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Factors associated with retention among a cohort of patients classified as pre-anti-retroviral treatment (pre-ART) in HIV care and treatment program in South Africa

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Title: Factors associated with retention among a cohort of patients classified as pre-Anti-Retroviral Treatment (pre-ART) in HIV Care and Treatment Program in Swaziland.

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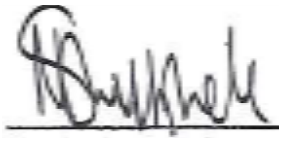
A research report submitted to the School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirements for the degree of Master of Public Health in the field of Health Systems and Policy

November, 2018

Johannesburg, South Africa

DECLARATION

I, Dr Nomthandazo Lukhele, hereby declare that this research report is my own work. I am submitting it in partial fulfilment of the requirements for the Master of Public Health degree in the field of Health Systems and Policy at the University of the Witwatersrand, Johannesburg. I further confirm that this work has not been submitted for any other degree or examination to this or any other University.



Date: 6 November, 2018

DEDICATION

This research report is dedicated to my loving Husband Webster and three children (Mukelwe, Siphiwo and Owethu) who believed in me and allowed me to sacrifice family time and finances to pursue this Master's Degree. It is also dedicated to my parents who have always been there for me and laid a good foundation that propelled me to always pursue academic excellence.

ABSTRACT

Background

Early enrolment and retention of people living with HIV in care and treatment services is one of the important pillars for a successful care and treatment program. Retaining patients in HIV care has been a noted challenge in sub-Saharan Africa. This study sought to identify baseline socio-demographic and clinical factors that influence retention of adult patients enrolled in HIV chronic care from pre-ART. The findings and conclusions drawn from this study will inform policy and programme decisions that improve retention.

Methods:

This was a retrospective clinical cohort study using routinely collected data from a record review conducted in 15 public health clinics in Swaziland in the period from 1st April 2012 – 30th June 2012. Baseline clinical and socio-demographic characteristics of a cohort of patients (n=510) enrolled for pre-ART were used. The primary outcome was retention at three, six, and 12 months. For descriptive analysis, frequencies and proportions, and medians and interquartile ranges were calculated. Bivariate and multivariate logistic regression model and survival analysis were conducted to measure retention rates with associated factors and also to control for confounders. In both cross tabulation and multivariate analysis, a p-value of <0.05 was considered statistically significant in explaining observed differences. Data analyses were performed using Stata 13.

Results:

Women were the majority (78%) of patients enrolling for HIV chronic care (starting with pre-ART) and 37% were pregnant. The median CD4 count at enrolment was 357 cells/mm^3 (IQR 216 - 546) and 89% had no clinical complaints at time of enrolment and were either in WHO clinical stage I and II. About a quarter (24%) of patients were lost within the first three months after the initial clinical visits. About half, of the patients 52%, 49% and 46%, were retained in HIV care at 3, 6 and 12 months respectively post-enrolment. The probability of being retained decreased with time. At 12 months patients had a 50% chance of being retained [S_t= 0.50, 95% CI (0.45-0.54)].

The socio-demographic and clinical factors that were significantly associated with retention among men were baseline CD4 count and age. Men who had a CD4 count greater than 500 cells /mm^3 were less likely to be retained in care compared to men with CD4 count < 350 cells/mm^3 (odds ratio (OR) = 0.38, (95% CI 0.61 – 0.94, P-value, 0.04) at three months and, OR= 0.22, (95% CI 0.05– 0.93, P-value, 0.04), at 12 months). Men who were 30 years and older were more likely to be retained in HIV care compared to younger men less than 30 years (. OR = 3.4, (95% CI 1.32 – 8.70, p= 0.01) at three months and, OR= 4.05 (95% CI 1.51-10.80, p= 0.005) at 6 months and OR= 3.17 (95% CI 1.23- 8.16, p= 0.02) at 12 months.

Among females, baseline CD4 count, marital status and not being pregnant were significantly associated with retention. Women who were single were less likely to be retained in HIV care compared to those who were married at all retention points: at three months, OR = 0.43 (95% CI 0.26 – 0.71, p = 0.001), at six months OR= 0.62, (95% CI 0.38 – 1.00, p = 0.05) and at 12 months, OR 0.56= 95% CI 0.38 – 1.00, p = 0.05). Women with CD4 count greater than 500 cells / mm^3 were 47% less likely (OR 0.53, 95% CI 0.30 – 0.91, P=0.02) to be retained in HIV care compared to women with CD4 count < 350 cells/ml. At three months non-pregnant women were 1.69 times more likely (OR 1.69, 95% CI 0.99 – 2.6, P=0.056) to be retained in HIV care compared to pregnant women.

Conclusion and recommendations

Retention rates among patients enrolling for HIV care starting with pre-ART were found to be relatively low, with only one in two retained in care. Loss-to- follow-up was the common reason for not being retained in care. Most patients were lost during the first three months especially soon after the day of enrolment. Baseline CD4 count and age among men, and baseline CD4 count, marital and pregnancy status among women, were the factors associated with retention in HIV care after 12 months. Patients most likely to be lost from care were those assessed as ineligible to initiate ART with a CD4 count >500 cell/mm^3, young men, single and pregnant women.

To improve retention rates, adopting and implementing the Treat All policy, where all people living with HIV are eligible to initiate ART regardless of CD4 count is recommended. In addition, building the capacity of health care workers to provide quality psychosocial assessment, counselling and support is essential. More focus should be placed on retaining

patients not initiated on ART in the first three months. Real-time electronic HIV care data systems with unique patient identifiers may also improve data quality and tracking of patient outcomes. Further research is also needed to evaluate the effectiveness of the current national patient follow-up strategies and Treat All policy in improving retention rates in HIV care.

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Finally I take this opportunity to thank my Pastor Bishop J.V. Hlatshwako whose prayers also got me this far. May God Richly bless you all!!

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ABBREVIATIONS

ANC- Antenatal care

ART – Antiretroviral Therapy

BMI- Body-Mass Index

EC- Expert Patients (peer educator)

HIV – Human Immunodeficiency Virus

HTC- HIV Testing and Counseling

IPT- Isoniazid prophylactic therapy

LTFU - Lost to follow up

NARTIS- Nurse led ART Initiations

PEPFAR – President's Emergency Plan for AIDS Relief

PLHIV- People Living with HIV

PMTCT – Prevention of Mother To Child Transmission of HIV

PI – Principal Investigator

POC – Point of Care CD4 testing

PHC – Primary Health Care

RHMT – Regional Heath Management Team

SDG- Sustainable Development Goals

SOP – Standard Operating Procedure

TB- Tuberculosis

WHO- World Health organization

UNAIDS-Joint United Nations Programme on AIDS

CHAPTER 1: INTRODUCTION

1.1 Background

HIV has been a global epidemic, especially in Southern and East African countries (1). Globally there has been political commitment to HIV epidemic control first through the millennium development goals (MDGs) and recently through the Sustainable Development Goals (SDGs). To fast track ending HIV/AIDS, UNAIDs set the 90-90-90 goals, which requires that 90% of people living with HIV know their status, 90 % of those diagnosed HIV positive are initiated on lifelong antiretroviral treatment (ART) and 90%of those on ART treatment are retained virally suppressed in care (2). Ending the AIDS epidemic is also part of the 2030 global agenda. Important milestones include reducing new HIV infections, as well as HIV related mortality and morbidity. A public health approach is required to increase HIV services (prevention and treatment services) coverage and attainment of the global goals with a particular focus on addressing the needs priority populations (2-5).

In 2016, about 36.7 million people globally, were living with HIV worldwide (34.5 million adults 15 years and older and 2.1 million children < 15 years) and over half (52%) of them in the Southern and East Africa region (1). The majority of people living with HIV are women and girls aged 15 years and above (17.8 million) (1). In 2016, new infection among adults 15 years and older declined from 1.9 million in 2010 to 1.7 million people newly infected with HIV in 2016 (11% decline). However, globally, there are still about 5000 new HIV infections each day. More than half (64%) of the new infections are in sub Saharan Africa of which about 37% are among young people aged 15- 24 years. Of those newly infected 15-24 year old, 60% are young girls and women (1).

HIV related deaths also declined by about 48% since 2005 (1). The East and Southern African region is making significant strides to control the epidemic when compared to other regions of the world. The region has the highest ART coverage rates, where six out of ten people are on antiretroviral therapy and there has been the greatest decline in the number of AIDS-related deaths. Death fell by 42% between 2010 and 2016 (1)**.** Globally**,** ART scale up has been a significant contributor to the noted decline in new infections and mortality rates (1, 3).

1.1.1 Overview of Care and Treatment services including Pre-ART care for people living with HIV

Care for people living with HIV (PLHIV) should start before they start ART, as soon as they are diagnosed with HIV (3, 6, 7). Early enrolment and retention in care is one of the important pillars for a successful care and treatment program (2, 3, 5, 7, 8). The HIV care and treatment package includes HIV testing and counseling services, pre-ART services, ART treatment initiation, ART refill and clinical and laboratory monitoring services. Pre-ART refers to the pre-treatment period that starts when a person tests HIV positive to the point commencement of ART (6, 7, 9, 10). Pre-ART care comprises of a package of health interventions provided during the pre-ART period. These include assessment of patient's eligibility for starting ART, serial routine laboratory investigations, e.g. CD4 counts, screening for TB and other opportunistic infections, provision of prophylactic treatment mainly cotrimoxazole and Isoniazide prophylactic therapy (IPT), nutritional assessment and therapy and ongoing adherence review and psychosocial support (6, 7, 9) .

The main aim of pre-ART care is to retain patients in the pre-treatment period in care and ensure that they are timely initiated on antiretroviral therapy (10). Once patients are initiated on ART they still have to be retained in care for life to improve their clinical outcomes as well as achieve epidemic control at national and global level (7, 10-12).

1.1.2 HIV/AIDS in Swaziland: Prevalence and overview of Care and treatment services

Swaziland is one of the countries in Southern Africa heavily affected by the HIV epidemic. With only a population of 1.4 million people, the national HIV prevalence among adults 15 years and older is about 27 % (2016) (32.8% for females and 20.4 % for males) (13).The country has a generalized epidemic with no statistically significant variation in prevalence in the four regions of Swaziland. Over the past five years the HIV incidence has declined from 2.4% (2011) to 1.4% (2016) among the population aged 15 years and above (13). The HIV incidence is higher (1.3) among young women aged 15-24 years compared to incidence for men (0.8) in similar age group (13).

The government of the Kingdom of Swaziland is committed to achieving the global UNAIDS 90-90-90 targets by 2020 and ending aids by 2030. In 2016, 84% of people living with HIV

knew their HIV status, of those 87.4% were initiated on ART treatment and 91.9% of those on treatment and retained in ART care were virally suppressed (13).

1.1.2.1 Swaziland ART Program strategies

Interventions that are key to the success of the ART program since its inception in 2003 included rapid decentralization of services from the hospitals to primary health care clinics. The country also introduced task shifting from solely doctor-led ART initiations to include nurse-led ART initiations (NARTIS) in 2010. Comprehensive pre-ART services were also introduced in 2010 (6). The Pre-ART care services that were provided from 2010 until the current time (2018) includes ART eligibility assessments using either CD4 or WHO clinical staging at every clinic visit. Those found eligible to start ART are prioritized to ensure that initiation of ART is not delayed. In 2012 a patient was eligible to initiate ART if clinically assessed as WHO stage 3 or 4 or had a CD4 count < 350 cells/mm^3 (6). In addition, all clinics providing Pre-ART and ART services have access to laboratory services.

1.1.2.2 Overview of the process of enrolling HIV positive patients into Pre-ART in Swaziland at time of study (2012).

In Swaziland it is standard practice that patients with a proof of an HIV positive test results are enrolled for pre-ART care soon after HIV diagnosis irrespective of CD4 count or WHO stage, preferably on the same day of HIV diagnosis in all health facilities (hospitals and clinics)(6, 9). During enrolment an HIV chronic care file is opened for the patient. In this file the initial clinical visit and all other subsequent visits of each patient are recorded. This HIV chronic care file includes records of all pre-ART visits, ART initiations and ART refill visits in addition to adherence and laboratory visits. Socio demographic details of the patients are recorded on the outside cover of the chronic care file. The same patient socio demographic and baseline clinical characteristics are then transferred into a Pre-ART register (6, 9, 14).

A patient is said to be enrolled once they have the chronic care file opened for them and allocated a unique number from the pre-ART register. Enrolled patients are scheduled to come for HIV clinical visit at least once in three months. Those found eligible to start ART often have more frequent visits to ensure that initiation of ART is not delayed. Those assessed as not eligible to start ART are to be retained in pre-ART care until they also become eligible.

Patients who miss clinical visit appointments by three days or more are followed up by expert client / peer educators through a cellphone call and or home visits (6, 9, 14). Enrolled patient are also given a green booklet that stays with them. This booklet is a summary of all clinical visit dates and is meant to remind patients of their next visit date. The HIV chronic care files and registers remains in the facility as primary tool for clinical monitoring and programme evaluation purposes. *Figure 1* below gives an overview of Swaziland's HIV chronic care framework.

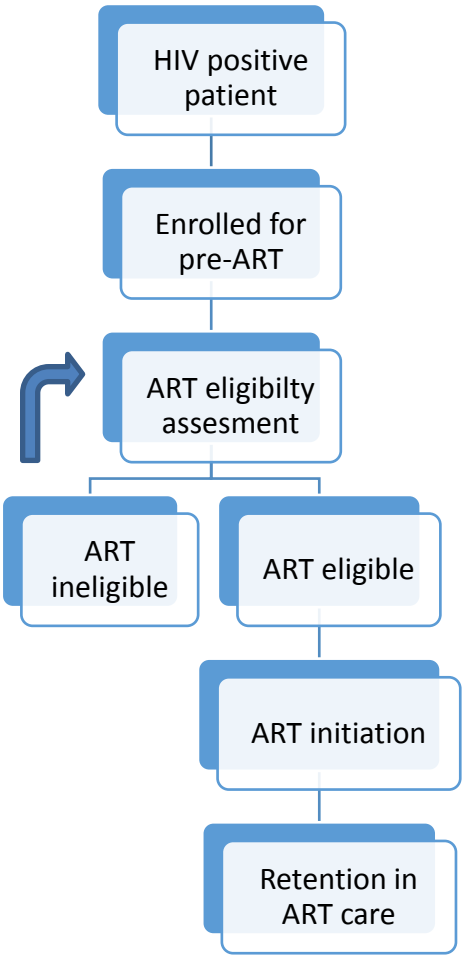

Figure 1: Overview of the HIV continuum of care framework in Swaziland

1.2 Problem Statement

The HIV chronic care pathway is a cascade that starts when someone tests HIV positive followed by pre-ART and subsequently to ART care. The main aim is to ensure that all people living with HIV (PLHIV) are tested, timely initiated on ART treatment once eligible and retained virally suppressed in lifelong quality care to decrease HIV related morbidity, mortality and HIV transmission at population level (2, 3, 11, 15).

