

**ASSESSMENT OF PREDICTORS OF SURVIVAL IN PATIENTS LIVING WITH HIV/AIDS AFTER THE ADVENT OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY IN ADDIS ABABA ETHIOPIA.**

By

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**A thesis submitted to the school of graduate studies of Addis Ababa University, Medical Faculty, School of Public Health in partial fulfillment of the requirement for the Degree of Masters of Public Health in Epidemiology (MPHE).**

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**ADDIS ABABA UNIVERSITY  
SCHOOL OF GRADUATE STUDIES**

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## **DEDICATION**

To my mother W/o Meymuna Mohammed, to my brothers and sister, especially Mrs Tofik Bedru and Miss Asma Bedru.

## ABSTRACT

**BACKGROUND:** The introduction of highly active antiretroviral therapy in 1996 dramatically improved survival and quality of HIV-infected patients in the industrialized world. This survival benefit of HAART in HIV infection has been well studied in the developed world. In resource-poor settings, where such treatment was started only recently, limited data exist on treatment results. More over mortality have been high particularly in the first month of initiating ART and factors contributing to this high mortality are poorly understood.

**OBJECTIVE:** To asses predictors of survival in PLWHA after the advent of HAART.

**METHODS:** A historical cohort study was conducted in Zewditu Hospital located in Addis Ababa, Ethiopia. Patient's records enrolled between March, 2005 to July, 2008 were reviewed consecutively using patients ART unique identification number as a reference. Different documents for the same patient were triangulated in case of odd values, non logical or missed data. Deaths from all AIDS related cause occurring during the follow-up period were identified from physician reports or registration by drug adherence counselor. Univariate analysis was used to describe patient's baseline characteristics. Actuarial table was used to estimate survival after intiation of ART, and log rank test was used to compare survival curves. Cox proportional-hazard regression was used to calculate the bivariate and adjusted hazard rate and then determine independent predictors of time to death.

**RESULT;** One thousand seventy patients on ART were followed for a median of 34 month (IQR 6, 36.25). The mean age was 36.4 and the median weight of the cohort at the initiation of ART was 51kg (IQR, 45-60kg).The median CD4 count was 94cells/ $\mu$ l (IQR, 46-154). The estimated mortality was 24.9%, 29%, 31.7%, 33.1%, 33.5, and 34% at 6, 12, 18, 30, and 48 months respectively. After adjustment, the independent significant predictors of not surviving in patients living with HIV/AIDS after initiation of ART remain poor ART adherence (AHR=3.92[95%CI=3.13, 4.90]),Advanced WHO staging (AHR=2.47[95%CI= (1.58, 3.81)], being unemployed (AHR=1.87[95%CI= 1.49, 2.34]), moderate anemia (AHR=1.86[95%CI=1.35, 2.56), and Low CD4 count (AHR=1.85[95%CI= 1.35, 2.52]).

**CONCLUSION;** A careful monitoring of patients with low CD4+ ,advanced WHO staging, moderate anemia and unemployed particularly during the first 3 months of HAART is necessary. Tracing poorly adhered patients and giving them drug counseling is crucial to improve their survival.

## **I. Introduction**

### **1.1. Background information**

Acquired immune deficiency syndrome (AIDS) is one of the most destructive epidemics the world has ever witnessed. Ethiopia is a low income country in East Africa with rapid growing population at a rate of 2.7% per year since 2000 and one of the seriously affected countries in sub-Saharan Africa, with more than 1.3 million people living with HIV and an estimated 277,800 people requiring treatment. Average life expectancy at birth is also relatively low at 48 (47 for males and 49 for females) and is further expected to decline to 49.4 years if present HIV infection rates continue(1). To scale up the national response, HIV/AIDS policy was formulated by minister of health (MOH) and adopted by the council of minister in 1998. In 2003, the Government of Ethiopia introduced its ART programme with the goal of reducing HIV-related morbidity and mortality, improving the quality of life of people living with HIV and mitigating some of the impact of the epidemic (4).

In 2005, Ethiopia launched free ART; over 71,000 were initiated on ART by the end of November 2006 and some 241 hospitals and health centers are now providing HIV care and treatment services in regions of the country (1). Four interventions have been implemented to prolong the survival of PLWHA which includes ART supply and use, PCP prophylaxis, MAC prophylaxis and care by physician specializing in HIV (4).

Ethiopia is currently decentralizing HIV care and treatment services to selected health centers. Efforts have been made to demystify HIV care and ART by developing standardized and simplified clinical tools, reference materials, and job aids. Building the capacity of clinical nurses to prescribe first-line ARVs for stable patients and provide primary chronic HIV care including ART was pioneered in 2006. Ethiopia is also piloting the use of trained non-health professional counselors (1). ART includes at least three compatible anti-retroviral agents. In the past, doctors prescribed anti-HIV drugs one at a time (monotherapy), it was discovered that these drugs are far more effective when three or more are taken at the same time. This is because triple combination therapy attacks HIV at two (or three) different points in its life cycle at the same time, greatly reducing the chance that virus with resistance to one drug will be able to carry on copying themselves(4).

## 1.2. Statement of the problem

The human immunodeficiency virus (HIV) has created an enormous challenge worldwide. Since its recognition, HIV has infected close to 70 million people, and more than 30 million have died due to acquired immunodeficiency syndrome (AIDS). More than 66% of the 40 million people living with HIV/AIDS are in sub-Saharan Africa, where AIDS is the leading cause of death. Undisputable fact is that 14,000 people in Sub-Saharan Africa are being infected daily with HIV and 11,000 are dying every day due to HIV/AIDS related illnesses(5).

HAART has provided dramatic reductions in hospitalization and mortality rates. It has also increased the quality of life for many individuals living with this disease. Unfortunately, new advances in therapies have also brought a host of complications, many of which affect body habitus. Fat redistribution syndromes have created a new stigma associated with these emerging side effects of therapy. ARV has enormous benefits and challenges. The challenges include resistance, affordability, toxicity and adherence (4, 5).

Since the introduction of HAART, the incidence of most AIDS-defining opportunistic infections has dramatically decreased; the number of AIDS related death declined and slowed patient progression from HIV to AIDS. Although some studies demonstrate that the incidence of HIV-related wasting syndrome has also declined in the HAART era, data from the Nutrition for Healthy Living (NFHL) cohort show that weight loss and wasting are still common in HIV-infected persons and that even a 5% weight loss in 6 months markedly increases the risk of death(4,6,7,8).

Access to ARV drugs will improve survival and quality of PLWHA. This has been shown in developed countries and in very few middle-income countries where more affordable drugs are available. Where enough drugs are available to take several combinations, people are still doing well after 7-8 years with good adherence to treatment. Few studies have examined the effect of ART in Africa, and experiences from Europe and North America are not necessarily applicable to such settings. However, early reports from ART programs in resource-limited settings have been promising, with virological efficacy comparable to industrialized countries. Nevertheless, mortality has been high, particularly the first months after initiating ART, and factors contributing to this high mortality are poorly understood. In Europe and north America, the majority of those who started ART in 1996 and who have taken it ever since are still alive. In developing world, although early

signs are promising, we don't know if the same level of success is as sustainable as in richer nations. This is because patients in richer nations have usually taken several combinations of drug since starting ART. When one combination fails, another is available to replace it. This will be less easy in the developing world, because the cost of ARV used for 'second line' treatment is higher than is the cost for first line treatment. It is important that where second line drugs are not available, people with HIV and their communities are prepared for the possibility that treatment may fail (2). 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 (8, 9).

ART is still new in Africa. Many important questions related to the best use of ART remain unanswered, including for example, when is the best time to start therapy, which are the best drug to use, how long will treatment keep people alive, Is the treatment effective in general HIV populations and what factors predict the survival of PLWHA after the initiation of ART? The dynamics of the restoration of predictors of survival under these circumstances are not well understood. Although the relationship between survival and its predictors such as virus load, low CD4 count, anemia, and body mass index has been described, the independent predictors of survival in PLWHA, as well as the interaction of these identifiers, in the general HIV-infected population after the advent of HAART remain poorly characterized. The main aim of this study is then to answer some of the above questions directly or indirectly and fill the information gap by assessing the predictors of survival in PLWHA after the advent of HAART in Zewditu Hospital. Further more it will provide empirical evidence for program planner, decision makers and ART program implementer at the different level by enabling them to access a base line data on predictors of survival on PLWHA after the advent of HAART. More over it will be a paramount important to curb the horizon of the disease. And it provides baseline information that will assist in the development of a system for tracking adherence, improving quality of life and survival.

## **II. Literature review**

### **2.1. Burden of adult HIV /AIDS problem and Ethiopian Scenario of HAART**

Globally 39.4 million peoples are living with HIV/AIDS. Adults contribute 37.2 million (33.8-41.7 million). About five million peoples are newly infected of which 4.3 are adults. More than 95% of new infections are in developing countries. Over six million need ART but 350,000-400,000 treated in developing countries. The introduction of highly active antiretroviral therapy in 1996 dramatically improved the prognosis for HIV-infected patients in the industrialized world. Until recently, however, access to treatment has been severely limited in developing countries, where the majority of people with HIV/AIDS live. By December 2006, two million people in low- and middle-income countries were receiving ART, but this was still only 28% of those estimated to be in urgent need of it (8).

In Ethiopia, 47% of the total populations is aged 15 to 49 years. The highest HIV prevalence occurs in the age group 15-24. HIV infections occurring in adults between 15 to 49 years account for 90 % of all infections. According to single point prevalence estimates (HAPCO), Adult prevalence (%) By 2008 in Male=1.8, Female =2.6, Total=2.2, by 2010, Male=1.9, Female =2.9, Total=2.4. Annual AIDS deaths by year 2008, Male= 25,206, Female=33,084, Total=58,290 and by year 2010, Male= 12,024, Female= 16,049, Total= 28,073. ART needs, 289,734 by 2008 and 397,818 by 2010. As of March 2009, 189,267 started ART of which 177,041 (Adults >14 years) In Addis Ababa, Adult prevalence (%)=7.9 by 2008 and 9.2 by 2010. Annual AIDS deaths=5,761 by 2008 and 3,977 by 2010. ART needs is 48,846 by 2008 and 70,097 by 2010 (2, 3). In Addis Ababa, 60,922 PLWHA enrolled, 35,515 PLWHA started and 26,643 PLWHA are currently on ART. The total person on 1st line regimen is 101,683 of which 96,488 are adults. The total number of persons on 2<sup>nd</sup> line regimen is 1,034 and 984 in adult. Among adults on the 1st line regimen, 39,066 on d4t(30)-3TC-NVP, 5,125 on d4t(40)-3TC-NVP, 19,954 on d4t(30)-3TC-EFV, 2,282 on d4t(40)-3TC-EFV, 17,290 on AZT-3TC-NVP, and 12,771 on AZT-3TC-EFV. The rest 1.01% are on 2nd regimen (27 on ABC-ddI-LPV/R, 6 on ABC-ddI-NFV, 107 on TDF-ddI-LPV/R, 28 on TDF-ddI-NFV, and 816 on others unspecified) (3).

### 2.3. Estimates of survival of PLWHA

According to Degu J, mortality rate in ART+ group was 15.4/100PYO and most of the death occurred during the first three month. Alfred C etal estimated t he probability of being alive on ART at 6, 12 and 18months as 89.8%, 83.4% and 78.8% respectively. Robert etal in other hand revealed the cumulative mortality rate at 12 months was 2.9%.Frank J. etal estimated mortality rates ART<sup>+</sup> were 15.4 and 56.4 deaths per 1000 person-years. Lisa M. etal showed persons with OI, 67% were alive at least 36 months and 77% were alive at least 24month. Egger etal also showed the cumulative 75% survival from cryptococcal related mortality at 54 month. Chottanapund S etal estimated the survival rates at 12, 24, and 36 months were 92.8%, 87.4%, and 85.4%.

In a study conducted in Tanzania, 95 patients (29.7%) died during the follow-up period, among whom 59 died within 3 months of starting ART. Estimated mortality was 19.2, 24.5, 29.0, 35.2 and 40.7% at 3, 6, 12, 24 and 36 months, respectively. Mortality was found to be high, with the majority of death occurring with in three month of starting ART (7)

The CD4 counts gradually declines over several years, with a more accelerated decline 1.5 to 2 years before an AIDS defining diagnosis. HIV RNA concentrations in plasma show an intial “burst” during acute infection and then decline to a “set point” as a result of seroconversion and development of immune response. The viral load correlates with the rate of CD4 decline (4% decline/year/log<sub>10</sub>/copies/ml).With continued infection, HIV RNA levels gradually increase. In untreated patients, the median survival after the CD4 count fallen to <200 cells/mm<sup>3</sup> is 3.7 years. The median survival after an AIDS defining complication is 1.3 years (1).

