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Failure to Initiate Antiretroviral Therapy, Loss to Follow-up and Mortality among HIV-infected Patients during the Pre-ART period in Uganda

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Abstract

Background—Delays and failures in initiation of antiretroviral therapy (ART) among treatment eligible patients may compromise the effectiveness of HIV care in Africa. An accurate understanding, however, of the pace and completeness of ART initiation and mortality during the waiting period is obscured by frequent losses to follow-up.

Methods—We evaluated newly ART-eligible HIV-infected adults from 2007 to 2011 in a prototypical clinic in Mbarara, Uganda. A random sample of patients lost to follow-up was tracked in the community to determine vital status and ART initiation after leaving the original clinic. Outcomes among the tracked patients were incorporated using probability weights, and a competing risks approach was used in analyses.

Results—Among 2,633 ART-eligible patients, 490 were lost to follow-up, of whom a random sample of 132 was tracked and 111 (84.0%) had outcomes ascertained. After incorporating the outcomes among the lost, the cumulative incidence of ART initiation at 30, 90 and 365 days after eligibility was 16.0% (95% CI: 14.2–17.7), 64.5% (95% CI: 60.9–68.1), and 81.7% (95% CI: 77.7–85.6). Death prior to ART was 7.7% at one year. Male sex, higher CD4 count, and no education were associated with delayed ART initiation. Lower CD4 level, malnourishment and travel time to clinic were associated with mortality.

Conclusions—Using a sampling-based approach to account for losses to follow-up revealed that both the speed and completeness of ART initiation were sub-optimal in a prototypical large clinic

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in Uganda. Improving the kinetics of ART initiation in Africa is needed to make ART optimally effective.

Keywords

Antiretroviral therapy; Africa; loss to follow-up; mortality

INTRODUCTION

For HIV-infected patients with indications for antiretroviral therapy (ART) in Africa, timely ART initiation during this period of high clinical risk is essential to effective and efficient care. Initiating ART, however, even for patients who have already been tested and enrolled into treatment programs, requires overcoming significant psychological, socio-structural, and operational barriers. First, patients must first accept their diagnosis in order to make rational choices about prioritizing care, but stigma and denial may take time to overcome [1]. Second, disclosure of HIV status to family and friends can ease the burden of taking a life-long medication, but patients also fear that disclosure may lead to hostility or rejection [2]. Third, requirements for multiple adherence counseling sessions before ART initiation and for "treatment supporters" present at many clinics may improve medication adherence after initiation, but these processes may inadvertently magnify barriers to ART initiation for patients unable meet these criteria [3]. Fourth, patients often reside far away from the clinic, and therefore travel time and costs as well as competing priorities from work and childcare may delay completion of pre-ART evaluation [4,5].

The magnitude and consequences of failures or delays in ART initiation are incompletely understood because loss to follow-up between eligibility and ART initiation (i.e., unknown outcomes) is high – from 15% to greater than 50% -- in many African clinics [6–12]. "Loss to follow-up," however, is not in and of itself a patient outcome, but rather an artifact of what the clinics can conveniently observe, and yields limited actionable public health information. Meaningful outcomes, hidden by loss to follow-up, include deaths prior to ART initiation; "silent" transfers (including possibly ART initiation at new sites); and disengagement from care with failure to start ART. Understanding outcomes in the group classified as "lost to follow-up" among patients already identified as eligible for ART is needed in order to assess the magnitude of delays and failures in ART initiation, the rate of death during the waiting period, and reasons for disengagement from care before ART initiation.

In this paper, we examine delays and failures of ART initiation in a clinic-based cohort of ART-eligible patients over a four-year period in rural Uganda. To address the selection bias potentially introduced by loss to follow-up, we identified a random sample of lost patients, intensively sought their outcomes in the community and used these outcomes to reclassify outcomes among all lost patients. We have previously applied this approach to evaluate outcomes among patients who had already initiated ART [5,13]. In the current paper, we apply this approach to recover valid estimates of the magnitude and determinants of ART initiation, deaths, and disengagement from in a population of ART-eligible patients.

METHODS

Patients

We evaluated HIV-infected adults with a CD4 count based indication for ART (i.e., CD4 + T-cell ≤ 250 /μl in contemporaneous Uganda National Guidelines) between Oct. 1, 2007 and Jan. 27, 2011 at the Immune Suppression Syndrome (ISS) Clinic in Mbarara District in southwestern Uganda. Of note, the study population includes both patients who were enrolled in the clinic before October 1, 2007 but who were not ART eligible until after this

date. The ISS Clinic is a "prototypical" scale-up ART clinic in that the patient volume is high (up to 150 visits a day is common), no routine HIV RNA testing is available, and it is supported by the Uganda Ministry of Health through implementing partners of the US President's Emergency Fund for AIDS Relief (PEPFAR). In this analysis, observation began on the date of first CD4 ≤ 250 /μl, and patients were followed until time of death, loss to follow-up (defined as 60 days late for last scheduled appointment), ART initiation or closure of database on January 27, 2011. Among those lost to follow-up, a random sample was selected for tracking in the community to obtain updated data on vital status, ART use, and HIV care either through contact with the patient directly or a close relation of the patient when the patients could not be found in person [5]. The size of the sample was determined by operational capacity: we tracked as many patients as we could with available resources.