Globally, the challenge with the HIV care pathway is that it is a leaky cascade. This is because, not all people living with HIV are linked to pre-ART care immediately after testing HIV positive (10, 11, 16-18). Those who are linked often do so at a late stage when the immune suppression is advanced and they start seeing symptoms of illness (17, 19-22). Another major challenge is the high attrition rate among pre-ART patients (10, 11, 17, 18).

In sub Saharan Africa, the overall pre-ART retention rate is estimated at 33% (10). The highest attrition for pre-ART care happen early, within the first six to twelve months of enrolment (10, 11, 18, 20-25). Lost pre-ART patients end up not initiating ART or come back to initiate ART late and at an advanced stage of the HIV disease (20-22, 26, 27). Delayed ART initiation, results in poor health outcomes, increased risk of mortality, and HIV transmission at population level (19, 20, 22, 27-31). Even after ART initiations retaining patients in lifelong care remains a challenge in sub-Saharan Africa (16, 18).

The Swaziland HIV program reports good retention rates for patients who are 15 years and older that are improving each year (77 % in 2012, 88% in 2013, and 92% in 2014) for patients who are already on ART (32). However retention rates among pre-ART patients is not known as data is not routinely monitored.

1.3 Justification for the study

Globally and nationally, there have been innovations aimed at advancing the decentralization of quality HIV/AIDS services including pre-ART care to primary health care facilities or clinics (5, 6). This is to improve access to HIV services and minimize losses throughout the continuum of HIV care. Swaziland has been scaling up HIV testing at both facility and community levels. All patients who have tested HIV positive have to be linked and retained in pre-ART care to optimize their health outcomes (6). However, national data on pre-ART retention is not available

and no study has been conducted to determine retention rates and factors influencing retention among patients enrolling for care and treatment services starting from pre-ART care.

The aim of the study was to determine the retention rates among a cohort of adults HIV positive adults enrolled for HIV care starting with pre-ART and also determine the patients baseline socio demographic and clinical factors associated with retention in care at clinic level in Swaziland over a 12 month period. Although literature on this subject is rich from Sub-Saharan African countries especially South Africa, such information does not exist in Swaziland. The wide variation in retention definitions, ART eligibility criteria and the timing and package of the pre-ART care makes generalizability of findings difficult. In addition, most studies focused on either retention of pre-ART patients up to initiation or retention rates among ART patients. Very few studies followed a cohort of patients from the pre-ART period all the way to ART care and also segregating patient retention outcomes by sex.

This study is unique in Swaziland because, it focuses on following patients from the time they enroll for pre ART care (post testing HIV positive) for a period of 12 months to determine retention rates and factors associated with retention.

The findings and conclusions drawn from this study will assist the Swaziland national ART program to come up with strategies to improve retention of patients enrolled for pre-ART care, by targeting interventions to address specific needs of identified population groups at specific time points of the HIV chronic care pathway. The study results will also give insight to what the country needs to do; to accelerate meeting the 90-90-90 UNAIDS targets by 2020 and ending aids by 2030. It will also help generate future research questions, and make clear recommendations on how the country can strengthen "Treat All" policy and differentiated service delivery to improve retention in HIV care and for better treatment outcomes.

Study findings will be shared with the participating facilities, Manzini region Health Management Team (RHMT), the National ART program, policy makers and planners to strengthen the accelerated delivery and access to uninterrupted HIV treatment services.

1.4 Research Question, Study Aim and Objectives

1.4.1 Research question

Are there patient baseline factors/characteristics associated with retention among patients enrolling for HIV care and treatment services starting with pre-ART care?

1.4.2 Study aim

The aim of this study was to determine factors associated with retention at 12 months after enrolment, among a cohort of patients classified as pre-Anti-Retroviral Treatment (pre-ART) at enrolment in an HIV Care and Treatment Program in Manzini region, Swaziland.

1.4.3 Specific objectives

1. To describe socio-demographic characteristics (age, sex, marital status, level of education, employment status and patients nearest clinic) of a cohort of patients enrolled for pre-ART care at clinic level in the period from 1st April 2012– 30th June 2012.
2. To describe baseline clinical characteristics (CD4 count, WHO staging, BMI and pregnancy status for females only) of a cohort of patients enrolled for pre-ART care at clinic level in the period from 1st of April 2012 – 30th June 2012.
3. To describe retention rates of a cohort of women and men enrolled for pre-ART care at clinic level at three, six, and 12 months post enrolment.
4. To describe the time to disengaging in HIV care and to determine the associated factors for women and men enrolled in pre-ART care in the period from 1st April 2012 – 30th June 2012.
5. To determine the relationship between socio demographic and baseline clinical characteristics and retention in care at three, six, and 12 months post enrolment among women and men.
6. To provide recommendations towards strengthening retention of patients enrolled for pre-ART care at clinic level in, Swaziland.

1.5 Literature Review

This section focuses on extensive literature review of scientific journal and or publication to gather more evidence on the determinants of retention in pre-ART to collaborate the findings of this study.

1.5.1 Pre-ART definitions and package of care

Pre-ART period refers to the interval between HIV diagnoses and the time ART is initiated. Assessment of patients for ART eligibility is a key service element in pre-ART care (33). This has to be repeatedly done until a patient is declared ART eligible and start ART (33). Retaining all HIV diagnosed patients in pre-ART care is important so as to allow timely initiation of ART treatment and avoid HIV related mortality due to late presentation (10, 11, 22, 23).

Different follow up studies, used varied eligibility criteria and differing definitions of retention which makes generalizing study findings to other settings difficult (10, 11, 16, 17, 21-24, 26, 34-38). Some studies defined eligibility based on level of CD4 count or WHO clinical staging. A CD4 $\leq$ 200 or 250 or 350 cells / m^3, WHO stage 3 and or 4. Retention in pre-ART is defined using latest CD4 in the past 6 months or 12 months, using appointment schedules or initiating ART, not dead or lost to follow up (10, 11, 16, 17, 21-24, 26, 34-38) .

For example, in South Africa, patients are enrolled for pre-ART after the first ART eligibility assessment is done (24, 39). Often, pre ART care will be for those patients who were assessed as ineligible for ART after the first ART eligibility assessment and they would be followed up until they are subsequently assessed as eligible for ART or until they initiate ART (24, 39). This therefore means that in those settings where patients who were assessed as eligible for ART even if they might have not initiated ART are not enrolled to pre ART care but followed at an ART program (24). In Swaziland, all patients (including TB patients and pregnant women) are enrolled for pre-ART care immediately after testing HIV positive even before the ART eligibility assessment is done. In effect, for Swaziland pre-ART patients comprises both patients who are eligible for ART initiations and those who not eligible (4). Once eligible patients are initiated, the same clinic continues to provide ART care and the same patient clinical record is used for documentation.

1.5.2 Overview of retention rates in HIV care (Pre-ART and or ART care)

Literature shows that along the continuum of HIV care, most patients are lost in pre-treatment period (10, 11, 17, 40). These patients are often lost early within the first 12 months with many not honouring the subsequent visits post enrolment. Loss-to-follow-up is the main reason patients are not retained in care and not so much deaths or being transferred out (10, 21, 24, 26). The longer patients remain ineligible to initiate ART (remain in pre-ART care) the more likely they are not to be retained in care (23). While mortality rates have been reported to be low, they are however higher in patients assed as eligible to initiate ART especially if they did not start ART treatment immediately. ART initiation generally improves retention rates and also is associated with lower death rates (16).

Most cohort studies assessed retention rates from enrolment into pre-ART care up to 60 months (10, 11, 16, 17, 21-24, 26, 34-38). The earliest study end point was at six months followed by 12 months and longest being at 60 months. Patients not in care were either dead, transferred out or lost-to-follow-up. There are studies that followed different cohorts of patients coming to enroll for pre-ART up until they initiated ART (10, 16) or from the time they initiate ART up to a specified period (16) or reported on retention rates at each stage of the care cascade as defined by Rosen et al. (2011) separately (10, 11, 16, 17, 21-24, 26, 34-38). Stage 1 (from HIV testing to receipt of CD4 count. Rosen suggested that studies on pre-ART retention must report retention rates in three stages: Stage 1 (from HIV testing to receipt of CD4 count results or clinical staging), Stage 2 (from staging to ART eligibility), or Stage 3 (from ART eligibility to ART initiation) (10).

A systematic review of studies conducted in Sub-Saharan Africa from 2006 -2011 estimated that retention rates from HIV diagnosis through to ART initiation to be about 17%, with the range from 10th percentile to 90th percentile being 7%- 32%. A study conducted at Temba Lethu HIV clinic in Johannesburg South Africa. Reported that among patients who were assessed as eligible to start ART between March 2010 and August 2012 about 28% initiate ART and remain in care for at least two years. Retention rates for patients assessed as ineligible to initiate ART after HIV diagnosis were estimated to be even lower (16). It was noted that in the Themba Lethu study 85% of the study participants were eligible to initiate ART after testing.

1.5.2.1 Attrition rates

Among patients not yet initiated on ART the greatest reason for not being in care was mainly attributed to being lost-to-follow-up rather than death or being transferred out (21, 23, 26). A study conducted in Zambezia Province, Mozambique reported that among a cohort of pre-ART patients (n=13,968) registered for care, 66% were lost to follow up, 1.8% died and only 0.1 % were transferred out 12 months post enrollment for pre-ART care. This means only 32.3% of the patients were retained in the 12 months (23). Another large cohort study (n=55,789) conducted in four Sub-Saharan HIV programs in three countries (Kenya, Uganda and Malawi) studied predictors of mortality and lost-to-follow-up among pre-ART patients. The study reported that being lost from Pre-ART care due to death occurred far less frequently than due to other reasons. In the same study under reference, the mortality rate was 3.9 per 100 person - years (95 % CI 3.7- 4.5) while the lost-to-follow-up rate was at 28.3 per 100 person - years (95 % CI 27.8- 28.8) (21). In India, 63.8 % of pre-ART patients ineligible to start ART were retained in care after 4.5 years of follow up. Of those not retained in care, 90% of them were lost- to- follow- up and only 2.2 % due to deaths (26). In the same study high attrition rates were reported among patients who remain ineligible for ART initiation for longer follow - up period (26). Among Pre-ART patients lost from care some do come back at a later time (26).

Mortality rates are reported to be higher in the pre-treatment stage than after initiating ART, especially in patients with very low CD4 counts less than 200 (11, 20-22). A study conducted in Uganda, for six months followed pre-ART patients who were assessed as eligible to initiate ART but were not retained and hence not initiated on ART to determine their clinical outcomes. The median CD4 of patients who did not complete ART initiation preparation was 87 cell/mm^{3}compared to 187 cells/mm^3 among those who were retained in pre-ART care and eventually got initiated on ART. The study also found that pre-treatment mortality in this group that was not retained was very high, around 34 per 100 person - years in the first month of enrolment (22). Patients who were enrolled for pre-ART care within three months of HIV diagnosis had lower mortality rates than patients who were not. Eligible patients who completed all the necessary preparation and initiating ART within three months had lower mortality rates compared to those who did not. Among those initiated on ART, death was higher among those that were not virally suppressed six months post treatment (11, 22).

1.5.2.2 When are patients lost from care

Most of the attrition of patients not retained in HIV care, happened in the pre-ART stage rather than when patients were already initiated on ART (10, 11, 17, 18, 21, 24). Most patients were noted to be lost early within the first year of enrolment (10, 11, 20-24, 40). More than half of patients were lost within the first year in a study conducted in rural Mozambique (23). As revealed in studies conducted in Johannesburg South Africa, Kenya, Malawi and Uganda pre-ART patients (not eligible to start ART) often do not honour the first appointment post enrolment (21, 24).

1.5.3 Factors associated with Retention

Studies that seek to determine factors associated with retention in pre-ART and ART looked at a range of them. These range from socio-demographic to clinical factors including psychosocial structural and economic factors. These factors had differing influence on retention based on the study context and characteristics of participants. Factors such as sex, CD4 count, transport challenges, perceived good health and stigma were commonly found to influence retention in pre-ART, ART uptake and retention in ART care (22, 23, 37, 41). Very few studies segregated patient retention outcomes by sex.

1.5.3.1 Socio-demographic factors associated retention

1.5.3.1.1 Sex and retention

The literature is inconclusive about the influence of sex on retention. Several studies in sub-Saharan Africa, Central Africa and Asia have shown that men are more likely to be lost in care when compared to women (17, 21-24, 26, 41-43). In these studies the men presented late for enrolment in care often with very low CD4 count and in advance clinical stage (WHO stage 3 or 4 disease). A study conducted in Mozambique found that men had 32 % higher hazard of being lost to follow up within a 12 month period compared to women (23). In addition men were less likely to start ART (17). On the other hand there were also studies that reported that sex had no influence on retention. The men in those studies, were presenting for enrolment to pre-ART care with higher baseline CD4 (24, 37, 44).

