OPEN

Mortality Among HIV-Infected Adults on Antiretroviral Therapy in Southern Uganda

Dorean Nabukalu, BStat, MSc,[a] Constantin T. Yiannoutsos, PhD,[b] Aggrey Semeere, MBChB, MMed, MAS,[c] Beverly S. Musick, MS,[d] Teddy Murungi, BSc, PGD,[a] Jane Viola Namulindwa, MBChB,[a] Francis Waswa, BSc, MSc,[a] Gertrude Nakigozi, MBChB, MPH, PhD,[a] Nelson K. Sewankambo, MBChB, MSc, MMed,[e] Steven J. Reynolds, MD, MPH,[f,g] Tom Lutalo, PhD,[a] Fredrick Makumbi, PhD,[a] Godfrey Kigozi, MBChB, MPH, PhD,[a] Fred Nalugoda, PhD,[a] and Kara Wools-Kaloustian, MD[h]

Background: Monitoring and evaluation of clinical programs requires assessing patient outcomes. Numerous challenges complicate these efforts, the most insidious of which is loss to follow-up (LTFU). LTFU is a composite outcome, including individuals out of care, undocumented transfers, and unreported deaths. Incorporation of vital status information from routine patient outreach may improve the mortality estimates for those LTFU.

Settings: We analyzed routinely collected clinical and patient tracing data for individuals (15 years or older) initiating antiretroviral treatment between January 2014 and December 2018 at 2 public HIV care clinics in greater Rakai, Uganda.

Methods: We derived unadjusted mortality estimates using Kaplan–Meier methods. Estimates, adjusted for unreported deaths, applied weighting through the Frangakis and Rubin method to represent outcomes among LTFU patients who were successfully traced and for whom vital status was ascertained. Confidence intervals were determined through bootstrap methods.

Results: Of 1969 patients with median age at antiretroviral treatment initiation of 31 years (interquartile range: 25–38), 1126 (57.2%) were female patients and 808 (41%) were lost. Of the lost patients, 640 patient files (79.2%) were found and reviewed, of which 204 (31.8%) had a tracing attempt. Within the electronic health records of the program, 28 deaths were identified with an estimated unadjusted mortality 1 year after antiretroviral treatment initiation of 2.5% (95% CI: 1.8% to 3.3%). Using chart review and patient tracing data, an additional 24 deaths (total 52) were discovered with an adjusted 1-year mortality of 3.8% (95% CI: 2.6% to 5.0%).

Conclusions: Data from routine outreach efforts by HIV care and treatment programs can be used to support plausible adjustments to estimates of client mortality. Mortality estimates without active ascertainment of vital status of LTFU patients may significantly underestimate program mortality.

Key Words: ART, program evaluation, weighted mortality estimates, adult mortality, Uganda

(*J Acquir Immune Defic Syndr* 2024;95:268–274)

Received for publication April 10, 2023; accepted July 24, 2023.

From the [a]Rakai Health Sciences Program, Rakai, Uganda; [b]Indiana University, Fairbanks School of Public Health, Indianapolis, IN; [c]Infectious Diseases Institute, Makerere University, Kampala, Uganda; [d]Indiana University School of Medicine, Indianapolis, IN; [e]Makerere University College of Health Sciences, School of Medicine, Kampala, Uganda; [f]Division of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD; [g]Johns Hopkins University School of Medicine, Baltimore, MD; and [h]Department of Medicine, Indiana University School of Medicine, Indianapolis, IN.

This work is a product of the Fogarty IeDEA Mentorship Program funded by Fogarty under grant number; U01AI069911. The HIV treatment program in greater Rakai is funded by The U.S. President's Emergency Plan for AIDS Relief (PEPFAR).

The authors have no conflicts of interest to disclose.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jaids.com).

Correspondence to: Dorean Nabukalu, BStat, MSc, Rakai Health Sciences Program, Uganda Virus Research Institute, P.O. Box 49, Entebbe, Uganda (e-mail: dnabukalu@rhsp.org).

