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Incidence and predictors of attrition among adolescents on antiretroviral therapy in Public Hospitals, South Ethiopia: A multicenter retrospective follow-up study

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ABSTRACT

Objective Despite the increased access and utilization of the antiretroviral therapy resulted in reduction of acquired immunodeficiency syndrome related morbidity and mortality, attrition from antiretroviral therapy care among adolescents continue to be a critical challenge for antiretroviral therapy program effectiveness. Hence, determining the incidence of attrition and predictors among adolescents on antiretroviral therapy will help in improvement of the health of adolescents living with Human Immunodeficiency Virus.

Design A multi-center retrospective follow-up study.

Settings Public Hospital in south Ethiopia

Participants Adolescents (10-19 years) on antiretroviral therapy from January 01, 2014 to December 30, 2023 (n=434). The data was collected from patients' chart and electronic data records.

Primary outcome measures The occurrence of attrition (death and loss to follow-up) and predictors were evaluated by using Cox proportional hazards.

Results The overall incidence density of attrition was 3.33 (95% CI: 2.65, 4.18) per 100 PYO. Age 15 to 19 years (AHR=1.88; 95% CI: 1.12, 3.18), death of both the parents (AHR=2.19; 95% CI: 1.04, 4.61), no formal education (AHR=3.16; 95% CI: 1.48, 6.77), CPT non utilization (AHR=1.73; 95% CI: 1.03, 2.91), not changed regimen (AHR=6.16; 95% CI: 3.56, 10.66), and poor treatment adherence (AHR=5.16; 95% CI: 2.35, 11.32) were predictors of attrition.

Conclusion The incidence of attrition was comparable at the study setting. Moreover, older age, death of parents, no formal education, CPT non user, unchanged baseline regimen, and suboptimal treatment adherence were the identified predictors of attrition. Special attention should be given to old aged, no formal education, orphaned, and those with poor baseline clinical

characteristics. Moreover, early tracing of missed follow-up schedules, improving adherence support, and increasing contacting frequency in order to reduce attrition is highly encouraged.

STRENGTHS AND LIMITATIONS OF THIS STUDY

To estimate the incidence of attrition among HIV positive adolescents participated in the study, the study used a long follow-up period.

As attrition is a warning indicator for drug resistance, determining attrition is very important to monitor ART drug resistance.

Due to the retrospective nature of the study, the effect of some important predictor variables like; viral load and CD4 count, was not assessed because of incomplete record.

INTRODUCTION

Human immunodeficiency virus (HIV) is an infection that weakens the immune system by attacking white blood cells, with the most severe form being acquired immunodeficiency syndrome (AIDS). Antiretroviral therapy (ART) can be used to treat and prevent HIV [1].

In 2022, about 1.65 million adolescents aged 10-19 were living with HIV, and 34,000 AIDS-related deaths occurred among them, globally [2 3]. About 1.40 million, or 85%, of adolescents living with HIV (ALHIV) were from sub-Saharan Africa (SSA) [3]. Ethiopia is one the Sub-Saharan Africa countries with a total of 610,000 people living with HIV (PLHIV) and about 11,000 AIDS-related mortalities and 83% of those living with the disease were using ART [4].

The World Health Organization (WHO) defines adolescence as the period of life following childhood and preceding adulthood, precisely between the ages of 10 and 19 years. Adolescents' rapid physical, cognitive, and psychological development significantly impacts their emotions, thoughts, decisions, and interactions with their environment [5].

Attrition refers to the disruption in ART care, including lost patients, deaths, and those who stopped treatment, indicating progress towards achieving the 95-95-95 targets [6]. It continues to be a great public health problem among adolescents. Adolescents have significantly higher attrition rates from ART than adults without being privileged from and getting access to HIV care and treatment service, these results in relatively poorer outcomes [7].

Evidence from Global cohort collaboration reported that 30% and 3.9% of HIV positive adolescents were lost to follow-up and died worldwide, respectively [8]. Based on the studies conducted in different countries, the incidence of attrition from ART care among Adolescents was anticipated to be high. Studies done in Myanmar [9] and Thailand [10] revealed that attrition rates among ALHIV were determined to be 6.4 per 100 person years of observations (PYO) and 29.5%, respectively. Even though there is a paucity of evidence regarding the magnitude of attrition (a combination of lost follow-up and death) in Sub-Saharan Africa, a systematic review showed that 15.07% of ALHIV experienced attrition due to lost follow-up from ART after initiation of the treatment [11]. In Ethiopia, about 28.1% [12] of adolescents aged ten to nineteen years experienced attrition from HIV care and 11.1% attrite from care due to death [13]. Attrition of patients from HIV care and treatment after ART initiation is resulting in an increase in poor treatment outcomes, including drug resistance, increased health care costs, preventable onward HIV transmission, and avoidable morbidity and death [14]. It can weaken the continuing provision of the opportunistic infection prophylaxis, timely identification of treatment failure, and adverse events assessment [15]. In addition, attrition from HIV care also affected the 95-95-95 ambitious targets of UNAIDS which aimed at 95% viral suppression. Due to this impact of attrition, only 68% of PLHIV were virally suppressed and adolescents were highly in need of the lifelong treatment, care, and social support to have better treatment and health outcomes as they pass

through youth to adulthood [16]. Even though there is paucity in information on adolescent's viral suppression, 46% of children and adolescents were virally suppressed [17]. Attrition from the ART program can significantly impact households, often requiring orphaned children to assume responsibility for the household after the death of their young parents [18 19]. Factors associated with adolescent's attrition from HIV care and treatment including advanced HIV disease, low hemoglobin level, absence of social support, financial constraints, lower age, and year of ART initiation. Attrition is also associated with infection with tuberculosis (TB), non-disclosure, malnutrition, and Cotrimoxazole preventive therapy (CPT) utilization [9 14 20 21]. In order to minimize adolescents' attrition from HIV care and treatment service, different measures have been taken in Ethiopia. These include; decentralization of services, provision of ART drugs without charge, health education and counseling through community partners, and delivering phone text messages [14]. Attrition from care among ALHIV is continuously rising and continues to be a significant obstacle to ART program effectiveness despite the above-mentioned interventions.

According to WHO 2021 consolidated HIV guideline, total attrition (a combination of both death and loss to follow-up) is one of the early warning indicators and attrition ≥25% during reporting period is a warning sign of drug resistance [22]. Despite the country's growing adolescent population and high prevalence of adolescent HIV infections, Ethiopia's HIV/AIDS policies currently do not provide adequate regard to the unique needs of adolescents [7 23 24]. The current HIV care and treatment guideline in Ethiopia focused on young children (0 to 14 years of age) and adults (15 and above years old) and there are no guidelines specifically focusing on HIV care and treatment for ALHIV nationally [14]. Moreover, there is little indication of attrition from care among ALHIV on ART in Ethiopia, and none in the research settings. As a result, the purpose of

this study is to determine the incidence and predictors of attrition among adolescents on ART in South Ethiopia.

METHODS

Study design, period, and setting

A multi-center retrospective follow-up study was conducted in Gamo Zone and Ari Zones public hospitals in South Ethiopia from March 05, 2024 to April 05, 2024. Arba Minch town is the administrative center of the Gamo Zone. It is 505 Kilometer Southwest far from the capital city, Addis Ababa. Jinka town is the administrative center of Ari Zone in Southwest Ethiopia. It is about 563Km far from Addis Ababa. In these two zones there are two general and six primary public hospitals providing ART services with about 5,480 individuals currently on HIV care and treatment.

Population

All HIV positive adolescents (10-19 years) who were on ART in public hospitals of Gamo and Ari Zones were the source population. All randomly selected HIV positive adolescents (10-19 years) who were on ART in the public hospitals of Gamo and Ari Zones from January 01, 2014 to December 30, 2023 were the study population. All HIV positive adolescents (10-19 years) who were on ART and had at least one follow-up visit from January 01, 2014 to December 30, 2023 were included in the study. HIV-positive adolescents whose charts were with incomplete records (indicators of the outcome were not registered) were excluded from the study.

Sample size determination and sampling procedures

The sample size was determined by STATA software v14.0 for major predictor variables based on the following assumptions: Significance level (**α**) (two-sided) = 0.05, 95% confidence

interval, power of 80%, AHR = 1.58 for adolescents with HIV/TB co-infection who experienced attrition [25], standard deviation (variability) of covariates of interest = 0.5, the overall probability of event (attrition) (d) at the end of the study: 0.428 [25], and a 10% withdrawal probability was added for incomplete records yielding a total sample size of 434 to conduct the study.

First, in the two zones (Gamo and Ari) there are eight public hospitals; two General Hospitals and six Primary Hospitals. In these public hospitals, there are about 491 adolescents on ART from January 01, 2014 to December 30, 2023. The adolescents (10-19 years) was identified in each of the hospitals using medical record number (MRN) that was obtained from electronic data bases and patients charts was drown using the MRN. A sampling frame was developed by assigning codes to the identified medical records. Then proportional allocation was done to allocate the calculated sample size to each hospital. Finally, a simple random sampling technique was applied by using a computer-generated random number to include 434 eligible records of the study participants within the follow-up period (Figure 1).

Data collection tool, procedure, and personnel

Data were collected by using data extraction checklist developed in English from the standardized ART intake and follow-up forms from national HIV guideline [14], and by reviewing related literatures [8-13 21 25-30]. The follow-up period was from January 01, 2014 to December 30, 2023 and each participant can enter and leave the study at any time within the follow-up period. Adolescents who were categorized as LTFU during the study but were comeback to the care before the follow-up ends were counted as active because their coming back was the result of defaulter tracing intervention. The checklist contains socio-demographic, clinical and treatment-related characteristics of participants. The lists of study participants were taken from ART data clerk by using children's MRN or unique ART number. And charts of the adolescents were taken

from card rooms. Then data were collected by reviewing the registration books and patient follow-up charts by ten data collectors and eight supervisors.

Study variables

Dependent variable: Time to attrition, [Attrition as event and coded "1", and censored coded "0"]. Explanatory variables include: socio-demographic variables: Age, Sex, residence, educational status, and marital status of the adolescents; clinical-related variables: Entry point of care, WHO clinical staging, nutritional status, hemoglobin level, CD4 count, presence opportunistic infections, functional status, and disclosure status; and treatment-related variables: Type of baseline regimen, regimen change, treatment adherence, and CPT prophylaxis.

Operational definitions

Attrition (Event): If adolescents on ART were lost to follow-up or died within the follow-up period [31].

Censored: Adolescent on ART that were transferred out or alive and active on ART at the end of the study or turning 19 years of age [21 31].

Loss to follow-up: Adolescents that have not come for care for three or more consecutive months (≥90 days) after the last missed appointment for care and not registered as died or transferred out to other health facility [32].

Died: It refers to adolescents documented as "died" on the exit form of the patient.

Adherence**:** Is the extent to which an adolescent's behavior of taking ART medication with agreed-upon recommendations from a health-care provider. It was classified as; good: if ≥ 95% of the recommended doses were taken or ≤3 doses missed monthly, Fair: if 85-94% of the recommended doses were taken or 4-9 doses missed monthly, poor: if < 85% of the recommended doses were taken or ≥10 doses missed monthly [14].

Data quality assurance

Data were collected by health professionals who were trained on HIV comprehensive care and working on the clients' follow-up services. One day training was given to the data collectors (BSc in Public Health or Nursing) and supervisors (BSc in Public Health) on the way of reviewing charts and extract the needed data, study objectives, and keeping confidentiality. To check the consistency, completeness, and accuracy of the checklist, a pretest was conducted in Jinka General Hospital on 5% of the sample prior to the actual data collection. Necessary modifications was made accordingly prior to the starting of the actual data collection. The checklists was properly coded and numbered. The investigators and supervisors carried out a daily based data collection monitoring. Then appropriate feedback was given to the data collectors. After completing the data collection process, all the checklists was collected together and cross-checked for relevance.

Analysis

The data were checked, coded, cleaned, and then entered into Epi-Data version 3.1 before being exported to STATA version 14.0 for further management and analysis. An exploratory data analysis was performed to determine the presence of probable outliers, normality (by the Skewness and Kurtosis tests), and the level of missing values. Viral load and CD4 count showed missing values more than 30% and excluded from the analysis. Median, interquartile range, frequencies, and percentage was used for descriptive statistics. Person year of observation was used to compute the incidence density (Incidence of Attrition = [number of attrition/total number of person years of observation]*100). The Kaplan Meier curve was used to estimate survival time and compare survival experience among categories of predictor variables, and the significance of survival experience was checked using the log-rank test. A life table was

used to estimate the cumulative probability of survival at different time intervals. The Cox proportional hazards model was fitted after checking for proportional hazards assumption using graphical presentation (log-log plot), and Schoenfeld residual test (global test) (P-value=0.5585). To analyze the association between each independent variable and the outcome variable, a binary Cox proportional hazards model was fitted, and variables with a P-value < 0.25 in bivariable Cox regression were candidates for multivariable analysis. To find independent predictors of attrition, a multivariable Cox regression model with a backward likelihood ratio technique was built. The variance inflation factor (VIF) and tolerance was used to test for multicollinearity, the mean VIF = 1.23, showing no threat of multicollinearity. The Cox Snell residuals plot was used to assess the model's goodness of fit. The hazard function followed the 45-degree line very closely over time except for large values and fulfilled the assumption of Goodness of fit of the model. To identify statistically significant variables, AHR with a 95% confidence interval (CI) and matching P-value was used. The statistical significance was declared at the P-value < 0.05.

Patient and public involvement

None

RESULTS

Of 437 adolescents (10-19 years) who were initiated on ART from January 01, 2014 to December 30, 2023, the eight public hospitals, 409 were included in the analysis. The remaining 28 (14 due to incomplete data, 9 missing chart during data collection, and 5 clients with no follow-up after ART initiation) were excluded from the analysis because of not fulfilling the inclusion criteria.

Adolescent's sociodemographic characteristics

The median age of the adolescents included in the study was 14 with an interquartile range (IQR) of 12 to 18 years and of the study participants 213 (52.1%) were females. More than half of the adolescents were urban residents and for nearly half of the participants, both of their parents were alive. Regarding the marital status of the adolescents, majority (86.1%) were single and 16 (3.9%) were divorced after being married. Half, 206 (50.4%), of the adolescents participated in the study have attained primary educational status and only ten (2.4%) attained tertiary and above. More than two-third of the adolescent were students and nearly three percent, 12 (2.9%) of the participants were female sex workers (Table 1).

Table 1. Sociodemographic characteristics of adolescents on ART in public hospitals of Gamo and Ari zones, South Ethiopia, 2024

Variables	Categories	Frequency	Percentage (%)
Age (in years)	10-14	211	51.6
	15-19	198	48.4
Sex	Male	196	47.9
	Female	213	52.1
Residence	Urban	255	62.4
	Rural	154	37.7
Parent status	Both alive	200	48.9
	Either died	160	39.1
	Both died	49	12.0
Marital status	Single	352	86.1
	Married	41	10.0
	Divorced	16	3.9
	No formal education	77	18.8
	Primary	206	50.4

Educational status	Secondary	116	28.4
	Tertiary and above	10	2.4
Occupational status	Student	282	69.0
	Daily laborer	38	9.3
	Female sex worker	12	2.9
	No work/child	49	12.0
	Other	28	6.8

Adolescents' baseline clinical and treatment-related characteristics

Of the total adolescents enrolled to ART care during the follow-up period, 253 (61.9%), were entered to care through medical referral or linkage. The median weight of the adolescents was 26 kg with and IQR of 21kg to 40kg whereas the median height was 1.37menter with an IQR of 1.21meter to 1.50meter. The hemoglobin level of the majority, 381 (93.1%), of the adolescents participated in the study was greater or equal to 10g/dl. Regarding the WHO clinical staging, more than half 227 (55.5%) of the participants were in stage I and nearly five percent (4.7%) were with stage IV at the time of ART initiation. Of the study participants, 65 (15.9%) have history of tuberculosis infection at the start of the treatment initiation and more than ninety percent (93.9%) were treated for the infection. Of those treated for TB, 5 (8.3%) and 55 (91.7%), were treated by 2SRHZ/4RH and 2HRZE/4RH, respectively. Participants with history OIs other than TB accounts for less than twenty percent of the total participants and from these, pneumonia, 24 (34.8%) and diarrhea, 23 (33.3%) are among the commonly identified opportunistic infections other than TB. Nearly three-fourth, 298 (72.9%), of the adolescents has a working type of functional status. Two-third, 265 (64.8%), of the study participants disclosed their HIV status to others and the remaining keep their status secrete from others.

Regarding prophylaxis for prevention of opportunistic infections, 227 (55.5%) and 268(65.5%) took CPT and INH, respectively. During the follow-up time, 157 (38.4%) of the adolescents were initiated on Zidovudine, Lamivudine and Nevirapine containing regimen (AZT+3TC+NVP) at baseline while only 23 (5.6%) were initiated on AZT+3TC+EFV regimen, respectively. The duration on ART during the follow-up time is 63months with an IQR of 20month to 101months and more than half, 212 (51.8%), of the adolescents were stayed on ART for five years and above duration. Regarding treatment adherence, 331 (80.9%) had good adherence and 30 (7.3%) had fair treatment adherence. Reasons for fair or poor treatment adherence are known for only eight participants and the reasons are far distance, forgetting the drug, stigma, and others. The baseline regimen of 265 (64.8%) adolescents participated on the study was changed during the follow-up time and the main reason for the regimen change was availability of new drug, 150 (80.6%) (Table 2).

Table 2. Clinical and treatment-related characteristics of adolescents on ART in public hospitals of Gamo and Ari zones, South Ethiopia, 2024

Variables	Categories	Frequency	Percentage (%)
Mode of entry	VCT	77	18.8
	Medical referral/linkage	253	61.9
	Other	79	19.3
BMI for age	<-2SD	185	45.2
	≥-2SD	224	54.8
Hemoglobin level	<10g/dl	28	6.9
	≥10g/dl	381	93.1
WHO clinical staging	Stage I	227	55.5
	Stage II	56	13.7
	Stage III	107	26.1
	Stage IV	19	4.7

	Yes	65	15.9
History of Tuberculosis	No	344	84.1
Treated for TB (n=65)	Yes	61	93.9
	No	4	6.1
Treatment regimen for TB	2SRHZ/4RH	5	7.7
	2HRZE/4RH	55	84.6
	Unknown	5	7.7
History of opportunistic infections other than TB	Yes	74	18.1
	No	335	81.9
Functional status	Working	298	72.9
	Ambulatory	90	22.0
	Bedridden	21	5.1
Disclosure status	Yes	265	64.8
	No	144	35.2
CPT	Yes	227	55.5
	No	182	44.5
INH	Yes	268	65.5
	No	141	34.5
Type of initial regimen	TDF+3TC+EFV	60	14.7
	AZT+3TC+NVP	157	34.4
	TDF+3TC+DTG	69	16.9
	ABC+3TC+DTG	34	8.3
	AZT+3TC+EFV	23	5.6
	Other	66	16.1
Month on ART	< 1year	55	13.5
	1 to 4 years	142	34.7
	≥5 years	212	51.8
Adherence	Good	331	80.9
	Fair	30	7.3
	Poor	48	11.7

Regimen change	Yes	265	64.8
	No	144	35.2

Incidence of attrition among adolescents

The follow-up time was from January 1, 2014 to December 30, 2023 and the adolescents were followed for three months at minimum and 119 month at maximum and the median follow-up time was 67(IQR 23 - 108) months which yields a total of 2222.1 person-years of observation. The adolescents' mean survival time was 8.41 (95% CI: 8.09, 8.73) years. At the end of the follow-up, among the total study participants, 74 (18.1%) experienced the attrition (lost or died) and 335 (81.9%) were censored. The overall incidence density of attrition was 3.33 (95% CI: 2.65, 4.18) per 100 PYO. The cumulative probability of survival was 93.7%, 89.5%, 85.8%, and 84.7% at the end of 12, 24, 48, and 60 months, respectively as described by life table.

The stepwise decreasing Kaplan-Meier survival curve showed that it doesn't cross the survival function at survival probability of 0.5 (Figure 2). The log-rank test showed that there is a statistically significant difference in survival experience among the categories of the predictor variable including age, educational status, CPT prophylaxis, baseline regimen change, and drug adherence were.

It was identified that there is a statistically significant difference in survival time among adolescents among different categories of age group. Hence the mean survival time for adolescents aged 10 to 14 years was 8.71(95% CI: 8.32, 9.10) years and 8.08(7.56, 8.59) years, respectively. Adolescents on ART unchanged initial regimen have the lowest survival times, 6.36 (95% CI: 5.54, 7.18) when compared to adolescents whose baseline regimen was changed 9.16 (8.90, 9.43). In addition, there is a statistically significant difference in survival time among adolescents within different groups of treatment adherence levels. The mean survival time for adolescents with good treatment adherence was higher (8.96, 95% CI: 8.67, 9.25) than for those

with fair (7.48, 95% CI: 6.07, 8.89) and poor treatment adherence (5.55, 95% CI: 4.39, 6.72). Another categorical variable that was found to have a significant difference in attrition free survival time between its categories is initial regimen change. Adolescents whose baseline ART regimen was not changed have lower attrition free survival times (6.36, 95% CI: 5.54, 7.19) as compared to those whose regimen was changed (9.16, 95% CI: 8.90, 9.43) (Figure 3).

Predictors of attrition among adolescents

In bivariable analysis, age, marital status, parent status, educational status, occupation, entry mode to care, CPT prophylaxis, regimen change, drug adherence, disclosure of HIV-sero status, and type of baseline regimen the identified variables significantly associated with attrition at P-value of <0.25. In multivariable analysis, age, parent status, educational status, CPT prophylaxis, baseline regimen change, and drug adherence were significantly associated with attrition and found to be the independent predictors of attrition from ART care among adolescents at P-value <0.05. Hence, adolescents aged 15 years to 19 years had nearly two times (AHR=1.88; 95% CI: 1.12, 3.18) increased hazard of attrition from care when compared to their counterparts. Death of either or both the parents of the adolescents can increase the risk program attrition by two fold times, (AHR=2.07; 95% CI: 1.22, 3.52) and (AHR=2.19; 95% CI: 1.04, 4.61), when compared to adolescent whose both parents are alive, respectively. Attaining no formal education (AHR=3.16; 95% CI: 1.48, 6.77) and attaining primary educational status (AHR=2.47; 95% CI: 1.25, 4.89) can result in more than two times higher hazard of attrition among adolescents participated in the current study. Adolescents who did not took the CPT prophylaxis for prevention of opportunistic infection hand 1.73 times (AHR=1.73; 95% CI: 1.03, 2.91) increased hazard of experiencing ART program attrition than their counterparts. Adolescents whose baseline ART regimen was not changed are at six fold times (AHR=6.16; 95% CI: 3.56, 10.66)

higher risk of attrition. Poor or fair treatment adherence can increase the hazard of attrition by five (AHR=5.16; 95% CI: 2.35, 11.32) and six (AHR=6.02; 95% CI: 3.52, 10.29) time when compared to adolescents with good treatment adherence, respectively (Table 3).

316 **Table 3.** A multivariable cox-proportional analysis of predictors of attrition among adolescents on ART in public hospitals of Gamo
317 and Ari zones, South Ethiopia, 2024

Variables	Categories	Attrition status		Incidence rate per 100 PYO (95% CI)	CHR (95% CI)	AHR (95% CI)	P-value
		Yes (Event)	No (Censored)				
Age (in years)	10-14	33 (15.6)	178 (84.4)	2.6 (1.8, 3.7)	1	1	
	15-19	41 (20.7)	157 (79.3)	4.3 (3.2, 5.8)	1.60 (1.01, 2.53)	1.88 (1.12, 3.18)	**0.018**
Parent status	Both alive	27 (13.5)	173 (86.5)	2.5 (1.7, 3.6)	1	1	
	Either died	37 (23.1)	123 (76.9)	4.5 (3.3, 6.2)	1.81 (1.10, 2.99)	2.07 (1.22, 3.52)	**0.007**
	Both died	10 (20.4)	39 (79.6)	3.3 (1.8, 6.1)	1.37 (0.66, 2.88)	2.19 (1.04, 4.61)	**0.040**
Marital status	Single	61 (17.3)	291 (82.7)	3.1 (2.4, 3.9)	1	1	
	Married	8 (19.5)	33 (80.5)	4.7 (2.4, 9.4)	1.45 (0.69, 3.03)	0.75 (0.34, 1.67)	0.479
	Divorced	5 (31.2)	11 (68.8)	8.2 (3.4, 19.7)	2.55 (1.02, 6.37)	0.79 (0.29, 2.14)	0.648
Educational status	No formal education	25 (32.5)	52 (67.5)	8.4 (5.7, 12.4)	4.94 (2.50, 9.76)	3.16 (1.48, 6.77)	**0.003**
	Primary	36 (17.5)	170 (82.5)	3.3 (2.4, 4.6)	2.09 (1.11, 3.94)	2.47 (1.25, 4.89)	**0.009**
	Secondary and above	13 (10.3)	113 (89.7)	1.5 (0.9, 2.7)	1	1	
Occupational status	Student	37 (13.1)	245 (86.9)	2.2 (1.6, 3.0)	1	1	
	Daily laborer	5 (13.2)	33 (86.8)	2.5 (1.1, 6.1)	1.14 (0.45, 2.89)	1.00 (0.34, 2.95)	0.995
	No work/child	20 (40.8)	29 (59.2)	11.5 (7.4, 17.8)	4.50 (2.59, 7.83)	1.48 (0.62, 3.51)	0.374
	Other	12 (30.0)	28 (70.0)	7.2 (4.1, 12.7)	3.11 (1.62, 5.98)	1.45 (0.61, 3.47)	0.403
Entry mode	VCT	16 (20.8)	61 (79.2)	3.7 (2.3, 6.0)	1	1	

	Medical referral	47 (18.6)	206 (81.4)	3.6 (2.7, 4.8)	0.98 (0.55, 1.73)	0.84 (0.46, 1.52)	0.555
	Other	11 (13.9)	68 (86.1)	2.2 (1.2, 4.1)	0.63 (0.29, 1.38)	0.55 (0.24, 1.24)	0.147
CPT prophylaxis	Yes	37 (16.3)	190 (83.7)	2.7 (1.9, 3.5)	1	1	
	No	37 (20.3)	145 (79.7)	4.7 (3.4, 6.5)	1.74 (1.09, 2.77)	1.73 (1.03, 2.91)	**0.038**
ART regimen	TDF+3TC+EFV	6 (10.0)	54 (90.0)	1.8 (0.8, 4.0)	0.29 (0.10, 0.88)	0.89 (0.25, 3.11)	0.856
	AZT+3TC+NVP	32 (20.4)	125 (79.6)	3.0 (2.1, 4.2)	0.47 (0.20, 1.08)	0.65 (0.25, 1.73)	0.391
	TDF+3TC+DTG	18 (26.1)	51 (73.9)	13.6 (8.6, 21.6)	1.63 (0.68, 3.94)	1.62 (0.53, 4.94)	0.398
	ABC+3TC+DTG	7 (20.6)	27 (79.4)	7.3 (3.5, 15.3)	1	1	
	AZT+3TC+EFV	6 (26.1)	17 (73.9)	4.2 (1.9, 9.3)	0.66 (0.22, 1.98)	0.96 (0.27, 3.36)	0.949
	Other	5 (7.6)	61 (92.4)	1.1 (0.5, 2.7)	0.17 (0.05, 0.57)	0.44 (0.12, 1.58)	0.208
Regimen change	Yes	31 (11.7)	234 (88.3)	1.7 (1.2, 2.4)	1	1	
	No	43 (29.9)	101 (70.1)	11.1 (8.3, 15.0)	6.04 (3.70, 9.85)	6.16 (3.56, 10.66)	**<0.001**
Disclosure	Yes	41 (15.5)	224 (84.5)	2.8 (2.1, 3.8)	1	1	
	No	33 (22.9)	111 (77.1)	4.3 (3.1, 6.1)	1.53 (0.97, 2.41)	1.58 (0.95, 2.62)	0.075
Adherence	Good	39 (11.8)	292 (88.2)	2.1 (1.5, 2.9)	1	1	
	Fair	9 (30.0)	21 (70.0)	5.4 (2.9, 10.5)	2.52 (1.22, 5.22)	5.16 (2.35, 11.32)	**<0.001**
	Poor	26 (54.2)	22 (45.8)	12.6 (8.6, 18.5)	5.60 (3.40, 9.22)	6.02 (3.52, 10.29)	**<0.001**

DISCUSSION

The study was conducted to determine incidence density and predictors of attrition among adolescents on ART. At the end of the follow-up, among the total study participants, 74 (18.1%) experienced attrition. The overall incidence density of attrition was 3.33 (95% CI: 2.65, 4.18) per 100 PYO. Moreover, older age, death of either or both of the parents, attaining no formal education and attaining primary educational status, not taking the CPT prophylaxis, unchanged baseline ART regimen, and poor or fair treatment adherence were the identified predictors of attrition among adolescents on ART.

