CLINICAL OUTCOMES AND PATIENT RETENTION IN THE ANTIRETROVIRAL ROLL-OUT PROGRAMME AT LETABA HOSPITAL, LIMPOPO PROVINCE, SOUTH AFRICA.

A research report submitted to the Faculty of Health Science, University of the Witwatersrand, in partial fulfilment of the requirements for the M FAM MED degree.

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DECLARATION

I**,** Dr Matshehla Mary-Anne Lebogang Semenya declare that this research report is my own work. It is being submitted for the degree of Master of Family Medicine at the University of the Witwatersrand, Johannesburg. It has never been submitted before for any degree or examination at this or any other University.

Signed.....28th day of October 2013

ABSTRACT

Background

The roll-out of antiretroviral drugs in South Africa started in March 2004. In Mopani district, a rural district of Limpopo Province, the roll-out programme commenced in October 2004. While many resources were invested in this program, no study has assessed the clinical outcomes in this rural district. In addition, most studies conducted in South Africa were conducted in urban and tertiary settings. Assessing clinical outcomes is important in determining whether the program is making the desired clinical difference in the lives of the patients and may serve as feedback into the program for quality improvement purposes.

Methodology

The study was a retrospective record review of patients who were initiated on antiretroviral (ARV) treatment between December 2007 and November 2008. A structured questionnaire was used to collect data from 124 patient's files and data was collected up to November 2011. The data collected included patients' socio-demographic characteristics, clinical outcomes (CD4 count, viral load, presence of opportunistic infections, adverse effects and hospital admissions recorded at 6, 12, 24 and 36 months), the number of patients who were still attending the ARV clinic at 36 months and the reasons why patients are no longer attending the clinic. Data was analysed with Epi-Info and STATA.

Results

Of the 124 patients, 69% were females, 28% males and 3% did not have their sex specified. The majority of the patients were between 30 and 49 years. There was a significant improvement in CD4 count and viral load between baseline and all time-periods after the initiation of ARV treatment. The mean CD4 count at baseline was 128

cells/mm^3; it increased to 310 cells/mm^3 at 6 months, 380 cells/mm^3 at 12 months and 470 cells/mm^3 at 24 months. By 6 months, 67% of the patients had achieved viral suppression, but at 24 months, patients started having viral rebound. During the study, 20 patients fell pregnant and four patients fell pregnant twice. Overall, pregnant patients had a significantly higher viral load compared to non-pregnant patients (p-values = 0.015 at 6 months, 0.002 at 12 months and 0.027 at 24 months). Seventy two percent of patients were retained in the program at 36 months. Of the 28% that were no longer attending the clinic, 11.3% were transferred to other institutions, 6.5% were down referred to clinics, 3.2% died, 3.2% defaulted and 3.2% were lost to follow-up.

Conclusion

This study shows that good clinical outcomes can be achieved within an antiretroviral roll-out program in a rural hospital. The biggest magnitude of clinical benefits was observed in the first six months after the initiation of ARV treatment with threats of viral rebound thereafter. There was good patient retention at 36 months after initiation of ARV treatment and a significant difference in viral load between pregnant and non-pregnant patients. The high rate of unplanned pregnancy signifies the need to place closer attention to family planning among female patients on antiretroviral treatment.

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NOMENCLATURE AND DEFINITION OF TERMS

AIDS - Acquired Immunodeficiency Syndrome

ARV - Antiretroviral

ART - Antiretroviral Treatment

Clinical Outcomes - CD4 Count (Cluster of differentiation 4, T- helper lymphocytes)

- Viral load
- Weight gain
- Opportunistic infections
- Adverse effects
- Hospital admissions

D4T –Stavudine

Defaulter – Patients who do not present at the clinic for up to 3 months

EFZ – Efavirenz (EFV)

HIV – Human Immunodeficiency Virus

HAART – Highly Active Antiretroviral Therapy

KPA – Key Priority Area

LTFU - Lost to follow-up (Patients not presenting at clinic for more than 3 month without known reason)

M&E – Monitoring and Evaluation

NSP- National and Strategic Plan

PI- Protease Inhibitors

PMTCT- Prevention of mother-to-child transmission

Regimen 1a- Stavudine (d4T), Lamivudine (3TC) and Efavirenz (EFV)

Regimen1b- Stavudine, Lamivudine and Nevirapine (NVP)

Regimen 2- Zidovudine (AZT), Didanosine (ddI) and Lopinavir/ritonavir (kaletra)

TAC- Treatment Action Campaign

TDF- Tenofovir

UNAIDS- Joint United Nations Programme on HIV/AIDS

Undetectable Viral Load- Viral load less than 50 copies/mm^3

Unspecified- Not recorded in the patient's file

Virological failure -Inability to achieve or maintain suppression of viral load to <400 copies/mm^3

WHO- World Health Organisation

CHAPTER 1: INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) was first recognised as a new and distinct clinical entity in 1981.[1] According to the Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO), an estimated 39, 5 million people were living with the Human Immunodeficiency Virus (HIV) by the end of 2006. Of these, about 63% of all people, living with HIV resided in the Sub-Saharan region and 59% were women.[2]

In South Africa, it was estimated that 0.8 % of the South African population was living with HIV in the early 1990s. Thereafter, the prevalence of HIV increased and several studies conducted on women attending antenatal clinics estimated that 30.2% pregnant women were living with HIV in 2005.[3] In the general population however, an estimated 10.8 % people over 2 years and 16.2% among the 15-49 years were living with HIV by the end of 2005. During this period, the prevalence of HIV in Limpopo Province was 8% and 8.8% in 2008.[4]

There was a lot of controversy around HIV/AIDS policies in South Africa in 2000. This was due to the reluctance of the then Minister of Health and the president of South Africa to adopt a public sector plan for treating HIV/AIDS with antiretroviral(ARV) treatment. They expressed doubts about whether HIV caused AIDS; they promoted good general nutrition, and discouraged antiretroviral therapy (ART) because of toxicity. However, in 2002, the South African cabinet affirmed the policy that "HIV causes AIDS" and in March 2003, the Treatment Action Campaign (TAC) laid a charge of manslaughter against the Health Minister for not rolling out ARVs; and against the Trade and Industry Minister for stopping production of generic ARVs in South Africa.[5] In November 2003, the cabinet voted to make ARVs available in the public sector after having several deliberations with TAC.[6]

The roll-out of ARVs started in Gauteng Province in March 2004 followed by other provinces. By the end of December 2005, there were 204 ARV sites in the nine provinces and by the end of 2006, Limpopo Province had twenty-three operational ARV rollout sites, of which three were in Mopani District. [7] These three sites were in Letaba Hospital, C.N Phatudi Hospital (a district hospital which is about 20 km from Letaba Hospital) and Grace Mugodeni Health Centre (which is about 28 km from Letaba Hospital). In addition to the government sector, several private profit and non-profit centres offered ARVs.

Although many resources were invested in the rollout of ARVs in South Africa, few studies have evaluated the clinical outcomes and the proportion of patients retained in the program. Studies that have done these were conducted in urban and tertiary settings, where clinical resources and support are better than in rural areas and the roll-out sites closer to academic centres. These urban studies demonstrated that patients who are started on ARVs could have good clinical outcomes (where the CD4 count increases, the viral load decreases, weight increases and the opportunistic infections decreases) and most had good patient retention.[8,9,10,11,12] These are some of the indicators that were used to assess the effectiveness of ARVs. Whether these good clinical outcomes can be obtained in the rural setting where resources and clinical support are not easily available, is the focus of the current study. The current study therefore aimed to determine the clinical outcomes and the extent of patient retention in the ARV roll-out program at Letaba hospital. It was hoped that the findings of this study would inform the development of interventions that can be used for clinical quality improvement at the ARV clinic at Letaba hospital and in similar rural ARV clinic settings.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

This chapter presents the current knowledge about the clinical outcomes of ARV treatment programs and highlights gaps in knowledge that necessitated this study. This chapter is laid out in three sections: the process of literature search, presentation of the literature on ART and clinical outcomes, and conclusions from the literature review.

2.2 Literature search

The following Internet search engines were utilised to search for relevant literature:

- PubMed (The United States Library of Medicine)
- Department of Health website
- Cochrane Library
- Google scholar
- Google

The Witwatersrand Medical Library was also used to search for available printed literature sources. Several search words used for the literature search included: “CD4 count”, “viral load”, “opportunistic infections”, ‘‘ART rollout’’, “monitoring and evaluation of ARV roll out sites”, “Global and South African HIV statistics”, “clinical outcomes of HAART”, “record keeping in ARV roll out sites”, “adherence”, “compliance”, “cost of HIV care”, ‘‘effects of pregnancy on viral load and CD4 count’’, and “retention in ARV roll-out sites”. The literature search was conducted using several combinations of these search words and relevant articles were obtained and appraised for validity, importance, usefulness and applicability. The search yielded more than a thousand articles, of which about 150 with similar variables to the present study were selected. The abstracts were then used to further select articles that were relevant, reliable and those with similar methodology to the present study. Approximately 60 articles were finally selected and appraised.

Many studies were available on clinical outcomes, adherence and retention, but there were very few studies evaluating ARV roll-out programmes. Even fewer studies were conducted in rural areas in South Africa, and no studies were conducted in Limpopo Province.

2.3 Presentation of Literature

The literature will be laid out under the following topics:

1. Clinical outcomes of ARV treatment
2. Adherence to ARV treatment
3. Patient retention in the ARV program
4. ARV treatment roll-out programme
5. Monitoring and Evaluation of the ARV treatment program

2.3.1 Clinical outcomes of ARV treatment

There are a number of studies in the literature on clinical outcomes of patients on ARV treatment. Most studies have reported on CD4 count, viral load, weight gain, presence of opportunistic infections and adverse effects, as key clinical outcomes of ARV treatment.[8,10,11,12,13,14] The subsections that will follow will review literature on these outcomes of ARVs.

2.3.1.1 CD4 count

CD4 cells are a type of white blood cells that fight infections. [15] The CD4 count measures the number of CD4 cells/mm^3 in the blood. HIV targets CD4 cells by binding to the surface of CD4 cells, then enters the CD4 cell and continues to replicate while inside, leading to the destruction of the CD4 cells. A normal CD4 count ranges from 600 to 1200 cells/mm^3.[16] There are factors other than HIV that can affect the CD4 count; these include infections, time of the day, smoking, stress, sex (women tend to have a higher CD4 count than men by about 100 cells) and the laboratory used.[17] Along with viral load, the CD4 count helps in the assessment of the immune status of the patient, guides treatment and predicts the prognosis. CD4 is therefore a good clinical outcome measure.

Studies have shown a variation in the improvement of CD4 count results after the initiation of ARV. The average improvement ranged from 68 to 165 cells/mm^3, the patient's CD4 count increased for all time periods but the biggest magnitude was in the first 6 months. After 6 months of ARV, the CD4 count increased at a slower rate. [8,13, 14,18] Studies that followed up patients for a longer duration and had a large number of patients tended to have higher mean CD4 rise as demonstrated by the studies conducted in South Africa, Rwanda and Malawi. [13,8,18,19,20] In a South African study conducted in Khayelitsha, mean CD4 increased from 95 cells/mm^3 at baseline to 404 cells/mm^3 at 32 months. The strength of the study was a large sample size of 929, completeness of data and the fact that patients were monitored closely and non-compliant patients were picked up early and given intense adherence counselling.[19] While in the Cambodia study, the CD4 count increased from 11 cells/mm^3 at baseline to 274 cells/mm^3 in 24 months. The patients had lower baseline CD4, implying that they had very sick patients. The intense education and counselling given to the patient might have contributed to the significant improvement in the CD4 count. In the Sanne study (2009), the baseline CD4 cell count was 87 cells/mm^3 and after 6 months, the CD4 cell count was above 200 cells/mm^3 in almost all the patients. The study had a large sample size of 7583, time-to-event data was collected prospectively and it was conducted in a well-resourced programme. Missing data was one of the limitations in the study.[8]

In the beginning of ARV treatment rollout, doctors were the only category of health care professionals that were prescribing ART. Due to the shortage of doctors and the need to increase access for patients needing treatment, task shifting was introduced.[13] The task of prescribing ARVs was shifted from doctors to nurses so that more patients can be treated. However, there was fear that the clinical outcomes of HIV care may be jeopardised by this task shifting. In a study evaluating Nurse-centred ART in Rwanda, the mean CD4 count of patients started on ARV treatment increased by between 79 and 128 cells/mm^3.[13] Though nurses managed the patients, the outcomes were good and comparable to centres where patients were managed by doctors. Even though the study had a large sample size and the nurses were given intense training; the selection of the sites, nurses and of the patients was not done randomly. There was selection bias as only centres that offered relatively favourable conditions like strong management and adequate staffing were selected. The

positive results might have been influenced by these favourable conditions. This undermines the external validity of the study and the ability of the results to be generalised to the rest of the population where the conditions might not be favourable. This is an important consideration for rural settings, where there are poor resources.

