Determinants of Long Term Survival of Patients initiated on HAART at The AIDS Support Organization, Uganda

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Keywords

Antiretroviral therapy

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ABSTRACT

It is well documented that mortality rates have decreased and the survival of HIV and AIDS patients has been prolonged since the introduction of highly active antiretroviral therapy (HAART) in 1996. Although HAART has dramatically improved the prognosis of HIV disease, some HIV patients on HAART still die of HIV related illnesses. It is important to understand what these factors are in order to mitigate the impact on these factors on patient survival and achieve better outcome for these patients. The aim of this study was to determine risk factors for long term survival of patients on HAART in Uganda.

Data for 2,244 out of 30,000 clients receiving care and treatment at TASO Entebbe was retrospectively analyzed. TASO Entebbe is a non-governmental HIV clinic that provides care and treatment to HIV positive clients. Long term survival in this case was defined as survival for more than 5 years after initiation on HAART. Logistic regression and survival analysis were conducted.

Female clients had a 12% lower risk of death compared to the male clients (AHR=0.88 [CI: 0.443-0.936]). Clients that had pulmonary TB had 1.3 times higher risk of death compared to clients that did not have pulmonary TB (AHR=1.33 [CI: 1.162-2.733]). Clients initiated at CD4 cell counts less than 250 cells/µl had almost 7 times higher adjusted odds of death compared to those initiated at CD4 cell counts greater than 500 cells/µl (AOR= 6.95 [CI: 2.882-16.744]) and clients initiated at CD4 cell counts between 250 cells/µl and 500 cells/µl almost 3 times higher adjusted odds of death compared to clients initiated at CD4 cell counts greater than 500 cells/µl (AOR 2.56 [CI: 1.004-6.520]).

It is recommended that an aggressive HIV testing strategy be put in place to facilitate early identification of HIV positive patients. Early identification would enable early initiation into HAART well before the CD4 cell counts fall below 500 cells/µl. The observed higher risk of mortality amongst men suggests interventions to promote early HIV testing and treatment initiation amongst men. The observed high risk of mortality for patients with pulmonary TB, calls for aggressive TB case finding and treatment of positive in order to reduce the HIV/TB related mortality.

DECLARATION

I declare that *Determinants of Long Term Survival of Patients initiated on HAART at The AIDS Support Organization, Uganda* is my own work, that it has not been submitted before for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged as complete references.

Signed: Awor **Date: 22nd March 2017**

Awor Anna Colletar

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CHAPTER ONE
INTRODUCTION

1.1 Background

HIV/AIDS remains an important public health problem despite significant efforts worldwide to combat the disease (Pavlova-McCalla et al., 2012). In 2014, approximately 36.9 million people worldwide were thought to be infected with HIV. The vast majority of this number live in low- and middle- income countries (AIDSinfo, 2014). Sub-Saharan Africa is the most affected region, with 25.8 million people living with HIV in 2014; which accounts for almost 70% of the total new HIV infections globally (WHO, 2014). Although the global HIV prevalence is estimated at 0.8% in 2014, there are variations across regions ranging from a low of 0.1% in the Middle East and North Africa to a high of 4.8% in sub-Saharan Africa (WHO, 2014). Left untreated, HIV/AIDS is inevitably fatal, with a median survival time from sero-conversion of 8 to 10 years (Sabin, 2013). It is well known that mortality rates have decreased and survival of HIV patients has been prolonged since the introduction of highly active antiretroviral therapy (HAART) in 1996 (Stein et al., 2006; Murphy et al., 2001; Hogg et al., 1999).

HAART has dramatically changed the prognosis of HIV disease (Jaggy et al., 2003) and the clinical benefits of HAART for HIV/AIDS patients, in terms of mortality reduction and improved quality of life is well documented (Braitstein et al., 2006; Egger et al., 2002). In resource-poor countries, access to antiretroviral therapy (ART) has improved between 2009 and 2014 and mortality rates among treated patients have declined substantially (Azin, 2010). In 2014, 14.9 million people living with HIV were receiving antiretroviral therapy (ART) globally, of which 13.5 million were receiving ART in low- and middle-income countries (WHO, 2014). This achievement has been mainly due to two reasons:

i) reduction of the cost of anti-retroviral (ARV) drugs which led to an increase in access and availability of HIV treatment in Sub-Saharan Africa;
ii) the implementation of WHO guidelines promoting scaling-up by task shifting for clinical decision-making to less specialised health-care workers facilitated increases in provision of both care and treatment to HIV patients (Gilks et al., 2006).

HIV patients are now surviving longer and it has been noted that long-term survival in HIV-positive populations with access to effective HIV prevention, care and treatment appears to be

approaching that of the general population (van Sighem et al., 2010). This was observed in a large study in rural South Africa, which showed that adult life expectancy rose from 49.2 years in 2003 (before ART became widely available) to 60.5 years in 2011 (Bor, Herbst, Newell, & Bärnighausen, 2013). Studies have shown declining rates of HIV-related deaths compared to non-HIV related deaths since the introduction of HAART (Lohse et al., 2007; d'Arminio et al., 2007). The annual number of people dying from HIV-related causes has decreased by 29% in recent years from 1.7 million in 2009 to 1.2 million in 2014 (WHO, 2014). However, the number of HIV related deaths is still high compared to other regions: 66% of the global HIV related deaths occur in sub-Saharan Africa.

Treatment of patients with HIV/AIDS is complex with chronic pathologies associated with immunodeficiency, chronic viral infection and socio-behavioral factors (McManus et al., 2012). These pathologies include opportunistic infections, neoplasms and organ systems pathologies that affect patients with HIV/AIDS (Levy, 2009). The severity of these pathologies depends on the level of immunity of the patients, with patients having lower immunity experiencing worse outcomes. Observational cohort studies have shown that the probability of staying alive on HAART largely depends on adherence to treatment and the degree of immunodeficiency at the time of HAART initiation (McManus et al., 2012). In particular patients that adhere to treatment have been known to have better prognosis. While biomedical factors associated with long term survival of patients on ART are well documented, socio-economic and behavioral factors are not well documented. Beyond clinical parameters, pre-existing characteristics of individuals such as demographics, socioeconomic status, mental disorders or substance abuse might also affect the rate of recovery after ART initiation, and therefore survival.

Like other countries in sub-Saharan Africa, Uganda continues to bear a huge burden of HIV/AIDS with an estimated 1.6 million people living with HIV/AIDS in 2014 (UNAIDS, 2014). In Uganda the ART coverage was about 76.5% in 2013 for adults while the provision of cotrimoxazole prophylaxis to prevent opportunistic infections has a higher coverage (94%). Despite this high coverage of patients on ART, about 63,000 persons living with HIV (PLHIV) were estimated to have died of AIDS-related causes in 2012. In Uganda, HIV positive patients are initiated on

HAART based on CD4 cell counts cut off of 350 cell/µl, WHO clinical stage, hemoglobin level and the total lymphocyte count.

1.2 Problem Statement

Since the introduction of HAART there are reductions in HIV-related deaths, as well as increased life expectancy for newly diagnosed HIV patients. One reason for this increase, is the scale up of HAART enabling eligible HIV access and initiate HAART promptly. Although HAART has improved the survival of HIV infected patient, compared to patients in high-income countries, patients in resource-poor countries have higher mortality rates (Shibre, Bekele, & Abera, 2014). To minimize such HIV related deaths, there is need to identify risk factors and potential causes of death. Existing knowledge of factors associated with survival of HIV patients has majorly been done in patients not yet initiated on HAART. The studies have also mostly focused on relatively small cohorts, and that were followed over a short time period. In addition, the few studies done in sub-Saharan Africa have been conducted on patients managed by public health facilities. Better knowledge of prognostic factors would allow closer follow-up of and more targeted interventions for HIV positive patient initiated on HAART; thus reducing excess mortality. There is need therefore to understand factors associated with survival for patients that have been initiated into HAART particularly in a non-government health facility setting.

1.3 Outline of the thesis

A brief background to the study and the research problem that the study sought to investigate was presented in chapter 1. Literature in relation to survival of HIV positive patients initiated in HAART, the conceptual framework that guided the study, aims and objectives of the study are presented in chapter 2. The methodology used, study population, data management, analysis and the ethical consideration are presented in chapter 3. The results from the analysis of patient data are presented in chapters 4 and 5: univariate and bivariate analysis are presented in chapter 4 while results from the multivariate models fitted to the data are presented in chapter 5. In chapter 6 the discussion of results and recommendations are presented.

CHAPTER TWO
LITERATURE REVIEW

2.1 Introduction

This chapter presented a review of literature pertaining to factors associated with survival of HIV positive patients initiated into HAART. In the first part a review of literature around the relationship between different demographic factors, socio-economic factors and behavioral factors and clinical factors and survival on HAART is presented. The focus then shifts to the second part which reviews literature on the conceptual framework that was used in the current study.

Knowledge on HIV/AIDS and factors that predict long term survival of HIV infected patients initiated on HAART are changing rapidly (AIDSinfo, 2014). Although factors that determine mortality in patients before the introduction of HAART are well documented, the effects of these factors with the introduction of HAART especially in resource poor settings have not been fully investigated. The factors that have been found to affect mortality for patients on ART include: viral load, CD4 cell counts, total lymphocytes, body mass index (BMI) and adherence. Although these factors tend to be similar across the world, there are some striking differences in their relative frequency between well-resourced and resource-poor settings.

2.1 Demographic factors associated with survival on HIV treatment

Studies have shown that survival on ART is affected by a number of demographic factors. On the whole mixed results have been found. Highlighted below are findings of various studies with regards to how demographic factors affect survival of patients on HAART.

2.1.1 Gender

Studies have shown mixed results in relation to the association of gender and survival of patients on HAART have been found. For example, a study in a rural health center in Cameroon found that male subjects had almost double the risk for mortality compared to females (HR 1.73; 1.37–2.19) (Isidore et al., 2009). Several authors described gender differences in ART outcomes (Sterling et al., 2001; Moore et al., 2002; Kremer & Sonnenberg-Schwan 2003; Perez-Hoyos et al., 2003), while others found no gender differences associated with ART (Egger et al., 2002; Bourgeois et al., 2005; Nicastri et al., 2005; Braitstein et al., 2006). Potential factors that have

been found to contribute to gender differences in relation to survival on HAART include differences in treatment adherence, risk behavior, financial accessibility, and early access to antiretroviral treatment (Le Coeur et al., 2007), which could all explain better survival. Especially for men stigma, family and work responsibilities may impact access to treatment. Consequently, men are more immune compromised at HAART initiation compared to women (Cornell et al., 2009).

2.1.2 Age

Age at diagnosis and age at ART initiation have been found to be associated with the rate and extent of immunologic recovery (Li et al., 2011). The effects of aging on survival therefore need to be considered in addition to the effects of increased duration of illness (McManus et al., 2012). There remains a need to better understand long-term survival in aging. It has been found that the relative risk of death within 5 years after an HIV diagnosis was greater for persons who were older at the time of diagnosis compared to those who were younger (Jevtović et al., 2007). However, this effect was more evident for patients with CD4 cell counts less than 350 cells/µl compared to patients with CD4 cell counts of greater than 350 cells/µl. Studies have also found that age at sero-conversion seems to have become a less important prognostic factor for progression to AIDS since the introduction of HAART (Jevtović et al., 2007). This is perhaps surprising since reconstitution of immune function is likely to be more difficult in older people given that clients over the age of 50 years are less likely to have their CD4 cell counts increased when receiving HAART (Steinman, 1986, Grabar et al., 2004).

2.2 Socioeconomic factors

Studies observing populations before the introduction of HAART found that socioeconomic factors were not significantly associated with HIV-related mortality (Pavlova-McCalla et al., 2012). In the post-HAART period various socioeconomic factors were inconsistently associated with HIV/AIDS mortality risk in studies adjusting for HAART use. Queries whether the social and economic situations of HIV-infected individuals explain variations in the disease progression and survival are supported by the framework of social production of disease and political economy of health (Pavlova-McCalla et al., 2012). According to this framework, a person's relative social and

economic positioning shapes behavior, and the relationship between subordinate-dominant groups affects patterns of disease through material and social inequalities (Zierler & Krieger, 1997).

2.3 Behavioral factors

The behavioral factors that have been found to be associated with survival on ART include use of alcohol and other drugs as well as tobacco use.

2.3.1 Alcohol and other drugs use

Studies of alcohol use in HIV infected patients have resulted in conflicting and limited information regarding prevalence, as well as the effects of alcohol use on HIV replication, disease progression and response to ART (Maria et al,. 2003). Heavy alcohol users receiving antiretroviral therapy were twice as likely to have CD4 cell counts below 500 cells/µl compared to light or non-drinkers (OR 2.31 [95% CI: 1-5.5] and HAART-treated heavy alcohol users were four times less likely to achieve a positive virological response (OR 4.13 [95% CI, 1.2-17] (Maria et al., 2003). Henrich et al. (2007) examined association of alcohol abuse and injection drug use (IDU) with the immunologic and virological responses to highly active antiretroviral treatment (HAART) in urban community health clinics. In a linear regression model adjusted for age, gender, and baseline CD4 cell count, history of IDU only and a combination of alcohol abuse and IDU were associated with a lesser increase in CD4 cell count after HAART compared with those with neither alcohol nor IDU. The possible reason for this is that alcohol consumption may impact response to antiretroviral therapy through its alterations of immune responses, augmented by nutritional deficiencies that can further compromise the immune system, as well as its potential effect on adherence to treatment (Maria et al., 2003).

2.3.2 Tobacco use

Chronic manifestations such as cancers or cardiovascular diseases are becoming an emerging problem among HIV-infected persons in industrialized countries (Lewden et al., 2005). Tobacco consumption in HIV/AIDS patients from industrialized countries has been shown to be elevated and higher than in the general population with approximately half of patients being regular smokers (Antoine et al., 2009). Recent reports emphasized that tobacco industries are entering actively the market of low-resource countries, including Africa, in order to compensate for their

losses in the Northern Hemisphere at a time when the demand in these countries is decreasing (Cherif, 2005). Tobacco smoking is associated with poorer response to antiretroviral therapy and worse disease progression in HIV/AIDS patients especially women (Reynolds, 2009). An analysis of 924 participants starting HAART in women's Interagency HIV study showed that women who smoked cigarettes had poorer virological and immunological response to HAART, lower CD4 cell counts, higher HIV viral loads, a 36% greater likelihood of developing AIDS-defining illnesses, and a 53% higher risk of death compared with non-smokers. The rate of specifically AIDS-related death was similar (Feldman et al., 2006). The authors concluded that some of the benefits provided by HAART are not revealed in cigarette smokers, and emphasized the need for smoking cessation efforts targeting HIV positive women (Feldman et al., 2006). In a study conducted by the University of Miami, the researcher found that HIV positive smokers response to HAART decreased by 40% as measured through drug levels in the body, CD4 cell counts and viral loads.

