

AN ASSESSMENT OF CLINICAL CARE AND
OUTCOMES OF HIV INFECTED PATIENTS ON
ANTIRETROVIRAL THERAPY, USING
THERAPY-EDGE DATABASE AT ST. JOSEPH'S
HOSPITAL, ROMA – LESOTHO

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DECLARATION

I, Ufok Juliana SAMSON-AKPAN declare that this research report is my own work. It is being submitted for the degree of Master of Family Medicine in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

Signature:..... Date: 26th September 2013

DEDICATION

To my mother Madam Akon Tom Umoh (1923-2010) who exhibited foresight and invested greatly in the empowerment of the girl child through quality education and to my husband Enobong Sonny Samson-akpan(Snr) (1942-2012) for his support of quality education.

ABSTRACT

Background

The high prevalence of HIV has been a major cause for concern in Lesotho and the clinical course has witnessed some service lapses, complications and deaths. The researcher was therefore motivated to conduct this study with the aim to assess care and outcomes offered to HIV patients at St. Joseph's Hospital. The objectives were to describe patient socio-demographic and clinical characteristics at initiation of antiretroviral therapy, to describe clinical parameters of haemoglobin, AST, CD4 count levels as outcome proxy of care and to analyze the rate and predictors of patient retention and lost to follow-up.

Methods

A retrospective cohort study of 1060 patients initiated on ART at the Thusong ART Clinic in St. Joseph's Hospital, Roma between August 2005 and July 2008 was conducted. Relevant documentation was captured from the patients' clinical records hard copy files onto the Therapy-Edge (TE) database tool used. Patient confidentiality was respected. The dataset was closed on 31st October 2012. Data were analyzed using STATA version 11.

Results

The total number of patients enrolled during the study period of August 2005 – July 2008 was 1060. The findings on the patients studied showed that 99.5% were Sotho with the majority of 70.2% being female. Patients in the age group of 16-35 years were 22.2%, in the age groups of 36-55 years and >55 years were 58.3% and 19.5% respectively. Median age was 43 years. Employed persons were 24.3%, students were 2.3%, unemployed persons were 44.8% and 28.6% were of unknown employment status. On WHO classification, 18.1% was WHO Stage I, 34.6% was Stage II, 43.4% was Stage III and 3% was Stage IV. Median weight at enrollment was 55.6kg. Baseline CD4 count < 50 cells/mm³ was 13.3%, count of 50 – 199 cells/mm³ was 43.2%, CD4 count ≥ 200 cells was 38.7%. Patients with Hb <10g/dl were 17.3%. On patient retention over a period of about 6 years, 57% of the patients were still alive

and in care, 11.3% had been transferred out to the health centers and clinics, 29.5% were lost to follow up. It is noteworthy that only 2.2% were recorded as dead.

Conclusion

The study showed that more than half of the HIV patients on ART were female, thus suggesting better access to care and health seeking behaviour. Clinical parameters of haemoglobin, AST, CD4 cell counts used to monitor progress over follow-up period showed results comparable with other similar studies. Baseline CD4 count, WHO stage, age, gender and employment status were agreeable with studies in other settings to predict those lost to follow-up (LFTU). The low percentage of documented deaths suggests that some deaths may have been included in LTFU.

Better documentation, staff training and retention, decentralization of care and proper follow-up measures are steps in the right direction for better ART monitoring and outcomes.

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ABBREVIATIONS

AIDS – Acquired immunodeficiency syndrome
ART – Anti-retroviral Therapy
AST – Aspartate aminotransaminase
AZT - Zidovudine
BMI – Body Mass Index
d4T – Stavudine
EFV - Efavirenz
HAART – Highly Active Anti-retroviral Therapy
HB - Haemoglobin
HIV – Human Immunodeficiency Virus
IQR – Inter-quartile range
KG - Kilogramme
LTFU – Lost To Follow-Up
ML – milliliter
MOH – Ministry of Health
MOH&SH – Ministry of Health and Social Welfare
NVP - Nevirapine
PEP – Post Exposure Prophylaxis
PHC – Primary Health-care Clinic
PMTCT – Prevention of Mother To Child Transmission
3TC - Lamivudine
TE – Therapy-Edge-HIVTM
TB - Tuberculosis
UNAIDS – United Nations Programme on HIV/AIDS
WITS – University of the Witwatersrand
WHO – World Health Organization

CHAPTER 1: INTRODUCTION

UNAIDS 2010 estimates show that 34 million people were living with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and more than 30 million had died since the beginning of the epidemic about 30 years ago^{1,2}. Lesotho is a small mountainous kingdom completely surrounded by the Republic of South Africa. It has a population of 1.87 million and has an HIV prevalence of 23.6%, the third highest in the world, after Swaziland and Botswana^{1,2,3}. In 2010, 2.7 million new infections worldwide were reported and more than half of these were in Sub-Saharan Africa. AIDS is the single largest cause of mortality in Africa, with 1.2 million death reported in 2010^{1,4}.

The Government of Lesotho is committed to the scaling-up of anti-retroviral therapy^{5,6} to those eligible for treatment as reports from Sub-Saharan Africa have confirmed the success of other scale-up efforts and have provided evidence that highly active antiretroviral therapy (HAART) can save the lives of many people living with HIV and AIDS^{7,8}. The Ministry of Health 2007 statistics in Lesotho shows 24,700 clients receiving antiretroviral therapy out of the estimated 56,000 in need of ART, unlike in the previous year where the total was less than 10,000 that received highly active antiretroviral therapy⁹. St. Joseph's Hospital is a district hospital with 120 in-patient beds including out-patient and emergency Medical, Surgical, Paediatric, Obstetrics and Gynaecology, Maternal and Child Health, HIV/AIDS services among others. Support services of laboratory, pharmacy and x-ray are present and functioning. The emergence of HIV and AIDS has markedly increased the burden of disease on the population and the influx of patients to the hospitals and clinics. The current National Scale-up of ART through the 'know your status' (KYS) campaign strategy¹⁰ has contributed to sudden increase of patients in all antiretroviral therapy centers in the country. This situation has put added strain on the health workers.

The mission of St. Joseph's Hospital is to deliver quality services in all departments to the community. Accurately recorded patient records are an important part of achieving this goal to provide quality clinical care. St Joseph's Hospital ART center follows a routine that

patients socio-demographic and clinical characteristics are documented. Patients who test positive for HIV are immediately sent for CD4 count. The criteria for eligibility for ART initiation was CD4 count below 200 cells/mm³ and was used during the study period - August 2005-July 2008. Eligible patients are made to start pre-initiation work-up for ARVs. The work-up plan includes 3 counseling sessions on disclosure, nutrition and positive living and stress management, adherence for the patient and his/her treatment supporter (buddy). This could take one to four weeks depending on the patient's preparedness to attend. The patient is assessed for any opportunistic infections and tuberculosis must be excluded before commencement of ARVs. Opportunistic infections are treated on their own merit before initiation or in conjunction with ARVs. A regimen for HIV/TB co-infection is also followed. Clinical improvement is defined as improvement in functional capacity as measured by the Karnofsky Performance scale used from August 2005 to December 2006 or the Performance Function scale of work, ambulatory or bedridden on the HIV Care/ART card of the Government of Lesotho ART scaling up plan⁶ – in use from January 2007, CD4 cell count response to HAART recorded as an expected increase of 50 cells/mm³ by 6 months on treatment (Renaud 1999, Le Moing 2002)^{11,12}, increase of body mass index (BMI) to the normal range (18.5 – 25kg/m²)¹³ within one year of treatment. In St Joseph's Hospital weight is used. Other clinical parameters used are haemoglobin estimation and liver function tests including aspartate aminotransaminase (AST). Follow-up appointments are scheduled periodically or as necessary. This routine is as contained in the Government of Lesotho ART scaling up plan⁶.

