MINI-DISSERTATION

EVALUATION OF TREATMENT PROGRESSION AMONGST PATIENTS INITIATED ON ANTIRETROVIRAL THERAPY AT THE UNIVERSITY OF LIMPOPO, SOUTH AFRICA

by

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DEDICATION

This is dedicated to all those whom have moulded, supported and encouraged me in those developmental years – including my parents Maria and the late father Simon. My late grandparents Nicodemus and Flora Mollo, including my late uncles Lesiba George Mollo and Piet Karel Mollo, I am who I am because of you.

DECLARATION

I, **Tshepho Jan Maselela**, solemnly declare that the mini-dissertation hereby submitted to the University of Limpopo for the degree of Masters of Public Health has never been submitted by me or any other person at this or any other University, that this is my own work in design and execution, that I am aware of the implications of plagiarism as academic dishonesty, and that all sources of reference used have been duly acknowledged.

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Signature Date

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I would like to thank God of Grace, without Him, nothing is possible.

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ABSTRACT

Background:

Human Immunodeficiency Virus (HIV) has affected all parts of the world, and as of 2019, more than 76 million people have been infected by HIV. South Africa has the largest population of people living with human immunodeficiency virus (HIV) in the world and the highest infected group were aged 24 to 49, and females had the highest percentage in viral load suppression for all age groups. HIV infection leads to advanced loss of CD4 T cells and the roll out of antiretroviral therapy (ART) has bring about in significant cutbacks in HIV-associated complications by recovering the CD4+ T cell count. Some patients may not be successful in attaining this result, and some may accomplish it only after a number years of treatment. The disease progression and the health conditions amongst People Living with HIV-AIDS (PLWA) has improved substantially in the past two decades. The purpose of this study was to evaluate the disease progression of the patients initiated on ART from 2017 to 2019 at the University of Limpopo Health Centre, in Limpopo province.

Methodology:

A descriptive retrospective investigation was carried out which followed a quantitative approach in which secondary data from medical files of 259 patients initiated on ART at University of Limpopo Health Centre was used. where outcomes of ART initiation assessed and evaluated in association with characteristics of patients. Data analysis was done using the STATA statistical software version 12 for Windows (STATA Corporation, College Station, Texas). Frequency tables were used to make comparisons between groups for continuous and categorical variables using student t-test, and chi-square test. P-value less than 0.05 at 95% confidence level were regarded as significant.

Results:

The research finding revealed 80.0% of the study participants were females and the mean age group of participants diagnosed HIV positive was 28.28 years with standard deviation of ±7.5. The mean of the CD4 count cells at baseline for females was 411.4 cells/μL while for males was 341.2 cells/μL (*p=0.212*). The mean CD4 count cells at last ART visit for females was 613.7 cells/μL while for males was 452.9 cells/μL

(*p<0.001*). There has been significant increase of the CD4 cell count from the baseline to the last ART visit as it is noted in the increase in proportion of patients with CD4 cell count of more than 500 in all the years. The proportion of patients with baseline CD4 cell count of 200 to 350 (moderate immunodepression) were high in 2019 and 2017 at 40.6% and 40.3% respectively. Majority of the patients were transferred out to other facilities at 79.4% as most patients are students and only 2.3% mortality rate has been reported for the study period. Majority of the patients initiated on ART at University of Limpopo were in WHO stage 2 at 45.5% followed by those in stage 3 and stage 1 at 22.2% and 21.8% respectively. Patients who were 24 years or older were 1.1 times more likely to have improved CD4 cell count at the last date of ART visit as compared to younger patients but not statistically significant while males were 3.5 times more likely to have improved CD4 cell count at the last date of ART visit as compared to females which was statistically significant. Patients who were initiated on ART at WHO stage 4 were 6.67 more likely to have improved CD4 cell count at the last date of ART visit as compared to those who were initiated on ART at WHO stage 1.

Conclusion:

The treatment progression in the study setting was found to be convincing and acceptable which is similar to the findings reported in other studies in many other countries. The significance of CD4 cell counts monitoring for HIV patients cannot be overemphasised. This study recommends a strengthened testing and treatment programme targeted males amongst the university community, enhance provider-provider relationship when patients are transferred out to other health facilities, enhance the collection of baseline and progressive data on both the CD4 cell count and viral load.

Key concepts:

Antiretroviral therapy, CD4 cell count, Viral load, HIV infection, University Health Centre

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LIST OF ABBREVIATIONS

ADCs	AIDS-defining cancers
AIDS	Acquired Immuno-Deficiency Virus
ARV	Antiretroviral Therapy
CD4	Cluster of Differentiation 4
COP18	18TH Conference of the Parties
CVD	Cardiovascular Disease
DoH	Department of Health
FDC	Fixed Dose Combination
FSW	Female Sex Worker
HAART	Highly Active Antiretroviral Therapy
HCT	HIV counselling and testing
HIV	Human Immuno-Deficiency Virus
HSRC	Human Science Research Council
ICT	Information and Communication Technology
ICU	Intensive Care Unit
LTFU	Loss to Follow Up
NCD	Non-communicable Diseases
PLWHA	People Living with HIV/AIDS
RNA	Ribonucleases
RWHAP	Ryan White HIV/AIDS program
SSA	Sub-Saharan Africa
SPSS	Statistical Package for Statistical Social Sciences
TB	Tuberculosis
TREC	Turfloop Research Ethics Committee
VL	Viral Load
WEBDHIS	Website District Health Information Software

DEFINITION OF CONCEPTS

Antiretroviral therapy – drugs that interfere with the replication of retroviruses like HIV and used to stop the progression of HIV disease by reducing the viral load and thereby allowing some recovery of the immune system (Lu, Wu, Yarla, Xu, Ding & Lu, 2018). In the context of this study, antiretroviral therapy will refer to the approved treatment for HIV in South Africa.

Characteristics – attribute in people that are able to provide formal and logical analysis and may be used as the basis of generalizations about classes and other statements that transcend individuality (Stedman, 2018). In the context of this study, characteristics will refer to the socio-demographics of HIV positive patients initiated on ART which could be categorised by age, gender, marital status, educational level and work status.

Treatment progression – evaluation to assess results in defaulting, loss to follow up (LTFU), viral load suppression, co-morbidities and mortality rate of patients on ARV therapy (Zingoni, Chirwa, Todd & Musenge, 2019). In the context of this study, the treatment progression will refer to the improvement in the CD4 cell count from the baseline assessment as compared to the last date for ART visit.

CHAPTER ONE

1.1 Introduction and background

Human Immunodeficiency Virus (HIV) has affected all parts of the world, and as of 2019, more than 76 million people have been infected by HIV (Cunningham & Zeirhut, 2020). According to Cunningham, et.al (2020), as of end of 2019, World Health Organization (WHO) has reported 33 million HIV related deaths and 38 million people are living with HIV, of which 1.8 million being children. The management of disease progression has seen introduction of HIV treatments since in the late 1995, with the first generation of HIV protease inhibitors becoming commercially available (Heather, 2017). The introduction of Highly Active Antiretroviral Therapy (HAART) - a medication regimen used to manage and treat human immunodeficiency virus type 1 (HIV-1) had immediate and profound (Lu, Wu, Yarla, Xu, Ding & Lu, 2018). HIV treatment has improved substantially since the introduction of Antiretroviral Therapy (ARV) (Smith, Brinkman, Geerlings, Smit, Thyagarajan & Sighem et al., 2015)

Approximately 1.2 million people aged 13 or older were living with HIV as of 2011 in the United States and the HIV incidence has remained stable for the past decade with approximately 50,000 new diagnoses annually (Schafer, Albrecht, Dillingham, Hogg, Jaworsky & Kasper et al., 2017). A quarter of HIV-infected persons, are being diagnosed with clinical and/or immunologic acquired immune deficiency syndrome (AIDS) within 3 months and a third within a year, of HIV diagnosis. It was also found that the median CD4 cell count at first presentation for care has increased in recent years, but remains below 350 cells/mm^3 for more than half of U.S. patients (Lopes, Eron Jr, Mugavero, Miller & Napravnik, 2017). Notably, nonurban regions are the only areas with increasing AIDS diagnoses in the United States with the south-eastern region of the country representing the current epicentre of HIV incidence (21, 893 new diagnoses in 2014) and prevalence (402, 681 prevalent cases as of 2013) (Schafer et al., 2017).

Approximately 83% of an estimated 2.1 million adolescents (age 10–19 years) globally were living with HIV in sub-Saharan Africa by 2013 (Mark, Armstrong, Andrade, Penazzato, Hatane & Taing et al., 2017). In Kenya, approximately 72% of adults in need of ART were receiving it which contributed to the improved survival and quality

of life and 380,000 deaths were estimated to have been averted due to ART between 2000 and 2013 (Mukui, Ng'ang'a, Williamson, Wamicwe, Vakil & Katana et al., 2016). A systematic review study of adult and paediatric patients who started ART in clinics and treatment programmes in sub-Saharan Africa found that mortality in these patients decreased substantially over time, with a corresponding increase in undocumented transfers to other clinics and in the rate of interrupting therapy (Zürcher, Mooser, Anderegg, Tymejczyk, Couvillon & Nash et al., 2017). In Ethiopia men had a significantly higher risk of loss to follow-up than women, and aggravated by occupational mobility, alcohol and drug use (Bucciardini, Tatarelli, Hilawe, Fragola, Lucattini & Halifom et al., 2019).

In 2017 South African (SA) population living with HIV was 7 920 000 and out of those infected 4 402 000 were on HAART. The highest infected group were aged 24 to 49, and females had the highest percentage in viral load suppression for all age groups (Zuma, 2019). The goal of initiating ART is to supress the virus so that it does not multiply, while considering outcomes of improved or strengthened immune system and decreasing the risk of more transmissions. The Joint United Nations Programme on HIV/AIDS (UNAIDS) targeted towards elimination of HIV in 2014 includes the diagnosis of 90% of HIV infected individuals, access to treatment for 90% of identified HIV infected persons, and 90% viral suppression among those initiated on treatment (Bulage, Ssewanyana, Nankabirwa, Nsubuga, Kihembo & Pande et al., 2017; Zürcher, 2017). In Limpopo province, Letaba Hospital HIV Clinic study indicated an adherence outcome to be unsatisfactory at 87%, which falls less than the 95% recommended by WHO. However, one can argue that it remains higher than the 61% of the overall province (Mabunda, Ngamasana, Babalola, Zunza & Nyasulu., 2019).

