

https://dspace.org/

Sex differences in treatment outcomes among adolescents and young adults initiated on ART in Johannesburg, 2016-2017

Kwinda, Zwannda

2025

University of the Witwatersrand, Johannesburg

https://hdl.handle.net/10539/48041

Kwinda, Zwannda . (2025). Sex differences in treatment outcomes among adolescents and young adults initiated on ART in Johannesburg, 2016-2017 [Master`s dissertation, University of the Witwatersrand, Johannesburg]. WIReDSpace. https://hdl.handle.net/10539/48041

Downloaded from a DSpace repository. https://dspace.org/

UNIVERSITY OF THE WITWATERSRAND



Sex differences in treatment outcomes among adolescents and young adults initiated on ART in Johannesburg, 2016-2017

NAME: KWINDA ZWANNDA

STUDENT NUMBER: 786532

A research report submitted to the Faculty of Health Sciences, University of Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree of Master of Science in Epidemiology and Biostatistics

May 2025

Supervisor: Ms Idah Mokhele, Senior Researcher, HE^{2}RO

Co-supervisor: Dr Ntombizodwa Ndlovu, Lecturer, Wits School of Public Health

DECLARATION

I, Zwannda Kwinda, declare that this research project report, which I hereby submit for the degree of Master of Science in Epidemiology and Biostatistics in the School of Public Health, at the University of the Witwatersrand, is my work and has not been submitted for any qualification at this or any other institution.

Signature: Z.R. Kwinda Date: 30 May 2025

DEDICATION

This research report is dedicated to my daughter, Mulamuleli, for being the greatest inspiration for me to work harder, my parents for always supporting and motivating me to do better, and to God for His guidance and abundant love throughout my journey of completing this project.

ABSTRACT

Background

Despite the scale-up of antiretroviral therapy (ART) in South Africa, there is limited evidence on how this expansion has benefited male and female adolescents and young adults aged 15 to 24 years (AYAs) at the beginning of the universal test and treat (UTT) era in 2016. This study aims to evaluate sex-specific drivers of HIV treatment outcomes among AYAs 12 months after ART initiation at the start of the UTT era.

Methodology

A retrospective cohort study was conducted using routine patients' data from the Therapy Edge database. Descriptive statistics were performed to compare baseline socio-demographic and clinical characteristics between male and female AYAs. Fisher's exact test was conducted to assess the association between the baseline characteristics and the study outcome variables: viral load (VL) suppression and retention in care. A generalized mixed-effects model (GLMM) was used to identify sex-specific drivers of ART outcomes.

Results

The analysis revealed a higher VL suppression rate among females (74.5%) than males (60.0%). Along with an impressive retention to care rate of 99.1%, there was only one female participant who was deceased 12 months post-ART initiation. Baseline education level was identified as a predictor of VL suppression for both male (RR:1.43, CI:1.07-1.91, P=0.02) and female (RR:0.72, CI:0.61-0.86, p<0.01) AYAs. Additionally, the ART regimen was a predictor specifically for females (aRR:0.01, CI:0.10 - 0.20, p<0.01).

Conclusion

The results highlighted sex disparities in VL suppression among AYAs and demonstrated strong retention in care at the beginning of the UTT era. The findings indicate that baseline education level, and ART regimen should be considered for improved HIV treatment outcomes. Future research should explore sex-inclusive interventions to support sustained VL suppression AYAs.

ACKNOWLEDGMENTS

Firstly, I would like to thank my supervisors, Ms. Idah Mokhele and Dr. Zodwa Ndlovu, for their guidance and support throughout this research, from protocol development to the completion of the research report. I appreciate their patience, and I will forever be indebted to making them proud.

I would like to thank all the lecturers and staff of the School of Public Health at the University of the Witwatersrand for their valuable contribution and willingness to assist in completing this qualification.

I am grateful to the National Research Fund (NRF) for awarding me a scholarship that provided financial support to help me finish my studies.

To my classmates who became friends, Idah, Marceline, Innocent, Themba and Zisiwe. Thank you for your support, encouragement, and always motivating me to work hard through my study.

Table of Contents

Declaration I
Dedication II
Abstract III
Acknowledgments IV
Table of Contents V
List of figures VII
List of tables VIII
Abbreviations IX
Chapter 1 – Introduction 1
1.1. Background 1
1.2. Problem statement 2
1.3. Justification 3
1.4. Aims and objectives 3
1.4.1. Research Question 3
1.4.2. Aim 3
1.4.3. Objectives 3
Chapter 2 – Literature review 5
2.1. Epidemiology of HIV among Adolescents and Young Adults 5
2.2. The Universal Test and Treat strategy and ART outcomes 6
2.3. Predictors of Treatment Outcomes 7
Chapter 3 - Methods 10
3.1. Study setting and design 10
3.1.1. Study design 10
3.1.2 Study population and setting 10
3.2. Sampling 11
3.2.1. Inclusion criteria 11
3.2.2. Exclusion criteria 11
3.3. Data management 11
3.3.1. Data extraction and cleaning 11
3.3.2. Variables 12
3.3.2.3. Confounders 14
3.4. Data analysis 14
3.4.1. Descriptive analysis 14
3.4.2. Association of socio-demographic and clinical characteristics with treatment outcomes 12 months after ART initiation, stratified by sex 14
3.4.3. Baseline explanatory variables that are predictors for treatment outcomes 15

3.5. Ethical considerations 16
Chapter 4 - Results 17
4.1. Descriptive analysis 17
4.1.1. Study population 17
4.1.2. Baseline socio-demographic characteristics 19
4.1.3. Baseline clinical characteristics 19
4.2. Association of socio-demographic and clinical characteristics with treatment outcomes 12 months after ART initiation, stratified by sex 21
4.2.1. Retention in care 21
4.2.2. VL suppression 22
4.2.3. Baseline explanatory variables that are predictors for treatment outcomes 24
Chapter 5 - Discussion 28
5.1. Introduction 28
5.1.1. Description of the Study Population ..... **Error! Bookmark not defined.**
5.1.2. Factors associated with retention in care at 12 Months after ART initiation 29
5.1.3. Drivers for VL Suppression and ART outcomes Differences Between Males and Females 30
5.2. Limitations and strengths 32
5.2.1. Strengths 32
5.2.2. Limitations 33
Chapter 6 - Conclusions and recommendations 35
References 36
Appendix 1: Assessment of missing data using Little's MCAR test 42
Appendix 2: Variance inflation factor (VIF) to assess multicollinearity 44
Appendix 1: Ethics clearance certificate 45
Appendix 2: Signed plagiarism declaration 46

LIST OF FIGURES

Figure 4.1: A flow chart for the selection of patients eligible for the study between 01 September 2016 and 30 September 2017 (N=117) 18

LIST OF TABLES

Table 3.1: A list of baseline socio-demographic and clinical variables used in this study 13

Table 4.2: Association of socio-demographic and clinical characteristics with VL suppression 12 months after ART initiation, stratified by sex, for study participants attending Themba Lethu clinic, 2016-2017 (n=71) 23

Table 4.3: Univariate analysis of socio-demographic and clinical factors associated with VL suppression 12 months after ART initiation for study participants in attending Themba Lethu clinic, (2016-2017; n=71) 25

Table 4.4: Multivariables (GLMM) results showing socio-demographic and clinical factors associated with VL suppression in patients attending Themba Lethu clinic, (2016-2017; n=71) 26

ABBREVIATIONS

ABC	Abacavir
ABYM	Adolescent Boys and Young Men
AGYW	Adolescent girls and young women
AYAs	Adolescents and young adults aged 15-24 years
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine transaminase
ART	Antiretroviral therapy
ARV	Antiretroviral
AST	Aspartate transaminase
BMI	Body mass index
DREAMS	Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe
EFV	Efavirenz
FTC	Emtricitabine
Hgb	Haemoglobin
HIV	Human Immunodeficiency Virus
HPTN	HIV Prevention Trials Network
HTS	HIV Testing Services
HIVSS	HIV Self-Screening
d4T	Lamuvudine
3TC	Lamivudine
LFTU	Lost to follow-up
NVP	Nevirapine,
PLHIV	People living with HIV
SD	Standard deviation
SSA	Sub-Saharan African
TDF	Tenofovir Diproxil Fumarate
UNAIDS	Joint United Nations Programme on HIV and AIDS
UTT	Universal Test and Treat
VL	Viral load
WHO	World Health Organization
YOLO	You Only Live Once

CHAPTER 1 – INTRODUCTION

1.1. Background

Human Immunodeficiency Virus (HIV) remains a significant global health challenge, with an estimated 39 million people living with HIV (PLHIV) worldwide[1]. In 2022 alone, approximately 1.3 million new HIV cases were reported[2]. South Africa bears the highest burden of HIV, with 8.2 million PLHIV and 210,000 new HIV cases were recorded in 2021[1,3]. The country has implemented the world's largest antiretroviral therapy (ART) program, with over 5.5 million people initiated on ART, a testament to the progress that can be achieved with concerted efforts.[1,3]. Notably, since the launch of the South African National ART Program in 2003, the number of HIV/AIDS-related deaths has declined by 58% between 2007 and 2018[4]. This shift has transformed HIV from a fatal illness into a manageable chronic disease, significantly extending the lifespan of PLHIV[1,3,5].

In 2015, South Africa adopted the United Nations Programme on HIV/AIDS (UNAIDS) 90-90-9 targets, which were later changed to 95-95-95 in 2020. The 95-95-95 target aims to diagnose 95% of all PLHIV, ensure that 95% of diagnosed individuals begin sustained ART, and achieve VL suppression in 95% of those undergoing treatment by 2025[6]. This is to assist the country in reaching the Sustainable Development Goal (SDG) of ending AIDS by 2030[6]. To complement this, South Africa implemented the World Health Organization (WHO) recommended Universal Test and Treat (UTT) strategy to accelerate progress toward these targets. The UTT strategy is aimed at ensuring that all PLHIV are offered ART on the same day of diagnosis, regardless of CD4 count, to achieve viral suppression and improve treatment outcomes[7].

The introduction of UTT assisted the country in reaching the first 95 in 2023[8]. Despite UTT's success in enhancing early diagnosis, linkage to care, and improving ART outcomes, disparities in ART outcomes across populations persist[9]. Adolescents and young adults (AYAs) aged 15 to 24 years still face treatment-related challenges, including poor retention in care due to loss to follow-up (LTFU)[10,11]. This occurs when a patient misses a scheduled clinic visit or ART refill and fails to return within 60 or 90 days[12]. A study conducted in eight clinics in KwaZulu-Natal, South Africa, reported that AYAs had a 1.65 times higher risk of attrition compared to

the older age group[13]. Factors contributing to the sex disparities in ART outcomes include the effectiveness of ART regimens and the social, demographic, and clinical characteristics of patients, such as age, sex, education, income, geographical location, CD4 count, and BMI [14,15].