INTRODUCTION

Assessing patient care outcomes is a key component in monitoring and evaluating clinical programs in both resource-replete and resource-limited settings. Numerous challenges complicate these efforts, the most insidious of which is loss to follow-up (LTFU) among program clients. LTFU thwarts efforts to assess outcomes of care among patients receiving antiretroviral treatment (ART), particularly in resource-limited settings where there is a dearth of alternative systems (eg, vital statistics registries, real-time locating systems) to assess the outcomes of patients who drop out of the program where they initiated care.[1–4] LTFU is an umbrella term representing many outcomes, such as undocumented "silent" transfers (transferring to other clinics without the knowledge of the program), discontinuation of care, and unreported death. Unreported deaths, in particular, have been documented to be as high as 40%, a year after ART initiation among those LTFU patients.[3] Hence, any assessment of program effectiveness including evaluation of interventions, policies, and guidelines at local, national, or regional levels is significantly affected by lack of information on outcomes among patients who are LTFU.

In sub-Saharan Africa, as we get close to 95-95-95 by 2025 and ending AIDS by 2030, knowing all outcomes in the cohort becomes arguably more important. LTFU (and underreporting of deaths) remains an important issue partly driven by a steep increase in the number of patients starting ART after expansion of care and attendant decreases in staff-to-patient ratios.[5,6] There is also a documented increase in transfer to other clinics in recent years because of the improved availability of care options as ART delivery has been scaled up.[7,8] One would anticipate that the outcomes of patients who remain out of care are significantly different from those who have re-engaged in care elsewhere, although both types of patients appear as having been lost to their previous program. In the case of true disengagement from care, LTFU patients may be at higher risk of death.[9,10] Consequently, estimates of mortality commonly reported by ART programs in low-income and middle-income countries are likely an underestimate of the true mortality rate.[1,5,11,12] Therefore, it is important to ascertain what happened to patients who are LTFU and then appropriately adjust for true outcome status of those LTFU as one evaluates ART treatment outcomes.

Two studies in the early ART scale-up period found between 20% and 60% of LTFU patients had died within 6 months of ART initiation.[3,13] Even within the Treat All era, we anticipate that mortality will be higher among those who are LTFU than for patients who continue care within their clinic of origin. Thus, overall mortality rate estimates will be significantly affected by the degree to which patient outcomes are adjusted for unseen deaths among patients who are LTFU. The accuracy of HIV care outcome estimates is expected to be low if adjustments for unseen mortality are not undertaken.

Tracing of patients who have missed an appointment is desirable, but it is not always practical as part of routine program monitoring and evaluation. As we approach HIV epidemic control, many programs (including the President's Emergency Plan for AIDS Relief) routinely track clients who have missed visits through community outreach as part of their patient retention efforts and, in the process, obtain information on vital status and engagement in care among a subset of patients who have missed clinic visits. Information from these encounters can be used to adjust overall estimates of patient outcomes through weighting the outcomes of those traced within survival analyses.[14–16] Augmenting data from routine clinical care with information obtained through outreach efforts can improve the accuracy of mortality estimates.[14,17]

We show how real-world program tracing data can be combined with routinely collected clinical data to improve mortality estimation among adults at the Rakai Health Sciences Program (RHSP) clinics located at Kalisizo and Kasaali in South Western Uganda.

METHODOLOGY

Study Design, Setting, and Population

We analyzed clinical and patient tracing data prospectively collected on a cohort of adult patients initiating ART at clinics in greater Rakai, Uganda, from 2014 to 2018. This study was approved, as part of the East Africa International Epidemiology Databases to Evaluate AIDS (IeDEA-EA) Consortium, by the Indiana University Institutional Review Board and the Uganda Virus Research Institute Research Ethics Committee. The Indiana University Institutional Review Board and the Uganda Virus Research Institute Research Ethics Committee waived the written informed consent requirement because the analysis used deidentified routinely collected patient-level data.

With support from the President's Emergency Plan for AIDS Relief through the U.S. Centers for Disease Control and Prevention, RHSP supports comprehensive services at 2 public HIV care clinics at Kalisizo and Kasaali. RHSP is 1 of 9 HIV care and treatment programs that contribute data to the IeDEA-EA consortium.

Routine, free-of-charge HIV care and treatment services offered at the RHSP clinics include pre-ART adherence counseling, same-day ART initiation (initiating ART the same day they test and receive HIV-positive results), monthly return appointment visits up to 6 months after ART start, and viral load assessment at 6 months post-ART initiation. Virally suppressed patients are then given appointments every 3 months, whereas nonsuppressed patients continue with monthly appointments until virally suppressed.

