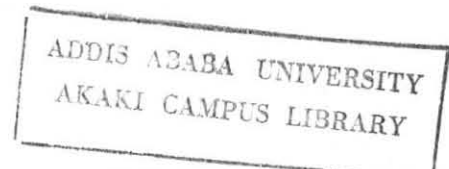




ADDIS ABABA UNIVERSITY
COLLEGE OF DEVELOPMENT STUDIES
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***FACTORS AFFECTING SURVIVAL STATUS OF HIV PATIENTS
FOLLOWING ANTIRETROVIRAL THERAPY PROGRAM IN DEMBI
DOLLO HOSPITAL, WEST ETHIOPIA***

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***A thesis submitted to Office of Graduate Programs of Addis Ababa
University in partial fulfillment of the requirement for the degree of
Master of Population Studies (Concentration on Reproductive Health)***

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**Addis Ababa University
School of Graduate Studies**

This is to certify that the thesis prepared by **Dame Kedir** entitled: “*Factors Affecting Survival Status of HIV Patients Following Antiretroviral Therapy Program in Dembi Dollo Hospital, West Ethiopia*” and Submitted to Partial Fulfillment of the requirements for the Degree of Master of Science (Population Studies) complies with the regulations of the University and meets the accepts standards with respect to originality and quality.

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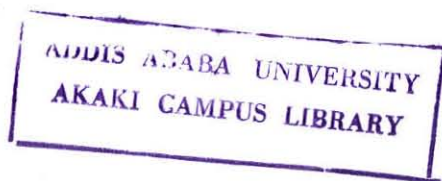

Chair of the Department of Graduate Program Coordinator

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Abstract

Factors affecting survival status of HIV patients following antiretroviral therapy program in Dembi Dollo Hospital, West Ethiopia

Dame Kedir (Bsc)

Addis Ababa University, 2013

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The introduction of HAART has brought about a significant reduction in the morbidity and mortality of patients with HIV infection. However, the mortality rate of patients treated with HAART is still very high in resource-constrained settings. The study has reviewed patients' forms and follow up cards of 491 patients treated with HAART in Dembi Dollo Hospital from 2010-2012. The minimum follow up time was 2 month and the maximum was 36 months. Kaplan-Meier survival curves and Log-Rank test were used to compare the survival experience of different groups of patients and proportional hazards Cox model was used to explore factors affecting survival of patients which directly linked with increased risk of mortality. The overall mean estimated survival time of patients was 33.8 months. Poverty is one of the most determinant factors affecting survivals of patients in study area. Moreover, laboratory and clinical factors are associated with increased risk of mortality. Fear of stigma is one of the barriers to uptake treatment persistently. Food support program is necessary for all of patients to have better survival experience.

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Acronyms

AIDS	Acquired Immunodeficiency Syndrome
ANOVA	Analysis of Variance
ART	Antiretroviral therapy
ARV	Antiretroviral
BMI	Body Mass Index
CI	Confidence Interval
D4T	Stavudine
EFV	Efavirenz
FGD	Focus Group Discussion
HAART	Highly Active Antiretroviral Therapy
HCT	HIV Counseling and Testing
HGB	Hemoglobin
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
IDU	Injection Drug Use/User
LR	Likelihood Ratio
NEV	Neveapine
NNRTI	Non-Nucleotide Reverse Transcriptase Inhibitor
NRTI	Nucleotide Reverse Transcriptase Inhibitor
OI	Opportunistic Infection
PI	Protease Inhibitors
PLWHA	People Living with HIV/AIDS
PMTCT	Prevention of Mother to Child Transmission
PYO	Person Years of Observation
RTI	Reverse Transcriptase Inhibitors
TB	Tuberculosis
TLC	Total Lymphocyte Count
VCT	Voluntary Counseling and Testing
WHO	World Health Organization
ZDV	Zidovudine

CHAPTER ONE

1. INTRODUCTION

1.1 Background of the study

AIDS is one of the most destructive epidemics in the world, Cumulative worldwide mortality associated with HIV and AIDS has been estimated at 3.1 million. Although only 10% of the world's population lives in sub Saharan Africa, the region is nevertheless home to around two-thirds of the world's HIV-infected people, In 2007, an estimated 22.5 million adults and children in the region were living with HIV/AIDS and 1.6 million died, representing 76% of global AIDS deaths (1).

The total number of people living with HIV worldwide continued to grow in 2008, reaching an estimated 33.4 million which was more than 20% higher than the number in 2000, and the prevalence was roughly threefold higher than in 1990. Moreover, 2.7 million became newly infected and 2 million died due to AIDS in 2008 alone. Sub-Saharan Africa remains the most heavily affected region, accounting for 71% of all new HIV infections and AIDS related deaths globally in 2008 (2).

In Ethiopia more than 1.3 million people living with HIV and an estimated 277,800 people requiring treatment. In 2003 the government of Ethiopia introduced ART program with the goal of reducing HIV related morbidity and mortality, improving quality of life of people living with HIV and mitigating some of the impact of epidemic, In 2005 Ethiopia launched free ART and over 71, 000 were initiated by the end of November 2006 and 261 hospitals and health centers are now providing HIV care and treatment services in regions of the country. In Ethiopia the adult prevalence of HIV was estimated

to be 2.2% in 2008(3).

Adult HIV prevalence in 2009 was estimated to be between 1.4% and 2.8% in the country. The last single point estimate exercise which was done in 2007, estimated urban and rural prevalence of 7.7% and 0.9%, respectively, for 2009. Prevalence was 1.8% for males and 2.8% for females, and women accounted for 59% of the HIV-positive population. According to the 2007 single point estimate, there were an estimated 1,116,216 people living with HIV in 2009, of which 336,160 were eligible for ART. There were an estimated 131,145 new HIV infections and 44,751 AIDS-related deaths of which females accounted for 57% of the total infections and deaths. The total estimated number of HIV-positive pregnant women and annual HIV positive births in the same year were 84,189 and 14,140, respectively. There were an estimated 72,945 children less than 15 years old living with HIV, out of which 20,522 needed ART. Due to the combined effect of poverty and AIDS, more than 5.4 million children under the age of 18 years were orphaned out of which 855,720 (16%) lost at least one parent due to AIDS (4).

The introduction of HAART has greatly improved the survival of HIV/AIDS infected people. HAART reduces morbidity and mortality by suppression of viral replication, restoration and preservation of immune function, and prevention of drug resistance. Mortality among patients on HAART is associated with high baseline levels of HIV RNA, WHO stage III or IV at the beginning of treatment, low body mass index, severe anemia, low CD4 cell count, type of ART treatment, cotrimoxazole prophylaxis, gender, resource-poor setting and poor adherence to HAART. The benefits of highly active antiretroviral therapy (HAART) in the treatment of HIV infection have been well

described including viral suppression, CD4 lymphocyte repletion, and durable reductions in AIDS related opportunistic diseases and death. However, the durability of the effectiveness of HAART remains to be delineated. Factors that limit the success of HAART include poor therapy adherence, regimen complexity, viral resistance, pharmacodynamic interactions, drug tolerability and toxicity, therapy costs, and presence of co morbid conditions such as substance abuse and addiction (5).

As things stand today in the country, the provision of free antiretroviral drugs is taken as one of the treatment options to reduce the effects/consequences of the epidemic. In this regard the HIV Counseling and Testing (HCT) program has shown considerable improvement both in terms of service expansion as well as utilization. The number of health facilities providing ART reached 512 in December 2009. A total of 5.8 million people (53% male) received HIV counseling and testing in 2008/09, this is a 22% increase from the previous year. ART coverage increased from 46% in 2008 to 53% in 2009. As of end of 2009 there were a total of 241,236 people ever started ART and 176,644 currently on ART. Females accounted for 57.9% of ART clients. A total of 11,000 children were ever started ART, including 8,761 currently on ART as of December 2009. ART coverage for children was 43%. However, lost to follow up to ART service was 28% by the end of 2008 which is a major challenge (6).

1.2 Statement of the problem

It is a well known fact that Ethiopia is one of the countries attacked by the HIV/AIDS epidemic. The epidemic has claimed the lives of the country's adult that would otherwise have contributed immensely to the country's development in many respects. Ever since the first infections were identified in the country, a lot has been

done both by the government and other stake holders to curb the effect of the disease specially to suppress the risk of transmission. Numerous researches have also been conducted that tried to address many of the issues that arise in connection with the HIV epidemic. One thing that should, however, be noted is that many of these research works mainly focused on the assessment of the prevalence and the study of the numerous prevention measures that should be undertaken to stop or reduce the spread of the epidemic. Little attention seems to have been given to study the situation of those living with the virus. Especially when seen in light of the current situation in the country where we have over 1 million individuals living with the virus in 2008/2009 only (7), it is important that research works focus on the study of PLWHA situation. This is more so when we see the large number of HIV positive people who are following ART.

Thus, it should be stated at this juncture that researches should be conducted to evaluate the effectiveness of the free antiretroviral drugs treatment option. Though research work is not non-existent in this area, many of them focused on the study of drug adherence. Many of the factors that can possibly affect the survival status of people who are in ART follow up remain unstudied. And in most cases these studies were limited to urban areas mainly Addis Ababa.

The effectiveness of HAART could vary from region to region (this variation is also generally a reflection of the variation that exists between and within countries and regions as regards HIV prevalence and its epidemiological patterns) because of the difference in background disease burden (such as tuberculosis or intestinal parasites),

viral subtypes, and possible genetic differences in drug metabolism. However, such arguments are based on little data from the resource-limited settings (5).

Given this as a back drop, this thesis will focus on the consideration of some of the possible factors/variables that may possibly influence the survival status of people who are following ART in West Ethiopia. The study of these factors will provide information to put in place efficient ART system that will take into account the huge cost that is involved in the system. It is the fact that little has been done on the factors that influence the survival status people, given that he/she is already HIV positive following ART and also the current health policy give priority for prevention than treatment of disease.

1.3 Objective of the Study

1.3.1 General Objective

To assess factor affecting survival status among PLWHA who are on HAART treatment in Dembi Dollo Hospital.

1.3.2 Specific Objectives

The specific objectives of the study are:

1. To estimate the survival pattern of HIV patients treated with HAART.
2. To compare survival time among the different groups of HIV patients treated with HAART; and
3. To determine the factors and/or covariates that affect the survival of HIV patients treated with HAART.

Research Questions

Based on the stated research problem the research focused on:

- Which social, economic and demographic variables affect the chance of survival of HIV positive people under the HAART program in DDH?
- What are the health care related factors that influence the survival of ART clients?

1.4 Significance of Study

The survival benefit of highly active antiretroviral therapy (HAART) in HIV infection and its impact on the incidence of opportunistic infections have been well studied in the developed World. In resource-poor settings, where such treatment was started only recently, limited data exist both on treatment results and on how to carry out such interventions. As a result, the existing treatment guidelines and recommendations are based on data from the developed world (9). The study will give some evidence and information for governmental and non -governmental organizations which work in the area of HIV/AIDS specifically on ART at national, regional and district level by providing basic information on factors affecting survival of PLWHA and started ART treatment.

The relevance and significance of the study pointed out like:-

1. The findings from this study will be expected to give information for public health practitioners and stakeholders who are working in the areas of giving care, support and treatment for HIV/AIDS patients.
2. The findings of this study will provide empirical evidence for program

planners, decision makers and ART program implementers at different levels by enabling them to access a baseline data on predictors of survival on PLWHA after the advent of HAART.

3. The study will also aid HIV patients by providing information about those socio- demographic factors and baseline clinical/laboratory characteristics, which have influence on the survival of patients, so that they can improve their quality of life accordingly.
4. It is also believed that results of the research will be used as a basis for further study in the area.

1.5 Limitation of the study

1. The study is conducted based on secondary data which might have incomplete and biased information.
2. The study was restricted to adults, and results might not be applicable to infants and children.
3. Underestimation of mortality due to lost to follow up patients excluded in the study. In addition to this all deaths are assumed to be caused by AIDS.
4. The study includes only baseline values of the variables. i.e. CD4 cell count stability or improvement, weight lose or gain, viral load, Body Mass Index, treatment switches or substitute , number of missed appointments, which are associated to mortality of AIDS patients, are not included in the study.
5. Selection bias is possibly introduced during secondary data collection because patients with incomplete records were excluded

6. Generalizability is questionable as important predictors of survival in other studies such as viral load and BMI were not considered.

1.6 Strength of the study

- ❖ Study was carried out in the farthest Hospital from Addis Ababa
- ❖ Retrospective cohort study
- ❖ The study gives an insight for researchers especially in carrying out prospective study.

CHAPTER TWO

2. LITERATURE REVIEW

2.1 Burden of HIV/AIDS globally and ART use in Ethiopia

Globally HIV /AIDS burden and situation of HAART program in Ethiopia context globally 33.3 million people are living with HIV/AIDS about 2.6 million people are newly infected and of this more than 95% of new infection are in developing .many of them needing ART (2) in sub- Saharan Africa 1.8 million people became infected in 2009(2) in the industrialized world the introduction of HAART in 1996 dramatically improved the prognosis for HIV infected (10) until recently however access to treatment has been severely limited in developing countries where the majority of people with HIV live in sub-saran Africa only 37% of people eligible for treatment where able to access life saving medicines in 2009(8).

A study in the US conducted from January 1994 through June 1997 which evaluated 1255 patients who were using antiretroviral revealed that mortality among the patients declined from 29.4 per 100 person-years in 1995 to 8.8 per 100 person-years in the second quarter of 1997. The incidence of major opportunistic infections (OI) also declined from 21.9 per 100 person-years in 1994 to 3.7 per 100 person-years by mid-1997. There were also reductions in mortality and incidence of opportunistic infections regardless of sex, race, age, and risk factors for transmission of HIV (9).

ART changes the natural history of HIV infection. Results from medical studies on HAART have been extremely impressive. Since its introduction in 1996, mortality and morbidity rates in HIV-infected individuals in countries with widespread access to HAART have plummeted. The use of antiretroviral medicines dramatically reduced

AIDS related illnesses and death in countries where these drugs are widely accessible (10). Although the treatments are not a cure and continue to present new challenges with respect to side-effects and drug resistance ART as disease modifying therapy for established HIV infection has produced dramatic effects on morbidity and mortality among HIV-infected patients. As a result of the widespread use of ART, the HIV/AIDS pandemic which was once regarded as an infectious disease with an almost universal fatal outcome has been transformed into a manageable chronic infectious disease (11, 12).