The researcher has chosen this study because the high prevalence of HIV was a major cause for concern and called for implementation of effective control programs as a matter of urgency. Skilled human resource capacity and material resources are called into play to make an impact. ART centers offer the basic services of counseling, testing, treatment, care and support and the clinic needs an organized work team with necessary and appropriate skills to be able to function well¹⁴. In the course of clinical care, our ART center had witnessed some complications and deaths. The researcher was thus motivated to find out whether optimal clinical treatment was offered and received, given the prevailing circumstances in St Joseph's Hospital. Therapy-Edge-HIVTM computerized system has been used as a tool to assist in this

study as it is a networking database system which measures quality of care, identifies best practices and answers to the effectiveness through diagnostic testing in chronic illnesses such as HIV and AIDS¹⁵.

In St. Joseph's Hospital, an access spreadsheet from SolidarMed (a Swiss NGO) was used by a clerk to enter patient data. Assessment had never been done in St. Joseph's hospital and the researcher is going to undertake this task to assess clinical care for the outcomes observed so that quality services can be provided.

This study is justifiable in that St. Joseph's hospital in its first 3 years of ART had counseled and tested 10,000 clients out of which 2,600 were HIV positive and were enrolled in care. Of these, 1,060 were on antiretroviral therapy¹⁶. Therapy-Edge data system was the tool used in this study to capture data from patients' clinical files and saved for analysis of the quality of care so far offered to HIV patients at St. Joseph's Hospital. The system had been introduced to Thusong ART clinic through the researcher who had been given initial orientation of the software by Right to Care - a non-profit organization involved in the implementation of the ART Treatment Program in South Africa. TE was installed on-site in May 2009 and the researcher and data capturers were trained on its use.

The findings will hopefully serve as evidence to support interventions which are appropriate for quality assurance in the management of HIV patients.

CHAPTER 2: LITERATURE REVIEW

UNAIDS report (2010) on global AIDS epidemic show that 34 million people (range 31.6 – 35.2 million) were estimated to be living with HIV and AIDS – a huge rise from around 8 million in 1990, and more than 30 million had died from AIDS related causes since the beginning of the epidemic^{1,2,3,4}. There were 2.7 million (range 2.4 – 2.9 million) new infections worldwide and more than half of these (1.9 million) were in Sub-Saharan Africa^{1,2}. Also, in 2010, 1.2 million Africans died of AIDS^{1,4} thus making AIDS the single largest cause of mortality in Africa^{1,4}. The overall growth of the epidemic has stabilized in recent years as shown by the steady decline of annual incidence of HIV infections. This has been attributed to the significant increase in the number of people receiving anti-retroviral therapy leading to the decline in the number of AIDS-related deaths^{1,2,3,4}. This had been largely proven in Botswana which has one of the highest HIV incidences in the world and a successful nationwide roll-out and scale-up of antiretroviral therapy had led to a decline in AIDS related mortality¹⁷.

In the Sub-Saharan African region, Lesotho has an HIV adult (aged 15-49 years) prevalence of 23.6% and is the third highest in the world, after Swaziland (25.9%) and Botswana (24.8%)^{1,2,3,18}. South Africa comes fourth^{19,20} on the list with 17.8% prevalence rate, but has the largest population of 5.6 million²¹ living with HIV and AIDS in the world^{1,4,19,20,21}. In other sub - regions like Northern and Southern Asia, the epidemic has remained relatively stable and largely concentrated among high risk groups like sex workers, while in Eastern Europe and Central Asia, the number of people living with HIV and AIDS has more than tripled since the year 2000^{1,4}. More females than males are reported to be infected with HIV. Muula et al states 2.3 : 1.2 female to male ratio,²² Maskew M states 66.3% female infection²³. The UNAIDS Global Report 2012 on AIDS epidemic informs that women represent 58% of the people living with HIV in sub-Saharan Africa and that more than half of the adults with HIV in Lesotho are women²⁴. The World Health Organization (WHO) had responded to the challenge of rapid decentralized care of antiretroviral therapy (ART) by instituting the Integrated Management of Adult and Adolescent Illness (IMAI), where there is collaboration with capacity building institutions globally to elaborate standardized training materials in the training of health cadres on HIV and AIDS treatment and care. IMAI has shown great

potential in scaling up capacity and entry into treatment as well as care, prevention and other services as reported by WHO^{25,26}. Lesotho's AIDS effort is now guided by the National HIV and AIDS Strategic Plan 2011/12 – 2015/16²⁷ with the intention to reverse the epidemic by reducing new infections by 50%, strengthening coping mechanisms for vulnerable people and providing antiretroviral treatment and care for all those in need²⁷. For those on treatment, good response to HAART is necessary. In their different studies, Renaud et al and Moing et al showed that CD4 cell count response to HAART is an expected increase of at least 50 cells/mm³ by six months on treatment^{11,12}. The studies by Lawn et al and Brennan et al state that low CD4 count is the largest predictor of death^{28,29}. The study of Toure et al on rapid scaling of ART in Cote d'Ivoire showed that aside from old age being associated with death during early follow-up, other associated risk factors were lower baseline CD4 cell count, higher WHO clinical stage, low haemoglobin and low body mass index³⁰.

On patient retention rates, Rosen et al. systematically reviewed 32 publications reporting on 33 cohorts (74,192 patients in 13 countries) and found the weighted mean retention rates as 79.1%, 75.0% and 61.6% at 6, 12, and 24 months respectively and came to the conclusion that ART programs in Africa have retained about 60% of their patients at the end of 2 years³¹. On lost to follow-up, Fox et al states that mortality is substantially underestimated among patients lost to follow-up despite limited tracing³². Transportation costs are reported in the studies of Tuller et al and also by Miller et al to be one of the major determinants of lost to follow-up^{33,34}.

The Thusong ART clinic currently uses hard copy files to store clinical records. Therapy-Edge-HIVTM (TE) employed in this study is an electronic patient management system which stores clinical data in a relational database. It graphically tracks and automatically processes a patient's clinical data through an extensive knowledge base of pharmacological and clinical information created and maintained in collaboration with expert HIV clinicians and researchers¹⁵.

2.1. Definition of Terms

HIV Prevalence – is the percentage of the population living with HIV.

HIV Incidence – is the number of new HIV infections.

CD4 cells – These are T helper/inducer lymphocytes with CD4 receptors and are important cells which regulate and control aspects of the immune system.

Defaulter – Patient who does not attend a scheduled appointment including fill-up pharmacy visits.

Lost to follow-up – Patient who is more than three months late after scheduled appointment. This would be confirmed if the out-reach team is unable to locate patient via phone call/s or/and home visit.

Patient retention - defined as proportion of patients alive and in care at the end of the study period.

HAART naive – Patients who have not been previously exposed to HAART.

Viral load (VL) suppression – Viral load decreases to below the level of detection (400 copies/ml) by reference laboratory estimations.

Anaemia – Haemoglobin (Hb) value below 11.5g/dl (women) and 12.9 g/dl (men).

CHAPTER 3: METHODOLOGY

3.1 Study Aim and Objectives

3.1.1 Aim

To assess the clinical care and outcomes of HIV patients on antiretroviral therapy from August 2005 to July 2008 using TE database in St. Joseph's Hospital.

3.2. Objectives

1. To describe patient socio-demographic and clinical characteristics at initiation of antiretroviral therapy.
2. To describe the longitudinal record of selected clinical parameters as an outcome proxy of the clinical care of patients initiated on ART:
 - Haemoglobin level
 - AST level
 - CD4 count level
3. To analyze the rate and predictors of patient retention and lost to follow-up.

