



# Retention in Care, Loss to Follow-up and Associated Patient Characteristics: A Retrospective Cohort Study among Adults Receiving Antiretroviral Therapy from Urban Health Facilities in Ghana

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## Abstract

**Introduction:** Assessing treatment outcomes among persons receiving antiretroviral therapy (ART) for human immunodeficiency virus (HIV) infection is important for clinical and public health decisions. Although Komfo Anokye Teaching Hospital and Suntreso Government Hospital have offered ART to several patients for more than a decade, their treatment outcomes have not been well reported. We aimed at investigating retention in care, loss to follow-up, and patient characteristics associated with these outcomes among HIV-infected adults receiving ART from two urban treatment sites in the Ashanti Region of Ghana in order to design interventions to improve therapy outcomes.

**Materials and method:** We conducted medical records review (MRR) from September to December 2020 among HIV-infected patients receiving ART from two urban ART sites in Kumasi, Ghana. Patients were eligible if they were adults aged  $\geq 20$ -years and had taken ART for  $\geq 3$ -years as of December 2019. Retention in care, loss to follow-up (LTFU) and mortality among our study patients were investigated from ART initiation up to 3-years. In this study, retention of patients in care was defined as actively attending clinic and picking ARVs within the follow-up period. Loss to follow-up was defined as having discontinued clinic attendance and ARVs pick-up for more than 90 days after the last scheduled visit. Logistic regression analyses were performed to study the treatment outcomes and their associated patient characteristics.

**Results:** Of the 370 patients whose medical records were reviewed, 258 (69.7%) were female, 260 (70.3%) were retained in ART up to 3-years, 29.7% were lost to follow-up of whom 9.1% were confirmed dead. Overall mortality was therefore 2.7%. Being employed (AOR 2.55,  $p = 0.015$ , 95% CI 1.201-5.4.414), female (AOR 1.319, CI 95% 0.754-2.310), divorced (AOR 1.266, CI 95% 0.506-3.166) and having primary level of education (AOR 1.539, CI 95% 0.915-2.590) were associated with greater odds of being retained in care.

**Conclusion:** Although mortality among our study cohort was low and about 70% were retained in ART up to 3-years, loss to follow-up was high, especially within the first 6 months. Effective follow-up interventions are required to reduce LTFU during the first 6 months of treatment and among younger adults, patients with secondary and tertiary education as well as single and married patients who were less likely to be retained in care.

## Keywords

Antiretroviral therapy, Treatment outcomes, Retention in care, Loss to follow-up, Ashanti Region, Ghana

## Introduction

The efficacy of antiretroviral medicines (ARVs) for prolonging life of persons living with human immunodeficiency virus (HIV) infection has not been in doubt [1]. As the world continues to await a cure for HIV infection, ART remains a life-long venture but retention in antiretroviral therapy (ART) programs has been a significant challenge to persons receiving ART [2,3]. Many large and small studies have

reported ART outcomes such as survival or retention in care, loss to follow-up, mortality as well as immunologic and virologic response to ART. Previous studies have reported overall treatment retention rate of 65% within 2-4-years of ART [4,5] and 86% after 4-years of ART [6]. A study of large data from 42 countries has estimated retention in ART at month 36, to be 68%, with regional retention rate of 65% for Africa, 80% for Asia, 64% for Latin America and the Caribbean [5]. Meta-analysis of large data from 45 studies in Ethiopia

has revealed that pooled magnitude of retention in clinical care was 70.65%, with overall magnitude of loss to follow-up (LTFU) being 15.17% [7].

Other researchers have reported among a Ghanaian cohort that after 3-years of follow-up, overall LTFU from ART was 31%, with 67% of such cases occurring within the first 12 months of treatment [8]. It has been determined that independent predictors of attrition from ART programs include male sex, being younger adult, single, divorced or separated [9]. According to Alvarez, et al. 2013, being female was associated with reduced risk of attrition but being single, illiterate and aged < 25-years-old were associated with increased risk of LTFU [10]. Studies from sub-Saharan Africa show that the cumulative incidence of attrition from ART programs can be up to 35% in 3-years of follow-up [5].