2.4 Clinical factors

HIV RNA (viral load) and CD4 T lymphocyte (CD4) cell counts are the two surrogate markers of antiretroviral treatment (ART) responses and HIV disease progression that have been used for decades to manage and monitor HIV infection (AIDSinfo, 2014). In the case of viral load, patient's pre-ART viral load level and the magnitude of viral load decline after initiation of ART provide prognostic information about the probability of disease progression CD4 cell counts provides information on the overall immune function of an HIV-infected patient (Murray, Elashoff, Iacono-Connors, Cvetkovich, & Struble, 1999). The measurement is critical in establishing thresholds for the initiation and discontinuation of opportunistic infection prophylaxis and in assessing the urgency to initiate ART (AIDSinfo, 2014).

2.4.1 Baseline CD4 cell counts at HIV Diagnosis

CD4 cell count is an important immunologic marker of progression of HIV infection and a key predictor of mortality (Egger et al., 2002; WHO, 2006). CD4 cell counts should be measured in all patients at entry into care. It is the key factor in determining the need to initiate opportunistic infection prophylaxis. The current World Health Organization treatment guidelines recommend initiation of ART before the CD4 cell counts reaches less than 500 cells/µl (WHO, 2013). A study in Serbia showed that the proportion of patients with a baseline CD4 cell counts below 100 cells/µl

at HIV diagnosis were 6 times more likely to die compared to those that had CD4 cell counts greater than 100 cells/µl (OR = 6.2 [CI: 1.8-21.0]) (Jevtović et al., 2007). Another study conducted in Durban, South Africa, indicates that CD4 cell counts below 50 cell/µl at diagnosis was the strongest predictor of mortality in HIV patients after they started ART (Ojukutu et al., 2008). Studies have also found that mortality was roughly two times higher for patients who began ART with a severe immune-depression (CD4 cell counts less than 50 cell/µl) (Isidore et al., 2009; Kabugo et al., 2005; Laurent et al., 2005b; Sterne et al., 2005; Crum et al., 2006; Etard et al., 2006; Kheang, 2006; Egger, 2007). It has been noted that patients starting treatment at low counts probably never reach CD4 cell counts anywhere near normal. This adds to the weight of evidence that starting treatment earlier, before CD4 cell counts falls below 350 cells/µl could lead to better survival (Huges et al., 2007). The level of CD4 cell count at the commencement of HAART has an impact on immunological recovery, with higher CD4 cell counts resulting into favorable treatment outcomes.

2.4.2 WHO staging

The clinical staging and case definition of HIV for resource-constrained settings were developed by the WHO in 1990 and revised in 2007. Staging is based on clinical findings that guide the diagnosis, evaluation, and management of HIV/AIDS, and it does not require a CD4 cell counts. This staging system is used in many countries to determine eligibility for antiretroviral therapy, particularly in settings in which CD4 cell counts testing is not available. Clinical stages are categorized as 1 through 4, progressing from primary HIV infection to advanced HIV/AIDS. WHO staging of patients at initiation have been found to be associated with survival; for example, a study in Ethiopia to determine survival and predictors of mortality among adult patients on HAART found that WHO stage 4 at baseline was an independent predictor of survival (Tadele et al., 2014). Similar findings have been reported in other studies in Tanzania and Cameron in which patients who enrolled into HAART at WHO stage 4 had twice the hazard of death (Johannessen et al., 2008; Sieleunou et al., 2009) compared to patients enrolled into HAART at WHO stage 1.

2.4.3 Opportunistic infections

When a patient's CD4 cell counts fall below 200 cells/µl, opportunistic infections with bacteria and other pathogens become common (Janeway et al., 2005). Koenig et al., (2009) found that

patients with AIDS who receive a diagnosis of TB during the first months after ART initiation had a mortality rate of 27%, which was 3 times higher than that among other patients. According to Manosuthi et al., (2006), patients who were initiated into ART more than 6 months after TB diagnosis had higher mortality rate than those who initiated ART less than 6 months after TB diagnosis. A study conducted in Durame Hospital, Ethiopia, showed that patients with positive TB test had 3.9 times higher risk of death compared to patients with negative TB test results (Gezahegu, 2011).

There are many opportunistic infections and co-infections that impose significant burdens of morbidity and mortality; among the most important are Hepatitis B (Hoffmann and Thio, 2007), Hepatitis C (Rockstroh and Spengler, 2004) and Human herpesvirus-8 (strongly associated with Kaposi sarcoma) (Malope et al., 2007). Perhaps the two most important co-infections to consider in sub-Saharan Africa are tuberculosis (TB) and malaria (WHO, 2007).

2.4.4 Viral Load

Viral load has been considered one of the most important indicator of initial and sustained response to ART and should be measured in all HIV-infected patients at entry into care, at initiation of therapy, and on a regular basis thereafter (AIDSinfo, 2014). A systematic review of data from clinical trials involving thousands of participants established that decreases in viral load following initiation of ART are associated with reduced risk of progression to AIDS or death (Marschner et al., 1998).

2.4.5 ART Regimen

Antiretroviral drugs currently comprise six distinct classes and over 20 individual agents. The nucleoside analogues, or *nucleoside reverse transcriptase inhibitors* (NRTIs), were the first class of Anti-Retroviral (ARV) agents that were developed (Portsmouth, Stebbing and Gazzard 2003). The ARVs worked by inhibiting reverse transcriptase enzymes that support the multiplication of the virus. So when inhibited the virus cannot multiply. The two additional classes of ARVs in routine use are *protease inhibitors*, which act by inhibiting the cleaving of HIV particles from host cells (Wynn *et al.*, 2004), and *non-nucleoside reverse transcriptase inhibitors* (NNRTIs), which bind directly to and thus inhibit reverse transcriptase. A study to evaluate long-term survival of

HIV-infected patients treated with HAART in Serbia and Montenegro found that the use of regimens containing protease inhibitors and two *non-nucleoside reverse transcriptase inhibitors* was associated with long-term survival (OR 9.0, 95% CI 2.2-35.98) (Jevtović et al., 2007). Simultaneous use of all three drug classes was also predictive of long-term survival (OR 7.4, 95% CI 2.2-25.1). In the same study, long time survivors took more drugs and had more regimen switching than patients who died. Use of HAART composed of three *nucleoside reverse transcriptase inhibitors* or *nucleoside reverse transcriptase inhibitors* with a *non-nucleoside reverse transcriptase inhibitors* did not lead to difference in survival between subgroups (Jevtović et al., 2007).

2.4.6 Cotrimoxazole prophylaxis

Being put on cotrimoxazole prophylaxis was found to improve the survival probability of the patients on HAART significantly (Tadele, Shumey, & Hiruy, 2014). This could be due to the benefit from cotrimoxazole in the prevention of the classic opportunistic infections, such as Pneumocystis pneumonia, toxoplasmosis, bacterial pneumonia sepsis and diarrhea (Mermin et al., 2004). The same study also found that daily cotrimoxazole prophylaxis was associated with reduced morbidity and mortality and had beneficial effects on CD4 cell counts and viral load.

2.4.7 Body Mass Index

Malnutrition is a significant factor affecting human immunodeficiency virus (HIV) care and treatment in resource limited settings (Semba, Darnton-Hill, & De-Pee, 2010). Adequate diet is believed to be important for adherence to antiretroviral therapy (ART) as patients with inadequate nutrient intake are known to have more frequent opportunistic infections compared to patients with adequate food intake. A study in Zambia shown that provision of food assistance to HIV-infected adults on ART had an incentivizing effect which can improve medication adherence, particularly among patients recently initiated on treatment (Tirivayi, Koethe, & Groot, 2012). Lack of essential micronutrients in particular contributes to the depletion and dysfunction of CD4 cells counts and malnourished patients may have suboptimal response to treatment when (ART) is initiated (Koethe, Jenkis, Shepherd, Stinnette, & Sterling, 2011). BMI is an integral part of anthropometric assessments, a widely used indicator to assess nutritional status (Frid, Thors, Rosenblad, & Nydahl, 2013). A study conducted in rural Malawi showed that individuals who were severely

malnourished defined as BMI less than 16 kg/m^2 had six times higher risk of dying compared to patients with BMI greater than 16 kg/m^2 (Zachariah et al., 2006). Similar results were observed in a study conducted in Cameroon showed that BMI less than 18 kg/ m^2 had three times higher risk of death than patients with BMI greater than 18.5 kg/m^2. In a study conducted in Ethiopia, a BMI less or equal to 18.5 kg/m^2 was significantly associated with overall mortality. A BMI between 15 and 18.5 kg / m^2 was related to a 1.5 times higher risk of death compared to BMI greater than 18.5 kg /m^2 (HR = 1.57). This risk rose to three times more for those with a BMI less than 15 kg / m^2 (Degu et al., 2006).

2.4.8 Hemoglobin levels

A study in Ethiopia found that anemia was a strong predictor of mortality among adult patients on HAART (Shibre et al., 2014). A study conducted in Tanzania shows anemia as a strong predictor of mortality; patients with severe anemia had nearly 15 times higher risk of dying during the first year on ART as compared to those with a normal hemoglobin level (Asgeir et al., 2008). In Malawi, patients with hemoglobin levels less than 8.5 g/dl had two times more risk of death compared with patients with hemoglobin level greater than 8.5 g/dl (Zachariah et al., 2006).

2.4.9 Adherence to HAART

According to published research from the United States, HAART adherence predicts treatment response and progression to AIDS and death (Kitahata et al., 2004). Findings showed that higher levels of adherence to HAART were significantly associated with longer time to virologic failure, greater increase in CD4 cell counts and lower risk of progression to clinical AIDS or death (Fielden et al., 2008; Gross et al., 2006; Kitahata et al., 2004). After controlling for other factors, patients with low adherence had over five times the risk of disease progression than patients with moderate adherence or patients with high adherence. There was no significant difference in the risk of progression between patients with moderate and high levels of adherence. Patients who progressed to AIDS or death had significantly higher viral loads and lower CD4 cell counts than patients who experienced virological failure, but did not progress, the authors concluded (Kitahata et al., 2004). Poor adherence at the initiation of HAART had significant association with mortality in this study which was congruent with previous study conducted in Addis Ababa (Bedru & Worku, 2010) and Malawi (Zachariah et al., 2006). Researches also revealed that good adherence was significantly

correlated with high general health perception scores, and overall quality of life component scores (Abrogoua et al., 2012). Although adherence to HAART has been associated with optimal viral suppression, the impact of different levels of adherence on long-term clinical outcomes has not been determined.

2.5 Conceptual Framework

The conceptual framework used to guide the study explains the interaction between the independent intermediate and the dependent/expected outcome in the study (Figure 1). The independent variable comprises of dimensions that include the demographic, socio economic factors of the study population, the intermediate factors include biomedical and behavioral factors that interact with the demographic and social economic factors to determine survival of the patients on HAART. It was assumed that the biomedical factors and behavioral factors act as intermediate variables that affected the survival of patients on HAART.

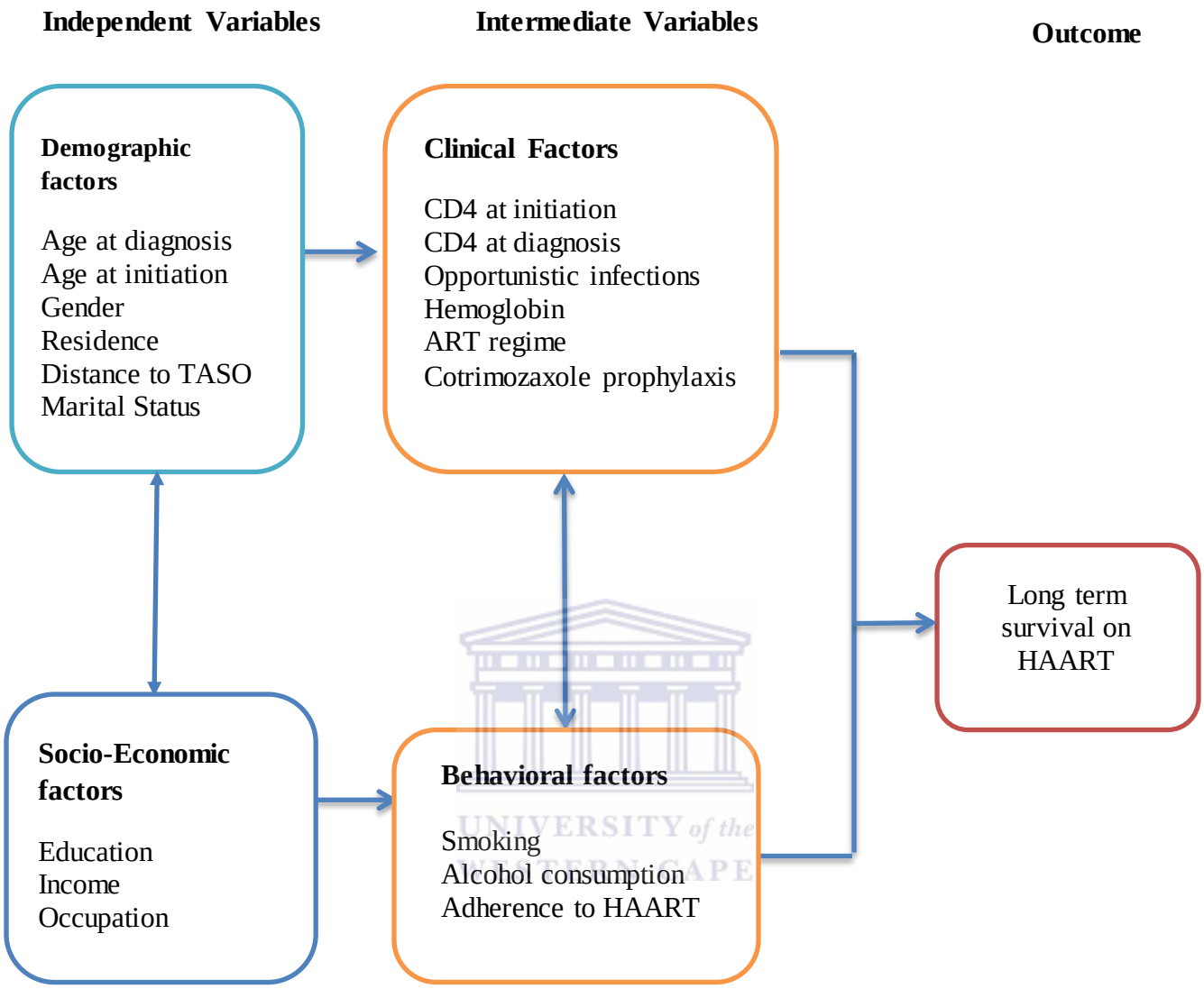

Figure 1.1: Conceptual Framework

CHAPTER THREE
METHODOLOGY

3.1 Study design

Secondary data of patient data accessing HIV care and treatment at the TASO Entebbe clinic was performed. The TASO Entebbe client database contains information of over 30,000 HIV positive clients that access HIV services at the clinic. The data used for the study was extracted from the TASO HIV patient database for only 2,244 clients that have enrolled into HAART. Data in relation to HIV treatment is collected over the patient's lifetime. TASO was selected for this study because it was one of the first HIV care and treatment center in Uganda to provide ARV to HIV patients. The study was based on the cohort of HIV-infected patients initiated on HAART at the TASO center from June 2004 to June 2014.

