INCIDENCE AND PREDICTORS OF LOSS TO FOLLOW-UP AMONG ADULT HIV PATIENTS ON ANTIRETROVIRAL THERAPY AT PUBLIC HEALTH FACILITIES IN METEKEL ZONE, NORTH WEST ETHIOPIA.

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A RESEARCH THESIS SUBMITTED TO THE DEPARTMENT OF EPIDEMIOLOGY, FACULTY OF PUBLIC HEALTH, JIMMA UNIVERSITY; IN PARTIAL FULFILLMENT FOR THE REQUIREMENT FOR THE DEGREE OF MASTERS OF PUBLIC HEALTH IN EPIDEMIOLOGY.

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Abstract

Background:

Antiretroviral therapy services have rapidly expanded, yet one of the main causes of HIV/AIDS programs' underwhelming results—drug resistance, morbidity, and mortality-is "lost to follow-up." Studies carried out in various parts of the country reveal a high incidence and inconsistent contributing factors. However, the study area's information about the incidence and determinants of loss to follow-up is not adequately addressed.

Objective: To assess incidence and predictors of loss to follow-up among HIV-infected adults receiving antiretroviral treatment at public health facilities in Metekel zone, Northwest Ethiopia.

Methods: A retrospective cohort study at the institution was carried out from June 20 to July 5, 2022. Between June 28, 2017, and June 27, 2022, 540 adults who were receiving antiretroviral therapy at public health facilities in the Metekel zone were contacted. Data from the patient's chart were collected using a data abstraction tool. Based on the proportion of ART follow up at public health institutions, the samples from registration were chosen using a straightforward random sampling procedure. Epi Data version 3.1 was used to clean, enter, and export data, which was then exported to STATA 15 for analysis. To calculate the mean survival time and the difference in loss to follow-up between categorical variables, Kaplan-Meir curves and the log-rank test were used.

Result: In this study overall incidence rate of loss to follow-up were 15.12 (95% CI: 12.9-17.6) per 100 person-year. Significant predictors of loss to follow-up were; having tuberculosis at baseline [AHR=2.12, 95% CI, (1.33−3.38)], being underweight at baseline [AHR=5.36, 95% CI, (3.46–8.31)], poor adherence to antiretroviral treatment [AHR =2.14, 95% CI, (1.32−3.46)] and viral load result of >1000 copies/mL [AHR =2.71, 95% CI, (1.55 −4.72)].

Conclusion and recommendation: The finding of this study showed that the incidence of loss to follow-up among adults receiving antiretroviral therapy was high as compared to previous studies. Hence, special emphasis and close follow-up should be given to patients those having tuberculosis at baseline, poor adherence level, underweight at baseline and recent high viral load in the first year of treatment initiation.

Keywords: Antiretroviral therapy, HIV, Loss to follow up, Northwest Ethiopia

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Abbreviations and Acronyms

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
ASM	Appointment Spacing Model
BMI	Body Mass Index
CD4	Cluster for Differentiation 4 (Type of T-lymphocytes)
CPT	Cotrimoxazole preventive therapy
EDHS	Ethiopian Demographic and Health Survey
EPHIA	Ethiopia's population-based HIV impact assessment
HIV	Human Immune deficiency Virus
HR	Hazard Ratio
IRB	Institutional review board
LTFU	Loss to Follow-up
NHEAPR	National HIV Estimation and Projection report
IQR	Interquartile range
OI	Opportunistic Infections
PY	Person-years
PLWHIV	People Living With HIV
TB	Tuberculosis
UNAIDS	United Nations Program on HIV/AIDS
USAID	United States Agency for International Development
W H O	World Health Organization

CHAPTER ONE: INTRODUCTION

1.1. Background

The standard definition of loss to follow-up (LTFU) is when patients fail to take an Antiretroviral Therapy(ART) refill for ≥ 180 days since the last clinic visit, and this definition is used for program monitoring and evaluation worldwide. It allows comparison of the programs and minimizes misclassification of patients(1). However, according to World Health Organization (WHO) lost to follow up in antiretroviral therapy service utilization, it is an administrative classification indicating that patients did not register as death or transferred to another facility but ceased to engage in the continuum of care and who had no contact for three consecutive months or longer after the last appointment for antiretroviral refills (2).

The loss to follow-up among Human Immune deficiency Virus (HIV) infected patients is related to ART adherence and is becoming an increasing problem in sub-Saharan Africa as the ART program is expanding; this has resulted in a decrease in the clinician-to-patient ratio (4,5). According to the United States Agency for International Development (USAID) fast-track strategy 95% of people on ART should achieve sustained viral suppression with good adherence and retention to ART follow up(6). But poor retention in care and lost to follow-up are great challenges in achieving this target(7).

Lost to follow up was also highly associated with early death among adults on ART (8). A systematic review conducted in sub-Saharan Africa in 2015 determined LTFU as the most common cause of attrition from HIV care (59%) followed by death (41%) and median attrition at 12, 24 and 36 months was 22.6%, 25% and 29.5% respectively. Retention was also decreased from 86.1% at 6 months to 64.6% at 36 months(9). Retention in care continues to be a challenge among HIV-infected adults, in Ethiopian health facilities(19). Ethiopia has currently a large internally displaced population in the areas where they have been displaced which poses a greater challenge for those on ART service and in the region retention in care continues to be a challenging (5).

The goal of antiretroviral therapy is to restore immune function, maintain maximal suppression of viral replication, reduce HIV-related morbidity and mortality, improve quality of life and prolong survival(3). Ethiopian government launched fee-based ART in 2003 and free-based ART in 2005, tend and delivered as part of the comprehensive HIV/AIDS care(10). The Federal Ministry of Health currently recommends ART care based on the 2018 revised National Guideline(3).

1.2.Statement of the problem

Several studies revealed that the magnitude of LTFU among patients living with HIV was estimated to be high. The finding in Asia, the trend of loss to follow-up among HIV- positive patients who received ART was 9%(11). In sub-Saharan Africa, five years of retrospective follow-up revealed that 24.6% were lost to follow-up(12). In a retrospective study conducted in Uganda, the incidence of LTFU was 26.7 per 100 person-years and in Nigeria, 23.9% were LTFU(13,14).

In Ethiopia, the incidence of LTFU varies from 3.7 per 100 person-years to 26.6 per 100 person-months across different settings(15,16). In Benishangul Gumuz the annual HIV progress report particularly in the Metekel zone showed a significant amount of patients who are on ART were undergoing LTFU in ART care(17).

The rapid expansion of ART significantly improved the survival and quality of life of people by reducing the mortality rate secondary to HIV (18). Due to this, the number of people receiving HIV treatment has increased intensely in recent years, particularly in resource-poor countries (2). Despite this remarkable achievement, significant numbers of adults who drop out of care at various points have remained challenging along the treatment pathway(15,19).

According to the United States Agency for International Development (USAID) people on ART were targeted to achieve 95% sustained viral suppression(20,21). Though, a loss to follow-up affects the performance of the 95–95–95 ambitious targets that aims at attaining 95% of virally suppressed patients on ART and this is interference to ART follow-up lower the success of the treatment of ART and thus leads to a decrease in the number of CD4 cell counts and increases the number of viral counts and still a great challenge in achieving this target, Likewise, patients who are not retained due to loss to follow–up are likely to develop a high viral load, which increases the risk of infecting others(22–24).

LTFU from the ART service has a great negative impact on HIV patients. It can negatively affect the immunological benefits of ART and rise in AIDS-related morbidity, mortality, and hospitalization, and it also results in serious consequences such as drug toxicity, treatment failure due to poor adherence, and drug resistance(11,25). It also poses a serious challenge to program implementers and constitutes an inefficient use of scarce resources like treatment(26,27).

Multiple factors may also contribute to LTFU at ART service according to different studies which are associated with baseline sociodemographic factors like (age, sex, educational status, marital

status, religion, occupational status, residence), baseline clinical and laboratory (CD4 count, viral load, Hemoglobin), WHO clinical stages, functional status, and having an opportunistic infection at enrolment) treatment-related factors taking ART regimen, prophylaxis, not disclosing their status to anyone, adherence, not having a primary caregiver, distance from the health facility, nutritional status, and type of facility were significantly associated with LTFU (15,19,26–39).

In Ethiopia even with the implementation of free highly active antiretroviral treatment, implemented decentralization of services and task shifting, role shifting of ART programs, appointment spacing model(ASM), fixed-dose combinations, integrating and linking service, delivering HIV services to adolescents, patient monitoring, and involvement of case managers and adherence supporters significantly increased HIV/AIDS infected people's retention, reducing morbidity and mortality through viral load suppression and improved adherence(1,40–42).

Despite the efforts to reduce the rate of LTFU among HIV patients who are put on ART follow-up, it continued to be a challenge in HIV/AIDS care, almost half of all HIV patients have undetected viral loads, and as a result, the number of people who are loss to follow-up is higher than the number of people who start new care(43).

Even though the availability of ART program at Health center and hospitals, studies conducted in different parts of the country shows a high incidence of loss to follow-up and inconsistencies regarding factors that contribute (32,44). While most were single facility-based studies and were conducted in relatively previous cohorts(45). Currently, the Ethiopian government's HIV/AIDS National Strategic plan 2025 targeted a 95% HIV viral load suppression rate for people on ART care and treatment for ending the AIDS epidemic by 2030(5,46).To succeed in this plan, recent data related to the incidence and predictors of LTFU are crucial.

Ministry of Health recommends a differentiated service delivery system like; treatment taking varying from monthly to six-month intervals (ASM), test-and-treat approach it increases the number of people starting ART, reduces mortality, and reduce both mother-to-child transmission, reduce transmission to HIV-negative partners and viral load testing is a gold standard, a sensitive and earlier indicator of treatment failure it gives great emphasize by the latest revised national guideline (1). Furthermore, the impact of these new HIV/AIDS initiatives such as viral load status, ASM, and a test-and-treat approach was not considered in previous different cohort studies.

As one of the emerging and pastoralist regions and war prone area, Benishangul Gumuz shared the lion's share of a high incidence of loss to follow-up in Ethiopia and the region suffered greater challenge to give ART service in recent years(18).

The extent of non-retention of treatment and factors that contribute to it can differ from one location to the other. Besides this, predicting factors for the loss to follow-up, in the study area, are not narrated or not well addressed. Therefore, this study aims to assess incidence and predictors of loss to follow-up among adult HIV patients on ART at public health facilities in Metekel Zone.

1.3. Significances of the study

There was a growing concern about the increasing rates of loss to follow-up among HIV positive adults starting antiretroviral therapy; that leads to further disease progression, transmission, and cause for mortality and morbidity. The finding of this study will help in the achievement of the HIV/AIDS National Strategic plan 2025 targeted a 95% HIV viral load suppression rate for ending the AIDS epidemic by 2030.

Additionally it will help the Health facilities, zonal, regional health officials, and non-governmental organizations for planning health strategies, and interventions in antiretroviral therapy service. The finding of the study will help health care providers to recognize main predictors, prioritize intervention areas and implement key interventions around the time of loss to follow-up and improved care for continual reduction of morbidity and mortality among HIV-care services. Finally, it will be helpful for health professionals and interested bodies to use data as reference data for researchers.

CHAPTER TWO: LITERATURE REVIEW

2.1. Incidence of the lost to follow up among Adults on ART

Studies have been conducted in countries to determine the incidence and predictors of loss to follow up among HIV-positive adults on ART. In a study done on long-term antiretroviral therapy in Latin America and the Caribbean the cumulative incidence of LTFU five years after ART initiation was 12.1-15.3)/100 PY and 18.2% (47,66) in the African region, the rate of LTFU ranges between 10 to 26 per 100 PY, and the rate of LTFU increases with additional years on ART(30).In addition, a study conducted in a different part of Africa shows that the incidence of LTFU was 2.4 per 100 in Kenya,7.5 to 26.7 per 100 in Uganda, and 26 per 100 in Malawi(14,33,48,49).

A retrospective cohort study done in Uganda finding suggests that the cumulative incidence of LTFU increased with the duration of follow-up from 8.9% at 6 months to 20.2% at 48 months(31). Other similar studies in South Africa revealed that the incidence rate of LTFU was 103 per 1000 person-years in the first year on ART and increased to 405 per 1000 person-years in the eighth year of taking ART(30).

In Ethiopia, institution-based retrospective cohort studies conducted to determine the incidence of LTFU among HIV-positive adults on ART showed that it varies from place to place the result shows incidence rate was 3.7 per 100 PY in Debre Markos (16) 10.9%, and 12.26% in Gonder (19,32), 13.45% in Bichena (44), 8.2 per 100 person-years in Axum(35), 26.6% in Jigjiga Ethiopia(15), 8.8 per 1000 person-months in Mizan-Teferi and 10.5 per 100 PY in Hadiya south Ethiopia (37,66). In a study conducted in Axum, 41% of LTFU, occurred within the first six months of ART initiation(35). In Gonder, lost follow-up was highest in the first 12 months of ART follow-up,15.1per100 PY of observation(19), and similarly high at 1st year in the northwest Amhara, 27.41/100 PYs (44). The proportion of LTFU according to different study is 40.8% in the study done in Bichena health center (44),19.2% in Gondar Specialized Hospital (19),17.3% in Jigjiga Eastern Ethiopia(15), 20.8% in Hadiya zone, southern Ethiopia(71) and 9.8% in Axum(16).

