(COMPLETED RESEARCH)

LOSS TO FOLLOW-UP OF HIV POSITIVE PATIENTS WHO INITIATED ANTIRETROVIRAL THERAPY BETWEEN 2012 - 2017 AT SHILUVANA LOCAL AREA, GREATER TZANEEN SUB-DISTRICT, LIMPOPO PROVINCE.

by

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MINI-DISSERTATION

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Abstract

Background:
The provision and success of Antiretroviral therapy (ART) depend on monitoring and evaluation of treatment programmes which should be assessed during regular patient follow-ups. The treatment of HIV infection can only be effective if patients are retained in care and programme monitoring is adequately undertaken to understand the effectiveness of the emerging treatment. The outcome of patients lost to follow-up (LTFU) has received relatively little attention and it is predicted that these patients may have stopped taking antiretroviral drugs, resulting in high morbidity and mortality. The provision of ART was introduced into South African public health facilities in 2003 and therefore, attention has shifted from the immediate need to get patients into care, to the long-term challenges of keeping patients in care and on treatment. The objective of the current study was to determine the trends at which HIV-positive patients become LTFU on the ART programme at Shiluvana Local Area's six clinics in the Greater Tzaneen Sub-District, Limpopo Province, South Africa.

Methods: A retrospective cohort study approach was used and data was collected from the database of patients who were LTFU from 2012 – 2017 in the electronic data management system of the District Health Information System. Data was collected from 1161 patients. Data analysis was done using SPSS version 25, in which categorical data was presented using frequencies and percentages and comparisons between groups was done using Chi-square test for categorical data, and Student's t-test for continuous data. *A p-value of <0.05* was considered statistically significant. Univariate regression analysis was done to determine the contributory factors to LTFU for a period of more than 3 months.

Results: The mean age of the study population was 36.5 years old ranging from 16 years to 87 years old and the age distribution of people who were LTFU for ART showed a significant association (*p = 0.001*). The study participants' distribution by gender revealed that majority were females at 71.4%. The study findings also revealed there was a statistically significance difference in health status of the study population and majority of the LTFU were in the younger age group. The CD4 count

of LTFU patients showed a statistically significance difference and majority of the LTFU in patients with a CD4 count of less than 200 were in younger age group also. The TB/HIV co-infection in the study population showed a statistically significance difference and majority of LTFU in the study did not have TB/HIV co-infection. The WHO clinical HIV staging in the study population did not show a statistically significance difference. Marital status, TB/HIV co-infection and WHO clinical staging were found to be a strong predictor of LTFU of more than 3 months.

Conclusion: The study findings bring with them a number of recommendations such as there is a need to have a standardised tracking method of patients who migrate to other health facilities for their ART treatment. This will provide more accurate information regarding LTFU levels and reduce the misclassification of patients. The age group which is affected by LTFU in all variables was in the 20 – 34 years' age group. This is of great concern, as this is the age group who are economically active and should contribute to the future economy of the country. It is therefore recommended that a greater focus should be placed in this age group, with policies and programmes that bring them into ART and retain them there.

Lastly, educational campaigns, in a form of pamphlets and posters to emphasize adherence to ART and the importance of remaining on ART within designated health facilities. In conclusion, patients should be retained in care for as long as possible to prevent the prevalence of the ARV resistant virus that can impact negatively on the ART programme.

Keywords: Antiretroviral treatment**.** Human immunodeficiency virus, Loss to follow-up, socio-demographic.

DECLARATION

I declare that the mini dissertation "Loss to follow-up of HIV positive patients who initiated antiretroviral therapy between at Shiluvana local area, Greater Tzaneen sub-district, Limpopo Province" hereby submitted by me to the University of Limpopo, for the Degree of Master of Public Health, has not been previously submitted by me for a degree to this University or another university. I also declare that this is my own work except where I have stated otherwise, in design and in execution, and that all materials contained herein are duly acknowledged. I have followed the required conventions in referencing the thoughts and ideas of others.

Signed_____

Date _____

DEDICATION

My dedication goes to all health workers who work tirelessly and the government, making ART available to all patients infected with, and affected by, HIV, which improved their lives, including curbing the number of those who are orphaned due to the HIV pandemic.

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prayed and praised me for studying, even though she is not educated, she believes that education is the key to success that empowers everyone, especially a girl child, to become independent, thank you mother for encouraging and believing in me.

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DEFINITIONS OF CONCEPTS

Antiretroviral – drugs that interfere with the replication of retroviruses like HIV and are used to stop the progression of the HIV disease by reducing the viral load and thereby allowing some recovery of the immune system (National Department of Health (NDoH, 2015). In this study antiretroviral will be defined as above.

Adherence – means adhering to a treatment regimen; for the patient it means, taking all the pills and doses in accordance with the manner prescribed by the doctor clinician, and also means maintaining certain lifestyle patterns (e.g. stop smoking and alcohol intake), attending follow-up appointments, collecting all prescriptions, maintaining a healthy diet and other therapeutic behaviour (NDoH, 2015; Lekoloane, 2014). In this study, adherence will be defined as above.

Disclosure – is a process whereby a client revealing or shares the results of his /her HIV status whether positive or negative with partner, or family/friend they trust (NDoH2016). In this study disclosure will be defined as the patient voluntarily reveals his /her HIV status to any friend, partner or family member for support.

Loss to follow-up – is when 180 days or more since a patient's last clinic visit have passed (Chi, Yiannoutsos, Westfall, Newman, Zhou, Cesar, Brinkhof, Mwango, Balestre, Carriquiry, & Sirisanthana, 2011). In this study, loss to follow-up will be defined as when three or more calendar months have passed since a patient's the last clinic attendance without the patient having antiretroviral treatment or without having taken a dose of their treatment; and they are not yet classified as dead or transferred out.

Retention – is defined as the process of continuous participation and engagement in HIV medical and ART care (Holtzman, CW, Brady, KA & Yehia, 2015). In this study, retention in care will be defined as the process where the patient continues to honour appointment regularly for treatment collection and continues to participate in ART and medical care as expected by the healthcare providers and HIV medical care protocols and guidelines.

LIST OF ABBREVIATIONS

AIDS   :   Acquired Immune Deficiency Syndrome

ART   :   Antiretroviral Therapy

CART   :   Combination Antiretroviral Therapy

CD4   :   Cluster of Differentiation 4 (glycoprotein expressed on the surface of T-Helper Cells)

HIV   :   Human Immunodeficiency Virus

LFTU : Loss to Follow-Up

NDoH : National Department of Health

NIMART : Nurse Initiated and Management of Antiretroviral Therapy

PLWA : People Living with HIV/AIDS

PMTCT : Prevention of Mother to Child Transmission

SSA : Sub-Saharan Africa

SPPS : Statistical Package for Social Sciences

UNAIDS : The Joint United Nations Programme on HIV and AIDS

VL : Viral Load

WHO : World Health Organization

CHAPTER1. ORIENTATION OF THE STUDY

• **Introduction and background**

The human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) remains a public health issue on all continents. Globally, an estimated 36.9 million people were living with HIV by the end of 2014 (UNAIDS, 2014; World Health Organization (WHO), 2015). Of this number, 2 million people were newly infected with HIV in 2014, and the Sub–Saharan African region remains the most affected region in the world, with 25.8 million people living with HIV/AIDS (PLWA) accounting for almost 70% of the global total of new HIV infections (WHO, 2015). HIV/AIDS poses an unprecedented challenge to communities, nations and states across Africa, which includes a challenge to human survival, human rights and human development (Poku, 2017).

The incidents of HIV infections are declining in many countries across Sub-Saharan Africa, even though this region remains the continent's most affected HIV and AIDS area, with an estimated 22.9 million PLWA. This number of PLWA accounts for more than two-thirds of new HIV infections globally (Baral & Phaswana-Mafuya, 2012; UNAIDS, 2010). HIV remains functionally incurable; however, antiretroviral therapy (ART) can facilitate PLWA to have a complete and productive life. A public health concern is the provision and uptake of ART, which is still limited in most parts of Sub-Saharan Africa (Baral & Phaswana-Mafuya, 2012). South Africa currently has the highest HIV-infection burden in the world, with an estimated 6.3 million people infected with the virus in 2012 (UNAIDS, 2014).

A major intervention which has been undertaken in many resource-limited settings is the roll out of ART to millions of PLWA. This has brought about a significant improvement in the care for PLWA over the past two decades and has affected prognosis and life expectancy globally (Geng, 2011). South Africa has the largest HIV treatment programme in the world. This programme was found to be larger than

the size of programmes in India, Zimbabwe, Kenya and Mozambique combined. It was reported that by March 2014 over 3 million people in South Africa were on treatment (WHO, 2017).There was a nationwide rollout of antiretroviral treatment programmes in the country in 2004, and since then, life expectancy has increased from 53.4 to 62.5 years of age in 2015 (WHO, 2017). Clinics were accredited as ARV sites in order to promote accessibility to all infected with HIV.