1.2 Problem Statement

The disease progression and the health conditions amongst People Living with HIV-AIDS (PLWA) has improved substantially in the past two decades. Robust estimates of how these improvements have affected prognosis and life expectancy are of utmost importance to patients, clinicians, and health-care planners (Trickey, May, Vehreschild, Obel, Gill & Crane et al., 2017). However, the success of national antiretroviral therapy (ART) programs in expanding access to treatment for HIV/AIDS in low- and middle-income countries is undisputed (Fox, 2015). Some studies have

reported improvements in overall survival and changing causes of death, with proportionately fewer AIDS-related deaths in more recent years (Domingues & Waldman, 2014; Trickey et al., 2017), but none has investigated trends in prognosis after starting ART by calendar period at an academic institution of higher learning.

South Africa has the largest ART programme in the world recorded at to 62% of the 7,7 million of people living with HIV in the country. (UNAIDS, 2019). The HIV students HIV prevention strategies are bearing positive outcome with a prevalence of 3.4% which WHO (2019) describe as being below the country national prevalence . However to continue and maintain these positive outcome, it is important that an understanding of antiretroviral therapy treatment of progression in universities is prioritized. Women continue to make large proportion of university student communities. UNAIDS (2019) reported that HIV prevalence among young women is nearly four times greater than that of young men. South African National AIDS Council (2018) reporting that 540,000 young women were living with HIV, compared to 180,000 young men. The researcher has noted that the disease progressions of patients initiated on ART were not evaluated and analysed and as such decided to conduct this study at the University Health Centre.

1.3 Literature Review

Literature review is a critical and analytical account of the existing research on a topic of study (Massaro, Dumay & Guthrie, 2016) . In this literature review, the following themes are of discussion in chapter 2: global burden of HIV, characteristics of patients initiated on ART globally, Africa and locally in SA, co-morbidities, defaulting rate, Loss to Follow Up, viral suppression and mortality amongst these patients.

1.4 PURPOSE OF THE STUDY

The purpose of undertaking this study is to evaluate disease progression of patients initiated on ART with an aim to inform the Limpopo Health Department and University Health Centre about strengthening, monitoring and evaluation strategies of the patients on ART.

1.4.1 Aim of the Study

The aim of the study is to evaluate the disease progression of the patients initiated on ART from 2017 to 2019 at the University of Limpopo, in Limpopo province.

1.4.2 Objectives of the study

- To categorize the demographics of patients initiated on ART from 2017 to 2019 at the University Health Centre, in the Limpopo Province.

- To evaluate temporal trends in baseline clinical characteristics (CD4 cell count and WHO staging) of patients initiated on ART from 2017 to 2019 at the University Health Centre, in the Limpopo Province

- To determine the proportion of new patients on ART and those who were transferred in during the course of treatment

- To determine the association between the demographics of patients initiated on ART and their treatment progression from 2017 to 2019 at the University Health Centre, in Limpopo Province.

1.5 Research question

How are patients on ART at the University Health Centre, in Limpopo Province progressing in relation to ART treatment?

1.6 Research methodology

In this study, the research question was addressed using quantitative research approach. Quantitative research is an inquiry into social or human problem based on testing a theory composed of variables, measured with numbers, and analysed with statistical procedures, to determine the predictive generalisations of the theory (Creswell, 2013). A more detailed approach to the study methodology is described further in Chapter three which focuses on research design; study site; population and sampling; data collection; data analysis; reliability and validity; and lastly how to minimise bias.

1.7 Ethical consideration

The research proposal was submitted to the Turfloop Research Ethics Committee (TREC) for ethical clearance and was approved, and the certificate is included in document as Annexure A.

1.8 Significance of the Study

The study findings will benefit the University Health and Wellness Centre and the Department of Higher Education and the Department of Health in the understanding of the characteristics of patients on ART including their treatment progression with an aim to improve on the monitoring and evaluation of treatment programmes, which is assessed during regular patient follow-up. The findings will provide clarifications within a university setting to the health professionals on the treatment progressions who provide health services to ART patients. The findings will be sort of a guide to improve or better the service rendered currently.

1.9 Conclusion

This chapter has provided the scientific foundation of the study. The background, aim and objectives were explained. An outline of the literature review which serve to support the rationale, is discussed in the next chapter, i.e., Chapter Two and the methodology which will be detailed in chapter 3.

CHAPTER TWO
LITERATURE REVIEW

2.1 Introduction

Literature review is a critical and analytical account of the existing research on a topic of study (Massaro, Dumay & Guthrie, 2016). The researcher underwent a systematic and thorough identification and review of different literatures that we found to be relevant to the research topic. The literature search was carried out using the libraries and the various internet sources (from Pubmed, Medline and Google Scholar). A number of studies were then obtained and reviewed to gain existing knowledge on the various themes relating the research topic. In this literature review, the following themes are of discussion: global burden of HIV, characteristics of patients initiated on ART globally, Africa and locally in SA, co-morbidities, defaulting rate, Loss to Follow Up, viral suppression and mortality amongst these patients.

2.2 The burden of HIV

Globally 75 % of PLWHA knew their status at the end of 2017 and among those, 79% were accessing ARVs, and 81% of people accessing treatment had suppressed viral loads (Prabhu, Harwell & Kumarasamy, 2019). Sub-Saharan Africa accounts for 71% of the PLWHA worldwide (Ebogo-Belobo, Simeni, Nnouma, Loubou, Abamé & Hapi et al., 2019). Among African countries SA accounts 25% PLWHA (Ayele, Tessema, Amsalu, Ferede & Yismaw, 2018). Sufficient adherence to achieve lifetime suppression of HIV viral replication is possible with modern antiretroviral regimens, further supporting the strategy of maximising diagnosis of HIV and ART initiation, for personal and public health benefit to curb spread of the virus (Monroe, Lau, Mugavero, Mathews, Kenneth & Mayer et al., 2017).

2.3 The initiation of antiretroviral treatment

All PLWHA with detectable viral load, regardless of their CD4 cell count, should begin ART as soon as possible after diagnosis to prevent disease progression, improve clinical outcomes, and limit transmission with rare exception (Günthard, Saag, Benson, Del Rio, Eron & Gallant et al., 2016). Globally, remarkable progress has been made in improving access to ARVs whereby treatment coverage of 65% (9.7 million people) was achieved by end of 2012 compared to the 2015 target of 15 million agreed

by United Nations Member States in June 2011 (WHO 2013a; Baggaley, Dalal, Johnson, Macdonald, Mameletzis & Rodolph et al., 2016). All PLWHA already on ART, 16% (1.6 million people) put on ART in 2012 alone. In SSA which constitutes 69% of HIV infections globally, access to ART increased from 50,000 to more than 7.5 million between 2002 and 2012 (Mutasa-Apollo, Shiraishi, Takarinda, Dzangare, Mugurungi & Murungu et al., 2014; WHO 2013a).

2.4 The global characteristics of patients initiated on ART

In a study conducted amongst 18 European and North American HIV cohorts, it was found that during 84 621 person-years, 2106 (2%) patients died in the first year after starting ART (24.9 per 1000 person-years). The study further reported that 81 608 (92%) individuals remained in the study for more than 1 year. Of this, 2302 (3%) died during 153 813 person-years (15.0 per 1000 person-years). Further 4594 (5%) patients were lost to follow-up during the first year after starting ART and 6674 patients (8%) were lost-to follow-up during the second and third years (Trickey, May, Vehreschild, Obel, Gill & Crane et al., 2017; Schanzer, Antoniou, Kwong, Timmerman & Yan, 2018). In a study conducted amongst the seven participating U.S. HIV clinical sites, found that poor socio-economic status had significant impact in treatment outcomes, especially to those co-infected with TB-HIV. Both heavy alcohol drinking and frequent binge alcohol drinking were associated with less retention in HIV care (Monroe *et al*., 2017).

Postorino, Luciani, Mangano, Carpentieri, Scerbo and Priamo et al., (2015) found in their cohort study that of the 34% of patients presenting with AIDS in Italy, 43% were diagnosed at <350 cells/μL of CD4 cell counts. The major risk factors to these were sexual transmission and intravenous drug use (Postorino et al., 2015). However, a worrying trend was observed in Argentina regarding poor or limited disease progression despite showing retention in HIV care and treatment amongst HIV patients. Argentina is still in poor situations in terms of HIV patient's progress despite availability of ART and free care (Freitas, Avellino-Silva, Gutierrez, Durigon, Pereira & Litivinoc et al., 2018). According to Freitas et al (2018), youth born with HIV presented poor immune status after transition from paediatric to adult care.

2.5 Characteristics of patients initiated on ART in Africa

In SSA, the main mode of transmission is through heterosexual sex, and vertical transmission in children population (Kharsany & Karim, 2016) . HIV infections tend to be higher among wealthier individuals in rural areas and urban found to be higher among lower income communities (Ayele et al., 2018). Studies done in SSA showed that insufficient access to nutritious food tend to be associated with HIV risk behaviours among women (Ayele et al., 2018). In Ethiopia 160 cases of patients on WHO clinical stage 3-4 lived with their families or renting, perceived ART having many side effects.

The use of alcohol was high amongst this group, also not disclosing to their partners (Hønge, Jespersen, Aunsborg, Mendes, Medina & Silva et al., 2016). Despite high prevalence of HIV in SSA, the percentage of PLWHA taking ART regularly as prescribed is low (Yaya, Landoh, Saka, Wasswa, Aboubakari & N'Dri et al., 2014). Zimbabwe found that low baseline weight and WHO stage IV were linked to increase likelihood of becoming lost to follow up (Prabhu et.al.,2019). A longitudinal study conducted in Tanzania hospital showed that mycobacteria prevalence was low in patients who are HIV and has been on HAART for over 1 year (Kharsany & Karim, 2016).