The clinics have a supportive Peer Smart system whereby a person living with HIV (PLHIV) with a history of very good ART adherence voluntarily supports other PLHIV by encouraging and guiding them to good health-seeking behavior. The number of Peer Smart volunteers (patients enrolling into the care program are introduced to the Peer Smart program and actively provide the information necessary for the peers to trace them in the community) per clinic depends on the volume of patients. Patients are outreached a day after missing a scheduled visit. The tracing process starts with a phone call. If the patient does not have a phone, does not respond to the phone call, or does not report to clinic on the day agreed on during a previous phone contact, a Peer Smart volunteer, embedded in the community, is tasked to trace the patient in the community at his/her residential address to ascertain their vital status and see that they return to care. The result of the tracing is recorded on paper client locator forms designed by the clinics for use in tracing patients who missed appointments. These are then placed in paper files of the patient.

For this study, patients were classified as LTFU if, according to the electronic health records (EHR), they had missed their last scheduled visit before the end of study (December 31, 2018). All PLHIV who were enrolled between 2014 and 2018 (inclusive) at the RHSP clinics at Kalisizo and Kasaali at or after the age of 15 years were ART naïve at enrollment and at ART initiation were included in this study. All patients were followed from ART initiation until death, transfer-out, or administrative censoring depending on which occurred first.

Data Collection and Management

Data were collected as part of routine clinical care through standardized data collection instruments and then entered into the Uganda national electronic patient database.[18] Vital status included in the program database was generally ascertained through passive death reporting. Deidentified data were transferred from electronic patient database of the program to the IeDEA-EA Regional Data Center in Indianapolis, where they underwent data quality checks.

The paper files for patients who were identified as having missed their last visit before December 31, 2018, were located, and information on tracing, vital status, and dates of death or transfer were abstracted and recorded on a customized data collection form (see Appendix I, Supplemental Digital Content, http://links.lww.com/QAI/C213). As part of tracing, all attempts to locate patients are documented, and therefore, any information indicating that an attempt was made to locate the patient was considered a tracing or outreach event. This included a completed outreach form (ie, Peer Smart form, client locator form, or entry in the missed appointment register) or notes in the patient files showing that a phone call or home visit was made.

Notations indicating the patient's death without evidence that an outreach attempt was made were considered as having been "passively" ascertained by the program (ie, obtained through routine means) and were not coded as a death obtained through tracing. Some of these deaths, however, were not part of the electronic record because of a data entry error, so this vital status information was treated differently, during the analysis, as compared with death information available in the program's EHR (see "Statistical Analyses" section for more details). Data from the customized study form were entered into a REDCap database specifically created for this study and were exported to statistical software for analysis along with the EHR data available from routine clinical care.

Definitions of Patient Outcomes

The primary outcome of interest in this study was patient death after ART initiation. We distinguish between a "passively ascertained" death, as documented on the patient's record with no evidence of tracing, versus an "actively ascertained" death, which is a death ascertained during a tracing encounter or a death which is not part of the clinics' EHR system which were discovered through chart review.

Statistical Analyses

Descriptive statistics of baseline continuous and categorical patient characteristics were summarized and compared through Wilcoxon and χ^2 tests, respectively. Two analyses were performed: unadjusted analysis, using the passively ascertained deaths available in the EHR, and an adjusted analysis, which accounts for all deaths identified during tracing. Unadjusted estimates of cumulative incidence of mortality were determined through Kaplan–Meier methods. Data from patients who were LTFU were censored at the last completed clinic visit. Adjusted estimates were obtained through weighting schemes[14] applied to the data from the sample of outreached patients to represent the outcomes among all patients with missed visits, including those who were never traced, and thus, their outcomes remained unknown. Outcomes among patients who were LTFU and whose vital status was successfully ascertained through tracing and chart review were assigned a weight equal to the inverse proportion of those with known vital status (numerator) among all LTFU patients (denominator).[19] Patients who were not LTFU and whose vital status was known at database closure were assigned a weight equal to 1.[19] Only data on patients who were not LTFU and those LTFU patients whose vital status was obtained through tracing or chart review were kept in the analysis.[14] As the Frangakis and Rubin asymptotic variance estimate is difficult to calculate,[14] we used bootstrap methods for computing 95% confidence intervals (CIs) for the mortality estimates.[20,21] *P* values for comparisons between various patient groups (eg, male versus female patients) were generated through permutation tests.[22] All analyses were performed using Stata version 17 (StataCorp, College Station, TX). All analytical code is provided as part of the Supplemental Digital Content, http://links.lww.com/QAI/C220 accompanying this paper.