This study reported that the incidence density of attrition was 3.33 per 100 PYO. This finding is low than the retrospective cohort studies conducted in Thailand [10] and Myanmar [9] which reported a 295.2 per 1000 PYO and 6.4 per 100 PYO incidence of attrition, respectively. It is also lower than the findings from cohort studies done in India [29] and South Africa [28] which showed that the incidence of attrition due to lost to follow-up among ALHIV were 4.4 per 100 PYO and 7.2 per 100 PYO, respectively. Whereas, the incidence of attrition due to death were 4.9 per 100 PYO [29] and 1.2 per 100 PYO [28], respectively. This finding is also lower than the result from the retrospective cohort study done in Ethiopian which showed that the incidence of attrition due to LTFU was 4.86 per 100 PYO [12]. This discrepancy may be due to the large sample size used in the previous studies [9 10 28 29]. Also a long follow-up time [9], the difference in socio-demographic characteristics of the study participants and improvement in the current health care system than former times may also contribute to the inconsistence. Another reason for the variance may be due to the difference in the operational definition of LTFU, it's defined as; if the last appointment was missed for ≥12 months [10] and difference in study design [28]. Moreover, there was a difference in study population, for young adults were included in the studies done in

Thailand [10] and South Africa[28] and study done in Ethiopia [12] included children whose age less than 10 years. The result of this study is in line with the studies done previously in Tanzania [26] and Ethiopia [12] showed that the incidence of attrition due to death was 3.8 per 100 PYO and 2.29 per 100 PYO, respectively. The reason behind this consistency in Ethiopia might be due to uniformity in follow-up charts and data recording formats in the ART program prepared by the Ethiopian Federal Minister of Health [14].

In contrary, the overall incidence density of attrition as reported by the current study is slightly higher than studies conducted among adolescents living with HIV in South Africa [28] and Ethiopia [13] which reported that the incidence of attrition due to death was 1.2 per 100 PYO and 1.52 per 100 PYO, respectively. This may be due to difference in study population; the study conducted in South Africa additionally included young adults aged 20 to 28 years [28]. It may also be because of difference in study design [28], and large sample size [13 28]. In addition, the divergence may be explained by difference in Sociodemographic characteristic of study participants and longer follow-up period of the current study.

Adolescents aged 15 years to 19 years had nearly two times increased hazard of attrition from care when compared to their counterparts. This finding is consistent with result from previous studies done in India [29], South Africa [30], and Uganda [21] which reported an increased risk of attrition with increased age (15-19 years). The reason might be because older adolescents started ART at advanced immunodeficiency stage and also large amount of adolescents lost from ART care as they transition from pediatric care to adult care [30 33 34].

Educational status of the adolescents was one of the identified predictors of attrition by the current study. Attaining no formal education or primary educational status can result in more than two times higher hazard of attrition compared with those attained secondary and above

educational level as reported by this study. This is consistent with a study conducted in Amhara region, Ethiopia [13]. This might be because adolescents who attained higher educational status were well informed and aware about the benefit of retention in care and the effect of attrition on their health.

Death of either or both the parents of the adolescents can increase the risk program attrition by two fold times when compared to adolescent whose both parents are alive, respectively. This finding is consistent with finding from studies conducted in Ethiopia [13 35]. However, the study done in Ethiopia [35] targeted on children aged 0 to 14 years. The reason for this could be due to lack of caregivers' role in providing proper feeding, drug administration, and supervision, collective with the social and economic disruption resulted from death of the caregivers [36]. In addition, adolescents living with widowed caregiver or on their own were considerably more likely to be depressed than their peers and may experience attrition from care [37].

The other predictor of attrition among HIV-positive adolescents is non-utilization of CPT prophylaxis. Hence, adolescents who did not took the CPT prophylaxis for prevention of opportunistic infection hand 1.73 times increased hazard of experiencing ART program attrition than their counterparts. Similar finding was reported by studies done in Ethiopia [13 38] among which one was conducted among children[38]. This might be due to the fact that CPT administration can prevent the occurrence of OIs among HIV positive individuals and will reduce AIDS-related mortality and improves life quality [39]. Moreover, provision of CPT prophylaxis is an effective and simple intervention for reducing morbidity and increase retention rates in ART Program [40].

Adolescents whose baseline ART regimen was not changed are at six fold times higher risk of attrition. This is supported by study done in Ethiopia [13] and contrary with the study done in

Namibia [20]. The study done in Namibia [20] reported that adolescents whose regimen was changed to second or third line regimen were at higher hazard of attrition. This could be due to most of the old regimens have adverse effects that boost the progression of HIV-infection to AIDS stage and lead to succeeding complications. An AZT-based ART regimen is associated with the development of anemia, which has an extra effect on the patient's immune system [41]. The highest attrition was occurred among adolescents on AZT-based regimen which was 43.2% as reported by the current study.

Furthermore, treatment adherence was one of the identified factors associated with attrition among HIV positive adolescents. It was identified that poor or fair treatment adherence can increase the hazard of attrition by five and six time among HIV positive adolescents when compared to adolescents with good treatment adherence, respectively. This result was supported by finding from previous studies done in Ethiopia [13 35]. However, the source population of one of the studies done in Ethiopia [35] was children age 0 to 14 years. This can be due to the fact that fair or poor adherence can lead to higher viral load, drug resistance, and poor treatment outcomes. This can also result in decreased CD4 levels, the progression of AIDS, and an increase in OIs, all of which cause attrition [42].

CONCLUSION

The incidence of attrition was comparable at the study setting. Moreover, older age, death of either or both of the parents, attaining no formal education and attaining primary educational status, not taking the CPT prophylaxis, unchanged baseline ART regimen, and poor or fair treatment adherence were the identified predictors of attrition among adolescents on ART. Special attention should be given to old aged, no formal education, orphaned, and those with poor baseline clinical characteristics. Moreover, early tracing of missed follow-up schedules,

improving adherence support, and increasing contacting frequency in order to reduce attrition is highly encouraged. To address the effect of important clinical and sociodemographic variables, a longitudinal prospective study was needed.

Contributors TGG, TMT, and FM were responsible for the design of the study. TGG, FM, TMT, and AAS conducted the research. SS and SWK supervised data collection. TGG completed the statistical analyses and drafted the manuscript. TGG, FM, and TMT contributed to the writing of the manuscript. All authors read and approved the submitted version.

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Patient consent for publication Not applicable

Ethical approval Prior to data collection, the document was submitted to the Arba Minch College of Health Sciences' institutional ethical review board (IRB) for ethical assessment and approval. Ethical approval letter was obtained from IRB with reference number AMCHS/01/20/33/0. An official support letter was received from the Gamo and Ari Zones Health Departments. The letter of cooperation was submitted to hospital authorities, and permission was sought to have full access to the information. Individual informed consent/assent was not obtained from the participants or guardians because the study is a retrospective study that requires record review without physical contact with the participants, which was waived by the IRB.

Data availability statement Data are available upon reasonable request.

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REFERENCES

1. WHO. HIV and AIDS Fact sheet; 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/hiv-aids. Accessed 13 July 2023.
2. UNAIDS. Young people and HIV; 2023. Available at: https://www.unaids.org/sites/default/files/media_asset/young-people-and-hiv_en.pdf Accessed September 09, 2023.
3. UNICEF. UNICEF Data: Adolescent HIV prevention; 2023. Available at : https://data.unicef.org/topic/hivaids/adolescents-young-people/ Accessed September 09, 2023
4. UNAIDS. HIV and AIDS estimates country factsheet 2022 - Ethiopia; 2022. Available from: https://www.unaids.org/en/regionscountries/countries/ethiopia. Accessed September 09, 2023.
5. WHO. World Heath Organization: Adolescent health; 2023. Available from: https://www.who.int/health-topics/adolescent-health#tab=tab_1 Accessed September 25, 2023.

6. Organization WH. Consolidated HIV strategic information guidelines: driving impact through programme monitoring and management. 2020
7. Auld AF, Agolory SG, Shiraishi RW, et al. Antiretroviral therapy enrollment characteristics and outcomes among HIV-infected adolescents and young adults compared with older adults—seven African countries, 2004–2013. *Morbidity and Mortality Weekly Report* 2014;63(47):1097.
8. Kariminia A, Law M, Davies MA, et al. Mortality and losses to follow-up among adolescents living with HIV in the Ie DEA global cohort collaboration. *Journal of the International AIDS Society* 2018;21(12):e25215.
9. Htun T, Kyaw K, Aung T, et al. Attrition during pre-ART and ART time periods among adolescents enrolled in Integrated HIV Care Programme in Myanmar, 2005–2017. *Epidemiology & Infection* 2019;147
10. Teeraananchai S, Puthanakit T, Kerr SJ, et al. Attrition and treatment outcomes among adolescents and youths living with HIV in the Thai National AIDS Program. *Journal of virus eradication* 2019;5(1):33-40.
11. Leshargie CT, Demant D, Burrowes S, et al. The proportion of loss to follow-up from antiretroviral therapy (art) and its association with age among adolescents living with HIV in sub-Saharan Africa: a systematic review and meta-analysis. *Plos one* 2022;17(8):e0272906.
12. Jerene D, Abebe W, Taye K, et al. Adolescents living with HIV are at higher risk of death and loss to follow up from care: Analysis of cohort data from eight health facilities in Ethiopia. *PloS one* 2019;14(10):e0223655.
13. Leshargie CT, Demant D, Burrowes S, et al. Incidence and predictors of mortality among adolescents on antiretroviral therapy in Amhara Region, Ethiopia: a retrospective cohort analysis. *BMJ open* 2022;12(11):e063879.
14. Ethiopia F. National consolidated guidelines for comprehensive HIV prevention, care and treatment. *Addis Ababa: Fmoh* 2018:1-238.
15. Geng EH, Nash D, Kambugu A, et al. Retention in care among HIV-infected patients in resource-limited settings: emerging insights and new directions. *Current Hiv/aids Reports* 2010;7:234-44.
16. UNAIDS. IN DANGER: UNAIDS Global AIDS Update 2022. Geneva: Joint United Nations Programme on HIV/ AIDS; 2022. Licence: CC BY-NC-SA 3.0 IGO.
17. UNCEF. 2023 Global Snapshot on HIV and AIDS: Progress and priorities for children, adolescents and pregnant women; 2023. Available from: https://www.childrenandaids.org/sites/default/files/2023-11/231130%20UNCEF_HIV_Global_Snapshot_2023UPDATED_0.pdf. Accessed on January 15, 2024.
18. Booysen F, Bachmann M, Matebesi Z, et al. The socio-economic impact of HIV/AIDS on households in South Africa: pilot study in Welkom and Qwaqwa, Free State Province. *Retrieved March* 2004;26:2009.
19. Booysen F, Van der Berg S. The role of social grants in mitigating the socio-economic impact of HIV/aids in two free state communities 1. *South African Journal of Economics* 2005;73:545-63.
20. Munyayi FK, van Wyk BE. Determinants and rates of retention in HIV care among adolescents receiving antiretroviral therapy in Windhoek, Namibia: a baseline cohort analysis. *BMC Public Health* 2023;23(1):1-12.
21. Okoboi S, Ssali L, Yansaneh AI, et al. Factors associated with long-term antiretroviral therapy attrition among adolescents in rural Uganda: a retrospective study. *Journal of the International AIDS Society* 2016;19:20841.
22. Organization WH. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach; 2021. Licence: CC BY-NC-SA 3.0 IGO: World Health Organization.

23. Judd A, Sohn AH, Collins IJ. Interventions to improve treatment, retention and survival outcomes for adolescents with perinatal HIV-1 transitioning to adult care: moving on up. *Current opinion in HIV and AIDS* 2016;11(5):477-86.
24. Neilan AM, Karalius B, Patel K, et al. Association of risk of viremia, immunosuppression, serious clinical events, and mortality with increasing age in perinatally human immunodeficiency virus–infected youth. *JAMA pediatrics* 2017;171(5):450-60.
25. Tesha E-D, Kishimba R, Njau P, et al. Predictors of loss to follow up from antiretroviral therapy among adolescents with HIV/AIDS in Tanzania. *PloS one* 2022;17(7):e0268825.
26. Amour MA, Shayo GA, Matee MM, et al. Predictors of mortality among adolescents and young adults living with HIV on antiretroviral therapy in Dar es Salaam, Tanzania: a retrospective cohort study. *Journal of the International AIDS Society* 2022;25(2):e25886.
27. Lamb MR, Fayorsey R, Nuwagaba-Biribonwoha H, et al. High attrition before and after ART initiation among youth (15–24 years of age) enrolled in HIV care. *AIDS (London, England)* 2014;28(4):559.
28. Nglazi MD, Kranzer K, Holele P, et al. Treatment outcomes in HIV-infected adolescents attending a community-based antiretroviral therapy clinic in South Africa. *BMC infectious diseases* 2012;12:1-7.
29. Nimkar S, Valvi C, Kadam D, et al. Loss to follow-up and mortality among HIV-infected adolescents receiving antiretroviral therapy in Pune, India. *HIV medicine* 2018;19(6):395-402.
30. Okonji EF, Wyk BV, Mukumbang FC. Two-year retention in care for adolescents on antiretroviral therapy in Ehlanzeni district, South Africa: a baseline cohort analysis. *AIDS care* 2023;35(3):374-84.
31. Nimwesiga C, Taremwa IM, Nakanjako D, et al. Factors Associated with Retention in HIV Care Among HIV-Positive Adolescents in Public Antiretroviral Therapy Clinics in Ibanda District, Rural South Western Uganda. *HIV/AIDS-Research and Palliative Care* 2023:71-81.
32. Organization WH. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach: World Health Organization 2016.
33. Enane LA, Davies M-A, Leroy V, et al. Traversing the cascade: urgent research priorities for implementing the 'treat all'strategy for children and adolescents living with HIV in sub-Saharan Africa. *Journal of virus eradication* 2018;4:40-46.
34. Meloni ST, Agaba P, Chang CA, et al. Longitudinal evaluation of adherence, retention, and transition patterns of adolescents living with HIV in Nigeria. *PLoS One* 2020;15(7):e0236801.
35. Guyo TG, Toma TM, Haftu D, et al. Proportion of Attrition and Associated Factors Among Children Receiving Antiretroviral Therapy in Public Health Facilities, Southern Ethiopia. *HIV/AIDS-Research and Palliative Care* 2023:491-502.
36. Vreeman RC, Ayaya SO, Musick BS, et al. Adherence to antiretroviral therapy in a clinical cohort of HIV-infected children in East Africa. *PLoS One* 2018;13(2):e0191848.
37. Sengendo J, Nambi J. The psychological effect of orphanhood: a study of orphans in Rakai district. *Health transition review* 1997:105-24.
38. Chanie ES, Tesgera Beshah D, Ayele AD. Incidence and predictors of attrition among children on antiretroviral therapy at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, 2019: Retrospective follow-up study. *SAGE Open Medicine* 2022;10:20503121221077843.
39. Collini P, Obasi A. Cotrimoxazole prophylaxis: BMJ publishing Group Limited London, 2006.
40. Vitoria M, Granich R, Banda M, et al. Implementation of co-trimoxazole prophylaxis and isoniazid preventive therapy for people living with HIV. *Bulletin of the World Health Organization* 2010;88:253-59.

41. Gebremedhin KB, Haye TB. Factors associated with anemia among people living with HIV/AIDS taking ART in Ethiopia. *Advances in hematology* 2019;2019
42. Organization WH. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach: World Health Organization 2021.

Figure legends

Figure 1. Schematic presentation of the sampling procedure to assess the incidence and predictors of attrition among adolescents on ART in public hospitals of Gamo and Ari zones, South Ethiopia, 2024

Figure 2. The overall Kaplan-Meier survival estimate showing the time until free of attrition among adolescents on ART in public hospitals of Gamo and Ari zones, South Ethiopia, 2024

Figure 3. Kaplan-Meier survival estimates of time until attrition free of the main predictor variables among adolescents on ART in public hospitals of Gamo and Ari zones, south Ethiopia, 2024

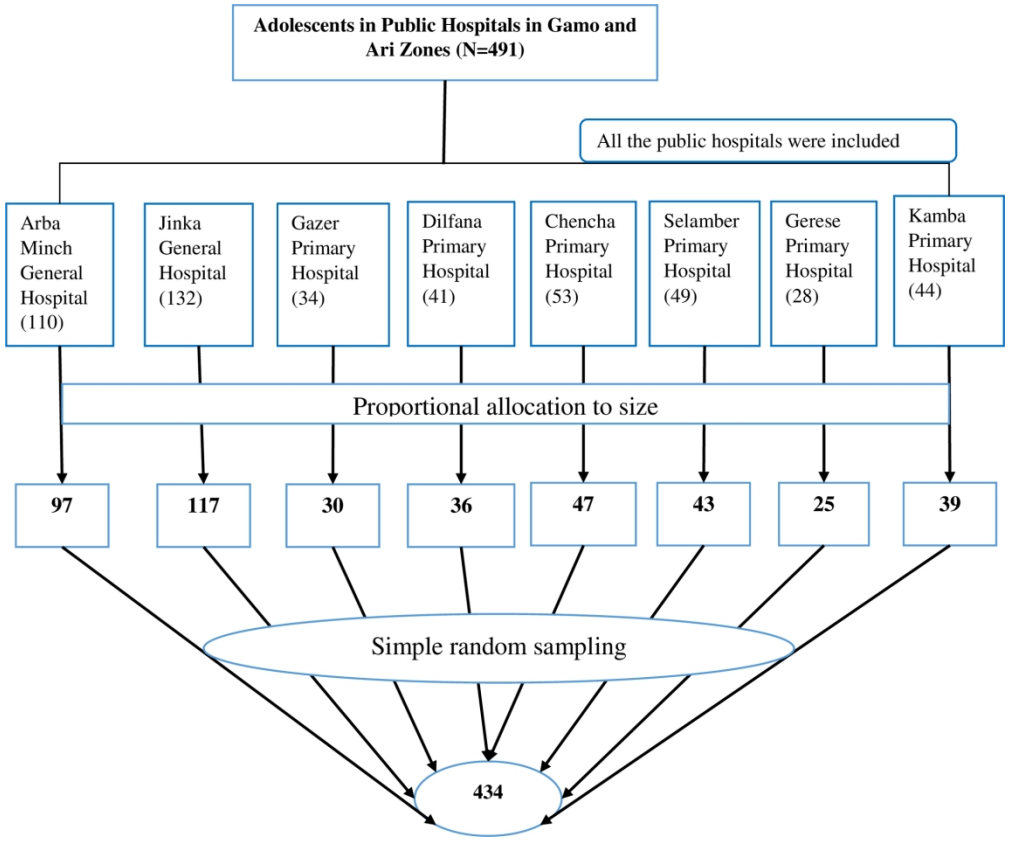

Figure 1. Schematic presentation of the sampling procedure to assess the incidence and predictors of attrition among adolescents on ART in public hospitals of Gamo and Ari zones, South Ethiopia, 2024

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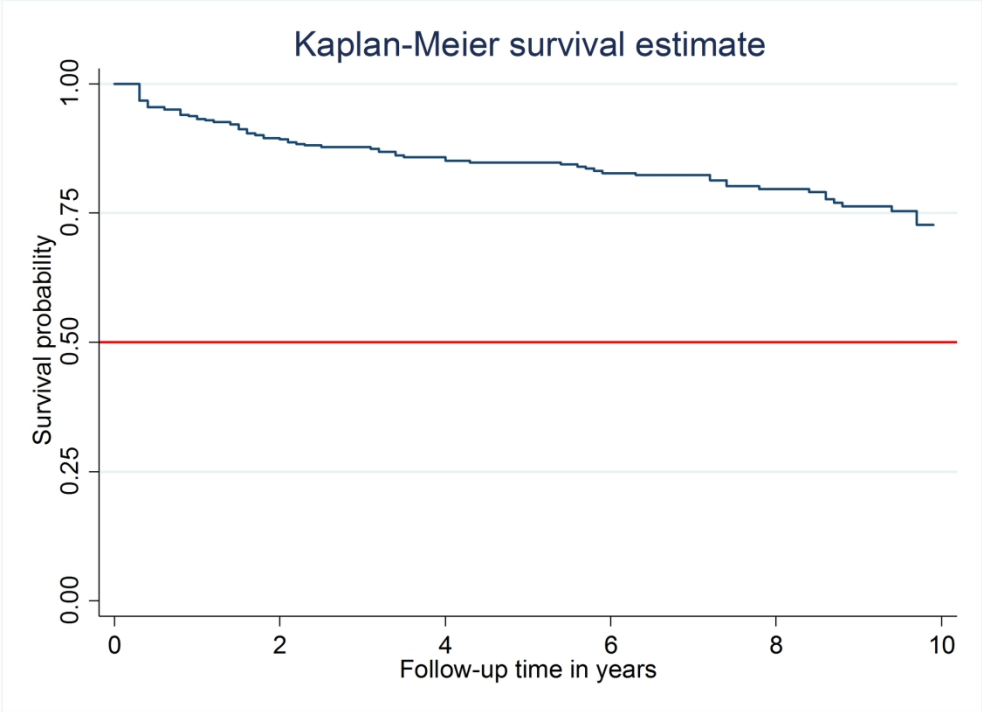
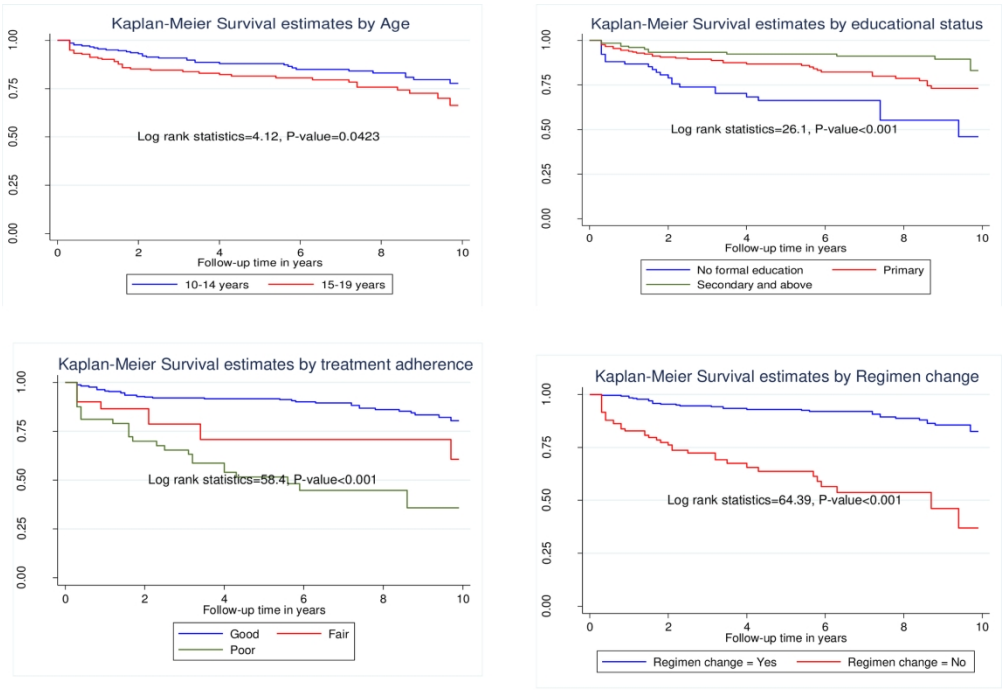


Figure 2. The overall Kaplan-Meier survival estimate showing the time until free of attrition among adolescents on ART in public hospitals of Gamo and Ari zones, South Ethiopia, 2024

484x353mm (118 x 118 DPI)



[1]

Figure 3. Kaplan-Meier survival estimates of time until attrition free of the main predictor variables among adolescents on ART in public hospitals of Gamo and Ari zones, south Ethiopia, 2024

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Incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in Public Hospitals, South Ethiopia: A multicenter retrospective follow-up study

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Incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in Public Hospitals, South Ethiopia: A multicenter retrospective follow-up study

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ABSTRACT

Objective This study aimed to determine the incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in public hospitals, South Ethiopia.

Study design A multi-center retrospective follow-up study was conducted and Cox proportional hazards model was used to identify predictors of the study outcome variable (attrition).

Settings The study was conducted in eight Public Hospitals (two general and six primary hospitals) in south Ethiopia.

Participants Adolescents (10-19 years) on antiretroviral therapy from January 01, 2014 to December 30, 2023 (n=434). The data was collected from patient's charts and electronic data records.

Outcome Variable The primary outcome was time to attrition and the secondary outcome was predictors of attrition.

Results The overall incidence density of attrition was 3.33 (95% Confidence Interval (CI): 2.65, 4.18) per 100 Person Year of Observation (PYO). Age 15 to 19 years (Adjusted Hazard Ratio (AHR)=1.88; 95% CI: 1.12, 3.18), death of both the parents (AHR=2.19; 95% CI: 1.04, 4.61), no formal education (AHR=3.16; 95% CI: 1.48, 6.77), Cotrimoxazole Prophylaxis Therapy (CPT) non utilization (AHR=1.73; 95% CI: 1.03, 2.91), not changed regimen (AHR=6.16; 95% CI: 3.56, 10.66), and poor treatment adherence (AHR=5.16; 95% CI: 2.35, 11.32) were predictors of attrition.

Conclusion Attrition was identified to be a significant public health problem in study settings. Moreover, old age, parental death, not attending formal education, not using CPT, unchanged baseline regimen, and suboptimal treatment adherence predict attrition. Hence, special attention should be given to older adolescents, those with no formal education, orphaned, and with poor

baseline clinical characteristics. Likewise, early tracing of missed follow-up schedules, improving adherence support, and increasing contacting frequency to reduce attrition are highly encouraged.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- As attrition is a warning indicator for drug resistance, determining attrition is very important to monitor ART drug resistance and the current study used a long follow-up period to do so.
- The current study provided evidence on predictors of attrition for adolescents that can be important and used to improve adolescent's HIV-related services.
- The effect of some important predictor variables like; viral load and CD4 count, was not assessed because of incomplete records.
- Adolescents whose charts were lost and those with incomplete records were excluded from the analysis which may under or overestimate the attrition.