2.6 Characteristics of patients initiated on ART in South Africa

South Africa has approximately 25% of PLWHA and serve as the highest country with HIV rate compared to other African countries (Ayele et al., 2018). The proportion of PLWHA being aware of their status in Female Sex Workers (FSW) is higher than in general population, however the survey done among FSW in urban areas contradict the outcome (Hakim, MacDonald, Hladik, Zhao, Burnett & Sabin et al., 2018). Furthermore, in a study conducted at a public primary health care clinic in Johannesburg of South Africa, found that with attrition, there were no significant differences in the risk of virologic suppression among patients on a Fixed Dose Combination (FDC) compared to those on multi-pills. These findings were observed at both 6 and 12 months where patients on a FDC presented marginally higher rates of suppression with no discernible differences in risk (Van Der Walt, Lancaster & Shean, 2016.).

The qualitative study conducted in the informal settlement at Tshwane regarding provision of reproductive health services and prevention of HIV and AIDS reported that women were not getting adequate services in reproductive healthcare, and this might put them at risk of sexually transmitted infections (STIs), HIV and mostly teenage pregnancy (Mataboge, Beukes & Nolte ,2015).

The healthcare professional as participants in Mataboge et al (2015) reported that policies in place are also affecting services negatively, hence education not given due to shortage of staff. Nevertheless, findings were limited to one informal settlement.

2.7 The treatment progression of patients initiated on ART

According to Rahman, Vaidya and Zou (2016) HIV treatment program improved outcomes remarkably on patients concerning maintenance of treatment intake and viral load suppression and Co-infections such as TB, which does affect outcomes of HIV treatment. Van Der Walt, Lancaster and Shean (2016) reported lack of collaborative Care of HIV/TB healthcare leading to inappropriate or unsatisfactory care given to those co-infected patients. Individuals who start ART and achieve viral load suppression on a first-line regimen had incidence of first viral results being low (Monroe et al., 2017).

2.7.1 Defaulting on Antiretroviral Therapy

Psychosocial and interpersonal factors were associated with adherence to care behaviours, and further research recommended on gender and culture specific in improving adherence to care behaviours (Davis, McCrimmon, Dasgupta, Gilbert, Terlikbayeva, Hunt, Primbetova, Wu, Darisheva & El-Bassel, 2018). Adolescence is a stage whereby transformation is intense for this PLWHA. The adherence of these groups has shown to be low (Ngeno, Waruru, Inwani, Nganga, Wangari & Katana et al., 2019). However, the study done in Kenya has shown that treatment program in place has reduced mortality and LTFU (Ngeno et al., 2019).

PLWHA do not only face stigma but also economic constraints as well as social challenges, which affect negatively to their treatment. Yehia et al (2015) depicted that in most cases patients from rural areas do not adhere to treatment than those in urban areas. Health facilities in other rural areas are distant from where patients are, and that result in poor health outcomes and high chances of incomplete adherence to ART.

Achieving universal treat coverage will require strong support linkage to HIV care. The stigma outlined as primary barrier to care and support for PLWHA (Yehai et al., 2015). The study conducted in Boucher, O'Brien, Baxter, Fitzgerald, Liddy and Kendall (2019) associated defaulting with unskilled occupation, marital disharmony, small family size, low to middle class socioeconomic status, smoking and unsatisfactory conduct of health personnel. There are limited studies from literature on the rates of ART defaulter.

2.7.2 Loss to follow up

Patients who are Lost to follow-up after initiation of ART are common in Africa and are a substantial impediment to understanding the effectiveness of promising treatment programs (Geng, Bangsberg, Musinguzi, Emenyonu, Bwana & Yiannoutsos et al., 2010). Discontinuation of treatment by patients cause the high risk of illness and death due to AIDS-related conditions. Rosen, Sydney, Matthew & Christopher, 2017). Between 15% and 40% of patients are lost within the first year of ART (Geng et al., 2010). In SA, findings in one public hospital and clinic was 31% of patients who defaulted soon after ART initiation had died, 25% had transferred out to another health facility and 44% had discontinued treatment voluntarily or could not be found (Rosen et al., 2017).

The study done by the Davis et al (2018) in central Asia, Kazakhstan verified potential strategies that intervention such as electronic reminders, linkage to drug treatment services and patient navigation do enhance adherence. One of the electronic reminders in South Africa is TIER.NET. The reviewed automated technology has been reliable to assist patients adhere to their regimen and decrease health cost as well as increase in adherence rates. (Davis et al., 2018). However, implementation of Information and Communication Technology (ICT) monitoring system requires sufficient infrastructure, operating cost, adequate staff and training to be functional and sustainable (Avery, Mills & Stephan ,2017).

Loss to follow-up differed between regions; rates were lowest in Central Africa and highest in East Africa (Drain, Dorward, Bender, Lillis, Marinucci, & Sacks, 2019). Study done by Bucciardini, Tatarelli, Hilawe, Fragola, Lucattini and Halifom et al., (2019) at Ethiopia showed that men had a significantly higher risk of loss to follow-up than

women did. Ethiopian men have high occupational mobility, men often experience alcohol and drug abuse, which notoriously decreases care adherence, male are usually associated with ideals of strength and well-being that may reinforce HIV-related stigma and may hinder men's access to healthcare services. Nevertheless, limitations of the study are that some of the patients classified as LTFU might have died.

2.7.3 Viral suppression

The goal of initiating ART is to supress the virus so that it does not multiply, while considering outcomes of improved or strengthened immune system and decreasing the risk of more transmissions. Monitoring of clinical response to ART uses viral load because it enables earlier and more accurate detection of treatment failure before immune system deteriorate further (Maina, Bonney, Bukusi, Sedegah, Lartey & Ampofo, 2015; Parekh, Ou, Fonjungo, Kalou, Rottinghaus, Puren & Alexander et al., 2018). The study done in United States reported that after testing viral load, frequent follow-ups made which re-enforce adherence resulting in improved quality of life. The VL testing for adults and adolescents with HIV is at entry into care, 2 to 8 weeks after ART initiation and repeated every 4 to 8 weeks until VL suppressed to less than 200 copies/mL and repeated every 3 to 4 months for those adherents to treatment with consistently suppressed VL (Eisinger, Dieffenbach & Fauci, 2019).

WHO HIV updated guidelines 2017 recommend routine viral load testing conducted at 6 and 12 months after ART initiation and every 12 months thereafter (WHO, 2017) South Africa is currently using the same guideline as recommended by WHO. Nevertheless, CD4 cell count risk charts developed and validated in a South African cohort study were reported useful in settings that continue with no access to VL testing (Koller, Fatti, Chi, Keiser, Hoffmann & Wood et al., 2017; Koller et al., 2017). The study done in SSA countries highlighted some of the challenges noted since the scale up of viral load monitoring (Lecher et al., 2015). It included difficulty with specimen transport, equipment breakdown, personnel shortage, weak laboratory information management and infrastructure. The funding for VL testing equipment's and well-equipped laboratory in the healthcare system is still needed in achieving 90/90/90 strategy(Drain et al., 2019).

2.8 Co-morbidities among patient initiated on ART

PLWHA are more prone to opportunistic infections, thus even other conditions observed (Van Der Walt, Lancaster & Shean, 2016). According to Van der Walt et al (2016), TB accounts for 19.6% HIV/AIDS deaths, followed by other conditions such as corpulmonale, Diabetes Mellitus (DM), pneumonia, liver disease and epilepsy. HIV associated inflammation triggered by some protease inhibitors induce metabolic dysfunction hence results in chronic inflammation causing this comorbidity such as hypertension, diabetes, bone diseases, stroke and other vascular diseases (Serrão, Piñero, Velez, Coutinho, Maltez & Lino et al., 2019). The greater burden turns to increase with age in PLWHA than those who are not infected (Cohen & Torres, 2017). Most common lifestyle diseases such as myocardial infarction, coronary revascularization, stroke, congestive heart failure and amputation for peripheral artery disease (Durand, Chartrand-Lefebvre, Baril, Trottier, Trottier & Harris et al., 2017) caused most deaths. However, this diseases condition was more of public problem, not isolated to PLWHA (Ballocca, Gill, D'Ascenzo, Marra, Cannillo & Bonora et al., 2016).

Cancer is another comorbid of its risk factor is CD4 cells of less than 50 cells per mm2 to 350-499 cells per mm2 (Ebogo-Belobo et al., 2019). Cancer-specific mortality was significantly elevated in HIV-infected in the United States, often found to be colorectal, pancreas, larynx, lung, melanoma, breast, and prostate (Coghill, Shiels & Suneja, Engels, 2015). According to Chinula, Moses and Gopal (2017) Kaposi Sarcoma, Cervical cancer and Non-Hodgkin lymphoma are the most common cancer related to PLWHA in SSA.

2.9 Mortality among Antiretroviral Therapy patients

Surveillance data for death and cause of death are important, as mortality is a key maker of the effectiveness of a country strategy and should be a standardised indicator in international HIV reporting (Laursen, Erikstrup, Wejse & Bissau, 2016). In Asia, a steady reduction observed in Pacific with 39%, western, central Europe and North America 36% and the Caribbean 23% reduction. In Latin America, where ARV coverage has been relatively high and AIDS-related mortality relatively low for many years, the reduction in deaths over the past seven years was 12% (Ayele et al., 2018).

Laursen et al (2016) reported a global decline in deaths from AIDS-related illness has noticed in huge numbers in SSA. The decline was 42% from 2010 to 2017 in eastern and southern Africa. Post-apartheid South Africa had decreased mortality in less than two decades of democracy. The disparities in health and survival chances by income had a negative influence mostly to those who are poor (Haal, Smith & Doorslaer, 2018). In 1997, 14.5% of deaths attributed to HIV/AIDS; this number peaked in 2006 at 41.9% and decreased to 29.1% by 2012 (Pillay, Van Wyk, Msemburi, Dorrington, Laubscher & Groenewald et al., 2019).Despite the higher disease burden among women, more men living with HIV are dying (Ayele et al., 2018).