RESULTS

Cohort Composition

We studied 1969 patients from the 2 study clinics who met the inclusion criteria (Fig. 1). Of these, 808 patients had missed their last appointment before database closure on December 31, 2018; 640 were from RHSP clinic at Kalisizo; and 168 were from Kasaali, as shown in Figure 1. Per study protocol, the files of these 808 patients were sought, and 640 patient files (79.21%) were found, retrieved, and reviewed for information on patient tracing. Of the 1969 patients, 161 (8.18%) had either transferred to another clinic or migrated to a known location. Of these, 23 patients (1.17%) were captured as transferred out by routine means, whereas transfer status on the rest was ascertained through tracing.

Among the 1969 adult patients included in this analysis, the median age at ART initiation was 31 years (interquartile range [IQR]: 25–38) and 57% were female (Table 1). Nearly 72% of the patients were from the RHSP clinic at Kalisizo. At ART initiation, most of the patients (78%) had World Health Organisation (WHO) clinic stage 1 disease and a median CD4 count of 318 cells/mm^3 (IQR: 165–478).

We observed 52 deaths, and of these, 28 (53.8%) were passively ascertained deaths and were entered in the program's EHR. An additional 24 deaths were actively ascertained, 3 through chart reviews and the rest through the patient tracing program (Fig. 1). The 1-year unadjusted mortality estimate after ART initiation was 2.5% (95% CI:

