

Predictors of Mortality among Adult People Living with HIV and Its Implications for Appointment Spacing Model Approach Care in Southwest Ethiopia.

Aderajew Nigusse Teklehaymanot (✉ aderajewnu@gmail.com)

Jimma University College of Public Health and Medical Sciences

Tefera Belachew Lemma

Jimma University

Esayas Kebede Gudina

Jimma University

Masrie Getnet

Jimma University College of Public Health and Medical Sciences

Demuma Amdisa

Jimma University College of Public Health and Medical Sciences

Lelisa Sena Dadi

Jimma University College of Public Health and Medical Sciences

Research

Keywords: Adult, Appointment Spacing Modals, ART, PLWHA, Predictors, Jimma zone

Posted Date: June 17th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-35093/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Introduction:

Antiretroviral Therapy has markedly improved survival of people living with human Immune virus. Yet, the full potential benefits of the therapy depend on understanding of predictors of mortality among PLWHA. The aim of this study was to assess predictors of mortality among adult PLWHA in Jimma Zone Public Hospitals.

Methods

A retrospective cohort study was conducted among 676 adult PLWHA who enrolled to ART clinic from September 1st, 2012 - August 30, 2016. Multivariable Cox Regression analysis was used to identify predictors of mortality using 95% confidence interval (CI) and at P value ≤ 0.05 cut of point.

Results

The total person-time contributed was 28,209 person-months with an overall mortality incidence rate of 11 per 1000 person-months observation. The cumulative mortality incidence among females over the study period was 16.8% (64/382). The predictors of mortality were found severe Undernourishment (AHR: 3.7; 95% CI: 1.6, 6.7) and moderate malnutrition (AHR: 2.5; 95% CI: 1.7, 7.5) at base line, younger age (AHR:2.1; 95% CI: 1.7, 3.3), female (AHR: 2.8; 95% CI: 2.1,4.6), single (AHR: 2.6; 95% CI: 1.8, 3.8), divorced (AHR: 2.4; 95% CI: 1.3,3.9) Illiterate (AHR: 2.5; 95% CI: 1.9, 4.8), lack of disclosure (AHR: 3.6; 95%: 1.7, 9.5), WHO clinical stage IV (AHR: 3.7; 95% CI: 1.7, 5.3), seeking treatment out of catchment area (AHR:3.6; 95% CI: 1.5,5.4), rural residence (AHR:2.1; 95% CI:1.4, 3.3), and immunological failure (AHR:1.7; 95% CI: 1.3, 2.7).

Conclusions

Poor nutritional status at baseline, advanced HIV disease, occurrence of treatment failure, female sex, substance use disorders, lack of social support, immunological failures, clinical failures, and younger age, low level of education and poor physical access to healthcare facility were found to be important predictors of mortality. Intervening, those factors as routine and part of “appointment spacing model care” can improve survival of PLWHA.

Introduction

Human Immunodeficiency virus (HIV) is a global epidemic, which affects individuals of all ages, sexes, races and income status (1). Globally, between 1980 and 2015, about 78 million people were infected and half of them have died of the disease (2). According to the 2016 report of Global Burden of Diseases

(GBD 2016), worldwide 38.8 million people had HIV infection; 2.1 million people had been newly infected and 1.2 million died due to the virus in 2015 (3). The Africa continent contributes about 11% of the global population (2). Yet, the highest proportions of HIV infection have been recorded in sub-Saharan Africa (SSA) and Southern Africa countries in particular (4).

Ethiopia is among African countries hard hit by the HIV pandemic (5). The overall prevalence of the disease among adults, pregnant women and, women who had multi sexual partners was reported to be 0.9%, 0.4%, and more than 6%, respectively (6). The prevalence among women (1.2%) was twice that of men (0.6%), seven times in urban residence (2.9%) compared to rural settings (0.4%). The burden of HIV varies from region to region, ranging from < 0.1% in Somali Region to 4.8% in Gambela Region (ref?). In 2016, a total of 19,743 people were died of AIDS and about 792,840 children lost either or both of their parents due to AIDS (7, 9).

To alleviate the impact of HIV/AIDS, Ethiopia introduced ART in 2003 for the first time at cost of patients, and two years later ART started to be provided for free (8, 10, and 11). Following the 3 by 5 program, 535,069 PLWHA who had 'ever started' ART and 375,811 PLWHA who did not yet started ART were put on ART in more than 1000 health facilities in 2014/5 (8). Subsequently, report of 2017 revealed that HIV incidence, AIDS related mortality and overall HIV prevalence were fallen by 95%, 73% and 29%, respectively (12).

Ethiopia has also been implementing prevention, treatment and care interventions. The prevention activities include voluntary counseling and testing (VCT), prevention of mother to child transmission (PMTCT), behavioral change communication and community mobilization. The treatment and care theme encompasses ART, laboratory monitoring, provider initiated testing and counseling (PITC), nutritional support, palliative care and home-based care activities (8, 13). Despite the efforts devoted to limit the impact of HIV, still numerous gaps and challenges remain unsolved. Among others, timely initiation of ART, retention in care and prevention of HIV related mortality, narrowing significant inequities in ART coverage, which varies between children (23%) versus adults (60%), females (54%) versus male (69%), and disparities among regions ranging from 5.6–93% are worth mentioned (9,14).

To help HIV patients fully benefit from ART, attain national goals and use resources most effectively, Ethiopia uses the HIV continuum care (HCC) framework initially incepted by the Centers for Disease Control and prevention (CDC) in Atlanta, USA, in 2013 (16). The HIV continuum care is a series of stages from the time a person is diagnosed with HIV through assessment for ART eligibility, retention in care, and immunologic success and virological suppression via treatment adherence towards reduction of mortality and ART care success out comes (17,18,19). Many activities have been attempted to address negative ART care outcomes (10). Nevertheless, there have been challenges at every stage of the HCC. These include late HIV care presentation (LP) (20, 21), discontinuation of ART (22, 23), poor ART adherence (24, 25), immunologic (26, 27), clinical (28), treatment (23, 28) and virological failures (29, 30).

Currently, Ethiopia is implementing a new care approach known as “appointment spacing model care (ASM)”, which mainly focuses on a few visits of hospitals (two times per year) and comprehensive care at a time. However, there are still massive challenges pertaining to ART program regardless of the efforts being devoted by both governmental and non-governmental organizations (31). Consequently, patients usually experience different unintended health care outcomes such as loss of many from the ART schedules (32), failure to recover their immunity (33) and deaths from the disease (34, 35).

The overall picture shows that research is lacking to identify key factors that lead to negative ART care outcomes, including mortality. Furthermore, studies conducted in Africa have revealed that factors affecting ART care are beyond individual level. The factors are related to health care institutions such as lack of ART trained health professionals (31–34), and lack of quality care (35–38); community level factors such as stigma (39,40) and traditional healing (41–44); and program level factors such as political commitment (45,46) and lack of coordinated HIV care activities (47). Nevertheless, comprehensive study has not been carried out in Ethiopia to adequately address the challenges of ART care from the viewpoints of stakeholders. Therefore, the aim of this study was to assess predictors of mortality among adult PLWHA in Jimma Zone Public Hospitals.

Cohort Description

Study Setting and period

The study was conducted in the Jimma zone five public hospitals (Jimma Medical Center, Shenen Gibe, Agaro, Seka and Limmu-Genet hospitals). Jimma zone is one of the 20 administrative zones in Oromia Regional State located in southwest Ethiopia. Jimma Medical Center is the only tertiary hospital in southwest Ethiopia. The other four hospitals are primary hospitals with catchment population of about a million each. At the time of the study, a total of 11,186 adults and 2,683 children were in chronic HIV care at the hospitals. The data was collected from February 15/2018 to March 16/2018 and the study involved patients on chronic HIV care at the hospitals during period of 01 September 2012 to 30 August 2016.

