ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES SCHOOL OF PUBLIC HEALTH

Assessment of time to recurrence of opportunistic infections in people living with HIV/AIDS, in Debre Markos town, East Gojam zone, North West Ethiopia, in 2013. (Retrospective Cohort study)

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Table of Contents

ACKNOWLEDGMENT I

ACRONYMS and ABBREVIATIONS V

ABSTRACT VI

1. Introduction ..... - 1 -

1.1 Back ground ..... - 1 -

1.1.1 Epidemiology of HIV/AIDS ..... - 1 -

1.1.2 Antiretroviral therapy accessibility ..... - 1 -

1.2 statement of the problem ..... - 2 -

1.3 Significance of the study ..... - 3 -

2. Literature review ..... - 4 -

2.1 Factors associated with OI occurrence ..... - 4 -

2.1.1 ART and its adherence ..... - 4 -

2.1.2 CD4 count ..... - 4 -

2.1.3 OI prophylaxis ..... - 5 -

2.1.4 socio-demographic, WHO clinical stage and other factors ..... - 6 -

3. Objective ..... - 7 -

3.1 General objective ..... - 7 -

3.2 Specific objective ..... - 7 -

4. Methods ..... - 8 -

4.1 Study design ..... - 8 -

4.2 Study area and period ..... - 8 -

4.3 Source population ..... - 8 -

4.3.1 Study population ..... - 8 -

4.4 Sample size determination ..... - 9 -

4.5 Sampling procedure ..... - 10 -

4.6 Data collection ..... - 10 -

4.6.1 Data collection instrument ..... - 10 -

4.6.2 Study variables ..... - 11 -

4.6.3 Data collection procedure……..……..……..……...……-11-
4.7 Operational Definition……..……..……...…….……-12-
4.8 Data processing and analysis……...…….…….-14-
4.9 Data quality management……..……....-14-
4.10 Ethical consideration……..……..…..…….-14-
4.11 Dissemination of result……...……..……...-15-
5. Result……...……...…….-16-
5.1 Socio demographic characteristics……...….-16-
5.2 Clinical, laboratory and treatment information's……..-16-
5.3 Magnitude of any OI recurrence……....-17-
5.4 Survival analysis……..……..-19-
6. Discussion……...…….……...-32-
7. Strength and Limitation…….……..……-34-
7.1 Strength of the study……..……-34-
7.2 Limitations of the study…….……..…..-34-
8. Conclusion and recommendation…….……...……-35-
9. References……...-37-
ANNEXES……...……...……-41-
ANNEXE I Information and Consent form…….…-41-
Annex II: Questionnaire…….…….……-45-

List of Figures and Tables

Figure1: Profile of PLHIV enrolled for cohort between 25 March 2007 and 24 March 2013 in Debre Markos town, Amhara region, Ethiopia----------49

Figure 2: kaplan-meier survival estimation of time to free of OI recurrence in PLWHA in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013----------21-

Figure 3: kaplan-meier survival estimation of time to free of OI recurrence in pre-ART and ART PLWHA in Debre Markos town, east Gojam zone, Ethiopia between 25 March 2007 and 24 March 2013----------21-

Figure 4: kaplan-meier survival estimation of time to free of OI recurrence for different base line and follow up characteristics in PLWHA in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013----------25-

Table 1: cumulative incidence and incidence rate of recurred OIs in pre-ART and ART PLWHA in Debre Markos town, Ethiopia between 25 March 2007 and 24 March 2013----------18 -

Table 2: The actuarial life table estimation of cumulative progression to recurrence of OI in PLHIV in Debre Markos town, Ethiopia between 25 March 2007 and 24 March 2013----------20-

Table 3: Bi-variate cox proportional hazard model of the association between base line and follow up characteristics and OI recurrence in study participants' in Debre Markos town, east Gojam zone, Ethiopia between 25 March 2007 and 24 March 2013----------26-

Table 4:multi-variants cox proportional hazard model of the association between base line and follow up characteristics and OI recurrence in study participants' in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013----------30-

ACRONYMS and ABBREVIATIONS

AHR	Adjusted Hazard Rate
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
ARV	Antiretroviral
BMI	body mass index
CI	Confidence Interval
CMV	Cytomegalovirus
CNS	Central Nervous System
D/m/Y	Date, Month, Year
ETB	Ethiopian birr
HAART	Highly Active Anti-Retroviral Treatment
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
HSV	Herpes Simplex Virus
MAC	Mycobacterium avium complex
OI	Opportunistic Infection
PCP	Pneumocystis Carinii Pneumonia
PLHIV	People Living With HIV infection
PLWHA	People Living With HIV/AIDS
SPH	School of Public Health
TB	Tuberculosis
WHO	World Health Organization

ABSTRACT

Introduction*:* According to 2011 Ethiopian demographic health survey the national adult HIV prevalence is 1.5 %. In the same survey, HIV prevalence was 2.2% in the Amhara Region. In the region of North West Ethiopia, 88.9% of pre-ART PLWHA has any type of OI at initiation of ART. Different studies showed the effect of ART improves time to death of PLWHA however, little is known about its effect on improving time of recurrence of OI and factors associated with it and magnitude of the recurrence. Hence this study will be used to plan resources needed for chronic HIV/AIDS care and to identify factors affecting patients' survival.

Objective: To assess time to recurrence of OIs and factors associated with it and to determine magnitude of recurrence in PLWHA in Debre Markos town in 2013.

Method: Institution based comparative retrospective cohort study were used and the required sample size was 536. All 18 years old and above PLWHA who were on chronic HIV care in Debre Makkos town health institutions was the source population for the study. Study participants were selected from the list of PLWHA attending the public health facilities using simple random sampling procedure by data collectors who are working in ART clinic. Univariate analysis was used to describe patients' baseline and follow up characteristics. Actuarial life table and Kaplan-meier survival was used to estimate survival and log rank test was used to compare survival curves. Cox proportional-hazard regression model was used to calculate the uni-variate and adjusted hazard rate and to determine independent predictors of time to recurrence of OI.

Result: Among study participates 66% were females and the median age was 32 years. Most of them were urban 70.1%, orthodox 92.4%, not educated 44%, married 43.3% and employed 20%. During a median of 43 person weeks follow up OIs recurred in three quarter (75.7%) study participants. The Incidence rate of OI recurrence was 13.1(95 CI: 11.9-14.5) per 1000 person weeks. Using the Kaplan-meier survival estimation the median time of survival was 57 weeks. After adjusted for covariates the significant predictors for survival were marital status, occupational status, follow up CD4 count, base line Hgb value, ART exposure status, base line ART adherence status, base line and follow up prophylaxis exposure status and follow up prophylaxis adherence status,

Conclusion and recommendation: Governmental and non-governmental organizations working on HIV/AIDS should give especial attention for risk groups like widowed, not taking treatment/ adhere ART or prophylaxis while continuing HIV care for all PLWHA.

1. Introduction

1.1 Back ground

1.1.1 Epidemiology of HIV/AIDS

In 2011 according to the latest estimates from UNAIDS: globally approximately 34 million people were living with HIV (1, 2). New HIV infections have declined by more than 21% since their peak in 1997 (2). Still, there were about 2.2 million new infections in 2011, 500 000 fewer than the 2001 (3).

Globally, women constituted half (50%) the adults (15 years and older) living with HIV in 2010 but more than half (59%) in sub-Saharan Africa (1, 2).

Since the beginning of the epidemic nearly 30 million people have died of AIDS-related causes (1, 2, 4), in 2011 the annual number of people dying from AIDS-related causes worldwide was estimated 1.7 million (3).

At end of 2010 about 22.9 million which is 67% of those living with HIV/AIDS globally are in Africa though only about 12% of the world's population lives in the region(2). In terms of mortality, the region represents about 79% of AIDS mortality globally (5), the estimated mortality from AIDS related illnesses at end of 2010 are 1.2 million (2).

According to 2011 Ethiopian demographic health survey the overall national adult (age 15-49) HIV prevalence is 1.5 % which is similar with 2005 Ethiopian demographic health survey that was 1.4 %. Peak HIV prevalence occurred in Women (1.9 %) than men (1.0 %), in both sexes with the highest wealth quintile (3.9 %), in age group of 30-34 women (3.7 %) and 35-39 of men (3%), in urban areas (4.2 %) than in rural areas (0.6 %), in employed (2.2 %) than unemployed (1.4 %), in those who attended secondary school (3.1 %) than those with less education or with more than a secondary school education, among regions highest in Gambela (6.5 %) and in Addis Ababa (5.2 %) (6).

In Amhara region, according to 2011 Ethiopian demographic health survey HIV the prevalence was 2.2%. In age group of 15-24 years the prevalence was 0.4% and 0.2% for women and men respectively (6).

1.1.2 Antiretroviral therapy accessibility

According to UNAIDS report introduction of Combination antiretroviral therapy in 1996 has led to dramatic reductions in morbidity and mortality from HIV/AIDS ; and access to ART has increased in recent years, rising from less than half a million (400 000) people on treatment in

2003 (1) to 8 million people in 2011 (54% coverage of people eligible to treatment based on the 2010 WHO guidelines on initiating treatment at a CD4 count <350 cells per mm3 (7), a 25-fold increase since 2003) (3) though people eligible for ART increase in the same way from 9.6 million in 2009 to about 10.4million in 2010 (1, 2). Similarly the number of health facilities providing ART show a threefold increase from 7700 in 2007 to 22 400 at the end of 2010 (2).

In all regions, ART access growth rates were lower than 25% from 2009 to 2010, the smallest percentage increase in the number of people receiving ART was seen in Latin America (11% increase) and the greatest increase was seen in Sub-Saharan Africa (30% increase from 3 911 000 in December 2009 to about 5 064 000 in 2010) with coverage of 49% in 2010 (2).

In Ethiopia the fee based and universal free access Antiretroviral (ARV) treatment was started in 2002/3 and 2004/5 respectively. The country uses decentralizing the ARV treatment service provision to the level of Health centers and private Health facilities for fast expansion of the service, in 2009/10 enabling 402 Health centers and 20 private Health facilities to provide ARV treatment free of charge (8). Out of all ART clients 58% (102,379) were female. In terms of drug combination, the majority of patients are on the 1st line regimen (d4T-3TC-NVP), while only 1% (1,079) of the patients has switched to a 2nd line regimen (9).

In Amhara region in 2009/10 the number of people on ART was 64,648 which is 60.2% coverage from 107,414 people who require ART (8).

1.2 statement of the problem

Human Immunodeficiency Virus (HIV) infection leads to acquired immunodeficiency syndrome (AIDS) and major causes of morbidity and mortality of such patients are OIs caused by viral, bacterial, fungal and parasitic pathogens (10). OIs can occur in up to 40% of PLHIV with a CD4 count less than 250/mm3 (11).

In North India, TB was the commonest OI (71%) followed by candidiasis (39.3%), *PCP* (7.4%), cryptococcal meningitis and cerebral toxoplasmosis (3.7% each) (12). In southern India the most common OIs at enrollment of pre-ART have pulmonary tuberculosis (14%) and PCP (6%) but after initiating HAART that was 6% for pulmonary tuberculosis, 3% for toxoplasmosis, *PCP* and extra pulmonary tuberculosis (13).

A national study in Ethiopia showed HIV patients' had OIs like Herpes Zoster scar (19.3%), pulmonary tuberculosis (5.2%) and pneumonia (5.2%) and Some patients (2%) had more than one neurologic complications of HIV/AIDS (14). In Northwest Ethiopia, a study at Felegehiot

hospital in pre-ART HIV patients' showed 88.9% of them have common OIs (chronic diarrhea (38.6%), TB(34.5%), herpes zoster (30.7%), Oro-pharyngeal candidiasis (14%), pneumonia (3.5%) and other sexually transmitted infections (12.5%)) (15). Another study in similar area also showed 82.4% pre-ART HIV patients' was present with different type of OIs at start of therapy (16). Similar study in North West Ethiopia at Gondar University Hospital also showed 7.5% of the HIV patients' had pulmonary tuberculosis (17) and study in similar area of Gondar College of Medical Sciences Hospital also showed 8.3% of HIV patients' had Cryptococcal meningitis(18). A study in Southen Ethiopia at Hawassa Referral Hospital also showed 22.7% of HIV patients' had Chronic diaherae (19).