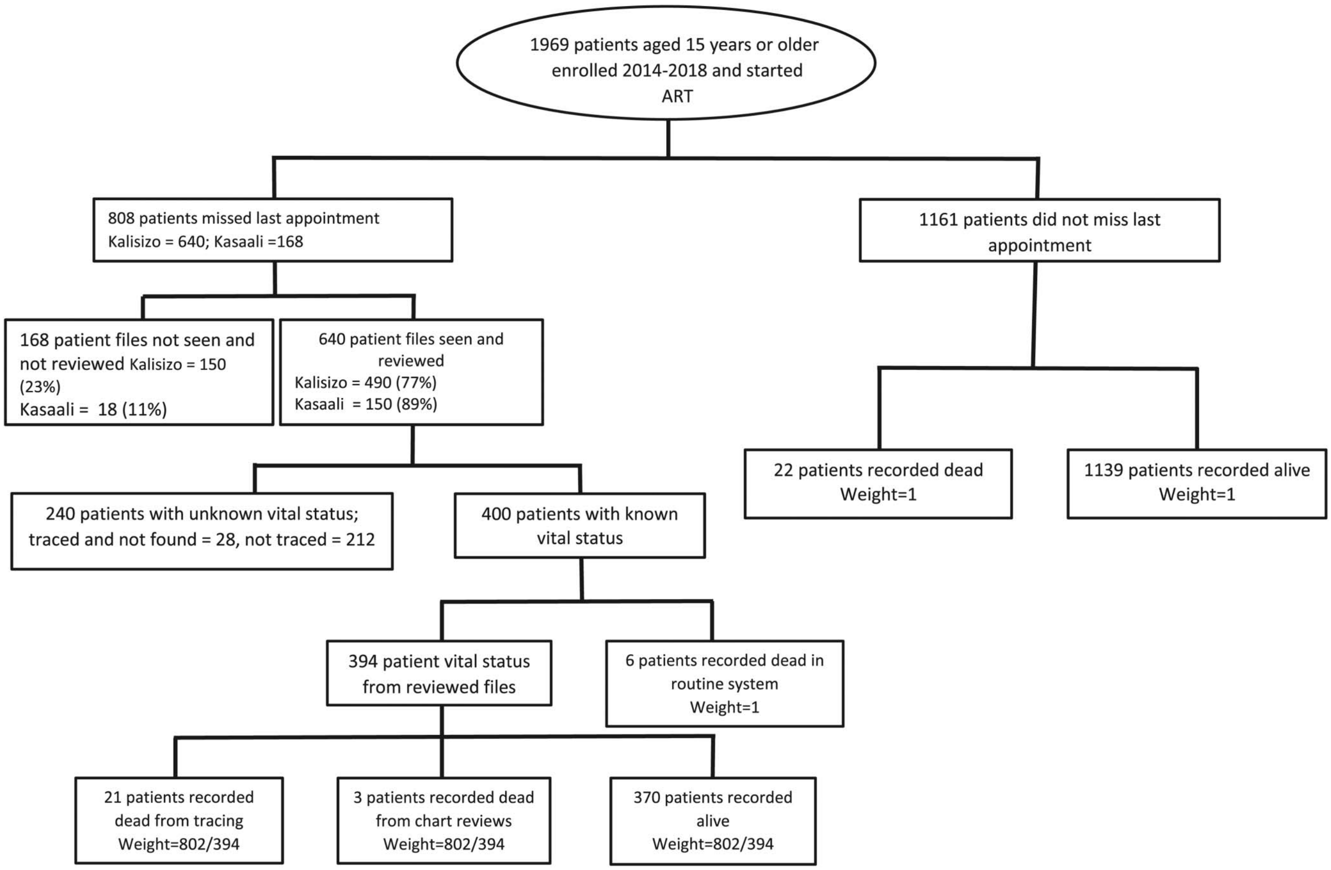

FIGURE 1. Cohort composition and vital status data source.

1.8% to 3.3%). After updating deaths through tracing, adjusted 1-year mortality estimate, produced by the Frangakis and Rubin approach,[14] was 3.8% (95% CI: 2.6% to 5.0%; Table 2). Adjusted 1-year mortality was significantly higher in male patients (6.0%; 95% CI: 3.6% to 8.4%) compared with female patients (2.0%; 95% CI: 0.9% to 3.0%; log-rank *P* value = 0.001) and higher in patients who initiated ART at WHO stages 3 or 4 (combined 1-year mortality 17.9%; 95% CI: 9.1% to 26.7%), compared with those initiating ART at WHO stages 1 or 2 (2.5%; 95% CI: 1.5% to 3.5%) while there was no significant difference in 1-year mortality rates among different age groups and between patients enrolled in the 2 clinics, as presented in Table 2.

The overall unadjusted and adjusted estimates of cumulative mortality over time, along with 95% bootstrap-generated confidence intervals, are shown in Figure 2.

TABLE 1. Characteristics of the Cohort by Missed Last Visit Status

Characteristic	Overall N = 1969	Patient Subgroup: Did Not Miss Past Visit N = 1161	Patient Subgroup: Missed Past Visit N = 808
Age at ART start (yrs), median (IQR)	31 (25–38)	31 (26–38)	30 (25–36)
Sex female, N (%)	1126 (57.2)	673 (58.0)	453 (56.1)
Clinic, N (%)			
RHSP at Kalisizo	1414 (71.8)	774 (66.7)	640 (79.2)
Kasaali clinic	555 (28.2)	387 (33.3)	168 (20.8)
Maximum WHO stage before ART start, N (%)			
Stage 1	1531 (78.4)	936 (81.5)	595 (73.9)
Stage 2	266 (13.6)	130 (11.3)	136 (16.9)
Stage 3	96 (4.9)	53 (4.6)	43 (5.3)
Stage 4	60 (3.1)	29 (2.5)	31 (3.9)
CD4 count at ART start (cells/m), median (IQR)	318 (165–478)	328 (168–473)	310 (152–488)

TABLE 2. Unadjusted and Adjusted Mortality Estimates at 1 Year After ART Initiation