3.2 Study Setting

TASO is an indigenous HIV/AIDS service organization in Uganda founded in 1987 (TASO, 2013). The premise on which TASO was found was based on people that were unified by common experiences faced when encountering HIV/AIDS at a time of high stigma, ignorance and discrimination. TASO has since evolved into a Non-Governmental Organization with eleven service centres and four (4) regional offices, covering most parts of Uganda. Through the years, TASO has cared for a cumulative number of over 300,000 PLHIV and has provided support to over 1,000,000 members of their families in form of economic empowerment, provision if school fees and food support. Out of the total number of PLHIV under the care of TASO, 66,851 are receiving life prolonging Anti-retroviral drugs (ARV). The study population were patients in the in one of the centres: Entebbe TASO centre. The selection of this centre was based on its proximity to the student.

3.3 Aim of the study

The aim of this study was to determine risk factors associated with long term survival of patients on HAART in TASO Entebbe in Uganda.

The objectives of the study were:

1. To determine demographic factors associated with long term survival of patients on HAART.

2. To determine socioeconomic factors associated with long term survival of patients on HAART.
3. To determine biomedical factors associated with long term survival of patients on HAART.
4. To determine how changes in key biomedical parameter impact on survival of patients on HAART.

3.4 Study population and sampling

TASO Entebbe has over 30,000 clients in care. In order to satisfy the 10year cohort criteria, the study sample was selected from clients that had been initiated into HAART between 2004 and 2005. A total of 2,244 clients had been initiated on HAART during this period. The sample size was determined based on difference in mortality rates between 2 groups (LTS and STS). The parameters used was based on a study in Taiwan (Fang et al., 2006) where it was found that 5-year survival rate was 58% in patients who had already developed AIDS at diagnosis (AIDS group), and 89% in those who had not (non-AIDS group). In order to determine factors associated with survival the sample size n is given by:

$$n = Z^2[p(1-p)]/e^2$$

n is the required sample size

p null hypothesis proportion=0.58

e required size of standard error: using significance=1.96; SE = 0.05

This gives a sample size of 374 patients

Inclusion criteria

- Patients who are 15 years and older.
- Patients that have been initiated HAART between 2004 to 2005
- Patients that are still accessing care and have not been lost to follow up

3.5 Data collection

Two TASO client databases, one consisting of demographic socioeconomic and the other clinical data of patients receiving HIV care and treatment services at TASO Entebbe clinic was used in this study. The database containing clinical data of the patients was much larger since it contained data on clinical outcomes of the clients collected over the years. In order to create the dataset used for this study, the two data sets were merged using patient unique identification numbers in the two files.

3.5.1 Dependent variables

The date of initiation into HAART was defined as the date in which the patient was started on HAART at TASO center. This date has been selected because the study focused on survival on HAART. Therefore, to have a uniform definition of the start dates, the date thus of initiation on HAART was used. Two dependent variables were analyzed: survival status and survival time.

3.5.1.1 Survival status

Patients were grouped into 2 categories:

1 – If still alive on HAART after 5 years;

0 – if died before being 5 years on HAART

3.5.1.2 Survival time

Survival time can be broadly defined as the time to the occurrence of a given event of interest, in the case of this study the death of a person. The survival time for a patient initiated on HAART (measured in days) was defined as the number of days from the date of initiation on HAART to the date of death or end of the study period, which was 31st June 2014.

3.5.2 Independent variables

The independent variables in the study included: demographic, socioeconomic, and behavioral and clinic characteristics of the study population. Under the *demographic characteristics,* gender, age at diagnosis, age at initiation of HAART, distance from the health facility, marital status and pregnancy was collected. Under the *socio-economic characteristics,* type of employment, religion and the highest level of education attained by the patients. Under the *behavioral characteristics,* alcohol, drug use and tobacco use were collected, under the clinical factors CD4 cell counts at

diagnosis, CD4 cell counts at initiation, adherence defined as monthly ARV medication refill rates, opportunistic infections including TB, cancer including kaposi sarcoma, cryptococci meningitis, ART regime and hemoglobin was collected.

3.6 Data Analysis

Data from the TASO database was extracted into an excel sheet. This was the imported into SAS software in which all the analysis was done

Descriptive analysis of the client included in this study was conducted. Factors analyzed included demographic, social economic, behavioral and medical characteristic of the selected respondents. Frequency distributions for categorical variables were computed while means, median and inter quartile range were computed for continuous variables.

For the fixed period analysis, the outcome variable was defined by the survival status of the clients,
1- if client is still alive 5 years after initiation into HAART;
0 - if clients died within 5 years after initiation into HAART

With this definition a dichotomous variable was created and used as the depended variable in the analysis. Contingency table analysis was employed at the bivariate stage of analysis to determine the association between the various categorical independent variables. Chi-square statistic used to test the hypothesis of equality of survival between the survival status of patients, across levels of each demographic, socio-economic and health variables. For continuous independent variables t-test was used to determine the factors associated with survival. The hypothesis of equal survival for groups was rejected if the observed level of significance, p, was less than 0.05.

The Kaplan-Meier or the Product Limit method was used in the bivariate analysis of survival time. Survival time defined as the number of days from the date of the patient's HAART initiation to the date of death. Cases that were still alive and those lost to the follow-up were considered censored observations.

Two models were used in the multivariate analysis in this study: a logistic regression model was used to determine factors associated with survival in the fixed period survival of patients initiated

on HAART: the Cox proportional hazards model was used to determine the factors associated with survival time.

At the multivariate level, the logistic regression to identify variables associated with survival status. The logistic model handles cases when the survival time is discrete or known only for a few discrete intervals (Hosmer *et al.*, 1989). With HAART survival having significantly increased, a five year fixed period was selected for this study. Since fixed period survival times is the outcome variable the logistic regression model is the most appropriate for the analysis.

The dependent variable, y, is binary defined by:

$$y = \begin{cases} 1 & if\ dead\ within\ five\ years\ of\ diagnosis \\ 0 & still\ alive\ five\ years\ after\ diagnosis \end{cases}$$

The major short coming of the logistic regression model is its failure to take into consideration censored observations. The model is applied to a situation where full period of the event is fully observed which was not the case in this study. The model also assumes fixed follow-up periods. Due to these shortcomings of the logistic regression model which is that it cannot analysed censored data (people still alive at the end of the study), a Cox regression model was also used to assess factors associated with survival times on HAART.

The Cox proportional hazards model was used to identify variables associated with survival time. These response variables in turn depended on a variety of factors (predictors). For this study, the response variable was the survival time, measured in days from the date of HAART initiation to the date of death or censorship (if lost to follow-up or alive by June 2014).

3.7 Reliability and Validity

Reliability refers to dependability or a way a tool such as the questionnaire produce similar results in different circumstances if nothing changes (Sarantakos, 1998). While validity is an indication of the extent to which an instrument measures what we think it is supposed to measure (Sarantakos, 1998). For this study, the data extraction tool was designed by the researcher to collect information in regard to the study objectives. The data was also extracted by the researcher herself to ensure reliability.

3.8 Generalizability

Since TASO provides the same standard of care as any other facilities providing ART care and treatment, these finding can be generalized to other settings within Uganda.

3.9 Ethics considerations

Ethics clearance to conduct this study was obtained from the Senate Research Committee of University of Western Cape and the TASO Research Ethics Committee. Permission for data abstraction was obtained from TASO. Although secondary data was used, privacy and confidentiality and data protection rules were adhered to throughout the study. No harm was anticipated harm to the clients in this study since names or personal identification numbers of HIV/AIDS patients were not included in the data extraction sheet (Appendix 1). After signing a confidentiality clause with TASO, the student was allowed to extract patient data with the assistance of the TASO data Manager.

Although the results of this study may not have direct benefit to individual patients, on the whole, these results may be used to improve care for patients initiated on HAART by providing a criterion for identifying patients that may be predisposed to short term survival, thus improving HIV programming and patient management at TASO as a whole.

CHAPTER FOUR

RESULTS

4.1 Introduction

From the client database, 31,701 clients accessed HIV services at the TASO center, with a total of 8,441 clients initiated on ART. In order to obtain a 10 year cohort required for this study, only the number of clients initiated into HAART between 2004 and 2005 were considered: giving a total of 2,648 clients.

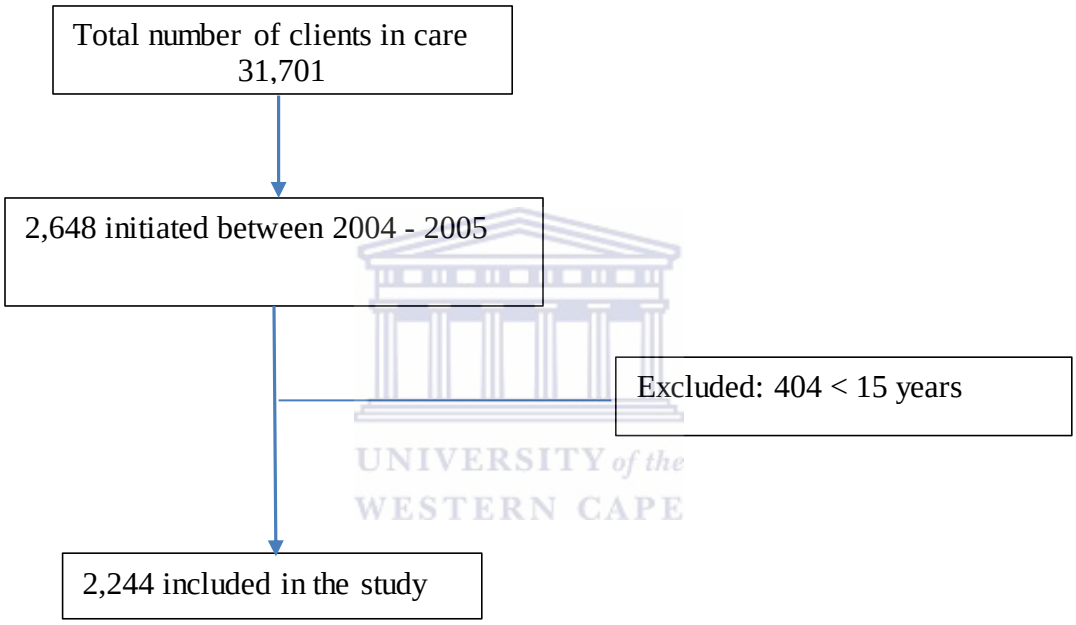

Figure 4.1: Patient Acquisition Flow Chart

4.1.1 Sociodemographic characteristics of the study respondents

Tables 4.1 shows the sociodemographic characteristics of the study respondents. There were more females than males in the study (64% vs. 36%). The majority (54.8%) of the clients had an upper primary level of education; 28.6% has secondary school level of education, 4.7% tertiary level education; while 11.8% had no education. With regard to the marital status, 44% reported being married; 24% separated and 23% were widowed. Most of the clients reported their religion as Christian (76%), with 43% identifying as Catholic and 33% as Anglican; while Muslims and other religions accounted for 23% of the clients. Just under a quarter (24%) of the clients were unemployed, with the others stating their employment status as housewives (4%), peasants,

engaged in subsistence farming (11%), vendors (16%) and paid employees (12%), casual laborers (28.2%) and students (0.6%). With regards to the distance to the clinic; majority of the clients (63%) resided within 20 km from the clinic, 19.2% resided within 21-35 km from the clinic; 13.4% resided within 36-75 km and 5% resided over 75 km from the clinic. The mean age of clients in the study was 36 years with the majority (77%) between 25-44 years of age. The same trend was observed for the age at initiation in which about 90% of the clients initiated were aged between 25-54 years. Only 4% of the patients reported ever having used tobacco in the past, no client reported that they were currently using tobacco and only 7% of the clients used alcohol and drugs.

4.1.2 Clinical Characteristics of the study respondents

Table 4.2 shows the clinical characteristics of the study respondents. The median time between diagnosis and initiation on HAART was 309 days, with an interquartile range (IQR) of 78-785 days. More than half the clients diagnosed with HIV/AIDS (55%) were initiated into ART within one year; 19% were initiated within 1-2 years after diagnosis, and 27% more than two years after diagnosis. In general, 60% of the clients who were diagnosed with HIV at this clinic had low CD4 cell counts less than 250 cells/µl). In this study, CD4 cell counts change was defined as the difference between highest CD4 cell counts attained by the client after initiation and client CD4 cell counts at HAART initiation. Based on the CD4 cell counts change, 62% of the clients achieved CD4 cell counts change greater than 250 cell/µl.