3.3. Study Design

This was a retrospective cohort study of patients initiated on ART at the Thusong ART Clinic in St. Joseph's Hospital between August 2005 and July 2008. Clinical chart record review was conducted. The dataset was closed on 31 October 2012.

3.4. Study Setting

The study site was St. Joseph's District Hospital in Roma, Lesotho which serves a population of about 115,000 in the Roma Health Service Area (HSA)³⁵. Its ART Clinic (Thusong) which was opened in August 2005 had enrolled about 4,000 HIV-infected adults in care and provided antiretroviral treatment to over 2,000 of these individuals using the Lesotho National ART Treatment Guidelines³⁶ by the time this research commenced. Lesotho ART Guidelines

and the ART scaling up plan were in force during the study period, 2005-2008 and the criteria for initiation of ART was $CD4 < 200 \text{ cells/mm}^3$.^{36,6}

3.5. Study Population

The study population comprised of all HIV infected adult patients enrolled in care at the St Joseph's Hospital ART clinic (Thusong) from August 2005 to July 2008.

3.6. Study Sample

The study sample consisted of all individuals initiated on ART at the Thusong ART clinic between August 2005 and July 2008 who met the inclusion criteria.

3.6.1. Inclusion Criteria

- HIV-infected adults aged 16 years and above
- HAART-naive individuals at the time of initiation

3.6.2. Exclusion Criteria

- HIV positive patients who are not eligible for initiation of HAART on the basis of $CD4 > 200 \text{ cells/mm}^3$
- HIV positive patients who have been transferred into the study site already on treatment
- Post Exposure Prophylaxis (PEP)
- PMTCT programme patients on AZT prophylaxis.

3.7. Data Collection and Storage

The data described in the objectives was captured from patients' clinical record hard copy files and captured electronically on Therapy-Edge-HIVTM by trained data capturers and quality controlled by the researcher. Therapy-Edge-HIVTM (TE) stores clinical data electronically in a relational database, graphically tracks and automatically processes a patient's clinical data through a knowledge base of pharmacological and clinical information created and maintained in collaboration with expert HIV clinicians and researchers¹⁵.

Patient demographics entered excluded the patient's name for confidentiality purposes.

3.7.1. Measurement

Relevant documentation was captured from the patients' clinical record files onto the TE system. Data that was not documented was absent in TE as it was done retrospectively, as opposed to prospective study where there may be opportunity to revisit and correct any mistakes or errors. Data capturing errors may occur due to possible differences in terminologies in the TE data system and the manual files coupled with the possibility of teething problems of a newly introduced system. Poor quality record keeping and documentation in the manual files may bring about missing necessary data. All these can pose as limitations to proper assessment of patients' risk and prognosis.

3.7.2. Data Analysis

Data were analyzed using STATA version 11.

Patient socio-demographic and clinical characteristics of the cohort were described using proportions for categorical variables and medians (with Inter-quartile range) for continuous variables. Person-time accrued from the date of ART initiation until the earliest of: (1) death; (2) loss to follow-up; (3) transfer out; or (4) close of the dataset on 31 October 2012. Proportions for the different clinical outcomes (WHO stage and CD4 level) were compared at baseline, 6 months, 12 months and at the end of the study period – approximately 4 years after the date of the last ART initiation. Kaplan-Meier curves were used to compare LTFU stratified by each of the categorical variables. The crude rate and adjusted hazard ratios (aHR) of LTFU were estimated using Cox proportional hazards models. In the multivariate analysis, each of the potential predictors – gender, age, baseline CD4 count, WHO clinical stage and occupational status was adjusted against each other. The proportionality assumption was checked (using log (-log (survival)) over time for each covariate) and was not violated. All statistical tests were 2 –sided and alpha level was set at 5%.

3.7.3. Ethical Consideration

Permission to conduct the research was granted by the Human Research Ethics Committee of the University of the Witwatersrand, and the Ministry of Health and Social Welfare of Lesotho as well as St. Joseph's Hospital.

Identifying data from patient clinical records were removed to respect anonymity and patient confidentiality. Every patient enrolled for ART signs an informed consent. Consent for HIV/AIDS treatment seeks to undergo HIV testing and treatment and to obtain confidential medical opinion and/or recommendation. The consent form contains the information that an explanation of the condition has been made to the patient and he/she has understood and has agreed that HIV and other tests be conducted and that ARVs be provided and taken as advised.

The result of the test (or treatment) may be anonymously used for purposes of research and/or data collection, provided that such information is de-identified with sufficient safeguards. The agreement is done freely and voluntarily and the patient is free to withdraw his/her consent at any stage.

CHAPTER 4: RESULTS

4.1. Socio-Demographic and Clinical Characteristics

The characteristics at enrollment for ART from August 2005 to July 2008 were documented (Table 1). During this period - 2005 – 2008, a total of 1060 patients were enrolled.

The majority, 1056 (99.5%) of the patients enrolled were Sotho, 745 (70.2%) were female and 315 (28.8%) were male. On marital status, 587 (55.3%) were married, 157 (14.8%) were single, 224 (21.1%) were widowed, 90 (8.5%) were separated and 2 (0.2%) were unknown. Employed persons (include self) showed 258 (24.3%), student 24 (2.3%), unemployed 475 (44.8%), and 303 (28.6%) were of unknown employment status.

Patients in the age group of 16-35 years were 235 (22.2%), in the age group of 36-55 years were 618 (58.3%) and over 55 years were 207 (19.5%). Median age (IQR) was 43 (35-52) years. WHO Stage I was 192 (18.1%), Stage II was 367 (34.6%), Stage III was 460 (43.4%), and Stage IV was 32 (3%). WHO staging was missing in 9 (0.85%) persons.

Median weight at enrollment was 55.6kg (49-60.1). Baseline CD4 count below 50 (<50) cells/mm³ accounted for 141 (13.3%), 50-199 cells/mm³ was 458 (43.2%), a count of 200 cells and above was 410 (38.7%) and 51 (4.8%) baseline record was missing. Median CD4 (IQR) was 167 cells/mm³ (74-290).

Baseline haemoglobin below 10gm/dl was 183 (17.3%), 10gm/dl and above was 735 (69.3%) and 142 (13.4%) baseline record was missing. Median Hb (IQR) was 11.6gm/dl (10.3-13.1). Of those on ART regimen, 109 (10.3%) were on EFV-3TC-d4T, 421 (39.7%) were on EFV-3TC-AZT, 164 (15.5%) were on NVP-3TC-d4T, 220 (20.7%) were on NVP-3TC-AZT and

those on any other regime were 146 (13.8%). These results are summarized in the Table 1 below.

Table 1: Characteristics at enrolment among 1060 patients initiating ART at St. Joseph's Hospital, Roma - Lesotho, 2005 – 2008

Characteristics at ART* enrolment	Summary
Total enrolment for 2005 – 2008 study period	1060
Lesotho, n (%)	1056 (99.5%)
Female, n (%)	745 (70.2%)
Black race, n (%)	1007 (94.9%)
missing race	53 (5.1%)
Pregnant, n (%)	3 (0.3%)
Marital status: Married, n (%)	587 (55.4%)
Single, n (%)	157 (14.8%)
Widowed, n (%)	224 (21.1%)
Separated, n (%)	90 (8.5%)
Unknown, n (%)	2 (0.2%)
Occupation	
Employed (includes self), n (%)	258 (24.3%)
Student, n (%)	24 (2.3%)
Unemployed, n (%)	475 (44.8%)
Unknown, n (%)	303 (28.6%)
Hb* < 10 g/dl, n (%)	183 (17.3%)
≥ 10 g/dl, n (%)	735 (69.3%)
missing Hb, n (%)	142 (13.4%)
CD4 < 50 cells/mm ³ , n (%)	141 (13.3%)

