Understanding Clinical Retention Effects on Mortality in North America with a Nested Trial Approach

Poster Q-09

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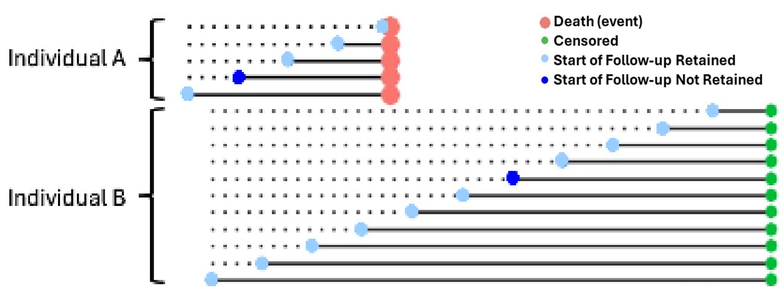
BACKGROUND

- **Goal:** Further explore the association between retention and mortality
- Previous work looked at time-fixed retention definitions (retained in both of the first 2 years) and we enhanced this by implementing a nested trial approach with time-updated and lagged retention

METHODS

- **Population:** People with HIV (PWH), ≥18 years old, enrolling in 13 NA-ACCORD clinical cohorts, surviving and enrolled until at least January 1, 2012. Excluded PWH missing demographic or care data, and with unknown date of death. Ended follow-up on December 31, 2023
- **Retention:** At least 2 encounters within 12 months, ≥ 90 days apart in the prior year
- **Outcome:** All-cause mortality where ascertainment relied on cohort/site-specific practices, most of which included Social Security Disability Insurance (SSDI) and National Death Index (NDI) linkage.
- **Statistical Analysis:** Multivariable weighted Cox Regression Model to estimate hazard ratios and 95% confidence intervals (CIs) for mortality by retention status
  - Created probability of treatment (retention) weights using logistic regression.
    - **Time-updated and lagged covariates**: age, year in care, CD4 count (<200, 200-499, ≥500, Unknown cells/μL), viral suppression (HIV RNA <200 copies/mL), AIDS diagnosis, ART receipt status, hypertension diagnosis, and diabetes diagnosis
    - **Time-fixed variables**: sex, HIV transmission risk, race/ethnicity, and NA-ACCORD site
  - Used a nested trials approach and created multiple episodes/baselines per individual with retention status and weights incorporating covariates updated on a yearly basis (**Figure 1**)

Figure 1. Schematic representing the contribution of person-time at risk for the event (all-cause mortality) in a hypothetical nested trial design.

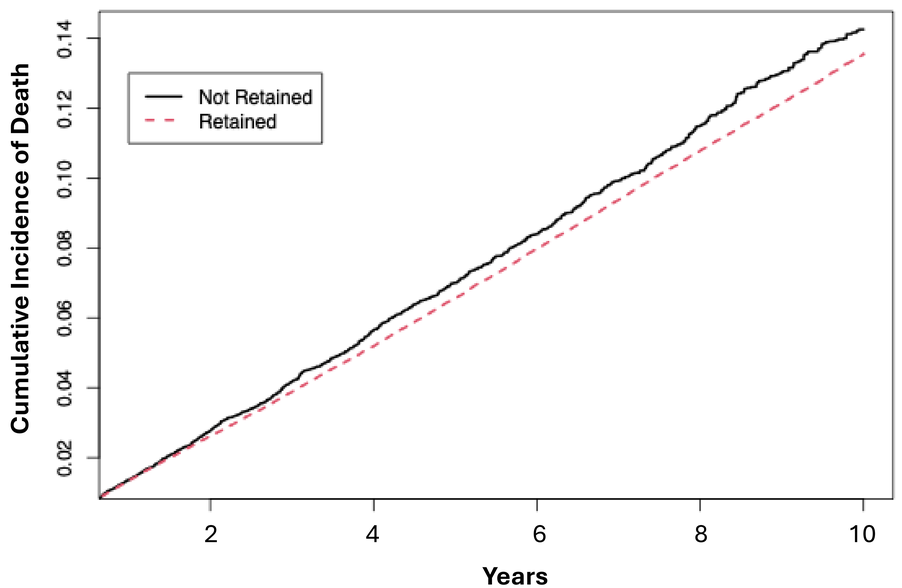


Clinical retention is slightly protective against all-cause mortality when using analytic approaches that accommodate a time-varying exposure, contrary to results from more typical time-fixed/cross-sectional approaches

Table 1. Time-to-Event Analysis

	N = 73,099
Number of events (%)	6,985 (9.6%)
Median Follow-up Time (years)	7.5
Total Person time (years)	562,554
Event Rates/1,000 Person-Years (95% Confidence Interval)	12.42 (12.13, 12.71)
Hazard Ratio from Nested Trial Model (95% Confidence Interval)	**0.94 (0.87, 1.00)**

Figure 2. Adjusted cumulative incidence of death for those people with HIV enrolled in clinical care within the NA-ACCORD comparing those retained in previous year to those not retained.



RESULTS

- Among 73, 099 PWH contributing 562,554 person-years, mean baseline age was 44 years (SD: 11.8), 80% were male, 43% non-Hispanic black, 60% men who have sex with men, and 11% people who inject drugs
- The weighted hazard ratio suggests a protective effect, but it is not statistically significant **(Table 1**)
- The risk of mortality is lower for those retained in care **(Figure 2**)
- Time-updated retention effect estimate is different than a previous analysis using a time-fixed retention analysis, which suggested a non-protective (harmful) association

CONCLUSIONS

- Slightly protective (non-significant) association between clinical retention and risk of mortality
- Time-updated retention provided a different effect estimate than a model with time-fixed retention, which suggests models using time-fixed retention measures may not accurately capture engagement patterns that predict key long-term outcomes
- Future research should address these gaps and adapt retention definitions to better quantify the quality of HIV care

LIMITATIONS AND NEXT STEPS

- This is an observational study and though we controlled for potential confounders, residual confounding may still be present
- We are considering additional outcomes including viral suppression

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