It is essential to note that the UTT strategy is a vital component of case finding, linkage to care, and improved ART outcomes. However, sex-related barriers may contribute to disparities in ART outcomes between adolescent girls and young women aged 15 to 24 years (AGYW) and adolescent boys and young men aged 15 to 24 years (ABYM). Given that AGYW have the highest risk of HIV incidence and are three times more likely to acquire HIV than their male counterparts[16,17]. Understanding sex differences in ART outcomes at the start of the UTT era, is important for determining whether both male and female AYAs benefited from the UTT. Additionally, this will enable the tailoring of interventions aimed at improving ART outcomes for this vulnerable population, thereby helping the country reach the 95-95-95 target.

1.2. Problem statement

South Africa remains off track in achieving the UNAIDS 95-95-95 targets to end AIDS by 2030, with AYAs, and children continuing to lag behind[1]. While significant efforts have been invested in expanding case finding, treatment, and care services, AYAs show poorer retention in care and lower rates of viral load suppression[1,18]. Notably, ART coverage among AGYW remains suboptimal, with only 56.9% of AGYW receiving ART in 2021, compared to 70% coverage in the general population[19]. Although AYAs account for 6.8% of the total population of PLHIV, they represent 80% of the annual HIV incidence, which impacts the country's achievement of the 95-95-95 target[1,3]. Despite the introduction of various strategies aimed at improving ART outcomes, there remains a critical gap in understanding whether the challenges faced by AYAs are similar across sexes, and whether these interventions sufficiently account for sex-specific differences linked to social, demographic, and clinical characteristics.

To implement responsive and equitable interventions, it is necessary to revisit the early implementation of the UTT strategy and assess how AYAs, especially AGYWs, performed during this critical period. Without a clear understanding of the initial barriers and accelerators

to treatment retention and viral suppression, efforts to strengthen ART programs risk overlooking this vulnerable population and sex-specific needs.

1.3. Justification

This study aimed to examine the association between sex and treatment outcomes among AYAs and explore the key factors contributing to the relationship at the start of UTT era. By identifying the drivers of sex-specific disparities in ART retention and viral suppression, the findings provide insights into potential barriers and facilitators of successful treatment outcomes during the early implementation of the UTT era. Understanding the factors that contributed to positive or suboptimal outcomes at the onset of UTT is essential as the country approaches the final year of achieving the 95-95-95 targets. These insights will help guide targeted interventions to optimize ART programs and ensure that both AGYW and ABYM receive effective HIV care. The study's findings will contribute to strengthening HIV treatment strategies and informing policies aimed at improving retention and viral suppression for AYAs in high-burden settings, thereby supporting efforts of ending AIDS by 2030.

1.4. Aims and objectives

1.4.1. Research Question

Do HIV treatment outcomes differ between male and female AYAs (AGYW and ABYM), who initiated ART at the onset of the UTT era in Johannesburg, South Africa, 12 months after treatment initiation?

1.4.2. Aim

To determine sex differences in HIV treatment outcomes defined as VL retention in care and VL suppression among AYAs who were initiated on ART at the onset of the UTT era in Johannesburg, South Africa, 2016-2017.

1.4.3. Objectives

1. To describe the baseline socio-demographic and clinical characteristics of AGYWs and ABYMs 12 months after ART initiation in Johannesburg, between September 1, 2016, and September 30, 2017.
2. To compare 12-month treatment outcomes (i.e., retention in care and VL suppression) between AGYWs and ABYMs 12 months after ART initiation in Johannesburg between September 1, 2016, and September 30, 2017.
3. To assess predictors of 12-month retention in care and VL suppression for AGYWs and ABYMs 12 months after ART initiation in Johannesburg between September 1, 2016, and September 30, 2017.

CHAPTER 2 – LITERATURE REVIEW

2.1. Epidemiology of HIV among Adolescents and Young Adults

South Africa has the largest ART program globally, which contributed to a 51% reduction in HIV incidence in the general population between 2017 and 2019[19,20]. However, AYAs remain at high risk, with an HIV incidence of 0.7% compared to 0.6% in the general population[21]. Among AGYW, the incidence is even higher, at 1.2%, nearly four times that of their male counterparts (0.3%) [19,20,22].

Despite significant progress in HIV prevention and treatment, AYAs in South Africa continue to experience disproportionately high HIV incidence and suboptimal ART outcomes[22–24]. In 2020, more than 1,000 new HIV incidence occurred among AGYW each week, exceeding the National Strategic Plan (NSP) target of fewer than 800 per week[22]. The NSP is a multi-year policy and implementation framework that guides the country's response to HIV, tuberculosis (TB), and sexually transmitted infections (STIs)[9]. The NSP and studies report that factors such as age-disparate relationships, sex-based violence, and socio-economic disparities contribute to the sustained high HIV burden among AGYW[9,16,25].

Multiple studies have identified key drivers of HIV transmission among AGYW, including early sexual debut, multiple sexual partners, transactional sex, and limited access to prevention services[26–28]. In response, South Africa has implemented several HIV prevention programs, including the Determined, Resilient, Empowered, AIDS-Free, Mentored, and Safe (DREAMS) initiative, which integrates biomedical, behavioural, and socio-economic interventions[29]. However, despite these comprehensive prevention efforts, AGYW remain at high risk. A study conducted in KwaZulu-Natal reported an HIV incidence of 4.1% among AGYW exposed to the DREAMS program, compared to 1.5% in the general population[30].

This ongoing high risk of HIV among AGYW highlights the need to examine ART outcomes in this high-burden context. While significant strides have been made in increasing ART

coverage, the effectiveness of these interventions for AGYW and ABYM remains insufficiently explored, particularly at the onset of UTT era. The UTT strategy, launched in South Africa in 2016, aims to expand access to ART, improve retention in care, and achieve VL suppression across all populations[31]. While evidence suggests that UTT has led to increased ART coverage[8,9,32], there is limited research assessing whether this expansion has improved treatment outcomes among AGYW, particularly compared to ABYM. Understanding the association between sex and ART outcomes in HIV-burdened settings is critical for optimizing intervention strategies and ensuring equitable treatment success.

2.2. The Universal Test and Treat strategy and ART outcomes

The UTT strategy, a significant development in South Africa's public health landscape in 2016, eliminated CD4 count thresholds for treatment initiation[31]. Thereby, expanding ART access to all PLHIV regardless of clinical stage[7]. A study reported that early ART initiation under UTT significantly reduced HIV transmission, as demonstrated in the HPTN 052 trial, which reported a 96% reduction in transmission among sero-discordant couples when ART was initiated early[33].

A study conducted in Gauteng reported that only 36.4 % of the population who were aware of their HIV status were on ART between 2010 and 2012[14]. However, most PLHIV were not treated early, increasing their risk of morbidity and mortality[34]. Before the implementation of the UTT strategy, AYAs were less likely to qualify for ART initiation due to the National HIV treatment guidelines which required a CD4 count below 500 cells/mm^3 for eligibility[35]. Newly infected, sexually active AYAs are often asymptomatic with higher CD4 counts at diagnosis, a phase known as clinical latency, during which the virus replicates without showing clinical signs[36].

While the UTT strategy has increased ART coverage nationwide, research indicates significant disparities in retention and viral suppression rates between AYAs and the older populations[10]. Studies suggest that while UTT has improved ART access, young people, particularly AGYW, continue to face significant barriers to effective care[37–39]. For example, before UTT

implementation, only 36.4% of HIV-positive AYAs in Gauteng were on ART, highlighting the structural challenges in accessing treatment[26]. Following the introduction of UTT, ART coverage improved, but retention challenges, particularly among AYAs, persisted[38,39].

Retention in care remains a crucial factor for achieving and maintaining sustained viral suppression and preventing drug resistance. A study at the Themba Lethu Clinic in Johannesburg demonstrated that AYAs retained in care were more likely to achieve viral suppression and immune restoration than those who were LTFU[38]. However, a multi-site study in KwaZulu-Natal revealed that AYAs had a 1.65 times higher risk of attrition compared to older age groups, with stigma, long clinic waiting times, and lack of youth-friendly services identified as key barriers[18].

The implementation of UTT has had a transformative effect on ART coverage. Yet, the continued challenges in retention and viral suppression for AYAs necessitate a more in-depth understanding of the barriers specific to this age group.

2.3. Predictors of Treatment Outcomes

The association between sex and ART outcomes is a critical yet underexplored area of research in the UTT era. Emerging studies suggest that biological, social, and structural factors contribute to disparities in ART outcomes between AGYW and ABYM[40,41]. Although some studies have shown that AGYW may have better ART adherence compared to ABYM, they still face significant socio-economic and structural barriers that impact their treatment success[38,39].

Studies indicate that AGYW tend to have better retention rates compared to ABYM, though both groups face challenges such as stigma, negative healthcare provider attitudes, and socio-economic hardships[10,38]. Sex-specific barriers to ART adherence, including the fear of disclosure and intimate partner violence, are critical in understanding ART outcomes in this population[28,37].

Socioeconomic factors such as low levels of education, unemployment, and geographic location profoundly impact ART adherence and retention among AYAs[42]. Evidence indicates that individuals with primary education or no education often display reduced health literacy, which can lead to misunderstanding about HIV and ART[42]. A lack of understanding of the importance of ART adherence and management can ultimately hinder treatment effectiveness[10].

Related studies reported that unemployed patients are more likely to struggle with consistent ART adherence due to financial difficulties. These challenges included the cost of transportation to healthcare facilities and purchasing nutritious food, vital for maintaining adherence to ART regimens and good health outcomes[43]. While patients in urban areas have access to health care facilities with advanced resources, the population in rural areas often faces barriers associated with transportation and access to adequate healthcare services[44]. This is particularly pronounced among AGYW, who may also have limited autonomy in accessing healthcare services without the support of caregivers or partners[45].

AYAs, especially AGYW, often report that the healthcare system does not provide youth-friendly services, which include long waiting times, a lack of privacy, and healthcare providers who are not adequately trained to handle adolescent-specific issues[46]. These factors exacerbate the challenge of improving retention and viral suppression rates in this vulnerable group. Furthermore, Adolescents transitioning to adult HIV care face disruptions in treatment due to several factors, including inadequate status disclosure, fear of navigating the healthcare facility, limited self-advocacy for adherence, and poor health literacy[23,47]. These disruptions often result in a loss of continuity in treatment, leading to higher rates of attrition and treatment failure[23].