On average, 6 life-years will be saved per person treated, if individuals primarily enter ART programmes when symptomatic. If individuals are recruited to programmes while still healthy and are frequently monitored, and CD4+ cell counts are used to help decide when to initiate ART, three times as many are expected to be treated, and average life-years saved among those treated increases to 15. Initiating ART at higher CD4+ cell counts than WHO recommends leads to more life-years saved, but disproportionately more years spent on ART The overall impact of ART programmes will be limited if rates of diagnosis are low and individuals enter care too late. Frequently monitoring individuals at all stages of HIV infection and using CD4 cell count information to determine when to start treatment can maximize the impact of ART and improve survival (12). In other study, the

cumulative 75% survival (free) from relapse duration was 41.9 months in ART group ( $P < 0.01$ ). The 75% survival from cryptococcal-related mortality in no-ART group was 6.4 months whereas  $>54$  months for ART group ( $P < 0.01$ ), ART was the only factor that associated with lower relapse and mortality rate ( $P < 0.01$ ). ART significantly reduced relapse and mortality rate from cryptococcosis in HIV-infected patients (14). The probability of progression to AIDS or death at 3 years ranged from 3.4% (2.8-4.1) in patients in the lowest-risk stratum for each prognostic variable, to 50% (43-58) in patients in the highest-risk strata. The CD4 cell count at initiation was the dominant prognostic factor in patients starting HAART (15).

Survival rates at 1, 2, and 3 years after TB diagnosis were 96.1%, 94.0%, and 87.7% for ART+ group and 44.4%, 19.2%, and 9.3% for ART- group (log-rank test,  $P < 0.001$ ) (16).

## **2.4. Predictors of survival**

### **2.4.1. socio-demographic predictors**

Fat loss is more common reported in men than women. Older peoples are more likely to report both central fat gain and fat loss from the arms, legs, and face (1). Other studies showed that females have significantly higher survival rates than males in WHO stage 1, 2 and 3 (both  $P < 0.0001$ ) and borderline in stage 4 ( $P = 0.076$ ). More over the Cox model revealed a death hazard ratio (males vs. females) of 1.70 (95% confidence interval 1.35–2.15) after controlling for WHO clinical stages, body mass index and age. More men than women were also lost to follow-up in all occupations except health workers. (8, 11). Advanced age is other significant predictors of survival (15, 18).

### **2.4.2. Base line clinical and laboratory predictors**

Studies in well resourced countries have shown that after 3 years on a combination of non-nucleoside reverse transcriptase inhibitor (NRTIs) and a protease inhibitor (PI), 30-40% of people will develop body fat change (lipodystrophy)(1).

The study in Tanzania rural hospital revealed that the significant independent predictors of mortality are moderate and severe anemia (log rank test,  $P < 0.001$ ), thrombocytopenia, and severe malnutrition (log rank test,  $P < 0.001$ ) (8). According to a study conducted in Derban, however revealed that factors predicting higher mortality rates among PLWHA were oral thrush,

TLC<1200/ml, BMI less than 18.5 kg/m<sup>2</sup>, anemia, WHO clinical stages III or IV and presence of prolonged diarrhea at baseline. However, only low TLC and low BMI were associated with increased mortality both in the pre-HAART (BMI, P = 0.016; TLC, P= 0.009) and in the HAART groups (BMI, P = 0.017; TLC, P = 0.039) while anemia was not associated with increased mortality in either group (pre-HAART, log-rank = 2.2, P = 0.14; HAART, Log-rank = 2.1, P = 0.14) (9).

HAART improved survival and decreased tuberculosis incidence to a level similar to that achieved in the developed countries during the early years of HAART. This relative reduction in mortality and tuberculosis is encouraging news. However, both the mortality and the tuberculosis incidence rates were higher in this resource limited setting. More over A baseline CD4 cell count <50/μl was a significant predictor of mortality (HR 3.70, 95% CI 1.96 – 7.14, p<0.0001) .A history of oral candidiasis and cryptococcal meningitis also conferred an increased mortality risk (HR 3.17, 95% CI 1.70 – 5.87, p=0.0002 and HR 2.76, 95% CI 1.07 – 7.10, p=0.03). Patients with a history of tuberculosis (pulmonary or disseminated) were not at a significantly increased risk of death (HR 1.16, 95% CI 0.65 – 2.08, p=0.62). A history of herpes zoster and P. jirovecii pneumonia was also not associated with increased mortality (HR 0.73, 95% CI 0.31 – 1.73, p=0.48 and HR 1.11, 95% CI 0.45 – 2.80, p=0.82). Patients with a CD4 cell count <50/μl had a 3-fold higher risk of mortality (HR 3.08, 95% CI 1.54 – 5.88, p=0.001) and those with a history of oral candidiasis a 2.5-fold increased risk (HR 2.58, 95% CI 1.37 – 4.88, p=0.003) (8). In a comparison of patients treated in industrialized and poor countries, a large difference in mortality was noted. This was linked to lower baseline CD4+ cell counts (12% mortality if < 50/mcL), concomitant tuberculosis, and lack of free care (10).

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 haemoglobin and low CD4 cell count; during follow-up: low CD4 cell count and persistently detectable viral load (14). 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/microL, adjusted hazard ratios were 0.74 (95% CI 0.62-0.89) for 50-99 cells/microL, 0.52 (0.44-0.63) for 100-199 cells/microL, 0.24 (0.20-0.30) for 200-349 cells/microL, and 0.18 (0.14-0.22) for 350 or more CD4 cells/microL. Baseline HIV-1 viral load was associated with a higher probability of progression only if 100,000 copies/microL or above. Other independent predictors of

poorer outcome were advanced age, infection through injection-drug use, and a previous diagnosis of AIDS (15).

### **2.4.3. Medication and ART regimen predictors**

The main cause of treatment failure are preexisting resistance, limited potency of regimen, imperfect adherence, poor absorption of drug, rapid elimination, and drug-drug interaction which lead to persistent viral replication and drug failure (1). A study by Anna C. showed that AZT is unsuitable for populations that have a high prevalence of anemia and low CD4+ cell counts, as the incidence of severe anemia (grade IV) was 6.6% during the first 3 months of treatment with AZT plus 3TC plus tenofovir (TDF). The ddI plus 3TC combination is well tolerated, as in industrialized countries. d4T is part of the first-line ART regimen recommended by WHO since the first guidelines were released in 2002. From then on, it has been integrated in the protocols of most national HIV programs in resource-limited countries and is now used by hundred of thousands of patients worldwide. However, d4T is no longer recommended in Western countries because of its longer-term toxicity profile that includes, for example, the long-term potential for the disfiguring lipoatrophy complication. In resource-limited countries, peripheral neuropathies are the main reason for changing d4T during the first months of treatment, but the importance of lipoatrophy as a reason for abandoning d4T later in treatment is still to be determined in cohorts from resource-poor settings (10).

Antiretroviral therapy substantially reduces mortality rate among HIV/TB-coinfected patients. Initiation of ART within 6 months of TB diagnosis is associated with greater survival. The 5-year risk of AIDS or death (death alone) from the start of HAART ranged from 5.6 to 77% (1.8-65%), depending on age, CD4 cell count, HIV-1-RNA level, clinical stage, and history of injection drug use. From 6 months the corresponding figures were 4.1-99% for AIDS or death and 1.3-96% for death alone. Triple ART, detectable viral load, CD4 count at base line, and change in CD4 count were important in predicting CD4 counts <200 cells/ $\mu$ l. (16, 18).

Significant risk factors associated with mortality included WHO stage IV disease, a baseline CD4 cell count under 50 cells/ $\mu$ l and increasing grades of malnutrition. Individuals who were severely malnourished [body mass index (BMI) < 16.0 kg/m<sup>2</sup>] had a six times higher risk of dying in the first 3 months than those with a normal nutritional status. Among individuals starting ART, the BMI and

clinical staging could be important screening tools for use to identify and target individuals who, despite ART, are still at a high risk of early death (20).

Individuals with incomplete CD4 T cell recovery to  $<500$  cells/microL had more advanced HIV-1 infection at baseline. CD4 T cell changes during the first 3-6 months of ART already reflect the capacity of the immune system to replenish depleted CD4 T lymphocytes (21).

#### **2.4.4. Risk behavior predictors**

Non-adherent patients who initiated HAART when the CD4+ cell count was  $0.200$  to  $0.349 \times 10^9$  cells/L had statistically elevated mortality rates (adjusted relative hazard,  $2.56$  [95% CI,  $1.36$  to  $4.84$ ];  $P = 0.004$ ) compared with adherent patients who initiated HAART at a CD4+ cell count of  $0.350 \times 10^9$  cells/L or greater. However, compared with adherent patients who initiated HAART at a CD4+ cell count of  $0.350 \times 10^9$  cells/L or greater, adherent patients who initiated HAART when the CD4+ cell count was  $0.200$  to  $0.349 \times 10^9$  cells/L had statistically similar mortality rates (adjusted relative hazard,  $0.82$  [CI,  $0.45$  to  $1.49$ ];  $P > 0.2$ ). Delaying HAART until the CD4+ cell count falls to  $0.200 \times 10^9$  cells/L does not increase the mortality rate in HIV-infected patients with good medication adherence. Mortality rates increase if HAART is initiated below  $0.200 \times 10^9$  cells/L. Also, nonadherent patients have higher mortality rates than adherent patients with similar CD4+ cell counts. Above a CD4+ cell count of  $0.200 \times 10^9$  cells/L, medication adherence is the critical determinant of survival, not the CD4+ cell count at which HAART is begun (17).

### **III. OBJECTIVE**

#### **3.1. GENERAL OBJECTIVE**

- To assess predictors of survival in Patients living with HIV/AIDS after the advent of HAART.

#### **3.2. SPECIFIC OBJECTIVE**

1. To estimate the time to death of PLWHA who are on HAART.
2. To compare the time to death among the different groups of PLWHA after the advent of HAART.
3. To determine independent predictors of survival in PLWHA after initiation of HAART.

## **IV.METHODOLOGY**

### **4.1. Study area and period**

Zewditu Hospital is one of the general specialized hospitals in Addis Ababa Ethiopia. The hospital gives different specialized clinical services for millions inhabitants from different part of the country. it also provides patient care and treatment for HIV/AIDS related opportunistic infection, provider initiative counseling and testing (PIHCT) for TB, Follow up of complicated case of TB patients and transfer to health center for DOTS. More over the hospital initiates ART and provide prophylaxis (cotrimoxazole and INH). The ART program of the hospital was started in July 2003.Zewditu hospital has been providing ART service to all patients coming from all regions between 2003 and 2004.The free ART program started in March 2005. Adult patients are eligible for ART based on WHO recommendation criteria. A total of 14,841 patients have been enrolled since February 2009. Eight thousands nine hundred patients ever started on ART.A total of 5,445 adult patients are currently on ART. The hospital uses intake form, follow up form, registers (Pre-ART register and ART register), monthly report form, cohort report form, pharmaceutical and laboratory report form and different referral paper tool to monitor the patients. Patients are seen at two weeks after ART initiation and then routinely every month for clinical assessment and ART dispensing. Among HIV patients currently on ART, 844 are on d4t-3TC-NvP, 679 on d4t-3TC-EFV, 1548 on AZT-3TC-NVP, 1266 on AZT-3TC-EFV,55 others and 11 on second line ART treatment. Out of 4,626 started ART, 46 %( 2126) had TB co-infection. The current ART distribution by sex is 50%.The ART case team in the hospital include medical doctors(2), regular nurse(5), advanced ART nurse(3), pharmacist(1), druggist(2), laboratory technician(3), pediatric physician(1), data clerk(2), and adherence supporter(5)(25).This study was conducted from January, 2009 to May, 2009.

### **4.2. Study design**

A historical institutional based cohort study was conducted in Zewditu hospital to assess predictors of survival in PLWHA receiving antiretroviral therapy.

### **4.3. Population**

#### **4.3.1. Source population**

All adult living with HIV /AIDS and started antiretroviral therapy in Addis Ababa public hospitals..

#### **4.3.2. Study population**

Those patients fulfilling the following criteria at Zewditu ART center

Inclusion criteria

- HIV-positive adults aged 14 years or older who started ART since March 2005
- HIV patients with complete intake form, registers, and follow up form.

Exclusion Criteria include

- Diagnosis made out side the hospital will be excluded(Transfer in)
- Patient with incomplete recording of base line and follow up data
- loss to follow up (drop, lost)
- competing cause of death
- Women who were pregnant at the time of ART initiation or PMTCT
- Lactating mother in WHO stage I or II who started ART exclusively to prevent vertical transmission.
- Diabetes, thyroid disease, or any malignancies other than Kaposi sarcoma.

### **4.4 Sample size determination and sampling technique**

#### **4.4.1 Sample size determination**

The sample size was calculated using two sample proportion formulas in Epi-Info version 3.3 for windows. Calculation was based on the assumption that type I error of 5%, power of 80% and one exposed (death) to two non-exposed (survive) allocation ratio. The most significant predictors of survival were used. We took the maximum sample among the most significant predictors of mortality in most literatures Initially the sample size was determined by mild to moderate malnutrition but the

height of the patients was not recorded totally at the time of ART initiation. Therefore we forced to take the next predictors i.e. WHO staging to calculate the final sample size needed.