	Method for Estimating Mortality			
	% Mortality Estimate (95% CI)			
	Unadjusted		Adjusted	
Characteristic	Mortality Estimates	Log-Rank P	Mortality Estimates	Log-Rank P
Overall	2.5 (1.8 to 3.3)		3.8 (2.6 to 5.0)	
Sex		0.001		0.001
Female	1.5 (0.8 to 2.5)		2.0 (0.9 to 3.0)	
Male	3.7 (2.5 to 5.5)		6.0 (3.6 to 8.4)	
Age		0.055		0.187
Younger than 25 yrs	1.1 (0.4 to 2.9)		1.5 (0.0 to 2.9)	
25–50	2.9 (2.1 to 4.0)		4.5 (2.9 to 6.1)	
Older than 50 yrs	1.6 (0.2 to 11.1)		1.5 (−1.5 to 4.5)	
Clinic		0.404		0.561
Kalisizo	2.6 (1.8 to 3.7)		3.9 (2.6 to 5.3)	
Kasaali	1.9 (0.9 to 3.9)		3.3 (0.8 to 5.7)	
Maximum WHO stage before ART start		0.001		0.001
Stages 1 and 2	1.6 (1.1 to 2.4)		2.5 (1.5 to 3.5)	
Stages 3 and 4	11.5 (7.2 to 18.2)		17.9 (9.1 to 26.7)	

DISCUSSION

We present data from 2 IeDEA-EA supported PEPFAR-funded clinics in greater Rakai, Uganda. We show how existing clinical data can be supplemented by vital status information from routine outreach of patients who are LTFU. Such data are available in many HIV care and treatment programs in our setting but are not always included in the EHR. Analysis of these data allows adjustment of mortality estimates.[14] This method of mortality adjustment (based on data collected during the active follow-up of patients) has been performed by other studies within Uganda[23,24] and globally.[10,16,25] All studies acknowledge the importance of active follow-up in program evaluation. As in those studies, our analyses showed that at different time points and over the entire follow-up period, adjusted mortality estimates were significantly higher based on active follow-up compared with unadjusted estimates obtained when data from clinic records alone were analyzed. This implies that mortality may be significantly underestimated in cases where only clinic records are used, as is the case in most monitoring and evaluation reports. This in turn will translate into potentially overestimating the positive impact of care and treatment programs or the implementation of new guidelines such as universal Test and Treat[19,24] (also known as "Treat All"). From our study, 1 year after the start of ART, mortality estimated from the routine records was 2.5% compared with 3.8% when information from the tracing program was included. These findings support inclusion of tracing data and are consistent with findings from other settings.[1,9,16,19]

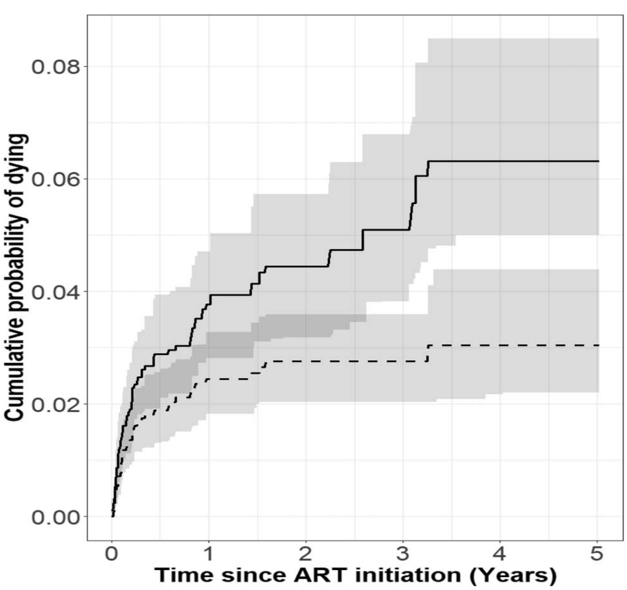

FIGURE 2. Unadjusted (dashed) and adjusted (solid) mortality estimates with 95% CI for adult patients living with HIV/AIDS initiated on ART in 2 RHSP clinics from 2014 to 2018.

Although our findings are consistent with previous studies and are not novel per se, this study provides several contributions to the record of the global response to the HIV/AIDS pandemic. First, it is one of the few studies addressing patient mortality in the Treat All era (ie, after 2017). Second, this study did not use enhanced data collection through a research protocol but relied on data already collected through the existing program infrastructure. From this perspective, our study and attendant materials, included in the Supplemental Digital Content, http://links.lww.com/QAI/C220, outline an approach whereby programs can use extant patient tracing data to supplement their routine programmatic data to derive more accurate estimates of indices of program effectiveness, such as patient mortality. Incorporating data from active follow-up, we were able to get closer to the true mortality rate among our program clients.