INTRODUCTION

Human immunodeficiency virus (HIV) continues to be the critical public health problem of the globe. In 2022, about 1.65 million adolescents aged 10-19 were living with HIV, and 34,000 AIDS-related deaths occurred among them, globally [2 3]. About 1.40 million, or 85%, of adolescents living with HIV (ALHIV) were from sub-Saharan Africa (SSA) [3]. Ethiopia is one of the Sub-Saharan African countries with a total of 610,000 people living with HIV (PLHIV) and about 11,000 AIDS-related mortalities [4].

Attrition refers to the disruption in ART care, including lost patients, deaths, and those who stopped treatment, indicating progress towards achieving the 95-95-95 targets [5]. It continues to be a great public health problem among adolescents. Adolescents have significantly higher

attrition rates from ART than adults without being privileged and getting access to HIV care and treatment services, these results in relatively poorer outcomes [6].

Evidence from Global cohort collaboration reported that 30% and 3.9% of HIV-positive adolescents were lost to follow-up and died worldwide, respectively [7]. Based on the studies conducted in different countries, the incidence of attrition from ART care among Adolescents was anticipated to be high. Studies done in Myanmar [8] and Thailand [9] revealed that attrition rates among ALHIV were determined to be 6.4 per 100 PYO and 29.5%, respectively. Evidence from a systematic review conducted in Sub-Saharan Africa reported that 15.07% of ALHIV experienced attrition due to lost follow-up from ART after initiation of the treatment [10]. In Ethiopia, about 28.1% [11] of adolescents aged ten to nineteen years experienced attrition from HIV care and 11.1% attrite from care due to death [12]. Attrition of patients from HIV care and treatment after ART initiation is resulting in an increase in poor treatment outcomes, including drug resistance, increased health care costs, preventable onward HIV transmission, and avoidable morbidity and death [13]. It can weaken the continuing provision of opportunistic infection prophylaxis, timely identification of treatment failure, and adverse events assessment [14]. In addition, attrition from HIV care also affected the 95-95-95 ambitious targets of UNAIDS which aimed at 95% viral suppression. Due to this impact of attrition, only 68% of PLHIV were virally suppressed and adolescents were highly in need of lifelong treatment, care, and social support to have better treatment and health outcomes as they pass through youth to adulthood [15]. Even though there is a paucity of information on adolescent viral suppression, 46% of children and adolescents were virally suppressed [16]. Attrition from the ART program can significantly impact households, often requiring orphaned children to assume responsibility for the household after the death of their young parents [17] [18]. Predictors of adolescent's attrition from HIV care and

treatment including advanced HIV disease, low hemoglobin level, absence of social support, financial constraints, lower age, and year of ART initiation. Attrition is also predicted by infection with tuberculosis (TB), non-disclosure, malnutrition, and Cotrimoxazole preventive therapy (CPT) utilization [8 13 19 20].

To minimize adolescents' attrition from HIV care and treatment services, different measures have been taken in Ethiopia. These include; decentralization of services, provision of ART drugs without charge, health education and counselling through community partners, and delivering phone text messages [13]. Attrition from care among ALHIV patients remains a significant challenge to ART program effectiveness, necessitating assessment of incidence and predictors for effective retention strategies[21].

According to the WHO 2021 consolidated HIV guideline, total attrition is one of the early warning indicators and attrition ≥25% during the reporting period is a warning sign of drug resistance [23]. Despite the country's growing adolescent population and high prevalence of adolescent HIV infections, Ethiopia's HIV/AIDS policies currently do not provide adequate regard to the unique needs of adolescents [6 24 25]. Ethiopia's current HIV care and treatment guidelines primarily target young children and adults, lacking a national focus on HIV care and treatment for ALHIV [13]. Moreover, there is little indication of attrition from care among ALHIV on ART in Ethiopia, and none in the research settings. As a result, the purpose of this study is to determine the incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in Public Hospitals, South Ethiopia.

METHODS

Study design, period, and setting

A multi-center retrospective follow-up study was conducted in Gamo Zone and Ari Zones public hospitals in South Ethiopia from March 05, 2024, to April 05, 2024. Arba Minch town is the administrative center of the Gamo Zone. It is 505 Kilometers Southwest far from the capital city, Addis Ababa. Jinka town is the administrative center of Ari Zone in Southwest Ethiopia. It is about 563Km far from Addis Ababa. In these two zones, there are two general and six primary public hospitals providing ART services with about 5,480 individuals currently on HIV care and treatment among which adolescents account for 1,041. These health facilities provide different services (Outpatient department service, Inpatient department services, Emergency services, Maternal and Child Health services, Dental treatment, Ophthalmic service, and follow-up services) to the community in their catchment area and nearby woredas and zones. The estimated total population in the two zones was 2,127,970. Among these the adolescent population account for 410,059.

Population

All HIV-positive adolescents (10-19 years) who were on ART in public hospitals of Gamo and Ari Zones were the source population. All randomly selected HIV-positive adolescents (10-19 years) who were on ART in the public hospitals of Gamo and Ari Zones from January 01, 2014, to December 30, 2023, were the study population. All HIV-positive adolescents (10-19 years) who were on ART and had at least one follow-up visit from January 01, 2014, to December 30, 2023, were included in the study. HIV-positive adolescents whose charts were with incomplete records (indicators of the outcome were not registered) were excluded from the study.

Sample size determination and sampling procedures

The sample size was determined by STATA software v14.0 for major predictor variables using Cox model comparing one slope to the reference value based on the following assumptions: Significance level (**α**) (two-sided) = 0.05, 95% confidence interval, power of 80%, AHR = 1.58 for adolescents with HIV/TB co-infection who experienced attrition [26], standard deviation (variability) of covariates of interest = 0.5, the overall probability of event (attrition) (d) at the end of the study: 0.428 [26], and a 10% withdrawal probability was added for incomplete records yielding a total sample size of 434 to conduct the study.

First, in the two zones (Gamo and Ari) there are eight public hospitals; two General Hospitals (Jinka and Arba Minch General Hospitals) and six Primary Hospitals (Chencha, Selamber, Kamba, Gerese, Dilfana, and Gazer Primary Hospitals). In these public hospitals, 437 adolescents were on ART between January 01, 2014, and December 30, 2023. The adolescents (10-19 years) were identified in each hospital using medical record numbers (MRNs) obtained from electronic databases, and patient charts were drawn using the MRNs. The total number of adolescents identified in the hospitals is very close to the calculated sample size; all their charts were screened for eligibility by considering the inclusion criteria, and 409 eligible charts were included in the analysis (Figure 1).

Data collection tool, procedure, and personnel

Data were collected by using a data extraction checklist developed in English from the standardized ART intake and follow-up forms from national HIV guideline [13], and by reviewing related literature [7-12 20 26-31]. The follow-up period was from January 01, 2014, to December 30, 2023, and each participant can enter and leave the study at any time within the follow-up period. Adolescents who were categorized as LTFU during the study but were come back to the care

before the follow-up ends were counted as active because their coming back was the result of defaulter tracing intervention. The checklist contains socio-demographic, clinical and treatment-related characteristics of participants. The lists of study participants were taken from the ART data clerk by using children's MRN or unique ART numbers. Charts of the adolescents were taken from card rooms. Then data were collected by reviewing the registration books and patient follow-up charts by ten data collectors and eight supervisors.

Study variables

The dependent variable was time to attrition and the predictor variables included: socio-demographic variables: Age, Sex, residence, educational status, and marital status of the adolescents; clinical-related variables: Entry point of care, WHO clinical staging, nutritional status, hemoglobin level, CD4 count, presence opportunistic infections, functional status, and disclosure status; and treatment-related variables: Type of baseline regimen, regimen change, treatment adherence, and CPT prophylaxis.

Operational definitions

Attrition (Event) is if adolescents on ART were lost to follow-up or died within the follow-up period [32]. Whereas, censored is if adolescents on ART that were transferred out or alive and active on ART at the end of the study or turning 19 years of age [20 32]. Loss to follow-up is if an adolescent has not come to care for ≥3 consecutive months (≥90 days) after the last missed appointment and is not registered as died or transferred out to other health facilities [33]. However, adolescents were counted as died if he/she documented or registered as "died" on the exit form of the patient. Adherence is the extent to which an adolescent's behavior of taking ART medication with agreed-upon recommendations from a health-care provider. It was classified as; good: if ≥ 95% of the recommended doses were taken or ≤3 doses missed monthly, Fair: if 85-

94% of the recommended doses were taken or 4-9 doses missed monthly, poor: if < 85% of the recommended doses were taken or ≥10 doses missed monthly [13]. Regimen change is if the ART regimen given to the adolescent at the time of treatment initiation was changed to other regimen types different from the baseline one. An adolescent is a study participant whose age was precisely between 10 and 19 years [22].

Data quality assurance

Data were collected by health professionals who were trained in HIV comprehensive care and working on the clients' follow-up services. One day orientation was given to the data collectors (BSc in Public Health or Nursing) and supervisors (BSc in Public Health) on the way of reviewing charts and extracting the needed data, study objectives, and keeping confidentiality. To check the consistency, completeness, and accuracy of the checklist, a pretest was conducted in Jinka General Hospital on 5% of the sample before the actual data collection. Necessary modifications (adding of the % option for viral load and removing the "presence of co-morbidity other than opportunistic infection" because it was absent for all the pre-test charts) were made accordingly before the starting of the actual data collection. The checklists were properly coded and numbered. The investigators and supervisors carried out daily data collection monitoring. Then appropriate feedback was given to the data collectors. After completing the data collection process, all the checklists were collected together and cross-checked for relevance.

Analysis

The data were checked, coded, cleaned, and then entered into Epi-Data version 3.1 before being exported to STATA version 14.0 for further management and analysis. Exploratory data analysis was performed to determine the presence of probable outliers, normality (by the Skewness and Kurtosis tests), and the level of missing values. Viral load and CD4 count showed missing values

of more than 30% and were excluded from the analysis. Median, interquartile range, frequencies, and percentages were used for descriptive statistics. Person year of observation was used to compute the incidence density (Incidence of Attrition = [number of attrition/total number of person-years of observation]*100). The Kaplan-Meier curve was used to estimate survival time and compare survival experience among categories of predictor variables, and the significance of survival experience was checked using the log-rank test. A life table was used to estimate the cumulative probability of survival at different time intervals. The Cox proportional hazards model was fitted after checking for proportional hazards assumption using the Schoenfeld residual test (global test) (P-value=0.5585) (Supplemental File 1). To analyze the association between each independent variable and the outcome variable, a binary Cox proportional hazards model was fitted, and variables with a P-value <0.25 in bivariable Cox regression were candidates for multivariable analysis. To find independent predictors of attrition, a multivariable Cox regression model with a backward stepwise likelihood ratio technique was built. The variance inflation factor (VIF) and tolerance were used to test for multicollinearity, the mean VIF = 1.23, showing no threat of multicollinearity. The Cox Snell residuals plot was used to assess the model's goodness of fit. The hazard function followed the 45-degree line very closely over time except for large values and fulfilled the assumption of Goodness of fit of the model (Figure 2). To identify statistically significant variables, AHR with a 95% confidence interval (CI) and matching P-value was used. The statistical significance was declared at the P-value < 0.05.

Patient and public involvement

None

RESULTS

Adolescent's sociodemographic characteristics

Of 437 adolescents (10-19 years) who were initiated on ART from January 01, 2014, to December 30, 2023, in the eight public hospitals, 409 were included in the analysis with a completeness rate of 94%.

The median age of the adolescents included in the study was 14 with an interquartile range (IQR) of 12 to 18 years and of the study participants, 213 (52.1%) were females. More than half of the adolescents were urban residents. Regarding the marital status of the adolescents, a majority (86.1%) were single and 16 (3.9%) were divorced after being married. Half, 206 (50.4%), of the adolescents who participated in the study have attained primary educational status and only ten (2.4%) attained tertiary and above. About three percent (2.9%) of the participants were female sex workers (Table 1).

Table 1. Sociodemographic characteristics of HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Variables	Categories	Frequency	Percentage (%)
Age (in years)	10-14	211	51.6
	15-19	198	48.4
Sex	Male	196	47.9
	Female	213	52.1
Residence	Urban	255	62.4
	Rural	154	37.7
Parent status	Both alive	200	48.9
	Either died	160	39.1
	Both died	49	12.0
	Single	352	86.1

Marital status	Married	41	10.0
	Divorced	16	3.9
Educational status	No formal education	77	18.8
	Primary	206	50.4
	Secondary	116	28.4
	Tertiary and above	10	2.4
Occupational status	Student	282	69.0
	Daily laborer	38	9.3
	Female sex worker	12	2.9
	No work/child	49	12.0
	Other *	28	6.8

Notes; *Other: merchant, housewife, farmer

Adolescents' baseline clinical and treatment-related characteristics

Of the total adolescents enrolled on ART care during the follow-up period, 253 (61.9%), were entered to care through medical referral or linkage. The hemoglobin level of the majority, 381 (93.1%), of the adolescents who participated in the study was ≥10g/dl. Regarding the WHO clinical staging, more than half 227 (55.5%) of the participants were in stage I at the time of ART initiation. Of the study participants, 65 (15.9%) have a history of tuberculosis infection at the start of the treatment initiation. Participants with a history of OIs other than TB account for less than twenty percent of the total participants and from these, pneumonia, 24 (34.8%) and diarrhea, 23 (33.3%) are among the commonly identified opportunistic infections. Two-thirds, 265 (64.8%), of the study participants disclosed their HIV status to others and the remaining kept their status secret from others. Regarding prophylaxis for the prevention of opportunistic infections, 227 (55.5%) and 268(65.5%) took CPT and INH, respectively. During the follow-up time, 157 (38.4%) of the adolescents were initiated on Zidovudine, Lamivudine and nevirapine-containing regimen (AZT+3TC+NVP) at baseline. The median duration of ART during the

follow-up time was 63 months with an IQR of 20 months to 101 months. Regarding treatment adherence, 30 (7.3%) had fair treatment adherence. Reasons for fair or poor treatment adherence are known for only eight participants and the reasons are far distance, forgetting the drug, stigma, and others. The baseline regimen of 265 (64.8%) adolescents who participated in the study was changed during the follow-up time and the main reason for the regimen change was the availability of a new drug, 150 (80.6%) (Table 2).

Table 2. Clinical and treatment-related characteristics of HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Variables	Categories	Frequency	Percentage (%)
Mode of entry	VCT	77	18.8
	Medical referral/linkage	253	61.9
	Other*	79	19.3
BMI for age	<-2SD	185	45.2
	≥-2SD	224	54.8
Hemoglobin level	<10g/dl	28	6.9
	≥10g/dl	381	93.1
WHO clinical staging	Stage I	227	55.5
	Stage II	56	13.7
	Stage III	107	26.1
	Stage IV	19	4.7
History of Tuberculosis	Yes	65	15.9
	No	344	84.1
Treated for TB (n=65)	Yes	61	93.9
	No	4	6.1
Treatment regimen for TB	2SRHZ/4RH	5	7.7
	2HRZE/4RH	55	84.6
	Unknown	5	7.7
History of opportunistic infections	Yes	74	18.1

other than TB	No	335	81.9
Functional status	Working	298	72.9
	Ambulatory	90	22.0
	Bedridden	21	5.1
Disclosure of HIV status to the adolescent	Yes	265	64.8
	No	144	35.2
CPT	Yes	227	55.5
	No	182	44.5
INH	Yes	268	65.5
	No	141	34.5
Type of initial regimen	TDF+3TC+EFV	60	14.7
	AZT+3TC+NVP	157	34.4
	TDF+3TC+DTG	69	16.9
	ABC+3TC+DTG	34	8.3
	AZT+3TC+EFV	23	5.6
	Other**	66	16.1
Month on ART	< 1year	55	13.5
	1 to 4 years	142	34.7
	≥5 years	212	51.8
Adherence	Good	331	80.9
	Fair	30	7.3
	Poor	48	11.7
Regimen change	Yes	265	64.8
	No	144	35.2
Viral Load (n=205) in copies/ml	Below 1000	180	87.8
	1000 and above	25	12.2
CD4 count (n=281) in cells/mm^3	≤200	50	17.8
	200-350	47	16.7
	≥350	184	65.5

Notes; *Other: Dried Blood Spots, index case testing, and self-referral **Other: ABC+3TC+EFV, ABC+3TC+LPV/r, TDF+3TC+ATV/r,

Incidence of attrition

The follow-up time was from January 1, 2014, to December 30, 2023, and the adolescents were followed for 0.3 years at minimum and 9.9 years at maximum. The median follow-up time was 5.6(IQR 1.9 - 9) years which yields a total of 2222.1 person-years of observation. The adolescents' mean survival time was 8.41 (95% CI: 8.09, 8.73) years. At the end of the follow-up, among the total study participants, 74 (18.1%) experienced attrition (11.7% were lost and 6.4% died) and 335 (81.9%) were censored (11.0% were transferred out and 70.9% were alive and on ART at the end of follow-up). The overall incidence density of attrition was 3.33 (95% CI: 2.65, 4.18) per 100 PYO. The incidence of attrition was 4.50 (95% CI: 3.42, 5.93) per 100 PYO in General Hospitals and 2.11 (95% CI: 1.40, 3.18) per 100 PYO in Primary Hospitals, respectively. The cumulative probability of survival was 0.9368, 0.8953, 0.8576, and 0.8469 at the end of 12, 24, 48, and 60 months, respectively as described by the life table.

The stepwise decreasing overall Kaplan-Meier survival curve didn't cross the survival function at a survival probability of 0.5 (Figure 3). The log-rank test showed that there is a statistically significant difference in survival experience among the categories of the predictor variable including age, educational status, CPT prophylaxis, baseline regimen change, and drug adherence.

It was identified that there is a statistically significant difference in survival time among adolescents among different categories of age groups. Hence, the mean survival time for adolescents aged 10 to 14 years was 8.71(95% CI: 8.32, 9.10) years and 8.08(7.56, 8.59) years, respectively. In addition, the rate of attrition among older adolescents was higher which was 4.30 (95% CI: 3.17, 5.85) when compared to the counterparts. Adolescents on ART unchanged initial regimen have the lowest survival times, 6.36 (95% CI: 5.54, 7.18) when compared to adolescents

whose baseline regimen was changed 9.16 (8.90, 9.43). In addition, there is a statistically significant difference in survival time among adolescents within different groups of treatment adherence levels. The mean survival time for adolescents with good treatment adherence was higher (8.96, 95% CI: 8.67, 9.25) than for those with fair (7.48, 95% CI: 6.07, 8.89) and poor treatment adherence (5.55, 95% CI: 4.39, 6.72). Another categorical variable that was found to have a significant difference in attrition-free survival time between its categories is initial regimen change. Adolescents whose baseline ART regimen was not changed have lower attrition-free survival times (6.36, 95% CI: 5.54, 7.19) as compared to those whose regimen was changed (9.16, 95% CI: 8.90, 9.43) (Figure 4).

Predictors of attrition among adolescents

In bivariable analysis, age, marital status, parent status, educational status, occupation, entry mode to care, CPT prophylaxis, regimen change, drug adherence, disclosure of HIV-sero status, and type of baseline regimen were predictors of attrition at a p-value of <0.25. In multivariable analysis, age, parent status, educational status, CPT prophylaxis, baseline regimen change, and drug adherence were predictors of attrition among adolescents at p-value <0.05. Hence, adolescents aged 15 years to 19 years had nearly two times (AHR=1.88; 95% CI: 1.12, 3.18) increased hazard of attrition from care when compared to their counterparts. The death of either or both of the parents of the adolescents increases the risk of program attrition by two-fold, (AHR=2.07; 95% CI: 1.22, 3.52) and (AHR=2.19; 95% CI: 1.04, 4.61), when compared to adolescent whose both parents are alive, respectively. Attaining no formal education (AHR=3.16; 95% CI: 1.48, 6.77) and attaining primary educational status (AHR=2.47; 95% CI: 1.25, 4.89) can result in more than two times higher hazard of attrition among adolescents participated in the current study. Adolescents who did not take the CPT prophylaxis for

prevention of opportunistic infection hand 1.73 times (AHR=1.73; 95% CI: 1.03, 2.91) increased the hazard of experiencing ART program attrition than their counterparts. Adolescents whose baseline ART regimen was not changed are at six-fold times (AHR=6.16; 95% CI: 3.56, 10.66) higher risk of attrition. Poor or fair treatment adherence can increase the hazard of attrition by five (AHR=5.16; 95% CI: 2.35, 11.32) and six (AHR=6.02; 95% CI: 3.52, 10.29) times when compared to adolescents with good treatment adherence, respectively (Supplemental File 2).

DISCUSSION

The study was conducted to determine the incidence of attrition and its predictors of attrition among HIV-infected adolescents receiving ART. At the end of the follow-up, among the total study participants, 74 (18.1%) experienced attrition. The overall incidence density of attrition was 3.33 (95% CI: 2.65, 4.18) per 100 PYO. Moreover, older age, parental death, attaining no formal education and primary educational status, non-CPT utilization, unchanged baseline ART regimen, and suboptimal treatment adherence were predictors of attrition among adolescents receiving ART.

This study reported that the incidence density of attrition was 3.33 per 100 PYO. This finding is lower than the retrospective cohort studies conducted in Thailand [9] and Myanmar [8]. It is also lower than the findings from cohort studies done in India [30] and South Africa [29]. This finding is also lower than the result from the retrospective cohort study done in Ethiopia [11]. This discrepancy may be due to the large sample size used in the previous studies [8 9 29 30]. Also, a long follow-up time [8], the difference in socio-demographic characteristics of the study participants and improvement in the current healthcare system than former times may contribute to the inconsistency. Another reason for the variance may be due to the difference in the operational definition of LTFU, it's defined as; if the last appointment was missed for ≥12 months [9] and

difference in study design [29]. Moreover, there was a difference in the study population, young adults were included in the studies done in Thailand [9] and South Africa [29] and the study done in Ethiopia [11] included children whose age is less than 10 years. The result of this study is in line with the studies done previously in Tanzania [27] and Ethiopia [11]. The reason behind this consistency in Ethiopia might be due to uniformity in follow-up charts and data recording formats in the ART program prepared by the Ethiopian Federal Minister of Health [13].

On the contrary, the overall incidence density of attrition as reported by the current study is slightly higher than studies conducted among adolescents living with HIV in South Africa [29] and Ethiopia [12]. This may be due to differences in the study population; the study conducted in South Africa additionally included young adults aged 20 to 28 years [29]. It may also be because of differences in study design [29], and large sample size [12 29]. In addition, the divergence may be explained by differences in the sociodemographic characteristics of study participants and the longer follow-up period of the current study.

Adolescents aged 15 years to 19 years had nearly two times increased hazard of attrition from care when compared to their counterparts. This finding is consistent with results from previous studies done in India [30], South Africa [31], and Uganda [20] which reported an increased risk of attrition with increased age (15-19 years). The reason might be because older adolescents started ART at the advanced immunodeficiency stage and also a large amount of adolescents lost from ART care as they transition from pediatric care to adult care [31 34 35].

Educational status of the adolescents was one of the identified predictors of attrition by the current study. Attaining no formal education or primary educational status can result in more than two times higher hazard of attrition compared with those attained secondary and above educational level as reported by this study. This is consistent with a study conducted in Amhara

region, Ethiopia [12]. This might be because adolescents who attained higher educational status were well-informed and aware of the benefit of retention in care and the effect of attrition on their health.

Death of either or both the parents of the adolescents can increase the risk program attrition by two-fold times when compared to adolescents whose both parents are alive, respectively. This finding is consistent with findings from studies conducted in Ethiopia [12 36]. However, the study done in Ethiopia [36] targeted children aged 0 to 14 years. The reason for this could be due to the lack of caregivers' role in providing proper feeding, drug administration, and supervision, collectively with the social and economic disruption resulting from the death of the caregivers [37]. In addition, adolescents living with widowed caregivers or on their own were considerably more likely to be depressed than their peers and may experience attrition from care [38].

The other predictor of attrition among HIV-positive adolescents is non-utilization of CPT prophylaxis. Hence, adolescents who did not take the CPT prophylaxis for prevention of opportunistic infection had 1.73 times increased hazard of experiencing ART program attrition than their counterparts. A similar finding was reported by studies done in Ethiopia [12 39] among which one was conducted among children [39]. This might be due to the fact that CPT administration can prevent the occurrence of OIs among HIV-positive individuals reduce AIDS-related mortality and improve life quality [40]. Moreover, the provision of CPT prophylaxis is an effective and simple intervention for reducing morbidity and increasing retention rates in ART Program [41].

Adolescents whose baseline ART regimen was not changed are at a six-fold times higher risk of attrition. This is supported by a study done in Ethiopia [12] and contrary to the study done in Namibia [19]. The study done in Namibia [19] reported that adolescents whose regimen was changed

to a second or third-line regimen were at higher hazard of attrition. This could be due to most of the old regimens having adverse effects that boost the progression of HIV infection to the AIDS stage and lead to succeeding complications. An AZT-based ART regimen is associated with the development of anemia, which has an extra effect on the patient's immune system [42]. The highest attrition was occurred among adolescents on AZT-based regimen which was 43.2% as reported by the current study.

Furthermore, treatment adherence was one of the identified predictors of attrition among HIV-positive adolescents. It was identified that poor or fair treatment adherence can increase the hazard of attrition by five and six times among HIV-positive adolescents when compared to adolescents with good treatment adherence, respectively. This result was supported by findings from previous studies done in Ethiopia [12 36]. However, the source population of one of the studies done in Ethiopia [36] was children aged 0 to 14 years. This can be due to the fact that fair or poor adherence can lead to higher viral load, drug resistance, and poor treatment outcomes. This can also result in decreased CD4 levels, the progression of AIDS, and an increase in OIs, all of which cause attrition [43].

CONCLUSION

Attrition was identified to be a significant public health problem in the study setting. Moreover, old age, parental death, not attending formal education, not using CPT, unchanged baseline regimen, and suboptimal treatment adherence predict attrition. Special attention should be given to the old aged, no formal education, those orphaned, and those with poor baseline clinical characteristics. Moreover, early tracing of missed follow-up schedules, improving adherence support, and increasing contacting frequency to reduce attrition are highly encouraged. To

address the effect of important clinical and sociodemographic variables, a longitudinal prospective study was needed.

Contributors TGG, TMT, and FM were responsible for the design of the study. TGG, FM, TMT, and AAS conducted the research. SS and SWK supervised data collection. TGG completed the statistical analyses and drafted the manuscript. TGG, FM, and TMT contributed to the writing of the manuscript. TGG is responsible for the overall content as guarantor. All authors read and approved the submitted version.

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Patient consent for publication Not applicable

Ethical approval Prior to data collection, the document was submitted to the Arba Minch College of Health Sciences' institutional ethical review board (IRB) for ethical assessment and approval. An ethical approval letter was obtained from IRB with reference number AMCHS/01/20/33/0. An official support letter was received from the Gamo and Ari Zones Health Departments. The letter of cooperation was submitted to hospital authorities, and permission was sought to have full access to the information. Individual informed consent/assent was not obtained from the participants or guardians because the study is a retrospective study that requires record review without physical contact with the participants, which was waived by the IRB.