The majority of clients (89.7%) had normal hemoglobin levels (greater than 8g/dl). The majority of clients were also on first line ART regimens (96%). The majority of the clients (73.6%) were on ZDV/3TC based regimen, 13% on TD4/3TC and 11% of the clients were on DT4/3TC were 11%, Most clients (87%) reported optimal adherence to ART. The reasons given by the 13% of the clients who reported poor adherence included: forgetting to take the drugs (42%), stock outs (31%); side-effects (10%); medicine fatigue (6%); toxicity (4%) and provider instruction to stop taking medication (2%). A quarter of clients reported having experienced side effects over the course of ART: neuropathy (71%); anemia (15%), rashes (15%); and jaundice (2%).

Majority of the clients in the study (85%) reported having had an opportunistic infection. Preurigo was the commonest opportunistic infections (69%); followed by oral candidiasis (36%),

pulmonary TB (27%), esophageal candidiasis (16%), cryptococci meningitis (6.2%), toxoplasmosis (5%), kaposi sarcoma (2.3%) and pneumocystis pneumonia (1%).

Of all the clients, 53% reported having used family planning, with condoms being the commonest type of family planning methods (71%), followed by depo provera (17%); and permanent methods (1%). With regards to pregnancy, 30% of the female clients got pregnant of which only 20% reported having enrolled into PMTCT.

Table 4.1 Sociodemographic character ristics of the study respondents (N=2,244)

Characteristics		n	%
Gender	Female	1,439	64.1
	Male	805	35.9
Education	None	260	11.8
	Primary level	1,208	54.8
	Senior Secondary level	630	28.6
	Tertiary Level	104	4.7
Marital status	Single	136	6.2
	Married	983	44.7
	Separated	532	24.2
	Divorced	36	1.6
	Widowed	514	23.4
Religion	Anglican	723	33.5
	Catholic	922	42.7
	Muslim	248	11.5
	Other	268	12.4
Type of employment	None	465	24.0
	Casual Laborer	546	28.2
	Housewife	73	3.8
	Paid Employee	214	11.1
	Peasant	221	11.4
	Student	11	0.6
	Vendor	318	16.4
	Other	86	4.5
Distance to health facility (in km)	1-5	405	18.6
	6-10	506	23.3
	11-20	457	21.0
	21-35	417	19.2
	36-75	292	13.4
	>75	98	4.5

Characteristics		n	%
Age at diagnosis (years)	15-24	179	8.0
	25-34	942	42.0
	35-44	782	34.9
	45-54	251	11.1
	55+	90	4.0
Age at ART initiation (years)	15-24	115	5.2
	25-34	857	38.4
	35-44	864	38.5
	45-54	300	13.2
	55+	108	4.8
Used tobacco	Yes	34	4.1
Used alcohol and drugs	Yes	167	7.4

Table 4.2: Clinical characteristics of th e study respondents (N=2,244)

Characteristics		n	%
Length of time between diagnosis and ART initiation (in years)	<1	1226	54.6
	1-2	418	18.6
	>2	600	26.8
Baseline CD4 cell counts (cells/µl)	<250	1335	59.6
	250-500	615	27.4
	500+	219	13.0
CD4 cell counts change (cells/µl)	<100	242	13.8
	100<250	422	24.1
	250-500	360	20.5
	500+	730	41.6
Baseline hemoglobin (g/dl)	<8	185	10.3
	8+	1619	89.7
ART Regimen	D4T/3TC	238	10.6
	TD4/3TC	294	13.1
	ZDV/3TC	1721	76.3
ART adherence	Yes	1952	87.0
Reason for missing ART dosage	Forgot	68	3.0
	Stock out	50	2.2
	Side effects	6	0.3
	Provider instruction	3	0.1
	Medicine fatigue	9	0.4
	Other reasons	16	0.7
Experienced ART side-effects	Yes	579	25.8
Side effects	Anemia	86	14.9
	Neuro	411	71.1
	Jaundice	4	0.7

Characteristics		n	%
	Rash	85	14.7
Had opportunistic Infections	Yes	1897	84.5
Pulmonary TB	Yes	598	26.7
Had Extra-pulmonary TB	Yes	85	3.8
Had Preurigo	Yes	1548	69.0
Had Cryptococci	Yes	139	6.2
Had Kaposi Sarcoma	Yes	51	2.3
Had Esophagus Candida	Yes	351	15.6
Had Oral Candida	Yes	800	35.7
Had Pneumocystis Pneumonia	Yes	25	1.1
Had Toxoplasmosis	Yes	106	4.7
Client on Family planning	Yes	1187	52.90
Type of Family planning	Condoms	853	71.96
	Implants	32	2.7
	Injection	200	16.9
	Other types of FP	21	1.8
	Permanent	6	0.5
	Pill	75	6.3
Client Pregnant	Yes	441	30.7
Client on PMTCT	Yes	86	19.50

4.2 Univariate Analysis

At the univariate level, two models were fitted to the data: the logistic model using fixed period survival (5 years) and the Cox regression model (for survival time) each of the demographic and socioeconomic factors of the respondents were individually fitted into the model to assess individual association with survival outcomes.

4.2.1 Logistic Regression

Logistic regression model was fitted to the data to assess the association between the respondent characteristic and five-year survival. The odds ratios were used to assess the probability of mortality compared to the reference category. All tests were conducted at 5%.

4.2.1.1 Five-year survival by sociodemographic characteristics of the study respondents

Table 4.3 shows five-year survival by sociodemographic characteristics of ART clients. Female clients had 39% lower odds of death within 5 years after initiation into ART compared to the male clients (OR=0.61; CI: 0.48-0.78). Clients who ever used tobacco had 4 time higher odds of death compared to those that never used tobacco (OR =3.91 [CI: 1.96-7.89]). No significant associations were observed between education, religion, marital status, type of employment, age at diagnosis with HIV, age at initiation on HAART, having used alcohol and drugs and death within 5 years.

Table 4.3: Five-year survival by sociodemographic characteristics of the study respondents (N=2,244)

Characteristics		Dead within 5 years (%) (n=315)	Alive after 5 years (%) (n=1,929)	Crude Odds Ratio (95% Confidence interval)
Gender	Female	54.0	46.0	*0.610 (0.479-0.776)
	Male	65.8	34.2	Ref
Education	None	12.4	11.7	Ref
	Primary level	55.7	54.7	0.963(0.659-1.409)
	Secondary level	28.0	28.7	0.924(0.611-1.395)
	Tertiary Level	3.9	4.9	0.762(0.381-1.524)
Marital status	Single	6.8	6.1	1.218(0.716-2.072)
	Married	46.1	44.4	1.136(0.831-1.552)
	Separated	22.9	24.4	1.028(0.718-1.470)
	Divorced	2.6	1.5	1.906(0.834-4.357)
	Widowed	21.6	23.6	Ref
Religion	Anglican	31.4	33.8	0.801(0.542-1.184)
	Catholic	42.8	42.6	0.867(0.596-1.261)
	Muslim	11.8	11.4	0.889(0.549-1.437)
	Other	14.1	12.1	Ref
Type of employment	None	25.8	22.8	1.409(0.912-2.175)
	Casual Laborer	31.8	27.7	1.491(0.979-2.270)
	Housewife	3.8	3.8	1.283(0.604-2.728)
	Paid Employee	10.5	11.2	1.217(0.716-2.068)
	Peasant	9.7	11.7	1.078(0.629-1.849)
	Student	1.1	0.4	3.032(0.769-11.964)
	Vendor	13.1	17.0	Ref
	Other	4.1	4.5	1.186(0.575-2.445)
Distance to health facility (km)	1-5	22.5	18.0	1.775(0.878-3.588)
	6-10	20.9	21.0	1.389(0.689-2.800)
	11-20	17.6	19.4	1.406(0.694-2.848)
	21-35	12.9	13.5	1.280(0.627-2.616)

	Characteristics	Dead within 5 years (%) (n=315)	Alive after 5 years (%) (n=1,929)	Crude Odds Ratio (95% Confidence interval)
	36-75	22.5	22.3	1.356(0.650-2.829)
	>75	3.3	4.7	Ref
Age at diagnosis (years)	15-24	6.0	8.3	*0.475 (0.235-0.959)
	25-34	41.6	42.0	0.646 (0.373-1.118)
	35-44	34.9	34.8	0.655 (0.376-1.140)
	45-54	11.8	11.1	0.692 (0.371-1.290)
	55+	5.7	3.7	Ref
Age at ART initiation (years)	15-24	4.8	5.2	0.803(0.379-1.700)
	25-34	36.2	38.5	0.821(0.472-1.429)
	35-44	39.7	38.3	0.905(0.522-1.572)
	45-54	14.0	13.3	0.920(0.501-1.691)
	55+	5.4	4.7	Ref
Used tobacco	Yes	4.1	1.1	3.9111(1.93-7.89)
Used alcohol and drugs	Yes	9.5	90.5	1.377(0.9098-2.0838)

4.2.1.2 Five-year survival by clinical characteristics of the study respondents

Table 4.4 shows five-year survival by clinical characteristics of ART clients. No significant differences were observed between lengths of time between diagnosis and initiation to HAART and CD4 at diagnosis and the odds of death. In relation to baseline CD4 clients, clients who has a CD4 cell count less than 250 cells/µl had 13 times higher odds of death (OR= 12.721 [CI: 5.607-28.858]) compared to clients with a baseline CD4 of greater than 500 cells/µl. Clients who has a CD4 cell count between 250 cells/µl and 500 cells/µl had 2 times higher odds of death (OR= 2.181 [CI: 0.890-5.342]) compared to clients with a baseline CD4 of greater than 500 cells/µl, however this was not significantly different.

Clients who had a CD4 cell count change of between 100-250 cells/µl had 83% lower odds of death (OR= 0.171 [CI: 0.085-0.344]) compared to clients with a CD4 cell count change of less than 100 cells/µl. Clients who has a CD4 cell count change of between 250 cells/µl and 500 cells/µl had 94% lower odds of death (OR= 0.064 [CI: 0.023-0.175]) compared to clients with a CD4 cell

count change of less than 100 cells/µl. Clients who has a CD4 cell count change greater than 500 cells/µl had 77% lower odds of death (OR= 0.229 [CI: 0.109-0.478]) compared to clients with a CD4 cell count change of less than 100 cells/µl. Clients with a baseline heomoglobin level of less than 8 g/dl had 3 times higher odds of death (OR= 3.131 [CI: 2.046-4.789]) compared to clients with a baseline greater than 8 g/dl.

In relation to ART regimen, being on ZDV/3TC was used as the reference category because it was the regimen that most clients were on. Clients on DT4/3TC has a significantly 9 times higher odds of death (OR= 8.92 [CI: 6.61-12.03]) compared to clients on ZDV/3TC.

Clients that had pulmonary TB had almost double the odds of death (OR=1.64 [CI: 1.27-2.11]) compared to clients that did not have pulmonary TB. Clients that had cryptococci meningitis while on HAART had more than double the odds of death compared to clients that did not have cryptococci meningitis (OR=2.38 [CI: 1.60-3.55]). Clients that had Kaposi Sarcoma while on HAART had almost 3 times higher odds of death compared to clients that did not have Kaposi sarcoma (OR 2.90 [CI: 1.58-5.30]). Clients that had esophageal candidiasis had almost double the odds of death while on HAART compared to clients that did not have esophageal candidiasis (OR= 1.71 (CI: 1.58-2.30). While clients that had oral candidiasis had 1.5 times higher odds of death (OR= 1.47 [CI: 1.15-1.87]) compared to clients that did not have oral candidiasis. However, clients that had preurigo while on HAART had 51% lower odds of death compared to clients that did not have preurigo (OR =0.49 [CI: 0.39-0.63]). Female clients who got pregnant while on HAART had 51% lower odds of death compared to clients that did not get pregnant (OR = 0.508[CI: 0.34-0.76]).

Adherence to ART, enrollment on PMTCT for pregnant HIV positive women, having low baseline level of hemoglobin (below 8g/dl), reported having opportunistic infections, in particular pneumocystis pneumonia, toxoplasmosis and extra-pulmonary TB, being on family planning were not significantly associated with five-year survival on ART.

Table 4.4: Five-year survival by clinical characteristics of study respondents (N=2,244)

Characteristics		Dead within 5 years (%)	Alive after 5 years (%)	Crude Odds Ratio (95% Confidence Interval)
Length of time between diagnosis and ART initiation (years)	<1	6.3	8.3	1.228 (0.929-1.639)
	1-2	41.6	42.0	1.105 (0.764-1.599)
	>2	34.9	34.8	Ref
Baseline CD4 cell counts (cells/µl)	<250	89.5	54.7	12.721 (5.607-28.858)
	250-500	8.6	30.5	2.181 (0.890-5.342)
	500+	1.9	14.8	Ref
CD4 cell counts change (cells/µl)	<100	6.9	14.3	Ref
	100<250	3.5	24.5	0.171 (0.085-0.344)
	250-500	7.8	21.4	0.064 (0.023-0.175)
	500+	81.9	38.8	0.229 (0.109-0.478)
ART Adherence	Yes	87.0	89.1	0.816 (0.571-1.168)
Baseline hemoglobin (g/dl)	<8	23.9	9.1	3.131 (2.046-4.789)
	8+	79.1	90.9	Ref
Experienced ART side-effects	Yes	28.3	25.4	1.157 (0.887-1.509)
ART Regimen	D4T/3TC	37.4	6.2	8.919 (6.611-12.033)
	TD4/3TC	8.6	13.8	0.917 (0.599-1.405)
	ZDV/3TC	54.0	79.9	Ref
On first line	Yes	95.5	95.8	1.212 (0.638-2.302)
Opportunistic Infections	Yes	13.8	15.3	1.125(0.817-1.550)
Pulmonary TB	Yes	35.6	25.2	1.638(1.273-2.109)
Extra-pulmonary TB	Yes	4.8	3.6	1.328(0.751-2.350)
Preurigo	Yes	54.9	71.2	0.491(0.385-0.626)
Cryptococci meningitis	Yes	11.8	5.3	2.384(1.603-3.545)

Characteristics		Dead within 5 years (%)	Alive after 5 years (%)	Crude Odds Ratio (95% Confidence Interval)
Kaposi Sarcoma	Yes	5.1	1.8	2.896(1.583-5.297)
Esophageal Candida	Yes	22.5	14.5	1.714(1.278-2.297)
Oral Candida	Yes	43.5	34.4	1.470(1.154-1.872)
Pneumocystis Pneumonia	Yes	1.9	1.0	1.952(0.774-4.926)
Toxoplasmosis	Yes	3.2	5.0	0.626(0.323-1.214)
Client on Family planning	Yes	8.9	17.8	0.398(0.310-0.511)
Client Pregnant	Yes	19.4	32.2	0.508(0.342-0.757)
Client on PMTCT	Yes	6.1	20.6	0.248(0.058-1.054)

4.2.2 Kaplan Meier and Cox Proportional Hazards Model

Time to death were compared through survival analysis using the Kaplan-Meier method using the log-rank test. Cox proportional hazards regression models were used to estimate the magnitude of association by hazard ratios (HRs), with their respective 95%CIs.