CHAPTER THREE
METHODOLOGY

3.1 Introduction

In this study, the research question was addressed using quantitative research approach. Quantitative research is an inquiry into social or human problem based on testing a theory composed of variables, measured with numbers, and analysed with statistical procedures, to determine the predictive generalisations of the theory (Creswell, 2013). This quantitative approach was descriptive cross-sectional study, where outcomes of ART initiation was assessed and evaluated in association with characteristics of patients.

3.2 Research Design

The research followed a retrospective and quantitative approach that primarily focused on the use of secondary data obtained from pre-existing patient files to develop an objective conclusion in addressing the research question. In this research the numerical data, characteristic of quantitative research, was essential in establishing associations between variables.

3.1 Study site

The study site/setting is an important component of a research study. The nature, context, environment, and logistics of the study setting may influence how the research study is carried out (Majid, 2018). The study was conducted at the University of Limpopo Health and Wellness Centre, which is located in Mankweng Township, 40 kilometres east of City of Polokwane. The University is situated in the foothills of the Hwiti (Wolkberg range) midway between Polokwane and Magoebaskloof (Maphakela, 2019). The University has an enrolment estimated at 20 000 registered students and has a staff compliment estimated at 1500 employees.

The clinic is situated at the footpath of the popular Gate 2 in the western side of the University, which students use as an access point when going to respective shops and using public transport. The absolute location of the Health and Wellness Centre is recorded as follows 23° 53′ 37.374″ S, 29° 44′ 6.644″ E and with the physical address as: Health and Wellness Centre, University Road Mankweng-E, Polokwane Rural,

Limpopo, South Africa, 0727. World Health Report (2000) emphasises the significance of having the right skill mix of health professionals in a health care facility. Skill mix describes the mix of posts, grades or occupations including the combinations of activities or skills needed for each job within the organization. The clinic skill mix at the study site included the following:

Table 3-1: Staff compliment illustrating Skill mix at University of Limpopo Health and Wellness

Professional Category	Number of Officials	Specialised training
Professional Nurse	6	All NIMART trained
Pharmacist	1	
Social Worker	1	
Health Promoter	1	
HIV Counsellor	2 (1 provided by NDOH	
Condom Distributor	1 – from DOH	
Contract Professional Nurse	4	COVID-19

The clinic provides comprehensive and integrated health care services to both the students and university staff. However, very critical patients requiring specialised care are referred to Mankweng Hospital or Pietersburg Hospital. The clinic ensures that students and staff that might seek medical attention avoid local queues from the Community clinic and misses their academic classes and takes leave of absence.

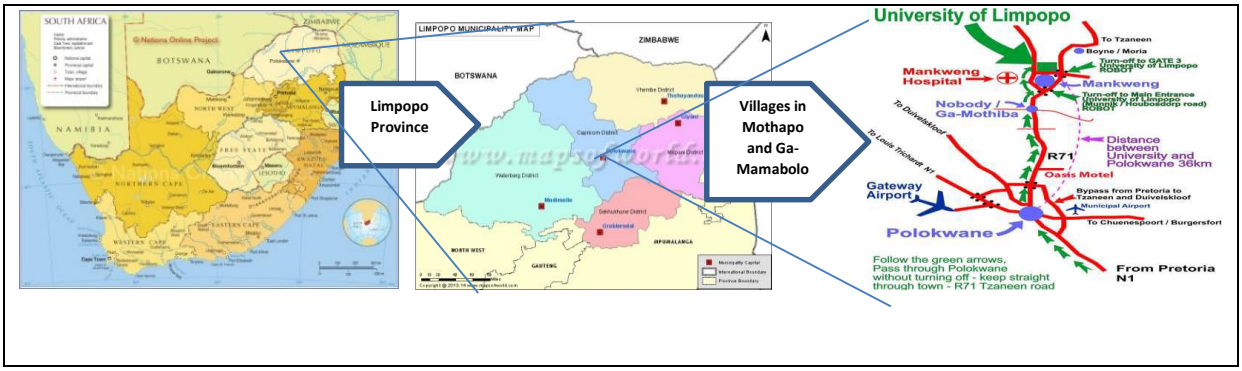

Figure 3-1: Maps of South Africa and the Limpopo Province showing the University of Limpopo located within Polokwane Municipality in Capricorn District, (adapted from Maphakela, 2016)

3.2 Population and Sampling

3.2.1 Population

Population composed of all individuals that are of interest to the researcher (Cozby & Bates, 2015). The population in this study refers to all 386 PLWHA files that has detailed demographic, clinical, diagnosed and treatment history kept at the University Health centre from January 2016 to December 2020.

3.2.2 Sampling technique and sample size

Sampling is a process through which individuals selected from target population (Martinez-Mesa, González-Chica, Duquia, Bonamigo & Bastos, 2016). The sample method involves taking a representative selection of the population and using the data collected as research information (Aydin, Kaplan, Atilgan & Gürel, 2019). It has also been described as a representative “taste” of a group as it ensures that sample is a representative of a population (Mooney & Garber, 2019). Sampling enables the researcher to make a precise estimate of the standard error, which helps in obtaining information concerning some characteristic of the population (Singh, 2015; Chaudhuri & Dutta, 2018).

3.2.3 *Sampling of participants*

3.2.3.1 Sampling size determination

Sampling size refers to mathematical process of deciding, before a study begins, how many subjects studied (A dictionary of epidemiology, 2014). Sample size in this research was taken from Tier.net database of ART patients from the 2016 to 2020 at the University Health Centre.

St $$n = \frac{N}{1 + N(e)^2}$$

Where

- n is the sample size
- N is the population size of ART patients in a year
- *e* is the sampling error (5%)

The total patients initiated on ART for the period 2017 to 2019 were 386 with a distribution of 111 patients on ART in 2017, 143 patients on ART in 2018 and 132

patients on ART in 2019. Therefore, the sample was distributed proportional to the size of the population in each year as per Table 2 below.

Table3-2: Distribution of Sample Size per year.

2017	2018	2019
$n = \frac{111}{1+111(0.05)^2}$ $n = \frac{111}{1+0.278}$ n=**86**	$n = \frac{143}{1+143(0.05)^2}$ $n = \frac{143}{1+0.358}$ n=**105**	$n = \frac{132}{1+132(0.05)^2}$ $n = \frac{132}{1+0.33}$ n=**99**

3.2.4 Sampling procedure

Probability sampling method, sometimes called random sampling, was used in the current study. The researcher should know the sample universe from which the sample is drawn in this sampling method. Under this sampling design every item of the universe has an equal chance of inclusion in the sample (Elfil & Negida, 2017; Sharma, G., 2017). Stratified random sampling technique, which is a modification of the simple random sampling, was applied (Sharma, 2017). A stratified random sampling involves dividing the entire population into homogeneous groups called strata (plural for stratum).

The Health Centre provided data on the patients initiated in the Antiretroviral Therapy programme during the period 2017 to 2019. Stratified random sampling requires that data be divided into various sub-groups (strata) sharing common characteristics like age, sex, race, income, education, and ethnicity. The researcher used the year of enrolment into the ART programme as a common characteristic and had that as a stratum, indicating that three strata's (2017, 2018 and 2019) were created to sampling the study population. A random sample was taken from each strata. The advantages are it assures representation of all groups in the population needed. The characteristics of each stratum can be estimated and comparisons can be made. It also reduces variability from systematic sampling.

Therefore, random samples were selected from each stratum which are years from 2017 to 2019. This assisted in obtaining an effect size from each strata separately, as if it was a different study. Therefore, this means that a total of 290 records were

sampled for the study period being the year 2017 to 2019. In each stratum, a random sampling technique was used to select patient's records. Sampling procedure commenced once the institutions have granted permission for collected data.

3.2.4.1 Inclusion Criteria

Inclusion criteria are set of predefined characteristics used to identify subjects who will be included in the research study (Encyclopaedia of Research Design, 2010). In this study, the inclusion criteria are HIV positive patient files, which were kept at ART clinic at the University Health Centre from 2017 to 2019.

3.2.4.2 Exclusion Criteria

Exclusion criteria refers to a set of predefined definitions that is used to identify subjects who will not be included or who will have to withdraw from a research study after being included (Encyclopaedia of Research Design,2010). In this study, the exclusion criteria were PLWHA medical records from 2017 to 2019 not having detailed healthcare worker clinical notes, laboratory blood report, geographical information, patients who died and transferred to another clinic within this specified period.

3.3 Data sources and data collection

Data collection is the process of gathering information in a meaningful and reliable manner (A dictionary of epidemiology, 2014). The data for the current study was extracted by the computer from the Tier.net system which will be accessed from the Department of Health. The following information was planned to be extracted: age, sex, marital status, level of education, baseline WHO stage, viral load, CD4 cell count and co-morbidities. See APPENDIX 4 for detailed collection tool. The data was cleaned using Microsoft Excel spread sheet and exported to the STATA statistical software version 12 for Windows (STATA Corporation, College Station, Texas) for analysis. Unfortunately, the available records at the health centre did not have enough information on viral loads and the co-morbidities, therefore these information was excluded during analysis.

The data collection method omits the need of participants or assistants. The researcher was the sole and principal person who collected the data. No data collection training was conducted; the researcher only took factual data from the

participant files. Data was managed in a storage system i.e. hard drive, compact disc and file for hard copies. The data storage system was made accessible to only the researcher and supervisors to ensure that participants' confidentiality was ensured.

3.4 Data analysis

Data analysis is an on-going process during research which involves analysing participant information through using analysis guidelines or software (Creswell, 2013)**.** Data was extracted to a Microsoft word excel spread sheet and then transferred to STATA statistical software version 12 for Windows (STATA Corporation, College Station, Texas) for analysis. Assistance in analysing the results was sought from the Statistician at the University of Limpopo. Categorical variables are presented as percentages and frequencies while continuous variables are presented as mean, median and standard deviation.