Data availability statement Data are available upon reasonable request.

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REFERENCES

1. WHO. HIV and AIDS Fact sheet; 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/hiv-aids. Accessed 13 July 2023.
2. UNAIDS. Young people and HIV; 2023. Available at: https://www.unaids.org/sites/default/files/media_asset/young-people-and-hiv_en.pdf Accessed September 09, 2023.

3. UNICEF. UNICEF Data: Adolescent HIV prevention; 2023. Available at : https://data.unicef.org/topic/hivaids/adolescents-young-people/ Accessed September 09, 2023

4. UNAIDS. HIV and AIDS estimates country factsheet 2022 - Ethiopia; 2022. Available from: https://www.unaids.org/en/regionscountries/countries/ethiopia. Accessed September 09, 2023.

5. Organization WH. Consolidated HIV strategic information guidelines: driving impact through programme monitoring and management. 2020

6. Auld AF, Agolory SG, Shiraishi RW, et al. Antiretroviral therapy enrollment characteristics and outcomes among HIV-infected adolescents and young adults compared with older adults—seven African countries, 2004–2013. *Morbidity and Mortality Weekly Report* 2014;63(47):1097.

7. Kariminia A, Law M, Davies MA, et al. Mortality and losses to follow-up among adolescents living with HIV in the Ie DEA global cohort collaboration. *Journal of the International AIDS Society* 2018;21(12):e25215.

8. Htun T, Kyaw K, Aung T, et al. Attrition during pre-ART and ART time periods among adolescents enrolled in Integrated HIV Care Programme in Myanmar, 2005–2017. *Epidemiology & Infection* 2019;147

9. Teeraananchai S, Puthanakit T, Kerr SJ, et al. Attrition and treatment outcomes among adolescents and youths living with HIV in the Thai National AIDS Program. *Journal of virus eradication* 2019;5(1):33-40.

10. Leshargie CT, Demant D, Burrowes S, et al. The proportion of loss to follow-up from antiretroviral therapy (art) and its association with age among adolescents living with

HIV in sub-Saharan Africa: a systematic review and meta-analysis. *Plos one* 2022;17(8):e0272906.

11. Jerene D, Abebe W, Taye K, et al. Adolescents living with HIV are at higher risk of death and loss to follow up from care: Analysis of cohort data from eight health facilities in Ethiopia. *PloS one* 2019;14(10):e0223655.
12. Leshargie CT, Demant D, Burrowes S, et al. Incidence and predictors of mortality among adolescents on antiretroviral therapy in Amhara Region, Ethiopia: a retrospective cohort analysis. *BMJ open* 2022;12(11):e063879.
13. Ethiopia F. National consolidated guidelines for comprehensive HIV prevention, care and treatment. *Addis Ababa: Fmoh* 2018:1-238.
14. Geng EH, Nash D, Kambugu A, et al. Retention in care among HIV-infected patients in resource-limited settings: emerging insights and new directions. *Current Hiv/aids Reports* 2010;7:234-44.
15. UNAIDS. IN DANGER: UNAIDS Global AIDS Update 2022. Geneva: Joint United Nations Programme on HIV/ AIDS; 2022. Licence: CC BY-NC-SA 3.0 IGO.
16. UNCEF. 2023 Global Snapshot on HIV and AIDS: Progress and priorities for children, adolescents and pregnant women; 2023. Available from: https://www.childrenandaids.org/sites/default/files/2023-11/231130%20UNCEF_HIV_Global_Snapshot_2023UPDATED_0.pdf. Accessed on January 15, 2024.
17. Booysen F, Bachmann M, Matebesi Z, et al. The socio-economic impact of HIV/AIDS on households in South Africa: pilot study in Welkom and Qwaqwa, Free State Province. *Retrieved March* 2004;26:2009.

18. Booysen F, Van der Berg S. The role of social grants in mitigating the socio-economic impact of HIV/aids in two free state communities 1. *South African Journal of Economics* 2005;73:545-63.

19. Munyayi FK, van Wyk BE. Determinants and rates of retention in HIV care among adolescents receiving antiretroviral therapy in Windhoek, Namibia: a baseline cohort analysis. *BMC Public Health* 2023;23(1):1-12.

20. Okoboi S, Ssali L, Yansaneh AI, et al. Factors associated with long-term antiretroviral therapy attrition among adolescents in rural Uganda: a retrospective study. *Journal of the International AIDS Society* 2016;19:20841.

21. WHO. Global update on HIV treatment 2013: results, impact and opportunities: WHO report in partnership with UNICEF and UNAIDS. Avaialble from: https://iris.who.int/bitstream/handle/10665/85326/9789241505734_eng.pdf;jsessionid=B98E988DF5509E1C12576852805B8403?sequence=1. Acessed on July 23, 2023. . Geneva: WHO.

22. WHO. World Heath Organization: Adolescent health; 2023. Available from: https://www.who.int/health-topics/adolescent-health#tab=tab_1 Accessed September 25, 2023.

23. Organization WH. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach; 2021. Licence: CC BY-NC-SA 3.0 IGO: World Health Organization.

24. Judd A, Sohn AH, Collins IJ. Interventions to improve treatment, retention and survival outcomes for adolescents with perinatal HIV-1 transitioning to adult care: moving on up. *Current opinion in HIV and AIDS* 2016;11(5):477-86.

25. Neilan AM, Karalius B, Patel K, et al. Association of risk of viremia, immunosuppression, serious clinical events, and mortality with increasing age in perinatally human immunodeficiency virus–infected youth. *JAMA pediatrics* 2017;171(5):450-60.

26. Tesha E-D, Kishimba R, Njau P, et al. Predictors of loss to follow up from antiretroviral therapy among adolescents with HIV/AIDS in Tanzania. *PloS one* 2022;17(7):e0268825.

27. Amour MA, Shayo GA, Matee MM, et al. Predictors of mortality among adolescents and young adults living with HIV on antiretroviral therapy in Dar es Salaam, Tanzania: a retrospective cohort study. *Journal of the International AIDS Society* 2022;25(2):e25886.

28. Lamb MR, Fayorsey R, Nuwagaba-Biribonwoha H, et al. High attrition before and after ART initiation among youth (15–24 years of age) enrolled in HIV care. *AIDS (London, England)* 2014;28(4):559.

29. Nglazi MD, Kranzer K, Holele P, et al. Treatment outcomes in HIV-infected adolescents attending a community-based antiretroviral therapy clinic in South Africa. *BMC infectious diseases* 2012;12:1-7.

30. Nimkar S, Valvi C, Kadam D, et al. Loss to follow-up and mortality among HIV-infected adolescents receiving antiretroviral therapy in Pune, India. *HIV medicine* 2018;19(6):395-402.

31. Okonji EF, Wyk BV, Mukumbang FC. Two-year retention in care for adolescents on antiretroviral therapy in Ehlanzeni district, South Africa: a baseline cohort analysis. *AIDS care* 2023;35(3):374-84.

32. Nimwesiga C, Taremwa IM, Nakanjako D, et al. Factors Associated with Retention in HIV Care Among HIV-Positive Adolescents in Public Antiretroviral Therapy Clinics in

Ibanda District, Rural South Western Uganda. *HIV/AIDS-Research and Palliative Care* 2023:71-81.

33. Organization WH. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach: World Health Organization 2016.

34. Enane LA, Davies M-A, Leroy V, et al. Traversing the cascade: urgent research priorities for implementing the 'treat all'strategy for children and adolescents living with HIV in sub-Saharan Africa. *Journal of virus eradication* 2018;4:40-46.

35. Meloni ST, Agaba P, Chang CA, et al. Longitudinal evaluation of adherence, retention, and transition patterns of adolescents living with HIV in Nigeria. *PLoS One* 2020;15(7):e0236801.

36. Guyo TG, Toma TM, Haftu D, et al. Proportion of Attrition and Associated Factors Among Children Receiving Antiretroviral Therapy in Public Health Facilities, Southern Ethiopia. *HIV/AIDS-Research and Palliative Care* 2023:491-502.

37. Vreeman RC, Ayaya SO, Musick BS, et al. Adherence to antiretroviral therapy in a clinical cohort of HIV-infected children in East Africa. *PLoS One* 2018;13(2):e0191848.

38. Sengendo J, Nambi J. The psychological effect of orphanhood: a study of orphans in Rakai district. *Health transition review* 1997:105-24.

39. Chanie ES, Tesgera Beshah D, Ayele AD. Incidence and predictors of attrition among children on antiretroviral therapy at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, 2019: Retrospective follow-up study. *SAGE Open Medicine* 2022;10:20503121221077843.

40. Collini P, Obasi A. Cotrimoxazole prophylaxis: BMJ publishing Group Limited London, 2006.

41. Vitoria M, Granich R, Banda M, et al. Implementation of co-trimoxazole prophylaxis and isoniazid preventive therapy for people living with HIV. *Bulletin of the World Health Organization* 2010;88:253-59.

42. Gebremedhin KB, Haye TB. Factors associated with anemia among people living with HIV/AIDS taking ART in Ethiopia. *Advances in hematology* 2019;2019

43. Organization WH. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach: World Health Organization 2021.

Figure legends

Figure 1. Flow chart for study participants recruitment to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Figure 2. Cox-Snell residual plot for model fitness to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Figure 3. The overall Kaplan-Meier survival estimate showing the time until free of attrition among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Figure 4. Kaplan-Meier survival estimates of time until attrition free of the main predictor variables among adolescents on ART in public hospitals, south Ethiopia, 2024.

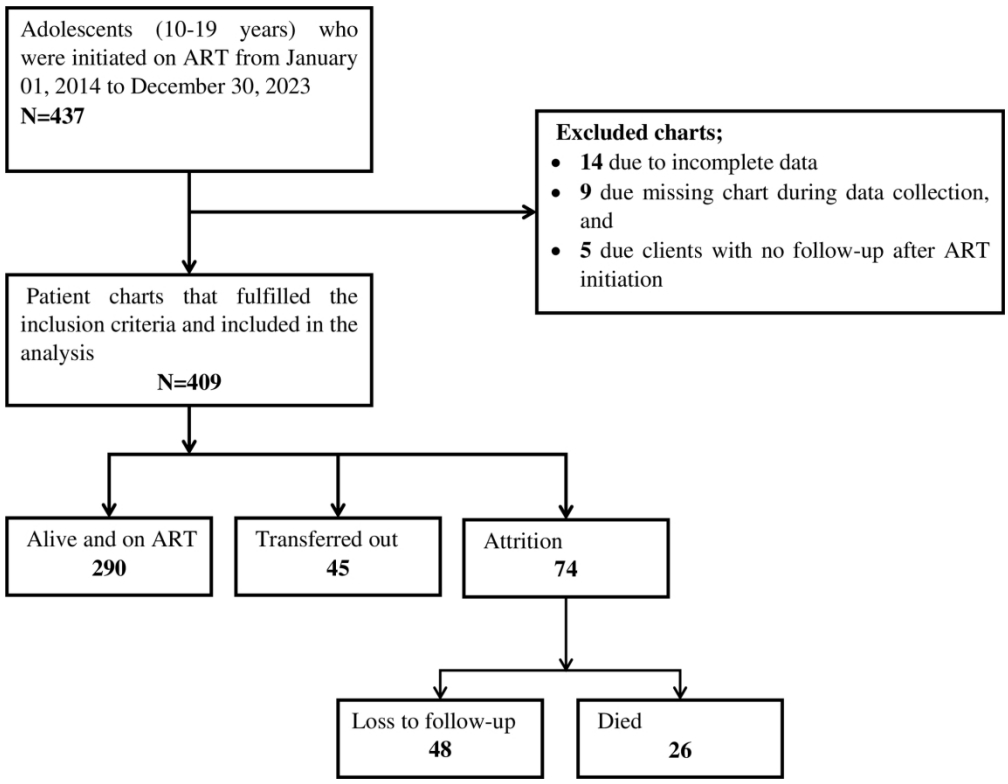

Figure 1. Flow chart for study participants recruitment to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

190x146mm (300 x 300 DPI)

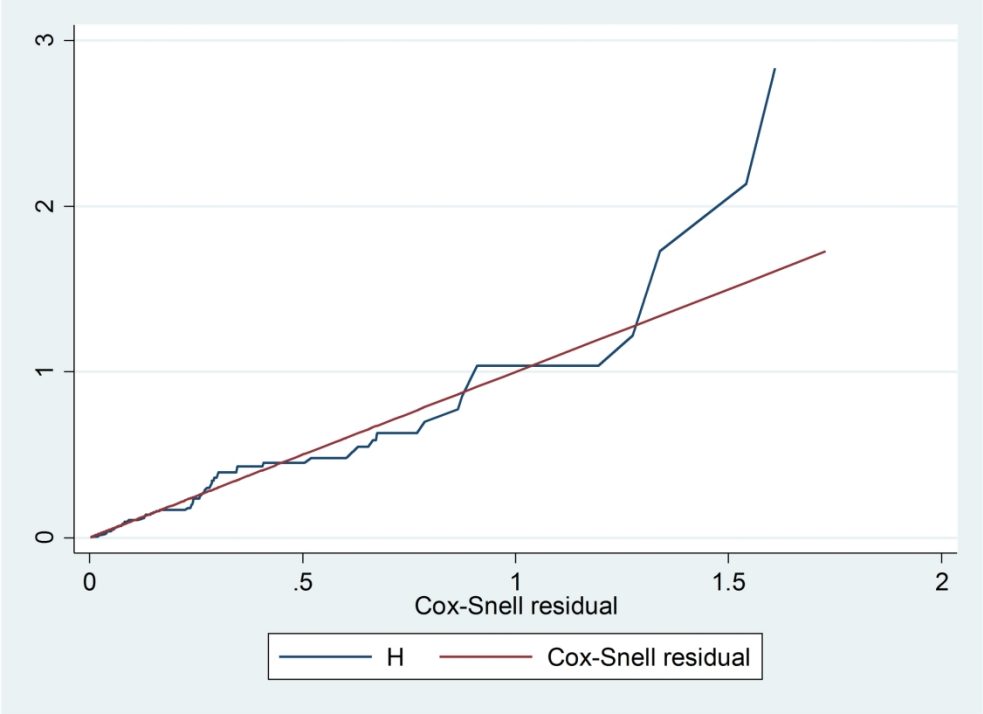

Figure 2. Cox-Snell residual plot for model fitness to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

484x353mm (118 x 118 DPI)

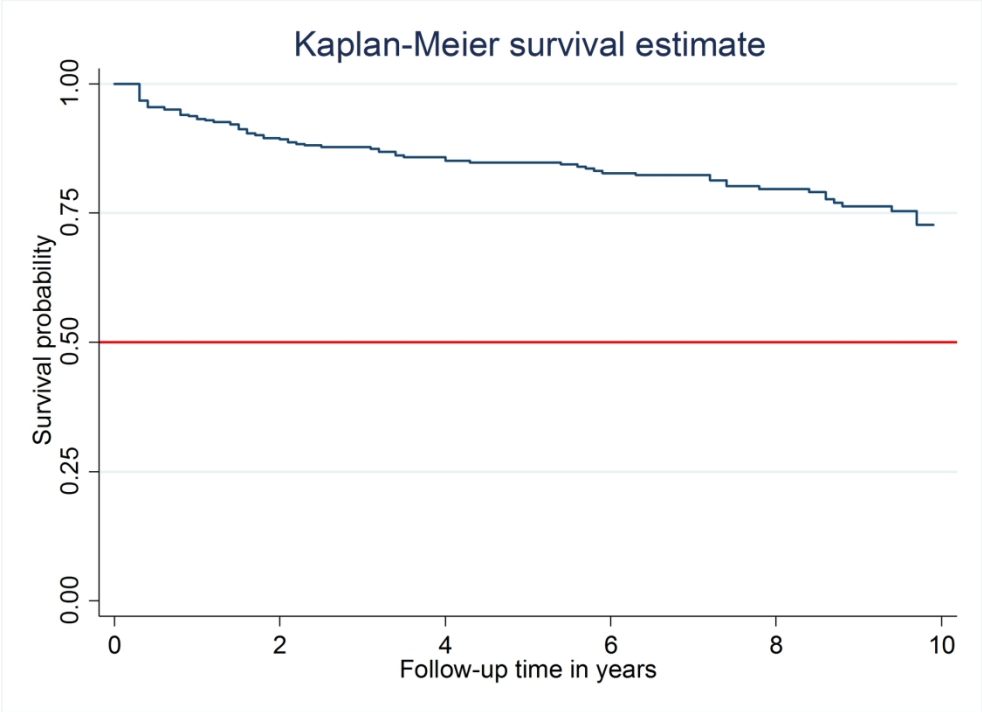

Figure 3. The overall Kaplan-Meier survival estimate showing the time until free of attrition among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

484x353mm (118 x 118 DPI)

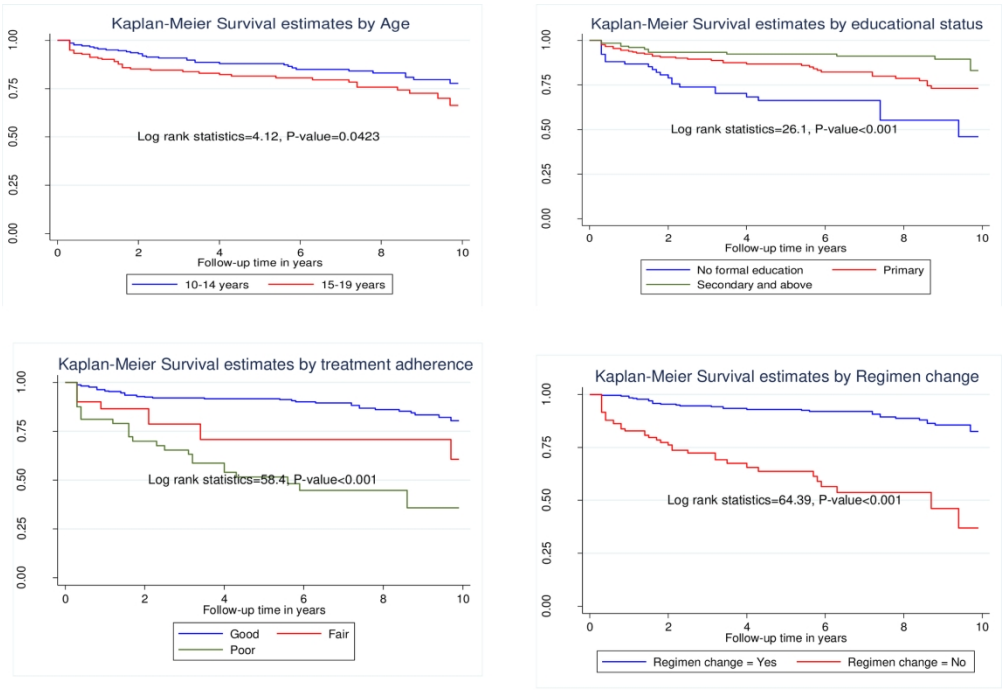

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Figure 4. Kaplan-Meier survival estimates of time until attrition free of the main predictor variables among adolescents on ART in public hospitals, south Ethiopia, 2024.

190x141mm (300 x 300 DPI)

Supplemental File 1. Test of proportional-hazards assumption to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in public health hospitals, south Ethiopia, 2024

Variables	Categories	X^2	DF	P-value
Age	15-19	1.17	1	0.2801
Parent status	Either died	0.14	1	0.7096
	Both died	1.82	1	0.1771
Educational status of caregiver	No formal education	2.65	1	0.1035
	Primary	1.38	1	0.2398
CPT prophylaxis	No	1.54	1	0.2147
Adherence	Fair	0.38	1	0.5398
	Poor	0.00	1	0.9710
Regimen change	No	0.28	1	0.5982
Global test		7.76	9	0.5585

Supplemental File 2. Multivariable cox-proportional analysis of predictors of attrition among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Variables	Categories	Attrition status		Incidence rate per 100 PYO (95% CI)	CHR (95% CI)	AHR (95% CI)	P-value
		Yes (Event)	No (Censored)				
Age (in years)	10-14	33 (15.6)	178 (84.4)	2.6 (1.8, 3.7)	1		
	15-19	41 (20.7)	157 (79.3)	4.3 (3.2, 5.8)	1.60 (1.08, 2.53)	1.88 (1.12, 3.18)	**0.018**
Parent status	Both alive	27 (13.5)	173 (86.5)	2.5 (1.7, 3.6)	1		
	Either died	37 (23.1)	123 (76.9)	4.5 (3.3, 6.2)	1.81 (1.19, 2.98)	2.07 (1.22, 3.52)	**0.007**
	Both died	10 (20.4)	39 (79.6)	3.3 (1.8, 6.1)	1.37 (0.63, 2.84)	2.19 (1.04, 4.61)	**0.040**
Marital status	Single	61 (17.3)	291 (82.7)	3.1 (2.4, 3.9)	1		
	Married	8 (19.5)	33 (80.5)	4.7 (2.4, 9.4)	1.45 (0.69, 3.03)	2.75 (0.34, 7.67)	0.479

	Divorced	5 (31.2)	11 (68.8)	8.2 (3.4, 19.7)	2.55 (1.02, 6.37)	0.79 (0.29, 2.14)	0.648
Educational status	No formal education	25 (32.5)	52 (67.5)	8.4 (5.7, 12.4)	4.94 (2.56, 9.76)	2.16 (1.48, 3.77)	**0.003**
	Primary	36 (17.5)	170 (82.5)	3.3 (2.4, 4.6)	2.09 (1.16, 3.95)	1.47 (1.25, 1.89)	**0.009**
	Secondary and above	13 (10.3)	113 (89.7)	1.5 (0.9, 2.7)	1		
Occupational status	Student	37 (13.1)	245 (86.9)	2.2 (1.6, 3.0)	1		
	Daily laborer	5 (13.2)	33 (86.8)	2.5 (1.1, 6.1)	1.14 (0.45, 2.89)	1.00 (0.34, 2.95)	0.995
	No work/child	20 (40.8)	29 (59.2)	11.5 (7.4, 17.8)	4.50 (2.59, 7.83)	1.48 (0.62, 3.51)	0.374
	Other *	12 (30.0)	28 (70.0)	7.2 (4.1, 12.7)	3.11 (1.68, 5.98)	1.45 (0.61, 3.47)	0.403
Entry mode	VCT	16 (20.8)	61 (79.2)	3.7 (2.3, 6.0)	1		
	Medical referral	47 (18.6)	206 (81.4)	3.6 (2.7, 4.8)	0.98 (0.55, 1.73)	0.84 (0.46, 1.52)	0.555

	Other **	11 (13.9)	68 (86.1)	2.2 (1.2, 4.1)	0.63 (0.2[illegible], 1.35)	[illegible].55 (0.24, [illegible].24)	0.147
CPT prophylaxis	Yes	37 (16.3)	190 (83.7)	2.7 (1.9, 3.5)	1		
	No	37 (20.3)	145 (79.7)	4.7 (3.4, 6.5)	1.74 (1.0[illegible], 2.77)	[illegible].73 (1.03, [illegible].91)	**0.038**
ART regimen	TDF+3TC+EFV	6 (10.0)	54 (90.0)	1.8 (0.8, 4.0)	0.29 (0.1[illegible], 0.86)	[illegible].89 (0.25, [illegible].11)	0.856
	AZT+3TC+NVP	32 (20.4)	125 (79.6)	3.0 (2.1, 4.2)	0.47 (0.2[illegible], 1.08)	[illegible].65 (0.25, [illegible].73)	0.391
	TDF+3TC+DTG	18 (26.1)	51 (73.9)	13.6 (8.6, 21.6)	1.63 (0.6[illegible], 3.91)	[illegible].62 (0.53, [illegible].94)	0.398
	ABC+3TC+DTG	7 (20.6)	27 (79.4)	7.3 (3.5, 15.3)	1		
	AZT+3TC+EFV	6 (26.1)	17 (73.9)	4.2 (1.9, 9.3)	0.66 (0.2[illegible], 1.98)	[illegible].96 (0.27, [illegible].36)	0.949
	Other***	5 (7.6)	61 (92.4)	1.1 (0.5, 2.7)	0.17 (0.05, 0.55)	[illegible].44 (0.12, [illegible].58)	0.208
Regimen change	Yes	31 (11.7)	234 (88.3)	1.7 (1.2, 2.4)	1		

	No	43 (29.9)	101 (70.1)	11.1 (8.3, 15.0)	6.04 (3.70, 9.86)	6.16 (3.56, 10.66)	**<0.001**
Disclosure of HIV status	Yes	41 (15.5)	224 (84.5)	2.8 (2.1, 3.8)	1		
	No	33 (22.9)	111 (77.1)	4.3 (3.1, 6.1)	1.53 (0.96, 2.43)	1.58 (0.95, 2.62)	0.075
Adherence	Good	39 (11.8)	292 (88.2)	2.1 (1.5, 2.9)	1		
	Fair	9 (30.0)	21 (70.0)	5.4 (2.9, 10.5)	2.52 (1.22, 5.22)	5.16 (2.35, 11.32)	**<0.001**
	Poor	26 (54.2)	22 (45.8)	12.6 (8.6, 18.5)	5.60 (3.40, 9.21)	6.02 (3.52, 10.29)	**<0.001**

Notes; *Other: merchant, housewife, farmer; **Other: Dried Blood Spots, index case testing, and self-referral ***Other: ABC+3TC+EFV, ABC+3TC+LPV/r, TDF+3TC+ATV/r,

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Incidence of attrition and predictors among HIV-infected adolescents receiving antiretroviral therapy in Public Hospitals, South Ethiopia: A multicenter retrospective follow-up study

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ABSTRACT

Objective This study aimed to determine the incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in public hospitals, South Ethiopia.

Study design A multi-center retrospective follow-up study was conducted and Cox proportional hazards model was used to identify predictors of the study outcome variable (attrition).

Settings The study was conducted in eight Public Hospitals (two general and six primary hospitals) in south Ethiopia.

Participants Adolescents (10-19 years) on antiretroviral therapy from January 01, 2014 to December 30, 2023. The data was collected from patient's charts and electronic data records.

Outcome Variable The primary outcome was time to attrition and the secondary outcome was predictors of attrition.

Results The overall incidence density of attrition was 3.33 (95% Confidence Interval (CI): 2.65, 4.18) per 100 Person Year of Observation (PYO). Age 15 to 19 years (Adjusted Hazard Ratio (AHR)=1.88; 95% CI: 1.12, 3.18), death of both the parents (AHR=2.19; 95% CI: 1.04, 4.61), no formal education (AHR=3.16; 95% CI: 1.48, 6.77), Cotrimoxazole Prophylaxis Therapy (CPT) non utilization (AHR=1.73; 95% CI: 1.03, 2.91), not changed regimen (AHR=6.16; 95% CI: 3.56, 10.66), and poor treatment adherence (AHR=5.16; 95% CI: 2.35, 11.32) were predictors of attrition.