Measurements

Sociodemographic and clinical information was collected in the course of routine care by providers using standardized paper forms from the Uganda Ministry of Health and supplemented by forms developed at the clinic. Data are then subsequently hand-entered into an Open MRS database. Diagnosis of tuberculosis at time of eligibility was defined as any documentation of clinical or microbiologic tuberculosis in the nine months before or 30 days after ART-eligibility. Malnourishment was defined by standardized WHO criterion of a body mass index < 18.5 kg/m^2. For the sample of lost patients, a patient tracker went into the community to ascertain outcomes using a standardized questionnaire. Key information sought included vital status and date of death, if applicable. Patients found in person were asked whether they had seen a doctor or nurse for HIV care in the proceeding 90 days, whether they were on ART (defined as any ART within the last 14 days), and if so, when they started ART.

Analyses

In the clinic population as originally observed (i.e., without incorporating outcomes obtained through tracking a sample of the lost patients), we estimated the incidence of loss to follow-up through one year after ART-eligibility (defined as 60 or more days late for an appointment). New patients not on ART are typically asked to return in 2 to 4 weeks after their first visit and established patients with CD4 levels above treatment thresholds not on ART are customarily asked to return in 1 to 4 months. For this estimate we used the cumulative incidence approach in which ART initiation and deaths were considered competing events [14–16]. We also analyzed the group of patients who were lost to follow-up and subsequently successfully tracked to estimate the cumulative incidence of mortality from time of last clinic visit using the Kaplan-Meier approach, the hazard of mortality after last clinic visit, and the predictors of mortality using a proportional hazards regression.

We then analyzed the entire clinic population in which we used the outcomes discovered through tracking a random sample of lost patients to represent outcomes in all lost patients. Loss to follow-up that is differential on either the outcome alone or on outcomes and exposures of interest is a well-recognized cause of bias. Conceptually, incorporating outcomes of the sample of successfully tracked patients addresses the effects of differential loss to follow-up by replacing unknown outcomes with known outcomes in a representative sample which allows recovery of unbiased estimates. Statistically, lost patients with outcomes ascertained through tracking were given a weight inverse to the sampling probability, lost patients without updated outcomes were assigned a weight of zero, and all patients who remain under observation at the clinic receive a weight of one [13,17]. Operationally, consider a hypothetical clinic population of 10,000 patients in which 1000 patients are lost to follow-up and in which the ascertainer seeks 100 of the lost patients and successfully finds outcomes in 90. In this example, after tracking, 910 patients have

outcomes that remain unknown (900 of whom were lost and never sought and 10 of whom were unsuccessfully sought). They are given a weight of zero and effectively removed from the analysis. The 90 patients who were initially lost to follow-up but then successfully sought (and who therefore now have known outcomes) are used to represent the 910 without known outcomes through a weight of 10.1 (910/90). The patients who remain under observation are assigned a weight of one (thus representing only themselves), as their outcomes are by definition completely known.

In this sample-weighted population, we used the cumulative incidence method to estimate the incidence of ART initiation (at the original or any other clinic), mortality prior to ART initiation, and disengagement from care (defined as 90 days without a visit to any facility) over the first year after ART eligibility for the entire clinic population. For the specific outcome of disengagement from care (and its complement "retention in care"), we assumed that care utilization among those interviewed in person represented all lost patients who were alive. Therefore, patients who were lost and interviewed in person were additionally weighted in inverse proportion to the probability that a living patient was interviewed in person. Confidence intervals for weighted descriptive estimates were obtained through bootstrapping.

We conducted two proportional hazards regressions of the reweighted data: one to identify factors associated with ART initiation and the second to identify factors associated with mortality – both in the entire clinic population. Predictor selection was guided by the desire to evaluate the influence of as many predictors as possible but avoid colliders and overfitting. Missing predictor data was addressed with multiple imputation [18,19] under the "missing at random" assumption. Of note, multiple imputation was not used to address missing outcome data, a problem that we addressed with the sampling-based approach. All analyses were conducted in Stata version 11.1 (College Station, TX). Ethical approval was granted by the University of California, San Francisco and the Mbarara University of Science and Technology.