Regarding ART-related mortality, analyses of 18 published cohort studies have revealed that between 8% and 26% of patients offered ART in sub-Saharan Africa die within the first year of treatment [11], with 14% dying within the first 3 months [4]. Some other researchers have reported that ART-associated rates of mortality during the initial stages of treatment were higher in low income settings [5,12]. Assessing ART outcomes among persons living with HIV is therefore important for clinical and public health decisions but results of ART outcomes of our study sites have not been previously reported. We aimed at investigating retention in ART, loss to follow-up, mortality and patient characteristics associated with these outcomes among patients receiving ART from two urban ART programs in Ghana in order to design interventions to improve treatment outcomes.

## Materials and Method

### Study setting and population

The study was conducted at two antiretroviral treatment sites in the Ashanti Region of Ghana namely Komfo Anokye Teaching Hospital (KATH) and Suntreso Government Hospital (SGH) both in Kumasi. The study sites are similar in operations since they use national treatment guidelines and receive supplies of antiretroviral medicines and other logistics from government without cost to the individual facilities and patients. The two sites are located approximately 2.5 km apart in the second largest city of Ghana and therefore have urban characteristics. As a teaching hospital, KATH receives patients from different parts of the country (including persons living with HIV/AIDS) through a referral system. As part of its clinical services, SGH runs sexually transmitted infections (STI) clinic where patients who test positive for HIV are offered ART. The study population was made up of HIV-infected adults aged  $\geq$  20-years who were receiving ART as at December 2019. To qualify for inclusion, patients were additionally expected to have taken ART for  $\geq$  3-years and had the required information in their medical records for review. Patients who initiated ART in other facilities but were transferred to the study sites were excluded from the study.

### Sample size estimation

We used sample size calculation formula recommended

by Bill Godden 2004 [13], with input from Rose, Spinks & Canhoto, 2015 [14] to calculate required sample size from an estimated population of 7,200 HIV-infected adults receiving clinical care from the two facilities. The minimum sample size required was 365 folders but in order to make room for any possible data insufficiency from some of the records the number of folders to be reviewed was increased to 385.

### Data collection process

A data collection tool designed in Microsoft excel was used to extract selected patients' details from their hospital records. Quota random sampling technique was used to apportion the number of folders to be reviewed from each study site. The apportioned number of folders for each study site was collected from patients who initiated treatment in the year 2014, 2015, 2016 and 2017. We conducted medical records review (MRR) among our study patients to investigate patient retention in care, loss to follow-up, mortality and patient characteristics such as age, gender, educational, marital and occupational background associated with these outcomes. Within the age category we divided the patients into three groups described as young adults (20-40-years), middle-aged adults (41-60-years) and older adults (61-80-years). For each participant, the required data were extracted to cover a period of 3-years starting from the day of ART initiation. For patients who died or were lost to follow-up in the course of treatment, their data were extracted from the day of ART initiation to the last date of clinic attendance. Data collection was done between September and December 2020.

In this study retention of patients in ART was defined as actively attending clinic and refilling ARVs within the follow-up period. Loss to follow-up of a patient was defined as having discontinued clinic attendance and ARVs pick-up for more than 90 days after the last scheduled visit. Patients who defaulted treatment for any length of time but had returned to continue ART within the 3 years of follow-up were considered to be retained in care.

### Data management and analysis

Participants' data collected from the two study sites were aggregated and entered into Stata version12 software for analysis. Descriptive statistics were carried out on variables such as age, gender, marital, occupational and educational backgrounds of study patients in relation to their treatment outcomes such as retention in care, loss to follow-up and

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**Table 1:** Patient characteristics, retention in care and loss to follow-up from urban ART program in Ghana.