I.e

$$\text{Let } P = \frac{p_1 + rp_2}{1+r} \text{ and } r = n_2/n_1$$

$$n_1 = \frac{\left[ [Z_{\alpha/2} \sqrt{\left(1 + \frac{1}{r}\right) p(1-p)} + Z_{\beta} \sqrt{p_1(1-p_1) + p_2\left(\frac{1-p_2}{r}\right)}] \right]^2}{(p_1 - p_2)^2}$$

Where;

P1=proportion of death among non exposed.

P2=proportion of death among exposed

$\alpha$ =level of significance,  $Z_{\alpha/2}$ =1.96 at 95%CI

Power=80%=1- $\beta$ ,  $Z_{\beta}$ =1.28

n=the minimum required sample size in each group

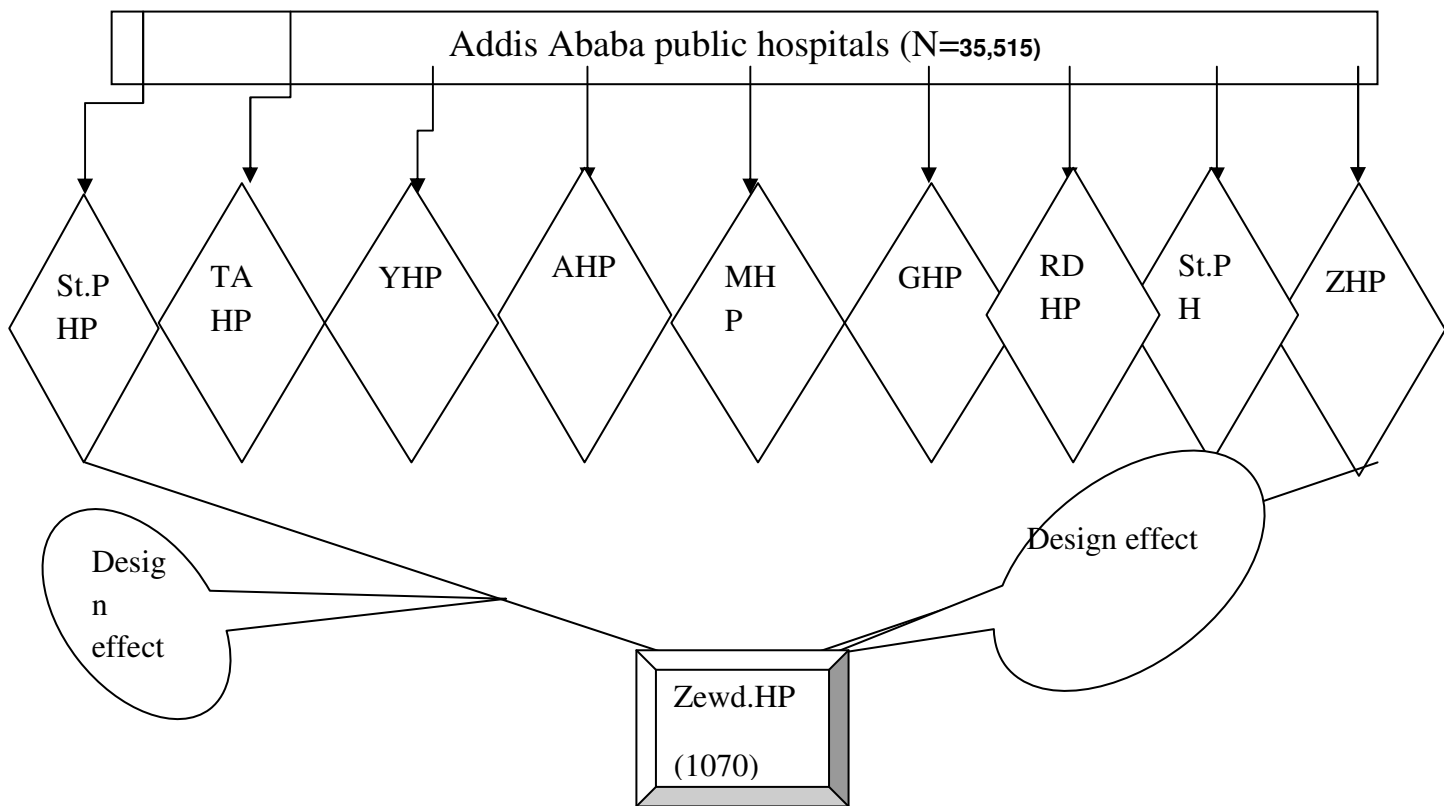
Table 4.1 The estimated sample size of the most significant predictors of survival in PLWHA after initiation of ART from different previous studies

Predictors	Hazard rate	Proportion of death among exposed	Proportion of death among non exposed	n <sub>1</sub> (alive)	n <sub>2</sub> (death)	Total
1.Sex(male vs female)	1.60	39.2	25.6	266	132	398
2.WHO clinical staging VI vs I-III	1.46	36.2	20.40	476	238	714
3.BMI						
a. severe vs normal	2.12	46.9	15.1	51	25	76
b. mild to moderate vs normal	1.27	21.9	15.1	720	360	1,080
4.TLC(<0.6vs≥1.2)	1.72	60.0	25.3	48	24	72
5.platelet(<150vs≥150)	2.3	46.2	25.3	121	61	182
6.CD4(<50 vs>50)	3.09	24	8	124	62	186
7.employment status (no/yes)	1.42	19	11	448	224	672
8.oral candidiasis(yes/no)	2.59	22	11	260	130	390 <sub>15</sub>

Finally WHO staging was selected which give a sample size  $n_1$  (alive) =476, and  $n_2=238$ . This sample size was further multiplied by 1.5 design effect. The final sample size was then calculated as active ( $n_1$ ) =710 and death ( $n_2$ ) =360 resulting the total sample size as **1070**

### 3.4.2. Sampling technique

There are nine hospitals in Addis Ababa. First those hospitals with no ART clinic or started ART recently were excluded. During Pretest, we found that some hospitals started ART recently and give follow up care for patients transferred from other hospitals especially from Zewditu hospital. Moreover Zewditu hospital is the pioneer in giving ART service not only in Addis Ababa but also in Ethiopia.



We selected Zewditu Hospital purposely to get optimal follow up period as it is pioneer in starting free ART program in the country and adequate sample especially death with a good data handling system is in place. More over, some of the patients taking ART in other hospital were transferred from this hospital as revealed during pre-test. Patient's records were reviewed consecutively. Different documents for the same patients were triangulated in case of odd values, non logical data or missed data. First the profiles of all patients on ART b/n March, 2005 and July, 2008 were evaluated. Then after los to follow up, drop out, PMTCT, deaths with competing cause, transfer out or patients started ART since August 2008 or before March 2005 or with incomplete data were excluded. Finally samples were selected consecutively starting from March 2005 up to September 2008 using Patient's ART unique identification numbers. If the selected sample was excluded already, the next consecutive number was included.

#### **4.5. Data collection procedure**

##### **4.5.1. Variable**

##### **4.5.1.1. Independent variable**

The independent variables are

- Socio-demographic characteristics as age, religion, sex, educational level, ethnicity, marital status, dependent children at home , employment
- Base line clinical, laboratory and ART information-past opportunistic illness, Tb test and treatment, ART treatment, CD4count, chemoprophylaxis (cotrimoxazole, INH...), drug allergies ,BMI,WHO clinical staging, Hgb, T-cell lymphocyte count, side effects and ALT/AST.
- Social condition as religious/supportive care, HIV serostatus disclosure, spouse and children condition and sero status
- Knowledge on ART and HIV
- Sexual risk behavior
- Addiction
- ART and treatment

#### **4.5.1.2. Dependent variables**

The main out come measure is cumulative survival rates from the initiation of triple-drug antiretroviral therapy to May 2009

#### **4.5.2. Questionnaire**

The questionnaire consists of the following items;

- Socio-demographic data
- Base line clinical, laboratory and ART data
- Social support and condition
- Sexual risk behavior
- Addiction
- ART and treatment
- Knowledge on HIV and ART
- Follow up data

#### **4.5.3. Data collection and quality control**

A data collection form was developed from the ART entry and follow up form being used in the ART clinic. Pre-testing was under taken in Yekatit and St.Paulos hospital (located in Addis Ababa which are also giving ART service) before the actual data collection took place and some minor modification was done accordingly. the data then collected by reviewing pr-ART register, lab request, monthly cohort form, follow up form, ART intake form, patient's card, and death certificate complemented by registration by home visitors or calling by drug adherence supporters. The most recent laboratory results before starting ART used as a base line values. If there is no pre-treatment laboratory test, however, results obtained with in one month of ART initiation used. If two results obtained with in a month, the mean was used.

Three advanced ART nurses, who were trained on Comprehensive HIV care, collected the data. Two ART physicians supervised the data collectors. A total of two-day intensive training was given for all supervisors and data collectors. The over all activity was controlled by the principal investigator of the study. Data quality was controlled by designing the proper data collection materials and pre-

testing, through continues supervision .All completed data collection form was examined for completeness and consistency during data management, storage, cleaning and analysis. The data was entered and cleaned by trained data clerk and principal investigator respectively before analysis.

#### 4.6. Data considerations, analysis and processing

Data was entered to Epi-Info 3.3 for windows and analyzed using SPSS version 16.0 for windows. The data was cleaned and edited before analysis. Data exploration was undertaken to see if there were odd codes or items that were not logical and then subsequent editing was made. We described the patient cohort characteristics in terms of mean/median value for continuous data and percentage for categorical data.

**The main end point in this study was death from all AIDS related causes** .Deaths was ascertained by reviewing the death certificates, medical registration in the hospital, or registration by ART adherence supporter through calling using the registered phone number or visiting to home.. And individuals alive and on ART at the end of the study period were censored. Finally, the out come of each subject was dichotomized in to censored or death.

Survival analysis was used to measure the association of patient's characteristics with time from ART initiation to death. Actuarial table was used to estimate survival after the advent of ART, and log rank tests also used to compare survival curves .Bivariate Cox regression analysis was used to determine the association b/n independent variable with survival. Multivariate analysis for the whole group using stepwise Cox proportional hazard model was used to identify independent predictors of survival. Multicollinearity was checked using Spearman's correlation coefficient. Based on this, past CNS toxoplasmosis, functional status at base line, past or base line TB, oral candidiasis and past weight loss were not entered in to the final model as they were collinear to WHO staging .Total Lymphocyte Count was also excluded from the final model as it was collinear to base line CD4 count. Base line social condition, risk behaviors, and knowledge on HIV/AIDS, prophylaxis and adherence were not entered in to the regression model as they were missed commonly and not reliable. Age and sex of the cohort were also included in the model irrespective of their association to survival as they are the most common confounding variable in epidemiology and they are associated with survival by previous studies(1,8, 11,21,,22).Each variable was checked to fit the model using step wise Cox regression analysis. First Bivariate and at last only those variables that showed

statistically significant associations with the out come on multivariate model building was retained in the model. P-value less than or equal to 5% was considered as significant.

#### **4.7. Ethical Consideration**

Permission to undertake the study obtained from the Office of Institutional Review Board of Medical Faculty, Addis Ababa University and Addis Ababa health office. Official letter of co-operation was written to concerned bodies in St.paulos, Zewditu, and Yekatit hospital. The information was collected using secondary data in the ART clinic. Home visiting or calling was used only when it was impossible to ascertain the out come of the patients using records. Informed consent was obtained from each participant during home visiting or calling.

#### **4.8. Operational Definition**

**Asymptomatic**; without symptoms. Usually used in the HIV/AIDs literature to describe a person who has a positive reaction to one of several tests for HIV antibodies but who shows no clinical symptoms of the disease.

**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 or advanced ART nurse

**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 or Nurse

**Good Adherence**; if the percentage of missed dose is between >95 %(<= 2 doses of 30 doses or <3 dose of 60 dose) as documented by ART physician or Nurse.

**HAART**; The name given to treatment regimens recommended by leading HIV experts to aggressively suppress viral replication and progress of HIV disease.

**Immunodeficiency**; break down in immuno-competence to resist or fight off infections.

**Lost**; if a patient discontinued ART for at one to three month as recorded by ART physician or advanced ART nurse.

**NNRTI**; inhibit an enzyme used by HIV called ‘reverse transcriptase’.

**NRTI** ;Nucleoside Reverse Transcriptase inhibitor that bind to the active site of the HIV reverse transcriptase stopping the production of HIV RNA.

**Lipodystrophy**; change in body fat distribution (fat gain or fat loss)

**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 or Nurse

**Protease Inhibitor (PI)**; antiviral drugs that act by inhibiting the virus protease enzyme.

**Reverse transcriptase** ;enzyme of HIV converts the single –stranded viral RNA in to DNA.

**Survival** ; lack of experience of death

**Viral Load**; the quantity of HIV RNA in the blood.

**Wasting**: profound involuntary weight loss of greater than 10% of baseline body weight plus either chronic diarrhea or chronic weakness and intermittent or constant) in the absence of a concurrent illness or condition other than HIV infection that could explain the findings (e.g., cancer, tuberculosis, cryptosporidiosis, or other specific enteritis) as documented by Physician or advanced ART nurse.

**WHO staging system**; a classification of the clinical stage of HIV disease developed by the world health organization.

