92 (33.2) | 185 (66.8) | |
| Gender | Male | 17 (35.4) | 31 (64.6) | 0.880 |
| | Female | 150 (40.3) | 222(59.7) | |
| ART start date | 2016-18 | 134 (37.4) | 224 (62.6) | 0.132 |
| | 2019-20 | 33 (53.2) | 29(46.7) | |
| Baseline CD4 Count (in cell/$mm^3$) | <350 | 90 (40) | 135(60) | 0.669 |
| | >350 | 77 (39.9) | 116 (60.2) | |
| Baseline WHO Clinical Stage | Stage I | 149 (38.9) | 234 (61.1) | 0.435 |
| | Stage II | 4 (80) | 1 (20) | |
| | Stage III | 14 (43.8) | 18 (56.3) | |
| | Stage IV | 0 (0) | 0 (0) | |
| Duration on ART (in months) | <12 | 25 (34.7) | 47 (65.3) | 0.742 |
| | 12-24 | 36 (37.5) | 60 (62.5) | |
| | >24 | 106 (42.1) | 146 (57.9) | |
| ART Regimen | NNRTI | 152 (39.8) | 230 (60.2) | 0.670 |
| | PI | 5 (47.1) | 7 (64.2) | |
| | Not recorded | 10 (38.5) | 16 (61.5) | |

| | |
|---|---|
| ART | Antiretroviral Treatment |
| LTFU | Lost to follow up |
| NNRTI | Non-Nucleoside Reverse Transcriptase Inhibitor |
| PI | Protease Inhibitor |

# CHAPTER 5: DISCUSSION

## 5.1 INTRODUCTION

This chapter discusses factors associated with viral suppression and retention in care rates at selected primary health care facilities in the Mitchells Plain sub-district.

## 5.2 VIRAL SUPPRESSION RATE AMONG ADOLESCENTS ON ART

The current study found that 73.6% of adolescents on ART at selected primary health care facilities in the Mitchells Plain sub-district had viral suppression at 6 months, however it declined over time; this fell short of the UNAIDS' 95% target. These results are similar to the findings of a study conducted in Ehlanzeni district, Mpumalanga, where viral suppression of 74% was reported (Okonji *et al.,* 2021). However, the viral suppression rate of our study was below the one found in similar studies undertaken in Cameroon and Uganda, which was 88.2% (Djiyou *et al.,* 2023). The difference might be due to varying interventions in addressing the needs of adolescents. Countries such as Cameroon have developed adolescent-specific activities such as group counselling and support groups; these are critical in ensuring that adolescents adhere to their treatment.

## 5.3 CHARACTERISTICS OF ADOLESCENTS ON HIV TREATMENT

This study consisted of more female than male adolescents, which is in line with a study conducted in the Eastern Cape that consisted of more female adolescents (Haghighat et al., 2021). Similarly, South Africa's public sector's study had more female adolescent participants (Maskew et al., 2019). The higher proportion of female adolescents in this study is a reflection of the high prevalence of HIV among female adolescents globally (UNAIDS, 2016).

The current study showed that more older adolescents were on ART than younger adolescents (66% vs 25.7%), and this was similar to Van Wyk's discovery in the Western Cape Metropole (Van Wyk *et al.,* 2020). The high proportion of adolescents in this study reflects an increase in the number of older adolescents that are on HIV care and treatment in South Africa (Maskew et al., 2019). Furthermore, the aging population of perinatally infected adolescents and the rising number of older adolescents that seek HIV care have an impact on the increase in older adolescents (Maskew et al., 2019).

Our study revealed that 60% of adolescents were on ART for more than 24 months. The duration of this treatment is slightly below the 71.5% that Kadima et al. (2019) found in their study in Uganda. Further, another study conducted among adolescents and children in Kenya also found a high percentage (91.9%) of adolescents who had remained on ART for more than 24 months (Tsikhutsu *et al.*, 2022).

## 5.4 SOCIODEMOGRAPHIC CHARACTERISTICS AND VIRAL SUPPRESSION

In this study, older adolescents had a higher viral suppression rate than younger adolescents, and this was statistically significant. These findings were congruent with a study conducted among adolescents in the United States (Judd *et al.*, 2017). However, Njuguna *et al.* (2020) found that older adolescents and younger adolescents had poorer viral load outcomes compared to young adults. Young adolescents are more likely to take better care of themselves because they are more experienced in the ART programme.