2.3.1.2 Viral load

Viral load test is a quantitative measurement of HIV nucleic acid, reported as copies/mm^3.The latest tests can measure values as low as 40-50 copies/mm^3 (reported as undetectable) and as high as 1 million copies / mm, depending on the laboratory used.[17] There are no magic numbers for viral load and the goal of treatment is to reduce it to undetectable levels. The viral load provides important information that is used in combination with the CD4 cell count to monitor the status of HIV disease, to guide recommendations, to monitor the effects of ARV treatment and to predict the future course of HIV.[16,21] Viral load is therefore another good clinical outcome measure. After the initiation of ARV treatment, the viral load is expected to drop and be undetectable by six months. [22] Studies have shown a varied response of viral load after the initiation of ARV treatment, with the percentage of patients who achieve an undetectable viral load by 12 months ranging between 45 and 90%. [8,9,14,10,23,24] Even though patients achieved viral suppression after initiation, there was a trend of increasing virological treatment failure with increasing duration on ARV treatment. [8,10] This was also demonstrated in a study conducted in Johannesburg, where good virological outcomes were achieved at the onset but subsequently, 9.4% had viral rebound within one year, 16.8% within two years and 20.6% within three years. Studies that were conducted over a longer period, with larger sample size and used time-to-event demonstrated increasing virological failure with time.[8] Cross sectional studies conducted over a short period of time terminated before the viral rebound can be demonstrated and did not show this trend.

2.3.1.3 Weight gain

Weight gain is another clinical outcome reported in a number of studies. There was significant mean weight gain ranging between 1.5 and 4.3 kg in the first six months after initiating ARV treatment. Beyond six months, there was a positive trend towards weight gain but the increases were not statistically significant. [11,13] Possible explanations provided for this increases are; after the initiation of ARV treatment, patients feel better and their appetite improves. As the opportunistic infections decrease, the metabolic rate decreases - encouraging weight gain; ARV treatment also contributes to metabolic adverse effects, which include elevated cholesterol and triglycerides, insulin resistance and centripetal redistribution of body fat.[16]

2.3.1.4 Opportunistic infections

Opportunistic infections are infections that take advantage of the weak immune system.[25] There is a correlation between CD4 count and HIV-associated opportunistic infections. The type and severity of opportunistic infections that patients experience often depends on the level of the CD4 count, with certain HIV-associated diseases being common when the CD4 count reaches certain levels. Below is a summary of the correlation between opportunistic infections and CD4 count:[10,25]

>500 cells/mm^3

- Immunity is minimally affected
- Recurrent vaginal candidiasis

200- 500 cells/mm^3

- Pulmonary tuberculosis
- Herpes zoster
- Oropharyngeal candidiasis

< 200 cells/mm^3

- Pneumocystis jiroveci
- Mucocutaneous herpes simplex
- Cryptosporidium
- Oesophageal candidiasis
- Milliary/extrapulmonary tuberculosis

<100 cells/mm^3

- Cerebral toxoplasmosis
- Cryptococcal meningitis

<50 cells/mm^3

- Cytomegalovirus
- Disseminated mycobacterium avium intracellulare (MAC)

This correlation between opportunistic infections and CD4 count is used to decide on clinical prophylaxis to reduce the incidence and the severity of opportunistic infections. After the initiation of ARV treatment, the immune system recovers and the incidence of opportunistic infections decreases dramatically.[10, 24, 25]

2.3.1.5 Adverse effects

Adverse drug reaction is a broad term referring to an unwanted, uncomfortable or dangerous effect that a drug may have.[16] Adverse effects are common in patients on ARVs. The percentage of patients found to have adverse effects ranged from 44% to 76% in the literature, with between 2.8 and 5.3% requiring a regimen change. [11,13,14] Dizziness,

peripheral neuropathy and rash were reported to be the most common side effects. Studies that were conducted over a longer period reported peripheral neuropathy as the commonest side effect, while those conducted over a shorter period reported dizziness, rash, headache and nausea/vomiting to be the most common.[8,9,11,14] This might be because peripheral neuropathy manifests after patients have been on treatment for a longer period in contrast to dizziness, nausea/vomiting and headache, which manifests earlier and get better with time as the patient is accustomed to the drugs. The side effects can range from mild tolerable to life-threatening effects. Symptomatic therapy can be given for some side effects, but if they get worse or become intolerable, drugs will need to be switched. For life- threatening side effects, all treatment will need to be interrupted and certain drugs should never be used on the same patient again.[22] An article on the challenges of limited formulary states that toxicities to antiretroviral therapy make long-term adherence to therapy difficult for patients.[26] The article further states that in resource-poor settings, where there are limited drug options, when and how to change therapy are especially difficult problems. A larger formulary is needed to allow changes and use of drugs that are less toxic because toxicities have the capacity to discourage patients, undermine adherence and reduce the effectiveness of ARVs in resource-poor nations.

A study was conducted in Rwanda assessing the quality of life in HAART-treated HIV positive patients with body fat redistribution. The findings indicated that HAART-treated patients with body fat redistribution experienced lower quality of life than their HIV-infected counterparts without body fat alterations.[27] Therefore although the benefits of antiretroviral therapy cannot be underestimated, the psychological and social impact of the associated body fat changes cannot be ignored.[27] Looking for side effects, explaining them to the patients and switching treatment early is important in enhancing compliance. The limitation of the study was the fact that the study was cross-sectional, conducted over one year with a once off interview on quality of life. Quality of life is subjective and may change over time. There are a number of factors that affect quality of life, poverty is one of them and this particular study was conducted in a poor community.

2.3.2 Adherence to ARV treatment

As shown by the studies above, the introduction of ARV treatment yielded good clinical outcomes but patients tended to get viral rebound and treatment failure with time. It is important to investigate reasons for these in individuals as adherence is a very important predictor of undetectable viral load.[28,29] There are a number of factors that influence adherence. Amongst others are cost, adverse effects, social, cultural and psychological influences. [42] The South African National Antiretroviral Treatment guidelines advises that adherence should be assessed by doing pill count at each visit with an adherence goal of >95% and re-adherence is to be offered to patients with an adherence of <80% and for patients who miss their clinic visits.[22] This method is easy, but labour intense. The lay councillors can do the pill count and the doctor can review the results during consultation. Patients can be asked adherence questions and reasons for non-adherence. In the Van Oosterhout study, virological failure was associated with a positive response to non-adherence. Two adherence questions pertaining to having missed a tablet a day before or a week before the clinic visit correlated with sub therapeutic nevirapine plasma levels. In this study, interviews conducted on side effects indicated that 76% of patients experienced side effects and 3% mentioned side effects as a reason for non-adherence.[14]

2.3.3 Patient Retention

Patient retention in the treatment program is important for patients on ARV treatment to achieve optimal clinical outcomes, to ensure continuation of treatment, to monitor side effects and to identify treatment failure. In a large systematic review conducted in 2007 on 74,289 patients from resource-limited settings, it was estimated that about 50% of the patients initiated on ARV treatment were retained at 24 months. The analysis was updated in 2010 and the average retention was found to be 70% at 24 months and 64.8% at 36

months. In most studies, patients who were lost to follow up were not traced and there was a possibility that they might have continued on treatment at other treatment sites.[30]

Two studies were conducted in South Africa to investigate the reasons for loss to follow-up (LTFU) amongst patients in an Antiretroviral treatment programs in Johannesburg.[31,32] In these two studies the researchers identified patients who were lost to follow-up through chart reviews and then attempted to trace patients in order to ascertain the reasons for LTFU. In both studies, large proportions of patients (55% and 35%) could not be traced because contact information was either missing or incorrect. Of those who were successfully traced, large proportions were found to have died (27% and 48%) or to have continued ARV treatment at other facilities (14% and 17%). Those who were not in the above figures sighted reasons of financial difficulty (34% and 5%), lack of knowledge that ARV treatment is lifelong (percentage not reported), hospitalisation or illness (10% and 0%) and interruption of treatment by the doctor (11 and 0.6%) as reasons to be unable to come for follow-up. In South Africa although the patients get treatment free, there is a cost on transportation.

2.3.4 ARV treatment Roll-out.

ARV roll-out is also a vital topic even though it was not included in the present study. The South African government endorsed the use and roll-out of free ARVs in public health facilities in August 2003 after many debates, a legal case and marches by Treatment Action Campaign (TAC). There was also a commitment made by the government to provide ARVs to over a million people with HIV/AIDS by early 2008.[33] Even though ARV treatment roll-out started in March 2004; there has been a lot of delays and problems in accrediting public health facilities for ARV roll-out, providing appropriately trained health personnel and registering drugs. It is estimated that more than 330 000 deaths and about 35 000 infant HIV infections occurred between 2000 and 2005 due to HIV/AIDS denialism.[34] However, there has been much progress but the target of putting 1 million people on ARVs was not met by the end of 2009. There are no accurate estimates of the number of people on ARV treatment but it is estimated that about 700 000 were receiving

ARVs by 2009 and the number increased to 920 000 by 2010. There is a need to scale-up the number of people on treatment significantly in South Africa but this has serious cost implications because ARV drugs are expensive.

A study was conducted in G.F Jooste Hospital, Cape Town, in 2005 to determine the cost of care for inpatients and outpatients at a dedicated antiretroviral referral unit, to identify key epidemiological cost drivers and to examine the associated clinical and outcome data. The study was a prospective costing study on 48 outpatient and 25 inpatients for a period of one month. The results showed that the incremental cost per outpatient was R1280, 00 and R5802, 00 for inpatients. In summary, the study showed that the cost of providing secondary level care for on or immediately preceding ARV initiation can be significantly high.[35] The study was conducted about seven years ago and the current cost is expected to be much higher than the figures shown. A proposal was made that the budget should be included in the governments strategic planning, so that the services can be expanded to meet current needs and to avoid overcrowding in secondary level health services. Studies that cost ARV services need to be conducted in the primary health care setting, especially given that nurse-initiated ARV services have been found to be effective and could reduce the cost.

2.3.5 Monitoring and Evaluation of ARV roll-out programs

A National Strategic Plan (NSP) 2007- 2011was developed in May 2006 in South Africa.[36] The plan identified 19 goals that are needed to reach the NSP's aims. These were structured under four key priority areas (KPA). Key Priority Area 3 is about Research, Monitoring and Surveillance. The NSP 2007-2011 recognised monitoring and evaluation as an important policy and management tool. It is further said that national, provincial and district level indicators to monitor inputs, processes and outputs will be used to assess collective efforts. Some of the seven goals of Priority Area 3 that are relevant to this study are:

1. Develop and implement the M&E framework with appropriate indicators.
2. Create an enabling environment for research in support of the NSP.