RESULTS

Patient characteristics

Between October 1, 2007 and January 27, 2011, 2,633 patients first became eligible for ART as defined by immunological criteria (i.e., a CD4 count < or = 250 cells/μl). The median age was 32 years (IQR: 27–39) and 1,070 were men (40.6%). The median CD4 count at eligibility was 131 cells/μl (IQR: 53 to 198), 645 (24.5%) were WHO Stage 4 and 115 (4.4%) had a diagnosis of tuberculosis at eligibility. In 2,247 (85.3%) patients, the first CD4 count taken at the ISS Clinic was < 250 cells/μl, and we considered these patients eligible at the time of clinic enrollment (Table 1).

Tracking a sample of the patients lost to follow-up

The cumulative incidence of loss to follow-up at one year was 21.3% (95% CI: 19.6–23.0). Of the 490 patients lost to follow-up, we sought a random sample of 132 (27%) for tracking (Figure 1). In 111/132 (84.0%), updated information about vital status or care status was obtained. Among the 111 successfully tracked patients, 42 had died and the cumulative incidence of mortality one year after last clinic visit was 36.8% (95% CI: 28.2–47.0). The hazard, or instantaneous rate, of death was highest in the 60 days after last visit at 38/100 person-years, falling to 11/100 person-years from 60 to 180 days and to 8/100 person-years from 180 to 365 days after last visit (Figure 2). Of the 69 successfully tracked patients who were alive, in 22 cases (32%) the patient him or herself was interviewed and in 47 (68%), a sibling, spouse, close friend or other close acquaintance acted as the informant. Of 22

patients who were alive and found in person, 14 (64%) reported having seen a doctor or nurse for HIV care at a different facility within the last 90 days. The remaining 8 of 22 (36%) reported no recent contact with health care. In a proportional hazards regression of predictors of survival among those lost to follow-up, nearer district of residence, lower enrollment CD4 level, lower BMI and earlier calendar date of last visit were associated with higher mortality (Supplemental Digital Content 1).

Sample-weighted outcomes following ART eligibility

After incorporating the outcomes among the lost with probability weights, for the entire clinic population the cumulative incidence of ART initiation at 30, 90 and 365 days after eligibility was 16.0% (95% CI: 14.2 to 17.7), 64.5% (95% CI: 60.9 to 68.1), and 81.7% (95% CI: 77.7 to 85.6). The cumulative incidence of death prior to ART initiation at 30, 90 and 365 days following ART eligibility was 1.6% (95% CI: 0.05 to 2.5), 5.5% (95% CI: 2.8 to 8.1), and 7.7% (95% CI: 5.6 to 10.1). One year after eligibility, 10.0% of eligible patients were alive but had never started ART (Figure 3). The large majority of these patients not on ART after 1 year – 69.5% – were lost to follow-up from the ISS Clinic.

In multivariable analyses, higher age at enrollment and, notably, being unemployed were associated with faster ART initiation after adjustment for other socio-demographic and clinical factors. Male sex, higher CD4 count levels at presentation, having no formal education and being new to care at the time of eligibility were all associated with a decreased rate of ART initiation. In multivariate analysis to identify factors associated with mortality, malnutrition, lower CD4 level at clinic enrollment, greater travel time from residence to clinic and district of residence was associated with higher risk of mortality (Table 2).

DISCUSSION

Using a sampling-based approach to understand the experience of ART-eligible patients under routine program conditions in Uganda where loss to follow-up is high, we found that about 1 in 5 patients eligible for ART by CD4 count did not initiate ART one year after eligibility, and that 1 in 12 died during awaiting ART initiation. We identified a number of patient (CD4 level, male sex), system (whether or not you were new to care at the time of ART eligibility) and structural factors (travel time) to be associated with the rate of ART initiation as well as in a separate analysis, mortality, which shed light on the multi-dimensional determinants of barriers to effective care. These observations were made through application of a sampling-based approach in a clinic-based cohort to address biases presented by loss to follow-up. This approach strengthens both internal validity and external validity since the data come from a “real world” setting.

Although there is no absolute criterion about how soon eligible patients should start ART, our estimate of time to ART initiation demonstrates two concerning features. First, ART initiation is not rapid – at 60 days only 50% of eligible patients had initiated. In particular, a large fraction of eligible patients were classified as WHO Stage 3 or 4 and therefore likely had active opportunistic infections. These patients would likely benefit from ART initiation within 14 days as suggested by ACTG protocol 5164 [20]. Second, uptake of ART remained incomplete one year after eligibility. The ISS Clinic, like most clinics in Africa, typically required 2–3 counseling sessions before ART initiation and also a treatment supporter. In resource-limited settings, these requirements may magnify barriers to ART initiation even though they may strengthen adherence. Failure to achieve this last step of ART initiation is tantamount to a failed investment in testing and linkage.