The other problem among the HIV sero-positive individuals were dual, triple OIs and other co-infections, a study in India showed that the most frequent dual infections were chronic diarrhea and Oral- candidiasis (28.92%), Oral- candidiasis and TB (25.49%), chronic diarrhea and TB (21.08%), HSV-2 and Oral- candidiasis (19.11%), HSV-2 and Cytomegly Virus (14.21%), Hepatitis-B Virus and HSV-2 (3.92%); among the commonest triple infections: Oral-candidiasis, TB, chronic diarrhea (14.21%), HSV-2, CMV, Oral- candidiasis (10.78%), HSV-2, CMV, chronic diarrhea (8.34%) and HSV-2, CMV, TB (6.86%) (20)

1.3 Significance of the study

Different studies showed the effect of ART improves time to death of PLHIV (21-23) but as far as our knowledge concerned its effect on improving time of recurrence of OI and factors associated with it and magnitude of recurrence is not studied in our country. Hence this study will be used to plan resources needed for chronic HIV/AIDS care and to identify factors affecting patients' survival time. The evidence is expected to be used by governmental and non - governmental organizations working HIV/AIDS or mainstreaming it in order to inform policy makers and medical practitioners**.**

2. Literature review

2.1 Factors associated with OI occurrence

Different studies showed that many factors like ART and its Adherence, OI Prophylaxis, CD4 count, WHO clinical staging, Socio-demographic factors, Functional status and Weight/BMI are associated with OI occurrence (11, 16, 21-22, 26-36)

2.1.1 ART and its adherence

ART initiation reduces OI occurrence, increase mean CD4 count which is one of the predictor for OI occurrence (16, 24-25). A one year follow-up study after ART initiation in North West Ethiopia shows OIs dropped from 82.4% patients present with different type of OIs at start of therapy to only 6.7% with an overall reduction of OIs occurrence by 91.9% (90.4% in males and 94.2% in females). Patients also showed immunological change from 132.883 mean CD4/mm3 count to 335.87 mean CD4/mm3 with mean increase of 203.0 cells/mm3 (16).

The HIV cohort study in Switzerland showed ART reduces incidence of any OI from 15.1 per 100 person months in 6 months before ART therapy to 7.7, 2.6 and 2.2 in the first 3, 6 and 9-15 months respectively after starting treatment (26). Another cohort study also showed that the introduction of ART decreased the incidence of PCP by 94%, CMV by 82%, and MAC by 64%, as presenting AIDS events. The same study also showed decrease in the incidence of events consequent diagnosis of AIDS by 84% for PCP, 82% for CMV, and 97% for MAC (22). Similarly other cohort study in Italy showed Initiation of ART within 2 months after toxoplasmic encephalitis diagnosis had a 3-fold reduction in the risk of developing a new OI compared with those who delayed therapy (relative hazard, 0.36; 95% CI, 0.15–0.86) (23). Another cohort study also showed that HAART reduces the incidence of severe OIs by 21% during the first 6 months and 28% during subsequent follow-up after adjusting for CD4 count (27).

Treatment adherence is one of the challenges in the failure of HAART which is chance for OI progression(11, 28). Poor ART adherence has resulted in lower CD4 increase (the mean increase in good adherence was estimated 184.81 while in poor adherence it was only 78.12 (28).

2.1.2 CD4 count

The HIV cohort study in Switzerland showed the baseline CD4 count is one of the predictor for OI progression; compared with CD4 counts above 200 x 10^6/L, the hazard ratio for developing OIs was 2.5 for counts between 51 and 200 x 10^6/L and 5.8 for counts below 50 x 10^6/L at

baseline. A rise in CD4 count by 50 x 10^6/L or more by 6 months reduced subsequent OIs with hazard ratio of 0.32 (26).

Another cohort study also showed the baseline CD4 cell count was strongly associated with OI development after ART initiation. Compared with patients starting HAART with less than 50 CD4 cells/_L, adjusted hazard ratios were 0·74 for 50–99 cells/_L, 0·52 for 100–199 cells/_L, 0·24 for 200–349 cells/_L and 0·18 for 350 or more CD4 cells/_L (29). Another cohort study also showed higher CD4 cell count was associated with a reduction of risk of new OI progression, with a hazard ratio compared with 100 cells/ml of 0.35 for counts 200 cells/ml, 0.81 for counts 200 to 350 cells/ml, 0.74 for counts 350 to 500 cells/ml, and 0.96 for counts 500 cells/ml or above (30). A similar cohort study in France shows severe OIs are higher at lower CD4 count (relative risk 5.37 for counts $\leq$ 50 and 2.42 for counts 51-200) at multivariate analysis (27). Similar cohort study also showed the risk of toxoplasmic encephalitis occurrence was increased by 30% for each 50-cell decrease in CD4+ cell count, independent of antiretroviral (23).

2.1.3 OI prophylaxis

A critical appraisal in 2011 showed primary prophylaxis with Trimethoprim-sulfamethoxazole is preventing life-threatening OIs like PCP, toxoplasmosis, and bacterial infections (31). Another Meta-analysis in 2010 about Cotrimoxazole also showed reduction of the risk of PCP and Tuberculosis (in people who are tuberculin skin test positive).Primary prophylaxis with anti-tuberculosis regimens seems more effective at reducing the incidence of active tuberculosis at 1 to 3 years in adults who are HIV and tuberculin skin test positive (32).

An experimental study in Ugandan Adults about Cotrimoxazole prophylaxis showed its effect on prevention of OIs like diarrhea for PLHIV who are continue taking it for CD4 count above 200 cells/lL after ART initiation. Compared to those remaining on cotrimoxazole, patients who discontinued had a relative risk of diarrhea of 1.8 (P= 0.001) and at least 1 episode of diarrhea (P= 0.001) occurred in 14% continued verses 25% discontinued. Participants who discontinued cotrimoxazole were more likely to be diagnosed with a respiratory tract infection (40% vs 29%; P: 0 .002) (33). Another experimental study also showed Cotrimoxazole is preventing PCP (RR 0.59 (*P* 0 .03)) (34). OIs were lower for patients on HAART plus cotrimoxazole treatment compared cotrimoxazole alone (relative risk 0.72 for >6 month and 0.79 for 0-6 month) at multivariate analysis (27).

2.1.4 socio-demographic, WHO clinical stage and other factors

A cohort study showed that age was significant predictor for OI occurrence, per 10 year increase the hazard ratio was 0.8 (26). Other cohort study also showed female sex increases the risk of toxoplasmic encephalitis in multivariate logistic regression analysis (23). In contrary, a study in Thailand showed male gender and low body weight were significantly associated with higher incidence of OIs after ART (21). A cohort study in United states showed older age, female gender, being unemployed were associated with significantly higher odds of OIs like herpes simplex virus-2 infection at multivariate analysis (35).

A cohort study in India showed functional status of the patients have positive and negative correlation with WHO disease stage ($r = 0.365$, $P = < 0.0001$) and with CD4 count ($r = -0.198$, $P = 0.012$) respectively and hemoglobin levels are negatively correlated with WHO staging ($P = <0.001$) in which those are proxy predictor of OI occurrence (36).

3. Objective

3.1 General objective

To assess time to recurrence of OIs and factors associated with it and to determine magnitude of recurrence in PLWHA in Debre Markos town, Ethiopia in 2013.

3.2 Specific objective

1. To determine magnitude of recurrence of any OIs in pre-ART and ART PLWHA in Debre Markos town in 2013
2. To assess time to recurrence of any OIs after treatment of any preceding OIs in PLWHA in Debre Markos town in 2013.
3. To assess factors associated with time to recurrence of any OIs after treatment of it in PLWHA in Debre Markos town in 2013.

4. Methods

4.1 Study design

Institution based comparative retrospective cohort study from March 25, 2007 up to March 24, 2013 was conducted by using quantitative research method.

4.2 Study area and period

The study was conducted in Debre Markos town governmental health institutions among 8,974 adult PLHIV included to chronic HIV care/ ART follow up between 25 March 2007 and 24 March 2013.

Debere Markos town is a capital city of East Gojam zone having a total population size of 86,767. It is found in the North West part of the country bounded by *Gozamen woreda* in the North, South, and East, and Aneded Woreda in the West. It covers an area of 6 million square meters and located on the main road of Addis Ababa-Bahir Dar and 300 km away from Addis Ababa the capital city of Ethiopia and 265 km from Bahir Dar capital city of Amhara regional state.

Debre Markos town has one referral hospital that serves more than 3.5 million people in the zone and nearby zones and adjacent region as well. There are three public health centers in which one is providing ART service for the HIV/AIDS patients on the other hand, two NGO clinics and other private clinics do not provide ART service.

4.3 Source population

All 18 years old and above people living with HIV/AIDS having chronic HIV care /ART follow up in Debre Markos town health institutions providing ART service were the source populations for the study.

4.3.1 Study population

All adult peoples living with HIV/AIDS who had chronic HIV care/ART follow up in Debre Makkos town health institutions providing ART service; fulfill the inclusion criteria and willing to participate in the study were included in the study.

Inclusion criteria

- Age above or equal to 18 years old

- ❖ PLWHA who develop OI and taking standard treatment according to the Ethiopian Ministry of Health guideline

Exclusion criteria

- ➢ A patient who take treatment for OI but not returned at least once to health institution for follow up.
- ➢ PLHIV who did not develop any OI while registered on HIV care/ART follow up form in ART clinic.
- ➢ The follow up format is incompletely documented when treatment for OI is given or on consecutive follow up.
- ➢ Pregnant and lactating mothers who are not on ART but taking zidovidine for PMTCT of HIV/AIDS

4.4 Sample size determination

The sample size was calculated based on the assumption of 95% confidence interval and 80% power with ratio of one to one for ART and pre-ART PLWHA using the commonest OI (TB) which is 6% and 14 % for ART and pre-ART PLWHA respectively from previous study (21). EPI INFO version 3.5.3 was used to calculate the required sample size using the following formula (37)

$$n = \frac{\left[Z_{\alpha}\sqrt{(1+1/m)\bar{p}(1-\bar{p})} + Z_{\beta}\sqrt{p_0(1-p_0)/m + p_1(1-p_1)}\right]^2}{(p_0 - p_1)^2}$$

$$\bar{p} = \frac{p_1 + m\,p_0}{m+1}$$

Where

n: minimum sample size required for each group

m: ratio of pre-ART and ART PLHIV

P0: probability of event in pre-ART

P1: probability of event in ART

α=level of significance

$Z_{\alpha}/2$=1.96 at 95% confidence interval

Power=1-β=80%, Z_{β}=1.282

The calculated sample size was 488 (244 for ART and pre-ART). After adding 10%contingency the sample was 536.8 ~ 536.

4.5 Sampling procedure

Study participants who fulfilled the inclusion criteria in the study area were identified by data collectors from list of PLHIV who were on HIV care/ART follow up from governmental ART clinics. The historical data has 3 features, pre-ART PLHIV who stay on chronic HIV care and then start ART and continue chronic HIV care, PLHIV directly begin ART and continue chronic HIV care and currently pre-ART PLHIV who were on chronic HIV care. Then from these historical data to prepare sampling frame for pre-ART and ART PLWHA we used the following method. PLWHA who fulfill the inclusion criteria both on pre-ART and ART history was given separate code and then selected by lottery method for odd and even codes. But PLWHA who full fill the inclusion criteria either on pre-ART or ART history was given separate code. Then the sampling frame was prepared by adding the two separate codes i.e. the code selected by lottery and the code given for full filling the inclusion criteria either the pre-ART or ART history. Then selection was made by applying simple random sampling procedure using random number table (figure1in annex). Since the needed data is available on study participants' treatment card and HIV care/ART follow up form, the selected study participants' willingness to allow extraction of the data was asked by data collectors. Additionally in order to reduce falsely survival increment study participants were asked by data collectors about treatment history for OIs out of the follow up health institution and willingness for extraction of the data in the respective health institution was asked. Willingness to participate in the study was asked when PLWHA come to health institution for follow up or treatment or by using registered address on follow up form like phone number or kebele, house number which was used to get to their home and the ART adherence supporter groups were also used to trace study participants.