Critically, the provision and success of ART depend on monitoring and evaluation of treatment programmes which should be assessed during regular patient follow-ups. When programme monitoring is not adequately undertaken, the effectiveness of the emerging treatment will not be understood (Geng 2011; Mwale, 2016; Zhou, Tanuma, Junko & Lim, 2012). The outcome of patients lost to follow-up (LTFU) has received relatively little attention. These patients may have stopped taking antiretroviral drugs, resulting in high morbidity and mortality (Brinkhof, Pujades-Rodriguez & Egger, 2009). Therefore, attention has shifted from the immediate need to get patients into care, to the long-term challenges of keeping patients in care and on treatment (Fox, Brennan, Maskew, MacPhail & Sanne, 2010). The objective of the current study is to characterise the population that is discontinuing follow-up ART at a rural clinic. Being a resource-constrained setting, the results of the study will help inform future service delivery processes to improve outcomes.

• **Research problem**
Long-term regular follow-up of ART is an important component of HIV care. Patients who are LTFU while on treatment compromise their own health and the long-term success of ART programmes. The researcher noted that there is a high uptake of HIV patients on the ART programme in the Shiluvana Local Area which has brought about a significant improvement in the health of the PLWA. However, the challenge encountered in this area is the monitoring of the HIV patients, as high number of patients are LTFU in care and treatment. In this local area, there are an estimated 2 703 patients who were LTFU between January 2012 and December 2017, as captured in the District Health Information System (DHIS) for the Mopani District. The breakdown of patients per clinic who were LTFU was high and unfortunately those patients who are unaccounted for, might have died or might be alive and taking treatment elsewhere (Fox et al, 2010). This will eventually impact on the

performance of the ART programme, resulting in increased morbidity, mortality and ART programme failure. The current study aims to characterise the patients who are LTFU at the Shiluvana Local Area clinics

1.3. Purpose of the study

1.3.1. Aim of the study

The aim of the current study was to investigate the LTFU of HIV-positive patients who initiated antiretroviral therapy in health facilities within the Shiluvana Local Area six clinics in Greater Tzaneen Sub-District in the Limpopo Province.

1.3.2. Objective of the study

- To describe the socio-demographic factors of LTFU patients who initiated ART at Shiluvana Local Area Clinics from 2012 – 2017.
- To determine the trends of LTFU patients in the Shiluvana Local Area six clinics of Greater Tzaneen, in the Limpopo Province.
- To determine the relationship between socio-demographic and clinical factors, with the duration of LTFU for patients who initiated ART at Shiluvana Local Area six clinics from 2012 – 2017.

1.4. Research question

What is the proportion of LTFU among patients who initiated antiretroviral therapy (ART) from 2012 – 2017 in the Shiluvana Local Area six clinics of Greater Tzaneen Sub-District, in the Limpopo Province?

1.5. Literature review

According to Brink (2011), a literature review is a scholarly paper which includes current knowledge including substantive findings, as well as theoretical and methodological contributions to a particular topic of interest, that is consulted in order to put the research problem into context. In this study, literature was sourced from various journals, theses and research articles which assisted the researcher to learn what other researchers have already reported about the research problem which the researcher was interested in studying. In the current study, the researcher reviewed the literature in the topics of LTFU for patients who initiated ART, and which will be discussed in detail in Chapter 2.

1.6. Research methodology.

Creswell (2013) and Brink and Van der Walt (2013), define research methodology as the procedure that is used to study a topic, which includes data collection, analysis and the interpretation of data in a systemic approach. A quantitative study design, using a retrospective cohort study was carried out among HIV-infected patients who initiated ART and where LTFU during the period of 2012 – 2017 at Shiluvana Local Area's six clinics. Details of the research methodology will be discussed further in Chapter 3.

1.7. Significance of the study.

The significance of the study is that it may contribute to the solutions used in addressing the problems relating to the LTFU of patients in the ART programme. Further details will be discussed in Chapter 5

1.8. Chapter outline of the study.
- **Chapter 1. The orientation of the study,** the introduction and background on HIV-infected patients, the roll out of ART to the HIV-infected patients, and the challenges faced in ensuring that patients are retained in care. The chapter further covers the research problem, aim, objectives, definitions of terms, and the significance of the study.
- **Chapter 2** reviews the literature from different studies on the topic of LTFU in other resource-limited areas.
- **Chapter 3** outlines the research methodology used in the study, including the research design, research setting, population, sampling, data collection and analysis.
- **Chapter 4** presents the result of the study.
- **Chapter 5** presents the discussions about the findings, limitations of the study and the recommendations.

1.9. Conclusion

This chapter focused on the orientation of the study, the problem statement, the aim of the research, the methodology used in the study, and the significance of the study literature review in relation to LTFU in the patients who initiated ART globally.

CHAPTER 2: LITERATURE REVIEW

This chapter includes a definition of LTFU for patients who initiate ART, and provides a summary of work done globally, including on the African continent and other parts of South Africa, and in the Limpopo Province in particular. Loss to follow up is generally defined as when 3 calendar months or longer have passed from the last clinic attendance by a patient without the patient having antiretroviral treatment in hand or without have taken a dose of their treatment, and they are not yet classified as dead or transferred out (Geng, 2011). Therefore, this will be the definition to be used in the current study.

2.1 Introduction

The new strategy for fighting the HIV epidemic, involving the implementation of the test and treat strategy comes with the potential challenges of ART adherence, retention to care and LTFU among the ever-growing number of patients initiated to treatment. There is a need for strict monitoring and evaluation; in order to achieve the 90–90–90 strategic goals set by UNAIDS (Mberi, Kuonza, Dube, Nattery, Manda & Summers, 2015). Evaluating the outcomes of patients initiated on ART is critical; however, outcomes are generally only based on patients who remain in care. High rates of LTFU diminish treatment options and substantially limit the effectiveness of ART strategies (Wang, Losina, Stark, Munro, Walensky, Wilke, Martin, Freedberg & Wood, 2011).

2.2. Definition of Loss to Follow-up

It is critical for HIV-infected patients who have started ART to visit clinical centres or health facilities regularly so that disease progression and the patients' responses to combined antiretroviral therapy (cART) are monitored (Keiser, Anastos, Schechter, Balestre, Myer, Boulle, Bangsberg, Touré, Braitstein, Sprinz & Nash, 2008). These visits should include giving important information to patients on minimising the risk of disease progression and transmission. Despite this need for regular monitoring, LTFU in HIV cohort studies were common occurrences and frequently reported.

The definition of LTFU tends to vary (Grimsrud, 2015; Mocroft, Kirk, Aldins, Chies, Blaxhult, Chentsova, Vetter, Dabis, Gatell & Lundgren, 2008). This literature review revealed that globally, there is no universal definition for classifying patients as LTFU (Chi et al., 2011). In a multi-study conducted using data from several areas (located in North-eastern, Midwestern, Southern and Western United States of America) LTFU was defined as having no patient visits for at least six months (Fleishman, Yehia, Moore, Korthuis, Gebo & HIV Research Network, 2012). Previous studies of HIV-infected patients have defined LTFU as no patient visit for a period of 12 months, or as failure to show up within 4 months of a scheduled appointment, or as having presented data on LTFU without including the definition (Mocroft et al., 2008). LTFU was generally defined as when three calendar months or longer have passed from the last clinic attendance, without the patient having antiretroviral treatment in hand or without have taken a dose of their treatment, they were not yet classified as dead or transferred out of the ART programme (Geng 2011; Berheto et al., 2014). For the purpose of this study, the definition of LTFU includes patients who may be dead or alive; those who are alive may have self-transferred themselves to another ART clinic, or may not be on any ART treatment anywhere. (Megerso,Garoma, Tolosa Eticha, Daba, Tarekegn & Habtamu, 2016).

2.3 The global burden of LTFU of patients on ART

The treatment of HIV infection can only be effective if patients are retained in care (Geng, 2011). Retention of patients in care is a key strategy of achieving the global 90–90–90 strategy (Jamieson & Kellerman 2016). An increased LTFU of patients who were initiated on ART would render the strategy unachievable. LTFU was found to be a global problem (Harries, 2010). The Asia-Pacific Database provided the following data for the patients who were LTFU: Australia – 2034; Thailand – 47 000; Bangkok – 10 400; Philippines – 1 781; India – 411 037; Singapore – 308 433. The burden of LTFU is also experienced in China, where 45% – 48% patients were found to be LTFU (McManus, Petoumenos, Brown, Baker, Russell, Read, Smith, Wray, Giles, Hoy, Carr & Law, 2015). The study included 6 852 person-years (PY) where 15% of the patients died and 15.5% were LTFU (Alvarez-Uria, Naik, Pakam & Middle, 2013).

2.4 The burden of LTFU in patients on ART in Africa.

Even though the extraordinary scale-up of HIV testing, care and treatment programmes in Sub-Saharan Africa over the past decade has resulted in more than 19 million persons accessing ART, the effectiveness of these programmes has been significantly hindered by high levels of attrition across the HIV care continuum (Elul, Lamb, Lahuerta, Abacassamo, Ahoua, Kujawski, Tomo & Jani, 2017). Patients who are LTFU are common in different African countries which pose an obstacle to the effectiveness of the ART programmes (Geng, Bangsberg, Musinguzi, Emenyonu, Mwebesa, Constantin, Yiannoutsos, Glidden, Steven, Deeks, & Martin, 2013). In Uganda from 2004 to 2007, it was found that between 30% and 39% of patients were LTFU (Geng et al., 2013). In a study conducted in Côte d'Ivoire, it was found that LTFU occurs to all patients of all ages, including children, adults and pregnant women, but that there was a low LTFU of 2.5% in females and 5.5% in their partners (Schechter, Bakor, Kone, Robinson, Lue & Sentura, 2014). In Kenya, 57% of the youth aged between 15 and 21 were found to be LTFU and of these patients, 29% were LTFU immediately after enrolment (Ojwang', Pennera, Blata, Agot, Bukusi & Cohena, 2015) In Nigeria, western Kenya it was found that females were more LTFU than their males partners (De la Mata, Sun Ly, Van Nguyen, Merati, Thanh, Lee, Yong Choi, Ross, Law & Tek Ng, 2017). In a study conducted in Cameroon, it was found that higher risk of LTFU was related to being having a CD4 count > 200, being women of younger age and pregnant at the last clinic visit, and 8.4 % women were LTFU and 7.1 % men (Gwynn, Fawzy, Viho, Wu, Abrams& Nash, 2015).