We identified patient, structural and operational factors associated with the rate of ART initiation that point to actionable gaps in public health ART delivery. Previous cross-sectional analyses have found that male sex is a consistent predictor of late stage presentation among HIV infected persons in Africa [21], and in this analysis men appear to start ART almost 30% more slowly than women after adjusting for presentation CD4 level. Further research on the psychological aspects of male health care behavior in Africa is needed. Patients with no education, most of whom are likely to be illiterate, started ART at a slower rate. Patients without education should be flagged as a vulnerable group who may require additional assistance to successfully navigate the health care system. Unemployed patients initiated ART faster. Work responsibilities have been identified as a barrier to retention in previous work and therefore likely explain diminished ART initiation rates [5]. Exploration of alternative initiation strategies that are part community-based, using peer educators or "community adherence groups" are needed to enable access health care without jeopardizing the livelihoods of patients [22,23]. Finally, we found an interesting programmatic effect: patients who are new to care at eligibility are initiated on ART faster than patients who become eligible after already being in care. This is likely because patients already in care receive longer return visits since they appear to be "stable." Yet, this introduces a longer interval to their next visit when they do become eligible by CD4 count criteria. Randomized trails of both community-based peer advocates and SMS technology have been shown to reduce HIV RNA rebound in Africa for patients already on ART. These evidence-based strategies should be explored as methods to facilitate ART initiation newly eligible patients as well.

This analysis identified four factors associated with mortality that can be used to guide clinical attention to high-risk patients. The CD4 level at ART eligibility is a consistent predictor of mortality and likely reflects opportunistic infections already in progress at the time of ART initiation. Rolling out enhanced diagnostics for smear-negative tuberculosis, *C. neoformans* and other common infections is critical in preventing these deaths [24,25]. A body mass index < 18.5 kg/m^2 conferred a threefold rise in the rate of death even after adjusting for CD4 level, TB diagnosis, and other sociodemographic factors. These patients likely represent a mix of individuals with undiagnosed infections as well as persons with macro-nutritional deficiency. Food supplementation in this subset of patients may improve survival and wider dissemination of nutritional interventions may improve outcomes [26–28]. Travel time from residence to clinic was associated in a dose response relationship to survival. This finding suggests that addressing geographic and physical accessibility through decentralization may merit greater prioritization as a strategy to make treatment delivery more effective [29,30].

This study has certain limitations. First, although our sample was formally a random subset of the lost to follow-up, not all outcomes were ascertained, and therefore the reweighted estimates may be biased. We believe given more than 80% of outcomes were ascertained, the opportunity for bias is not large. Second, although we believe the ISS Clinic is representative of large ART programs in Africa, processes are likely better than the "average clinic" because of its affiliation with Mbarara University and membership in the IeDEA consortium. If true, this would imply that the shortcomings with uptake of ART are even more concerning than those we observed here.

In summary, we used a sampling-based approach – which allows us to maximize validity with a highly generalizable patient population – to understand uptake of ART among eligible patients at a scale-up clinic in Uganda. This approach is broadly feasible. On-site start up costs for three months to track 120 patients was is approximately 5,000 dollars. This includes 1,200 dollars for a motorbike, 600 dollars per month as salary for the ascertainer, 500 dollars for fuel, 500 dollars per month for other consumables and administrative costs.