2.2. Predictors of loss to follow up among HIV positive adults on ART

2.2.1. Baseline socio-demographic predictors

There were identified significant factors associated with LTFU. These include sex, young age, occupations, educational level, marital status, phone number, residence, and religion. The age of

the adult is considered a predictor of LTFU according to different studies. Findings from a study done in Asia show LTFU was significant with age > 50 years(51). A retrospective cohort study conducted in India revealed that age between 15-19 years was 2.4 times higher hazard ratio risk factor for LTFU(52). In studies from South Africa, those in the age 18 to 35 group were 2 times more likely to lost compared to other ages(39). In Kenya, younger ages between 15-30 were the other risk factor for LTFU(53) and a study conducted in Gonder northwest suggests that the hazard of LTFU is 2 times higher among adults whose age is between 15–30 years (19).

In a retrospective study done in Uganda, the male gender was a risk ratio of 1.8 times lost than the female(14), another similar study conducted in Nigeria Being male was also risked to LTFU(54), a study finding on the Predictors of loss to follow up in Jigjiga eastern Ethiopia revealed that Patients with a male sex hazard ratio of 2.1 times risk factor for LTFU(15).

Educational status was the risk factor for LTFU according to a study conducted Democratic Republic of Congo those who attained secondary or higher education levels were 1.6 had a higher hazard of being LTFU(55). A study done in South Africa showed that being self-employed was an HR of 13.9 times more a significant risk factor for LTFU(30), similar study conducted in Oromia, Ethiopia being day laborers was a significant factor for LTFU on ART services(56).

Studies conducted in sub-Saharan countries showed that marital status was significantly associated with LTFU(57). And being a Muslim was a hazard ratio of 1.3 risks for LTFU according to a study done in Accra, Ghana(58).

The rural residence is also another significant socio-demographic variable. A previous study conducted in the Oromia region showed that the odd of rural residents was 2.35 times increased the risk of loss to follow-up in ART in contrast, a retrospective cohort study finding in Debre Markos northwest of Ethiopia showed that, rural residence was HR of 0.6 fewer risks for lost to follow-up (38,56). In a retrospective cohort study in Masaka, Uganda not having a registered phone number were HR 1.52 times the risk factor for LTFUP among ART service(31), and similar findings were reported in northwest Ethiopia (34,38).

2.2.2.Clinical and laboratory-related predictors

CD4 count is a significant risk factor for LTFU. A cohort study done in sub-Saharan Africa suggest that reduced total CD4 lymphocyte count was a risk factor for lost to follow-up (12). A similar cohort study done in Ghana indicates that having CD4 <250 cells/ml was HR 1.45 times

higher risk factor for LTFUP. However, a similar study conducted in Kenya showed that the lower CD4 <200 cells/ml count were 0.58 less risk for LTFU(28,58). In Ethiopia, a study conducted in the Oromia region suggests that patients with baseline CD4 <350 cells/mL were significantly associated with LTFU, though, a retrospective cohort study in Gonder, northwest having CD4 count between 201–349 cells/μL HR of 0.58 were less risk for LTFU (32,56).

Retrospective cohort study findings from Malawi show that being in World Health Organization (WHO) clinical stage 3 and Stage 4 were 1.35 and 1.87 times the hazard ratio for LTFU respectively. And Similar study conducted in Debre Markos northwest Ethiopia also reported that WHO clinical stage IV were a 2.8 hazard ratio of loss to follow-up in ART(33,38).

A Cohort study conducted in sub-Saharan Africa revealed that reduced hemoglobin concentration among ART was 1.9 times the risk for predictors for lost(57). As well as a similar study done in Uganda having anemia had a higher risk of LTFU in ART(14). Regarding viral load concentration, a Study conducted in Asia reviled that viral load ≥ 1000 copies/mL is 1.86 times the risk for Lost to follow up compared with viral load < 1000 copies(51). As well as in a study done in woldia, Ethiopia low viral load count <1000 copies/mL were a protective effect for LTFU (59).

2.2.3. ART, Nutritional and other medication-related predictors

ART regimen was a significant variable in studies conducted in Ethiopia, taking AZT-3TC-NVP medication at the start of ART was a significant predictor of lost to follow-up in the studies done in northwest Ethiopia(19,35). According to a study conducted in Gonder northwest and southern Ethiopia not taking opportunistic prophylaxis like Isoniazid (INH), preventive therapy were 4.57 and 2.15 times the hazard risk for LTFU from ART service respectively (19,34). And not receiving Cotrimoxazole preventive therapy (CPT) were 2.66 times the hazard risk for LTFU(19).

The presence of opportunistic infection was a risk factor for being lost to follow-up, a sub-Saharan Africa: a systematic review and meta-analysis conducted studies shows that tuberculosis co-infection were significantly associated with early LTFU(29). A retrospective cohort study conducted in northwest Ethiopia finding revealed that being smear-positive pulmonary TB was 2 times the risk for lost(35). But, in a study conducted in Indonesia among Tuberculosis Infection and HIV Patients found that TB infection did not have a significant association with LTFU after ARV initiation(60).

A study done on Long-term loss to follow-up in Asia also showed that hepatitis C confection was another factor for being lost from ART service(51). Poor adherence level was also a significant factor for LTFU. A study done in Accra, Ghana, and Malawi revealed that poor adherence to counseling was 1.4 and 4.5 times a significant risk for loss to follow up, respectively(33,58), and also a study conducted in woldia, southern Ethiopia and Oromia showed that those whose poor adherence level was increased risk of LTFU(16,56,59).

The study done in the Democratic Republic of Congo and Jigjiga, eastern Ethiopia shows the relationship between the non–disclosure HIV status and LTFU was 2.8 times more likely a higher chance of being lost to follow-up from ART service(15,55).

but, studies done in Ghana revealed that not disclosing their HIV status was a less likely hazard for time lost to follow-up(58). Not having primary caregivers was the independent predictor of loss to follow-up from ART services in a study done in southwest Ethiopia(34). A study done in Malawi indicates that distance from health Facilities and patients' living areas had a greater hazard of being LTFU compared to patients near the site(61). Longer distance travel between home and hospital was the other predictor factor for lost to follow up according to a study conducted in southwest Ethiopia(34).

Nutritional status has been positively linked with LTFU. A study done in Malawi shows Adults who are body mass index (≤ 18.4) were 1.2 times at the risk for LTFU as compared to BMI >18.5 among ART patients(33). Likewise, a study conducted in northwest and southwest Ethiopia shows being underweight to be a significant predictor of LTFU from ART service(32,34).

A study conducted in Arba Minch, southern Ethiopia shows a baseline weight greater than 60 kilograms, was more likely to be lost from treatment(16). A retrospective follow-up study conducted in northwest and southern Ethiopia showed that being's ambulatory functional status was 1.94 and 2.4 times the risk for LTFU respectively(33,68). In addition, a study conducted in Oromia Ethiopia showed that those whose bedridden functional status was 2.16 had an increased risk of LTFU(56). A retrospective follow-up study conducted at primary health care facilities and hospitals in south Ethiopia LTFU was higher in hospitals than in health centers. it suggests that LTFU rates were 9.0 and 10.9 per 100 PY of observation in health centers and hospitals, respectively(45). But a similar study showed that the likelihood of LTFU in the health center were higher than in hospital(23).

2.3. Conceptual framework

The following conceptual framework shows an association between independent variables with a dependent variable which is developed after reviewing kinds of literatures(12,14–16,31,32,36–39,48,56,62–66). According to this literature, Socio-demographic, ART and other medications, baseline clinical and laboratory, nutritional status, and facility type variables affect adults LTFU in the continuum of HIV care.

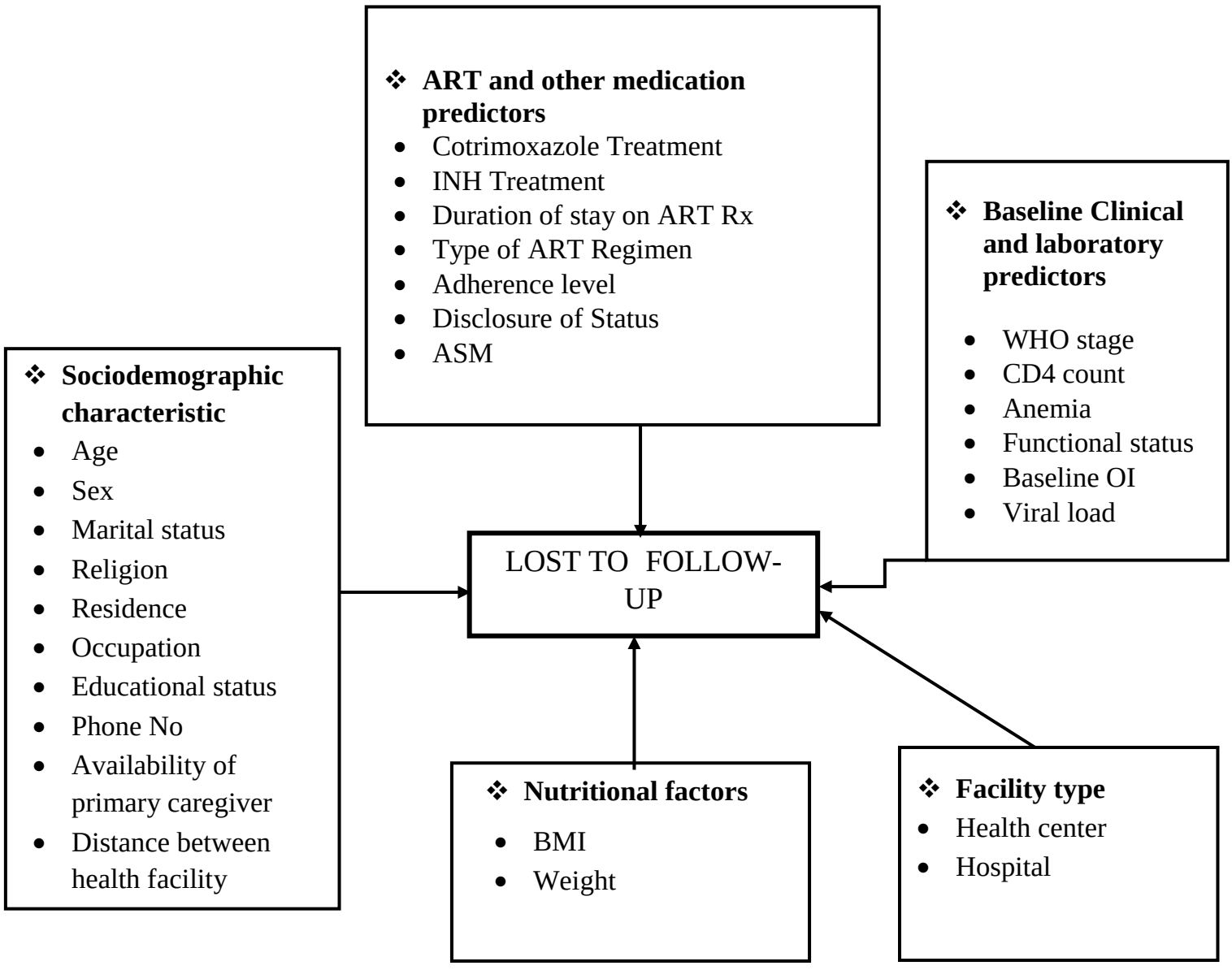

Figure 1 Conceptual framework for the incidence and predictors of lost to follow-up among adults on antiretroviral therapy.

Source: Adapted after reviewing literatures (12,14–16,31,32,36–39,48,56,62–66).

CHAPTER THREE: OBJECTIVES

3.1. General objective

- To assess incidence and predictors of loss to follow-up among HIV-infected adults receiving antiretroviral treatment from June 28/2017, to June 27/2022, at public health facilities in Metekel zone, Northwest Ethiopia, 2022.

3.2. Specific objectives

- To estimate the incidence of loss to follow-up among HIV-infected adults receiving antiretroviral treatment at public health facilities in Metekel zone, Northwest Ethiopia, 2022.
- To identify predictors of loss to follow-up among HIV-infected adults receiving antiretroviral treatment at public health facilities in Metekel zone, Northwest Ethiopia, 2022.

