To estimate the association between different patterns of engagement and subsequent mortality, we analyzed the temporal dynamics of patient retention and the heterogeneity in patient behaviors. Retention in HIV care is widely suboptimal across sub-Saharan Africa with patients frequently transitioning in and out of HIV care. Current analyses often (1) reduce highly-dimensional retention histories into cross-sectional summaries (i.e., LTFU) and (2) obscure patient heterogeneity behind population-level averages. Better characterization of these complex longitudinal retention patterns may help uncover distinctive patient engagement behaviors and improve our ability to target interventions for a diverse population. For example, similar retention patterns may point to similar challenges to remaining in care.

We used group-based trajectory analysis—a form of latent class analysis—to better understand the temporal dynamics of patient retention and the heterogeneity in patient behaviors.

Study Objectives

- To identify subgroups with distinct patterns of adherence and retention among patients newly started on ART in Zambia.
- To identify predictors of belonging to subgroups with a specific engagement trajectory.
- To estimate the association between different patterns of engagement and subsequent mortality.

Methods

Study Population

- HIV-infected adults newly started on ART between Aug 1, 2013 and Feb 1, 2015 at one of 64 clinics supported by the Centre for Infectious Disease Research in Zambia (CIDRZ).

- We used data on patient characteristics, clinical history, and visit history from the national electronic medical record system for HIV care (SinCare). We actively traced a random sample of patients LTFU (>90 days late for last visit) using a multistage sampling approach to ascertain mortality.

Analyses

- We used group-based trajectory analysis to identify patient subgroups that followed distinct longitudinal trajectories with regards to two outcomes (defined at every 30 day interval): (1) Medication possession ratio (MPR) over the past 3 months and (2) LTFU Status (>90 days late to the last appointment).

- Group-based trajectory analysis assumes that the population is made of distinct, but unobserved subpopulations with different behavioral patterns (form latent class analysis).

- Observed outcomes are used to estimate (1) the shape of the trajectory for each group and (2) the population-level distribution of each group.

- Number of groups is unknown a priori and final model chosen after systematic assessment of various specifications based on BIC.

- Other Model Specifications: (1) Time zero was data of ART initiation, (2) Patients censored at the time of death, transfer, or end of observation (i.e., July 31, 2015), (3) Excluded patients with less than 180 days of observation time (i.e., early deaths, transfers) in order to allow individuals sufficient time to differentiate into a trajectory, and (4) Used sampling weights to account for tracing outcomes.

Predictors of trajectory group membership and risk of mortality by trajectory group membership:

- We used the BCH method to identify associations between trajectory group membership and individual patient characteristics or outcomes. (1) Estimate each individual’s probability of belonging to each trajectory group given their observed outcomes (i.e., posterior probability), (2) Assign individuals to the trajectory group they are most likely to belong to based on posterior probabilities, and (3) Weight observations by the inverse of their classification error (i.e., the probability that they were assigned to that trajectory group when they belong to another) to account for misclassification of group membership.

- Predictors of trajectory group membership: Multinomial Logistic Regression including individual and group-level characteristics.

Motility Risk by Trajectory Group: (1) Survival analysis stratified by trajectory group with bootstrapped confidence intervals (time zero was date of ART initiation, administrative censoring at the time of transfer or end of observation, and (2) Adjusted Poisson regression to estimate incidence rate ratios (Cox PH model inappropriate due to non-proportional hazards).

- Models weighted to account for both classification error and sampling

- Multiple imputation (n=20) to address missingness in predictor variables

Results

Trajectory Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Consistently High MPR and retention (28.0%)</th>
<th>Suboptimal adherence early with late recovery, but consistent retention (22.0%)</th>
<th>Gradually decreasing MPR and retention (21.3%)</th>
<th>Early nonadherence/LTFU without recovery (8.5%)</th>
<th>Late nonadherence/LTFU without recovery (10.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean Classification Error (i.e., probability of being assigned to the “true” trajectory group): 0.912

Entropy for Overall Model: 1.957 (indicates good separation between trajectory groups)

Results (cont.)

Risk of Mortality by Trajectory Group

<table>
<thead>
<tr>
<th>Group</th>
<th>Consistently High MPR and retention (28.0%)</th>
<th>Suboptimal adherence early with late recovery, but consistent retention (22.0%)</th>
<th>Gradually decreasing MPR and retention (21.3%)</th>
<th>Early nonadherence/LTFU without recovery (8.5%)</th>
<th>Late nonadherence/LTFU without recovery (10.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Further studies should extend this approach to better understand longitudinal changes in viral suppression.

Conclusions

- Characterizing the heterogeneity in longitudinal retention trajectories provides a richer understanding of patient behavior and patterns of retention that may be obscured by cross-sectional assessments of bias to follow-up.

- Different retention behaviors are associated with substantially different risk of mortality.

- There is an urgent need to better understand both the baseline and longitudinal drivers of these heterogeneous engagement behaviors.

- Deeper understanding of the drivers of this heterogeneity in patient behaviors could be used to better target interventions to patients when they need them.

Implications

- This work was supported by the University of California San Francisco–Glendale Institute of Virology and Immunology Center for AIDS Research (CFAR) and the University of California San Francisco–Glendale AIDS Health Disparities Research Center (grant numbers P30 AI027766, the National Institute of Allergy and Infectious Diseases [T32 AI000530], National Institute of Mental Health [K24 AI134413 to EHG], and the Bill and Melinda Gates Foundation [OPP10907]).

This work was supported by the University of California San Francisco–Glendale Institute of Virology and Immunology Center for AIDS Research (CFAR) Implementation Science Working Group, an NIH-funded program (grant number P30 AI027766), the National Institute of Allergy and Infectious Diseases [T32 AI000530], National Institute of Mental Health [K24 AI134413 to EHG], and the Bill and Melinda Gates Foundation [OPP10907].