Mwale (2016) stated that most patients in Zambia, who were LTFU, were associated with patients' factors. In Zambia, a study conducted in Kabwe revealed that 56% were LTFU due to health system, social and economic factors that need to be addressed in order to achieve the third USAID strategic goal that 90% of patients who initiated on ART should be virally suppressed, resulting in the end of the HIV pandemic. In a study conducted in Ethiopia, it was concluded that one in five adult patients, were LTFU (Gesesew, Ward, Woldemicheal & Mwanri, 2017).

Study conducted in Uganda in Wakiso village, 60.5% were females, 43.6 % were below the age of 30 years and 50.1% were married and 33.4% had no documented outcome and were considered LTFU, while their outcome was not known and most

reasons for being LTFU were stigmatisation, long waiting hours especially those who were receiving treatment at hospital when compared with those who were taking treatment at health facilities (Opio, Semitala. Kakeeto, Sendula, Okimat, Nakafeero, Nankabirwa, Kamaragi & Kalyango, 2019). Patients were LTFU at different stages of ART initiation, with some patients who were LTFU even at pre ART period. This was also found in a study done in Nigeria, where 74.9% of patients were LTFU at the pre-ART period (Agolory, Odafe, Swaminathan & Dokubo, 2017).

In a study conducted in Guinea-Bissau, one-third of the patients were LTFU immediately before ART initiation; others were LTFU one year after ART initiation and during the 7-year observation, more than half were LTFU after initiation for different reasons (Honge, Jespersen, Nordentoft & Da Silva, 2013). In a study conducted in Malawi in 2012, it was found that about 440 out of every 1000 HIV patients were LTFU over five years (Estill, Tweya, Egger, Wandeler, Feldacker, Johnson, Blaser, Vizcaya, Phiri & Keiser, 2014). Mozambique has an HIV prevalence of 11.5% among adults with more than 1.5 million PLWA by the end of 2012. Almost one-third of these PLWHA who had started ART were either dead or LTFU (Decroo, Koole, Remartinez, dos Santos, Dezembro, Jofrisse, Rasschaert, Biot & Laga, 2014. In a study conducted in the University of Gondar, it was found that patients aged between 15–30 years were likely to be LTFU compared to older patients which was most likely to be due to socio-demographic factors such as age, occupation, as they have to do daily labour and baseline health functional status; ambulatory patients were more likely to be LTFU than those who were not ambulatory (Berheto, Haile & Mohammed, 2014; Teshale, Tsegaye & Wolder. 2020).

2.5 The South African context of patients who are LTFU on ART

The provision of ART was introduced into South African public health facilities in 2003 which was 3 years after community mobilisation and a Constitutional Court ruling (Karim & Karim, 2010). Patients who are LTFU after initiation of ART are common in Africa and are a substantial impediment to understanding the effectiveness of promising treatment programmes (Karim & Karim, 2010).

Discontinuation of treatment by patients has been shown to cause a high risk of illness and death due to AIDS-related conditions – between 15% and 40% were lost

within the first year of ART (Geng, Bangsberg, Musinguzi, Emenyonu, Mwebesa, Bwana, Constantin, Yiannoutsos, Glidden, Steven, Deeks & Martin, 2010). In South Africa, it has been found that in one public hospital, 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 (Geng et al., 2010). These findings were similar to another study conducted in a public primary healthcare clinic in South Africa. Although ART has dramatically reduced morbidity and mortality for PLWA and increased life expectancy from 53.4 to 62.59 WHO, 2017), incomplete treatment adherence was the major cause of treatment failure, development of drug resistance, HIV disease progression and death (Grimsrud, Cornel, Schomaker, Fox, Orrell, Prozesky, Stinson, Tanser, Egge &Myer, 2016; McManus et al., 2015; Miller et al., 2010).

South Africa was found to have a high number of LTFU patients. In a study conducted in Gugulethu, Cape Town, it was found that both pregnant women and non-pregnant women were at risk of LTFU at pre and on treatment stages. It was found that 19.8% of pregnant women and 17.1% of non-pregnant women were LTFU. This was due to having to deal on an emotional level with the recent HIV-positive diagnosis, difficulty in disclosing the information to their spouse and family members, or lack of preparedness before starting their treatment (Balogum, Melomni, Igwilo, Roberts, Okafor, Folasade, Phyllis & Kanki, 2019 ;Kaplan, Orelli, Zwane, Bekker & Wood, 2008). In KwaZulu-Natal in South Africa, LTFU of 38.1% has been shown to occur at the pre-ART stage (Evangeli, Newell & McGraths, 2016).

2.6 The burden of LTFU in patients on ART in Limpopo.

Loss to follow up (LTFU) is a global problem that needs strict monitoring in order to succeed in the management of PLWHA. Patients who are not monitored regularly and continue to miss their clinic appointments, or running out of treatment, are at high risk of illness, drug resistant HIV and death due to HIV/AIDS related diseases (Mberi et al., 2015). In a study that was conducted in Limpopo at the Thekganang ART clinic, Mathebula (2014) stated that patients who were LTFU had similar reasons to those in other studies conducted by other authors. These included patient-related issues, systemic and psychological issues, relocation due to

employment, transport costs, fear of disclosure, stigma and other issues already mentioned, it was found that 57.1% of male and 42.9% female patients were found to be LTFU.

2.7. Factors contributing to LTFU of patients on ART.

There are several factors contributing to LTFU. These factors include, among others, recent diagnosis, social barriers, cultural barriers, economic barriers, non-disclosure, long waiting times at clinics, unclear follow-up instructions from heath care workers, financial constraints (impacting on transport costs and travel to health facilities),these are part of economic barriers and gender inequalities, where husbands have control over women(Asiimwe et al., 2015; Evangeli et al.,2016; Geng, 2011; Kaplan et al., 2008; Mberi et al., 2015; 2016; Schechter et al., 2014). Societal norms and values do contribute to patients becoming LTFU as amongst others the society they live in do not accept any form of medicines except traditional ones (Sam-Agudu, Pharr, Bruno, Cross, Cornelius & Okonkwo et al., 2017; Nangobi, 2018). There are structural factors such as distance to their treatment centres, long waiting hours at the treatment centres are found to hinder the smooth flow on regular follow ups even the staff attitude is found to contribute to patients missing their appointments eventually lead to the patients missing their appointments for months and eventually becomes LTFU (Tusubira, Akiteng, Nakirya, Nalwoga, Ssinabulya & Nalwadda et al., 2020; Mwangi, 2017).

Other challenges are that patients are confronted with negative healthcare attitudes, child care responsibilities, stigma related to HIV (internalised and external), lack of support from family members and spouses, medication regimen, faith healing and cultural beliefs, mental illness, use of herbal medicines, deteriorated health, shortage of ART at times, shortage of food to support adherence, as well as migration of patients due to employment and side-effects (Mberi et al., 2015; Schechter et al., 2014; Zurcher, Mooser & Andeggeg, 2017).

2.8 Public health intervention to reduce and prevent ART patients' LTFU.

LTFU poses public health challenges in the world, in resource-limited settings due to increased morbidity and mortality rates (Geng, 2011). To respond to these challenges, HIV care programmes have to be accessible, sustainable and should

have continuity with well-trained healthcare providers who will be able to serve those in need (Geng, 2011; Mwale, 2016; Mberi et al., 2015). Public health planners need to find a way to meet patients halfway. Primary health models need to be re-engineered to meet the needs of the patients. These models could include community ART stations, group medications pick-ups, hybrid models of home and clinic-based care, and subsidisation of transportation costs. All these aspects would help in patient retention to care (Geng, 2011). In addition, it is important to identify all patients who were LTFU and develop a strategy to trace and bring them to treatment. By using a tracing team or computer software to track patients who have self-transferred to other ART sites and transfer them out of the system, will enable the healthcare system to have a true reflection of those who are really LTFU (Harries, Zachariah, Lawn & Rosen, 2010).

Extensive counselling for supporting lifelong adherence to medication and retention is a key to treatment understanding and continuation. This could involve the use of radio announcements, reminding patients to collect their medications, develop ART stations at workplaces, as well as pick up points of pre-packed ART at schools, shops or community-based entities, other than the clinic or hospital settings (Harries et al., 2010). In addition, Holtzman et al., (2015) and Mwale (2016) stated that other appointment scheduling, clinic experiences, transportation costs, pharmacy services, medication side-effects, health beliefs and health literacy, were also contributory factors related to the level of LTFU by patients.