4.6 Data collection

4.6.1 Data collection instrument

Data abstraction format was developed from federal ministry of health HIV care/ART follow up form which is used in the ART clinic and also the patient's card. The format includes the following check list

- Socio demographic characteristics (sex, age, residence, marital status, Occupational status, educational status)

- ART and chemoprophylaxis information (ARV drug treatment, drug adherence, line of treatment regimen, prophylaxis treatment and its adherence)
- Laboratory information (CD4 count, hemoglobin value)
- Clinical information (WHO clinical staging, weight, height, OIs (name and count treated at one time), other chronic diseases like diabetes mellitus, hypertension, cardiac disease)
- Functional status (working, ambulatory, bedridden)

4.6.2 Study variables

Dependent variable

- Time to recurrence of any type of OIs

Independent variable

- Socio demographic (age, sex, religion, residence, occupation, educational status, marital status)
- clinical, laboratory, ART and chemoprophylaxis information
- Functional status (working, ambulatory, bedridden)

4.6.3 Data collection procedure

The data was collected by reviewing HIV care/ART follow up form, laboratory request and patients' card. If PLWHA develop OI before completing treatment of preceding OI while the patient is on study, the time of treatment which is nearest to end of the study was used as the starting time for study. If laboratory results (CD4 count, Hgb) are not found during OI treatment the most recent to the study laboratory results before treatment of OI were used as base line predictors. Length of follow up for each study participant was varied because of different enrollment time.

Re-occurrence of OI was confirmed by reviewing HIV care/ART follow-up form or patient card or by asking study participant during data collection period about treatment history for OIs out of the follow up health institution. The health status was assured by asking the study participants when s\he come to ART clinic for follow up or asking using registered address on follow up form like phone number or kebele, house number which was used to get to their home and the ART adherence supporter groups were also used to trace study participants.

Individuals who change from unexposed to exposed, drop-out/loss follow-up/transferred out/dead by any disease other than OI/cause of death not confirmed during study period or not develop OI at end of the study period were censored. The final outcome of each subject was dichotomized into censored or recurrence of any type of OI.

Three data collectors and one supervisor who have direct experience and work on ART clinic was recruited for data collection and supervision respectively and they were selected in collaboration with the manager of hospital and head of the health centre. Data collectors and supervisors were trained by the principal investigator. The training was conducted in the gathering room of the hospital during weekends by getting permission from the hospital authorities.

The training focused on objective of the study, selection of exposed and unexposed, confidentiality of information and the contents of the questionnaire in detail. Further training was offered to supervisors on data quality management.

4.7 Operational Definition

Pre-ART PLHIV: the person who was HIV positive confirmed but not eligible for ART.
ART PLHIV: the person who was HIV positive confirmed and started ART.
Survival: lack of any type of OI recurrence

Censored: no recurrence of any type of OI in study participant during follow up on study; but future recurrence is not sure

Re-occurrence: happening\diagnosis of any type of OIs by health personals working in ART clinic after completing the preceding treatment of any type of OI.

Drop out: if a PLHIV on HIV care lost to follow-up for more than three months as recorded by ART health personnel.

Lost to follow-up: if PLHIV on HIV care not seen for equal to or more than one month as recorded by ART health personnel.

Transferred-out: if PLHIV on HIV care in one health institution shift to other health institution.

Good Adherence: if PLHIV adherent $\geq$ 95 % that is the percentage of missed dose is < 2 doses of 30 doses or <3 dose of 60 dose) as documented by ART health personnel.

Fair Adherence: if PLHIV adherent 85-94 % that is the percentage of missed dose is 3-5 doses of 30 doses or 3-9 dose of 60 dose) as documented by ART health personnel.

Poor Adherence: if PLHIV adherent <85% that is the percentage of missed dose is ≥ 6 doses of 30 doses or >9 dose of 60 dose) as documented by ART health personnel.

4.8 Data processing and analysis

Each abstraction format was given a code and was entered in to EPI INFO version 3.5.3 statistical package and it was exported to SPSS 16.0 and STATA 11 statistical package for analysis of statistical inferences. Data cleaning and editing were made before analysis.

The patient cohort characteristics like age, CD4 count, hemoglobin value, time to re-occurrence of any OIs and BMI were described in terms of mean/median value and characteristics like sex, residence, marital status, Occupational status, educational status, WHO clinical staging, ART adherence, line of ART regimen, prophylaxis treatment and its adherence, Functional status, final outcome of study (censored or re-occurrence of any type of OIs) were described in terms percentages, tables, graphs.

Cumulative incidence and incidence rate of OI were calculated at end of the study. Incidence rate was calculated by dividing total events to person-weeks. The actuarial life table and Kaplan Meier survival was used to estimate survival time and log rank test was used for categorical variables to compare survival curves across each strata. Some Continuous variables were changed in to categorical variables using the previous research category. Before running the Cox regression model assumption of proportional-hazard and multi-colinearity was checked. Assumption of proportional-hazard was checked by Schoenfeld residual with p-value ≥0.1(α=10%) and the assumption was not violated. Multi-colinearity was checked using Pearson correlation, tolerance/variance inflation factor and we found that base line ART regimen was highly correlated with follow up ART regimen ($r=0.809$, $p<0.0001$) so that further analysis in the final model were not done for base line ART regimen. Similarly follow up Hgb value were excluded in final model because of its correlation with base line Hgb value ($r=0.598$, $p<0.0001$) and it was done in only 10.8% of study participants. Exclusion of redundant variables was done to stabilize final model and to improve precision of estimation. Cox proportional-hazard model was used to calculate the uni-variate and Multivariate adjusted hazard rate and to determine independent predictors of survival. In Multi-variate cox proportional hazard model, only those

variables which were associated with time to recurrence of any OI with p-value $\leq$ 0.2 in uni-variate analysis and not collinear were entered to the final model.

4.9 Data quality management

To maintain data quality training was given for data collectors and for supervisors. Properly designed data collection material was developed from Ethiopian federal ministry of health HIV care/ ART follow-up form and patients' card. Incompletely recorded follow up formats were excluded from abstraction.10% of the sample was randomly selected and the data was re-abstracted by the supervisor to check the reliability and consistency of data and accordingly correction was made. Supervision was carried out on daily base to check completeness, consistency both by the supervisor and by principal investigator to keep the quality of data. Correctly complete abstraction format was collected from data collectors by supervisor and was submitted to principal investigator.

The data was entered by one trained data clerk and 10% of the data was re-entered by the principal investigator to clean data before analysis. In addition at the end of data entry data cleaning was done using frequencies, cross tabulations, sorting and listing to check missed values and outliers. Errors identified were corrected by revising the original abstracting format.

4.10 Ethical consideration

The proposal was submitted to the School of Public Health Addis Ababa University ethical committee for ethical approval and clearance. Permission was also obtained from the concerned bodies of East Gojam zone and Debre Markos town Health Department and the responsible bodies of hospital and health centers. Although the study was conducted by reviewing medical records of individual patients, the patient was not subjected to any harm as far as the confidentiality and anonymity is maintained. To protect confidentiality, health professionals working in ART clinic of Debre Markos health centers and referral hospital prepared the sampling frame and extracted the data from medical records. In addition no personal identifier was extracted on medical records and the recorded data was not accessed by a third person. The abstraction was only used for planning purpose of the research. Informed consent was obtained from study participants to get permission to extract data from their medical records. To get study participants who were not coming to the ART clinic for follow up during data collection period, in addition of using already registered address like phone number, kebele, house number on follow up form, ART adherence supporter groups were also used to trace them. For study

participants who were severely ill with coma or having hearing impairment or died before data collection period while included in the study period the nearest relatives (family) or legal representatives were asked to give permission to extract on medical records.

4.11 Dissemination of result

The final report of the study was presented and discussed in School of Public Health, College of Health Sciences, and Addis Ababa University. Finally the results of the study will be disseminated to School of Public Health, Ethiopian Public Health Association, Federal Ministry of Health, Regional health bureau, East Gojam zone and Debre Markos town health department, Debre Maros hospital and health centre and for other interested governmental and non-governmental organizations. Moreover, effort will be made to publish the output in a peer reviewed journal.

5. Result

In this historical cohort study, between 25 March 2007 and 24 March 2013 8,974 PLWHA 18 years age and above were evaluated. Five hundred thirty six PLWHA who were on pre-ART and ART with 1:1 ratio each consisting 268 were followed for a total of 30971 person weeks and median of 43 person weeks. The minimum and maximum person week follow-up was 2 and 258 respectively. The study assessed magnitude and time to recurrence of OIs in pre-ART and ART PLWHA and also baseline and follow up predictors of time to recurrence in PLWHA.

5.1 Socio demographic characteristics

In study 66% (354) females and 34% (182) males were participated. Their median age was 32 year (IQR=26-40) in which 92% (493) were below age group of 50 years. Most of the study participants were urban by residence 70.1% (376), orthodox 92.4% (495), not educated 44% (236), married 43.3% (232) and employed 20% (107) (table 3).

5.2 Clinical, laboratory and treatment information's

At base line, three quarter of the study participants (74.6%=400) had one episode of OI and most (39.9% =214) of them had WHO Clinical stage III OI. All most all study participants (97.1%=394) had no any chronic diseases like hypertension, diabetes mellitus and others (table 3).

With regarding to functional status most of study participants were working both at base line 78% (418) and at follow up 87.1% (471) (table 3).

Study participants base line and end line mean (SD) values for body mass index were 19(±3.1) and 19.8(±3.1) respectively. The base line median values for CD4 count and hemoglobin were 280 (IQR=150-410) and 11(IQR=9.8-13) respectively and their end line median values were 384(IQR=237-478) and 12.5(IQR=11-13.5) respectively.

Most of the study participants were taking prophylaxis both at base line (82.6%=443) and at follow up (84.5%=453) and all most all of them had good drug adherence status both at base line (93.7%=415) and at follow up (93.2%=422). Among prophylaxis drugs almost all of the participants were taking Cotrimoxazole both at base line (95.5%=423) and at follow up (96.7%=439) (table 3).

Half of the study participants (50%=268) were taking ART both at base line and at follow up. All participants were on first line ART regimens in which about one third were taking

TDF+3TC+EFV regimen both at base line (37.7%=101) and at follow up (39.6%=106). All most all study participants had good antiretroviral drug adherence both at base line (94% =252) and follow up (94.4% =253) (table 3).

5.3 Magnitude of OI recurrence

During follow up OIs recurred in three quarter study participants 75.7% (95 CI: 72-79.2) (406) and the rest were censored 24.3% (130). Cumulative incidence of recurrence was 74.6% (69.2-79.6) (200) in Pre-ART and 76.9% (71.5-81.6) (2006) ART PLWHA. In Chi-square test the Cumulative incidence of recurrence was not statistically significant different in the overall or each type of OI in Pre-ART and ART PLWHA (table 1).

The Incidence rate of any type of OI recurrence was 13.1(95 CI: 11.9-14.5) per 1000 person weeks, which differs by ART exposure status that was 15.7(95 CI: 13.6-18) and 11.4(95 CI: 9.9-13) per 1000 person weeks in pre-ART and ART PLWHA respectively.

In the study area mostly recurred OIs were recurrent Upper respiratory tract infection 13.6% (73), chronic diarrhea 9.7% (52), pneumonia 8.5% (46), oral candidiasis 8% (43), herpes zoster 7.1% (38) though their Cumulative incidence and the common recurred OI was different in pre-ART and ART PLWHA (table 1).