3. Conduct regular surveillance.[36]

Monitoring and Evaluation in HIV care and support is still new and the development of effective monitoring tools is in the early stages.[37] A study was conducted in Malawi with the aim of describing the supervision, monitoring and evaluation strategies used to assess the delivery of antiretroviral therapy during a nationwide scale-up of treatment in Malawi. This study demonstrated the importance of early supervision for sites that are starting to deliver antiretroviral treatment, and showed the value of combining data collection with supervision.[38] Without supervision, errors in data will not be identified and corrected. Making monitoring and supervisory visits to delivery sites was seen to be essential for tracking the national scale-up delivery of antiretroviral treatment. Another study was conducted in Malawi, to assess the quality of data aggregated by antiretroviral treatment clinics. This study reported that 82, 000 patients were enrolled in its free National ART programme.[39] In comparison to South Africa there were approximately 460, 000 people on treatment by 2007.[4] Data compiled by the Ministry of Health supervisory team was compared to the quarterly aggregate data for April to June 2006 compiled and reported by the ART facilities. The study also examined whether site characteristics such as facility-type, burden (maximum number of new patients the clinic can start on ARV treatment each month), length of time providing treatment and the number of data clerks were associated with complete and accurate data in site reports. The results of this study showed that 70% of the sites provided complete data for all six case-registration fields in the site report. The aggregates for the number starting ARVs because of tuberculosis history and patient occupation were less likely to be complete with 24 -26% of sites having incomplete data and 80% of the sites had complete data on outcomes. Several factors were associated with data quality. These included a higher burden (starting more patients each month), having dedicated clerks for record keeping, having a visit by a zonal ARV treatment supervisor, location, having provided ARVs for a longer period of time and non- rural setting.[39]

2.4 Conclusion

Literature shows that after the initiation of ARV treatment, good clinical outcomes can be achieved as shown with the increase in CD4 count, a decrease in viral load, increase in

weight and the decrease in opportunistic infections. The biggest improvement in clinical outcomes occurs in the first 6 months. Even though patients had good virological outcomes in the early stage, there was a trend of virological failure with time. Literature also suggest that ARV treatment programs have good patient retention. Currently available studies were conducted in well-resourced and mostly urban settings. The few studies conducted in resource poor settings were conducted outside of South Africa. To bridge this gap in knowledge, the current study therefore aims to determining the clinical outcomes in the anti-retroviral clinic, Letaba Hospital; a typical rural hospital in South Africa.

CHAPTER 3: METHODS

3.1 Aim

The aim of this study was to determine the clinical outcomes and the extent of patient retention in an antiretroviral roll-out programme at Letaba Hospital.

3.2 Objectives

a) To describe the socio-demographic characteristics of patients attending the antiretroviral clinic
b) To determine the clinical outcomes of patients attending the ARV roll-out clinic at 6, 12, 24 and 36 months, with clinical outcomes defined as the CD4 count, the viral load, the burden of opportunistic infections and the side effects of ARV treatment.
c) To determine the outcomes of follow-up of patients initiated at the ARV rollout program, specified as: the proportions of patients retained in the program at 6, 12, 24, 36 months; the proportion that died; the proportion transferred to other facilities and the proportion lost to follow-up.
d) To explore the relationships between selected patient characteristics and the specified clinical outcomes.

3.3 METHODOLOGY

3.3.1 Study Design

The study was a retrospective, record review of patients' medical records.

3.3.2 Site of Study

The study was conducted at Letaba Hospital, a level 2 hospital in Mopani District. The hospital is situated in a rural area, about 18km from Tzaneen town in the Greater Tzaneen

Municipality. As a referral hospital, it caters for the 1.1 million people who reside in the district. According to a community survey conducted by Statistics South Africa in 2007, the population of Limpopo Province was 5 238 286, of which 1 068 568 were in the Mopani District and 349 087 in the Greater Tzaneen Municipality.[40] The hospital receives referrals from two immediate community health centres and 18 surrounding clinics. In addition, six district hospitals (Van Velden, Kgapane, C N Phatudi, Sekororo, Maphuta Malatji, Nkhensani Hospitals) and one specialised hospital (Evuxakeni Mental Hospital) refer patients to Letaba Hospital. The ART clinic is known as Nyeleti Clinic and it started operating in October 2004. By 2007, one thousand five hundred patients were attended at the clinic monthly, while five hundred patients were already initiated on ARV treatment. At the time of the study in 2007/8, the clinic operated with three professional nurses, one staff nurse, seven lay counsellors and two data capturers. One or two doctors from departments in the hospital are allocated to provide medical services at the clinic daily.

3.3.3 Study Population

All adult patients who received antiretroviral treatment at Nyeleti Clinic and were initiated at the clinic between December 2007 and November 2008 were eligible to be included in the study. The clinic statistics estimated the number of patients to have been registered at the clinic during the study period to be 687.

3.3.4 Sample and Sampling method

The minimum number of medical records required for the study was 124. This sample size was calculated with the help of a statistician based on the following formula.

$n = \frac{Z^2 p(1-p)}{e^2}$,where p is the prevalence of HIV in Limpopo Province(8.8%),[3] Z is the confidence interval which is 95%, e is the sampling error which is 5% and n in the required sample number.

All patients who were enrolled at the clinic were entered into a register. A systematic sampling method was used to select every third file from the register. The first file was

randomly selected. If a sampled file did not meet the inclusion criteria, the next file was selected and the sampling continued (every third file) until the required sample size was achieved.

Inclusion criteria:

- Patients who were 18 years and older.
- Patients who were initiated on treatment at Letaba Hospital.

Exclusion Criteria:

- Patients who were referred from other sites.
- Files not found

3.3.5 Data Collection

Information was extracted from files that met the selection criteria and recorded onto a data collection sheet. A coding system was used on the data collection sheet to enable the researcher to go back to the files for further clarity where necessary, and to avoid re-selection of the same files. The data collection sheet was developed by the researcher guided by the study objectives and it included the following information:

Section 1 – Patient's socioeconomic demographics such as age, residential address, sex, race, level of education, employment and marital status.

Section 2 - Clinical Outcomes (CD4 count, viral load, presence of opportunistic infections, hospital admission and adverse effects recorded at 6, 12, 24 and 36 months).

Section 3 – Information about patient retention (Checked if the patient is still attending the clinic. If not, is patient transferred, down referred, defaulted, deceased or lost to follow-up?).

3.4 Pilot Study

A pilot study was conducted at the ARV clinic of C.N Phatudi Hospital. This hospital is a district hospital in Mopani District, situated about 23 kilometres from Letaba Hospital.

Twenty-five patient's files were used for the pilot study. The pilot study helped to test if the data collection sheet was effective in collecting the data required, check if the required data was available and if the study was feasible. The results of the pilot study were not included in this study.

3.5 Analysis

A statistician assisted with the analysis of the data. The data collected was entered into Epi-Info ™ version 6. Descriptive statistics was done in which frequencies, means, proportions and percentages were determined. For further data analysis, data was imported into STATA version 9.0-computer software. 2x2 tables were used to compare groups using ANOVA, t-tests, Chi-squared test and Fisher-exact test where cell count were less than five. A comparison of the outcomes (CD4 count and viral load) was done for the following groups- sex (male v/s female), education level (none/primary, secondary and tertiary), employment (employed v/s unemployed), different age groups and for pregnant v/s non-pregnant. Patient retention was estimated as the proportions of patients still attending the clinic at set times and reasons for no longer attending the clinic were also identified. Associations were tested for between socio-demographic variables and clinical outcomes. P-value <0.05 was considered as statistically significant.

3.6 Ethical consideration

The research protocol was approved by the Human Research and Ethics Committee at the University of Witwatersrand (Clearance certificate number M110485). Permission to conduct the study was granted by the Provincial Research Committee of Limpopo and Chief Executive Officer of Letaba Hospital. Patients were not directly involved as the research was a record review. Confidentiality of the data collected was maintained as the data collection sheet was anonymous, codes were used for identification and only the researcher, the supervisor and the statistician had access to the data.

CHAPTER 4: RESULTS

4.0 Introduction

The results are presented under the following headings:

1) Socio-demographic characteristics
2) Co-morbid diseases
3) Clinical outcomes (CD4 count, viral load, presence of opportunistic infections and adverse effects)
4) Patient retention
5) Associations between socio-demographic characteristics and clinical outcomes.

4.1 Socio-demographic characteristics.

Hundred and twenty-four patient's files were sampled amongst those who presented at the clinic between December 2007 and November 2008. Due to missing information and incomplete documentation of certain information, "n" is not always equal to 124 in the results presented below.

4.1.1 Sex distribution

Of the 124 patient files sampled, 85 (69%) were females, 35 (28%) males while 4 (3%) did not have their sex specified. Figure 1 below shows the sex distribution of the patients.

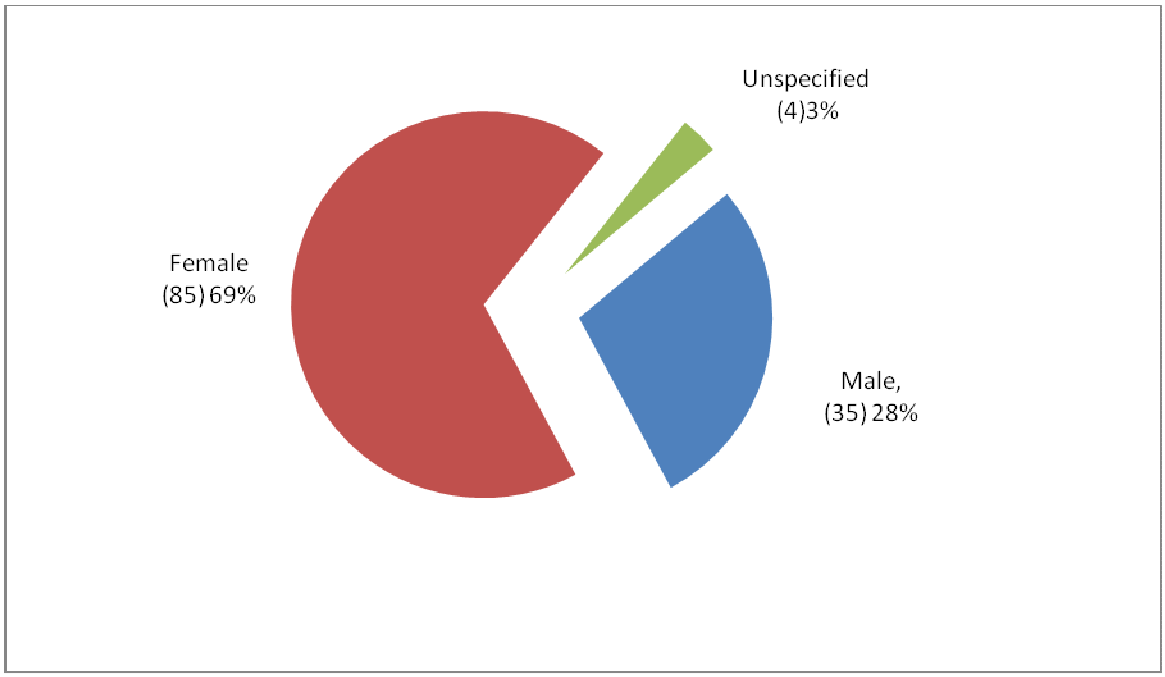

Figure 1: Sex distribution

4.1.2 Age distribution

The ages of the patients ranged between 21 and 72 years. The mean age was 41 years and about 2/3 were below 50 years of age. Only 5% were above the age of 60. As noted in figure 2 below, the majority of patients fall in the age groups of 30-49years.