	50-199 cells/mm ³ , n (%)	458 (43.2%)
	≥ 200 cells/mm ³ , n (%)	410 (38.7%)
	missing CD4, n (%)	51 (4.8%)
Weight	< 50 kg, n (%)	349 (32.9%)
	≥ 50 kg, n (%)	711 (67.1%)
Age	16-35 years	235 (22.2%)
	36-55 years	618 (58.3%)
	> 55 years	207 (19.5%)
WHO	Stage I, n (%)	192 (18.1%)
	Stage II, n (%)	367 (34.6%)
	Stage III, n (%)	460 (43.4%)
	Stage IV, n (%)	32 (3.0%)
	missing WHO Stage, n (%)	9 (0.85%)
Regimen:	EFV-3TC-d4T, n (%)	109 (10.3%)
	EFV-3TC-AZT, n (%)	421 (39.7%)
	NVP-3TC-d4T, n (%)	164 (15.5%)
	NVP-3TC-AZT, n (%)	220 (20.7%)
	Other	146 (13.8%)
Age (years), median (IQR)		43 (35 -52)
Hb* g/dl, median (IQR)		11.6 (10.3 – 13.1)
CD4 count , median (IQR)		167 (74 – 290)
Weight kg, median (IQR)		55.6 (49 - 60.1)

*ART – antiretroviral therapy, Hb-haemoglobin, EFV-efavirenz, 3TC-lamivudine, d4T-stavudine, AZT-zidovudine, NVP-nevirapine, IQR-inter-quartile range. Values may not add to 100% due to missing observations

4.2. Outcomes at the end of follow-up period

After a median follow-up period of 5.3 years (IQR 4.6-6.1), the 1060 patients contributed 5172.7 person-years of follow-up. Table 2 demonstrates that at the end of this period, 604 (57%) of the patients were still alive and in care, 120 (11.3%) had been transferred out, 313 (29.5%) were confirmed lost to follow up and 23 (2.2%) were recorded to have died. This figure is an underestimation of deaths, and patients that died may have been included in the lost to follow up group.

Table 2: Outcomes at end of follow-up among 1060 patients initiating ART at the St. Joseph's Hospital - Roma, Lesotho, 2005 – 2008

Characteristics at end of follow-up	n (%)
Alive and in-care	604 (57%)
Transferred out	120(11.3%)
Lost to follow-up	313 (29.5%)
Dead	23 (2.2%)

4.3. Longitudinal evolution of selected clinical parameters over follow-up

Figures 1 - 3 graphically depict the evolution of the selected parameters shown in Table 3.

The selected parameters included CD4 cell count, Haemoglobin and AST estimations. Over the follow-up period, the median (IQR) ranges were: CD4 – between 152 (84-265) and 499 (371-757) cells/mm³; Haemoglobin – between 11.8 (10.3-12.8) and 13.6 (11.9-14.5) g/dl. CD4 count and Haemoglobin are seen to gradually increase over the follow-up period. The AST does not show appreciable variation with median IQR – between 20 (14-33) and 27.5 (16-39) IU/L.

Table 3: Selected clinical parameters over follow-up

Time period (years)	CD4 count (cells/mm ³) median (IQR)	Haemoglobin (g/dl) median (IQR)	AST (IU/L) Median (IQR)
0	152 (84-265)	11.8 (10.3-12.8)	20 (14-33)
0.6	204 (115-316)	11.6 (10.3-12.8)	23 (15-37)
1	244 (163-361)	12.6 (11.7-13.7)	23 (16-36)
2	309 (217-413)	13.1 (12.2-14.2)	22 (15-32)
3	348 (245-480)	13.4 (12.5-14.5)	23.5 (18-33)
4	402 (270-543)	13.5 (12.6-14.5)	23 (17.2-33.1)
5	437 (312-628)	13.3 (12.3-14.3)	24.7 (17-34)
6	499 (371-757)	13.6 (11.9-14.5)	27.5 (16-39)