Table 1: Cumulative incidence and incidence rate of recurred OIs in pre-ART and ART PLWHA in Debre Markos town, Ethiopia between 25 March 2007 and 24 March 2013.

Recurred OI	Pre-ART (268)		ART(268)		p-value	PLWHA (536)	
	Frequency (CI*(95% CI))	IR (95% CL)	Frequency (CI*(95% CI))	IR (95% CI)		Frequency (CI*(95% CI))	IR (95% CI)
Recurrent Upper respiratory tract infection	35(13.1(9.4-17.5))	2.7(1.9-3.8)	38(14.2(10.4-18.8))	2.1(1.5-2.9)	0.905	73(13.6(10.9-16.7))	2.4(1.9-3)
chronic diarrhea	30(11.2(7.8-15.4))	2.3(1.6-3.4)	22(8.2(5.3-12))	1.2(0.8-1.8)	0.249	52(9.7(7.4-12.4))	1.7(1.3-2.2)
Pneumonia	21(7.8(5.0-11.5))	1.6(1.0-2.5)	25(9.3(6.3-13.3))	1.4(0.9-2)	0.73	46(8.5(6.4-11.2))	1.5(1.1-2)
oral candidacies	22(8.2(5.3-12))	1.7(1.1-2.6)	21(7.8(5-11.5))	1.2(0.72-1.8)	0.905	43(8(6-10.6))	1.4(1-1.9)
herpes zoster	18(6.7(4.2-10.2))	1.4(0.8-2.2)	20(7.5(4.7-11.1))	1.1(0.7-1.7)	0.806	38(7.1(5.1-9.5))	1.3(0.9-1.7)
EPTB	15(5.6(3.3-8.9))	1.2(0.7-1.9)	16(6(3.6-9.3))	0.9(0.5-1.4)	0.916	31(5.8(4-8))	1(0.7-1.4)
minor muco-cutanous manifestation	13(4.9(2.7-8))	0.1(0.51.7-)	15(5.6(3.3-8.9))	0.8(0.5-1.4)	0.919	28(5.2(3.6-7.4))	0.9(0.6-1.3)
PTB	10(3.7(1.9-6.6))	0.8(0.4-1.4)	13(4.9(2.7-8))	0.7(0.4-1.2)	0.722	23(4.3(2.8-6.3))	0.7(0.5-1.1)
PCP	12(4.5(2.4-7.5))	0.9(0.5-1.6)	9(3.4(1.7-6.1))	0.5(0.2-0.9)	0.605	21(3.9(2.5-5.8))	0.7(0.4-1)
Genital/oral ulcer	8(3(1.4-5.6))	0.6(0.3-1.2)	6(2.2(0.9-4.6))	0.3(0.1-0.7)	0.750	14(2.6(1.5-4.2))	0.5(0.3-1.2)
Toxoplasmosis	6(2.2(0.9-4.6))	0.5(0.2-1)	5(1.9(0.7-4.1))	0.3(0.09-0.6)	0.954	11(2.1(1.1-3.5))	0.4(0.2-0.6)
Encephalopathy	4(1.5(0.5-3.6))	0.3(0.08-0.8)	7(2.6(1.1-5.1))	0.4(0.2-0.8)	0.569	11(2.1(1.1-3.5))	0.4(0.2-0.6)
Wasting syndrome	8(3(1.4-5.6))	0.6(0.3-1.2)	3(1.1(0.3-3))	0.2(0.03-0.5)	0.203	11(2.1(1.1-3.5))	0.4(0.2-0.6)
Cryptococal meningitis	3(1.1(0.3-3))	0.2(0.05-0.7)	8(3(1.4-5.6))	0.4(0.2-0.9)	0.241	11(2.1(1.1-3.5))	0.4(0.2-0.6)
Persistent generalized lymphadenopaty	6(2.2(0.9-4.6))	0.5(0.2-1.4)	3(1.1(0.3-3))	0.2(0.03-0.5)	0.332*	9(1.7(0.8-3.1))	0.3(0.01-0.6)
Others	7(2.6(1.1-5.1))	0.5(0.2-1.1)	9(3.4(1.7-6.1))	0.5(0.2-0.9)	0.799	16(3(1.8-4.7))	0.5(0.3-0.8)
Total [#]	200(74.6(69.2-79.6))	15.7(13.6-18)	206(76.9(71.5-81.6))	11.4(9.9-13)	0.614	406(75.7(72-79.2))	13.1(11.9-14.5)

IR: incidence rate per 1000 person weeks

CI*- cumulative incidence
CI-confidence interval
[#] row total is not sum of column values due to occurrence more than one OI in some study participants
* P-value is Fisher's Exact test because of 50% of the expected cell values are less than 5.

5.4 Survival analysis

A total of 536 PLWHA were followed for a median of 43 (IQR=20.25-75.75) person weeks. The minimum, maximum and total person weeks follow up was 2, 258 and 30971 respectively. According to the Kaplan-meier survival estimation the median time of survival was 57 weeks (95% CI: 51.66-62.34). The actuarial life table analysis showed that most (11.8%=63) OIs recurred from 10-20 weeks. The cumulative proportion of free from any OI recurrence up to week 20 was 81%. The cumulative proportion of free from OI recurrence up to week 250 was 1% (table 2).

The median time of survival was different in pre-ART and ART PLWHA, that was 52 (95% CI: 45.24-58.76) and 64 (95% CI: 54.87-73.13) weeks respectively (figure 3).

Table 2: The actuarial life table estimation of cumulative progression to recurrence of OI in PLWHA in Debre Markos town, Ethiopia between 25 March 2007 and 24 March 2013.

Interval Start Time	Number Entering Interval	Number Withdrawing during Interval	Number of any OIs recurred	Cumulative Proportion Surviving at End of Interval	Hazard Rate
0	536	16	38	.93	.01
10	482	12	63	.81	.01
20	407	20	41	.72	.01
30	346	17	35	.65	.01
40	294	12	38	.56	.01
50	244	16	32	.49	.01
60	196	8	33	.40	.02
70	155	4	29	.33	.02
80	122	6	21	.27	.02
90	95	2	6	.25	.01
100	87	1	14	.21	.02
110	72	2	7	.19	.01
120	63	2	6	.17	.01
130	55	0	5	.16	.01
140	50	2	4	.14	.01
150	44	1	6	.12	.01
160	37	0	7	.10	.02
170	30	3	6	.08	.02
180	21	0	4	.06	.02
190	17	0	0	.06	.00
200	17	2	4	.05	.03
210	11	2	1	.04	.01
220	8	1	3	.03	.05
230	4	0	1	.02	.03
240	3	0	1	.01	.04
250	2	1	1	.00	.10

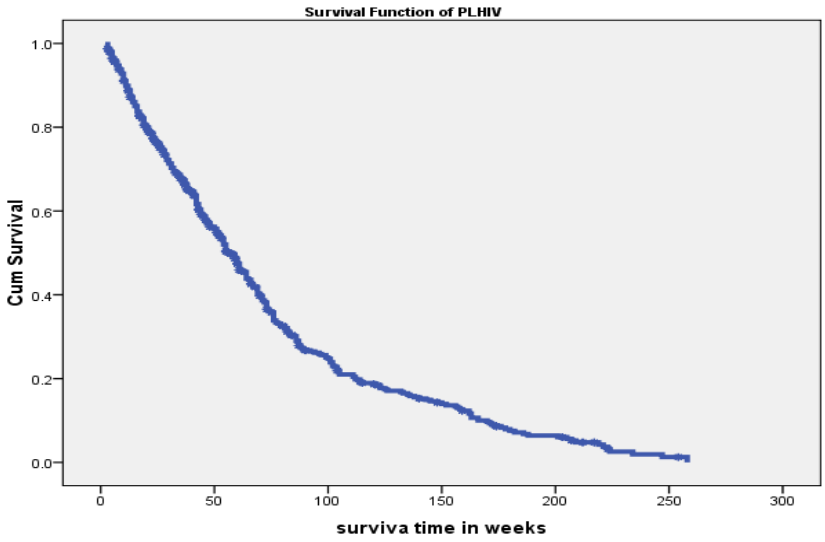

Figure 2 kaplan-meier survival estimation of time to free of OI recurrence in PLWAH in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013.

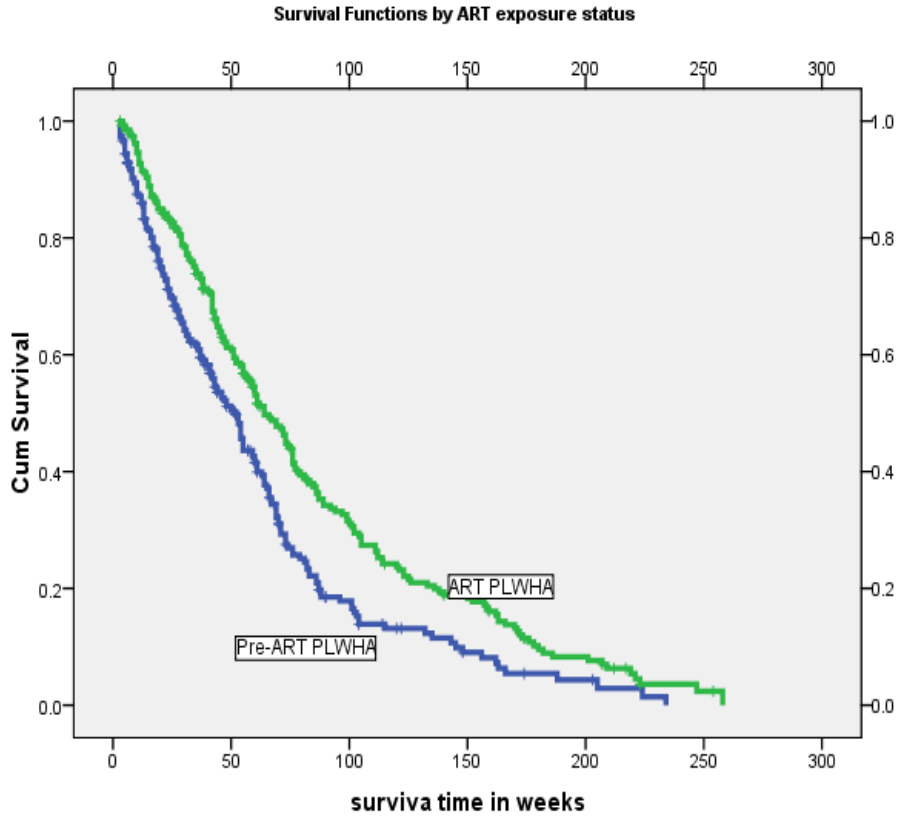

Figure 3 kaplan-meier survival estimation of time to free of OI recurrence in pre-ART and ART PLWAH in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013.

At base line and follow up significant difference in time to recurrence of OI in log rank test among categorical variables strata were seen in marital status (p=0.001), educational status (p<0.0001), occupational status (p<0.0001), base line CD4 count (p=0.0084), base line Hgb value (p<0.0001), follow up Hgb value (p=0.01), follow up Body mass index (p=0.008), base line functional status (P=0.044), follow up functional status (p=0.006), ART exposure status (p<0.0001), base line prophylaxis exposure status (p<0.0001), follow up prophylaxis exposure status (p=0.003), base line ART adherence status (p<0.0001), follow up ART adherence status (p<0.0001), base line prophylaxis adherence status (p=0.001) and follow up prophylaxis adherence status (p<0.0001) (table 3). The figure below shows survival time for some variables.