CHAPTER FOUR: METHODS AND MATERIALS

4.1. Study area and period

Metekel zone is one of the three zones found in Benishangul Gumuz Regional State. It is bordered on the south and southwest by Kamashi, on the west by Sudan, and the north and east by the Amhara region. The administrative center of the Metekel zone is Gelgel belles which is located 540 km Northwest of Addis Ababa. Administratively, the zone is structured into seven districts and 1 town administration that are (Gelgel belles, Mandura, Pawie, Wombera, Debati, Bullen, Dangur, and Guba), based on the 2007 E.C Ethiopian census, the total population of the zone was estimated to be 484,118, of whom 256,030 were men and 228,088 are women. The majorities of 278,752 of the population lives in rural areas and are economically dependent on farming.

The zone has three hospitals (one General Hospital and 2 primary Hospitals), 21 health centers, and 168 health posts. Currently among these facilities, 1 General hospital and 8 health centers were providing ART services based on the revised 2018 National Guideline. Nowadays, 3,187 HIV patients are actively following ART services in the zone. Among those 96% of the follow-up were Adults(67).

The study period was from June 20 to July 05, 2022. Among chart records of adults registered from June 28, 2017, and June 27, 2022. This period is selected to have a nearest five years of follow-up study periods and more or less full implementation of recently updated standardized formats, documentation, and recording system in a regular manner were much be improved in the nearest years.

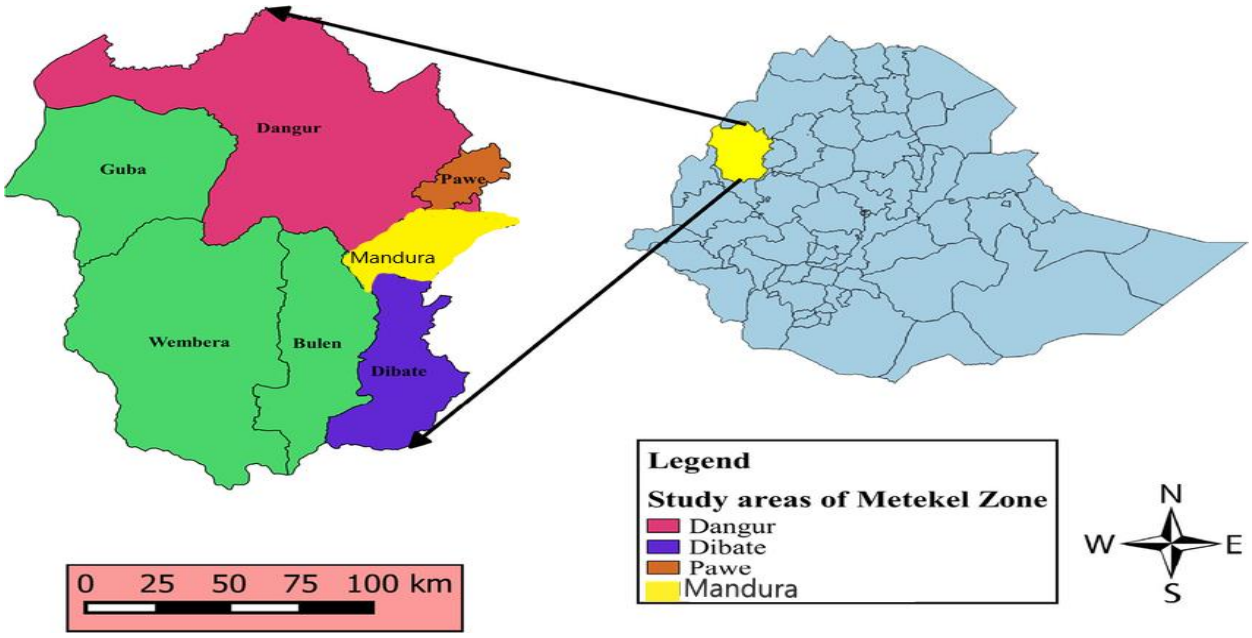

Figure 2.https://www.researchgate.net/figure/Map-of-Ethiopia-Metekel-zone-and-study-districts

4.2. Study design

An institution-based one group cohort study design was employed.

4.3. Population

4.3.1. Source population

- All HIV patients age ≥ 18 years who are on HIV care at public health facilities in Metekel zone, Northwest Ethiopia, between June 28, 2017, and June 27, 2022.

4.3.2. Study population

- A randomly selected all HIV-positive adults who initiated antiretroviral therapy on HIV care at selected public health facilities in Metekel zone, Northwest Ethiopia, between June 28, 2017, and June 27, 2022.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

All adult HIV positive age ≥ 18 years patients who had at least 1- month(28day) follow-up after ART initiation between June 28, 2017, and June 27, 2022.

4.4.2. Exclusion criteria

Patients with incomplete baseline and follow-up information at least (sociodemographic variable, who's date of ART initiation and date of the last visit not well recorded), and Patients transferred in from other health facilities were excluded due to incomplete baseline and follow up information.

4.5. Sample size determination, sampling technique, and procedures

4.5.1. Sample size determination

The sample size was determined for Cox proportional regression by using the Schoenfeld formula for survival analysis in STATA statistical package, Version 15 based on considering the following assumptions:

$$E = \frac{(Z_{\alpha/2}+Z_{\beta})^2}{[\ln(HR)]^2\,[p(1-p)]},\ N = \frac{Event}{probablity\ of\ Event} \quad \text{----------(67)}$$

- Significance level (α) (two-sided) =0.05, $Z_{\alpha/2} = 1.96$
- Power = 80%; $\beta = 0.2$, $Z_{\beta=}$ 0.842
- HR = hazard ratio was used from studies conducted in northwest and south Ethiopia(71,68).
- E = number of event (lost).
- p = proportion of variability among covariates (for 1:1 allocation) = 0.5
- L=probability of lost was used from the study conducted in northwest and south Ethiopia(71,68).
- It was assumed that no subject was anticipated to withdraw from the follow-up.
- Finally, a 10% non-response rate (NRR) for an incomplete chart will be added.
- Hence, the largest sample for the objective was 549 used.

Table 1.Sample size calculations for predictors of LTFU among HIV-infected adults receiving antiretroviral treatment at public health facilities in Metekel zone, Northwest Ethiopia, 2022

S. No	Predictor variables	Parameters		sample size	NRR (10%)	Final sample	Reference
		AHR	L				
1	Functional status (bedridden)	2.4	0.105	391	39	430	(71)
2	WHO clinical staging (Stage IV)	2.09	0.116	499	50	549	(68)

Finally, the largest sample size (N=549) of the minimum sample of the current study was selected.

4.5.2. Sampling technique

The study was carried out in Metekel Zone Districts at public health facilities that regularly offer ART services. ART services are currently provided in the study area by eight health centers, and one public hospital. A straightforward simple random sample procedure was used to choose one public health hospital and three health centers from this group. Based on the existing ART service provided by each facility, the sample size for each selected health facility was distributed proportionately. Records of antiretroviral therapy clients who initiated antiretroviral treatment between June 28, 2017, to June 27, 2022 were selected in each health facility and then, the sampling frame was generated by using the unique ART for eligible records. Finally, a computer-generated simple random sampling technique was employed to recruit a predetermined study participant into the study as follows (figure 3).

The sampling frame was generated using the unique ART number and the database was entered into Excel. Then, the required sample size of 549 ART services number was selected randomly by a computer-generating method. Finally, the selected medical charts were followed for five years.

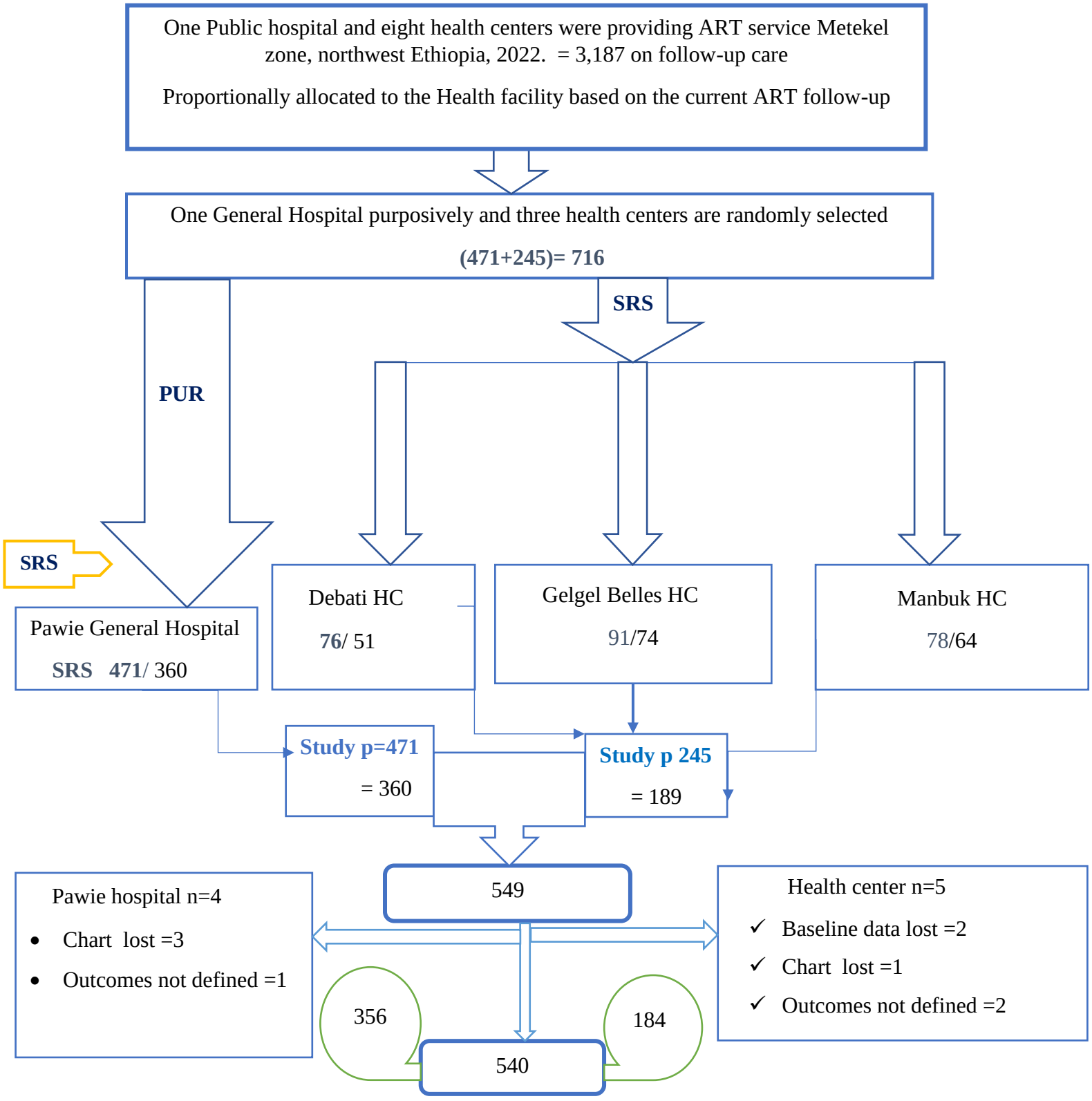

Figure 3.Schematic presentation of sampling procedure at public Health facilities in Metekel zone, Northwest Ethiopia, 2022.

4.6. Data collection procedures

Data collection procedure: Data were collected based on a data abstraction tool adapted from the ART intake form, register, and follow-up form from the standardized ART entry that is currently used by the ART clinics of the study health facilities(1) and by reviewing different literature.

Data Source: The data for this research was secondary data recorded routinely by the data clerk at each health facility for clinical monitoring and evaluation purposes and entered into an electronic database and follow-up medical records during the follow-up time ART.

Patient intake form, follow-up card, and ART registers, as well as the electronic information database, was used as data sources. Other clinical charts including laboratory test results was also use to collect the CD4 cell and viral load counts. District Health Information System 2 (DHIS2) record numbers was used to identify individual patient cards or their data in the electronic database.

Socio-demographic characteristics, baseline and follow-up clinical and laboratory data, and the primary outcome variable (LTFU) from antiretroviral therapy follow-up care after initiation of treatment, confirmed by reviewing ART register, SMART care, follow-up card at the health center and hospital, noted by ART adherence supporters was collected from patient cards.

The starting point for retrospective follow-up was the time from the first patient's enrolment to regular HIV care in the clinic and the endpoint was the date lost or censored (outcome other than lost) from ART services during the study period (June 28,2017, to June 27/ 2022). The data was collected by five trained health professionals (two for hospital and one for health centers) who have trained and experienced on recently updated 2018, comprehensive ART Guideline at selected health facilities and supervised by two senior Bachelor Degree holder nurse.

4.7. Study variables

4.7.1. Dependent variable

The dependent variable is lost to follow-up from ART services.
LTFU from ART service was an event of interest (coding was "1" for lost and "0" for censored).

4.7.2. Independent variables

The independent variables were age, sex, marital status, educational status, religious status, residence, occupational status, the distance between home and health facilities, registered phone number, WHO clinical stage, functional status, CD4 cell count, viral load, the occurrence of opportunistic infections (OIs), disclosure status, active tuberculosis (TB), length of follow-up, Isoniazid (INH) initiation, Cotrimoxazole preventive therapy (CPT) initiation, body mass index (BMI), (weight)Kg, availability of primary caregiver, type of ART regimen, anemia, adherence on ART, and ASM utilization to ART care.