Patient And Public Involvement

A five-year retrospective open cohort study was conducted to assess the predictors of mortality and the implication of appointment spacing model approach care among PLWHA in Jimma zone public hospitals. This retrospective cohort study has assessed whether the risk of expected outcome was different by the exposure of interest using existing data (48).

Hence, two groups who were known to be either exposed or not exposed to the factor of interest in a specific time frame were compared on the basis of outcomes of interest. The hazard risk is used as measures of estimation of the relative risk (50).

The research question of this study is in line with the Ethiopian Public Health research plan developed through multiple consultative processes involving broader stakeholders including patient representatives. We plan to disseminate the research findings through the national HIV, TB and Nutrition research conferences involving researchers, policymakers, stakeholders and affected communities.

Enrolment Procedures

A total of 676 adult PLWHA was randomly selected from All adult (≥ 18 years old) who were on chronic care follow up. The Sample size was estimated using two population proportions formula. Based on BMI measurement, those PLWHA, who had undernourishments at the initiation of ART were considered to be exposed (n_1) whereas those who had normal BMI were taken to be non-exposed group (n_2). Accordingly, 281 exposed and 395 non-exposed samples were estimated, implying total of 676 samples of PLWHA for the study.

The study population was all adult PLWHA enrolled in ART care in the selected hospitals. Patients with unknown nutritional status at ART initiation, those who defaulted, those with incomplete information and those transferred out to other facilities were excluded from the study.

Recruitment and informed consent procedures take place within the Ethiopian HIV Program clinics; any client's clinical records who present to hospital are approached by a Doctors/nurse or another allied healthcare provider and asked whether they are willing to speak to a research assistant about participating in a research project.

If a client is agreeable, a research assistant meets with them to explain the purpose, context and methods for this cohort study, and reviews the informed consent form to determine whether the person is interested, willing and able to participate. The results were also maintained using aggregated report rather than individual characteristics in any aspect of the data throughout all steps and manuscript preparation. These data were not identifiable; therefore informed consent was not required.

Data source and collection procedure

Medical records were reviewed from February 15/2018-murch 16/2018 covering a period of five years (from 01 September 2012 to 30 August 2016).

Using appropriate case reporting format prepared in English. The data were collected by 10 BSc professional nurses using data collection format. All the five hospitals have an electronic patient database called Comprehensive Care Centre Patient Application Database (C-PAD). C-PAD is Electronic Medical Records (EMR) system database that contains patients' both clinical and non-clinical information. This was the main source of data in this study. Data were extracted using a data extraction check list from the database. When data were incomplete, we tried to refer the patients' cards, registration and log books using patient medical record number and ART registration number.

Data processing and analysis

Cleaned and coded data were entered to EPI-data version 3.14, and then exported to SPSS version 20.0 for analysis. Kaplan Meier (KM) survival function and Log rank test was used to test the statistical difference in the KM curves. Bivariate Cox regression analysis was done to estimate the unadjusted Hazard Ratios (HRs). Independent variables with $P \leq 0.25$ at bivariate analysis level were entered into the multivariable Cox regression model to control potential confounders. Finally, variables, which have $P \leq 0.05$ and non-null values within respective confidence intervals (CIs) at multivariable analysis were considered to be independent predictors of mortality among the PLWHA.

Results:

Socio demographic Characteristic of Adult PLWHA in Jimma zone Public Hospitals

In this study, records of 382 (56.5%) females and 294 (43.4%) males were reviewed. The mean age of the study participants at the time of ART initiation was 30.4 years (\pm SD 7.4); 487 (72%) were between 25 and 44 years of age. More than half (55.6%) of them were married and 132 (19.5%) of them were divorced ones. Most of the participants (79.3%) reported to have attended at least a primary school. About 61% of the participants (412) were urban residents and 128 (18.9%) were living outside the catchment area of the respective hospitals. Nearly two-third (66.3%) of the study participants reported to have had persons taking care of them. Disclosure of their HIV diagnosis to family member was reported by 68.9% of the participants. About 80% (540) and 58.6% of the study participants reported to have used Khat and alcohol respectively (Table 1).

Table 1
Socio demographic Characteristic of Adult PLWHA in Jimma
zone Public Hospitals, September 2012 –August 2016

Variables	Classification	Number	Percent
Sex	Male	294	43.4
	Female	382	56.5
Age group	18–24	97	14.3
	25–34	244	36.1
	35–44	243	35.9
	45–54	72	10.6
	> 55	20	2.9
	Marital status	Single	92
	Married	376	55.6
	Divorced	132	19.5
	Widowed	77	11.3
Level of Education	Illiterate	140	20.7
	Primary	271	40.1
	Secondary	190	28.1
	12 and above	75	11.1
Religion	Orthodox	322	47.6
	Muslim	265	39.2
	Protestant	84	12.4
	Catholic	5	0.7
Occupation	G/Employed	159	23.5
	Self employed	322	47.6
	Unemployed	86	12.7
	Other	100	11.1
Residence	Urban	412	60.9
	Rural	264	39.1
Catchment area	In catchment	548	81.1

Variables	Classification	Number	Percent
	out of Catchment	128	18.9
Have Care giver	Yes	448	66.3
	No	228	33.7
Disclosure	Yes	467	68.9
	No	211	31.1
Hx of alcohol	Yes	397	58.6
	No	281	41.4
Hx of Chew <i>khat</i>			
	Yes	540	79.6
	No	138	20.4

Baseline clinical status of PLWHA who were on ART care

Regarding the baseline medical and nutritional status of PLWHIV who were ART, 339 (50.1%), 192 (28.4%) and 145(21.4%) were started on ART on the basis of clinical, CD4 count, and both clinical and CD4 count approaches, respectively. One hundred eighty (26.6%) and 201 (29.7%) of them respectively had severe and moderate malnutrition at ART initiation. Two hundred six (30.5%) and 34 (5.0%) PLWHA was classified as either WHO clinical stage III or IV respectively. Regarding functional status, 63.0% of the study participants were in working condition (Table 2).

Table 2
Baseline medical and nutritional status of ART users, September 2012 –
August 2016

Variables	Categories	Number	Percent
Eligibility criteria	Clinical only	339	50.1
	CD4 count only	192	28.4
	Clinical and CD4 count	145	21.4
BMI at baseline	1/Not malnourished	395	58.4
	2/Moderate	181	26.8
	3/Severe malnutrition	100	14.8
	Not recorded	21	3.1
Weight category	≤ 40 kg	460	68.0
	41–60 kg	118	17.5
	> 61 kg	98	14.5
WHO clinical stage	Stage I	190	28.1
	Stage II	246	36.4
	Stage III	206	30.5
	Stage IV	34	5.0
Functional status	Working	426	63.0
	Ambulatory	216	31.9
	Bedridden	34	5.0
History of any OI	Yes	487	72.0
	No	189	27.5
History of TB	No	333	49.3
	INH prophylaxis	102	15.0
	With treatment/re-treatment	240	35.5
Baseline AFB result	Negative	484	71.6
	Positive	138	20.4
	Not recorded	54	7.9

Four hundred eighty-seven (72.0%) of the participants had history of opportunistic infections (OIs) at ART initiation. TB was the most common OI identified contributing for 35% of the OI cases (pulmonary TB – 29% and extra pulmonary TB – 6%). However, 71.6% patients on TB treatment were negative for Acid Fast Bacilli (AFB). The other OIs were diarrhea 101 (21.0%), chronic diarrhea (18.0%) and Herpes zoster (12.0%) (Fig. 1).