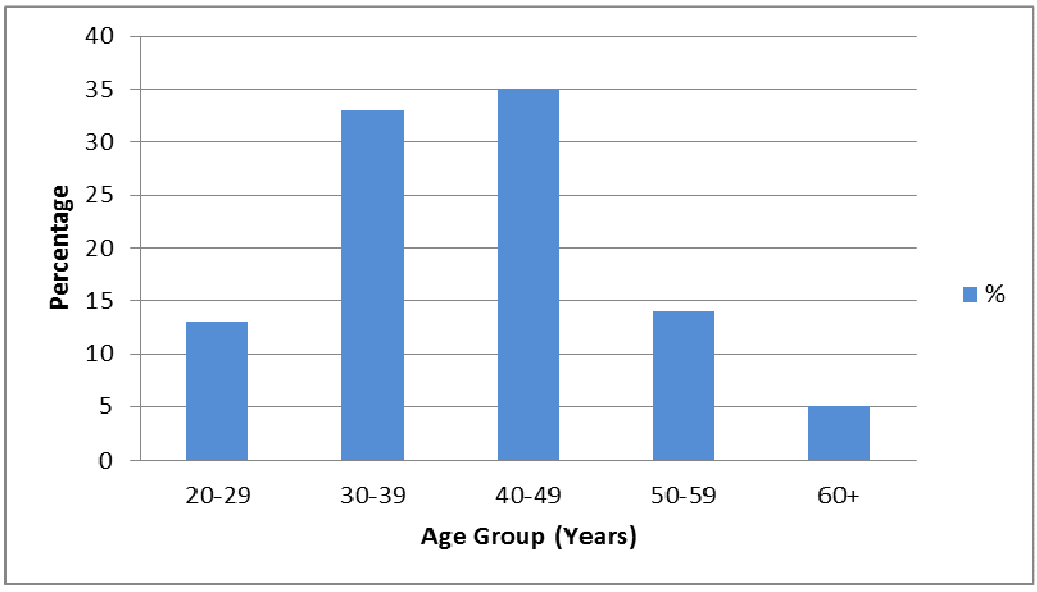

Figure 2: Age distribution

4.1.3 Race

All the patients who were sampled were Black South Africans. The clinic sees predominantly African patients.

4.1.4 Marital Status

The majority of the patients 61 (49%) in the study were single, 41(33%) married, 7 (6%) were divorced, 6(5%) were widowed and 9 (7%) had their marital status unspecified. Figure 3 below shows the marital status distribution.

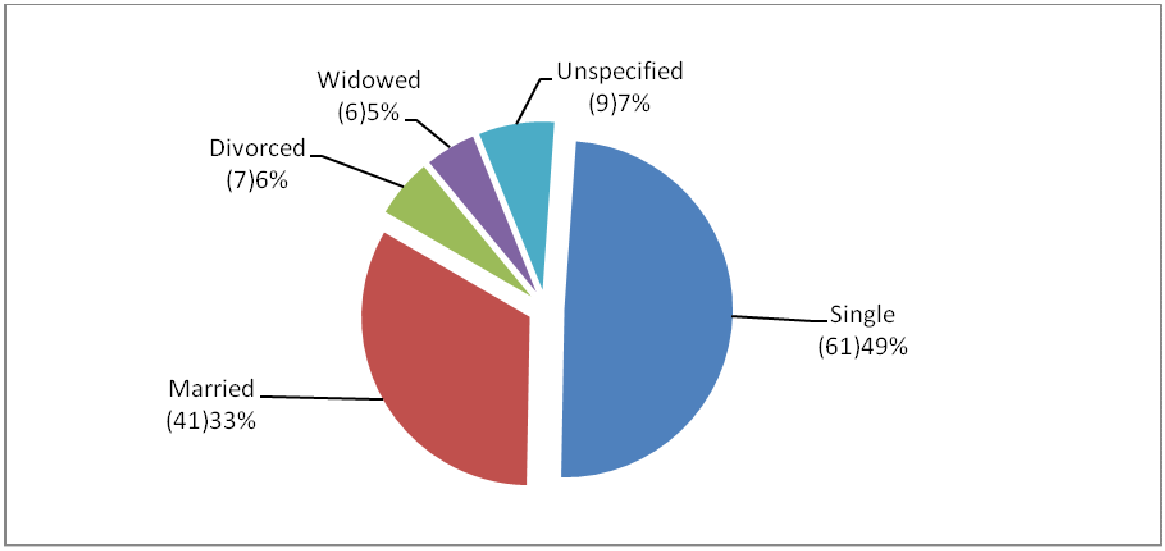

Figure 3: Marital status distribution

4.1.5 Employment status

Out of the 124 patients sampled, the majority 69(56%) were unemployed, 15(12%) were employed and 40 (32%) were unspecified. Figure 4 below shows the employment status of the patients.

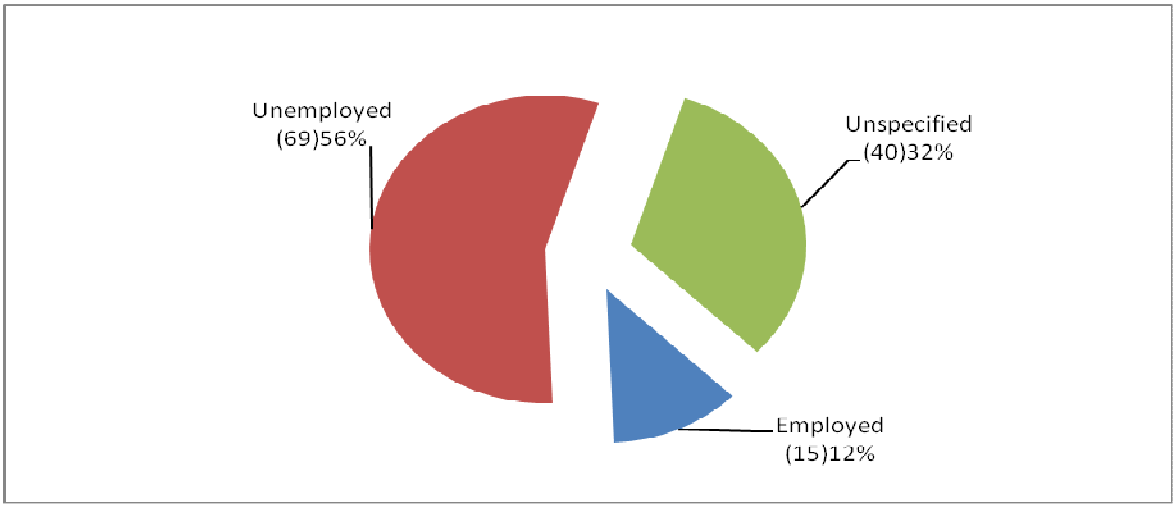

Figure 4: Employment status

4.1.6 Education level

Twenty-seven (22%) patients had no education or only went up to primary school, 35(28%) secondary school and 4 (3%) went up to tertiary. For a large number of patients 58(47%), the education level was not specified. Table 1 below shows the education levels for the study participants.

Table 1: Education level

Education level	Frequency	Percentage
Unspecified	58	47%
None/primary	27	22%
Secondary	35	28%
Tertiary	4	3%

4.1.7 Distance between place of residence and the hospital

The majority of patients, 59 (47.6%) lived less than 10 km to the hospital while 40 (32%) lived between 10-20km and 25 (20%) lived more than 20km to the hospital. Figure 5 below shows the distance from residence to the hospital.

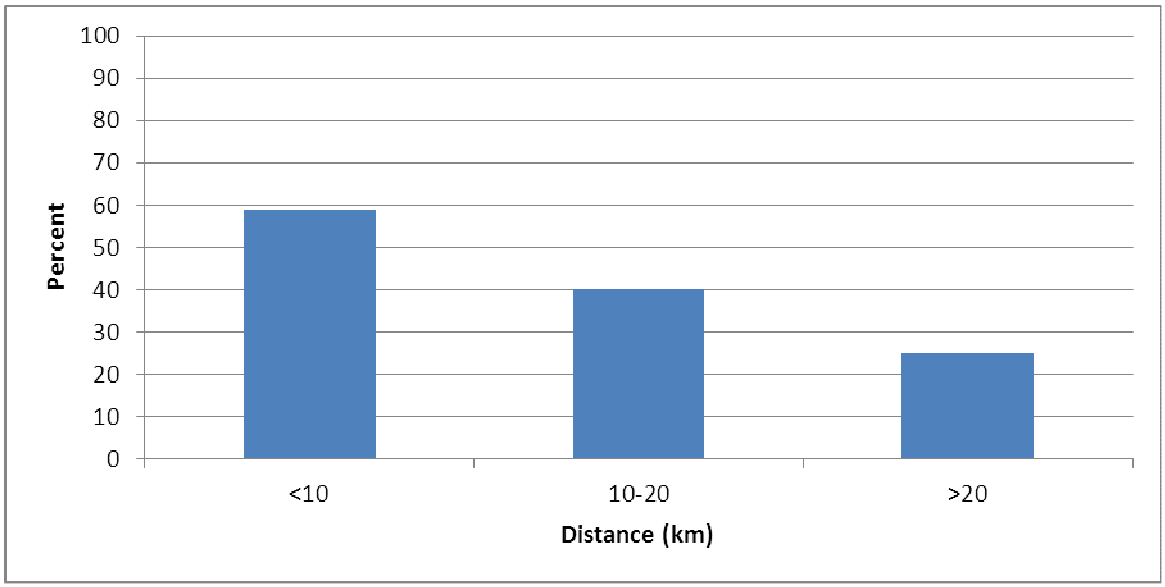

Figure 5: Distance from place of residence to hospital

4.2 Co-morbidities

Forty-two (34%) patients had co-morbidities, with 7 (16%) patients having more than one co-morbidity. Twenty female patients fell pregnant and four patients fell pregnant twice during the study period. Table 2 below shows the frequency of co-morbidities.

Table 2: Frequency of co-morbidities

Co-morbidity	No. of patients
Pregnancy	20
Arthritis	13
Hypertension	5
COPD	2
Diabetes	1
Cancer	1
Peptic Ulcer Disease	1
Depression	1
Cardiac	1
Obesity	1
Epilepsy	1

4.3 Drug Regimen at baseline, 6, 12, 24 and 36 months

At baseline 120 (97%) patients were started on drug regimen 1a and only 4 (3%) were started on regimen 1b. At 6 months, regimens were changed for 5 (4%) patients due to intolerable side effects and for one patient (0.8%) who fell pregnant. At 12 months regimens were changed for 8 (7 %) patients, 12 (11 %) at 24 months and for 10 patients (12%) at 36 months.

4.4 Clinical outcomes

4.4.1 CD4 count

Of the 124 patients files sampled only 119 CD4 count results (96%) were available at baseline, 102 (83%) at 6 months, 101 (87%) at 12 months and 78 (70%) were available at 24 months. The mean CD4 count was 128 cells/mm^3 at baseline; it increased to 310 cells/mm^3 at 6 months, 380 cells/mm^3 at 12 months and 470 cells/mm^3 at 24 months. At baseline, 110 (93%) of patients had a CD4 count of 200 cells/mm^3 or less. From six

months the majority of patients had CD4 counts of >200 cells/mm^3. There was a statistically significant improvement with regard to CD4 count at baseline versus all other time periods ($p < 0.05$). When comparing CD4 count at 6 months with 12 months, and 12 months with 24 months, the increase was not statistically significant but there was a positive trend. Table 3 below shows the CD4 count results at all time periods.