4.8. Operational definition

- **Lost to follow-up**: Those who were not taking an ART refill for 3 months or longer from the last attendance for a refill and not yet classified as 'dead' or 'transferred-out 'on patient chart(38).
- **Time to Lost to follow-up**: Was the time interval between the dates of ART initiation to the last missed appointment (LTFU)(34).
- **Event**: LTFU from ART in the follow-up period (between June 28, 2017, to June 27, 2022).
- **Censored**: defined as Individuals who died while on ART, individuals transfer out to other health institutions after beginning of the study and individuals on ART at the end of the study were considered as censored(39).
- **Retention:** patients who were known to be alive and receiving ART(1).
- **Functional status**: will be classified into the following categories: 1).Working-able to perform usual work, 2).Ambulatory-able to perform activity of daily living, and 3).Bedridden –not able to perform activity of daily living(1).
- **Adherence Status**

  1. Good (≥95%): Missing <3 doses out of 30 doses or missing <4 doses out of 60 doses
  2. Fair (85-95%): Missing 3-5 doses out of 30 doses or missing 4-9 doses out of 60 doses
  3. Poor (<85%): Missing >6 doses out of 30 doses or missing >9doses out of 60 doses(1).
- **Disclosure:** in this study is defined as disclosure of the status that is being HIV positive to at least one individual(19).
- **Death**: Those patients who recorded as "dead" on the adults' medical card(1).
- **Transferred out:** Those patients who were formally transferred out to another health facility(1).

- **Transfer in**: Those patients who were formally transferred out from other health facilities and entered the health Facility accordingly(1).
- **Follow up form:** is thus designed to follow patients in a systematic manner starting from the time of enrollment (irrespective of the stage of the patient at enrollment) for chronic care through ART to capture key information in each visit(1).
- **Distance:** measured by kilometer length between the health facility and patient resident home, distance > 5 kilometers and distance < 5 kilometers(17).
- **Incomplete record**: Baseline sociodemographic characteristics patient chart with missed Age and Sex not available during data collection were not included.

4.9. Data processing and analysis

Data were checked for completeness and consistency, it was entered into Epi Data manager 3.1 and then exported to STATA version 15 for cleaning, coding and for further analysis. Exploratory data analysis was carried out to check the levels of missing values and the presence of outliers.

Descriptive statistics, frequencies and percentage for categorical variables and summary statistics for continuous data (mean with standard deviation in normally distributed data or median with IQR for the data not normally distributed) was used to characterize the study population.

Kaplan-Meier (KM) curves to estimate survival time and compare survival (or hazard) rate between categories of variables was done. Moreover, the Log-Rank test (Mantel-Cox test) was used to assess for a statistically significant difference in survival (hazard) rate between categories of variables. The life table was used to estimate the cumulative probability of survival at different time intervals (every 12 months) and p-value <0.05 in the log-rank test were indicating there is a statistically significant difference in survival (or hazard) rate. Incidence density rate of lost to follow up was calculated per 100 Person years of observation. In this study, we have determined the incidence of LTFU by taking the denominator as person year (PY).

Cox proportional hazard model was carried out to identify predictors of lost to follow up among ART care. The finding of this study showed that a graphical presentation of categorical variables were parallel and the proportional hazard assumptions were checked using Schoenfeld residual test (global test) with a value of p>x2=0.2737(Annex VI). Variables significant at a p-value of less than 0.25 in the bivariable Cox regression analysis was a candidate variable to enter into the final multivariable Cox regression analysis. Adjusted Hazard Ratio (AHR) with respective 95% CI was

used to determine strength of association, and p-value < 0.5 was used statistical significance. Cox proportional hazard model for its fitness to the data was cheeked using cox Snell residuals, in which the hazard function follows the 45-degree line (Annex VII). Generally, it can conclude that the final model fits the data successfully. Finally the data was presented in text, tables, and figures.

4.10. Data quality management

Data quality was assured by careful designing of data abstraction tools, recruitment of data collectors, and supervisor who have previous experience. Pretest was tested at Jawi Hospital on (5%) 27 charts to check for appropriateness and consistency and the necessary modification was made on the final data extraction format. In addition to this, training was given for data collectors and supervisors on data collection tools and data collection procedures for one day. Data collectors were supervising closely by the supervisor and principal investigator (PI) daily throughout the data collection period to ensure the quality of the data. After completion of the data, the completeness and consistency of each questionnaire was checked by the PI and the supervisor daily.

4.11. Ethical consideration

Ethical clearance for the study was obtained from the Ethical Review Board (ERB) of Jimma University Institute of Health (JUIH). Permission to undertake the study was obtained from every relevant authority in Metekel Zone Health Department and health facilities heads. Finally, the objective of the study was explained to the coordinator and ART staff of health facilities. Privacy of respondents was maintained by using non-personal identifiers such as patients' medical registration numbers and unique ART numbers was used to distinguish study subjects during data reviewing and extraction process.

4.12. Dissemination plan

The result of the study was presented and submitted to Jimma University, faculty of public health department of epidemiology as partial fulfillment of Masters of Public Health in Epidemiology. It is also planned to communicate the finding with health facilities and respective Zonal health departments and Regional Health Bureau with documentation and possibly with the presentation. Efforts will be applied to present the finding in locally or internationally held symposiums, workshops, and conferences. Also, efforts will be made to publish the paper in an internationally reputable journal.

5 RESULTS

Data were reviewed for a total of 549 clients whose records were screened from Metekel zone public health facilities enrolled in antiretroviral therapy care during the period from June 28, 2017 to June 27, 2022, of which 540 clients were eligible and included in the study with a response rate of 98.3%. From the total review record, 356 (65.93%) from Pawie General Hospital, 72 (13.33%) from Gelgel Beles Health Center, Manbuk and Dibati health centers account for 63 (11.67%) and 49 (9.04%), respectively. A further nine (9) cards were not included those with outcomes not defined Chart lost and important baseline line data missed.

5.1 Socio-demographic characteristics of the patients

The mean age of participants was 35.7 (SD±12.41) years old and the highest number of study participants were in the age group of 25–34 years (29.3%). Of the total reviewed records, 304 (56.3%) were females, and 428 (79.3%) were urban dwellers. Orthodox Christians made up the majority of the study population (347, or 64.3%), followed by Muslims (140, or 25.9%) and Protestants (7.4%). The majority 227 (42%) of the patients had at least primary school education and 161 (29.8%) of the patients had no formal education.

Regarding marital status, the highest percentage (57.6%) corresponds to married clients, and about 152 (28.1%) were unmarried, but those who either got separated, divorced, or widowed sum up to less than 15% of the total cohort. Concerning occupation, 247 (45.74%) of the study participants were farmers, 110 (20.4%) were merchants, and 9.1% were daily-laborers.

The majority of respondents 478 (88.5%) were disclosed to someone else, and regarding the availability of telephones, 508 (94%) of the study participants had cell phone contact. Among antiretroviral therapy care attendants, 371 (68.7%) travel more than five kilometers to reach the health facility. Among the reviewed records, the majority of the respondents 96.4% had available care giver and 478 (87.96%) of the clients had known partner HIV status (Tabe2).

Table 2 Baseline socio-demographic characteristics among HIV-positive adults on ART at public health facilities in Metekel zone, Northwest Ethiopia, 2022.

Socio demographic Variables	Categories	Frequency	Percent (%)
Age	18-24 years	122	22.6
	25-34 years	158	29.7
	35-44 years	130	24.1
	≥45 years	130	24.1
Sex	Male	236	43.7
	Female	304	56.3
Residence	Urban	428	79.3
	Rural	112	20.7
Marital status	Single	152	28.1
	Married	311	57.6
	Divorced	59	10.9
	Widowed	7	1.3
	Separated	11	2
Religion	Orthodox	347	64.3
	Muslim	140	25.9
	Protestant	40	7.4
	Catholic	13	2.4
Level of education	No education	161	29.8
	Primary	227	42
	Secondary	134	24.8
	Tertiary	18	3.3

Table 2 (Continued)

Occupation	Sex worker	6	1.1
	Driver	15	2.78
	Daily laborer	49	9.1
	Merchant	110	20.4
	Farmer	247	45.7
	Government	62	11.5
	Self employed	38	7
	Others	13	2
Distance of ART clinic	< 5 KM	169	31.3
	≥ 5 KM	371	68.7
HIV disclosure status	Disclosed	478	88.5
	Not disclosed	371	68.7
Partner HIV status	Known	475	87.96
	Unknown	65	12.04
Availability of care giver	Yes	521	96.4
	No	19	3.6
Telephone contact	Yes	508	94
	No	32	6

Others; house wife, soldiers

5.2 Baseline Clinical and laboratory related characteristics of Adult on ART

Out of total respondents, 315 (58.3%) were linked to antiretroviral therapy care from VCT, and more than four-fifths (83.7%) of the patients started antiretroviral therapy at working functional status and one-fourth (25%) of the respondents were categorized under WHO clinical stage at an advanced WHO stage of either stage III or IV. Among the participants, 15.4% of the reviewed records had a most recent CD4 count of less than 350 cells/ml. Relating to hemoglobin level the majority of the study participant 490(90.7%) started antiretroviral therapy at a hemoglobin level of >10 g/dL.

On the other point concerning the recent viral load status of the participants, 28 (5.2%) had a viral load result greater than 1000 copies copies/mL. Among 540 patient charts that had documentation on past history of tuberculosis, 45 (8.33%) patients had a history of tuberculosis treatment (Table 3).A total of 43 (7.9%) of the study participants had been diagnosed with tuberculosis (TB) at the initiation of antiretroviral therapy, and more than one-third 191 (35.4%) had an opportunistic infection (OI), of which 38.5% had pneumonia, followed by tuberculosis 35.5%, herpes zoster10.7%, oral thrush 8.3% and diarrhea 6.6%.

Table 3 Baseline Clinical and laboratory related characteristics of Adult on ART at public health facilities in Metekel zone, Northwest Ethiopia, 2022.

Variables	Categories	Frequency	Percent (%)
ART linkage point	VCT	315	58.3
	OPD	117	21.7
	IPD	9	1.7
	MCH	36	6.7
	Tb/other	63	11.7
Recent CD4 count	< 350 cells/ml	83	15.4
	≥ 350 cells/ml	457	84.6
Baseline functional status	Functional	452	83.7
	Ambulatory	78	14.4
	Bedridden	10	1.8
WHO clinical stage at baseline	Stage I	394	72.96
	Stage II	8	1.48
	Stage III	100	18.52
	Stage IV	38	7.04
Presence of opportunistic infection	Yes	191	35.4
	No	349	64.6
Tuberculosis at baseline	Yes	43	7.96
	No	497	92.4
History of TB treatment	Yes	45	8.33
	No	495	91.67
Viral Load count at 6 month	Not eligible/<6month	89	16.4
	≤1000 copies/mL	423	78.3
	>1000 copies/mL	28	5.2
Baseline Hemoglobin	≤10 g/dL	50	9.3
	>10 g/dL	490	90.7

5.3 ART, nutritional status and other related characteristics of Adult on ART

The majority, 323 (59.8%) of participants were on the TDF-3TC-EFV (1e) regimen and 161 (29.8%) of the original regimen were changed to other regimens for various reasons, mainly due to the availability of new drugs, some minor adverse drug reactions and virologic failure. Among the reviewed records 23(4.26%) had fair and 39(7.22%) had poor adherence to Antiretroviral treatment. From the total chart reviewed 243 (45%) of them were underweight (<18.5 kg/m2) according to their body mass index and out of the total respondents, 403 (74.63%) were recent body weight of ≤60kg. Regarding ASM utilization of the study participants from the reviewed record more than half (324, 60%) had utilized ASM among the study participants (Table 4).

Table 4 ART, nutritional status and other related characteristics of Adult on ART at public health facilities in Metekel zone, Northwest Ethiopia, 2022.

Variables	Categories	Frequency	Percent (%)
IPT treatment at baseline	Yes	330	61.1
	No	210	38.9
Body mass index	<18.5 kg/m2	243	45
	≥18.5 kg/m2	297	55
Cotrimoxazole prophylaxis	Yes	338	62.6
at baseline	No	202	37.4
Recent body weight	≤60 kg	403	74.63
	>60 kg	137	25.37
Initial ART regimen	TDF+3TC+EFV	323	59.81
	AZT+3TC+EFV	5	0.93
	TDF+3TC+DTG	212	39.6
Experience of regimen change	Yes	112	20.7
	No	428	79.2
Reason for change	Due to toxicity	12/112	10.7
	Virology failure	11/12	9.8
	New drug	89/112	79.4
	Clinical/Immunologic failure/other	0/161	0
Recent ART adherence to Rx	Good	478	88.52
	Fair	23	4.26
	Poor	39	7.22
Appointment spacing model	Yes	324	60
	No	216	40

5.4 Incidence of lost to follow-up of HIV-positive adults

A total of 540 patients on ART were followed for a minimum of 0.9 and a maximum of 59.9 months of the follow-up period. The total follow up period was 12,625.53 person-months (1,037.0 person-years) of observation with a median follow-up period of 1.72 years (IQR 0.87-2.84). At the end of the follow-up period, a total of 157 (29.1%) (95% CI: 25.38-33.06) patients experienced loss to follow-up, and 383 (70.9%) were censored. Out of those censored, 11 (2%) died, and 28 (5.2%) were transferred out. At the end of five years, 344 (63.7%) of respondents had been retained to ART.

