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# Risk factors and true outcomes for lost to follow-up individuals in an antiretroviral treatment programme in Tete, Mozambique

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**Summary** Scale-up of antiretroviral therapy (ART) in sub-Saharan Africa is a major public health priority, but ensuring long-term adherence to treatment is a growing concern. The objectives of this retrospective study were to determine risk factors and true outcomes for individuals lost to follow-up in a routine HIV/AIDS care programme in Tete, Mozambique. Between May 2002 and August 2007, 2818 individuals were initiated on ART and 594 (21%) considered lost to follow-up were actively traced. Risk factors for being lost to follow-up were: age between 16 and 35 years [odds ratio (OR) = 1.4, $P = 0.009$]; CD4 count <50 cells/$\mu$l (OR = 1.7, $P < 0.001$); time on ART <3 months (OR = 3.6, $P < 0.001$); tuberculosis infection (OR = 2.5, $P < 0.001$); and Kaposi's sarcoma infection (OR = 5.9, $P < 0.001$). Sixty-four percent (380/594) of patients lost to follow-up could not be traced. Of the 214 (36%) that could be traced, 118 (55%) were dead, 43 (20%) were transferred out, 7 (3%) were misclassified and 46 (22%) were true defaulters. Active tracing should be conducted routinely to better understand the reasons for defaulting and to provide evidence for action. Early mortality may be reduced by enrolling patients in care as early as possible and providing optimal adherence counselling in the first months.


## 1. Introduction

Scale-up of antiretroviral therapy (ART) in sub-Saharan Africa has resulted in 1.3 million individuals on treatment by the end of 2007, but still less than 50% of people in need of treatment are receiving it. Providing treatment to those in need remains the priority, but ensuring long-term adher-

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ence to treatment is a growing concern. A recent systematic review reported that only 60% of patients are still in care after 2 years in sub-Saharan Africa.[1]

Patients no longer in care are usually categorized as transferred to another facility, dead or lost to follow-up. Routine tracing of patients lost to follow-up is crucial to improve retention in ART programmes and ascertain true outcomes as part of monitoring and evaluation. Active tracing of lost to follow-up patients from programmes in South Africa and Malawi found that approximately 50% of patients were actually dead.[2,3] Understanding the reasons for defaulting from a programme helps to identify barriers to care. Reasons for loss to follow-up have included financial restraints such as transport and clinic costs.[4] In a study from Kenya, pregnancy, older age, advanced AIDS and adherence problems during the first 2 months were risk factors for loss to follow-up.[5] The objectives of this retrospective study were to determine possible risk factors and true outcomes for individuals lost to follow-up in a routine HIV/AIDS care programme in Tete province, Mozambique.

## 2. Materials and methods

### 2.1. Study site

The study site was the Tete Provincial Hospital (TPH) located in Tete, Mozambique (population 1.4 million), where the HIV prevalence is estimated to be 19% (15- to 49-year-olds).[6] The Provincial Health Department (Direcção Provincial de Saúde, or DPS), in collaboration with Médecins Sans Frontières (MSF) initiated ART provision in 2002 at TPH. No systematic tracing was done. By 2007, 21% of all individuals initiated on ART were documented as lost to follow-up. All treatment protocols were approved by DPS and complied with WHO guidelines. All HIV care, including ART, was provided free of charge. Patients entered the programme through voluntary testing and counselling (VCT), or inpatient and outpatient referrals. Standard follow-up included clinical and laboratory investigations at initiation of ART, at 2 weeks, at 1 month, and then monthly for the first 6 months. After 2005, stable patients were seen every 3 months thereafter. Additional visits with a counsellor were scheduled for patients with poor adherence to try to prevent defaulting. From September to November 2007, all patients initiating ART between May 2002 and August 2007 and documented as lost to follow-up were actively traced to ascertain their true outcomes.

### 2.2. Data collection and statistical analysis

Paper records were used for all visits to the HIV clinic. In addition, an electronic database was used for routine monitoring and evaluation of patients on ART. Loss to follow-up was defined by absence from the clinic for more than 60 days after the last expected visit. A 'true defaulter' was defined as a patient who was lost to follow-up, traced, and found to be alive but no longer in our ART programme. Individuals identified as lost to follow-up were actively traced by a team of office staff and community health workers. Hospital archives were searched for missing paper records at least twice. If a volunteer knew a patient outcome was 'dead' or 'transferred', this was recorded and that individual was not traced further. When possible, home visits were made. Patients found alive and defaulting were encouraged to return.