1.5.3.1.2 Age and Retention

The literature shows mixed results about whether age was associated with retention in pre-ART and ART. In the studies where age was associated with retention, older age was associated with being retained in either pre-ART and ART care (17, 21, 23, 25, 35) . Younger patients under the age of 30 were more likely to be lost from care compared to older patients (23). Most young patients are lost to follow up before ART initiation than after ART initiation. A study conducted in sub-Saharan Africa (Kenya, Malawi, Uganda), found that among positive patients not yet initiated on ART, mortality and Lost-to-follow-up rates decreased in older age groups with a 10 years unit increase aHR=0.84 (95 % CI 0. 82-0.86) within the first six months and a similar pattern was reported for the period 6 months to 60 months (21). However after ART initiation patients older than 50 years have a higher likelihood of death after ART initiation than younger age groups (35). In some studies (Western Cape and India) age had no effect on retention in HIV care study (22, 26, 44).

1.5.3.1.3 Education and retention

The literature has reported mixed findings on the relationship between education and retention in HIV care. Patients with no formal education had a higher risk of being lost to follow compared to those with some form of education (23, 26). Education had no effect on retention in pre-ART care in a study conducted in Cape Town, South (44).

1.5.3.1.4 Employment status and retention

The literature is equivocal about the influence of employment status on retention. In a Johannesburg study, patients in employment were more likely to be retained in care and they were more likely to honor the first clinical visit post enrolment compared to those that were not employed(24). In Mozambique, among those employed, administrative workers had half the odds of being lost to follow up while domestic workers and small merchandise workers had slightly higher odds (23). Qualitative reports from patients lost from care have found that competing work priorities as a well as the need to take time off from work were contributing factors to not being retained in care (23, 41). Employment had no effect on retention in Cape Town study (44).

1.5.3.1.5 Marital status and retention

Marital status has been reported as having no association with retention in HIV care in most studies (17, 24, 44, 45) . The studies have differing proportion of patients who were married. For

example in At Helen Joseph Hospital HIV clinic (a large public clinic) in Johannesburg, South Africa a very low proportion (21%) of patients reported being married, while in a study conducted in Anantapar, a rural district in India) 72 % of the participants were married (24, 26). However widows had better retention rates than married women in Mozambique and India (23, 26).The widows from India and Mozambique received nutritional food packages which were not received by the single of married groups.

1.5.3.1.6 Socio-economic status and retention in care

A general observation from literature reviewed revealed that low socio economic status as a predictor of not being retained in care. Patients from rural or poor setting had a higher chance of being lost to follow up (17, 22, 23, 26, 37, 41). In India it was reported that being homeless, illiterate and coming from rural and poor community, not near town were associated with lost to follow up (26). In Mozambique lack of education and absence of electricity in the home were associated with lost to follow up (23). In addition qualitative research cited to a greater extent lack of transport to reach facilities. Long distance from facilities, fear of stigma and discrimination by family or community members, competing responsibilities (subsistence farming and domestic work) and need to take time off work as contributing factors to high attrition from pre-ART care and low ART uptake (22, 23, 37, 41). Literature shows that patients from ≥10 KM radius to clinic are more likely to be lost (41).

1.5.3.2 Clinical Factors Associated with retention

1.5.3.2.1 Baseline CD4 count level and retention

Baseline CD4 count is the initial CD4 that is done soon after a patient test HIV positive and is used to determine patient immune status and eligibility for ART initiation at the time of HIV diagnosis or enrolment for HIV chronic care. Patients with an ART eligible CD4 count are more likely to be retained in care when compared to those with non-eligible CD4 count (17, 20, 21, 24, 45). Those with high baseline CD4 count above 350 cells/m^3 are more likely to be lost from care due to lost to follow up while those who are very severely immuno-compromised with very low CD4 count are more likely to be lost from care due to death especially if they don't initiate ART (17, 20, 21, 24, 45).

Over the past 10 years, WHO guidance on when to initiate PLHIV on ART has been changing allowing more people to initiate ART early. Before 2009, the ART eligibility criteria indicated

that patients with a CD4 ≤ 200 cell/mm^3 were eligible to initiate ART. The guidelines were revised to indicate that anyone with a CD4 ≤ 350 cell/mm^3 and later CD4 ≤ 500 cells/mm^3 were eligible to initiate ART in 2009 and 2013 respectively (7, 46, 47). More recently the 2016 guidance from WHO recommended countries to adopt a treat all policy, where by all people living with HIV are eligible to initiate ART regardless of CD4 count or WHO stage (8). Swaziland therefore adopted the treat all policy recommendation from the 1st October 2016. However during the time of the study (2012), in Swaziland patients were eligible to start ART when the CD4 count was ≤ 350 cell/mm^3 or when they had a WHO III or IV condition irrespective of CD4 count (6).

Earlier studies on factors associated with retention in pre-ART care used a CD4 count level of ≤ 200-250 cell/mm^3 and WHO stage III and IV condition to define ART eligibility. However the studies conducted around 2011 and beyond used CD4 ≤ 350 cells/mm^3 to mark eligibility in addition to clinical stage in line with the evolving recommendations on eligibility from WHO. From the literature patients assed as ART eligible by whatever criteria have been reported to be positively associated with retention in both pre-ART and ART care (21, 34). Having an ART eligible CD4 < 350 cells/mm^3 was associated with a greater odds of being retained in HIV care at 12 months(34). However in this group, lost to care among patients not initiated on ART was observed as higher in patients with very low CD4 count less than 200 cells/mm^3(11, 17, 21). This was the case in a sub-Saharan Africa, where a systematic review and meta- analysis from 29 studies (17). In this review the median CD4 at baseline was 154-274 cells/mm^3 (17). Similar findings were noted in another study conducted in Kenya, Malawi Uganda in Sub Saharan Africa. This study prospectively followed patients enrolled from 1st of January 2004 to 31st December 2010 for 60 months post enrolment for HIV care until they initiated ART, transferred out or died. The median CD4 count in the study under reference was 261 cells/mm^3(21). The study reported that patients with CD4 < 50 cells/mm^3 were more likely to be lost in care due to death or be lost to follow up compared to those with CD4 > 500 cells/mm^3 at 0-6 months and at six months to 60 months (21). In Mozambique, it was observed that patients with baseline CD4 > 50 and > 500 cells/mm^3 and 41% and 5% greater hazard ratio ($p < 0.01$) of being lost in care compared to those with CD4 > 350 cells/mm^3 (23). Similar findings were also reported in two retrospective cohort studies conducted in America at the University of Alabama, Birmingham HIV/AIDS outpatient clinic and at a Public hospital in Johannesburg South Africa. Both studies

found that poor retention in pre-ART care was associated with having a high baseline CD4 count (≥ 350 cells/mm^3) (24, 25). Patients who had a higher CD4 > 350 cells/mm^3 were less likely to honour the first clinical visit post enrolment when compared to those that have CD4 count < 350 cells/ mm^3 and become lost in care (24).

Retention of patients initiated on ART is better than those not on ART (11, 44). In Western Cape, South Africa a community based cross-sectional survey reported a 12 month retention rate of 94 % for patients on ART compared to 43% for patients who were on pre-ART care(44). A large study (n=11036) conducted in rural South Africa, looked at the effect of immediate versus deferred ART eligibility (with intention to treat) on 12 month retention. The baseline CD4 was used to define eligibility, where by patients with CD4 < 350 cells/mm^3 were assessed as eligible to start ART. The study found that having an ART eligible baseline CD4 count was associated with an increase in 12 months retention by 18 % percent points (95% CI 11-23 P < 0.001) compared to having higher CD4 counts which meant that they were not eligible for ART (34). In addition having an ART eligible CD4 count at baseline was associated with a 25 percentage point (95 % CI 20-31 P <0.001) increase in ART initiation within six months compared to those not eligible for ART initiation.

However even though initiating ART improves retention, the challenge is a majority of the ART eligible do not initiate HAART within six months of HIV diagnosis (34). It is estimated that among patients who had baseline CD4 counts taken, only 18% would have initiated ART regardless of CD4 count, 57% would have not initiate ART regardless of CD4 count and 25% would have initiated ART if CD4 count < 350 cells/mm^3 but not if it was > 350 cells/mm^3. This means that many factors and not just only patients CD4 count influence ART uptake.

A study conducted in India reported that the level of CD4 count at time of enrolment was not significant predictor of retention this finding was different from the finding from southern Africa mentioned above. This study followed a pre-ART cohort for a longer period of 4.5 years compared to the other studies (26).

1.5.3.2.2 Pregnancy status and retention

Prevention of mother to child transmission of HIV (PMTCT) is one of priority interventions aimed at reducing the HIV incidence. However there are few studies on retention in Pre-ART /ART care that included pregnant women. Those that did, reported that pregnant women were

more likely to present with early disease as evident by high baseline CD4 count and they were more likely to be lost from care and not initiate ART (37, 38).

1.5.3.2.3 WHO Clinical staging and retention

Differing reports on the influence of WHO staging on retention in HIV care. In sub-Saharan Africa it was observed that patients with advanced clinical disease especially WHO clinical stage 3 and 4 were more likely to be lost to follow up or to die (21). One study conducted in Mozambique reported that that patients assessed as having WHO clinical stage III and IV condition were more likely to be retained in care compared with those with WHO stage I (23). In the studies where having a WHO stage 3 or 4 condition was associated with low retention the participants had very low CD4 count and mortality rates were higher in the pre-treatment group (21). On the other hand where they were retained it was mainly because those with WHO stage 3 or 4 condition were eligible to initiate ART and initiating ART kept them retained (23). Other studies did not report any significant association between WHO stage and retention (22).

1.5.3.2.4 Tuberculosis and Retention

Few studies looked at specific effect of TB diagnosis on retention in Pre-ART/ART care. Conflicting findings of the effect of TB diagnosis and retention between facilities based versus community based research has been noted. A study conducted in four HIV programs in Sub Saharan Africa reported that patients diagnosed with TB at time of enrolment to care (pre-ART/ART) were associated with higher mortality and Lost-to-follow-up rates (21). Similarly the presence of a previous history of TB was reported to be associated with increased likelihood of being lost to follow up (36). However on a different note previous history of TB was not associated with 12 months retention in a community survey conducted in Western Cape, South Africa (44).

CHAPTER 2: METHODOLOGY

2.1 Study Design

This was a retrospective cohort study. A cohort was formed from clinical records of HIV positive patients enrolled into HIV care and treatment services (starting with pre-ART care) during the period from 1st April to 30th June 2012 in 15 primary health care clinics in the Manzini region of Swaziland. The clinical patient records were reviewed for a period of 15 months to determine baseline socio-demographic and clinical factors associated with retention in HIV care (either Pre-ART or ART care) at three, six, and 12 months, post enrolment. The retrospective data review allowed this study to be conducted despite the limited time and financial constraints.

2.2 Study setting

The study was conducted in 15 (ten Government and five mission owned) primary health clinics (Luyengo, Mahlangatsha, Cana, Mpuluzi, Bhahwini, Mangcongco, Lamvelase, Gebeni, Sigcineni, Bhekinkosi, Mliba, Mkhulamini, Mafutseni, Ngculwini, Bulunga) in the Manzini Region of Swaziland. Manzini is one of the four regions that make Swaziland. It is also the region with the highest population and HIV prevalence compared to the other regions of the country (50).

The 15 clinics selected for the study represented all the public clinics that provided a comprehensive package of HIV care and treatment services free of charge, to both adults and children as per the national guidelines at the time of study period. These facilities also used the National HIV care monitoring tools, namely pre- ART register, chronic care files, patient held green booklet and appointment registers.

The HIV care and treatment package included HIV testing and counseling services, pre-ART services, ART treatment initiation, ART refill and clinical and laboratory monitoring services. Seven out of the fifteen clinics had on-site point of care CD4 measuring machines and phlebotomist. At the time of study, patients were eligible to initiate ART if they had a CD4 count < 350 cells/mm^3 or had a WHO stage III or IV disease (12).

The HIV care and treatment services are mainly provided by the clinic nurses with mentoring support at least once per month from PEPFAR supported implementing partners and doctors from nearby hospital. Very sick patients needing doctors' attention are often referred to the

nearby hospital. All the clinics had an expert patient (peer educator) who provided adherence and psychosocial support to patients. The expert patients also had the responsibility of identifying and tracking patients who miss HIV care clinic appointments either by cellphone calls or home visits.

In Swaziland HIV care and treatment services are coordinated by the National HIV program. The program is the one responsible for formulating policies, guidelines and monitoring and evaluation tools for HIV service provision. The program also accredit facilities to be ART refilling and initiating sites, trains health workers and monitor program performance country wide. The National office works closely with the Regions. HIV service provision in the region is coordinated and implemented under the leadership of the regional health management team. The RHMT has to ensure that National policies and guidelines are implemented in the region. They are the ones to provide or advocate for resources for successful service provision.

Permission to gain access to conduct the study was sort from the Swaziland national HIV program and from the regional clinic supervisors of the study sites. An approval letter was signed by the National ART coordinator and then given to regional clinic supervisors and all the study clinics at time of arrival to help gain access to sites.

2.3 Study population

The study population consisted of a cohort of HIV positive patients who were enrolled into HIV care and treatment services (starting from pre-ART care) care from the 1st of April 2012 to 30 June 2012 in 15 study clinics of Manzini region in Swaziland. The study involved a retrospective review of their clinical records.

2.3.1 Inclusion criteria

Clinical records of all patients from 15 years and older (≥ 15 years) who tested HIV positive and enrolled for pre-ART care regardless of their CD4 count value during the period of 1st April 2012– 30th June 2012. These included;

1. Patients who tested HIV positive even before the 1st of April 2012 as long as they enrolled into pre-ART care) within the study period, 1st April 2012– 30th June 2012.
2. Antiretroviral treatment naïve patients

3. Transfer-in patients from other clinics were also included as long as they had a file and first pre-ART enrolment clinical intake record (baseline clinical data) available and within the study period, 1st April 2012– 30th June 2012.

2.3.2 Exclusion criteria

The following groups of patients were excluded from the study;

1. Clinical records of patients who were younger than 15 years old
2. Patients with missing chronic care (clinical) file clinical
3. Patients who had the first clinical intake record (baseline clinical data) missing from the available chronic care file.
4. Patients who were already on antiretroviral treatment.