Therefore, the overall incidence density rate of loss to follow-up was estimated to be 15.12 (95% CI: 12.9-17.6) per 100 person-years of observation. However the incidence density of lost to follow-up is quite different based on duration point in treatment, in the first-year follow-up is high, it shows a general pattern of declines over the five years follow-up as 17.76/100 person-years (95% CI: 14.2-22.1) at the first year, 16.9 /100 person-years (95% CI: 12.8-22.1) at the second year, 9.6 /100 person-years (95% CI: 5.9-15.5) at the third year, and 6.4/100 person-years (95%CI: 2.6-15.1) at 4th year, however, the incidence of lost to follow-up was high, 9.7 100 person-years (95% CI: 2.4-38.9) at the end of the 5th year follow-up.

The mean survival time of the entire cohort was found to be 42.8 months (95% CI: 40.6-44.9). Regarding time to follow up in this study, the cumulative survival probability at the end of the first year was 0.84, while it was 0.71, at the 2nd, and 0.55 follow-up 5th years (Table 4).

The overall Kaplan–Meir survival function estimate showed that most of the loss to follow-up from the initial ART regimen occurred in the earlier year of ART initiation, which declined in the later year of follow-up (figure 5).

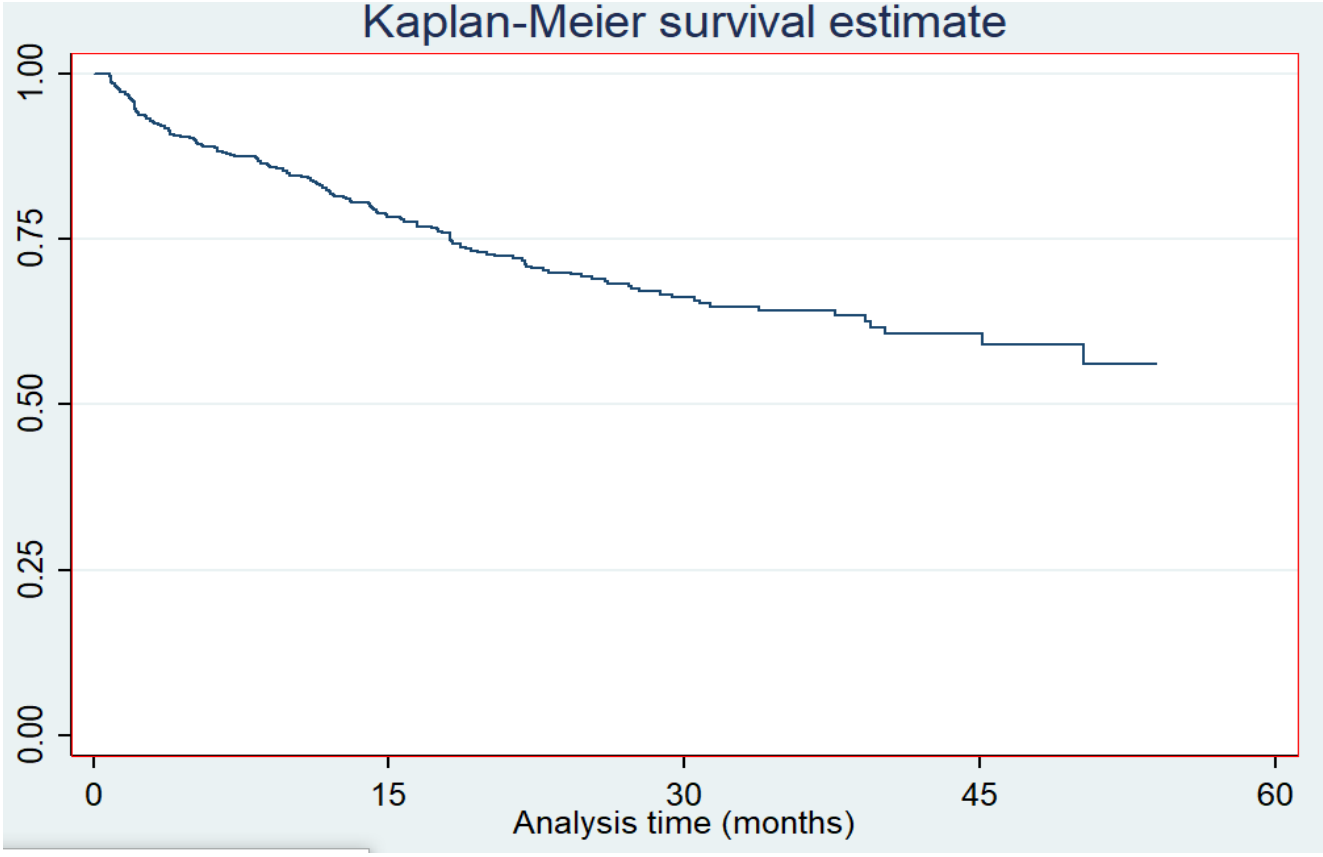

Figure 4 The Kaplan–Meier estimate of the loss to follow-up among adult patients ART patients enrolled to ART care at public health facilities in Metekel zone, Northwest Ethiopia from 2017-2022.

Table 5 Life table on the incidence rate of loss to follow-up among adult HIV patients at public health facilities in Metekel zone, Northwest Ethiopia, 2022.

Interval	Beg. total	LTFU	withdraw	At risk	Proportion of surviving	Cum.proportion of surviving
0-1st year	540	81	80	500	0.84	0.84
1-2nd year	379	52	93	332.5	0.84	0.71
2-3rd year	234	17	100	184	0.91	0.64
3-4th year	117	5	66	84	0.94	0.60
4-5th year	46	2	44	24	0.92	0.55

LTFU: loss to follow-up; Beg. Beginning; cum: cumulative.

5.4 Predictors of LTFU among HIV-positive adults

To assess the predictors of loss to follow-up, both bivariable and multivariable cox regression analyses were applied. From bivariable cox regression analysis, predictors with p values less than or equal to 0.25 were considered as the candidate variables for multivariable cox regression analysis.

According to the findings of the bivariate analysis, the following candidate variables of loss to follow-up were: residence, disclosure status, partner HIV status, presence care giver, telephone contact/relative, distance to reach health facility, baseline opportunistic infection, presence of tuberculosis at baseline, history of tuberculosis treatment, taking of Cotrimoxazole preventive therapy at baseline, presence of Pneumonia at baseline, adherence status, body mass index (BMI), recent CD4, recent viral load status, and recent weight.

Finally, four predictors were found to be statistically significant with loss to follow-up during multivariable cox proportional regression analysis at 95% confidence level (Table 6): presence of having tuberculosis at baseline, poor adherence level, being underweight (moderate and severe) at baseline, and recent high viral load status.

The study indicated that patients diagnosed with tuberculosis at baseline had a 2.12 times higher risk of loss to follow-up than individuals who were tuberculosis negative with an adjusted Hazard Ratio (AHR = 2.12, 95% CI, 1.33−3.38). The risk of loss to follow-up among those with poor adherence to Antiretroviral therapy was higher as compared to those with good adherence, in which participants with poor adherence had a 2.14 times higher risk of loss to follow-up than participants with good adherence (AHR 2.14, 95% CI 1.32–3.46).

Underweight patients with a body mass index of < 18.5 kg/m2 at baseline were 5.36 times more likely to have loss to follow-up than those with a body mass index of ≥18.5 kg/m2 (AHR, 5.36, 95% CI 3.46-8.31). The hazard of loss to follow-up was also higher among adults with recent viral load results of >1000 copies/mL, who had a risk of loss to follow-up by 2.71 (AHR = 2.71, 95% CI, 1.55−4.72) times as compared to those with < 1000 copies/mL.

In this historical cohort, those study participants who had tuberculosis at baseline had a lower survival time as compared to those who did not have tuberculosis at baseline. The mean survival time for those having tuberculosis was 24.4 months (95% CI: 17.6-31.2) and the mean survival time for those without tuberculosis was 44.3 months (95% CI: 42.1- 46.5).

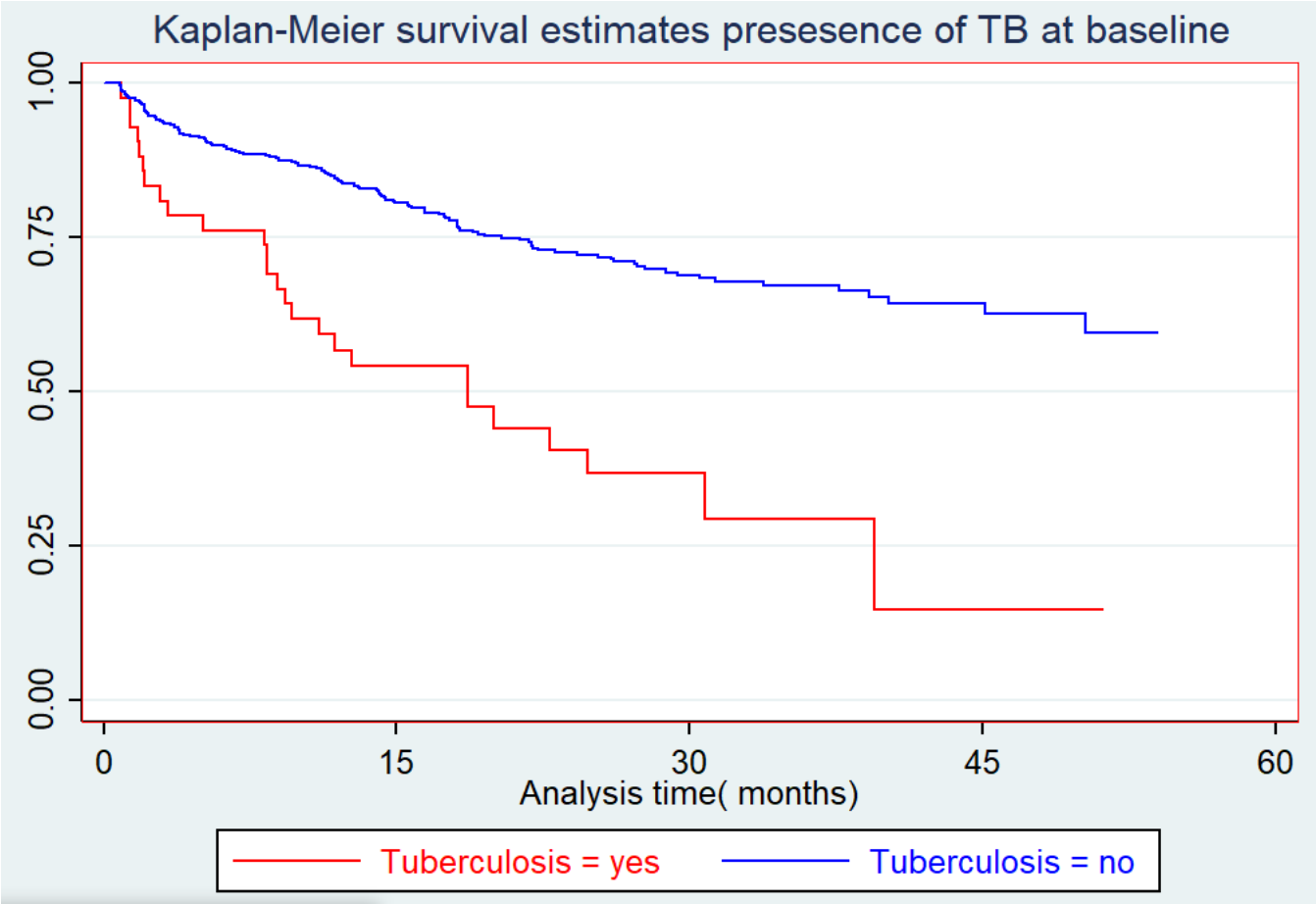

Figure 5 The Kaplan–Meier estimate of the loss to follow-up in TB among adult patients attending the ART clinic at public health facilities in Metekel zone, Northwest Ethiopia, 2022.

The mean survival time for those who were underweight (<18.5 kg/m2) was found to be 29.3 months (95% CI: 26.2- 32.3), compared to 54.22 months (95% CI: 52.2-56.2), for those who were BMI ≥18.5 kg/m2).