Statistical analysis was performed using Stata 10 (Stata Corp., College Station, TX, USA). Baseline characteristics were described using medians and interquartile ranges (IQRs) for continuous variables and counts and percentages for categorical data. Patient time to loss to follow-up was calculated from initiation of ART. A Kaplan-Meier plot was used to describe time to loss to follow-up and logistical regression was used to determine risk factors for loss to follow-up. Variables considered in the analysis for loss to follow-up and mortality included age, gender, baseline CD4 count <50 cells/μl, WHO stage (stages 1 and 2 vs. 3 and 4), mode of entry (VCT, or inpatient/outpatient referral), active Kaposi's sarcoma and active tuberculosis at last follow-up visit. Factors with a $P$-value < 0.1 on univariate analysis were included in a multivariate model. All tests and confidence intervals were considered to be significant at $P \leq 0.05$.

## 3. Results

Between May 2002 and August 2007, 2818 individuals were initiated on ART. At the beginning of the active tracing, 594 (21%) were considered lost to follow-up. Demographic characteristics of the entire study population are detailed in Table 1. Median follow-up period was 13.1 (IQR 3.9—26.0) months. The median follow-up time for those lost to follow-up was 3.5 months (IQR 0.5—11.8). Among those lost to follow-up, 263 (44%) were male and 509 (86%) were in WHO stages 3 or 4. Median baseline CD4 count for those lost to follow-up was 105 (45—177). Eighty-five (48%) were lost to follow-up within 3 months of ART initiation. Time to loss to follow-up is shown in Figure 1. On multivariate analysis, factors significantly associated with loss to follow-up were: age between 16 and 35 years [odds ratio (OR) = 1.4, $P$ = 0.009]; CD4 count <50 cells/μl (OR = 1.7, $P$ < 0.001); time on ART <3 months (OR = 3.6, $P$ < 0.001); concurrent tuberculosis infection (OR = 2.5, $P$ < 0.001); and concurrent Kaposi's sarcoma infection (OR = 5.9, $P$ < 0.001) (Table 2).

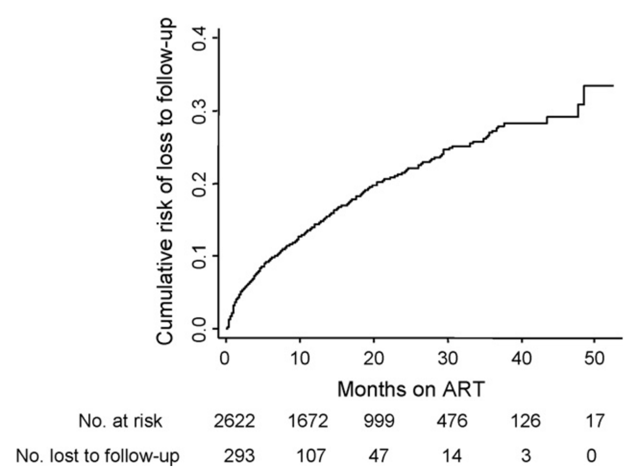


**Figure 1** Cumulative risk for loss to follow-up from an antiretroviral programme in Tete, Mozambique (excluding 190 patients lost to follow-up after the first visit).

**Table 1** Baseline characteristics of patients enrolled in an antiretroviral therapy (ART) programme, Tete, Mozambique, 2002–2007.

| | Total cohort | Lost to follow-up |
|---|---|---|
| Total | 2818 (100) | 594 (21.1) |
| Males | 1212 (43.0) | 263 (44.3) |
| Age on starting ART (years) | 34 (27–42) | 32 (26–40) |
| Median baseline CD4+ count (cells/μl) | 130 (68–198) | 105 (45–177) |
| Baseline CD4 <50 cells/μl | 285 (10.1) | 83 (14.0) |
| WHO clinical staging on starting ART | | |
| Stage 1 | 252 (8.9) | 45 (7.6) |
| Stage 2 | 243 (8.6) | 32 (5.4) |
| Stage 3 | 1392 (49.4) | 288 (48.5) |
| Stage 4 | 880 (31.2) | 221 (37.2) |
| Unknown WHO stage | 51 (1.8) | 8 (1.3) |
| Follow-up time on ART (months) | 13.1 (3.9–26) | 3.6 (0.5–11.8) |

Continuous variables are given as medians (interquartile range). Ordinal and discrete variables are given as *n* (%).

Sixty-four percent (380/594) of patients lost to follow-up could not be traced (Figure 2). Poor patient information was a major problem, with charts missing (145, 24%) or containing incorrect or incomplete information (77, 13%). Of the 214 (36%) that could be traced, 118 (55%) were dead, 43 (20%) were transferred out, 7 (3%) were misclassified (they were still in ART care), and 46 (22%) were true defaulters.

