FACTORS ASSOCIATED WITH VIROLOGIC FAILURE AMONG ADULT PATIENTS ON ANTIRETROVIRAL TREATMENT AT SELECTED HEALTH-CARE FACILITIES, LIMPOPO PROVINCE

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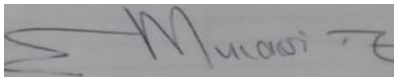
DECLARATION

I, **Mulaisi Tshimangadzo Ephraim**, declare that the dissertation for the Master's degree in Nursing at University of Venda, entitled ***"Factors associated with virologic failure among adult patients on antiretroviral treatment at selected health-care facilities, Limpopo Province."*** hereby submitted by me, has not previously been submitted for a degree at this or any other institution, that this is my own work in design and in execution, and that all material contained herein has been duly acknowledged.

Signature  **Date: 22/04/2021**

DEDICATION

This study is dedicated to:

My late mother Berlina Ntombi Sunduza and father Mulaisi Nyambeni Nathaniel, as well as my wife Mulaisi Precious and children Mulaisi Mahlatsi, Mulaisi Ndivho, Mulaisi Ronewa, and the rest of my family and friends, for their encouragement, and support throughout the study. This study is also dedicated to all HIV-positive patients experiencing virological failure, with the hope that this study will improve the quality of care to help them maintain their health.

In memory of my beloved mother, Ntombi, father, Nathaniel, and grandmother, Npfariseni.

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LIST OF ACRONYMS AND ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Treatment
ARV(s)	Antiretroviral Medication
HAART	Highly Active Antiretroviral Treatment
HIV	Human Immunodeficiency Virus
HTS	HIV Testing Services
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitor
PI	Protease-Inhibitors
UNAIDS	United Nations Organization on Acquired Immunodeficiency Syndrome
VCT	Voluntary Counseling and Testing
VF	Virological Failure
VL	Viral Load
WHO	World Health Organization

ABSTRACT

The Human Immunodeficiency Virus (HIV) is a lentivirus (a subgroup of retrovirus) that causes HIV infection and over time causes Acquired Immune Deficiency Syndrome. Highly Active Antiretroviral Therapy (HAART) is the medication whose main function is to hinder the progress from HIV into AIDS. It was introduced in Western countries in 1996. The main goal of HAART is to achieve maximal viral suppression.

A quantitative, descriptive, and cross-sectional research design was used to describe factors associated with HIV treatment failure. Clinical records were reviewed retrospectively using the purposive sampling as per inclusion and exclusion criteria of adults who are living with HIV (67 males and 184 females) making a total of 251. These adults commenced their ARV's treatment between April 2003 and December 2018 at 4 selected facilities. Data were collected using self-developed check list. All data were collected using data from an existing electronic patient management system (tier.net). The 251-checklist was then analyzed utilizing the Statistical Package for Social Sciences (SPSS, version 28). Descriptive statistics were used to analyze and describe and summarized data.

Results: association of gender and virologic failure of the adult patients experiencing virologic failure were females with 73.3% and males with 26.7%. With regards to CD4 count: 23.1% of adult patients had the CD4 count of <100 cells/mm on ART initiation, 26.9% had 100 – 200 cells/mm, 31.1% had 201 -350 cell/mm, and 18.9% had >350 cells/mm. WHO clinical staging on ART initiation was 34.3% for stage 01, 36.8% for stage 02,22.8% for stage 03 and 6% for stage 04. ART start regimen; regimen 1a accounted for 92%, followed by 5.9% for regimen 1b and 1.9% for regimen 2. TB and HIV co-infection at ART initiation resulted in 19.2% of the clients experiencing treatment failure as they TB during ART initiation. Viral load results at 12-month were 55.8% for 0 – 1000 copies/ml, 12.9% for 1000 – 10000 copies/ml, 23.5% for 100000 – 1000000 copies/ml and 1.4% for >1000000 copies. Missed appointments: 9.2% clients never missed appointment, 6.4% missed 01 month appointment, 21.6% missed 02 months appointments, 27.9% missed 03 months appointments and 34.7% missed more than 3 months appointments. Lost to follow up: 42% have not been lost to follow-up during the last 24 months, 12% lost to follow-up for 3 months, 15.6% lost to follow-up for 4 months, 17.2% lost to follow-up for 5 months, 4.4% lost to follow-up for 6 months and 8% lost to follow-up for more than 6 months.

Prolonged duration on ART: 4.9% of the clients experiencing virologic failure have been on ART for 2 years, 7.8% for 3 years, 9% for 4 years, 12% for 5 years and 66.1% for more than 5 years.

All ART doctors/nurses should assess these patients' latest viral load results during each visit and assess for signs of treatment failure.

Keywords: Factors, HIV virological failure, HIV treatment, adult patients, Antiretroviral treatment

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CHAPTER 1

OVERVIEW OF THE STUDY

INTRODUCTION

HIV is a human immunodeficiency virus that targets the immune system and weakens the human defense system against infections that human with healthy immune system can fight off (WHO, 2021). The virus gradually destroys the immune system targeting the cd4 cells, over time HIV comes into the most advanced stage of infection acquired immunodeficiency syndrome (AIDS), which can take many years to develop if the virus is not treated, depending on the individual immune system (WHO, 2021) The cornerstone of HIV treatment is highly active antiretroviral therapy (HAART), which achieves maximum viral replication suppression (Rathbun, 2018). Despite HAART, some patients have an increase in viral load, which frequently leads to the selection of resistant viral variants and disease progression (Adult antiretroviral therapy guidelines 2017). Treatment failure is defined as a plasma viral load of more than 1000 copies/ml after three months, as determined by two consecutive viral load assays with adherence support (WHO, 2021). Before it can be judged that an ART regimen has failed, an individual must have been on it for at least 6 months (WHO, 2019). HAART, on the other hand, entails the administration of at least three antiretroviral drugs in tandem to achieve maximum viral suppression (WHO, 2017).

1.1 BACKGROUND OF THE STUDY

Global HIV and AIDS statistics and features:

In June 2021, 28.2 million individuals worldwide had access to antiretroviral treatment. In 2020, 37.7 million people worldwide were infected with HIV (UNIAIDS, 2021). In the year 2020, 3.7 million individuals worldwide were living with HIV, including 36 million adults. In 2020, 84% of all HIV-positive people in the world were aware of their status. Furthermore, 87% of people who knew their HIV status were receiving antiretroviral treatment, with 90% having suppressed viral load and 10% having an unsuppressed viral load (UNIAIDS, 2021).

Regional HIV and AIDS statistics and 90 90 90 progress:

At the end of 2020, 5.8 million people were living with HIV in Asia and the Pacific. 76% of adults living with HIV in Asia and the Pacific were aware of their HIV status. In 2020, 64% of adults living with HIV in the area received antiretroviral treatment. The number of HIV-positive people who have achieved viral suppression has increased from 45% in 2017 to 61% by 2020 (UNIADS, 2021).

At the end of 2020, around 20.6 million people in eastern and southern Africa were living with HIV, 19.5 million of people living with HIV were adults from the age of 15 and above. 90% of all HIV-positive adults in the area knew there HIV status, 78% of people living with HIV were receiving antiretroviral treatment (UNIADS, 2021). The number of HIV-positive patients who were on treatment and has achieved viral suppression has increased from 52% in 2017 to 72% by 2020 (WHO 2021, UNIAIDS, 2021). In Botswana, 370 000 people were living with HIV in 2020. 362 500 people living with HIV were adults age 15 and above. Those living with HIV who knew their status made up 91%, those living with HIV and were on treatment made up 87%, and those living with HIV who were virally suppressed made up 85% (UNIAIDS, 2020). As a result, Botswana is close to meeting the 90-90-90 testing and treatment targets. In 2020, there were 1 390 200 adults living with HIV infection in Uganda; adults living with HIV who knew their status made up 91%, those living with HIV who were on treatment made up 90%, and those who were virally suppressed made up 82% (UNIADS, 2021).

In 2020, there were 1 400 000 people living with HIV infection in the United Republic of Tanzania; 1 240 000 of all people living with HIV Tanzania were adults age 15 and above. 84% of people living with HIV know their HIV status, 82% of those living with HIV were on treatment (UNIAIDS, 2021). According to the findings of a research done in Tanzania on HIV virological failure and drug resistance in a cohort of HIV-infected people, virological failure occurred at a rate of 14.9%. Lower CD4 count and non-adherence to ART were both predictors of virological failure. Early ART initiation and adequate adherence are critical for first-line ART success and durability in these settings (Hawkins, at al., 2016).

With an estimated 7.8 million people living with HIV in 2020, South Africa has the world's largest and most visible HIV epidemic. 7 490 000 people living with HIV were adults age 15 and above, people living with HIV who knew their status account for 92% of those living with the virus; those on treatment account for 72%, and those who are virally suppressed account for 66% (UNAIDS, 2020). South Africa has the world's biggest antiretroviral therapy (ART) program, which is mostly funded by local resources. The nation currently spends more than R22.9 billion on its HIV and AIDS program each year (UNAIDS, 2018). In 2014, South Africa adopted the 90 90 90 HIV targets, which aim to ensure that by 2020, 90% of people living with HIV are aware of their status, 90% of people diagnosed with HIV are receiving sustained antiretroviral therapy, and 90% of people receiving antiretroviral therapy have viral suppression.

A systemic review and meta-analysis study conducted by Lailulo (2020), on factors associated with antiretroviral treatment failure among people living with HIV on antiretroviral treatment in resource-poor setting. The results indicated that antiretroviral treatment failure

was nearly 6 times higher among patients who had a history of poor adherence to antiretroviral treatment as compared to patients with a good history of antiretroviral treatment adherence. The chances of antiretroviral treatment failure was almost 5 times higher among patients with cd4 <200 cells compared to those with cd4 >200 cells (Lailulo, 2020). The study highlighted that poor adherence and low cd4 cells were associated with antiretroviral treatment failure (Lailulo, 2020).

A prospective cross sectional study conducted by Bereda (2021), on prevalence and factors influencing First Line antiretroviral treatment failure among adult patients at antiretroviral treatment clinic of Mettu karl referral hospital. The results of the study highlighted the duration on antiretroviral treatment of >6 years and a baseline WHO clinical stage 3/4 were associated with first line antiretroviral treatment failure among adult patients (Bereda (2021)).

An observational cohort study conducted by Drova (2017), at Sedibeng, Gauteng Province, Gert Sibande, Mpumalanga Province, Ugu & King Cetshwayo District, KwaZulu-Natal Province, Alfred Nzo, Eastern Cape Province. The goal of the study was to find out what variables are linked to an unsuppressed viral load (>1000 copies/mL) in patients who have been on first-line ART for 6 months or more, in order to guide interventions to improve viral load suppression in patients who use public healthcare in South Africa. The findings revealed that 85% of patients on ART for more than six months with a viral load on record were virally suppressed, which is close to the national aim of 90% of ART patients being virally suppressed (90-90-90 targets). Being a male gender and/or child/adolescent at the time the patient started ART, being on ART for a duration of more than 5 years, patients with CD4 cell count of less than 100 at the time of initiation and patients who were on TB treatment were found to be the greatest predictors of unsuppressed viral load (Drova, 2017).

1.2 PROBLEM STATEMENT

HIV and AIDS remain a serious developmental concern for South Africa, which continues to have one of the world's highest HIV prevalence rates. In 2014, South Africa set the 90-90-90 targets for HIV, with the goal of ensuring that out of all the people living with HIV, 90% of them know their status, out of all the people who know theirs status, 90% of them should be on ART, lastly out of all the people on ARV's, 90% of them by 2020 should be virally suppressed. The researcher is a professional nurse who works with HIV patients, and he has seen a high percentage of patients who are failing to respond to the first-line ART regimen. In September 2016, South Africa began implementing universal test and treat (UTT) with the hope that they can attain the UNIADS 90 90 90 targets by 2020. The UTT requirements state that all HIV-positive clients should be put on antiretroviral treatment

(ART), clients who test positive for HIV are to be enrolled on antiretroviral treatment (ART), and those who satisfy the criteria are started on first-line medication straightaway (Onoya, at,al,. 2021). Because of the large number of clients registered on ART, the Blouberg sub-District has a significant number of facilities with suppression rates below 90%, with a total suppression rate of 85%. Some facilities have a total of 831 patients under their care, with 82% suppression rate 12 months after commencing ART. Some of the facilities contain a substantial number of virologically unsuppressed clients; 549 clients had their blood tested for viral load; 465 were virologically suppressed, with an 85% suppression rate 12 months after commencing ART. Other facility in Blouberg sub-District began implementing ARVs program in 2009, though the rate of suppression is still around 85%.