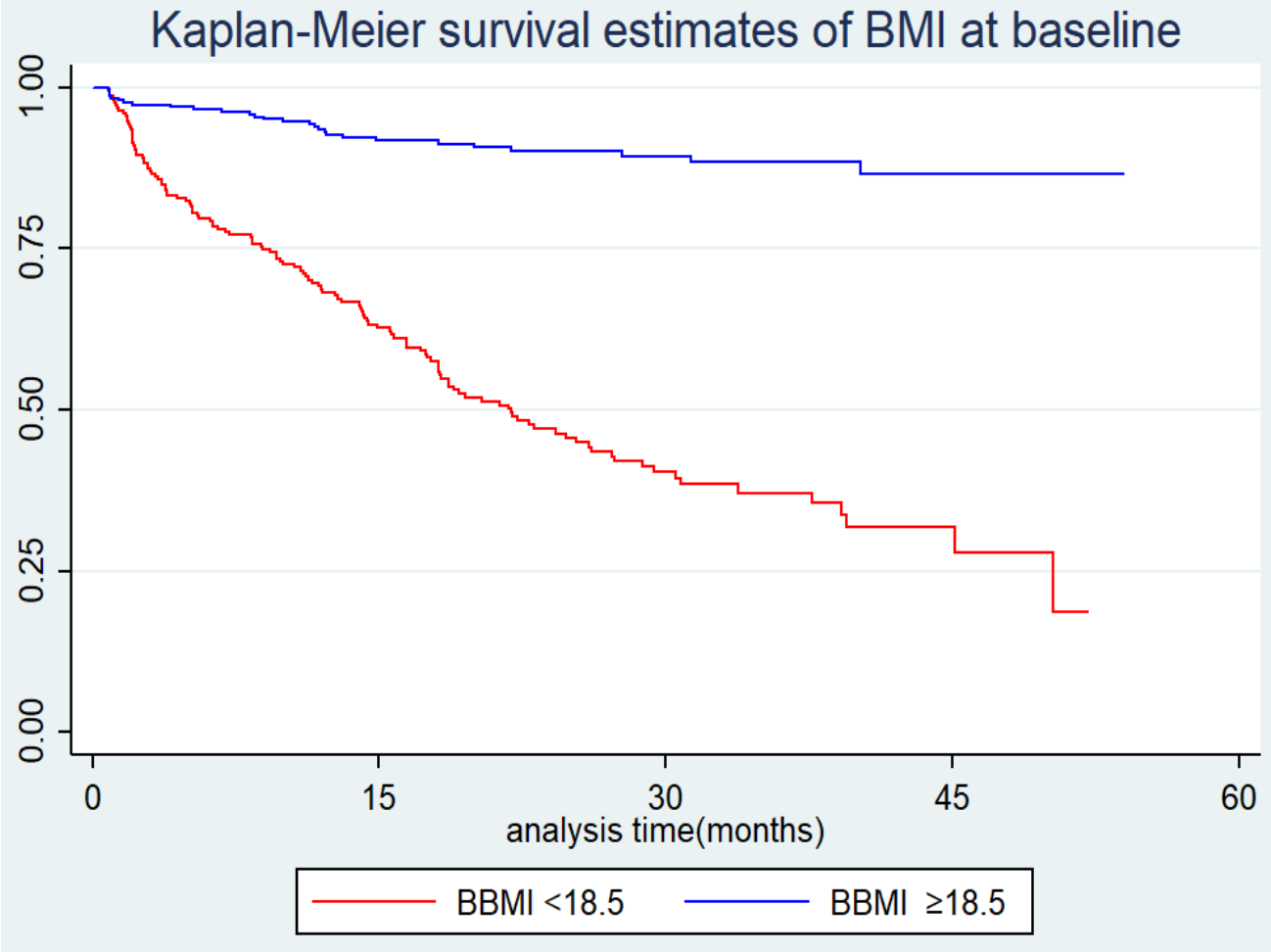

Figure 6 The Kaplan–Meier estimate of the loss to follow-up in BMI among adult patients attending the ART clinic at public health facilities in Metekel zone, Northwest Ethiopia, 2022.

The mean survival time for those who have been poor adherence level was found to be 20.7 months (95% CI: 15.4- 24.7), as compared to those who were good adherence level with a mean survival time of 44.3 months (95% CI: 42.1- 46.6) months.

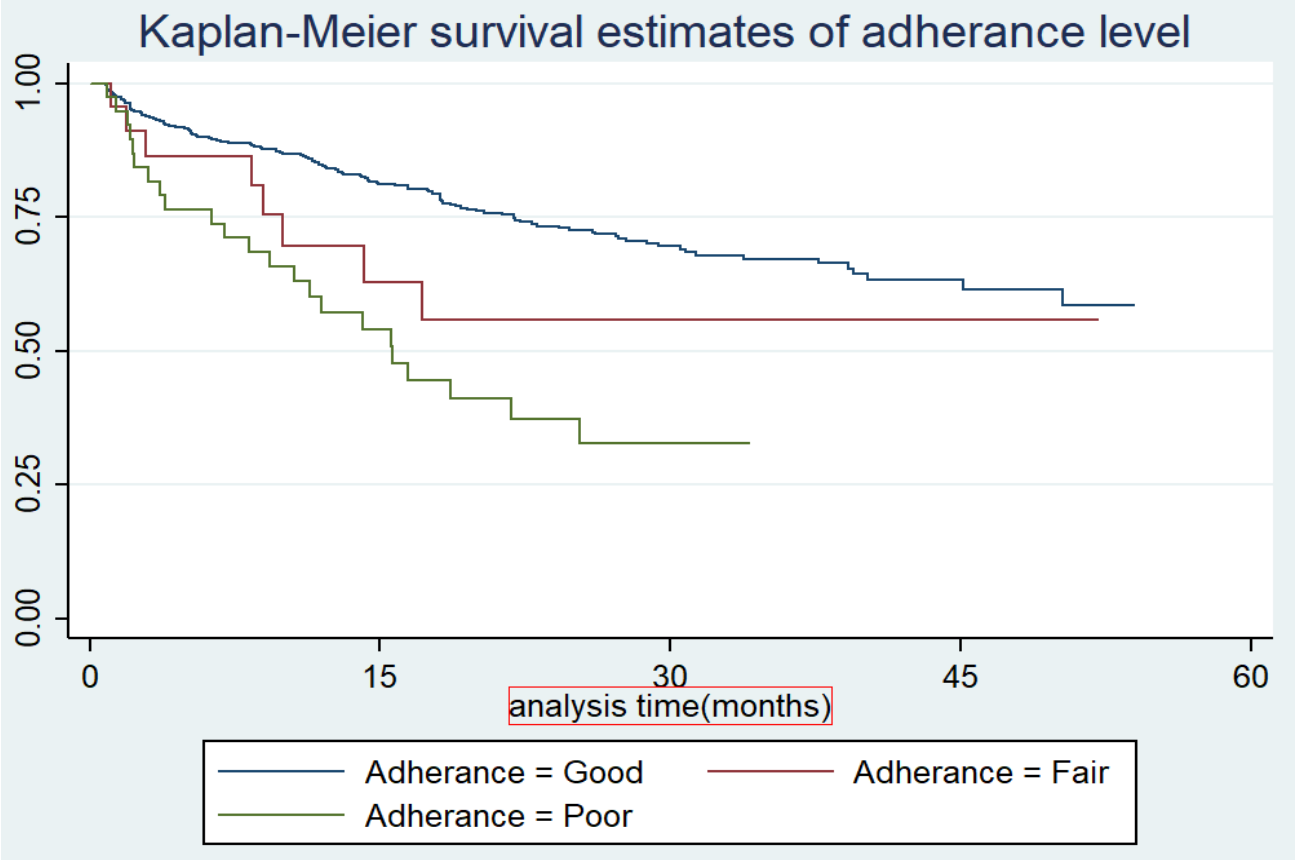

Figure 7: Kaplan–Meier estimates of loss to follow-up by adherence level among adult patients on attending the ART clinic at public health facilities in Metekel zone, Northwest Ethiopia, 2022.

The mean survival time for those who have a high viral load was found to be 21.1months (95% CI: 12.8- 29.3), as compared to those who had a low viral load with a mean survival time of 44.07 months (95% CI: 41.8-46.8).

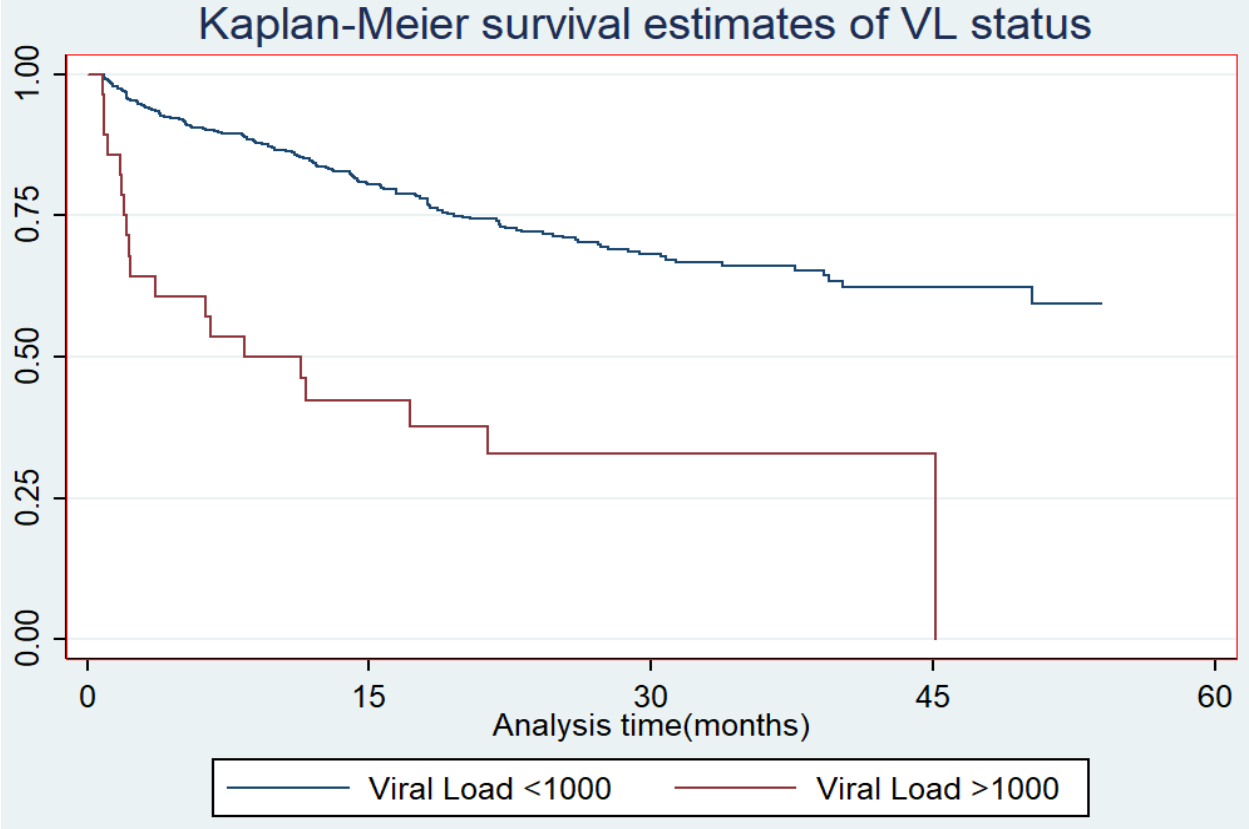

Figure 8 Kaplan–Meier estimates of loss to follow-up by viral load status level among adult patients on attending the ART clinic at public health facilities in Metekel zone, Northwest Ethiopia, 2022.