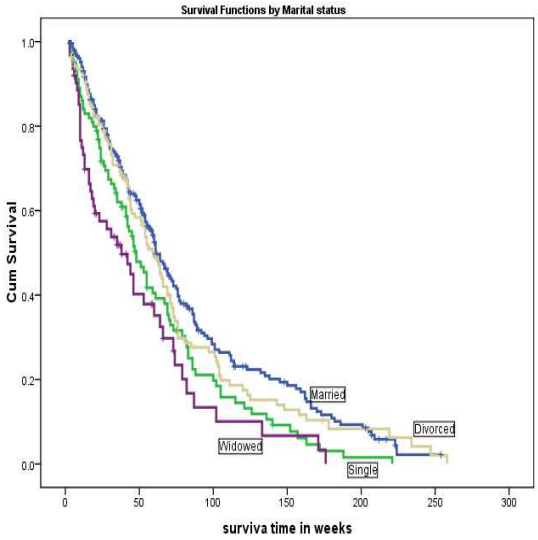

Figure 4.1 kaplan-meier survival estimation of time to free of OI recurrence in PLWAH by marital status in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013

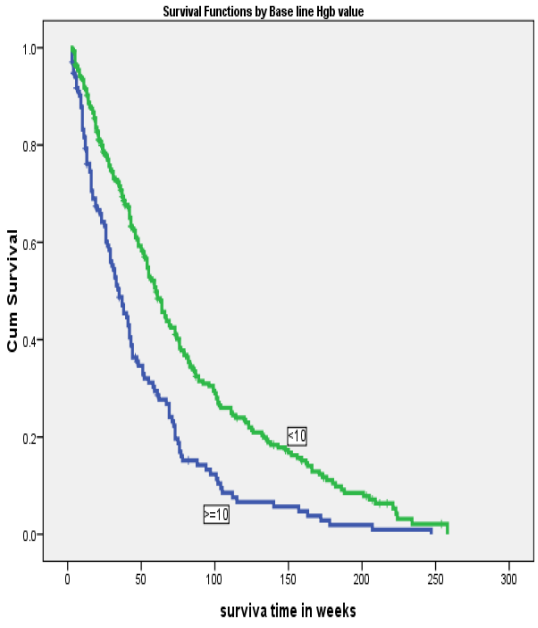

Figure 4.2 kaplan-meier survival estimation of time to free of OI recurrence in PLWAH by base line Hgb value in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013.

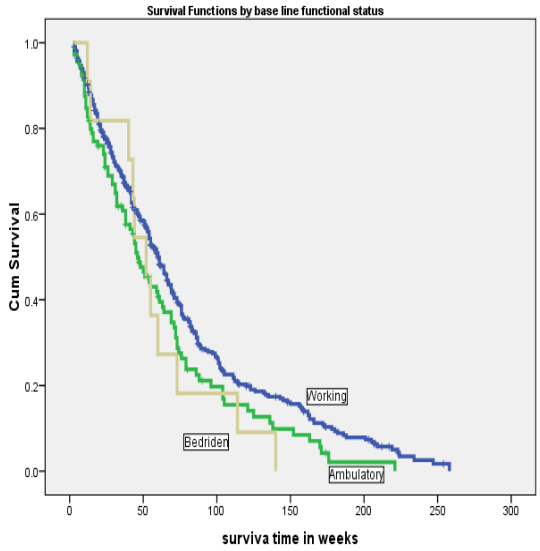

Figure 4.3 kaplan-meier survival estimation of time to free of OI recurrence in PLWAH by base line functional status in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013.

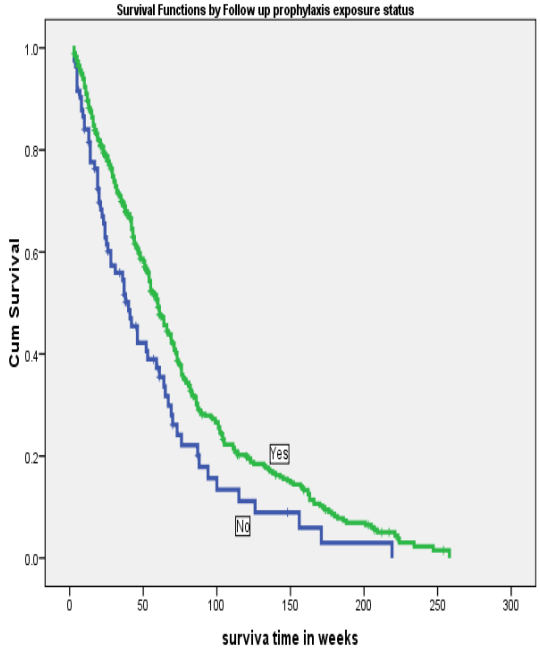

Figure 4.4 kaplan-meier survival estimation of time to free of OI recurrence of PLWHA by follow up prophylaxis exposure status in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013.

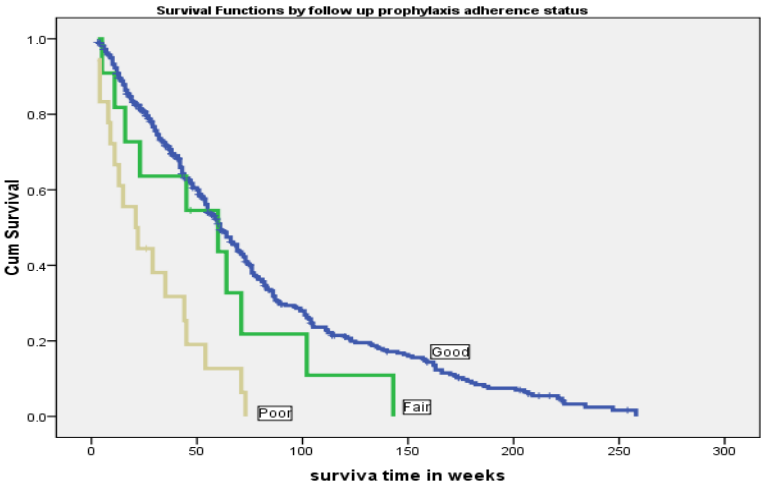

Figure 4.5 kaplan-meier survival estimation of time to free of OI recurrence in PLWAH by follow up prophylaxis adherence status in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013.

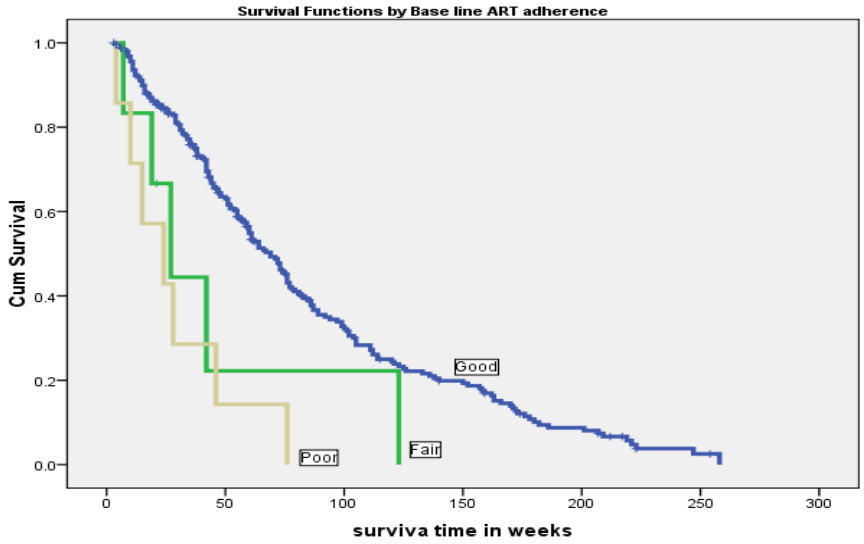

Figure 4.6 kaplan-meier survival estimation of time to free of OI recurrence in PLWAH by base line ART adherence status in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013.

Figure 4 kaplan-meier survival estimation of time to free of OI recurrence for different base line and follow up characteristics in PLWHA in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013.

In uni-variate cox-regression analysis the base line and follow up characteristics significantly ($p<0.05$) associated with survival time were marital status, educational status, occupational status, base line and follow up CD4 count, base line and follow up Hgb value, follow up Body mass index, base line and follow up functional status, ART exposure status, base line and follow up prophylaxis exposure status, base line and follow up ART adherence status, Base line ART regimen, base line and follow up prophylaxis adherence status (Table 3).

In Multi-variate cox proportional hazard model, only those variables which were associated with survival with p-value ≤ 0.2 and not collinear were entered to the final model. After adjustment for covariates, significant predictors reducing survival (risks for recurrence) were being widowed than married by 2.177 times, fair follow up prophylaxis adherence than good adherence by 7.272 times, fair base line ART adherence than good adherence by 14.832 times. And the significant predictors that improve survival (prevent recurrence) were divorced than married by 0.566 times, compared to farmer being merchant, employed and student by 0.301, 0.218 and 0.15 times respectively, having base line hemoglobin value of $\geq$ 10 g/dl than <10 by 0.421 times, compared $\leq$100 cells/μl CD4 count having 351-499 and $\geq$500 follow up CD4 count by 0.385 and 0.321 times respectively, taking prophylaxis at baseline and at follow up by 0.546 and 0.488 times respectively, taking ART by 0.522 times (table 4). When follow up CD4 count increase by 50 cells/μl survival was increased by 0.905 times ($P<0.0001$), and when base line Hgb value increase by 5 g/dl survival was increased by 0.660 times ($p=0.004$) after adjusted for other variables.

Table 3 Bi-variate cox proportional hazard model of the association between base line and follow up characteristics and OI recurrence in study participants' in Debre Markos town, east Gojam zone, Ethiopia between 25 March 2007 and 24 March 2013.

Characteristics	Any type OI recurred		Total (%)	p-value≠	CHR(95 CI)	p-value for CHR
	Yes (%)	No (%)				
Age group(years)				0.824		
<50	375(92.4)	118(90.8)	493(92)		1	
≥50	31(7.6)	12(9.2)	43(8)		1.042 (0.722-1.504)	0.8253
Sex				0.571		
Male	275(67.7)	79(60.8)	354(66)		1	
Female	131(32.3)	51(39.2)	182(34)		1.062(0.862-1.308)	0.573
Residence				0.233		
Urban	290(71.4)	86(66.2)	376(70.1)		1	
Rural	116(28.6)	44(33.8)	160(29.9)		1.14(0.918-1.416)	0.237
Marital status				0.001		
Married	172(42.4)	60(46.2)	232(43.3)		1	
Single	85(20.9)	17(13)	102(19)		1.418(1.092-1.84)	0.0088*
Divorced	103(25.4)	37(28.5)	140(26.1)		1.106(0.865-1.414)	0.4236
Widowed	46(11.3)	16(12.3)	62(11.6)		1.832(1.32-2.543)	0.0003*
Religion				0.634		
Orthodox	337(92.9)	118(90.8)	495(92.4)		1	
Protestant	9(2.2)	3(2.3)	12(2.2)		0.794(0.409-1.541)	0.496
Muslim	20(4.9)	9(6.9)	29(5.4)		0.855(0.545-1.342)	0.496
Educational status				<0.0001		
Not educated	184(45.3)	52(40)	236(44.4)		1	
Primary	122(30.1)	28(21.5)	150(27.6)		0.917(0.727-1.155)	0.461
Secondary	71(17.5)	24(18.5)	95(17.7)		0.744(0.563-0.984)	0.038*
Tertiary	29(7.1)	26(20)	55(10.3)		0.454(0.305-0.675)	<0.0001*
Occupational status				<0.0001		
Farmer	73(18)	25(19.2)	98(18.3)		1	
Merchant	69(17)	19(14.6)	88(16.4)		0.427(0.305-0.600)	<0.0001*
Employed	69(17)	38(29.2)	107(20)		0.345(0.245-0.484)	<0.0001*
Daily laborer	68(16.7)	17(13.1)	85(15.9)		0.864(0.62-1.205)	0.390
House wife	42(10.3)	11(8.5)	53(9.9)		0.661(0.45-0.97)	0.034*
Unemployed	70(17.3)	18(13.9)	88(16.4)		0.918(0.661-1.276)	0.612
Student	15(3.7)	2(1.5)	17(3.2)		0.576(0.328-1.012)	0.055
Chronic disease				0.883		
No	394(97.1)	126(96.9)	520(97)		1	
Yes	12(2.9)	4(3.1)	16(3)		1.365(0.749-2.489)	0.310
Base line treated OI number 1	312(76.8)	88(67.7)	400(74.6)	0.304	1	
≥2	94(23.2)	42(32.3)	136(25.4)		1.128(0.896-1.423)	0.308