With regards to the 90 90 90, the researcher discovered a gap in the Blouberg sub-District, which had a suppression rate of 85%. This implies that 15% of clients in the Blouberg sub-district are on treatment but not yet virally suppressed. The treatment aims to maintain viral suppression. Virologically suppressed clients have the lowest risk of infecting others. In the Blouberg sub-district, 15% of clients are on treatment yet remain infected, posing a risk of transmission of the resistant virus. Other provinces and hospitals have performed research on the variables that contribute to HIV treatment failure among people on first-line antiretroviral treatment, but Blouberg Municipality has not. Given the foregoing, the researcher determined that a study in the Blouberg Municipality was required.

1.3 THE RATIONALE OF THE STURDY

HIV and AIDS remain a serious developmental concern for South Africa, which continues to have one of the world's highest HIV prevalence rates. In 2014, South Africa set 90 90 90 targets for HIV, with the goal of ensuring that, out of all the people living with HIV, 90% of them know their status, out of all the people who know theirs status, 90% of them should be on ART, lastly out of all the people on ARV's, 90% of them by 2020 should be virally suppressed. The viral load suppression rate in South Africa is 66% of patients living with HIV who are virally suppressed (UNIAIDS, 2021). This suggests that, despite current attempts to sustain viral suppression, South Africa failed to reach the UNIAIDS 90 90 90 targets by 2020. Different studies have been conducted on virological failure in HIV positive people on ART in Limpopo and South Africa, but not much has been done in the recommended locations.

1.4 STUDY PURPOSE AND OBJECTIVES

1.4.1 Purpose

The purpose of the study was to:

To determine the factors associated with virologic failure among adult patients on antiretroviral treatment at selected health-care facilities, Limpopo Province.

1.4.2 Objectives

The objectives of the study were to:

- To describe the correlation of antiretroviral treatment failure with the demographic variable's routinely measured at the clinic namely age and gender of all adult patients on antiretroviral treatment with virologic failure at selected health care facilities.
- To describe the correlation of antiretroviral treatment with the clinical variables routinely measured at the clinic visits namely WHO clinical stage, cd4 count, viral load, presence of co-infection and adherence of adult patients on antiretroviral therapy with virologic failure at selected health care facilities.

1.5 SIGNIFICANCE OF THE STUDY

The number of individuals with significant treatment failure may be decreased, which may benefit participants and communities. Clients may be able to stay on first line for longer, which may enhance their quality of life. First-line regimen is a simplified and less toxic drug combination harmonized for the management of HIV, retaining clients in this line may improve adherence. The second-line combination's pill burden might be lowered, and viral load could be controlled, lowering the number of new infections. More patients may stay on the first-line regimen as a result of this research, which might assist the Department of Health to enhance the quality of life. The DoH may gain some insights on the phenomenon and develop strategies to improve the first-line retention.

Thus, fewer people might be switched to the second line. The second-line regimen is more expensive and increases the pill burden; thus, the DoH will save more funds. The body of knowledge might get more details of the phenomenon, as the study might be able to come up with new ideas to be added to the body of knowledge and may form the basis of further research to improve on the phenomenon. The policy makers or designers may benefit, as they will be able to adjust the policy to be more user-friendly, to booth the caregivers and the clients. The new policy that may be developed might be more beneficial to all the users and might improve the quality of care.

1.6 THEORETICAL FRAMEWORK

A theoretical framework is a blue print or guide for the researcher (Adom, 2018). The overall aim of the theoretical framework is to guide researcher findings more meaningful (Adom, 2018). A framework is the overall conceptual underpinning of a study.

Health Believe Model (HBM)

The Health Belief Model (HBM) is a tool that is used by the scientists to try and predict the health behaviors (Boskey, 2022). The HBM is derived from psychological and behavioral theory with the basis that the two components are one: this modeling is based on one's desire; the desire to not get ill or to get well if ill already, and the belief that one can take specific action that will prevent or cure illness (Wayne, 2019). The HBM proposes that one's own believes about health predicaments, perceived benefits of action, and self-efficacy together with barriers to action accounts for the engagement or lack of it thereof in health-promoting behaviors. When the HBM is applied correctly, it provides a structured assessment of data about patients abilities and if patients are motivated to change their health status (Wayne, 2019).

1.7 DEFINITION OF TERMS

- **Adults**

An adult is a mature, fully developed person. A legal adult is a person who has attained the age of majority and is thus considered autonomous, self-sufficient, and accountable for their acts. The normal age of legal adulthood is 18, yet this varies depending on legal rights and country (Simpson, 2020).

- **Antiretroviral treatment (ARVs)**

Anti-retroviral treatments (ARVs) these are therapeutic drugs that aids in the reduction of HIV levels in the patient. These drugs are categorized based on their mechanism of action, and their categories are namely: fusion inhibitors, non-nucleoside reverse transcriptase inhibitors (NNRTI), nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs) and protease-inhibitors (PI) (WHO, 2017).

In this study, antiretroviral treatment (ARVs) refers to any combination of different groups of ARVs in use which includes fusion inhibitors, non-nucleoside reverse transcriptase inhibitors (NNRTI), nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs) and protease-inhibitors (PI).

- **ART regimen First Line**

The initial combination of antiretroviral drugs is prescribed for an eligible HIV-infected patient. The recommended regimen for adults is made of 3 drugs, 2 NRTIs and 1 NNRTI (WHO, 2017).

In the present study, ART first line refers to the adult's initial combination of antiretroviral drugs prescribed for an eligible HIV-infected patient.

- **Human Immunodeficiency Virus (HIV)**

Human Immunodeficiency Virus (HIV) is a retrovirus that primarily infects vital components of the human immune system and is the virus that causes AIDS (WHO, 2017).

- **HIV Virologic failure**

HIV virologic failure is defined as persistent Viral Load (VL) >1000 copies/mL on two consecutive occasions, two months apart, with intensive adherence support between the two tests (DOH, 2015).

In the present study, HIV virologic failure will be referred to as adults persistent viral load >1000 copies/mL on two consecutive occasions, two months apart, with adherence support between the two tests 12 months after starting treatment.

1.8 SUMMARY

In this chapter the question of the research study was introduced and the concepts were defined and described. The overview of HIV/AIDS and ARV's together with virological failure descending from the global views to bub-Sahara and narrowed down to South Africa was discussed. The problem statement, purpose, objectives and significance of the study were indicated together with the theoretical framework of the study. The next chapter focuses on literature review.

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

Literature review is a process of reading, analyzing, evaluating, and summarizing scholarly materials about a specific topic. Its purpose is to summarize, synthesize, and analyze other people's ideas. A literature review is a critical examination of previous research that is relevant to the work you are doing (Creswell, 2019). The purpose of this chapter is to evaluate the evidence on variables linked to virologic failure in adult antiretroviral patients. The primary goal of a literature review is to familiarize the reader with the study in question as well as other researchers work on comparable topics.

2.2 ADDRESSING THE PROBLEM OF HIV

HIV is divided into two types: HIV-1 and HIV-2; of the two types of HIV, HIV-1 is the most common, and about 95% 0f people living with HIV around the world have HIV-1 (Seladi-schulma, 2021). HIV-1 is a type of retrovirus that is believed to have originated from a common virus in chimpanzees; it is believed that the virus was transmitted to humans when they come into contact with the blood of the chimpanzee they had hunted. When a human is infected with HIV, the virus begins to infect a specific type of immune system called cd4 cells; these are cells that are responsible for helping to coordinating the body's immune response (Seladi-schulma, 2021). When HIV is not treated with antiretroviral treatment, the virus continues to deplete the cd4 cells and it becomes harder for the immune system to deal with infections and certain types of cancers, the latest stage of HIV infection is called AIDS (Saladi-schulman, 2021).

With an estimated 37.7 million people living with HIV globally in 2020, the human immunodeficiency virus (HIV) pandemic remains a serious global public health concern (UNAIDS, 2021). In 2020, 1.5 million people got newly infected with HIV, 680 000 people died of AIDS-related diseases, and AIDS related mortality has declined by 53% since 2010 (UNAIDS, 2021).

In Eastern and Southern Africa, there were 20.6 million people living with HIV in 2020. Women and girls account for more than half (59%) of the overall number of people living with HIV in the region (WHO, 2019). Eastern and southern Africa account for more than half of all HIV infections worldwide 54.6% (UNAIDS, 2021). As a result of this public health issue, countries in Eastern and Southern Africa began implementing and scaling up ART in the public sector. This rapid scaling up of antiretroviral treatment (ART) has been one of

Eastern and Southern Africa's success stories in the fight against the HIV epidemic, with coverage rising from roughly 2% in 2003 to more than 78% in 2020. (UNAIDS, 2021).

2.3 ADDRESSING THE PROBLEM OF HIV VIROLOGIC FAILURE

The objective of highly active antiretroviral treatment (HAART) is to utilize at least three antiretroviral drugs in combination to achieve maximum viral suppression (DOH, 2019). In the context of HAART, however, if HIV patients do not adhere to medication, their odds of sustaining sustained viral suppression are reduced, leading to a rise in viral load, a condition known as virological failure (WHO, 2019). When a person on treatment has a viral load of more than 1000 copies/ml on two occasions two months apart in South Africa, it is deemed as virological failure, and the complete adherence concerns are addressed (DOH, 2019). According to WHO (2019) the early alarming signs indicating drug resistance has been identified as virological failure, moreover since SA's individuals under drug resistance monitoring, thus in this setting it is highly feasible to consider measuring virological failure as a resistance surrogate

At the end of 2020, about 27.5 million people worldwide were accessing antiretroviral treatment (WHO, 2021). However it also poses a threat in public health that could render null and void the benefits these therapies provides, provided new infection takes place wherein HIV virus strains which has genetic resistance characteristics over current therapies is acquired (WHO, 2021). Minimizing the spread of resistant strand of HIV is vital aspect for the broader global response. There have been remarkable reductions in rates of mortality and morbidity where HAART has been made available to HIV-infected people together with an increased quality of life, and a shift in the perspective of HIV infection from a death sentence to a manageable chronic condition (WHO, 2017).

2.4 THE 90–90–90 TARGETS

The 90-90-90 targets are that out of all the people living with HIV, 90% of them know their status, out of all the people who know theirs status, 90% of them should be on ART, lastly out of all the people on ARV's, 90% of them by 2020 should be virally suppressed. Modeling exercises that was conducted by Marinda (2020) stipulated that achieving the 90-90-90 targets could minimize the figures of new infections such that by 2030 we have achieved the HIV/AIDS epidemic control. WHO, in 2015 came with the recommendation which states that people who test positive for HIV should be initiated on ART same day, which is commonly known as universal test and treat (UTT) approach. South Africa by September 2016 issued out the UTT treatment guidelines for all public healthcare sectors following the adoption of UTT.

According to UNIAIDS (2021) South Africa is said to have contributed about 20% of the 37.7 million global population of people living with HIV (PLHIV), this contribution is from South Africa's 7.8 million estimated number of PLHIV in the country. In the very same year, the modeling of the 90-90-90 global indicator were derived from the 92% of PLHIV who knew their status, out of the total population of 72% of the people who knew their status, 79% of them were on treatment and 66% of the people who were on treatment were virological suppressed (UNIAIDS, 2021). For South Africa according to the 2015 Tembisa model, the estimates puts the indicators at 85.5% of the population which knew their status of HIV, and 56.9% for the ones on ART who know their status of HIV, lastly 78.4% for those on treatment were virological suppressed.

2.5 CULTURAL BELIEFS ON HIV/AIDS

- **Practices involving blood or other body fluids**

Scarification, male circumcision, and genital tattoos have all been implicated as possible sources of infection, particularly when done on groups. Through several theoretical mechanisms, female genital cutting (FGC) is frequently argued to be predisposed to HIV infection (Tholoana, 2011). The operation is historically conducted in a variety of methods, ranging from clitoral prepuce removal to vulva excision and partial closure of the vaginal introitus (Tholoana, 2011). HIV might theoretically be transferred directly through the use of septic instruments or through the practitioner's blood being injected into the female's open wounds (Tholoana, 2011).