Figure 4.2 shows the Kaplan Meier survival curve by gender. Table 4.5 shows five-year survival by sociodemographic characteristics of ART clients. Female clients had a higher median survival of 353 (IQR: 120-1159) days compared with males with 240 (IQR: 84-824) days: (p=0.0295). The risk of death among female clients was 22% lower compared to male clients (HR= 0.78 [CI: 0.62-0.98]). No significant associations were observed between education, marital status, religion, source of income, age at diagnosis with HIV, age at initiation on HAART, used tobacco, alcohol and drug use and survival on HAART.

Figure 4.2: Kaplan–Meier survival curve by Gender of the respondents

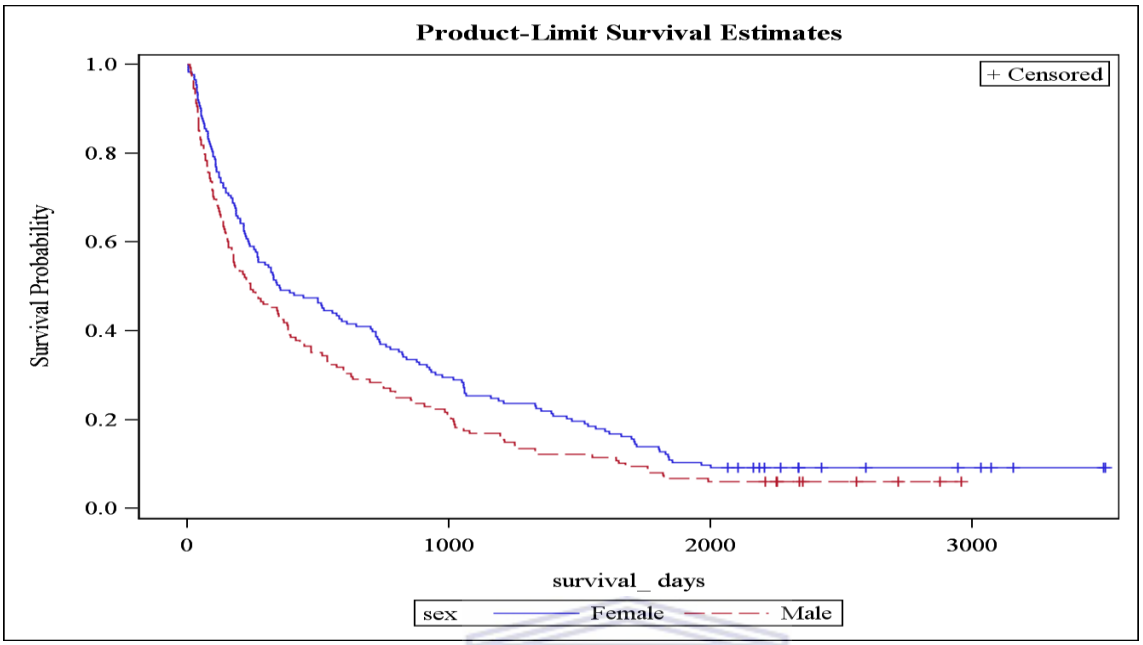

Table 4.5: Five-year survival by sociodemographic characteristics of the study respondents (N=2,244)

Characteristics		Dead within 5 years (%)	Median Survival (IQR)	Unadjusted hazard ratio
Gender	Female	54.0	353(120-1159)	0.776(0.617-0.976)
	Male	65.8	240(84-824)	Ref
Education	None	12.4	301(110-822)	Ref
	Primary	21.2	268(97-994)	0.838(0.576-1.220)
	Secondary	34.5	280(96-1006)	0.908(0.607-1.358)
	Tertiary Level	3.9	794(325-1336)	0.529(0.273-1.025)
Marital status	Single	6.8	422(169-1261)	0.709(0.410-1.226)
	Married	46.1	245(90-1006)	0.920(0.684-1.237)
	Separated	22.9	385(136-1021)	0.786(0.561-1.100)
	Divorced	2.6	201(116-589)	0.794(0.380-1.656)
	Widowed	21.6	347(95-923)	Ref
	Other	1.6	875(719-1200)	0.715(0.288-1.775)
Religion	Anglican	31.4	341(112-1055)	0.976(0.679-1.402)
	Catholic	42.8	342(97-1022)	1.038(0.734-1.469)
	Muslim	11.8	175(78-499)	1.550(0.979-2.454)
	Other	14.1	338(98-1064)	Ref
Type of employment	None	25.8	272(110-974)	0.979(0.648-1.479)
	Casual Laborer	31.8	234(98-732)	1.123(0.751-1.677)
	Housewife	3.8	325(109-1519)	0.847(0.406-1.766)
	Paid Employee	10.5	226(112-887)	1.151(0.686-1.930)
	Peasant	9.7	387(112-1064)	0.925(0.552-1.551)
	Student	1.1	499(126-779)	1.190(0.365-3.885)

Characteristics		Dead within 5 years (%)	Median Survival (IQR)	Unadjusted hazard ratio
	Vendor	13.1	212(78-1015)	Ref
	Other	4.1	181(70-875)	0.924(0.468-1.825)
Distance to health facility (km)	1-5	22.5	325(90-1015)	1.106(0.550-2.223)
	6-10	20.9	330(116-1015)	1.131(0.563-2.271)
	11-20	17.6	269(62-822)	1.135(0.563-2.289)
	21-35	12.9	472(148-1261)	1.053(0.518-2.140)
	36-75	22.5	319(126-794)	1.280(0.617-2.656)
	>75	3.3	144(65-1250)	ref
Age at diagnosis (years)	15-24	6.0	350(136-906)	0.899(0.471-1.714)
	25-34	41.6	225(92-747)	1.107(0.674-1.818)
	35-44	34.9	389(116-1012)	0.983(0.595-1.624)
	45-54	11.8	369(79-1434)	0.781(0.443-1.378)
	55+	5.7	549(185-1059)	ref
Age at ART initiation (years)	15-24	4.8	506(142-1055)	1.019(0.509-2.042)
	25-34	36.2	209(96-584)	1.366(0.818-2.279)
	35-44	39.7	385(116-1056)	1.012(0.608-1.685)
	45-54	14.0	386(88-1270)	0.905(0.514-1.594)
	55+	5.4	548(86-1059)	Ref
Used tobacco	Yes	4.1	350(77-984)	1.138(0.770-1.680)
	No	95.9	319(103-1015)	Ref
Used Alcohol and Drugs	Yes	9.5	350(97-1399)	0.553(0.105-2.901)
	No	90.5	319(231-392)	

Figure 4.3 shows Kaplan Meier survival curves for length of time between HIV diagnosis and initiation on HAART. Clients initiated on HAART within 1 year after diagnosis with HIV had a median survival time of 202 (IQR: 81-732) days; clients initiated on HAART between 1 year and 2 years after diagnosis with HIV had median survival was 519 (IQR: 112-1057) days; and clients initiated after 2 years had median survival of 344 (IQR: 22-1635) days. Clients initiated on HAART within 1 year of diagnosis had almost twice the hazard of death compared to clients initiated 2 years after diagnosis with HIV (HR= 1.94 [CI: 1.21-3.10], this risk was significantly higher.

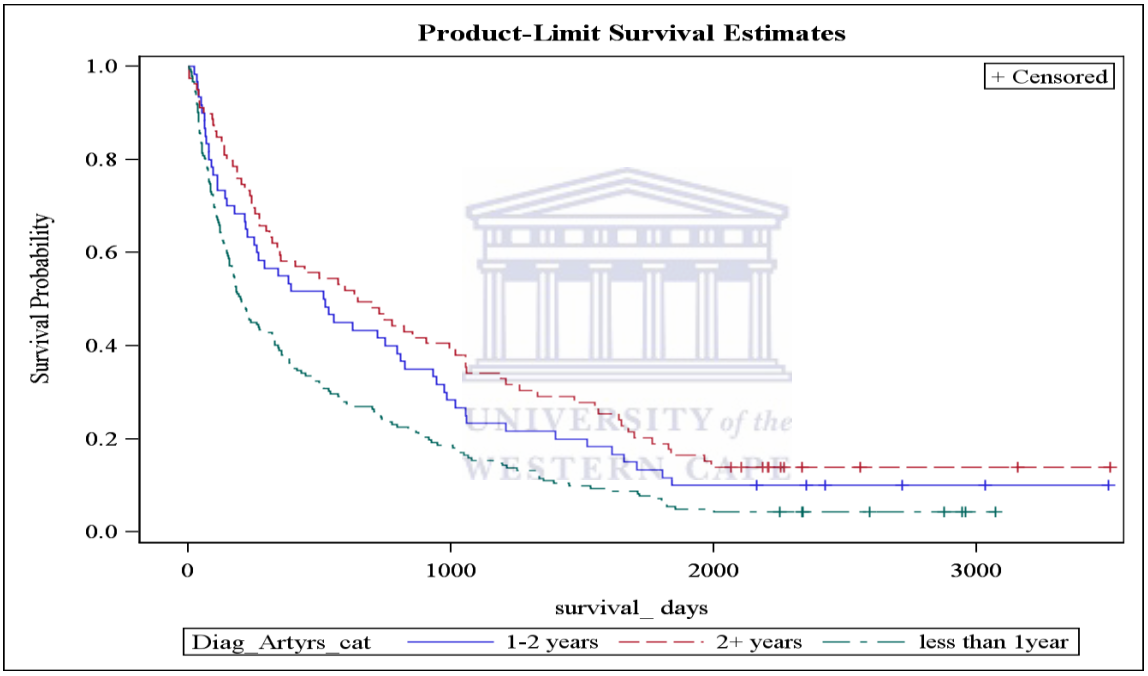

Figure 4.3. Kaplan-Meier Survival curve by Length of time between Diagnosis and Initiation to HAART of the study respondents

With regard to CD4 cell counts at diagnosis, clients with CD4 cell counts less than 250 cells/µl had a median survival time of 271(IQR: 96-887) days, clients with CD4 cell counts between 250 cells/µl and 500 cells/µl had a median survival time of 758 (IQR: 177-1674) days, majority of clients with CD4 cell counts between 250 cells/µl and 500 cells/µl at diagnosis were still alive after 10 years on HAART. Clients diagnosed at CD4 cell counts less than 250 cells/µl had almost 5 times higher hazard of death compared to clients diagnosed at CD4 cell count greater than 500 cells/µl (HR= 4.75 [CI: 1.77-12.78]), this difference was significant (p=0.0020).

Clients with CD4 cell counts change between the baseline and the highest CD4 attained of less than 100cells/µl had a median survival time of 532 (IQR: 325-839) days; clients with CD4 cell counts change between 100 cells/µl and 250 cells/µl had a median survival time of 504 (IQR:250-1150) days, clients with CD4 cell counts change between 250 and 500 cells/µl had a median survival time of 1,659 days, majority of clients with CD4 change above 500 cells/µl were still alive so the median survival could not be computed. With regards to CD4 change (defined as the change in CD4 count between baseline CD4 and the highest CD4 attained over the client's lifetime), clients who had a CD4 cell counts change of less than100 cells/µl and CD4 cell counts change between 100 cells/µl but less than 250 cells/µl both had a higher hazard of death compared to the reference category of CD4 cell counts change less than 100 cells/µl (HR= 0.24 [CI: 0.087-0.651]) and (HR= 0.45 [CI: 0.141-1.409]) and (HR= 2.34 [CI: 0.80-6.85]) respectively.

Clients who were on DT4/3TC had a median survival time of 149 (IQR: 62-325) days; clients on TD4/3TC had a median survival time of 1,331 (IQR: 535-1,842) days; and clients on ZDV/3TC had a median survival time of 499 (IQR: 144-1250) days. Figure 4.4 shows the Kaplan Meier analysis of survival time and ART regiments. Significant association was observed between survival on HAART and regimen ($p<0.0001$). Compared to clients on ZDV/3TC based regimens, client on DT4/3TC had almost three times higher hazard of death (HR= 2.64 [CI: 2.04-3.41]). While clients on TD4/3TC a significantly 46% lower hazard of death: (HR= 0.54 [CI: 0.35-0.84]).