In this study, female adolescents had a higher viral suppression rate compared to male adolescents, though this was not statistically significant. In addition, researchers found that female adolescents were more likely to attain VLS than male adolescents in a study conducted in Ehlanzeni district, South Africa (Okonji *et al.*, 2021). In contrast, the results of a two-year longitudinal study revealed that there was no difference in viral suppression between male and female adolescents (Mapangisana *et al.*, 2021).

## 5.5 CLINICAL CHARACTERISTICS AND VIRAL SUPPRESSION

There was no statistically significant association between CD4 and viral suppression; however, adolescents with CD4 of less than 350 cell/mm$^3$ achieved higher viral suppression compared to those with CD4 above 350 cell/mm$^3$. Martelli *et al.* (2019); Mwangi and van Wyk (2021) reported that having a CD4 greater than 350 cell/mm$^3$ was significantly associated with viral suppression in studies conducted among adolescents in Tanzania and Kenya, respectively. A study conducted in Cambodia among ALHIV also discovered that a CD4 greater than 672 was associated with high viral suppression (Chhim *et al.*, 2018). Adolescents with higher CD4 are likely to be well; therefore, their positive treatment outcomes motivate them to remain in care.

Adolescents who initiated treatment at WHO clinical stage II had a higher viral suppression than those initiated at WHO clinical stages I and III, although this did not reach statistical

significance. In line with this study, research conducted among children and adolescents found that adolescents who initiated treatment at WHO clinical stage III were less likely to attain viral suppression (Mutagonda *et al.*, 2022). In contrast, a study undertaken in the Cape Town metropolitan area discovered that adolescents who started treatment at higher WHO clinical stages (Stages III & IV) had higher rates of VLS, even though this did not reach a statistical significance (Van Wyk *et al*., 2020). Those that are in higher WHO clinical stages are usually sicker and more likely to adhere to treatment, hence the higher VLS among these patients.

Adolescents who were on treatment for less than 12 months had higher rates of VLS than those who were on treatment for 12 months or more, and this was statistically significant. Congruent with the findings of this study, Fokam *et al.* (2021) revealed that adolescents who were on treatment for a duration of 12 months or less were more likely to attain VLS. Further, Okonji *et al.* (2021) discovered that adolescents who had been on treatment for 18– 24 months were less likely to attain VLS. It is said that patients who are on treatment for longer than 12 months may experience treatment fatigue accompanied by poor adherence to treatment, which may result in unsuppressed VL.

Adolescents who were on the NNRTI regimen had higher viral suppression compared to those who were on the PI regimen, and this reached statistical significance. However, researchers in Zimbabwe and Tanzania discovered that adolescents who were on the NNRTI regimen were more likely to be unsuppressed (Jackson *et al.*, 2022; Mchomvu *et al*., 2022). Another study in Kenya discovered that adolescents on a PI-based regimen were more likely to attain VS compared to those on the NNRTI regimen (Tsikhutsu *et al.*, 2022). The PI regimen is more potent than the NNRTI regimen, which explains why patients on it may have VLS. Further, the PI regimen is usually offered as a second-line treatment to ART patients, who are more likely to adhere to treatment.

### 5.6 RETENTION IN CARE AMONG ADOLESCENTS ON ART

The study reports on low retention in care and associated factors for adolescents aged 12–19 years enrolled on ART in selected primary healthcare facilities in the Mitchells Plain sub-district over a 24-month period. The current study found a RiC rate of only 34% of adolescents in Mitchells Plain sub-district after a 24-month period on ART care, and this reached statistical significance. This is in line with the findings of a study conducted in Cape

Town, which found a RiC of 36% after 24 months of treatment (Van Wyk *et al*., 2020). However, this is low compared to the findings of a systematic review conducted in high- and low-income countries; this review reported remaining in care rates that ranged from 37% to 94.7% (Ritchwood *et al.*, 2020). The reported retention in care rate was significantly lower than the 90.2% reported by Tsikhutsu *et al.* (2022) in their Kenyan study. In the South African context, factors such as overcrowding in clinics, perceived stigma and poor ART readiness have been found to increase the risk of poor retention in care among adolescents on ART (Pry *et al*., 2020). On the other hand, adolescents and youth staff training and implementation of adolescent and youth-friendly services have been shown to promote engagement in care among adolescents (Okonji *et al*., 2020).