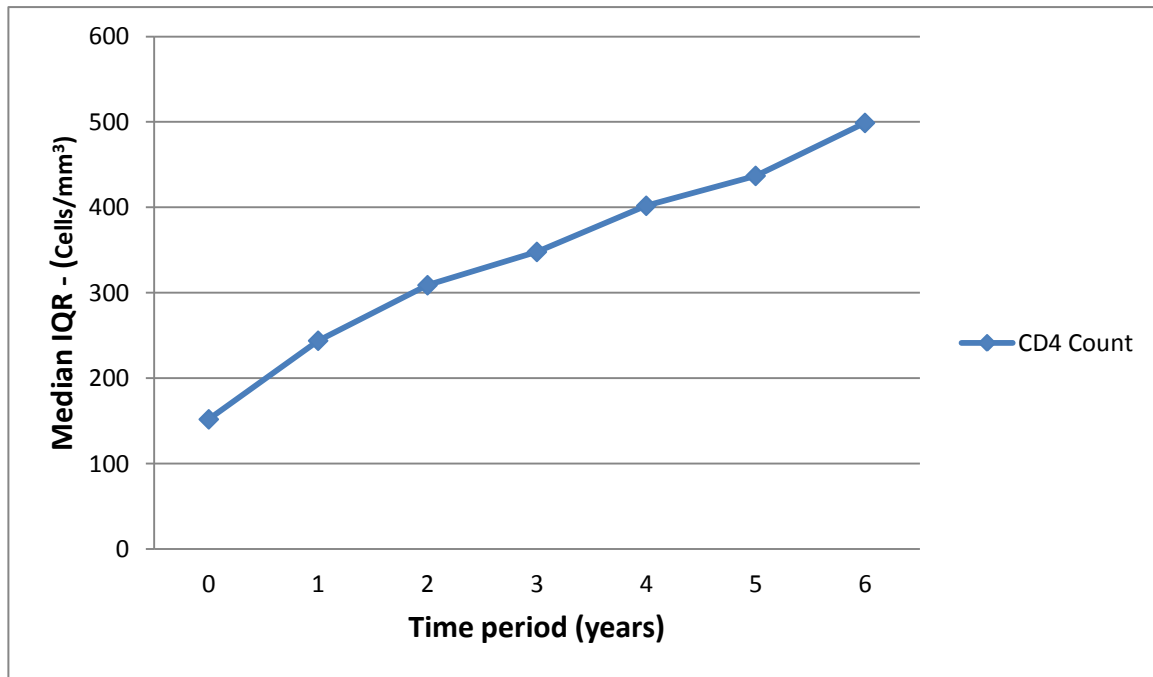


Figure 1: Longitudinal evolution of CD4 count over follow-up

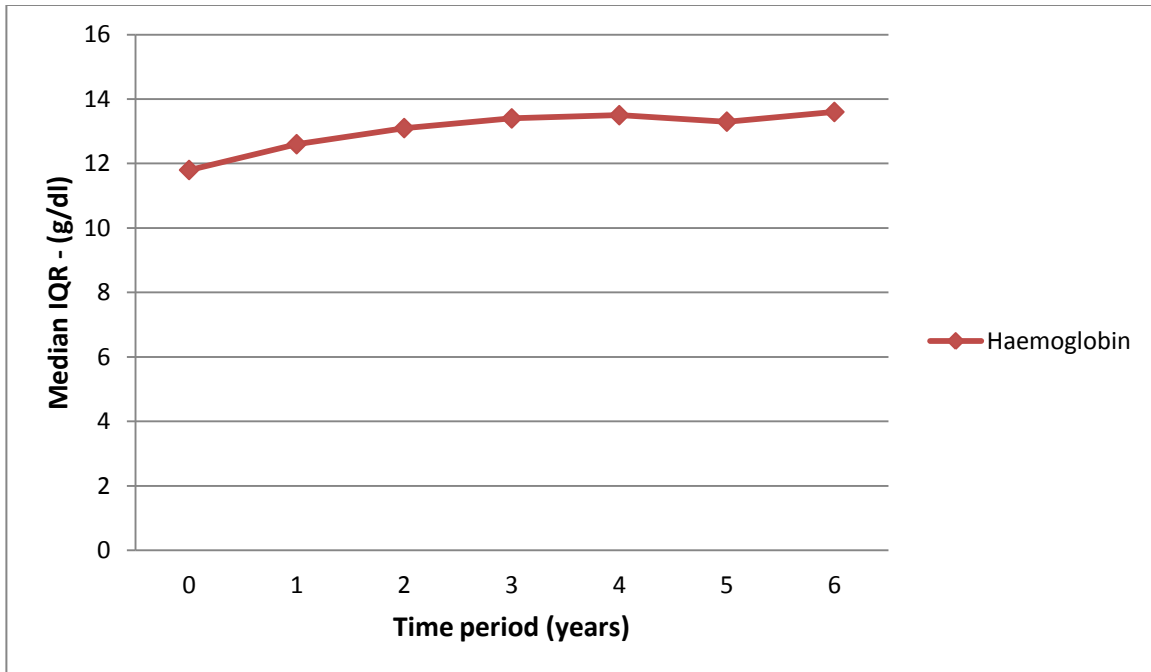


Figure 2: Longitudinal evolution of haemoglobin over follow-up

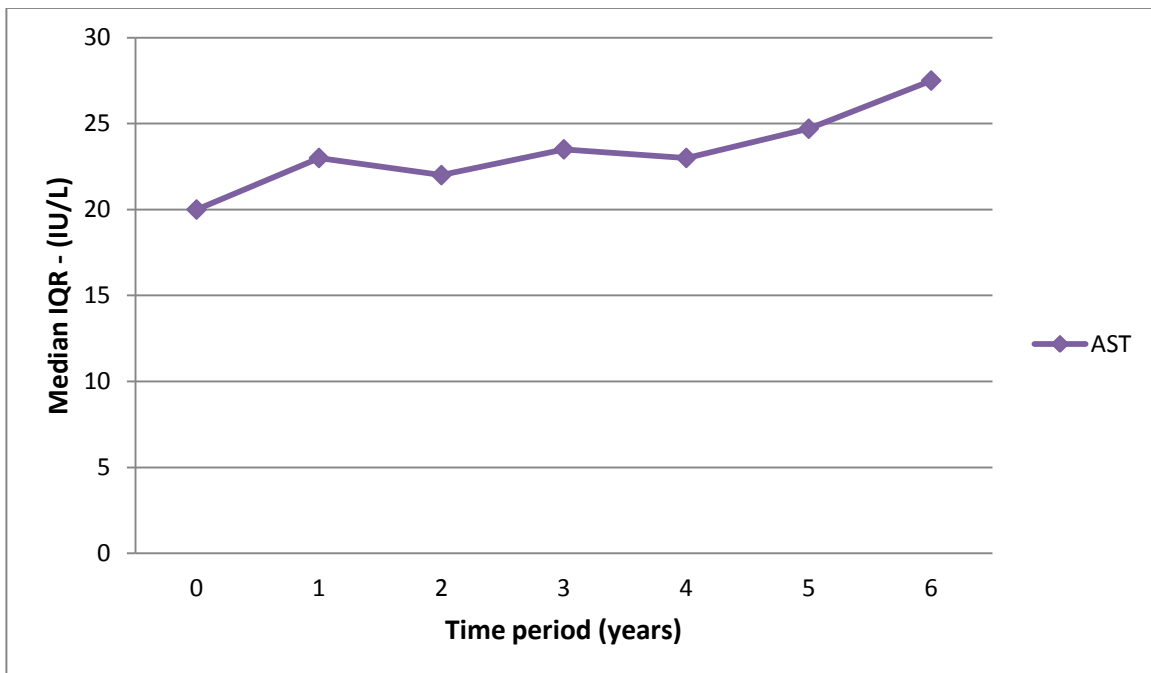


Figure 3: Longitudinal evolution of AST over follow-up

4.4. Patient retention versus lost to follow-up (LTFU)

By the end of the follow-up period, 604 (57%) of the patients were still alive and retained in care and 313 (29.5%) were confirmed lost to follow up (Table 2).

Figure 4 below shows a Kaplan-Meier survival curve illustrating overall patient retention in the cohort.

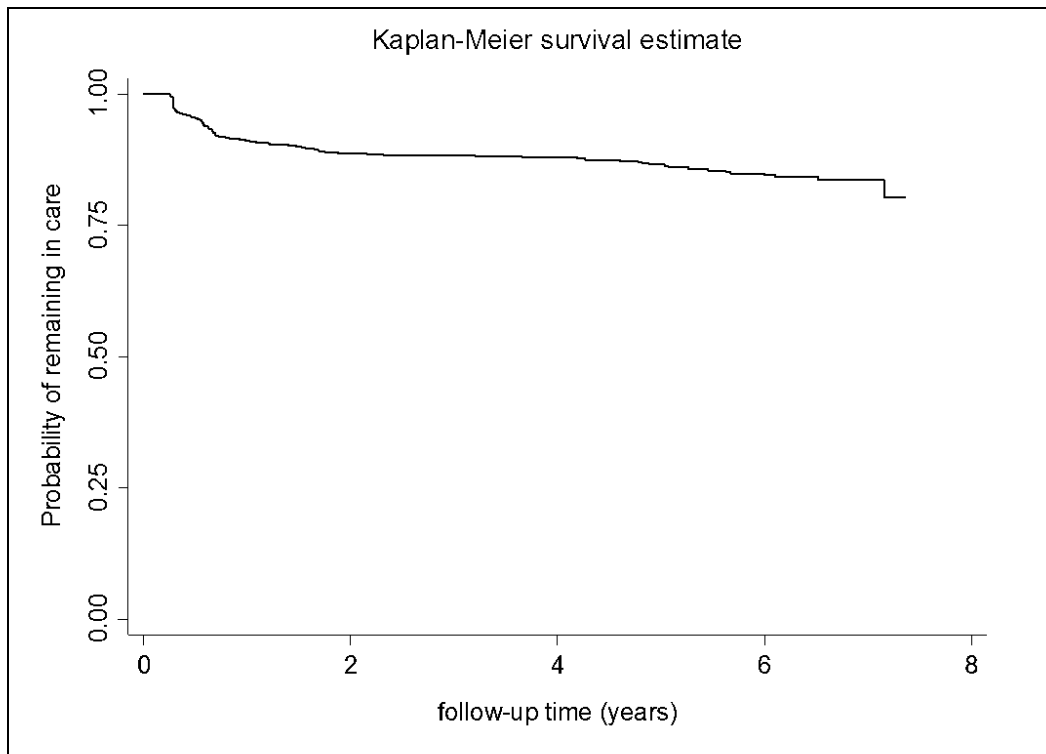


Figure 4: Kaplan-Meier survival curve on overall patient retention

4.5. Predictors for lost to follow-up (LTFU)

Some parameters at enrollment were used in the attempt to predict loss to follow up. These included gender, age group, employment status, WHO stage and baseline CD4 count. In the univariate analysis of predictors of loss to follow-up (LTFU), male gender seemed to increase the risk of being LTFU (crude HR 1.38, 95% CI 0.99 – 1.92), however these estimates marginally approached statistical significance (p-value 0.06). After adjustment, the magnitude of this association was stronger and was statistically significant, adjusted HR 2.35, 95% CI