Male circumcision has been found as a cultural element that protects men (Gazimbi, et al., 2019). The benefit of voluntary male medical circumcision (VMMC) is to reduce the spread of HIV. The VMMC program has been used with intend to reduce the spread of HIV in the Eastern and Southern Africa (Luseno, 2021). WHO and UNIAIDS recommended VMMC to be offered as part of comprehensive package of HIV prevention in high prevalence settings like Eastern and Southern Africa.

- **Religion and religiosity**

South Africa has the largest religious affiliation which is the Christian church, these Christian churches has been involved in the HIV epidemic since it was identified in the 1980 (Alio, et al., 2019). The church stand on sexuality is that you can only have sex inside of marriage, hence the traditional common relationship practices are of having multiple sexual partners outside of marriage, these leaves the church with the complex relationship with HIV/AIDS (Alio, et al., 2019). In South Africa churches reaction toward HIV varies from silently ignoring

HIV to openly condemning those who have been having multiple partners and the need for them to repent thir sins, these condemnations result in stigma against the HIV disease and its victims (Alio, et al., 2019)

In some churches disclosing HIV status may lead to rejection and criticism from the Christian community, and also keeping silent about positive HIV status may undermine the person's ability to cope with the infection (Alio, at al., 2019. In some case the person level of religiosity, that is their faith and belief, has been found to influence the person to look to religious leader for a spiritual healing rather than taking treatment, these type of practice can make a person to stop taking treatment in the hopes that they will receive a spiritual healing (Alio, at al., 2019)

- **Gender relations and norms**

In Sub-Saharan Africa, where HIV rates in women are significantly higher than in males, culturally sanctioned gender relations play an especially important role in the HIV/AIDS epidemic (UNAIDS, 2017). Gender Based Violence (GBV) have been found to be associated with disparity in HIV prevalence between genders, GBV contribute to an estimated 20% to 25% of new HIV infection in young woman (Klaas, at al., 2018). Gender inequalities and economic superiority of men over woman have significant health implications in the spread of HIV infection, according to South African National AIDS Coucil (SANAC) HIV prevalence among young woman in South Africa to be nearly four times higher than of men of the same age (Klass, at al., 2018). In 2016 young woman between the age of 15 – 24 made up to 37% of all new HIV infection in the country (Klass, at al., 2019).

The inequitable gender norms has been observed to have a negative health outcome related to HIV infection and HIV prevention, inequitable gender norms include; men should have the power to make all major decisions for the house hold, woman are to solely responsible for bringing kids to the household or pregnancy prevention, the husband have the right to be physically violent with the wife if she does not obey his commands (Pulerwits, 2019). The inequitable gender norms in some case allows men to have multiple sexual partners, intimate partner violence, less condom use or no condom use depending on the men (Pulerwits, 2019).

2.6 THE KEY COMPONENTS AND CONSTRUCTS OF HBM

- **Perceived Susceptibility**

When coming to HBM perceived susceptibility is the first concept, this concept deals with the individuals beliefs regarding the possibility of acquiring health condition (Wayne, 2019). Once perception that a problem relating to health is personal it will enhance ones decision making towards protecting self against such health a problem (Boskey, 2022). In order for

that to occur one ought to be exposed to knowledge and understanding which sharpens the perception of how one becomes vulnerable to a particular health condition. These individuals who perceive themselves as proned to virological failure are often likely to can execute measures which can protect themselves from virological failure (Boskey, 2022).

- **Perceived Severity**

This HBM is the second concept that deals with one's beliefs pertaining to the severity of a condition and the consequences thereof (wayne, 2019). This concept bring to spot light that though one can be susceptible of a condition, that alone guarantees not that one will fill the edge to make use of preventive measures against such a condition, save if such an individual is bearing the knowledge of social and severe physical implication the condition has. When one gets to understand the vast negative outcome of a condition, one often feels the edge to act according to the prescribed measures to can avoid the consequences (Boskey, 2022). People ought to consider HIV virological failure as a serious condition that bears detrimental outcome to one's physical and social life, prior to one welcoming preventative measures against HIV virological failure.

- **Perceived Benefits**

This refers to the beliefs of one self when coming to the efficacy of recommended action to can aid in the reduction of risk relating to the impact (Wayne, 2019). An individual ought to have a positive mindset that particular recommended actions if executed as per recommendations it can reduce the complications of the condition (Boskey, 2022). The HBM places on the table that adhering and complying to ARV's as per guidelines it can lead to the reduction of HIV virological failure

- **Perceived Barriers**

These barriers focus on the benefit of an individual in relations to the cost of the behavior which an advice aligns with (Boskey, 2022). There are diverse barriers that can hinder one from acting accordingly as to can avoid certain outcome(s). The barriers may be due to the costs of an action which need to be taken, the duration it will take prior to meeting desired outcome(s), personal character and the demography though not only limited to such. Hence if an individual can therefore reach a point wherein he/she realizes that he/she can overcome the barrier by certain means, such an individual is more likely to can opt for the actions which need to be executed (Boskey, 2022).

- **Cues to Action**

The cues to action HBM refers to encounters that and individual faces be if personal or environmental and the likes that can fuel an individual to comply with certain prescribed action (Boskey, 2022). This comes to play when an individual gets to have an edge to do as one is told by believing it will help ease the situation. Cues to action often requires some sorts of motivation on the parties involved to can have the willpower and to do as per prescribed action having concern about health matters and being submissive to health care which is believed to can alleviate one's condition.

- **Self-Efficacy**

This concept in the HBM is all about being confident with self, to can act/respond accordingly against an unpleasant situation and any setbacks that can be encountered (Wayne, 2019). One ought to be confident enough to can take any action, sustain such action until desired outcome(s) is/are met, likewise with HIV virological failure, patient's ought to be confident enough that they will act accordingly to prevent such (Boskey, 2022).

Factors related to HIV virological failure and its implications

In the South Africa, virological failure is defined as failure to achieve or sustain suppression of HIV viral load less than 1000 copies/ml, and virology suppression is defined as a confirmed viral load of below 1000 copies (NDOH, 2019). There are a number of causes of HIV virologic failure namely: poor adherence to antiretroviral treatment, poor drug absorption of the antiretroviral treatment, adverse drug interactions and infection with drug resistant HIV (Orrell, at al., 2020). Study conducted by Desalegn (2021), on determinants of antiretroviral treatment failure, the study findings was that there was a higher chance of developing treatment failure among; those who were initiated on antiretroviral treatment at an advance stage (WHO clinical stage 3 or 4), those who were initiated on antiretroviral treatment while their cd4 cells was <100, those with the history of antiretroviral treatment discontinuation for more than 1 month and those with the history of poor adherence to antiretroviral treatment.

The goal of antiretroviral treatment is to suppress the viral load replication, restore the immune response, halt in the disease progression, increase the survival rate, reduce morbidity and improve the quality of life (Lenjiso, at al., 2019). Failure to reduce the HIV viral load can lead to severe consequences this include the following: the evolution of drug resistance HIV that can be spread causing new infection to be resistant, immunological and clinical failure that can make an infected person to develop life threatening co-infections, increase in HIV related death and clients experiencing antiretroviral treatment

failure will need to be switched to more expensive antiretroviral treatment that will be more expensive for the department of health to sustain (Lenjiso, at al., 2019).

2.8 SUMMARY

This chapter discussed the literature review section which focused on addressing the problem of HIV, addressing the problem of HIV virologic failure, the 90–90–90 targets, and cultural beliefs on HIV/AIDS. The next chapter described the research methodology section.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 INTRODUCTION

This chapter discusses research methodology, which lays out a logical research process as well as the techniques and procedures that are used to answer the study's purpose and objectives. The study's goal was to find out what variables were linked to virologic failure in adult antiretroviral treatment patients in Limpopo Province's health-care institutions.

3.2 RESEARCH APPROACH

Quantitative research approach was employed in this study of the phenomenon, this approach is an investigation which is done systematically making use of mathematical calculation, statistical approach or computerization to can evaluate the results and prove the theory/hypothesis (Creswell, 2019). This was chosen by the researcher as the measure to evaluate data via usage of statistics to obtain the final results that could be generalized. Quantitative approach was used to determine diverse factors which may be related to virological failure when coming to adults patients who are on ARV's treatment at selected health-care facilities in Limpopo Province.

3.3 RESEARCH DESIGN

A cross-sectional design was adopted, which is a form of observational study design based on retrospective review. In cross-sectional investigations, cross-sectional regression is commonly used to determine the existence and size of causal effects of one independent variable on a dependent variable of interest at a specific moment in time. In cross-sectional research study design, the researcher assesses the outcome and exposures simultaneously in the study participants. The records of participants were chosen based on the study's inclusion and exclusion criteria. A cross-sectional design was chosen because participants in cross-sectional research are only recruited based on the study's inclusion and exclusion criteria at a single moment in time. Following the study to assess the causal relationship which exists between both variables of interest at a given point in time, the researcher was able to assess the relationship between both variables.

3.4 STUDY SETTING

The setting will be at the Blouberg sub-district in Capricorn District of Limpopo province of South Africa. According to the Statistics South Africa poverty trends report (2017), Eastern Cape and Limpopo Province have remained among the poorest provinces since 2011.

Limpopo Province has 5 Districts: Mopani, Vhembe, Capricorn, Waterberg, and Great Sekhukhune.

Figure 3.1: Geographical map of Capricorn District

The Blouberg sub-District is located in the Capricorn District of the Limpopo Province, in northern South Africa, near the borders of Zimbabwe and Botswana. There are 24 clinics, 4 mobile clinics, and 2 health facilities in the Blouberg sub-district. The rural area dominates the Blouberg sub-district, which has a population of at least 172601 people in 2016. The villages are surrounded by mountains, and residents travel to the health facility in personal cars, taxis, and carts. Blouberg is a hot area, with yearly rainfall ranging from 380 to 550mm, with the majority of rain falling during the summer months. Boreholes provide pure water to the villages, which they may drink and use. Since 2009, several health-care facilities have been designated as antiretroviral treatment roll-out sites. During the trial period, all treatment-eligible patients are started on ART at these clinics. Hellen Franz Hospital is a reference facility for Blouberg Health Care Facilities.

3.5 STUDY POPULATION

3.5.1 Population

A population, according to Zeiler (2018), is the complete group that fits the criterion that the researcher is investigating. According to Creswell (2019), a population is the total number of cases in research that match a specific set of criteria. According to Burns and Grove (2016), a population is defined as all potential participants who meet the sampling requirements for inclusion in a research project. All adult HIV clients aged 18 and above who were experiencing virologic failure 24 months after starting ART at Blouberg Municipality were included in this research.

TABLE 3.1: POPULATION FRAME ADULTS REMAINING IN CARE AT BLOUBERG SUB-DISTRICT FACILITIES JUNE 2018 (BLOUBERG SUB-DISTRICT TIER.NET 2018).

Name of the facility	Total adult client experiencing treatment failure	Total number of adults clients remaining in care	Facility viral suppression rate
Alldays Clinic	69	620	89%
Ambergate Clinic	25	282	91%
Blouberg CHC	101	674	85%
Buffelshoek Clinic	121	673	82%
Burgerecht Clinic	6	79	92%
De Vrede Clinic	35	319	89%
Gideon Clinic	4	175	98%
Goedentrou Clinic	10	89	88%
Grootdraai Clinic	13	166	92%
Indermark Clinic	68	574	88%
Kibi Clinic	37	269	86%
Krantzplaas Clinic	6	30	80%
Kromhoek Clinic	11	176	94%
Lesfontein Clinic	40	267	85%
Montz Clinic	11	95	88%
My Darling Clinic	27	113	79%
Ratshaatshaa CHC	38	380	90%
Rosenkrantz Clinic	25	170	85%

Sadu Clinic	13	44	69%
Schoongezicht Clinic	15	156	90%
Seakamela Clinic	149	830	82%
Taaibos Clinic	38	320	88%
Towerfontein Clinic	38	274	86%
Uitkyk Clinic	00	35	100%
Zeist Clinic	11	135	92%

3.5.2 Target Population

According to Creswell (2019) target population refers to a specific group of participants/persons of interest which the researcher longs to generalize the outcome over. The participants in this research were all adult HIV patients aged 18 and above who were exhibiting virologic failure 24 months after ART at designated health care institutions in the Blouberg sub-District of Limpopo Province.

3.6 Sample and sampling

3.6.1 Sample

A sample is a subset of a wider set of population elements deliberately selected by the researcher to participate in a research study, and it comprises the elements of inquiry from a defined population (Creswell, 2019). A sample is a representative sample of the study's target population. In this study, the sample for each health institution was recruited from a pool of HIV-positive people who had failed to respond to treatment and satisfied the inclusion criteria.