Despite the expansion of ART access under the UTT strategy, evidence regarding its impact on ART outcomes among AGYW and ABYM remains limited. This is a critical gap in our understanding, as much of the existing literature has focused on overall ART uptake rather than sex-specific differences in treatment success[48]. Our study aims to fill this gap by analyzing the association between sex and ART outcomes, as well as identifying the factors that contribute

to these differences in a high HIV-burden setting. Understanding the drivers of sex-specific differences in ART outcomes will provide valuable insights into developing targeted interventions to improve ART retention and viral suppression among AYAs. The findings of this research have the potential to significantly impact the field by contributing to the refinement of existing intervention strategies and optimizing care models for AGYW and ABYM. This potential impact should instill a sense of hope and anticipation in the audience, as it ultimately supports the achievement of South Africa's goals for controlling the HIV epidemic.

CHAPTER 3 - METHODS

3.1. Study setting and design

3.1.1. Study design

The study employed a retrospective cohort design, utilizing routine secondary data from the medical records of patients who initiated ART between 01 September 2016 and 30 September 2017 at Themba Lethu Clinic, an HIV clinic situated within a tertiary hospital in Johannesburg, South Africa.

3.1.2 Study population and setting

The study population included AYAs living with HIV who had initiated ART between 1 September 2016 and 30 September 2017 at Themba Lethu Clinic in Johannesburg, Gauteng province, South Africa. Data from 2016 to 2017 remain valuable in HIV research as a historical baseline for UTT implementation, enabling the assessment of progress and shifts in key indicators such as viral suppression, and retention in care. While HIV treatment and prevention evolve quickly, comparing these older data with current figures allows us to evaluate the impact of recent interventions, detect persistent disparities in vulnerable populations, and assess whether prior barriers still affect ART outcomes.

Themba Lethu Clinic is an urban government clinic located inside a provincial hospital called Helen Joseph in the Johannesburg Metropolitan Health District in the Gauteng Province, South Africa[49,50]. Gauteng has the largest population in South Africa and the highest number of local and international migrants compared to other provinces.[3]. In 2016, most (37%) of Gauteng residents lived in the City of Johannesburg, and 14% of the city's population were adolescents and young adults aged 15-24[3]. In 2017, 81% of people knew their HIV status, 67% initiated ART, and 88% were virally suppressed among the population of the City of Johannesburg[16].

Themba Lethu Clinic was initially established to provide ART to PLHIV as a valuable resource for research on ART roll-out, which is necessary for a resource-limited setting such as South Africa 45[49]. The clinic follows the South African National Department of Health's policies and Guidelines for providing HIV treatment and care, which were utilized during the study period,

between September 1, 2016, and September 2017. Patients' medical records at this clinic were maintained electronically in a database system called Therapy-Edge-HIVTM. The electronic medical record system is an electronic database that captures all routinely collected patient information, including demographic and clinical characteristics, clinic visit details, ART regimen, laboratory test results, and co-infections. Data from the Therapy-Edge-HIVTM system has been instrumental in-patient management and has significantly contributed to epidemiological and health economics evidence aimed at optimizing HIV care and treatment outcomes.

3.2. Sampling

The study initially planned to include all AYAs from the Therapy-Edge-HIVTM database who initiated ART between 01 September 2016 and 30 September 2017 at Themba Lethu Clinic. While the intention was to include the whole eligible cohort to minimize selection bias and allow comprehensive analysis, many patients were excluded from the final analysis due to missing outcome data. As a result, the final sample was a subset of the initial eligible cohort which might have affected the generalizability and introduced selection bias. These limitations were considered in the analysis and interpretation of the results.

3.2.1. Inclusion criteria

The study included AYAs who had never received ART, were not pregnant at the time of ART initiation, started ART between 1 September 2016 and 30 September 2017, and had information for their 12-month visit if retained in care

3.2.2. Exclusion criteria

Patients excluded from the study were those transferred to the Themba Lethu clinic from other healthcare facilities and those who were initiated on ART at the Themba Lethu clinic outside the study period. Eligible patients with missing information on ART initiation date and sex were also excluded.

3.3. Data management

3.3.1. Data extraction and cleaning

Data was obtained from Therapy-Edge-HIV™ database in password protected comma-separated values (CVS) file. The data abstraction process began with submitting a data request to the gatekeeper of the Therapy-Edge-HIV™ database. The gatekeeper extracted the required data elements listed in table 3.1. Patients' identifiers such as names, identity number and home address were removed to ensure anonymization. Extracted data were saved as a password protected CVS file. The data was exported, and all data cleaning and statistical analyses were conducted using STATA 15TM (STATA-Corp, 2017, College Station, TX, USA).

As shown in appendix 1, the dataset was assessed for completeness, and Little's Missing Completely at Random (MCAR) test was performed to evaluate the nature of the missing values. The null hypothesis was not rejected with a p-value greater than 0.05 (p-value = 0.11), indicating that the missing data were missing completely at random (MCAR). The missingness was unrelated to any patterns in the data and was likely random; this could be due challenges with clinic scheduling, inconsistent documentation, and lack of adherence to scheduled VL monitoring visits. Observations with excessive missing values (greater than 50%) were excluded from the analysis. Duplicate entries were identified and removed to prevent overrepresentation. Inconsistencies in variable formats, such as date and categorical entries, were standardized to maintain uniformity. During the analysis, outliers were excluded. Explanatory and outcome variables were coded into fewer categories for better comparability, as shown in Table 3.1.

3.3.2. Variables

3.3.2.1. Outcome variables

This retrospective cohort study assessed treatment outcomes 12 months after ART initiation, regardless of whether the 12-month visit occurred within the period from 1 September 2016 to 30 September 2017, as the analysis considered a 12-month follow-up window from the date of ART initiation

1. VL suppression was the outcome variable in the study: A VL suppression cut-off value recommended by the South African National Department of Health of less than 50 copies/ml, also referred to as undetectable VL, was used in the study[12]. VL test results

dated nine to 15 months after ART initiation, considered as 12-month VL, were included in the study.

2. Retention in care: Defined as being alive and in care versus no longer in care (i.e., lost to follow-up (LTFU), deceased, or transferred out). LTFU was defined as having missed a clinic appointment in the form of a clinic assessment, ART pick-up, or counsellor visit by 90 days or more after the scheduled date.

3.3.2.2. Explanatory variables

During analysis, socio-demographic and clinical variables were transformed into categorical variables as shown in Table 3.1.

Table 3.1: A list of baseline socio-demographic and clinical variables used in this study

Variables		Categories
Socio-demographic variables	Age groups (years)	1=15-18 (in secondary school), 2=19-21 (in further training institutions), 3=22-24 (employed or Job seeking)
	Sex	0=Female, 1=Male
	Ethnicity	0=Black African, 1=Other
	Nationality	1=South African, 2=Non-South African
	Marital Status	0=Not married, 1=married
	Education Level	1=Primary school or less, 2=Secondary school, 3=Post-matric
	Employment status	0=Employed, 1=Unemployed
Clinical variables	Baseline WHO staging:	1= I-II (asymptomatic to mild symptoms) 2= III-IV (advanced to severe symptoms)
	Baseline Body mass index (BMI) *(kg/m^2)*	0= under-weight (<18.5 kg/m^2) 1= normal (18.5 to 25.0 kg/m^2) 2= over-weight (25.0 to 30.0 kg/m^2) 3= obese (>30 kg/m^2)
	Baseline CD4 *(cells/mm^3)*	1 ≤ 250.0 2 = 250.0-349.9 3 = 350.0-499.9 4 ≥ 500.0
	Baseline Haemoglobin (Hgb) *(g/dL)*	1= <8.0 2= ≥8.0
	Baseline Aspartate transaminase (AST) *(IU/L)*	1= < 40.0 2= ≥ 40.0
	Baseline Alanine aminotransferase (ALT) *(IU/L)*	1= < 40 2= ≥ 40.0
	Baseline Lactate levels *(mmol/L)*	1=0.0 - 2.4 2= 2.5 – 4.0 3=≥4.0

	ART regimen	1 = first-line ART regimens for adolescents and adults in 2016 and 2017 [Tenofovir Diproxil Fumarate (TDF) + Lamivudine/ Emtricitabine (3TC/FTC) + Efavirenz/Nevirapine (EFV/NVP)] 2= Other (include: d4T+3TC+EFV/LPVr, 3TC+LPVr+ABC, AZT+3TC+EFV, 3TC+RTV/TDF+ABC+ATV, AZT+3TC+LPVr, AZT+3TC+RTV+ATV, RTV+TDF+ATV+EMT, or LPVr+TDF+EMT)

3.3.2.3. Confounders

Baseline variables considered as confounders in this study included: I. HIV WHO staging: This variable determines the patient's prognosis and affects treatment options[7,35].

I. I.CD4 count and age: They are predictors of disease progression and treatment response.
II. Education level: This variable is related to understanding treatment instructions, which impact adherence.
III. Marital status: This serves as a proxy for social support, which can impact treatment adherence.

3.4. Data analysis

3.4.1. Descriptive analysis

Patients' clinical and socio-demographic characteristics at baseline, i.e., at ART initiation, were stratified by sex to examine the distributional differences in these characteristics. Continuous variables were summarized using means and standard deviation (SD), while frequencies and proportions were used to summarize categorical variables. Marital status, AST levels, and WHO HIV stage were not recorded for over 50% of our study participants. Consequently, these variables were excluded from the final analysis.

3.4.2. Association of socio-demographic and clinical characteristics with treatment outcomes 12 months after ART initiation, stratified by sex

Fisher's Exact test was conducted to assess the association between sex and VL suppression for each explanatory variable, 12 months after ART initiation. Fisher's exact test was used because the observed frequencies in most contingency table cells were less than five. The comparison was not made for the retention in care outcome variable as all except one patient were retained; therefore, the data were skewed. The characteristics of the one patient not retained 12 months after ART initiation are described in the text.

3.4.3. Baseline explanatory variables that are predictors for treatment outcomes

A generalized linear mixed model (GLMM) was used to evaluate the effects of clinical and socio-demographic variables on VL suppression for each sex. The GLMM was chosen because it accommodates non-normal outcome distributions and accounts for correlations within groups and variability across groups[51]. The validity of the GLMM relies on the data being MCAR, which was assessed using Little's MCAR test in this study (appendix 1). The Little's MCAR test is performed by applying a Chi^2 test to the missing data to determine whether they are unrelated to the observed or unobserved data. This assumption ensured that the chosen model provided robust and reliable estimates while effectively handling missing data without introducing bias. Crude risk ratios (cRRs) with 95% confidence intervals were reported.