Table 6 Bivariable and multivariable Cox regressions among HIV-positive adults on ART at public health facilities in Metekel zone, northwest Ethiopia, 2022

Predictors	Category	LTFU	Censored	Crude HR 95% CI	P .Value	Adjusted HR95% CI
Residence	Urban	118	310	1		
	Rural	39	73	1.30(0.90-1.87)	0.152	1.23(0.82-1.83)
Disclosure status	Disclosed	130	348	1		
	Not disclosed	27	35	1.77(1.16-2.68)	0.007	1.40(0.85-2.30)
Partner HIV status	Known	132	343	1		
	Unknown	25	40	1.59(1.03-2.44)	0.034	1.66(0.98-2.89)
Presence of Care giver	Yes	147	374	1		
	No	10	9	2.15(1.13-4.09)	0.019	1.04(0.51-2.13)
Telephone contact	Yes	137	364	1		
	No	20	19	1.78(1.11-2.84)	0.016	1.15(0.67-1.99)
Distance from facility	<5 KM	35	134	1		
	≥ 5KM	122	249	1.67(1.15-2.44)	0.007	1.14(0.76-1.70)
Opportunistic infection at Baseline	Yes	70	121	1.44(1.05-1.98)	0.023	1.40(0.95-2.05)
	No	87	262	1		
Tuberculosis at Baseline	Yes	26	17	2.94(1.93-4.49)	<0.001	**2.12(1.33-3.38)**
	No	131	366	1		
History of TB treatment	Yes	36	21	2.50(1.65-3.79)	<0.001	1.44(0.91-2.29)
	No	121	362	1		
Baseline Cotrimoxazole therapy	Yes	76	262	1		
	No	81	121	2.15(1.57-2.95)	<0.001	1.27(0.88-1.82)

Table 6 (continued)

Baseline Pneumonia	Yes	31	16	3.82(2.56-5.69)	<0.001	1.39(0.84-2.28)
	No	126	367	1		
Adherence status	Good	126	352	1		
	Fir	8	15	1.64(0.80-3.35)	0.175	1.40(0.66-2.97)
	poor	23	16	3.05(1.95-4.77)	<0.001	**2.14(1.32-3.46)**
Body mass index	<18.5	129	114	7.40(4.90-11.1)	<0.001	**5.36(3.46-8.31)**
	≥18.5	28	269	1		
Recent CD4	<350 cells/mm	35	48	1.96(1.34-2.86)	<0.001	1.26(0.84-1.89)
	≥350 cells/mm	122	335	1		
Recent viral load	<1000	138	374	1		
	≥1000	19	9	4.06(2.51-6.58)	<0.001	**2.71(1.55-4.72)**
Recent weight	<60	140	263	3.14(1.90-5.20)	<0.001	1.63(0.95-2.77)
	≥60	17	120	1		

KEY

CHR: Crude Hazard Ratio

AHR: Adjusted Hazard Ratio

CI: Confidence Interval

P-value: is from Cox-regression model for crude and adjusted for all predictors in the model

Reference: 1

Significantly associated predictors are shown with bold

6 DISCUSSION

In this study, the overall incidence of LTFU for adults was 15.12 per 100-person years of observation which is consistent with studies done in Lain and Caribbean countries with an incidence rate of (12.1-15.3)/100 person-year(47), and in the study done in Bichena health center 13.45%(44), 10.9 and 12.26 PY in Gondar Specialized Hospital Northwest Ethiopia (19.32).

On the other hand this finding is higher as compared to studies conducted in Asia 9 per 100-person years (12), 7.5 per PY in Uganda (31), 2.4 per 100 PY in Kenya (48), 3.7 per 100 person-years in Debre Markos (38), 5.3per 100 person-years in arbaminch(16), 6.4 per person-months southern Ethiopia (34), 8.8 per 1000 person-months in Mizan-Teferi (37), 10.5 per 100 person-years in Hadiya south Ethiopia (71),and 8.2 per 100 PY in Axum (35).

The discrepancy might be clarified by differences in the study settings because the study area for current study is a war-prone area for the past years till now and suffered a large number of internally displaced population in the areas where they have been displaced which poses a greater challenge for those on ART service, health-seeking behavior, lack of reporting of death events that could be considered LTFU. In addition patients transferring out without giving prior notice to the caregiving health institutions where they initially registered may be another reason and as one of pastoralist region lengthy travel distances to get health service probably the other factor for lost to follow-up.

On the contrary, this evidence is lower than findings in sub-Saharan Africa 24.6% (12), 26.7 per 100 person-years in Uganda and 23.9% loss to follow-up were in Nigeria, (13,14), and 26.6 per 100 person-months in Jigjiga town, Eastern Ethiopia, (15). It might result from the current rapid expansion and availability of potent antiretroviral treatment. The other possible reason might be the difference in sample size and study period, difference in the follow-up period, and the sociodemographic characteristics of the study participants and the beginning of the test and the start of ART criteria may be the other possible reasons.

In addition to the incidence rate, proportion of LTFU in this study was 29.1%, which was lower than studies conducted in the study done in Bichena health center, Northwest Ethiopia 40.8%(44). On the other hand this finding is also higher than studies done in Gondar Specialized Hospital Northwest Ethiopia,19.2% (19), in Jigjiga Eastern Ethiopia(15), 20.8% in Hadiya zone, southern Ethiopia(50) and Axum(16). The LTFU in our study turned out to be higher than those of the

preceding reports because of travel costs patients had to cover to reach clinics. That means our study area is relatively under developed and sparsely populated with limited infrastructure and resources which are directly or indirectly related to health service delivery and access. As could be noted from the findings of multivariable findings, the presence tuberculosis at baseline, poor adherence level, under nutrition (BMI <18.5 kg/m2), and high viral load were independent predictors of LTFU.

Patients with TB at baseline had a 2.12 times higher risk of LTFU than those who were TB negative at baseline. This finding is consistent with other previous studies that have been conducted in Axum Ethiopia(35) and in studies conducted in sub-Saharan Africa(69). These may be patients who were co-morbid with tuberculosis always had overlapping toxicity when using any multidrug therapy and adverse reactions to antiretroviral drugs are also common, and there are significant overlaps in the toxicity profiles of the first-line anti-tuberculosis and antiretroviral drugs(73).

Patients with TB at baseline had a 2.12 times higher risk of LTFU than those who were TB negative at baseline. This finding is consistent with other previous studies that have been conducted in Axum Ethiopia(35) and in studies conducted in sub-Saharan Africa(69). These may be patients who were co-morbid with tuberculosis always had overlapping toxicity when using any multidrug therapy and adverse reactions to antiretroviral drugs are also common, and there are significant overlaps in the toxicity profiles of the first-line anti-tuberculosis and antiretroviral drugs(73).

Furthermore, it is conceivable that individuals with TB/HIV co-infection may face greater pill burdens, necessitating a greater commitment to adhere to all prescribed treatments. In contrast, in the study conducted in Indonesia among tuberculosis Infection and HIV Patients found that TB infection did not have a significant association with LTFU after ART initiation(60). The possible difference might be related to the implementation of the TB-HIV collaboration program and strengthen regular monitoring of TB/HIV client.

This study also found that undernourished patients with a BMI < 18.5 kg/m2 were 5.36 times at higher risk of LTFU as compared with those with a BMI ≥18.5 kg/m2. This finding is similar to that of previous studies in Lilongwe, Malawi, Southern Ethiopia, and Gondar, Northwest Ethiopia (32–34). The possible explanation for this might be that due to the treatment failure secondary to the compromised immune system (70). In addition, it might be related to the effects of HIV

because it highly affects the nutritional status and is related to the occurrence of poor appetite, impaired nutritional absorption, increased basal metabolic rate, and the occurrence of opportunistic infections (9).

The risk of LTFU among those with poor adherence was higher as compared to those having good adherence, in which participants with poor had a 2.14 times higher risk of LTFU than participants with good adherence. This was supported by studies conducted in Ghana, Malawi (33,58) and Gonder, woldia, Arbaminch and Oromia (16,18 ,56,59). The possible reason could be patients with poor adherence may have socio-demographic, economic and clinical problems that affect their adherence initially, which further affects retention in care (72). Due to non-adherence, clients have discontinued their lifelong ART treatment due to poor drug and clinical adherence, which resulted in high viral load, treatment failure, an easy probability of contracting OIs, and then they would have died.

The hazard of LTFU was also higher among adult those with recent viral load result of >1000 copies/mL higher the risk of LTFU by 2.71 times as compared to those with <1000 copies/ml. The exciting result from this study revealed that recorded low VL of below ≤1000 copies/mL prevented the hazard of LTFU. This is in line with a study done woldia, Ethiopia(59) Asia (51) the justifiable reason that VL measurement is an indicator of successful medication adherence to clients and a suppressed viral load result is less risk of LTFU(70).

In addition, this finding indicates the need for expansion to viral load testing sites to attain universal access to timely viral load monitoring to avoid premature switching of clients to either second or third line ART regimen, which is more toxic and not as effective as the first line regimen and a high viral load can lead to a low CD4 cell count when the CD4 count is low, the risk of developing an illness or infection is higher that leads to lost from follow up(9).

On the other hand such as sex, age, marital status, WHO clinical stage, anemia, CD4 count, CPT, INH and functional status were not significantly associated with lost to follow up, even though they were significant in other previously conducted studies. Possible explanation for the difference might be the number differences among participants with the characteristics of difference in previous study and our study also; the younger age group could be more mobile than the older one and may face the fear of discrimination and stigma. Furthermore, possible reason that ambulatory

patients are more likely to be lost to follow up from antiretroviral treatment could be due to the social, economic, and financial influences that are caused by their inability to work.

This study's findings provide us in integrating with many stakeholders with ART services, which improves LTFU for meeting the second and third 95 ambitious targets and lowers HIV/AIDS prevalence by keeping clients.

6.1 Strengths and Limitations of the study

Strengths

The strength of this study is it is conducted after the implementation of the updated guidelines, which is different from earlier studies. The other strength of this study is the majority of earlier studies were not carried out at multi-center facilities and this study encompasses selected functioning public health institutions located within the Metekel zone, from health centers up to general hospital.

Limitations

As a retrospective cohort study and depends on individual secondary data (chart review) unable to control the quality of the data and some of the data lack accuracy and completeness during the time of data collection, different people are involved at different times in patient care and data entry on charts at different years, selection bias is possibly introduced during exclusion of incomplete registries and lost charts, some exposure variable measurements varied with time and potential misclassification that arises from long study periods that were made might be a setback to this study.

Variables, like income, behavioral factors and satisfaction level healthcare system were not considered as predictor variables, as well as the follow-up period in the present study is relatively short and the results may not be applicable to longer follow-up periods.

7 Conclusion and Recommendations

7.1. Conclusion

The study finding showed that the incidence of lost to follow up among adults receiving antiretroviral therapy was high when compared with a majority of previous studies. A majority of the loss to follow-up occurred within the first year of ART initiation. The main positive predictors of lost to follow up were the presence of having tuberculosis at baseline, under nutrition (BMI <18.5 kg/m2), poor adherence level, and high viral load (>1000 copies/mL).

7.2. Recommendations

Despite high access to ART and decentralized care has been available nowadays, still lost to follow up from ART care is a concerning issue. Lost to follow up from ART care has to be reduced to achieve long term success for the ART program. According to the finding, the following recommendation was forwarded.

To Regional Health Bureau

- Basic and refreshment training should be provided for Health care providers on tuberculosis early detection, under nutrition, high viral load, and poor adherence to treatment.

To Zonal Health Department and District Health Office

- To give attention on early detection and management for patients poor clinical and laboratory baseline data like; tuberculosis, high viral load, under nutrition (BMI <18.5 kg/m2) and poor adherence to treatment.

For Non-governmental organization

- Strengthen provision of Therapeutic and Supplemental foods it will help those people on ART on under nutrition (BMI <18.5 kg/m2).

For health care provider

- To reduce lost to follow-up, it's crucial to closely monitor HIV-positive people on ART, especially during the first six months and a year.
- It is crucial to increase TB screening for early diagnosis and ensure close follow-up and comprehensive counseling among patients receiving ART therapy.
- For a patient with a high viral load count, the health care provider needs to strengthen Enhanced Adherence support/counseling (EAS) to ART and consideration should be given to continuing proper regular monitoring of viral load as well as send viral load test per schedule.
- The study suggests the need for improving adherence counseling, early tracking of missed appointments, and decreasing the frequency of follow-up and adequate counseling.
- The health worker shall provide continuous nutrition assessment, care, and give supplementary Therapeutic and Supplemental foods for under nutrition and support to reduce patients' LTFU from ART care.
- Health care providers working in ART clinic should give greater attention for data recording since data are crucial in patient monitoring and follow up.

To researchers

- Better to retrospective study was a full of inevitable incomplete information, so better to conduct prospective cohort study design to address behavioral factors, socioeconomic status and incomplete records. Furthermore, a qualitative study should be applied to obtain information from LTFU patients themselves by tracing them and the health service quality and satisfaction level of patients need to be addressed.

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ANNEX

Annex-I: Information sheet and consent form English version

Participant information sheet and informed consent form for health facilities administrators.

My name is _____. I am working as a data collector for the research being conducted to assess incidence of lost to follow up and its predictors among adult people living with HIV who initiate ART in this facility by **Temesgen Desalegn** who is MPH in Epidemiology student in Faculty of Public Health, Jimma University. I kindly request you to lend me your attention to explain to you the study and study participants.

Title of The Research Project: To assess incidence of lost to follow up and its predictors among adult people living with HIV who initiate ART at public facilities in Metekel zone, northwest Ethiopia.

Name of the Organization: Institute of Health, faculty of public Health, Jimma University

Name of the Sponsor: Government

Introduction: This information sheet was prepared for this health institution administration and ART coordinating office. The aim of this information sheet was to make clear the above body about the research project, data collection procedure and to get permission to undertake the research.

Purpose of research: The main aim of this study is to write a thesis as a partial requirement for the fulfillment of a master's degree in Epidemiology for the principal investigator. Moreover, the result of the study will be used as evidence and input for the public health facilities and other governmental and non-governmental organizations working on ART care.

Procedure: To achieve the above objective all HIV positive adults starting from Jun 28 2017 to Jun 27, 2022 will be included in the study.

Risk and discomfort: By participating in this research there was no risk encountered to whom document is reviewed for data extraction.