CHAPTER 3: RESEARCH METHODOLOGY

3.1. Introduction

In this chapter the researcher reports on how the study was conducted and includes the study design, site identification, sampling methods, data collection and analysis.

3.2. Research method

Creswell (2013) defines research methodology as the procedure that is used to study a topic, which includes data collection, analysis and the interpretation of data in a systemic approach.

3.2.1 Research design

A quantitative research method was used to investigate the rate of LTFU among patients who initiated ART in the Shiluvana Local Area's six clinics from 2012 to 2017, of Greater Tzaneen Sub-District, in the Limpopo Province. Quantitative research focuses on gathering numerical data and generalising it across groups of people to explain a particular phenomenon (Leavy, 2017). The advantage of using a quantitative research approach is the fact that it involves a large number of participants. This enhances the generalisation of the results and means that the research can be replicated, analysed and compared to similar studies. The outcomes of quantitative research provide summaries of data that support generalisations about the phenomenon under study, and this allows for greater accuracy and objectivity of the research findings. A retrospective study subject is generally measured once; the intention is to establish associations between variables (Leavy, 2017). In the current study, records of HIV-infected patients who were initiated on to treatment at Shiluvana Local Area clinics ART programme, and became LTFU between January 2012 and December 2017, were retrospectively investigated.

3.2.2. Research Site

The Limpopo Province is situated in the far northern part of South Africa and is one of nine Provinces of the country. Structurally, the healthcare system in Limpopo Province is composed of the Provincial Department of Health, under the political leadership of a Member of Executive Council (MEC), who is responsible for healthcare service delivery. The Limpopo Province, like other provinces in South Africa, has several health districts with limited management authority. There are 5 health districts in Limpopo Province (Capricorn, Waterberg, Greater Sekhukhune, Mopani and Vhembe). They are responsible for supporting and coordinating the provision of primary health care and district hospital services, including the payment of public healthcare workers. Primary healthcare services are delivered via the district health system which is the cornerstone of health policy in South Africa (Maimela, Alberts, Modjadji, Choma, Ntuli & van Geertruyden, 2016)

This study was conducted in the Shiluvana Local Area clinics, which is situated in the Greater Tzaneen Municipality, which is in the Mopani District of Limpopo Province in South Africa. Administratively, the Mopani District has five sub-districts, namely: Ba-Phalaborwa, Greater Tzaneen, Maruleng, Greater Letaba and Giyani sub-districts. The Greater Tzaneen Sub-District is a rural settlement, with a population of 390100 which is 0.74% of total South Africa (Statistics South Africa (StasSA) 2011). Shiluvana Local Area is made up of six primary healthcare facilities which are Lenyenye Clinic, Maake Clinic, Mokgoboya Clinic, Lephepane Clinic and Moime Clinic and Shiluvana Community Health Centre (CHC), and one secondary health facility which is the Dr CN Phatudi Hospital. This hospital was the only health facility offering ART services in the Sub-District before the year 2011. Once the hospital started experiencing a high number of patients, the clinics were accredited as ART sites and patients were down referred for ART collection to their nearest accredited clinics. These health facilities are sparsely distributed and are situated in different catchment areas. These 6 clinics are situated between 5 km and 20 km from the Dr CN Phatudi Hospital.

3.2.3. Research Population

The study population is the entire group of persons or objects of interest to the researcher that meets the criteria which the researcher is interested in studying (Brink, 2011). In this study, the population was all records of HIV-positive patients who were enrolled in the antiretroviral treatment programme in health facilities from January 2012 to December 2017, within the Shiluvana Local Area, which totalled 5109 patients. Table 3.1 presents the number of patients who were retained in care and those LTFU per clinic which was used to calculate the sample size.

Table 3.1: Number of Patients Retained in Care and LTFU per Facility

Facility Name	Number Retained in care	Number LTFU patients
Lenyenye	1441	505
Maake	842	449
Mokgoboya	468	106
Lephepane	776	451

Moime	503	249
Shiluvana CHC	1079	943
Total	5109	2703

Source: DHIS, 2018 from Limpopo Province

3.2.4. Sample size and sampling technique

A consecutive sample of HIV-positive patients LTFU was filtered from the database from January 2012 to December 2017. A minimum sample size of 1160 was required for the study. This was calculated based on the sampling error of 5%, 95% confidence interval and a total of 2703 LTFU in January 2012 to December 2017 (District Health Information System Statistics). The formula below was used to calculate the sample size for the study (Singh et al., 2014):

Where

- n is the sample size
- N is the population size of patients LTFU
- *e* is the sampling error (5%)

The sample was distributed proportional to the size of the population in each health facility as per Table 3.2

Table 3.2: Distribution of Sample Size per Facility.

Lenyenye Clinic	Maake Clinic	Mogoboya Clinic
n = n = n=**223**	n = n = n=**211**	n = n = n=**83**
Lephepane Clinic	**Moime Clinic**	**Shiluvana CHC**

n =	n =	n =
n =	n =	n =
n=**211**	n=**153**	n=**280**

The principle which was used to select the patients' records from the electronic register was systematic random sampling. The patients' records were selected at regular intervals based on a sampling fraction. The sampling fraction was 2 which were calculated as (population size ÷ sample size). Therefore, the first patient record was selected at random, based on the sampling fraction then subsequent units were chosen at equal intervals of 2. If the sampled record did not meet the inclusion criteria, then that record was excluded, and the next record was selected. The systemic sampling process continued until the required sample size of 1161 was achieved in the different health facilities.

3.2.5. Inclusion criteria: Eligibility criteria for inclusion in the analysis

Records of HIV-positive patients who have been enrolled in health facilities, initiated on ART, aged 15 years and older, who were LTFU within the Shiluvana Local Area between January 2012 and December 2017, were included in this study. The researcher classified LTFU patients as those patients who had 3 or more calendar months passed from the last clinic attendance, without the patient having antiretroviral treatment in hand or without have taken a dose of their treatment, and who were not yet classified as dead or transferred out (Grimsrud, 2015).

3.2.6. Exclusion criteria: Eligibility for exclusion in the analysis

Records which were excluded in this study were of HIV-positive patients not initiated on ART at Shiluvana Local Area, those who honoured their clinic appointments, those who were transferred out to other ART clinics and those who died between January 2012 and December 2017.

3.3. Data source and Collection

Data collection is the process of gathering information that is used to answer the research question. Data for this study was secondary data extracted from the electronic patient management system called *Tier.net*. This computer system is used to capture the information of patients on ART on each follow-up visit, for monitoring

and evaluation purposes. Data records relating to patients with an HIV diagnosis, who met the ART eligibility criteria according to the national ART initiation guidelines of CD4 cells/mm², or WHO stage (III or IV) prior to 2012, and later those with CD4 of 350 cells/ mmor WHO stage (III or IV) were eligible for ART initiation. These patients were followed up until they were LTFU from 2012 – 2017. Patients who met the definition of LTFU after the specified period, were identified as LTFU, and were eligible for analysis. The following patient information was extracted from the database: age, sex, marital status, level of education, religion, baseline WHO stage, viral load and CD4 cell count, history of TB/HIV co-infection, baseline functional and ART regimen at the start and period of LTFU after ART initiation.

3.4. Data Analysis

Once the data was captured, it was cleaned using a Microsoft Excel spread sheet and exported to the statistical software, SPSS (version 25) for analysis. Categorical data was presented using frequencies and percentages, whilst continuous data was presented using means and standard deviations. Comparisons between groups (the groups were categorised by WHO staging, viral load, CD4 cell count, co-infection with TB and duration on ART prior LTFU) was done using Chi-square test for categorical data, and Student's t-test for continuous data. *A p-value* of *<0.05* was considered statistically significant.

Univariate regression analysis was done to determine the contributory factors to LTFU for a period of more than 3 months. 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 duration of LTFU in months and the independent variables were socio-demographic factors of patients who were classified as LTFU.

3.5. Reliability and validity.

Reliability and validity are major issues 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 (LoBiondo-Wood & Haber, 2014).

3.5.1. Reliability

Reliability relates to the consistency of a measure, the ability of an instrument to measure the attribute of a variable consistently (LoBiondo-Wood & Haber, 2014). In the current study reliability was ensured by checking the available data for correctness and data accuracy was ensured by using WHO and Department of Health standard guidelines for checking outliers in the data. Repeatability in the current study means that if the researchers obtain findings from a similar group, if others repeat the same study, they should get exactly the same results as in the current study

3.5.2. Validity.

Validity is defined as the extent to which a concept is accurately measured in a quantitative study. Validity in research can be obtained in several ways, including face validity, content validity, predictive validity and concurrent validity and construct (Ramos, Montez, Tripp, Ng, Gill, & Hung 2,014). In this study the researcher focused on content validity that ensured that it measured all the aspects of the intended concept, LTFU, and the construct validity ensured that inferences can be drawn about the result to the general population of the study.

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 (Pannucci & Wilkins, 2010). In this study the researcher minimised selection bias by selecting only HIV-positive patients' records who initiated ART and have become LTFU during the period 2012 – 2017, in the Shiluvana Local Area. Interpretation bias was minimised by interpreting only the variables in the data collection tool. Reporting bias was

minimised by reporting findings as they are, either positive or negative. Publication bias will be minimised by publishing in peer reviewed journals.