2.4 Sampling

The study was conducted in 15 primary health care clinics because they made up all the public clinics in Manzini region at the time of study that were offering comprehensive HIV services which include, HTC, pre-ART and ART services as depicted in the national guidelines. In addition these facilities also used the national standardized tools to monitor services. These clinics were also a good representative of patients and clinical practices in both rural and urban settings.

From each facility the pre-ART register was used to identify and retrieve clinical files/records of all patients enrolled into HIV care and treatment services (including pre-ART) in the period 1 April 2012 – 30 June 2012 (3 months). Each patient clinical record was the unit of analysis. All records of patients who met the inclusion criteria from each clinic were included in the study.

For the minimum sample size calculation the formulae $n = \frac{Z^2 p(1-p)}{d^2}$ was used. Where z = Normal standard deviation (1.96), p = Proportion of patients enrolled into pre- ART that are likely to be retained estimated at 33% in sub-Saharan Africa, d = required precision of 5%.

= $\underline{(1.96)^2 * 0.33 * 0.67}$ = 340 clinical records

$(0.05)^2$

On average, each clinic enrolled at least 15 patients each month into pre-ART care. All the patients who enrolled for pre-ART care in the study period, 1st April 2012– 30th June 2012 from the 15 clinics were included in the study. The sample size had adequate power to answer the study objectives.

2.5 Data Management and Analysis

2.5.1 Data collection process

The study facility pre-ART register and the patient chronic care (clinical) files were the two main data source documents for the study.

The register captures baseline data as transferred or copied from the patients chronic care file. Hence, the two have similar baseline socio demographic and clinical information, the difference is that the patient file include data on subsequent clinical follow up visits for both pre-ART and ART care including laboratory test and other investigations yet the register captures only baseline data and is periodically updated to mark pre-ART patients outcomes e.g. those patients who started ART, were transferred out or died. The pre-ART register also allows for sequential allocation of unique Pre-ART numbers to each client entering chronic care and has opened an HIV chronic care file. The pre-ART number usually starts with the initials of clinic name followed by the sequential number. This pre- ART number is documented on the outside cover of the patients file and is used by the facility for filing purposes.

2.5.1.1 Identification of study participants

In each study site, the pre-ART register was used by principal investigator and research assistant to identify all the patients enrolled for pre-ART care during the study period 1st April 2012- 30 June 2012.

A total of 805 patients were registered on pre-ART register in the period from 1 April to 30 June 2012. File retrieval was attempted on all the 805 patient files using the patient unique clinic filing number. However, 104 files could not be located in the facility as they were missing hence 701 patient records were found and reviewed. Out of the 701 files, data was collected from 510 patient records as shown in *Figure 2 below.*

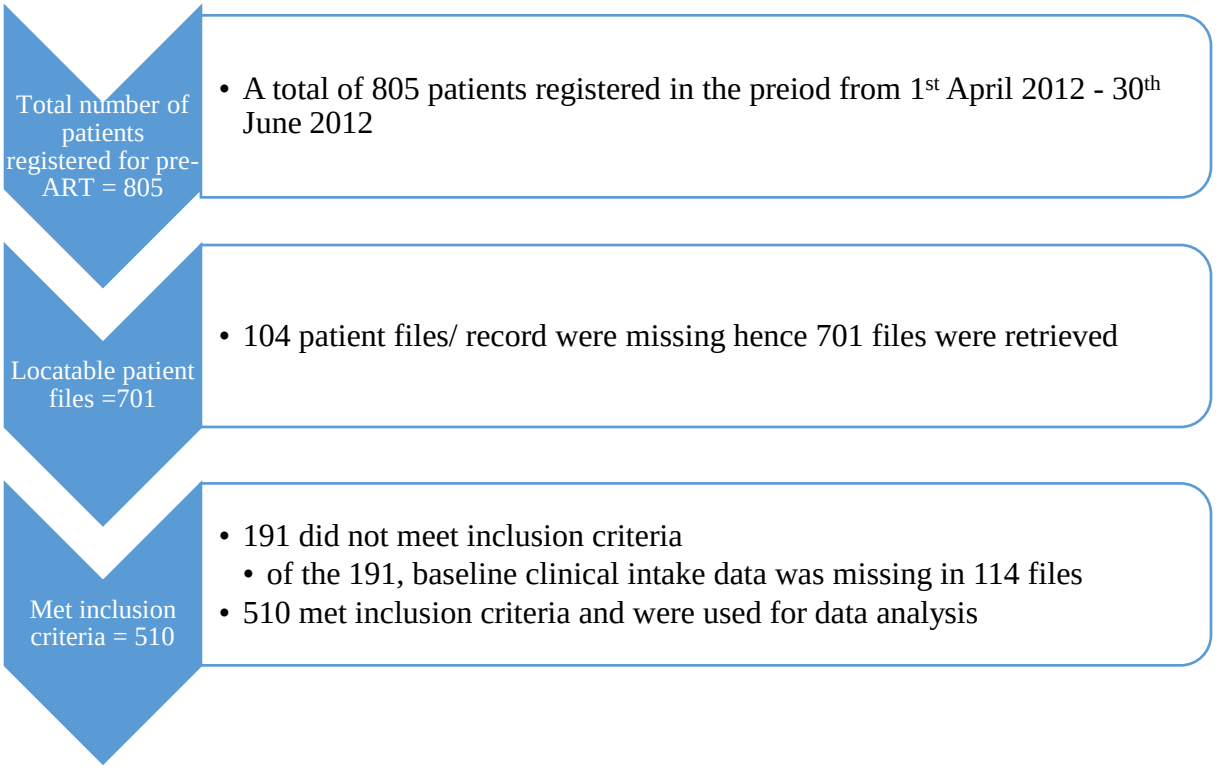

Figure 2: Flow chart for final sample of files used for data abstraction

2.5.1. 2 Collection of Baseline socio demographic, clinical and retention data

The patient's chronic care file (n=510) was the primary data source. A data extraction tool was developed and used to collect data on studied variables from each patient clinical file. The clinical record review was done from January – August 2014. Data from all recorded clinical visits was extracted as long as it was within the 15 months of study data collection.

To standardize collected data, the first intake visit date from the patient file was taken as the pre-ART enrolment date. To it, 15 months was added manually or electronically using a preset formulae on the excel sheet to mark/ determine study data collection end point. Even though the pre-ART register and the chronic care file had similar baseline data the chronic care file was used as the main data source. Where the clinical file was missing baseline data from the Pre-ART register was not used as it did not have follow up visit data.

Data was collected by the principal investigator and a trained research assistant. The research assistant was a lay person who has previous experience in research data collection and basic computer skills. However, the process of data collection using the paper based extraction tool was found to be time consuming. An electronic excel spread sheet was created to allow real time

data entry on the study variables. Collected data from the paper tools was also entered on this excel sheet. Completed study forms were kept in a locked cabinet by the principal investigator. The excel file was also protected with password only known by the principal investigator and research assistant.

2.5.2 Study Variables and Measurement

2.5.2.1 Study Variables

Primary outcome: Retention in care was the outcome variable of interest. A patient was considered to be retained in care if he/she attended the clinic for either pre-ART/ ART medicine collection, laboratory testing and or clinical review and was not documented as "dead, "stopped treatment" or "transferred- out" at three, six and 12 months post enrolment. A patient was considered lost to follow up if they have not attended an appointment at one of the three time points or did not have any visit in the last three months from time of analysis and was not documented as dead or transferred out.

Secondary outcome: Was the time to being lost-to-follow- up. The last facility visit date was used as an outcome date and LTFU defined as ≥3 months without a visit date after 12 months from the enrolment date.

Baseline Covariates

The main covariates were;

1. *Baseline socio demographic characteristics* of patients *enrolled into pre-ART care at clinic level in the period 1st April 2012– 30th June 2012* such as age, sex, marital status, level of education and employment status and patients nearest clinic.
2. *Baseline clinical characteristics of patients enrolled into pre-ART care at clinic level in the period 1st April 2012– 30th June 2012.* These describe the patient clinical findings on the day of the first (intake) pre-ART clinical visit or consultation. It includes the patient's first CD4 count value, functional status, BMI, WHO staging, as well as pregnancy (for women) and TB status at enrolment.

2.5.3 Data Management

Table 1 below describes how study variables were categorized. Most of the collected data were categorical however numerical variables such as age, level of education, BMI and CD4 count were categorized for description purposes and to allow for bivariate and multivariate analysis.

Table 1: Transformation of study variables

Categorized Variable	Description	Bivariate and Multivariate analysis transformed categories
Socio-demographic Variables		
1. Sex	Male Female	Same
2. Age*	15-19 20-29 30-39 40+	≤30 <30
3. Marital status*	Single Married Widowed Divorced	Single Married Widowed & divorced
4. Level of education	Primary - (Grade 1-Grade7) Secondary - (Form 1-Form 3) High school (Form 4-Form5) Tertiary – (any training after form5) Has never been to school	Same
5. Employment Status	Employed Not Employed	Same
6. Enrolled at nearest clinic	Yes No	Same
7. Functional status	Working Ambulatory Bedridden	same
8. Body Mass Index	< 18.5 (underweight) 18.5- 24.9 (normal) 25-29.9 (overweight) ≥ 30 (obese	Same
9. WHO Staging	Stage I, II III IV	Same
10. CD4 count*	<100 100-200 201-350 351-500 >500	≤ 350 351-500 >500
11. Pregnant*(females only)	Yes No	Yes No

*Variable used in multivariate analyses

The categorical variables were coded to prepare for quantitative data analysis. Missing data and non-applicable responses were also coded so that every variable slot was filled. Comments were also inserted on the excel cell as per need. The patients name and last name were not captured but only the pre-ART number was used as a unique patient identifier. There was no duplication of numbers within the facility and among all study sites as the initials of the clinics were all different.

At the end of each data collection session, the PI and research assistant cross checked their work to ensure enhanced data quality. This was done by randomly checking at least 10% of total entered data.

2.5.3 Data Cleaning

Collected data from PI and research assistant were merged and entered in Microsoft Excel where data cleaning was done. The study database was reviewed for validity, accuracy and completeness. Manual and automated reviews of the study database were carried out before analysis to assess the extent to which abstracted data was valid e.g. within study period with the right study population. Data was also checked for completeness and accuracy. Client records that had key fields missing (e.g., pre-ART enrolment date, date of birth, clinical visit dates, etc.) or outlying or inconsistent data (e.g. out-of-chronology dates where a follow up visit was recorded on a date that preceded enrolment) were identified and excluded from study.

As data was being entered quality checks were conducted to ensure that the data was within the plausible range especially for continuous variables and dates. Frequency tables for all the variables were generated and checked for consistency, outliers and for missing data.

The principal investigator had to go back to the facility to verify or re-collect data. If key missing or inconsistent data were not resolvable (e.g. error in the original source document) a comment was added on the excel sheet. Data with discrepancies that could not be corrected were noted as not correctable and hence were left as missing.

Cleaned data was then imported to Stata Version 13 (Stata Corporation, College Station, TX, USA) for analysis.

2.5.4 Statistical Analysis

The covariates in this study (n = 510) were patient socio-demographic and clinical characteristics at baseline with the primary outcomes being retention at three, six, and 12 months and time to being lost to follow up.

For the descriptive analysis, variables' frequencies and proportions, medians and interquartile ranges, mean and standard deviation were calculated at three, six, and 12 months intervals, respectively. Pearson's Chi squared or Fisher's exact statistical tests were used to determine the association between categorical variables (socio demographic and clinical) and retention at three, six and 12 months, respectively.

Confounding factors consisting of significant baseline socio demographic (marital status Occupational status) and clinical (baseline CD4 count and Pregnancy status) covariates were modeled in multivariate logistic regression to determine patient factors associated with retention. All estimates were reported in terms of odds ratios or hazard ratios and 95% confidence interval with corresponding P-values.

For the survival analysis, the outcome of interest was retention at 12 months. Patients who were diagnosed HIV positive and enrolled into pre-ART care had a primary outcome of attrition, defined as time from pre-ART enrolment to occurrence of an unfavourable endpoint loss from care (which include transferred out and death). The last facility visit date was used as an outcome date and loss from care defined as ≥ three months without a visit date after 12 months from the enrolment date. Right censoring occurred for patients who were initiated on ART.

Kaplan Meier curves were used to describe survival time (retention) over a period of 12 months post enrolment into HIV chronic care (pre-ART care). Cox proportional hazard model was used to determine the association between the significant covariates (socio-demographic factors and baseline clinical factors) and retention at 12 months respectively.

In both the multivariate logistic regression and Cox proportional hazard model, a P-value of <0.05 was considered statistically significant. Results findings were segregated by sex. A P-value of 0.1 was used to determine entry of variable in the final model. The goodness of fit test was done for each final model. *Table 2* below, gives a summary of the data analysis plan

Table 2: Data analysis plan

Study objective	Variables	Analysis
To describe (1) the socio-demographic and (2) clinical characteristics of a cohort of patients enrolled for pre-ART care at clinic level in the period 1st April - 30th June 2012.	**Independent Variables** *Categorical Variables* Socio-demographic; Age, sex, marital status, level of education and employment status and patients nearest clinic. Clinical; Functional status, BMI, WHO staging, CD4 count , and pregnancy status (for women) and TB *Continuous Variables* Socio-demographic; Age Clinical; CD4 count , BMI, **Dependent variable** Retention at three , six and 12 months respectively	Frequencies and proportions Medians and interquartile ranges Mean and standard deviation
(3)To determine the proportion retained among a cohort of men and women enrolled for pre-ART care at clinic level at three, six, and 12 months post enrolment		Frequencies and proportions
(4) To describe the time to Lost-to-follow-up and to explore the associated factors for women and men enrolled in pre-ART care in the period from 1st April – 30th June 2012.		Kaplan Meier curves Cox proportional hazard regression model
(5) To determine baseline socio demographic and clinical factors associated with retention at three, six, and 12 months post enrolment.		Bivariate analysis Chi-square test or Fischer exact Univariate and multivariate Logistic regression model Assessed goodness of fit of final model.

2.6 Ethics

Ethics approval was obtained from the University of Witwatersrand Ethics committee and from the Swaziland Scientific and Ethics Committee. A letter of approval to do the study in Swaziland using routinely collected data was provided by the Swaziland National ART coordinator's office to enable access to the facilities selected for this study.