Furthermore, comparison of categorical variables was done using a Chi-Squared test, whereas continuous variables were compared using a t-test. P-value of <0.05 was considered statistically significant.

Univariate regression analysis was done to determine the contributory factors to treatment outcomes. Univariate regression analysis is a type of regression analysis used to distinguish a distribution of a dependent variable from a distribution of several independent variables. A dependent variable is a variable which depends on the independent variables and is an outcome or result of the influence of the independent variable. An independent variable is defined as a variable which probably causes, influences or affects outcomes (Creswell ,2013). The dependent variable in the current study was treatment outcome (treatment progression) and the independent variables were patient demographic factors.

3.5 Reliability and validity

Internal and external validity in research are the two main principles for gauging the validity of research designs, examining causal propositions (Matt, Brewer & Sklar, 2010). Internal validity is the extent to which a study provides an unbiased estimate of the true value, while external validity occurs if the results apply to the population identified in the study question (Arora & Schriger, 2009).

3.5.1 Reliability

Reliability and validity are a major issue when it comes to research, indeed failure to assure the validity and/or reliability of the findings may cause the research to be questioned or, even worse, to be rejected as invalid (Trochim, 2012). Reliability refers to the consistency and/or repeatability of the measurement (Maimela,2016). The data extraction tool was cross-checked by the supervisor for consistency in the results. Reliability was maintained through excluding patients records that are incomplete and has errors. The data extraction tool was not be changed to maintain reliability in the current study. Repeatability in the current study meant that if another researcher conducts the study similar to this one, he or she should be able to repeat the study and get exactly the same results as the current study.

3.5.2 Validity

Validity refers to the degree to which the measurement procedure actually measures the concept that it is intended to measure (Bastos, Duquia, Ganzalez-Chica, Mesa & Bonamigo, 2014; Maimela, 2016). Validity in research can be obtained in several ways, including face validity, content validity, predictive validity and concurrent validity (Ramos, Montez, Tripp, Ng, Gill & Hung ,2014). In this study the focus was on content validity. Content validity in the current study was achieved by consulting with experts in the field to validate the data collection tool. The tool was piloted using few patient files to check if it was be able to collect what was aimed in the study after the ethical approval and permission to conduct the study had been received.

3.6 Bias

Bias is defined as any propensity, which prevents fair consideration of a request. In research it occurs when systematic error is introduced into sampling or testing by selecting or encouraging one outcome or answer over others (Panacci & Wilkins, 2010). Selection biases was minimised by using systematic random sampling to select patient files. Reporting bias was minimised by reporting exact findings. Interpretation bias was avoided by interpreting variables of interest only.

3.7 Ethical considerations

Research plays a pivotal role in the progress of inventions in medicines and medical technology (Khan, Sultana & Khan, 2012). Research ethics plays an important role, striving to make possible that any research study is conducted in due ethical procedures. Clinical research basically focuses on improving human health individually by improving current trends, methodologies and identifying innovative methods of treatment (Khan, Tareen & Sultan, 2016). Ethical lapses in research can significantly harm human subjects and in research ethics the basic aim of ethics is distinguishing between right and wrong, to recognize the wrong doings and try to avoid them from harming research subjects in any research study (Khan, Sultana & Khan, 2012). The current study was conducted in line with the South African Health Act 61 of 2003, to comply with the norms and standards, or guidelines, set for the conducting of research in terms of the National Health Act (Senkubuge & Mayosi, 2012).

3.7.1 Permission to conduct the study and ethical clearance

The proposal for this study was presented at University of Limpopo Department of Public Health, then submitted to the School of Healthcare Sciences and Faculty of Health Sciences' School Research Ethical Committee for further review before it was sent to Turfloop Research Ethics Committee (TREC) at University of Limpopo for ethical clearance approval. Permission to conduct the study was also sought from the University Heath Centre (Appendix 2 & 3).

3.7.2 Informed consent and voluntary participation

According to Gray (2009), informed consent means that the respondents should participate in the study of their own accord, and that they are free to withdraw from the study anytime should they wish to. In the current study, informed consent was not required because the study used secondary data.

3.7.3 Privacy, confidentiality and anonymity

From a legal perspective and research ethical considerations, the protection of privacy will be linked to the processing of personal data. Thus, the current research was conducted in accordance with basic considerations for data protection, such as personal integrity, privacy and responsible use and storage of personal data. Confidentiality means the nondisclosure of certain information except to another

authorized person. The concept of confidentiality applies that the information a person reveals to a professional is private and has limits on how and when it can be disclosed to a third party (Guraya, London & Guraya, 2014). Information provided by the health centre was kept confidential, stored and only the researcher and research supervisor had access to the storage system i.e. hard drive and file for hard copies. Patient identifiable information from the records were not revealed during research report writing. The health centre provided data electronically and to ensure that the anonymity of patient's records was maintained, files were not be labelled in patient's name but rather in unique identifiable numbers.

3.7.4 Respect and dignity

The researcher will base the research work on a fundamental respect for human dignity which is closely linked to individual inviolability. The researcher protected personal integrity of participants, preserve individual freedom and self-determination, respect privacy and family life, and safeguard against harm and unreasonable strain. To achieve that the patient's records, including patient's name were not displayed on the medical records but rather a unique identifiable numbers. In research ethics, this means that individuals have interests and integrity, which cannot be set aside in research in order to achieve greater understanding or to benefit society in other ways. Researchers must protect personal integrity, preserve individual freedom and self-determination, respect privacy and family life, and safeguard against harm and unreasonable strain.

3.7.5 Harm

The current study was using secondary data and there was no harm which would be caused as patients' names were not availed to the researcher and the study did not have any direct contact with the patients.

CHAPTER FOUR
INTERPRETATION AND PRESENTATION OF FINDINGS

4.1. Introduction

In this chapter, a summary of the findings reports on the results from the secondary data retrieved from the University Health Centre information management system, Consolidated Tier.Net Data system – a *HIV Electronic Register or eRegister.* The HIV Electronic Register is a 3-tier approach to monitoring which includes a paper-based system making up tier 1, an electronic version of the paper register as the middle tier or tier 2, and full electronic medical record software at the 3rd tier. These 3-tier approach allows the University and the Provincial Health Departments or ministries of health to strategically implement one of the three tiers in each of their facilities offering ART services.

The data was collected using full electronic medical record software, which allowed the researcher access to the variables of interest. The participants have been on ARVs for more than a year and their blood results were reviewed to see progress of their viral load and CD4 cell count. Based on the captured data on participants' progress on ARV treatment progression, allowed the researcher to analyse socio-demographic data and treatment and patients' virological and immunological status as established in their blood results.

The data was collected from the University's Consolidated Tier.Net Data system – a *HIV Electronic Register* which was analysed using the SPSS statistical package. The analysis was aimed at addressing the study objectives as included below

- To categorize the demographics of patients initiated on ART from 2017 to 2019.
- To determine the proportion of patients who were transferred in and transferred out during the course of treatment
- To evaluate progressive trends in baseline clinical characteristics (viral load, CD4 cell count and WHO staging), mortality rate and comorbidities of patients initiated on ART from 2017 to 2019
- To determine the association between the demographics of patients initiated on ART and their treatment progression from 2017 to 2019.

4.2. The demographics of patients initiated on ART from 2017 to 2019

The study population or sample characteristics from the current study are presented in Figure 4.1; Figure 4.2 and Table 4.1 below. Majority of the records were of females which accounted for 80.5% of the participants, as a result, it can be argued that there were more females receiving treatment than males.

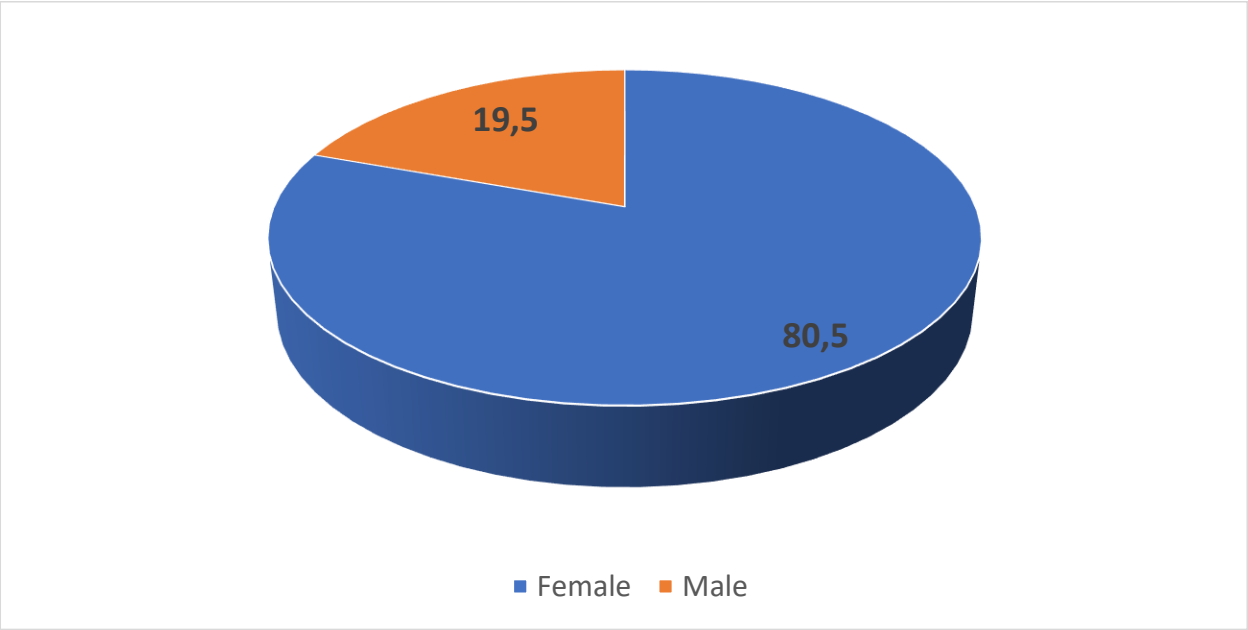

Figure 4.1: Gender distribution of HIV positive patients initiated on ART

Majority of participants were in age group 25 – 34 years at 58.6% followed by those in age group less than or equal to 24 years; 35 – 44 years then 45 – 54 years and lastly more than 55 years at 34.6%; 11.3% and 4.3% respectively as presented in Figure 4.2 below.