1.29 – 4.30 (p-value 0.006). Males had an approximately 2.4 fold risk of being lost to follow-up during this follow-up period. Older age, less advanced WHO clinical stage, seemed to be protective against being lost to follow-up. Older age seemed to be protective of being lost to follow-up though these estimates did not reach statistical significance, age group > 55 years vs. 16-35, adjusted HR 0.91, 95% CI 0.44-1.90 (p-value 0.80) and age group > 55 years vs. 36-55, adjusted HR 0.80, 95% CI 0.44-1.43 (p-value 0.44). For WHO clinical stage, risk for loss to follow-up for stages II and III vs. stage I were largely similar (adjusted HR 0.15, 95% CI 0.08-0.29 and adjusted HR 0.18, 95% CI 0.10-0.33 respectively) (all p-value <0.001) and lower for stage IV vs. stage I, adjusted HR 0.10, 95% CI 0.01-0.74 (p-value 0.02). The relationship with baseline CD4 count in this analysis did not demonstrate a clear trend. On adjustment for the other predictors, patients with lower baseline CD4 count had a trend towards higher risk of being likely to be lost to follow-up than those with higher CD4 count, though these estimates were not statistically significant. CD4 count < 50 cells/mm³ vs. CD4 count ≥200, adjusted HR 1.47, 95% CI 0.75-2.88 (p-value 0.26). For those with CD4 between 50 and 200, the association with being lost to follow-up seemed imprecise, adjusted HR 0.62, 95% CI 0.35-1.10 (p-value 0.10).

The occupational status of the patient showed no association with being lost to follow-up in this univariate analysis, though these estimates did not reach statistical significance. After adjustment, patients who were employed (or students) were almost 29% less likely to be lost to follow-up than the unemployed, adjusted HR 0.72, 95% CI 0.08-0.41 (p-value 0.03). Table 4 below shows the results of both the unadjusted and adjusted analysis.

Table 4: Predictors for LTFU

	cHR (95% CI)	p-value	aHR (95%CI)	p-value
Gender				
Female	1 (ref)		1 (ref)	
Male	1.38 (0.99 – 1.92)	0.06	2.35 (1.29-4.30)	0.006
CD4 count baseline				
≥200	1 (ref)		1 (ref)	
50 - 199	0.46 (0.31-0.69)	<0.001	0.62 (0.35-1.10)	0.10
<50	0.88 (0.53-1.45)	0.61	1.47 (0.75-2.88)	0.026
Age group				
16-35	1 (ref)		1 (ref)	
36-55	0.77 (0.54-1.12)	0.17	0.80 (0.44-1.43)	0.44
>55	0.57 (0.34-0.95)	0.03	0.91 (0.44-1.90)	0.80
WHO stage				
1	1 (ref)		1 (ref)	
2	0.14 (0.09-0.23)	<0.001	0.15 (0.08-0.29)	<0.001
3	0.23 (0.16-0.33)	<0.001	0.18 (0.10-0.33)	<0.001
4	0.22 (0.07-0.69)	0.01	0.10 (0.01-0.74)	0.02
Employed /Student				
No	1 (ref)		1 (ref)	
Yes	0.99 (0.63-1.54)	0.96	0.72 (0.08-0.41)	0.03

Figures 5, 6 and 7 are Kaplan-Meier curves illustrating patient retention by gender, baseline CD4 count category and WHO clinical stage.

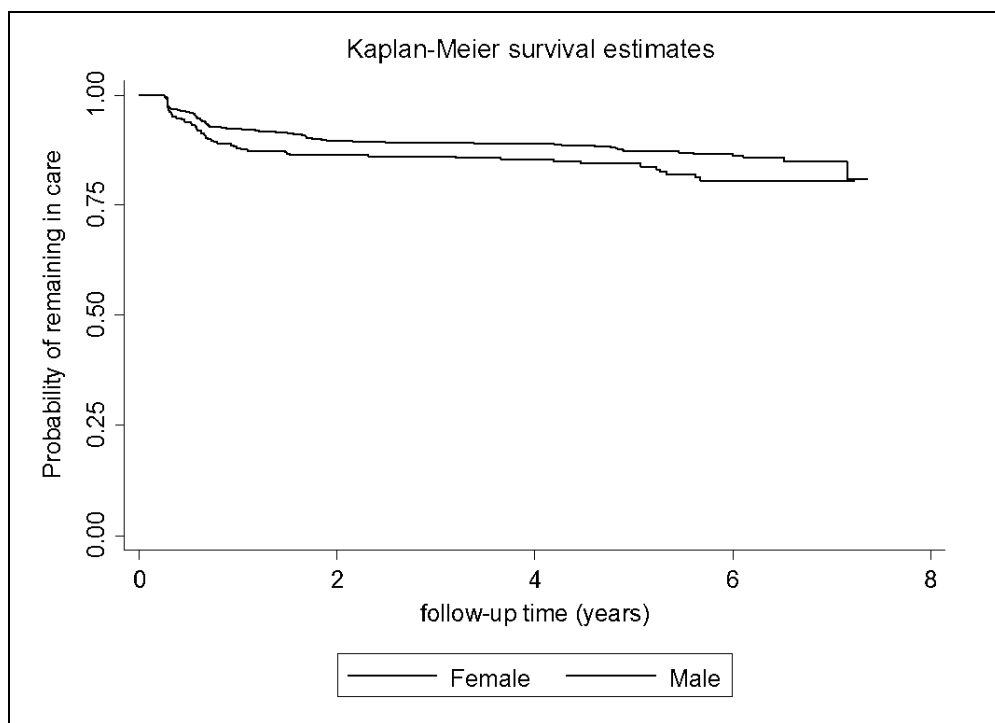


Figure 5: Kaplan-Meier estimates of patient retention stratified by gender

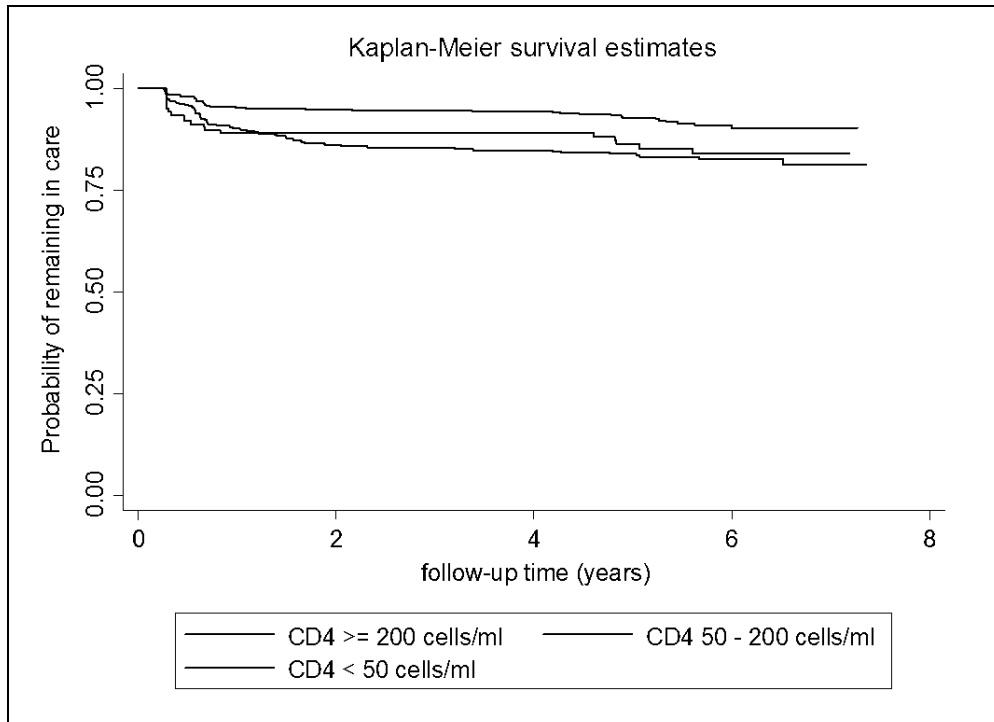


Figure 6: Kaplan-Meier estimates of patient retention by baseline CD4 count category