A regression model was not fitted for retention in care because it was a binary variable with one group containing only a single observation. The sample size for one category was too small; therefore, the model could not be run properly, making it impossible to determine the statistical significance of the predictor variables.

A backward stepwise regression model was employed to select variables for the final model, using a cut-off p-value of <0.2. The variables selected by the stepwise regression included regimen category, education level, and ALT. However, since stepwise regression can select variables based on chance, we also included additional variables essential for ART treatment outcomes from other related studies: employment status, age group, CD4 count, and BMI. All these variables were included in both the univariable and multivariable models.

The variance inflation factor (VIF) was calculated by regressing each chosen explanatory variable on all others to assess multicollinearity among them. Sex exhibited a VIF greater than

10, indicating a high level of collinearity with other predictor variables, as shown in Appendix 2. However, we could not remove it from the final model since it was the most important variable in the study.

Interaction between sex, age groups, education level, and employment status was also assessed by comparing models with and without interaction terms to determine if interactions significantly improved model fit. The likelihood ratio test was used to evaluate the statistical significance of each interaction term, and none were found to be significant (p-value < 0.05).

The final GLMM for VL suppression included the following variables: sex, education level, regimen category, CD4 count, ALT, and BMI. We performed a likelihood ratio test to assess our final model's goodness of fit. The final model was compared to a null model using the likelihood ratio test and examining pseudo R^2 values.

3.5. Ethical considerations

Permission to collect data at Themba Lethu Clinic was obtained from the Gauteng Department of Health, where the study was registered on the National Health Research Database (NHRD) (NDoH_202005_001). Ethical clearance was obtained from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, with clearance certificate number M200365 (Appendix 3). Confidentiality was ensured during data curation, and personal identifiers were removed before analysis. The collected data was used solely for this study.

CHAPTER 4 - RESULTS

4.1. Descriptive analysis

4.1.1. Study population

A flow diagram in Figure 4.1 shows that 42,320 patients were recorded on the Therapy-Edge-HIV™ database, with 10434 of them initiated within the study period. There were 42,203 patients who were not eligible to participate in the study and were excluded. Patients excluded in the study included individuals who had no documented ART start date, those initiated on ART outside of the study period, those transferred to Themba Lethu from another clinic during the study, patients who had received ART previously, patients younger than 15 years of age or older than 24 years, and patients who were found to be pregnant at the time of ART initiation. A total of 117 patients met the study eligibility criteria and were all included in the final analysis.

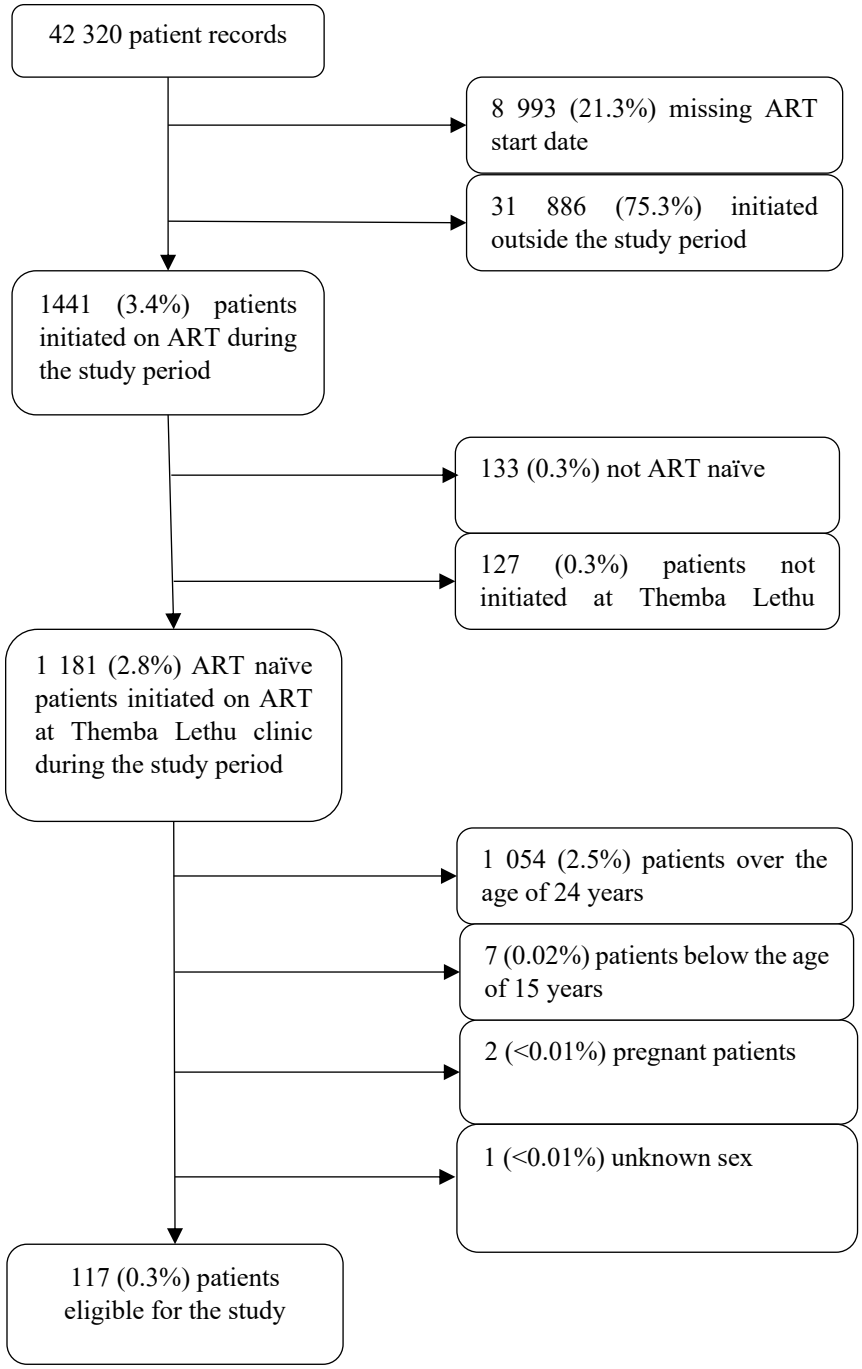


Figure 4.1: A flow chart for the selection of patients eligible for the study between 01 September 2016 and 30 September 2017 (N=117)

4.1.2. Baseline socio-demographic characteristics

Table 4.1 shows the baseline socio-demographic characteristics of patients included in the study. Of the 117 patients included in the analysis, 81 (69.2%) were female, with a mean age of 20.1 years (SD ± 2.0), and 36 (30.8%) males, with a mean age of 20.2 years (SD ±2.4). There were 107 (91.5%) black Africans, the majority were of South African nationality (n=110; 94.0%). The majority of patients (8; 70.9%) had secondary education, and a similar proportion of males and females had post-matric education (21.0% vs 22.2%). A larger proportion of patients (90; 76.9%) were employed, with a larger proportion of males (88.9%) compared to females (71.6). Conversely, unemployment was higher among females (n=18; 22.2%) compared to males (n=3; 8.3%),

4.1.3. Baseline clinical characteristics

Baseline clinical characteristics are shown in Table 4.1. At baseline, the mean Hemoglobin (Hgb) level was 13.1 g/dl (SD, ±0.2 g/dl); none of the male patients had a Hgb below 8.0 g/dl, while one female patient (n=1; 1.2%) had a Hgb level less than 8.0 g/dl. The mean baseline BMI was 24.3 g/dl (SD, ±0.8 g/dl). Most female patients (n=34; 42.0%) had a normal weight at the time of ART initiation, with the second largest proportion being obese (n=13; 16.1%). Among male patients, a majority (n=17; 47.2%) also had normal weight, while the second largest proportion was underweight (n=8; 22.2%). The mean baseline CD4 count was 438.3 cells/mm³ (SD ±29.5 cells/mm³). A larger proportion (n=34, 29.1%) of patients had a CD4 count exceeding 500.0 cells/mm³ at the time of ART initiation. Approximately 52.8% (n=42) of females had a CD4 count below 500.0 cells/mm³, including 13 (16.1%) who had a CD4 count below 250.0 cells/mm³. At baseline, the mean ALT was 30.8 mmol/L (SD 1.7), with 78 (66.7%) of patients having an ALT above 40 mmol/L. Most (88; 75.2%) patients were initiated on ‘TDF+EMT+EFV’ first-line ART regimens.

Table 4.1: Baseline socio-demographic characteristics of study participants attending Themba Lethu clinic, stratified by sex (2016-2017; n=117)

Variable	Category	Females	Males	Total
		n (%)	n (%)	n (%)
Total		81 (69.2)	36 (30.8)	117 (100)
Socio-demographic characteristics				
Age (years)	15-18	6 (7.4)	6 (16.7)	12 (10.3)
	19-21	33 (40.7)	17 (47.2)	50 (42.7)
	22-24	42 (51.8)	13 (36.1)	55 (47)
	Mean age (SD)	20.9 (2.0)	20.2 (2.4)	20.6 (0.2)
Nationality	South African	77 (95.1)	33 (91.7)	110 (94)
	Non-South African	4 (4.9)	3 (8.3)	7 (6)
Education level	Primary school or less	3 (3.7)	3 (8.3)	6 (5.1)
	Secondary school	58 (71.1)	25 (69.4)	83 (70.9)
	Post-matric	17 (21)	8 (22.2)	25 (21.4)
	Missing	3 (3.7)	− (−)	3 (2.6)
Race	Black African	74 (91.4)	33 (91.7)	107 (91.5)
	Other	2 (2.5)	1 (2.8)	3 (2.6)
	Missing	5 (6.2)	2 (5.6)	7 (6)
Employment status	Unemployed	18 (22.2)	3 (8.3)	21 (18)
	Employed	58 (71.6)	32 (88.9)	90 (76.9)
	Missing	5 (6.2)	1 (2.8)	6 (5.1)
Clinical characteristics				
Haemoglobin (mmol/L)	< 8,00	1 (1.2)	− (−)	1 (0.9)
	≥ 8,00	65 (80.3)	29 (80.6)	94 (80.3)
	Missing	15 (18.5)	7 (19.4)	22 (18.8)
	Mean Hgb (SD)	12.5 (0.2)	14.5 (0.4)	13.1 (0.2)
BMI (kg/m2)	Under-weight	5 (6.2)	8 (22.2)	13 (11.1)
	Normal	34 (42)	17 (47.2)	51 (43.6)
	Over-weight	17 (21)	1 (2.8)	18 (15.4)
	Obese	13 (16.1)	1 (2.8)	14 (12)
	Missing	12 (14.8)	9 (25)	21 (18)