We observed a strong relationship between death and loss to follow-up, which suggests that analyses of mortality in the pre-ART population based on passively ascertained vital status information likely biased and possibly severely so [31,32]. We found the rate and total uptake of ART was neither optimally fast nor complete. Factors associated with uptake identify groups of patients who may benefit from targeted interventions, namely, men and patients with little or no education. Enhanced program features such as point-of-care, distributed care sites, and text messages to notify patients already in care when they become eligible for ART may improve ART uptake and delivery and potentially survival. ART is highly efficacious; improving the utilization of ART under program conditions through implementation strategies can make this intervention more effective in routine care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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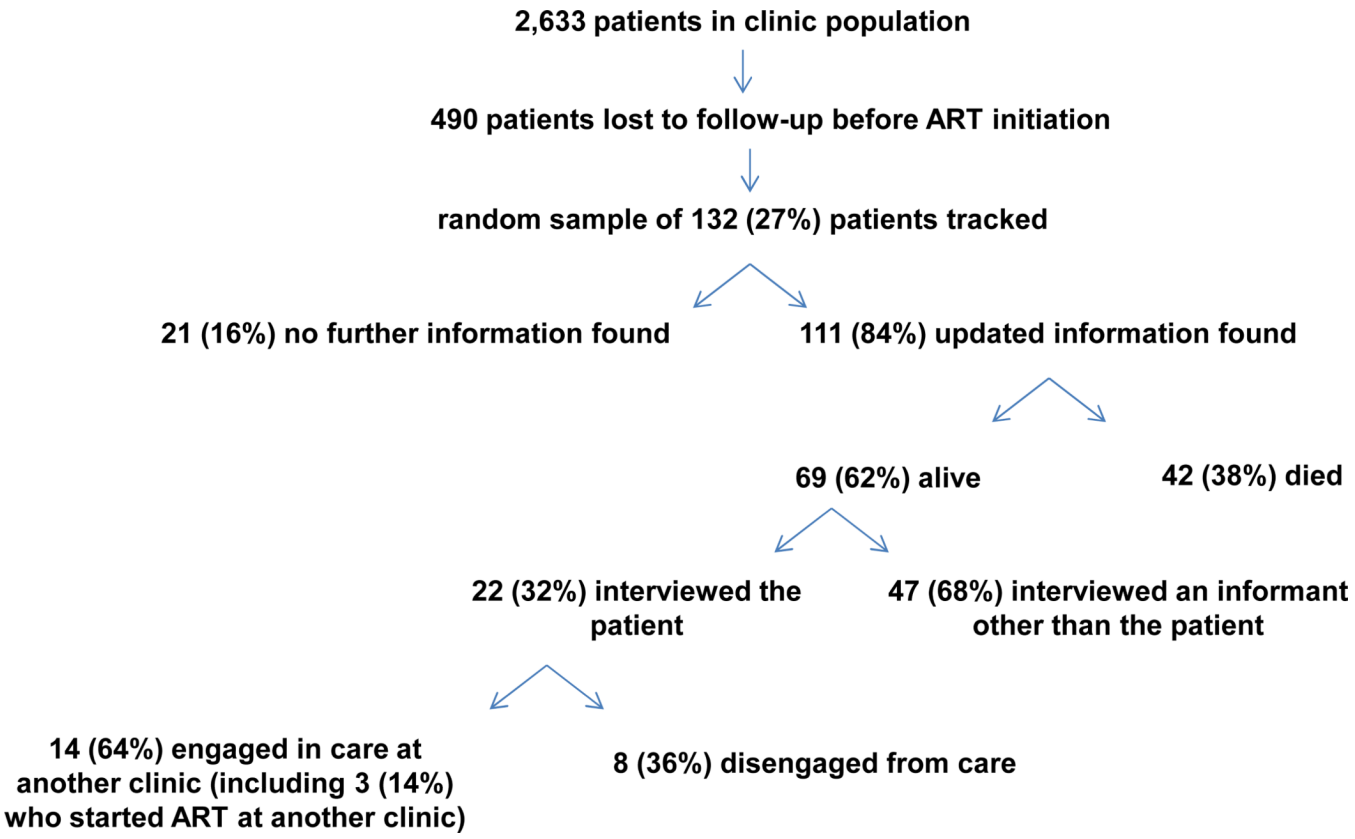

Figure 1.
Flow-chart depicting HIV-infected patients who became newly eligible for antiretroviral therapy according to CD4+ T-cell based criteria at the ISS Mbarara Clinic.

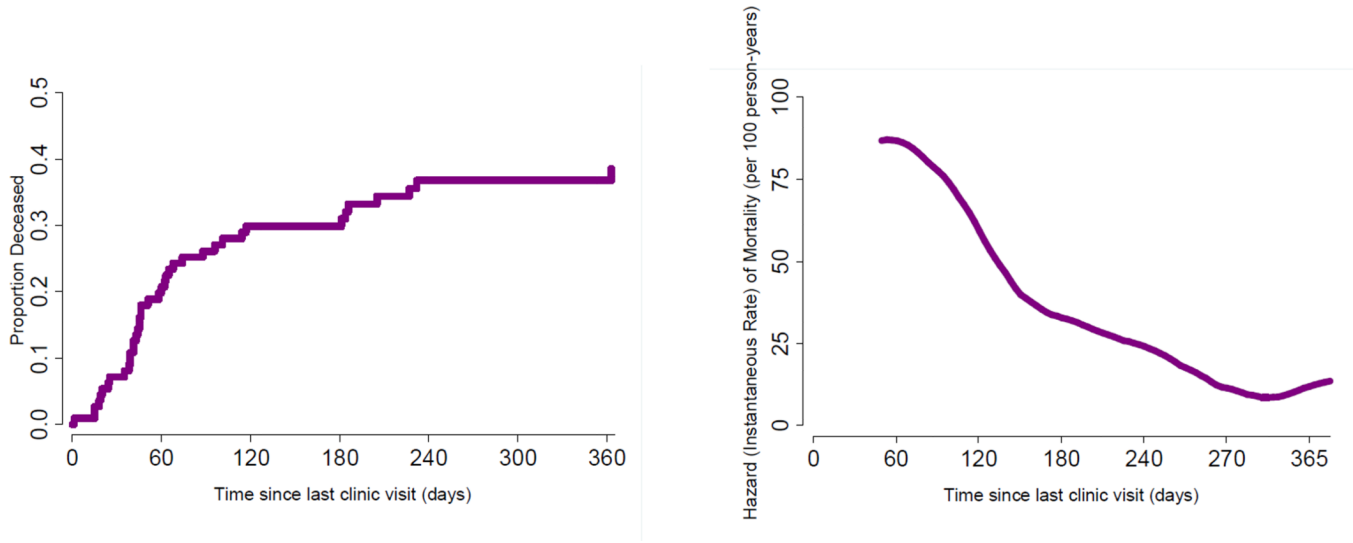

Figure 2.