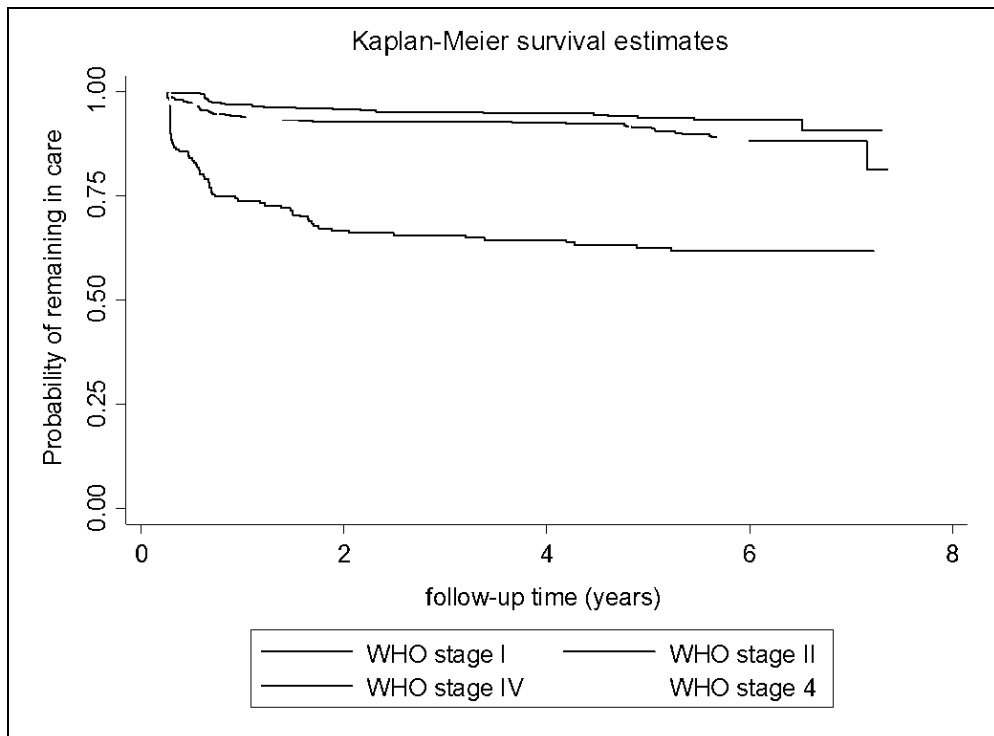


Figure 7: Kaplan-Meier estimates of patient retention by WHO clinical stage

CHAPTER 5: DISCUSSION

The results demonstrate that an overwhelming majority of the patients were female - 70.2%. Similar studies show that more females than males are infected with HIV but in differing proportions such as 2.3 : 1.2 female to male ratio stated by Muula et al²², 66.3% female infection by Maskew M²³. The UNAIDS Global Report 2012 informs that more than half of the adults with HIV in Lesotho are women²⁴. The situation of higher percentage of women can be attributed to the issue of uptake as more women than men are seen to access HIV services generally, as well as exhibiting health seeking behaviour^{37,38}. The particular scenario in Lesotho can also be due to the fact that the men are mostly migrant workers^{39,40} in South Africa and may register for ART outside of Lesotho. This may set female percentage of ART recipients much higher. In this study, 44.8% of those enrolled were unemployed and this could be due to poor economy of the country or a combination of poverty and HIV. UNAIDS 2012 reports that the impact of HIV epidemic on individual families and the country is felt in that adults become too sick to work and orphaned children are left to run households²⁴.

After a median follow-up period of 5.3 years, 57.5% were still alive and in care and 11.3% were transferred out to other clinics and health centers. The retention rate of 57.5% after 5 years follow-up in this study compares favourably to other studies in sub-Saharan Africa such as the systematic review of Rosen et al. They reviewed 32 publications reporting on 33 cohorts (74,192 patients in 13 countries) and found the weighted mean retention rates as 79.1%, 75.0% and 61.6% at 6, 12, and 24 months respectively and came to the conclusion that ART programs in Africa have retained about 60% of their patients at the end of 2 years³¹. The number of transfer-out patients still alive is not a part of this study. St Joseph's Hospital serves about 7 Health centers and outstation clinics in its Health Service Area to where most of the transfer outs were sent. This demonstrates a clinical care system with down-referral to nurse managed primary health-care clinic (PHC) for monitoring and treatment which is advocated in ART scale-up settings¹⁴. The utilization of such clinics has proved to decrease the burden on specialized doctor-managed ART clinic and patient outcomes appear to be

equal if not better than those achieved at ART clinics among stable patients as reported by Brennan et al⁴¹. Recently, in order to expand access to ART, governments have shifted focus from the down-referral model of care to a nurse-initiation and management ('NIM-ART') model^{42,43,44}.

This study recorded 29.5% of patients as lost to follow-up while only 23 (2.2%) were recorded as dead. This figure is an underestimation of deaths because patients that died may have been counted as lost to follow up. Males were also seen to have a 2.4 fold risk of being lost to follow-up. This calls for greater vigilance on follow-up and documentation of the findings on clinic attendance, home visits or findings by other acceptable locally convenient method like phoning. Weidle et al in their study in the urban primary health care setting of Lusaka, Uganda found 21% LTFU on account of not being seen after 30 days of pharmacy appointment date and 24 % LTFU in the first year⁴⁵. In the systematic review of 17 studies in sub-Saharan Africa, Brinkhof et al reported combined mortality of 46% on assessment of outcomes for patients lost to follow-up⁴⁶, while Zachariah et al reported 12.6% early mortality in their cohort⁴⁷. Geng et al in their study in tracking a sample of patients lost to follow-up came to the conclusion that the losses to follow-up represent one of the biggest barriers to global evidence based delivery of ART⁴⁸. The study of Fox et al gives evidence that 'mortality is substantially underestimated among patients lost to follow-up despite limited active tracing' and recommends linking to vital registration systems for accurate assessment³².

On selected clinical parameters over follow-up, haemoglobin estimation between 11.8 and 13.6 g/dl shows gradual increase over the time period, AST – between 20 and 27.5 IU/L does not show any detrimental variation and CD4 cell counts are seen to gradually increase over the follow-up period. These findings bear similarities with general findings in the literature and are consistent with treatment success. The opposite findings such as CD4 cell count ≤ 50 cells/mm³, haemoglobin ≤ 8 g/dl and increase in AST values above normal (0-45 IU/L for men and 0-35 IU/L for women) among others are cited by Ojikutu et al in their retrospective study as predictors of mortality⁴⁹. The study of Shah et al on haemoglobin and albumin as markers of HIV progression found out that women were more likely to be anaemic and hypoalbuminaemic pre-HAART, but post-HAART increases were similar to those of men and

came to the conclusion that both haemoglobin and albumin were strong independent prognostic factors for risk of AIDS and death regardless of gender⁵⁰.

CD4 count six monthly to yearly median IQR increase of between 35 and 65 cells/mm³ in the study is comparable to similar studies with clinical improvement outcomes. In 1999, Renaud and in 2002 Le Moing noted that CD4 cell count response to HAART is an expected increase of at least 50 cells/mm³ by six months on treatment^{11,12}. On adjustment for the other predictors, patients with lower baseline CD4 count showed a trend towards higher risk of being lost to follow-up than those with higher CD4 count. This finding supports the earlier submission that deaths were most likely recorded as lost to follow-up and is supported by the studies by Lawn and Brennan which note that low CD4 count is the largest predictor of death^{28,29}, even-though such effect is strongly modified by viral load suppression and period on ART²⁹. Unfortunately, in this study, viral load estimations were not employed generally due to cost constraints.