Laboratory profiles and treatment of PLWHA on ART

More than half, 353 (52.3%) of the study participants had hemoglobin level of less than 11 mg/dl at ART initiation. With regard to other laboratory parameters, 51.5% of them had normal liver functional test and 52.9% had CD4 cell count below 200 cells/ μ L.

Stavudine based regimens, 1a (d4T + 3TC + NVP) and 1b (d4T + 3TC + EFV), were the most common ART regimens used in 53% of the participants. Less than half, 286 (43.3%) of the study participants reported to have had good adherence to OI prophylaxis, whereas the rest had fair 241(35.7%) or poor 149 (22.0%) adherences (Table 3).

Table 3

Laboratory, clinical care and behavior related factors in the initiation of ART in Jimma zone Public Hospitals, Southwest Ethiopia, September 2012 – August 2016

Variables	Categories	Number	Percent
Adherence to Cotri at 6month	Good	286	42.3
	Fair	241	35.7
	Poor	149	22.0
ART regimen	1a (d4T + 3TC + NVP)	154	22.8
	1b (d4T + 3TC + EFV)	212	31.4
	1c (AZT + 3TC + NVP)	96	14.2
	1d (AZT + 3TC + EFV)	93	13.8
	1e (TDF + 3TC + EFV)	117	17.3
	1f (TDF + 3TC + NVP)	104	15.3
Liver functional test	Normal (0–50)	348	51.5
	Abnormal (> 50)	279	41.3
	Not done	49	7.2
CD4 count	< 200	358	52.9
	201–350	249	36.8
	> 350	69	10.2
Hemoglobin Level	< 11 mg/dl	353	52.5
	11.5–16 mg/dl	255	37.7
	> 17 mg/dl	68	9.8
Adherence to all clinical care 6 m	Good	264	39.0
	Fair	71	10.5
	Poor	341	50.4
Patient Status at death	Not Known	12	12.2
	Clinical failure	36	36.7
	Immunologic failure	24	24.4
	Virologic Failure	26	26.5

Cumulative Incidence and Incidence rate of mortality

Ninety-eight (14.5%) patients were died during the five-year of ART follow up period. The cumulative incidence among females was 16.8% (64/382). The total follow up time was 28,209 person-months when an overall incidence rate of 11 deaths per 1000 person-months was observed. The death rates among those PLWHA who had severe and moderate malnutrition were 5.7 and 2.9 deaths per 1000 person-months, respectively. The overall survival probability of the adult PLWHA was 86.6%. The overall estimated mean (\pm SD) survival time of adult PLWHA on ART follow up was 42.8 (SD = 17.8) months. In the five-year time interval, the highest mortality was observed during 18 to 24 months of follow up, followed by the months of 30 to 36 and 24 to 30, respectively. The lowest mortality was observed during the follow up period from 48 to 54 months followed by 54–60 months of follow up, followed and during the period 6 to 12 months (Table 4).

Table 4
Overall Life table of PLWHA on ART follow up in Jimma zone public Hospitals south west Ethiopia, September 2012 –August 2016

Interval	Beginning	Death/98	Lost/134	Survival	Sta/ error	95% CI
0–6	676	10	0	0.9783	0.0042	0.9766 0.9941
6–12	666	5	0	0.8781	0.0056	0.9639 0.9867
12–18	661	8	34	0.9325	0.0091	0.9209 0.9570
18–24	608	19	13	0.9211	0.0106	0.8965 0.9386
24–30	558	14	12	0.9022	0.0118	0.8763 0.9230
30–36	561	17	23	0.8853	0.0129	0.8582 0.9091
36–42	521	9	25	0.8748	0.0137	0.8451 0.8992
42–48	487	11	16	0.8608	0.0158	0.7289 0.8874
48–54	476	1	10	0.8500	0.0159	0.8157 0.8782
54–60	470	4	2	0.8453	0.0565	0.7096 0.9748

The overall probability of survival among adult PLWHA on follow up in Jimma zone public hospitals showed a decrement with an increment of WHO classification stages. Those PLWHA on ART follow up classified as WOH stage I, II, III and IV had a survival probability of 96.3%, 94.9%, 92.9%, 76.5% and 48.6%, respectively (Fig. 2).

Predictors of mortality among Adult PLWHA on art follow up

Adult PLWHA who suffered from severe malnutrition at baseline had nearly four times (AHR: 3.7; 95% CI: 1.6, 6.7) risk of death while those with moderate malnutrition had more than twice (AHR: 2.5; 95% CI: 1.7, 7.5) risk of dying early compared to those with normal BMI. The risk of early death was nearly three times higher among females (AHR: 2.8; 95% CI: 2.1, 4.6) compared to males. Deaths among single (AHR: 2.6; 95% CI: 1.8, 3.8), divorced (AHR: 2.4; 95% CI: 1.3, 3.9), and widowed (AHR: 2.3; 95% CI: 1.7, 3.7) PLWHA on

ART follow up were higher compared to married PLWHA on ART follow up. The risk of death among adults PLWHA decreases as educational status increases. The risk of death was more than two times among illiterate (AHR: 2.5; 95% CI: 1.9, 4.8) and those who attend primary school (AHR: 2.1; 95% CI: 1.8, 3.6) compared to PLWHA on ART follow up who attend secondary or above schools.

Those PLWHA who did not disclose their HIV status to anyone (family or friend) had more than three times (AHR: 3.6, 95% CI: 1.7, 9.5) risk of dying compared to those who have disclosed their HIV status. Those PLWHA on ART follow up who had lower body weight (< 40Kg) had nearly three times risk of dying compared to their counterparts (AHR: 1.8; 95% CI: 0.5, 3.7). Those adult PLWHA with TB Co-infection at the initiation of ART were nearly three times (AHR: 2.9, 95% CI: 1.5, 5.5) more likely to die within five years of treatment follow up period compared to those who did not have it. Individuals who were at stage IV HIV diseases (bedridden) at the initiation of ART were more than three times (AHR: 3.7, 95% CI: 2.4, 13.8) more likely to die within five years of treatment follow up period as compared to those with working functional status.

The risk of death was four times in those with elevated liver enzymes (> 50 IU/L) (AHR: 4.2; 95% CI: 2.4, 6.7) and nearly three times higher in those with OI (AHR: 2.5; 95% CI: 1.9, 7.1) compared to their counterparts. Those PLWHA on ART follow up whose causes of death confirmed to be clinical failure (AHR: 2.1; 95% CI: 1.4, 2.8) and immunological failure (AHR: 1.7; 95% CI: 1.3, 2.7) were two times at higher risk of wasting syndrome (severe malnutrition /stage three malnutrition and leading to death) within five year treatment follow up period compared to their counterparts. The risk of death was also found to be high among PLWHA living outside catchment area of the hospital (AHR: 3.6; 95% CI: 1.5, 5.4) compared to their counterparts (Table 5).