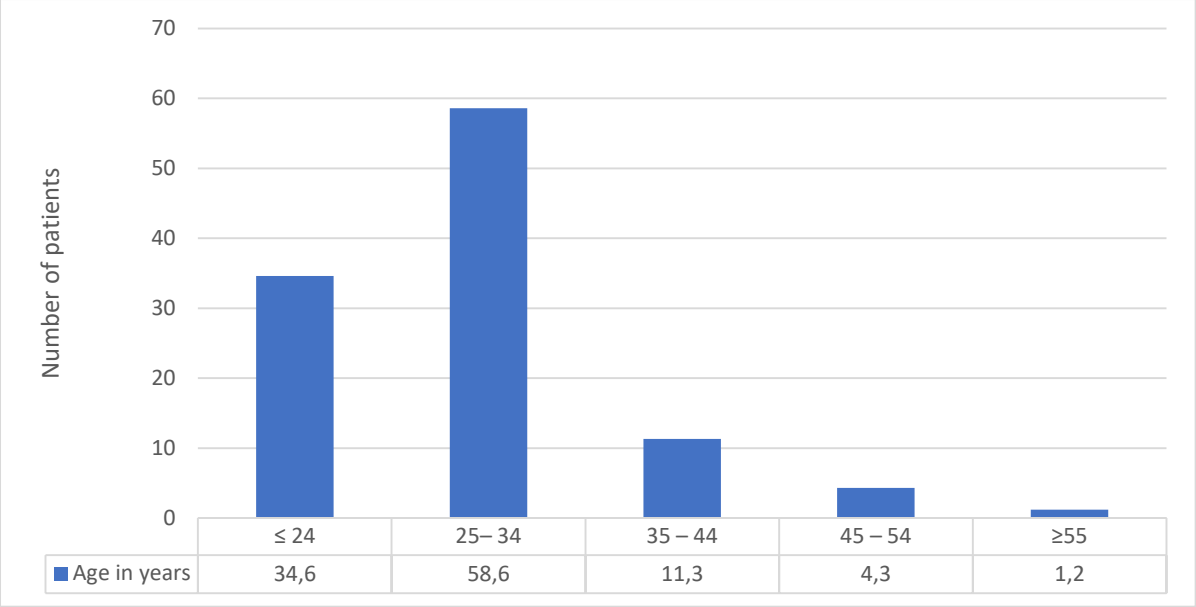

Figure 4.2: Age distribution of HIV positive patients initiated on ART

The mean age group of participants diagnosed HIV positive was 28.28 years with standard deviation of ±7.5 (females with mean age of 28.4 and males with mean age of 27.6) and there was no statistical significance difference between the age groups. The mean of the CD4 count cells at baseline for females was 411.4 cells/μL while for males was 341.2 cells/μL and there was no statistically significance between these two (*p=0.212*). The mean CD4 count cells at ART visit for females was 613.7 cells/μL while for males was 452.9 cells/μL and there was statistically significance between these two (*p<0.001*). Approximately 86 (33%) of participants were initiated in the ART programme with a CD4 cell count baseline of greater than 500 cells/μL Majority of the patients were transferred out to other facilities at 79.4% as most patients are students and only 2.3% mortality rate has been reported for the study period as presented in Table 4.1 below:

Table 4.1: Characteristics of HIV positive patients initiated on ART by gender

		Females (n= 207)		Males (n= 50)		P-value
		Mean	**±SD**	**Mean**	**±SD**	
Age		28.4	7.8	27.6	6.4	0.790
CD4 count cells baseline		411.4	257.6	341.2	174.3	0.212
CD4 count cells at last visit		613.7	263.2	452.9	210.2	<0.001
		n	**%**	**N**	**%**	**P-value**
Age in years	≤ 24	17	34.0	72	34.8	
	25– 34	27	54.0	98	47.3	
	35 – 44	4	8.0	25	12.1	0.790
	45 – 54	4	4.0	9	4.4	
	≥55	0	0.0	3	1.5	
Outcome						
	Active	43	86.0	0	0.0	
	LTF	0	0.0	6	2.9	0.046
	RIP	0	0.0	4	1.9	
	TFO	7	14.0	197	95.2	

Legend

LTF: Lost to Follow-up
RIP: Rest in Peace
TFO: Transferred Out

4.3 Temporal trends in baseline clinical characteristics (CD4 cell count and WHO staging) of patients initiated on ART from 2017 to 2019 at the University Health Centre, in the Limpopo Province

The Table 4.2 above presents the baseline CD4 cell count and WHO staging for HIV positive patients initiated on ART he WHO Clinical stage on initiation. Majority of patients were at having between 200 and 350 CD4 cell count (moderate immunodepression) at 36.7% followed by those who had CD4 cell count of more than 500 while only 14.1% had CD4 cell count of less than 200 (severe immunodepression). In comparison of gender a similar distribution has been witnessed like in general study participants but the difference was noted in females as those patients with CD4 cell count of more than 500 were second highest at 30.1% following those who had CD4 cell count of 200 to 350 (moderate immunodepression). The WHO staging analysis revealed that majority of the patients initiated on ART at University of Limpopo were in WHO stage 2 at 45.5% followed by those in stage 3 and stage 1 at 22.2% and

21.8% respectively. It should be noted that there was a statistical significance difference between gender (*p<0.001*) when considering WHO staging as majority of the participants were in WHO stage 3 were males at 46% followed by those in stage 4 at 28% while females were in majority at 56.5% followed by those in stage 1 and stage 3 at 27.1% and 16.4% respectively.

Table 4-2: The temporal trends of clinical baseline characteristics (CD4 cell count and WHO staging) of HIV positive patients initiated on ART

	Both sexes (n=257) n(%)	**Male (n=50) n(%)**	**Female (n=207) n(%)**	**p-value for trend**
Baseline CD4				
<200	27 (14.1)	6 (15.8)	21 (13.7)	0.212
200-350	70 (36.7)	17 (44.7)	53 (34.6)	
350-499	43 (22.5)	10 (26.3)	33 (21.6)	
>500	51 (26.7)	5 (13.2)	46 (30.1)	
WHO staging				
Stage 1	56 (21.8)	0 (0.0)	56 (27.1)	<0.001
Stage 2	117 (45.5)	0 (0.0)	117 (56.5)	
Stage 3	57 (22.2)	23 (46.0)	34 (16.4)	
Stage 4	14 (5.5)	14 (28.0)	0 (0.0)	
Unknown	13 (5.1)	13 (26.0)	0 (0.0)	

Figure 4.2 below presents the comparison of baseline CD4 cell count and CD4 cell count at last ART visit per year. There has been significant increase of the CD4 cell count from the baseline to the last ART visit as it is noted in the increase in proportion of patients with CD4 cell count of more than 500 in all the years. The proportion of patients with baseline CD4 cell count of 200 to 350 (moderate immunodepression) were high in 2019 and 2017 at 40.6% and 40.3% respectively as presented in Figure 4.2 below.

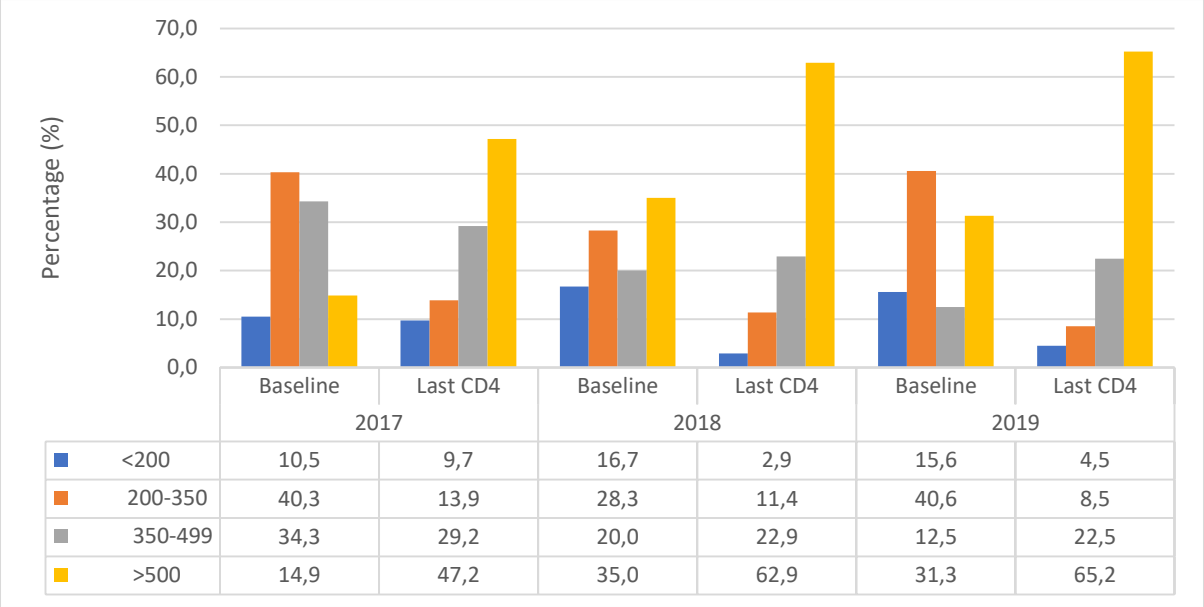

Figure 4.3: CD4 cell count of ART patients at baseline as compared to last date of ART visit stratified by year

4.4 The proportion of new patients on ART and those who were transferred in during the course of treatment

Table 4.3 summarises the proportions of participants were transferred in and out of the University of Limpopo ART programme. Approximately 74% were new patients initiated on ART at the University of Limpopo ART programme and of there was no statistical significance difference in gender and different age groups. However, there was a statistical significance difference in baseline CD4 cell count as majority of the new patients initiated on ART were having CD4 cell count between 200 and 350 at 35.9% while those who were transferred were at 40.6%. There was no statistical significance difference in WHO staging.