3.6.2 Sampling

According to Creswell (2019), sampling is all about selecting a specific group of population to can serve as the ones which represent the overall population. Sampling refers to the researcher's selection of specific cases for the study (Creswell, 2019). The researcher chose data from all adult HIV clients aged 18 and above who were having virologic failure 24 months after initiating ART at designated health care institutions in the Blouberg sub-District of Limpopo Province for this study.

3.6.2.1 Sampling of health care facilities

Non-probability sampling with purposive sampling was used to select 4 facilities with high statistics of patients with virologic failure. Following the 90 90 90 strategy, which calls for; out of all the people living with HIV, 90% of them know their status, out of all the people who know theirs status, 90% of them should be on ART, lastly out of all the people on ARV's, 90% of them by 2020 should be virally suppressed, and due to the high number of clients enrolled on ART and remaining on care 24 months after staining antiretroviral treatment. The researcher purposefully selected facilities that had 85% suppression rate or less also looking at the facilities with minimum total clients remaining in care of 250 and above. Facilities with virological suppression rate of >85% and facilities with <250 total clients remaining in care were excluded. Seakamela clinic has a total of 830 adult clients remaining in care and an 82% suppression rate, Blouberg Health Centre has a total of 674 adult clients remaining in care and ans 85% suppression rate, Buffelshoek clinic has a total of 673 adult clients remaining in care and an 82% suppression rate, and Lesfontein clinic, has a total of 267 adult clients remaining in care and an 85% suppression rate. These facilities were chosen based on the lowest viral suppression rate (less than 85%) and the highest number of clients. The chosen facilities provide a significant contribution to the Blouberg sub-District municipality's total suppression rate of 83%. The majority of Blouberg's facilities are now at or over 90% capacity. However, none of the top five facilities with a big number of clients are above 90%, contributing to the enormous number of clients who are experiencing treatment failure.

TABLE 3.2: SAMPLING FRAME OF THE SELECTED FACILITIES REMAINING IN CARE JUNE 2018 (BLOUBERG SUB-DISTRICT TIER.NET 2018).

Name of the facility	Total adult client experiencing treatment failure	Total number of adults clients remaining in care	Facility viral suppression rate
Seakamela clinic	149	830	82%
Buffelshoek Clinic	121	673	82%

Blouberg health center	101	674	85%
Lesfontein clinic	40	267	85%
Total	411	2444	83%

3.6.4 Inclusion criteria

Eligibility criteria for inclusion in the analysis:

- All records of adult HIV patients aged 18 and above who have a viral load (VL) of >1000 copies/mL, 24 months or more after starting ART and have been on treatment for 24 months or longer in the selected facilities.
- All records of adult HIV patients aged 18 and above who had a viral load (VL) of >1000 copies/mL, 24 months or more after initiating antiretroviral treatment (ART) at selected facilities Blouberg sub-District Limpopo Province in June 2021.
- All records of adult HIV patients aged 18 and above who had a viral Load (VL) of >1000 copies/mL, 24 months or more after initiating ART and continuing in care at chosen institutions on the 20th of June 2021.

3.6.5 Exclusion criteria

- All the records of HIV clients less than 18 years of age
- All the records of all adult HIV clients with viral load (VL) >1000 copies/mL, 24 months or more after starting treatment and has less than 24 months on ART
- All the records of adult clients with no documented viral load results

3.7 MEASUREMENT INSTRUMENT

After extensively examining the literature on the variable of interest, the researcher created a checklist. The researcher was led by the literature in developing a checklist. The study's checklist was created with the goal of acquiring chosen data lists from the current patient monitoring system (ePMS) (tier.net) database at selected Blouberg municipality health care institutions. Since 2011, the designated facilities have been using this computerized database. It is South Africa's primary computerized reporting system for HIV patient care. The paper-based ART patient care form/folder, which is filled by doctors and nurses at each

patient interaction, is the system's data source. Demographic data, baseline laboratory results, follow-up laboratory findings, HAART regimen at commencement, starting HAART regimen, duration on HAART, adherence, age at HAART initiation, TB status at HAART beginning, and history will be abstracted from the electronic system.

3.8 PRE-TEST

Pre-testing was used to identify if the instrument package was able to gather all the information that it is intended to gather and for editing questions that were missing on the data collection tool. It also assisted to estimate the time and the cost that was involved (Pandey, 2021). A pre-test was conducted at Blouberg health center. The researcher requests permission to complete the checklist from the facility management. All the records of clients experiencing treatment failure were systematically reviewed and all the records selected were coded. During pre-testing the instrument was able to collect all the information available on tie.net system, henceforth the researcher decided to include findings from the pre-test results. The findings of the pre-test results were included in the main study.

3.9. MEASURES TO ENSURE VALIDITY AND RELIABILITY

3.9.1 Validity

Validity is about how the method which was utilized to measure what the researcher intended to measure if it proves to be highly accurate (Creswell, 2019). According to Burns and Groove (2016), stipulates that validity highly focuses on the accuracy together with the truthfulness of the findings in a scientific manner. To ensure validity is satisfied, the instrument which is to be used to measure the effect should be able to cover all relevant points of interests which need to be measured. In this study validity was ensured by observing the items in the measuring instrument making sure it meets all the criterion of the content which is desired to be measured.

3.9.2 Reliability

According to Sürücü (2020) reliability refers to how consistent is the measure, likewise as by Middleton (2019), who stated that reliability is about how vast the measurement of the particular phenomenon continues to give results which are consistent and stable. In this study, reliability was ensured by applying the test-retest reliability or simply stability. It is the degree to which values are consistent through any repeated test. This was ensured by managing or administering the test two times to the identical set of themes and then correlates the two measurements at each time. The pre-test information collected was

compared with the data collection information collected to see if there are any inconsistencies.

3.10. Data collection method

According to Burns and Grove (2016), data collection is the precise, systematic gathering of information relevant to the research purpose or the specific objectives and questions of a study**.**

3.10.1 Plan for data collection

A pre-test was used to begin the preparation for data collection. After receiving ethical clearance from the University of Venda Research Ethics Committee, clearance number: SHS/20/DC/47/0412 and permission to conduct the study from the Limpopo Province's Department of Health's Ethics Committee, as well as the sub-district manager at the Blouberg health center, the researcher began the data collection process. The researcher coordinated data collection dates and times with the health-care administrators. The researcher requested permission to access tier.net and complete the checklist from the facility management and data capture. The arrangements will be made with the facility management for the researcher to collect data at the time when the facility is not busy. All the records of clients experiencing treatment failure were systematically reviewed based on the required information from the checklist. Checklists were completed in response to what was found on the records regarding the information or variables needed. All the records selected were coded for anonymity. This was done with the intention of acquiring chosen data lists from the current patient monitoring system (ePMS) (tier.net) database held at various health care institutions in the Blouberg municipality. The researcher always adhered to the COVID-19 regulations to prevent the spread of infections by sanitizing, keeping a 1.5m distance with personnel who will be assisting to retrieve the records, and wearing a mask. Records also place risk for COVID-19 infections. Therefore, non-sterile gloves were also used when handling the records.

3.10.2 Plan for data management and analysis

3.10.2.1 Data management

The data was backed up and kept in a secure location under lock and key with password security. Each selected record was assigned a codename, which was used to discuss data throughout the study.

3.10.2.2 Data analysis

Data was received from the tier.net ePMS and transferred to a Microsoft Excel-based spreadsheet for cleaning, coding, and analysis. The researcher then went on to verify for completeness, errors, and to tidy them all up. After that, the data was imported into the IBM SPSS 28 statistical software tool for further analysis. The statistical software was able to read the nominal data since it was coded. In this study, descriptive and inferential statistics were utilized. Each group's variables were organized into categories. The groups' respective variables were then statistically compared. Frequencies and cross-tabulation were used to apply descriptive statistics.

3.11 ETHICAL CONSIDERATIONS

Appropriate authorization were consulted with in order to be granted permission to execute the sturdy and the ethical clearance assuring that ethical standards shall be upheld during the course of the study. The DOH and DOH facilities provided verbal and written informed consent. All of the information gathered was kept strictly confidential. To identify individual patient records, no names were utilized; instead, only codes were used. Password protection was installed on the computer that was used for data entry and analysis. The participants rights were protected, their records and the standards of high level of confidentiality were sustained, anonymity also eliminating any aspect that can cause harm following the guidance of Pesut (2020). The researcher took into consideration the fundamental principles of ethical research which include justice, beneficence, and respect for human dignity.

The researcher adhered to the following ethical standards:

3.11.1 Permission and ethical clearance

This research was submitted to the School's Higher Degree Committee and the Advanced Nursing Department. The proposal will be presented to the Higher Degree Committees of the Executive School and the University. Ethical clearance was sought from the University of Venda Research Ethics Committee, and permission to conduct the study were obtained from the Department of Health Limpopo Province, relevant district, and the management at the Blouberg health care facilities.

3.11.2 Confidentiality and anonymity

The Office of Personnel Management was notified of the right to privacy and the procedures that would be taken to guarantee that this principle was not violated. The OPM was assured

that the data acquired from their facilities would be kept confidential, and that the data would be collected and evaluated in a private room. Anonymity and confidentiality were used to preserve privacy (Pesut, 2020).

Anonymity refers to the researcher's act of keeping the subjects' identities a secret regarding their participation in the study (Pesut, 2020). Anonymity was maintained by not utilizing real names on individual patient records; instead, each patient record was given a codename that would be utilized throughout the study for analysis. Individual patient records will be kept secure for follow-up if need arise.

Confidentiality refers to the researcher's obligation to keep all data collected during the study confidential and unavailable to others (Pesut, 2020). The selected facility OPM was assured that data collected from their facilities will be kept locked in a secure safe place where no unauthorized person would gain access to the study data.

3.12 DELIMITATION OF THE STUDY

The study was confined to data of individuals at specific facilities who met the inclusion criteria. Only factors linked to HIV virologic failure were considered. This is due to the fact that the research is restricted to a single sub-district and a few facilities in the Limpopo Province. Different clinicians may have entered the data into patient charts in different ways, resulting in measurement bias due to coding mistakes. Similarly, the data capturers in charge of inputting data from paper-based charts into the electronic system might have made mistakes, resulting in measurement bias.

3.13 PLAN FOR DISSEMINATION OF RESULTS

A research report is a written scientific document produced by a researcher as a result of a study or inquiry (Pandey, 2021). The completed report will be peer-reviewed, and a copy submitted to the University of Venda library for academic use. The copy will be available online and during seminars at the University of Venda. Results will be published in the form of articles in accredited journals.

3.14 SUMMARY

This chapter main focal point was to outline the research methodology used by the researcher to carry out the study, explain how the data was collected and analyzed, outlined also who were the participants and what sampling technique was put to use in the study. The following chapter will focus on data analysis, data presentation and interpretation of the results.

CHAPTER 4

DATA ANALYSIS AND DISCUSSION OF FINDINGS

4.1 INTRODUCTION

The outcomes of data obtained from tier.net were discussed in this chapter. The data was collected from all records on tier.net of adult HIV clients aged 18 and above who had a viral load (VL) of above >1000 copies/mL, 24 months after starting treatment at selected health care facilities and met the selection criteria. Data was analyzed with the help of a statistician using IBM SPSS Statistics version 28. Descriptive statistics were presented in the form of graphs, cross-tabulations, and other graphs.

4.2 PRESENTATION OF STUDY FINDINGS AND DISCUSSIONS

Data collected was presented with the aid of figures and tables.

4.2.1 Social Demographic

As indicated in the table below, this data included social demographics. For the study, a total of 251 adult patient records were chosen, with 184 female adult patients and 67 male adult patients. The patients were at least 15 years and older.

4.2.2 Factors associated with virologic failure

4.2.2.1 Association of gender and virologic failure

There was a need to determine the association of gender and virologic failure to enable the researcher to make their biographical inferences.

TABLE 4.1: ASSOCIATION OF GENDER AND VIROLOGIC FAILURE

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	67	26.7	26.7	26.7
	Female	184	73.3	73.3	100.0
	Total	251	100.0	100.0	

Table 4.1 shows the relationship between gender and virologic failure. According to the findings, females accounted for 73.3% patients who had virologic failure, while men accounted for 26.7% patients who experienced virologic failure.