## 4. Discussion

We report the results of a large-scale loss to follow-up tracing for a district ART programme in rural Mozambique. This is the first published study from Mozambique on loss to follow-up in ART delivery. Overall, loss to follow-up was 21%. On active tracing, we found that over half of patients were actually dead, a finding consistent with reports from other sub-Saharan Africa programmes.[2,3] In our study patients with a CD4 count <50 cells/μl were 1.7 times more likely to be lost to follow-up. Several studies have found an association between low immune status and death as the cause of loss to follow-up, suggesting that the most vulnerable patients are precisely those who are most likely to be lost-to-care.[5] In our study patients with concurrent tuberculosis were 2.5 times as likely to be lost to follow-up, consistent with a study from South Africa.[3] Earlier initiation of ART may reduce mortality in co-infected patients.[7] Patients with Kaposi's sarcoma were five times as likely to be lost to follow-up. Kaposi's sarcoma is the most common AIDS malignancy and has also been found to be associated with high rates of mortality in ART programmes.[8] Patients who were lost to follow-up were more than three times as likely to have been on ART for <3 months. This points to the need to reinforce adherence support measures and clinical management during the first few months, particularly for those who start treatment with a low baseline CD4.

The main limitation of our study was that almost two-thirds of patients who were initially classified as lost to follow-up could not be traced. Many paper records were

**Table 2** Adjusted associations between baseline characteristics and loss to follow-up for patients enrolled in an antiretroviral therapy (ART) programme, Tete, Mozambique, 2002–2007.

| | Unadjusted | | | Adjusted | | |
|---|---|---|---|---|---|---|
| | Odds ratio | (95% CI) | *P*-value | Odds ratio | (95% CI) | *P*-value |
| Age (reference older than 35 years of age)[a] | | | | | | |
| 16–35 years | 1.5 | (1.3–1.9) | <0.001 | 1.4 | (1.1–1.9) | 0.009 |
| 0–15 years | 1.0 | (0.7–1.4) | 0.879 | 0.9 | (0.4–2.0) | 0.745 |
| Male | 1.1 | (0.9–1.3) | 0.483 | – | – | – |
| WHO stage (reference stage 1–2)[a] | | | | | | |
| Stage 3 | 1.4 | (1.1–1.9) | 0.013 | 1.3 | (0.9–2.0) | 0.133 |
| Stage 4 | 1.8 | (1.4–2.4) | <0.001 | 1.3 | (0.9–2.0) | 0.215 |
| Baseline CD4 count <50 cell/μl | 2.0 | (1.5–2.7) | <0.001 | 1.7 | (1.2–2.3) | 0.002 |
| VCT as entry point (reference IPD/OPD) | 0.7 | (0.5–0.9) | 0.002 | – | – | – |
| <3 months on ART | 5.0 | (4.1–6.1) | <0.001 | 3.6 | (2.7–4.8) | <0.001 |
| Concurrent tuberculosis infection | 5.0 | (3.7–6.8) | <0.001 | 2.5 | (1.6–3.9) | <0.001 |
| Concurrent Kaposi's sarcoma infection | 6.9 | (4.4–10.7) | <0.001 | 5.9 | (2.7–12.9) | <0.001 |

IPD: inpatient department; OPD: outpatient department; VCT: voluntary counselling and testing.
[a] At ART initiation.