## V.RESULT

Between January and May 2009 , 5,234 HIV patients ever started ART were evaluated (fig.6.1) .One thousand seventy(710 active and 360 death) non pregnant adult patients were included in the present study.Base line and follow up predictors of survival among HIV patients who started ART were assessed.Patients on ART were followed for a median of 34 month (IQR 6, 36.25).

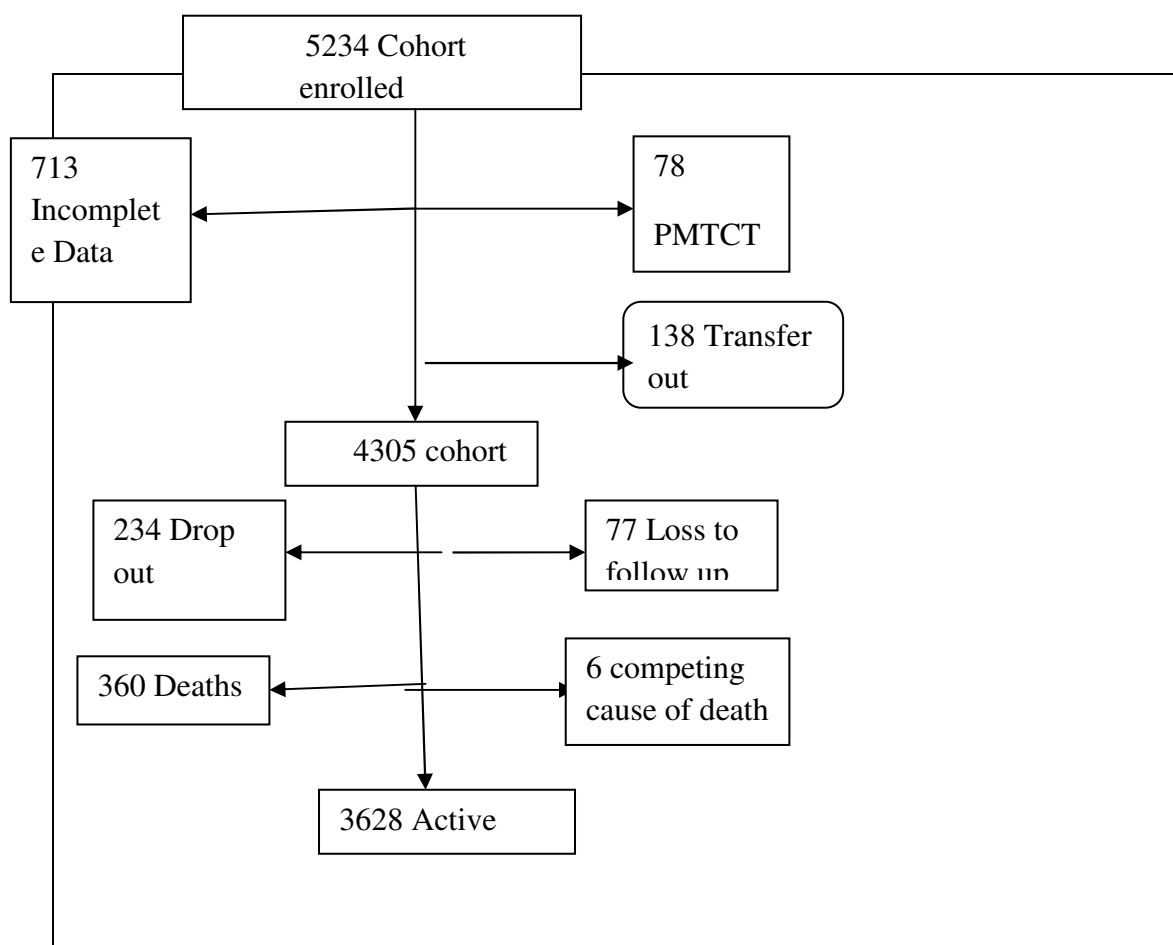


Fig. 6.1 Profile of enrolled cohort on ART enrolled between March, 2005 and July 29, 2008,  
Addis Ababa, Ethiopia

## I. Cohort Basic Characteristics

Among the cohort, 45% (483) of them were male and the mean age was 36.4(SD=9.83). Fifty three percent (568) of them were educated secondary and above, and 45% of the cohort were on marriage. Fifty eight percent (616) were unemployed. The median weight of the cohort at the initiation of ART was 51kg (IQR, 45kg-60kg). The mean Hemoglobin was 11.93(SD, 2.43) and the mean ALT level was 39.48 U/l. The median CD4 count was 94cells/ $\mu$ l (IQR, 46-154). The mean TLC was 1629.38cells/ $\mu$ l. Among the cohort, 90.9 %( 973) were given cotrimoxazole at the time of ART initiation. Fifty one percent (544) of the cohort were on WHO staging III, 14 %( 153) had TB co-infection and 54 %( 579) of them were on Zidovudine based ART regimen. Twenty percent (212) of the cohort were poorly adhered. Fifty one percent (308) of cohort didn't know their spouse HIV status. Sixty six percent (244) of cohorts had one or more casual sexual partner, and 43 %( 391) never used condom. Regarding substance use, 17 %( 142), 17 %( 142), 18.1 %( 148), and 9.3 %( 78) had been using Tobacco, alcohol, soft drugs and hard drugs moderately or more respectively. Moreover, 22.8 %( 188), 17.2 %( 142), 26.2% (215) and 24.3 %( 200) cohort had poor understanding of HIV disease, HIV/AIDS transmission, prophylaxis and treatment of Opportunistic illness, and ART medication and adherence respectively. Basic characteristics of the cohort were presented in table (6.1-6.5) below.

**Table 6. 1. Baseline Socio-demographic characteristics of the cohort studied (N = 1070 patients) in Addis Ababa, Ethiopia, from 1 March 2005 to 30 May 2009.**

Characteristics	Death(n=360)	Active(n=710)	Log rank test, p-value
<b>Gender</b>			
Male ( <i>n (%)</i> )	173(16%)	310(29%)	0.20
Female ( <i>n(%)</i> )	187(18%)	400(37%)	
<b>Age</b>			
<40	165(24%)	522(49%)	0.99
≥40	95(9%)	188(18%)	
<b>Religion*</b>			
Muslim	9(0.9%)	32(3%)	0.09
Orthodox	324(30.6%)	589(55.2%)	
Protestant	27(2.5%)	78(7.4%)	
<b>Educational status*</b>			
No education	46(4.4%)	57(5.4%)	0.03
Primary	150(14.2%)	236(22.3%)	0.09
Secondary	133(12.6%)	330(31%)	0.03
Tertiary	31(2.9%)	74(7%)	
<b>Marital status*</b>			
Never married	100(9.4%)	181(20%)	0.20
Married	150(14%)	334(31.3%)	
Separated	7(0.7%)	18(1.7%)	0.80
Divorced	51(4.8%)	71(6.6%)	0.03
Widowed	52(4.9%)	104(9.7%)	0.57
<b>Dependent children at home*</b>			
No	233(21.9%)	487(45.8%)	0.19
Yes	127(11.9%)	217(20.4%)	
<b>Employment status*</b>			
No	136(12.9%)	480(45.4%)	0.00
Yes	224(21.2%)	217(20.5%)	

**Table 6.2. Past opportunistic illness of the cohort studied (N = 1070 patients) in Addis Ababa, Ethiopia, from 1 March 2005 to 30 April 2009.**

Past opportunistic illness	Death(n=360)	Active (n=710)	log rank test, p-value
Candidiasis (oral)			
No	148(13.8%)	357(33.4)	
Yes	212(19.8%)	353(33%)	0.007
CNS Toxoplasmosis			
No	227(21.2%)	686(64%)	
Yes	133(12.4%)	24(1.7%)	0.000
Diarrhea			
No	181(17%)	406(38%)	
Yes	179(16.7%)	304(28.4%)	0.46
Herpes Zoster			
No	282(26.4%)	529(49.4%)	
Yes	78(7.2%)	181(17%)	0.243
Tuberculosis(PTB/EPTB)			
No	204(19%)	480(44.9%)	
Yes	156(14.6%)	230(21.5%)	0.001
Fever			
No	217(20.3%)	346(32.3%)	
Yes	143(13.4%)	364(34%)	0.001
Weight loss			
No weight loss	129(12%)	397(37%)	
<10% weight loss	48(4.5%)	199(18.6%)	0.153
≥10% weight loss	183(17.1%)	110(10.3%)	0.000
Other past opportunistic illness			
No	310(29%)	635(59%)	
Yes	50(4.7%)	75(7%)	0.11
Past Cotrimoxazole			
Yes	308(29%)	611(57%)	0.45

No	52(5%)	99(9%)	
Past Fasnsider			
No	94(9%)	20(2%)	0.00
Yes	266(25%)	690(65%)	
Past Fluconazole			
Yes	25(2%)	0	0.00
No	335(32%)	710(66%)	
Past INH			
Yes	6(0.6%)	5(0.5%)	0.13
No	354(33.1%)	705(64.5%)	

Table 6.3. Base line Clinical and laboratory information of the cohort studied (N = 1070 patients) in Addis Ababa, Ethiopia, from 1 March 2005 to 30 April 2009.

Base line clinical and laboratory presentation	Death(360)	Active(710)	log ran test, p-value
Weight at presentation* (median (25th - 75th quartiles)) (kg)	51(45-60)		0.000
Functional Status			
Working	39(4%)	318(30%)	0.000
Ambulatory	135(13%)	310(29%)	
Bedridden	186(17%)	82(8%)	
WHO staging			
Stage I or II	24(2%)	126(12%)	0.007
Stage III	147(14%)	397(37%)	
Stage IV	189(18%)	197(18%)	
Baseline laboratory studies (mean (SD))			
Haemoglobin (g/dl) <sup>  </sup>	11.93(2.43)		0.000
ALT (U/l) <sup>**</sup>	39.48(37.96)		0.988
AST (U/l) <sup>††</sup>	42.95(39.51)		0.000
TLC( cells/ $\mu$ l)	1629.38(959.03)		0.000
CD4 count (median (25th - 75th quartiles)) (cells/ $\mu$ l)	94(46-154)		0.000
Base line Cotrimoxazole (n (%))			
Yes	329(31%)	644(60%)	0.403
No	31(3%)	66(6%)	
Base line Fansider (n (%))			
Yes	59(6%)	7(0.7%)	0.000
No	301(28%)	703(66)	
Base line INH (n (%))			
Yes	17(2%)	0	0.000
No	343(32%)	710(66%)	

Base line Fluconazole (n (%))	17(2%)	6(0.6%)	0.000
Yes	343(32%)	704(65.4%)	
No			
ART regimen			0.004
D4T-3TC-NVP	101(9%)	157(15%)	
D4T-3TC-EFV	118(11%)	203(19%)	
AZT-3TC-NVP	64(6%)	190(18%)	
AZT-3TC-EFV	77(7%)	160(15%)	
ART regimen			0.001
Stavudine Based	141(13.2%)	350(32.7%)	
Zidovudine based	219(20.5%)	360(33.6%)	
TB Co- infection			0.000
No	270(25%)	647(60%)	
Yes	90(8%)	63(6%)	
ART Adherence			0.000
Good	191(18%)	667(62%)	
Poor	169(16%)	43(4%)	

\*missed variables

Table 6.4. Social condition and Risk behavior of the cohort studied (N = 1070 patients) in Addis Ababa, Ethiopia, from 1 March 2005 to 30 April 2009.