Table 3: CD4 count

	Baseline	6 months	12 months	24 months
<50	19 (16%)	2 (2%)	3 (3%)	2 (3%)
50-100	27 (23%)	11 (11%)	4 (4%)	4 (5%)
101-200	64 (54%)	16 (15%)	16 (16%)	7 (9%)
>200	9 (7%)	73 (71%)	78 (77%)	65 (83%)
Mean CD4	128	310	380	470
Total no.(n)	119	102	101	78

Baseline v/s 6 months ($p<0.05$); baseline v/s 12 months ($p<0.005$); baseline v/s 24 months ($p<0.005$)

4.4.2 Viral load

Of the 124 patients files sampled only 77 (62%) viral load results were available at baseline, 101(82%) at 6 months, 100 (86%) at 12 months and 79 (71%) at 24 months. The viral load results ranged from 0 to 1200000 copies/mm^3. At baseline only 7% of patients had a viral load of <50 copies/mm^3, the majority of patients (81%) had a viral load of more than 400 copies/mm^3. The number of patients with viral load <50 copies/mm^3 increased significantly to 67% at 6 months, 61% at 12 months and 63% at 24 months. Results of viral load are shown in table 4 below.

Table 4: Viral load

	Baseline	6 months	12 months	24 months
<50	5 (7%)	68 (67%)	61 (61%)	50 (63%)
50-400	9 (12%)	17 (17%)	18 (18%)	10 (13%)
401-5000	20 (26%)	16 (16%)	12 (12%)	7 (9%)
5000+	43 (55%)	-	9 (9%)	12 (15%)
Total	77	101	100	79

Baseline v/s 6 months ($p<0.05$); baseline v/s 12 months ($p<0.005$); baseline v/s 24 months ($p<0.005$)

4.4.3 Weight gain

There was significant weight gain between baseline and 6 months ($p=0.0063$). For the rest of the study period there was a positive trend but the increase was not statistically significant. Table 5 below shows the mean weight and p-values per time.

Table 5: Weight gain

	Mean +/- sd	p-value
Baseline	57.4 +/-13.9	Baseline
6months	62.1+/-12.6	Baseline v/s 6months (0.0063)
12months	62.3+/-12.3	6 months v/s 12months (0.91)
24 months	63.3+-14.6	12 months v/s 24 months (0.61)

4.4.4 Opportunistic infections

At baseline 68 (58.4%) patients had opportunistic infections, the number decreased to 55 (44%) at 6 months, 39 (31, 5%) at 12 months and 19 (15.3%) at 24 months. Twenty-nine (23.4%) patients had more than one opportunistic infection. Table 6 below shows the list of opportunistic infections and their frequencies during the study period.

Table 6: Description of opportunistic infections

	0-6 months n=68	6-12 months n=55	12-24 months n=39	24-36 months n=19
Gastroenteritis	18% (12/68)	11% (6/55)	15% (6/39)	21% (4/19)
Tuberculosis	28% (19/68)	20% (11/55)	5% (2/39)	5% (1/19)
Oral thrush	31% (21/68)	4% (2/55)	15% (6/39)	5% (1/19)
Skin rash	10% (7/68)	18% (10/55)	5% (2/39)	1% (2/19)
Upper respiratory tract infections	22% (15/68)	44% (24/55)	44% (17/39)	42% (8/19)
Otitis media	3% (2/68)	7% (4/55)	3% (1/39)	5% (1/19)
Lower respiratory tract infections	3% (2/68)	2% (1/55)	15% (6/39)	5% (1/19)
Meningitis	-	-	3% (1/39)	3% (1/39)

4.4.5 Side-effects

During the study period, 74(59%) patients experienced side-effects. By six months 21 (16.9%) patients had side-effects, 46 (37%) by 12 months, 40 (32.2%) by 24 months and 32(25.8%) by 36 months. The most common side effect was skin rash, manifesting in 52% of the patients who presented with side-effects at 6 months, 74% at 12 months, 38% at 24 months and 41% at 36 months. The incidence of skin rash was highest during the 6-12 months period, and then it started decreasing after 12 months. The second commonest side effect was peripheral neuropathy with 38% at 6 months, 59% at 12 months, 63% at 24 months and 53% at 36 months. Peripheral neuropathy increased after six months, with the highest increase between 12-24 months. Three (8%) patients developed lactic acidosis at 12-24 months during the entire study period. Table 7 below shows the frequency of side effects per time period.

Table 7: Commonest side effects

	0-6 months	6-12 months	12-24 months	24-36 months
Peripheral Neuropathy	38% (8/21)	59% (27/46)	63% (25/40)	53% (17/32)
Skin Rash	52% (11/21)	74% (34/46)	38% (15/40)	41% (13/32)
Gastrointestinal	-	7% (3/46)	8% (3/40)	9% (3/32)
Lactic Acidosis	-	-	8% (3/40)	-
Dizziness	4% (1/21)	4% (2/46)	-	-
Lipodystrophy	-	-	3% (1/40)	3% (1/32)

4.4.6 Hospital admissions

Nine (7.2%) patients were admitted to hospital during the entire study period. Three of these nine patients admitted were admitted twice. There were seven admissions during the 0-6 months period, the admissions decreased to 4 during the 6-12 months and to 1 during 12-24 months.

4.5 Outcomes of follow up

4.5.1: Patient retention

At 6 months 123 (99%) of the 124 patients were retained in the program, 116 (93%) at 12 months, 111 (90%) at 24 months and 85 (72%) at 36 months. Figure 6 below shows the number of patients retained per time period.

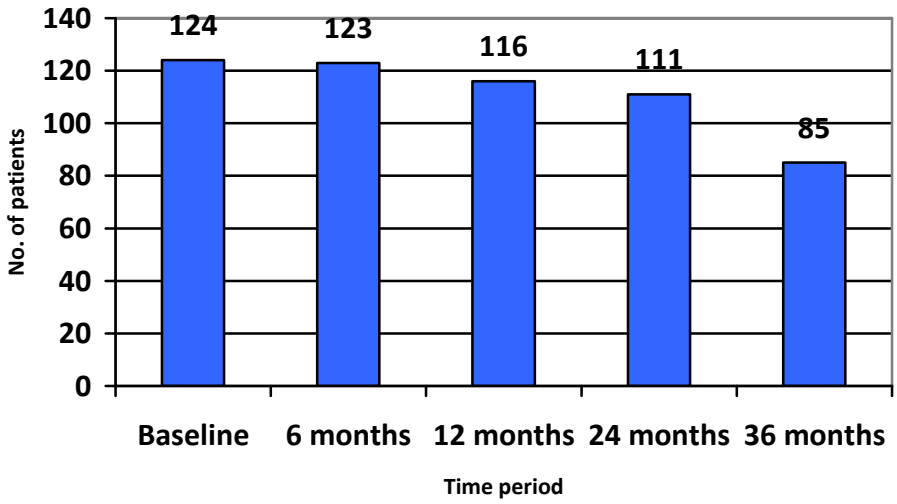

Figure 6: Number of patients retained per time period

4.5.2: Reasons for dropping out of ARV programme

Of the 33 (28%) patients that were no longer attending Nyeleti, 14(43%) were transferred to other institutions, 8 (24%) were down- referred to clinics, 4(12%) died, 4(12%) defaulted and 3(9%) were lost to follow-up. Figure 7 below shows the reasons for patients no longer attending the clinic

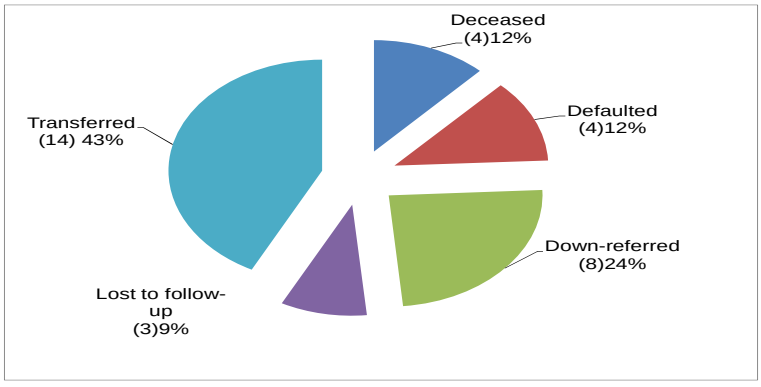

Figure 7: Reasons for dropping out of the ARV programme

4.6 Association of socio-demographics and clinical outcomes.

4.6.1 Association between CD4 count and age

No significant difference was observed in relation to CD4 count and age at baseline (p=0.27), 6 months (p=0.72), 12 months (p=0.89) and 24 months (p=0.19). In all age groups the majority of patients had a CD4 count of 200 cells/mm^3 and less at baseline and a CD4 >200 cells/mm^3 at 6, 12 and 24 months. Table 8 below illustrates the association between CD4 count and age.

Table 8: CD 4 count by age

		Age (years)			
		<30	30-49	50+	p-value
Baseline	<50	3 (19%)	14 (17%)	2 (9%)	0.27
	50-100	6 (38%)	19 (24%)	2 (9%)	
	101-200	7 (44%)	42 (52%)	15 (68%)	
	>200	0 (0%)	6 (7%)	3 (14%)	
6 months	<50	0 (0%)	2 (3%)	0 (0%)	0.72
	50-100	1 (7%)	10 (14%)	0 (0%)	
	101-200	3 (21%)	10 (14%)	3 (19%)	
	>200	10 (72%)	50 (69%)	13 (81%)	
12 months	<50	0 (0%)	3 (4%)	0 (0%)	0.89
	50-100	1 (7%)	3 (4%)	0 (0%)	
	101-200	3 (21%)	10 (15%)	3 (17%)	
	>200	10 (72%)	53 (77%)	15 (83%)	
24 months	<50	0 (0%)	2 (4%)	0 (0%)	0.19
	50-100	1 (14%)	1 (2%)	2 (13%)	
	101-200	1 (14%)	6 (11%)	0 (0%)	
	>200	5 (71%)	46 (83%)	14 (87%)	

4.6.2 Association between CD4 count and sex

No significant difference was observed in relation to CD4 count and sex at baseline p=0.18, 6 months p=0.83, 12 months p=0.59 and 24 months p=0.23. In both sex groups the majority of patients had a CD4 count of 200 cells/mm^3 and less at baseline and a CD4 >200 cells/mm^3 at 6, 12 and 24 months. Although not statistically significant, more proportions of women tended to have higher CD4 counts. Table 9 below illustrates the association between CD4 count and sex.

Table 9: CD 4 count by sex

		Gender		
		Male	Female	p-value
Baseline	<50	9 (28%)	10 (12%)	0.18
	50-100	8 (25%)	19 (23%)	
	101-200	13 (41%)	48 (58%)	
	>200	2 (6%)	6 (7%)	
6 months	<50	1 (4%)	1 (1%)	0.83
	50-100	3 (11%)	8 (11%)	
	101-200	5 (18%)	11 (16%)	
	>200	19 (68%)	51 (72%)	
12 months	<50	1 (3%)	2 (3%)	0.59
	50-100	1 (3%)	3 (4%)	
	101-200	7 (24%)	9 (13%)	
	>200	21 (70%)	55 (80%)	
24 months	<50	2 (9%)	0 (0%)	0.23
	50-100	1 (6%)	3 (6%)	
	101-200	2 (9%)	5 (9%)	
	>200	17 (77%)	45 (85%)	

4.6.3 Association between CD4 count and level of education

Education level was not significantly related to CD4 count at baseline (p=0.13), 6 months (p=0.24), 12 months (p=0.34) and 24 months (p=0.94). At baseline, the majority (>75%) of the patients had a CD4 count below 200 cells/mm^3 in all educational levels, while at 6, 12 and 24 months the majority (70% or more) had a CD4 count of above 200 cells/mm^3 in all educational levels. Table 10 below shows the association between CD4 and education level.