Table 5

Predictors mortality among Adult PLWHA in Jimma zone Public Hospitals, South west Ethiopia, 2012 – August 2016

Variables	Classification	Death 98 (%)	Censored 578 (%)	CHR (95%)	AHR (95%)	P value
Age group	18–24	40(40.8)	57(9.8)	4.1 (1.5,11.3)	2.1 (1.7, 3.3)	0.01
	25–34	23(23.5)	221(38.2)	2.3 (1.8, 6.6)	0.8(0.3, 2.4)	0.04
	35–44	10(10.2)	232(40.1)	1	1	
	45–54	8(8.2)	64(11.1)	2.1 (1.4,16.3)	0.9 (0.4, 9.3)	0.38
	> 55	17(17.3)	4(0.7)	3.7 (0.8, 6.6)	1.8 (0.8, 7.6)	0.02
Sex	Male	34(34.7)	260(44.9)	1	1	
	Female	64(65.3)	318(55.0)	3.1(1.5, 5.5)	2.8 (2.1,4.6)	0.03
Marital status	Married	9 (9.2)	36(6.2)	1	1	
	Single	56(57.1)	367(63.5)	4.3(2.0, 7.9)	2.6 (1.8, 3.8)	0.01
	Divorced	14 (14.3)	118(20.4)	4.1(2.2, 7.2)	2.4 (1.3, 3.9)	0.02
	Widowed	19 (19.4)	58(10.0)	3.6 (2.5, 6.7)	2.3 (1.7, 3.7)	0.03
Education Level	Illiterate	53(54.1)	87(15.1)	5.7(3.3,9.8)	2.5 (1.9, 4.8)	0.00
	Primary(1–8)	26 (26.5)	242(41.9)	2.5(1.6, 6.7)	2.1 (1.8, 3.6)	0.01
	Secondary(9– 12)	15 (15.3)	24(4.2)	1.5 (1.1, 5.3)	0.5 (0.3, 3.6)	0.21
	college	4(4.1)	71(12.3)	1	1	
Disclosure status	Yes	17 (17.3)	450(77.9)	1	1	
	No	211(31.)	128(22.1)	5.6 (4.3,11.4)	3.6 (1.7, 9.5)	0.03
BMI	Normal	6 (6.1)	240(41.5)	1	1	
	Moderate malnutrition	31(3.1)	298(51.6)	3.6 (2.3,9.4)	2.5(1.7, 7.5)	0.01
	Severe malnutrition	61(6.1)	40(6.9)	5.6 (4.3,8.3)	3.7 (1.6, 6.7)	0.01
Functional status	Working	29 (29.6)	372(64.4)	1	1	

Variables	Classification	Death 98 (%)	Censored 578 (%)	CHR (95%)	AHR (95%)	P value
	Ambulatory	37 (37.8)	189(32.7)	1.3 (1.9, 3.6)	1.04(0.9, 2.2)	0.04
	Bedridden	32 (32.6)	17 (2.9)	6.1 (4.7,18.6)	3.7(2.4,13.8)	0.03
TB-co infection	No TB	19 (19.4)	224(38.8)	1	1	
	INH Prophylaxis	21 (21.4)	172 (29.8)	1.2 (0.8, 3.1)	1.1(0.7, 2.9)	0.04
	TB treatment	58 (59.2)	182(31.5)	4.5 (3.5, 7.8)	2.9(1.5, 5.5)	0.02
Weight	< 40 kg	52 (53.1)	408 (70.6)	4.6(1.9, 6.7)	1.8(0.5, 3.7)	0.01
	40–60 kg	30 (30.6)	88(15.2)	1.1(0.7, 2.4)	0.7(0.4,1.7)	0.04
	> 60 kg	16 (16.3)	82(14.2)	1	1	
WHO clinical stage	Stage I&II	8(8.2)	394(68.2)	1	1	
	Stage III	58 (59.2)	177(30.6)	3.5(2.1, 5.4)	1.7 (1.4, 3.2)	0.01
	Stage IV	32 (32.6)	7 (1.2)	7.1(3.8, 11.8)	3.7 (1.7, 5.3)	0.00
CD4 count	< 200	57 (58.2)	301 (52.1)	4.2 (1.5,10.3)	2.3(1.8, 6.3)	0.01
	201–350	28 (28.6)	221 (38.2)	2.3 (0.8, 6.6)	1.7(0.6, 4.9)	0.02
	> 350	13 (13.2)	56 (9.7)	1.60(1.04, 2.)	1	
follow up within Catchment area	yes	19 (19.4)	524(90.7)	1	1	
	No	79(80.6)	54(9.3)	6.9 (3.9, 9.2)	3.6 (1.5, 5.4)	0.01
Have Care giver	Yes	17 (17.3)	401(69.4)	1	1	
	No	81(82.7)	177(30.6)	4.9(1.2, 4.9)	2.9 (2.0,17.2)	0.03
Residence	Urban	24 (24.4)	338(58.5)	4.10(1.5,11.3)	1	

Variables	Classification	Death 98 (%)	Censored 578 (%)	CHR (95%)	AHR (95%)	P value
	Rural	74 (75.6)	240(41.5)	2.3 (0.8, 6.6)	2.1(1.4, 3.3)	0.02
alcohol and Kchat use	Yes	68(69.4)	329(56.9)	3.6 (1.1,2.6)	1.8 (1.4, 5.4)	0.03
	No	30(30.6)	249(43.1)	1	1	
infection	Yes	92(93.9)	395(68.3)	5.9 (3.9, 9.3)	2.5 (1.9, 7.1)	0.03
	No	7(6.1)	183(31.7)	1	1	
Patient Status	Not Known	12 (12.2)	156(26.9)	1	1	
	Clinical failure	36 (36.7)	142(24.6)	4.1 (1.5,10.3)	2.1 (1.4, 2.8)	0.02
	Immunologic failure	24 (24.5)	127(21.9)	2.4(0.7, 5.6)	1.7 (1.3, 2.7)	0.02
	Virologic Failure	26 (26.5)	153(26.5)	2.8(1.3,3.7)	1.7 (1.3, 2.3)	0.02
ART regimen	1A	24(24.5)	136(23.5)	1	1	
	1B	18(18.4)	204(35.3)	1.8(0.7, 3.3)	1.3(0.1, 3.5)	0.04
	1C	21(21.4)	85(14.7)	4.1 (1.5,11.3)	2.3 (1.8, 7.2)	0.03
	1D	15(15.3)	88(15.2)	3.1 (1.7,10.1)	1.3(1.0, 8.8)	0.03
	1E	11(11.2)	122(21.1)	1.9(0.5, 5.6)	1.5(1.3,8.4)	0.41
	1F	9(9.2)	105(18.2)	1.7(0.4,9.4)	0.6(0.2, 7. 3)	0.04
Liver F test	Normal (0–50)	12(12.2)	267(46.2)	1	1	
	Abnormal (>50)	69(70.4)	284(49.1)	6.4(3.8, 7.4)	4.1(2.4, 6.7)	0.01
	Not done	17(17.3)	32(5.5)	1.7(1.5,9.3)	0.6(0.2, 6.4)	0.04

Discussion

ART Program has created a significant change in improving both health status and life expectance of PLWHA. However, first-line drug resistance and death from HIV related causes are quiet formidable challenges in Sub-Saharan Africa, including Ethiopia. In this study, 14.9% cumulative incidence of HIV mortality was reported in patient on ART. This is lower than finding of a study conducted in Debre-Markos, west Ethiopia (49). The variation could be due to the fact that in the earlier study, participants were

recruited both from health centers and hospitals and the service from health Center is not comprehensive as Hospital.

The study revealed that mortality was found to be higher among (65.3%). This finding is in line with the national EDHS data (2016) in which the prevalence of HIV infection among females was two times higher than males (50). Studies from African countries also support this finding. The prevalence of HIV related death among female and male was reported to be 6.5% and 4.7% in Kenya (51), and 7.5% and 4.3% in Uganda (52), respectively. The fact that rates of HIV infection and death among women are higher imply not only gender difference but also gender inequality, leaving women more vulnerable to its impact, which implies the need for strengthening HIV care and support more among females to curb the challenge.

