**Working title:**

Loss to follow-up and silent transfers among HIV patients in central Mozambique: an observational study

**Introduction:**

* Rationale for the study
* How it fills an evidence gap
* Previous literature on the topic, especially systematic reviews

Patient retention is critical for the success of HIV treatment programs. In central Mozambique, Inguane et al. (2016) estimated the one-year patient retention rate to be only 18 percent [1]. However, some patients reported as lost to follow-up (LTFU) might still receive care at a different health facility, but were not registered as having transferred to that facility. These “silent transfers” result in underestimated retention rates, leading to the perception that HIV patients utilize health services less than they truly do. Previous research on LTFU patients focuses largely on determining unbiased mortality rates among the HIV-positive population. These studies generally use a random sample [2, 3] or census [4, 5] of LTFU patients, and are highly resource intensive. There is scant literature on the topic of inter-facility transfer [6, 7].

We propose two novel methods for estimating loss to follow-up in a way that accounts for silent transfers. Both methods avoid the need to track LTFU patients directly, instead characterizing all other aspects of patients’ interactions with the health system and estimating the rate of LTFU deductively. The first method makes use of aggregated information collected by health facilities, such as the rate of enrollment in antiretroviral (ARV) treatment. The second method utilizes pharmacy records to track how often individual patients pick up their ARV medications and transfer between facilities. In the proposed study, we will demonstrate these approaches by estimating the rate of loss to follow-up among facilities in central Mozambique.

1. [**https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4956731/**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4956731/)
2. [**https://www.ncbi.nlm.nih.gov/pubmed/26424542**](https://www.ncbi.nlm.nih.gov/pubmed/26424542)
3. [**http://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(15)00015-6/fulltext**](http://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(15)00015-6/fulltext)
4. [**https://www.ncbi.nlm.nih.gov/pubmed/15076249**](https://www.ncbi.nlm.nih.gov/pubmed/15076249)
5. [**http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0001725**](http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0001725)
6. [**https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3895621/**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3895621/)
7. [**https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2948795/**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2948795/)

**Methods and analysis:** (full description of the study design)

* How the sample will be selected
* Interventions to be measured [not applicable]
* The sample size calculation (drawing on previous literature) with an estimate of how many participants will be needed for the primary outcome to be statistically, clinically and/or politically significant
* What outcomes will be measured, when and how
* A data analysis plan.

Notes:

* Need to get the number of health facilities (each type) in the Beira corridor. Because it’s not defined by an administrative region like province, we need to come up with a systematic way to decide which facilities are in the sample.

*Study population and data sources*

The population of interest consists of all patients taking antiretroviral treatment for HIV/AIDS in the Beira Corridor of Mozambique. We chose this area because it represents a relatively closed system; that is, patients rarely transfer into or out of the region for HIV care. The selected facilities would approximately represent different types of health facilities with respect to referral, e.g., Beira Central Hospital, District Hospitals, and health centers.

From health facility data, we would obtain the ART enrollment rate, the number of active ART patients, mortality rate among active patients. In the patient survey, we would ask how many and which facilities they have visited in the past year, and in which facility they first began ART.

When direct tracking LTFU patients is not feasible, an alternative approach is to measure everything else and calculate what is left over. The system we aim to characterize is shown in Figure 1. This can be represented as a system of differential equations or a Markov chain analysis.

* F1, F2 and F3 are facility types (e.g. referral hospital, district hospital, health center),
* The red letters “B” through “G” are rates of transfer between the facility types,
* F4 represents facilities outside of the region,
* “I” is the rate of transfer to facilities outside of the region,
* “A” is the rate of enrollment for HIV treatment,
* “J” is the mortality rate among active HIV patients in the region,
* “H” is the rate of losing patients to follow-up.

Figure 1. Rates of enrollment, mortality, loss to follow-up and facility transfer among HIV patients

The key point is to set up a study in which “I” is negligible by choosing a set of health facilities that represent a closed system. The enrollment rate *A* can be calculated as the total enrollment at all facilities (including double counting of patients) divided by the average number of facilities visited by HIV patients. The enrollment rate for each type of health facility (not shown) is the overall enrollment rate *A* multiplied by the proportion of patients who were first initiated on ART at the facility type. All other transition rates (inter-facility transfers and mortality) are obtained directly from the health facilities or the patient survey.

The overall rate of loss to follow-up *H* can be calculated as the enrollment rate *A* minus the mortality rate *J* (Equation 1).

H = A – (I + J) [Equation 1]

The same calculation can be made for each facility type *F1*, *F2* and *F3* using their specific enrollment and mortality rates, and the rates of transfer into and out of the facility type. For example, for facility type F1, the equation is:

HF1 = (AF1 + B + G) – (I + JF1 + C + F)

Adding more complexity to the model may be useful, for example, accounting for urbal/rural and male/female distinctions. This would necessitate an increase in sample size.

To report the results in number of patients, we apply these rates to the number of active patients reported by each facility type.

*Limitations*

This method minimizes the need to gather information from LTFU patients directly. However, it necessarily assumes that the number of facilities visited by LTFU patients in one year is the same as the number of facilities visited by active patients.

The main limitation is that we do not directly measure the parameter of interest: the rate of loss to follow-up. Rather, we measure everything else and estimate LTFU deductively. For that reason, this approach is subject to many sources of bias. The final results depend on all of the other information being accurate, an assumption that may be difficult to defend in a developing country where data quality tends to be low.

**Ethics and dissemination**

* Ethical and safety considerations and any dissemination plan (publications, data deposition and curation) should be covered here.