Table 10: CD4 count by education level

		Educational Level			
		None/Primary	Secondary	Tertiary	p-value
Baseline	<50	4 (16%)	6 (18%)	2 (50%)	0.13
	50-100	9 (36%)	9 (27%)	1 (25%)	
	101-200	12 (48%)	15 (44%)	0 (0%)	
	>200	0 (0%)	4 (12%)	1 (25%)	
6 months	<50	0 (0%)	0 (0%)	1 (25%)	0.24
	50-100	2 (9%)	1 (4%)	0 (0%)	
	101-200	5 (22%)	5 (18%)	1 (25%)	
	>200	16 (70%)	22 (79%)	2 (50%)	
12 months	<50	0 (0%)	1 (3%)	0 (0%)	0.34
	50-100	0 (0%)	1 (3%)	0 (0%)	
	101-200	5 (25%)	2 (7%)	1 (25%)	
	>200	15 (75%)	26 (87%)	3 (75%)	
24 months	<50	1 (7%)	0 (0%)	0 (0%)	0.94
	50-100	1 (7%)	1 (5%)	0 (0%)	
	101-200	1 (7%)	2 (11%)	0 (0%)	
	>200	12 (81%)	16 (84%)	4 (100%)	

4.6.4 Association between CD4 count and employment status.

No significant difference was observed in respect to CD4 count and employment status at baseline (p=0.2), 6 months (p=1.00), 12 months (p=0.4) and 24 months (p=0.23). Table 11 shows the relationship between employment status and CD4 count.

Table 11: CD 4 count by Employment Status

		Employment Status		
		Employed	Unemployed	p-value
Baseline	<50	3 (21%)	10 (15%)	0.20
	50-100	2 (14%)	19 (29%)	
	101-200	6 (43%)	33 (50%)	
	>200	3 (21%)	4 (6%)	
6 months	<50	0 (0%)	0 (0%)	1.00
	50-100	1 (7%)	5 (9%)	
	101-200	3 (21%)	11 (19%)	
	>200	10 (71%)	41 (72%)	
12 months	<50	0 (0%)	1 (1%)	0.41
	50-100	0 (0%)	3 (5%)	
	101-200	0 (0%)	9 (16%)	
	>200	14 (100%)	45 (78%)	
24 months	<50	1 (8%)	0 (0%)	0.23
	50-100	0 (0%)	3 (7%)	
	101-200	0 (0%)	4 (9%)	
	>200	12 (92%)	37 (84%)	

4.6.5 Association between viral load and age

There was no statistically significant association between viral load and age at baseline. At baseline 85% of patients in the 50+ age group had a viral load of > 5000 copies/mm^3 compared to 55% for age group 30-49 years and 31% for age group of < 30 years (p=0.09). However, there was a statistically significant association between viral load and age at 6 months, 83% of patients in the 50+ age group had a viral load of < 50copies/mm^3, compared to 65% for 30-49 years and 58% for the <30 age group (p=0.032). At 12 months (p=0.13) and 24 months (p=0.48) there was no significant difference between viral load v/s age. Table 12 below shows the association between viral load and age.

Table 12: Viral load by age

		Age (years)			
		<30	30-49	50+	p-value
Baseline	<50	1 (8%)	4 (8%)	0 (0%)	0.09
	50-400	1 (8%)	8 (16%)	0 (0%)	
	401-5000	7 (54%)	11 (22%)	2 (15%)	
	>5000	4 (31%)	28 (55%)	11 (85%)	
6 months	<50	7 (58%)	46 (65%)	15 (83%)	0.032
	50-400	0 (0%)	16 (23%)	1 (6%)	
	401-5000	5 (42%)	9 (13%)	2 (11%)	
	>5000	0 (0%)	0 (0%)	0 (0%)	
12 months	<50	7 (64%)	40 (57%)	14 (74%)	0.13
	50-400	1 (9%)	16 (23%)	1 (5%)	
	401-5000	0 (0%)	10 (14%)	2 (11%)	
	>5000	3 (27%)	4 (6%)	2 (11%)	
24 months	<50	3 (50%)	38 (66%)	9 (60%)	0.48
	50-400	1 (17%)	6 (10%)	3 (20%)	
	401-5000	0 (0%)	7 (12%)	0 (0%)	
	>5000	2 (33%)	7 (12%)	3 (20%)	

4.6.6 Association between viral load and sex

There was no statistically significant association between viral load and sex at baseline (p=0.12), 6 months (p=0.82), 12 months (p=0.77) and 24 months (p=0.93). Even though the association was not statistically significant, a higher percentage of males tended to have viral loads > 5000 copies/mm^3 compared to females. Table13 below shows the association between viral load and sex.

Table 13: Viral load by sex

		Male	Female	p-value
Baseline	<50	1 (4%)	4 (8%)	0.12
	50-400	2 (9%)	7 (14%)	
	401-5000	2 (9%)	16 (31%)	
	>5000	18 (78%)	24 (47%)	
6 months	<50	22 (73%)	44 (64%)	0.82
	50-400	5 (17%)	12 (17%)	
	401-5000	3 (10%)	13 (19%)	
	>5000	0 (0%)	0 (0%)	
12 months	<50	16 (59%)	43 (61%)	0.77
	50-400	5 (19%)	13 (19%)	
	401-5000	3 (11%)	9 (13%)	
	>5000	3 (11%)	5 (7%)	
24 months	<50	15 (63%)	34 (63%)	0.93
	50-400	3 (13%)	7 (13%)	
	401-5000	3 (12%)	4 (7%)	
	>5000	3 (12%)	9 (17%)	

4.6.7 Association between viral load and education

There was no statistically significant association between viral load and level of education at baseline (p=1.00), 6 months (p=0.90), 12 months (p=0.83) and 24 months (p=0.13). For all levels of education, the majority of the patient had a viral load of more than 5000 at baseline and, at 6, 12, 24 months most patients had a viral load below 50 copies/mm^3. Table 14 below demonstrates the association between viral load and level of education.

Table 14: Viral load by level of education

		Educational Level			
		None/Primary	Secondary	Tertiary	p-value
Baseline	<50	1 (6%)	1 (6%)	0 (0%)	1.00
	50-400	2 (12%)	2 (12%)	0 (0%)	
	401-5000	2 (12%)	2 (12%)	0 (0%)	
	>5000	9 (53%)	8 (47%)	2 (67%)	
6 months	<50	17 (74%)	21 (68%)	3 (100%)	0.94
	50-400	4 (17%)	5 (16%)	0 (0%)	
	401-5000	2 (9%)	5 (16%)	0 (0%)	
	>5000	0 (0%)	0 (0%)	0 (0%)	
12 months	<50	11 (55%)	16 (59%)	3 (100%)	0.82
	50-400	4 (20%)	7 (26%)	0 (0%)	
	401-5000	4 (20%)	2 (7%)	0 (0%)	
	>5000	1 (5%)	2 (7%)	0 (0%)	
24 months	<50	8 (53%)	15 (71%)	4 (100%)	0.16
	50-400	4 (27%)	0 (0%)	0 (0%)	
	401-5000	1 (7%)	1 (5%)	0 (0%)	
	>5000	2 (13%)	5 (24%)	0 (0%)	

4.6.8 Association between viral load and employment status

There was no statistically significant association between viral load and employment status, with p-values of (p=0.38) at baseline, (p=0.90) 6 months, (p=0.23) 12 months, (p=0.60) at 24 months. In both employed and unemployed patients the majority had a viral load of >401 copies/mm^3 at baseline and that < 50 copies/mm^3 at 6, 12 and 24 months. Table 15 below shows the association between viral load and employment status.

Table 15: Viral load by Employment Status

		Employment Status		
		Employed	Unemployed	p-value
Baseline	<50	0 (0%)	3 (7%)	0.38
	50-400	2 (22%)	3 (7%)	
	401-5000	3 (33%)	13 (28%)	
	>5000	4 (44%)	27 (59%)	
6 months	<50	10 (77%)	39 (67%)	0.90
	50-400	2 (15%)	10 (17%)	
	401-5000	1 (8%)	9 (16%)	
	>5000	0 (0%)	0 (0%)	
12 months	<50	9 (69%)	31 (67%)	0.23
	50-400	1 (31%)	3 (15%)	
	401-5000	0 (0%)	10 (14%)	
	>5000	0 (0%)	5 (8%)	
24 months	<50	9 (68%)	31 (67%)	0.60
	50-400	1 (8%)	3 (7%)	
	401-5000	2 (15%)	3 (7%)	
	>5000	1 (8%)	9 (20%)	

4.6.9 Association of viral load with pregnancy status.

There was a statistically significant association between viral load of pregnant compared to non-pregnant women at 6 months (p=0.015), 12 months (p=0.002) and 24 months (p=0.027). Pregnant women were more significantly likely to have a higher viral load than non-pregnant women. Table 16 below shows the association of viral load for pregnant versus non- pregnant women.

Table 16: Viral load for pregnant v/s non-pregnant

		Pregnant		
		No	Yes	p-value
Baseline	<50	4 (10%)	0 (0%)	0.46
	50-400	7 (17%)	0 (0%)	
	401-5000	12 (29%)	4 (40%)	
	>5000	18 (44%)	6 (60%)	
6 months	<50	35 (69%)	9 (53%)	0.015
	50-400	11 (22%)	1 (6%)	
	401-5000	5 (10%)	7 (41%)	
	>5000	0 (0%)	0 (0%)	
12 months	<50	38 (73%)	5 (29%)	0.002
	50-400	9 (17%)	4 (24%)	
	401-5000	4 (8%)	5 (29%)	
	>5000	1 (2%)	3 (18%)	
24 months	<50	29 (69%)	5 (42%)	0.027
	50-400	3 (7%)	4 (33%)	
	401-5000	2 (5%)	2 (17%)	
	>5000	8 (19%)	1 (8%)	

4.6.10 Association between "distance between place of residence and hospital" and patient retention.

There was no statistically significant association between distance from the place of residence to the hospital and patient retention. Table 17 below shows the relationship between the distance to place of residence and the proportion of patient retained.

Table 17: Association between distance and patient retention.

Distance	Not retained	Retained	P value
<10 km	17 (52%)	38 (45%)	0.46
10-20 km	8 (24%)	31 (37%)	
20+ km	8 (24%)	16 (19%)	

CHAPTER 5: DISCUSSION

5.0 Introduction

This chapter discusses the results of the study, compares them to the literature and highlights the implications for clinical practice and public health.

5.1 Participant sociodemographics

The study was conducted in a rural area in Limpopo. The majority of patients in the study (69%) were females, compared to 28% males and 3% were unspecified. The age ranged from 21 to 72 years, with a mean of 41 years and the majority of patients were in age group 30-49 years. These findings are similar to a number of studies where the patients were predominantly female and the mean age of the participants was between 30 and 49 years. [8,11,13,14,41] The findings are similar to the Mcphail and the Hudspeth studies, where the majority of patients were female and men presented at older ages and with more advanced disease.[11,31] Efforts are therefore to be made by the government in getting men to seek help on their health more often and to do so early. Late presentation in advanced disease states have implications for the overall prognosis and survival outcomes, especially given that several studies on reasons for loss to follow-up in South Africa have found that patients who were found to have died, had very low mean CD4 counts.[20,31,42,43] .

Most of the patients in the study were females in the working and child bearing age group (67%). The majority of the patients (56%) were unemployed even though most were in the working age group. Thirty two percent were unspecified and only 12% were employed. This compares to the Sanne study where 56% of the patients were unemployed.[8] The Sanne study was conducted in an urban area with a much larger sample size. Although the reasons for unemployment were not explored, HIV disease might be contributing to the high unemployment rate since patients may be dismissed because of absenteeism or they become too sick to continue working. Those who are employed would also need to take time off from work to go for regular consultations, follow-up and collection of medications. This has a negative impact on the South African economy and some patients

lose salaries on days absent from work. In the present study, thirty two percent of the patient's employment status was not specified, signifying poor record keeping. These unspecified data could have affected the results, as it was not included in the analysis.