Patient's clinical information was kept confidential. Only the patient's pre-ART number and not the name was used as a patient identifier during data collection. Collected data was used solely for the purpose of this study and only the research team had access to it. Data was locked by a password that was only known by the principal investigator and research assistant.

All data will continue be stored in a password protected file known by only the study investigator for two years after the final report is produced.

CHAPTER 3: STUDY RESULTS

The aim of this study was to determine patient baseline characteristics associated with retention among a cohort of patients (≥ 15years) classified as pre-ART at enrolment in an HIV Care and Treatment Program in Manzini Region, Swaziland. This was a retrospective cohort study that examined patients enrolled for pre-ART care between 1st April 2012 – 30th June 2012. Clinical records of the pre-ART cohort were reviewed for a period of 15 months to determine baseline socio-demographic (sex, age, marital status, level of education, and employment status, patients nearest clinic), and clinical factors (functional status, Body Mass Index, TB status, WHO staging, CD4 count, and pregnancy status among women) associated with retention in HIV care (either Pre-ART or ART care) at three, six and 12 months.

3.1 Description of the baseline characteristics of the Pre-ART cohort

3.1.1 Baseline socio-demographic characteristics

Table 3 below presents a description of baseline socio-demographic characteristics of the study population (n=510). The characteristics are sex, age, marital status, level of education, employment status, and patients' nearest clinic.

Over three-quarters of the cohort were females (78%) while 22% were males. The study participants were young, with a median age of 29 years (IQR; 27-37 years), and their ages ranged from 15 to 80 years. Half (50%) of the patients were in the age group 20-29 years, followed by the 30-39 years age group (23%) and then those aged 40 years and above (21%). Adolescents aged 15-19 years accounted for 6% of the study population. In terms of marital status, 54% of the patients were single, 42% were married and five percent were previously married (4.4% widowed and 0.4% divorced).

On level of education just over half (51%) of the patients had secondary and high school education, 37% had primary school education. About one in 10 of the patients had never been to school and only one percent had tertiary level education. Furthermore, about 4 out of 5 (77%) of the study patients were not employed. Furthermore, 91% of the study participant reported that the clinic they were enrolled at was their nearest clinic.

Table 3: Baseline socio-demographic characteristics of the Pre-ART Cohort (n = 510) at enrolment

Characteristics	n	%
Sex (n= 510)		
Females	398	78.0
Males	112	22.0
Age in years (n=510)		
Median age	29 (IQR:27-37)	
Females only	28 (IQR:23-35)	
Males only	33 (IQR:27- 44)	
Age group		
15-19	30	5.9
20-29	255	50.0
30-39	118	23.1
40+	107	21.0
Marital status (n=500)		
Single	268	53.6
Married	208	41.6
Widowed	22	4.4
Divorced	2	0.4
Level of Education (n=359)		
Primary	133	37.1
Secondary	116	32.3
High school	68	18.9
Tertiary	5	1.4
Has never been to school	37	10.3
Employment status (n=422)		
Employed		
Non-employed	97	23.0
	325	77.0
Enrolled at nearest clinic (n=504)		
Yes	458	90.9
No	46	9.1

4.1.2 Baseline clinical characteristics

Table 4 below presents the baseline clinical characteristics of the study population (n=510). The baseline clinical characteristics included functional status, BMI, TB status, WHO staging, CD4 count and pregnancy status.

When assessing the functional status of the patients, about nine out of 10 (89%) of the study participants at enrolment were found to be clinically stable, able to carry out their day to day activities normally, and without any physical limitations. The ambulatory population accounted for 11% of enrolled patients. These had energy levels that only allowed them to walk but not enough to conduct any chores. Less than one percent of the enrolled patients were bedridden.

Nutritional assessment using body mass index (BMI) calculation revealed that one-in-two (52%) of the study population had normal weight with BMI 18.5 – 24.9. Those who were overweight accounted for 28% with BMI 25-29.9 and 14 % were obese with a BMI $\geq$ 30. Very few patients (5%) were underweight with BMI < 18.5. The mean BMI was 25 with a standard deviation of 4.9.

A majority of the patients (90%) were classified as being WHO stage I or II, which means they had no or very minor opportunistic infections. One out of ten (10%) study patients had opportunistic infections that classified them as WHO stage III or IV. These opportunistic infections are a marker of moderate to severe immune suppression. Most patients screened negative for TB (86 %) with 13% identified as presumptively TB patients and only two percent were already diagnosed with active TB disease at enrolment.

A good proportion of the study population 410 (89%) had a baseline CD4 count at enrolment. At the time of enrolment, the CD4 eligibility cut-off point for ART initiation was set at less than 350 cells/mm^3or being classified as having a WHO stage III or IV condition, respectively.

About half (51%) of the patients had CD4 count above the cut-off point (greater than 350 cells/mm^3) of being initiated on ART. This means that the almost other half (49 %) of the study population was eligible for ART initiation. In addition, about 1 in 5 (22 %) were at an advanced immunosuppression with CD4 $\leq$ 200 cells/mm^3. The overall median CD4 count was 357 (IQR: 216-546) cells/mm^3. The median CD4 count for females was 404 (IQR: 236- 583) and for men it was 270 (IQR: 176-397).

There were 398 female participants with a documented pregnancy status, and of whom 37%, (127) were pregnant at the time of enrolment.

Table 4: Baseline clinical characteristics of the Pre-ART cohort at enrolment (n = 510)

Characteristics	Frequency (n)	Percentage (%)
Functional status (n=433)		
Working	385	88.9
Ambulatory	47	10.9
Bedridden	1	0.2
BMI (n=419)		
Mean	25 (SD = 4.9)	
Median	24 (IQR:22-28)	
BMI categories		5.3
< 18.5 (underweight)	22	52.5
18.5- 24.9 (normal)	220	28.4
25-29.9 (overweight)	119	13.8
≥ 30 (obese)	58	
WHO staging (n=467)		
I	317	67.9
II	103	22.1
III	42	9.0
IV	5	1.0
TB status (n=443)		
Screen TB Negative	380	85.8
Screen TB Positive	56	12.6
With Active TB disease	7	1.6
Baseline CD4 count = CD4 cells/mm^3 (n=462)		
Median CD4 count	357 (IQR: 216-546)	
Median CD4 count (females only)	404 (IQR: 236-583)	
Median CD4 count (males only)	270 (IQR: 176-397)	
CD4 categories		
<100	43	9.3
100-200	61	13.2
201-350	123	26.6
351-500	90	19.5
>500	145	31.4
Pregnant (Female patients only; n=341)		
Yes	127	37.2
No	214	62.8

3.2 Measures of association between baseline socio-demographic and clinical characteristics and retention in HIV care at three, six and 12 months.

3.2.1 Measure of association between baseline socio-demographic characteristics and retention in care at three, six and 12 months: Bivariate analysis.

Table 5 presents results from bivariate analysis between patient's baseline Socio-demographic and retention at three, six and 12 months respectively.

3.2.1.1 Age and retention at three, six and 12 months

In general, a large proportion of older patients (≥ 30 years) were retained in HIV care compared to younger patients (< 30 years) at three, six, and 12 months respectively. The proportion of patients retained in care in the different age groups decrease with time with the greatest loss being noted at three months. Among patients less than 30 years old: retention was 44% at three months, 42% at six months and 39% at 12 months, respectively. Among patients ≥ 30 years, 63%, 58%, 56% were retained at three, six and 12 months respectively. The noted difference in proportion of patients retained in care in each age category was statistically significant at all three time points; (retained at three months, among patients < 30 years old 44%, among patients ≥ 30 years old 63 % P < 0.001; retained at six months < 30 years 42%, ≥ 30 years old, 58 % P < 0.01; retained at 12 months < 30 years old 39 %, ≥ 30 years old 56%, P < 0.001).

3.2.1.2 Marital status and retention at three, six and 12 months

Investigating the association between marital status and retention revealed that the category of singles had the least proportion of patients retained in HIV care. Less than half (45%, 45%, 41%) of them were retained in HIV care at three, six and 12 months, respectively compared to the proportion retained in the married (62%, 54%,52%); divorced and widowed groups (50%, 50%, 50%) in the same time points. However, the association between marital status and retention in HIV care was statistically significant at three months and 12 months only, (Proportion of patient retained in HIV care by marital status at three months; married 62%, single 45 %, widowed and divorced 50 % P value < 0.001, at six months: married 54%, single 45 %, widowed and divorced 50 % P value < 0.139, at 12 months married 52%, single 41%, widowed and divorced 50 % P value < 0.044). Similarly to the trend observed with age groups, the retention rates also declined with time.

The rest of the socio demographic factors (Sex, level of education, employment status and nearest clinic of patient) examined in this study did not show any statistically significant association with retention in HIV care at three, six and 12 months.

Table 5: Association between baseline socio-demographic characteristics and retention in HIV care at three, six, and 12 months

Characteristics	Retention outcomes at 3 months			Retention outcomes at 6 months			Retention outcomes at 12 months		
	Retained n (%)	Not Retained n(%)	p-value	Retained n (%)	Not Retained n (%)	p-value	n (%)	Not Retained n (%)	p-value
Total (n=510)	266 (52)	244 (48)		250 (49)	260 (51)		236 (46)	274 (54)	
Sex (n= 510)									
Females	203 (51)	195 (49)		191 (48)	207 (52)	0.381	182 (46)	216 (54)	
Males	63 (56)	49 (43)	0.326	59 (53)	53 (47)		54 (48)	58 (52)	0.641
Age in years (n=510) *Age groups*									
< 30 years	125 (44)	160 (56)	<0.00	119 (42)	166 (58)		110(39)	175 (61)	
30+ years	141 (63)	143 (37)	1*	131 (58)	148 (42)	<0.00	126 (56)	99 (44)	<0.00
Marital status (n=500)									
Married	128 (62)	80 (38)	0.002	113 (54)	95 (46)	0.139	109 (52)	99 (48)	0.044
Single	121 (45)	147 (55)		121 (45)	147 (55)		110 (41)	158 (59)	
Widowed & divorced	12 (50)	12 (50)		12(50)	12 (50)		12 (50)	12 (50)	
Level of Education (n=359)									
Primary	72 (54)	61 (46)		64 (48)	69 (52)		58 (44)	75 (56)	
Secondary	57 (49)	59 (51)		54 (47)	62 (53)	0.788	51 (44)	65 (56)	0.855
High school	33 (49)	35 (51)	0.849	30 (44)	38 (56)		29 (43)	39 (57)	
Tertiary	3 (60)	2 (40)		2 (40)	3 (60)		3 (60)	2 (40)	
Has never been to school	21 (57)	16 (43)		21 (57)	16 (43)		19 (51)	18 (49)	
Occupation (n=422)									
Employed	51 (53)	46 (47)	0.795	55 (57)	42 (43)	0.132	50 (52)	47 (48)	0.141
Non-employed	166 (51)	159 (49)		144 (44)	181 (56)		140 (43)	185 (57)	
Enrolled at Nearest clinic (n=504)									
Yes	239 (52)	219 (48)	0.779	224 (49)	234 (51)		211 (46)	247 (54)	0.61
No	25 (54)	21 (46)		25	21 (46)	0.482	23 (50)	23 (50)	

*Statistically significant p-value < 0.05

3.2.2 Measures of association between baseline clinical characteristics and retention in care at three, six and 12 months: Bivariate analysis

Table 6 below depicts the summary of the bivariate analysis between patients' baseline clinical factors and retention.

3.2.2.1 CD4 count and retention

At three months the highest proportion of patients retained in HIV care were those with CD4 ≤ 350 cells/mm^3 and the least retained group was among those with baseline CD4 > 500 cells/mm^3 (proportion retained at three months, CD4 ≤ 350 cells/mm^3- 64.3%, 351-500 cells/mm^3- 57.8% , > 500 - 45.5% P=0.02). A similar observation was also noted at six and 12 months (proportion retained at six months CD4 ≤ 350 cells/mm^3, 61.7%, 351-500 cells/mm^3– 48.9%, > 500 cells/mm^3 - 45.5% P=0.005 and lastly at 12 months CD4 ≤ 350 cells/mm^3; 58.6%, 351-500 – 44.4%, > 500 cells/mm^3, 43.5% P=0.006). The baseline CD4 count was noted to have a statistically significant association with retention in HIV care at three, six and 12 months, respectively.

3.2.2.2 Pregnancy status and retention

With regard to pregnancy status, in general, non- pregnant women compared to pregnant women had the highest proportion of women retained in care at three, six and 12 months, respectively. Retention at three months was 44.9% for pregnant women versus 55.1% for non-pregnant P < 0.067; retention at six months was 36.2% for pregnant women and 54.7% for non-pregnant women; and at 12 months retention for pregnant women was 35.4% and 52.3% for non-pregnant women. A significant association was also noted between pregnancy status and retention at six and 12 months.

The patients' functional status, Body Mass Index, TB status and WHO status were found not to be significantly associated with retention in HIV care at three, six, and 12 months in this study.

Table 6: Association between baseline clinical characteristics and retention in HIV care at three, six and 12 months.