In this study, the highest number of deaths was noticed in the 2nd and 3rd years of follow up. This could be attributed to eligibility criteria, change of guideline for ART initiation and project driven approach care as well as using test and treat immediately, regardless of CD4 count and WHO clinical staging (53, 54). The other reason may be because of Ethiopia doesn't implement strict follow up care (55) for patients with good adherence at 1st year and 2nd the trust in and awareness of modern medicine was poor, and conversely high in traditional medicine, which patients could consider as an alternative option (56, 57), and the presents of nutrition by prescription program and accessibility of ART was deprived during the period as compared to today. On the other hand, mortality declined in years 2015 and 2016 as compared with earlier years. This might be because of improvement, accessibility and awareness of ART users and service providers by the Federal Ministry of Health (58). Marital status was significantly associated with the survival status of ART users. Those who were not married were more affected by HIV related death compared to married ones. This finding is similar to finding of a study done in developing countries (59, 65). This might be due to the fact that those adult PLWHA who were out of marriage were at higher risk of exposure to unhealthy lifestyles, as well as they might have been challenged with stigma and discrimination emanated from the community, which can in turn lead to poor compliance to treatment. Lack of or minimal participation in any working opportunity to generate income can push them to more risks compared to individuals who have social and family support. On the other hand, those who were not married might have wider sexual network, which leads to super infection of HIV and infections of sexually transmitted diseases that can result in double burden increasing risk of mortality.

Mortality was also found to be higher among adult PLWHA who had developed immunologic failure, in WHO clinical stages III and IV, with low CD4 count, with moderate to severe malnutrition, in poor functional status and with impaired liver function test compared to their counterparts in the five year follow up period. These findings are in line with other studies (80 – 65). This indicates that those vulnerable PLWHA to having an advanced stage of the disease are usually accompanied by multiple challenges and co-morbidities. In addition, such outcome indicates a very low performance to meet the expected UNAIDS targets for Ethiopia by 2020 in spite of the fact that Ethiopia has launched “appointment spacing model approach care (few/two visit per year of clinics by PLWHA)”.

In this study, mortality was higher among adult PLWHA who had developed immunologic failure, WHO clinical stages III and IV, low CD4 count, severe and moderate malnutrition, bed ridden in functional status and abnormal liver function test results compared to their counterparts in the five year follow up period. These findings are in line with other studies (80 – 65). This indicates that those vulnerable PLWHA to having an advanced stage of the disease are usually accompanied by multiple challenges, co-morbidities and humble prediction of outcome. In addition, such outcome indicates a very low performance to meet the expected UNAIDS targets for Ethiopia by 2020 in spite of the fact that Ethiopia has launched “appointment spacing model approach care (few/two visit per year of clinics by PLWHA)”.

In this study, death rates were higher among patients with HIV who had baseline Liver Function Test, ART Regimen, TB-Coinfection, Alcohol and Kchat use) and rural Residence, advanced baseline WHO clinical stage, and who developed clinical, virological and immunologic failure as compared with their counterparts. This finding is in line with studies in Axum, Jinka, North west Ethiopia, and south west Ethiopia (66–69). This similarity could be explained because of the same ART care system and similar sociocultural conditions in study population. In addition this similarity could be termed through the document, these PLWHA are defenseless for advanced stage of disease escorted by numerous health problem outcomes, like underprivileged for bad prediction and following mortality as end outcome.

Strengths And Limitations

This study has some limitations. First, it is a one zone public hospitals study which limits its national representativeness. Second, it has been used patient records, which limits the number of variables included into the models. Thirdly, the data we used are secondary data and cannot incorporate other possible predictors of HIV-related mortality such as drug resistance, substance abuse, unspecified OIs, House hold food security status, Livelihood status and other possible confounders

As strength of this study only focusing on cost and stigma and discrimination doesn't give sense unless, the health system is working on the crucial change of quality health care, life expectancy of clients, quality of life, understanding that all patient didn't have same livelihood in Economical states, cultural, residence, support, ART retention, Access to health care and Information, level of understanding to HIV care, and fear of inadvertent disclosure due to having a large volume of medication and concerns regarding safety and storage of medication for prolonged periods at home.

Conclusions

In conclusion, the incidence of HIV mortality was 11 deaths per 1000 person- months, whereas most deaths (20%) occurred during the 18–24 month follow up period interval. Females are at higher probability of dying from AIDS related causes. Marital status, functional status, education level, disclosure of HIV status, having care givers/support, abnormal test of liver function, presence of opportunistic infection, malnutrition were found to be independent predictors of AIDS related mortality.

These findings imply that applying an action/intervention towards these leading cases of mortality as routine and as part of the new approach care “appointment spacing model care (ASMC)” can reduce mortality and can be a sustainable clinical care other than project driven intervention of HIV care. Except children less than 14 years old, pregnant women and clients other than good adherence (not stable per World Health Organization criteria) were enrolled in the ASMC approach care in Ethiopia, which minimizes the direct and indirect cost of frequent visit, stigma and discrimination of clients.

But, from this study only focusing on cost and stigma and discrimination doesn't give sense unless, the health system is working on the crucial change of quality health care, life expectancy of clients, quality of life, understanding that all patient didn't have same livelihood in Economical states, cultural, residence, support, ART retention, Access to health care and Information, level of understanding to HIV care, and fear of inadvertent disclosure due to having a large volume of medication and concerns regarding safety and storage of medication for prolonged periods at home.

The models also require ongoing evaluation and further adaptation in order to address gaps, such as reaching clients who are at high risk of loss to follow up. Improving access to health services, including ART, and support for retention in care is enhanced by decongestion of high-volume clinics. This takes place through decentralization of services to, for example, community service outlets, and through task shifting beyond hospital/Health center-initiated management of ART (HIMART) by deploying community cadres such as community health workers, peer educators and PLWHA.

Abbreviations

AIDS: Acquired Immunodeficiency Syndrome, **AFB:** Acid Fast Bacilli, **ART:** Antiretroviral Therapy, **ASMC:** Appointment spacing model care, **BMI:** Body mass index, **EDHS:** Ethiopian Demographic Health survey, **GFFA:** Global Fund to fight AIDS, **ART:** Highly Active Antiretroviral Therapy, **HAPCO:** Prevention and Control Office, **Hg:** Hemoglobin, **HIV:** Human immunodeficiency virus, **KM:** Kaplan Meier, **MSC:** Management Science for Health, **OI:** Opportunistic Infection, **TB:** Tuberculosis, **WHO:** World Health Organization.

Declarations

Ethical Approval and consent to participants

Waiver of the consent was obtained from the office of institutional ethical review board (IRB) of the Institute of Health Jimma University and the reference number was (IHRPG/807/17). The data access permission was obtained from Jimma zone five public hospitals (Jimma Medical Center, Shenen Gibe, Agaro, Seka and Limmu-Genet hospitals) board. We extracted an anonymised data from the record and no participant was taken part in the study. The data and collected information was kept and locked in a filing cabinet with the key only accessible to principal investigator (PI) and the computer files were protected with passwords that only the PI knows. We couldn't use any individual-level data from inception

to this manuscript. The results were also maintained using aggregated report rather than individual characteristics in any aspect of the data throughout all steps and manuscript preparation. These data were not identifiable; therefore informed consent was not required.

Consent for publication:

Not required

Availability of data and materials:

all data revealed to the study are included in the article or the data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they do not have competing interest.