Benefits: the research has no direct benefit for the patient whose record was reviewed but the indirect benefit for the participant and all others had a great impact for planning.

Confidentiality: The information collected from this research project was kept confidential and information about data that were collected by this study was stored without names, in addition, it was not revealed to anyone except the principal investigator and was kept locked with key and the data were collected by trained nurses who work in the ART clinic.

Contact address: This research project will be reviewed and approved by the ERB of the Institute of Health, Jimma University. If in any case, you want to know more information about the research and its undertakings, you can contact the committee through the address of the advisor and /or principal investigator.

Principal investigator: Temesgen Desalegn (BSc in PH) Mobile phone:

Tel: +251911679322/921114459 Email tame9142@gmail.com

Advisors:

1. Mrs. Chaltu Fikru (BSc, MPHE, Assistant professor) Jimma University, Faculty of Public Health, Department of Epidemiology.

Advisor Tel: +251-917-764-828, (Email: fikruc@yahoo.com.)

2. **Mr. Abraham Lomboro (BSc, MPHE)**: Jimma University, Faculty of Public Health, Department of Epidemiology.
   Advisor Tel: +251-920-991-831, (Email: abrish4466@gmail.com)

Permission: lastly you are kindly requested to permit and forward your permission to the concerned body in your institution to get the data clerk and other responsible body.

Declaration of Informed Voluntary Consent:

I have read/was read the participant information sheet. I have clearly understood the purpose of the research, the procedures, the risks and benefits, issues of confidentiality, the right of participation and the contact address for any queries. I have been given the opportunity to ask any questions for things that may have been unclear. I was informed that I can terminate the study at any time. Therefore, I declare my voluntary consent to permit this study to be conducted in this institution with my signature as indicated below.

Signature of health facilities administrator: _____

Name: _____ Date: _____

Signature of Principal Investigator: _____

Name: Temesgen Desalegn **Date: _____**

Thank you for your cooperation!!

Annex II- Data abstraction sheet/Check list

This checklist was prepared for the collection of socio-demographic, clinical, treatment and outcome related information that are important for the assessment of LTFU and predictors of LTFU who initiate antiretroviral therapy at public facilities in Metekel zone. All this information was retrieved from the clients ART and pre-ART registration book and from individual patient card without mentioning the name of clients. This information was collected by health care providers (BSc nurses) and data clerk working in the ART clinic of the health facility.

Part I. Socio demographic Characteristics

Serial Number	**Socio demographic Characteristics**	**Coding classification**	**Skip**
101	Age	Age in years_____	
102.	Sex	1.Male 2.Female	
103.	Residence	1._____ (Urban) 2._____(Rural)	
104.	Marital status	1. Single 2. Married 3. Divorced 4. Widowed 5. Separated	
105.	Religion	1. Orthodox 2. Muslim 3. Protestant 4. Catholic 5. Others specify _____	
106.	Level of education	1.No education 2.Primary 3.Secondary 4.Tertiary	

107.	Occupation	1. Sex worker 5. Farmer. 2. Driver 6. Government 3.Daily labor 7 Self-employed 4. Merchant 8. Others	
108.	Distance of ART clinic	_____ km from home	Measured by distance from residence
109.	HIV disclosure status	1. Disclosed 2. Not disclosed	
110.	Partner's HIV status	1.Known 2.Unknown	
111.	Availability of care giver	1.Yes 2.No	
112	Telephone contact of client or relatives	1.Yes 2. No	

PART- II Base line Clinical and Laboratory characteristics of Patients

Serial Number	**Clinical characteristics**	**Coding classification**	**Skip**
201.	ART linkage point	1. VCT 2. OPD 3. IPD 4. MCH 5. Others	
202.	Treatment modality	1.previous Modality 2.Test and treat	
203.	Baseline Body weight	_____Kg	
204.	Baseline BMI	_____ kg/m2	

205.	CD4 count at base line/recent	_____Cells/mm^3		
206.	Baseline WHO Clinical stage	1.CLINICAL STAGE I 2.CLINICAL STAGE II 3.CLINICAL STAGE III 4.CLINICAL STAGE IV		
207.	Baseline Hemoglobin	_____ gm/dL		
208.	Baseline Opportunistic infection presence	1.Yes 2.No		If 2 skip to 212
209.	Type of Opportunistic infection	1.Pneumonia	1.yes 2.No	
		2.Pulmonary tuberculosis	1.yes 2.No	
		3.Upper RTI	1.yes 2.No	
		4.Diarrhea	1.yes 2.No	
		5.Unexplained Fever	1.yes 2.No	
		6.Herpes zoster	1.yes 2.No	
		7.Oral candidacies	1.yes 2.No	
		8.Skin dermatitis	1.yes 2.No	
		9.Other*_____	1.yes 2.No	
210.	Cotrimoxazole Preventive Therapy (CPT) at baseline	1.Yes 2.No		
211.	TB treatment at baseline	1.Yes 2.No		
212.	IPT treatment at baseline	1.Yes 2.No		
213.	Baseline functional status	1.Functional 2.Ambulatory 3.Bedridden		

214.	Initial ART regimen	1.TDF+3TC+EFV 2.AZT+3TC+EFV 3.AZT+3TC+NVP 4.TDF+3TC+NVP 5.TDF+3TC+DTG 6.Other_____		
215.	Initial ART change	1.Yes 2.No		
216.	If yes Reason for change regimen	1.Side effect	1.yes 2.No	
		2.TB treatment	1.yes 2.No	
		3.Clinical failure	1.yes 2.No	
		4.Immunological failure	1.yes 2.No	
		5.Virologic failure	1.yes 2.No	
		6.New drug available	1.yes 2.No	
		7.Due to new TB infection	1.yes 2.No	
		8.Other_____	1.yes 2.No	

Part- III HIV care and ART Follow-up form information

Serial Number	**Characteristics**	**Coding classification**	**Skip**
301.	Date confirmed HIV positive	(--------/----------/----------)	
302.	Starting date of ART	(--------/----------/----------)	
303.	Last follow up date	(----------/----------/----------)	
304.	Recent CD4 count	_____Cells/mm^3	
305.	Last Viral load count	1. Not eligible 2. ≤1000 copies/mL 3. >1000 copies/mL	

306.	Recent ARV adherence to treatment	1. Good (≥95%) 2. Fair (85-94%) 3. Poor (<85%)		
307.	Reason for fair/poor adherence	1. Toxicity/side effects	1.yes 2.No	
		2. Forgot	1.yes 2.No	
		3. Felt better	1.yes 2.No	
		4. Too ill	1.yes 2.No	
		5. Stigma	1.yes 2.No	
		6. Travelling problem	1.yes 2.No	
		7. Others specify-----	1.yes 2.No	
308.	Client was on ASM	1.Not eligible 1.yes 2.No		
309.	Current status	1. Alive 2. Dead 3. Lost follow up 4. transfer to other health facility		

Annex-III: Assurance of principal investigator

The undersigned agrees to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the Faculty of Public Health in effect at the time of grant is forwarded as the result of this application.

Name of the student: Temesgen Desalegn Balda

Date: _____ Signature: _____

Approval of advisor(s)

1. Mrs. Chaltu Fikru (BSc, MPHE, Assistant professor)
   Date: _____ Signature: _____
2. Mr. Abraham Lomboro (BSc, MPHE)
   Date: _____ Signature: _____

Cox-proportional hazard assumption test

To apply the cox regression model, it has to be checked proportional hazed assumption effect of the covariate on the hazard ratio remains constant over time. It was tested by using Schoenfeld residual test and a graphical presentation.

1. Schoenfeld residual test: it is a statistical test to assess the proportional hazard assumption which says the null hypothesis hazard rate over time is constant and if the statically P-value is less than 0.05 null hypothesis is not rejected and the proportional hazard assumption will be failed.

Annex VI: Test of proportional-hazards assumption (estat, phtest) for HIV/ADIS infected adult who were on ART in Metekel zone public health facilities, northwest Ethiopia, 2022.

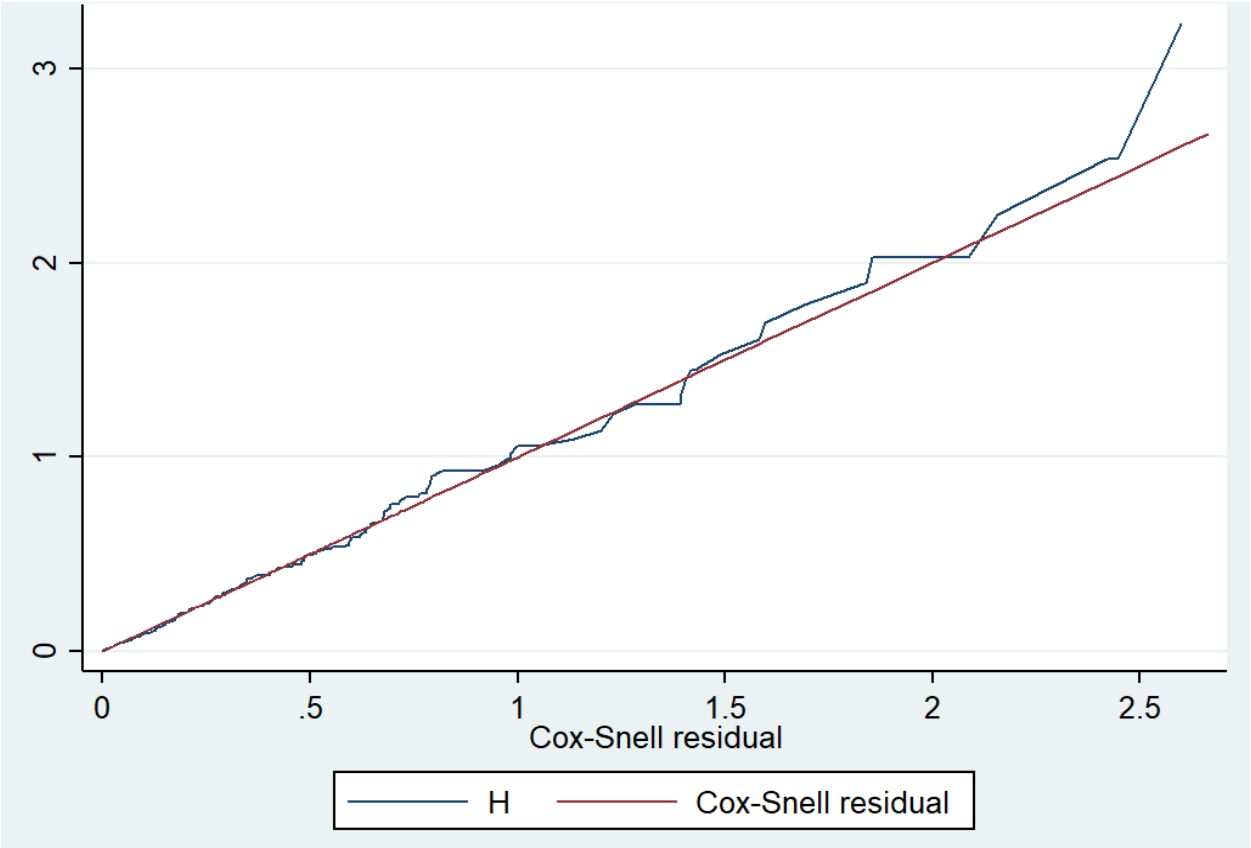
	Chi 2	Df	Probab>Chi 2
Global test	19.50	16	0.2737

2. log-log plot: for two data sets if the distance between two curves is parallel then the proportional hazard assumption is satisfied it is a graphical test of plotting *–log(-log(survival*)) versus time graph.

Model Adequacy

After fitting the cox proportional hazard model the adequacy of the model was checked by Nelson Aalen cumulative hazard with Cox-Snell residual. The predict command was used to generate the Cox-Snell residuals from the model. The graph showed that the hazard function follows the 45-degree line closely over time. Hence, it was possible to conclude that the final model fits the data well.

Annex VII: Cox-Snell residual cumulative hazard graph for HIV/ADIS infected adult who were on ART in Metekel zone public health facilities, northwest Ethiopia, 2022.



Annex-IV: Declaration

I, the undersigned, Master of Public Health in Epidemiology student declare that this thesis my original work in partial fulfillment of the requirement for the degree of Master of Public Health in Epidemiology.

Name: Temesgen Desalegn Balda

Signature: _____ Date _____

Place of submission: Department of Epidemiology, Faculty of Public Health, Institute of Health, Jimma University.

Date of Submission: _____

This thesis work has been submitted for with the approval as university advisor(s).

Advisors Name	**Signature**	**Date**
1. Mrs. Chaltu Fikru (BSc, MPHE, Assistant Professor)	_____	_____
2. Mr. Abraham Lomboro (BSc, MPHE)	_____	_____

Approval of Internal examiner

Name of internal examiner	**Signature**	**Date**
1. Mr. Lata Fekadu (MSc.)	_____	_____

Thanks a lot