Conclusion Attrition was identified to be a significant public health problem in study settings. Moreover, old age, parental death, not attending formal education, not using CPT, unchanged baseline regimen, and suboptimal treatment adherence predict attrition. Hence, special attention should be given to older adolescents, those with no formal education, orphaned, and with poor baseline clinical characteristics. Likewise, early tracing of missed follow-up schedules,

improving adherence support, and increasing contacting frequency to reduce attrition are highly encouraged.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- As attrition is a warning indicator for drug resistance, determining attrition is very important to monitor ART drug resistance and the current study used a long follow-up period to do so.
- The current study provided evidence on predictors of attrition for adolescents that can be important and used to improve adolescent's HIV-related services.
- The effect of some important predictor variables like; viral load and CD4 count, was not assessed because of incomplete records.
- Adolescents whose charts were lost and those with incomplete records were excluded from the analysis which may under or overestimate the attrition.

INTRODUCTION

Human immunodeficiency virus (HIV) continues to be a critical global public health problem. In 2022, about 1.65 million adolescents aged 10-19 were living with HIV, and 34,000 AIDS-related deaths occurred among them, globally [1 2]. About 1.40 million, or 85%, of adolescents living with HIV (ALHIV) were from sub-Saharan Africa (SSA) [2]. Ethiopia is one of the Sub-Saharan African countries with a total of 610,000 people living with HIV (PLHIV) and about 11,000 AIDS-related mortalities [3].

Attrition refers to the disruption in ART care, including lost patients, deaths, and those who stopped treatment, indicating progress towards achieving the 95-95-95 targets [4]. It continues to be a great public health problem among adolescents. Adolescents have significantly higher

attrition rates from ART than adults without being privileged and getting access to HIV care and treatment services, these results in relatively poorer outcomes [5].

Evidence from Global cohort collaboration reported that 30% and 3.9% of HIV-positive adolescents were lost to follow-up and died worldwide, respectively [6]. Based on the studies conducted in different countries, the incidence of attrition from ART care among Adolescents was anticipated to be high. Studies done in Myanmar [7] and Thailand [8] revealed that attrition rates among ALHIV were determined to be 6.4 per 100 PYO and 29.5%, respectively. Evidence from a systematic review conducted in Sub-Saharan Africa reported that 15.07% of ALHIV experienced attrition due to lost follow-up from ART after initiation of the treatment [9]. In Ethiopia, about 28.1% [10] of adolescents aged ten to nineteen years experienced attrition from HIV care and 11.1% experienced attrition from care due to death [11]. Attrition of patients from HIV care and treatment after ART initiation is resulting in an increase in poor treatment outcomes, including drug resistance, increased health care costs, preventable onward HIV transmission, and avoidable morbidity and death [12]. It can weaken the continuing provision of opportunistic infection prophylaxis, timely identification of treatment failure, and adverse events assessment [13]. In addition, attrition from HIV care also affected the 95-95-95 ambitious targets of UNAIDS which aimed at 95% viral suppression. Due to this impact of attrition, only 68% of PLHIV were virally suppressed and adolescents were highly in need of lifelong treatment, care, and social support to have better treatment and health outcomes as they pass through youth to adulthood [14]. Even though there is a paucity of information on adolescent viral suppression, 46% of children and adolescents were virally suppressed [15]. Attrition from the ART program can significantly impact households, often requiring orphaned children to assume responsibility for the household after the death of their young parents [16 17]. Predictors of adolescent attrition from

HIV care and treatment include advanced HIV disease, low hemoglobin level, absence of social support, financial constraints, lower age, and year of ART initiation. Attrition is also predicted by infection with tuberculosis (TB), non-disclosure, malnutrition, and Cotrimoxazole preventive therapy (CPT) utilization [7 12 18 19].

To minimize adolescents' attrition from HIV care and treatment services, different measures have been taken in Ethiopia. These include; decentralization of services, provision of ART drugs without charge, health education and counseling through community partners, and delivering phone text messages [12]. Attrition from care among ALHIV patients remains a significant challenge to ART program effectiveness, necessitating assessment of incidence and predictors for effective retention strategies[20].

According to the WHO 2021 consolidated HIV guideline, total attrition is one of the early warning indicators, and attrition ≥25% during the reporting period is a warning sign of drug resistance [21]. Despite the country's growing adolescent population and high prevalence of adolescent HIV infections, Ethiopia's HIV/AIDS policies currently do not provide adequate regard to the unique needs of adolescents [5 22 23]. Ethiopia's current HIV care and treatment guidelines primarily target children and adults, lacking a national focus on HIV care and treatment for ALHIV [12]. But this adolescent population is with rapid physical, cognitive, and psychological development significantly impacts their emotions, thoughts, decisions, and interactions with their environment and even affects their engagement in ART program [24]. Moreover, there is little indication of attrition from care among ALHIV on ART in Ethiopia, and none in the research settings. As a result, the purpose of this study is to determine the incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in Public Hospitals, South Ethiopia.

METHODS AND MATERIALS

Study design, period, and setting

A multicenter retrospective follow-up study was conducted in Gamo Zone and Ari Zones public hospitals in South Ethiopia from March 05, 2024, to April 05, 2024. Arba Minch town is the administrative center of the Gamo Zone. It is 505 Kilometers Southwest far from the capital city, Addis Ababa. Jinka town is the administrative center of Ari Zone in Southwest Ethiopia. It is about 563Km far from Addis Ababa. In these two zones, there are two general and six primary public hospitals providing ART services with about 5,480 individuals currently on HIV care and treatment among which adolescents account for 1,041. These health facilities provide different services (Outpatient department service, Inpatient department services, Emergency services, Maternal and Child Health services, Dental treatment, Ophthalmic service, and follow-up services) to the community in their catchment area and nearby woredas and zones. The estimated total population in the two zones was 2,127,970. Among these the adolescent population account for 410,059.

Population

All HIV-positive adolescents (10-19 years) who were on ART in public hospitals of Gamo and Ari Zones were the source population. All randomly selected HIV-positive adolescents (10-19 years) who were on ART in the public hospitals of Gamo and Ari Zones from January 01, 2014, to December 30, 2023, were the study population. All HIV-positive adolescents (10-19 years) who were on ART and had at least one follow-up visit from January 01, 2014, to December 30, 2023, were included in the study. HIV-positive adolescents whose charts were with incomplete records (indicators of the outcome were not registered) were excluded from the study.

Sample size determination and sampling procedures

The sample size was determined by STATA software v14.0 for major predictor variables using Cox model comparing one slope to the reference value based on the following assumptions: Significance level (**α**) (two-sided) = 0.05, 95% confidence interval, power of 80%, AHR = 1.58 for adolescents with HIV/TB co-infection who experienced attrition [25], standard deviation (variability) of covariates of interest = 0.5, the overall probability of event (attrition) (d) at the end of the study: 0.428 [25], and a 10% withdrawal probability was added for incomplete records yielding a total sample size of 434 to conduct the study.

First, in the two zones (Gamo and Ari) there are eight public hospitals; two General Hospitals (Jinka and Arba Minch General Hospitals) and six Primary Hospitals (Chencha, Selamber, Kamba, Gerese, Dilfana, and Gazer Primary Hospitals). In these public hospitals, 437 adolescents were on ART between January 01, 2014, and December 30, 2023. The adolescents (10-19 years) were identified in each hospital using medical record numbers (MRNs) obtained from electronic databases, and patient charts were drawn using the MRNs. The total number of adolescents identified in the hospitals is very close to the calculated sample size; all their charts were screened for eligibility by considering the inclusion criteria, and 409 eligible charts were included in the analysis (Figure 1).

Data collection tool, procedure, and personnel

Data were collected by using a data extraction checklist developed in English from the standardized ART intake and follow-up forms from national HIV guideline [12], and by reviewing related literature [6-11 19 25-30]. The data was collected from the charts of the adolescents who were initiated on ART care between January 01, 2014, to December 30, 2023. Adolescents who were categorized as LTFU during the study but were come back to the care before the follow-up ends

were counted as active because their coming back was the result of defaulter tracing intervention. The checklist contains the socio-demographic, clinical, and treatment-related characteristics of participants. The lists of study participants were taken from the ART data clerk by using children's MRN or unique ART numbers. Charts of the adolescents were taken from card rooms. Then data were collected by reviewing the registration books and patient follow-up charts by ten data collectors and eight supervisors.

Study variables

The dependent variable was time to attrition and the predictor variables included: socio-demographic variables: Age, Sex, residence, educational status, and marital status of the adolescents; clinical-related variables: Entry point of care, WHO clinical staging, nutritional status, hemoglobin level, CD4 count, presence opportunistic infections, functional status, and disclosure status; and treatment-related variables: Type of baseline regimen, regimen change, treatment adherence, and CPT prophylaxis.

Operational definitions

Attrition (Event) is if adolescents on ART were lost to follow-up or died within the follow-up period [31]. Whereas, censored is if adolescents on ART that were transferred out or alive and active on ART at the end of the study or turning 19 years of age [19 31]. Loss to follow-up is if an adolescent has not come to care for ≥3 consecutive months (≥90 days) after the last missed appointment and is not registered as died or transferred out to other health facilities [32]. However, adolescents were counted as died if he/she documented or registered as "died" on the exit form of the patient. Adherence is the extent to which an adolescent's behavior of taking ART medication with agreed-upon recommendations from a health-care provider. It was classified as; good: if ≥ 95% of the recommended doses were taken or ≤3 doses missed monthly, Fair: if 85-

94% of the recommended doses were taken or 4-9 doses missed monthly, poor: if < 85% of the recommended doses were taken or ≥10 doses missed monthly [12]. Regimen change is if the ART regimen given to the adolescent at the time of treatment initiation was changed to another regimen type different from the baseline one. An adolescent is a study participant whose age was precisely between 10 and 19 years [24].

Data quality assurance

Data were collected by health professionals who were trained in HIV comprehensive care and working on the clients' follow-up services. One day orientation was given to the data collectors (BSc in Public Health or Nursing) and supervisors (BSc in Public Health) on the way of reviewing charts and extracting the needed data, study objectives, and keeping confidentiality. To check the consistency, completeness, and accuracy of the checklist, a pretest was conducted in Jinka General Hospital on 5% of the sample before the actual data collection. Necessary modifications (adding the % option for viral load and removing the "presence of co-morbidity other than opportunistic infection" because it was absent for all the pre-test charts) were made accordingly before the starting of the actual data collection. The checklists were properly coded and numbered. The investigators and supervisors carried out daily data collection monitoring. Then appropriate feedback was given to the data collectors. After completing the data collection process, all the checklists were collected together and cross-checked for relevance.

Statistical Analysis

The data were checked, coded, cleaned, and then entered into Epi-Data version 3.1 before being exported to STATA version 14.0 for further management and analysis. Exploratory data analysis was performed to determine the presence of probable outliers, normality (by the Skewness and Kurtosis tests), and the level of missing values. Viral load and CD4 count showed missing values

of more than 30% and were excluded from the analysis. Median, interquartile range, frequencies, and percentages were used for descriptive statistics. Person year of observation was used to compute the incidence density (Incidence of Attrition = [number of attrition/total number of person-years of observation]*100). The Kaplan-Meier curve was used to estimate survival time and compare survival experience among categories of predictor variables, and the significance of survival experience was checked using the log-rank test. A life table was used to estimate the cumulative probability of survival at different time intervals. The Cox proportional hazards model was fitted after checking for proportional hazards assumption using the Schoenfeld residual test (global test) (P-value=0.5585) (Supplemental File 1). To analyze the association between each independent variable and the outcome variable, a binary Cox proportional hazards model was fitted, and variables with a P-value <0.25 in bivariable Cox regression were candidates for multivariable analysis. To find independent predictors of attrition, a multivariable Cox regression model with a backward stepwise likelihood ratio technique was built. The variance inflation factor (VIF) and tolerance were used to test for multicollinearity, the mean VIF = 1.23, showing no threat of multicollinearity. The Cox Snell residuals plot was used to assess the model's goodness of fit. The hazard function followed the 45-degree line very closely over time except for large values and fulfilled the assumption of Goodness of fit of the model (Figure 2). To identify statistically significant variables, AHR with a 95% confidence interval (CI) and matching P-value was used. The statistical significance was declared at the P-value < 0.05.

RESULTS

Adolescent's sociodemographic characteristics

Of 437 adolescents (10-19 years) who were initiated on ART from January 01, 2014, to December 30, 2023, in the eight public hospitals, the chart of 409 adolescents fulfilled the inclusion criteria and were reviewed.

The median age of the adolescents included in the study was 14 with an interquartile range (IQR) of 12 to 18 years and of the study participants, 213 (52.1%) were females. More than half of the adolescents were urban residents. Regarding the marital status of the adolescents, a majority (86.1%) were single and 16 (3.9%) were divorced after being married. Half, 206 (50.4%), of the adolescents who participated in the study have attained primary educational status and only ten (2.4%) attained tertiary and above. About three percent (2.9%) of the participants were female sex workers (Table 1).

Table 1. Sociodemographic characteristics of HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Variables	Categories	Frequency	Percentage (%)
Age (in years)	10-14	211	51.6
	15-19	198	48.4
Sex	Male	196	47.9
	Female	213	52.1
Residence	Urban	255	62.4
	Rural	154	37.7
Parent status	Both alive	200	48.9
	Either died	160	39.1
	Both died	49	12.0
	Single	352	86.1

Marital status	Married	41	10.0
	Divorced	16	3.9
Educational status	No formal education	77	18.8
	Primary	206	50.4
	Secondary	116	28.4
	Tertiary and above	10	2.4
Occupational status	Student	282	69.0
	Daily laborer	38	9.3
	Female sex worker	12	2.9
	No work/child	49	12.0
	Other *	28	6.8

Notes; *Other: merchant, housewife, farmer

Adolescents' baseline clinical and treatment-related characteristics

Of the total adolescents enrolled in ART care during the follow-up period, 253 (61.9%), were entered into care through medical referral or linkage. The hemoglobin level of the majority, 381 (93.1%), of the adolescents who participated in the study was ≥10g/dl. Regarding the WHO clinical staging, more than half 227 (55.5%) of the participants were in stage I at the time of ART initiation. Of the study participants, 65 (15.9%) have a history of tuberculosis infection at the start of the treatment initiation. Participants with a history of OIs other than TB account for less than twenty percent of the total participants and from these, pneumonia, 24 (34.8%), and diarrhea, 23 (33.3%) are among the commonly identified opportunistic infections. Two-thirds, 265 (64.8%), of the study participants disclosed their HIV status to others and the remaining kept their status secret from others. Regarding prophylaxis for the prevention of opportunistic infections, 227 (55.5%) and 268(65.5%) took CPT and INH, respectively. During the follow-up time, 157 (38.4%) of the adolescents were initiated on Zidovudine, Lamivudine, and nevirapine-containing regimen (AZT+3TC+NVP) at baseline. The median duration of ART during the

follow-up time was 63 months with an IQR of 20 months to 101 months. Regarding treatment adherence, 30 (7.3%) had fair treatment adherence. Reasons for fair or poor treatment adherence are known for only eight participants and the reasons are far distance, forgetting the drug, stigma, and others. The baseline regimen of 265 (64.8%) adolescents who participated in the study was changed during the follow-up time and the main reason for the regimen change was the availability of a new drug, 150 (80.6%) (Table 2).

Table 2. Clinical and treatment-related characteristics of HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Variables	Categories	Frequency	Percentage (%)
Mode of entry	VCT	77	18.8
	Medical referral/linkage	253	61.9
	Other*	79	19.3
BMI for age	<-2SD	185	45.2
	≥-2SD	224	54.8
Hemoglobin level	<10g/dl	28	6.9
	≥10g/dl	381	93.1
WHO clinical staging	Stage I	227	55.5
	Stage II	56	13.7
	Stage III	107	26.1
	Stage IV	19	4.7
History of Tuberculosis	Yes	65	15.9
	No	344	84.1
Treated for TB (n=65)	Yes	61	93.9
	No	4	6.1
Treatment regimen for TB	2SRHZ/4RH	5	7.7
	2HRZE/4RH	55	84.6
	Unknown	5	7.7
History of opportunistic infections	Yes	74	18.1

other than TB	No	335	81.9
Functional status	Working	298	72.9
	Ambulatory	90	22.0
	Bedridden	21	5.1
Disclosure of HIV status to the adolescent	Yes	265	64.8
	No	144	35.2
CPT	Yes	227	55.5
	No	182	44.5
INH	Yes	268	65.5
	No	141	34.5
Type of initial regimen	TDF+3TC+EFV	60	14.7
	AZT+3TC+NVP	157	34.4
	TDF+3TC+DTG	69	16.9
	ABC+3TC+DTG	34	8.3
	AZT+3TC+EFV	23	5.6
	Other**	66	16.1
Month on ART	< 1year	55	13.5
	1 to 4 years	142	34.7
	≥5 years	212	51.8
Adherence	Good	331	80.9
	Fair	30	7.3
	Poor	48	11.7
Regimen change	Yes	265	64.8
	No	144	35.2
Viral Load (n=205) in copies/ml	Below 1000	180	87.8
	1000 and above	25	12.2
CD4 count (n=281) in cells/mm^3	≤200	50	17.8
	200-350	47	16.7
	≥350	184	65.5

Notes; *Other: Dried Blood Spots, index case testing, and self-referral **Other: ABC+3TC+EFV, ABC+3TC+LPV/r, TDF+3TC+ATV/r,

Incidence of attrition

The follow-up time was from January 1, 2014, to December 30, 2023, and the adolescents were followed for 0.3 years at minimum and 9.9 years at maximum. The median follow-up time was 5.6(IQR 1.9 - 9) years which yields a total of 2222.1 person-years of observation. The adolescents' mean survival time was 8.41 (95% CI: 8.09, 8.73) years. At the end of the follow-up, among the total study participants, 74 (18.1%) experienced attrition (11.7% were lost and 6.4% died), and 335 (81.9%) were censored (11.0% were transferred out and 70.9% were alive and on ART at the end of follow-up). The overall incidence density of attrition was 3.33 (95% CI: 2.65, 4.18) per 100 PYO. The incidence of attrition was 4.50 (95% CI: 3.42, 5.93) per 100 PYO in General Hospitals and 2.11 (95% CI: 1.40, 3.18) per 100 PYO in Primary Hospitals, respectively. The cumulative probability of survival was 0.9368, 0.8953, 0.8576, and 0.8469 at the end of 12, 24, 48, and 60 months, respectively as described by the life table.

The stepwise decreasing overall Kaplan-Meier survival curve didn't cross the survival function at a survival probability of 0.5 (Figure 3). The log-rank test showed that there is a statistically significant difference in survival experience among the categories of the predictor variable including age, educational status, CPT prophylaxis, baseline regimen change, and drug adherence.

It was identified that there is a statistically significant difference in survival time among adolescents among different categories of age groups. Hence, the mean survival time for adolescents aged 10 to 14 years was 8.71(95% CI: 8.32, 9.10) years and 8.08(7.56, 8.59) years, respectively. In addition, the rate of attrition among older adolescents was higher which was 4.30 (95% CI: 3.17, 5.85) when compared to the counterparts. Adolescents on ART unchanged initial regimen have the lowest survival times, 6.36 (95% CI: 5.54, 7.18) when compared to adolescents

whose baseline regimen was changed 9.16 (8.90, 9.43). In addition, there is a statistically significant difference in survival time among adolescents within different groups of treatment adherence levels. The mean survival time for adolescents with good treatment adherence was higher (8.96, 95% CI: 8.67, 9.25) than for those with fair (7.48, 95% CI: 6.07, 8.89) and poor treatment adherence (5.55, 95% CI: 4.39, 6.72). Another categorical variable that was found to have a significant difference in attrition-free survival time between its categories is initial regimen change. Adolescents whose baseline ART regimen was not changed have lower attrition-free survival times (6.36, 95% CI: 5.54, 7.19) as compared to those whose regimen was changed (9.16, 95% CI: 8.90, 9.43) (Figure 4).

Predictors of attrition among adolescents

In bivariable analysis, age, marital status, parent status, educational status, occupation, entry mode to care, CPT prophylaxis, regimen change, drug adherence, disclosure of HIV-sero status, and type of baseline regimen were predictors of attrition at a p-value of <0.25. In multivariable analysis, age, parent status, educational status, CPT prophylaxis, baseline regimen change, and drug adherence were predictors of attrition among adolescents at p-value <0.05. Hence, adolescents aged 15 years to 19 years had nearly two times (AHR=1.88; 95% CI: 1.12, 3.18) increased hazard of attrition from care when compared to their counterparts. The death of either or both of the parents of the adolescents increases the risk of program attrition by two-fold, (AHR=2.07; 95% CI: 1.22, 3.52) and (AHR=2.19; 95% CI: 1.04, 4.61), when compared to adolescent whose both parents are alive, respectively. Attaining no formal education (AHR=3.16; 95% CI: 1.48, 6.77) and attaining primary educational status (AHR=2.47; 95% CI: 1.25, 4.89) can result in more than two times higher hazard of attrition among adolescents participated in the current study. Adolescents who did not take the CPT prophylaxis for

prevention of opportunistic infection hand 1.73 times (AHR=1.73; 95% CI: 1.03, 2.91) increased the hazard of experiencing ART program attrition than their counterparts. Adolescents whose baseline ART regimen was not changed are at six-fold times (AHR=6.16; 95% CI: 3.56, 10.66) higher risk of attrition. Poor or fair treatment adherence can increase the hazard of attrition by five (AHR=5.16; 95% CI: 2.35, 11.32) and six (AHR=6.02; 95% CI: 3.52, 10.29) times when compared to adolescents with good treatment adherence, respectively (Supplemental File 2).

DISCUSSION

The study was conducted to determine the incidence of attrition and its predictors of attrition among HIV-infected adolescents receiving ART. At the end of the follow-up, among the total study participants, 74 (18.1%) experienced attrition. The overall incidence density of attrition was 3.33 (95% CI: 2.65, 4.18) per 100 PYO. Moreover, older age, parental death, attaining no formal education and primary educational status, non-CPT utilization, unchanged baseline ART regimen, and suboptimal treatment adherence were predictors of attrition among adolescents receiving ART.

This study reported that the incidence density of attrition was 3.33 per 100 PYO. This finding is lower than the retrospective cohort studies conducted in Thailand [8] and Myanmar [7]. It is also lower than the findings from cohort studies done in India [29] and South Africa [28]. This finding is also lower than the result from the retrospective cohort study done in Ethiopia [10]. This discrepancy may be due to the large sample size used in the previous studies [7 8 28 29]. Also, a long follow-up time [7], the difference in socio-demographic characteristics of the study participants, and improvement in the current healthcare system than former times may contribute to the inconsistency. Another reason for the variance may be due to the difference in the operational definition of LTFU, it's defined as; if the last appointment was missed for ≥12 months [8] and

difference in study design [28]. Moreover, there was a difference in the study population, young adults were included in the studies done in Thailand [8] and South Africa [28] and the study done in Ethiopia [10] included children whose age is less than 10 years. The result of this study is in line with the studies done previously in Tanzania [26] and Ethiopia [10]. The reason behind this consistency in Ethiopia might be due to uniformity in follow-up charts and data recording formats in the ART program prepared by the Ethiopian Federal Minister of Health [12].

On the contrary, the overall incidence density of attrition as reported by the current study is slightly higher than studies conducted among adolescents living with HIV in South Africa [28] and Ethiopia [11]. This may be due to differences in the study population; the study conducted in South Africa additionally included young adults aged 20 to 28 years [28]. It may also be because of differences in study design [28], and large sample size [11 28]. In addition, the divergence may be explained by differences in the sociodemographic characteristics of study participants and the longer follow-up period of the current study.

Adolescents aged 15 years to 19 years had nearly two times increased hazard of attrition from care when compared to their counterparts. This finding is consistent with results from previous studies done in India [29], South Africa [30], and Uganda [19] which reported an increased risk of attrition with increased age (15-19 years). The reason might be because older adolescents started ART at the advanced immunodeficiency stage and also a large amount of adolescents lost from ART care as they transition from pediatric care to adult care [30 33 34].

The educational status of the adolescents was one of the identified predictors of attrition by the current study. Attaining no formal education or primary educational status can result in more than two times higher hazard of attrition compared with those attained secondary and above educational level as reported by this study. This is consistent with a study conducted in Amhara

region, Ethiopia [11]. This might be because adolescents who attained higher educational status were well-informed and aware of the benefit of retention in care and the effect of attrition on their health.

Death of either or both the parents of the adolescents can increase the risk program attrition by two-fold times when compared to adolescents whose both parents are alive, respectively. This finding is consistent with findings from studies conducted in Ethiopia [11 35]. However, the study done in Ethiopia [35] targeted children aged 0 to 14 years. The reason for this could be due to the lack of caregivers' role in providing proper feeding, drug administration, and supervision, collectively with the social and economic disruption resulting from the death of the caregivers [36]. In addition, adolescents living with widowed caregivers or on their own were considerably more likely to be depressed than their peers and may experience attrition from care [37].

The other predictor of attrition among HIV-positive adolescents is non-utilization of CPT prophylaxis. Hence, adolescents who did not take the CPT prophylaxis for prevention of opportunistic infection had 1.73 times increased hazard of experiencing ART program attrition than their counterparts. A similar finding was reported by studies done in Ethiopia [11 38] among which one was conducted among children [38]. This might be because CPT administration can prevent the occurrence of OIs among HIV-positive individuals reduce AIDS-related mortality and improve life quality [39]. Moreover, the provision of CPT prophylaxis is an effective and simple intervention for reducing morbidity and increasing retention rates in ART Program [40].

Adolescents whose baseline ART regimen was not changed are at six-fold times higher risk of attrition. This is supported by a study done in Ethiopia [11] and contrary to the study done in Namibia [18]. The study done in Namibia [18] reported that adolescents whose regimen was changed to a second or third-line regimen were at higher hazard of attrition. This could be due to most of

the old regimens having adverse effects that boost the progression of HIV infection to the AIDS stage and lead to succeeding complications. An AZT-based ART regimen is associated with the development of anemia, which has an extra effect on the patient's immune system [41]. The highest attrition has occurred among adolescents on AZT-based regimens which was 43.2% as reported by the current study.

Furthermore, treatment adherence was one of the identified predictors of attrition among HIV-positive adolescents. It was identified that poor or fair treatment adherence can increase the hazard of attrition by five and six times among HIV-positive adolescents when compared to adolescents with good treatment adherence, respectively. This result was supported by findings from previous studies done in Ethiopia [11 35]. However, the source population of one of the studies done in Ethiopia [35] was children aged 0 to 14 years. This can be because fair or poor adherence can lead to higher viral load, drug resistance, and poor treatment outcomes. This can also result in decreased CD4 levels, the progression of AIDS, and an increase in OIs, all of which cause attrition [42].

As attrition is a warning indicator for drug resistance, determining attrition is very important to monitor ART drug resistance and the current study used a long follow-up period to do so. The current study provided evidence on predictors of attrition for adolescents that can be important and used to improve adolescent's HIV-related services. Despite the strengths, the current study has some limitations; the effect of some important predictor variables like; viral load and CD4 count, was not assessed because of incomplete records. In addition, adolescents whose charts were lost and those with incomplete records were excluded from the analysis which may under or overestimate the attrition.

CONCLUSION

Attrition was identified to be a significant public health problem in the study setting. Moreover, old age, parental death, not attending formal education, not using CPT, unchanged baseline regimen, and suboptimal treatment adherence predict attrition. Special attention should be given to the old aged, no formal education, those orphaned, and those with poor baseline clinical characteristics. Moreover, early tracing of missed follow-up schedules, improving adherence support, and increasing contacting frequency to reduce attrition are highly encouraged. To address the effect of important clinical and sociodemographic variables, a longitudinal prospective study was needed.