The conclusions from these results are encouraging. Geng et al[19] estimated a 7.5% of 1-year mortality rate after ART initiation based on data up to 2008 from a research study conducted in a similar HIV care and treatment program in southern Uganda. A subsequent study incorporating data up to 2015 from clinics throughout the IeDEA-EA Consortium reported an unadjusted estimate of 1-year mortality of 2.7% and an adjusted estimate incorporating patient tracing of 7.1%,[24] which was very close to the 2008 estimate of 7.5%. Our adjusted estimate of a 3.8% of 1-year mortality suggests that mortality among patients newly starting ART may have been reduced by as much as 50%, from 7.5% to 3.8% during the previous 10-year period. Without the adjustment, this would have been erroneously overestimated from 7.5% to 2.5%.

There are some limitations in this study. Only 79% of patient files sought were located and reviewed. Thus, we did not find all the records from patients who were LTFU. As such, residual selection bias may be present. On one hand, if the patients who were not found were sicker and at higher risk of death, this would result in this study underestimating mortality rates. However, if the patients who were not found were healthier and thus perhaps more mobile to pursue work outside of their initial catchment, our study may have overestimated mortality rates. In addition, the clinics in this study were not sampled from a larger pool of clinics but rather represent a convenience sample, so our results may not be representative of the Western region of Uganda or, more broadly, East Africa. Another limitation is our assumption that patients who transferred to other clinics had the same outcomes as patients who remained in care in the programs considered in this study. Although this is a plausible situation, given the level of standardization of national care and treatment protocols throughout Uganda, patients frequently experience disruptions in their continuity of care during the period of transition from one program to another, which may have an adverse impact on patient clinical outcomes.[24] From this perspective, even our adjusted mortality estimate may be underestimating true mortality in our client population. This study looked at all-cause mortality in PLHIV, but some mortality may be due to risks other than HIV and changes in mortality estimates may be due to changes in mortality in the general population. One recommendation for further study is exploring HIV cause-specific mortality in this clinic cohort.

The principal strength of our study is the use of vital status data, which is often ignored when reporting program outcomes, on a large portion of patients who have missed appointments. These data allowed us to substantially and upwardly revise our routine mortality estimates by incorporating additional information on these patients.

CONCLUSIONS

Mortality estimates from routinely available ART program data can be significantly underestimated because existing data are not linked to patient records in a substantial portion of patients who are lost to the program. As Uganda approaches HIV epidemic control, ascertaining outcome status of those "LTFU" becomes arguably more important —also understanding risk factors for poor outcomes (eg, mortality), so these can be reduced. Although, with the rapid scale-up of HIV care and treatment programs, census approaches that canvass all lost patients are impractical for large programs following thousands of patients, utilization of tracing data to adjust estimates through statistical modeling is a viable and pragmatic way to monitor and evaluate such programs.

ACKNOWLEDGMENTS

The authors acknowledge the efforts of the RHSP monitoring and evaluation team, the clinical and records personnel at the two clinics for the support rendered in retrieving patient charts. The Rakai Health Sciences Program management for their administrative and financial support. The IeDEA team for the mentorship.