Author Information

ANT

MPH in RH, assistance professor in the Department of population and Family Health, Faculty of Public Health, Jimma University, Ethiopia

TBL

MD, MSC in human nutrition, PhD in human nutrition, professor of human nutrition, postgraduate Directorate, Jimma University, Ethiopia

EKG

MD, Internist, PhD of infectious Disease, associated professor in the Departments of Internal Medicine, Jimma Medical Center, Jimma University, Ethiopia

MG

BSC in Biostatistics, MSC in Biostatistics, assistance professor in the Department of Epidemiology, Faculty of Public Health, Jimma University, Ethiopia

DA

BSC in Health Education and behavioral science, MPH in health education and behavioral science in the Department of Health Behaviors and Society, Faculty of Public Health, Jimma University, Ethiopia

LSD

MPH in Public Health, PhD in Epidemiology, associated professor, department head of Epidemiology in the Faculty of Public Health, Jimma University, Ethiopia

Funding:

This manuscript didn't have any 'Funding opportunity for publication services, Even though Jimma University institute of health was funded for proposal preparation, tool development, data collection, data entry and analysis. The views presented in the article are that of the author and are not views of the funding organization.

Authors' contributions:

all authors have read and approved the final manuscript. ANT and LSD: Involved in the inception, design, data acquisition, analysis and interpretation, and wrote the manuscript. EKG and TBL: Participated in design, data acquisition and analysis, administrative matters and reviewed the manuscript. MG and DA: Participated in data acquisition, data management and analysis as well as critically reviewed the manuscript. All authors are responsible for the overall content of this paper.

Acknowledgements:

All study hospitals are greatly acknowledged for the information they provided. Research assistants are also appreciated for collecting, supervising and encoding the data. Jimma University Institute of health is highly acknowledged for covering the cost of the study.

References

1. Moore RD. Epidemiology of HIV Infection in the United States: Implications for Linkage to Clinical Infectious Diseases 2011; 52(2):S208-S13.
2. The Global HIV/AIDS Epidemic: AIDS.gov; 2013, accessed, 01April, 2015.
3. Wang H, Wolock TM, Carter A, et al. Estimates of global, regional, and national incidence, prevalence, and mortality of HIV, 1980-2015: the Global Burden of Disease Study 2015. *Lancet HIV* 2016;3(8):361-87.
4. The gap report. Geneva, Switzerland, 2014.
5. CSA, ICF. Ethiopian Demographic Health Survey 2016. Addis Ababa and Calverton: Central Statistical Agency (Ethiopia) and ICF International, 2018:36-41
6. Max R, Hannah R. "HIV / AIDS": OurWorldInData.org; 2018 [cited 2018 13 September]. Accessed 13 September 2018.

7. Profiles of 41 Development Partners in Ethiopia. Addis Ababa: Development Assistance Group (DAG) Ethiopia, 2015.
8. Assefa Y, Gilks CF, Lynen L, et al. Performance of the Antiretroviral Treatment Program in Ethiopia, 2005-2015: strengths and weaknesses toward ending AIDS. *Int J Infect Dis* 2017;60:70-76.
9. EHNRI, MOH. HIV Related Estimates and Projections for Ethiopia. Addis Ababa: Ethiopian Health and Nutrition Research Institute and Ethiopian Ministry of Health, 2012.
10. Carpenter CC, Fischl MA, Hammer SM, et al. Antiretroviral therapy for HIV infection in Updated recommendations of the International AIDS Society-USA panel. *Jama* 1997;277(24):1962-9.
11. Mekonnen Yared, Rachel Sanders, Senait Tibebe, et al. Equity and Access to ART in Ethiopia. USA: USAID, 2010.
12. UNAIDS. Ending AIDS: Progress towards the 90–90–90 targets. Geneva: UNAIDS, 2017. 26. MOH. Country Progress Report on the HIV Response: Federal Democratic Republic of Ethiopia. Addis Ababa, Ethiopia: Ministry of Health, 2014.
13. Assefa Y, Damme W, and Mariam D. Toward Universal Access to HIV Counseling and Testing and Antiretroviral Treatment in Ethiopia: Looking Beyond HIV Testing and ART *AIDS Patient Care & STDs* 2010;24(8):521-25
14. Gilks C, Crowley S, Ekpini R, et al. The WHO public-health approach to antiretroviral treatment against HIV in resource-limited settings. *Lancet* 2006;368(9534):505-10
15. UNAIDS. Getting to Zero selected as World AIDS Day theme Geneva, Switzerland 2011 [cited 2018 15 June].
16. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: what's new? Geneva, Switzerland: World Health Organization, 2015.
17. Kranzer K, Govindasamy D, Ford N, et al. Quantifying and addressing losses along the continuum of care for people living with HIV infection in sub-Saharan Africa: a systematic *Journal of the International AIDS Society* 2012;15(2):17383.
18. Gardner EM, McLees MP, Steiner JF, et al. The Spectrum of Engagement in HIV Care and its Relevance to Test-and-Treat Strategies for Prevention of HIV Infection. *Clinical Infectious Diseases* 2011;52(6):793-800.
19. Cheng W, Tang W, Han Z, et al. Late Presentation of HIV Infection: Prevalence, Trends, and the Role of HIV Testing Strategies in Guangzhou, China, 2008-2013. *AIDS* 2016;2016:1631878
20. Jeong SJ, Italiano C, Chaiwarith R, et al. Late Presentation into Care of HIV Disease and Its Associated Factors in Asia: Results of TAHOD. *AIDS Res Hum Retroviruses* 2016;32(3):255-61.
21. Mitiku I, Arefayne M, Mesfin Y, et al. Factors associated with loss to follow-up among women in Option B+ PMTCT programme in northeast Ethiopia: a retrospective cohort *Journal of the International AIDS Society* 2016;19(1):20662.

22. Thelma ET, Anna Marie Celina GG, Ekaterina VK, et al. Factors Associated with Loss to Follow-up during Treatment for Multidrug-Resistant Tuberculosis, the Philippines, 2012– *Emerging Infectious Disease journal* 2016;22(3)
23. Tesfahuneygn G, Medhin G, Legesse M. Adherence to Anti-tuberculosis treatment and treatment outcomes among tuberculosis patients in Alamata District, northeast Ethiopia. *BMC Research Notes* 2015;8: 503.
24. Nabukeera-Barungi N, Elyanu P, Asire B, et al. Adherence to antiretroviral therapy and retention in care for adolescents living with HIV from 10 districts in Uganda. *BMC infectious diseases* 2015;515-20.
25. Bezalem Eshetu Yirdaw, Wenchekeo E. Immunological recovery time of adult AIDS patients on ART: A case study at Felege-Hiwot Referral Hospital, Bahir-Dar, Ethiopia. *Ethiop J Health Dev* 2014;28(2):126-35.
26. Kokeb M, Degu G. Immunological Response of HIV-Infected Children to Highly Active Antiretroviral Therapy at Gondar University Hospital, North-Western Ethiopia. *Ethiop J Health Sci* 2016;26(1):25-30.
27. Zheng J, Zhao D. Clinical, immunological, and virological outcomes of pediatric antiretroviral therapy in central China. *BMC Research Notes* 2014;7:419-426
28. Petersen ML, van der Laan MJ, Napravnik S, et al. Long term consequences of the delay between virologic failure of highly active antiretroviral therapy and regimen modification. *AIDS (London, England)* 2008;22(16):2097-106.
29. Purchase S, Cunningham J, Esser M, et al. Keeping kids in care: virological failure in a paediatric antiretroviral clinic and suggestions for improving treatment outcomes. *African journal of AIDS research : AJAR* 2016;15(3):301-9.
30. Berhanemeskel E, Beedemariam G, Fenta TG. HIV/AIDS related commodities supply chain management in public health facilities of Addis Ababa, Ethiopia: a cross-sectional survey. *Journal of pharmaceutical policy and practice* 2016;9:11.
31. Assefa Y, Alebachew A, Lera M, Lynen L, Wouters E, Van Damme W. Scaling up antiretroviral treatment and improving patient retention in care: lessons from Ethiopia, 2005-2013. *Globalization and Health*. 2014;10:43-
32. Fetzer BC, Hosseinipour MC, Kamthuzi P, Hyde L, Bramson B, Jobarteh K, et al. Predictors for mortality and loss to follow-up among children receiving anti-retroviral therapy in Lilongwe, Malawi. *Tropical medicine & international health*. 2009;14(8):862-9.
33. Davies MA, Moultrie H, Eley B, Rabie H, Van Cutsem G, Giddy J, et al. Virologic failure and second-line antiretroviral therapy in children in South Africa—the leDEA Southern Africa collaboration. *Journal of acquired immune deficiency syndromes (1999)*. 2011;56(3):270-8.
34. Jerene D, Endale A, Hailu Y, Lindtjorn B. Predictors of early death in a cohort of Ethiopian patients treated with ART. *BMC infectious diseases*. 2006;6:136.
35. .Koye DN, Ayele TA, Zeleke BM. Predictors of mortality among Adults on Antiretroviral Therapy at a referral hospital, Northwest Ethiopia: a retrospective follow up study. *BMC Pediatr*. 2012;12:161.