This indicates that virologic failure affects more female clients on ART than male clients. Additional research in South Africa Drova (2017), Lekoloana (2014), and Temitope (2012) as well as other investigations in North Ethiopia complement these findings (Gizachew, 2018). According to the findings of this study, more than 60% of clients who experienced virologic failure were females. However, the findings in this study are significantly higher in comparison with other studies conducted in South Africa. The percentage of females who experienced virologic failure in Temitope in 2012, Lekoloana in 2014 and Drova in 2017 amounted to 68.66%, 63.8% and 69% respectively. The results of the study revealed that the female gender influenced virologic failure, this concurs with findings in similar studies by Gizachew (2018). The results show that females have higher association with virologic failure than males. Therefore, the findings of this study confirm that gender is associated with virologic failure.

4.2.2.2 CD4 count

TABLE 4.2: CD4 COUNT ON ART INITIATION

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 100	55	21.9	23.1	23.1
	100 – 200	64	25.5	26.9	50.0
	201 – 350	74	29.5	31.1	81.1
	> 350	45	17.9	18.9	100.0
	Total	238	94.8	100.0	
Missing	System	13	5.2		
Total		251	100.0		

The CD4 count of the patients at the time of ART commencement is shown in Table 4.2. The findings show that on ART commencement, 23.1% patients had a CD4 count of less than 100 cells/mm, of which 26.9% had 100 – 200 cells/mm, 31.1% had 201 – 350 cells/mm, and 18.9% had >350 cells/mm. These findings reveal that at the time of ART commencement, 81.1% patients with virologic failure had a CD4 count of less than 351 cells/mm. As a result of these observations, the researcher concluded that there is a link between CD4 level and virologic failure. As a result, a low CD4 count at the start of ART is linked to virologic failure.

TABLE 4.3: CD4 COUNT ON ART INITIATION GENDER CROSS-TABULATION

		Gender		Total
		Male	Female	
CD4 at start of ART	< 100	19	36	55
	100 - 200	20	44	64
	200 - 350	17	57	74
	> 350	7	38	45
Total		63	175	238

Table 4.3 shows the gender cross-tabulation CD4 count at the start of ART. The CD4 count of patients on ART initiation for females in this study ranged from 100 cells/mm (20.5%), 100–200 cells/mm (25 %), 201–350 cells/mm (32.5 %), to >350 cells/mm (21.7%). Males' CD4 count on ART commencement was 100 cells/mm (30.1%), 100–200 cells/mm (31.7%), 201–350 cells/mm (26.9%), and >350 cells/mm (11.1%) respectively. The relationship between virologic failure and CD4 count was shown to be gender specific. The study found that CD4 count on ART commencement ranged from 201 to 350 cells/mm in 57 female adult patients with virologic failure, whereas CD4 count on ART initiation ranged from 100 to 200 cells/mm in 20 male adult clients with virologic failure.

Table 4.2 shows that on ART commencement, more than 81% of adult clients experiencing virologic failure had a cell count of <351 cells/mm. Patients who were started on ART when their CD4 count was between 201 and 350 cells/mm had a 31% probability of suffering virologic failure as revealed by Gizachew (2018) and Jobanputra (2015). Furthermore, Bezabih (2019) claimed that patients who were initiated on ART at an advanced stage of HIV/AIDS and had a CD4 count of less than 100 cells per millimetre were four times more likely to develop virologic failure.

Clients were formerly started on ART based on WHO clinical staging; however, in 2006, WHO suggested that clients with a CD4 count of less than 200 be started on ART regardless of staging (WHO, 2015). Since then, the standard for Baseline CD4 has risen from 200 to 250. The South African Department of Health updated ART Guidelines in 2013 that increased the value of the starting CD4 to 350. The South African Department of Health introduced Universal Test and Treat in 2016, which meant that all clients starting in 2016 were treated regardless of their CD4 level.

4.2.2.3 WHO clinical staging on ART initiation

TABLE 4.4: WHO CLINICAL STAGE ON ART INITIATION

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	stage 01	86	34.3	34.4	34.4
	stage 02	92	36.7	36.8	71.2
	stage 03	57	22.7	22.8	94.0
	stage 04	15	6.0	6.0	100.0
	Total	250	99.6	100.0	
Missing	System	1	.4		
Total		251	100.0		

The WHO clinical staging on ART initiation is presented in Table 6. According to the findings of this study, WHO clinical staging for patients starting ART was 34.3% for stage 01, 36.8% for stage 02, 22.8% for stage 03, and 6% for stage 04. These findings show that stages 1 and 2 are strongly linked to virologic failure.

According to the findings, 71.1 % of adult patients with virologic failure were in WHO clinical stages 1 and 2 at the time of ART commencement. These findings are comparable to Bereda's research (2021), wherein the findings were that 68.4% of clients experiencing antiretroviral treatment failure base line WHO clinical stage was 1 and 2. However, the findings in this study are significantly greater in comparison. Furthermore, this study differs greatly from study done by Wendie (2020), in which a larger percentage of participants 66.4% were classified as WHO clinical stage 3 or stage 4, and the study conducted by Brhane (2020) where a higher percentage 67.5% of patients were classified as WHO clinical stage 3 or stage 4.

4.2.2.4 ART start regimen

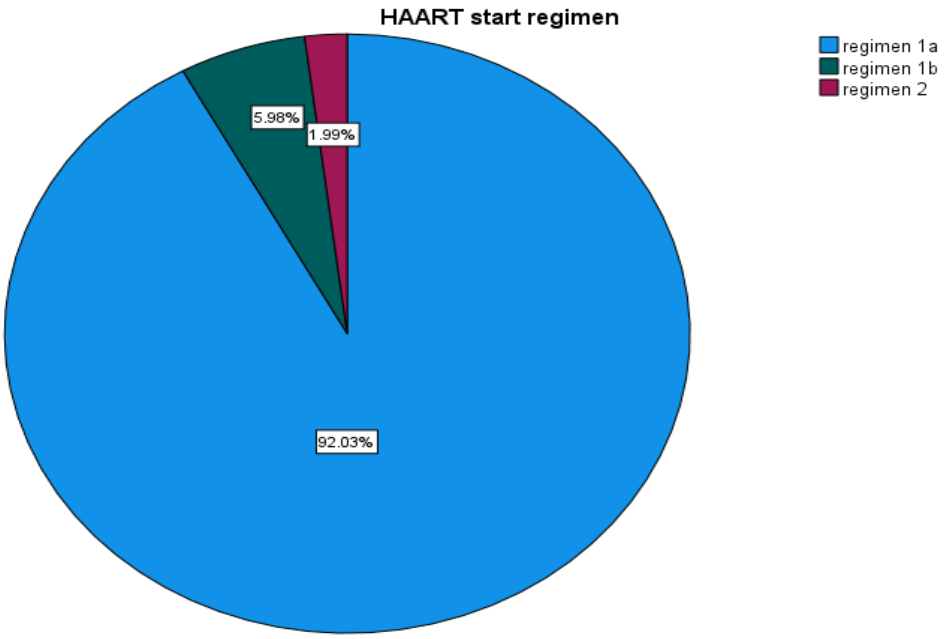

Figure 4.2: ART start regimen

The treatment regimen at the time of ART initiation is shown in Figure 4.2. According to the findings, the majority of patients who began ART on regimen 1a were 92% followed by 5.9% for regimen 1b and 1.9% for regimen 2. The findings reveal that individuals who were initiated on ART regimen 1a had a higher risk of virologic failure.

According to the findings, the majority of adult patients having virologic failure (92%) were started on ART on regimen 1a. These findings are consistent with those of a study conducted by Haas (2020), the findings indicated that the majority of clients experiencing antiretroviral treatment failure were 91.3% regimen 1a, 7.2% regimen 1b and 1.2% regimen 2. The findings reveal that ART regimen 1a is linked to virologic failure.

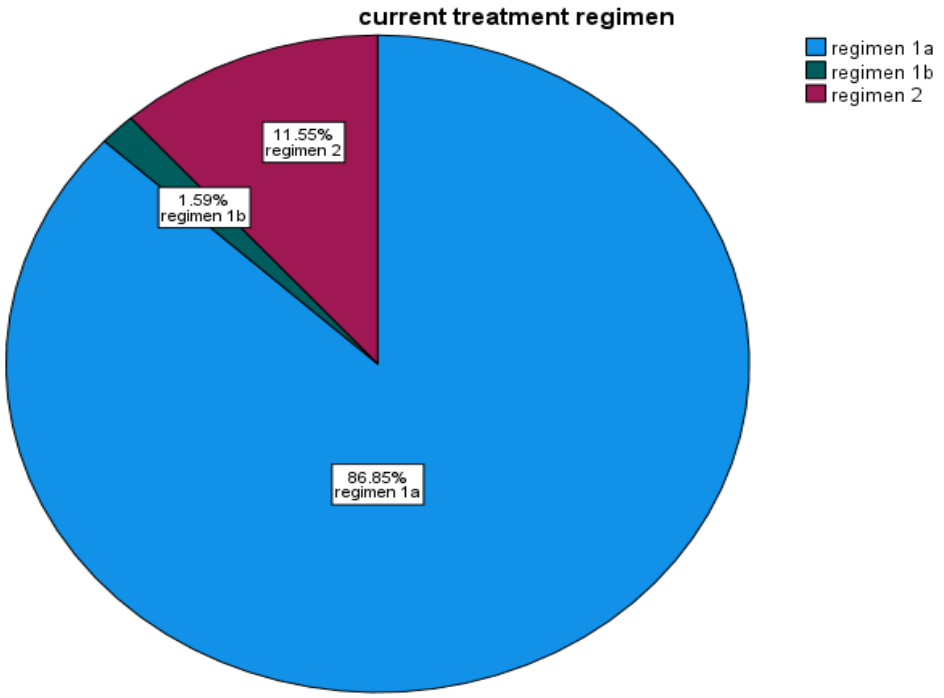

Figure 4.3: Current treatment regimen

Figure 4.3 shows the current treatment regimens of clients who have had virologic failure. The results show that the majority of the clients' current treatment regimens were regimen 1a (86.9%), regimen 2 (11.5%), and regimen 1b (1.5%). There is a significant change between the ART start regimen and the current regimen. The number of clients on the second line is growing, while the number of clients on the first line is decreasing. This also means that 11.5% of clients are having virologic failure as a result of second-line treatment, often known as regimen 2.

The foundation of most regimens is either a non-nucleoside reverse transcriptase inhibitors (NNRTIs), a protease inhibitors (PI), or an integrase inhibitor (Spencer, 2005). The backbone is usually made up of two NRTIs (Nucleoside Reverse Transcriptase Inhibitors) (advanced clinical file 2016). Unless there are contraindications, Regimen 1a is the primary choice for commencement. Regimen 1a has always altered the NRTIs, with stavudine being the most commonly substituted medication (d4T). The original regimen 1a was D4T/3TC/EFV, which was later replaced owing to adverse effects such as peripheral neuropathy, lipodystrophy, and lactic acidosis. Due to these adverse effects, stavudine (d4T) was phased out and replaced with TDF; the new first-line regimen 1a which became TDF/3TC/EFV, which was later changed into a fixed-dose combination known as TDF/FTC/EFV. Regimen 1a was chosen as the first regime. If a client fails regimen 1a or 1b, they are sent to the second-line regimen, or regimen 2. (DoH, 2019).

In the event of renal failure, ABC or AZT could be used to replace TDF, depending on contraindications (DoH, 2019). The first-line regimen was started on 92% of all virologic failure patients, followed by regimen 1b with 5.9% and regimen 2 with 2%. (1.9%). This indicates that 11.6% of the population is presently on regimen 2 and experiencing virologic failure where an increase has been noted since the commencement regimen where 1.9% of the population used regime 2 to treat virologic failure (1.9 percent). This means that more than 10% of clients with virologic failure had already been transferred to second-line or regimen 2.