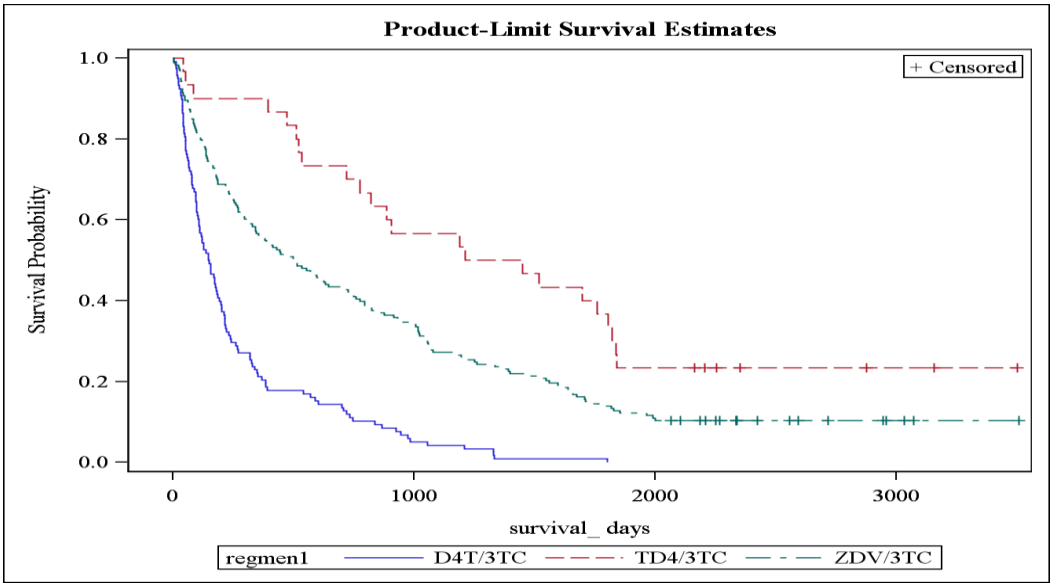

Figure 4.4. Kaplan–Meier survival curve by HAART Regimen

Clients that had opportunistic infections had a median survival time of 165 (IQR: 73-699) days while those that did not have opportunistic infections had a median survival time of 341 (IQR: 112-1056). Clients that had opportunistic infections while in HAART had a 1.4 times higher hazard of death compared to those that did not had opportunistic infections (HR= 1.45 [CI:1.07-1.95] p= 0.0164). Clients that had pulmonary TB while on HAART had a median survival time of 362(126-1329) days while clients that did not have pulmonary TB had a median survival time of 280(96-867). Clients that had pulmonary TB had 1.4 times higher hazard of death (HR= 1.36 [CI: 1.07-1.72]) compared to clients that did not have pulmonary TB while in HAART.

Clients that had extra-pulmonary TB had a median survival time of 1006 (IQR: 134-1,803) days while those that did not have extra-pulmonary TB had a median survival time of 296 (98-949) days. Clients that had extra-pulmonary TB had 53% lower hazard of death compared to clients that did not have extra-pulmonary TB (HR= 0.47 [CI: 0.275-0.809]). Clients that had preurigo had a median survival time of 535 (IQR: 148-1391) days while those that did not have preurigo had a median survival time of 196 (IQR: 74-547). Clients that had preurigo had a 47% lower hazard of death while on HAART compared to clients that did not have preurigo (HR = 0.530 [CI: 0.419-0.669]).

Clients that had pneumocystis pneumonia had a median survival time of 315 (IQR: 236-320) days while those that did not have pneumocystis pneumonia had a median survival time of 325 (IQR: 97-1015). No significant association was observed between survival on HAART and pneumocystis pneumonia although clients that had pneumocystis pneumonia had 52% lower hazard of death (HR= 0.48 [CI: 0.249-0.940]) compared to clients that did not have pneumocystis pneumonia.

Clients that had toxoplasmosis, had a median survival time of 1042 (362-1.963) days, while those that did not have toxoplasmosis had a median survival time of 296 (IQR: 97-984) days. Clients that had toxoplasmosis had a lower hazard of death compared to clients that did not have toxoplasmosis had a 52% lower hazard (HR= 0.48 [CI: 0.249-0.940]).

Clients that had used family planning had a median survival time of 538 (IQR: 96-1535) days while those who had not used FP had a median survival time of 262 (IQR: 108-839). Client that had used FP had a significantly 30% lower hazard of death compared to not using family planning (HR= 0.701 [CI*:* 0.54-0.902]).

No association was observed between ART adherence, baseline hemoglobin level, being on first line ART, preurigo, Cryptococci meningitis, Kaposi Sarcoma, esophageal candidiasis, oral candidiasis and hazard of death.

Table 4.6: Five-year survival by clinical characteristics of study respondents (N =2,244)

Characteristics		Dead within 5 years (%)	Median Survival (IQR)	Unadjusted hazard ratio
Length of time between diagnosis and ART initiation (years)	<1	54.6	202(81-732)	1.937(1.210-3.102)
	1-2	18.6	519(112-1057)	1.240(0.744-2.066)
	>2	26.8	344(22-1635)	ref
Baseline CD4 cell counts (cells/µl)	<250	89.5	271(96-887)	4.751(1.766-12.783)
	250-500	8.6	758(177-1674)	2.339(0.799-6.846)
	500+	1.9	-	Ref
CD4 cell counts Change (cells/µl)	<100	81.9	532(325-839)	Ref
	100<250	7.8	504(250-115	0.238(0.087-0.651)
	250-500	3.5	1659(33-.)	0.445(0.141-1.409)
	500+	6.8	1819	1.339(0.490-3.653)
ART Adherence	Yes	87.0	325(109-914)	1.189(0.848-1.666)
	No	13.0	139(33-1519)	Ref
Baseline Hemoglobin (g/dl)	<8	23.9	331(56-1330)	1.330(0.888-1.990)
	8+	79.1	785(181-1716)	Ref
ART Regimen	D4T/3TC	10.6	149(62-325)	2.638(2.043-3.405)
	TD4/3TC	13.1	1331(535-1842)	0.541(0.348-0.839)
	ZDV/3TC	76.3	499(144-1250)	Ref
On first line	Yes	95.90	276(97-939)	1.066(0.598-1.901)
	No	4.10	1519(1050-1805)	Ref
Had Opportunistic Infections	Yes	84.5	165(73-699)	1.355(1.065-1.724)
	No	15.5	341(112-1056)	Ref
Pulmonary TB	Yes	35.6	362(126-1329)	0.472(0.275-0.809)
	No	64.4	280(96-867)	Ref
Extra-pulmonary TB	Yes	4.8	1006(134-.)	0.530(0.419-0.669)

Characteristics		Dead within 5 years (%)	Median Survival (IQR)	Unadjusted hazard ratio
	No	95.2	296(98-949)	Ref
Preurigo	Yes	54.9	535(148-1391)	0.893(0.630-1.266)
	No	45.1	196(74-547)	Ref
Cryptococci meningitis	Yes	11.8	265(126-946)	0.861(0.512-1.448)
	No	88.2	330(97-1022)	Ref
Kaposi Sarcoma	Yes	5.1	348(78-1015)	1.077(0.819-1.417)
	No	94.9	319(106-1015)	Ref
Esophageal Candida	Yes	22.5	280(112-1015)	1.233(0.978-1.553)
	No	77.5	323(98-1010)	Ref
Oral Candida	Yes	43.5	270(98-1184)	0.941(0.419-2.115)
	No	56.5	341(106-809)	Ref
Pneumocystis Pneumonia	Yes	1.9	315(236-320)	0.483(0.249-0.940)
	No	98.1	325(97-1015)	Ref
Toxoplasmosis	Yes	4.7	1042(362-.)	0.701(0.54-0.902)
	No	95.3	296(97-984)	Ref
Client on Family planning	Yes	52.90	538(96-1535)	1.937(1.210-3.102)
	No	47.1	262(108-839)	Ref

4.4 Multivariate Analysis

Two models were fitted to the data: logistic regression and cox proportional hazards regression model. A purposeful selection of predictor variables for the final multivariate analysis was done. The models included either variables that were tested to be significant at $P \leq 0.20$ in univariate analyses (Hosmer, Lemeshow, & May, 2008) or which were pre-determined to be clinically important. P-values were two-sided and those $P \leq 0.05$ were considered to be statistically significant. Age at which the client was diagnosis with HIV and marital status were forced into the multivariate models based on a-priori assumptions of the importance of these variables.

4.4.1 Logistic regression

Table 4.7 shows the result of the multivariate logistic analysis and sociodemographic characteristics of the respondents. Females respondents were 13% times less likely to die within 5 years of HAART initiation compared to the male clients AOR (0.87 [CI: 0.556-0.857] p=0.0366).

Table 4.7: Five year survival and sociodemographic characteristics of the study respondents (N=2,244)

Characteristics		Dead within 5 years (%)	Alive after 5 years (%)	Crude Odds	Adjusted Odds ratios
Gender	Female	54.0	46.0	0.610(0.479-0.776)	0.869(0.556-0.857)
	Male	65.8	34.2		
Education	None	12.4	11.7	Ref	
	Primary level	55.7	54.7	0.963(0.659-1.409)	
	Secondary level	28.0	28.7	0.924(0.611-1.395)	
	Tertiary level	3.9	4.9	0.762(0.381-1.524)	
Marital status	Single	5.2	5.3	1.067(0.594-1.920)	
	Married	46.1	44.4	1.136(0.831-1.552)	
	Separated	22.9	24.4	1.028(0.718-1.470)	
	Divorced	2.6	1.5	1.906(0.834-4.357)	
	Widowed	21.6	23.6	Ref	
	Other	1.6	0.8	2.224(0.783-6.318)	
Religion	Anglican	31.4	33.8	0.801(0.542-1.184)	
	Catholic	42.8	42.6	0.867(0.596-1.261)	
	Muslim	11.8	11.4	0.889(0.549-1.437)	
	Other	14.1	12.1	Ref	
Type of Employment	None	25.8	22.8	1.409(0.912-2.175)	
	Casual Laborer	31.8	27.7	1.491(0.979-2.270)	
	Housewife	3.8	3.8	1.283(0.604-2.728)	
	Paid Employee	10.5	11.2	1.217(0.716-2.068)	
	Peasant	9.7	11.7	1.078(0.629-1.849)	

Characteristics		Dead within 5 years (%)	Alive after 5 years (%)	Crude Odds	Adjusted Odds ratios
	Student	1.1	0.4	3.032(0.769-11.964)	
	Vendor	13.1	17.0	Ref	
	OTHER	4.1	4.5	1.186(0.575-2.445)	
Distance to health facility(km)	1-5	22.5	18.0	1.775(0.878-3.588)	
	6-10	20.9	21.0	1.389(0.689-2.800)	
	11-20	17.6	19.4	1.406(0.694-2.848)	
	21-35	12.9	13.5	1.280(0.627-2.616)	
	36-75	22.5	22.3	1.356(0.650-2.829)	
	>75	3.3	4.7		
Age at diagnosis (years)	15-24	6.0	8.3	0.475(0.235-0.959)	
	25-34	41.6	42.0	0.646(0.373-1.118)	
	35-44	34.9	34.8	0.655(0.376-1.140)	
	45-54	11.8	11.1	0.692(0.371-1.290)	
	55+	5.7	3.7	Ref	
Age at ART initiation (years)	15-24	4.8	5.2	0.803(0.379-1.700)	
	25-34	36.2	38.5	0.821(0.472-1.429)	
	35-44	39.7	38.3	0.905(0.522-1.572)	
	45-54	14.0	13.3	0.920(0.501-1.691)	
	55+	5.4	4.7	Ref	
Used tobacco	Yes	4.1	1.1	3.9111(1.93-7.89)	4.252(0.69-26.296)
	No	95.9	98.9		
Used Alcohol and drugs	Yes	9.5	90.5	1.377(0.909-2.084)	
	No	7.1	92.9		

Table 4.8 shows the result of the multivariate logistic analysis of clinical characteristics of the respondents and five year survival.

In relation to baseline CD4 clients, clients who has a CD4 cell count less than 250 cells/µl had 7 times higher odds of death (AOR= 6.947 [CI: 2.882-16.744]) compared to clients with a baseline CD4 of greater than 500 cells/µl. Clients who has a CD4 cell count between 250 cells/µl and 500 cells/µl had 3 times higher odds of death (AOR= 2.559 [CI: 1.004-6.520]) compared to clients with a baseline CD4 of greater than 500 cells/µl.

Clients who had a CD4 cell count change of between 100-250 cells/µl had 93% lower odds of death (AOR= 0.047 [CI: 0.015-1.153]) compared to clients with a CD4 cell count change of less than 100 cells/µl. Clients who has a CD4 cell count change of between 250 cells/µl and 500 cells/µl had 80% lower odds of death (AOR= 0.196 [CI: 0.095-0.403]) compared to clients with a CD4 cell count change of less than 100 cells/µl. Clients who has a CD4 cell count change greater than 500 cells/µl had 80% lower odds of death A(OR= 0.200 [CI:0.092-0.434]) compared to clients with a CD4 cell count change of less than 100 cells/µl. Clients who suffered from side effects of HAART had a 3 times higher odds of death (AOR= 2.704 [CI: 1.683-4.344]) compared to clients who did not have any side effects from HAART.

Client on DT4/3TC had almost 4 times higher adjusted odds of death: (AOR= 3.63 [CI: 1.893-6.978]) compared to clients on ZDV/3TC based regimens, clients on TD4/3TC had almost 2 times higher adjusted odds of death: (AOR= 1.47 [CI: 0.829-2.596]) compared to clients on ZDV/3TC based regimens. Clients that had pulmonary TB had almost 2 times adjusted odds of death compared to clients that did not have pulmonary TB (AOR= 1.75 [CI: 1.109-2.770]). Clients that had preurigo had a 49% lower adjusted odds of death while on HAART compared to clients that did not have preurigo (AOR= 0.510 [CI: 0.324-0.803]). Clients that had cryptococci meningitis had almost 3 times higher adjusted odds of death while on HAART compared to clients that did not have meningitis (AOR= 2.53 [CI:1.111-5.775]).

A non-significant association was observed between five year survival and baseline hemoglobin levels, having Kaposi Sarcoma, esophageal candidiasis, oral candidiasis; having used family planning clients who had low HB.