Variables	Death(360)	Active(710)
<b>Spouse HIV status*</b>		
Not Applicable	36(6%)	37(6.2%)
Not Asked	0	6(1%)
Negative	19(3.2%)	32(5.3%)
Positive	42(7%)	119(19.9%)
Unknown	142(23.7%)	166(27.7%)
<b>General concern*</b>		
No	54(9.1%)	126(21.2)
Yes	159(26.7%)	255(42.9%)
<b>Casual sexual partner*</b>		
No	41(11.1%)	85(23%)
1	41(11.1%)	71(19.2%)
2	35(9.5%)	45(12.2%)
3	10(2.7%)	15(4.1%)
<u>≥</u> 3	14(3.5%)	13(3.8%)
<b>Condom use*</b>		
Not applicable	37(5.5%)	76(11.3%)
Never	167(19.9%)	226(33.3%)
Rarely	17(2.5%)	15(2.2%)
Some times	30(4.5%)	48(7.1%)
Mostly	8(1.2%)	14(2.1%)
Always	6(0.9%)	27(4%)
No response	1(0.1%)	2(0.3%)

\*missed variables

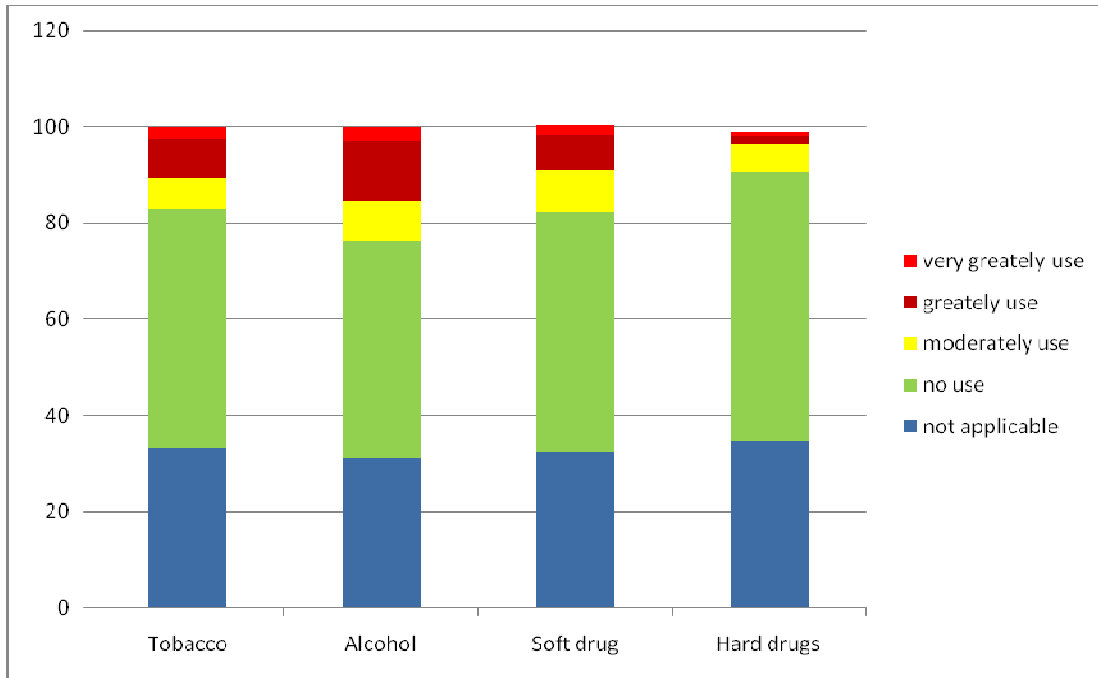


Fig. 6.2 Substance use of the cohort studied (N = 1070 patients) in Addis Ababa, Ethiopia, from 1 March 2005 to 30 April 2009

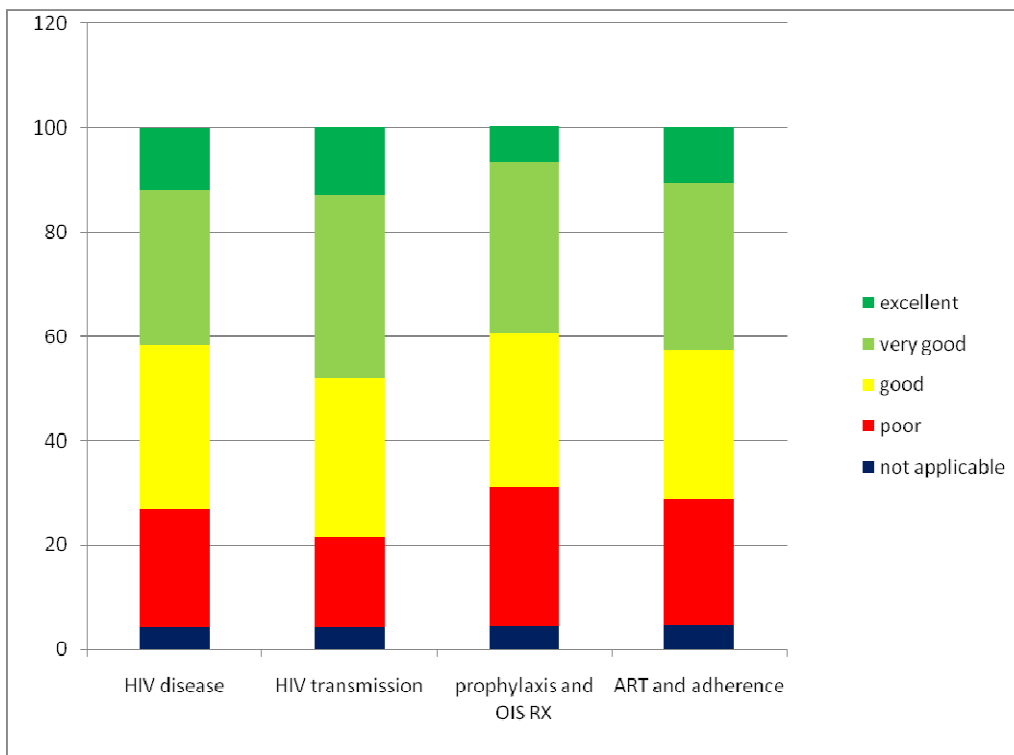


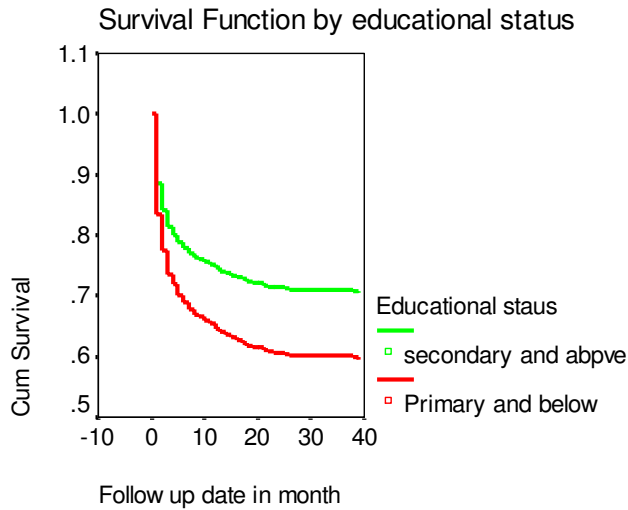
Fig 6.3 Knowledge on HIV/AIDS and ART of the cohort studied (N = 1070 patients) in Addis Ababa, Ethiopia, from 1 March 2005 to 30 April 2009.

## Survival Analysis

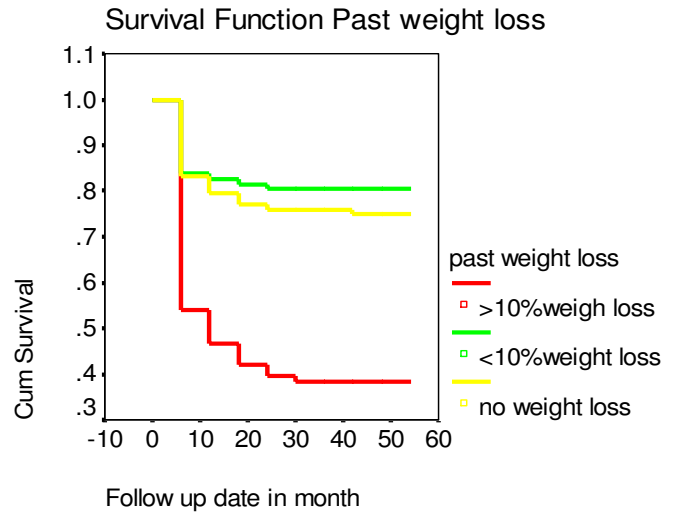
A total of 1070 cohort were followed for median of 34 month. The median follow up was 34 month and the minimum was 1 month and the maximum was 48 month. Three hundred sixty (33.6%) of them were died of whom 55.6 %( 200) were died with in 3 month (HR=0.069) and the rest 66.4% were active up to the end of last censored date. The estimated mortality was 24.9%, 29%, 31.7%, 33.1%, 33.5, and 34% at 6, 12, 18, 30, and 48 months respectively.

Table 6.5. Actuarial Table estimates of the cumulative progression to death for 1070 cohort starting ART b/n March 1, 2005 up to July 29, 2008. The diminishing number of patients at risk at each subsequent time interval is due to death or being censored as of April 2009.

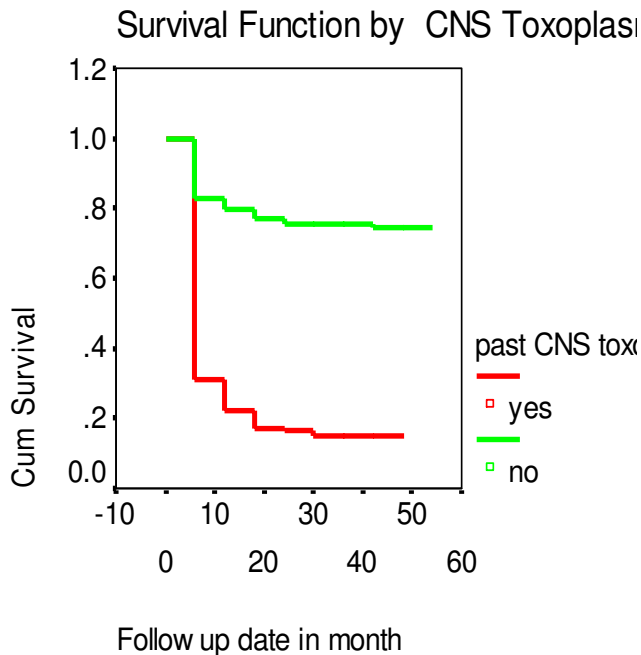
Interval start time in month	No of patients entering the interval	Number of death	Cumulative proportion of survival	Hazard Rate
.0	1070	266	0.751	0.047
6.0	804	44	0.710	0.009
12.0	760	29	0.683	0.007
18.0	721	15	0.669	0.004
24.0	704	4	0.665	0.001
30.0	690	0	0.665	0.000
36.0	376	2	0.660	0.001
42.0	126	0	0.660	0.000
48.0	15	0	0.660	0.000



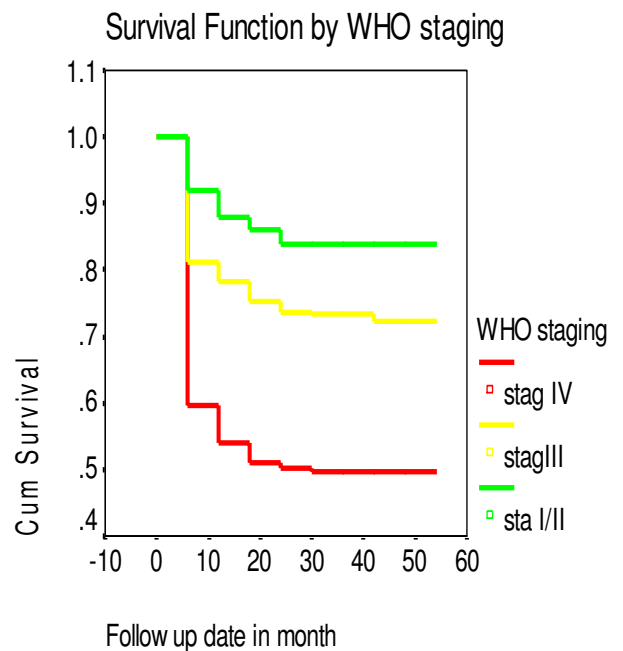
6.4.1. Patients with primary education or below were at high risk of death compared to others (log rank test,  $p < 0.01$ )



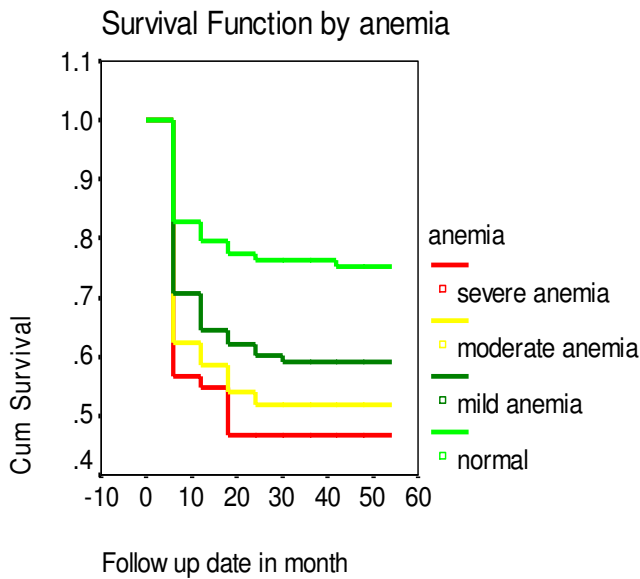
6.4.3. Patients with >10% weight loss were at high risk of death compared to others (log rank test,  $p < 0.01$ ).



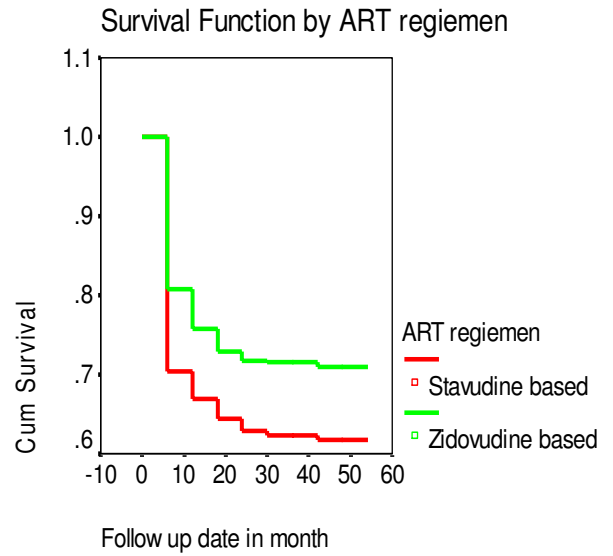
6.4.2. Patients with past history of CNS Toxoplasmosis were high risk of death compared to others (log rank test,  $p < 0.01$ ).