4.2.2.5 TB and HIV co-infection at ART initiation

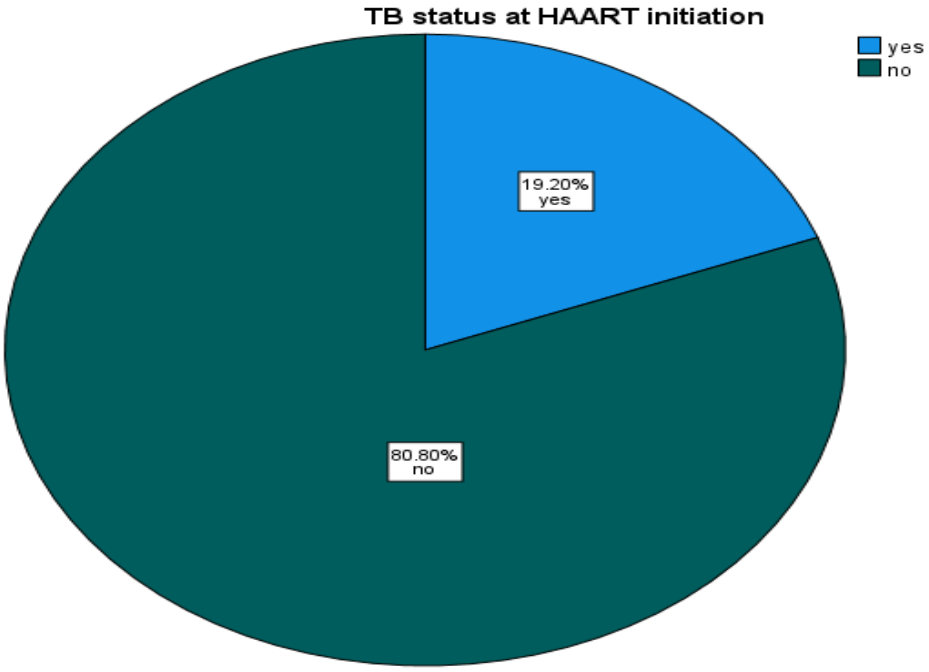

Figure 4.4: TB and HIV co-infection at ART initiation

Figure 4.4 depicts the co-infection of TB and HIV at the time of ART commencement. According to the findings of this study, 19.2% of patients who failed to respond to ART had TB at the time of commencement. These findings suggest that there is a link between tuberculosis and virologic failure.

These findings are comparable to those of Zenebe (2021) and Bereda (2021), 21.7% and 54.9% of clients experiencing antiretroviral treatment failure had TB co-infection respectively. The findings reveal that clients with TB at the time of ART commencement had a significantly higher risk of treatment failure, comparing to those with no TB co-infection. with 19% of those who experience treatment failure having TB at the time of ART commencement.

4.2.2.6 Viral load results at 12-month

TABLE 4.5: 12-MONTHS VIRAL LOAD

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0 – 1000	121	48.2	55.8	55.8
	1000 – 10000	28	11.2	12.9	68.7
	10000 – 100000	51	20.3	23.5	92.2
	100000 – 1000000	14	5.6	6.5	98.6
	> 1000000	3	1.2	1.4	100.0
	Total	217	86.5	100.0	
Missing	System	34	13.5		
Total		251	100.0		

Table 4.5 shows the 12-month viral load findings for clients who have virologic failure: (55.8%) 0 – 1000 copies/ml, (12.9%) 1000 – 10000 copies/ml, (23.5%) 100000 – 1000000 copies/ml, and (1.4%) >1000000 copies/ml. This suggests that more than 44% of the clients who are experiencing treatment failure had viral load readings of >1000 copies/ml during their 12-month follow-up. These results indicate that there is a significant association between the 12-month viral load of >1000 and virologic failure.

These findings are comparable to those of Waju's research (2021), 20% of clients experiencing antiretroviral treatment had a viral load results of >1000, despite the fact that the results of these study are substantially low. According to the findings of this study, more than 44% of clients who experienced virologic failure after a 12-month viral load test had >1000 copies/ml. In 2014, South Africa set 90, 90, 90 HIV objectives, with the goal of ensuring that by 2020: 90% of people living with HIV will know their status, 90% of people diagnosed with HIV infection will receive long-term antiretroviral treatment, and 90% of people on antiretroviral medication will have viral suppression (DOH, 2014). The findings demonstrate that during a 12-month viral load test, over 44% of the population did not achieve viral load reduction. According to similar research, two-thirds of patients (66.6%) who failed to suppress at their initial viral load assessment went on to have virological failure (Lekoloana, 2014). Virological failure has been identified by WHO as one of the early warning

signs of drug resistance; and in this setting, it is more feasible to measure as a surrogate for resistance, especially since the South African HIV treatment guidelines currently do not provide for individual patient monitoring for resistance testing (WHO, 2015).

4.2.2.7 Missed appointments

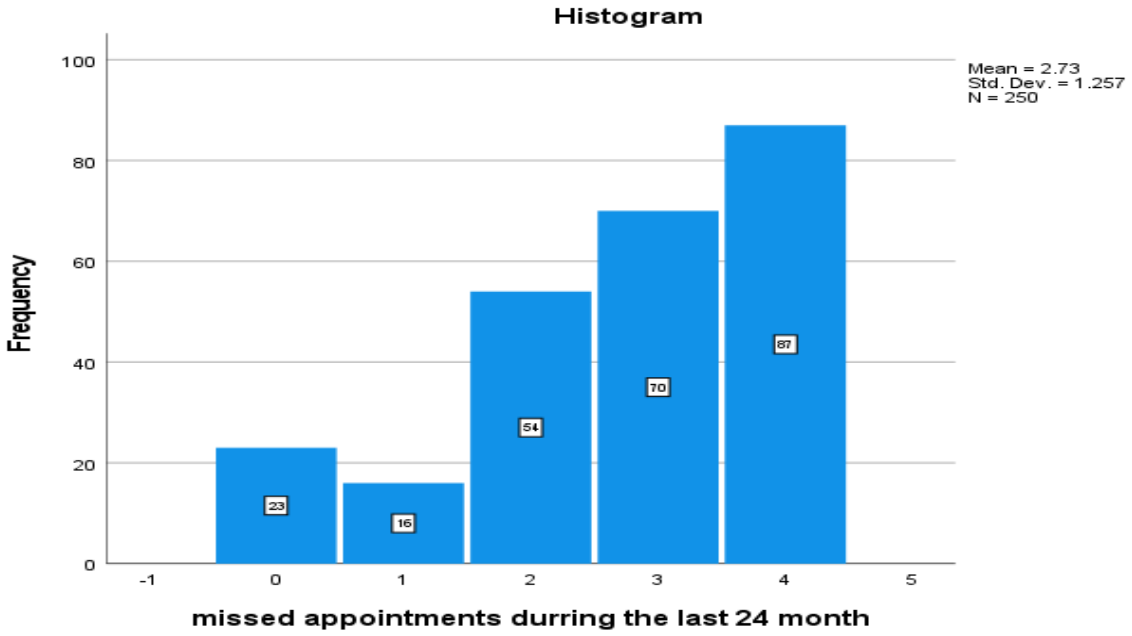

Figure 4.5: Missed appointments during the last 24 months

Figure 4.5 depicts missed appointments during the last 24 months. According to the findings, 9.2% of clients never missed an appointment, 6.4% missed a first-month appointment, 21.6% missed a second-month appointment, 27.9% missed a third-month appointment, and 34.7% missed more than three months visits. There is a link between missed appointments and virologic failure, and the number of clients who experience virologic failure rises as the number of missed appointments rises. Only around 10% of clients have never missed an appointment in the previous 24 months.

The results indicate that more than 90% of clients who are experiencing treatment failure have had treatment interruption. These findings concur with the findings of the study conducted by Jemberu (2020) and Bisetegn (2020), 35.9% and 55% of clients experiencing antiretroviral treatment failure had treatment interruptions respectively. Most of the clients experiencing treatment failure have missed 1 month or more appointments, with the largest percentages of those who have missed 3 months or more (62.6 %). The studies conducted by Muthiani (2010), indicate that the likelihood of developing virological failure was 7.3-fold higher among patients with poor ART-medication adherence during adherence-

enhancement counseling than those with good adherence. According to the findings, more than 90% of clients who are experiencing treatment failure have had their therapy interrupted. These findings are significantly higher in comparison than those of other study conducted by Bisetegn (2020), 55% had treatment interruption. The majority of clients who are experiencing treatment failure have missed one or more appointments for a month or more, with the biggest proportion missing three months or more (62.6%). As a result, individuals must be encouraged to keep appointments or return for follow-up visits as advised by the medical officers. The benefits of keeping appointments should be emphasized, and they should also be made aware of the drawbacks.

4.2.2.8. Lost to follow up

TABLE 4.6: LOSS TO FOLLOW-UP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no lost to follow-up	107	42.6	42.8	42.8
	Lost to follow-up for 3 months	30	12.0	12.0	54.8
	Lost to follow-up for 4 months	39	15.5	15.6	70.4
	Lost to follow-up for 5 months	43	17.1	17.2	87.6
	Lost to follow-up for 6 months	11	4.4	4.4	92.0
	more than 6 months	20	8.0	8.0	100.0
	Total	250	99.6	100.0	
Missing	System	1	.4		
Total		251	100.0		

Table 4.6 presents the loss to follow-up during the last 24 months. The results indicate that 42% have not been lost to follow-up during the last 24 months, 12% lost to follow-up for 3 months, 15.6% lost to follow-up for 4 months, 17.2% lost to follow-up for 5 months, 4.4% lost to follow-up for 6 months and 8% lost to follow-up for more than 6 months. More than 57%

of the clients experiencing virologic failure have a history of loss to follow-up during the last 24 months. There is significance association between lost to follow-up and virologic failure.

According to the findings, over 57% of clients who are experiencing virologic failure had been lost to follow-up for 3 months or more in the previous 24 months. These findings are much higher than those of Temitope (2012), who found that 21.61% of patients did not return to the clinic for three months or more and thereby defaulted on treatment. More than half of the clients who fail to complete treatment have a history of being lost to follow-up. Poor adherence results in low levels of antiretroviral effect in the body, which leaves the body unable to block viral replication, eventually leading to virologic failure (Jamberu, 2020).

4.2.2.9 Prolonged duration on ART

TABLE 4.7: DURATION ON ART

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	2 years	12	4.8	4.9	4.9
	3 years	19	7.6	7.8	12.7
	4 years	22	8.8	9.0	21.6
	5 years	30	12.0	12.2	33.9
	> 5 years	162	64.5	66.1	100.0
	Total	245	97.6	100.0	
Missing	System	6	2.4		
Total		251	100.0		

Table 4.7 presents the duration on ART for adult clients. The results indicate that 4.9% of the clients experiencing virologic failure have been on ART for 2 years, 7.8% have been on ART for 3 years, 9% have been on ART for 4 years, 12% have been on ART for 5 years and 66.1% have been on ART for more than 5 years. This shows that the majority of clients who are experiencing treatment failure have been on treatment for more than 5 years. There is an association between virologic failure and prolonged duration on ART simply because the number of clients experiencing treatment failure increases with the duration on treatment.

More than 66% of the population experiencing treatment failure had more than 5 years on treatment.

According to the findings, the majority of clients who are experiencing virologic failure (78.3%) have been on treatment for 5 years or longer. These findings are consistent with those of Bayu (2017) and Feleke (2020), 74.5% and 55.5% of clients experiencing antiretroviral treatment failure. The frequency of individuals who develop virologic failure rises as treatment continues. More than 78% of people who experienced treatment failure had been on treatment for 5 years or more. Longer treatment duration has been linked to HIV virologic failure, as the percentage of patients who failed therapy increased with treatment length as observed in this study (Getawa, 2020).

TABLE 4.8: DURATION ON ART PER GENDER

		Gender		
		Male	Female	Total
duration on ART	2 years	4	8	12
	3 years	3	16	19
	4 years	6	16	22
	5 years	10	20	30
	> 5 years	42	120	162
Total		65	180	245

Table 4.8 presents the duration on ART per gender, the results shows that 42 (64.6%) of the male population who are experiencing treatment failure have more than 5 years on treatment. Whereas 120 (66.6%) of the female population who are experiencing treatment failure have more than 5 years on treatment. The duration on ART is similar for all the genders which indicates that virologic failure increase with prolonged duration on ART.

This trend is similar for males and females. The duration on ART per gender, indicates that 80% of male population who are experiencing treatment failure have 5 years or more on treatment. In addition, 77.7% of the female population who are experiencing treatment failure have 5 years or more on treatment. Prolonged duration on treatment has proven to be associated with HIV virologic failure since percentage of treatment failure in this study increases with duration on treatment (Getawa, 2020).