Table 4.8: Five year survival and clinical characteristics of the study respondents (N=2,244)

Characteristics		Dead within 5 years (%)	Alive after 5 years (%)	Crude Odds	Adjusted Odds ratios
Length of time between diagnosis and ART initiation (years)	<1	6.3	8.3	1.228(0.929-1.639)	
	1-2	41.6	42.0	1.105(0.764-1.599)	
	>2	34.9	34.8		
Baseline CD4 cell counts (cells/µl)	<250	89.5	54.7	12.721(5.607-28.858)	6.947(2.882-16.744)
	250-500	8.6	30.5	2.181(0.890-5.342)	2.559(1.004-6.520)
	500+	1.9	14.8	Ref	
CD4 cell counts Change(cells/µl)	<100	6.9	14.3	Ref	
	100<250	3.5	24.5	0.171(0.085-0.344)	0.047(0.015-1.153)
	250-500	7.8	21.4	0.064(0.023-0.175)	0.196(0.095-0.403)
	500+	81.9	38.8	0.229(0.109-0.478)	0.200(0.092-0.434)
ART Adherence	Yes	87.0	89.1	0.816 (0.570-1.168)	0.484(0.267-0.877)
	No	13.0	10.9		
Baseline hemoglobin level (g/dl)	<8	23.9	9.1	3.131(2.046-4.789)	
	8+	79.1	90.9		
Experienced ART-effect	Yes	28.3	25.4	1.157(0.887-1.509)	2.704(1.683-4.344)
	No	71.7	74.6		
ART Regimen	D4T/3TC	37.4	6.2	8.919(6.611-12.033)	3.633(1.892-6.978)
	TD4/3TC	8.6	13.8	0.917(0.599-1.405)	1.467(0.829-2.596)
	ZDV/3TC	54.0	79.9	Ref	
On first line	Yes	95.5	95.8	1.212(0.638-2.302)	
	No	3.5	4.2	Ref	
Opportunistic Infections	Yes	13.8	15.3	1.125(0.817-1.550)	
	No	86.2	84.7		
Pulmonary TB	Yes	35.6	25.2	1.638(1.273-2.109)	1.753(1.109-2.770)

Characteristics		Dead within 5 years (%)	Alive after 5 years (%)	Crude Odds	Adjusted Odds ratios
	No	64.4	74.8		
Extra-pulmonary TB	Yes	4.8	3.6	1.328(0.751-2.350)	
	No	95.2	96.4		
Preurigo	Yes	54.9	71.2	0.491(0.385-0.626)	0.510(0.324-0.803)
	No	45.1	28.7		
Cryptococci meningitis	Yes	11.8	5.3	2.384(1.603-3.545)	2.533(1.111-5.775)
	No	88.2	94.7		
Kaposi Sarcoma	Yes	5.1	1.8	2.896(1.583-5.297)	2.169(0.663-7.092)
	No	94.9	98.2		
Esophageal Candida	Yes	22.5	14.5	1.714(1.278-2.297)	8.830(0.424-1.623)
	No	77.5	85.5		
Oral Candida	Yes	43.5	34.4	1.470(1.154-1.872)	1.467(0.911-2.363)
	No	56.5	65.6		
Pneumocystis Pneumonia	Yes	1.9	1.0	1.952(0.774-4.926)	
	No	98.1	99.0		
Toxoplasmosis	Yes	3.2	5.0	0.626(0.323-1.214)	
	No	96.8	95.0		
Client on Family planning	Yes	8.9	17.8	0.398(0.310-0.511)	0.852(0.533-1.360)
	No	91.1	80.2		
Client Pregnant	Yes	19.4	32.2	0.398(0.310-0.511)	
	No	80.6	67.8		
Client on PMTCT	Yes	6.1	20.6	0.248(0.058-1.054)	
	No	93.9	79.4		

4.4.2 Multivariate Cox regression analysis

According to the results of the multivariate cox regression model (table 4.9), the sex of the clients was significantly associated with survival time on HAART. Female clients had a 12% lower risk of death compared to the male clients (aHR=0.88 [CI: 0.443-0.936]) this difference was significant (p=0.0356). Clients with primary education had 50% lower risk of death compared to clients with no education (aHR= 0.50 [CI: 0.217-1.102]) clients with secondary level education had 63% lower risk of death compared to clients with no education: (aHR= 0.27 [CI: 0.118-0.601]), clients with Higher Institution had 88% lower risk of death compared to clients with no education: (aHR =0.12 [CI: 0.048-0.649-0.949]). Significant difference in survival time were observed between clients with secondary and higher institution level of education compared to clients with no education (p=0.0015; p=0.0090 respectively).

Table 4.9: Survival time and sociodemographic characteristics of the study respondents (n=2,244)

Characteristics		Dead within 5 years %	Alive after 5 years %	Unadjusted hazard ratio	Adjusted hazard ratio
			%		
Gender	Female	54.0	46.0	0.776(0.617-0.976)	0.882(0.443-0.936)
	Male	65.8	34.2	Ref	
Education	None	12.4	11.7	Ref	
	Primary	21.2	21.1	0.963(0.659-1.409)	0.489(0.217-1.102)
	Secondary	26.4	25.9	0.924(0.611-1.395)	0.266(0.118-0.601)
	Higher Institution	3.9	4.9	0.762(0.381-1.524)	0.117(0.048-0.649)
Marital status	Single	5.2	5.3	0.709(0.410-1.226)	
	Married	46.1	44.4	0.920(0.684-1.237)	
	Separated	22.9	24.4	0.786(0.561-1.100)	
	Divorced	2.6	1.5	0.794(0.380-1.656)	
	Widowed	21.6	23.6	Ref	
	Other	1.6	0.8	0.715(0.288-1.775)	
Religion	Anglican	31.4	33.8	0.976(0.679-1.402)	
	Catholic	42.8	42.6	1.038(0.734-1.469)	
	Muslim	11.8	11.4	1.550(0.979-2.454)	
	Other	14.1	12.1	Ref	
Type of employment	None	25.8	22.8	0.979(0.648-1.479)	
	Casual Laborer	31.8	27.7	1.123(0.751-1.677)	
	Housewife	3.8	3.8	0.847(0.406-1.766)	
	Paid Employee	10.5	11.2	1.151(0.686-1.930)	
	Peasant	9.7	11.7	0.925(0.552-1.551)	
	Student	1.1	0.4	1.190(0.365-3.885)	
	Vendor	13.1	17.0	Ref	
	OTHER	4.1	4.5	0.924(0.468-1.825)	

Distance to health facility(km)	1-5	22.5	18.0	1.106(0.550-2.223)	
	6-10	20.9	21.0	1.131(0.563-2.271)	
	11-20	17.6	19.4	1.135(0.563-2.289)	
	21-35	12.9	13.5	1.053(0.518-2.140)	
	36-75	22.5	22.3	1.280(0.617-2.656)	
	>75	3.3	4.7	ref	
Age at diagnosis (years)	15-24	6.0	8.3	0.899(0.471-1.714)	
	25-34	41.6	42.0	1.107(0.674-1.818)	
	35-44	34.9	34.8	0.983(0.595-1.624)	
	45-54	11.8	11.1	0.781(0.443-1.378)	
	55+	5.7	3.7	ref	
Age at ART initiation(years)	15-24	4.8	5.2	1.019(0.509-2.042)	
	25-34	36.2	38.5	1.366(0.818-2.279)	
	35-44	39.7	38.3	1.012(0.608-1.685)	
	45-54	14.0	13.3	0.905(0.514-1.594)	
	55+	5.4	4.7	Ref	
Used tobacco	Yes	4.1	1.1	1.066(0.598-1.901)	
	No	95.9	98.9		
Used alcohol and drugs	Yes	9.5	90.5	1.138(0.770-1.680)	
	No	7.1	92.9		

The result of the analysis between survival time and length of time between diagnosis and initiation into HAART, showed that clients initiated on HAART within 1 year and those initiated on HAART within 1 to 2 years after diagnosis with HIV both had higher risk of death compared to clients initiated on HAART more than 2 years after diagnosis with HIV. Those initiated on HAART within 1 year after diagnosis with HIV had almost twice the risk of death compared to clients initiated more than 2 years after diagnosis: (aHR= 1.96 [1.006-3.821] p=0.0479); client initiated on HAART between 1 and 2 years after had almost double the risk compared to clients initiated on HAART more than 2 years after diagnosis with HIV: (aHR=1.83 [CI: 0.794-4.235]). Although client initiated on HAART between 1 and 2 years after diagnosis with HIV had almost two times the risk of death, this was also not significant (p=0.1558).

Compared to clients on ZDV/3TC based regimens, client on DT4/3TC had a 5 times higher risk of death (aHR=4.79 [CI: 2.499-9.162] p=0.0003). While clients on TD4/3TC had 58% lower risk of death compared to clients on ZDV/3TC based regimens (aHR=0.42 [CI: 0.191-0.922] p<0.0001). Clients that had suffered from an opportunistic infection had almost 4 times higher risk of death compared to those that had not suffered from opportunistic infections, (aHR= (3.65 [1.603-8.291] p=0.002). Clients that suffered from pulmonary TB had 1.3 higher risk of death compared to clients that did not suffer from pulmonary TB (aHR=1.33 [CI: 1.162-2.733] p=0.0014). However, clients that had suffered from preurigo had 56% lower risk of death while on HAART compared to clients that had not suffered from preurigo (aHR=0.44 [CI: 0.236-0.744] p=0.0044).

No significant association was observed between CD4 at diagnosis, extra-pulmonary TB, oral candidiasis, toxoplasmosis being on FP and risk of death while on HAART.

Table 4.10: Survival time and Clinical characteristics of study respondents (N=2,244)

Characteristics		Dead within 5 years %	Alive after 5 years %	Unadjusted hazard ratio	Adjusted hazard ratio
Length of time between diagnosis and ART initiation (years)	<1	6.3	8.3	1.937(1.210-3.102)	1.961(1.006-3.821)
	1-2	41.6	42.0	1.240(0.744-2.066)	1.833(0.794-4.235)
	>2	34.9	34.8		
Baseline CD4 cell counts (cells/µl)	<250	89.5	54.7	4.751(1.766-12.783)	2.150(0.513-9.004)
	250-500	8.6	30.5	2.339(0.799-6.846)	1.435(0.349-5.898)
	500+	1.9	14.8	Ref	
CD4 cell counts Change (cells/µl)	<100	6.9	14.3	Ref	
	100<250	3.5	24.5	0.238(0.087-0.651)	0.129(0.045-0.368)
	250-500	7.8	21.4	0.445(0.141-1.409)	0.778(0.237-2.559)
	500+	81.9	38.8	1.339(0.490-3.653)	0.531(0.173-1.628)
ART Adherence	Yes	87.0	89.1	1.8889(0.933-3.823)	
	No	13.0	10.9	Ref	
Baseline hemoglobin (g/dl)	<8	23.9	9.1	1.330(0.888-1.990)	
	8+	79.1	90.9		
Experienced ART-effect	Yes	28.3	25.4	0.624(0.477-0.817)	1.117(0.635-1.687)
	No	71.7	74.6		
ART Regimen	D4T/3TC	37.4	6.2	2.638(2.043-3.405)	4.785(2.499-9.162)
	TD4/3TC	8.6	13.8	0.541(0.348-0.839)	0.420(0.191-0.922)
	ZDV/3TC	54.0	79.9	Ref	
Opportunistic Infections	Yes	13.8	15.3	1.445(1.070-1.952)	3.645(1.603-8.291)
	No	86.2	84.7		
Pulmonary TB	Yes	35.6	25.2	1.355(1.065-1.724)	1.332(1.162-2.732)
	No	64.4	74.8		
Extra-pulmonary TB	Yes	4.8	3.6	0.472(0.275-0.809)	0.690(0.225-2.006)
	No	95.2	96.4		
Preurigo	Yes	54.9	71.2	0.530(0.419-0.669)	0.438(0.236-0.744)
	No	45.1	28.7		
Cryptococci meningitis	Yes	11.8	5.3	0.893(0.630-1.266)	
	No	88.2	94.7		
Kaposi Sarcoma	Yes	5.1	1.8	0.861(0.512-1.448)	
	No	94.9	98.2		

Characteristics		Dead within 5 years %	Alive after 5 years %	Unadjusted hazard ratio	Adjusted hazard ratio
Oeso Candida	Yes	22.5	14.5	1.077(0.819-1.417)	
	No	77.5	85.5		
Oral Candida	Yes	43.5	34.4	1.233(0.978-1.553)	1.121(0.432-1.193)
	No	56.5	65.6		
PNEUMOCYSTIS PNEUMONIA	Yes	1.9	1.0	0.941(0.419-2.115)	
	No	98.1	99.0		
Toxoplasmosis	Yes	3.2	5.0	0.483(0.249-0.940)	0.592(0.215-1.626)
	No	96.8	95.0		
On Family planning	Yes	8.9	17.8	0.701(0.54-0.902)	1.244(0.758-2.040)
	No	91.1	80.2		
Client Pregnant	Yes	19.4	32.2	0.508(0.3415-0.787)	
	No	80.6	67.8		

4.5 Summary

This chapter presented results of the analysis data from respondents included in the study. At the univariate level, gender, HB levels, having used tobacco, having had cryptococci meningitis, Kaposi sarcoma, esophageal or oral candidiasis were associated with five-year survival. Length of time between diagnosis and initiation into HAART, having suffered from opportunistic infections specifically extra pulmonary TB, toxoplasmosis, preurigo and using family planning were associated with survival time. At the multivariate level, factors associated with five-year survival included having tobacco use, having had cryptococci meningitis, Kaposi sarcoma, having had esophageal candidiasis, while those associated to survival time were; education, length of time between diagnosis and initiation into HAART and having had opportunistic infections. Factors that affected both five year and survival time included gender, baseline CD4 cell counts, CD4 cell counts change, ART regimen, having had pulmonary TB.

CHAPTER FIVE

DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

The main objective of the study was to investigate the effect of demographic, social-economic and health factors and changes in the health factors on five-year survival and survival time for patients initiated into HAART. Two models were fitted to the data in order to achieve this objective. This chapter presents the discussion, conclusion and recommendation from the findings in chapters 4 and 5.

5.2 Demographic and Socioeconomic characteristics associated with survival on HIV treatment

The gender of the client was found to be associated with survival both at the bivariate level and at the multivariate level. This finding is similar to those in other studies in which the female gender showed lower risk of mortality compared to males; a higher proportion of male client had died by the 5th year compared to women, and the male clients also had lower median survival compared to female clients. Mixed results with regard to gender and survival on HAART have been shown, a study conducted in Cameroon to determine survival in AIDS patients on antiretroviral therapy in a rural center in the Far-North Province found male sex to be a predictor of mortality with a risk almost double that of female sex (HR= 1.73 [CI: 1.37–2.19]) (Isidore et al., 2009). Another study to evaluate gender-related mortality for HIV-infected patients on highly active antiretroviral therapy (HAART) in rural Uganda also found that female HIV-infected patients on HAART showed a tendency towards lower mortality after adjusting for baseline demographic variables and CD4 cell count (Alibhai et al., 2010). A number of authors have also found gender differences in ART outcomes (Sterling et al., 2001; Moore et al., 2002; Kremer & Sonnenberg-Schwan 2003; Perez-Hoyos et al., 2003). However, some studies have found no association between gender and survival on HAART (Egger et al., 2002; Bourgeois et al., 2005; Nicastri et al., 2005; Braitstein et al., 2006). Reasons for better survival by females was in a study in Thailand, that showed that women had more and earlier access to antiretroviral treatments (Le Coeur et al., 2007), which could explain better survival. In general, women have better health seeking behaviors than men.