Table4-3: The proportions of participants transferred in and out of the University of Limpopo ART programme

	New patients (n=190; 73.9%)	Transfer in (n=67; 26.1%)	p-value for trend
Gender	**n(%)**	**n(%)**	
Males	36 (19.0)	14 (20.9)	**0.729**
Females	154 (81.1)	53 (79.1)	
Age in years			
≤ 24	66 (34.7)	23 (34.3)	0.199
25– 34	95 (50.0)	30 (44.8)	
35 – 44	21 (11.1)	8 (11.9)	
45 – 54	5 (2.6)	6 (9.0)	
≥55	3 (1.6)	0 (0.0)	
Baseline CD4			
<200	19 (12.0)	8 (25.0)	0.048
200-350	57 (35.9)	13 (40.6)	
350-499	41 (25.8)	2 (6.3)	
>500	42 (26.4)	9 (28.1)	
WHO staging			
Stage 1	38 (20.0)	18 (26.9)	0.066
Stage 2	94 (49.5)	23 (34.3)	
Stage 3	42 (22.1)	15 (22.4)	
Stage 4	10 (5.3)	4 (6.0)	
Unknown	6 (3.2)	7 (10.5)	

4.5 The association between the demographics of patients initiated on ART and their treatment progression from 2017 to 2019 at the University Health Centre, in Limpopo Province

In the context of this study, the treatment progression will refer to the improvement in the CD4 cell count of above 500 cells/μL from the baseline assessment as compared to the last date for ART visit. Therefore, patients who were 24 years or older were 1.1 times more likely to have improved CD4 cell count at the last date of ART visit as compared to younger patients but not statistically significant while males were 3.5 times more likely to have improved CD4 cell count at the last date of ART visit as compared to females which was statistically significant. Patients who were initiated on ART at WHO stage 4 were 6.67 more likely to have improved CD4 cell count at the last date of ART visit as compared to those who were initiated on ART at WHO stage 1 as presented in Table 4.4 below.

Table 4-4: The univariate logistic regression of determine the association between sociodemographic and treatment progression

Variables		OR (95% CI)
Age		
	<24 years	Reference (1)
	≥24 years	1.09 (0.63 – 1.90) [a]
Gender		
	Female	Reference (1)
	Male	3.54 (1.77 – 7.08)*
WHO stage		
	1	Reference (1)
	2	0.63 (0.33 – 1.19)[a]
	3	0.97 (0.46 – 2.02)[a]
	4	6.67 (0.92 – 14.57)*

Values are reported as odds ratios (95%CI); * significant *at p<0.05;* ** significant *at p<0.005;* *** significant *at p<0.001*, [a]Not significant

4.3. Chapter Summary

This chapter presented and described the results of the study in tables and figures. The data were analysed to illustrate the characteristics of the study participants using descriptive statistics. The disease progression in response to the anti-retroviral therapy using markers were analysed using descriptive statistics. The following section, Chapter 5, presented the summary of the research findings, the limitations of the study, proposed recommendations, and conclusions.

CHAPTER FIVE
INTERPRETATION AND PRESENTATION OF FINDINGS

5.1 Introduction

The aim of the study was to evaluate the disease progression of the patients initiated on ART from 2017 to 2019 at the University of Limpopo's Health and Wellness Centre in Limpopo province. The study used a quantitative research study approach. This chapter summarises the findings and discussions made, gives conclusions about the disease progression of the patients initiated on ART from 2017 to 2019 at the University of Limpopo. This chapter examines in depth the observed evidence found in our study and considers this in the contexts of the other research in this study area. Finally, the strength and weakness including the limitations of the study are discussed and the implications for further research and clinical and public health practice are described

5.2 Demographics of the patients

The study found that majority of the participants were female and the female-male ratio enrolled in the ARV treatment was found to be consistent with the general population in many countries with females in majority (Furin, Miller & Lesia, 2012; Mosha, 2020). Fonner, Mbwambo, Kennedy and Sweat (2020) affirms that females will remain in majority in the ARV treatment programme as it emanates from the outcome of the targeted female HIV testing including antenatal care. The findings are corroborated by Mosha (2020) affirming that the females contract the HIV at a younger age than males. Fonner, et al. (2020) cautions that in Sub-Saharan countries gender inequities are key drivers of the HIV epidemic thus increasing risk for women.

The reported mean age of patients was 22 years and males were found to be older in the current study which concurs with a study conducted in the sub-Saharan region which revealed that younger men engage in risky sexual behavior making them the highest risk of becoming newly infected with HIV (Akullian, Bershteyn, Klein, Vandormael, Bärnighausen & Tanser; 2017). However, Akullian et al (2017) suggest that women contract HIV at a younger age. The current study findings revealed that there was no statistical significance difference between the age groups and majority of the patients transferred out to other facilities which concurs with a study conducted

in Jigjiga University from Ethiopia (Adugna, Walid, Yerega & Muktar, 2020). This similarity is mainly due to the fact that most patients are students at University and at the end of their studies they are no longer part of the University community. On contrary our study reported lower mortality rate and lost to follow up as compared to other studies (Adugna et al., 2020; Khan, Achappa, Kulkarni, Holla, Dsouza & Unnikrishnan et al., 2022).

4.6 Temporal trends in baseline clinical characteristics (CD4 cell count and WHO staging) of patients initiated on ART

HIV infection leads to advanced loss of CD4 T cells (Motayo, Olusola, Faneye, Aturaka, Oluwasemowo & Ogiogwa, 2017) and the roll out of ART has brought about in significant cutbacks in HIV-associated complications by recovering the CD4+ T cell count. Some patients may not be efficacious in attaining this result, and some may accomplish it only after numerous years of treatment (Motayo et al., 2017; Gelba, Fikadu, Legesse, Wubet, Yesuf & Abera et al., 2020). The current study findings revealed that majority of patients had moderate immunodepression while the least portion of patients had severe immunodepression which concurs with study findings from conducted in in Yaoundé, Cameroon by Mbakam et al (2021) which reported that at initiation on ART, majority of patients had moderate and severe immunodepression respectively. The benefits of joint ART are well acknowledged in literature and after initiation of ART most patients experience an increase in CD4 cell count which reduces the risk of HIV related events and death (Mugo, Shkedy, Mwalili, Awoke, Braekers, Wandede & Mwachari, 2022). This is also supported by the findings in this current study and therefore, changes in CD4 count cell constitute an important component in patient monitoring and evaluation of treatment response as these patients do not have access to routine viral load testing.

The WHO staging analysis revealed that majority of the patients initiated on ART at University of Limpopo were in WHO stage 2 followed by those in stage 3 and stage 1 at respectively which concurs with a study conducted in Dilla University Referral Hospital, Dilla, Southern Ethiopia (Birhane, Loha & Alemayehu, 2021) even though the study participants in the Ethiopian study were general population and not University students mainly. In this Ethiopian study, few opportunistic infections were recorded and majority these were tuberculosis. It is unfortunate that in the current

study, opportunistic infections were not clearly recorded and therefore left out in the analysis. Early initiation of ART regardless of WHO stage has a fundamental effect for clinical prognosis and improved survival (Fiorentino, Nishimwe, Protopopescu, Iwuji, Okesola & Spire et al., 2021). This is supported by WHO guideline and early initiation of ART regardless of WHO stage is considered as one way of preventing the occurrence of opportunistic infections among HIV patients (Abdu, Ali, Anteneh, Yesuf, Birhanu & Mohamed et al., 2021; Fiorentino et al., 2021).

4.7 Proportion of new patients on ART and those who were transferred in during the course of treatment

Within the ART programmes it is difficult to determine the proportion of people retained on ART long-term mainly because individuals classified as lost to follow-up, may have self-transferred to another HIV treatment programme, or may have died without been reported at the ART programme (Haas, Zaniewski, Anderegg, Ford, Fox & Vinikoor et al., 2018). In the current study, 259 patients were initiated on ART between January 2016 and December 2019 and majority of the patients were new patients initiated on ART. During the treatment period in the current study majority of the patients were transferred out and this is mainly because the Centre caters for majority students and it is expected as the students complete their studies will be transferred out. Females in the current study remained in the majority of those transferred out supported by the study conducted by Nglazi et al., (2013).

South Africa introduced Universal Test and Treat (UTT) in September 2016 as a response to World Health Organization (WHO, 2015) recommendation that all People Living with HIV-AIDS (PLWA) including those with CD4 cell counts >500 cells/μL be included in ART. In the current study, it was found that the mean of the CD4 at ART initiation was at 411,53 cells/μL for females and was 341,12 cells/μL for males. This is critical as the Health Centre has illustrated the implementation of the policy considering that there were a number of participants who were initiated in the ART programme with a CD4 cell count baseline of greater than 500 cells/μL. However, Dorward, Sookrajh, Gate, Khubone, Mtshaka and Mlisana et al., (2020) caution that people with CD4 cell counts >500 cells/μL are less motivated to adhere to ART which may lead to high drop-out and ultimately death in the long run. The University Health centre is demonstrating the acceptance of the uptake and treatment of patients upon

testing positive for HIV as obligated by UTT policy. Despite the early initiation of females on the ART, the study found that majority of females are still being initiated with a baseline greater than 500 cells/µL which is supported by Giles, Achhra, Abraham, Haas, Gill and Po et al., (2018) who affirms that in their epidemiological review study found that the median CD4 cell count at ART initiation was, in all cases, lower in men compared to women in each region and time period with the exception of Asia-Pacific sites and North America from 2010 onwards.