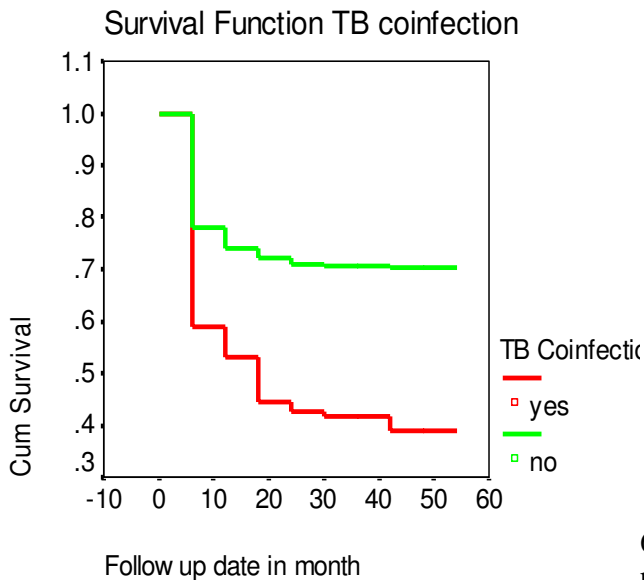
6.4.4. Patients at advanced WHO stage (III/IV) were at high risk of death compared to others (log rank test,  $p < 0.01$ )



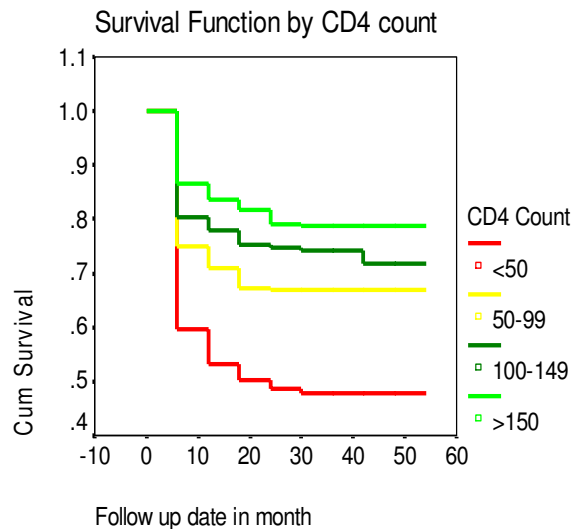
6.4.5. Patients with severe /moderate anemia were at high risk of death compared to others(log rank test, $p<0.01$ ).



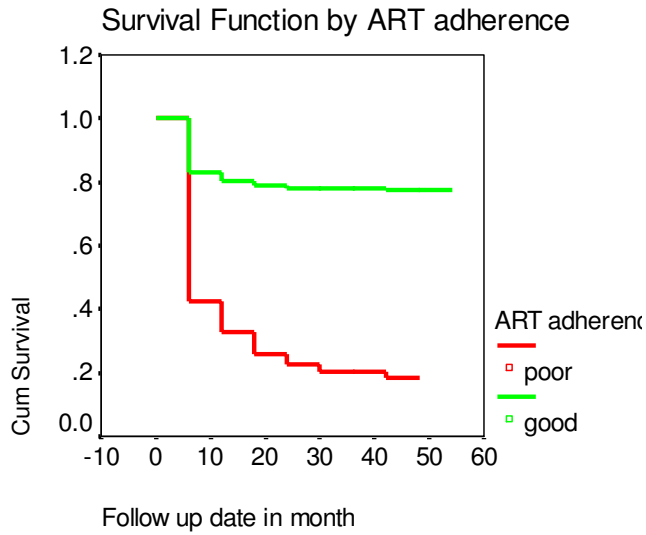
6.4.7. Patients taking stavudine were at high risk of death compare to others ((log rank test, $p<0.05$ ).



6.4.6. Patients with TB co infection were at high risk of death compared to others(log rank test, $p<0.01$ ).



6.4.9. Patients with <50 Cd4 count were at high risk of death compared to others(log rank test, $p<0.01$ )



6.4.10. Poorly adhered patients were at high risk of death compared to others (log rank test,  $p < 0.01$ ).

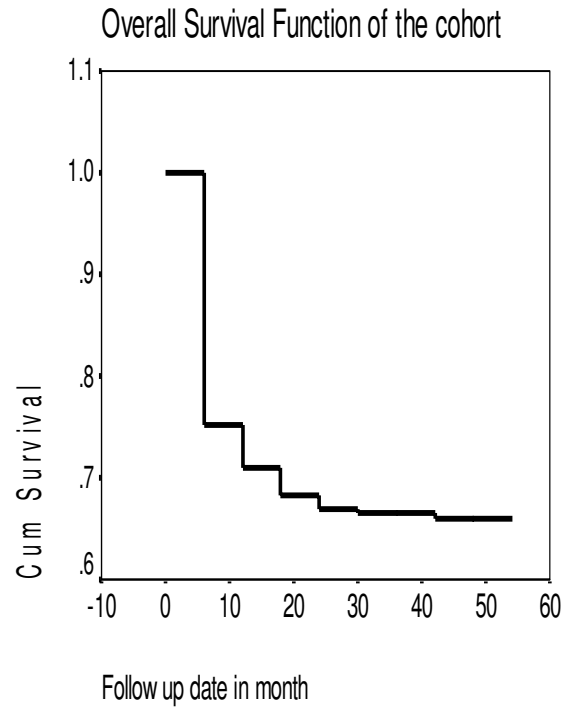
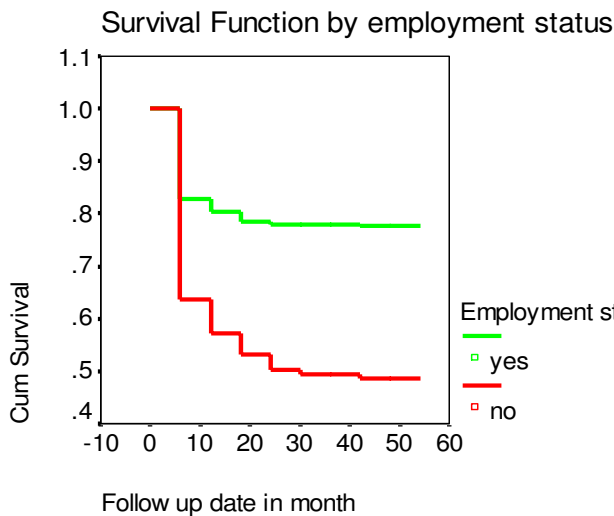


Fig. 6.5. Over survival curve of the cohort starting ART b/n March 1, 2005 up to July 29, 2008, showing rapid decline in the first 6 month of ART intake. Survivorship drops off rapidly especially in the first 3 months.



6.4.11. Unemployed patients were at high risk of death compared to other (log rank test,  $p < 0.01$ ).

Fig 6.4 Acturial curve of the cohort according to base line characteristics for the cohort starting ART b/n March 1, 2005 up to July 29, 2008.

**Table 6.7. Bivariate Cox-regression analysis of the cohort studied (N = 1070 patients) in Addis Ababa, Ethiopia, from 1 March 2005 to 30 April 2009.**

<b>Predictor</b>	<b>Crude HR(95% CI)</b>
<b>Age</b>	
<40	1
≥40	1(0.79,1.26) <sup>#</sup>
<b>Gender</b>	
Male	1.14(0.93,1.41) <sup>#</sup>
Female	1
<b>Educational Status</b>	
Primary and below	1.49(1.21,1.83) <sup>^</sup>
Secondary and above	1
<b>Religion</b>	
Muslim	1
Orthodox	1.76(0.91,3.42) <sup>#</sup>
Protestant	1.20(0.57,2.56) <sup>#</sup>
<b>Dependent children at home</b>	
No	1
Yes	1.15(0.93,1.43) <sup>#</sup>
<b>Marital status</b>	
Married	1
Never married	1.19(0.92,1.52) <sup>#</sup>
Widowed	1.10(0.80,1.51) <sup>#</sup>
Divorced	1.44(1.05,2.0) <sup>*</sup>
<b>Employment Status</b>	

<b>No</b>	2.67(2.16,3.31)^
<b>Yes</b>	1
<b>Candidiasis(oral)</b>	
<b>No</b>	1
<b>Yes</b>	1.34(1.08,1.65)^
<b>CNS Toxoplasmosis</b>	
<b>No</b>	1
<b>Yes</b>	5.62(4.51,7.00)^
<b>Diarrhea</b>	
<b>No</b>	1
<b>Yes</b>	1.23(1.00,1.52)#
<b>Past Herpes Zoster</b>	
<b>No</b>	1
<b>Yes</b>	0.86(0.67,1.12)#
<b>Past Tuberculosis(PTB/EPTB)</b>	
<b>No</b>	1
<b>Yes</b>	1.44(1.17,1.78)^
<b>Pat Fever</b>	
<b>No</b>	1
<b>Yes</b>	0.70(0.56,0.86)#
<b>Weight loss</b>	
<b>No weight loss</b>	1
<b>&lt;10% weight loss</b>	0.79(0.56,1.09)#
<b>≥10% weight loss</b>	3.19(2.54,4.0)^

<b>Past Cotrimoxazole prophylaxis</b>	
No	0.97(0.73,1.30)#
Yes	1
<b>Base line Cotrimoxazole prophylaxis</b>	
No	1.06(0.74,1.54)#
Yes	1
<b>WHO staging</b>	
Stage I or II	1
Stage III	1.81(1.18,2.79)^
Stage IV	3.99(2.61,6.10)^
<b>Functional Status</b>	
Working	1
Ambulatory	3.08(2.16,4.41)^
Bedridden	9.55(6.75,13.52)^
<b>TB Co- infection at base line</b>	
No	1
Yes	2.27(1.79,2.89)^
<b>Total Lymphocyte Count</b>	
>1200	1
600-1200	1.43(1.12,1.82)^
<600	2.16(1.56,3.00)^
<b>CD Count(cells/μl)</b>	
≥150	1
100-149	1.31(0.91,1.87)#

<b>50-99</b>	1.68(1.22, 2.32)^
<b>&lt;50</b>	3.02(2.25,4.06)^
<b>Anemia</b>	
<b>Normal Anemia</b>	1
<b>Mild Anemia</b>	1.87(1.47,1.2.38)^
<b>Moderate Anemia</b>	2.36(1.75,3.18)^
<b>Severe anemia</b>	2.71(1.80,4.08)^
<b>ART Adherence</b>	
<b>Good</b>	1
<b>Poor</b>	5.09(4.12,6.29)^
<b>ART regimen</b>	
<b>Zidovudine based</b>	1
<b>Stavudine based</b>	1.43(1.15,1.76)^

---

Note: #=P>0.05, \*=p<0.05, ^= p<0.01

**Table 6.8. Multivariate Cox-regression analysis and model fit of the cohort studied (N = 1070 patients) in Addis Ababa, Ethiopia, from 1 January 2005 to 30 April 2009.**

Predictors	Crude HR(95% CI)	Adjusted HR(95% CI)
<b>Age</b>		
<40	1	1
≥40	1(0.79,1.26) <sup>#</sup>	0.93,(0.73,1.19) <sup>#</sup>
<b>Gender</b>		
Male	1.14(0.93,1.41) <sup>#</sup>	1.08(0.87,1.34) <sup>#</sup>
Female	1	1
<b>Educational Status</b>		
Primary and below	1.49(1.21,1.83) <sup>^</sup>	1.23(0.99,1.53) <sup>#</sup>
Secondary and above	1	1
<b>Employment Status</b>		
No	2.67(2.16,3.31) <sup>^</sup>	1.87(1.49,2.34) <sup>^</sup>
Yes	1	1
<b>Marital status</b>		
Married	1	1
Never married	1.19(0.92,1.52) <sup>#</sup>	1.13(0.87,1.46) <sup>#</sup>
Widowed	1.10(0.80,1.51) <sup>#</sup>	1.00(0.72,1.37) <sup>#</sup>
Divorced	1.44(1.05,2.0) <sup>*</sup>	1.11(0.80,1.55) <sup>#</sup>

<b>WHO staging</b>		
<b>Stage I or II</b>	1	1
<b>Stage III</b>	1.81(1.18,2.79)^	1.32(0.85,2.05)#
<b>Stage IV</b>	3.99(2.61,6.10)^	2.45(1.58,3.81)^
<b>CD Count(cells/μl)</b>		
<b>≥150</b>	1	1
<b>100-149</b>	1.31(0.91,1.87)#	1.39(0.97,2.01)#
<b>50-99</b>	1.68(1.22, 2.32)^	1.41(1.01,1.97)#
<b>&lt;50</b>	3.02(2.25,4.06)^	1.85(1.35,2.52)^
<b>Anemia</b>		
<b>Normal Anemia</b>	1	1
<b>Mild Anemia</b>	1.87(1.47,2.38)^	1.30(1.00,1.69)#
<b>Moderate Anemia</b>	2.36(1.75,3.18)^	1.86(1.35,2.56)^
<b>Severe anemia</b>	2.71(1.80,4.08)^	1.99(1.12,2.67)*
<b>ART Adherence</b>		
<b>Good</b>	1	1
<b>Poor</b>	5.09(4.12,6.29)^	3.92((3.13,4.90)^
<b>ART regimen</b>		
<b>Zidovudine based</b>	1	1
<b>Stavudine based</b>	1.43(1.15,1.76)^	0.92(0.73,1.16)#

Note: #=P>0.05, \*=p<0.05, ^= p<0.01

In bivariate Cox regression analysis, age, sex, religion, dependent children at home, past diarrhea, past herpes zoster, past fever, past or base line cotrimoxazole prophylaxis and ALT were not associated with survival (Table 6.7). However, educational status, marital status, unemployed, oral candidiasis, past CNS toxoplasmosis, past TB co-infection, weight loss, functional status, WHO staging, CD4 count, TB co-infection at base line, Anemia, lymphopenia (TLC < 600), ART regimens and poor ART adherence were all associated with survival (as it shown in Table 6.7).