In Ethiopia 47% of the total population is aged 15 to 49 years. The highest prevalence occurs in the age group 15-24, 90% of HIV infection occurs in adults between 15-49 years. In Ethiopia 443,964 PLWHA enrolled, 246,347 PLWHA started treatment and 179,183 are currently on ART. The total person on 1st line regimen is 166,444 of which 156,083 are adults. The total number of persons on 2nd line regimen is 1000 of which 865 are adult. Antiretroviral medications are designed to inhibit the reproduction of HIV in the body. The main effect of antiretroviral treatment is to suppress viral replication, allowing the individual's immune system to recover and protect him/her from the development of AIDS and death. In other words what this means is that if ART is effective, the deterioration of the immune system and the onset of AIDS can be delayed for years thereby improving the quality of life of the victims. Standard ART (also known as HAART) consists of the use of at least three ARV drugs to maximally suppress the HIV virus and stop the progression of HIV disease (12, 13).

2.2 Factors affecting survival

To identify prognostic indicators of survival at different CD4+ cell levels, independent of HAART, among IDUs a study was conducted in Baltimore. The outcome of interest was HIV- related death, defined as death after an AIDS diagnosis or a diagnosis of another infectious disease such as sepsis or endocarditic. Analysis using the Cox proportional hazards model showed that prior hospitalization and AIDS diagnosis were independent consistent risk factors for HIV mortality, whereas outpatient/emergency room (ER) visits, sepsis or endocarditic and alcohol use were significantly associated with higher mortality, specifically for the low CD4 count group. It was also shown that survival among HIV-infected IDUs improved since the introduction of HAART, although utilization of HAART was incomplete (14).

Study conducted in the far north province of Cameroon showed that survival probability was 77% at 1 year [95% CI: 75–80] and 47% at 5 years [95% CI: 40–55]. The median survival time was 58 months. CD4 count, hemoglobin, BMI, sex and clinical stage at enrolment were independent predictors of mortality. Patients with a baseline CD4 count <50 cells/mm³ presented a mortality risk twice as high as those with >50 cells/mm³ (HR 1.85). A BMI between 15 and 18.5 kg/m² was related to a 1.5 times higher risk of death than a BMI >18.5 kg/m² (HR= 1.57). This risk rose to three times more for those with a BMI <15 kg/m². Patients in stage III and IV were two to four times more likely to die than patients in stage I and II. Men were at nearly twice the risk of death as women (HR = 1.7). Patients with hemoglobin <8.5 g/dl had two times more risk of death than those with a hemoglobin rate >8.5 g/dl (15).

In a study of 421 Italian patients with AIDS who were followed for up to 30 months, a hemoglobin level of 8 to, 11g/dL was associated with a relative risk of dying of 1.9 (95%CI 1.3–2.8) and a hemoglobin level of 8 g/dL was associated with a relative risk of dying of 2.9 (95% CI 1.9–4.5) compared with patients having a hemoglobin level of above 11 g/dL at the time of diagnosis of AIDS (18). WHO stage IV diseases, however, was found to be a strong predictor of mortality in all studies reporting on this (16).

In three studies comparing patients with WHO stage IV disease at baseline with those with WHO stages I–III, WHO stage IV was associated with more than a doubling in the hazard of death (summary hazard ratio, 2.2; 95% CI, 1.5–3 (1). The mortality hazard ratio (HR) of those with a baseline BMI <18 compared with those with a baseline BMI >18 was 3.4 (95% CI, 3.0–3.9). The median survival time of those presenting with a BMI <16 was 0.8 years, in contrast to a median survival of 8.9 years for those with a baseline BMI >22. Baseline BMI <18 remained a highly significant independent predictor of mortality after adjustment for age, sex, co-trimoxazole prophylaxis, tuberculosis, reported wasting at diagnosis, and baseline CD4+ cell count (adjusted HR = 2.5, 95% CI 2.03.0) (17).

Female patient had significantly lower age, higher prevalence of heterosexual contact and lower prevalence of intravenous drug use as risk factors for HIV infection than male subjects. They were also reported to have higher previous exposure to antiretroviral therapy, higher CD4 cell counts and lower viral loads than male individuals (18, 19).

7.14), a hemoglobin concentration ≤ 8 g/dl (HR 1.23, 95% CI 1.08 - 1.40), a history of oral candidacies (HR 3.17, 95% CI 1.70 - 5.87) and a history of cryptococcal meningitis (HR 2.76, 95% CI 1.80 - 19.2). A CD4 cell count $< 50/\mu\text{l}$ (HR 3.08, 95% CI 1.54 - 5.88) and a history of oral candidacies (HR 2.58, 95% CI 1.37 - 4.88) remained significant in multivariate analysis (26, 27).

A study was conducted in Tanzania with the objective of assessing mortality and to identify predictors of mortality in HIV-infected patients starting ART in one rural hospital. The study used Kaplan-Meier models to estimate mortality and Cox proportional hazards models to identify predictors of mortality and it was found that male sex, severe malnutrition and WHO stage IV were associated to progression to death and no such associations were found for age, religion, education level and active TB in the univariable analysis (28,29). A similar retrospective cohort study in northern Thailand, which used the same method of analysis, also revealed that sex, age group, registered year, clinical status, CD4 group, and ARV drug group were all significantly related to death in the univariable analysis, but the association with sex and age group was not significant in the multivariate analysis (30).

To assess the effect of adherence to HAART on survival (30, 31) has conducted a retrospective cohort study on 897 Ugandan patients who are treated with HAART between May 2004 and December 2006. Kaplan-Meier curves and Cox proportional hazards regression model were used in the analysis. In this study, which found out that non-adherence to HAART was significantly associated with mortality, it was shown that patients with a CD4 count of less than 50 cells/ mm^3 had a higher risk of mortality (HR = 4.3; 95% CI: 2.22–5.56) compared to patients with a CD4 count

Compared with younger patients, older patients were more likely to be on non nucleoside reverse transcriptase inhibitors based versus protease inhibitor based regimens (42 vs.29%, $P<0.01$). Older patients had fewer AIDS-defining opportunistic infections (22 vs.31%, $P<0.01$), but higher mortality (36 vs. 27%, $P=0.04$) and shorter survival (25th percentile survivor function 36.2 vs.58.5 months, $P=0.02$) than younger patients (20).The analysis in Nigeria demonstrates Male gender (HR,1.77,CI,1.15_2.75, $P<0.010$), age less than 30 years old (HR ,1.65, CI ,1.07_2.53, $P<0.023$), CD4 count less than 50 (HR,3.28, CI,2.20_4.89,PB=0.0001),co-infection with HIV and TB(HR=3.53,CI, 2.36_5.28, PB=0.0001),and unemployment/unknown occupation (HR,1.79, CI,1.21_2.66) were significantly associated with increased risk of death (21,22).

Significant risk factors associated with mortality included WHO stage IV disease, a baseline CD4 cell count under 50cells/ μ l and increasing grades of malnutrition. Individuals who were severely malnourished [body mass index (BMI) < 16.0 kg/m] had a six times higher risk of dying in the first 3 months than those with a normal nutritional status (23).

Study conducted in Thailand showed that the Survival rates at 1, 2, and 3 years after TB Diagnosis were 96.1%, 94.0%, and 87.7% respectively for ART+ group and 44.4%, 19.2%, and 9.3% respectively for ART- group (log-rank test, $P<0.001$). Among patients in ART+ group, the patients who delayed ART $\geq$ 6 months after TB diagnosis had a higher mortality rate than those who initiated ART<6 months after TB diagnosis ($P=0.018$, hazard ratio=2.651, 95% confidence interval=1.152-6.102) (24, 25).

Study conducted in south Africa reveals that the strongest predictors of mortality were a CD4 cell count <50/ μ l (hazard ratio (HR) 3.70, 95% confidence interval (CI) 1.96-

equal to or greater than 50 cells/mm³ (HR = 2.4; 95% CI: 1.79–2.38).

A collaborative analysis of prospective studies which includes 13 cohort studies from Europe and North America assessed the Prognosis of 12,574 adult HIV-1-infected patients who were on HAART (32). The end points considered were progression to a new AIDS-defining disease or death and to death alone. The prognostic model that generalized best was a Weibull model, stratified by baseline CD4 cell count and transmission group. Baseline CD4 cell count was strongly associated with the probability of progression to AIDS or death: compared with patients starting HAART with less than 50 CD4 cells/μl, adjusted HRs were 0.74 (95% CI: 0.62–0.89) for 50–99 cells/μl, 0.52 (95% CI: 0.44–0.63) for 100–199 cells/μl, 0.24 (95% CI: 0.20–0.30) for 200–349 cells/μl, and 0.18 (95% CI :0.14–0.22) for 350 or more CD4 cells/μl. Other independent predictor of poorer outcome was advanced age (33, 34).

Another study which included 1,308 patients on HAART was conducted in rural Malawi. The study used Product-limit estimates (Kaplan-Meier) to assess the probability of survival and Cox model to assess the independent predictors of death after initiation of HAART. Low BMI, WHO stage IV, male sex, and baseline CD4 count lower than 50 cells/μl were independent determinants of death in the first 6 months. However, age at HAART initiation and regimen types are not significantly associated with early death (35).

To assess the incidence of mortality, clinical characteristics and outcome of co-infection with HIV and TB, (36) conducted a cross-sectional study of co-infected cases reported from nine domestic hospitals throughout mainland China. Treatments for TB and HIV were provided to 241 patients and mortality attributable to co-infection was

reported for 15.8% of the cases. Immune function among most patients was suppressed based on reduced CD4 cell counts. HIV/TB co-infection was related to high mortality even when HAART and/or drug therapy for TB was provided. It was found that fever, fatigue, and weight loss were experienced by the majority of HIV/TB patients (87.6%, 61.0% and 60.2%, respectively), making these the leading clinical symptoms among co-infected patients. Another study conducted in Baltimore USA also revealed that, accounting for potential confounders, including CD4 cell count and viral load, the hazard of AIDS-related death was 2.4 times more for the person-time with TB compared to the person-time without TB (37,38).

A cohort study in Abidjan in which 792 adults started ART, with a median CD4 cell count of 252 cells/ml and were followed for a median of 8 months, showed that patients who experienced severe morbidity had higher risks of mortality, virological failure and immunological failure. Other independent risk factors for mortality and/or severe morbidity were at baseline: high viral load, advanced clinical stage, past history of tuberculosis, low BMI, low hemoglobin and low CD4 cell count; and during follow: low CD4 cell count and persistently detectable viral load (39).

To evaluate sex differences in HIV disease progression before (pre-1997) and after (post-1997) the introduction of HAART, a study which investigated 6,923 seroconverters from a collaboration of 23 HIV seroconverter cohort studies from Europe, Australia, and Canada was conducted. Within a competing risk framework, the authors used Cox proportional hazards models allowing for late entry to evaluate sex differences in time from HIV seroconversion to death, to AIDS, and to each first AIDS-defining disease and death without AIDS. While no significant sex differences were

found before 1997, from 1997 onward, women had a lower risk of AIDS and death than men did. Compared with men, women also had lower risks of AIDS dementia complex, tuberculosis, Kaposi's sarcoma, lymphomas, and death without AIDS. According to this research sex differences in HIV disease progression have become larger and statistically significant in the era of HAART, supporting a stronger impact of health interventions among women (40).

Although the consensus is that gender does not influence HIV progression, its relevance may depend on the setting. In a Spanish study, conducted to study gender differences in HIV progression to AIDS and death in a cohort of HIV infected injection drug users (IDUs), Kaplan-Meier methods and Cox regression adjusting for gender, age, and calendar period fitted as time dependent covariates were employed. Of the 929 IDU, 24.7% were women. ART was initiated in 44% of women and 34% of men. Risk of AIDS was lower in women in both univariate and multivariate analyses although it is not statistically significant. In general, the study concluded that HIV progression was lower in female IDUs before and after the introduction of HAART and their uptake of ART was higher than male IDUs (41).

Population-based, prospective cohort study was conducted on 3,116 antiretroviral naive HIV- infected patients in a province-wide HIV/AIDS treatment program in British Columbia, Canada, to compare survival rates among HIV-infected patients initiating HAART with and without a history of injection drug use. The main outcome measure of the study is all-cause mortality. Of the 3,116 patients, 915 were IDUs (29.4%), 579 were female (18.6%), and the median age was 39.4 years.

Treatment with HAART was initiated between August 1, 1996, and June 30, 2006. The median duration of follow-up was 5.3 years for IDUs and 4.3 years for non-IDUs. Patients were followed up until June 30, 2007. At 84 months after the initiation of HAART, the product limit estimate of the cumulative all-cause mortality rate was similar between the IDUs (26.5%) and non-IDUs (21.6%) (Wilcoxon $P=0.47$). The time-updated Cox regression also showed that, the hazard ratio of mortality was similar between IDUs and non-IDUs after adjustment for baseline CD4 cell count, adherence, and physician experience. In general injection drug use was not associated with decreased survival among HIV-infected patients initiating HAART in this study (42).

In Uganda a retrospective cohort of 427 HIV-1 patients who were initiated on ART was studied to establish the effect of AIDS defining complexes (ADCs) on immunological recovery among patients initiated on ART. Kaplan-Meier survival curves were employed to estimate median times, log rank test to compare different categories and Cox proportional hazard models were used at multivariate analysis. The median time to gaining 50 CD4 cells/ μ l from the baseline value after ART initiation was longer in the ADC group (9.3 months) compared to the non-ADC group (6.9 months) (log rank test, $p = 0.027$). At multivariate analysis after adjusting for age, sex, baseline CD4 count, baseline HIV viral load, total lymphocyte count and adherence level, factors that shortened the median time to immunological recovery after ART initiation were belonging to the non-ADC group ($HR = 1.31$, $p = 0.028$), adherence to ART of $\geq 95\%$ ($HR = 2.22$, $p = 0.001$) and a total lymphocyte count ≥ 1200 cells/ mm^3 ($HR = 1.84$, $p = 0.003$). A low baseline CD4 count of ≤ 200 cells/ μ l ($HR = 0.52$, $p = 0.001$) was associated with longer time to immunological recovery. There was no interaction between low CD4 counts and ADC group. Patients with

ADCs take longer to regain their CD4 counts due to the defect in the immune system. This may prolong their risk of morbidity and mortality (43).

A prospective cohort study conducted to determine the long-term incidence of TB and associated risk factors among individuals receiving HAART in South Africa found that risk of TB was independently associated with CD4 cell count < 100 cells/ml ($P = 0.04$), WHO stage III or IV disease ($P = 0.01$) and age < 33 years ($P = 0.01$). Risk of TB was not independently associated with plasma viral load, previous history of TB, low socioeconomic status or sex. Despite similar virological responses to HAART, blood CD4 cell count increases were much smaller among patients who developed TB than among those who remained free of TB (44).