Cumulative incidence and hazard (instantaneous rate) of mortality among treatment-eligible, HIV-infected patients who were lost to follow-up after date of last clinic visit, N=111

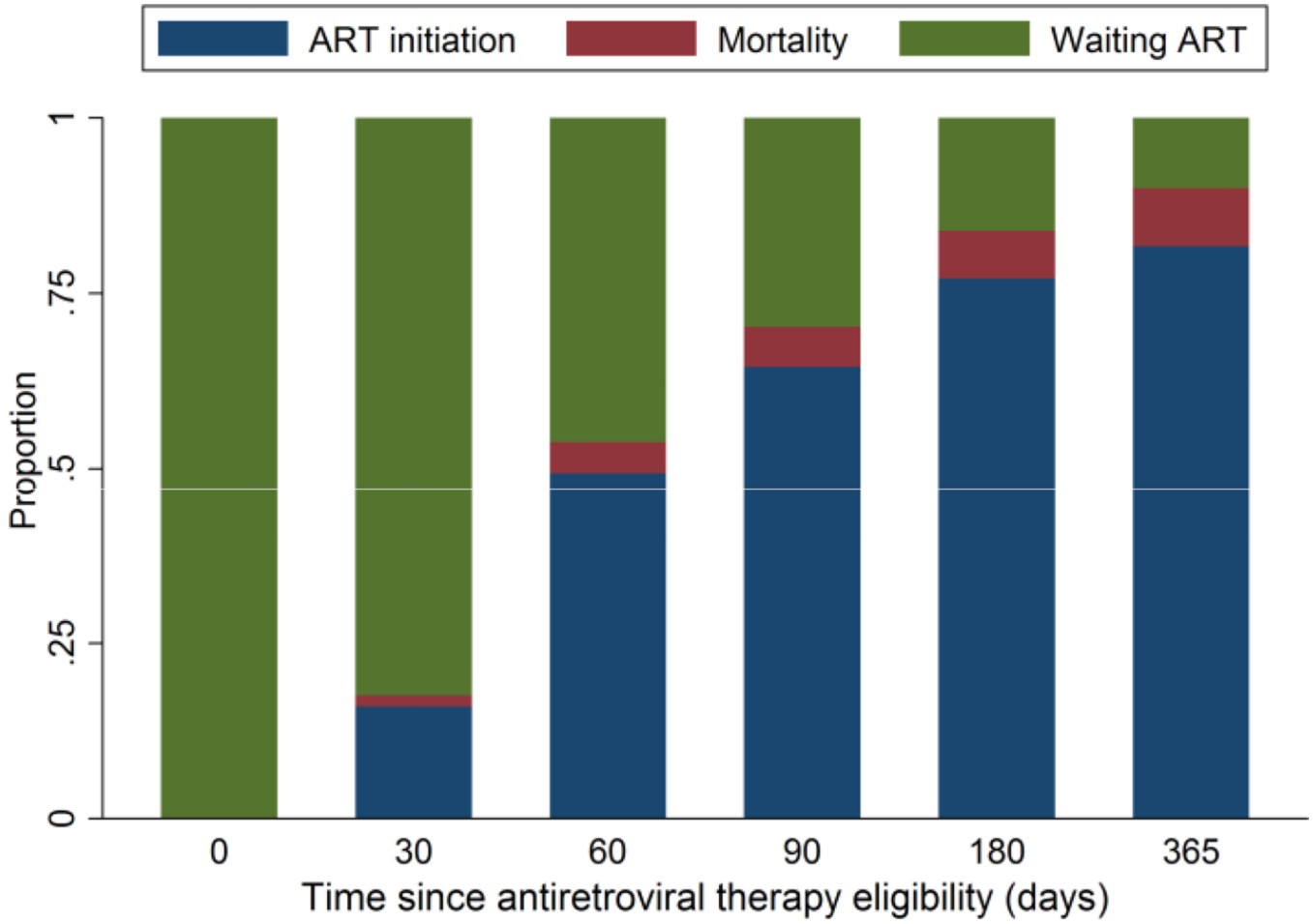

Figure 3.
Proportions of patients who initiate ART, died before ART initiation and awaiting ART following the date of first treatment-eligible CD4+ T-cell level at the ISS Mbarara Clinic, N=2,633

Table 1

Patient characteristics among all patients eligible for antiretroviral therapy by CD4 criteria at the ISS Clinic in southwestern Uganda from October 1, 2007 to January 27, 2011 and among those lost to follow-up, a random sample of the lost and those who had outcomes successfully ascertained among the lost.

