Declining Mortality in Patients on ART Lost to Follow-up in sub-Saharan Africa: Systematic Review and Meta-Analysis

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Background

- Anti-retroviral therapy (ART) has become widely available in low income countries with a high burden of HIV and AIDS, including in sub-Saharan Africa.
- Loss to follow-up (LTFU) is a common outcome in ART programs that hinders the ability to monitor key indicators of program effectiveness, such as mortality.
- Outcomes in patients LTFU can be determined by active tracing or linkage to mortality registries.
- A previous meta-analysis of tracing studies showed that mortality among successfully traced/linked patients was 40% (95% CI: 33% to 48%).[1]

Objectives

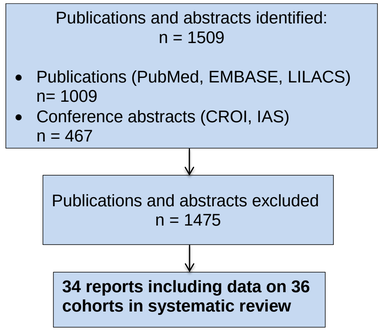
- We systematically reviewed tracing studies of adult and pediatric patients on ART in sub-Saharan Africa who were reported as LTFU to analyze changes in mortality over calendar time and rates of transfer from initial clinics to other clinics.

Methods

Data sources

- PubMed, EMBASE, LILACS databases and conference abstracts.

Figure 1



Inclusion criteria and data selection

- Published tracing studies where patients LTFU on ART in sub-Saharan Africa were actively traced or linked to vital registries
- Elegibility assessment by two independent reviewers
- Discrepancy resolution by third reviewer

Data extraction

- Data were extracted in duplicate and double-entered.

Statistical analysis

- We calculated exact binomial 95% confidence intervals for proportions.
- We used random-effects meta-analysis and meta-regression on logit transformed data to examine trends over time in mortality and transfers to other clinics.

Results

Characteristics of studies

- Figure 1 shows the process of identifying eligible studies. 36 cohorts were included.

	Studies n=36 (%)
Region	
West Africa	2 (5.6%)
East Africa	11 (30.6%)
Central Africa	1 (2.7%)
Southern Africa	22 (61.1%)
Setting	
Rural	5 (13.9%)
Urban	27 (75%)
Urban & rural	4 (11.1%)
Population	
Adults	30 (83.3%)
Children	4 (11.1%)
Adults & children	2 (5.6%)
Tracing method	
Telephone calls	2 (5.6%)
Home visits	13 (36.1%)
Combined approaches (Telephone calls, home visits, and social networks)	14 (38.9%)
Linkage to the civil registry	7 (19.4%)

Table 1: Characteristics of studies

- Definitions of LTFU varied from not seen for several weeks to not seen for over six months.
- Patients were traced by different methods (Table 1). In some studies in the Republic of South Africa, tracing was done by linkage to the civil registry.
- An estimated 31.5% (95% CI: 23.4% to 39.6%) were traced but not found.

Meta-regression analyses

- Mortality among patients LTFU declined over time (Figures 2,3). In meta-regression, mortality in adults and children combined declined from 53.1% in 2003 to 19.8% in 2010 (p=0.003).
- Mortality over all years was 36.8% in adults and 20.6% in children (p=0.034).
- Transfer out was reported in 18 studies. The proportion of patients transferred was 26.0% (95% CI: 21.7% to 30.4%) with no change with calendar year.
- The median CD4 cell count at the start of ART was reported in nine studies. Median counts increased from 71 cells/µL to 138 cells/µL.

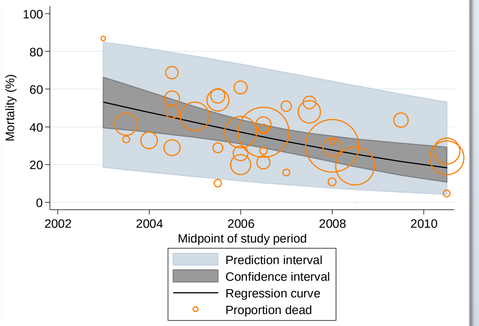
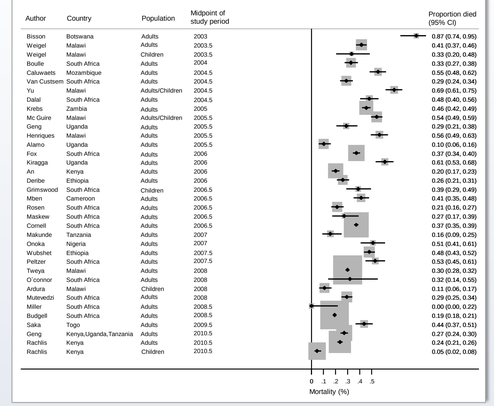


Figure 2. Estimated change in mortality over time among patients LTFU and successfully traced. Circle size is inversely proportional to the variance of estimates.

Figure 3. Forest plot of mortality among patients LTFU and successfully traced in 36 cohorts from sub-Saharan Africa



Conclusions

- Mortality among patients LTFU declined substantially with the scale up of ART in sub-Saharan Africa.
- This decline in mortality might be explained by an earlier start of ART, at higher CD4 cell counts.
- It does not appear to be explained by an increase in transfers to other clinics.

References

1.Brinkhof, M.W., M. Pujades-Rodriguez, and M. Egger, *Mortality of patients lost to follow-up in antiretroviral treatment programmes in resource-limited settings: systematic review and meta-analysis.* PLoS ONE, 2009. **4**(6): p. e5790.

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