3.7. Ethical consideration

3.7.1. Permission to collect data

Ethical clearance was required before the researcher could collect data to answer the research question. According to Creswell (2013), research involves collecting data from people and therefore, before commencing the study, the researcher should get permission from the Institutional Review Board Committee that provides protection to the study population against human rights violation. In this study, ethical clearance for conducting the study was obtained from Turfloop Research Ethics Committee (TREC). The ethical clearance certificate, number TREC/68/2019-PG is attached as Appendix C. Ethical principles were considered and followed according to the requirements of the Limpopo University Research Committee, Written permission to conduct the study was received from both the Provincial and District Offices of the Limpopo Department of Health, attached as Appendix D. Written informed consent was not feasible as the study used secondary data from an electronic database and patients' health records. Validity and reliability were maintained throughout the study.

3.7.2. Confidentiality and anonymity.

Confidentiality can be guaranteed when the researcher pledges not to share private collected information with others (Barbie, 2013). Confidentiality was maintained by making sure that all the records were kept safe after extraction from the main database at the District Office. The personal identity of the files was not used in order to maintain anonymity. Only unique identifiers were allocated to each record and the collected information was not linked to any patient record.

3.7.3. Privacy

The study did not involve direct contact with patients or interviewing of patients. Therefore, maintenance of privacy in the context of the study was not needed.

3.7.4. Harm

In any study, the wellbeing of the participants should be secured to avoid harm, be it physical, emotional, social or spiritual. The current study involved the use of secondary data and there was no contact with any HIV-positive patients, and therefore, protection from harm was not applicable.

3.8. Conclusion

In this chapter, the methodology used to collect and analyse data was outlined. A quantitative research approach was used to explore the socio-demographic factors, and the trends for which patients were LTFU in the Shiluvana Local Area's six clinics from 2012 – 2017.

CHAPTER 4: PRESENTATION AND INTERPRETATION OF THE FINDINGS

4.1 Introduction.

Chapter 4 of the study presents a summary of the results and data analysis on the various variables used for data collection, to answer the study objectives. The study objectives were as follows:

- To describe the socio-demographic factors of patients who were LTFU who initiated ART at the Shiluvana Local Area Clinics from 2012 to 2017.
- To determine the trends for patients became LTFU in the Shiluvana Local Area, of the Greater Tzaneen Sub-District, in the Limpopo Province.
- To determine the association between socio-demographic and clinical factors with the duration of LTFU patients, who initiated ART at Shiluvana Local Area Clinic from 2012 to 2017.

4.2. Gender distribution.

Figure 4.1: Gender Distribution of the Study Population

The study participants' distribution by gender revealed that majority were females at 71.4%, compared to males at 28.6% (Figure 4.1).

Figure 4.2: Age Distribution of the Study Population Stratified by Gender

The mean age of the study population was 36.5 years old ranging from 16 years to 87 years old. The age distribution of people who were LTFU for ART showed a significant association (*p = 0.001),* as illustrated in Figure 4.2 above and Table 4.1 below. The highest proportion of the study population was females aged 20 – 34 years and 35 – 44 years, at 52.9% and 24.9%, respectively. For males, the highest proportion of the study population was aged 35 – 44 years and 20 – 34 years, at 33.6% and 32.6%, respectively.

4.3. Socio-demographic of the LTFU study population

The study population distribution by marital status revealed that there was a statistically significant difference between the categories of marital status at *p-value = 0.001.* In the category of married, the majority of LTFU were in the age groups 35 – 44 years, at 45.5% followed by the age groups 20 – 34 years, 45 – 54 years and 55 years and above, at 29.3%, 20.6% and 4.6%, respectively. In the category of single, the majority of LTFU were in the age groups 20 – 34 years at 66.7% followed by the age groups 35 – 44 years, 45 – 54 years and less than 20 years, at 19.9%, 6.3% and 5.8%, respectively. In the category of divorced, the majority of LTFU were in the age group 45 – 54 years, at 47.2%, followed by the age groups 35 – 44 years, 20 – 34 years and 55 years and above, at 35.9%, 11.9% and 5.7%, respectively. In the category of widowed, the majority of LTFU were in the age groups 55 years and above, at 75.7%, followed by the age groups 45 – 54 years, 35 – 44 years and 20 – 34 years at 15.2%, 5.1% and 4%, respectively, as illustrated in Table 4.2 below.

The educational status showed a statistically significance difference at *p-value <0.001* and the majority of LTFU were seen in age group 55 years and above in those with no schooling at 44.5%, followed by the age group 45 – 54 years at 21.9%. In the category of those with a primary school education, the majority of the LTFU were in the age group 20 – 34 years at 37.5%, followed by the age groups 35 – 44 years and 45 – 54 years, at 33.7% and 18.4%, respectively. In the category of those with a secondary school education, the majority of the LTFU were in the age group 20 – 34 years at 65.7%, followed by the age group 30 – 44 years and 45 – 54 years,

at 25.7% and 6%, respectively. In the category of those with a tertiary education, the majority of the LTFU were in the age group 20 – 34 years at 66.7%, followed by the age groups 45 – 54 years at 33.3%, as illustrated in Table 4.1 below.

The religious status also showed a statistically significance difference at *p-value <0.001.For Christians,* the majority of LTFU were seen in age group 20 – 34 years at 50.4%, followed by age group 35 – 44 years at 28.2% and 13.3%, respectively and in the category of Muslims, the majority of LTFU were in the age group 55 years and above at 57.1%, followed by the age groups 35 – 44 years and 45 – 54 years, at 28.6% and 14.3%, respectively. In the category of other religions, the majority of LTFU were in the age group 20 – 34 years at 42.54%, followed by age groups 35 – 44, 55 years and above, 45 – 54 years, at 26.2%, 15.9% and 13.3%, respectively, as illustrated in Table 4.1 below.

Table 4.1: Socio-demographic Characteristics of the Study Population

Variable		n	Age (years)					p-value
			<20 n (%)	20–34 n (%)	35–44 n (%)	45–54 n (%)	55+ n (%)	
Gender								
	Male	337 (28.7)	6(1.8)	110(32.6)	113(33.6)	61(18.2)	46(13.7)	0.001
	Female	837 (71.3)	32(3.8)	443(52.9)	209(24.9)	96(11.5)	57(6.8)	
Marital status								
	Married	369 (31.4)	0(0.00)	108(29.3)	168(45.5)	76(20.6)	17(4.6)	<0.001
	Single	653 (55.6)	38 (5.8)	435(66.7)	130(19.9)	41(6.3)	8 (1.2)	
	Divorced	53 (4.5)	0(0.00)	6(11.3)	19(35.9)	25(47.2)	3(5.7)	
	Widowed	99 (8.4)	0(0.00)	4(4.0)	5(5.1)	15(15.2)	75(75.7)	
Educational level								
	No Education	155 (13.2)	1(0.7)	24(15.5)	27(17.4)	34(21.9)	69(44.5)	<0.001
	Primary	496 (42.2)	27(5.4)	186(37.5)	167(33.7)	91(18.4)	25(5.0)	
	Secondary	520 (44.3)	10(1.9)	341(65.7)	128(25.7)	31(6.0)	9(1.7)	
	Tertiary	3 (0.3)	0 (0.0)	2(66.7)	0 (0.0)	1(33.3)	0(0.00)	
Religious status								

Christian	730 (62.3)	29 (4.0)	368 (50.4)	206 (28.2)	97 (13.3)	30 (4.1)	<0.001
Muslim	7 (0.6)	0 (0.0)	0 (0.0)	2 (28.6)	1 (14.3)	4 (57.1)	
Other religions	435 (37.1)	9 (2.1)	185 (42.5)	114 (26.2)	58 (13.3)	69 (15.9)	

4.4. Clinical characteristics of the study population

The study findings revealed that there was a statistically significance difference in health status of the study population at *p-value <0.001*. Majority of the LTFU were in the age group 20 – 34 years at 48.9%, followed by the age groups 35 – 44 years, 45 – 55 years and 55 years and above, at 27.5%, 12.8% and 7.3%, respectively. In the category of bedridden, the majority of LTFU were in the age group 20 – 34 years at 37.4%, followed by the age groups 35 – 44 years, 45 – 54 years and 55 years and above at 27.5%, 17% and 16.5%, respectively, as illustrated in Table 4.2 below.

The CD4 count of LTFU patients showed a statistically significance difference at *p-value<0.001*. In all CD4 count categories, the majority of LTFU were seen in the age group 20 – 34 years. The majority of the LTFU in patients with a CD4 count of less than 200 were in the age group 20 – 34 years at 40%, followed by age groups 34 – 44 years, 45 – 54 years and 55 years and above, at 30%, 16.4% and 11.8%, respectively. A similar trend was seen in the category of CD4 count of between 200 and 349, wherein the majority of the LTFU were in the age group 20 – 34 years at 46.5%, followed by the age groups 34 – 44 years, 45 – 54 years and 55 years and above, at 28.7%, 14.1% and 6.8%, respectively. In the category of CD4 count of between 350 and 499, the majority of the LTFU were in the age group 20 – 34 years at 56.5%, followed by the age groups 35 – 44 years, 55 years and above and 45 – 54 years, at 24%, 9% and 7%, respectively. In the category of CD4 count of greater or equal to 500, the majority of the LTFU were in the age group and 20 – 34 years at 57%, followed by the age groups 34 – 44 years, 45 – 54 years and 55 years and above, at 21.1%, 11.3% and 5.6%, respectively, as illustrated in Table 4.2 below.