	Mean BMI (SD)	25.8 (1.0)	20.5 (0.7)	24.3 (0.8)
CD4 count (cells/mm^3)	≤ 250,00	13 (16.1)	9 (25)	22 (18.8)
	250,10-349,90	13 (16.1)	4 (11.1)	17 (14.5)
	350,00-499,90	16 (19.8)	3 (8.3)	19 (16.2)
	≥ 500,00	22 (27.2)	12 (33.3)	34 (29.1)
	Missing	17 (21)	8 (22.2)	25 (21.4)
	Mean CD4 (SD)	459.9 (35.0)	388.9 (54.8)	438.3 (29.5)
ALT (mmol/L)	< 40,00	53 (65.4)	25 (69.4)	78 (66.7)
	≥ 40,00	13 (16)	4 (11.1)	17 (14.5)
	Missing	15 (18.5)	7 (19.4)	22 (18.8)
	Mean ALT (SD)	30.7 (2.1)	31.1 (3.2)	30.8 (1.7)
First-line ART regimen	TDF+EMT+EFV	64 (79.0)	24 (66.7)	88 (75.2)
	Other	17 (21.0)	12 (33.3)	29 (24.8)

4.2. Association of explanatory variables with treatment outcomes 12 months after ART initiation, stratified by sex

4.2.1. Retention in care at 12-month follow-up

At 12 months after ART initiation, only one patient was no longer in care (deceased), while the remaining 116 patients were still alive and in care. The deceased patient was a South African black female aged between 15 and 18 years. She was employed and had secondary education as the highest level of education. At ART initiation, she was underweight, had an Hgb level above 8 g/dL, an ALT level below 40 mmol/L, and a baseline CD4 count between 250 and 350 cells/mm³, and was initiated on a TDF+EMT+EFV first-line regimen.

The distribution of baseline characteristics for patients who were alive and in care 12 months after initiating ART remained similar to that described in the baseline analysis presented in Table 4.1.

4.2.2. VL suppression at 12-month follow-up

Table 4.2 presents the socio-demographic and clinical characteristics of the study participants stratified by VL suppression. Of the 117 patients in our study, 71 (60.7%) had VL results measured 12 months after ART initiation. Of those missing VL results 12 months after ART initiation, 44.4% (n=16) were males and 37.0% (n=30) were females. Over a third (38.0%) had normal BMI, 54.0% had ALT more than 40 mmol/L, 66.0% were initiated on TDF+EMT+EFV ART regimen, and over a quarter (26.0%) had CD4 count, less than 250.0 cells/mm^3.

At 12 months after ART initiation, patients exhibited sex differences in VL suppression based on socio-demographic and clinical characteristics. However, these differences were insignificant for all variables except the regimen category. VL suppression was more prevalent in females (n=38; 74.5%) than in males (n=12; 60.0%) during the first 12 months of initiating ART. For both males and females, VL suppression was highly prevalent among individuals with a secondary school education level, those who were employed, those with a normal BMI, a CD4 count greater than 500 cells/mm3, ALT below 40 mmol/L, and Hgb above 8 mmol/l. Nevertheless, the association between these explanatory variables and VL suppression was not statistically significant. At 12 months post-ART initiation, there was a statistically significant association between VL suppression and the type of regimen on which ABYM were initiated (p-value < 0.01). Most (6; 75.0%) of the males who did not achieve VL suppression were initiated on other ART regimens that were not first-line.

Table 4.2: Association of socio-demographic and clinical characteristics with VL suppression 12 months after ART initiation, stratified by sex, for study participants attending Themba Lethu clinic, 2016-2017 (n=71)

Variable	Category	Male			Female		
		Suppressed n=12	Unsuppressed n=8	P-value	Suppressed n=38	Unsuppressed n=13	P-value
		N (%)	N (%)		N (%)	N (%)	
Age-group (years)	15 to 18	2 (16.7)	1 (12.5)	0.58	3 (7.9)	1 (7.7)	1.00
	19 to 21	4 (33.3)	5 (62.5)		19 (50.0)	7 (53.9)	
	22 to 24	6 (50.0)	2 (25.0)		16 (42.1)	5 (38.5)	
Education level	Primary school or less	0 (0.0)	1 (12.5)	0.59	2 (5.3)	0 (0.0)	0.14
	Secondary school	8 (66.7)	5 (62.5)		25 (65.8)	11 (84.6)	
	Post-matric	4 (33.3)	2 (25.0)		11 (28.9)	1 (7.7)	
	Missing	-	-		0 (0)	1 (7.7)	
Employment status	Unemployed	-	-		6 (15.8)	2 (15.4)	0.31
	Employed	12 (100.0)	7 (87.5)	0.40	31 (81.6)	9 (69.2)	
	Missing	0 (0.0)	1 (12.5)		1 (2.6)	2 (15.4)	
Haemoglobin (mmol/L)	< 8,00	-	-		-	-	0.66
	≥ 8,00	11 (91 7)	7 (87.5)	1.00	32 (84.2)	12 (92.3)	
	Missing	1 (8.3)	1 (12.5)		6 (15.8)	1 (7.7)	
BMI (kg/m^2)	Under-weight	1 (8.3)	2 (25.0)	0.89	3 (7.9)	0 (0.0)	0.72
	Normal	7 (58.3)	4 (50.0)		15 (39.5)	8 (61.5)	
	Over-weight	1 (8.3)	0 (0.0)		10 (26.3)	2 (15.4)	
	Obese	-	-		5 (13.2)	2 (15.4)	
	Missing	3 (25.0)	2 (25.0)		5 (13.2)	1 (7.7)	
CD4 count (cells/mm^3)	≤ 250,00	0 (0.0)	2 (25.0)	0.27	7 (18.4)	2 (15.4)	0.54
	250,10-349,90	1 (8.3)	2 (25.0)		7 (18.4)	3 (23.1)	

	350,00-499,90	3 (25.0)	0 (0.0)		5 (13.2)	4 (30.8)	
	≥ 500,00	6 (50.0)	3 (37.5)		13 (34.2)	2 (15.4)	
	Missing	2 (16.7)	1 (12.5		6 (15.8)	2 (15.4)	
ALT mmol/L	< 40,00	9 (75.0)	7 (87.5)	0.75	28 (73.7)	10 (76.9)	1.00
	≥ 40,00	2 (16.7)	0 (0.0)		5 (13.2)	2 (15.4)	
	Missing	1 (8.3)	1 (12.5)		5 (13.2)	1 (7.7)	
First-line ART regimen	TDF+EMT+ EFV	11 (91.7)	2 (25.0)	>0.00	35 (92.1)	9 (69.2)	0.06
	Other	1 (8.3)	6 (75.0)		3 (7.9)	4 (30.8)	

4.2.3. Baseline explanatory variables that are predictors for treatment outcomes

4.2.3.1. Univariable analysis of predictors of VL suppression

Table 4.3 presents the GLMM analysis evaluating the association between clinical and socio-demographic factors and VL in both AGYWs and ABYMs. Male participants with secondary education face a 1.43 times more likely to reach viral suppression than those with post-matric qualifications (RR=1.43; CI: 1.07-1.91; p=0.017). Female participants with a secondary level of education are 28% less likely to achieve VL suppression than those with a post-matric level of education (RR=0.72, 95%CI: 0.61-0.86, p<0.001). These results were statistically significant.

The data also indicated a higher likelihood of achieving VL suppression in overweight males, obese and overweight females, AYAs aged 19-21 years, males with a secondary education level, and AYAs with CD4 counts greater than 350 cells/mm3. Additionally, the risk of achieving VL suppression was lower among those with ALT levels exceeding 40 mmol/L and those initiated on other ART regimens. However, these results were not statistically significant at p <0.01.

Table 4.3: Univariate analysis of socio-demographic and clinical factors associated with VL suppression 12 months after ART initiation for study participants in attending Themba Lethu clinic, (2016-2017; n=71)

Variable	Male (n= 20)		Female (n= 51)	
	RR (95% CI)	p-value	RR (95% CI)	p-value
Age (years)				
15 to 18	Reference			
19 to 21	1.43(0.67-1.23)	0.223	1.32(0.88-1.41)	0.329
22 to 24	1.93(0.71-1.78)	0.452	1.12(0.44-1.52)	0.412
Education				
Post-metric	Reference			
Secondary	1.43(1.07-1.91)	0.02#	0.72(0.61-0.86)	<0.01#
Primary or less	-	-	0.92(0.79-1.08)	0.321
BMI (kg/m^2)				
Under weight	Reference			
Normal	1(0.51-1.96)	1	1.09(0.47-2.51)	0.85
Overweight	1.33(0.74-2.39)	0.33	1.35(0.59-3.11)	0.48
Obese	1.33(0.74-2.39)	0.33	1.13(0.47-2.69)	0.79
Baseline CD4 count (cell/mm^3)				
<250	Reference			
250.1-349.9	1.88(0.54-6.51)	0.32	1.05(0.55-2.01)	0.89
350-499.9	2.5(0.83-7.52)	0.10	1.14(0.64-2.04)	0.65
≥500	1.94(0.61-6.19)	0.26	1.48(0.93-2.36)	0.10
ALT (mmol/L)				
<40	Reference			
≥40	0.92(0.39-2.21)	0.86	0.96(0.66-1.41)	0.84
ART regimen				
TDF + 3TC/FTC + EFV/NVP	Reference			
Other	0.38(0.12-1.22)	0.10	0.46(0.18-1.13)	0.09

- p value <0.01

4.2.3.2. Multivariable analysis of predictors of VL suppression

Table 4.3.2 presents the factors associated with VL suppression after controlling other variables. The analysis reveals that age was not a statistically significant predictor for either male or female AYAs. The results also show no evidence of association between BMI, baseline CD4, and ALT and viral suppression. Among males, young adults (19–21 years) are 1.8 times more likely to achieve VL suppression than adolescents, whereas among females, the probability is 15% lower, although neither association was significant. Education does not appear to have a notable effect, with males who completed secondary education having a 1% higher probability of VL suppression compared to those with post-matric education. Conversely, among females, secondary education is associated with a 10% lower likelihood of VL suppression compared to those with post-matric education, indicating a sex difference vy education level. However, this analysis was not statistically significant.

Among females, those on other regimens were 99% less likely to achieve viral suppression, and the result is statistically significant (aRR=0.01, 95% CI: 0.1-0.2). The ART regimen was not associated with viral suppression in male patients. In addition to the significant role of the ART regimen in both AGYW, no other variables showed a strong, statistically significant association.