Characteristics	Retention outcomes at 3 months			Retention outcomes at 6 months			Retention outcomes at 12 months		
	Retained n (%)	Not retained n(%)	p-value	Retained n (%)	Not retained n (%)	p-value	n (%)	Not retained n (%)	P-value
Total	266 (52)	244 (48)		250 (49)	260 (51)		236 (46)	274 (54)	
Functional Status (n=433)									
Working	210 (54.5)	175 (45.5)		198 (51.4)	187 (48.6)		185 (48.1)	200 (59.9)	
Ambulatory	23 (48.9)	24 (51.1)	0.438	20 (42.5)	27 (57.5)	0.249	18 (38.3)	29 (61.7)	0.247
Bedridden^	0 (0)	1 (100)		0(0)	1(100)		0 (0)	1 (100)	
BMI (n=419)									
< 18.5 (underweight)	13 (59.1)	9 (40.9)		12 (54.5)	10(45.5)		13 (59.1)	9 (40.9)	
18.5- 24.9 (normal)	129 (58.6)	91 (41.4)	0.258	122 (55.5)	98 (44.5)	0.460	114 (51.8)	106 (48.2)	0.679
25-29.9 (overweight)	59 (49.6)	60 (50.4)		56 (47.1)	63 (52.9)		56 (47.1)	63 (52.9)	
≥ 30 (obese)	37 (63.8)	21(36.21)		33 (56.9)	25 (43.1)		31 (53.5)	27 (46.5)	
TB (n= 433)									
Screen TB Negative	208 (54.7)	172(45.3)		196 (51.6)	184 (48.4)		180 (47.4)	200 (52.6)	
Screen TB Positive	27 (48.2)	29(51.8)	0.455	25 (44.6)	31 (55.4)	0.644	26 (46.4)	30 (53.6)	0.875
With Active TB disease	5 (71.4)	2(28.6)		3 (42.86)	4 (57.1)		4 (57.1)	3 (42.9)	
WHO Staging (n=467)									
I	171 (53.9)	146 (46.1)		165 (52)	152 (48)		160 (50.5)	157 (49.5)	
II	56 (54.4)	47 (45.6)	0.937	49 (47.6)	54 (52.4)	0.829	42 (40.8)	61 (59.2)	0.361
III	22 (52.4)	20 (47.6)		22	20 (47.6)		20 (47.6)	22 (52.4)	
IV	2 (40)	3 (60)		2 (40)	3 (60)		2 (40)	3 (60)	
Baseline CD4 (cells/mm^3) n=462									
<350	146 (64.3)	81(35.7)		140 (61.7)	87 (38.3)		133 (58.6)	94 (41.4)	
351-500	52 (57.8)	38 (42.2)	0.002*	44 (48.9)	46 (51.1)	0.005*	40 (44.4)	50 (55.6)	0.006*
>500	66 (45.5)	79 (54.5)		66 (45.5)	79 (54.5)		63 (43.5)	82 (56.5)	
Pregnancy status(n=341)									
Yes	57 (44.9)	70 (55.1)	0.067	46 (36.2)	81 (63.8)	0.001*	45 (35.4)	82 (64.6)	0.002*
No	118 (55.1)	96(44.9)		117(54.7)	97 (45.3)		112 (52.3)	102 (47.7)	

^ Fischer exact test used *statistically significant p value< 0.05

3.2.3 Measure of association between baseline socio demographic and clinical characteristics and retention in care at three, six and 12 months using Multivariate logistic regression model

Overall, the study findings indicate that among all the baselines socio demographic and clinical characteristics, marital status, CD4 count level, and pregnancy status were the only variables significantly associated with retention in HIV care at three, six and 12 months. These variables were adjusted for in the multivariate logistic regression model. To control for the effects of pregnancy in the model, separate analysis was done for females and for males

Table 7 below depict the results (males and females respectively) of the final model with odds ratios to predict baseline socio demographic and clinical characteristics that had an influence on patients' retention at three, six and 12 months respectively.

3.2.3.1 Measures of association between baseline sociodemographic and clinical characteristics and retention in HIV care at three, six and 12 months among **female**: Multivariate logistic regression:

3.2.3.1.1 Marital status and Retention

Amongst females, marital status was the only socio demographic variable that significantly influenced retention in HIV care at three, six and 12 months when controlling for all other study variables. At three months single women were 57% less likely (OR 0.43, 95% CI 0.26 – 0.71, p=0.001) to be retained in HIV care compared to married ones. At six months again the single women compared to married ones were 38% less likely (OR 0.62, 95% CI 0.38 – 1.00, p = 0.05) to be retained in HIV care. At 12 months a pattern similar to that at three and six months was observed where single women compared to married ones had a 44% less likelihood (OR 0.56, 95% CI 0.38 – 1.00, p = 0.05) to be retained in HIV care at 12 months. Being widowed or divorced was not significantly associated with retention.

3.2.3.1.2 CD4 count and Retention

With regard to baseline clinical factors, CD4 count was significantly associated with retention in HIV care at three months among females. Patients with CD4 count greater than 500 cells / mm^3 were 47% less likely (OR 0.53, 95% CI 0.30 – 0.91, P=0.02) to be retained in HIV care compared to women with CD4 count < 350 cells/mm^3. A CD4 count level between 350 – 500 cells/mm^3 was not significantly associated with retention among females at three months.

3.2.3.1.3 Pregnancy status and Retention

At three months non-pregnant women were 69% more likely (OR 1.69, 95% CI 0.99 – 2.6, P=0.056) to be retained in HIV care when compared to pregnant women although the findings were not statistically significant. At six and 12 months pregnancy seems to be the only significant predictor of retention when controlling for all the socio demographic and clinical factors analyzed in this study. Non-pregnant women were also twice more likely to be retained in care at six and 12 months (at six months - OR 2.31, 95% CI 1.41 – 3.80, P= 0.001 and at 12 months OR 2.05, 95% CI 1.25 – 3.62, P= 0.004) when compared to pregnant women. Although the influence of pregnancy was not significant at three months, the direction was similar to what was observed at six and 12 months.

The other socio demographic (age, level of education, employment status, and patients' nearest clinic) and clinical characteristics, functional status, Body Mass Index TB status, WHO clinical staging) had no significant influence on retention at three, six and 12 months among females.

3.2.3.2 Measures of association between baseline sociodemographic and clinical characteristics and retention in HIV care at three, six and 12 months among **Males**: Multivariate logistic regression

3.2.3.2.1 Age and retention

Unlike in females, age significantly influenced retention in HIV care at three, six, and 12 months amongst males. In general men who were 30 years and older were more likely to be retained in HIV care when compared to younger men less than 30 years in all three time points. At three months, men who were 30 years and older compared to those less than 30 years were 3.4 times more likely (OR 3.4 , 95% CI 1.32 – 8.70 , p= 0.01) to be retained in HIV care, four times more likely (OR 4.05 , 95% CI 1.51-10.80, p= 0.005) at six months and 3.17 times more likely (OR 3.17 , 95% CI 1.23-8.16 , p= 0.02) at 12 months to be retained in HIV care.

3.2.3.2.2 CD4 count and retention

With regard to baseline clinical factors, CD4 count was significantly associated with retention in HIV care at three months among males in the multivariate analysis. Men who had a CD4 count greater than 500 cells / mm^3 were 62% less likely (OR 0.38, 95% CI 0.61 – 0.94, P-value, 0.04) to be retained in care compared to men with CD4 count < 350 cells/mm^3. At six months men who had a CD4 count from 350 - 500 cells/ mm^3 were 66% less likely (OR 0.34, 95% CI 0.20 – 1.00, P-value, 0.05) to be retained in HIV care compared to men with CD4 count < 350

cells/mm^3. Unlike at three months it is worth noting that CD4 > 500 cells/mm^3 had no significant influence on retention on men when controlling for the clinical and socio demographic factors at six months. At 12 months, with regard to CD4 count level a similar pattern was observed at three months. Men who had a CD4 count greater than 500 cells / mm^3 were 88% less likely (OR 0.22, 95% CI 0.05– 0.93, P-value, 0.04) to be retained in HIV care compared to men with CD4 count < 350 cells/mm^3. Again, a CD4 count level between 350 – 500 cells/mm^3 was also not significantly associated with retention among males at 12 months.

The other socio demographic (marital status, level of education, employment status, and patients' nearest clinic) and clinical characteristics (functional status, Body Mass Index TB status, WHO clinical staging) had no significant influence on retention at three, six and 12 months among males.

3.2.3.3 Summary of key findings from the multivariate logistics regression model

Among females, marital status and pregnancy status were associated with retention in care at three, six and 12 months respectively. At all the three time points single women compared to married women were less likely to be retained in HIV care when compared to married women. Similarly, non-pregnant women were more likely to be retained in HIV care at three, six and 12 months. The CD4 count level only showed significant influence on retention at three months only, with women with CD4 > 500 cells/mm^3 having a less likelihood of being retained in HIV care compared to women with CD4 < 350 cells/mm^3. Unlike among men age did not influence retention in care for females.

Among men, age was a significant predictor of retention at three, six and 12 months respectively. With older men ≥ 30 years being more likely to be retained compared to younger men < 30yrs old. With regard to CD4 count, similar to women, a CD4 count > 500 cells/mm^3 was significantly associated with lesser odds of being retained at three months and 12 months compared to patients with CD4 less than 350 cells/mm^3. However a CD4 > 500 cells/mm^3 had no influence on retention at six months. At six months. men who had a CD4 count between 350 - 500 cells/mm^3 were 66 % less likely (OR 0.34, 95% CI 0.20 – 1.00, P-value, 0.05) to be retained in care compared to men with CD4 count < 350 cells/mm^3

.

Table 7: Multivariate logistic regression models of baseline factors associated with retention in HIV care at three, six and 12 months ***for females****.*

Baseline characteristics	**Retention at 3 months**		**Retention at 6 months**		**Retention at 12 months**	
	OR [95% CI], P value	**aOR [95% CI], P value**	**OR [95% CI], P value**	**aOR [(95% C], P value**	**OR [95% CI], P value**	**aOR [95% CI], P value**
Marital status						
Married (reference)	1	1	1	1	1	1
Single	**0.48 [0.31- 0.72],0.001***	**0.43[0.26-0.71], 0.001***	**0.57 [0.38- 0.86], 0.008***	**0.62 [0.38- 1.00], 0.05***	**0.52 [0.34-0.79], 0.002***	**0.56 [0.34 - 0.91], 0.02***
Widowed & Divorced	0.70 [0.27-1.83], 0.469	0.42 [0.12- 1.54], 0.19	1.10 [0.42 - 2.87], 0.85	0.89 [0.24- 3.3], 0.86	0.93 [0.36- 2.41], 0.89	0.92 [0.25 - 3.41], 0.91
Baseline CD4 count = CD4 cells/mm^3 CD4 categories						
*<350 (reference)	1	1	1	1	1	1
350-500	0.76 [0.43 - 1.36], 0.36	0.90 [0.46 – 1.77], 0.77	0.68 [0.38- 1.19], 0.177	0.88 [0.44 – 1.68], 0.67	0 .56 [0.34 - 0.92], 0.02	0.71 [0.363-1.38], 0.31
>500	**0.51[0.32-0.82], <0.006***	**0.53 [0.30–0.91], 0.02***	**0.54 [0.34 – 0.86],0.009***	0.61 [0.35 – 1,04], 0.07	**0.54 [0.36-0.83] ,< 0.01***	0.73 [0.43 – 1.77], 0.27
Pregnancy status (females only)						
Yes (reference)	1	1	1	1	1	1
No	1.51 [0.97 - 2.35], 0.06	**1.69 [0.99- 2.6], 0.053***	**2.12 [1.35- 3.33], 0.001***	**2.31 [1.41- 3.8], 0.001**	**2.00 [1.77 – 3.14], 0.03***	**2.05[1.25 – 3.62], 0.004**
Age						
<30 years (reference)	**1**	1	1	1	1	1
≥ 30 years	**1.88 [1.25 - 2.84], 0.002***	1.26 [0.74 – 2.15], 0.40	1**.78 [1.19 - 2.7], 0.005***	1.00 [0.59- 1.71], 0.97	**1.91[1.27 – 2.87], 0.002***	1.13 [0.67 – 1.90], 0.66

*statistically significant p value< 0.05

Table 8: Multivariate logistic regression model of baseline factors associated with retention in HIV care at 3, 6 and 12 months ***for males.***

Baseline characteristics	**Retention at 3 months**		**Retention at 6 months**		**Retention at 12 months**	
	OR [95% CI], P value	**aOR [95% CI], P value**	**OR [95% CI], P value**	**aOR [95% CI], P value**	**OR [95% CI], P value**	**aOR [95% CI], P value**
Marital status						
Married	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
Single	0.66 [0.31- 1.44],0.30	0.87 [0.33 - 2.27], 0.78	1.36 [0.63 - 2.92], 0.43	2.54 [0.95 - 6.80], 0.06	1.22 [0.56 - 2.62], 0.66	1.93 [0.76 - 4.92],0.17
Widowed & Divorced	0.40 [0.61- 2.63], 0.34	0.27 [0.03 - 2.22], 0.22	0.25 [0.03 - 2.40], 0.23	0.19 [0.02 - 2.08], 0.17	0.78 [0.12 - 5.15], 0.80	0.67 [0.08 - 5.42], 0.71
CD4 cells/mm^3						
CD4 categories						
*<350	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
350-500	0.78 [0.28 - 2.14], 0.63	0.80 [0.27 – 2.34], 0.69	0.41 [0.15 - 1.10], 0.08	**0.34 [0.20-1.00], 0.05***	0.60 [0.22 - 1.60], 0.31	0.55 [0.19-1.54], 0.26
>500	**0.24 [0.06 - 0.88], 0.03***	**0.38 [0.61–0.94], 0.04***	0.54 [0.18 - 1.90],0.34	0.54 [0.14 - 1.97], 0.35	**0.22 [0.05 - 0.88], 0.03***	**0.22 [0.05 – 0.93], 0.04***
Age						
<30 years	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
≥ 30 years	**3.33 [1.50– 7.33], 0.003***	**3.4 [1.32– 8.70], 0.01***	**2.57 [1.17 - 5.59], 0.02**	**4.05[1.51-10.80], 0.005***	**2.6 [1.18 – 5.71], 0.02***	**3.17 [1.23- 8.16], 0.02***

* Statistically significant at 95% Confidence interval (P- value <0.05)

3.2.3 Factors associated with time to being lost to follow up: Survival Analysis.

Table 9 and *Figure 3* below describe the overall survival rates at 12 months after enrolment in HIV care. This study found that the probability of having patients retained in HIV care at 12 months post enrolment was about one-in-two (253/510). The study also noted that at three months (90 days), patients had a 66% chance of being retained, a survival function [0.66, 95 % CI (0.61-0.69)], and 174 patients (34%) were lost from HIV care. The greatest loss was on the first day as about nearly quarter (24%) of patients - 121 patients out of 510 study population - never honoured subsequent visits after the initial clinical visit. At six months (180 days) post enrolment ,an additional 7% (39 patients) were lost from HIV care, bringing the survival function to [0.58, 95 % CI (0.54-0.62)]. Between six months and 12 months a further 5% (44 patients) were lost from HIV care, bringing the total survival function down to 50% [0.50, 95% CI (0.45-0.54)].