Base line WHO stage				0.627		
I	63(15.5)	12(9.2)	75(14)		1	
II	149(36.7)	65(50)	214(39.9)		0.902(0.671-1.212)	0.473
III	159(39.2)	46(35.4)	205(38.3)		0.831(0.619-1.114)	0.216
IV	35(8.6)	7(5.4)	42(7.8)		0.994(0.623-1.426)	0.781
Body mass index (kg/m^2) [B.]				0.47		
<=18.4	188(46.3)	54(41.5)	242(45.2)		1	
18.5-22.9	170(41.9)	60(46.2)	230(42.9)		0.888(0.721-1.10)	0.2702
>=23	48(11.8)	16(12.3)	64(11.9)		0.873(0.634-1.202)	0.4047
CD4 count (cells/µl) [B.]						
<=100	25(6.2)	10(7.7)	35(6.5)	0.04	1	
101-199	34(8.4)	14(10.8)	48(9)		0.454(0.270-0.765)	0.003*
200-350	80(19.7)	21(16.1)	101(18.8)		0.682(0.434-1.071)	0.096
351-499	124(30.5)	35(26.9)	159(29.7)		0.732(0.475-1.128)	0.158
>=500	143(35.2)	50(38.5)	193(36)		0.568(0.37-0.872)	0.010*
Hemoglobin (g/dl) [B.]				<0.0001		
<10	120(36.4)	14(21.9)	134(34)		1	
>=10	210(63.6)	50(78.1)	260(66)		0.559(0.445-0.701)	<0.0001*
Functional status [B.]				0.044		
Working	307(75.6)	111(85.4)	418(78)		1	
Ambulatory	88(21.7)	19(14.6)	107(20)		1.319(1.094-1.674)	0.0226*
Bed ridden	11(2.7)	-	11(2)		1.426(0.718-2.605)	0.2488
Prophylaxis exposure [B.]				<0.0001		
No	72(17.7)	21(16.2)	93(17.4)		1	
yes	334(82.3)	109(83.8)	443(82.6)		0.544(0.421-0.704)	<0.0001*
Prophylaxis Adherence [B.]				0.001		
Good	308(92.2)	107(98.2)	415(93.7)		1	
Fair	11(3.3)	-	11(2.5)		1.555(0.852-2.441)	0.1506
poor	15(4.5)	2(1.8)	17(3.8)		2.417(1.428-4.089)	0.001*
Prophylaxis type [B.]				0.236		
otrimoxazole	318(95.2)	105(96.4)	423(95.5)		1	
INH	9(2.7)	2(1.8)	11(2.5)		0.693(0.355-1.351)	0.2814
Fluconazole	1(0.3)	1(0.9)	2(0.5)		0.287(0.040-2.046)	0.2128
Combination of any prophylaxis	6(1.8)	1(0.9)	7(1.5)		0.616(0.273-1.390)	0.2433
ART [B.]				<0.0001		
No	200(49.3)	68(52.3)	268(50)		1	
yes	206(50.7)	62(47.7)	268(50)		0.681(0.559-0.831)	<0.0001*

ART regimens ¥ [B.]				0.088		
D4T+3TC+NVP	55(26.7)	7(11.3)	62(23.1)		1	
D4T+3TC+EFV	19(9.3)	2(3.2)	21(7.8)		1.00(0.592-1.689)	0.9999
AZT+3TC+NVP	60(29.1)	6(9.7)	66(24.6)		1.202(0.829-1.743)	0.3311
AZT+3TC+EFV	11(5.3)	1(1.6)	12(4.6)		1.890(0.982-3.637)	0.0566
TDF+3TC+EFV	61(29.6)	41(66.1)	101(37.7)		1.579(1.076-2.317)	0.0197*
TDF+3TC+NVP	-	5(8.1)	6(2.2)		0.01(0.001-100.1)	0.9881
ART adherence [B.]				<0.00		
Good	194(94.2)	61(98.4)	255(95.2)	01	1	
Fair	5(2.4)	1(1.6)	6(2.2)		2.152(0.882-5.249)	0.092
poor	7(3.4)	-	7(2.6)		3.894(1.814-8.357)	<0.0001*
Body mass index (kg/m^2) [F.]				0.008		
<=18.4	151(37.2)	38(29.2)	189(35.3)		1	
18.5-22.9	196(48.3)	64(49.3)	260(48.5)		0.874(0.706-1.081)	0.2142
>=23	59(14.5)	28(21.5)	87(16.2)		0.621(0.458-0.842)	0.0022*
CD4 count (cells/µl) [F.]				0.55		
<=100	13(4.8)	5(5.7)	18(5)		1	
101-199	31(11.4)	7(8)	38(10.7)		0.583(0.304-1.117)	0.104
200-350	93(34.3)	33(37.9)	126(35.2)		0.526(0.293-0.942)	0.031*
351-499	75(27.7)	26(29.9)	101(28.2)		0.457(0.251-0.830)	0.010*
>=500	59(21.8)	16(18.5)	75(20.9)		0.428(0.233-0.787)	0.006*
Hemoglobin (g/dl) [F.]				0.01		
<10	11(23.4)	-	11(19)		1	
>=10	36(76.6)	11(100)	47(81)		0.412(0.203-0.833)	0.0136*
Functional status [F.]				0.006		
Working	345(85)	126(96.9)	471(87.9)		1	
Ambulatory	51(12.5)	3(2.3)	54(10.1)		1.588(1.183-2.132)	0.0021*
Bed ridden	10(2.5)	1(0.8)	11(2)		1.317(0.702-2.472)	0.3909
Prophylaxis exposure [F.]				0.003		
No	63(15.5)	20(15.4)	83(15.5)		1	
Yes	343(84.5)	110(84.6)	453(84.5)		0.666(0.508-0.873)	0.0032*
Prophylaxis Adherence [F.]				<0.00 01		
Good	316(92.1)	108(98.2)	424(93.6)		1	
Fair	10(2.9)	1(0.9)	11(2.4)		1.488(0.792-2.797)	0.217
poor	17(5)	1(0.9)	18(4)		3.475(2.116-5.707)	<0.0001*
Prophylaxis type [F.]				0.663		
Cotrimoxazole	331(96.5)	108(98.2)	439(96.9)		1	
INH	6(1.7)	1(0.9)	7(1.5)		0.666(0.295-1.506)	0.3289
Fluconazole	2(0.6)	-	2(0.4)		1.644(0.409-6.613)	0.484
Combination	4(1.2)	1(0.9)	5(1.2)		0.861(0.321-2.312)	0.7664

of any prophylaxis ART [F.]				<0.00		
No	200(49.3)	68(52.3)	268(50)	01	1	
Yes	206(50.7)	62(47.7)	268(50)		0.681(0.559-0.831)	<0.0001*
ART regimens ¥ [F.]				0.071		
D4T+3TC+NVP	51(24.8)	6(9.7)	57(21.3)		1	
D4T+3TC+EFV	17(8.3)	1(1.6)	18(6.7)		1.164(0.670-2.023)	0.5898
AZT+3TC+NVP	59(28.6)	6(9.7)	65(24.3)		1.083(0.740-1.584)	0.6828
AZT+3TC+EFV	11(5.3)	1(1.6)	12(4.5)		1.820(0.942-3.516)	0.0745
TDF+3TC+EFV	66(32)	40(64.5)	106(39.5)		1.406(0.962-2.055)	0.0783
TDF+3TC+NVP	2(1)	8(12.9)	10(3.7)		0.301(0.073-1.239)	0.0963
ART adherence [F.]				<0.00		
Good	189(91.7)	61(98.4)	250(93.3)	01	1	
Fair	7(3.4)	1(1.6)	8(3)		2.003(0.939-4.274)	0.072
Poor	10(4.9)	-	10(3.7)		4.214(2.205-8.054)	<0.0001*

[B.=] *at base line*
[F.=] *at Follow up*
[≠] log rank test p-value
**significant at α=5%*
CHR=crude hazard rate
¥ d4T: Stavudine; 3TC: Lamivudine; NVP: Nevirapine; EFV: Efavirenz; AZT: Zidouvudine; TDF: Tenofovir disoproxil fumarate

Table 4 multi-variate cox proportional hazard model of the association between base line and follow up characteristics and OI recurrence in study participants' in Debre Markos town, east Gojam zone between 25 March 2007 and 24 March 2013.

Characteristics	AHR(95 CI)	P value
Marital status		
Married	1	
Single	1.246(0.831-1.869)	0.287
Divorced	0.566(0.379-0.844)	0.005*
Widowed	2.177(1.30-3.644)	0.003*
Educational status		
Not educated	1	
Primary	1.337(0.899-1.987)	0.151
Secondary	1.086(0.658-1.793)	0.747
Tertiary	1.050(0.498-2.215)	0.898
Occupational status		
Farmer	1	
Merchant	0.301(0.170-0.531)	<0.0001*
employed	0.218(0.118-0.404)	<0.0001*
Daily laborer	0.792(0.466-1.345)	0.388
House wife	0.551(0.297-1.028)	0.058
Unemployed	0.599(0.349-1.028)	0.063
Student	0.150(0.059-0.384)	<0.000*
Base line Hemoglobin (g/dl)		
<10	1	
>=10	0.421(0.288-0.616)	<0.0001*
Follow up body mass index (kg/m^2)		
<=18.4	1	
18.5-22.9	1.045(0.736-1.484)	0.805
>=23	0.815(0.507-1.312)	0.400
ART		
No	1	
yes	0.522(0.347-0.784)	<0.002*
Follow up ART regimens ¥		
D4T+3TC+NVP	1	
D4T+3TC+EFV	0.448(0.147-1.363)	0.157
AZT+3TC+NVP	0.640(0.318-1.288)	0.211
AZT+3TC+EFV	1.137(0.269-4.816)	0.861
TDF+3TC+EFV	0.473(0.222-1.009)	0.053
TDF+3TC+NVP	1.332(0.207-8.552)	0.763

	Base line		Follow up	
	AHR (95 CI)	P- value	AHR (95 CI)	P- value
CD4 count (cells/µl)				
<=100	1		1	
101-199	0.463(0.190-1.126)	0.089	0.559(0.238-1.313)	0.182
200-350	0.585(0.262-1.306)	0.191	0.680(0.309-1.496)	0.338
351-499	0.604(0.255-1.429)	0.251	0.385(0.170-0.874)	0.022*
>=500	0.519(0.216-1.245)	0.142	0.321(0.141-0.731)	0.007*
Functional status				
Working	1		1	
Ambulatory	1.990(0.667-1.469)	0.961	1.119(0.673-1.861)	0.664
Bed ridden	0.978(0.361-2.647)	0.965	1.495(0.569-3.929)	0.414
Prophylaxis exposure				
No	1			
yes	0.546(0.326-0.914)	0.021*	0.488(0.275-0.867)	0.014*
Prophylaxis Adherence				
Good	1		1	
Fair	0.919(0.156-5.406)	0.925	7.272(1.308-40.446)	0.023*
poor	2.956(0.311-28.144)	0.346	3.588(0.521-22.692)	0.194
ART adherence				
Good	1		1	
Fair	14.833(1.858-118.41)	0.011*	1.908(0.377-9.665)	0.435
poor	6.636(0.305-144.600)	0.229	1.814(0.091-36.343)	0.697

**significant at α=5%*

AHR=adjusted hazard rate

¥ d4T: Stavudine; 3TC: Lamivudine; NVP: Nevirapine; EFV: Efavirenz; AZT: Zidouvudine; TDF: Tenofovir disoproxil fumarate

6. Discussion

In this historical cohort study, more than three quarter of the participants had recurrence of OIs. Cumulative incidence of recurrence was not significantly different (p=0.614) in Pre-ART and ART PLWHA which was 74.6% and 76.9% respectively. This study's finding of Cumulative incidence of OI recurrence in pre-ART PLWHA was slightly lower than the study in North West Ethiopia, in which 82.4% patients present with any type of OIs at start of ART (16) and a study in similar area of Northwest Ethiopia**,** a study at Felegehiot hospital in pre-ART HIV patients' was 88.9% at ART enrolment (15). The smaller in magnitude was due to inclusion of all Pre-ART PLWHA who were on chronic HIV care and treated for any type of OIs but the previous studies (15, 16) assessed the magnitude in only Pre-ART PLWHA who was enrolled for ART which might increases the magnitude because ART enrollment was done using WHO clinical staging and CD4 count.