Contributors TGG, TMT, and FM were responsible for the design of the study. TGG, FM, TMT, and AAS conducted the research. SS and SWK supervised data collection. TGG completed the statistical analyses and drafted the manuscript. TGG, FM, and TMT contributed to the writing of the manuscript. TGG is responsible for the overall content as guarantor. All authors read and approved the submitted version.

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Patient consent for publication Not applicable

Ethical approval Before data collection, the document was submitted to the Arba Minch College of Health Sciences' institutional ethical review board (IRB) for ethical assessment and approval. An ethical approval letter was obtained from IRB with reference number AMCHS/01/20/33/0. An official support letter was received from the Gamo and Ari Zones Health Departments. The letter of cooperation was submitted to hospital authorities, and permission was sought to have full access to the information. Individual informed consent/assent was not obtained from the participants or guardians because the study is a retrospective study that requires record review without physical contact with the participants, which was waived by the IRB.

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REFERENCES

1. UNAIDS. Young people and HIV; 2023. Available at: https://www.unaids.org/sites/default/files/media_asset/young-people-and-hiv_en.pdf Accessed September 09, 2023.
2. UNICEF. UNICEF Data: Adolescent HIV prevention; 2023. Available at : https://data.unicef.org/topic/hivaids/adolescents-young-people/ Accessed September 09, 2023

3. UNAIDS. HIV and AIDS estimates country factsheet 2022 - Ethiopia; 2022. Available from: https://www.unaids.org/en/regionscountries/countries/ethiopia. Accessed September 09, 2023.

4. Organization WH. Consolidated HIV strategic information guidelines: driving impact through programme monitoring and management. 2020

5. Auld AF, Agolory SG, Shiraishi RW, et al. Antiretroviral therapy enrollment characteristics and outcomes among HIV-infected adolescents and young adults compared with older adults—seven African countries, 2004–2013. *Morbidity and Mortality Weekly Report* 2014;63(47):1097.

6. Kariminia A, Law M, Davies MA, et al. Mortality and losses to follow-up among adolescents living with HIV in the Ie DEA global cohort collaboration. *Journal of the International AIDS Society* 2018;21(12):e25215.

7. Htun T, Kyaw K, Aung T, et al. Attrition during pre-ART and ART time periods among adolescents enrolled in Integrated HIV Care Programme in Myanmar, 2005–2017. *Epidemiology & Infection* 2019;147

8. Teeraananchai S, Puthanakit T, Kerr SJ, et al. Attrition and treatment outcomes among adolescents and youths living with HIV in the Thai National AIDS Program. *Journal of virus eradication* 2019;5(1):33-40.

9. Leshargie CT, Demant D, Burrowes S, et al. The proportion of loss to follow-up from antiretroviral therapy (art) and its association with age among adolescents living with HIV in sub-Saharan Africa: a systematic review and meta-analysis. *Plos one* 2022;17(8):e0272906.

10. Jerene D, Abebe W, Taye K, et al. Adolescents living with HIV are at higher risk of death and loss to follow up from care: Analysis of cohort data from eight health facilities in Ethiopia. *PloS one* 2019;14(10):e0223655.

11. Leshargie CT, Demant D, Burrowes S, et al. Incidence and predictors of mortality among adolescents on antiretroviral therapy in Amhara Region, Ethiopia: a retrospective cohort analysis. *BMJ open* 2022;12(11):e063879.

12. Ethiopia F. National consolidated guidelines for comprehensive HIV prevention, care and treatment; 2018. Addis Ababa: Fmoh 2018:1-238. Available from: https://www.afro.who.int/sites/default/files/2019-04/National%20Comprehensive%20HIV%20Care%20%20Guideline%202018.pdf. Accesed on September 12, 2023.

13. Geng EH, Nash D, Kambugu A, et al. Retention in care among HIV-infected patients in resource-limited settings: emerging insights and new directions. *Current Hiv/aids Reports* 2010;7:234-44.

14. UNAIDS. IN DANGER: UNAIDS Global AIDS Update 2022. Geneva: Joint United Nations Programme on HIV/ AIDS; 2022. Licence: CC BY-NC-SA 3.0 IGO.

15. UNCEF. 2023 Global Snapshot on HIV and AIDS: Progress and priorities for children, adolescents and pregnant women; 2023. Available from: https://www.childrenandaids.org/sites/default/files/2023-11/231130%20UNCEF_HIV_Global_Snapshot_2023UPDATED_0.pdf. Accessed on January 15, 2024.

16. Booysen F, Bachmann M, Matebesi Z, et al. The socio-economic impact of HIV/AIDS on households in South Africa: pilot study in Welkom and Qwaqwa, Free State Province. *Retrieved March* 2004;26:2009.

17. Booysen F, Van der Berg S. The role of social grants in mitigating the socio-economic impact of HIV/aids in two free state communities 1. *South African Journal of Economics* 2005;73:545-63.

18. Munyayi FK, van Wyk BE. Determinants and rates of retention in HIV care among adolescents receiving antiretroviral therapy in Windhoek, Namibia: a baseline cohort analysis. *BMC Public Health* 2023;23(1):1-12.

19. Okoboi S, Ssali L, Yansaneh AI, et al. Factors associated with long-term antiretroviral therapy attrition among adolescents in rural Uganda: a retrospective study. *Journal of the International AIDS Society* 2016;19:20841.

20. WHO. Global update on HIV treatment 2013: results, impact and opportunities: WHO report in partnership with UNICEF and UNAIDS. Avaialble from: https://iris.who.int/bitstream/handle/10665/85326/9789241505734_eng.pdf;jsessionid=B98E988DF5509E1C12576852805B8403?sequence=1. Acessed on July 23, 2023. . Geneva: WHO.

21. Organization WH. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach; 2021. Licence: CC BY-NC-SA 3.0 IGO: World Health Organization.

22. Judd A, Sohn AH, Collins IJ. Interventions to improve treatment, retention and survival outcomes for adolescents with perinatal HIV-1 transitioning to adult care: moving on up. *Current opinion in HIV and AIDS* 2016;11(5):477-86.

23. Neilan AM, Karalius B, Patel K, et al. Association of risk of viremia, immunosuppression, serious clinical events, and mortality with increasing age in perinatally human immunodeficiency virus–infected youth. *JAMA pediatrics* 2017;171(5):450-60.

24. WHO. World Heath Organization: Adolescent health; 2023. Available from: https://www.who.int/health-topics/adolescent-health#tab=tab_1 Accessed September 25, 2023.

25. Tesha E-D, Kishimba R, Njau P, et al. Predictors of loss to follow up from antiretroviral therapy among adolescents with HIV/AIDS in Tanzania. *PloS one* 2022;17(7):e0268825.

26. Amour MA, Shayo GA, Matee MM, et al. Predictors of mortality among adolescents and young adults living with HIV on antiretroviral therapy in Dar es Salaam, Tanzania: a retrospective cohort study. *Journal of the International AIDS Society* 2022;25(2):e25886.

27. Lamb MR, Fayorsey R, Nuwagaba-Biribonwoha H, et al. High attrition before and after ART initiation among youth (15–24 years of age) enrolled in HIV care. *AIDS (London, England)* 2014;28(4):559.

28. Nglazi MD, Kranzer K, Holele P, et al. Treatment outcomes in HIV-infected adolescents attending a community-based antiretroviral therapy clinic in South Africa. *BMC infectious diseases* 2012;12:1-7.

29. Nimkar S, Valvi C, Kadam D, et al. Loss to follow-up and mortality among HIV-infected adolescents receiving antiretroviral therapy in Pune, India. *HIV medicine* 2018;19(6):395-402.

30. Okonji EF, Wyk BV, Mukumbang FC. Two-year retention in care for adolescents on antiretroviral therapy in Ehlanzeni district, South Africa: a baseline cohort analysis. *AIDS care* 2023;35(3):374-84.

31. Nimwesiga C, Taremwa IM, Nakanjako D, et al. Factors Associated with Retention in HIV Care Among HIV-Positive Adolescents in Public Antiretroviral Therapy Clinics in Ibanda District, Rural South Western Uganda. *HIV/AIDS-Research and Palliative Care* 2023:71-81.

32. Organization WH. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach: World Health Organization 2016.

33. Enane LA, Davies M-A, Leroy V, et al. Traversing the cascade: urgent research priorities for implementing the 'treat all'strategy for children and adolescents living with HIV in sub-Saharan Africa. *Journal of virus eradication* 2018;4:40-46.

34. Meloni ST, Agaba P, Chang CA, et al. Longitudinal evaluation of adherence, retention, and transition patterns of adolescents living with HIV in Nigeria. *PLoS One* 2020;15(7):e0236801.

35. Guyo TG, Toma TM, Haftu D, et al. Proportion of Attrition and Associated Factors Among Children Receiving Antiretroviral Therapy in Public Health Facilities, Southern Ethiopia. *HIV/AIDS-Research and Palliative Care* 2023:491-502.

36. Vreeman RC, Ayaya SO, Musick BS, et al. Adherence to antiretroviral therapy in a clinical cohort of HIV-infected children in East Africa. *PLoS One* 2018;13(2):e0191848.

37. Sengendo J, Nambi J. The psychological effect of orphanhood: a study of orphans in Rakai district. *Health transition review* 1997:105-24.

38. Chanie ES, Tesgera Beshah D, Ayele AD. Incidence and predictors of attrition among children on antiretroviral therapy at University of Gondar Comprehensive Specialized

Hospital, Northwest Ethiopia, 2019: Retrospective follow-up study. *SAGE Open Medicine* 2022;10:20503121221077843.

39. Collini P, Obasi A. Cotrimoxazole prophylaxis: BMJ publishing Group Limited London, 2006.

40. Vitoria M, Granich R, Banda M, et al. Implementation of co-trimoxazole prophylaxis and isoniazid preventive therapy for people living with HIV. *Bulletin of the World Health Organization* 2010;88:253-59.

41. Gebremedhin KB, Haye TB. Factors associated with anemia among people living with HIV/AIDS taking ART in Ethiopia. *Advances in hematology* 2019;2019

42. Organization WH. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach: World Health Organization 2021.

Figure legends

Figure 1. Flow chart for study participants recruitment to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Figure 2. Cox-Snell residual plot for model fitness to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Figure 3. The overall Kaplan-Meier survival estimate showing the time until free of attrition among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Figure 4. Kaplan-Meier survival estimates of time until attrition free of the main predictor variables among adolescents on ART in public hospitals, south Ethiopia, 2024.

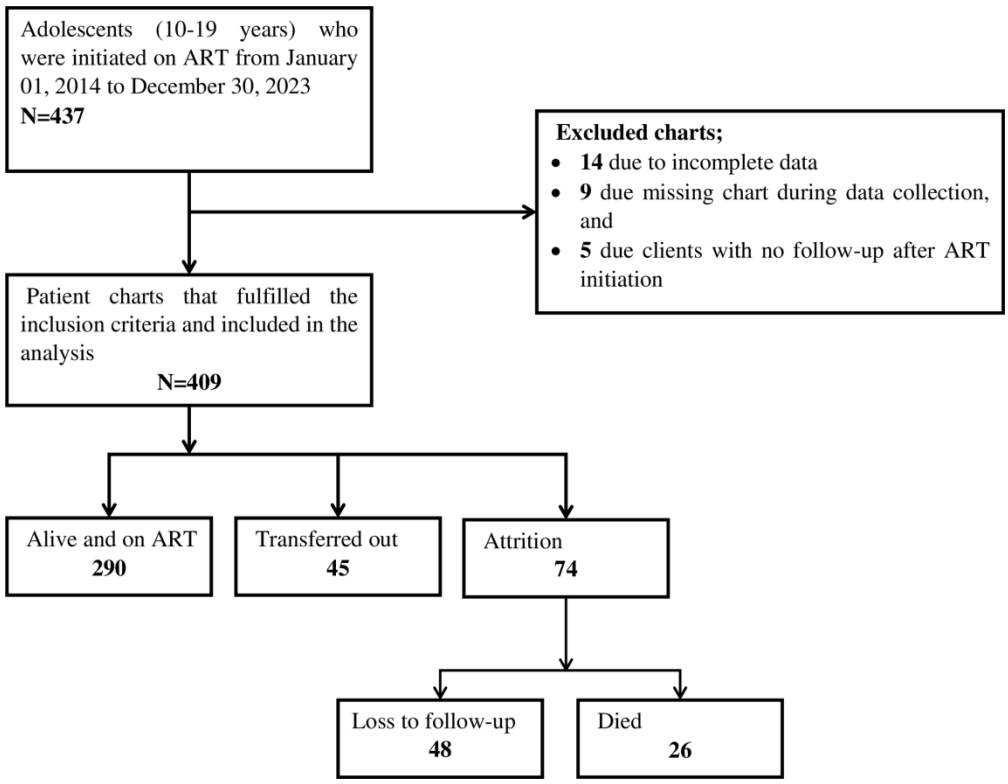

Figure 1. Flow chart for study participants recruitment to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

190x146mm (300 x 300 DPI)

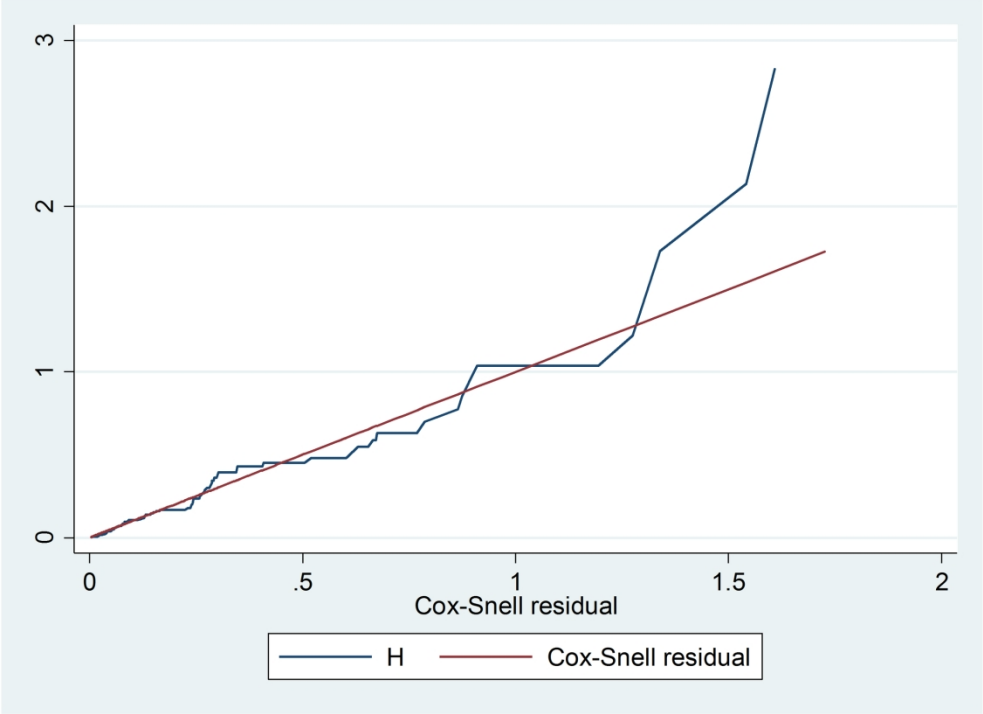

Figure 2. Cox-Snell residual plot for model fitness to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

484x353mm (118 x 118 DPI)

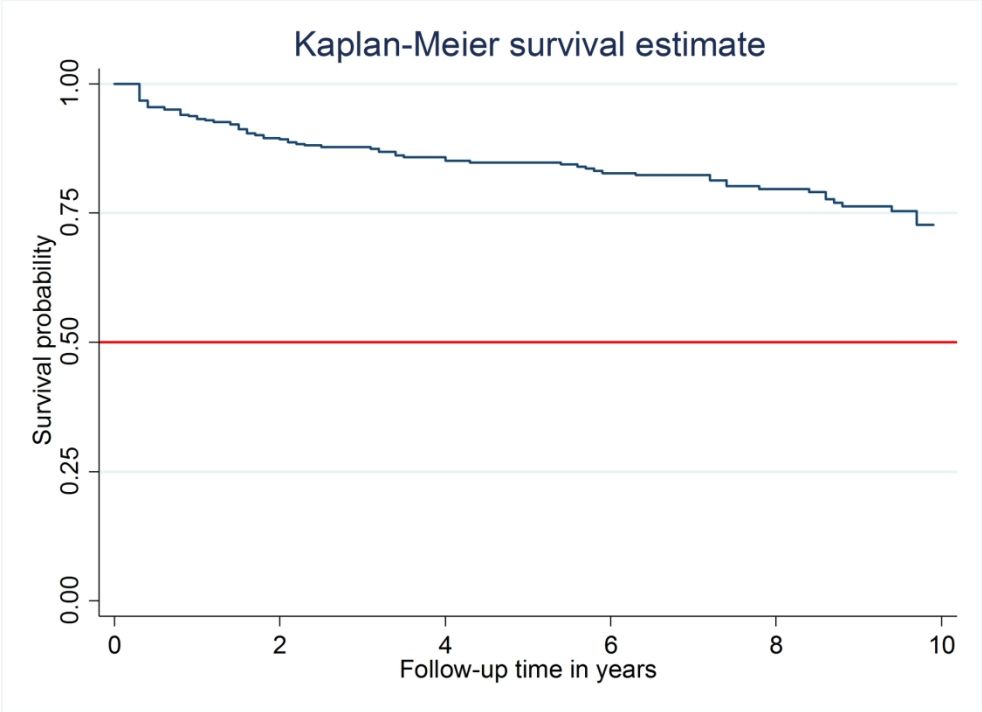

Figure 3. The overall Kaplan-Meier survival estimate showing the time until free of attrition among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

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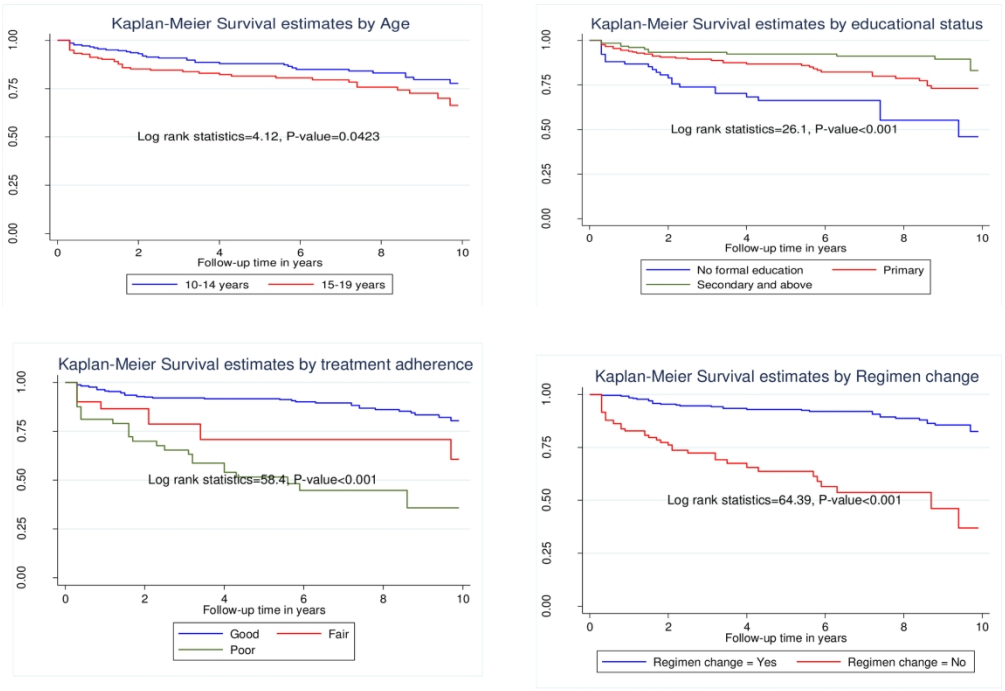

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Figure 4. Kaplan-Meier survival estimates of time until attrition free of the main predictor variables among adolescents on ART in public hospitals, south Ethiopia, 2024.

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Supplemental File 1. Test of proportional-hazards assumption to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in public health hospitals, south Ethiopia, 2024

Variables	Categories	X^2	DF	P-value
Age	15-19	1.17	1	0.2801
Parent status	Either died	0.14	1	0.7096
	Both died	1.82	1	0.1771
Educational status of caregiver	No formal education	2.65	1	0.1035
	Primary	1.38	1	0.2398
CPT prophylaxis	No	1.54	1	0.2147
Adherence	Fair	0.38	1	0.5398
	Poor	0.00	1	0.9710
Regimen change	No	0.28	1	0.5982
Global test		7.76	9	0.5585

Supplemental File 2. Multivariable cox-proportional analysis of predictors of attrition among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Variables	Categories	Attrition status		Incidence rate per 100 PYO (95% CI)	CHR (95% CI)	AHR (95% CI)	P-value
		Yes (Event)	No (Censored)				
Age (in years)	10-14	33 (15.6)	178 (84.4)	2.6 (1.8, 3.7)	1		
	15-19	41 (20.7)	157 (79.3)	4.3 (3.2, 5.8)	1.60 (1.08, 2.53)	1.88 (1.12, 3.18)	**0.018**
Parent status	Both alive	27 (13.5)	173 (86.5)	2.5 (1.7, 3.6)	1		
	Either died	37 (23.1)	123 (76.9)	4.5 (3.3, 6.2)	1.81 (1.19, 2.98)	2.07 (1.22, 3.52)	**0.007**
	Both died	10 (20.4)	39 (79.6)	3.3 (1.8, 6.1)	1.37 (0.63, 2.84)	2.19 (1.04, 4.61)	**0.040**
Marital status	Single	61 (17.3)	291 (82.7)	3.1 (2.4, 3.9)	1		
	Married	8 (19.5)	33 (80.5)	4.7 (2.4, 9.4)	1.45 (0.69, 3.03)	2.75 (0.34, 7.67)	0.479

	Divorced	5 (31.2)	11 (68.8)	8.2 (3.4, 19.7)	2.55 (1.02, 6.37)	0.79 (0.29, 2.14)	0.648
Educational status	No formal education	25 (32.5)	52 (67.5)	8.4 (5.7, 12.4)	4.94 (2.56, 9.76)	2.16 (1.48, 3.77)	**0.003**
	Primary	36 (17.5)	170 (82.5)	3.3 (2.4, 4.6)	2.09 (1.16, 3.95)	1.47 (1.25, 1.89)	**0.009**
	Secondary and above	13 (10.3)	113 (89.7)	1.5 (0.9, 2.7)	1		
Occupational status	Student	37 (13.1)	245 (86.9)	2.2 (1.6, 3.0)	1		
	Daily laborer	5 (13.2)	33 (86.8)	2.5 (1.1, 6.1)	1.14 (0.45, 2.89)	1.00 (0.34, 2.95)	0.995
	No work/child	20 (40.8)	29 (59.2)	11.5 (7.4, 17.8)	4.50 (2.59, 7.83)	1.48 (0.62, 3.51)	0.374
	Other *	12 (30.0)	28 (70.0)	7.2 (4.1, 12.7)	3.11 (1.68, 5.98)	1.45 (0.61, 3.47)	0.403
Entry mode	VCT	16 (20.8)	61 (79.2)	3.7 (2.3, 6.0)	1		
	Medical referral	47 (18.6)	206 (81.4)	3.6 (2.7, 4.8)	0.98 (0.55, 1.73)	0.84 (0.46, 1.52)	0.555

	Other **	11 (13.9)	68 (86.1)	2.2 (1.2, 4.1)	0.63 (0.2[illegible], 1.35)	0.55 (0.24, 1.24)	0.147
CPT prophylaxis	Yes	37 (16.3)	190 (83.7)	2.7 (1.9, 3.5)	1		
	No	37 (20.3)	145 (79.7)	4.7 (3.4, 6.5)	1.74 (1.0[illegible], 2.77)	1.73 (1.03, 2.91)	**0.038**
ART regimen	TDF+3TC+EFV	6 (10.0)	54 (90.0)	1.8 (0.8, 4.0)	0.29 (0.1[illegible], 0.86)	0.89 (0.25, 3.11)	0.856
	AZT+3TC+NVP	32 (20.4)	125 (79.6)	3.0 (2.1, 4.2)	0.47 (0.2[illegible], 1.08)	0.65 (0.25, 1.73)	0.391
	TDF+3TC+DTG	18 (26.1)	51 (73.9)	13.6 (8.6, 21.6)	1.63 (0.6[illegible], 3.91)	1.62 (0.53, 4.94)	0.398
	ABC+3TC+DTG	7 (20.6)	27 (79.4)	7.3 (3.5, 15.3)	1		
	AZT+3TC+EFV	6 (26.1)	17 (73.9)	4.2 (1.9, 9.3)	0.66 (0.22, 1.98)	0.96 (0.27, 3.36)	0.949
	Other***	5 (7.6)	61 (92.4)	1.1 (0.5, 2.7)	0.17 (0.05, 0.55)	0.44 (0.12, 1.58)	0.208
Regimen change	Yes	31 (11.7)	234 (88.3)	1.7 (1.2, 2.4)	1		

	No	43 (29.9)	101 (70.1)	11.1	(8.3, 15.0)	6.04	(3.70, 9.86)	6.16	(3.56, 10.66)	**<0.001**
Disclosure of HIV status	Yes	41 (15.5)	224 (84.5)	2.8 (2.1, 3.8)		1				
	No	33 (22.9)	111 (77.1)	4.3 (3.1, 6.1)		1.53	(0.97, 2.43)	1.58	(0.95, 2.62)	0.075
Adherence	Good	39 (11.8)	292 (88.2)	2.1 (1.5, 2.9)		1				
	Fair	9 (30.0)	21 (70.0)	5.4 (2.9, 10.5)		2.52	(1.22, 5.22)	5.16	(2.35, 11.32)	**<0.001**
	Poor	26 (54.2)	22 (45.8)	12.6	(8.6, 18.5)	5.60	(3.40, 9.21)	6.02	(3.52, 10.29)	**<0.001**

Notes; *Other: merchant, housewife, farmer; **Other: Dried Blood Spots, index case testing, and self-referral; ***Other: ABC+3TC+EFV, ABC+3TC+LPV/r, TDF+3TC+ATV/r,

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Incidence of attrition and predictors among HIV-infected adolescents receiving antiretroviral therapy in Public Hospitals, South Ethiopia: A multicenter retrospective follow-up study

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ABSTRACT

Objective This study aimed to determine the incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in public hospitals, South Ethiopia.

Study design A multi-center retrospective follow-up study was conducted and Cox proportional hazards model was used to identify predictors of the study outcome variable (attrition).

Settings The study was conducted in eight Public Hospitals (two general and six primary hospitals) in south Ethiopia.

Participants Adolescents (10-19 years) on antiretroviral therapy from January 01, 2014 to December 30, 2023 (n=409). The data was collected from patient's charts and electronic data records.

Outcome Variable The primary outcome was time to attrition and the secondary outcome was predictors of attrition.