The overall median survival time was 364 days IQR (18-366 days). The median survival time for females (361, IQR (3-366) days) was slightly lower than that for males (366 days IQR (44-366) days)).

Table 9: Summary of survival function at 12 months

Time (t) in days	Beginning total	Lost	Probability of being retained (S_t)
1	510	121	0.76 [0.72 - 0.80]
90	337	53	0.66 [0.61 - 0.69]
180	298	39	0.58 [0.54 - 0.62]
366	253	44	0.50 [0.45 - 0.53]

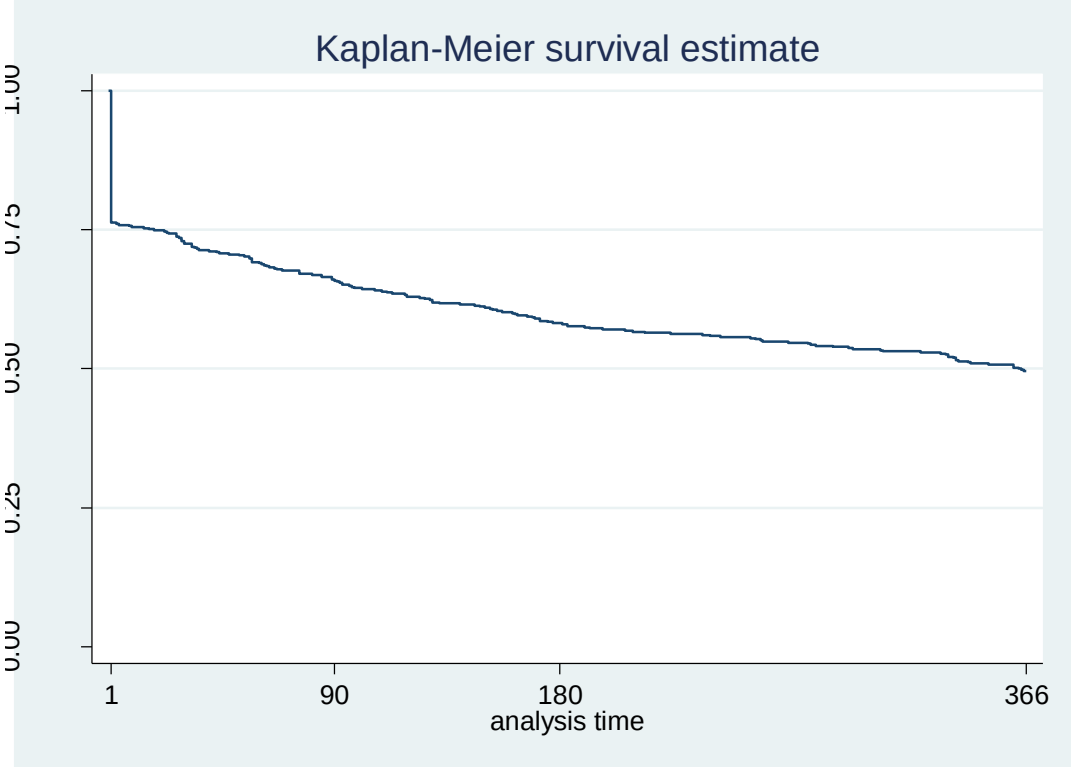

Figure 3: Survival function curve for retention at 12 months

3.2.4.1 Measures of association between Socio-demographic and baseline clinical characteristics and survival (retention) in HIV care at 12 months.

Table 10 and Table 11 show the relationship between the baseline social-demographic and clinical characteristics (marital status, age and pregnancy status (females only) with probability of surviving after 12 months. From the multivariate cox regression model, none of the study baseline sociodemographic and clinical factors showed statistical significance with time to being lost to HIV care at 12 months.

Table 10: Multivariate Cox regression models of baseline factors associated with retention in HIV care at 12 months ***for females****.*

Baseline clinical characteristics		**Crude HR, (95 % CI) P- value**	**Adjusted sHR**
Marital status	Married	*Reference*	*Reference*
	Single	**1.45 (1.08-1.95) 0.01***	1.31(0.93 – 1.86) 0.13
	Widowed and divorced	0.80 (0.34 -1.74) 0.58	1.00 (0.36 -2.80) 0.99
Baseline CD4 count	< 350	*Reference*	*Reference*
(cells/mm^3)	350-500	1.26 (0.84 - 1.90) 0.25	0.90 (0.57-1.44) 0.67
	>500	1.19 (0.85 - 1.68) 0.32	1.02 (0.70- 1.49) 0.90
Pregnancy status	Pregnant	R*eference*	*Reference*
	Not pregnant	**0.73 (0.55 – 0.99) 0.04***	0.72 (0.51 - 1.01) 0.67
Age group	< 30 years	*Reference*	*Reference*
	≥ 30 years	**0.59 (0.44-0.80) 0.001***	0.79 (0.54 - 1.17) 0.24

* Statistically significant at 95% Confidence interval (P- value <0.05)

Table 11: Multivariate Cox regression models of baseline factors associated with retention in HIV care 12 months ***for males****.*

Baseline clinical characteristics		**Crude HR, (95 % CI) P- value**	**Adjusted HR**
Marital status	Married	*Reference*	*Reference*
	Single	1.02 (0.42- 1.58) 0.93	0.81 (0.42- 1.58) 0.55
	Widowed and divorced	1.64 (0.49 -5.51) 0.42	1.80 (0.41 -7.99) 0.44
Baseline CD4 count = CD4	< 350	*Reference*	*Reference*
	350-500	1.10 (0.52 – 2.36) 0.79	1.09 (0.51 – 2.34) 0.81
	>500	2.13 (0.96 – 4.73) 0.06	2.05 (0.92 – 4.58) 0.08
Age group	< 30 years	*Reference*	*Reference*
	≥ 30 years	**0.55 (0.33-0.96) 0.04***	0.55 (0.28 - 1.06) 0.08

* Statistically significant at 95% Confidence interval (P- value <0.05)

CHAPTER 4: DISCUSSION OF RESULTS

The aim of this study was to determine factors associated with retention at 12 months after enrolment, among a cohort of patients classified as pre-Anti-Retroviral Treatment (pre-ART) at enrolment in an HIV Care and Treatment Program in Manzini region, Swaziland. The study found that, less than half (46%) of the study participants were retained in HIV care at 12 months post enrolment. Most of the patients who were not retained were lost within the first three months with many not honouring subsequent scheduled clinical appointments soon after enrolment.

The baseline socio-demographic and clinical factors that were associated with retention among women were: marital status, CD4 count and pregnancy status and among men it was age and CD4 count. All patients (men and women) with CD4 count > 500cell/mm^3 and single women were less likely to be retained in care compared to those with CD4 < 350 cell/mm^3 and married women respectively. Non pregnant women and older men ≥30 years were more likely to be retained in HIV care compared to pregnant and younger men, respectively. The other baseline factors (sex, level of education, employment status, nearest from clinic, WHO staging, BMI, TB status) were not associated with retention. In this study, there were very few reported deaths and transfer out but more patients who were lost to follow up.

4.1 Retention rates and factors associated with retention

A general observation noted from this study is that majority of patients that enroll for HIV care were women compared to men. This is a common finding that has been reported in other studies conducted in Southern Africa (10, 17, 21-23, 26). This is a result of the high incidence and prevalence rate of HIV among young women and a better health seeking behavior (1, 2, 13).

From this study it was also noted that just about half (46%) of the study participants enrolling for HIV chronic care were retained after a year of follow up. While the retention rates observed in this study are still relatively low, they are however higher than retention rates reported from similar studies from other countries including Sub-Saharan Africa (10, 16, 23, 26, 34, 36, 37, 44). From literature review the retention rates varied. This is largely due to the fact that different follow up studies, used varied ART eligibility criteria and differing definitions of retention (10,

11, 16, 17, 21-24, 26, 34-38). While in this study we used appointment dates keeping as a marker of retention, other studies were using presence of up to date CD4 results as an indicator of retention if patient was not reported dead or lost to follow up (10, 11, 16, 17, 21-24, 26, 34-38). Observing the clinical visit dates may have contributed to higher retention rates as it underestimates the laboratory system challenges of blood sample collection and return of laboratory result that may have a negative influence on retention. Appointment dates keeping is largely a reflection of patient's adherence habits to treatment plans. If we had used the presence of latest CD4 count as a marker of retention the rates would have been lower as point of care CD4 testing is only conducted for patients enrolling care to help quickly determine eligibility status.

The differing definitions of retention in different studies also make generalizability of findings difficult. To overcome this variation Rosen et al. (2011) defined three stages that can be studied and be used to define retention (10). However, the Rosen definitions were not entirely applicable in this study. There was no HIV testing data and in Swaziland, all patients qualify to enroll for pre-ART enrolment regardless of eligibility criteria as long as they have a positive HIV diagnosis. In addition, the same clinic settings and monitoring systems apply for both pre-ART and ART patients. Hence, this study followed patients throughout the continuum of care, from the time they enrolled into pre-ART care for a period of 12 months (including patients who eventually initiated ART in the 12 months period) in accordance to the Swaziland standard of practice (6, 9).

There was a noted cumulative decline in retention rates over the 12 months period but the greatest loss was noted within the first three months post enrolment into HIV care. This was observed despite the fact that at the time of the study, Swaziland was already implementing some of the programmatic strategies that have been proven in previous studies to improve retention such as increasing ART eligibility criteria from ≤ 200 to ≤ 350 cells/mm^3. Availability of POC CD4 testing at baseline, clinical mentoring support, prescribing prophylactic CTX treatment to pre-ART patients, and telephone and community follow up system for patients who missed appointments and decentralization of services (6, 10, 14).

Majority of the patients who were dropped of HIV care did not honor subsequent appointments after the initial visit. As a result, they did not complete the necessary ART eligibility assessment

or initiation preparations. This finding is consistent with most studies that showed that patients are lost soon after enrolment for HIV chronic care (17, 21-24, 26, 38).

Furthermore, studies have also reported that most of the patients not retained in care are lost-to-follow-up with very few reported deaths or transfer-outs. This finding is consistent with the study results as mortality rates were relatively lower than other studies done in the Sub-Saharan region (21, 23). The death rates have declined mainly because in recent years HIV testing coverage has rapidly expanded, eligibility thresholds increased from CD4 $\leq$ 200 to $\leq$ 350 and then to $\leq$ 500 cells/mm^3, and eventually to treat all, resulting in more patients enrolling for HIV chronic care and initiating ART much earlier. In addition, coupled with higher baseline CD4 count, patients who enroll in HIV chronic care early have less chances of developing severe opportunistic infection like TB that eventually result in premature deaths (21, 37, 51)

This study results also showed that the baseline CD4 count level is a significant predictor of being retained in HIV care regardless of sex. In both males and females, CD4 count is inversely associated with retention in HIV care. Patients who had a baseline CD4 count less than 350 cells/mm^3 were more likely to be retained in HIV care compared to those with higher baseline CD4 count above 500 cells/mm^3. This finding is consistent with other studies that showed patients with lower CD4 count and eligible for ART were more likely to be retained in HIV care (21, 34). In this study setting patients with CD4 less than a 350 cells/mm^3 at time of study were also eligible to initiate ART hence more likely to be retained. The challenge with this finding is that patients with higher CD4 counts ≥350 cells/mm^3 are lost from care and only return when their immune system have deteriorated and feel sick. This is not good as it leads to poor health outcomes as observed in some studies (26). In 2016, the country adopted the treat all policy in response to the scientific evidence and WHO recommendations that recommended early ART initiation for all people diagnosed with HIV regardless of CD4 count or WHO staging (8). This policy has the potential to improve retention as patients will initiate ART early.

In this study, the comparatively higher median CD4 count 357 cells/mm^3 (IQR 216 -546 cells/mm^3) at baseline, the proportion of eligible patients that eventually initiated ART all contributed to the low occurrence of opportunistic infections such as TB and low death rates, resulting in higher overall retention rates. However, loss due to mortality may also be relatively low possibly because the study was conducted at primary health care level where most sick

patients are referred to regional hospitals or health centers for further investigations and management.

In this study, patients' sex was found not to be a predictor of retention in HIV care. This was a surprising finding as most studies done in Southern Africa have reported that being male was associated with a greater likelihood of being lost from both pre-ART and ART care (17, 21, 22, 34, 42). A common finding reported in these studies was that men were diagnosed and presenting for enrolment into HIV care with very severe immune suppression (low CD4 counts) or with advanced disease hence were more likely to be lost due to mortality (17, 21, 22, 34).

Our findings are similar to a study conducted in Johannesburg, South Africa where the baseline median CD4 count was even higher 458 (IQR 394– 585) than the one we reported in this study and also in Malawi where the median CD4 count was slightly lower than the one observed in this study 294 (IQR 173-474) but still higher than the others (37, 39). A possible reason for the noted difference in this study is that the participants presented with much higher median CD4 count at enrolment compared to the ones reported in other studies. A general observation in all the studies, however is that men tend to enroll for pre-ART care with much lower baseline CD4 count compared to women (17, 21, 22, 34, 42).

In this study, among men unlike in women, age was a significant predictor of retention at all time periods of HIV care, with older men ≥ 30 years being more likely to be retained in HIV care than younger men < 30 years old. Other studies have reported similar findings even though they did not segregate results by sex (17, 21, 23, 25, 34, 35). It is not so clear why young patients are lost in HIV care. Some qualitative studies have reported socio-structural reasons such distance from health facility, availability and cost of transport to health care services as potential contributing factors to patients being lost to care. This study did not ascertain why patients were lost, or those eligible did not initiate ART. However it can be assumed that the similar psycho social reasons may have contributed to the retention rates observed. Another report indicated that feeling healthy as a cause for delayed care and fear of stigma and discrimination by family members or community. Knowing somebody who is living with HIV improved retention (22, 23) .