This study revealed being unemployed than employed was hazard for survival (AHR 1.962, 95% CI: 1.224-3.145) which is in harmony with the cohort study in United states (35).
This study showed taking ART reduces hazard of OI recurrence (AHR 0.522, 95% CI: 0.347-0.784) which is supported by different studies (16, 22-25, 26-27). The one year follow-up study after ART initiation in North West Ethiopia showed ART reduces any OIs occurrence by 91.9% (16). Other cohort study in Italy also showed Initiation of ART within 2 months after toxoplasmic encephalitis diagnosis had a 3-fold reduction in the risk of developing a new OI compared with those who delayed therapy (relative hazard, 0.36; 95% CI, 0.15–0.86) (23). HAART reduces the incidence of severe OIs by 21% during the first 6 months and 28% during subsequent follow-up after adjusting for CD4 count (27). The Swiss HIV cohort study in Switzerland also showed ART reduces incidence of any OI from 15.1 per 100 person months in 6 months before ART to 7.7, 2.6 and 2.2 in the first 3, 6 and 9-15 months respectively after starting treatment (26).
Anti-retroviral treatment adherence is one of the challenges in the failure of HAART which is chance for OI progression(11, 28). This study revealed base line fair ART adherence compared to good adherence was hazard (AHR 14.833, 95% CI: 1.858-118.41) for survival. This illustrates in addition of taking ART, its adherence is crucial to improve survival.

This study revealed survival time was enhanced by taking prophylaxis at baseline (AHR 0.546, 95% CI: 0.326-0.914) and at follow up (AHR 0.488, 95% CI: 0.275-0.867) and this result is in consistency with other studies (31-34). A critical appraisal in 2011 showed primary prophylaxis with Trimethoprim-sulfamethoxazole is preventing life-threatening OIs like PCP, toxoplasmosis, and bacterial infections (31). Another Meta-analysis in 2010 about Cotrimoxazole also showed reduction of the risk of PCP and Tuberculosis. Primary prophylaxis with anti-tuberculosis regimens seems more effective at reducing the incidence of active tuberculosis in PLWHA (32). An experimental study in Ugandan Adults with Cotrimoxazole prophylaxis showed its effect on prevention of OIs like diarrhea in PLWHA. Compared to those remaining on cotrimoxazole, patients who discontinued had a relative risk of diarrhea of 1.8 (P= 0.001) (33). Another experimental study also showed Cotrimoxazole is preventing PCP (RR 0.59, p= 0 .03) (34). This study revealed having higher follow up CD4 count prolongs survival time, compared $\leq$100 cells/μl the adjusted hazard rate were 0.385 (95% CI: 0.170-0.874) for counts 351-499 cells/μl and 0.321 (95% CI: 0.141-0.731) for counts $\geq$500 cells/μl and per 50 cells/μl follow up CD4 count increase, the hazard to OI recurrence was decreased by 0.905 times (P<0.0001) after adjusted for covariates. This result is in conformity with previous studies (23, 26-27,29-30). A cohort study in Europe showed higher CD4 cell count was associated with a reduction of risk of new OI progression, the hazard ratio compared with 100 cells/ml was of 0.35 (95% CI: 0.30–0.40) for counts 200 cells/ml, 0.81 (95% CI: 0.71–0.92) for counts 200 to 350 cells/ml, 0.74 (95% CI: 0.66–0.83) for counts 350 to 500 cells/ml, and 0.96 (95% CI: 0.92–0.99) for counts 500 cells/ml or above (34). The Swiss HIV cohort study in Switzerland also showed a rise in CD4 count by 50 x 10^6/L or more by 6 month reduced subsequent OIs with hazard ratio of 0.32 (95% CL: 0.2-0.52)(26) which is in agreement with current study. A similar cohort study in France also showed OIs were higher at lower CD4 count (relative risk 5.37 (95% CI 3.87-7.43) for counts $\leq$ 50 and 2.42 for counts 51-200) at multivariate analysis (27). Similar cohort study also showed the risk of toxoplasmic encephalitis occurrence was increased by 30% for each 50-cell decrease in CD4+ cell count, independent of antiretroviral (23).

7. Strength and Limitation

7.1 Strength of the study

The study design relatively gives strong power. The study was included both rural and urban population so generalizability for two populations is possible.

7.2 Limitations of the study

Some factors which affect time to recurrence was not accessed for extraction

Treatment history for OI out of follow-up health institution was not assured for patients who were dead and this might falsely increase time to recurrence.

Use of laboratory results which were most recent to study period for patients who have no laboratory results during OI treatment might not have the same result. This might result in some implication.

Estimated time to recurrence might be affected due to censor of study participant who drop-out/loss follow-up/transferred –out and exclusion of PLWHA who were taking treatment for OI but not returning at least once to the health institution for follow up, incomplete data recording at follow up form, and pregnant mothers who were not on ART but taking zidovidine.

8. CONCLUSION AND RECOMMENDATION

Since the introduction of free ART, more patients have been presented to HIV care and support. A number of PLWHA seeking HIV care are increasing through time in Debre Markos town health institutions to get care and treatment program. When more patients present to the care, it is challenging for the health care providers to predict the number of OIs recurred and the needed resources. Prior prediction about PLWHA who are at risk to OI recurrence to successfully manage them to improve survival is also tricky. Thus, based on this study the responsible authorities of health institution can predict the numbers of OIs recurred and the needed resources based on magnitude and time to recurrence. In addition health professionals can expect whose PLWHA are at risk for OI recurrence.

During a median of 43 person weeks follow up the median survival time of PLWHA was 57 weeks. OIs were recurred in three quarter study participants (75.7%). The overall Incidence rate of any OI recurrence was 13.1 per 1000 person weeks. This study identified the independent significant predictors that reduce (risk factors) and improve (preventive factors) survival time. Those risk factors were being widowed than married, non- adherence of ART and prophylaxis treatments. And the preventive factors were being divorced compared to married, having occupational status of merchant, employed and student compared to farmer, having ≥10 g/dl hemoglobin value, having CD4 count 351 cells/μl and above compared to ≤100 cells/μl, taking ART and prophylaxis treatments.

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

To hospitals and health centers with ART clinic (giving HIV care and support)

- A careful management of patients who are widowed than married, not adhering ART or prophylaxis is necessary.
- PLWHA should encourage to take ART and prophylaxis drugs and counseled to adhere to it properly
- Increasing the CD4 count and hemoglobin value, using nutrition and drug treatments is crucial to improve survival time.
- Preventive efforts should focus on high risk groups such as widowed, not adhering ART or prophylaxis.
- The ART care should be further enhanced to improve survival.

To Debre Markos town health office and other responsible organizations

- Encourage Health professionals to properly documenting patients' health care data being used for studies and for improving patient management especially hemoglobin, treated OI and its treatment.
- Give especial priority for PLWHA to be employed in governmental or non-governmental organizations or facilitate conditions to join merchant occupation.
- Further studies recommended for estimating economic losses for subsequent recurrence of OI.
- Recommend further observational studies with prospective design to ascertain the findings.

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ANNEXES

ANNEXE I Information and Consent form

Information and Consent form (English version)

A. Information Sheet

Greetings! My name is _____, I am health personnel working in Debre Markos hospital /health center ART clinic now I am collecting data from our PLHIV ART logbook for the research being conducted to assess time to recurrence of any OIs after treatment of any preceding OIs and factors associated with it and magnitude of recurrence in Debre Markos town, by Ato Habtamu Mellie who is the MPH student in Addis Ababa University. The study will be used to directly\indirectly expect social crisis, number of ART clinics needed and its burden, economic losses due to not working, costs for treatment or transportation based on time and magnitude of recurrence of OIs. The evidence is expected to be used by governmental and non -governmental organizations working HIV/AIDS or mainstreaming it in order to inform policy makers and medical practitioners. The data which is necessary for the study will be taken from your ART log book therefore; your willingness to use the recorded data in this study will be helped to achieve the stated benefits of the study and participation in the study is seen as vital citizenry and societal opportunities as well as contributions.

If you have any questions about this study you may ask me or the principal investigator

Habtamu Mellie Tel: 0912356496

E-mail: habtamumellie@yahoo.com

A. **Consent Form**

Based on the purpose and objectives of the study, 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. As the study will be conducted through review your medical records, it will not cause any harm as far as the confidentiality is kept. The information will be taken when you give permission, and participation is totally voluntary. 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\health center. On the other hand, there is no any special benefit by allowing your records to be used in the study.

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

1. NOT willing to extract data_____
   (End the session with thanks)
2. **Yes** willing to extract data _____
   (Appreciate and proceed to extract data)

Name and Signature of the data collector which shows that the respondent has consented (verbally) to take part in the study _____ _____

Signature: _____

Supervisor's Name: _____ Signature: _____

Name of the hospital/health center_____

Information and Consent form (Amharic version)

ሀ. ለጥናቱ ተሳታፊዎች መረጃ መስጫ ቅጽ

ሰላም ነህ\ወይ! ስሜ _____ ይባላል፡፡ በዚህ ሆስፒታል/ጤና ጣቢያ የኤች.አይ.ቪ/ኤድስ ክሊኒክ ውስጥ የምሠራ የጤና ባለሙያ ስሆን አሁን የኤች.አይ.ቪ/ኤድስ ተጓዳኝ በሽታዎች ተከስተዉ ከታከሙ በኋላ ዳግም የሚከሰቱበትን ጊዜ እና እዲከሰቱ ተፅዕኖ የሚያደርጉ ነገሮችን እንዲሁም በአካባቢው በአብዛኛው ዳግም የሚከሰቱ ተጓዳኝ በሽታዎች በሚል ርዕስ በአዲስ አበባ ዩኒቨርሲቲ ድህረ ምረቃ ተማሪ የሆኑት አቶ ሀብታሙ መሌ ለሚሰሩት ጥናት መረጃ ከኤች.አይ.ቪ/ኤድስ ተጓዳኝ በሽታ ታካሚዎች መዝገብ ላይ እየሰበሰብኩ ነው፡፡ የጥናቱ ውጤትም በቀጥታ\በተዘዋዋሪ መልኩ የኤች.አይ.ቪ/ኤድስ ተጓዳኝ በሽታ ተደጋጋሚ መከሰት የሚያመጣውን ማህበራዊ ቀውስ፣ ለበሽተኞች የሚያስፈልገውን የጤና ተቋም ቁጥርና በሱ ላይ የሚኖረውን ጫና፣ ስራ ባለመስራት፣ለህክምናና ለትራንስፖረት በሚከፈል ወጭ የሚኖረውን የኢኮኖሚ ድቀት ሳይንሳዊ ግምት ለመስጠት ያስችላል፡፡ ይህ መረጃም በኤች.አይ.ቪ/ኤድስ ዙሪያ ለሚሰሩ ብሔራዊ፣ ክልላዊና አካባቢያዊ የሆኑ መንግስታዊና መንግስታዊ ያልሆኑ ድርጅቶች፣ ሀኪሞች፣ ህግ አርቃቂዎች ይጠቀሙበታል ተብሎ ይታመናል፡፡ በመሆኑም ለጥናቱ አስፈላጊ የሆኑ መረጃዎች ከእርስዎ የኤች.አይ.ቪ/ኤድስ ክትትል መዝገብ ላይ ይወሰዳል፡፡ የአንተ\ች መረጃዎ እንዲወሰድ መፍቀድም ከላይ ለተጠቀሰው የጥናቱ ዓላማ መሳካት የጐላ አስተዋጽኦ ይኖረዋል፡፡ በጥናቱ መሳተፍም ሀገራዊና ማህበራዊ የሆነ ታላቅ አስተዋጽዖ አለው፡፡