Characteristic	Total clinic population (N=2,633)	Patients lost to follow-up (N=490)	Random sample of patients lost to follow-up (N=132)	Random sample of lost patients successfully tracked (N=111)
Age at enrollment -years, median (IQR)	32 (27–39)	31 (26–39)	32 (26–39)	32 (25–39)
Male sex, n (%)	1,070 (40.6)	221 (45.1)	68 (51.5)	60 (54.1)
Malnourished, n (%) *	780 (32.4)	190 (43.1)	55 (45.8)	49 (49.0)
BMI – (kg/m2), median (IQR) *	19.8 (17.9–22.4)	19.2 (17.2–21.1)	18.9 (16.8–20.8)	18.6 (16.7–20.3)
CD4 Count at eligibility- cells/μl, n (%)				
< 50	633 (24.0)	133 (27.1)	33 (25.0)	27 (24.3)
51–100	434 (16.5)	95 (19.4)	31 (23.5)	30 (27.0)
101–200	939 (35.7)	174 (35.5)	39 (29.6)	32 (28.8)
>200	627 (23.8)	88 (18.0)	29 (22.0)	22 (19.8)
Calendar date of ART eligibility	17-Apr-09 (27-Jun-08 to 26-Feb-10)	4-Dec-08 (16-May-08 to 12-Oct-09)	31-Aug-08 (30-Mar-08 to 14-Aug-09)	23-Sep-08 (3-Apr-08 to 1-Oct-09)
Diagnosis of tuberculosis at ART initiation, n (%)	115 (4.4)	30 (6.2)	7 (5.3)	7 (6.3)
Pregnant at ART eligibility	98 (3.72)	21 (4.3)	8 (6.6)	6 (5.4)
WHO Stage at presentation, n (%) †				
1	516 (20.2)	56 (13.3)	18 (15.8)	15 (15.3)
2	928 (36.4)	135 (32.1)	34 (29.8)	29 (29.6)
3	460 (18.1)	96 (22.8)	31 (27.2)	26 (26.5)
4	645 (25.3)	134 (31.8)	31 (27.2)	28 (28.6)
District of residence, n (%)				
Mbarara	1,287 (48.9)	228 (46.5)	70 (53.0)	59 (53.2)
Bushyeni	195 (7.4)	35 (7.1)	9 (6.8)	8 (7.2)
Isingiro	662 (25.1)	130 (26.5)	29 (22.0)	24 (21.6)
Other	489 (18.6)	97 (19.8)	24 (18.2)	20 (18.0)
No formal education, n (%) ‡	114 (5.2)	28 (7.0)	9 (8.3)	9 (9.9)

Characteristic	Total clinic population (N=2,633)	Patients lost to follow-up (N=490)	Random sample of patients lost to follow-up (N=132)	Random sample of lost patients successfully tracked (N=111)
Monthly income in Ugandan Shillings, n (%) [§]				
less than 100,000	1,706 (64.8)	320 (81.6)	81 (77.9)	66 (76.7)
100,000 – 250,000	326 (12.4)	56 (14.3)	16 (15.4)	13 (15.1)
250,001 – 500,000	55 (2.1)	8 (2.0)	4 (3.9)	4 (4.7)
500,001	58 (2.2)	8 (2.0)	3 (2.9)	3 (3.5)
Travel time from residence to clinic, n (%) [¶]				
less than 30 minutes	499 (20.7)	90 (20.0)	22 (18.2)	20 (19.8)
30–60 minutes	634 (26.3)	122 (27.1)	38 (31.4)	28 (27.7)
1–2 hours	772 (32.1)	129 (28.7)	33 (27.3)	27 (26.4)
2–3 hours	284 (11.8)	52 (11.6)	14 (11.6)	13 (12.8)
> 3 hours	219 (9.1)	57 (12.7)	14 (11.6)	13 (12.8)

[*] Missing in 220 (8.3%)

[†] Missing in 84 (3.2%)

[‡] Missing in 437 (16.6%)

[§] Missing in 489 (18.6%)

[//] Missing in 28 (3.0%)

[¶] Missing in 225 (8.5%)

Table 2

Factors associated with time to ART initiation and mortality.