The clients with the highest level of education had the higher median survival. The education level of the clients however did not significantly affect five-year survival on HAART. Education was found to significantly affect survival time; clients with higher level and lower primary level education having significantly lower risk of mortality compared to clients with no education. Implying that education of the client significantly affect survival at later stages of life. Mixed results have been found with the regard to education and mortality on HAART. The results in this study are similar to those found in different countries that indicated that education beyond a high school degree was a statistically significant protective factor for all-cause and HIV/AIDS-related mortality (McDavid, Ling, Song, & Hall, 2008; Silverberg, Leyden, Quesenberry, & Horberg, 2009), and one report showed no significant association with education. In this study education affected long term survival but not five-year survival implying that it affected survival in the long run, but not in the short term. The challenge that clients with no educated face could be the difficulty in reading and or understand medication instruction.

In this study, both client age at diagnosis and the age at initiation on HAART were not significantly affect both the five-year survival and survival time. Other studies have found similar result, for example, age at sero-conversion seems to have become a less important prognostic factor for progression to AIDS since the introduction of HAART, yet it is known that reconstitution of immune function is likely to be more difficult in older people (Steinman, 1986). However in this study, age was not an independent predictor of CD4 cell counts response to HAART unless at a threshold age of 50 years where according to studies they are less likely to have their CD4 cell counts increased during HAART (Grabar *et al.*, 2004).

According to a report published in the June 2006 *American Journal of Public Health*, tobacco smoking is associated with poorer response to antiretroviral therapy and worse disease progression in HIV/AIDS patients especially women. An analysis of 924 participants starting HAART in the Women's Interagency HIV Study; showed that patients who smoked cigarettes had poorer virological and immunological response to HAART, lower CD4 cell counts, higher HIV viral loads, a 36% greater likelihood of developing AIDS-defining illnesses, and a 53% higher risk of death compared with non-smokers; however, the rate of specifically AIDS-related death was similar (Feldman et al., 2006). These findings are similar to those in this study, patients who

reported having used tobacco had a lower median survival, a 3.9 higher risk of death, no significant association was observed between smoking and survival time. It should also be noted that although clients in this study had ever smoked, all of them reported not smoking after being diagnosed with HIV. In this study, although clients that consumed alcohol had a 1.3 and a 1.1 higher risk of death compared to clients that did not consume alcohol, these difference were not statistically significant. These findings are contrary to a number of studies that have found that heavy alcohol users receiving antiretroviral therapy were twice as likely to have CD4 cell counts below 500 than light or non-drinkers (OR 2.31 [CI: 1-5.5, p =0.03], and highly active antiretroviral therapy (HAART)-treated heavy alcohol users were four times less likely to achieve a positive virological response (OR 4.13 [CI: 1.2-17, p=0.04] (Maria et al., 2003, Henrich et al., 2007).

Marital status, religion, income of the clients, distance to the clinic were found not to significantly affect both the five-year survival and survival time. To date, research examining the role of SES on HIV/AIDS mortality has been scarce; according to Oakes and Rossi, this could be due to the difficulty of obtaining estimates of individual-level socioeconomic measures, the limited research could be due to measurement problems arising from the lack of conceptual clarity about the essential nature of social stratification and the absence of the application of sound measurement theory to the construction of socioeconomic measures in relation to health outcomes (Oakes & Rossi., 2003). The synthesis of the available up-to-date knowledge on the association between SES and mortality risk among people with HIV/AIDS indicates that SES affects patients' survival to a different extent in various population groups at distinctive points of disease progression.

5.2 Clinical factors associated survival on HIV treatment

Length of time between diagnosis and ART initiation clinic were found to significantly affect the survival time but not five-year survival. The shortest survival was observed for clients diagnosed and initiated within 1 year, implying that patients are identified late, when the disease has progressed. For survival time, before adjusting for other factors, client diagnosed and initiated within one year were twice more likely to die than those initiated later. At the multivariate level they were almost 3 times more likely to die that those initiated later. Although initiation between 1-2 years after diagnosis was associated with a higher hazard of death at the univariate level of analysis, the association was not significant at the multivariate level. Clients with CD4 cell counts

less than 250 cells/µl at diagnosed were found to have shorter survival, and were 7 times more likely to die within five years of diagnosis compared to those with CD4 cell counts greater than 500 cells/µl, while those with CD4 cell counts between 250 cells/µl and 500 cells/µl were 3 times more likely to die within five years of diagnosed compared to those with CD4 cell counts greater than 500 cells/µl. Baseline CD4 cell counts however did not affect survival time. The implication of this is that in the CD4 cell counts at diagnosed matter in the short term, this period is also the time when most death occur.

Although clients who were adherent had a higher median survival than patients who were not adherent, no significant association was observed between both the five year survival and survival time and adherence. Two studies conducted in Ethiopia and Malawi however revealed contrary results in which poor adherence at the initiation of HAART had significant association with mortality (Bedru & Worku, 2010) and Malawi (Zachariah et al., 2006). The reason could be due to the fact that majority of clients were adherent to ART. With increased adherence counselling which have been adopted in most countries as a standard of care, adherence levels have increased significantly.

Clients with normal hemoglobin levels at initiation had higher median survival that those who had lower levels. However, no significant association was observed between both the five year survival and survival time and HB levels at initiation. The regimen with the higher median survival was TD4/3TC, followed by ZDV/3TC and lastly D4T/3TC. The regimen the client was on affected both five year and survival time; while clients on D4T/3TC were 5 times more likely to die than clients on ZDV/3TC; being on TD4/3TC was found to be protective, with the probability of death as low as 37% less than for clients on ZDV/3TC. The finding of this study is similar to those of other studies. For example an evaluation study conducted in Serbia and Montenegro found that the use of regimens containing PIs and two NRTIs was associated with long-term survival (OR= 9.0, [CI 2.2-35.98], $P<0.001$) (Jevtović et al., 2007). Simultaneous use of all three drug classes was also predictive of long-term survival (OR= 7.4 [CI 2.2-25.1] $P<0.001$). In the same study, long time survivors took more drugs ($P<0.001$) and had more regimen switching than patients who died. Use of HAART composed of three NRTIs or NRTIs with an NNRTI did not differ between subgroups, while the use of classic HAART (two NRTIs+one PI) and HAART composed of all

three drug classes was significantly more common in the LTS subgroup (P=0.04 and 0.02, respectively).

Overall, clients that had opportunistic infections have significantly lower median survival compared to those that did not have any opportunistic infections. From the logistic regression, client that had opportunistic infections were 1.4 times more likely to die compared to those who did not, however no difference were observed at the multivariate level. It was also noted that having opportunistic infections did not affect survival time implying that opportunistic infections had an impact on survival in the short term. With regards to specific opportunistic infections, pulmonary TB and preurigo affected both five year and survival time. Being on family planning was found to affect both five-year survival and survival time. Being on family planning was found to be protective in both cases.

5.3 Summary

1. With regard to objective one of the study, gender of the client affected both five year survival and survival time after initiation on HAART. The education level of the clients had marginal effect at the bivariate level of analysis for survival time, however after adjusting for other factors, having no education, having secondary level education had higher risk for death while having a higher level of education was protective.

2. To determine social economic factors associated with long term survival of patients on HAART The education level of the clients had marginal effect at the bivariate level of analysis for survival time, however after adjusting for other factors having no education, senior 1-4 had higher risk for death while having a higher level of education was protective, having used tobacco also had an impact on survival.

3. To determine biomedical factors associated with long term survival of patients on HAART: Several biomedical and behavioral factor affected survival: length between diagnosis and initiation into HAART, CD4 cell counts at initiation, HB at initiation, ART regimen, having opportunistic infections: in particular, pulmonary TB, extra pulmonary TB, preurigo, cryptococci meningitis, kaposi sarcoma, esophagus and oral candidiasis, toxoplasmosis and being on family planning.

4. To determine how changes in key biomedical parameter impact on survival of patients on HAART; Changes in biomedical factors evaluated was change in CD4 cell counts between at initiation and the maximum CD4 cell counts attained thereafter by the client. The CD4 cell counts change affected both five-year survival and survival time in particular increase in CD4 cell counts was found to be protective.

5.4 Conclusions

This 10-year retrospective cohort study of AIDS patients on HAART provides insight in survival and its determinants in a non-governmental organization (NGO) managed setting. There are several predictors of mortality for patients on ART and although these determinants tend to be similar across the world, there are some striking differences in their relative frequency, e.g. the much lower baseline CD4 cell counts of patients starting ART in poor countries (Egger, 2007). Identifying the demographic, social economic, behavioral and biomedical variables, including how changes over time in these factors influence patient's survival after initiation on HAART improves understanding of the HAART program. Knowledge of these factors facilitates the identification of patients predisposing to dying early and therefore strategies to prolong their survival can be put in place. This knowledge therefore provides practical implications for managing HIV infected patients on ART in Uganda and other resource-limited settings.

5.5 Limitations

The limitation of this study was that the data being was from routine data collected during service provision to HIV positive patients under the care of TASO, usually such data are not consistently collected and the detail of the data collected was not defined in a way that applied to the definition as required in this study. This was overcome in this study through the creation of new variables were possible to suit the objectives of the study.

5.6 Recommendations

Length of time between diagnosis and ART initiation affected survival. The world health organization recommended earlier initiation of HIV+ patients into ART, this can only be possible if HIV positive patients are identified early. This will require that the government puts in place

strategies to test and identify people who are HIV positive and put in place mechanisms to link them into care. The biggest gap is at community level, there is need to strengthen linkage between the communities and the health facilities.

This study revealed that gender of the client affected survival of clients on HAART, with the female gender having better survival than male. The poor health seeking behavior of men may be a contributing factor and strategies need to be put in place to encourage male HIV+ clients to seek medical care earlier. Enhanced counselling should be provided to men and male friendly service made available.

The education level of clients is a predictor of mortality. It would be important that materials are translated into languages that clients understand and posters using pictures used to aid understanding especially for clients with low level of education.

Although in the long run having any opportunistic infections increases the risk of death, for patients newly initiated, health workers should be vigilant in the identification and treatment of all opportunistic infections but specifically pulmonary TB, preurigo, cryptococci meningitis, kaposi sarcoma, esophagus and oral candidiasis.

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APPENDIX I: Data Extraction Form

Patient ID _____

A. Demographic data

Date of Birth …./…../……..

Date of diagnosis…./…../…….. Age at diagnosis……

Date of initiation into HAART …./…../……Age at initiation of HAART……

Was client on cotrimozaxole before HAART initiation Yes [ ] No [ ]

Residence: _____Distance from TASO_____Kms

(Circle the appropriate code in the table below)

3. Marital Status:	**4. Sources of Income:**	**5. Education Level:**	**6. Religion:**
1. Married Mono.	1. None	1. None	1. Catholic
2. Married Poly	2. Paid employee	7. Pre Primary	2. Anglican
3. Cohabiting	3. Peasant	2. Lower Primary (P1-P4)	3. Muslim
4. Separated	4. Casual Laborer	3. Upper Primary (P5 - P7)	4. S.D.A
5. Divorced	5. Housewife	4. Senior 1 - 4	5. Pentecostal
6. Widowed	6. Vendor/Business	5. Senior 5 - 6	6. Orthodox
7. Never Married	person	6. Higher Inst. Of Learning	99. Other (Specify)
8. Minor	7. Dependent	99. Other (Specify)	
	99. Other (Specify		

7. Has the client ever smoked cigarettes? Yes [ ] No [ ]

8. Is the client currently smoking cigarettes? Yes [ ] No [ ]

9. Does the client drink alcohol? Yes [ ] No [ ]

B: Biomedical Factors at diagnosis and enrollment into HAART

	At diagnosis	At initiation on HAART	Lowest ever attained	Highest ever attained
CD4 cell counts				
Viral load				
Hemoglobin				
BMI				

C: FAMILY PLANNING ***(Tick or Circle the appropriate response)***

i) Is the Client Pregnant?

1. Yes…..
2. No……

ii) If **Yes,** Is Client on PMTCT?

1. Yes…..
2. No……

ii) If **NOT** pregnant, is Client on any contraceptive method?

1. Yes…..
2. No……
3. N/A…….

iv) Type of Family planning method

1. Condoms
2. Oral Pill
3. Depo. (Injection)
4. Implants
5. Other (specify)…….

D: ART MONITORING ***(Tick or Circle the appropriate response)***

i) Is client on ARVs? Yes [ ] No [ ] New [ ] Restarting [ ] Changed Regimen [ ]

ii) If YES Current ARV Regimen Code _____

iii) If CHANGED regimen please specify all other regimen taken before_____

E: SIDE EFFECTS OF ARVs

1. None
2. Anaemia
3. Neuropathy
4. Skin rash
5. Jaundice
6. Others(Specify) _____

F: NEW OPPORTUNISTIC INFECTIONS

OPPORTUNISTIC INFECTIONS	**Date1**	**Date2**	**Date3**
1. Cryptococcal Meningitis			
2. KS			
3. Pneumocystis Pneumonia			
4. Oesophageal Candidiasis			
5. Toxoplasmosis			
6. Extra PTB			
7. Cryptosporidium			
8. Recurrent oral Candidiasis			
9. Prurigo			
10. PTB			
11. None			
12. Others(Specify)			

G: ADHERENCE

i) Has the client ever miss out taking the ARVs? Yes [ ] No [ ]

ii) If yes, please fill in the table below:

Reasons for missing:

1. No supplies
2. Side effects
3. Forgot
4. Shared
5 Discontinued, Why? _____
6. Study Interruption
7. No Transport
8. Other (Specify) _____

Date	Reasons for missing (use the codes above fill in all that applies)

H: Survival status

i) What is the survival status of the client?

1. Dead
2. Alive

ii) If **DEAD**, indicate date of death ……/…../……

iii) If known, what was the cause (s) of death ……