36. Bhatta L, Klouman E, Deuba K, Shrestha R, Karki DK, Ekstrom AM, et al. Survival on antiretroviral treatment among adult HIV-infected patients in Nepal: a retrospective cohort study in Far-western region, 2006-2011. *BMC infectious diseases*. 2013;13:604.
37. Gils T, Bossard C, Verdonck K, et al. Stockouts of HIV commodities in public health facilities in Kinshasa: Barriers to end HIV. *PloS one* 2018;13(1):e0191294.
38. Jamieson D, Kellerman SE. The 90 90 90 strategy to end the HIV Pandemic by 2030: Can the supply chain handle it? *Journal of the International AIDS Society* 2016;19(1):20917.
39. Ankomah A, Ganle JK, Lartey MY, et al. ART access-related barriers faced by HIV-positive persons linked to care in southern Ghana: a mixed method study. *BMC infectious diseases* 2016;16(1):738.
40. Pellowski JA. Barriers to care for rural people living with HIV: A review of domestic research and health care models. *The Journal of the Association of Nurses in AIDS Care : JANAC* 2013;24(5):422-37.
41. Hontelez JA, Tanser FC, Naidu KK, et al. The Effect of Antiretroviral Treatment on Health Care Utilization in Rural South Africa: A Population-Based Cohort Study. *PloS one* 2016;11(7):e0158015.
42. Joseph D T, Lai Sze T, Brian H, et al. Enhancing Public Health HIV Interventions: A Qualitative Meta-Synthesis and Systematic Review of Studies to Improve Linkage to Care, Adherence, and Retention. *EBioMedicine*
43. Agbonyitor M. Home-based care for people living with HIV/AIDS in Plateau State, Nigeria: Findings from qualitative study. *Global Public Health* 2009;4(3):303-12.
44. Marya Viorst G, Linda M C, Charles M C, et al. Using the multiphase optimization strategy (MOST) to optimize an HIV care continuum intervention for vulnerable populations: a study protocol. *BMC public health* 2017;17:383.
45. Miho S, Belkis W, Gabrielle Om. Barriers to and Factors Facilitating Adherence to Antiretroviral Therapy from the Perspectives of Patients in Maqala City, Tigray Region, Nilo-Ethiopian Studies 2016;21:15-28.
46. Porter KE, Brennan-Ing M, Burr JA, et al. Stigma and Psychological Well-being Among Older Adults With HIV: The Impact of Spirituality and Integrative Health Approaches. *Gerontologist* 2017;57(2):219-28.
47. Shamila Suliman L. Integration of African traditional health practitioners and medicine into the health care management system in the province of Limpopo. *Uni* , 2010.
48. CSA, ICF. Ethiopian Demographic Health Survey 2016. Addis Ababa and Calverton: Central Statistical Agency (Ethiopia) and ICF International, 2018:36-41.
49. Abebe N, Alemu K, Asfaw T, et al. Survival status of HIV positive adults on antiretroviral treatment in Debre Markos Referral Hospital, Northwest Ethiopia: Retrospective cohort *Pan African Medical Journal* 2014;17doi: 10.11604/pamj.2014.17.88.3262.
50. Tso LS, Best J, Beanland R, et al. Facilitators and barriers in HIV linkage to care interventions: qualitative evidence Review *AIDS(London, England)* 2016;30(10):1639-

51. 2015 Kenya HIV estimates (MOH). Nairobi: Ministry of Health, 2015.
52. Uganda Population-Based HIV Impact Assessment UPHIA 2016–2017, 2017.
53. Kagee A, Remien RH, Berkman A, et al. Structural barriers to ART adherence in Southern Africa: Challenges and potential ways forward. *Glob Public Health* 2011;6(1):83-97.
54. Loeliger KB, Niccolai LM, Mtungwa LN, et al. Antiretroviral therapy initiation and adherence in rural South Africa: community health workers' perspectives on barriers and AIDS care 2016:1-12
55. Gesesew HA, Ward P, Woldemichael K, et al. Prevalence, trend and risk factors for antiretroviral therapy discontinuation among HIV-infected adults in Ethiopia in 2003-2015. *PloS one* 2017;12(6):e0179533.
56. Gesesew HA, Ward P, Woldemichael K, et al. Late presentation for HIV care in Southwest Ethiopia in 2003–2015: prevalence, trend, outcomes and risk factors. *BMC infectious diseases* 2018;18(1):59.
57. Gesesew H, Ward P, Hajito K, et al. Immunological failure in HIV-infected adults from 2003to 2015 in Southwest Ethiopia: A retrospective cohort study *BMJ Open* 2018;8:e017413.
58. Alemu A and Sebastian M, “Determinants of survival ´ in adult HIV patients on antiretroviral therapy in Oromiyaa, Ethiopia,” *Global Health Action*, vol. 3, p. 5398, 2010
59. EHNRI, MOH. HIV Related Estimates and Projections for Ethiopia. Addis Ababa: Ethiopian Health and Nutrition Research Institute and Ethiopian Ministry of Health, 2012.
60. WHO, *AIDS Epidemic Update 2017*, http://data.unaids.org/pub/report/2017/jc1784_epic_update_2017_en.pdf.
61. Kirschner D, Webb GF, Cloyd M. Model of HIV-1 disease progression based on virus-induced lymph node homing and homing-induced apoptosis of CD4+ lymphocytes. *Journal of acquired immune deficiency syndromes* (1999). 2000;24(4):352-62.
62. Moore RD. Epidemiology of HIV Infection in the United States: Implications for Linkage to Care. *Clinical Infectious Diseases*. 2011;52(suppl 2):S208-S13.
63. Damtew B, Mengistie B, Alemayehu T. Survival and determinants of mortality in adult HIV/AIDS patients initiating antiretroviral therapy in Somali region, Eastern Ethiopia. *Pan Afr Med J*. 2015; 22:1–8.
64. Ethiopian HIV/AIDS Prevention and Control Office Addis Ababa: HAPCO; 2000 [cited 2015 23 March].
65. Carpenter CC, Fischl MA, Hammer SM, Hirsch MS, Jacobsen DM, Katzenstein DA, et al. Antiretroviral therapy for HIV infection in 1997. Updated recommendations of the International AIDS Society-USA panel. *Jama*. 1997;277(24):1962-9.
66. Tadesse K, Haile F, Hiruy N. Predictors of Mortality among Patients Enrolled on Antiretroviral Therapy in Aksum Hospital, Northern Ethiopia: A Retrospective Cohort Study. *PloS one*. 2014;9(1):e87392.
67. Tachbele E, Ameni G. Survival and predictors of mortality among human immunodeficiency virus patients on anti-retroviral treatment at Jinka Hospital, South Omo, Ethiopia: a six years retrospective cohort study. *Epidemiol Health* 2016; 38.