Table 4.4: Multivariable (GLMM) results showing socio-demographic and clinical factors associated with VL suppression in patients attending Themba Lethu clinic, (2016-2017; n=71)

Variable	Multivariate (GLMM, n=71)			
	Male (n= 20)		Female (n= 51)	
	aRR (95% CI)	P-value	aRR (95% CI)	P-value
Age (years)				
15 to 18	Reference			
19 to 21	1.61 (0.47 - 4.16)	0.348	0.56 (0.85 - 1.42)	0.327
22 to 24	1.11(0.45 – 2.76)	0.375	0.45(0.85 – 1.55)	0.643

Highest Level of Education				
Post-matric	Reference			
Secondary school	1.01 (0.45 - 2.26)	0.98	0.90 (0.66 - 1.23)	0.51
Primary school or less	1	-	1.47 (0.73 - 2.94)	0.28
BMI (kg/m^2)				
Under-weight	Reference			
Normal	1.12 (0.23 - 5.47)	0.89	1.02 (0.70 - 1.48)	0.92
Over-weight	0.83 (0.17 - 4.08)	0.82	0.98 (0.60 - 1.61)	0.95
Obese	0.39 (0.04 - 3.45)	0.40	0.74 (0.44 - 1.27)	0.27
Baseline CD4 count (cell/mm^3)				
≤250	Reference			
250.1-349.9	1.95 (0.18 - 21.2)	0.58	1.03 (0.50 - 2.12)	0.93
350-499.9	0.67 (0.19 - 2.39)	0.54	1.34 (0.76 - 2.37)	0.31
≥500	0.90 (0.24 - 3.42)	0.88	1.44 (0.76 - 2.72)	0.27
ALT (mmol/L)				
<40	Reference			
≥40	1.34 (0.37 - 4.81)	0.65	1.08 (0.79 - 1.49)	0.62
ART regimen				
TDF + 3TC/FTC + EFV/NVP	Reference			
Other	0.23 (0.05 - 1.13)	0.07	0.01 (0.10 - 0.20)	<0.00[#]

CHAPTER 5 - DISCUSSION

5.1. Introduction

This retrospective cohort study aimed to determine sex differences in HIV treatment outcomes, specifically retention in care and VL suppression, among AYAs. The study participants were initiated on ART during the UTT era at Themba Lethu Clinic in Johannesburg (2016), South Africa, and followed up after 12 months to assess treatment outcomes. This chapter discusses the study findings, their scientific contribution, and their implications in the context of existing literature, highlighting the potential impact of these findings on future research and healthcare practices.

The key findings of this study were AYAs who initiated ART at the onset of the UTT policy exhibited better treatment outcomes at 12 months. Retention in care was generally high among AYAs during this period, with AGYWs achieving higher rates of viral load suppression compared to their male counterparts. Educational level was a significant predictor of VL suppression for both AGYW and ABYM, highlighting the role of health literacy in supporting adherence. Additionally, ART regimen type was an important driver of VL suppression specifically among AGYW.

The study population predominantly consisted of AGYW, accounting for 69.2%, while ABYM comprised only 31.8%. This sex disparity aligns with findings from the broader Themba Lethu cohort and other South African studies, which consistently report higher healthcare engagement among women than men[14,49]. Studies have attributed this to better health-seeking behaviour among females and the disproportionately higher HIV prevalence in AGYW, estimated at 10.4 per 1000 population compared to 3.5 per 1000 population in ABYM[19]. Additionally, HIV incidence remains markedly higher in AGYW (1.5 per 1000) than in ABYM (0.5 per 1000), reinforcing the observed overrepresentation of AGYW in ART programs[19,52]

5.2. Health status

The overall health status of participants at the initiation of ART was relatively good, with most having CD4 counts exceeding 400 cells/mm³, a standard BMI, and ALT levels below 40 mmol/L. These clinical parameters suggest a stable physiological profile and can be used to assess baseline health status, monitor treatment readiness, and anticipate potential complications during care[10]. This is because CD4 counts above this threshold indicate preserved immune function and are associated with a lower risk of opportunistic infections and HIV disease progression[7]. A normal BMI is associated with a reduced risk of overall health outcomes[35]. Additionally, ALT levels below 40 mmol/L suggest an absence of hepatic inflammation or injury, which is critical in individuals receiving medications with potential hepatotoxic effects such as ART[7,35].

Notably, 29.1% had CD4 counts above 500.0 cells/mm³, indicating early ART initiation under the UTT (Universal Test and Treat) policy, which recommends immediate initiation of ART for all HIV-positive individuals, regardless of their CD4 count. However, 18.8% of patients initiated ART with CD4 counts below 250 cells/mm³, signalling advanced HIV infection. Before UTT implementation, a significantly higher proportion (24.8%) of patients at Themba Lethu initiated ART at an advanced HIV disease stage (CD4 <50 cells/mm³)[49]. These findings underscore the success of the UTT strategy in facilitating earlier initiation of ART, thereby improving long-term treatment outcomes and instilling optimism for the future of HIV treatment.

Despite these improvements, the UNAIDS target of initiating 95% of PLHIV on ART by 2025 remains a challenge. This acknowledgment underscores the need for continued effort and innovation in HIV treatment[2,21]. Factors such as late diagnosis, poor linkage to care, and delayed ART initiation contribute to this challenge. Enhancing case-finding approaches is critical for early HIV diagnosis, linkage to care, and same-day ART initiation[31]. Moreover, understanding sex-specific clinical factors, such as CD4 and BMI, is crucial for informing and implementing tailored interventions to optimize ART long-term retention.

5.3. Retention in care

The study found a high overall retention rate, with 99.1% (116 patients) remaining engaged in care at 12 months post-ART initiation. This retention rate is higher than the 89% two-year retention reported in a previous Themba Lethu cohort study conducted during the UTT era[14]. Differentiated service delivery models, particularly multi-month dispensing (MMD), may have contributed to improved retention by reducing clinic visit frequency and making ART collection more convenient. This finding is supported by a multi-center randomized trial in Southern Africa, which reported over 90% retention with MMD implementation, highlighting patient demand for such approaches[53].

Despite the overall high retention rate, our study successfully identified sex disparities in treatment engagement as a significant concern. Consistent with existing research, we found that males were less likely to initiate early in care than females[44]. This disparity has been linked to lower health-seeking behaviour, employment-related barriers, and social stigma associated with ART among males[20]. In contrast, our study also highlighted the case of a female participant who died within 12 months of ART initiation. The AGYW had a baseline CD4 count below 400 cells/mm³, a factor consistently associated with increased risk of virologic failure and mortality within the first two years of ART[10,36].

5.4. Viral load suppression and ART outcomes

The findings demonstrate both expected and unexpected trends, revealing sex-based differences in VL suppression that warrant further exploration in the context of socio-demographic and clinical characteristics.

The overall VL suppression rates at 12 months were higher among females (74.5%) compared to males (60.0%). This contrasts with some previous studies in which males have been shown to experience poorer outcomes, often linked to delayed healthcare engagement and lower adherence to ART[39]. The current study found that females with tertiary education were more likely to achieve VL suppression than their male counterparts[33]. University and college campuses often offer integrated health services, including youth-friendly clinics and adherence

counseling, which may be particularly beneficial for young women in terms of both treatment and psychosocial support[46].

In contrast, young men tend to have fewer specialized services tailored to their needs, which may explain their lower VL suppression rates in this cohort. Lack of male-focused SRH services, including mental health support and tailored HIV care, may contribute to poorer engagement with ART[46]. The absence of these sex-specific services could also partly explain the trend in the current study, where females generally showed better treatment outcomes compared to males.

The study also found a statistically significant association between VL suppression and the ART regimen on which participants were initiated (p-value < 0.01). Most males (75.0%) who did not achieve VL suppression were initiated on ART regimens other than the first-line combination of TDF+FTC/3TC+EFV. These findings emphasize the importance of initiating patients, particularly ABYM, on first-line ART regimens to optimize virologic outcomes, as previous studies have shown that non-first-line regimens often have inferior virologic suppression and higher rates of treatment failure[12].

This highlights a critical need for careful selection of ART regimens, especially for ABYM who may have unique treatment challenges and adherence issues. The availability of a variety of ART regimens should not overshadow the importance of adhering to the most effective and recommended first-line ART regimen, which is more likely to lead to sustained VL suppression. Furthermore, this highlights the importance of introducing optimized first-line ART regimens, such as dolutegravir (DTG) based combinations, which have demonstrated superior efficacy, improved tolerability, fewer side effects, and a higher genetic barrier to resistance, ultimately improving the overall health outcomes of patients on ART[12]. The DTG-based regimens have shown significant promise in improving ART adherence among young people due to their fewer side effects and higher genetic barrier to resistance[35].

While socio-demographic factors such as education level, employment status, BMI, and baseline CD4 count showed trends in favour of VL suppression, the associations were not statistically significant. These findings are consistent with literature suggesting that adherence to ART, while influenced by social and demographic factors, may be more directly impacted by clinical and treatment-related factors, such as ART regimen choice and the quality of clinical support received[46]. Although not statistically significant, both male and female participants with secondary education, normal BMI, and CD4 counts above 500 cells/mm³ tended to have higher rates of viral suppression. These patterns, while not conclusive, may still offer insight into factors influencing ART outcomes.

Employment status was also not significantly associated with VL suppression in this study. However, employed males were more likely to benefit from MMD, which helps reduce the frequency of clinic visits and aligns with work schedules. MMD is a proven strategy to improve ART retention and adherence, particularly among employed individuals[39]. However, the absence of a strong statistical correlation between employment and VL suppression in this study may suggest that other factors, such as ART regimen, have a greater influence on treatment outcomes.

5.5. Strengths and limitations

Our study results should be interpreted considering several strengths and limitations,.

5.5.1. Strengths

The study included participants attending the Themba Lethu clinic, which provides healthcare services according to the South African Department of Health guidelines. The analysis was performed on routinely collected clinic data; hence, the study findings provide a profile of the actual population. Additionally, the analysis was conducted using data extracted from the electronic medical record system implemented at the facility for routine medical record management over many years. The study is one of the few studies that assessed sex differences in treatment outcomes among AYAs who initiated ART during the UTT era. The study employed the standard definition of treatment outcomes as outlined in the ART guidelines.