To determine the relationship between mortality risk and the CD4 cell response to ART, a cohort of 2,423 patients on ART and who had a median baseline CD4 105 cells/ μ l were observed for up to 5 years of ART in South Africa. Kaplan-Meier analyses were used to estimate cumulative mortality, univariate and multivariate mixed effect Poisson regression models were used to estimate the association between baseline risk factors, updated CD4 cell counts and viral load and the incidence of mortality. In addition Wilcoxon rank-sum tests were used to compare medians. Older age, WHO clinical stage 4, updated CD4 cell counts and detectable updated viral load measurements were all significantly associated with mortality risk in both the crude analyses and the multivariate model with the exception of male sex which is significant in the crude analysis only. However, updated CD4 cell counts were the variable most strongly associated with death (45).

Defaulting diminishes the immunological benefit of ART and increases AIDS-related morbidity, mortality and hospitalizations. In resource-constrained settings

where the health care services are not well developed, poor adherence to treatment and defaulting from treatment are the two major challenges that ART programs face (46). To determine the prevalence and factors associated with defaulting ART in Jimma, Ethiopia, unmatched case control study was conducted. Taking hard drugs (cocaine, cannabis and IV drugs), excessive alcohol consumption, being bedridden, living outside Jimma town and having HIV negative or unknown HIV status partner were independently associated with defaulting ART in the logistic regression analysis (47). A French study conducted to assess adherence to HAART in a cohort of patients infected by HIV through IDU has also shown that non-adherence was associated with younger age, alcohol consumption, frequency of negative life-events during the prior 6 months and active drug use after adjustment by logistic regression (48).

In the era of HAART, maximizing health-related quality of life has become a high priority of long-term management of HIV-infected individuals. To identify the predictors for lower quality of life among HAART-using HIV infected homosexual and bisexual men participants in 4 cities of USA, a longitudinal cohort study was conducted and predictors were assessed using the random effects model. Quality of life before HAART initiation was a strong predictor of quality of life subsequent to HAART initiation. Older age, lower socioeconomic status, less male sexual partners, no alcohol drinking, and more advanced HIV disease stage were significant predictors for lower physical health summary score. In addition, more outpatient visits, depression, amprenavir use, antiretroviral drug interruption, recreational drug use, and less social support were significantly associated with lower mental health summary score (43).

In south Ethiopia a series of studies were conducted on HIV infected patients to investigate the risk factors for HIV disease progression among untreated patients, to assess the effect of ART on patient mortality and tuberculosis incidence rate and to identify risk factors for mortality in patients treated with ART. Survival analysis methods such as log rank test, Kaplan Mayer and Cox regression models were employed in the study and the main outcome measures were time to death and time to diagnosis of tuberculosis. Among 207 untreated patients followed for a median duration of 19 months the mortality rate was 46 per 100 PYO, mortality increased with advanced disease stage and diarrhea, oral thrush and low total lymphocyte count were significant markers of mortality. In addition among 152 patients treated with HAART the overall mortality was 16.7 per 100 PYO. The highest death rate occurred in the first month of treatment. Being in WHO clinical stage IV and having $TLC \leq 750 / \text{mcL}$ were independent predictors of death but $BMI \leq 18.5 \text{ kg/m}^2$ at baseline was associated with death in univariate analysis. More over on the follow up data; decline in TLC, HGB and BMI was associated with death in univariate analysis only (48). Person year of observation (PYO) = number of observation multiplied by the number of years.

2.4 Operational Definition

CD4 count: a way of measuring immune-competency by counting the lymphocyte that carry the CD4 molecules.

Drop out: if a patient discontinued ART for at least three month as recorded by ART physician

Fair Adherence: if the percentage of missed dose is between 85-94 % (3-5 doses of 30 doses or 3-9 dose of 60 dose) as documented by ART physician

Good Adherence: if the percentage of missed dose is $>95 \%$ (< 2 doses of 30 doses or

<3 dose of 60 dose) as documented by ART physician.

Immunodeficiency: break down in immune-competence to resist or fight off infections.

Lost: if a patient discontinued ART for at one to three month as recorded by ART physician

Opportunistic infections: illness caused by various organisms, some of which usually do not cause disease in persons with healthy immune systems.

Poor Adherence: if the percentage of missed dose is between <85 %(> 6 doses of 30 doses or >9 dose of 60 dose) as documented by ART physician

Survival: Lack of experience of death

Competing Risks: Deaths from other causes

2.5 Conceptual Frame Work

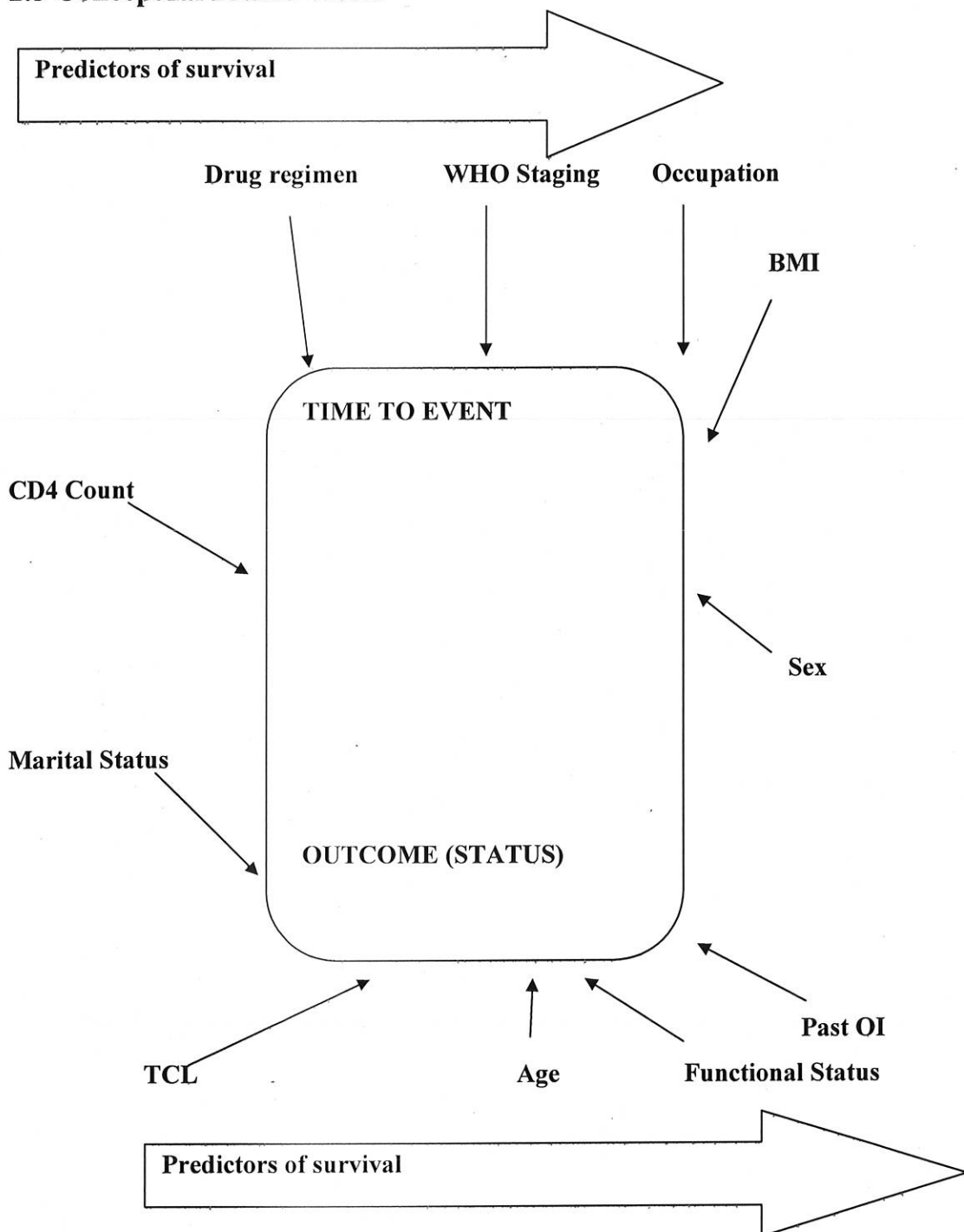


Fig: Modified and developed by author
(From: Tamasegen.A; 2008, Determinants of mortality and fertility)

CHAPTER THREE

3. METHODOLOGY AND DATA

3.1 Background of the study area

The study area is geographically located in Oromia regional state Kelem Wollega zone. The zonal capital town is DD, located 667Km from Addis Ababa. In Dembi Dollo town there is one zonal Hospital, one health center which give preventive, curative and rehabilitative service for the catchment area population. The town is crossed by high road coming from the center of country and characterized by high in and out flow transient people in order to purchase coffee and other things from the town. These movements assumed to expose people to high risk of HIV/AIDS. Currently there are four government Hospital and more than fifteen health center providing ART treatment service in the zone. So the researcher selected DDH as research area because it the place of born and the remotest area from Addis Ababa. ART clinics in DDH give ART service for HIV/AIDS patients, a total of 1939 have been enrolled, 1122 ever started ART, 100 patients dead and 754 patients are currently on ART. Therefore the study conducted in the Hospital from January 2013 to March 2013.

3.2 Study design and data types

A retrospective cohort study conducted in DDH to assess survival status of PLWHA who are on HAART. This retrospective cohort study, which reviews the patient intake forms and follows up charts of HIV/AIDS patients taking ART in DDH. In this study data collected from medical records under ART program about HIV positive peoples in DDH in collaboration with ART nurses and data clerk which is secondary data

type. In addition to this, qualitative method of data collection employed using semi-structured type of questionnaires and Focus Group Discussion.

Source population

All HIV/AIDS patients and started ART treatment in the Hospital are source of Population in this study. Those registered and effectively following ART service in the facility are assumed to be target population of the researcher.

Those patients fulfilling the following criteria included and excluded from the study.

Inclusion criteria:

- HIV positive adults aged 15yrs or older who started ART
- HIV positive patients with complete intake form, registers and follow up form

Exclusion criteria

- If diagnosis is made outside of health institution
- pregnant women at the time of ART initiation and lactating mother
- Loss to follow up

3.3. The Data

The data for this study were obtained from the ART clinic in DDH which is found in Dembi Dollo town. The Hospital serves as a teaching and referral centre for the population of DD zone and other adjacent zones and regions in West Ethiopia. It has a separate unit for the ART program. DDH launched ART treatment service in July 2003 for PLWHA who are financially strong and have the capability to pay for ART according to the national treatment guidelines. Later by the year 2005 the Hospital started to register and give free ART services for those who fulfill standard diagnostic criteria to start ART. In addition to adherence counseling and providing ART for HIV patients, the clinic also provides screening, follow up and referral

services for TB patients. All diagnosed HIV positive individuals from VCT, PMTCT or inpatient services were sent to the ART centre and registered. For those HIV patients, who were eligible to start ART according to the national treatment guideline, a unique ART number was given to each patient.

This study reviews patient's intake forms and follow-up cards of HIV patients taking HAART in DDH ART clinic. The patients' chart include the patient intake forms and follow-up cards, which are prepared by Federal Ministry of Health (FMOH) to be uniformly used by clinicians to simply identify and document clinical and laboratory variables. A sample of 491 patients taken from clinic, on which HAART was initiated between the times October 2003 and December 2010, were included in the study and they were followed up until December 30, 2012.

3.4. The methodology: Survival analysis

Survival analysis is the phrase used to describe the analysis of data in the form of a well-defined time origin until the occurrence of some particular event or end point. Generally, survival analysis is a collection of statistical procedures for data analysis for which the outcome variable of interest is time until an event occurs. The problem of analyzing time-to-event data arises in a number of applied fields such as medicine, biology, public health, epidemiology, engineering, demography and economics. In medical research, the time origin will often correspond to the recruitment of an individual into an experimental study, such as a clinical trial to compare two or more treatments. This in turn may coincide with the diagnosis of a particular condition, the commencement of a treatment regimen, or the occurrence of some adverse event. If the end point is the death of a patient, the resulting data are literally survival times. However, data of a similar form can be

obtained when the end point is not fatal, such as the relief of a pain, or the recurrence of symptoms. In this case the observations are often referred to as time-to-event data.

One of the most important differences between the outcome variables modeled via linear and logistic regression analyses and the time variable in the survival data is the fact that we may only observe the survival time partially. The variable time actually records two different things. For those subjects who experienced the event (most of the time death), it is the outcome variable of interest, the actual survival time.

However, for subjects who were alive at the end of the study, or for subjects who were lost to follow-up, time indicates the length of follow-up (which is a partial or incomplete observation of survival time). These incomplete observations are referred to as being censored.

Most survival analyses consider a key analytical problem called censoring. In essence, censoring occurs when we have some information about individual survival time, but we do not know the survival time exactly. Survival data are not in general amenable to standard statistical procedures, such as mean, standard deviation and ANOVA, used in statistical analysis and mostly they are positively skewed.

Descriptive methods for survival data

An initial step in the analysis of a set of survival data is to present numerical or graphical summaries of the survival times in a particular group. Such summaries may be of interest in their own right or as a precursor of a more detailed analysis of the data. Routine applications of standard formulas for measures of central tendency and variability will not yield estimates of the desired parameters when the data include

censored observations. In summarizing survival data there are two functions of central interest namely the survivor function and the hazard function.

3.5 Sample size determination and sampling technique

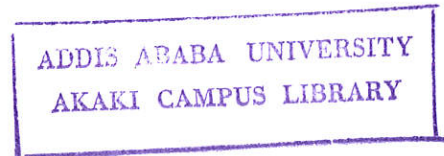
Sample size determination

Preliminary sample size determination is obtained by the collected information from the given population of HIV patients. So that sample size determination manipulated and retrieved using single population proportion formula as shown below. Sample size determination using single population proportion:

It takes as a basic requirement the total population size (N), the margin of error (E) and the tabulated value for 95% confidence coefficient ($Z_{\alpha/2}$),

Let p = sample proportion of death

θ = population proportion of death, then



A 95% CI for θ is ($\theta \pm Z_{\alpha/2} \text{S.E.}(\theta)/n$)

In this study the statistical level of significance ($\alpha=0.05$) and margin of error ($E=0.03$). Assuming margin of error $E=0.03$ because data is secondary type and there may be mistake in recording. The population proportion is estimated using the total of survival patient =754 and total of dead patients = 100 in the given total population size of $N=1939$ from January 2010 to December 2012 is calculated as

$$\theta = \frac{100}{754} = 0.1326$$

(Events), $1-\theta = 0.8674$ (Censored)

Assuming margin of error ($E=0.03$), $E = Z_{\alpha/2} \text{S.E.}(\theta)/n$

$$n = (Z_{\alpha/2})^2 \theta (1-\theta) / (E)^2$$

$$n = (1.96)^2 (0.1326) (0.8674) / (0.03)^2$$

$$n = 490.9, n \approx 491$$

Sampling Frame

Intending objective of the research leads to the area of HIV patients those found in DDH under the HAART follow up. Considering all things on the ART program, the study focused or generated on the patients who are regularly registered, transferred in, transferred out, died, lost and dropped out in the program from January, 2010 to December, 2012.