In multivariate Cox regression analysis, only those variables associated with survival and not collinear entered in to the final model. Age and sex of the cohort were also included in the model irrespective of their association to survival as they are the most common confounding variable. Each variables were checked to fit the model using Cox regression analysis. After adjustment, the independent significant predictors of not surviving in patients living with HIV/AIDS after initiation of ART remain poor ART adherence (AHR=3.92[95%CI=3.13, 4.90]), Advanced WHO staging (AHR=2.47[95%CI= (1.58, 3.81)], being unemployed (AHR=1.87[95%CI= 1.49, 2.34]), moderate anemia (AHR=1.86[95%CI=1.35, 2.56]), and Low CD4 count (AHR=1.85[95%CI= 1.35, 2.52]).

## VI. Discussion

In this historical cohort study, we found that the independent significant predictors of lesser survival in patients living with HIV/AIDS after initiation of ART were unemployed, advanced WHO staging, (IV), low CD4 count, anemia (moderate/severe) and poor adherence.

Survival difference based on baseline CD4 have been revealed in previous studies(1,8,9,12,13,15) .The median survival after CD4 count fallen to <200 cells/mm<sup>3</sup> and after an AIDS defining complications are 3.7 years and 1.3years respectively(1).Johanssent etal found high mortality with the majority of death occurring with in three months of starting ART. They estimated mortality rate 19.2% and 24.5% at 3 and 6 months. We also found almost the same pattern of high mortality rate with 18.7% and 24.9% of it occurring at 3 and 6 months. In the first 3 months after initiation of ART, patients had less cumulative survival. In the later month, patients were much more likely to survive their initial illness (Fig 6.3 and 6.4). According to Chottanapund S etal, the survival rate at 1,2 and 3 years after TB diagnosis were 96.1%,94%,and 87.7% for ART+ group and 44.4%,19.2% and 9.3% for ART- group(log ran test,P<0.001).Egger etal in the other hand estimated the cumulative 75% survival from cryptococcal related mortality in no ART group as 6.4 month where as 54 months for ART group. They concluded that ART significantly reduced relapse and mortality rate (P<0.01) (16). Degu J etal estimated mortality rate in ART+ group was 15.4/100PYO and most of the death occurred during the first three month. However according to a study carried out by Alfred C etal in Malawi, the probability of being alive on ART at 6, 12 and 18months was 89.8%, 83.4% and 78.8% respectively. 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 adherence and access while in our study, almost half of the cohort at WHO stage III, with poor adherence and high default rate. Robert etal showed cumulative mortality rate at 12 months was 2.9% .Frank J. etal also estimated mortality rates ART<sup>+</sup> were 15.4 and 56.4 deaths per 1000 person-years. According to Lisa M. etal among persons with OI, 67% were alive at least 36 months and 77% were alive at least 24month. Egger etal revealed cumulative 75% survival from cryptococcal related mortality at 54 month. Chottanapund S etal\_the survival rates at 12, 24, and 36 months were 92.8%, 87.4%, and 85.4%.This better survival in developed countries may be due to more affordable and enough

drugs availability. When one combination fails, another is available to replace it. This will be less easy in resource limited settings

Fat loss is more commonly reported in men than women and in older people (1).The hazard of death was significantly greater for person with greater than 40 years of age(1:15:22). Majority of recent studies showed females have significantly higher survival than males (1, 8, 11,22).In Our study, male have some what more mortality risk than females but it is not statistically significant (HR=1.14, 0.79-1.26, log ran test  $P>0.05$ ).Some studies justified this sex difference in survival by more men are lost to follow up and poorly adhered than females(8,11).But in our study loss to follow up were excluded and there was no association b/n gender and ART adherence(log ran test $>0.05$ ). Lack of statistically significant difference b/n sex and survival in our studies unlike better female's survival by recent studies might be due lesser access and availability of ART to females. In the other hand, a study on Zambian adults showed high mortality in women (HR=1.29) (21) while Robert etal showed no difference in mortality by age or sex (22). There is no also difference in survival by age in our study too.

Patients who were educated at most primary level had high risk compared to those secondary or above (log ran test,  $P<0.001$ ).But these is not consistent in multivariate analysis indicating educational level is not a strong predictors of survival in our study. Our study showed no difference in survival by religion, presence of dependent children, past diarrhea, past herpes zoster, and past fever. Likewise a study carried out in California showed risk of death is similar among ethnic groups but higher in person initially diagnosed with opportunistic illness (22). In our study, Divorced patients had high risk of death than married patients. More over divorced patients were poorly adhered compared to married patients (log ran test,  $P<0.05$ ). 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. In our study, Patients with oral candidiasis, CNS toxoplasmosis, past/base line tuberculosis, and  $>10\%$  weight loss/ were associated with high mortality. In line with our study, a history of oral candidiasis and CNS toxolasmosis conferred a high mortality rate (8, 9).Patients with a history of TB were not a significant risk of death (8) contrasting to our study which might be due to poor monitoring of HIV patients with TB co infection or poor ART adherence ( $p<0.05$ ) as a result of pills burden. High mortality in patients living with HIV/AIDS in poor countries was linked to concomitant TB infection (10).

Manosuthi et al also showed patients who delayed ART for greater than 6 months after TB diagnosis had a higher mortality rate than those who initiated ART less than 6 months after TB diagnosis. A history of herpes Zoster was not associated with mortality (8). This is also true in our study. Primary prophylaxis against pneumocystis carini Pneumonia was not associated with improved survival (22). The same finding was observed in our study. This lack of survival benefits associated with use of prophylaxis for PCP might indicate that physicians were dispensing cotrimoxazole mainly for high risk patients or because of other factors that this study was unable to control.

Anna et al showed AZT is unsuitable for population that have a high prevalence of anemia and low CD4 count but in our study patients treated with AZT based survived better than those treated with stavudine based ART regimen. This might be due to the difference in the incidence of severe anemia which was 6.6% in the above studies and 5% in our studies or due to other factors that need to be explored. Stavudine is no longer recommended in western countries because of its longer term toxicity profile that includes lipodystrophy(1, 10) But still it is part of the first line ART regimen recommended by WHO and being used by most national HIV program in resource limited countries like Ethiopia. Abandoning stavudine in the first line ART regimen is still need to be determined.

According to Johanssen et al, the significant independent predictors of mortality were CD4 count  $<50/\mu\text{l}$  at base line, moderate and severe anemia, thrombocytopenia and severe malnutrition (8). Ojikutu et al in other hand revealed that the independent factors predicting higher mortality rate were lymphopenia and low BMI both in ART+ and ART- group while anemia was not associated with increased mortality in either group(9). Anna et al also revealed a high mortality in poor countries was linked to lower base line CD4 count, concomitant TB infection, and lack of free care(10). In our study, the independent significant predictors of survival were unemployed, advanced WHO staging, low CD4 count base line ( $<50\mu\text{l}$ ), moderate anemia and poor ART adherence.

Moderate anemia remained one of the independent predictors of survival unlike severe anemia in our study. This might indicate undermining and poor monitoring of patients and care givers were giving more emphasis to severe case. Majority of the previous studies (8:10: 15: 20) identified low CD4 count was one of the independent predictors of mortality which is also consistent to our

finding. Even if different previous studies demonstrated BMI as one of the strong predictors of mortality (8, 9, 20), we 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. Total lymphocyte count was also excluded and we took CD4 count at base line as indirect serogate biomarker of high viral load. Advanced WHO staging was other strong predictors of survival in our study. This finding is also consistent with other previous studies (9:14: 20).

Non adherent patients who initiated HAART had statistically elevated mortality rate (AHR, 1.36-4.84) compared to adhered patients. More over medication adherence is the critical determinants of survival , not the CD4 cell count at which HAART begun(17).The same finding observed in our study in that the risk of death in non- adhered patients is 4 times higher compared to adhered patients.

## **VII. Strength and Limitation**

### **7.1. Strength**

- Underestimation of Mortality avoided by excluding drop out and lost to follow up
- Different documents were triangulated to ensure quality of data
- It can also complement the current endeavor by different sectors to combat HIV /AIDS
- It helps increase the quality of care given in the ART clinic.
- It may serve as a clue to study the effect of stavudine in resource limited setting like in Ethiopia
- It may serve as a bench mark for further evaluating WHO recommendation on initiation of HRTART in resource limited setting.
- It gives an insight for researchers especially in carrying out prospective cohort
- It may help as guiding tool during Comprehensive HIV/Care training and clinical mentoring of health professionals
- It gives a clue how effective ART was in resource limited settings like in Ethiopia

### **7.2. Limitation**

- Selection bias toward more severe illness since the study carried out at hospital
- The main limitation of this study was recall bias due to retrospective assessment of the patients.
- Using secondary data which might have incomplete data beside the endeavor.
- Use of CD4 as indirect serogate indicator instead of Viral load which might affect survival
- Generalizability is questionable as viral load and BMI were not considered

## **VIII. Conclusion and Recommendation**

Since the introduction of free ART, more patients have been presented to HIV care and support. A number of patients seeking ART is increasing through time in Zewditu hospital and are being enrolled to the hospital's care and treatment program based on the national ART treatment guideline. As more patients present to the care, it is critical and challenging for the health care providers to effectively monitor and manage the patients especially those who are at risk of death to improve their survival. This study has identified the independent significant predictors (risk factors) of survival in patients living with HIV/AIDS after initiation of HAART. These factors include being unemployed, low CD4 count at base line ( $<50\mu/l$ ), advanced WHO staging, moderate anemia, and poor adherence.

Based on this study finding, the following recommendations can be forwarded.

### **To HIV care and support providers (hospitals and health centers with ART clinic)**

1. Early recognition and managements of risk factors or clinical markers of survival in PLWHA.
2. Early initiation of ART prior to they develop clinical markers of survival will help to maximize clinical out come
3. A careful monitoring of patients with low CD4+ advanced WHO staging moderate anemia and unemployed is necessary particularly during the first 3 months of HAART.
4. Tracing poorly adhered patients and giving them drug counseling is crucial to improve survival.

5. Inculcating HGB in the WHO eligible criteria
6. Develop a way to control the completeness and reliability of base line and follow up data being collected.
7. Integrating the ART care with social support, IGA
8. IEC/BCC (Drug adherence, health care seeking....)
9. Intensive Drug counseling
10. Developing a multisectoral approach to improve patients survival

#### **To Addis Ababa Health office**

1. Giving in-service training for the health care giver on HIV/AIDS care and support especially on how to recognize and manage patients with high risk.
2. Monitor, evaluate and feed back the quality of service and care given to the patients either through assigning clinical mentoring or supportive supervision.
4. Further exploring specificity and sensitivity of WHO guideline in Ethiopia setting and modifying it based on the lessons learnt.
5. Increasing accessibility and utilization of ART to females.
6. Integrating the HIV care with other developmental organizations like NGOs, Religious leaders, community supporters etc in order to solve factors that directly or indirectly affect survival.
9. Empowering unemployed PLWHA either by income generating activities through micro-financing or sponsorship training.
11. Undergo further observational studies especially prospective study to complement this study

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**ANNEX I: QUESTIONNAIRE**

**INTRODUCTION:**

This patient information collection sheet is intended to assess predictors of survival of HIV/AIDS patients after the advent of Highly Active Antiretroviral Therapy in the ART unit of Zewditu Hospital, Addis Ababa, Ethiopia. The study will be conducted through reviewing secondary data and visiting the home/calling if the status of the patient is not recorded or found in the ART follow up form. The study is aimed to fill the information gap and provide empirical evidence for program planner, decision makers and ART program implementer at the different level by enabling them to access a base line data on predictors of survival. More over it will be a paramount important to curb the horizon of the disease. And it assists in the development of a system for improving the survival of PLWHA.

Date of review -----day-----month-----year

Name and signature of reviewer-----

Time Started \_\_\_\_\_ Time ended \_\_\_\_\_

Name and signature of the supervisor.....