68. Ravimohan S, Tamuhla N, Steenhoff AP. Early immunologic failure is associated with early mortality among advanced HIV-infected adults initiating antiretroviral therapy with active tuberculosis. *J Infect Dis* 2013;208(11):1784-93.
69. Reniers G, Blom S, Calvert C, et al. Trends in the burden of HIV mortality after roll-out of antiretroviral therapy in KwaZulu-Natal, South Africa: an observational community cohort *Lancet HIV* 2017;4(3):e113-e21.

Figures

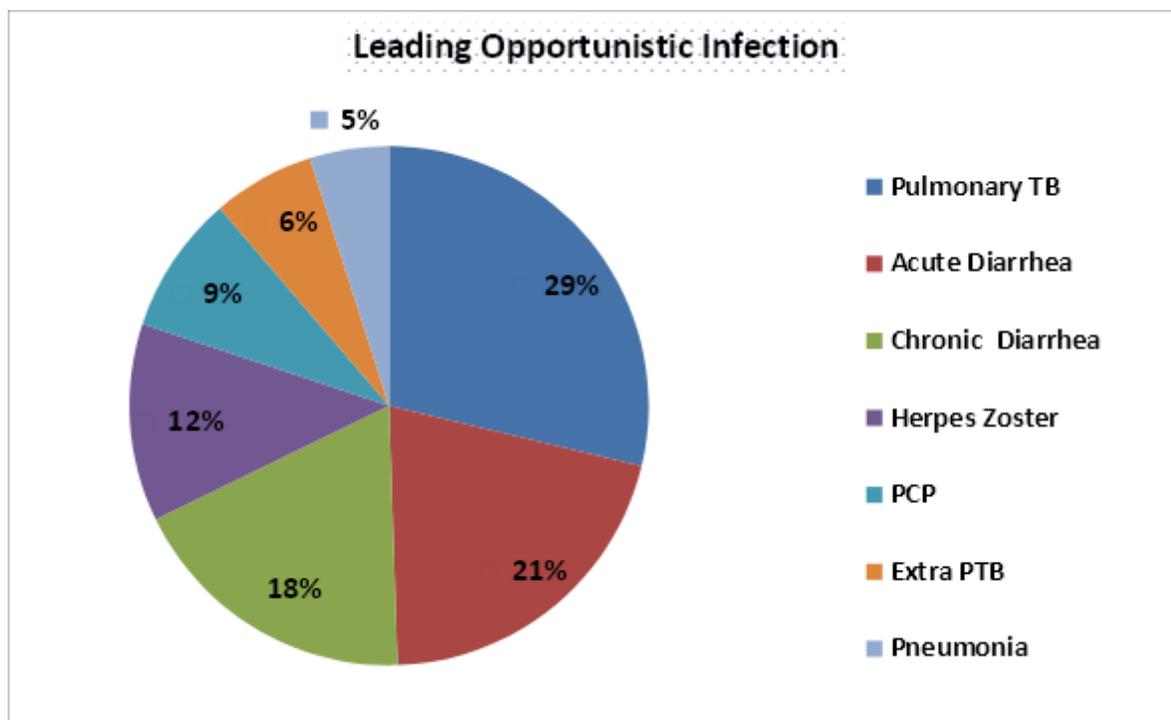


Figure 1

Leading opportunistic infection among adult PLWHA on ART, Jimma zone Public Hospitals, September 2012 – August 2016

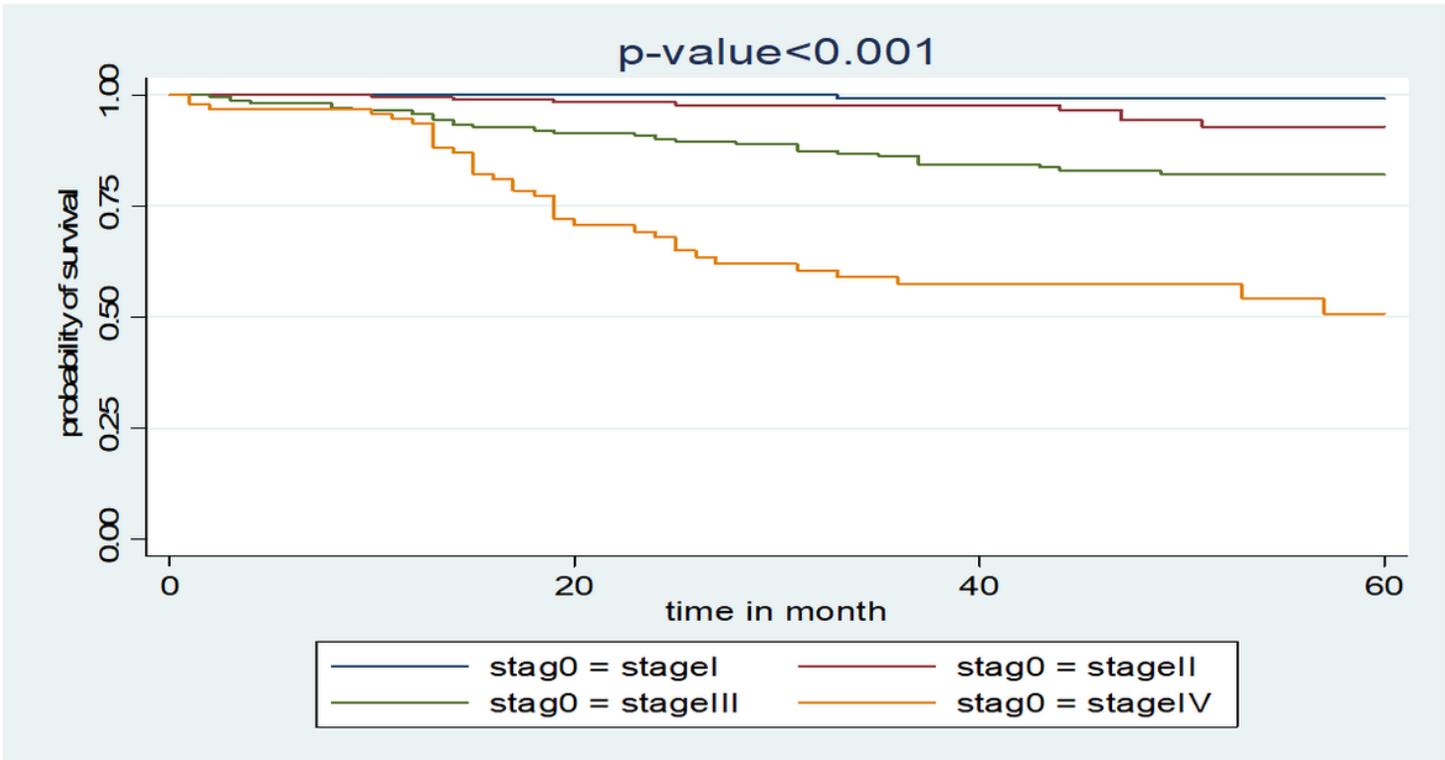


Figure 2

Kaplan Meier survival curve of PLWHA on ART follows up Jimma zone public hospitals by baseline WHO stages September 2012 – August 2016.