To further complicate matters, most of the patients in the study had a lower education level. Twenty two percent had no education while 28% went up to secondary school, only 3% went up to tertiary level and 47% were unspecified. South Africa has a high unemployment rate and in 2008 the national unemployment rate was 22.7%.[40] The lower the education level, the more difficult it will be to get employment. Those who get employment are more likely to do so in labor intense jobs which might pose a problem in patients who have ill health such as HIV disease. For a large number of patients, education level and employment status were not specified. This is in spite of the fact that the demographic form that is available in the patients file had space for the two variables. This poor record keeping needs to be addressed through training and supervision. There is a need for the staff members to understand the importance of good record keeping and the implications of poor records. Poor record keeping will also make it difficult for patients who are lost to follow-up to be traced.

The majority of females were in the child bearing age group and 20 patients (23.5 %) fell pregnant during the study period. In addition to strengthening family planning methods among patients, it is important to strengthen PMTCT to decrease the number of HIV infections in babies born to mothers who are HIV positive. It would be important to find out if the patients have disclosed their HIV status to their partners, if the partners have tested and if they are also on medication. Counseling needs to be strengthened, where condom use and safe sex should be stressed because unprotected sex will lead to re-infections and treatment failure.

On the question of the distance travelled to hospital, a large number of patients (47.6%) lived less than 10km to the hospital. Even though Letaba hospital is not a primary health care facility, a number of patients who qualify to be seen at primary health care are still attended to at Letaba hospital. It is one of the centers that started ARV roll out in 2004. It was followed by Grace Mugodeni health center in 2007 and the rest of the clinics started

from October 2010. With the devolution of ARV treatment to primary health care through NIMART (Nurse Initiated Management of Antiretroviral Treatment), patients are now initiated at primary health centers and those who are stable on treatment are down referred from Letaba hospital to their local clinics. This will also decrease the workload at the hospital and improve quality of care. Down referred patients will have better access to health care services as they will be treated at clinics in their villages. The problem of transportation will be eliminated for patients fit to walk because most clinics are within walking distance. It will also be easier for primary care practitioners to trace patients who otherwise would have been classified as LTFU.

5.2 Participant co-morbidities

In the study 42 (34%) patients had co-morbidities. Seven (16%) patients had more than one co-morbidity. The most common co-morbidity was pregnancy. Twenty patients fell pregnant during the study period, with 4 patients falling pregnant twice. During counseling patients should be encouraged to inform the health workers if they plan to fall pregnant so that they are advised to do so when their health status is optimal and drug regimens changed appropriately. Five (4%) patients were hypertensive, 1(0.8%) diabetic and 1(0.8%) had a cardiac problem. There are very few studies in the literature that reported on the prevalence of co-morbidities in patients on ARV treatment. The Reproductive Health and HIV Research Unit (RHRU) conducted a cross-sectional study where they reported similar results with the prevalence of hypertension between 2 and 12%, and diabetes at around 1%.[44] With the advent of ARV treatment, the life expectancy of HIV positive individuals is improved and non-HIV related illnesses of the cardiovascular and renal systems are emerging. Nephropathy and cardiomyopathy can be complications of hypertension, diabetes and HIV. Several drugs in HIV management (for example- tenofovir and co-trimoxazole) are also associated with renal disease.[45] Patients on ARV treatment who also have a chronic disease will be on multiple drugs and there is a risk of drug to drug interaction. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) and Protease inhibitors (PI) are metabolized by the cytochrome P450 enzyme (cyt P450) system. Drugs that induce or inhibit the cyt P450 enzymes may interfere with the metabolism of these drugs. PI's may also decrease the metabolism of the calcium channel

blockers, leading to increased serum concentrations which may increase risk of AV nodal blockade. HMG CoA reductase inhibitors used for the treatment of hyperlipidaemia compete with PI's for cyt P450; this may increase the serum concentration of HMG CoA reductase inhibitors increasing the risk of myopathy.[45,46] Patients with co-morbidities end up collecting all their chronic medication from the ARV site to avoid double trips to the hospital. If this is allowed to continue, the management of other chronic conditions should be done comprehensively according to guidelines. Drug interaction will be better monitored if patients collect all their chronic medication at the same site. The pill burden due to co-morbidities can also lead to poor adherence.[47] An effort is to be made to simplify drug regimens as much as possible to improve adherence.

5.3 Drug Regimen at baseline, 6, 12, 24 and 36 months

At baseline 97% of the patients were started on Regimen 1a and 3% on regimen 1b. This is in line with the 2004 South African National Antiretroviral treatment Guidelines where Regimen 1a and 1b were first-line therapy for adults[48] and also compares to the Brennan T.A and the Hudspeth studies where 89.4% and 92% of patients were started on regimen 1a respectively.[9,11] During the study period regimens were changed due to pregnancy, treatment failure and for intolerable side effects. In total 36(29%) patients were changed regimens during the study period where 6 (5%) were changed to other regimens at 6 months, 8 (7%) at 12 months, 12 (11%) at 24 months and 10 (12%) at 36 months.

Seventeen patients were changed due to side effects, of which 12 were changed due to peripheral neuropathy. By 6 months, 16.9% of the patient had side-effects. This increased to 37% at 12 months, 32.2% at 24 months and 25.8% at 36 months. The most common side effect was skin rash followed by peripheral neuropathy as shown in table 7. In the Van Oosterhout and the Sanne studies, peripheral neuropathy was the most common side effect followed by skin rash.[8,14] During data collection in the present study, it was difficult to decide whether the rash was due to side effects or skin pathology due to opportunistic infections because in most cases the cause was not recorded by the examining doctor. Skin rash as a side effect might be overrated. Peripheral neuropathy is associated with the use of D4T and Didanosine (ddI). All patients in this study were started on a regimen containing D4T and switched to AZT and TDF when the patient developed intolerable side-effects. In

most cases treatment-limiting toxicities occur early, but with D4T they continue to accumulate over time.[49] New ART guidelines were published in 2010 and D4T is no longer a first line drug.[22] This will significantly reduce the number of patients presenting with peripheral neuropathy as a side effect. It is of utmost importance to enquire about side effects, educate the patients and switch treatment early should the need arise.

Seventeen patients were changed due to pregnancy while 3 (15%) patients were diagnosed after 12 weeks and their regimens were not changed. Teratogenic effects were reported with the use of efavirenz in animal studies.[50] Recent studies have not confirmed the teratogenic effects in humans[51], however caution should still be exercised especially in the first trimester and less teratogenic drugs such as nevirapine considered.

5.4 Clinical outcomes

At baseline 93% of patients had CD4 count of 200 cells/mm^3 and below, the number decreased to 28% at 6 months, 23% at 12 months and 17% at 24 months. CD4 counts > 200 cells/mm^3 increased from 7% at baseline to 71% at 6 months, 77% at 12 months and 83% at 24 months. There was an improvement with regards to the CD4 count between baseline and all time periods, with the biggest magnitude of change in the first 6 months after the initiation of ARV treatment. The CD4 count increased at a slower rate after 6 months. The marked improvement in the first six months will encourage compliance and increase uptake in the ARV program. The mean CD4 count increased from 128 cells/mm^3 at baseline to 310 cells/mm^3 at 6 months, 380 cells/mm^3 at 12 months and 470 cells/mm^3 at 24 months. This compares to a number of studies where the mean CD4 count increased over time and is in line with the South African National Antiretroviral Guidelines where one of the goals of treatment is for the CD4 count to rise and remain above the baseline count.[8,11,13,14,20,22,48,52] The patients in this study had good immunological outcomes that are comparable to those found in studies conducted in urban settings.[9,10,12,19,49] There was also a significant improvement in viral load between baseline and all the time periods. The most significant improvement was between baseline and 6 months. By 6 months 84% of patients had suppressed viral load to </= 400, this compares to 90.8% in the Mcphail study.[32] Sixteen percent of patients had virological failure at 6 months, the number increased to 22% at 12 months and 24% at 24 months. This is viral rebound and the

percentage of patients with viral rebound usually increases over time. These were also the findings in the Sanne I.M and the Van Oosterhout studies.[8,14] Viral rebound is associated with poor adherence in the early phases of ART initiation and with resistance in the later phases.[19] Patients with viral rebound should be monitored closely and a trend observed over a period of time. This will increase the cost of treating the patient because more monitoring investigations will need to done to observe a trend and the patients might need to come more often for follow-up. Patients who have virological failure should be changed to second line treatment. This further limits the options should they fail on the second line drugs, as there are limited drug options in South Africa.

A major deficit was identified in this study, where at 24 months 19 (24%) patients had viral rebound with viral loads of >400 copies/mm^3, only 2 patients were followed up and changed to regimen 2 (second line drugs). Most of the patients were continued on a failing regimen without any intervention. This is caused by the fact that bloods are taken but results are not reviewed. This is a waste of resources, as bloods are sent to the laboratory to be processed and the hospital is billed. Expensive drugs are continued on patients with no clinical benefits. This amounts to clinical negligence and can result in poor adherence to treatment when patients realise that there is no improvement despite taking treatment. Maintaining patients on failing drug regimens also contributes to the development of drug resistance. [16] Studies have shown that if patients are monitored closely and adherence strengthened early in patients with viral rebound, fewer patients will have resistance.[19]A system needs to be introduced where red flags will compel clinicians to review results and take action whenever red flags are raised. Haematological results were unavailable because the bloods were not taken for most of the patients. This is worrying because results are supposed to be used to assess the effectiveness of the drugs and to monitor adverse effects. This is one of the weaknesses in this clinic. Patient education can assist in solving this problem. If patients are educated about their disease, disease monitoring and treatment, they will be able to remind the health care provider about the blood tests and trigger the review of investigation results. A documentation chart with current results and dates for the next tests can also be utilised. The chart can be kept in the patients file and should be reviewed at each visit by the health care professional.

There was a significant mean weight gain of +/- 4.7 kg between baseline and 6 months. For the rest of the study period there was a positive trend but the increase was not statistically significant. The results are similar to those found in the Shumbuso and the Hudspeth studies where there was a significant weight gain of up to 4.3 kg in the first six months and no significant increase from 6 to 24 months.[11,52] Weight gain in patients on ARV treatment is expected and it is very important for this weight gain to be monitored closely. As much as weight gain is a positive outcome in patients who are underweight, it can be a challenge if the patient gains a lot of weight and the Body Mass Index increases beyond 25 kg/$m^{2.}$ Obesity can reduce life expectancy, increase morbidity (due to diabetes and cardiovascular disease) and mortality.[24]

The number of opportunistic infections found in this study decreased over time after the initiation of ARV treatment. The number of patients with opportunistic infections decreased from 68 (58.4%) at 0-6 months, to 55 (44%) at 6-12months, 39 (31.5%) at 12-24months and 19(15.3%) at 24-36 months. This is one of the benefits of ARV treatment and these findings are similar to those that are reported in the literature, where the frequency of opportunistic infections decreases after the initiation of ARV treatment.[53, 10] After the initiation of ARV treatment, the CD4 count increases and the immune system recovers, reducing the incidence of the opportunistic infection and decreasing morbidity and mortality for the patient. As the CD4 continues to increase, certain prophylactic treatment will be stopped depending on the level of the CD4 count. This will also decrease the workload and the treatment cost. In the present study, the proportion of patients with upper respiratory infections (URTI) increased at 6-12 months and 12-24 months. There is no logical explanation why this rate would increase during these periods. This might be due to the fact that data was collected from files and there was no set criterion for the diagnosis of URTI. The rate might therefore be exaggerated.

During the entire study period, nine (7.2%) patients were admitted to hospital. Three of the nine patients were admitted twice. Most (7) of the admissions occurred during the 0-6 months period, followed by 4 at 6-12 months, 1 at 12-24 months and none at 24-36 months. The number of admissions was higher during the early stages of ARV treatment and it decreased over time on treatment. The finding is similar to that found in the Hudspeth study in which patients had fewer hospitalisations after ARV treatment

initiation. [11] In the early phases after ARV treatment initiation, the immune system is still weak and the body will still be susceptible to opportunistic infections. Patients with severe and life threatening infections may be admitted. As the immune system recovers and the body starts fighting infections, the incidence and the severity of opportunistic infections will decrease. This will also result in a decrease in the admission rate and further decrease in the cost of HIV management.