Sampling technique

Study participant selected by using systematic random sampling method by which one of random number in the Patient's ART unique identification numbers as a starting point and every number next to random number taken as a study participant if the data in registration book is incomplete the next number taken as a study participant. Profiles of all patients on ART assessed. Systematic random sampling method adapted as a sampling design for collecting a sample of patients based on their ART identification number and using the following procedures.

- ✓ Taking a simple random sampling from the given frame of the sample only for the first unit.
- ✓ Taking the total population and the sample size. Find the k value, $k = N/n$
- ✓ After such calculation for k, automatically select the remaining units in a definite sequence at equal spacing k (i.e. choose the 1st element and next the (k+1)th element)

Where n - is sample size taken

N - Is population size, k - Is the constant for equal sampling

3.6 Study Variables

In attempting to answer research questions, study conducted on identifying factor influencing Survival status of HIV positive people under the HAART program in DDH with the aim of:-

Identifying the socio-economic factors such as:

- Educational level
- Access to nutrition
- Psychological support
- Treated with respect and with complete considerations of human rights, privacy and confidentiality.
- Stigma and discrimination
- Residence
- Functional status

❖ Explore the variables among the demographic ones:

- Marital status
- Age
- Sex
- And others

❖ Among health care related ones :

- CD 4 count
- Weight of clients
- Partners HIV status
- WHO clinical stage
- TB treatment

Independent variable

The independent variables are:

- Socio demographic characteristics (age, sex, religion, ethnicity , marital status, Employment, educational status)
- Base line clinical, laboratory and ART information(opportunistic illness, WHO clinical staging, TB test and treatment, ART treatment, drug allergies, BMI, CD4count, side effects)
- ART treatment
- Follow up data

Dependent variables

The response/outcome variable is the survival time of HIV patients, the length of time from ART start date until the date of death/censor measured in months. The response variable, survival status has a binary assumption of two values (0) and (1) i.e. if the response is “0”, the individual patient is survive, and if it is “1”,the individual patient is dead , under the ART program.

The variables included in the study:

From the way of classifying data based on the association of the variables, this research includes both independent and dependent variables. The related dependent variable is the survival time of HIV positive people under HAART and it is measure of the association of the subject that reflects the effects of the independent variables which are listed as follows:

- Age in completed years
- Sex (Male, Female)
- Marital status (Never Married, Married, Others)
- Level of Education (No education, Primary, Secondary and above)

- Religion (Protestant, Catholic, Muslim, Orthodox, Others)
- Employment status (Farmer, Merchant, Gov't, Driver, Day laborer ,Unemployed, NGO)
- past opportunistic infection (yes, no)
- TB Co-infection (yes, no)
- HIV disclosure (yes, no)
- Risk behavior (Regular sexual partner, Casual or both sexual partner)
- Substance (Tobacco, Alcohol, Soft drugs) use (yes, no)
- Functional status (Working, Ambulatory and Bedridden)
- WHO clinical stage (Stage I or Stage II, Stage III and Stage IV)
- CD4 cells count of patients
- Weight of patients
- R e g i m e n (AZT-based, D4T-based)

Questionnaire

The checklist consists of the following data;

- Socio-demographic data
- Base line clinical, laboratory and ART data
- ART treatment
- Follow up data

3.7. Data collection procedure and quality control

Data was collected form ART entry and follow up form in the ART clinic. The researcher collect data by reviewing pre-ART register, laboratory request, monthly cohort form, and follow up form, ART intake form, patients' card and death certificate complemented by registration by home visitors. The most recent laboratory results before starting ART uses as base line value. If there is no pre-treatment laboratory test, results obtained within one month

of ART initiation used .Supervisors and data collectors trained for more than three days. The overall activity controlled by the principal investigator of the study. Data quality happens by designing the proper data collection materials and through continuous supervision. The data entered by trained data clerk and cleaned by principal investigator before analysis.

At the starting point of Antiretroviral treatment patient detailed socio-demographic health related facility was recorded on ART intake and follow up forms. Base line clinical and biological parameter including patients functional status, WHO clinical stage and CD4 cell count and others recorded. Patients expected to attend ART clinic on monthly basis. During each visit patient are provided with ART drugs for the up coming month and their status is assessed and recorded. The study uses log-book to retrieve secondary data. Based on the inclusion criteria 491 patients included in the study.

Data processing and analysis

Data analyzed using Stata version 12 and SPSS version 16.0 for windows. The data cleaning and editing took place before analysis. Patient cohort characteristics put in terms of mean/median value for continuous data and percentage for categorical data. Deaths confirmed by reviewing the

death certificates, medical registration in the hospital, or registration by ART adherence supporter through calling using the registered phone number and individuals alive and on ART at the end of the study period assumed to be censored. The outcome of each subject assumed to be dichotomized that is censored or death. Univariate analysis uses to describe patient's baseline characteristics of covariate. Actuarial (Life) table estimate survival after initiation of HAART, Kaplan–Meier curves to estimate survival probability and log rank test to compare survival curves. Cox proportional-hazard regression used to calculate the bivariate and adjusted hazard rate and then determine independent predictors of time to death.

3.8 Variable Selection Procedures

In many settings a variety of explanatory variables are measured and a major question in analyzing such data sets is how to incorporate these variables in the modeling procedure. An initial step in the model selection procedure is to identify a set of explanatory variables that have the potential for being included in the linear component of the proportional hazards model. Once a set of potential variables has been isolated, the combination of variables that has to be used in modeling the hazard function has to be determined. An important principle in statistical modeling is the hierarchic principle, and means that interactions should not be fitted unless the corresponding main effects are present. When the number of variables is relatively large, it can be computationally expensive to fit all possible models. In this situation, automatic routines for variable selection that are available in many software packages might seem an attractive prospect. These routines are based on forward selection, backward elimination or the combination of the two known as the stepwise procedure.

The model selection strategy depends to some extent on the purpose of the study. In a situation where the aim is to identify variables upon which the hazard function depends, instead of using the automatic variable selection procedures, the following procedure is recommended in (48).

1. The first step is fitting a univariable model for each of explanatory variables and identifying the variables that are significant at some level of significance. (A significance level from 20% to 25% is recommended in Hosmer and Lemeshow (1999)).
2. The variables that appear to be important from step 1 are then fitted together in a multivariable model. In the presence of certain variables others may cease to be important. Consequently, backward elimination is used to omit non significant variables from the model. Once a variable has been dropped, the effect of omitting each of the remaining

variables in turn should be examined.

3. Variables, which were not important on their own, and so were not under consideration in step 2, may become important in the presence of others. These variables are therefore added to

the model from step 2, with forward selection method. This process may result in terms in the model determined at step 2 ceasing to be significant.

4. A final check is made to ensure that neither no significant variable is eliminated from the model nor non significant variable is included in the model. At this stage the interactions between any of the main effects currently in the model can be considered for inclusion if the inclusion significantly modifies the model. For steps 2, 3 and 4 a level of significance around 10% is recommended in (48).

3.9 Ethical Considerations

The proposal submitted to the Institutional Review Board (IRB) of Addis Ababa University, Institute of Development Studies for approval. Following the approval by IRB, Official letter of co-operation written to concerned bodies by the College of Development Studies of Addis Ababa University. Study conducted through review of medical records, the individual patients had not subjected to any harm as far as the confidentiality is kept. To preserve the confidentiality, nurses working in ART clinic in DDH extracted the data from the medical records. Moreover, no personal identifier used on data collection form. The recorded data wouldn't accessed by a third person except the principal investigator, and kept confidentially.

CHAPTER FOUR

4. RESULTS AND DISCUSSION

4.1 Socio-demographic characteristics of cohort

The study was conducted between October 2012 and May 2013. It included 491 HIV patients, who started HAART in DDH from January 2010 to December 2012, about whom complete information related to the study covariates is available. Among the study subjects selected for this study, 250 were females, and 230 were married. When HAART was initiated, 99 patients were on WHO stage IV and 60 patients had bedridden functional status due to the severe progression of the disease. Among the study subjects, 49.1 % (241) of them were male and the mean age was 33.80 (sd=.315). About 49.7% (244) of them had primary education, 114(23.2) % of the study subjects were never married and 30.6 (114) were unemployed. The median weight of the study subjects was 56 kg .The median age of patients when HAART was initiated is 34 years.

4.2. Descriptive analysis

Base line and follow up predictors of survival among HIV patients who started HAART were assessed. The patients were followed up for a median of 36 months. The minimum follow up time was 2 month and the maximum was 36 months. . The median survival time is 45 months after initiation of HAART. More than 30 patients died during the follow up time of which 11 (19.6%) and 19 (33.9%) deaths occurred within tenth months and fifteen months of HAART, respectively. The overall mean estimated survival time of patients under the study was 33.8 (95% CI: 33.2- 34.4) months. Females have relatively lower survival time (33.2 months) than males (34.4 months).Patients with younger age (40 years or less) had survived for about 34.6 months while the mean survival time for older patients was 32.2 months. . Most of the patients 261 disclosed their HIV sero-status at least for one member of their family,184 of the patients had casual sexual partners and 115 not educated.

The median CD4 count at base line was 123cells/ μ l. The median weight of patients at base line when HAART was initiated were 56 kg, 64 %(330) were younger age less than 40 at the time of ART initiation, 42.4 %(208) had TB co infection and 43.8 %(215) were poorly or fair adhered. Initial ART regimen was d4t(30)-3TC-NVP in 58 patients (11.8%),AZT-3TC-NVP in 170 patients (34.6%),d4t(40)-3TC-NVP in 60 patients (12.2%) and 29 patients (5.9%) on AZT-3TC-EFV at ART initiation,117(23.8%) adults were in WHO stage III,99(20.2%) were in WHO stage IV and 275(56%) were in WHO stage I and II. Poor/fair adherence was reported in 215 (43.8%) Patients from these 45 patients poorly adhered due to forgetting, 70 patients by travelling problem and 100 patients by fear of stigma.

Table1: Socio-demographic characteristics of patients on HAART in DDH from January 2010 to December 2012(n=491).

Variables	Frequency(n=491)	Percentage(n=491)
Sex		
Female	250	50.9%
Male	241	49.1%
Age		
Less than 40 years	330	64.0%
40 and Above years	161	32.7%
Religion		
Protestant	118	24.0%
Catholic	37	7.5%
Orthodox	145	29.5%
Muslim	157	31.9%
Others	34	6.9%
Ethnicity		
Oromo	279	56.8%
Amhara	126	25.7%
Tigre	47	9.6%
Gurage	34	6.9%
Others	5	1.1%
Marital status		
Never married	114	23.2%
Married	230	46.8%
Others	147	29.9%
Employment status		
Farmer	134	27.2%
Merchant	19	3.9%
Gov't employee	83	10.4%
Driver	68	23.2%
Day laborer	51	5.8%
Unemployed	114	30.6%
NGO	12	2.4%
Educational Status		
No education	115	23.4%
Primary(1-8)	244	49.7%
Secondary and above	132	26.9%

Table 2: Clinical and laboratory information of patients on HAART in DDH from January 2010 to December 2012(n=491).

Variables	Frequency(n=491)	Percentage(n=491)
Functional Status		
Working	319	65.0%
Ambulatory	117	23.8%
Bedridden	55	11.2%
WHO staging		
Stage I or II	275	56.0%
Stage III	117	23.8%
Stage IV	99	20.2%
ART regimen		
D4T-3TC-NVP	137	27.9%
D4T-3TC-EFV	29	5.9%
AZT-3TC-NVP	170	34.6%
AZT-3TC-EFV	95	19.3%
others	60	12.2%
ART Adherence		
Good	276	56.2%
Fair or Poor	215	43.8%
HIV sero-status disclosure		
Wife/husband knew	43	8.7%
Own children	39	7.9%
Parent (s)	261	53.1 %
Brother (s) Sister (s)	55	11.2%
Relatives	44	8.9%
No body knew	34	6.9%
Others specify	15	3.1%
Risk behavior		
Regular	307	62.5
casual or both	184	37.5
TB co-infection		
No	283	57.6
Yes	208	42.4
Past OI		
Yes	326	66.4
No	165	33.6

From the total subjects under study 56 (11.41%) subjects died, from these 31.6% (31) died within 15 month and the rest 88.59% were active up to the end of last censored date. The estimated mortality was 3%, 7%, 8%, 10% and 13% at 10, 15, 20, 25 and 36 months, respectively.

Table 3: Actuarial (Life) Table estimates of the cumulative progression to death for 491 study subjects Starting HAART b/n 2010- 2012.

Interval Start Time(months)	The number of patients at beginning of the interval	Number With drawing during Interval	Cumulative Proportion Surviving at End of Interval	Hazard Rate
0 - 5	491	1	0.99	0.0004
5 - 10	490	11	0.97	0.0045
10 - 15	478	19	0.93	0.0083
15 - 20	441	5	0.92	0.0023
20 - 25	429	8	0.91	0.0039
25 - 30	402	3	0.90	0.0015
30 - 35	392	6	0.89	0.0032
35 - 40	361	3	0.87	0.0033

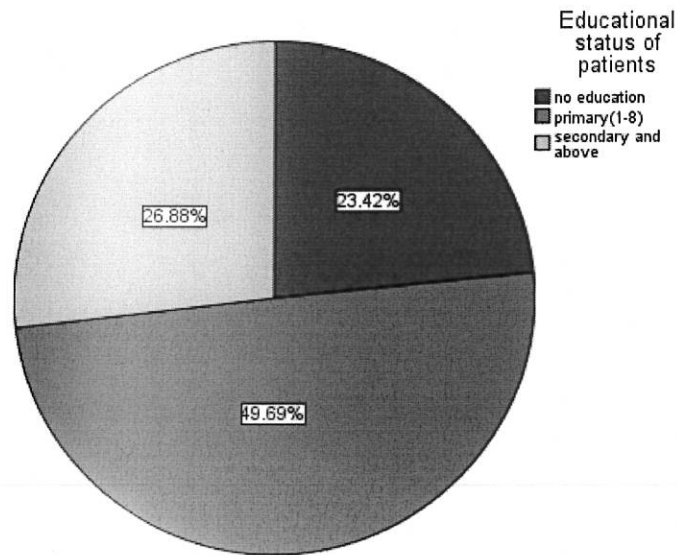


Figure 1: Educational status of the study subjects studied ($N = 491$ patients) in DDH, from January 2010 to December 2012.