Date.....

Total n<sub>o</sub> of records reviewed-----

**Reviewed Patient's card N<sub>o</sub> from \_\_\_\_\_ to \_\_\_\_\_**

Result:

a) Completed ----- b) Incomplete -----c) excluded-----

Action taken for the incomplete data \_\_\_\_\_ (please use additional blank paper if the space is not enough)

**Part I. Study subject's baseline information (to be filled from ART clinic intake form)**

**SECTION 1.SOCIO-DEMOGRAPHIC CHARACTERISTICS**

NO	QUESTIONNAIRE/ VARIABLE S	Coding categories	
102	Age of the patients	_____	
103	Sex:	1. Male          2. Female	
104	Ethnicity	1. Amhara      2. Oromo 3. Tigirie      4. Gurage 99. Other(specify) _____	
105	Religion	1. Muslim      2. Orthodox 3. Protestant   4. Catholic 99. Other (specify)-----	
106	Educational status	1. No education    2.primary 3. Secondary      4. Tertiary	
107	Occupational statuses	1. Farmer 2. Merchant 3. Governmental employee 4. Non-governmental employee 5. Day laborer 6. Jobless 7. driver 99. Others (specify)_____	
108	Marital status	1. Never married 2. Married 3. separated 4. Divorced 5. widowed	
109	Dependent children at home	1.yes  2.no	
110	region	1.tigray      2.afar   3.amhara	

		4.oromi 6.benshangul 12.gambella 14. AA	5.Somali 7.SNNPR 13.harar 15. diredawa	
<b>SECTION 2- Base line Clinical ,laboratory and ART information</b>				
NO	QUESTINAIRE/ VARIABLE S	CODING CATAGORIES		
<b>201</b>	Past opportunistic illness(list all mentioned)	0. no    1.candidiasis    2.CMV 3.Crypt.meningitis 4.Kaposisarcoma 5. Cryptosporiodiosis 6. Diarrehea 7. Diss.atypical myco. 8.Encephalopathy 9.fever                    10.herpes simplex 11. Minor mucocuan.man. 12.mycosis 13. PGL                    14. PCP    15.PML 16.pneumonia    17.salmonella 18.EPTB            19.toxoplasmosis 20. Wasting syndrome. 21.other specify_____		
<b>202</b>	Past Tb test	1.no 2..not determined                    3.positive 4.pos+1                                    5.Pos+2 6.Pos+3                                    7.unknown		
<b>203</b>	Past Tb treatment	1.no                    2.not determined 2.2SRHZ/6EH 3.2HRZES/1HRZE/5HRE 4.2HRZE/6HE		
<b>204</b>	Past ART treatment	1. no		

		2. 1a (30) =d4t (30)-3TC-NVP 2)1a (40) =d4t (40)-3TC-NVP 3) 1b (30) =d4t (30)-3TC-EFV 4) 1b (40) =d4t (40)-3TC-EFV 5) 1c= AZT-3TC-NVP 6) 1d=AZT-3TC-EFV 7)2 <sup>nd</sup> line regimens(2a/2b/2c/2d)	
<b>205</b>	past CD4 test	1. yes date[___/___/___] 2. no	
<b>206</b>	Past medications (check all)	1. no 2. cotrimoxazole 3. INH 4. Fluconazole 5. Othe médicaments-----	
<b>207</b>	height(cm) (look Vital signs part) at base line	_____	
<b>208</b>	weight(kg) at base line	_____	
<b>209</b>	functional status at base line	W. working A. Ambulatory B. bedridden	
<b>210</b>	WHO Clinical stage of HIV disease at base line	1.Stage I                      2.Stage II 3.Stage III                    4.Stage IV	
211	Hgb at base line	_____	
212	CD4 count at base line	_____date[___/___/___]	
213	WBC at base line	_____	
214	TLC at base line	_____	
215	ALT at base line	_____	
216	AST at base line	_____	

<b>SECTION 3- Base line Social condition</b>			
301	employment	1.working      2.working full time 3.working part time 4.not working /studying due to ill health 5. unemployed 6.other specify _____	
303	Religious /supportive care	1. no      b. yes	
304	HIV sero status disclosure	1.wife/husband 2.own child(ren) 3.parent(s) 4.brother(s)/sister(s) 5.relatives 6.no body knew 7.others specify _____	
305	Spouse information		
	1.condition of the husband/wife	a.health                      b.chronically ill c.dead                        d.unknown	
	2.HIV tested	a.not asked                      b.negative c. positive                      d. unknown	
	3.Tb tested	a. not asked                      b. negative c. positive                      d. unknown	
	4.was/is on Tb treatment	a. yes                              b. no	
	5. was/is on ART treatment	a. yes                              b. no	
306	General concern identified	1.financial issue	

		2.about the children 3.marital relation ship 4.family relations 5.beravement/grief 6.Hiv status disclosure 7.adherence to treatment 8.dietary problems 9.other specify_____	
<b>SECTION 4. Knowledge on HIV and ART</b>			
401	Attended HIV related health education in the past	1.yes 2.no	
402	Attended HIV related counseling session in the past	1.yes 2.no	
403	Understood of HIV disease	1.NA 3.+ 5.+++ 2.- 4.++	
404	Understood of HIV transmission	1.NA 3.+ 5.+++ 2.- 4.++	
405	Understood of prophylaxis and OI	1.NA 3.+ 5.+++ 2.- 4.++	
405	Understood of ART medication adherence	1. NA 3.+ 5.+++ 2.- 4.++	

<b>SECTION 5. Risk behavior</b>			
501	Had regular partner	1.yes	2.no
502	Had causal sexual partner	1.yes	2.no
503	If yes, no of causal partner in last 3 months	a.1 c.3	b.2 d.>3
504	Condom use	1.NA 3.rarly 5.mostly 7.no response	2.never 4.sometimes 6.always
505	Addictions		
	a. tobacco	1. NA      2.- 3. +      4. ++      5. +++	
	b. alcohol	1. NA      2.- 3. +      4. ++      5. +++	
	c.softdrugs(e.g.Khat,shisha, pills,etc)	1. NA      2.- 3. +      4. ++      5. +++	
	d.harddrugs(e.g.cocaine,morphine, iv drugs,etc)	. NA      2.- 3. +      4. ++      5. +++	
506	Barriers to ART adherence	1.stigma (from family and friends) 2.afraid of medications(side effects:”poison”) 3.doubt that medications will work 4.depressed/anxious 5.will forget to take medications	

		6.other specify_____	
507	Impression about mental condition	1. at ease      2. confused 3. depressed    4.anxious 5.suicidal	
<b>SECTION 6. ART and treatment</b>			
601	ARV eligibility criteria used	1.CD4 below 200 2.WHO stage IV 3.WHO stage I,II,and III with TLC $\leq$ 1200 4.residence of catchment area 5.no identified barriers for adherence	
602	OI prophylaxis at base line	0 .not given 1.cotrimoxazole 2.INH 3.fluconazole 4. others-----	
605	Regimen Recommended at base line	1)1a (30) =d4t (30)-3TC-NVP 2)1a (40) =d4t (40)-3TC-NVP 3) 1b (30) =d4t (30)-3TC-EFV 4) 1b (40) =d4t (40)-3TC-EFV 5) 1c= AZT-3TC-NVP 6) 1d=AZT-3TC-EFV 7)2 <sup>nd</sup> line regimens(2a/2b/2c/2d)	
<b>Part II. Patient's follow up information (to be filled from ART follow up</b>			

<b>form).Please document the current or the recent results</b>			
700	variables	Coding categories	
701	Date confirmed HIV +	[__ __ __]	
702	Eligible date	[__ __ __]	
704	Latest follow up date	[__ __ __]	
705	Duration in months since initiation of ART	_____ (wks/month)	
706	recent weight	_____ (in kg),date[__ __ __]	
707	recent functional status	W. working A. Ambulatory B. bedridden	
708	recent WHO staging	1.Stage I 2.Stage II 3.Stage III 4.Stage IV	
709	Tb screened recently	1. no 2. positive 3.. negative	
710	recent Tb prophylaxis	1. no 2. yes	
711	recent Tb treatment	1. no 2. yes	
712	recent Opportunistic infections	0. no 1.Zoster 2.bacterial pneumonia 3.Pulmonary Tb	

		<p>4.Extrapulmonary Tb</p> <p>5.oral /vaginal thrush</p> <p>6.mouth/genital ulcer</p> <p>7.chronic or acute diarrhea</p> <p>8.pneumocystis carini pneumonia</p> <p>9.CNS toxoplasmosis</p> <p>10.Cryptococcal meningitis</p> <p>11. others specify-----</p>	
711	cotrimoxazole	1. not given    2. good    3. fair    4. poor	
712	recent ARV adherence	1. good    2. fair    3. poor	If 1, skip to 714
713	Reason for fair or poor adherence	<p>1.toxicity/side effect            2.share with others</p> <p>3.forgot                                4.felt better</p> <p>5.too ill                                6.stigma disclosure</p> <p>7.drug stock out                    8.lost/run out of pills</p> <p>9.delivery/travel problems 10.inability to pay</p> <p>11.alcohol                              12.depression</p> <p>12.other specify_____</p>	
714	recent Dispense( code/dose)	<p>1)1a (30) =d4t (30)-3TC-NVP</p> <p>2)1a (40) =d4t (40)-3TC-NVP</p> <p>3) 1b (30) =d4t (30)-3TC-EFV</p> <p>4) 1b (40) =d4t (40)-3TC-EFV</p> <p>5) 1c= AZT-3TC-NVP</p> <p>6) 1d=AZT-3TC-EFV</p>	



		9.planned treatment interruption 10.other_____	
718	recent CD4 count	_____ [___/___/___]	
719	recent WBC	_____	
719	recent TLC	_____	
720	recent Hgb	_____	
721	recent ALT	_____	
722	recent AST	_____	
723	out come of the patients	1. active[___/___/___] 2.dead[___/___/___]	

**ANNEX II. Informed consent form and questionnaire (be used in home visiting or calling)**

**Introduction**

My name is \_\_\_\_\_. I am working with Abdo bedru who is doing a research as partial fulfillment for the requirement of Masters in Public Health at Addis Ababa University. This study is intended to assess predictors of survival of HIV/AIDS patients after the advent of Highly Active Antiretroviral Therapy in the ART unit of -----hospital in Addis Ababa, Ethiopia. The study is aimed to fill the information gap and provide empirical evidence for program planner, decision makers and ART program implementer at the different level by enabling them to access a base line data on predictors of survival. More over it will be a paramount important to curb the horizon of the disease. And it assists in the development of a system for improving the survival of PLWHA. The information will be collected through reviewing secondary data in the ART clinic and calling or visiting to the patient's home if the outcome of the patient is not recorded. We would like to assure you that the privacy and the confidentiality will strictly be secured throughout the study. All the information will be numbered and coded and the name will not be used throughout the research process. If a report of results is published, only information about the total group will appear. We are asking you for a little of your time, about five minutes, to help in this study. All your information will be numbered and your name will not be used. Your answers to any of the questions will not be given to anyone else and no reports of the study will ever identify you. The interview is voluntary. Your participation/ non-participation, or refusal to answer questions will have no effect now or in the future on services that you or any member of your family may receive from health service providers.

**Are you willing to participate in this study?**

Yes  No (end the interview)

Q.1.what is the current status of the patients?

- a) Dead
- b) alive

Q.2. If dead, when is the date of death? \_\_\_\_\_/\_\_\_\_/\_\_\_\_]

Name and signature of Interviewer-----

**ANNEX III. Informed consent form (Amharic version)**



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## **Acronyms**

**AIDS**; Acquired Immune Deficiency Syndrome.

**AHR**; Adjusted Hazard Rate

**ART**; Antiretroviral Therapy

**ARV**; Antiretroviral.

**AZT/ZDV**; Zidovudine

**CHR**; Crude Hazard Rate

**CI**; Confidence Interval

**CNS**; Central Nervous System

**d4t**; Stavudine,

**EFV**; Efaviren

**EPTB**; Extra Pulmonary Tuberculosis

**HAART**; Highly Active Antiretroviral Therapy.

**HAPCO**; HIV/AIDS Prevention and Control Office

**HIV**; Human Immunodeficiency Virus.

**HIV-1** ;Human Immunodeficiency Virus Type 1.

**HIV-2** ;Human Immunodeficiency Virus type 2.

**IQR**; Inter Quartile range

**MAC**; Mycobacterium Complex

**MOH**; Ministry Of health

**NNRTI**; Non-Nucleoside Reverse Transcriptase Inhibitor.

**NRTI** ;Nucleoside Reverse Transcriptase Inhibitor.

**NVP;** Nevirapine,

**PCP;** Pneumocystis Carini Pneumonia

**PI;** Protease Inhibitor.

**PLWHA;** Person/people Living with HIV/AIDS.

**PMTCT;** Pregnant Mother To Child Transmission

**PTB;** Pulmonary Tuberculosis

**3TC;** lamivudine

**TLC;** Total Lymphocyte Count

**WHO;** World Health Organization