4.8 The association between the demographics of patients initiated on ART and their treatment progression

According to the "All for Aids" guidelines (2016) baseline CD4 count is the most clinically used laboratory indicator of HIV progression useful in differential diagnosis. The CD4 count represents the immune system's ability to ward off infection. In the current study, patients males were more likely to have improved CD4 cell count at the last date of ART visit as compared to females which was statistically significant. This findings differs from the findings from the study conducted by Shoko and Chikobvu (2019). Baseline WHO staging acts as a marker of the progression of HIV as a disease at the time of initiation of ART (Temesgen, A., Gurmesa, A. and Getchew, Y., 2018). In this study most of the participants were in WHO stage 1 and 2 indicating the early stages of the disease. A concise review of previous literature indicated that limited studies were available on baseline WHO staging as a predictor of antiretroviral treatment success. However, the current study revealed that patients who were initiated on ART at WHO stage 4 were more likely to have improved CD4 cell count at the last date of ART visit as compared to those who were initiated on ART at WHO stage 1. The findings of this study are consistent with results obtained in a study in India, Thailand and Zimbabwe were baseline CD4 count less than 500 cells per mms were found to have higher odds of developing antiretroviral treatment failure (Chawana et al, (2014).

A study in China on predictors of ARV treatment failure found that there was an inverse correlation between WHO staging and CD4 cell count implying that the lower WHO stages were possibly associated with higher desirable CD4 counts (Kam, Teng & Shao, 2015). A review of previous literature also identified the major link of baseline WHO staging and treatment failure was being found in countries were initiation of ART

medication is dependent on WHO staging (Williamson, Jarvis, Panackal, Fisher, Molloy & Loyse et al., 2017.; Al Tariq, 2018).

4.9 Conclusion

The treatment progression in the study setting was found to be convincing and acceptable which is similar to the findings reported in other studies in many other countries. The significance of CD4 cell counts monitoring for HIV patients cannot be overemphasised (Lecher, 2015). The study reported that HIV disease can be managed better through treatment regimens composed of a combination of three or more antiretroviral (ARV) drugs. HIV treatment remains the critical intervention that the government must strengthen as it has demonstrated its role in suppressing viral load improving the CD4 cell count and above all keeping HIV positive people healthy (Ledergerber et al; 1999). Antiretroviral therapy can prevent HIV from progressing, and it's important that people diagnosed with HIV are initiated into the ART programme at an early stage. The study result concluded that male patients gain fewer CD4 cell counts as compared to female patients.

4.10 Limitations

The limitation of the study is that the findings will not be generalizable to the general population as only records from University of Limpopo Health Centre we used. Again the patients' records did not have enough information on opportunistic infections and viral loads therefore analysis on these variables were not done. This might spark a problem in view of the fact that only the University of Limpopo community were subjects and thus this might not be a true reflection of what other universities are experiencing in South Africa.

4.11 Recommendations

The recommendations of the study are based on various issues that emerged from the study findings and suggestions made by various studies reviewed. The proposed recommendations are as follows:

1. Recruitment of males in the University in the ART programme.

The UTT policy has removed CD4 criteria in order to increase timely uptake of ART, however our findings suggest that males remain limited in the ART initiated patients. It is therefore critical that the University introduce a project targeting males in the institution to recruit newly-eligible patients through improved testing, linkage, and initiation procedures to achieve a 90-90-90 targets

2. Retention of patients

Majority of the patients in the Health Centre ART programme are transferred out in a short term basis considering that the University lifespan is mostly related to students completing their studies. In order to retain the patients on treatment, the university must create a linkage programme of specifically students to their local or preferred clinic in six months before the completion of study. This will ensure that there is Health Centre support and facilitation of relationship with the receiving treatment Centre before finalization of Transferring out. Programme of support considering that retain in the ART

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Appendix 1: DATA COLLECTION TOOL

NB: There will be no interaction with patients however These are the list of questions the researcher (TJ MASELELA) will seek to answer while reviewing individual patient files

Date of HIV diagnosis:

Demographic

Gender					Male	Female
Age in years						
Marital status			Widowed	Divorced	single	Married
Student	**Yes**	**No**	Level of study	Undergraduate		Postgraduate
Staff member					Yes	No
Section B :						
Baseline CD4 cell count			<100	100-350	350-500	>500
(cells per cubic millilitre of blood)						
Baseline WHO clinical			Stage 1	Stage 2	Stage 3	Stage 4
Staging						
WHO clinical staging at time of treatment failure			Stage 1	Stage 2	Stage 3	Stage 4
Viral load			< 1 year		>1 year	
<1000 Copies						
>1000 Copies						

Section c

Co-infection with TB and duration of ART prior LTFU	< = 1	<3	>5
Number of co-morbid conditions	none	< 2	>3
Co-morbid diseases			
Hypertension			
Psychosis			
Diabetes			
Epilepsy			
Arthritis			
Hyper cholesterol			
Chronic depression			
Chronic dermatitis			

Appendix 2: REQUEST FOR PERMISSION TO CONDUCT RESEARCH

From: Maselela TJ
Student Number: 201952468
Cell Number: 082 697 9117
Email address: tshephomaselela@gmail.com

3 Katjiepiering Avenue
Flora Park
POLOKWANE
0699

To: The Director – Mr Norman Letebele
University of Limpopo Health and Wellness Centre

DATE : 25 February 2022

RE: REQUEST FOR APPROVAL TO CONDUCT A RESEARCH STUDY I.R.O MASELELA TJ

Dear Sir

I am currently registered for the degree in Master of Public Health (MPH) with the University of Limpopo. My supervisor is Prof E. Maimela. I have completed the course work and requires to undertake a research study as part of the fulfilment of the academic requirements of the qualification.

My research topic is, **"EVALUATION OF TREATMENT PROGRESSION AMONGST PATIENTS INITIATED ON ANTIRETROVIRAL THERAPY AT THE UNIVERSITY OF LIMPOPO, SOUTH AFRICA".**

The proposed study will be using information from the existing patient files for the period of January 2016 to December 2020. The following variables will be considered including demographics, diagnosis date, viral load and CD4 data, and clinical stage on initiation, treatment history, co-infections and co-morbidities. The data is available and existing in the University of Limpopo Health and Wellness Centre records. No participants will be interviewed in the study.

I commit that all data accessed will be handled with confidentiality and no patients will be identified in the sourcing of necessary data from the patient files.

Should you require any further information, please do not hesitate to contact my supervisor or me. Our contact details are as follows: *tshephomaselela@gmail.com or ericmaimela@ul.ac.za).* Upon completion of the study, I undertake to provide you with a copy of the dissertation.

Your permission to conduct this study will be greatly appreciated.

Yours sincerely

Maselela TJ

Date: 2022/02/25

Appendix 3: PERMISSION TO CONDUCT STUDY AT THE UNIVERSITY HEALTH CENTRE – THE MANAGER/DIRECTOR

Re: Request to conduct study iro Maselela TJ Inbox ×

Tshepho Maselela Fri, 25 Feb, 12:15

Good afternoon This serves to submit my request for approval to conduct the research study in the University of Limpopo Health and Wellness study. I have attach

Letebele, Norman <norman.letebele@ul.ac.za> Mon, 28 Feb, 12:46

to Seponono, Mapula, me, Eric

Dear Tshepho

Permission is granted to you to do your research work at the Student Health and Wellness Centre
Please be reminded that the data and information you collect is solely for the purpose of your study and not for public consumption without authorization from my office
You will be assisted by Sr Maunatlala but please report to the Acting Manager, Ms. Mampa, or myself on your arrival

kindly indicate in advance when you are coming

On Fri, Feb 25, 2022 at 12:16 PM Tshepho Maselela <tshephomaselela@gmail.com> wrote:

> Good afternoon
>
> This serves to submit my request for approval to conduct the research study in the University of Limpopo Health and Wellness study.
>
> I have attached herein the following:
> 1. Letter of Request

Appendix 4: Approval from Turfloop Research Ethics Committee (TREC)

University of Limpopo
Department of Research Administration and Development
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 3935, Fax: (015) 268 2306, Email: anastasia.ngobe@ul.ac.za

TURFLOOP RESEARCH ETHICS COMMITTEE

ETHICS CLEARANCE CERTIFICATE

MEETING: 23 February 2022

PROJECT NUMBER: TREC/29/2022: PG

PROJECT:

Title:	Evaluation of Treatment Progression amongst Patients Initiated on Antiretroviral Therapy at the University of Limpopo, South Africa.
Researcher:	TJ Maselela
Supervisor:	Prof. E Maimela
Co-Supervisor/s:	Mr. MP Kekana Ms. M Maphakela
School:	Health Care Sciences
Degree:	Master of Public Health

PROF P MASOKO
CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE

The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council, Registration Number: **REC-0310111-031**

Note:

i) **This Ethics Clearance Certificate will be valid for one (1) year, as from the abovementioned date. Application for annual renewal (or annual review) need to be received by TREC one month before lapse of this period.**

ii) **Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee, together with the Application for Amendment form.**

iii) **PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.**

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APPENDIX 5: Evidence of language editing

Tiyiselani & Rapetsoa scientific services

Article Publishing • Proof-reading • Editing

85 Compensatie
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Postnet Suite 179 • Private Bag X9307 •
Polokwane • 0700 Tel: 074 866 6914 • Fax:
0864154022

Date: 28 July 2022

To Whom it May Concern

I hereby confirm that I have proof-read the Master of Public Health mini-dissertation titled: **"evaluation of treatment progression amongst patients initiated on antiretroviral therapy at the University of Limpopo, South Africa"** authored by Mr TJ Maselela with student number **201952468**. The document has been edited and proofread for grammar, spelling, punctuation, overall style and logical flow. Considering the suggested changes that the author may or may not accept, at her discretion, each of us has our own unique voice as far as both spoken and written language is concerned. In my role as proof-reader, I try not to let my own "written voice" overshadow the voice of the author, while at the same time attempting to ensure a readable document. Please refer any queries to me.

Malatji MS