5.5 Patient retention

At 36 months, 85(72%) of the patients were still retained at the clinic. Of the 39 patients that were no longer attending the clinic, 14 (43%) were transferred to other institutions, 8(24%) were down-referred to clinics, 4 (12%) died, 4 (12%) defaulted and 3 (9%) were lost to follow-up. Most of the patients that were no longer attending the clinic were accounted for and only 6.4% had defaulted or were lost to follow-up. The findings were similar to the Brennan A.T study (a cohort study of 4476 patients) in which at 24 months 6.2% of the patients were lost to follow-up, 2.6% had died and 73.6% were retained.[9] In the Shumbuso F study, 80% of the patients were retained at 24 months. Even though Letaba hospital is in a rural area with limited resources, patient retention is comparable to studies conducted in better resourced centers. The high rate of retention will increase the patient and financial burden at the clinic as there are also new patients who are initiated on treatment. There might also be emergence of non-HIV related illnesses. This will need to be considered and factored in during budget reviews.

5.6 Relationships between socio-demographics, patient retention and clinical outcomes

Statistical association was tested between the distance between patients' residence and patient retention. There was no significant difference between distance from place of residence to the hospital and patient retention. The findings are different to those found in the literature. A review article by Geng E.H et al (2010) reported that distance to the clinic and transportation was found to be major barriers to patient retention in a variety of

settings in Africa and Asia. In rural Uganda, 50% of the patients cited lack of transportation and 42% excessive distance resulting in clinic absenteeism.[54] The high patient retention in the present study can be attributed to a number of factors including: good adherence counseling by the clinic staff, where patients are made to understand the importance of follow-up, positive staff attitude leading to high patient satisfaction rate (good patient- health worker relationship) and the temporary grant that was given to all patients with a CD4 < 200 cells/mm^3 for 12 months. The temporary grant is given to patients when they are weak and unable to work. The grant enables them to hire private transport when they are too weak to use public transport and they are counseled and empowered on ideas to use the grant to start sustainable means of making a living when the grant lapses .

Statistical association was tested between demographics and clinical outcomes. There was no significant association between CD4 count and age, sex, education level and employment status at all the time periods. There was no significant association between viral load and sex, education level and employment status. Even though there was no significant association between viral load and sex, a higher percentage of males tended to have a higher viral load. In a number of studies, men were found to have had a higher viral load than females. [8],[55] Men tend to access health care services late, when the disease is more advanced and the viral load higher. At baseline more than 80% of patients in the 50+ age group had viral load >5000 copies/mm^3 compared to 55% for age group 30-49 years and 31% for age group <30 years. This may be due to the fact there is low index of suspicion for HIV in older people by both the patients and health care providers, leading to late presentation at advanced stage and late diagnosis. There was a significant difference in viral load between the different age groups at 6 months. More than 80% of the patients in the 50+ age group had an undetectable viral load, compared to 65% for the age group 30-49 years and 58% for the < 30 age group. The patients in older age group had a significantly better viral load outcome than the younger age group at 6 months. This might be associated with good adherence, and might imply that older people had better adherence to treatment than younger ones.

There was an association between viral load and pregnancy. Non-pregnant women were more likely to have undetectable viral loads than those that fell pregnant, p=0.015 at 6

months, 12 months (p=0.002) and at 24 months (p=0.027). This is in contrast with what has been reported in the literature. In a study on the effects of pregnancy on immunological and virological outcomes of women on ARV treatment, there was no significant difference in the proportions of women with detectable viral load amongst those who fell pregnant and those who did not.[56] In pregnancy, the immune function is suppressed in both HIV-infected and uninfected women.[57] These changes have led to concern that the effects of pregnancy on HIV disease could accelerate the progression of the infection. Follow-up studies showed that that there was no significant difference in the rate of acceleration of disease between the two groups.[58]

5.7 Validity, reliability, bias and limitations

Validity refers to the extent to which a measure actually measures what it is meant to measure.[59] In ensuring validity in this study, the questionnaire was developed using information from the literature, guided by the supervisor and subjected to peer-reviewing by Family Physicians working in Letaba hospital. A pilot study was also conducted at C.N Phatudi hospital, a district hospital about 25 km from Letaba hospital, using twenty patient files. Appropriate corrections and adjustments were made to the questionnaire to ensure the validity and also to ensure that the research is feasible.

The sample size was calculated with the help of a qualified statistician and a systematic sampling method was used. These processes ensured that the results may be generalized to the study population and that sampling bias was eliminated. Using a statistically adequate sample size also ensured that type II error was eliminated.

Reliability refers to the degree of similarity of the information obtained when the measurement is repeated on the same subject or the same group.[59] The explicitness of the research methods used enhanced reliability.

The strength of the study was the fact that the record review covered a long period of time, enabling the trend in the clinical outcomes to be measured over time.

The biggest limitation of this study was the fact that the study was a record review. The researcher relied on the availability of information in the files. It was impossible to get

information that was not recorded in the file. Even though 124 patient's files were sampled at the beginning of the study, not all files contained all the information needed, resulting in missing data and therefore poor data quality.

Since the information was collected as recorded in the file; there was no way that the researcher could ascertain that the information was true. This might have introduced information bias and affected the results also.

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

This study found that ARV roll-out program in a rural hospital can produce both good patient retention and clinical outcomes, shown by the increase in CD4 count, decrease in viral load, increase in weight and the decrease in opportunistic infections. These good clinical outcomes in this rural setting were most pronounced in the first six months after ARV initiation. There was however a tendency to losing viral suppression after 24 months of ARV therapy.

Although there was good patient retention in this program 36 months after initiation of ART, unplanned pregnancies among female patients place them at risk for re-infection and virological failure. The finding that patients who fell pregnant during the study period had a higher viral load than those that did not indicates the need to give attention to family planning in the clinical management of patients on ARV treatment.

6.2 Recommendations

- A monitoring and evaluation programme which will ensure that guidelines and protocols are adhered to, should be developed to address the problem of health care providers not reviewing laboratory results. Such programs should identify priority indicators of clinical care and develop red-flags on non-compliance which persist on the system, until the problems are attended to.
- Regular audits on quality of record keeping need to be conducted and feedback given to individual health care practitioners to assist them in improve their record keeping.
- Patient education on family planning and safe sex, including condom use should be strengthened during clinic visits.

- Viral load testing should form part of PMCTC monitoring.
- A system needs to be developed to help in tracing the patients who are lost to follow up. Full patient contact details are to be recorded in the patients file. These should include the residential address and two contact telephone numbers. Patients return dates should be recorded in a book and patients who do not turn-up for their appointments should be contacted telephonically. If patients do not present at the clinic after the call, the home-based careers in the villages should be contacted to make a follow-up, failing which the clinic social worker should be requested to do a home visit and report back to the clinic.
- Given the risk of virological failure with time, support groups of people living with HIV disease should be encouraged to use the good clinical outcomes at the initial phase of ARV therapy to motivate patients to adhere strictly to treatment at later stage of treatment. Such encouragement can assist in addressing the inertia of not wanting to take treatment at later stages of therapy.

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APPENDICES

APPENDIX A: DATA COLLECTION SHEET

Code number

Demographic Information:

1. **Age:** _____yrs.
2. **Distance to Hospital: _____km.**
3. **Sex :** ❑ Male ❑ Female
4. **Race:** ❑African ❑White ❑Indian ❑Coloured
5. **Level of Education:** ❑ No education ❑ Primary ❑ Secondary ❑ Tertiary
6. **Marital Status** ❑ Single ❑ Divorced ❑Separated ❑ Married ❑ Widowed
7. **Employment** ❑ Employed ❑ Unemployed

Social Habits:

1. Drink alcohol ❑ Yes ❑ No
   If yes how much
   _____
2. Smoking ❑ Yes ❑ No
   If yes how many
   _____

Medical Record to be checked for the following:

	Baseline	**6months**	**12months**	**24months**	**36 months**
Date					
Viral Load(copies/$mm^{3)}$					
CD4 count(cells/$mm^{3)}$					
Drug Regimen					
Weight (kg)					
Height(cm)					

Opportunistic Infections

Oral thrush					
Tuberculosis					
Pneumonia					
Tumor/Cancer					
Skin Pathology					
Other					

Adverse effects

Peripheral neuropathy					
Skin rash					
Stevens Johnson syndrome					
GIT					
Hematological					
Lactic acidosis					
Lipo dystrophy					
Others					

	Baseline	**6months**	**12 months**	**24 months**	**36 months**
Are there any co-morbid disorders	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No
If yes, which of the following					
Diabetes					

Hypertension					
Epilepsy					
Asthma					
COPD					
Other					
Has the patient been admitted?	❑ Yes No ❑				
If yes,					
Diagnosis					
Outcome of admission.					
Is the patient honoring follow-up appointments?					
Is the patient compliant (pill count).					

Is the patient still attending Nyeleti Clinic ❑yes ❑no
If no, give reason below

Deceased ❑
Transferred ❑
Down-referred ❑
Defaulted ❑
Lost to follow-up ❑
Unknown ❑
Other_____

APPENDIX B: ETHICS CLEARANCE CERTIFICATE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Dr Mary-Anne M Semenya

CLEARANCE CERTIFICATE	**M110485**
PROJECT	Clinical Outcomes and Patient Rentention in an Antiretroviral Roll-Out Programme at Letaba
Hospital,	Limpopo Province, South Africa
INVESTIGATORS	Dr Mary-Anne M Semenya.
DEPARTMENT	Department of Family Medicine
DATE CONSIDERED	06/05/2011
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 22/07/2011 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Dr O Omole

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**
PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

APPENDIX C: PERMISSION BY PROVINCIAL RESEARCH COMMITTEE OF LIMPOPO.

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

Enquiries: Selamolela Donald Ref: 4/2/2

23 September 2011

Semenya MML

University of the Witwatersrand

Johannesburg

Greetings,

Re: Permission to conduct the study titled: Clinical outcomes and patient retention in an antiretroviral roll-out programme at Letaba Hospital, Limpopo Province, South Africa

1. The above matter refers.
2. Permission to conduct the above mentioned study is hereby granted.
3. Kindly be informed that:-
    - Further arrangement should be made with the targeted institutions.
    - In the course of your study there should be no action that disrupts the services
    - After completion of the study, a copy should be submitted to the Department to serve as a resource
    - The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible

Your cooperation will be highly appreciated

Head of Department

Department of Health

Limpopo Province

18 College Street, Polokwane, 0700, Private Bag x9302, POLOLKWANE, 0700
Tel: (015) 293 6000, Fax: (015) 293 6211/20 Website: http/www.limpopo.gov.za

APPENDIX D: PERMISSION BY LETABA HOSPITAL MANAGEMENT

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH AND SOCIAL DEVELOPMENT
LETABA PROVINCIAL HOSPITAL
TEL: O15 303 8200
FAX: 015 303 8421

Ref: 4/2/2
Enq: Dr M.J Muhlari
Date: 26 September 2011

Dr MML Semenya
Flat 33 Eco Ekhaya
TZANEEN
0850

RE: APPROVED FOR CONDUCTING A RESEARCH ON THE CLINICAL OUTCOMES AND PATIENT RETENTION IN AN ANTIRETROVIRAL ROLL-OUT PROGRAMME AT LETABA HOSPITAL, LIMPOPO PROVINCE, SOUTH AFRICA.

1. The above subject matter refers:

2. You are granted permission to conduct the above research at Letaba Provincial Hospital as per permission granted by the Head of Department, Limpopo Department of Health.

3. Hoping that you will find this in order.

.....
CHIEF EXECUTIVE OFFICER/LETABA HOSPITAL