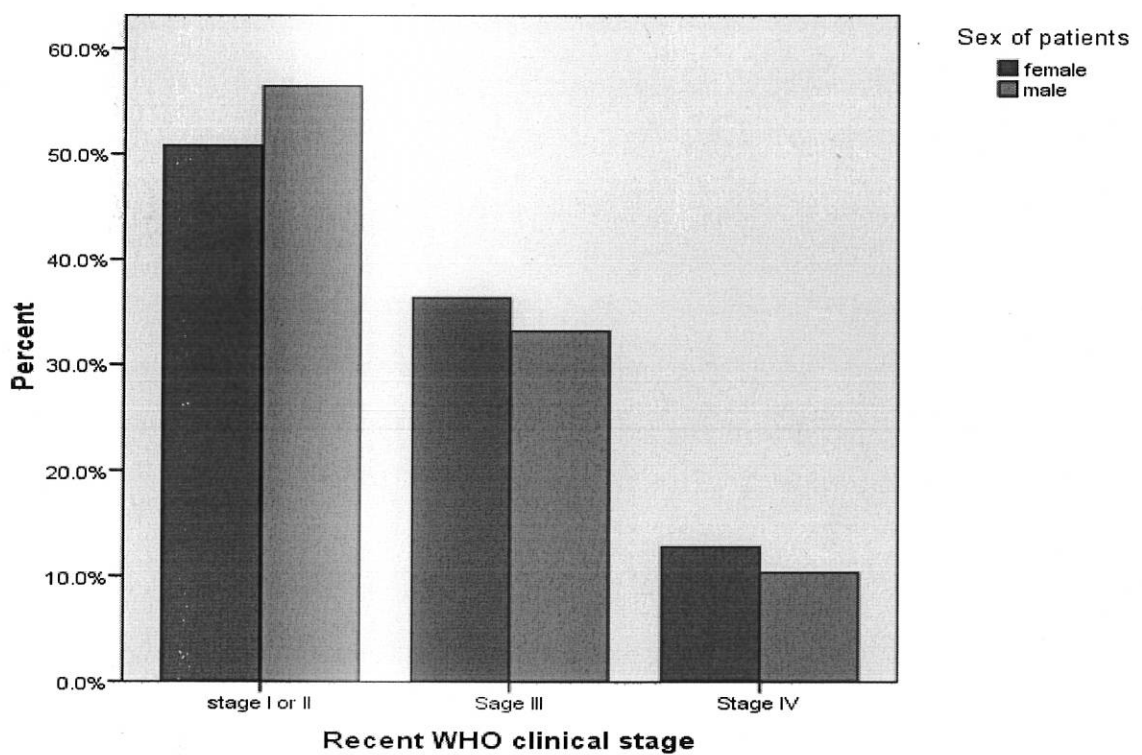
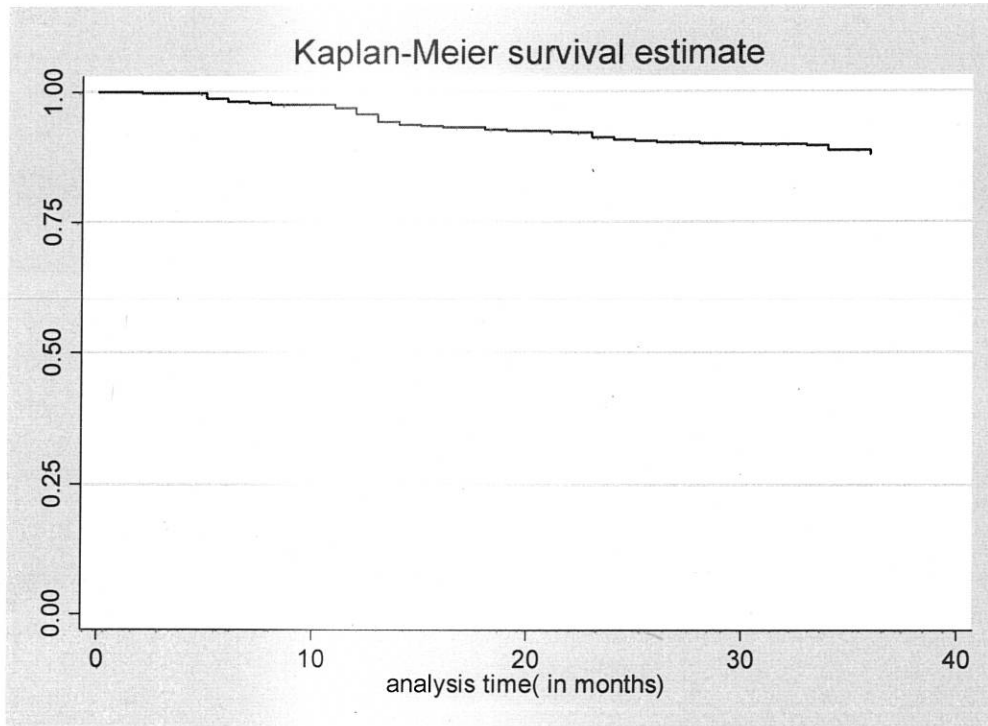


Figure 2: Recent WHO clinical stage stratified by sex of the study subjects studied ($N = 491$ patients) in DDH, from January 2010 to December 2012.

The graph of the estimate of overall Kaplan-Meier survivor function showed that most of the deaths occurred in the earlier months of HAART initiation and it declined in the later months of follow up. Separate graphs of the estimates of the Kaplan-Meier survivor functions, for different factors, have also been constructed in order to assess whether there is difference in survival experience between different groups of individuals. Most of the graphs did not show differences between different categories. However, relatively larger gaps are observed in covariates such as substance use, WHO clinical stage, functional status and TB co-infection. The graphs of Kaplan-Meier survival estimates based on different categories of factors substance used, WHO clinical stage, TB Co-infection, Risk behavior, functional status, educational status, level of adherence are also given in Figure 5 (Appendix).

Figure 3: The plot of the overall estimate of Kaplan-Meier survivor function of HIV patients treated with HAART in DDH 2012.



Log-rank test was performed to investigate the significance of the observed difference in the Kaplan-Meier estimates of the survivor functions among different categories of the factors. According to the log-rank test, there was no significant difference in survival experience between the various categories of sex, religion, level of education, employment status, and HIV disclosure status. However, the p-values of the log-rank test showed that the survival experience of patients in different categories of risk behavior, substance use, functional status, WHO clinical stage, marital status, past history of OI and TB co-infection differ significantly. Thus, those patients who had regular partner, who were not using substance (mostly alcohol), had working functional status, had good adherence, were in WHO clinical stage I or II, had no TB co-infection and who did not suffer from

opportunistic infections had better survival experience.

4.3. Results of Cox Proportional Hazard regression Model

In statistical modeling, when the number of variables is relatively large, it can be computationally expensive to fit all possible models. Thus, we fit bivariate models for each explanatory variable and assess their significance based on Wald χ^2 P-values. The results from bivariate Cox proportional hazard models are provided at Appendix (Table-5). The variables significant at 5% level of significance were age, sex, educational status, marital status, TB Co-infection, weight, functional status, WHO clinical stage, CD4 level count, substance used, risk behavior, and ARV adherence.

Next the variables which are found to be statistically significant at bivariate analysis are fitted together to assess their joint significance at multivariate analysis. For this purpose, we used back-ward variable selection procedures to obtain all the variables significant at 5% level of significance jointly. The variables significant at multivariate Cox Proportional Hazard Model analysis were age, weight, CD4 level count, substance used, functional status, risk behavior, and ARV adherence. Hence, the estimated values of the coefficients, Hazard Ratios and P-values of the explanatory variables on fitting the multivariate proportional Hazards Model to the data from HIV patients treated with HAART in DDH is presented in table 4.

Table 4: Estimated values of the coefficients, Hazard Ratio, 95%CI for the Hazard Ratio and P-values of the explanatory variables on fitting the multivariate Cox proportional Hazards Model to the data from HIV patients treated with HAART in DDH in 2012.

Factors/Covariates	Parameter estimate	Standard error	Wald χ^2	Df	P-value	Hazard Ratio	95%CI for Hazard Ratio	
Functional status(Vs W)	0.594	0.796	39.856	2	0.045			
Ambulatory	0.015	2.351	6.300	1	0.012	2.345	1.206	4.561
Bedridden			36.945	1	0.000	7.418	3.987	13.805
Weight of patients	-0.092	0.015	40.328	1	0.000	0.912	0.886	0.938
CD4 count	-0.005	0.001	37.930	1	0.000	0.995	0.993	0.997
Substance use(Vs No)	0.785	0.962	20.430	1	0.007	3.487	2.030	5.991
Tuberculosis co-infection(Versus No)	0.858	0.717	11.491	1	0.001	2.573	1.489	4.445
Risk Behavior(Versus Regular)	1.205	1.525	18.404	1	0.000	5.051	2.795	9.129
ARV Adherence(Versus Good)	0.920	0.962	18.404	1	0.000	3.653	2.022	6.601
Age of patients	0.042	0.061	49.213	1	0.022	3.019	2.001	6.056

NB: W=Working

The final step in model development strategy is consideration of interaction effects that may be useful in the improvement of the model. Thus, all the possible interactions of the variables were formed and the significance of adding each of the interactions in the main effects model, one at a time, is checked using the Wald test. However, the Wald test p-values in Table 6 indicate that none of them were found to be significant. Thus, the last model will be the one which contains only the main effects in Table 4.

4.5. Interpretation and Discussion of results

4.5.1 Interpretation

When the multiple proportional hazards Cox model is used in the analysis of survival data, the coefficient of a categorical explanatory variable in the model can be interpreted as the logarithm of the ratio of the hazard of death to the baseline (reference group) hazard. On the other hand, the coefficient for a continuous explanatory variable is the estimated change in the logarithm of the hazard ratio for a unit increase in the value of the explanatory variable after adjustment for the remaining variables in the model. Thus, the interpretation of those variables that were significant in the final proportional hazards model of HIV patients treated with HAART in DDH is as follows.

Age of patients at the start of HAART is found to have a significant effect on the survival status of patients (estimated HR=3.019, 95% CI: (2.001, 6.056), $p=0.022$). Since the estimated hazard ratio is greater than unity, other things being equal, the higher the age of a patient, the greater the hazard of death at any given time. Survival probability start to decline as the age patients increases because hazard of death tripled. In particular an increase of 1 year in age of patients increases the hazard rate of death by 3. The 95% CI also indicates that the hazard rate could be as low as 2 or as large as 6.056.

CD4 count is also another covariate which has a significant effect on the survival of patients (estimated HR=0.995, 95%CI: 0.993-0.997, $p=0.000$). The estimated hazard ratio for a 150cells/mm^3 increase CD4 count is $\exp^{(-0.005*150)} = 0.472$. The interpretation is that patients whose CD4 count is higher by 150 cells/mm^3 are dying at a hazard rate 53% lower than for patients with lower count. In addition to this

weight is another covariate which has a significant effect on then survival of patients (estimated HR=0.912, 95% CI: 0.886-0.938, P=0.000).

Estimated hazard ratio for a 5 Kilograms (Kg) increase in the weight of patients is $\exp^{(-0.092*5)} = 0.63$. The interpretation is that patient's whose weight increase by 5 Kilograms (Kg) dying at a hazard rate 37% lower than for patient's with the baseline of weight value. This shows that survival probability increases, for some unit increment of weight which indicates it has direct relationship with survival.

Substance use, functional status and TB co-infection are the three categorical variables that are found to be significantly associated with the survival status of patients in the fitted Cox regression model. The hazard ratio for substance use is 3.487. Thus, patients who are abusing substance have a 3.5 times higher risk of death than those that are not using substances. The confidence interval indicates that the risk of death for substance user patients could be higher by a quantity as large as 6 or as low as 3 than patients who are not using substance; $p = 0.007$. There was a decrease in survival rate of patients with TB co-infected after initiation of HAART. The probability of surviving for positive past TB test patients declines sharply in the first 10 months. Figure 5 (Appendix).

The estimated risks of death for a patient with ambulatory and bedridden functional status compared to those patients in a working functional status are 2.345 (95% CI: 1.206-4.561) and 7.418 (95% CI: 3.986-13.805) respectively. This means that the hazard rate of death for ambulatory and bedridden patients is 2.3 times and 7 times than that of working patients, respectively. Moreover, the estimated hazard ratio of bedridden functional status compared to ambulatory functional status is $\exp^{(0.594-(0.015))} = 3.065$ (95% CI: 1.53 to 4.75). Since confidence Interval does not contain 1, an individual whose functional status is bedridden has significantly higher hazard rate, at

any given time, than patients with ambulatory functional status. Thus, compared to patients with ambulatory functional status the hazard rate of bedridden patients is 3 times the hazard rate of ambulatory patients.

4.3 Qualitative approach

To understand factors affecting survival status of HIV positive patients in depth, we need to assess socio-demographic, economic, socio-cultural, and health care related factors of ART user at individual, community, programmatic, and structural levels. To address these issues the research analyzed the qualitative information generated through the FGDs and in-depth interviews with health care provider.

Factors influencing survival (ART use)

It is well known that ART treatment is one the major covariate that affects the survival of HIV patients. Hence the following findings emphasis on the factors that raised at individual, community, and health system levels to uptake treatment.

Individual Factors (Perceived and actual constraints)

Food support is one of motivating factor for HAART usage and adherence, especially to the severely ill, poor, and vulnerable patients who are on ART. Having access to adequate food is essential to treatment success, making nutritional support especially important to patients who are already vulnerable to food insecurity due to low socio-economic status and unemployment.

I can't take this drug with empty stomach. Because the daily diet I intake couldn't resist the drug side effects. Why can I burn my stomach and which cause me more damage than cure. -ART user, FGD participant.

Addictions to Khat, cigarettes, and alcohol emerged as individual-level barriers affecting survival.