Patient Characteristics	Patient Category (N = 370)	Retention in care	Loss to follow-up
Gender	Female 258 (69.3%)	188 (72.9%)	70 (27.1%)
	Male 112 (30.7%)	72 (64.3%)	40 (35.7%)
Age Group (Years)	21-40 200 (54.1%)	135 (67.5%)	65 (32.5%)
	41-60 160 (43.2%)	118 (73.8%)	42 (26.2%)
	61-80 10 (2.7%)	7 (70.0%)	3 (30.0%)
Occupation	Employed 333 (90%)	240 (72.1%)	93 (27.9%)
	Unemployed 37 (10%)	20 (54.1%)	17 (45.9%)
Education	Primary 199 (53.8%)	150 (75.4%)	49 (24.6%)
	Secondary 28 (7.6%)	16 (57.1%)	12 (42.9%)
	Tertiary 16 (4.3%)	8 (50%)	8 (50%)
	Uneducated 127 (34.3%)	86 (67.7%)	41 (32.3%)
Marital status	Divorced 72 (19.5%)	60 (83.3%)	12 (16.7%)
	Married 146 (39.5%)	91 (62.3%)	55 (37.7%)
	Single 89 (24.1%)	59 (66.3%)	30 (33.7%)
	Widowed 63 (17.0%)	50 (79.4%)	13 (20.6%)
ART initiation Regimen	AZT/3TC/EFV 88 (23.8%)	54 (61.4%)	34 (38.6%)
	AZT/3TC/NVP 109 (29.5%)	79 (72.5%)	30 (27.5%)
	TDF/3TC/EFV 114 (30.8%)	86 (75.4%)	29 (26.4%)
	TDF/3TC/NVP 59 (15.9%)	42 (71.2%)	17 (28.8%)

Note: TDF is tenofovir disoproxil fumarate, AZT is azidothymidine (zidovudine), 3 TC is lamivudine, NVP is nevirapine and EFV is efavirenz

mortality. Multivariate analysis was done using logistic regression to investigate the level of significance and associations between variables and treatment outcomes using odds ratios, p-values of < 0.05 and 95% confidence interval.

## Results

### Characteristics of study patients

The number of folders selected to be reviewed was 385 but 15 were rejected due to data insufficiency leaving a total of 370. The mean age of patients was 40.4-years (SD 9.29). Females constituted 69.7% (n = 258) of the 370 patients whose medical records were reviewed. Majority of the study patients 54.1% (n = 200) were 21-40 years-old, followed by 43.2% (n = 160) in the 41-60 years age group. Altogether the two age groups constituted 97.3% (Table 1). While 90% (n = 333) of the study patients were employed, 37 were unemployed. Approximately 88% of the study patients were either uneducated or had primary level of education. Only 12% had either secondary or tertiary education. While 39.5% were married, the remaining study patients were divorced (19.5%), single (24.1%) or widowed (17.0%).

### Retention in care and loss to follow-up from ART

Of the 370 study patients whose medical records were reviewed, 260 (70.3%) were retained in care up to 3-years but 110 (29.7%) were lost to follow-up at various times within the period (Table 1). Among the 258 females whose records

were reviewed, 27.1% (n = 70) were lost to follow-up while 35.7% (n = 40) of the males were also lost to follow-up. For patients aged 21-40 years described as younger adults, LTFU was 32.5% which was relatively higher than that of patients in the middle age group of 41-60 years with 26.2% LTFU. Although only 10% of the study patients were unemployed, LTFU of approximately 46% was recorded among this group as opposed to 27.9% LTFU recorded among the employed patients. Considering marital status, LTFU was high among married clients (37.3%) than those who were not married (single, divorced and widowed). The lowest LTFU rate of 16.7% was recorded among divorced clients followed by 20.6% for widowed patients (Table 1).

From logistic regression analysis results in Table 2, only employment status of study patients had statistically significant association with being retained in care. Employed patients (AOR 2.55, p = 0.015, 95% CI 1.201-5.4.414) had greater odds of being retained in care as compared to unemployed patients. The results however show that being female (AOR 1.319, CI 95% 0.754-2.310), divorced (AOR 1.266, CI 95% 0.506-3.166) and having primary education were associated with greater odds of being retained in care. Conversely, being younger adult with age 21-40-years (AOR 0.767, CI 95% 169-3.473), having secondary education (AOR 0.858, CI 95% 0.352-3.473), having tertiary education (AOR 0.830, CI 95% 0.263-2.621), being married (AOR 0.481, CI 95% 0.223-1.035), being single (AOR 0.583, CI 95% 0.273-1.222) and using tenofovir, lamivudine with efavirenz-TDF/3TC/