4.2.3 CONCLUSION

The results of the study indicate that the factors associated with antiretroviral treatment failure were, 77.3% females, CD4 of <351cells/mm on antiretroviral treatment initiation had 81% chance of developing virologic failure, 71.1% WHO clinical stage 1 and stage 2 on ART initiation, more than 44% history of viral load results of above 1000 copies/ml during their 12-month results, 90% missed at least 1 month or more appointment during the last 24-month visits, More than 78.3% treatment duration of 5 years or more. In this study these factors were highly associated with treatment failure

4.3 SUMMARY

In this chapter what was covered were the results of the study, these results were presented making use of figures and tables. Descriptive statistics in this chapter was made of use when coming to data analysis. The independent functions which are associated with virological failure were scrutinized using the inferential statistics. The results showed different factors that are associated with virological failure when coming to patients who are on ART and are adults.

CHAPTER 5

LIMITATIONS, RECOMMENDATIONS AND CONCLUSION

5.1 INTRODUCTION

Results of this study were presented in the previous chapter. This chapter presented the limitations, recommendations and conclusion of the research findings on factors associated with virologic failure among adult patients on antiretroviral treatment. It also pointed out the limitations of the study. Finally, recommendations based on the research findings and the conclusions of the study are proposed.

5.2 LIMITATIONS OF THE STUDY

The results cannot be generalized to neither the entire Limpopo Province or to the other provinces in South Africa since the study is limited to 4 clinics in the Limpopo Province. The population of the study was only limited to the Blouberg sub-district.

Due to the broad nature of this study, it was impossible to measure and investigate all aspects associated with HIV treatment failure at selected health care facilities. As such, this study may not be able to adequately explain some of the factors associated with HIV treatment failure since it was based on review of records. Consequently, the source document was only tier.net where some of the information may not have been captured at the facility by the data captures. And due to COVID-19 restrictions we were restricted from using clients' folders to access missing information. Only factors that were documented in the electronic data system were included in the study.

Selection bias as a result of the methodology as well as the inclusion and exclusion criteria may provide some bias on the results. Bias from loss to follow-up could not be controlled but the design of the study was to select a uniform sample in which loss to follow-up did not occur.

5.3 RECOMMENDATIONS

The following recommendations are made based on the findings of the study.

5.3.1 Association of gender and virologic failure

- Female patients exhibiting viral load of above 1000 should be identified promptly by PHC staff in the ART team from patient records by all the staff responsible for ART clients. All ART doctors and nurses should assess these patients' latest viral load results during each visit and assess for signs of treatment failure for instance falling CD4 counts, recurrence of opportunistic infections, and rising viral loads.

5.3.2 CD4 count

- The study recommended that patients who were initiated on ART while their CD4 count was less than 351cells/mm need to be monitored for treatment failure on each clinical visit. All ART doctors/nurses should assess for any indicators that can alert a concern to consider virological failure; the likes of increasing viral loads when one is on ART and opportunistic infections which is recurring.

5.3.3 WHO clinical staging on ART initiation

- The study recommended that patients who were initiated on ART while on WHO clinical stage 01 and 02, be monitored for treatment failure on each clinical visit. All ART doctors and nurses should assess any indicators that can alert a concern for consider virological failure; like increasing viral loads when one is on ART and opportunistic infections which is recurring.

5.3.4 TB and HIV co-infection at ART initiation

- TB and HIV co-infection are the most common prevalent factor associated with treatment failure among the male population. The study recommended that patients who were initiated on ART while they had TB and HIV co-infection, should be monitored closely during treatment initiation.

5.3.5 Viral load results at 12-month

- Develop a standard operating procedure to operationalize the national guidelines, with a clear step-by-step guide to manage the results for clients' viral load above

1000 and what to do when certain outcomes occur. Especially since ART care is shifted to health care staff with less expertise. The study recommends that all the clients who have viral load results of above 1000 be monitored closely and steps should be taken to ensure
that their viral load remain less than 1000.

5.3.6 Missed appointments and loss to follow up

- Appropriate measures should be taken by the ART team to improve medication use by these patients. The ART team manager should ensure the implementation of missing appointments and lost-to-follow-up SOP is available and followed by the whole team.
- Strengthening and continued support of counselling services, adherence clubs, community-based services, and outreach (patient tracer) services as they are central to the success of any ART program missing appointments and lost to follow up.
- Strengthening the community-based services and outreach (patient tracer) services to account for all the patients lost to follow up.

5.3.7 Prolonged duration on ART

- The study recommended that patients who are on ART for more than 5 years need to be monitored for treatment failure on each clinical visit.
- Strengthening and continued support of health education to these patients on the importance of ART as they are central to the success of any ART program.

5.3.8 Staff training

- Ensuring that there is a Centre in local areas which supports clinicians by providing mentorship to them in and out of all seasons.
- facilities to be empowered through in-service training on a standardised timely basis and when there are new guidelines to ensure that the staff uses recent recommendations at all times

5.3.9 Body of knowledge

- more research to be conducted to further understand HIV antiretroviral treatment failure among rural areas like Blouberg and come with interventions that will enable clinician's and clients to find the best way to manage antiretroviral treatment failure
- funds should be invested more in the study about treatment failure in rural areas and find a way to get to the time of HIV free generation and avoid the possibility of the new spread of resistant HIV
- the guidelines should be developed based on the practical application in aliment with the biomedical, structural and behavioural intervention in place at the facilities

5.4 CONCLUSION

The study intended to investigate factors associated with virologic failure among adult patients on antiretroviral treatment at selected health-care facilities, Limpopo Province. The study used quantitative approach with descriptive and cross-sectional design. This study found that the majority of patients experiencing virologic failure were females accounting for 77.3% and males accounting for 26.7%.

The study found that clients with CD4 count of <351cells/mm had 81% chance of developing virologic failure in comparison to those who were initiated when there was 351cells/mm and above. The study found that 71.1% of the adults experiencing treatment failure were on WHO clinical stage 1 and stage 2 on ART initiation. The findings of the study show that 19.2% of the clients experiencing treatment failure had TB during ART initiation. More than 44% of clients experiencing treatment failure had a history of viral load results of above 1000 copies/ml during their 12-month results. The results of the study indicate that 90% of all the clients have missed at least 1 month or more appointments during the last 24 month visits. More than 78.3% of patients experiencing virologic failure have been on treatment for 5 years or more. There is a need for health care workers to focus on this characteristic in order to prevent virologic failure/treatment failure.

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ANNEXURES

ANNEXURES A- Data collection tool

Data collection tool

Code number: Date:

Demographic information	
1. Sex:	[1] Male [2] female
2. Date of birth (dd/mm/yy)	
3. Care entry point	[1] Medical [2] Private sector [3] Self-referral [4] transfer in [5] PMTCT [6] Other
4. Marital status	[1] Married [2] Single [3] Divorced
5. Physical adress	[1] name of the place (specify) [2] Rural, township or suburbs (specify)
Background clinical and laboratory findings	
6. Date HAART started	
7. Clinical stage at start ART	[1] 1 [2] 2 [3] 3 [4] 4
8. CD4 at start ART Cells/mm3	
9. TB status at HAART initiation	
10. Did patient receive cotrimoxazole	[1] Yes

	[2] No
11. Previous viral load results	
HAART regimen history	
12. HAART regimen at start	[1] D4T/3TC/NVP [2] D4T/3TC/EFV [3] AZT/3TC/NVP [4] AZT/3TC/EFV [5] TDF/3TC/NVP [6] TDF/3TC/EFV [7] D4T/3TC/LPV/r [8] AZT/3TC/LPV/r [8] AZT/3TC/LPV/r [9] Other (Specify)_____
13. New regimen if applicable	[1] D4T/3TC/NVP [2] D4T/3TC/EFV [3] AZT/3TC/NVP [4] AZT/3TC/EFV [5] TDF/3TC/NVP [6] TDF/3TC/EFV [7] D4T/3TC/LPV/r [8] AZT/3TC/LPV/r [9] AZT/3TC/TDF/LPVr [10] Other (specify) ____
14. Duration on ART	
Adherence history	
15. Missed appointment	[1] less than 1 month (specify) [2] more than one month (specify)
16. Lost to follow up	[1] less than 3 month (specify) [2] more than 3 months (specify)

ANNEXURES B

Annexure : Information letter and Consent form

RESEARCH ETHICS COMMITTEE

UNIVEN Informed Consent

Annexure I

LETTER OF INFORMATION AND CONSENT FORM

Title of the Research Study: Factors associated with virologic failure among adult patients on antiretroviral treatment at selected health-care facilities, Limpopo Province

Principal Investigator/s/ researcher: Mulaisi Tshimangadzo Ephraim, Masters in Nursing Science

Co-Investigator/s/: **Supervisor/s**: Dr Raliphaswa N.S, Lecturer
Co-supervisor: Dr Ramakuela N.J, Lecturer
Co-supervisor: Dr Tshililo A.R , Lecturer

Brief Introduction and Purpose of the Study: The Human Immunodeficiency Virus (HIV) is a lentivirus (a subgroup of retrovirus) that causes HIV infection and over time Acquired Immune Deficiency Syndrome. Highly Active Antiretroviral Therapy (HAART) is the medication that slows down the progression from HIV to AIDS. It was introduced in Western countries in 1996. The main goal of HAART is to achieve maximal viral suppression. Treatment failure refers to a plasma viral load above 1000 copies/ml based on two consecutive viral load measurements after 3 months, with adherence support. An individual must have been taking ART for at least 6 months before it can be determined that a regimen has failed.

The purpose of this study is to determine the factors associated with virologic failure among adult patients on antiretroviral treatment at selected health-care facilities, Limpopo Province

Outline of the Procedures: Once the approval has been granted to conduct the study, the project will be explained to the facility OPM and relevant managers. The researcher will arrange with the health care management for the dates and time conducive to collect data. The study objectives, aims, benefits of the study will be explained to the facility OPM and relevant managers to gain trust and access to all relevant data system used. The structured data collection tool will be used aimed at gathering selected data list from existing patient

monitoring system (ePMS) (tier.net) database kept at selected health care facilities Blouberg municipality

Risks or Discomforts to the Participant: No risk

Benefit: The findings will be presented to the Department of Health in Limpopo province and in other workshops, national and international conferences. Findings will be published in the peer review accredited journals for possible publication.

Reason/s why the Participant May Be Withdrawn from the Study: participants can withdraw from the study anytime with no penalties.

Remuneration: no remuneration

Costs of the Study: none

Confidentiality: In this study the researcher will not share information gathered at research field with anyone outside research team, such as friends, close family members or any unauthorized persons. When reporting the data collected, the researcher will not use names or participants identities, coding and pseudonyms will be used.

Research-related Injury: none

Persons to Contact in the Event of Any Problems or Queries:

(Dr Raliphaswa N.S) Please contact the researcher (0723955603.), my supervisor (0822627809.) or the University Research Ethics Committee Secretariat on 015 962 9058. Complaints can be reported to the Director: Research and Innovation, Prof GE Ekosse on 015 962 8313 or Georges Ivo.Ekosse@univen.ac.za

General:
Potential participants must be assured that participation is voluntary and the approximate number of participants to be included should be disclosed. A copy of the information letter should be issued to participants. The information letter and consent form must be translated and provided in the primary spoken language of the research population

CONSENT

Statement of Agreement to Participate in the Research Study:

- I ……hereby confirm that I have been informed by the researcher, **Mulaisi Tshimangadzo Ephraim**, about the nature, conduct, benefits and risks of this study - Research Ethics Clearance Number: _,
- I have also received, read and understood the above written information (*Participant Letter of*

Information) regarding the study.

- I am aware that the results of the study, including personal details regarding my sex, age, date of birth, initials and diagnosis will be anonymously processed into a study report.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerized system by the researcher.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I understand that significant new findings developed during the course of this research which may relate to my participation will be made available to me.

Full Name of Participant Date Time Signature

I, …….. …… …… ……..

Mulaisi Tshimangadzo Ephraim herewith confirm that the above participant has been fully

Informed about the nature, conduct and risks of the above study.

Full Name of Researcher

…….. Date…….. Signature……..

Full Name of Witness (If applicable)

…….. Date …….. Signature……..

Full Name of Legal Guardian (If applicable)

…… Date…….. Signature……..

Please note the following:

Research details must be provided in a clear, simple and culturally appropriate manner and prospective participants should be helped to arrive at an informed decision by use of appropriate language (grade 10 level- use Flesch Reading Ease Scores on Microsoft Word), selecting of a non-threatening environment for interaction and the availability of peer counseling (Department of Health, 2004)

If the potential participant is unable to read/illiterate, then a right thumb print is required and an impartial witness, who is literate and knows the participant e.g. parent, sibling, friend,

pastor, etc. should verify in writing, duly signed that informed verbal consent was obtained (Department of Health, 2004).