He always tells me that he couldn't withdraw from Khat and Alcohol, which he believes antagonize with the drug. -Home-based care worker, FGD participant.

Social awareness and attitude toward Treatment

Awareness and positive attitude toward ART among community members positively influenced individuals' survival. Some self-motivated PLHIV encourage others in their community to test for HIV and use ART. This helped to lessen internal stigma that prevents PLHIV from seeking care.

It has become seven years since I started ART. Since then, I have been able to bring a number of patients to join our association and also seek care in health facilities. I use my story and experiences to convince others and most listened to me and trusted me a lot. -ART user, FGD participant.

Stigma toward PLHIV

Participants noted that stigma toward PLHIV in general and toward people using ART in particular are less severe than in the past, but discrimination still prevails in the society.

Disclosure of ART use to employers and workplace colleagues was singled out to be the most challenging thing to do. Losing jobs and being discriminated against in workplaces was repeatedly noted as a possible consequence of disclosure. Housemaids, sex workers, and those working in food and beverage establishments most frequently reported to have lost their jobs as a result of being seen using ART.

Last year, a women reported to our institution that a bar owner in this town sacked her from the job as she was accidentally seen by the bar owner taking ART. -Local NGO representative, Key informant.

Health System Factors

The reception and counseling by the health workers is excellent. They comfort us and encourage us to feel good. -on pre-ART, FGD participant.

On the negative side, long queues and long waiting times during their regular follow-up visits were among the common problems mentioned.

Indirect costs to use ART

Indirect costs for transportation to services, laboratory diagnosis, and drugs for opportunistic infections prove too great for many, forcing them to discontinue treatment.

We face difficulty to pay for diagnostic and treatments that are not available in the health centers including for x-rays, ultra-sound, and some important drugs. These and other services should be made available free for us in the health centers. -ART user, FGD participant.

Laboratory facilities and supplies

Frequent malfunctioning of the machines, overburdened by the workload and delay in repairing them emerged among the major problems.

There is only one CD4 machine that is adequate in the first place.

Moreover, it is out of service most often due to the frequent failures of the machine and associated delays in repairs. -Health worker, Key informant.

Power interruptions and supply shortages hamper the processing of blood samples, leading to spoilage, requiring patients to provide blood samples repeatedly

ART rooms in the health facilities

ART services are often provided in wards or sites in the health facilities that clearly identify patients' HIV status to others, hamper their right to privacy. This lack of anonymity prevents some PLHIV from using nearby ART facilities. Discontinuation

has of treatment has direct association with survival of patients. Therefore reasons for discontinuation (loss to follow up) ranged from issues related to lack of resources, situational factors, and to decisions made based on self-assessments of health.

Lack of resources

Most ART users are poor, and their access to resources, including food, is further limited by their HIV status.

Indirect Costs

Situational

Perceived and Actual Stigma

Treatment discontinuation due to fear of stigma and disclosure of ART use reported to be most common among sex workers, house maids, those working in food and beverage establishments, barber shops, and beauty salon. Some Orthodox and Islam followers discontinue ART during fasting seasons due to a desire to fulfill their religious obligation, as well as fear of stigma.

Self-assessment

Some patients make decisions to discontinue ART on their own based on self-assessment of treatment outcome

Side-effects

I discontinued treatment because I could not bear the pain of repeated and consistent vomiting whenever I took the tablets. -Discontinued ART user, FGD participant.

The skin rash, itching and vomiting when I started treatment were difficult to continue treatment and decided to leave the treatment. -Discontinued ART user, FGD participant.

4.5.2. Discussion of Results

This study identified variables/factors that significantly affect survival status of HIV patients. Identifying factors affecting survival status of HIV patients is very important to reduce higher risk of death for those taking ART during their consecutive follow up time. This retrospective cohort study found that the significant predictors' of death in patients living with HIV/AIDS after initiation of HAART was: older age, low CD4 count, low weight, substance use, ARV Adherence, being bedridden and ambulatory and co-Infection with TB. In addition to this WHO clinical stage, educational status, and marital status are only significantly associated with mortality in the bivariate analysis but not in the multivariable analysis. One of the outcomes deaths of patients was high in the earlier months of HAART initiation and it declined smoothly in the later months of follow up. Studies conducted in southern Ethiopia and Tanzania also revealed that the mortality rates were high within the first three months of follow up (29, 48-50). This may be caused due to the fact that most of the patients start HAART at the severe stage of the disease and fear of stigma. Mortality in the bivariate analysis but not in the multivariable analysis.

Study in Cameroon shows patients with a base line CD4 count ≤ 50 cells/mm³ presented a mortality risk twice as high as those with >50 cells/mm³ (24). Another study in Canada shows the hazard for the low CD4 count strata were higher CD4 < 50 cells/mm³, RH=6.07, 95% CI 4.11-8.97 relative to counts ≥ 200 cells/mm³. Majority of the previous studies (12: 13: 31) identified Low CD4 count was one of the independent predictors of mortality. This study result confirms that there is hazard difference for low and high CD4 counts this may be due to majority of the patients have immunity potential.

TB continues to be the leading cause of death in people living with HIV/AIDS. This study showed that TB increased the rate of mortality and reduces the survival probability. Patients co-infected with TB had nearly 2.5 times higher risk of dying while on ART compared to non-infected. Studies from Baltimore, USA and mainland China have also shown that TB is an independent predictor of mortality in patients on ART, after controlling for potential confounders, including CD4 cell count and viral load (33, 34). In the Baltimore study the hazard of AIDS related death was 2.4 times (95% CI: 1.2–4.7) more for the person-time with TB compared with the person-time without incident TB. A cohort study in Abidjan, Ivory Coast also found out that TB is a risk factor for immunological and virological failure, which leads to severe morbidity and mortality in adult patients treated with ART (35).

The functional status of patients can be seen as an indicator of the severity of the progression of the disease. Those patients who are in ambulatory and working functional status have the strength to work and engage themselves in household activities which may help them generate additional income and improve their quality of life. Even though patients who are staying in bed in Hospital are accessing medical care and support, cannot do anything by their own to create a stress-free environment for them selves. Thus, as expected, patients with ambulatory and bedridden functional status have lower survival probability than working patients.

Symptomatic disease (WHO stages III and IV) was associated with mortality in many studies (29, 40, and 42). However, our finding shows that WHO clinical stage is associated with mortality in the univariate analysis only, possibly reflecting differences in the accuracy of clinical staging or homogeneity of cohorts with respect

to this variable. Thus, in the univariable Cox regression, being WHO stage IV led to increased rate of mortality when compared to stage I and II.

Substance abuse is another significant predictor of survival in our study. Substance abuse was associated with mortality, non adherence to medication and lower quality of life in many studies (44, 46, and 47). Substance abuse may impair judgment and the ability to adopt and maintain routine medication use. Therefore, screening for drug abuse and excessive alcohol use, and supportive counseling and treatment for drug abuse might help in promoting long term adherence to ART.

Even though different previous studies demonstrated body mass index (BMI) as one of the strong predictors of mortality (32, 35 48-50), it was not possible to calculate BMI for patients since only the weight but not the height of the patients has been recorded at baseline. However, the study revealed that the weight of patients is significantly associated with survival and those patients having lower weight are at higher risk of mortality.

Compared to younger patients, older patients were more likely to have lower survival according to this study. Likewise, older age was also associated with increased rate of mortality and low quality of life and defaulting, which leads to mortality (42, 47). However in France a study demonstrated that younger age was associated with non adherence to ART (44). A study in Tanzania also showed that age is not significantly associated with mortality (29).

Study conducted in zewuditu Hospital shows the estimated mortality was 24.9%, 29%, 31.7%, 33.1%, 33.5, and 34% at 6, 12, 18, 30, and 48 months respectively (25). However according to a study carried out by Alfred C teal in Malawi, the probability of being alive on ART at 6, 12 and 18 months was 89.8%, 83.4% and 78.8% respectively (17). This study result shows estimated mortality

was 3%, 7%, 8%, 10% and 13% at 10, 15, 20, 25 and 36 months respectively(17). This survival difference might be due to majority of the patients start ART at WHO stage I and II; good follow up, low default rate, high drug access while in our study, almost quarter of the cohort at WHO stage III and high default rate and the study is conducted in rural hospital most of listed problems are observed in most of times. Study conducted in Singapore showed that patients of older age at diagnosis had a significantly higher risk of progression compared to younger patients' in addition older patients has higher mortality (36 vs. 27% $p=0.04$) and shorter survival 25th percentile survivor function (36.2 vs. 58.5 months, $p=0.02$) than younger patients (39).

This study result also shows similar progression this may be due to older aged patients progressed to AIDS at a faster rate and older patients may have a reduced capacity to generate new CD4 cells in response to viral killing. Patients who were educated at most primary level had high risk compared to those secondary or above(21) (log rank test, $P<0.001$). But these is not consistent result both in bivariate and multivariate analysis indicating educational level is not a strong predictors of survival in our study. Our study showed no difference in survival by religion, ethnicity and employment status. Likewise a study carried out in California showed risk of death is similar among ethnic groups.

In our study multivariate analysis indicating marital status is not strong predictors of survival, but study carried out in Uganda showed widowed patients had high risk of death than single not married patients. More over single not married patients were at high risk of mortality compared to married patients (log ran test, $P<0.01$). This difference might be due to married patients psychologically ready and get social support from their partner in adapting the illness and taking the drug correctly (19).

Study conducted in rural Malawi shows individuals who were severely malnourished [Body Mass Index (BMI) $<16\text{kg/m}^2$] had a six times higher risk of dying in the first three months than those with a normal nutritional status (27). Another Study in Cameroon shows BMI $\leq 15\text{kg/m}^2$ was related to three times higher risk of death than a BMI $>18.5\text{kg/m}^2$ in addition different previous studies demonstrated BMI as one of the strong predictors of mortality (19, 30), This study excluded it since only the weight not height of the patients has been recorded at base line. As a result we couldn't calculate BMI for each patient. Study conducted in Thailand clearly documented TLC was significantly associated with survival (40).

Study conducted in Uganda shows non adherent participants had a mortality of 42.5 deaths per 1000 person-years and after adjusting for age, sex and educational level were two times as likely to die as adherent participants (16, 41). In addition study conducted in Ethiopia the risk of death in non- adhered patients is 4 times higher compared to adhered patients (25). This was in agreement with this study results which indicate the risk of death in non- adhered patients is 3.5 times higher compared to adhere patients there which implies their strong association between being survive and ARV adherence.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATION

5.1. Conclusion

In this study we tried to identify factors affecting survival status HIV patients treated with HAART in DDH using the methods of survival analysis. The Kaplan-Meier results showed that the general mean estimated survival time of patients after HAART initiation is 33.8 months. The mortality rates high in the earlier months of HAART and tended to stabilize later. About 19.64% and 33.92% of the deaths occurred within tenth and fifteen months of HAART initiation, respectively.

Moreover, the results of the multivariable proportional hazards Cox regression model showed that lower CD4 count at the start of HAART, older age, TB co-infection, substance use and being of bedridden or ambulatory functional status has significant effect on survival HIV patients which is associated higher risk of mortality. Being on the primary education level, experience of past OI and being in WHO clinical stage IV are associated with increased rate of mortality in the crude (unvariable) analysis but not in the multivariable analysis. However, none of the socio-demographic variables have significant association with survival status of patients. Similarly disclosure status of patients and the type of drug regimen used at the start of treatment are not significantly associated with survival status of patients.

This study identified factors operating at individual, community, and health system levels, noting that individual or community-related barriers remain the biggest deterrents to ART use which has significant effects on the survival of patients. This does not, however, mean that the other barriers operating at health facility or policy

levels are less relevant. In fact, addressing barriers at all levels and throughout the treatment continuum is central to identify the major factors affect survival of patients. Barriers at the health facility level may prove to be the easiest to address, but they require significant resources and political concern.

5.2. Recommendation

- Careful follow up for poorly adhered patients and counseling them is crucial to improve survival
- Even though lower weight is associated with increased rate of mortality, the cause of having lower weight in patients is still not known. In this regard further studies need to be undertaken to determine the cause for having lower weight in patients under HAART. Also, the high mortality risk associated to older patients need be investigated.

Policy Level

- ❖ Enhancing food Support Programs ,especially for those having least income per day

Social Level

- ❖ Work to educate communities about HIV and ART to facilitate an enabling environment in which PLHIV will be more comfortable disclosing their status and accessing the services they need. Increasing access is closely linked to reducing stigma at the community level.
- ❖ Providing additional food support and transportation allowance for patients taking treatment far from facility

Facility and Health provision Level

- ❖ Solicit viable options to cover the cost for diagnosis, treatment, and drugs for opportunistic infections and other health problems of poor and bedridden patients

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on ART, including health insurance and social security.

- ❖ Plan ways to integrate ART services with the outpatient department within health facilities so that ART users access treatment without fear of stigma. Extend ART access to accommodate inmates and the homeless.
- ❖ Provide sufficient information about the side effects associated with ART use and the transitory nature of the side effects.
- ❖ Counsel and support patients with addictions such as alcohol, cigarettes, and Khat to quit these habits and continue using ART.

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APPENDIX

Table 5: Results of bivariate analysis fitted for HIV patients treated with HAART in DDH, 2012(n=491).