The study findings revealed that the TB/HIV co-infection in the study population showed a statistically significance difference at *p = 0.008*. The majority of LTFU in

the study did not have TB/HIV co-infection at 90.3% as compared with 9.7%of those having TB/HIV co-infection. In the category of patient records with TB/HIV co-infection, the majority of LTFU were in the age group 20 – 34 years at 36%, followed by the age groups 35 – 44 years, 55 years and above and 45 – 54 years, at 31.6%, 16.7% and 14%, respectively. Whereas, in the category of patient records without TB/HIV co-infection, the majority of LTFU were in the age group 20 – 34 years at 48.3%, followed by the age groups 35 – 44 years, 45 – 54 years and 55 years and above, at 27%, 13.3% and 7.9%, respectively. The study findings revealed that the WHO clinical HIV staging in the study population did not show a statistically significance difference at $p = 0.450$, as illustrated in Table 4.2 below.

Table 4.2: Clinical Characteristics of the Study Population.

Variable		n	Age (years)					p-value
			<20 n (%)	20–34 n (%)	35–44 n (%)	45–54 n (%)	55+ n (%)	
Health status								
	Ambulatory	992 (84.5)	35 (3.5)	485 (48.9)	272 (27.5)	127 (12.8)	72 (7.3)	0.000
	Bedridden	182 (15.5)	3 (1.7)	68 (37.4)	50 (27.5)	30 (16.5)	31 (17.0)	
CD4 count								
	<200	421 (35.4)	8 (1.9)	168 (40.0)	126 (30.0)	69 (16.4)	49 (11.8)	
	200–349	411 (35.3)	16 (3.9)	191 (46.5)	118 (28.7)	58 (14.1)	28 (6.8)	0.000
	350–499	200 (17.2)	7 (3.5)	113 (56.5)	48 (24.0)	14 (7.0)	18 (9.0)	
	550+	142 (12.2)	7 (4.9)	81 (57.0)	30 (21.1)	16 (11.3)	8 (5.6)	
HIV–TB co-infection								
	Yes	114 (9.7)	2 (1.8)	41 (36.0)	36 (31.6)	16 (14.0)	19 (16.7)	0.008
	No	1059 (90.3)	36 (3.4)	512 (48.3)	286 (27.0)	141 (13.3)	85 (7.9)	
WHO HIV stage								
	1	245 (20.9)	9 (3.8)	128 (52.2)	64 (26.1)	26 (10.6)	18 (7.4)	
	2	515 (43.9)	16 (3.1)	246 (47.9)	143 (22.8)	71 (13.8)	39 (7.4)	0.450
	3	302 (25.8)	11 (3.6)	131 (43.4)	82 (27.2)	41 (13.6)	37 (12.3)	
	4	110	2 (1.8)	47	33 (30.0)	18 (16.4)	10 (9.0)	

		(9.4)	(42.7)				

4.5. Trends in months in which patients became LTFU

Figure 4.3: Trends in Months in Study Population who were LFTU

The study findings revealed that the distribution of the study population who were LTFU in the category of months, had the greatest percentage in the more than 12 months category at 27.5% followed by the 7 – 12 months, less than 3 months and 3 – 6 months categories at 25.4%, 24.8% and 22.3%, respectively (Figure 4.3 above).

Figure 4.4: Trends in Months in Study Population who were LTFU, Stratified by Gender

The LTFU was higher in females at 71.4%, compared to males at 28.6%. Considering the duration of LTFU per gender it was highest in females in the period of more than 12 months at 27.2%, followed by the period of 7 – 12 months, less than 3 months and 3 – 6 months, at 25.7%, 24% and 23.1%, respectively. In males, the LTFU was highest in a period of more than 12 months at 28%, followed by period of less than 3 months, 7 – 12 months and 3 – 6 months, at 26.8%, 24.7% and 20.5%, respectively (Figure 4.4 above).

- **The relationship between socio-demographic factors and LTFU patients who were initiated on ART**

The study findings revealed that there was no significant relationship between gender, age, education and health status, and period of LTFU, in the study population. However, there was a statistically significant relationship between marital status and period of LTFU ($p = 0.036$) and between religion and period of LTFU ($p = 0.002$) as presented in Table 4.3 below.

Table 4.3: Relationship between Socio-demographic Factors and the Duration of LTFU

Variables	LTFU period in months				p-value
	<3	**3–6**	**7–12**	**>12**	
Gender					
Male	90 (26.8)	69 (20.5)	83 (24.7)	94 (27.9)	0.668
Female	201 (24.0)	193 (23.1)	215 (25.7)	228 (27.2)	
Age (years)					
<20	10 (26.3)	9 (23.7)	9 (23.7)	146 (26.4)	
20–34	146 (26.4)	137 (24.7)	124 (22.4)	89 (26.6)	
35–44	68 (21.1)	68 (21.1)	97 (30.1)	51 (32.5)	0.082
45–54	31(19.8)	31 (19.8)	44 (28.0)	26 (25.2)	
55+	36 (34.9)	17 (16.5)	24 (23.3	10 (26.3	
Marital status					
Single	178 (27.3)	144 (22.1)	159 (24.4)	18 (33.9)	
Married	67 (18,2)	87 (23.6)	106 (28.7)	109 (29.5)	0.036
Divorced	14 (26.4)	13 (24.5)	8 (15.1)	171 (26.2)	
Widow	32 (32.3)	18 (18.2)	25 (25.3)	24 (24.2)	
Education					
no education	46 (26.7)	30 (19.5	40 (25.8)	39 (25.2)	
primary	124 (25.0)	98 (19.7)	120 (24.2)	154 (31.1)	0.085
secondary	120 (23.1)	132 (25.4)	138 (26.6)	129 (24.9)	
tertiary	1 (33.3)	2 (66.7)	0 (0.00)	0 (0.00)	
Health status					
ambulatory	244 (24.6)	232 (23.4)	248 (25.0)	267 (26.9)	0.225
bedridden	47 (25.8)	30 (16.5)	50 (27.4)	55 (30.2)	
Religion					
Christian	156 (21.4)	156 (21.4)	203 (28)	215 (29.5)	
Muslim	3 (42.9)	2 (28.6)	3 (42.9)	0 (0.00)	0.002
other	133 (30.6)	104 (23.9)	91 (20.9)	107 (24.6)	

4.6. The relationship between the period of LTFU trends with TB/HIV co-infection and WHO clinical staging.

The study findings revealed that there was no significant relationship between clinical factors such as TB/HIV co-infection and CD4 count, with period of LTFU in the study population. However there was a statistical significance between clinical WHO staging and the period of loss to follow-up (p = 0.008) as presented in Table 4.4 below.

Table.4.4: Relationship of clinical factors and duration of LTFU

Variables	LTFU period in months				p-value
	<3	3–6	7–12	>12	
TB/HIV Co–infection					
No	261 (24.7)	239 (22.6)	273 (25.8)	286 (27.0)	0.623
Yes	30 (26.3	23 (20.2)	25 (21.9)	36 (31.6)	
WHO Staging					
1	51 (20.8)	45 (18.4)	61 (24.9)	88 (35.9)	
2	131 (25.5)	126 (24.5)	125 (24.3)	132 (25.7)	0.008
3	90 (29.8)	66 (21.9)	80 (26.5)	66 (21.9)	
4	19 (17.3)	25 (22.7)	30 (27.3)	36 (32.7)	
CD4 Count					
<200	103 (24.5)	88 (21.0)	112 (26.7)	117 (27.9)	
200–349	102 (24.8)	97 (23.6)	106 (25.8)	106 (25.8)	0.534
350–499	49 (24.5)	52 (26.0)	39 (19.5)	60 (30.0)	
550+	37 (26.1)	25 (17.6)	41 (28.9)	39 (27.5)	

Marital status was found to be a strong predictor of LTFU of more than 3 months, as those who were single and divorced were 1.3 times (*p = 0.001*) and 1.4 times (p = *0.003*), respectively, more likely to be LTFU than those who were married. TB/HIV co-infection was found to be a strong predictor of LTFU of more than 3 months since those who were co-infected were 0.24 less likely to be LTFU for more than 3 months (*p <0.001*). Lastly, WHO clinical staging was found to be a strong predictor of LTFU

of more than 3 months, as those who were in WHO clinical staging level 3 were 0.48 times less likely to be LTFU for more than 3 months.