5.5.2. Limitations

5.5.2.1. Missing data

Some patients in our study did not have VL results, leading to their exclusion from the analysis. We assumed the missing VL data were random, likely due to missed recording during their clinic visit, 12 months post-ART initiation. We used 9-15 months window to capture 12-month VL suppression, allowing for variability in clinic visit schedules and laboratory testing times while still reflecting patients' treatment status approximately one year after ART initiation.

The absence of VL results for some patients may have reduced the power of our study and introduced sampling bias, as most patients with recorded VL results were employed and initiated on the TDF+EMT+EFV first-line regimen. Factors potentially contributing to missing VL data include challenges with clinic scheduling, inconsistent documentation, and variable adherence to scheduled VL monitoring visits among patients, particularly those balancing employment or other commitments. Strengthening systems for routine VL monitoring and consistent data capturing would provide a more complete assessment of treatment outcomes among all patients.

5.5.2.2. Selection bias

Selection bias may have been introduced due to the exclusion of AYAs who had missing information on key baseline variables important for the inclusion criteria, such as ART initiation date and sex. Additionally, while AYAs account for 34% of the total South African population[3], the final study sample represented only 0.3% of the total patient population at Themba Lethu Clinic during the study period. The exclusion of a large proportion of potentially eligible clients may have resulted in a study population that is not fully representative of the broader AYA cohort. This could bias the findings toward those who were more engaged in care and had more complete records. As a result, the generalizability of the findings is limited. The outcomes observed in this selected group may not be a true representation of what AYAs initiated on ART experienced during the onset of UTT. These limitations are acknowledged and have been carefully considered in the interpretation of the study results.

5.5.2.3. Measurement of outcomes

We included all patients, whether alive and in care or no longer in care, in the analysis, effectively reducing survival bias. However, the study underestimated LTFU, as previous studies have reported high LTFU rates among adolescents within the first six months after the

initiation of ART. Additionally, this study likely overestimated ART outcomes, as it was conducted in a clinic nested within a Tertiary hospital, which is not a typical setting for the majority of ART sites in South Africa.

5.5.2.4. Generalizability

While the study focused exclusively on patients initiated on ART at Themba Lethu Clinic, an urban facility supported by specialized staff and researchers, the findings cannot be broadly generalized to other facilities or the general population of Gauteng. To ensure the applicability of our results, further studies should be conducted in clinics with similar profiles that reflect the primary care setting typical of South Africa's public healthcare facilities. This would help validate these findings and provide a more comprehensive understanding of ART outcomes across diverse healthcare contexts.

CHAPTER 6 - CONCLUSIONS AND RECOMMENDATIONS

The study revealed that AGYWs experienced better treatment outcomes compared to ABYM 12 months after initiating ART during the onset of UTT era. Although an overall VL suppression of 70.0% is lower than the WHO target of 95%, it is slightly higher than the 2024 national suppression rate of 67%. While VL suppression rates at 12 months post-ART initiation was relatively high, particularly among females, several factors influence treatment outcomes among AYAs. Sex-specific services, ART regimen selection, and social support structures play a critical role in determining success.

The findings suggest that AGYWs benefitted more from the UTT at its onset. The study also emphasises the importance of initiating AYAs, especially ABYMs, on optimised ART regimens to improve virologic outcomes. To improve progress toward the 95-95-95 targets, particularly among AYAs it is essential for the country to adopt strategies that promote equity in HIV care. This includes initiating AYAs on optimized ART regimens and ensuring access to comprehensive health literacy interventions, as education was shown to be a predictor of viral load suppression.

References

1. UNAIDS. UNAIDS data 2022 [Internet]. 2022. Available from: https://www.unaids.org/en/resources/documents/2023/2022_unaids_data
2. The path that ends AIDS: UNAIDS Global AIDS Update 2023. [cited 2025 Apr 7]; Available from: http://www.wipo.int/amc/en/mediation/rules
3. StatsSA. STATISTICAL RELEASE P0302. 2021; Available from: www.statssa.gov.za,info@statssa.gov.za,Tel+27123108911
4. StatsSA. Statistical release- Mid-year population estimates July 2018. Africa [Internet]. 2018;(P0302, July):1–22. Available from: http://www.statssa.gov.za/publications/P0302/P03022011.pdf
5. Maughan-Brown B, George G, Beckett S, Evans M, Lewis L, Cawood C, et al. HIV Risk Among Adolescent Girls and Young Women in Age-Disparate Partnerships: Evidence From KwaZulu-Natal, South Africa. J Acquir Immune Defic Syndr. 2018 Jun;78(2):155–62.
6. UNAIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic. 2020;
7. World Health Organization (WHO). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. 2016; Available from: https://www.ncbi.nlm.nih.gov/books/NBK374294/pdf/Bookshelf_NBK374294.pdf
8. Naomi model. HIV sub-national estimates viewer [Internet]. Available from: https://naomi-spectrum.unaids.org/?msclkid=c13808a3c15411ec81981271eefa903d
9. National Department of Health (NDOH). HIV REPORT 2021.indb [Internet]. 2021. Available from: www.dalro.co.za
10. Mbengue MAS, Chasela C, Onoya D, Mboup S, Fox MP, Evans D. Clinical predictor score to identify patients at risk of poor viral load suppression at six months on antiretroviral therapy: results from a prospective cohort study in Johannesburg, South Africa. Clin Epidemiol [Internet]. 2019;11:359–73. Available from: https://www.ncbi.nlm.nih.gov/pubmed/31191029

11. Nyakato P, Schomaker M, Fatti G, Tanser F, Euvrard J, Sipambo N, et al. Virologic non-suppression and early loss to follow up among pregnant and non-pregnant adolescents aged 15–19 years initiating antiretroviral therapy in South Africa: a retrospective cohort study. J Int AIDS Soc [Internet]. 2022 Jan 1;25(1):25870. Available from: /pmc/articles/PMC8760609/

12. South Africa National Department of Health. 2019 ART Clinical Guidelines for the Management of HIV in Adults, Pregnancy, Adolescents, Children, Infants and Neonates [Internet]. 2020. Available from: https://health.gov.za/wp-content/uploads/2020/11/2019-art-guideline.pdf

13. Dorward J, Sookrajh Y, Gate K, Khubone T, Mtshaka N, Mlisana K, et al. HIV treatment outcomes among people with initiation CD4 counts >500 cells/μL after implementation of Treat All in South African public clinics: a retrospective cohort study. J Int AIDS Soc [Internet]. 2020 Apr 1 [cited 2022 May 22];23(4):e25479. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/jia2.25479

14. Maskew M, Brennan AT, MacPhail AP, Sanne IM, Fox MP. Poorer ART outcomes with increasing age at a large public sector HIV clinic in Johannesburg, South Africa. J Int Assoc Physicians AIDS Care [Internet]. 2012 Jan;11(1):57–65. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3272319/

15. Onoya D, Sineke T, Mokhele I, Bor J, Fox MP, Miot J. Understanding the Reasons for Deferring ART Among Patients Diagnosed Under the Same-Day-ART Policy in Johannesburg, South Africa. AIDS Behav. 2021 Sep 1;25(9):2779–92.

16. HSRC. HIV impact assessment summary July 2018, the fifth South African national HIV prevalence, incidence, behaviour and communication survey [Internet]. 2018. Available from: http://www.hsrc.ac.za/en/departments/saph/HAST_National_HIV_Survey

17. Bello Pedzisai ndagurwa seyi Omogiate layout design B, Ekeh J, Republic M. Global aids monitoring report report. 2020; Available from: www.cesar-africa.com

18. Huerga H, Van Cutsem G, Ben Farhat J, Puren A, Bouhenia M, Wiesner L, et al. Progress towards the UNAIDS 90-90-90 goals by age and gender in a rural area of KwaZulu-Natal, South Africa: A household-based community cross-sectional survey. BMC Public Health. 2018 Mar 2;18(1).

19. UNAIDS. Factsheet 2022 [Internet]. 2022. Available from: https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf

20. Kharsany ABM, Cawood C, Lewis L, Yende-Zuma N, Khanyile D, Puren A, et al. Trends in HIV Prevention, Treatment, and Incidence in a Hyperendemic Area of KwaZulu-Natal, South Africa. JAMA Netw Open [Internet]. 2019 Nov 11 [cited 2025 May 5];2(11):e1914378. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6826647/

21. Pillay Y, Johnson L. World AIDS Day 2020: Reflections on global and South African progress and continuing challenges. S Afr J HIV Med. 2021;22(1):1205.

22. SANAC. Midterm review of the national strategic plan for HIV, TB AND STIs 2017-2022. 2019.

23. Anderson K, Muloiwa R, Davies MA. Treatment outcomes in perinatally infected hiv-positive adolescents and young adults after ≥10 yearon antiretroviral therapy. South African Medical Journal [Internet]. 2019;109(1):27–34. Available from: http://www.samj.org.za/index.php/samj/article/view/12508

24. Mathews C, Cheyip M, Beauclair R, Puren A, Lombard C, Jonas K, et al. HIV care coverage among HIV-positive adolescent girls and young women in South Africa: Results from the HERStory Study. South African Medical Journal. 2021;111(5).

25. Mabaso M, Sokhela Z, Mohlabane N, Chibi B, Zuma K, Simbayi L. Determinants of HIV infection among adolescent girls and young women aged 15-24 years in South Africa: a 2012 population-based national household survey.

26. Evan M, Risher K, Zungu N, Shisana O, Moyo S, Celentano DD, et al. Age-disparate sex and HIV risk for young women from 2002 to 2012 in South Africa. J Int AIDS Soc [Internet]. 2016 Dec;19(1):21310. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28364564

27. Maughan-Brown B, Venkataramani A, Kharsany ABM, Beckett S, Govender K, Lewis L, et al. Recently formed age-disparate partnerships are associated with elevated HIV-incidence among young women in South Africa. AIDS [Internet]. 2020 Jan;34(1):149–54. Available from: https://www.ncbi.nlm.nih.gov/pubmed/31483373

28. Maughan-Brown B, George G, Beckett S, Evans M, Lewis L, Cawood C, et al. HIV Risk Among Adolescent Girls and Young Women in Age-Disparate Partnerships: Evidence From KwaZulu-Natal, South Africa. J Acquir Immune Defic Syndr [Internet]. Fifth Edit. 2018 Jun 1;78(2):155–62. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29767637

29. Saul JI, Bachman G, Allen S, Toiv NF, Cooney C, Beamon A. The DREAMS core package of interventions: A comprehensive approach to preventing HIV among adolescent girls and young women. Available from: https://doi.org/10.1371/journal.pone.0208167.g001

30. Birdthistle I, Kwaro D, Shahmanesh M, Baisley K, Khagayi S, Chimbindi N, et al. Evaluating the impact of DREAMS on HIV incidence among adolescent girls and young women: A population-based cohort study in Kenya and South Africa. PLoS Med. 2021 Oct 1;18(10).