Covariates/factors	DF	Wald χ^2	P-values
Age	1	4.087	0.041
Sex	1	2.002	0.150
Ethnicity	4	0.005	0.944
Religion	4	0.925	0.336
Educational Status	2	3.401	0.036
Occupational Status	4	0.012	0.170
Marital Status	2	0.301	0.040
TB Co-infection	1	5.002	0.010
HIV Status Disclosure	1	1.031	0.251
Weight	1	5.190	0.001
Functional Status	2	5.603	0.018
WHO Clinical Stage	2	3.001	0.049
CD4 Level Count	1	4.110	0.025
Employment Status	1	0.176	0.674
Substance used	1	6.101	0.041
Risk Behavior	1	3.106	0.050
ARV Adherence	1	5.923	0.021
OI Prophylaxis	1	0.015	0.902
Hemoglobin Level	1	0.041	0.063

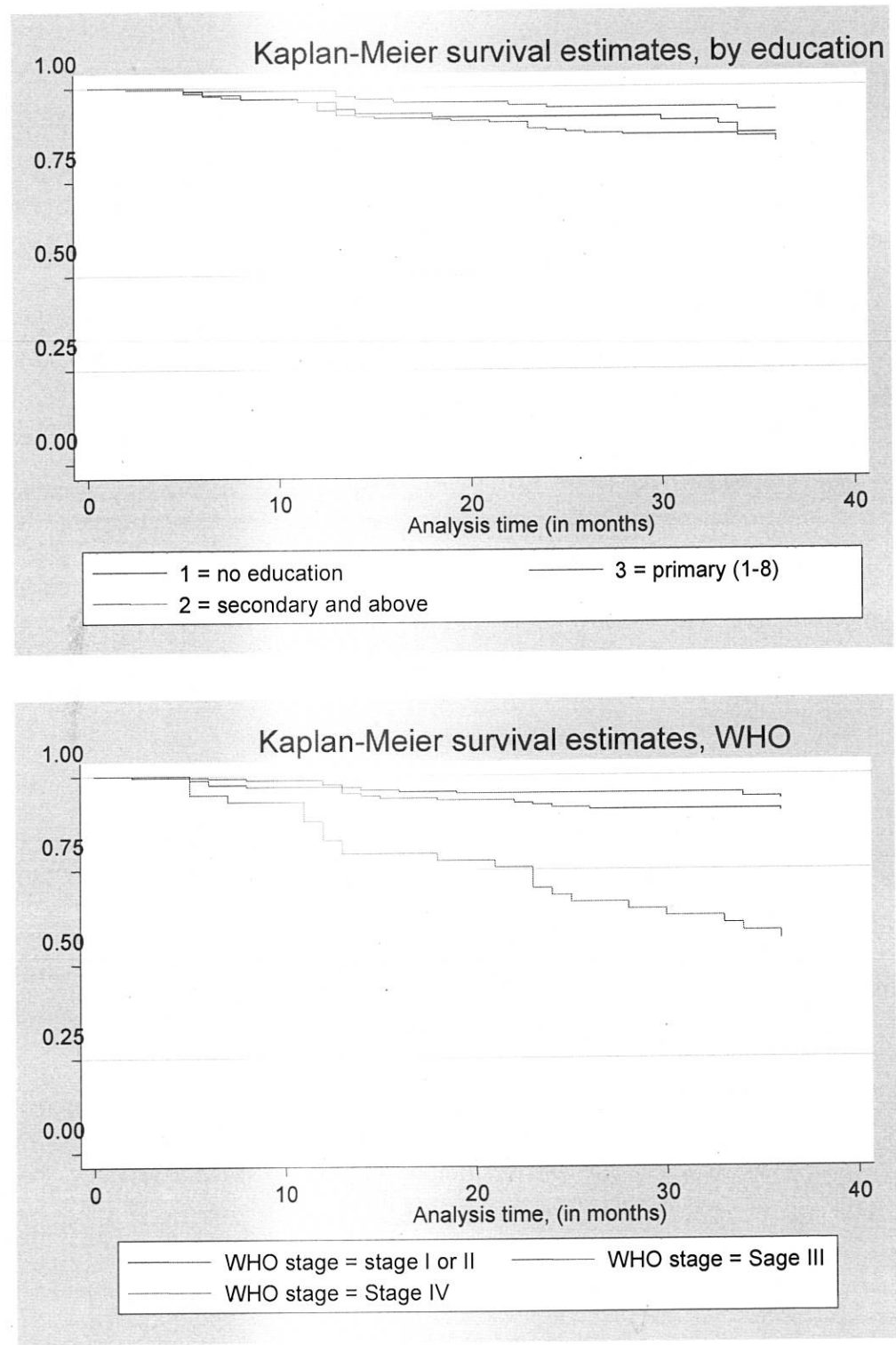
Table 6: Wald Statistics and corresponding P-values of possible interaction effects, added one at a time, to the variables included in the model.

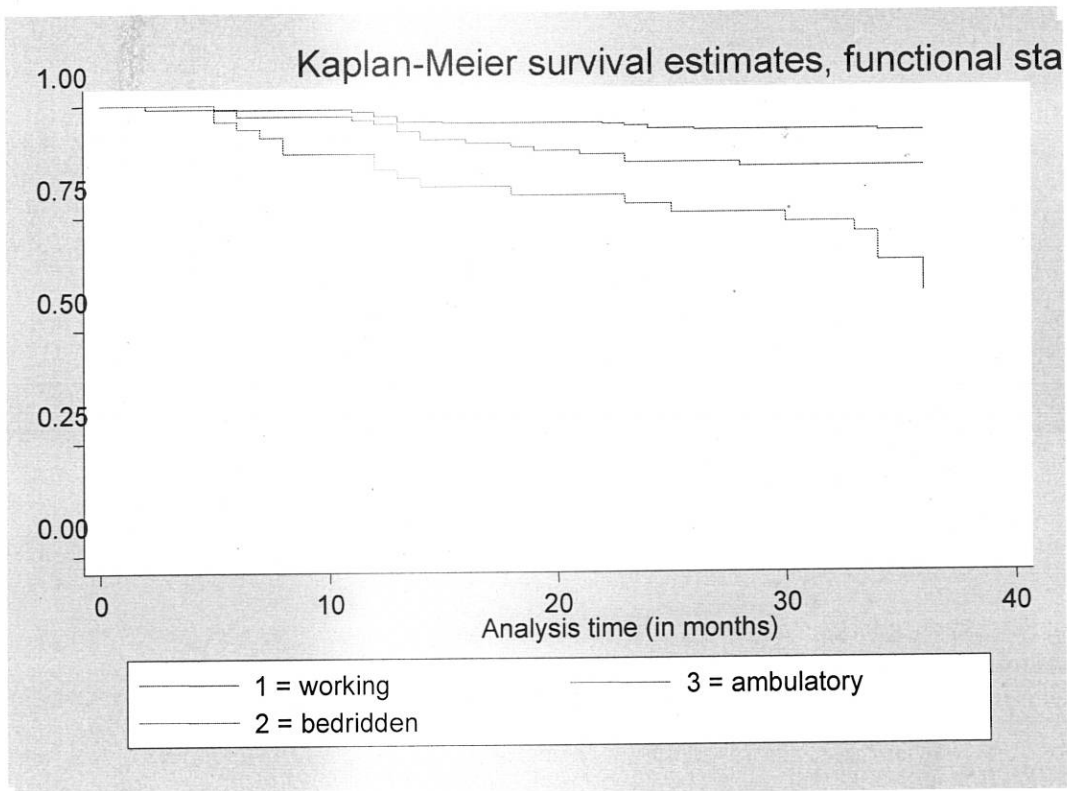
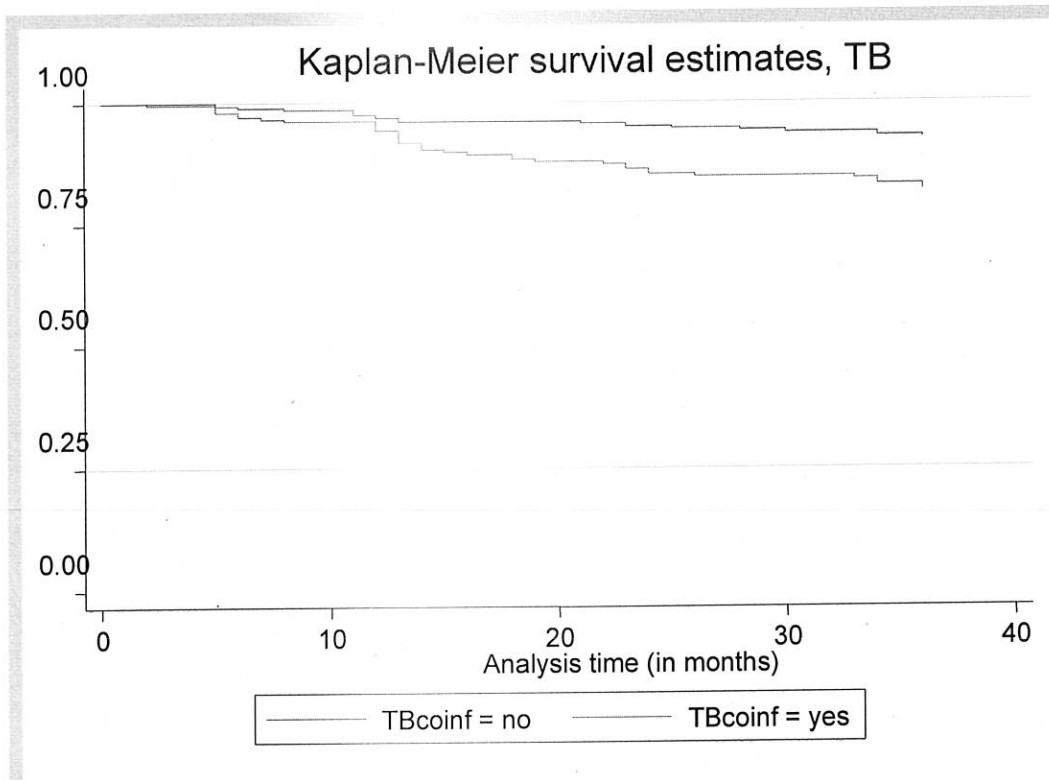
Interaction b/n covariate		DF	Wald χ^2	P-values
Functional Status	Weight	2	2.8879	0.0892
	CD4 count	2	0.2247	0.4864
	Substance use	2	0.2152	0.2927
	TB co-infection	2	1.0331	0.6355
	Risk Behavior	2	0.4841	0.7071
	ARV Adherence	2	0.4817	0.6427
	Age	2	0.3948	0.1293
Weight	CD4 count	1	0.1412	0.3656
	Substance use	1	0.9812	0.7107
	TB co-infection	1	1.2444	0.6011
	Risk Behavior	1	0.7669	0.6815
	ARV Adherence	1	0.8031	0.6905
	Age	1	3.9192	0.1409
CD4 count	Substance use	1	0.4849	0.6914
	TB co-infection	1	2.4013	0.0789
	Risk Behavior	1	0.3421	0.4378
	ARV Adherence	1	0.1691	0.5157
	Age	1	0.7464	0.4396
Age	Substance use	1	4.0906	0.0824
	TB co-infection	1	0.0803	0.5966
	Risk Behavior	1	3.9192	0.6427
	ARV Adherence	1	0.2444	0.7071
Substance use	TB co-infection	1	0.4811	0.4876
	Risk Behavior	1	0.3948	0.8209
	ARV Adherence	1	1.0657	0.0691
TB co-infection	Risk Behavior	1	0.0803	0.7769
	ARV Adherence	1	0.6176	0.6927
Risk Behavior	ARV Adherence	1	3.0021	0.0661

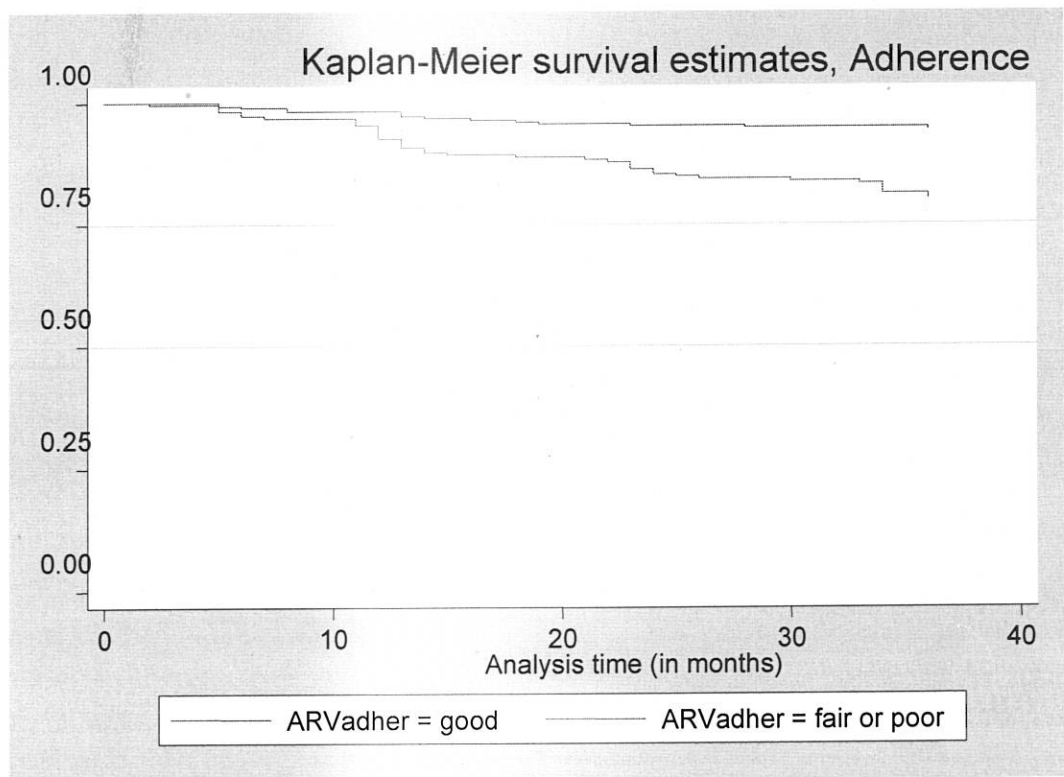
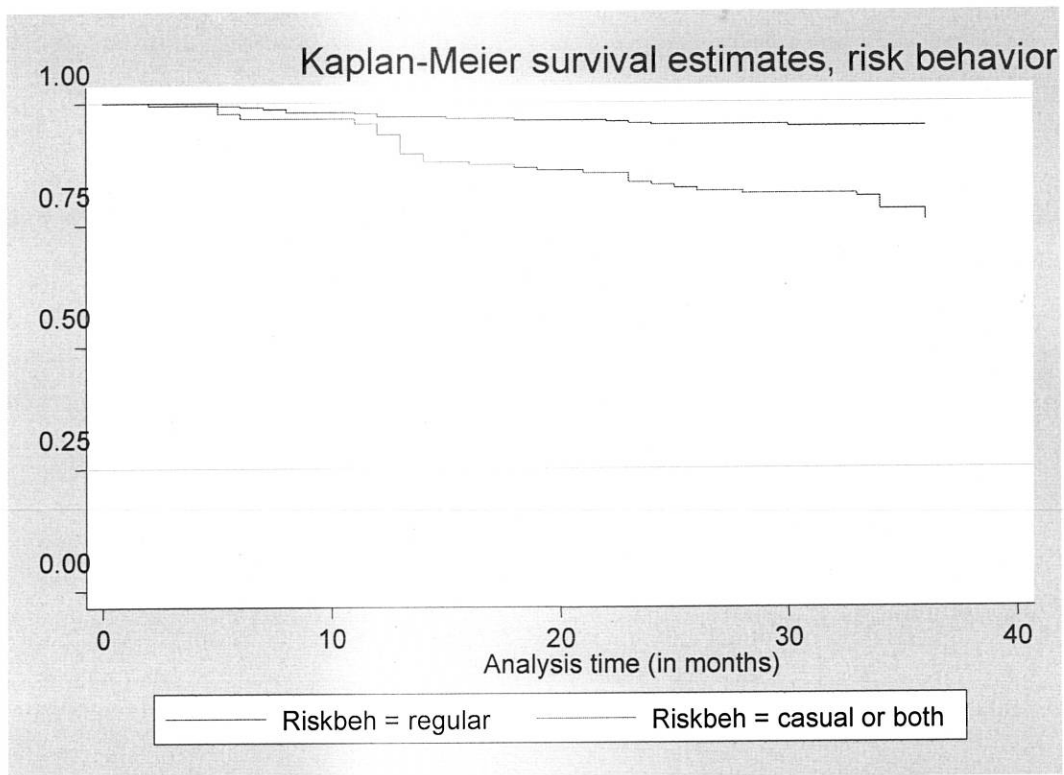
Table 7: Results of the Log –rank test for the categorical variables of HIV patients treated with HAART in DDH, 2012.