Table 4.5: Logistic Regression to Determine Predictors of LTFU for More Than 3 Months

	Univariate Logistic Regression	
Age	OR(95%CI)	p-value
<40 years	Ref	
≥40 years	0.05 (-0.20 – 0.30)	0.746
Gender		
Female	Ref	
Male	0.15 (-0.14 – 0.44)	0.321
Level of education		
None	Ref	
Primary	0.24 (-0.16 – 0.64)	0.243
Secondary	0.34 (-0.06 – 0.74)	0.097
Tertiary	0.17 (0.02 – 0.48)	0.891
Marital status		
Married	Ref	
Single	1.3 (0.8 – 2.1)	0.001*
Widowed	0.48 (-1.14 – 0.69)	0.156
Divorced	1.4 (0.8 – 2.4)	0.003*
Health status		
Ambulatory	Ref	
Bedridden	0.06 (0.04 – 0.30)	0.730
TB/HIV Co-infection		
No	Ref	
Yes	0.24 (0.07 – 0.43)	<0.001*
WHO Staging		

1	Ref	
2	0.26 (-0.63 – 0.47)	0.160
3	0.48 (0.08 – 0.87)	0.017*
4	0.23 (0.03 – 0.81)	0.438
CD4 Count		
≥500	Ref	
350 – 499	0.08 (-0.41 – 0.58)	0.744
200 – 349	0.70 (0.56 – 2.20)	0.769
<200	0.32 (0.07 – 0.52)	0.667

Significant

CHAPTER 5: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1. Introduction

The previous chapter presented and interpreted the results of the research study. In this chapter, the results will be discussed with reference to other scientific studies to reach conclusion and recommendations about the findings. This study utilised a quantitative approach for assessing the level of LTFU in ART at Shiluvana Local Area's six clinics.

5.2. Discussion

The introduction of antiretroviral treatment (ART) has contributed to the reduction of AIDS related mortality. However, patients who are LTFU from ART pose a significant problem to the public, healthcare services and the success of ART programmes in resource-poor settings (Berheto et al., 2014). The attainment of a successful ART programme is challenged by the development of drug resistance due to the number of patients who become LTFU in both low- and middle-income countries. LTFU increases morbidity and mortality among HIV-positive patients this results in their health deteriorating, their socio-economic status worsening, their lives do not getting better, they are not able to go back to work, they will always depend on social system and they will increase the burden on the health system (Asiimwe, et al., 2015). Generally since ART initiations, the lives of PLWHA have improved a great deal, but people still discontinue their treatment and become LTFU (Berherto et al., 2014).

The problem of LTFU is not only experienced in South Africa, but is experienced globally, as was evident in the reviewed literature. In this study, both men and women are found to be LTFU, although in different proportions. It was found that the prevalence of LTFU was higher for females compared to males in most studies, which is reflected in this study, as the findings revealed that 71.4% of LTFU were females compared to 28.6% who were male ($p = 0.001$). The study findings concur with findings from a study by Eyassu et al., (2016) conducted in South Africa, Kwa-Thema clinic where females were found to be more LTFU at 67.9% and males at 32.1%. In another study done in Uganda where the LTFU for females was 60.5% compared to that of males at 39.5 % (Opio et al., 2019), this study findings where female participants were more LFTU than the male participants which is consisted with and the current study indicate that the gender of participants has an influence in the rate of LTFU.. The findings of a study done in south-east Ethiopia is in contrast to the current study, as it reported a higher percentage of males that are LTFU at 60.9%, compared to females at 39.1%. In rural areas, this may the results of young men leaving the village in search for employment in an urban area, which renders them LTFU in their local treatment areas (Berheto et al., 2014).

The differences discussed above with respect to this study, it may be attributed to the fact that more females utilise health facilities than males as most males are expected to go to work, so they miss their scheduled appointments. Female social practices related to LTFU might be due to influences held by cultural, gender inequality, socioeconomic factors, family responsibilities (Gesesew et al., 2017) suggest that low literacy levels and higher usage of traditional medicines in females compared to males, may be associated with higher rates of LTFU, which concurs with the current study findings which reveal that these factors might have played an important role in hindering females' adherence to ART and treatment. A study done in Ethiopia showed that males were more likely to be LTFU than females were. A number of reasons were put forward for this difference: it was thought that males were using more addictive drugs than females were; males have to migrate in search of employment elsewhere; males may seek medical care later than females do; their health may have improved and, thus, they find it unimportant to come for follow-up visits; their health may have deteriorated and they were unable to return for their

appointments; or they might have died and their death was unreported, leading to LTFU (Lekoloana, 2014; Megerso, Garoma & Habtamu, 2017).

The mean age distribution of the study population was 36.5 years old, ranging from 16 years to 87 years. A substantial percentage of the study population who were LTFU, were in younger age group 20 – 34 years, within this age group 52.9% of the female age distribution and 32.5% of the male age distribution were situated here, which again reveals that females were found to be more LTFU than their male counterparts. The current study findings is comparable to the study done in Ethiopia, Western Kenya, Nigeria and Asia (De la Mata, et al., 2017), the younger study population were found to be more LTFU than their adult counterparts (Mergeso, et al., 2017) and a study conducted in Kisumu, Kenya support the current study where 79% females were found to be LTFU (Ojwang, et al., 2015).

In comparison with the studies done in Southwest Nigeria, Malawi and Western Kenya, in this study, younger females were found to be LTFU because of a fear of stigmatisation and discrimination, and they choose to collect treatment at clinics far from their nearest clinic to avoid being seen at an ART clinic near their homes. This, in turn, poses a challenge because of transportation costs to travel to far-away clinics, due to peer pressure among females themselves, result in missing their appointment schedule and end up LTFU. Another reason for being LTFU could be the result of increased mobility among the younger study population who are unmarried. All of this implies that being unmarried, a lack of support or staying far from an ART clinic, without committed spousal support, could result in patients not to remain in care and result in LTFU (Balogum,et al., 2019; Ojwang et al., 2015)

In studies conducted in Uganda and Western Kenya, it was found that male participants were more LTFU than female participants (Opio, et al., 2019). In contrast to the current study, males were found to be more LTFU than females especially in the age group of 35 – 44 at 33.6% against 24.9%, respectively, and the age group of 45 – 54 at 18.2% against 11.5%, respectively. It is similar in the >55 years (figure 4.2) where males are found to be more LTFU than their female counterparts. The differences may be attributable to the fact that males in this age group migrate from

the rural areas in search of employment in urban areas. The difference may also be a result of a lack of disclosure, stigmatisation, fear of discrimination or having no symptoms at ART initiation, which results in them stopping their ART.

The relationship between age categories and LTFU in the current study was significant, at *p = 0.001,* which concurs with the findings from a study by Opio et al., 2019 in Uganda where patients who were below the age of 30 years had a higher incidence of LTFU (32 per 1000 person months) as compared to patients 45 years and above(13 per 1000 person months. This could be due to the age group of 35 – 54 years old being more economically active, compared to the >55 age group. It might be assumed that the younger age group is still economically active or might have moved from schools to higher education, got married or might have found employment far away from their ART treatment clinics. These would all contribute to the patients becoming LTFU. Others might have seen an improvement in their health status resulting in them leaving their treatment. The finding of the current study was similar to the study done at the University of Gondar Comprehensive Specialized Hospital, where the younger study population were found to be more LTFU than the adult population (Asiimwe et al., 2015; Teshale, et al., 2020).

The study population distribution by marital status, revealed that there is a statistically significant difference between the categories of the marital status and LTFU with *p = 0.001*. The study revealed that the patients with the highest LTFU were those who were single, at 66.6%, within the 20 – 34 year age cohort. These results are comparable with the study findings by Mberi et al., 2015, in South Africa, conducted at the Tshepang ART Clinic, George Mukhari Hospital. The current study findings also concur with the findings of Eyassu, et al., 2015 which indicated that the study population who were single were more likely to be LTFU than the married study population. This might be attributed to the fact that the single, divorced and widowed study population do not have committed primary partners to support them through the treatment process, whilst others may be forced to work for their survival and so may not wish to disclose their status to anyone due to stigma and discrimination.

Married female people who are LTFU may fear disclosure to their of spouse for fear of spousal abuse or being subjected to cultural issues on women, which dictate that the spouse has to take a decision for the medical care of their partner (Mberi et al., 2015). Another reason for LTFU in the married research population is that they might have self–transferred to other clinics which were undocumented, this results in them registered as LTFU at the facility that they have left, whilst in fact they are receiving treatment at another facility (Zurcher, et al., 2017). This is a common occurrence in many ART clinics in South Africa in which undocumented transfers result in increased LTFU, which warrants improved and standardised procedures to track and report retention. This will help to accurately represent care engagement as well as capture undocumented transfers within the health system (Harries et al., 2010).

With respect to the educational status of the study population there was a statistically significant difference between the educational level of the study population and LTFU in the current study, at $p = 0.001$. It was found that the majority of those LTFU were those who were at age above 55 years and with no schooling. This was followed by those with primary education, in the age group of 20 to 34 years and those with secondary education in the same age group. The current study findings concur with that of several studies (Fox & Rosen, 2010; Alvarez-Uria et al, 2013) However, the current study findings are in contrast to a study conducted at the Tshepang ART Clinic, located at the Dr George Mukhari Hospital in South Africa, which reported that there was no relationship between age, sex or level of education and becoming LTFU (Mberi et al., 2015).

The scaling up of patients on ARV therapy continues in South Africa and the country is determined to ensure the realisation of the 90–90–90 strategy. This means that all patients who are HIV infected are initiated on ART, with the test and treat strategy being implemented in all facilities in South Africa (NDoH 2017). This strategy is aimed at ensuring that those patients who initiated ART are retained in care, to ensure viral suppression. However, there are challenges in ensuring that patients are retained in care as patients default their treatment and eventually become LTFU. These challenges can eventually render the ART programme ineffective as patients will develop drug resistant virus and will infect others with a drug resistant virus, and those infected will eventually fail in the first regimen of ART, leading to treatment

failure. This results in patients having to be switched to additional drugs in the second regimen which are more expensive than the first regimen. There can be potential higher mortality rate for HIV-positive patients, compared to a time when ART were not available resulting in the ART programmes will failure, due to new infections with the ARV resistant virus (Lekoloane, 2014).