## 5.7 SOCIO DEMOGRAPHIC CHARACTERISTICS AND RETENTION IN CARE

In this study, younger adolescents had higher retention in care rates than older adolescents, though this was not statistically significant. Similarly, a study conducted in Cape Town discovered that older adolescents had higher odds of being lost to follow-up compared to younger adolescents (Mulongeni *et al.*, 2019). In contrast, Jerene *et al.* (2019) found that older adolescents had higher retention in care rates than younger adolescents in studies conducted in Kenya and Ethiopia, respectively. Most younger adolescents are still under the care of their parents and are not yet exposed to the challenges faced by older adolescents; hence, they are more likely to remain in care.

This study showed that female adolescents had higher retention in care rates compared to their male counterparts. However, a study in Ethiopia discovered that male adolescents were more likely to remain in care than female adolescents (Jerene *et al.*, 2019). Similarly, studies in Kenya and South Africa found that more males than females remained in care (Okonji *et al.*, 2021; Kose *et al.*, 2022). In South Africa, females in general regularly attend clinics for other services, such as women's reproductive services; hence, it is easier for them to be retained in ART care.

Adolescents who had a CD4 <350 cell/mm$^3$ had high retention in care rates compared to those with CD4 counter that was above 350 cell/mm$^3$ and this was not statistically significant. In line with these findings, a study conducted in South Africa associated an increase in CD4 with lost to follow-up (Nyakato *et al.*, 2022). However, this finding is in contrast to the results of a study conducted by Okonji *et al.* (2021) in South Africa, which discovered that

adolescents with CD4 count above 350 cell/mm$^3$ had high retention in care rates compared to those with CD4 count less than 350 cell/mm$^3$. Patients with high CD4 count are usually well and stable, which may lead to poorer compliance with treatment compared to those with a lower CD4 count.

Adolescents who were classified as baseline WHO clinical stage II had higher retention in care rates compared to those on baseline WHO clinical stages I and III, and this did not reach statistical significance. This finding was congruent with the results of a study conducted in Cape Town, which also reported high RiC rates among adolescents classified as baseline WHO clinical stage II (Van Wyk *et al.*, 2020). Similarly, a study conducted in Kenya reported higher retention in care rates among adolescents classified as baseline WHO stage II compared to those classified as baseline WHO stage III or I (Kose *et al.*, 2022). Adolescents who are stable and healthy while on treatment are likely to remain on ART care, as they are motivated by their well-being and quality of life.

Adolescents who were on ART for more than 24 months had higher retention in care rates than those who were on ART for fewer than 24 months and this was not statistically significant. In line with the findings of this study, research conducted in South Africa and Nigeria found higher retention in care rates for adolescents who were on ART for more than 24 months and longer (Zanoni *et al.*, 2017; Meloni *et al.*, 2020). Experience on ART may be the reason that adolescents on treatment for more than 24 months show higher RiC rates. Adolescents on ART for longer periods of time are exposed to multiple sessions of adherence counselling, hence the ability to remain on treatment.



Adolescents who were on a PI-based regimen had higher retention in care rates compared to those who were on a NNRTI-based regimen; however, this difference was not statistically significant. In contrast, studies conducted in Thailand and Nigeria among adolescents discovered that adolescents who were on a PI-based regimen were associated with an increased risk of LTFU (Teeraananchai *et al.*, 2019; Meloni *et al.*, 2020). Another study undertaken in Nigeria also found that adolescents who were on PI-based regimen were significantly more likely to be LTFU compared to those who were on a 1$^{st}$ line regimen (Aliyu *et al.*, 2019). Patients on a PI-based regimen may experience worse treatment outcomes due to treatment failure; this might be the reason for their inability to remain on care.

# CHAPTER 6: RECOMMENDATIONS AND CONCLUSION

## 6.1 RECOMMENDATIONS

Interventions that seek to improve retention in care and VLS should be implemented. Moreover, policies must be put in place to optimise adherence and VLS among adolescents.

- Barriers to retention in care should be identified and addressed by healthcare officials.
- Further studies that use qualitative or mixed methods could be conducted to identify other predictors of retention in care and VLS, such as cultural, economic, religious and social factors.
- Adherence to ART is critical for VLS; it should be monitored at every visit to identify and address barriers to adherence for adolescents on ART.
- Facility staff should be trained on interventions that respond to the unique needs of adolescent patients. This training should be based on tailor-made interventions that are specific to the needs of adolescents.