This study did not employ body mass index because it could not be estimated due to absent height measurements in all files. All patients however had their weights recorded at baseline and on most visits. The trend over follow-up period for patients retained in care is gradual weight increase which is expected in improvement outcome. The occupational status of the patients showed no association with being lost to follow-up in the study analysis, but the estimates did not reach statistical significance. Patients who were employed (or students) in this study totaled 26.6% and these were about 29% less likely to be lost to follow-up than the unemployed who were 44.8% of those enrolled. In a poor country like Lesotho, even though ARVs are provided free, the patients need money for transportation to access it. Most of the patients reside in the mountain regions where the poor terrain makes access by car impossible. Health care workers are also faced with this problem. Such patients would have to trek long distances or use horse transport if available and affordable to access care⁵¹. The studies of Tuller et al and Miller et al cite transportation costs as one of the major determinants of lost to follow-up^{33,34}. Older age and less advanced WHO clinical stage seemed to be protective against being lost to follow-up. For older age seemingly protective of being lost to follow-up, the estimates did not reach statistical significance. The studies of Fox et al and Toure et al

showed older age to be associated with death during early follow-up. Also associated with risk were those with lower baseline CD4, higher WHO clinical stage, low Hb and BMI among others^{32,30} as found to be the case in this study. In industrialized countries, age has been consistently associated with blunted CD4 + T cell recovery on ART and also found to predict mortality in patients on ART as shown in the studies of Kaufmann et al, 2005⁵² and Egger et al, 2002⁵³ respectively. In Africa, due to greater prevalence of opportunistic infections like tuberculosis and the association between age and blunted immunologic recovery, the effect of age on mortality may be even more important than in industrial settings. The studies of Lawn et al, 2006⁵⁴ and Johannessen et al, 2008⁵⁵ show that low pre-ART CD4 count, advanced WHO clinical stage or low weight are associated with death.

5.1. Study Limitations:

This is a retrospective study which leaves no opportunity for mistake correction in the manual files. Data capturing errors may have occurred due to possible differences in terminologies in the TE data system and the manual files coupled with the fact that in St. Joseph's Hospital, this was new with teething problems. Poor quality record keeping and documentation in the manual files brought about missing necessary data, for example CD4 count were missing in 4.8% and haemoglobin in 13.4% of the patients studied. Other missing data included WHO stage in 0.85%, occupational status in 28.6%, race in 5.1% and marital status in 0.2% of the study population. Non estimation of viral load posed a limitation to proper assessment of patients' risk and prognosis.

6. CONCLUSION AND RECOMMENDATIONS

6.1. Conclusion

In using TE to retrospectively assess clinical care and outcomes of patients on ART, the researcher has been able to show that the clinical outcomes were comparable to other settings.

The following are the key findings:

- More than half of the HIV patients are female and this draws attention to the fact that men are not accessing care enough.
- More men than women are likely to be lost to follow-up which seems to point at lack of education on the epidemic .
- There is a possible underestimation of deaths because patients that died may have been counted as lost to follow up and this depicts defective follow-up and documentation system.
- Selected clinical parameters findings of Haemoglobin, AST and CD4 count over follow-up period for those in retention are consistent with treatment success outcome.
- Patients with lower baseline CD4 count were more likely to be lost to follow-up than those with higher CD4 count and this is consistent with similar studies.
- The employed (or students) were about 29% less likely to be lost to follow-up than the unemployed with possible financial constraints for transport to access ART care.
- Less advanced WHO clinical stage seemed to be protective against being lost to follow-up.
- Older age seemed to be protective of being lost to follow-up

6.2 Recommendations

The researcher puts up the following recommendations to St. Joseph's Hospital, Ministry of Health - Lesotho and institutions managing HIV-infected patients:

- Better documentation and record keeping including establishment of links with other systems³².
- TE training, real-time utilization in cooperation with Therapy-Edge – South Africa and dissemination of knowledge.
- Training and supervision in ART to include all appropriate cadres
- Retention of trained and skilled workers in ART
- Institution of proper follow up measures to include tracking of patients lost
- Institution of more affordable ways of access for patients to collect ART, for example, social grants, transport reimbursement or further decentralization of care
- Find strategies to start patients on ART whilst their CD4 count is closer to 200, rather than being very low. Such strategies could include more regular HIV testing, more frequent CD4 testing for those with high CD4 counts and more decentralization of care.
- More HIV awareness campaigns to target males.

APPENDIX 1: Ethical approval - WITS

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

R14/49 Dr UFOK J Sampson-Akpan

CLEARANCE CERTIFICATE

M090624

PROJECT

An Assessment of Clinical Care and Outcomes of Human Immunodeficiency Virus Patients on Anti-Retroviral Therapy, Using TherapyEdge Database at St Joseph's Hospital, Roma, Lesotho

INVESTIGATORS

Dr UFOK J Sampson-Akpan,

DEPARTMENT

Department of Family Medicine

DATE CONSIDERED

09.06.26

DECISION OF THE COMMITTEE*

Approved unconditionally

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

DATE

09.06.26

CHAIRPERSON



(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr M Maskew

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 2: Ethical approval – MOH&SW, Lesotho



Ministry of Health and Social
Welfare
P.O. Box 514
Maseru 100

1 February 2010

TO
Dr.U. Juliana Samson-akpan
SSR 023 NUL Quarters
PO Roma 18
Lesotho

Dear Dr.U.Juliana,

RE: PROTOCOL OF "An assessment of clinical care and outcomes of HIV patients on Antiretroviral therapy using THERAPYEDGE database at St. Joseph's hospital Roma-Lesotho".

Reference is made to your letter requesting ethical approval of the above mentioned study and the memorandum from the Director STI, HIV and AIDS dated 16 December 2009.

The Ministry of Health and Social Welfare Research and Ethics Committee having reviewed above references hereby authorizes you to conduct this study among the specified population. The study is authorized with the understanding that the protocol will be followed as stated. Departure from the stipulated protocol will constitute a breach of the permission.

Yours sincerely,


(Signature)

Dr. M. Moteetee
Director General of
Health Services and
Chairperson Research and
Ethics Committee

*Received with signature
29/1/2010*

APPENDIX 3: Permission to conduct Research - St. Joseph's Hospital

ST. JOSEPH'S HOSPITAL
P.O. Box 308
Roma – 180
LESOTHO.
Tel: +266 22340206 Fax: +266 22340341
E-mail: stjosephhospital@leo.co.ls

15th April 2009

Medical Superintendent
St. Joseph's Hospital
Roma 180

Dear Sir/Madam,

**PERMISSION TO CONDUCT RESEARCH ON AN ASSESSMENT OF
CLINICAL CARE AND OUTCOMES OF HIV PATIENTS ON
ANTIRETROVIRAL THERAPY, USING THERAPYEDGE DATABASE AT ST.
JOSEPH'S HOSPITAL, ROMA - LESOTHO.**

I am a postgraduate student in Family Medicine in the University of Witwatersrand – Johannesburg. I hereby apply for your permission to undertake a research on the above title in St. Joseph's Hospital, Roma on approval of my proposal by the Ethics Committee.

The specified data will be collected and entered into TherapyEdge-HIV™ data system for analysis thereafter. This system will be funded and installed by Right to Care which is funded by PEPFAR.

All information obtained will be used for research purposes and will be kept highly confidential.

The final product of this study will be submitted to the Hospital for the results to be utilized for necessary interventional measures.

Thank you.

Yours Sincerely

Dr. U. Juliana Samson-akpan

Permission given by : Dr K.G. HUGANZA
Designation : ACTING MEDICAL SUP.
Signature : [Signature]
Date : 15th APRIL 2009



APPENDIX 4: Protocol Amendment on Objectives - WITS



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