Even though the patients are being given ARV treatment for free in the South African health system, it is clear from the current study that they still disappear from the ART programmes and become LTFU, as Mberi et al., (2015) indicate. LTFU may be a result of death, which is unreported, or self-transfer to another ART clinic, also unreported. This may result in the misclassification of patients as there is no evidence as to whether they have died or are still alive, or whether they have stopped their treatment and so became LTFU (Mberi, et al., 2015).

The findings in the current study show a statistically significant relationship between the health status of the study population and LTFU *(p value = 0.000).* The participants who were bedridden at the start of their ART were less likely to be LTFU, compared to ambulatory patients at the start of their ART. The study findings concur with the study findings in Ethiopia which reported that there was a significant relationship between LTFU and those who were bedridden and ambulatory (Mergeso, et al., 2017). This could be due to the fact that for those who were very sick and bedridden, the ART had improved their health status and so they opted to remain in care. They may also have been financially and physically depended on others for care and were therefore effectively monitored by them, in comparison to those who displayed few or no symptoms, did not value the ART, and therefore left the treatment (Mergeso, et al., 2017).

The findings from a study done in Asia and Ethiopia (De La Mata et al., 2017; Essayu, et al., 2015) concurs with the current study findings that there was a statistically significant relationship between the age cohort of LTFU patients and CD4 Count *(p = 0.000).* Observed proportions of LTFU differed by CD4 count at ART initiation which concurs with a multicentre study finding from South Africa (Grimsrud et al., 2016). The highest proportion of observed LTFU was seen in patients with CD4 counts at ART initiation with <200 cells/µL and the lowest proportions was

observed in patients initiating ART with ≥300 cells/µL (Grimsrud et al., 2016). However, in a study conducted in Nigeria, there was a low LTFU rate in patient with baseline CD4 below 400 cell/mm^3, whilst those with baseline CD4 greater than 400 cell/mm^3, had a high LTFU rate (Babatunde et al., 2015; Gwynn, et al., 2015). These results differ with the findings of the current study. The CD4 count of LTFU patients showed a statistically significance difference at *p-value<0.00.*

The current study findings revealed that there was not a statistically significant different relationship between the WHO clinical HIV staging in the study population and LTFU. The current study revealed that the WHO clinical stage was worse (WHO stage III and IV) for the young adults, compared to older adults *(p <0.001),* which differs with findings from Western Kenya (Ojwang et al 2015).

The findings of the univariate logistic regression revealed that marital status (being single or divorced) was found to be a strong predictor of LTFU of more than 3 months, with single or divorced patients being more likely to be LTFU than those who were married. TB/HIV co-infection was also found to be a strong predictor of LTFU of more than 3 months, compared to those who are not co-infected. Lastly, the WHO clinical staging was found to be a strong predictor of LTFU of more than 3 months, as those who were in WHO clinical staging level 3 were less likely to be LTFU for more than 3 months. These findings are supported by the studies of Berheto et al (2014).

6. LIMITATIONS OF THE STUDY.

Only the medical records of the study population were analysed. The study population was not interviewed to find the reasons for them leaving their treatment and becoming LTFU. Data that was extracted from existing patients' records did not include reasons for LTFU information. In addition, the study did not include those who were LTFU at the pre-ART stage; had these been included, the estimate of LTFU may have been higher than in the current study.

7. RECOMMENDATIONS

In view of the findings, the researcher came up with the following recommendations:

- There is a need to have a standardised tracking method of patients who migrate to other health facilities for their ART treatment. This will provide more

accurate information regarding LTFU levels and reduce the misclassification of patients.

- The age group which is affected by LTFU in all variables was in the 20 – 34 year age group. This is of great concern, as this is the age group who are economically active and should contribute to the future economy of the country. It is therefore recommended that a greater focus should be placed in this age group, with policies and programmes that bring them into ART and retain them there.

- Lastly, educational campaigns, in a form of pamphlets and posters to emphasize adherence to ART and the importance of remaining on ART within designated health facilities.

8. CONCLUSION

In this study factors such as gender, education, age, WHO clinical staging, CD4 Count and TB/HIV co-infection influenced the level of LTFU of the patients was observed by the researcher. The younger age group in the age cohort of between 20 – 34 years were most commonly LTFU. There is a need to ensure that HIV-positive people in this age group are linked to ART facilities, provided with on-going counselling and support services, as well as social services that will help them remain in care and adhere to their treatment.

Tracing and tracking patients who are LTFU and, more importantly, standardising the monitoring and evaluation system need to be implemented in order to reduce the number of patients who are LTFU. Patients should be retained in care for as long as possible to prevent the prevalence of the ARV resistant virus that can impact negatively on the ART programme. The high rates of LTFU may diminish treatment options and substantially limit the effectiveness of ART strategies due to the possible emergence of ARV resistant viruses.

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APPENDIX: A Clinical and non-clinical characteristics of HIV infected patients initiated ART at Shiluvana Local Area from 2012 – 2017

Variables	Category	Coding
Age in years		
Sex	Male female	0 and 1
Marital status	Never married Married Divorced widowed	0 to 3
Education	No education Primary Secondary Tertiary	0 to 3
Religion	Christian Muslim	0 and 1
Baseline WHO stage	stage 1 Stage 2 stage 3 Stage 4	0 to 3
Baseline CD4 count	<200 200 - 349 350 – 499 ≥500	0 to 3
Viral Load	<400 >400	0 and 1
History of TB/HIV co-infection	No Yes	0 and 1
Baseline functional	Ambulatory bedridden	0 and 1
ART regimen at start	Reg. 1 Reg.2	0 and 1

APPENDIX B: Permission to apply for ethical clearance

University of Limpopo
Faculty of Health Sciences
Executive Dean
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 2149, Fax: (015) 268 2685, Email:kgakgabi.letsoalo@ul.ac.za

DATE: 15 November 2018

NAME OF STUDENT:	NKUNA SA
STUDENT NUMBER:	201730457
DEPARTMENT:	PUBLIC HEALTH
SCHOOL:	HEALTH CARE SCIENCE
QUALIFICATION:	MPH

Dear Student

FACULTY APPROVAL OF PROPOSAL (PROPOSAL NO. FHDC2018/7)

I have pleasure in informing you that your MPH proposal served at the Faculty Higher Degrees Meeting on the 15 November 2018 and your title was approved as follows:

Approved Title: "Loss to follow up on HIV Positive Patients who initiated antiretroviral therapy at Shiluvana local area, Greater Tzaneen Sub District, Limpopo Province".
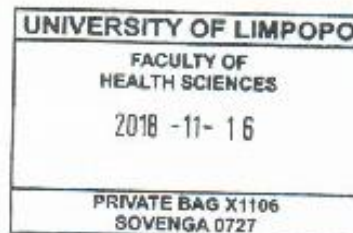
Note the following:

Ethical Clearance	Tick One
Requires no ethical clearance	
Proceed with the study	
Requires ethical clearance (TREC) (apply online)	
Proceed with the study only after receipt of ethical clearance certificate	√

Yours faithfully

MR K.J Letsoalo
Chairperson

UNIVERSITY OF LIMPOPO
FACULTY OF
HEALTH SCIENCES
2018 -11- 16
PRIVATE BAG X1106
SOVENGA 0727

CC: Supervisor: Dr E Maimela
      CO- Supervisor: Dr T.S Ntull

APPENDIX C: Ethical clearance certificate from 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: 06 March 2019

PROJECT NUMBER: TREC/68/2019: PG

PROJECT:

Title: Loss to follow up of HIV positive patients who initiated antiretroviral therapy at Shiluvana local area, Greater Tzaneen Sub-District, Limpopo Province.
Researcher: SA Nkuna
Supervisor: Dr E Maimela
Co-Supervisor/s: Dr TS Ntuli
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 D: Approval to conduct the study from Limpopo Department of Health

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH

Ref	:	LP_201907_015
Enquires	:	Mrs K. Letseparela
Tel	:	015-293 6028
Email	:	Kurhula.Hlomane@dhsd.limpopo.gov.za

Salome Annah Nkuna

PERMISSION TO CONDUCT RESEARCH IN DEPARTMENTAL FACILITIES

Your Study Topic as indicated below;

Loss to follow up of HIV positive patients who initiated antiretroviral theraphy at Shiluva local area, Greater Tzaneen Sub-District, 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

pp **Head of Department**

Date 26/08/19

Private Bag X9302 Polokwane
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Website: http/www.limpopo.gov.za

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APPENDIX E: Certificate from language editor

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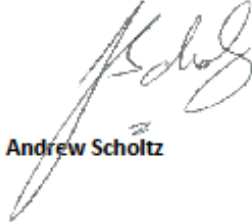Tel: 076 079 0214 • Fax: 086 216 7380

Date: 10 July 2020

To Whom it May Concern

I hereby confirm that I have proof-read the document entitled: "Loss to Follow Up of HIV-Positive Patients Who Initiated Antiretroviral Therapy Between January 2012 and December 2017 in the Shiluvana Local Area, Greater Tzaneen Sub-District, Limpopo Province" authored by Salome Annah Nkuna and have suggested a number of changes which 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.

Andrew Scholtz