Results The overall incidence density of attrition was 3.33 (95% Confidence Interval (CI): 2.65, 4.18) per 100 Person Year of Observation (PYO). Age 15 to 19 years (Adjusted Hazard Ratio (AHR)=1.88; 95% CI: 1.12, 3.18), death of both the parents (AHR=2.19; 95% CI: 1.04, 4.61), no formal education (AHR=3.16; 95% CI: 1.48, 6.77), Cotrimoxazole Prophylaxis Therapy (CPT) non utilization (AHR=1.73; 95% CI: 1.03, 2.91), not changed regimen (AHR=6.16; 95% CI: 3.56, 10.66), and poor treatment adherence (AHR=5.16; 95% CI: 2.35, 11.32) were predictors of attrition.

Conclusion Attrition was identified to be a significant public health problem in study settings. Moreover, old age, parental death, not attending formal education, not using CPT, unchanged baseline regimen, and suboptimal treatment adherence predict attrition. Hence, special attention should be given to older adolescents, those with no formal education, orphaned, and with poor

baseline clinical characteristics. Likewise, early tracing of missed follow-up schedules, improving adherence support, and increasing contacting frequency to reduce attrition are highly encouraged.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- As attrition is a warning indicator for drug resistance, determining attrition is very important to monitor ART drug resistance and the current study used a long follow-up period to do so.
- Evidence on the important predictors that can be used for intervention targeted at improving adolescents' HIV-related care and services was generated.
- The effect of some important predictor variables like; viral load and CD4 count, was not assessed because of incomplete records.
- Adolescents whose charts were lost and those with incomplete records were excluded from the analysis which may under or overestimate the attrition.

INTRODUCTION

Human immunodeficiency virus (HIV) continues to be a critical global public health problem. In 2022, about 1.65 million adolescents aged 10-19 were living with HIV, and 34,000 AIDS-related deaths occurred among them, globally [1 2]. About 1.40 million, or 85%, of adolescents living with HIV (ALHIV) were from sub-Saharan Africa (SSA) [2]. Ethiopia is one of the Sub-Saharan African countries with a total of 610,000 people living with HIV (PLHIV) and about 11,000 AIDS-related mortalities [3].

Attrition refers to the disruption in ART care, including lost patients, deaths, and those who stopped treatment, indicating progress towards achieving the 95-95-95 targets [4]. It continues to be a great public health problem among adolescents. Adolescents have significantly higher

attrition rates from ART than adults without being privileged and getting access to HIV care and treatment services, these results in relatively poorer outcomes [5].

Evidence from Global cohort collaboration reported that 30% and 3.9% of HIV-positive adolescents were lost to follow-up and died worldwide, respectively [6]. Based on the studies conducted in different countries, the incidence of attrition from ART care among Adolescents was anticipated to be high. Studies done in Myanmar [7] and Thailand [8] revealed that attrition rates among ALHIV were determined to be 6.4 per 100 PYO and 29.5%, respectively. Evidence from a systematic review conducted in Sub-Saharan Africa reported that 15.07% of ALHIV experienced attrition due to lost follow-up from ART after initiation of the treatment [9]. In Ethiopia, about 28.1% [10] of adolescents aged ten to nineteen years experienced attrition from HIV care and 11.1% experienced attrition from care due to death [11]. Attrition of patients from HIV care and treatment after ART initiation is resulting in an increase in poor treatment outcomes, including drug resistance, increased health care costs, preventable onward HIV transmission, and avoidable morbidity and death [12]. It can weaken the continuing provision of opportunistic infection prophylaxis, timely identification of treatment failure, and adverse events assessment [13]. In addition, attrition from HIV care also affected the 95-95-95 ambitious targets of UNAIDS which aimed at 95% viral suppression. Due to this impact of attrition, only 68% of PLHIV were virally suppressed and adolescents were highly in need of lifelong treatment, care, and social support to have better treatment and health outcomes as they pass through youth to adulthood [14]. Even though there is a paucity of information on adolescent viral suppression, 46% of children and adolescents were virally suppressed [15]. Attrition from the ART program can significantly impact households, often requiring orphaned children to assume responsibility for the household after the death of their young parents [16 17]. Predictors of adolescent attrition from

HIV care and treatment include advanced HIV disease, low hemoglobin level, absence of social support, financial constraints, lower age, and year of ART initiation. Attrition is also predicted by infection with tuberculosis (TB), non-disclosure, malnutrition, and Cotrimoxazole preventive therapy (CPT) utilization [7 12 18 19].

To minimize adolescents' attrition from HIV care and treatment services, different measures have been taken in Ethiopia. These include; decentralization of services, provision of ART drugs without charge, health education and counseling through community partners, and delivering phone text messages [12]. Attrition from care among ALHIV patients remains a significant challenge to ART program effectiveness, necessitating assessment of incidence and predictors for effective retention strategies[20].

According to the WHO 2021 consolidated HIV guideline, total attrition is one of the early warning indicators, and attrition ≥25% during the reporting period is a warning sign of drug resistance [21]. Despite the country's growing adolescent population and high prevalence of adolescent HIV infections, Ethiopia's HIV/AIDS policies currently do not provide adequate regard to the unique needs of adolescents [5 22 23]. Ethiopia's current HIV care and treatment guidelines primarily target children and adults, lacking a national focus on HIV care and treatment for ALHIV [12]. But this adolescent population is with rapid physical, cognitive, and psychological development significantly impacts their emotions, thoughts, decisions, and interactions with their environment and even affects their engagement in ART program [24]. Moreover, there is little indication of attrition from care among ALHIV on ART in Ethiopia, and none in the research settings. As a result, the purpose of this study is to determine the incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in Public Hospitals, South Ethiopia.

METHODS AND MATERIALS

Study design, period, and setting

A multicenter retrospective follow-up study was conducted in Gamo Zone and Ari Zones public hospitals in South Ethiopia from March 05, 2024, to April 05, 2024. Arba Minch town is the administrative center of the Gamo Zone. It is 505 Kilometers Southwest far from the capital city, Addis Ababa. Jinka town is the administrative center of Ari Zone in Southwest Ethiopia. It is about 563Km far from Addis Ababa. In these two zones, there are two general and six primary public hospitals providing ART services with about 5,480 individuals currently on HIV care and treatment among which adolescents account for 1,041. These health facilities provide different services (Outpatient department service, Inpatient department services, Emergency services, Maternal and Child Health services, Dental treatment, Ophthalmic service, and follow-up services) to the community in their catchment area and nearby woredas and zones. The estimated total population in the two zones was 2,127,970. Among these the adolescent population account for 410,059.

Population

All HIV-positive adolescents (10-19 years) who were on ART in public hospitals of Gamo and Ari Zones were the source population. All randomly selected HIV-positive adolescents (10-19 years) who were on ART in the public hospitals of Gamo and Ari Zones from January 01, 2014, to December 30, 2023, were the study population. All HIV-positive adolescents (10-19 years) who were on ART and had at least one follow-up visit from January 01, 2014, to December 30, 2023, were included in the study. HIV-positive adolescents whose charts were with incomplete records (indicators of the outcome were not registered) were excluded from the study.

Sample size determination and sampling procedures

The sample size was determined by STATA software v14.0 for major predictor variables using Cox model comparing one slope to the reference value based on the following assumptions: Significance level (**α**) (two-sided) = 0.05, 95% confidence interval, power of 80%, AHR = 1.58 for adolescents with HIV/TB co-infection who experienced attrition [25], standard deviation (variability) of covariates of interest = 0.5, the overall probability of event (attrition) (d) at the end of the study: 0.428 [25], and a 10% withdrawal probability was added for incomplete records yielding a total sample size of 434 to conduct the study.

First, in the two zones (Gamo and Ari) there are eight public hospitals; two General Hospitals (Jinka and Arba Minch General Hospitals) and six Primary Hospitals (Chencha, Selamber, Kamba, Gerese, Dilfana, and Gazer Primary Hospitals). In these public hospitals, 437 adolescents were on ART between January 01, 2014, and December 30, 2023. The adolescents (10-19 years) were identified in each hospital using medical record numbers (MRNs) obtained from electronic databases, and patient charts were drawn using the MRNs. The total number of adolescents identified in the hospitals is very close to the calculated sample size; all their charts were screened for eligibility by considering the inclusion criteria, and 409 eligible charts were included in the analysis (Figure 1).

Data collection tool, procedure, and personnel

Data were collected by using a data extraction checklist developed in English from the standardized ART intake and follow-up forms from national HIV guideline [12], and by reviewing related literature [6-11 19 25-30]. The data was collected from the charts of the adolescents who were initiated on ART care between January 01, 2014, to December 30, 2023. Adolescents who were categorized as LTFU during the study but were come back to the care before the follow-up

(Since this type of study looks back at the existing, records, the follow-up period is defined by the time frame in which the researcher can ascertain the outcome from the historical data) ends were counted as active because their coming back was the result of defaulter tracing intervention. The checklist contains the socio-demographic, clinical, and treatment-related characteristics of participants. The lists of study participants were taken from the ART data clerk by using children's MRN or unique ART numbers. Charts of the adolescents were taken from card rooms. Then data were collected by reviewing the registration books and patient follow-up charts by ten data collectors and eight supervisors.

Study variables

The dependent variable was time to attrition and the predictor variables included: socio-demographic variables: Age, Sex, residence, educational status, and marital status of the adolescents; clinical-related variables: Entry point of care, WHO clinical staging, nutritional status, hemoglobin level, CD4 count, presence opportunistic infections, functional status, and disclosure status; and treatment-related variables: Type of baseline regimen, regimen change, treatment adherence, and CPT prophylaxis.

Operational definitions

Attrition (Event) is if adolescents on ART were lost to follow-up or died within the follow-up period [31]. Whereas, censored is if adolescents on ART that were transferred out or alive and active on ART at the end of the study or turning 19 years of age [19 31]. Loss to follow-up is if an adolescent has not come to care for ≥3 consecutive months (≥90 days) after the last missed appointment and is not registered as died or transferred out to other health facilities [32]. However, adolescents were counted as died if he/she documented or registered as "died" on the exit form of the patient. Adherence is the extent to which an adolescent's behavior of taking ART

medication with agreed-upon recommendations from a health-care provider. It was classified as; good: if ≥ 95% of the recommended doses were taken or ≤3 doses missed monthly, Fair: if 85-94% of the recommended doses were taken or 4-9 doses missed monthly, poor: if < 85% of the recommended doses were taken or ≥10 doses missed monthly [12]. Regimen change is if the ART regimen given to the adolescent at the time of treatment initiation was changed to another regimen type different from the baseline one. An adolescent is a study participant whose age was precisely between 10 and 19 years [24].

Data quality assurance

Data were collected by health professionals who were trained in HIV comprehensive care and working on the clients' follow-up services. One day orientation was given to the data collectors (BSc in Public Health or Nursing) and supervisors (BSc in Public Health) on the way of reviewing charts and extracting the needed data, study objectives, and keeping confidentiality. To check the consistency, completeness, and accuracy of the checklist, a pretest was conducted in Jinka General Hospital on 5% of the sample before the actual data collection. Necessary modifications (adding the % option for viral load and removing the "presence of co-morbidity other than opportunistic infection" because it was absent for all the pre-test charts) were made accordingly before the starting of the actual data collection. The checklists were properly coded and numbered. The investigators and supervisors carried out daily data collection monitoring. Then appropriate feedback was given to the data collectors. After completing the data collection process, all the checklists were collected together and cross-checked for relevance.

Statistical Analysis

The data were checked, coded, cleaned, and then entered into Epi-Data version 3.1 before being exported to STATA version 14.0 for further management and analysis. Exploratory data analysis

was performed to determine the presence of probable outliers, normality (by the Skewness and Kurtosis tests), and the level of missing values. Viral load and CD4 count showed missing values of more than 30% and were excluded from the analysis. Median, interquartile range, frequencies, and percentages were used for descriptive statistics. Person year of observation was used to compute the incidence density (Incidence of Attrition = [number of attrition/total number of person-years of observation]*100). The Kaplan-Meier curve was used to estimate survival time and compare survival experience among categories of predictor variables, and the significance of survival experience was checked using the log-rank test. A life table was used to estimate the cumulative probability of survival at different time intervals. The Cox proportional hazards model was fitted after checking for proportional hazards assumption using the Schoenfeld residual test (global test) (P-value=0.5585) (Supplemental File 1). To analyze the association between each independent variable and the outcome variable, a binary Cox proportional hazards model was fitted, and variables with a P-value <0.25 in bivariable Cox regression were candidates for multivariable analysis. To find independent predictors of attrition, a multivariable Cox regression model with a backward stepwise likelihood ratio technique was built. The variance inflation factor (VIF) and tolerance were used to test for multicollinearity, the mean VIF = 1.23, showing no threat of multicollinearity. The Cox Snell residuals plot was used to assess the model's goodness of fit. The hazard function followed the 45-degree line very closely over time except for large values and fulfilled the assumption of Goodness of fit of the model (Figure 2). To identify statistically significant variables, AHR with a 95% confidence interval (CI) and matching P-value was used. The statistical significance was declared at the P-value < 0.05.

RESULTS

Adolescent's sociodemographic characteristics

Of 437 adolescents (10-19 years) who were initiated on ART from January 01, 2014, to December 30, 2023, in the eight public hospitals, the chart of 409 adolescents fulfilled the inclusion criteria and were reviewed.

The median age of the adolescents included in the study was 14 with an interquartile range (IQR) of 12 to 18 years and of the study participants, 213 (52.1%) were females. More than half of the adolescents were urban residents. Regarding the marital status of the adolescents, a majority (86.1%) were single and 16 (3.9%) were divorced after being married. Half, 206 (50.4%), of the adolescents who participated in the study have attained primary educational status and only ten (2.4%) attained tertiary and above. About three percent (2.9%) of the participants were female sex workers (Table 1).

Table 1. Sociodemographic characteristics of HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Variables	Categories	Frequency	Percentage (%)
Age (in years)	10-14	211	51.6
	15-19	198	48.4
Sex	Male	196	47.9
	Female	213	52.1
Residence	Urban	255	62.4
	Rural	154	37.7
Parent status	Both alive	200	48.9
	Either died	160	39.1
	Both died	49	12.0
	Single	352	86.1

Marital status	Married	41	10.0
	Divorced	16	3.9
Educational status	No formal education	77	18.8
	Primary	206	50.4
	Secondary	116	28.4
	Tertiary and above	10	2.4
Occupational status	Student	282	69.0
	Daily laborer	38	9.3
	Female sex worker	12	2.9
	No work/child	49	12.0
	Other *	28	6.8

Notes; *Other: merchant, housewife, farmer

Adolescents' baseline clinical and treatment-related characteristics

Of the total adolescents enrolled in ART care during the follow-up period, 253 (61.9%), were entered into care through medical referral or linkage. The hemoglobin level of the majority, 381 (93.1%), of the adolescents who participated in the study was ≥10g/dl. Regarding the WHO clinical staging, more than half 227 (55.5%) of the participants were in stage I at the time of ART initiation. Of the study participants, 65 (15.9%) have a history of tuberculosis infection at the start of the treatment initiation. Participants with a history of OIs other than TB account for less than twenty percent of the total participants and from these, pneumonia, 24 (34.8%), and diarrhea, 23 (33.3%) are among the commonly identified opportunistic infections. Two-thirds, 265 (64.8%), of the study participants disclosed their HIV status to others and the remaining kept their status secret from others. Regarding prophylaxis for the prevention of opportunistic infections, 227 (55.5%) and 268(65.5%) took CPT and INH, respectively. During the follow-up time, 157 (38.4%) of the adolescents were initiated on Zidovudine, Lamivudine, and nevirapine-containing regimen (AZT+3TC+NVP) at baseline. The median duration of ART during the

follow-up time was 63 months with an IQR of 20 months to 101 months. Regarding treatment adherence, 30 (7.3%) had fair treatment adherence. Reasons for fair or poor treatment adherence are known for only eight participants and the reasons are far distance, forgetting the drug, stigma, and others. The baseline regimen of 265 (64.8%) adolescents who participated in the study was changed during the follow-up time and the main reason for the regimen change was the availability of a new drug, 150 (80.6%) (Table 2).

Table 2. Clinical and treatment-related characteristics of HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Variables	Categories	Frequency	Percentage (%)
Mode of entry	VCT	77	18.8
	Medical referral/linkage	253	61.9
	Other*	79	19.3
BMI for age	<-2SD	185	45.2
	≥-2SD	224	54.8
Hemoglobin level	<10g/dl	28	6.9
	≥10g/dl	381	93.1
WHO clinical staging	Stage I	227	55.5
	Stage II	56	13.7
	Stage III	107	26.1
	Stage IV	19	4.7
History of Tuberculosis	Yes	65	15.9
	No	344	84.1
Treated for TB (n=65)	Yes	61	93.9
	No	4	6.1
Treatment regimen for TB	2SRHZ/4RH	5	7.7
	2HRZE/4RH	55	84.6
	Unknown	5	7.7
History of opportunistic infections	Yes	74	18.1

other than TB	No	335	81.9
Functional status	Working	298	72.9
	Ambulatory	90	22.0
	Bedridden	21	5.1
Disclosure of HIV status to the adolescent	Yes	265	64.8
	No	144	35.2
CPT	Yes	227	55.5
	No	182	44.5
INH	Yes	268	65.5
	No	141	34.5
Type of initial regimen	TDF+3TC+EFV	60	14.7
	AZT+3TC+NVP	157	34.4
	TDF+3TC+DTG	69	16.9
	ABC+3TC+DTG	34	8.3
	AZT+3TC+EFV	23	5.6
	Other**	66	16.1
Month on ART	< 1year	55	13.5
	1 to 4 years	142	34.7
	≥5 years	212	51.8
Adherence	Good	331	80.9
	Fair	30	7.3
	Poor	48	11.7
Regimen change	Yes	265	64.8
	No	144	35.2
Viral Load (n=205) in copies/ml	Below 1000	180	87.8
	1000 and above	25	12.2
CD4 count (n=281) in cells/mm^3	≤200	50	17.8
	200-350	47	16.7
	≥350	184	65.5

Notes; *Other: Dried Blood Spots, index case testing, and self-referral **Other: ABC+3TC+EFV, ABC+3TC+LPV/r, TDF+3TC+ATV/r,

Incidence of attrition

The follow-up time was from January 1, 2014, to December 30, 2023, and the adolescents were followed for 0.3 years at minimum and 9.9 years at maximum. The median follow-up time was 5.6(IQR 1.9 - 9) years which yields a total of 2222.1 person-years of observation. The adolescents' mean survival time was 8.41 (95% CI: 8.09, 8.73) years. At the end of the follow-up, among the total study participants, 74 (18.1%) experienced attrition (11.7% were lost and 6.4% died), and 335 (81.9%) were censored (11.0% were transferred out and 70.9% were alive and on ART at the end of follow-up). The overall incidence density of attrition was 3.33 (95% CI: 2.65, 4.18) per 100 PYO. The incidence of attrition was 4.50 (95% CI: 3.42, 5.93) per 100 PYO in General Hospitals and 2.11 (95% CI: 1.40, 3.18) per 100 PYO in Primary Hospitals, respectively. The cumulative probability of survival was 0.9368, 0.8953, 0.8576, and 0.8469 at the end of 12, 24, 48, and 60 months, respectively as described by the life table.

The stepwise decreasing overall Kaplan-Meier survival curve didn't cross the survival function at a survival probability of 0.5 (Figure 3). The log-rank test showed that there is a statistically significant difference in survival experience among the categories of the predictor variable including age, educational status, CPT prophylaxis, baseline regimen change, and drug adherence.

It was identified that there is a statistically significant difference in survival time among adolescents among different categories of age groups. Hence, the mean survival time for adolescents aged 10 to 14 years was 8.71(95% CI: 8.32, 9.10) years and 8.08(7.56, 8.59) years, respectively. In addition, the rate of attrition among older adolescents was higher which was 4.30 (95% CI: 3.17, 5.85) when compared to the counterparts. Adolescents on ART unchanged initial regimen have the lowest survival times, 6.36 (95% CI: 5.54, 7.18) when compared to adolescents

whose baseline regimen was changed 9.16 (8.90, 9.43). In addition, there is a statistically significant difference in survival time among adolescents within different groups of treatment adherence levels. The mean survival time for adolescents with good treatment adherence was higher (8.96, 95% CI: 8.67, 9.25) than for those with fair (7.48, 95% CI: 6.07, 8.89) and poor treatment adherence (5.55, 95% CI: 4.39, 6.72). Another categorical variable that was found to have a significant difference in attrition-free survival time between its categories is initial regimen change. Adolescents whose baseline ART regimen was not changed have lower attrition-free survival times (6.36, 95% CI: 5.54, 7.19) as compared to those whose regimen was changed (9.16, 95% CI: 8.90, 9.43) (Figure 4).

Predictors of attrition among adolescents

In bivariable analysis, age, marital status, parent status, educational status, occupation, entry mode to care, CPT prophylaxis, regimen change, drug adherence, disclosure of HIV-sero status, and type of baseline regimen were predictors of attrition at a p-value of <0.25. In multivariable analysis, age, parent status, educational status, CPT prophylaxis, baseline regimen change, and drug adherence were predictors of attrition among adolescents at p-value <0.05. Hence, adolescents aged 15 years to 19 years had nearly two times (AHR=1.88; 95% CI: 1.12, 3.18) increased hazard of attrition from care when compared to their counterparts. The death of either or both of the parents of the adolescents increases the risk of program attrition by two-fold, (AHR=2.07; 95% CI: 1.22, 3.52) and (AHR=2.19; 95% CI: 1.04, 4.61), when compared to adolescent whose both parents are alive, respectively. Attaining no formal education (AHR=3.16; 95% CI: 1.48, 6.77) and attaining primary educational status (AHR=2.47; 95% CI: 1.25, 4.89) can result in more than two times higher hazard of attrition among adolescents participated in the current study. Adolescents who did not take the CPT prophylaxis for

prevention of opportunistic infection hand 1.73 times (AHR=1.73; 95% CI: 1.03, 2.91) increased the hazard of experiencing ART program attrition than their counterparts. Adolescents whose baseline ART regimen was not changed are at six-fold times (AHR=6.16; 95% CI: 3.56, 10.66) higher risk of attrition. Poor or fair treatment adherence can increase the hazard of attrition by five (AHR=5.16; 95% CI: 2.35, 11.32) and six (AHR=6.02; 95% CI: 3.52, 10.29) times when compared to adolescents with good treatment adherence, respectively (Supplemental File 2).

DISCUSSION

The study was conducted to determine the incidence of attrition and its predictors of attrition among HIV-infected adolescents receiving ART. At the end of the follow-up, among the total study participants, 74 (18.1%) experienced attrition. The overall incidence density of attrition was 3.33 (95% CI: 2.65, 4.18) per 100 PYO. Moreover, older age, parental death, attaining no formal education and primary educational status, non-CPT utilization, unchanged baseline ART regimen, and suboptimal treatment adherence were predictors of attrition among adolescents receiving ART.

This study reported that the incidence density of attrition was 3.33 per 100 PYO. This finding is lower than the retrospective cohort studies conducted in Thailand [8] and Myanmar [7]. It is also lower than the findings from cohort studies done in India [29] and South Africa [28]. This finding is also lower than the result from the retrospective cohort study done in Ethiopia [10]. This discrepancy may be due to the large sample size used in the previous studies [7 8 28 29]. Also, a long follow-up time [7], the difference in socio-demographic characteristics of the study participants, and improvement in the current healthcare system than former times may contribute to the inconsistency. Another reason for the variance may be due to the difference in the operational definition of LTFU, it's defined as; if the last appointment was missed for ≥12 months [8] and

difference in study design [28]. Moreover, there was a difference in the study population, young adults were included in the studies done in Thailand [8] and South Africa [28] and the study done in Ethiopia [10] included children whose age is less than 10 years. The result of this study is in line with the studies done previously in Tanzania [26] and Ethiopia [10]. The reason behind this consistency in Ethiopia might be due to uniformity in follow-up charts and data recording formats in the ART program prepared by the Ethiopian Federal Minister of Health [12].

On the contrary, the overall incidence density of attrition as reported by the current study is slightly higher than studies conducted among adolescents living with HIV in South Africa [28] and Ethiopia [11]. This may be due to differences in the study population; the study conducted in South Africa additionally included young adults aged 20 to 28 years [28]. It may also be because of differences in study design [28], and large sample size [11 28]. In addition, the divergence may be explained by differences in the sociodemographic characteristics of study participants and the longer follow-up period of the current study.

Adolescents aged 15 years to 19 years had nearly two times increased hazard of attrition from care when compared to their counterparts. This finding is consistent with results from previous studies done in India [29], South Africa [30], and Uganda [19] which reported an increased risk of attrition with increased age (15-19 years). The reason might be because older adolescents started ART at the advanced immunodeficiency stage and also a large amount of adolescents lost from ART care as they transition from pediatric care to adult care [30 33 34].

The educational status of the adolescents was one of the identified predictors of attrition by the current study. Attaining no formal education or primary educational status can result in more than two times higher hazard of attrition compared with those attained secondary and above educational level as reported by this study. This is consistent with a study conducted in Amhara

region, Ethiopia [11]. This might be because adolescents who attained higher educational status were well-informed and aware of the benefit of retention in care and the effect of attrition on their health.

Death of either or both the parents of the adolescents can increase the risk program attrition by two-fold times when compared to adolescents whose both parents are alive, respectively. This finding is consistent with findings from studies conducted in Ethiopia [11 35]. However, the study done in Ethiopia [35] targeted children aged 0 to 14 years. The reason for this could be due to the lack of caregivers' role in providing proper feeding, drug administration, and supervision, collectively with the social and economic disruption resulting from the death of the caregivers [36]. In addition, adolescents living with widowed caregivers or on their own were considerably more likely to be depressed than their peers and may experience attrition from care [37].

The other predictor of attrition among HIV-positive adolescents is non-utilization of CPT prophylaxis. Hence, adolescents who did not take the CPT prophylaxis for prevention of opportunistic infection had 1.73 times increased hazard of experiencing ART program attrition than their counterparts. A similar finding was reported by studies done in Ethiopia [11 38] among which one was conducted among children [38]. This might be because CPT administration can prevent the occurrence of OIs among HIV-positive individuals reduce AIDS-related mortality and improve life quality [39]. Moreover, the provision of CPT prophylaxis is an effective and simple intervention for reducing morbidity and increasing retention rates in ART Program [40].

Adolescents whose baseline ART regimen was not changed are at six-fold times higher risk of attrition. This is supported by a study done in Ethiopia [11] and contrary to the study done in Namibia [18]. The study done in Namibia [18] reported that adolescents whose regimen was changed to a second or third-line regimen were at higher hazard of attrition. This could be due to most of

the old regimens having adverse effects that boost the progression of HIV infection to the AIDS stage and lead to succeeding complications. An AZT-based ART regimen is associated with the development of anemia, which has an extra effect on the patient's immune system [41]. The highest attrition has occurred among adolescents on AZT-based regimens which was 43.2% as reported by the current study.

Furthermore, treatment adherence was one of the identified predictors of attrition among HIV-positive adolescents. It was identified that poor or fair treatment adherence can increase the hazard of attrition by five and six times among HIV-positive adolescents when compared to adolescents with good treatment adherence, respectively. This result was supported by findings from previous studies done in Ethiopia [11 35]. However, the source population of one of the studies done in Ethiopia [35] was children aged 0 to 14 years. This can be because fair or poor adherence can lead to higher viral load, drug resistance, and poor treatment outcomes. This can also result in decreased CD4 levels, the progression of AIDS, and an increase in OIs, all of which cause attrition [42].