31. Department of Health - South Africa. Implementation of the universal test and treat strategy for positive patients and differentiated care for stable patients. 2016; Available from: https://sahivsoc.org/Files/22%208%2016%20Circular%20UTT%20%20%20Decongestion%20CCMT%20Directorate.pdf

32. Onoya D, Sineke T, Hendrickson C, Mokhele I, Maskew M, Long LC, et al. Original research: Impact of the test and treat policy on delays in antiretroviral therapy initiation among adult HIV positive patients from six clinics in Johannesburg, South Africa: results from a prospective cohort study. BMJ Open [Internet]. 2020 Mar 25;10(3). Available from: /pmc/articles/PMC7170559/

33. Celum C, Hosek S, Tsholwana M, Kassim S, Mukaka S, Dye BJ, et al. PrEP uptake, persistence, adherence, and effect of retrospective drug level feedback on PrEP adherence among young women in southern Africa: Results from HPTN 082, a randomized controlled trial. PLoS Med. 2021;18(6).

34. Dorward J, Sookrajh Y, Gate K, Khubone T, Mtshaka N, Mlisana K, et al. HIV treatment outcomes among people with initiation CD4 counts >500 cells/μL after implementation of Treat All in South African public clinics: a retrospective cohort study. J Int AIDS Soc

[Internet]. 2020 Apr 1;23(4). Available from: https://pubmed.ncbi.nlm.nih.gov/32319203/

35. Meintjes G, Moorhouse MA, Carmona S, Davies N, Dlamini S, Van Vuuren C, et al. Adult antiretroviral therapy guidelines 2017. South Afr J HIV Med [Internet]. 2017;18(1). Available from: https://sajhivmed.org.za/index.php/hivmed/article/view/776/969

36. Kufa T, Shubber Z, MacLeod W, Takuva S, Carmona S, Bor J, et al. CD4 count recovery and associated factors among individuals enrolled in the South African antiretroviral therapy programme: An analysis of national laboratory based data. PLoS One [Internet]. 2019 May 1;14(5):e0217742. Available from: https://www.ncbi.nlm.nih.gov/pubmed/31150489

37. Buh A, Deonandan R, Gomes J, Krentel A, Oladimeji O, Yaya S. Barriers and facilitators for interventions to improve ART adherence in Sub-Saharan African countries: A systematic review and meta-analysis. PLoS One [Internet]. 2023 Nov 1;18(11):e0295046. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10688728/

38. Clouse K, Pettifor AE, Maskew M, Bassett J, Van Rie A, Behets F, et al. Patient retention from HIV diagnosis through one year on antiretroviral therapy at a primary health care clinic in Johannesburg, South Africa. J Acquir Immune Defic Syndr [Internet]. 2013 Feb 1;62(2). Available from: https://pubmed.ncbi.nlm.nih.gov/23011400/

39. Maskew M, Technau K, Davies MA, Vreeman R, Fox MP. Adolescent retention in HIV care within differentiated service-delivery models in sub-Saharan Africa. Lancet HIV [Internet]. 2022 Oct 1;9(10):e726. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9927242/

40. Okonji EF, van Wyk B, Mukumbang FC, Hughes GD. Determinants of viral suppression among adolescents on antiretroviral treatment in Ehlanzeni district, South Africa: a cross-sectional analysis. AIDS Res Ther [Internet]. 2021 Dec 1;18(1). Available from: https://pubmed.ncbi.nlm.nih.gov/34627300/

41. Filiatreau LM, Pettifor A, Edwards JK, Masilela N, Twine R, Xavier Gómez-Olivé F, et al. Associations Between Key Psychosocial Stressors and Viral Suppression and

Retention in Care Among Youth with HIV in Rural South Africa. AIDS Behav [Internet]. 2021 Aug 1;25(8):2358–68. Available from: https://pubmed.ncbi.nlm.nih.gov/33624194/

42. Green D, Tordoff DM, Kharono B, Akullian A, Bershteyn A, Morrison M, et al. Evidence of sociodemographic heterogeneity across the HIV treatment cascade and progress towards 90-90-90 in sub-Saharan Africa - a systematic review and meta-analysis. J Int AIDS Soc [Internet]. 2020 Mar 1;23(3). Available from: https://pubmed.ncbi.nlm.nih.gov/32153117/

43. Mabunda K, Ngamasana EL, Babalola JO, Zunza M, Nyasulu P. Determinants of poor adherence to antiretroviral treatment using a combined effect of age and education among human immunodeficiency virus infected young adults attending care at Letaba Hospital HIV Clinic, Limpopo Province, South Africa. Pan Afr Med J [Internet]. 2019 Jan 1;32. Available from: https://pubmed.ncbi.nlm.nih.gov/31143342/

44. Dorward J, Mabuto T, Charalambous S, Fielding KL, Hoffmann CJ. Factors Associated With Poor Linkage to HIV Care in South Africa: Secondary Analysis of Data From the Thol'impilo Trial. J Acquir Immune Defic Syndr [Internet]. 2017 Dec 1;76(5):453–60. Available from: https://europepmc.org/article/MED/28961678

45. Donenberg G, Merrill KG, Atujuna M, Emerson E, Bray B, Bekker LG. Mental health outcomes of a pilot 2-arm randomized controlled trial of a HIV-prevention program for South African adolescent girls and young women and their female caregivers. BMC Public Health. 2021;21(1).

46. James S, Pisa PT, Imrie J, Beery MP, Martin C, Skosana C, et al. Assessment of adolescent and youth friendly services in primary healthcare facilities in two provinces in South Africa. BMC Health Serv Res [Internet]. 2018 Oct 22;18(1):809. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6198437/

47. Zanoni BC, Archary M, Sibaya T, Musinguzi N, Kelley ME, McManus S, et al. Development and validation of the HIV adolescent readiness for transition scale (HARTS) in South Africa. J Int AIDS Soc [Internet]. 2021 Jul 1;24(7). Available from: https://pubmed.ncbi.nlm.nih.gov/34235876/

48. Johnson LF, Dorrington RE, Moolla H. Progress towards the 2020 targets for HIV diagnosis and antiretroviral treatment in South Africa. South Afr J HIV Med. 2017;18(1).

49. Fox MP, Maskew M, Patrick MacPhail A, Long L, Brennan AT, Westreich D, et al. Cohort Profile: The Themba Lethu Clinical Cohort, Johannesburg, South Africa. Int J Epidemiol [Internet]. 2013 Apr 1;42(2):430–9. Available from: https://academic.oup.com/ije/article/42/2/430/733581

50. Fox MP, Maskew M, Brennan AT, Evans D, Onoya D, Malete G, et al. Cohort profile: The Right to Care Clinical HIV Cohort, South Africa. BMJ Open. 2017 Jun 1;7(6).

51. Meeyai S. Logistic Regression with Missing Data: A Comparison of Handling Methods, and Effects of Percent Missing Values. Journal of Traffic and Logistics Engineering [Internet]. 2016;4(2). Available from: http://www.jtle.net/uploadfile/2016/1108/20161108041850649.pdf

52. Human Science Research Counsil (HSRC). South African National HIV Prevalence, Incidence, Behaviour and Communication Survey [Internet]. 2017. Available from: www.rienner.com

53. Fatti G, Ngorima-Mabhena N, Tiam A, Tukei BB, Kasu T, Muzenda T, et al. Community-based differentiated service delivery models incorporating multi-month dispensing of antiretroviral treatment for newly stable people living with HIV receiving single annual clinical visits: a pooled analysis of two cluster-randomized trials in southern Africa. 2021; Available from: http://onlinelibrary.wiley.com/doi/10.1002/jia2.25819/full|https://doi.org/10.1002/jia2.25819

APPENDICES

Appendix 1: Assessment of missing data using Little's MCAR test

Table of missingness in the data

	Observed	Missing	% Missing
Age	116	2	1.7%
Sex	117	1	0.8%
Marital status	3	115	97.5%
Race	110	8	6.8%
Nationality	117	1	0.8%
Level of education	114	4	3.4%
Employment status	111	7	5.9%
Baseline WHO status	32	86	72.9%
BMI	97	21	17.8%
Baseline CD4	93	25	21.2%
Baseline Hg	96	22	18.6%
AST	8	110	93.2%
ALT	96	22	18.6%
Lactate	0	118	100.0%
Viral load	88	30	25.4%

Little's missing completely at random (MCAR) Test

Little's test evaluates whether data are MCAR.

H_0: The missing data are Missing Completely At Random (MCAR)

H_1: The missing data are **not** Missing Completely At Random (MCAR)

```
Little's MCAR test

Number of obs       = 118
Chi-square distance = 121.2338
Degrees of freedom  = 103
Prob > chi-square   = 0.1060
```

Since the p-value > 0.05, we fail to reject the null hypothesis and conclude that the data are missing completely at random.

Appendix 2: Variance inflation factor (VIF) to assess multicollinearity

Logistic model for VL_12months_Sup, goodness-of-fit test

```
       number of observations =       113
number of covariate patterns =       100
            Pearson chi2(77) =       120.52
                 Prob > chi2 =         0.0011
```

Variable	VIF	1/VIF
Sex	10.62	0.094186
regcat	9.98	0.100176
age_cat	3.93	0.254540
baselineCD4	3.67	0.272260
educ	3.50	0.285966
ALT	2.69	0.371147
employed	2.69	0.371260
BMI	2.10	0.476045
race	1.65	0.605922
Mean VIF	4.54	

Appendix 3: Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Miss Zwannda Kwinda

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M200365

NAME: (**Principal Investigator**)	Miss Zwannda Kwinda
DEPARTMENT:	Epidemiology and Biostatistics Wits School of Public Health Helen Joseph Hospital
PROJECT TITLE:	Sex differences in Anti-retroviral Therapy outcomes among adolescents and young adults initiated on Anti-retroviral Therapy in Johannesburg, 2016 - 2017
DATE CONSIDERED:	27/03/2020
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Ms Idah Mokhele
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	04/09/2020

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

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions.Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. I **agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **March** and will therefore be due in the month of **March** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 4: Signed plagiarism declaration

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

FACULTY OF HEALTH SCIENCES

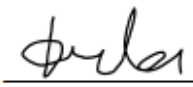
PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Zwannda Kwinda (Student number: 786532) am a student registered for the degree of MSc Epidemiology and Biostatistics in the academic year 2023.

I hereby declare the following:

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

Signature:  Date: 27 March 2024 [redacted]