REFERENCES

1. Braitstein P, Brinkhof MW, Dabis F, et al. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *Lancet*. 2006;367:817–824.
2. Geng EH, Bangsberg DR, Musinguzi N, et al. Understanding reasons for and outcomes of patients lost to follow-up in antiretroviral therapy programs in Africa through a sampling-based approach. *J Acquir Immune Defic Syndr*. 2010;53:405–411.
3. Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. *PLoS Med*. 2007;4:e298.
4. Wools-Kaloustian K, Kimaiyo S, Diero L, et al. Viability and effectiveness of large-scale HIV treatment initiatives in sub-Saharan Africa: experience from western Kenya. *AIDS*. 2006;20:41–48.
5. Boulle A, Bock P, Osler M, et al. Antiretroviral therapy and early mortality in South Africa. *Bull World Health Organ*. 2008;86:678–687.
6. Brinkhof MWG, Dabis F, Myer L, et al. Early loss of HIV-infected patients on potent antiretroviral therapy programmes in lower-income countries. *Bull World Health Organ*. 2008;86:559–567.
7. Amanyire G, Semitala FC, Namusobya J, et al. Effects of a multicomponent intervention to streamline initiation of antiretroviral therapy in Africa: a stepped-wedge cluster-randomised trial. *Lancet HIV*. 2016;3:e539–e548.
8. Nglazi MD, Kaplan R, Orrell C, et al. Increasing transfers-out from an antiretroviral treatment service in South Africa: patient characteristics and rates of virological non-suppression. *PLoS One*. 2013;8:e57907.
9. Bisson GP, Gaolathe T, Gross R, et al. Overestimates of survival after HAART: implications for global scale-up efforts. *PLoS One*. 2008;3:e1725.
10. Van Cutsem G, Ford N, Hildebrand K, et al. Correcting for mortality among patients lost to follow up on antiretroviral therapy in South Africa: a cohort analysis. *PLoS One*. 2011;6:e14684.
11. Stringer JSA, Zulu I, Levy J, et al. Rapid scale-up of antiretroviral therapy at primary care sites in Zambia: feasibility and early outcomes. *JAMA*. 2006;296:782–793.
12. Toure SS, Kouadio B, Seyler C, et al. Rapid scaling-up of antiretroviral therapy in 10,000 adults in Côte d'Ivoire: 2-year outcomes and determinants. *AIDS*. 2008;22:873–882.
13. Brinkhof MWG, Pujades-Rodriguez M, Egger M. Mortality of patients lost to follow-up in antiretroviral treatment programmes in resource-limited settings: systematic review and meta-analysis. *PLoS One*. 2009;4:e5790.
14. Frangakis CE, Rubin DB. Addressing an idiosyncrasy in estimating survival curves using double sampling in the presence of self-selected right censoring. *Biometrics*. 2001;57:333–342.
15. Raboud JM, Montaner JS, Thorne A, et al. Impact of missing data due to dropouts on estimates of the treatment effect in a randomized trial of antiretroviral therapy for HIV-infected individuals. Canadian HIV Trials Network A002 Study Group. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1996;12:46–55.
16. Yiannoutsos CT, An MW, Frangakis CE, et al. Sampling-based approaches to improve estimation of mortality among patient dropouts: experience from a large PEPFAR-funded program in Western Kenya. *PLoS One*. 2008;3:e3843.

17. Touloumi G, Pocock SJ, Babiker AG, et al. Impact of missing data due to selective dropouts in cohort studies and clinical trials. *Epidemiology*. 2002;13:347–355.
18. Tierney WM, Achieng M, Baker E, et al. Experience implementing electronic health records in three East African countries. *Stud Health Technol Inform*. 2010;160:371–375.
19. Geng EH, Emenyonu N, Bwana MB, et al. Sampling-based approach to determining outcomes of patients lost to follow-up in antiretroviral therapy scale-up programs in Africa. *JAMA*. 2008;300:506–507.
20. Chernick MR, Gonzãlez-Manteiga W, Crujeiras RM, et al. Bootstrap methods. In: Lovric M, ed. *International Encyclopedia of Statistical Science*. Berlin, Heidelberg: Springer Berlin Heidelberg; 2011:169–174.
21. Stine R. An introduction to bootstrap methods: examples and ideas. *Sociol Methods Res*. 1989;18:243–291.
22. Schemper M. A survey of permutation tests for censored survival data. *Commun Stat Theor Methods*. 1984;13:1655–1665.
23. Geng EH, Glidden DV, Emenyonu N, et al. Tracking a sample of patients lost to follow-up has a major impact on understanding determinants of survival in HIV-infected patients on antiretroviral therapy in Africa. *Trop Med Int Health*. 2010;15(suppl 1):63–69.
24. Geng EH, Odeny TA, Lyamuya RE, et al. Estimation of mortality among HIV-infected people on antiretroviral treatment in East Africa: a sampling based approach in an observational, multisite, cohort study. *Lancet HIV*. 2015;2:e107–e116.
25. Tweya H, Gareta D, Chagwera F, et al. Early active follow-up of patients on antiretroviral therapy (ART) who are lost to follow-up: the 'Back-to-Care' project in Lilongwe, Malawi. *Trop Med Int Health*. 2010;15(suppl 1):82–89.