ጥናቱን በተመለከተ ጥያቄ ካለዎት እኔን ወይም አጥኚውን አቶ ሀብታሙ መሌን ከታች በተጠቀሰዉ አድራሻ መጠየቅ ይችላሉ፡፡

ስልክ፡ 09-12-35-64-96

ኢ..ሜል habtamumellie@yahoo.com

ለ. ለጥናቱ ተሳታፊዎች የፈቃደኝነት መጠየቂያ ቅጽ

ከጥናቱ አላማ አንጻር አንተ/ቺ ለጥናቱ ከሚያስፈልጉ ሰዎች መካከል በእጣ የጥናቱ አካል በመሆን ተመርጠሃል/ሻል፡፡ አጥኚው እዚሁ ክሊኒክ ላይ የምሠራውን እኔን ለመረጃ ሰብሳቢነት የመረጠኝ የመረጃውን ምስጢራዊነት ለመጠበቅ ብሎ ነው፡፡ ማለትም ከክሊኒኩ ውጪ ያሉት በመረጃ ስብሰባ ወቅት ስምዎንና ሌሎች መረጃዎችን እንዳያዩ ሲባል ነው፡፡ ጥናቱ የሚደረገው ከኤች.አይ.ቪ/ኤድስ ክትትል መዝገብ ላይ ስለሆነ በእርስዎ ላይ ምንም ዓይነት ጉዳት አያመጣም፡፡ ከሕክምና መዝገብዎ ላይ መረጃ ሲወሰድ የእርስዎን ማንነት የሚገልጽ ስም እና ሌላ ምንም ዓይነት ነገር ወደ መጠይቁ አይሞላም፡፡ የተወሰደውም መረጃ ምስጢራዊነቱ ተጠብቆ ሙሉ በሙሉ ለምርምር ሥራ ብቻ ይሆናል፡፡ የሕክምና መረጃዎ ለምርምር ሥራ እንዳይውል የማድረግ መብት አለዎት፡፡ ነገር ግን መረጃዎ ለምርምር ሥራው ቢውል ጠቀሜታው የጎላ ነው፡፡ በጥናቱ ለመሳተፍ ፈቃደኛ ባይሆኑ በሕክምናዎት ላይ ምንም ዓይነት ጉዳት አይፈጠርብዎትም፡፡ በሌላ በኩል መረጃዎን በመስጠትዎ የሚያጡት የተለየ ጥቅም አይኖርም፡፡

መረጃው ለምርምር ሥራ ቢውል ፈቃደኛ ነዎት?

1. አይደለሁም_____

   መረጃቸው ለጥናቱ ሥራ እንዲውል አል ፈቀዱም

   (ውይይቱ በምስጋና ይጨረሳል)
2. አዎ

   (በምስጋና መረጃቸውን መሰብሰብ ይጀመራል)

የመረጃው ሰብሳቢዉ ስምና ፊርማ የጥናቱ ተሳታፊዎች መረጃቸውን ለጥናቱ ሥራ እንዲውል ፈቃደኛ መሆናቸዉን ያመለክታል _____

_____

ፊርማ _____

የአጥኚዉ ስምና_____ _____ ፊርማ _____

የጤና ተቋሙ ስም_____ _____

Annex II: *Questionnaire*

Study participant Identification number----------

Time of study participant enter into study (Date----------/month----------/year----------)

Time of study participant leave study or outcome occurred (Date--------/month--------/year-------)

Part-I SOCIO DEMOGRAPHIC CHARACTERISTICS

1. Age (----------) years
2. Residence
   - A. Urban
   - B. Rural
3. Sex
   - A. Male
   - B. Female
4. Religion
   - A. Orthodox
   - B. Protestant
   - C. Muslim
   - D. Others specify----------
5. Marital status
   - A. Married
   - B. Single
   - C. Divorced
   - D. widowed
6. Educational status
   - A. Not educated
   - B. Informal education
   - C. Grade 1-8
   - D. Grade 9-12
   - E. Above grade 12
7. Occupational status
   - A. Farmer
   - B. Merchant
   - C. Government employee
   - D. Day laborer
   - E. Other specify----------

Part-II Base line clinical and functional status information

8. **B**aseline treated opportunistic illness

A. herpes zoster
B. Wasting syndrome
C. chronic diarrhea
D. pulmonary tuberculosis
E. extra pulmonary tuberculosis
F. oral thrush
G. bacterial pneumoniaPCP
H. toxoplasmosis
I. Cryptococcal meningitis
J. Encephalopathy
K. Genital/oral ulcer
L. Other specify-------

9. Baseline number of OIs treated at one time

A. 1
B. 2
C. 3
D. Other write number--------

10. Has base line other chronic diseases like diabetes mellitus, hypertension, and cardiac disease?

A. Yes
B. No

11. Baseline WHO clinical staging

A. I
B. II
C. III
D. IV

12. Baseline Weight (----------) kg

13. Baseline Height (----------) cm

14. Baseline Functional status

A. Working
B. Ambulatory
C. Bed ridden

Part-III Base line laboratory and ART information

15. Baseline CD4 count (----------)

16. Baseline hemoglobin (Hgb) value (----------)

Part-IV Baseline ART and chemoprophylaxis's information

17. Is study participant on ART?

A. Yes
B. No

17.1 If the answer for question number 17 is yes, line of Regimens given

A. First line regimens (specify dispensed drugs/code ----------/----------/----------)

17.2 2nd line regimens(specify dispensed drugs/code ----------/----------/----------)

17.3 If the answer for question number 17 is yes, adherence level for ART

A. Good
B. Fair
C. Poor

18. At baseline type of OI prophylaxis given

A. Not given

A. Cotrimoxazole

B. INH

C. Fluconazole

D. Others specify----------

18.1 If prophylaxis given on question number 18, adherence level for prophylaxis

A. Good

B. Fair

C. Poor

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

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

20. Is opportunistic infections Re-occurred?

A. Yes

B. No

22.1 If the answer for question number 20 is yes, type of OIs occurred

A. herpes zoster

B. Wasting syndrome

C. chronic diarrhea

D. pulmonary tuberculosis

E. extra pulmonary tuberculosis

F. oral thrush

G. bacterial pneumonia

H. PCP

I. CNS toxoplasmosis

J. Cryptococcal meningitis

K. Encephalopathy

L. genital/oral ulcer

M. Other specify-------

21. Recent Weight in kg(----------) kg

22. Recent CD4 count (----------)

23. Recent hemoglobin (Hgb) value(----------)

24. Is study participant taking ART on follow up?

A. Yes

B. No

24.1 If the answer for question number 24 is yes, line of Regimens given

A. First line regimens (specify dispensed drugs/code ----------/----------/----------)

B. 2nd line regimens(specify dispensed drugs/code ----------/----------/----------)

24.1If the answer for question number 24 is yes, adherence level for ART on follow up

A. Good C. Poor

B. Fair

25. Follow up type of OI prophylaxis given

A. Not given
B. Cotrimoxazole
C. INH
D. Fluconazole
E. Others specify----------

25.1 If prophylaxis given on question umber 25, adherence level for prophylaxis

A. Good
B. Fair
C. Poor

A. Working
B. Ambulatory
C. Bed ridden

26. Follow up Functional status

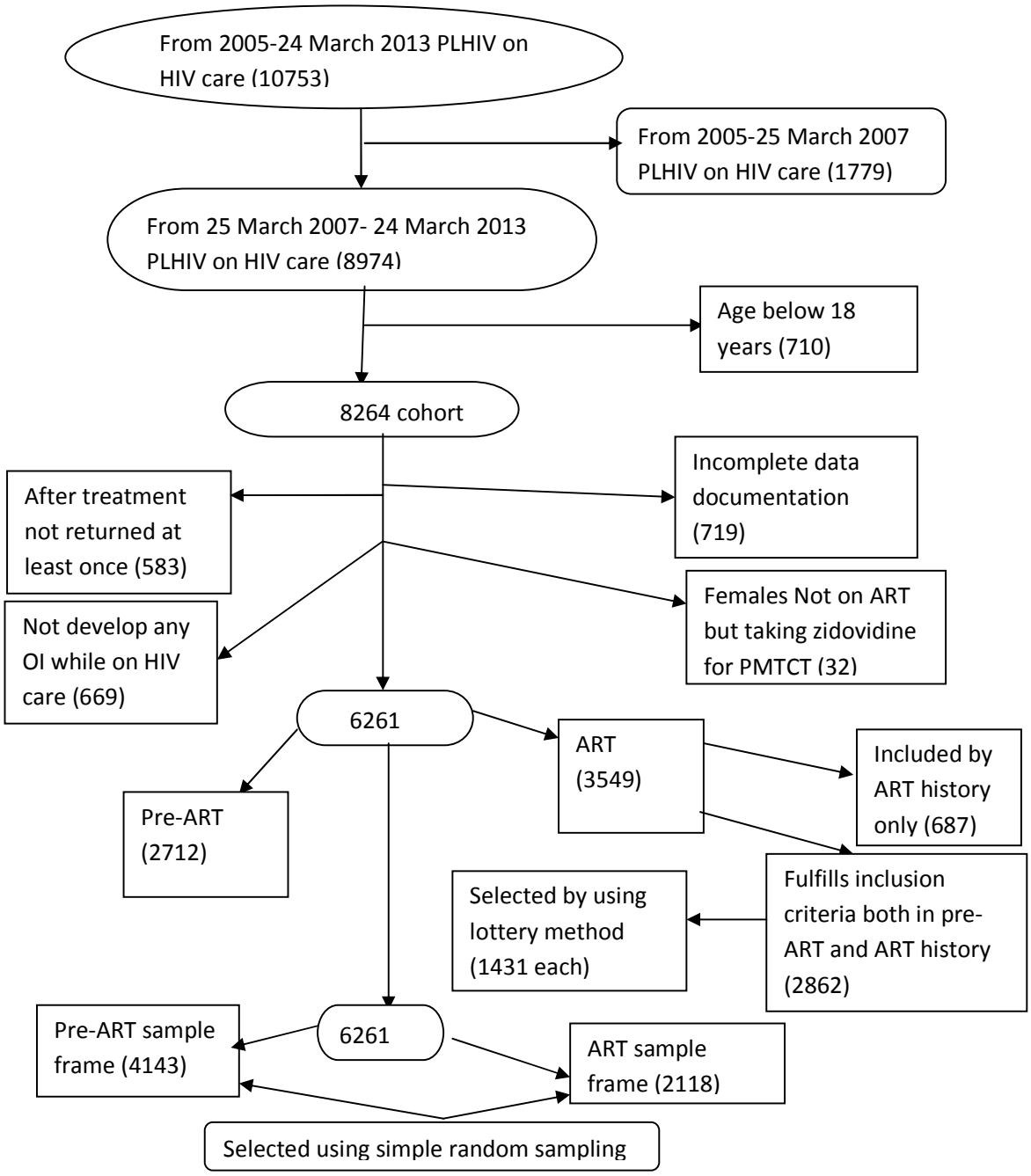

Figure1 Profile of PLHIV enrolled for cohort between 25 March 2007 and 24 March 2013 in Debre Markos town, Amhara region, Ethiopia.

ADDIS ABABA UNIVERSITY SCHOOL OF GRADUATE STUDIES

Assessment of time to recurrence of opportunistic infections in people living with HIV/AIDS, in Debre Markos town, East Gojam zone, North West Ethiopia, in 2013. (Retrospective Cohort study)

BY: Habtamu Mellie (BSC)

Approved by examining board

Chairman, SPH

Dr.Wakgari Deressa _____

Signature

Advisor

Dr. Getnet Mitkie _____

Signature

Examiner

_____ _____

Signature