Characteristic	ART Initiation				Mortality			
	Unadjusted HR and 95% CI	**P-value**	**Adjusted HR and 95% CI**	**P-value**	**Unadjusted HR and 95% CI**	**P-value**	**Adjusted and 95% CI**	**P-value**
Age at enrollment, per 10 years	1.10 (0.88–1.12)	0.955	1.11 (1.01–1.21)	0.032	1.26 (1.02–1.54)	0.030	1.17 (0.89–1.53)	0.256
Sex								
Female	Ref.				Ref.			
Male sex	0.71 (0.58–0.88)	0.002	0.73 (0.60–0.88)	0.001	2.04 (1.16–3.60)	0.014	1.44 (0.80–2.60)	0.225
Nutritional status								
Normal (i.e. ≥ 18.5 kg/m^2)	Ref.		Ref.		Ref.		Ref.	
Malnourished (i.e. < 18.5 kg/m^2)	0.88 (0.69–1.12)	0.302	0.86 (0.70–1.06)	0.153	4.70 (2.53–8.71)	<0.001	3.08 (1.61–5.89)	0.001
CD4 count at eligibility (cells/μl)		0.028		0.015		<0.001		0.025
0≤50	Ref		Ref.		Ref		Ref	
50≤100	0.64 (0.45–0.90)		0.61 (0.45–0.84)		1.09 (0.57–2.09)		0.97 (0.52–1.80)	
100≤150	0.73 (0.54–1.00)		0.78 (0.61–1.00)		0.27 (0.12–0.61)		0.36 (0.17–0.77)	
150≤200	0.63 (0.46–0.87)		0.70 (0.52–0.94)		0.27 (0.11–0.69)		0.52 (0.20–1.41)	
TB diagnosis at eligibility								
Absent	Ref		Ref.		Ref		Ref	
Present	0.82 (0.46–1.47)	0.505	0.83 (0.52–1.31)	0.428	1.24 (0.39–3.97)	0.710	0.71 (0.25–2.04)	0.529
Pregnant at ART eligibility								
No	Ref		Ref.		Ref		Ref	
Yes	1.33 (0.89–1.96)	0.158	0.97 (0.58–1.62)	0.900	1.36 (0.37–4.98)	0.639	3.41 (0.86–13.51)	0.081
WHO stage at presentation		0.190		0.354		0.001		0.092
1	Ref.		Ref.		Ref.		Ref.	
2	1.33 (1.02–1.75)		1.25 (0.97–1.59)		1.26 (0.34–4.66)		1.07 (0.30–3.85)	
3	1.19 (0.82–1.73)		1.25 (0.90–1.73)		4.12 (1.18–14.40)		2.15 (0.61–7.62)	
4	1.29 (0.96–1.73)		1.15 (0.84–1.56)		4.91 (1.48–16.25		2.76 (0.79–9.57)	
New to care at the time of eligibility	1.35 (1.06–1.71)	0.014	1.54 (1.22–1.94)	<0.001	2.95 (1.06–8.25)	0.039	2.03 (0.64–6.43)	0.227
District of residence		0.692		0.326		0.802		0.027
Mbarara	Ref.		Ref.		Ref.		Ref.	

Characteristic	ART Initiation				Mortality			
	Unadjusted HR and 95% CI	P-value	Adjusted HR and 95% CI	P-value	Unadjusted HR and 95% CI	P-value	Adjusted and 95% CI	P-value
Bushyeni	1.02 (0.61–1.70)		1.15 (0.75–1.74)		0.53 (0.13–2.15)		0.37 (0.09–1.49)	
Isingiro	1.14 (0.91–1.43)		1.23 (0.98–1.54)		0.96 (0.50–1.87)		0.45 (0.22–0.91)	
Other	1.02 (0.75–1.38)		1.07 (0.81–1.42)		0.81 (0.37–1.75)		0.36 (0.17–0.77)	
Education								
Any	Ref.		Ref.		Ref.		Ref.	
None	0.54 (0.30–1.00)	0.048	0.48 (0.27–0.87)	0.016	1.43 (0.47–4..43)	0.527	1.75 (0.51–6.03)	0.375
Monthly income in Ugandan Shillings		0.264		0.403		0.999		0.968
Less than 100,000	Ref.		Ref.		Ref.		Ref.	
100,000 – 250,000	0.87 (0.61–1.24)		1.02 (0.75–1.38)		1.01 (0.42–2.41)		1.21 (0.50–2.96)	
250,001 – 500,000	0.59 (0.25–1.40)		0.62 (0.26–1.47)		0.92 (0.14–6.22)		1.32 (0.20–8.87)	
500,001	1.38 (0.85–2.24)		1.40 (0.84–2.33)		0.88 (0.12–6.28)		0.93 (0.12–7.00)	
Employment status								
Employed	Ref.		Ref.		Ref.		Ref.	
Unemployed	1.30 (1.08–1.57)	0.006	1.27 (1.07–1.51)	0.006	0.94 (0.46–1.94)	0.866	0.96 (0.46–1.99)	0.911
Time travel from residence to clinic		0.678		0.268		0.045		0.027
Less than 30 minutes	Ref.		Ref.		Ref.		Ref.	
30–60 minutes	0.84 (0.60–1.18)		0.81 (0.61–1.07)		1.82 (0.60–5.46)		1.97 (0.63–6.16)	
1–2 hours	0.91 (0.67–1.24)		0.80 (0.60–1.07)		2.11 (0.74–6.02)		2.77 (0.87–8.86)	
> 3 hours	0.99 (0.73–1.33)		0.75 (0.55–1.02)		3.76 (1.34–10.57)		4.74 (1.52–14.99)	