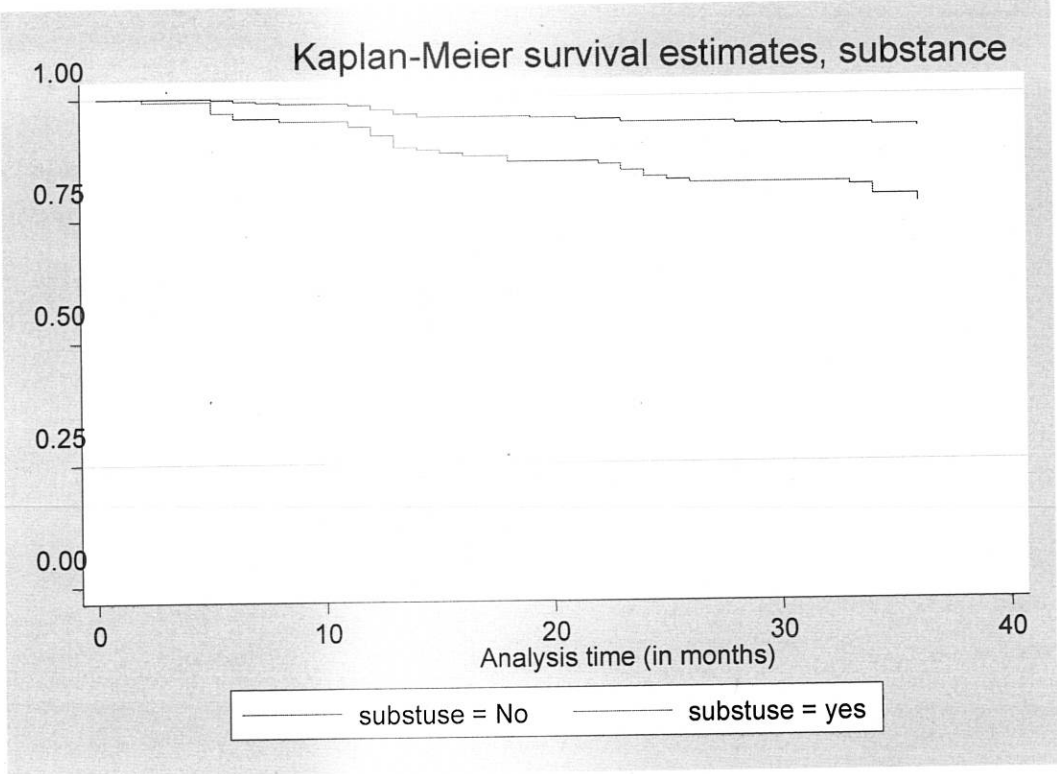
Covariates/factors	DF	Chi-square	P-values
Sex	1	0.11	0.7369
Ethnicity	4	2.05	0.3475
Religion	3	1.65	0.3679
Educational Status	2	0.61	0.4335
Occupational Status	4	0.93	0.6287
Marital Status	2	0.32	0.2865
TB Co-infection	1	14.38	0.0037
HIV Status Disclosure	1	0.03	0.8519
Functional Status	2	6.17	0.0130
WHO Clinical Stage	2	95.80	0.0000
Employment Status	1	0.21	0.6466
Substance used	1	5.56	0.0184
Risk Behavior	1	16.06	0.0019
ARV Adherence	1	5.76	0.0122

Figure 5: Plots of Kaplan-Meier survivor functions based on different factors, of HIV patients treated with HAART DDH, 2012.









Questionnaire

Date-----/month-----/year-----

Name of the hospital-----

Name of data collector----- signature-----

Name of supervisor-----signature-----

Part-I Socio-demographic characteristics

101. Age (-----) years

102. Sex 1.male

 2. Female

103. Religion

 1. Protestant

 2. Catholic

 3. Orthodox

 4. Muslim

 99. Others specify-----

104. Ethnicity

 1.Oromo 2. Amhara

 3. Tigire 4. Gurage

 99. Others specify-----

105. Marital status

 1. Single

 2. Married

 3. Divorced

 4. Widowed

 5.Separated

106. Educational status

1. Primary 2. Secondary
3. Tertiary 4. Not educated

107. Dependent children at home

1. Yes 2. No

108. Occupational status

1. Farmer 2. Merchant
3. Government employee 4. Non government employee
5. Day laborer 6. Driver
7. Commercial sex worker 8. Jobless

99. Other specify-----

Part-II Base line clinical, laboratory and ART information

201. past opportunistic

illness

1. No 2. CMV 3. PCP
4. PGL 5. PML 6. EPTB
7. Candidiasis 8. Diarrhea 9. Pneumonia
10. Herpes simplex 11. Kaposi sarcoma
12. Toxoplasmosis 13. Encephalopathy
14. Wasting syndrome 15. Herpes zoster
16. Other specify-

202. Weight at base line (-----) kg

203. Height at base line (-----) cm

204. Functional status at base line

1. Working 2. Ambulatory

3. Bed ridden

205. WHO clinical staging of HIV at base line

1. Stage II

2. Stage III 3.

Stage IV

206. Past TB test

1. No 2. Not determined

3. Positive 4. Negative

207. Past TB treatment

1. No 2.

2SRHZ/6EH

3. 2HRZES/1HRZE/5HRE 4. 2HRZE/6HE

208. Past medication

1. No 2.

Cotrimoxazole

3. INH 4. Other specify-----

209. CD4 count at base line (-----) date-----/-----/-----

210. Hgb count at base line -----

211. TLC count at base line-----

Part-III ART treatment

301. ART eligibility criteria

1. CD4<200

2. WHO stageIV

3. WHO stage II and III with TLC<1200

302. OI prophylaxis given

1. Not given 2. Cotrimoxazole

3. INH 4. Fluconazole

5. Others specify-----

303. Regimens given at follow up time

1. la(30)=d4t(30)-3TC-NVP

2. la(40)=d4t(40)-3TC-NVP

3. lb(30)=d4t(30)-3TC-EFV

4. lb(40)=d4t(40)-3TC-EFV

5. lc=AZT-3TC-NVP

6. ld=AZT-3TC-EFV

7. 2nd line regimens

Part-IV patient follow up information (filled from ART follow up form) recent results

401. Date confirmed HIV positive (-----/-----/-----)

402. Eligible date (-----/-----/-----)

403. Last follow up date (-----/-----/-----)

404. Duration since initiation of ART (----- month)

405. Recent weight (----- kg)

406. Recent functional status

1. Working 2. Ambulatory

3. Bedridden

407. Recent WHO staging

1. Stage II

2. Stage III

3. Stage IV

408. TB prophylaxis

1. No

2. Yes

409. TB screened

1. No

2. Negative

3. Positive

410. TB treatment

1. No

2. Yes

411. Opportunistic infections

1. No

2. Zoster

3. Pneumonia

4. Pulmonary TB

5. EPT

6. Oral thrush

7. genital/oral ulcer

8. Diarrhea

9. Cryptococcal meningitis

10. CNS toxoplasmosis

11. PCP

12. Others specify-----

412. Cotrimoxazole

1. Given
2. Not given

413. Recent ARV adherence

1. Good
2. Fair
3. Poor

414. Reason for fair/poor adherence

1. Toxicity/SE
2. Share with others
3. Forgot
4. felt better
5. Too ill
6. Stigma
7. Drug stoke out
8. Travelling problem
9. unable to pay
10. Alcohol
11. Depression
12. Others specify-----

415. Drug side effect

1. No
2. Nausea
3. Diarrhea
4. Fatigue
5. Headache
6. Numbness
7. Rash
8. Anemia
9. Fat change
10. Night mare
11. Dizziness
12. Others specify-----

416. Reason for regimen change

- | | |
|-----------------------|----------------------|
| 1. Not change | 2. Toxicity/SE |
| 3. Pregnancy | 4. Risk of pregnancy |
| 5. New drug available | 6. Drug out of stock |
| 7. Clinical failure | 8. New TB |
| 9. Other specify----- | |

417. Reason for stopping regimen

- | | |
|---|---------------------------|
| 1. Not stopped | 2. Pregnancy |
| 3. toxicity/SE | 4. Treatment failure |
| 5. Poor adherence | 6. Drug out of stock |
| 7. Lack of finance | 8. Other patient decision |
| 9. Planned treatment interruption 10. Other specify----- | |

418. Recent CD4 count (-----date-----/-----/-----)

419. Recent TLC count (-----)

420. Recent Hgb count (-----)

421. Current status 1.alive 2. Dead

Consent form (English version)

My name is _____, I am an ART clinic nurse working in Dembi Dollo Hospital ART clinic and now I am collecting data from our patients ART logbook for the research being conducted to assess factors affecting survival status of HIV/AIDS patients after initiation of antiretroviral treatment, by Ato Dame Kedir who is the MSC student in Addis Ababa University. You are selected as one of study subject by chance. The investigator employed me (from this ART clinic) for this data collection to maintain your data strictly confidential, We believe that the findings of this study will have some evidence and information for governmental and non - governmental organizations which work in the area of HIV/AIDS specifically on ART at national, regional and district level by providing basic information on factors affecting survival of PLWHA and started ART treatment.

Information which is necessary for the study will be taken from your ART log book. As the study will be conducted through review your medical records alone, it will not cause any harm as far as the confidentiality is kept. The information will be taken when you give permission, participation is totally voluntary.

Your willingness for your ART record information to be utilized in this study will help us achieve the stated benefits of the study. Your name and other personal identifiers will not be recorded on data collection form and the information that you give us will be kept confidential and will also be used for this study purpose only. You have full right not to let your information on ART logbook to be used for this study. But the information that would be taken will be quite useful for the study. You will not face any problem if you do not allow the information to be taken from your records and you will not also be denied of getting any medical services from the hospital. If you have any questions about this study you may ask me or the principal investigator **Dame Kedir** E-mail: **d.kedir@yahoo.com**. TELEPHONE: **0910-50-96-95**

Are you willing to let your information to be used for this study?

1. Yes 2. No

Signature of the interviewer which shows that the respondent has consented (verbally) to take part in the study.

Informed consent form (Afaan Oromo version)

Unka hayyamsiisa maamila qorannoo keesatti hirmaatanii ibsu.

Maqaan koo-----jedhama. Ogeessa fayyaa hojjetaa Hospitaala kanaa yommuun ta’u, qorannoo matadureeensaa namoota dawwaa HIV/AIDS fudhatan akka isaani umurii dheeraa jiraatan ykn hin jiranne wantootni murteessan maalfa’i jedhamu; Uunivaarsiiti Finfinneti barataa qayyabannoo Uummataa digirii lammaffaa kan ta’e obbo Damee Kadir qoratamuuf galmee wal’aanamtootaarraa funaanuuf jira . Qorataan Kun anaan Nama galmee kanarra hojjetu kan nafileef akka iccitiin wal’aanamtootaa eegamuuf jedheeti.Jechuun namoonni kiliinika kanaa ala jiran yommuu ragaa kana funaanan maqaa keessaniif ragoolee kan biraas akka hin argamneef jecha.Qorannoon kun bifa saayiinsaawa ta’een ragaa funaanee dhiyeessuudhaan, sagantaa ittisaaf qorannoo HIV maalirraa akka jiru madaaluuf akkasumas namoota vaayiraasii kanaa wajjin jiraataniif eegannoon addaa akka taasifamuufiif bu’aan isaa guddaadha jedhamee yaadama .Kanaafis ragooleen qorannoo kanaaf barbaadaman galmee ART kessaa funaanaama .Qorannoon kun galmeerraa fuudhatama waan ta’eef isin irratti miidhaa fidu tokko hin qabu .Ragaa kana yoo nuu eyyamtan kaayyoo qorannoo kanaaf buu’aansaa guddaa dha . Galmee keessan irra ragaan yommuu sassabamu maqaan keessaniif wantootni isin ibsan tokkollee hin fudhataman.Ragaan fudhatamu kun icciitiinsaa guuttumaa guutuuti eegamee qorannoo kana qofaaf oola. Ragaan keessan akka qorannoo kanaaf hin oolle dhorkuuf mirga qabdu; garuu ragaan kun qorannoo kanaaf yoo oolle bu’aansaa guddaadha. Ragaa keessan kana yoo qorannu yoo qorannaa kanaaf hin kennu jettan tajaajila yaalaa keessan irratti dhibbaa isinirran ga’u tokko hin jiru. Gama biraatiin ragaa kana waan kennitaniif bu’aa dhuunfaa /addaa argattan hin qabdan .Qorannaa kana ilaalchisee gaaffii yoo qabaattan ana ykn qorataa ol’aanaa (PI) gaafachuu ni dandeessu.

Ragaan kun akka qoraannoo kanaaf oluu fedha qabduu?

1. Eeyyee
- 2.lakkii

Ragaa kana eeyyamaniiru. Maqaa fi mallattooo nama ragaa funaanee-----

DECLARATION

I, the undersigned, declare that this thesis is my original work, has not been presented for degrees in any other University and all source materials used for the thesis have been duly acknowledged.

Name: Dame Kedir Nuna

Signature:  **Date:** 18/07/2013

Place: Center for Population Studies, Addis Ababa University.

This thesis has been submitted for examination with my approval as a University advisor.

Name: Yohannes Dibaba (Assist.Prof)

Signature: **Date:**

**Place: Dep't of Population & Family Health,
Jimma University**