## 6.2 CONCLUSION

This study found retention in care rates of adolescents on ART to be 34% over a period of 24 months and VLS rate was found to be 73.6%. This poor retention in care rate and VLS rate, which is similar to global trends, requires a programmatic focus on this vulnerable population group with tailor-made interventions in order to avoid the negative individual and public impact of these poor outcomes.

Some of the objectives of this study were to describe the baseline and clinical characteristics and to analyse these characteristics to determine risk factors for retention in care and VLS of adolescents on ART. Retention in care was found to have a relevant and significant association with current age. Significant associations were found between VLS and the following characteristics: current age and duration on ART. These associations may be considered in the process of adolescent ART programme design and any tailored interventions.

Our study shows that attaining the last 95 of the UNAIDS' 95-95-95 goal is still a long way off for adolescents on ART and retention in care is poor. In order to address this, public health officials must develop adolescent-specific interventions that will respond to the needs of adolescents.

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# APPENDICES

## APPENDIX 1: ETHICS CLEARANCE

29 November 2021

Mr A Meyile
School of Public Health
**Faculty of Community and Health Sciences**

**Ethics Reference Number:** BM21/10/5

**Project Title:** Assessment of treatment outcomes for adolescents on antiretroviral treatment at Mzamomhle clinic in the Cape Metropole, South Africa.

**Approval Period:** **19 November 2021 – 19 November 2024**

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project and the requested amendment to the project.

Any further amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

**Please remember to submit a progress report annually by 30 November for the duration of the project.**

For permission to conduct research using student and/or staff data or to distribute research surveys/questionnaires please apply via:
https://sites.google.com/uwc.ac.za/permissionresearch/home

*The permission letter must then be submitted to BMREC for record keeping purposes.*

The Committee must be informed of any serious adverse event and/or termination of the study.

*Ms Patricia Josias*
*Research Ethics Committee Officer*
*University of the Western Cape*

CITY OF CAPE TOWN
ISIXEKO SASEKAPA
STAD KAAPSTAD

CITY HEALTH

Dr Natacha Berkowitz
Epidemiologist: City Health

T: 021 400 6864 F: 021 421 4894
E: Natacha.Berkowitz@capetown.gov.za

13-04-2022

**RE: Assessment of treatment outcomes for adolescents on antiretroviral therapy at a public primary healthcare clinic in the Cape Metropole, South Africa. (9486)**

Dear Abongile Meyile

Your research request has been amended as per your request. Please refer to the subsequent pages for the approval of additional facilities or focus areas requested. Contact persons for each area requested:

**Mitchells Plain & Southern:** Mzamomhle Clinic, Crossroads 1 Clinic, Eastridge clinic, Lentegeur clinic, Satellite Mandalay, Phumlani clinic, Rocklands clinics, Tafelsig CDC, Weltevreden Valley, Westridge clinic

Contact Person: Mrs Soraya Elloker (Area South Manager)

Tel/Cell: (021) 400 3983/084 222 1478

Email: Soraya.elloker@capetown.gov.za

Please note the following:

1. All individual patient information obtained must be kept confidential.
2. Access to the clinic and its patients must be arranged with the relevant Manager such that normal activities are not disrupted.
3. A copy of the final report must be uploaded to https://web1.capetown.gov.za/web1/mars/ProjectClosure/UploadReport/0/9486 MARS within 6 months of its completion and feedback must also be given to the clinics involved.
4. Your project has been given an ID Number (9486). Please use this in any future correspondence with us.
5. No monetary incentives to be paid to clients on the City Health premises
6. If this research gives rise to a publication , please submit a draft before publication for City Health comment and include a disclaimer in the publication that "the research findings and recommendations do not represent an official view of the City of Cape Town "
7. As the research is approved as per submitted protocol, any changes to the protocol need to be submitted and approved by City Health prior to implementation.
8. We are currently not approving research for joint authority facilities (Dirkie Uys, Durbanville, Heideveld, Kasselsvlei, Nolungile, Nyanga, Parow, Ravensmead, Scottsdene) as they are in the process of being consolidated into one authority.

Thank you for your co-operation and please contact me if you require any further information or assistance.

Kind Regards

Dr Natacha Berkowitz Epidemiologist: City Health