Among females, marital status and pregnancy status were associated with retention in HIV care at three, six and 12 months respectively. At all three time points pregnant women were less likely to be retained in HIV care compared to married and or non-pregnant women, respectively. These

findings are consistent with results from studies conducted in Malawi and Mozambique, where it was reported that pregnant women were more likely to be lost from care, not complete ART eligibility assessment or initiate ART, mainly because they are diagnosed early and they self-rate their health status as good and seeing no need for Pre-ART/ ART care.

Other studies have also reported that patients who self-refer for HIV testing services tend to have better retention rates in HIV care if diagnosed positive than patients from provider initiated testing e.g. from outpatient departments including antenatal care (ANC) (38, 41). The poor retention outcomes among pregnant women cannot be taken lightly as it counteracts the goal of prevention of mother to child transmission of HIV. In Swaziland however, the mother to child transmission rate is on the decline as ART uptake among pregnant women diagnosed at ANC is improving and also because pregnant women are given the infant HIV prophylaxes from the first ANC visit (6, 9, 32, 50). Nonetheless, this study cannot ascertain if the pregnant women that were also lost from HIV care were also lost from ANC or PNC clinics. It can therefore be assumed that cited health system, socio economic and structural factors such as distance and availability of transport and long waiting time at ANC could be barriers to retention for both single and pregnant women (37, 41). From the literature one could not ascertain the reasons why married women are more likely to be retained than single women.

Regarding influence of employment and level of education on retention in HIV care, literature on this association shows a mixture of results depending on the context of the study. Similar to our findings, other studies found no association between employment status and level of education and retention in HIV care (44, 51). However, a study conducted in Johannesburg, South Africa reported better retention for those employed than those unemployed patients (39) . Poor retention rates were reported in rural Mozambique and India among those who were illiterate (23, 26). Other studies have also reported low BMI and advanced clinical stage as being associated with increased mortality and lost to follow up (21). In our study findings, however, these were not significant. A general observation is that factors associated with failure to initiate ART are similar to those linked with loss from pre-ART care and vice versa. These include being male, having a low CD4 count, failure to complete ART eligibility assessment, being non-eligible and self-rated poor state of health. These factors tend to be the same as those associated with lost-to-follow-up and death at any time point (21, 36, 37, 48). In addition, the presence of more risk

factors was associated with higher rates of being lost from HIV care than having none or fewer factors (38).

From qualitative research the reported cause of attrition are multifactorial, ranging from patient factors to socio-economic and structural factors. The commonly reported cause for poor attrition is transport cost and distance from health facility, followed by fear of stigma and discrimination following disclosure (22, 23, 42). Other reported reasons include being illiterate, coming from a rural or disadvantaged community with no home electricity (23, 26). Health system factors cited include staff shortages and long waiting time. perceived good health, fear of drug side effects, competing work priorities and need to take time off from work (23, 37, 42).

Recommended strategies to improve retention include decentralization of health service delivery, task shifting with peer navigators among health workers, and use of efficient technology that speed up acquisition uptake of HIV services and retention such mobile phones and point of care CD4 testing (37, 42, 52, 53). Swaziland was implementing these initiatives at the time of study, and retention rates were still comparatively lower than the expected standard benchmark. In addition, this study was conducted at clinic level where services have been decentralized. However, some facilities did not have the capacity to diagnose or treat TB-HIV co-infected patients.

In the Cox proportional hazard model, no patient factor (socio demographic or clinical) was found to be significantly associated with to loss-to-follow-up after 12 months of being in HIV care. Other studies have also reported same results of none of the patient factors having an influence on lost-to-follow-up after 12 months in care (44). This underscores the complex context and specific interplay of patient and socio structural factors influencing (26). Greater improvements in retention rates can be realized through a multi sectorial approach that addresses both the structural and socio-economic factors to complement the efforts of the Health sector in improving service coverage and quality of care.

4.2 Study Limitations

This study was not void of limitations. However, the limitations are not so severe as to discard the study findings and analysis. A major limitation of the study was the missing information in some clinical patient records. Another limitation is that, the study was conducted at primary health care level which are most manned by nurses with poor data entry skills and some of the treatment outcomes for referred clients were not recorded. Patient data was not sought at referral hospital and this may explain the low mortality rates reported in this study. Furthermore, patients who might have been classified as not retained in HIV care in the study period, could have returned but not captured in the system as patients move in and out of clinical care. On the other hand, some patients may be classified as retained in clinical care even after dropping-off for some time for whatever reason. In addition, lost patients could have died or re-enrolled for pre-ART in other sites. Other limitations included missing patients' reasons for not being retained in services or for not initiating ART if eligible. This information is key to addressing specific reasons and to provide evidence informed policy and programming in the health sector.

CHAPTER 5: CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

The aim of this study was to determine the factors associated with retention in HIV Care at 12 months after enrolment among a cohort of patients classified as pre-Anti-Retroviral Treatment (pre-ART) at enrolment in an HIV Care and Treatment Program in Manzini region, Swaziland.

The study was able to establish that, the socio demographic and clinical factors that were found to be significantly influencing retention in HIV care after 12 months among men were baseline CD4 count and age, and among females, it was baseline CD4 count, marital and pregnancy status. The other socio demographic factors (level of education, employment status, proximity to clinic) and clinical factors (functional status, Body Mass Index, TB status, WHO clinical staging) were not associated with retention in HIV care at any of the time frames (three, six and 12 months) of the study.

Retaining patients in HIV care was a challenge in the study sites, with only half of the study participants retained in HIV care in a period of 12 months post enrolment. Lost-to-follow-up was the common reason for not being retained in care than loss due to death or transfer out. Most patients were lost in the first three months, soon after the day of enrolment, with many not coming for subsequent scheduled visits. Patients most likely to be lost from HIV care include those assessed as ineligible to initiate ART, especially those presenting with higher CD4 count > 500 cells/mm^3, young men, single and pregnant women. Other plausible reasons for poor retention include lack of transport, high transport fees, poverty, stigma and discrimination and poor health staff attitude (22, 23, 37, 41).

Therefore, based on the aforementioned, the findings in this study can be generalized to other regions of Swaziland as the country has a generalized epidemic and a standard package of HIV care and service delivery. In addition, the results can also be generalized to other countries with similar populations, epidemic levels and socio economic status.

5.2 Recommendations

This study, the first of its kind in Swaziland has provided the baseline information to strengthen retention in HIV care and improve clinical outcomes of patients enrolled for pre-ART care at clinic level in Swaziland. There is need to use evidence to inform policy, programming, prioritization and resource allocation. In a bid to help the implementation of the findings, key recommendations targeted at policy, strategic, programme and research levels of the response are made, and these are:

a) Improve quality of psychosocial counselling and support; since patients are lost from care within the first three months post enrolment with many not honoring subsequent scheduled visit after the enrolment visit. Efforts to improve retention rates should therefore start from the day patients enroll into pre-ART care. These should include building the capacity of health care workers to provide quality psychosocial assessment, counselling and support. Equipping health care workers is essential in order to help them easily identify and address psycho-socio structural barriers (e.g. transport challenges, fear of stigma, and perceived healthy status) that may hinder patients from honoring subsequent clinical appointments. An additional goal of the psychosocial assessment and counseling would be to get the client self-motivated to adhere to treatment plan and be retained in ART care for life in order to achieve good clinical outcomes and HIV epidemic control. Particular focus should be on supporting young men, single and or pregnant women and all patients with higher CD4 count > 500 cells/mm^3 services. This is the most vulnerable and high risk group of patients that is not initiated on ART in the first three months.

b) Improve data systems and quality: Efforts to improve data systems and quality are also needed for accurate tracking of patient outcomes. In this study, quite a number of files could not be located, and some had key data elements missing and outcomes of referred clients were undocumented by referring sites. Implementing real-time electronic system with unique patient identifiers will reduce errors, improve the quality and flow of data, and ultimately improve timely tracking of patient outcomes, especially among referred clients between health facilities.

c) Multi sectorial strategies: Various literature shows that retention in HIV care is not only a result of patient factors but rather the interaction of patient factors with service provider as well as socio economic and structural factors, which are largely context specific. Commonly cited factors associated with poor retention includes lack of transport/ transport fees, poverty, stigma and discrimination and poor health staff attitude (26, 41). Therefore a multi sectorial approaches/strategies that addresses both the structural and socio-economic factors to complement the efforts of the health sector in improving in improving overall retention of clients enrolled in HIV care are recommended.

d) Research: Evaluation of current patient follow-up strategies: In the study, only half of patients were retained in HIV care. This finding is worrying when considering that Swaziland has standard operation procedures that guide follow-up of patients who do not honour appointments. Even though this study did not seek to determine if follow ups were made the study findings implies that the current practice is not as effective for the new enrolling pre-ART patients who may not initiate ART on the same day of testing or enrolment to care. Hence, there is need for research to evaluate the effectiveness of national patient follow-up strategies. Furthermore, there is need to study the effects of *Treat All* policy (including same day initiation) on retention especially on the population identified in this study as being at risk of being lost from HIV care; those presenting with higher CD4 count > 500 cells/mm^3 , young men, single and pregnant women.

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Annex 1: Definition of terms

These definitions have been adopted from Swaziland Ministry of Health. Patient linkage, retention and follow up in HIV care Standard operation Procedures. Mbabane, Swaziland: 2012.

Pre-ART - refers to the period that starts when a person tests HIV positive and ends when that person initiates ART.

Pre-ART care – comprises of a package of health interventions provided during the pre-ART period. These include assessment of patient eligibility for starting ART, serial routine laboratory investigations, e.g. CD4 counts, screening for TB and other opportunistic infections, provision of prophylactic treatment mainly cotrimoxazole and Isoniazide prophylactic therapy (IPT), nutritional assessment and therapy and ongoing counseling.

Enrolment into pre-ART care – a structured and active process of registering HIV positive individuals into the healthcare system of an HIV-care facility by issuing them with a unique patient identifier and opening clinical files (medical records) for them. This can be done before or after ART eligibility assessment.

Retention - a patient is said to be retained if he/she has attended the clinic within the last 90 days for medicine collection, laboratory testing and or clinical review and is not documented as "dead, "stopped treatment" or "loss-to-follow-up".

Lost to follow up- a patient is classified as "lost-to-follow-up" if they have not been to an HIV care clinic for more than 90 days since last appointment.

Missed appointments - patients who are more than three days but less than or equal to seven days late for their expected appointment.

Defaulters - patients who are more than 7 days, but less than or equal to 90 days, late for their expected appointment.

ART eligible – a patient is said to eligible to start ART if they are assessed as WHO stage 3 or 4 or have a CD4 count < 350 cells/mm^3.

ART eligibility assessment - the process of determining, using the clinical WHO staging and or CD4 count level, if a patient qualifies to start ART.

Annex 2: Data extraction sheet

General Information				
Name of Data collector				
Facility Name				Date of data collection: (dd/mm/yyyy)
Research No.				Pre-ART enrolment date ***(as appears on pre-ART register)***
Pre-ART No				
Transfer –In	yes	No		
Patient Socio Demographic details				
DOB (dd/mm/yyyy)				Sex:
Physical address/ area	Within catchment area			Outside catchment area
Occupation	Unemployed	Employed	Not stated	
Marital status	Married	Single	Widowed	Divorced
Education level	Primary	Secondary	High school	Tertiary
Nearest clinic				
Date Tested Positive				

Pre-ART Enrolment Visit: Baseline assessment					
Date of pre-ART baseline assessment **(*as appears on patient file)***(dd/mm/yyyy)					
Weight kg :	Height :	BMI:	MUAC	Functional status: Ambulatory Working Bedridden	
Active TB		No	Yes	Type:	
TB screening		Negative	Positive	Not done	
Pregnant		Yes	No	Last menstrual period (LMP) date dd/mm/yyy	LMP not stated
Substance history (*circle)*		Smoking: Yes No		Alcohol : Yes No Other :	
WHO stage at enrolment		1	2	3	Not stated
1st CD4 Result			Date taken (dd/mm/yyyy):		
Results from Pima machine		Yes	No		
ART eligible at enrolment		Yes	No		

Pre-ART care : Clinical visits						
Visit date dd/mm/yyyy	weight	CD4 result	CD4 from Pima (Y/N)	Date taken	TB Screening (pos/neg)	Next appointment date dd/mm/yyyy
1.						
2.						
3.						
4.						
5.						
6.						
7.						
8.						
9.						
10.						
11.						

General comments

ART Initiation Visit					
Date of ARTinitiation(dd/mm/yyyy)					Weight :
Height:	BMI:	MUAC:		Functional Status: Ambulatory Working Bedridden	
Active TB		No		Yes if yes date of TB treatment initiation	
TB screening		Negative		Positive	Screening not done
WHO stage		1	2	3	4	Stage not stated

CD4 Result		Results from Pima : Yes NO	
Pregnant	Yes	No	Last menstrual period (LMP) date dd/mm/yyyy
Substance history (*circle)*	Smoking: Yes No	Alcohol : Yes No	Other:
Return date (dd/mm/yyyy)			
Comments:			

ART Care : Clinical visits

Visit date	Weight	Functional status	WHO stage	CD4 count	Date taken	Next visit date
1.						
2.						
3.						
4.						
5.						
6.						
7.						

Clinical Outcomes			
Loss to follow	Yes	No	Last clinic visit date (dd/mm/yyyy):
initiated on ART	Yes	No	Date (dd/mm/yyyy):
Transfer -out	Yes	No	Date (dd/mm/yyyy):
Dead	Yes	No	Date (dd/mm/yyyy):

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M131174

NAME: (Principal Investigator) Dr Nomthandazo Lukhele

DEPARTMENT: School of Public Health
Health Systems and Policy

PROJECT TITLE: Factors Associated with Retention among a Cohort of Patients Classified as Pre-Anti Retroviral Treatment (Pre-ART) in an HIV Care and Treatment Programme in Swaziland

DATE CONSIDERED: 29/11/2013

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Dr Aziza Mwisongo

APPROVED BY:
Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 07/02/2014

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature

18/02/2014
M131174Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES