Sampling-Based Approach to Determining Outcomes of Patients Lost to Follow-Up in Antiretroviral Therapy Scale-Up Programs in Africa

To the Editor: Evaluating outcomes among the millions of HIV-infected patients starting antiretroviral therapy (ART) in settings with limited resources is key to understanding the effect of current treatment programs and guiding future strategies. Accurately assessing survival outcomes has been precluded by substantial numbers of patients not returning for care. One year after starting ART, 15% to 30% of patients are lost to follow-up.\(^1\),\(^2\) Only by determining the outcomes of those lost can true survival and program impact be understood. We present a sampling-based strategy to address this.

Methods. We evaluated all HIV-infected adults initiating ART in a rural clinic in Mbarara, Uganda, between January 1, 2004, and September 30, 2007. Each month, a tracker sought an unselected and consecutive sample of patients in the community who were lost to follow-up (a 6-month absence from clinic) to obtain their vital status. Naive and corrected estimates of cumulative incidence of mortality were determined with Kaplan-Meier techniques. In the naive estimate, only deaths passively recorded by the clinic through routine processes were included. In the corrected estimate, the updated vital status among the tracked sample of lost patients was used to represent outcomes among all those lost to follow-up by generating a probability weight (the ratio of all patients lost to follow-up to those lost and sampled with subsequent updated vital status) (FIGURE 1). Lost patients with sampling-updated vital status were assigned this weight, and all other lost patients were dropped from the analysis. This approach is equivalent to previously described methods.\(^3\) Comparisons of lost patients with and without vital status ascertainment were tested with \(\chi^2\) and \(t\) tests. Significance was set at \(P<.05\). Analyses were performed using Stata 10 (StataCorp, College Station, Texas). The study was approved by the institutional review boards of the University of California, San Francisco, and the Mbarara University of Science and Technology. Patients gave oral consent.

Results. A total of 3628 HIV-infected adults newly starting ART were evaluated. The median age was 35 years, 61% were women, and median pretherapy CD4 T-cell count was 95/mm\(^3\). Over a maximum of 3.75 years (median, 1.16 years; interquartile range, 0.42-2.11 years), 829 patients became lost to follow-up, of whom a sample of 128 was sought. Of these 128, we could ascertain the vital status of 111 patients (87%); 32 of 111 (29%) had died. Patients found by tracking (n=111) were similar in age (\(P=.66\)), sex (\(P=.84\)), and CD4 T-cell count (\(P=.44\)) to those who were lost and did not have vital status ascertained (n=718). Using the naive estimate, the cumulative incidence of death at 1, 2, and 3 years following ART was 1.7%, 2.1%, and 2.3%, respectively. After incorporating deaths from the tracked sample of lost patients (probability weight, 829/111), the corrected incidence of death at 1, 2, and 3 years was 7.5%, 10.3%, and 12.2%, respectively (FIGURE 2).

Comment. To address a critical barrier in evaluating ART scale-up, we used a sampling-based strategy to account for losses to follow-up. Searching for a sample of lost patients and determining vital status on a high percentage was feasible. Using just a single tracker to locate lost patients and simple calculations to derive corrected survival estimates, the pro-

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**FIGURE 1. Derivation of Probability Weights**

(A) Entire clinic population

(B) Patients lost to follow-up

(C) Patients sought by tracking

(D) Patients with vital status ascertained by tracking

The probability weight \(P_w\) allows a sample of patients who were lost to follow-up to represent all lost patients in subsequent survival analysis. Population A represents the entire clinic population, B represents all patients lost to follow-up, C is the sample of lost patients sought in the community, and D represents the sought-after lost patients who had their vital status ascertained. Vital status outcomes among those successfully sought (group D) are taken to represent outcomes among the remaining lost patients (group B—group D). Hence, the ratio of B/D is used to weight patients in group D to allow them to represent all lost patients.
cess is accessible and affordable. Incorporating updated outcomes from the tracked sample increased 5.3-fold the estimate of mortality at 3 years, an absolute difference of 9.9%.

Although our sample was unselected and consecutive, it was not random; hence, the corrected mortality estimates may potentially underestimate or overestimate true mortality. However, the lack of substantial differences in characteristics between the lost patients with and without tracking-updated vital status ascertainment suggests the sample was representative and unbiased. Formally sampling and tracking a random subset of lost patients should strengthen this strategy. Sampling is well suited to the resource limitations of global scale-up because the fraction of lost patients sought may potentially underestimate or overestimate true mortality.

The naive estimate is determined using those deaths passively reported during the course of routine clinical care. The corrected estimate uses vital status outcomes in the tracked sample of lost patients to represent vital status outcomes in all lost patients.

Figure 2. Naive and Corrected Mortality Estimates

The naive estimate is determined using those deaths passively reported during the course of routine clinical care. The corrected estimate uses vital status outcomes in the tracked sample of lost patients to represent vital status outcomes in all lost patients.

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