As attrition is a warning indicator for drug resistance, determining attrition is very important to monitor ART drug resistance and the current study used a long follow-up period to do so. The current study provided evidence on predictors of attrition for adolescents that can be important and used to improve adolescent's HIV-related services. Despite the strengths, the current study has some limitations; the effect of some important predictor variables like; viral load and CD4 count, was not assessed because of incomplete records. In addition, adolescents whose charts were lost and those with incomplete records were excluded from the analysis which may under or overestimate the attrition. Because of this incompleteness, only 409 study participants, which

is smaller than the calculated sample size, were included in the analysis, which might slightly underpower the study.

CONCLUSION

Attrition was identified to be a significant public health problem in the study setting. Moreover, old age, parental death, not attending formal education, not using CPT, unchanged baseline regimen, and suboptimal treatment adherence predict attrition. Special attention should be given to the old aged, no formal education, those orphaned, and those with poor baseline clinical characteristics. Moreover, early tracing of missed follow-up schedules, improving adherence support, and increasing contacting frequency to reduce attrition are highly encouraged. To address the effect of important clinical and sociodemographic variables, a longitudinal prospective study was needed.

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Patient consent for publication Not applicable

Ethical approval Before data collection, the document was submitted to the Arba Minch College of Health Sciences' institutional ethical review board (IRB) for ethical assessment and approval. An ethical approval letter was obtained from IRB with reference number AMCHS/01/20/33/0. An official support letter was received from the Gamo and Ari Zones Health Departments. The letter of cooperation was submitted to hospital authorities, and permission was sought to have full access to the information. Individual informed consent/assent was not obtained from the participants or guardians because the study is a retrospective study that requires record review without physical contact with the participants, which was waived by the IRB.

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REFERENCES

1. UNAIDS. Young people and HIV; 2023. Available at: https://www.unaids.org/sites/default/files/media_asset/young-people-and-hiv_en.pdf Accessed September 09, 2023.
2. UNICEF. UNICEF Data: Adolescent HIV prevention; 2023. Available at : https://data.unicef.org/topic/hivaids/adolescents-young-people/ Accessed September 09, 2023

3. UNAIDS. HIV and AIDS estimates country factsheet 2022 - Ethiopia; 2022. Available from: https://www.unaids.org/en/regionscountries/countries/ethiopia. Accessed September 09, 2023.

4. Organization WH. Consolidated HIV strategic information guidelines: driving impact through programme monitoring and management. 2020

5. Auld AF, Agolory SG, Shiraishi RW, et al. Antiretroviral therapy enrollment characteristics and outcomes among HIV-infected adolescents and young adults compared with older adults—seven African countries, 2004–2013. *Morbidity and Mortality Weekly Report* 2014;63(47):1097.

6. Kariminia A, Law M, Davies MA, et al. Mortality and losses to follow-up among adolescents living with HIV in the Ie DEA global cohort collaboration. *Journal of the International AIDS Society* 2018;21(12):e25215.

7. Htun T, Kyaw K, Aung T, et al. Attrition during pre-ART and ART time periods among adolescents enrolled in Integrated HIV Care Programme in Myanmar, 2005–2017. *Epidemiology & Infection* 2019;147

8. Teeraananchai S, Puthanakit T, Kerr SJ, et al. Attrition and treatment outcomes among adolescents and youths living with HIV in the Thai National AIDS Program. *Journal of virus eradication* 2019;5(1):33-40.

9. Leshargie CT, Demant D, Burrowes S, et al. The proportion of loss to follow-up from antiretroviral therapy (art) and its association with age among adolescents living with HIV in sub-Saharan Africa: a systematic review and meta-analysis. *Plos one* 2022;17(8):e0272906.

10. Jerene D, Abebe W, Taye K, et al. Adolescents living with HIV are at higher risk of death and loss to follow up from care: Analysis of cohort data from eight health facilities in Ethiopia. *PloS one* 2019;14(10):e0223655.

11. Leshargie CT, Demant D, Burrowes S, et al. Incidence and predictors of mortality among adolescents on antiretroviral therapy in Amhara Region, Ethiopia: a retrospective cohort analysis. *BMJ open* 2022;12(11):e063879.

12. Ethiopia F. National consolidated guidelines for comprehensive HIV prevention, care and treatment; 2018. Addis Ababa: Fmoh 2018:1-238. Available from: https://www.afro.who.int/sites/default/files/2019-04/National%20Comprehensive%20HIV%20Care%20%20Guideline%202018.pdf. Accesed on September 12, 2023.

13. Geng EH, Nash D, Kambugu A, et al. Retention in care among HIV-infected patients in resource-limited settings: emerging insights and new directions. *Current Hiv/aids Reports* 2010;7:234-44.

14. UNAIDS. IN DANGER: UNAIDS Global AIDS Update 2022. Geneva: Joint United Nations Programme on HIV/ AIDS; 2022. Licence: CC BY-NC-SA 3.0 IGO.

15. UNCEF. 2023 Global Snapshot on HIV and AIDS: Progress and priorities for children, adolescents and pregnant women; 2023. Available from: https://www.childrenandaids.org/sites/default/files/2023-11/231130%20UNCEF_HIV_Global_Snapshot_2023UPDATED_0.pdf. Accessed on January 15, 2024.

16. Booysen F, Bachmann M, Matebesi Z, et al. The socio-economic impact of HIV/AIDS on households in South Africa: pilot study in Welkom and Qwaqwa, Free State Province. *Retrieved March* 2004;26:2009.

17. Booysen F, Van der Berg S. The role of social grants in mitigating the socio-economic impact of HIV/aids in two free state communities 1. *South African Journal of Economics* 2005;73:545-63.

18. Munyayi FK, van Wyk BE. Determinants and rates of retention in HIV care among adolescents receiving antiretroviral therapy in Windhoek, Namibia: a baseline cohort analysis. *BMC Public Health* 2023;23(1):1-12.

19. Okoboi S, Ssali L, Yansaneh AI, et al. Factors associated with long-term antiretroviral therapy attrition among adolescents in rural Uganda: a retrospective study. *Journal of the International AIDS Society* 2016;19:20841.

20. WHO. Global update on HIV treatment 2013: results, impact and opportunities: WHO report in partnership with UNICEF and UNAIDS. Avaialble from: https://iris.who.int/bitstream/handle/10665/85326/9789241505734_eng.pdf;jsessionid=B98E988DF5509E1C12576852805B8403?sequence=1. Acessed on July 23, 2023. . Geneva: WHO.

21. Organization WH. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach; 2021. Licence: CC BY-NC-SA 3.0 IGO: World Health Organization.

22. Judd A, Sohn AH, Collins IJ. Interventions to improve treatment, retention and survival outcomes for adolescents with perinatal HIV-1 transitioning to adult care: moving on up. *Current opinion in HIV and AIDS* 2016;11(5):477-86.

23. Neilan AM, Karalius B, Patel K, et al. Association of risk of viremia, immunosuppression, serious clinical events, and mortality with increasing age in perinatally human immunodeficiency virus–infected youth. *JAMA pediatrics* 2017;171(5):450-60.

24. WHO. World Heath Organization: Adolescent health; 2023. Available from: https://www.who.int/health-topics/adolescent-health#tab=tab_1 Accessed September 25, 2023.

25. Tesha E-D, Kishimba R, Njau P, et al. Predictors of loss to follow up from antiretroviral therapy among adolescents with HIV/AIDS in Tanzania. *PloS one* 2022;17(7):e0268825.

26. Amour MA, Shayo GA, Matee MM, et al. Predictors of mortality among adolescents and young adults living with HIV on antiretroviral therapy in Dar es Salaam, Tanzania: a retrospective cohort study. *Journal of the International AIDS Society* 2022;25(2):e25886.

27. Lamb MR, Fayorsey R, Nuwagaba-Biribonwoha H, et al. High attrition before and after ART initiation among youth (15–24 years of age) enrolled in HIV care. *AIDS (London, England)* 2014;28(4):559.

28. Nglazi MD, Kranzer K, Holele P, et al. Treatment outcomes in HIV-infected adolescents attending a community-based antiretroviral therapy clinic in South Africa. *BMC infectious diseases* 2012;12:1-7.

29. Nimkar S, Valvi C, Kadam D, et al. Loss to follow-up and mortality among HIV-infected adolescents receiving antiretroviral therapy in Pune, India. *HIV medicine* 2018;19(6):395-402.

30. Okonji EF, Wyk BV, Mukumbang FC. Two-year retention in care for adolescents on antiretroviral therapy in Ehlanzeni district, South Africa: a baseline cohort analysis. *AIDS care* 2023;35(3):374-84.

31. Nimwesiga C, Taremwa IM, Nakanjako D, et al. Factors Associated with Retention in HIV Care Among HIV-Positive Adolescents in Public Antiretroviral Therapy Clinics in Ibanda District, Rural South Western Uganda. *HIV/AIDS-Research and Palliative Care* 2023:71-81.

32. Organization WH. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach: World Health Organization 2016.

33. Enane LA, Davies M-A, Leroy V, et al. Traversing the cascade: urgent research priorities for implementing the 'treat all'strategy for children and adolescents living with HIV in sub-Saharan Africa. *Journal of virus eradication* 2018;4:40-46.

34. Meloni ST, Agaba P, Chang CA, et al. Longitudinal evaluation of adherence, retention, and transition patterns of adolescents living with HIV in Nigeria. *PLoS One* 2020;15(7):e0236801.

35. Guyo TG, Toma TM, Haftu D, et al. Proportion of Attrition and Associated Factors Among Children Receiving Antiretroviral Therapy in Public Health Facilities, Southern Ethiopia. *HIV/AIDS-Research and Palliative Care* 2023:491-502.

36. Vreeman RC, Ayaya SO, Musick BS, et al. Adherence to antiretroviral therapy in a clinical cohort of HIV-infected children in East Africa. *PLoS One* 2018;13(2):e0191848.

37. Sengendo J, Nambi J. The psychological effect of orphanhood: a study of orphans in Rakai district. *Health transition review* 1997:105-24.

38. Chanie ES, Tesgera Beshah D, Ayele AD. Incidence and predictors of attrition among children on antiretroviral therapy at University of Gondar Comprehensive Specialized

Hospital, Northwest Ethiopia, 2019: Retrospective follow-up study. *SAGE Open Medicine* 2022;10:20503121221077843.

39. Collini P, Obasi A. Cotrimoxazole prophylaxis: BMJ publishing Group Limited London, 2006.

40. Vitoria M, Granich R, Banda M, et al. Implementation of co-trimoxazole prophylaxis and isoniazid preventive therapy for people living with HIV. *Bulletin of the World Health Organization* 2010;88:253-59.

41. Gebremedhin KB, Haye TB. Factors associated with anemia among people living with HIV/AIDS taking ART in Ethiopia. *Advances in hematology* 2019;2019

42. Organization WH. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach: World Health Organization 2021.

Figure legends

Figure 1. Flow chart for study participants recruitment to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Figure 2. Cox-Snell residual plot for model fitness to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Figure 3. The overall Kaplan-Meier survival estimate showing the time until free of attrition among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Figure 4. Kaplan-Meier survival estimates of time until attrition free of the main predictor variables among adolescents on ART in public hospitals, south Ethiopia, 2024.

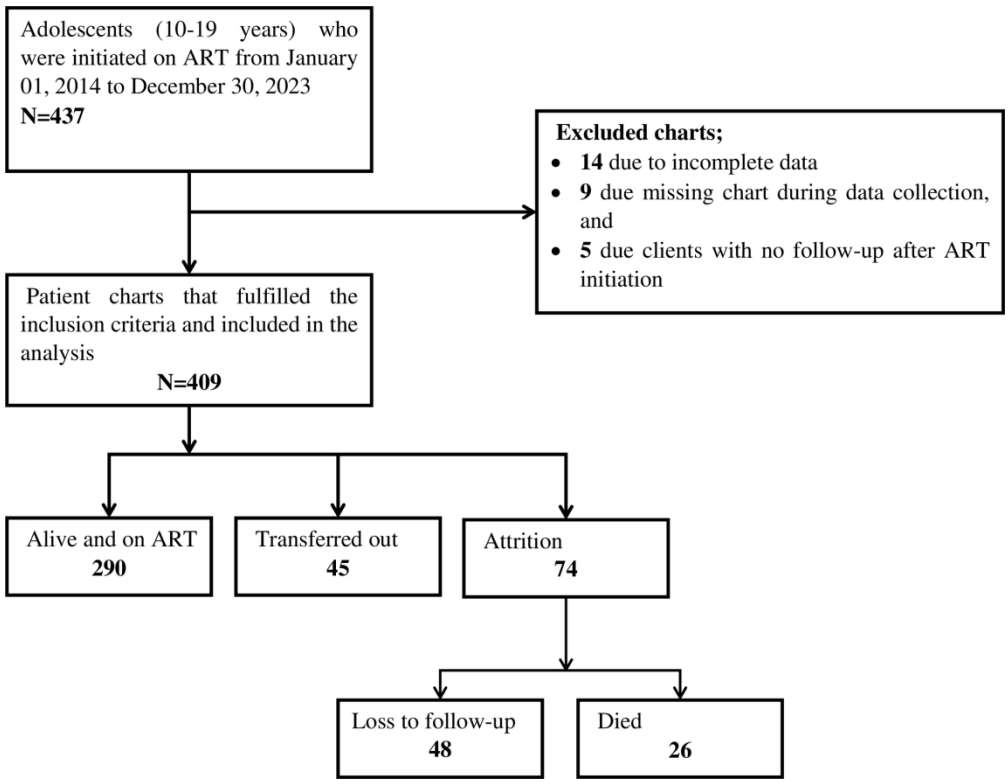


Figure 1. Flow chart for study participants recruitment to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

190x146mm (300 x 300 DPI)

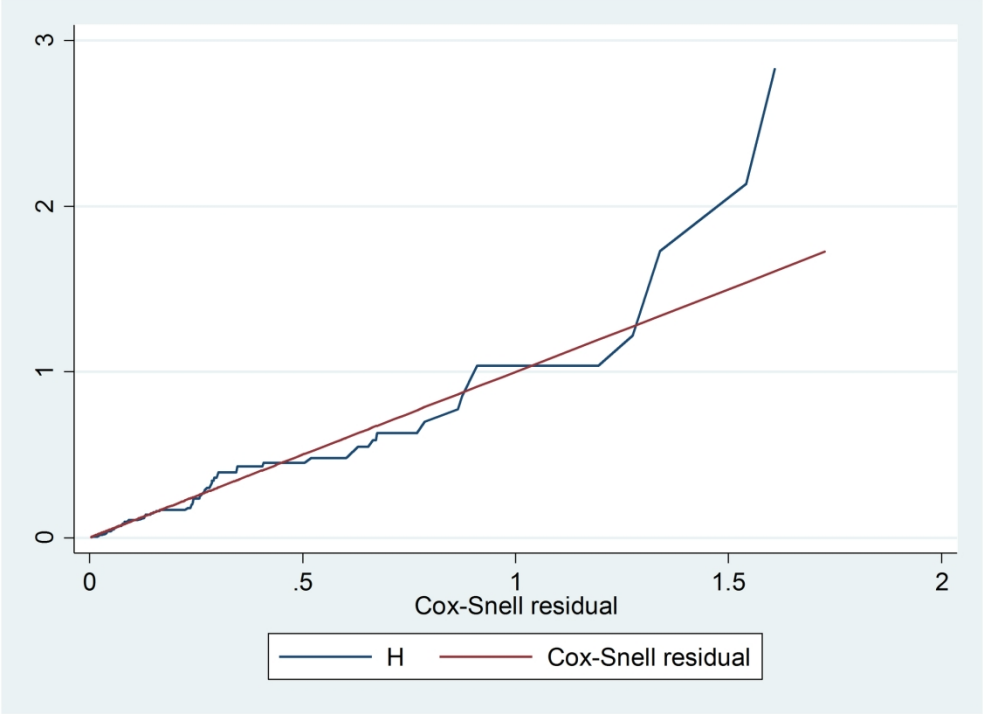


Figure 2. Cox-Snell residual plot for model fitness to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

484x353mm (118 x 118 DPI)

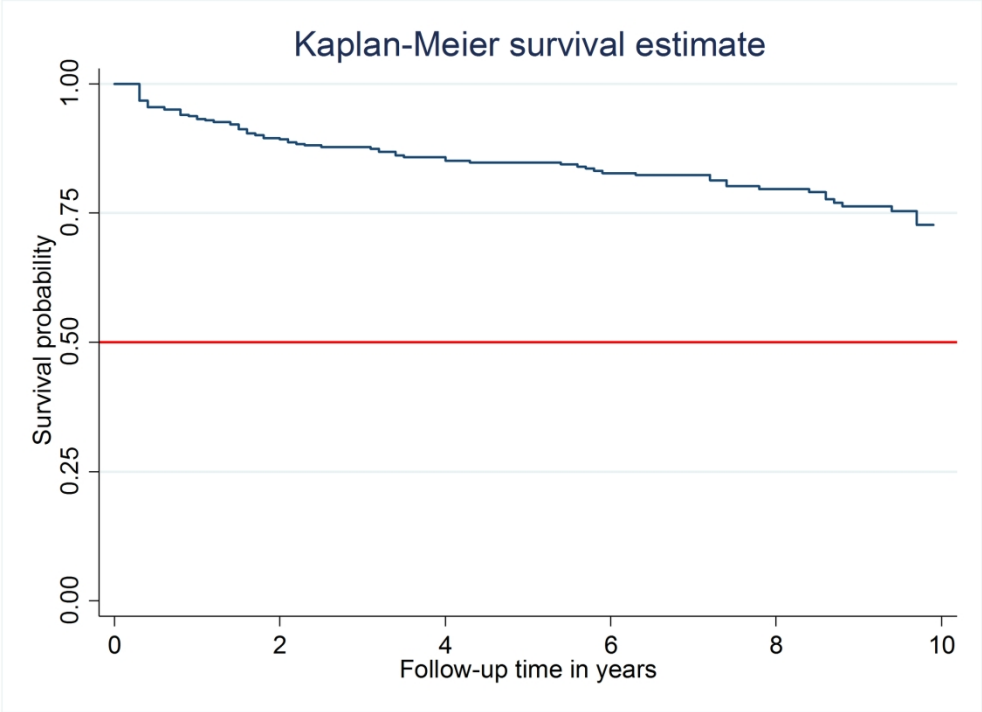
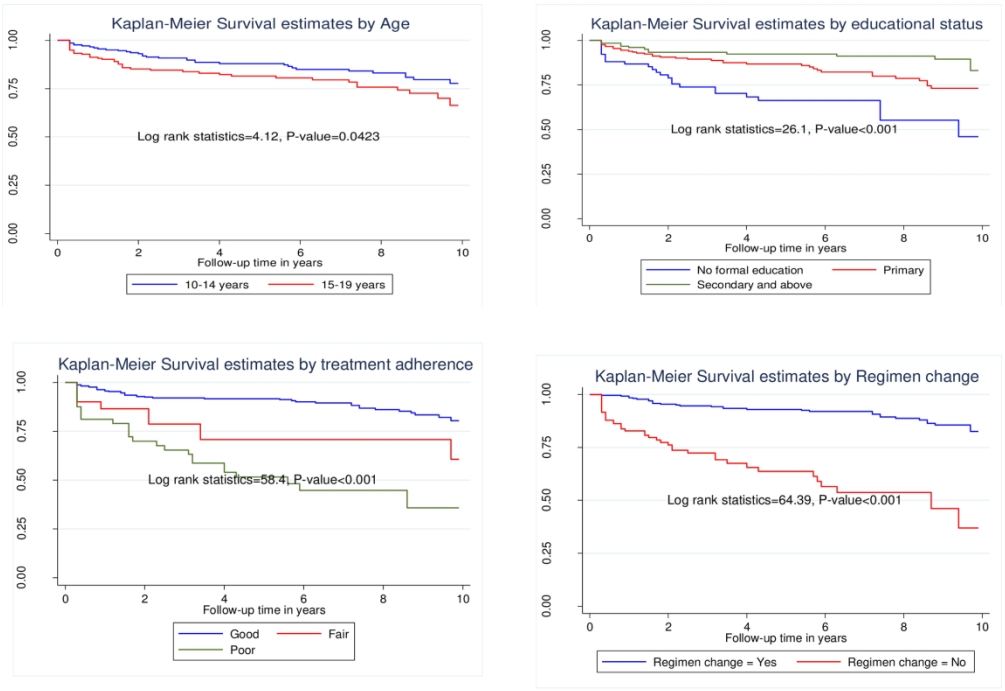


Figure 3. The overall Kaplan-Meier survival estimate showing the time until free of attrition among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

484x353mm (118 x 118 DPI)



[1]

Figure 4. Kaplan-Meier survival estimates of time until attrition free of the main predictor variables among adolescents on ART in public hospitals, south Ethiopia, 2024.

190x141mm (300 x 300 DPI)

Supplemental File 1. Test of proportional-hazards assumption to assess the incidence of attrition and its predictors among HIV-infected adolescents receiving antiretroviral therapy in public health hospitals, south Ethiopia, 2024

Variables	Categories	X^2	DF	P-value
Age	15-19	1.17	1	0.2801
Parent status	Either died	0.14	1	0.7096
	Both died	1.82	1	0.1771
Educational status of caregiver	No formal education	2.65	1	0.1035
	Primary	1.38	1	0.2398
CPT prophylaxis	No	1.54	1	0.2147
Adherence	Fair	0.38	1	0.5398
	Poor	0.00	1	0.9710
Regimen change	No	0.28	1	0.5982
Global test		7.76	9	0.5585

Supplemental File 2. Multivariable cox-proportional analysis of predictors of attrition among HIV-infected adolescents receiving ART in public hospitals, South Ethiopia, 2024

Variables	Categories	Attrition status		Incidence rate per 100 PYO (95% CI)	CHR (95% CI)	AHR (95% CI)	P-value
		Yes (Event)	No (Censored)				
Age (in years)	10-14	33 (15.6)	178 (84.4)	2.6 (1.8, 3.7)	1		
	15-19	41 (20.7)	157 (79.3)	4.3 (3.2, 5.8)	1.60 (1.08, 2.53)	1.88 (1.12, 3.18)	**0.018**
Parent status	Both alive	27 (13.5)	173 (86.5)	2.5 (1.7, 3.6)	1		
	Either died	37 (23.1)	123 (76.9)	4.5 (3.3, 6.2)	1.81 (1.19, 2.98)	2.07 (1.22, 3.52)	**0.007**
	Both died	10 (20.4)	39 (79.6)	3.3 (1.8, 6.1)	1.37 (0.63, 2.84)	2.19 (1.04, 4.61)	**0.040**
Marital status	Single	61 (17.3)	291 (82.7)	3.1 (2.4, 3.9)	1		
	Married	8 (19.5)	33 (80.5)	4.7 (2.4, 9.4)	1.45 (0.69, 3.03)	2.75 (0.34, 7.67)	0.479

	Divorced	5 (31.2)	11 (68.8)	8.2 (3.4, 19.7)	2.55 (1.02, 6.37)	0.79 (0.29, 2.14)	0.648
Educational status	No formal education	25 (32.5)	52 (67.5)	8.4 (5.7, 12.4)	4.94 (2.56, 9.76)	2.16 (1.48, 3.77)	**0.003**
	Primary	36 (17.5)	170 (82.5)	3.3 (2.4, 4.6)	2.09 (1.16, 3.95)	1.47 (1.25, 1.89)	**0.009**
	Secondary and above	13 (10.3)	113 (89.7)	1.5 (0.9, 2.7)	1		
Occupational status	Student	37 (13.1)	245 (86.9)	2.2 (1.6, 3.0)	1		
	Daily laborer	5 (13.2)	33 (86.8)	2.5 (1.1, 6.1)	1.14 (0.45, 2.89)	1.00 (0.34, 2.95)	0.995
	No work/child	20 (40.8)	29 (59.2)	11.5 (7.4, 17.8)	4.50 (2.59, 7.83)	1.48 (0.62, 3.51)	0.374
	Other *	12 (30.0)	28 (70.0)	7.2 (4.1, 12.7)	3.11 (1.68, 5.98)	1.45 (0.61, 3.47)	0.403
Entry mode	VCT	16 (20.8)	61 (79.2)	3.7 (2.3, 6.0)	1		
	Medical referral	47 (18.6)	206 (81.4)	3.6 (2.7, 4.8)	0.98 (0.55, 1.73)	0.84 (0.46, 1.52)	0.555

	Other **	11 (13.9)	68 (86.1)	2.2 (1.2, 4.1)	0.63 (0.2[illegible], 1.35)	[illegible].55 (0.24, [illegible].24)	0.147
CPT prophylaxis	Yes	37 (16.3)	190 (83.7)	2.7 (1.9, 3.5)	1		
	No	37 (20.3)	145 (79.7)	4.7 (3.4, 6.5)	1.74 (1.0[illegible], 2.77)	[illegible].73 (1.03, [illegible].91)	**0.038**
ART regimen	TDF+3TC+EFV	6 (10.0)	54 (90.0)	1.8 (0.8, 4.0)	0.29 (0.1[illegible], 0.86)	[illegible].89 (0.25, [illegible].11)	0.856
	AZT+3TC+NVP	32 (20.4)	125 (79.6)	3.0 (2.1, 4.2)	0.47 (0.2[illegible], 1.08)	[illegible].65 (0.25, [illegible].73)	0.391
	TDF+3TC+DTG	18 (26.1)	51 (73.9)	13.6 (8.6, 21.6)	1.63 (0.6[illegible], 3.91)	[illegible].62 (0.53, [illegible].94)	0.398
	ABC+3TC+DTG	7 (20.6)	27 (79.4)	7.3 (3.5, 15.3)	1		
	AZT+3TC+EFV	6 (26.1)	17 (73.9)	4.2 (1.9, 9.3)	0.66 (0.2[illegible], 1.98)	[illegible].96 (0.27, [illegible].36)	0.949
	Other***	5 (7.6)	61 (92.4)	1.1 (0.5, 2.7)	0.17 (0.05, 0.55)	[illegible].44 (0.12, [illegible].58)	0.208
Regimen change	Yes	31 (11.7)	234 (88.3)	1.7 (1.2, 2.4)	1		

	No	43 (29.9)	101 (70.1)	11.1 (8.3, 15.0)	6.04 (3.70, 9.86)	6.16 (3.56, 10.66)	**<0.001**
Disclosure of HIV status	Yes	41 (15.5)	224 (84.5)	2.8 (2.1, 3.8)	1		
	No	33 (22.9)	111 (77.1)	4.3 (3.1, 6.1)	1.53 (0.9[illegible], 2.43)	1.58 (0.95, 2.62)	0.075
Adherence	Good	39 (11.8)	292 (88.2)	2.1 (1.5, 2.9)	1		
	Fair	9 (30.0)	21 (70.0)	5.4 (2.9, 10.5)	2.52 (1.22, 5.22)	5.16 (2.35, 11.32)	**<0.001**
	Poor	26 (54.2)	22 (45.8)	12.6 (8.6, 18.5)	5.60 (3.40, 9.21)	6.02 (3.52, 10.29)	**<0.001**

Notes; *Other: merchant, housewife, farmer; **Other: Dried Blood Spots, index case testing, and self-referral; ***Other: ABC+3TC+EFV, ABC+3TC+LPV/r, TDF+3TC+ATV/r,