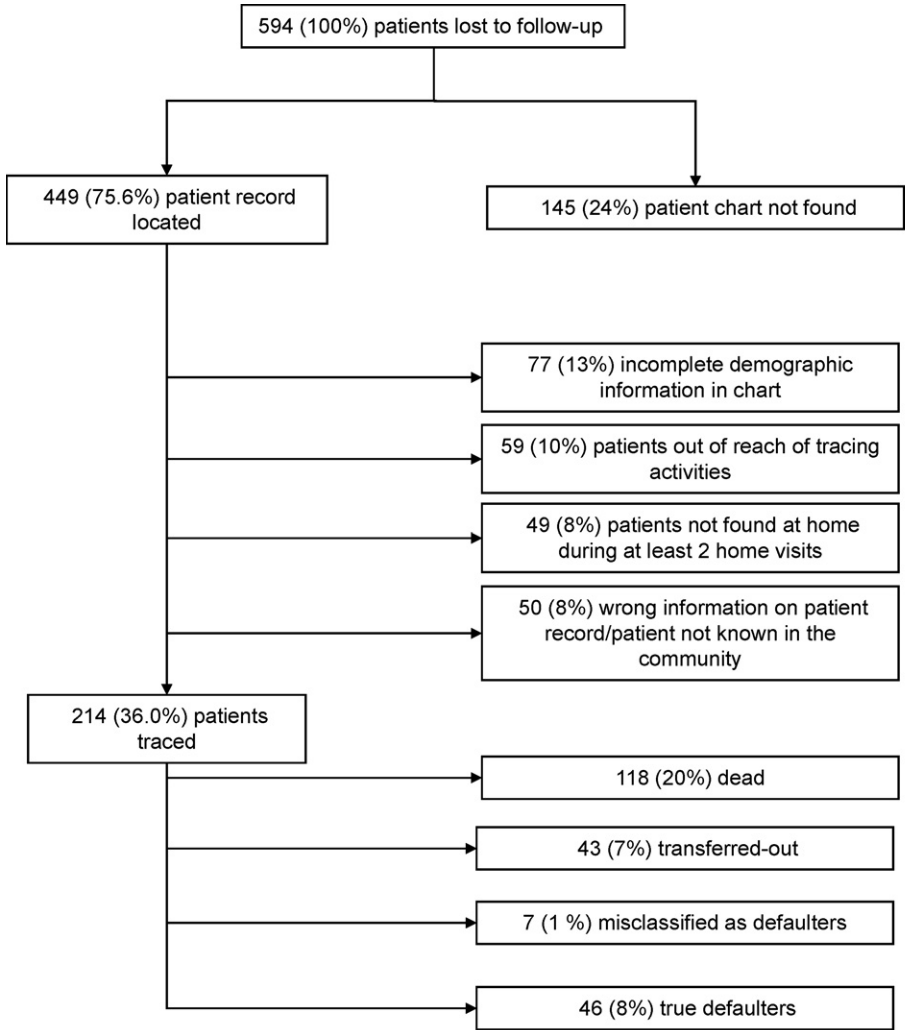


**Figure 2** Active tracing of patients lost to follow-up from an antiretroviral programme, Tete, Mozambique, 2002—2007.

missing, which may have been misfiled or lost, especially when the hospital archive was moved in 2007. The rapid scale-up of ART services outpaced the available human resources, resulting in poor record-keeping. Improved data-entry systems to ensure complete and accurate addresses of patients upon registration are essential. In the past, the programme depended on overworked counsellors to record demographic information. Partly as a consequence of this study, we have reinforced this aspect of the programme by reassigning this task to full-time receptionists, who ensure that all demographic data are correctly entered. An incorrect address in the paper record was a reason for being unable to trace some patients. Geographical proximity was a strict criterion for accessing care, but from 2002—2006 no other ART programmes existed in the province. We suspect that some non-residents gave false addresses in order to access care. Moreover, many patients were transferred out in 2007 during a rapid down-referral of stable patients to community clinic, which accounts for the high rate (20%) of transfers. Some patients may have been misclassified as lost to follow-up rather than transfers, and paper records may have been given to patients and therefore were missing during the tracing. In routine monitoring, it is important to conduct regular tracing of loss to follow-up patients. This way, these types of administrative errors can be identified early.

We believe our findings have a number of implications for managing loss-to-follow up in ART programmes in resource-constrained settings. First, active tracing should be conducted routinely to better understand the reasons for defaulting and to provide evidence for action. Knowing that the majority of lost to follow-up patients are likely to be dead, in our programme, death records from TPH are now being regularly reviewed to update the programme's database. Second, quantitative and qualitative analyses should be conducted to better understand the reasons for defaulting. Adequate paramedical staff such as counsellors are essential to provide patient education and adherence counselling and to conduct tracing activities within the communities. Finally, given that patients with low CD4 counts and active opportunistic infections are most likely to be lost to follow-up and that a large proportion of patients lost to follow-up have in fact died, much greater attention must be paid to reducing early mortality by enrolling people in care as early as possible and providing optimal adherence counselling in the first months.

**Authors' contributions:** All authors were responsible for the overall concept and design of the study; CC conducted the active tracing; FM and CC contributed to the data collection; FM and KC performed the data analysis; RM, NF and MB contributed to the intellectual content and writing of the paper; KC wrote the first draft of the paper. All authors reviewed and approved the final manuscript. KC is the guarantor of the paper.

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**Conflicts of interest:** None declared.

**Ethical approval:** General measures are provided at the Tete Provincial Hospital to ensure patient confidentiality, consent for HIV testing, and counselling and support for those who receive a positive HIV test result. The Mozambican National Health Science Research Committee provides general oversight and approval for the collection and use of routine programmatic data for monitoring and evaluation and did not require formal submission for ethical approval for this study, as it was undertaken as part of routine programme monitoring.

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