**Table 2:** Logistic regression analysis results of patients retained in urban antiretroviral therapy program in Ghana.

Patient characteristics	Number of patients retained in care	Adjusted odds ratio (AOR)	p-value	95% confidence interval
<b>Age (Years)</b>				
21-40 (n = 200)	135 (67.5%)	0.767	0.731	0.169-3.473
41-60 (n = 160)	118 (73.8%)	1.011	0.989	0.226-4.517
61-80 (n = 10)	7 (70.0%)	1.000		
<b>Sex</b>				
Female (n = 258)	188 (72.9%)	1.319	0.332	0.754-2.310
Male (n = 112)	72 (64.3%)	1.000		
<b>Education</b>				
Primary (n = 119)	150 (75.4%)	1.539	0.104	0.915-2.590
Secondary (n = 28)	16 (57.1%)	0.858	0.737	0.352-2.091
Tertiary (n = 16)	8 (50.0%)	0.83	0.751	0.263-2.621
Uneducated (n = 127)	86 (67.7%)	1.000		
<b>Marital status</b>				
Divorced (n = 72)	60 (83.3%)	1.266	0.613	0.506-3.166
Married (n = 146)	91 (62.3%)	0.481	0.061	0.223-1.035
Single (n = 89)	59 (66.3%)	0.538	0.139	0.237-1.222
Widowed (n = 63)	50 (79.4%)	1.000		
<b>Occupation</b>				
Employed (n = 333)	240 (72.1%)	2.55	0.015	1.201-5.414
Unemployed (n = 37)	20 (54.7%)	1.000		
<b>Regimen</b>				
AZT/3TC/EFV (n = 88)	54 (61.4%)	0.652	0.276	0.302-1.407
AZT/3TC/NVP (n = 109)	79 (72.5%)	1.125	0.759	0.531-2.385
TDF/3TC/EFV (n = 114)	86 (75.4%)	1.024	0.95	0.488-2.148
TDF/3TC/NVP (n = 63)	42 (71.2%)	1.000		

**Note:** TDF is tenofovir disoproxil fumarate, AZT is azidothymidine (zidovudine), 3 TC is lamivudine, NVP is nevirapine and EFV is efavirenz

**Table 3:** Loss to follow-up time among Ghanaian adults offered antiretroviral therapy in urban health facilities.

Loss to follow-up time/Months	No. of patients LTFU (N = 110)	% of patients LTFU
< 1 (NFUV)	22	20
00-06	30	27.3
07-12	15	13.6
13-18	13	11.8
19-24	9	8.2
25-30	17	15.5
31-36	4	3.6

EFV (AOR 0.652 CI 95% 0.302-1.407) were associated with reduced odds of being retained in ART up to 3-years.

Table 3 shows that out of the 110 patients who were lost to follow-up, 20% (n = 22) had no follow-up visit (NFUV) after treatment initiation. In other words such patients did not return to the hospital for continuation of care after initiation of ART. Cumulatively 47.3%, 60.9%, 72.7%, 80.9% and 96.4%

of patients were lost to follow-up within 6, 12, 18, 24 and 30 months of ART respectively.

### Mortality

A total of 10 (9.1%) deaths were recorded out of 110 patients who were lost to follow-up. Overall mortality of the study patients was therefore 2.7% within 3-years of ART. All the 10 deaths were recorded in patients' folders. No records of cause of death were found in folders. We did not conduct verbal autopsy to ascertain the cause of death.

### Discussion

In this study which we investigated retention in care, loss to follow-up and mortality among patients receiving antiretroviral therapy from urban health facilities in Ghana, the results show that being younger adult, having secondary or tertiary education, being married or single and using tenofovir, lamivudine with efavirenz (TDF/3TC/EFV) were associated with reduced odds of being retained in ART. The most significant limitations of the study were the retrospective design and incomplete documentation of some patients' details.

