USING MULTISTATE MODELS TO DISENTANGLE MORTALITY & LOSS TO FOLLOW-UP IN HIV+ PATIENTS

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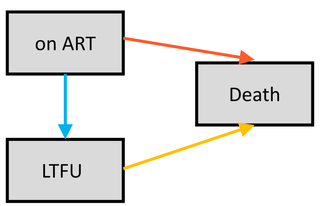
BACKGROUND

- Estimating mortality in HIV+ patients starting antiretroviral therapy (ART) is challenging because ART programmes often face substantial loss to follow-up (LTFU).
- Many studies ignore LTFU, leading to biased mortality estimates.
- Others correct using conventional methods which do not allow examining risk factors and mortality estimates separately for those LTFU and remaining in care.
- Multistate models can address this issue. They are widely used in epidemiology but have not been used in this context.
- Using data from rural northern Mozambique, we explored the use of multistate models to estimate mortality and risk factors for death in HIV+ patients starting ART.

METHODS

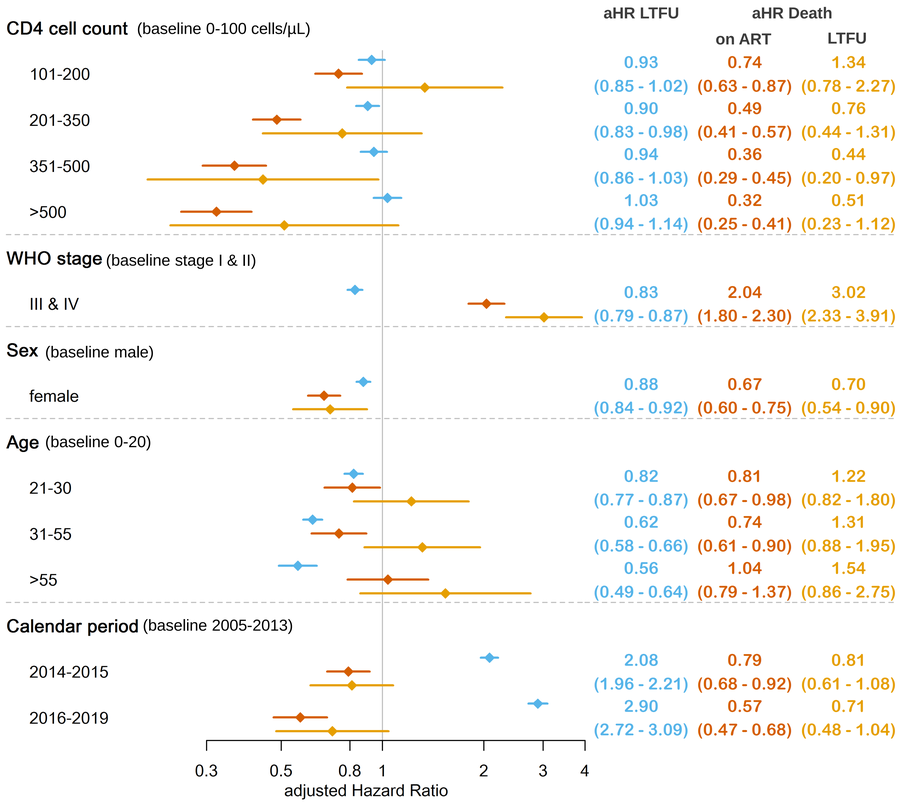
- We included HIV+ patients starting ART 2005-2018 in Ancuabe District, Mozambique where patients LTFU are traced by home visits.
- Risk factors were CD4 count, WHO stage, age, sex and calendar period (all at ART start).
- We used a multistate illness death model without recovery to describe progression of patients between initial state *on ART* through intermediate state *LTFU* to final absorbing state *Death*.
- We fit the "best" parametric survival model to estimate:
  - State transition hazards & probabilities
  - Associations with possible risk factors



- For transition *LTFU* → *Death* we up-weighted traced patients to represent all patients LTFU (weights = inverse of probability of being traced and found).

Multistate models are an attractive method to deal with ***LTFU*** when ***estimating mortality*** in ART facilities.

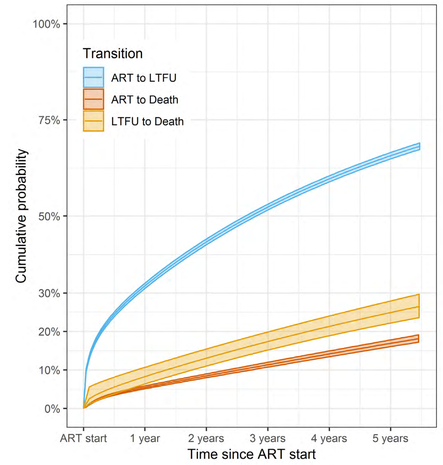
Figure 2: Adjusted Hazard Ratios (aHR) and 95% confidence intervals of risk factors for transition hazards



RESULTS

- A total of 17,342 patients were included. 1403 (8%) have died, 8817 (50%) were LTFU. 1342 (15%) of patients LTFU were traced and found, 46 (3.4%) of them had died.
- Crude cumulative probability of dying was higher in patients LTFU compared to those remaining in care (Figure 1). At 4 years after ART start, mortality was 14.1% (95% CI 13.5-14.9) in those in care vs. 21.3% (18.8-24.0) in those LTFU.
- Male sex, less advanced clinical stages, younger ages and starting ART in later calendar periods were all associated with an increased hazard of LTFU (Figure 2).
- For patients remaining in care, mortality was associated with lower CD4 cell counts, more advanced clinical stages, starting ART in earlier calendar periods and male sex (Figure 2).
- Results were similar for patients LTFU, but there was no association with calendar period, a more pronounced effect of WHO clinical stage on mortality and a less pronounced effect of CD4 count on mortality (Figure 2).

Figure 1: Cumulative transition probabilities



CONCLUSIONS

- Similar to conventional correction methods, multistate models allowed us to derive pooled mortality, but the models also provided estimates and risk factors separately for patients remaining in care and LTFU. They show that:
  - The clinics in Ancuabe District should give special attention to young and healthy patients: they are at increased risk of not returning to the clinic.
  - Risk factors for mortality are fairly similar among patients LTFU and patients remaining in care and include male sex, low CD4 cell counts and more advanced clinical stage.

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