If anyone makes a mistake completing this document e.g. a wrong date or spelling mistake, a new document has to be completed. The incomplete original document has to be kept in the participant's file and not thrown away, and copies thereof must be issued to the participant.

References:

Department of Health: 2004. *Ethics in Health Research: Principles, Structures and Processes*

http://www.doh.gov.za/docs/factsheets/guidelines/ethnics/

Department of Health. 2006. *South African Good Clinical Practice Guidelines*. 2nd Ed. Available at:

http://www.nhrec.org.za/?page_id=14

ANNEXURE C: Letter of requesting permission

To: DEPARTMENT OF HEALTH LIMPOPO PROVINCE

RE: APPLICATION FOR PERMISSION TO CONDUCT THE RESEARCH

The above matter refers:

I, **Mulaisi Tshimangadzo Ephraim** request permission to conduct research. The target group for the study will be records of HIV clients 18 years and above experiencing virologic failure. I am a student at the University of Venda and have registered for a Masters degree in nursing.

The title of the study is**:** "**Factors associated with virologic failure among adult patients on antiretroviral treatment at selected health-care facilities, Limpopo Province".**

The purpose of this study is to determine factors associated with virologic failure among adult patients on antiretroviral treatment at selected health-care facilities, Limpopo Province. The study will assist HIV clients experiencing virologic failure to get their virologic problem resolved without switching them to second line unnecessarily. It is also assumed that professional health care workers will be able to manage virologic failure with more caution.

Should there be issues that you want to be clarified, I am prepared to address them to your satisfaction.

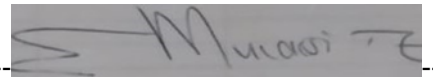
Researcher: Mulaisi TE 0658858691/0723955603
Supervisor: Dr Raliphaswa N.S (015 962 8000)

Co- supervisor: Dr Ramakuela N.J (015 962 8682)

Co- supervisor: Dr Tshililo A.R

I look forward to your favourable response.

Yours sincerely

----  ----------

Mulaise TE

ANNEXURE D: Letter of requesting permission

To: CAPRICORN DISTRICT, LIMPOPO PROVINCE

RE: APPLICATION FOR PERMISSION TO CONDUCT THE RESEARCH

The above matter refers:

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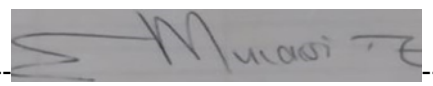
---  ----------

Mulaise TE

ANNEXURE E: Letter for requesting permission

To: BLOUBERG SUB-DISTRIC, CAPRICORN DISTRICT

RE: APPLICATION FOR PERMISSION TO CONDUCT THE RESEARCH

The above matter refers:

I, **Mulaisi Tshimangadzo Ephraim** request permission to conduct research. The target group for the study will be records of HIV clients 18 years and above experiencing virological failure. I am a student at the University of Venda and have registered for a Masters degree in nursing.

The title of the study is**:** "**Factors associated with virologic failure among adult patients on antiretroviral treatment at selected health-care facilities, Limpopo Province".**

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Researcher: Mulaisi TE 0658858691/0723955603

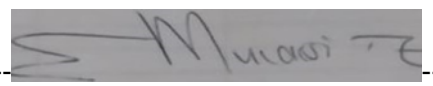
Supervisor: Dr Raliphaswa N.S (015 962 8000)

Co- supervisor: Dr Ramakuela N.J (015 962 8682)

Co- supervisor: Dr Tshililo A.R

I look forward to your favourable response.

Yours sincerely

---  ----------

Mulaise TE

ANNEXURE F: Ethical clearance letter

OFFICE OF THE DIRECTOR

NAME OF RESEARCHER/INVESTIGATOR:
Mr TE Mulaisi

STUDENT NO:
11583463

PROJECT TITLE: Factors associated with 'virologic failure among adult patients on antiretroviral treatment at selected healthcare facilities, Limpopo Province.

ETHICAL CLEARENCE NO: SHS/20/PDC/47/0412

SUPERVISORS/ CO-RESEARCHERS/ CO-INVESTIGATORS

NAME	INSTITUTION a DEPARTMENT	ROLE
Dr NS Raliphaswa	University of Venda	Supervisor
Dr NJ Ramakuela	University of Venda	Co - Supervisor
Dr AR Tshililo	University of Venda	Co - Supervisor
Mr. TE Mulaisi	University of Venda	Investigator — Student

Type: Masters Research

Risk: risk to humans, animals, environment, or a sensitive research area

Approval Period: December 2020 [i]- December 2022

The Human and Clinical Trails Research Ethics Committee (HCTREC) hereby approves your project as indicated above.

General Conditions

While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, please note the following.

- The project leader (principal investigator) must report in the prescribed format to the REC:
- Annually (or as othenvise requested) on the progress of the project, and upon completion of the project
- Within 48hrs in case of any adverse event (or any matter that interrupts sound ethical principles) during the course of the project' _ Annually a number of projects may be randomly selected for an external audit.
- The approval applies strictly to the protocol as stipulated in the application form, Would any changes to the protocol be deemed necessary during the course of the project„ the project leader must apply for approval of these changes at the REC. Would there be deviated from the project protocol without the necessary approval of such changes, the ethics approval is immediately and automatically forfeited.
- The date of approval indicates the first date that the project may be started. Would the project have to continue after the expiry date; a new application must be made to the REC and new approval received before or on the expiry date.
- In the interest of ethical responsibility, the REC retains the right to:
- Request access to any information or data at any time during the course or after completion of the project,
  - To ask further questions; Seek additional information; Require further modification or monitor the conduct of your research or the informed consent process.
  - withdraw or postpone approval if:
- Any unethical principles or practices of the project are revealed or suspected.

_ It becomes apparent that any relevant information was withheld from the REC or that information has been false or misrepresented. _ The required annual report and reporting of adverse events was not done timely and accurately, _ New institutional rules, national legislation or international conventions deem it necessary

ISSUED BY:

UNIVERSITY OF VENDA, RESEARCH ETHICS COMMITTEE Date Considered: September 2020

UNIVERSITY OF VENDA
OFFICE OF THE DIRECTOR
RESEARCH AND INNOVATION
2020 -12- 4

Name of the HCTREC Chairperson of the Committee: Prof MS Maputle

--Signature. MS Maputle

Private Bag X5050
Thohoyandou 0950

University of Venda
THOHOYANDOU, LIMPOPO PROVINCE, SOUTH AFRICA
PRIVATE BAG X5050, TELEPHONE (015) 962 8504/8313 FAX (015) 962 9050
"A quality driven finoncia/[y sustainable, rural-based Comprehensive University"

ANNEXURE G: Approval letter from Provincial Department of Health Polokwane

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

Department of Health

Ref : LP_2021-04-001
Enquires : Ms PF Mahlokwane
Tel : 015-293 6028
Email : Phoebe.Mahlokwane@dhsd.limpopo.gov.za

Tshimangadzo Ephraim Mulaisi

PERMISSION TO CONDUCT RESEARCH IN DEPARTMENTAL FACILITIES

Your Study Topic as indicated below**;**

Factors associated with virologic failure among adult patients on antiretroviral treatment at selected health-care facilities, Limpopo Province

1. Permission to conduct research study as per your research proposal is hereby Granted.
2. Kindly note the following:
    a. Present this letter of permission to the institution supervisor/s a week before the study is conducted.
    b. In the course of your study, there should be no action that disrupts the routine services, or incur any cost on the Department.
    c. After completion of study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
    d. The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
    e. The approval is only valid for a 1-year period.
    f. If the proposal has been amended, a new approval should be sought from the

Department of Health

g. Kindly note that, the Department can withdraw the approval at any time.

Your cooperation will be highly appreciated

_____

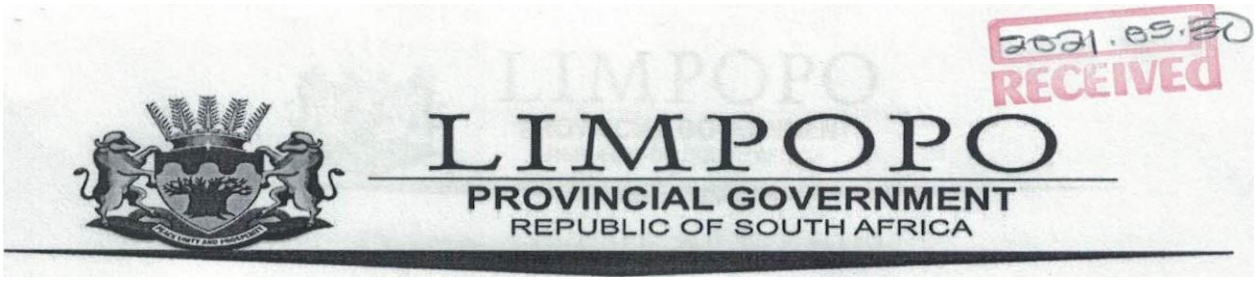
_____ 18/05/2021

Head of Department **Date**

Private Bag X9302 Polokwane
Fidel Castro Ruz House, 18 College Street. Polokwane 0700. Tel: 015 293 6000/12. Fax: 015 293 6211. Website: http/www.limpopo.gov.za

The heartland of Southern Africa – Development is about people!

ANNEXURE H: Approval letter from Capricorn District Limpopo Province



DEPARTMENT OF HEALTH CAPRICORN DISTRICT

REF : s.5/3/1/2
ENQ ; Makgaloa M.O TEL : 015
290 9252

FROM: DISTRICT EXECUTIVE MANAGER

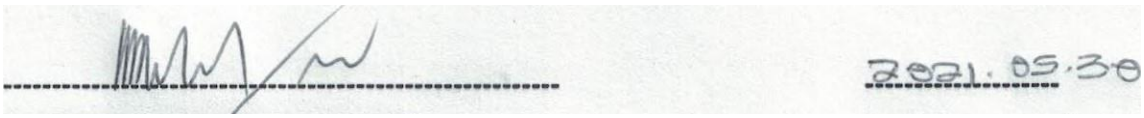
TO ; Mr. TE Mulaisi
UNIVERSITY OF VENDA
PRIVATE BAG X 5050
THOHOYANDOU
0950

CELL : 072 3955 603
EMAIL: mulaisitshimangadzo@gmail.com

SUBJECT : PERMISSION TO CONDUCT RESEARCH IN DEPARTMENTAL FACILITIES

The above matter refers:-

4. Permission to conduct the above research is hereby granted.
5. Kindly be informed that :
   - In the course of your research there should be no action that disrupts the services.
   - Kindly note that the Department can withdraw the approval at any time.
   - The approval is only valid for a I-year period.
6. Your cooperation will be highly appreciated.



DISTRICT EXECU IVE MANAGER DATE

Private Bag x9530, Polokwane, 0700, 34 Hans Van Resnberg ST, Polokwane 0700
Tel: (015) 290 9000, Fax: (015) 291 3260/1568 Website: http/vmw.limpopo.gov.za
CERTIFICATERESEARCH AND INNOVATION

ROSEMARY'S PROOFREADING
& EDITING SERVICES

+27 83 215 6445
Rosemarys.pes@gmail.com
1 Richards drive
Midrand, 1684

24 DECEMBER 2021

To Whom It May Concern:

RE: LANGUAGE EDITING

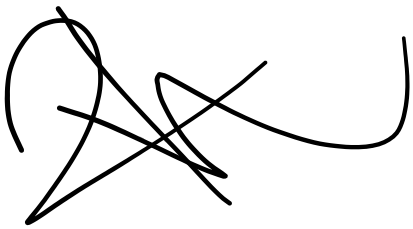
This letter serves as confirmation that language and technical editing was conducted by Rosemary's Proofreading and Editing Services. Further details of the study and the researcher have been provided below.

TITLE OF THE STUDY: "FACTORS ASSOCIATED WITH VIROLOGIC FAILURE AMONG ADULT PATIENTS ON ANTIRETROVIRAL TREATMENT AT SELECTED HEALTH-CARE FACILITIES, LIMPOPO PROVINCE".

Researcher: **MULAISI TSHIMANGADZO EPHRAIM**

Student number: 11583463

Kind Regards



R MALULEKE (CODER & LANGUAGE EDITOR)