The overall LTFU of 29.7% within 3 years of ART found in this study is almost equal to the results of Collini, et al. 2009 who obtained 31% of LTFU from Komfo Anokye Teaching Hospital (KATH). The marginal reduction in LTFU cases may be attributed to the enhanced counseling and follow-up efforts by the clinical care providers of the two health facilities. Our retention figure of 70.3% is however higher than that estimated for Africa (65%) by Fox & Rosen, 2015 [5]. The results of this study show that 64.3% males as compared to 72.9% females (AOR 1.319, 95% CI 0.754-2.310) were retained in care (Table 2). The trend is consistent with results of other researchers [15,16].

Table 1 shows that patients aged 21-40 years and 41-60 years constituted 97.3% (n = 360). Between the two age groups, loss to follow-up was higher (32%) among the 21-40-years age group implying reduced odds of retention in care (AOR 0.767 95% CI 0.169-3.373) than the 41-60-years group with 26.2% LTFU and relatively higher odds of being retained in care (AOR 1.011, 95% CI 0.226-4.517). These results are consistent with findings of Fatti, et al. 2014 that crude cumulative incidences of loss to follow-up on ART were higher among younger adults than older ones [17]. Although patients in the 61-80-years group also had 30% LTFU, they constituted only 2.7% of the study patients.

Regarding loss to follow-up and occupational background, the results show that employed patients (AOR 2.550, 95% CI 1.201-5.414) had higher odds of being retained in care as compared to unemployed patients who had higher LTFU of 46%. This situation is expected because unemployment has strong association with socio-economic status [18,19]. Although antiretroviral medicines could be picked by patients from their facility pharmacies of the study sites without out-of-pocket payment, financial challenges associated with transportation cost of visiting ART sites have been identified in other studies among patients of our study sites. The reduced odds of being retained in care among married patients (AOR 0.481 95% CI 0.223-1.035) as compared to the unmarried (single, divorced and widowed) could be interpreted on the basis that married clients find it difficult to disclose their HIV+ status to their sexual partners for fear of stigmatizing attitude, possible rejection and domestic violence especially among women [20,21]. Wolf, et al. 2014 have reported association between HIV-related stigma and LTFU [22].

Cumulative LTFU of 47.3% within the first six months of ART (which includes 20.7% of those who had no follow-up visits) is very alarming. These findings from our study support those of Zachariah, et al., 2006 [23] who recorded early attrition from treatment due to 12.6% deaths, of which 61% and 79% occurred within the first 3 months and 6 months of ART respectively.

Implications of the study results are worth considering. Of the 110 patients who were lost to follow-up, 10 had died leaving 100 (approximately) 27% of the study patients. The clinical, social and economic implications of 27% ART drop-outs without viral suppression need to be considered. Firstly, such persons have the potential to transmit HIV to sexual partners with whom they engage in unprotected sex [24]. Secondly, women of reproductive age among this group of

ART drop-outs have the potential to transmit HIV to their babies if they become pregnant and do not receive prevention of mother to child transmission (PMTCT) interventions [25]. Thirdly, ART non-adherent patients may develop resistant HIV strains which will in turn be transmitted to other persons. Since cost of treatment of resistant HIV infection is usually higher, health budgets in settings with resistant HIV strains are likely to increase [26]. Lastly, in the context of UNAIDS' 90 90 90 target [27,28] of HIV service delivery by the year 2020 and its extension to 95 95 95 by the year 2030 [29], the study sites may not be able to achieve the second and third targets of 95% patient retention and viral suppression unless pragmatic interventions are designed to achieve the target.

Although mortality among our study cohort was low and 70% were retained in ART up to 3-years, loss to follow-up was high especially within the first 6 months of therapy. We observed that being female, aged 41-60-years, employed and divorced were associated with increased odds of being retained in care. Effective follow-up interventions are required to reduce LTFU within the first 6 months of treatment and among younger adults, patients with secondary and tertiary education as well as single and married patients who were less likely to be retained in care.

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## Ethical Clearance and Consent to Participate

This work did not require ethical clearance and consent to participate because there were no human subjects involved.

## Conflict of Interest

The authors declare that there is no conflict of interest.

## Author Contributions

RKO participated in the study design, data collection and analysis and drafting of manuscript; BPA participated in the study design, data analysis and also edited the manuscript; JA, EF and RM also participated in the study design, data collection, analysis and preparation of the manuscript.

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