Mortality in the HIV Outpatient Study (HOPS), Trends and Risks 2007-2022

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BACKGROUND:

While persons with HIV (PWH) often survive into old age with ongoing ART use, tailoring interventions to optimize health and lifespan requires ongoing study of determinants of survival.

METHODS:

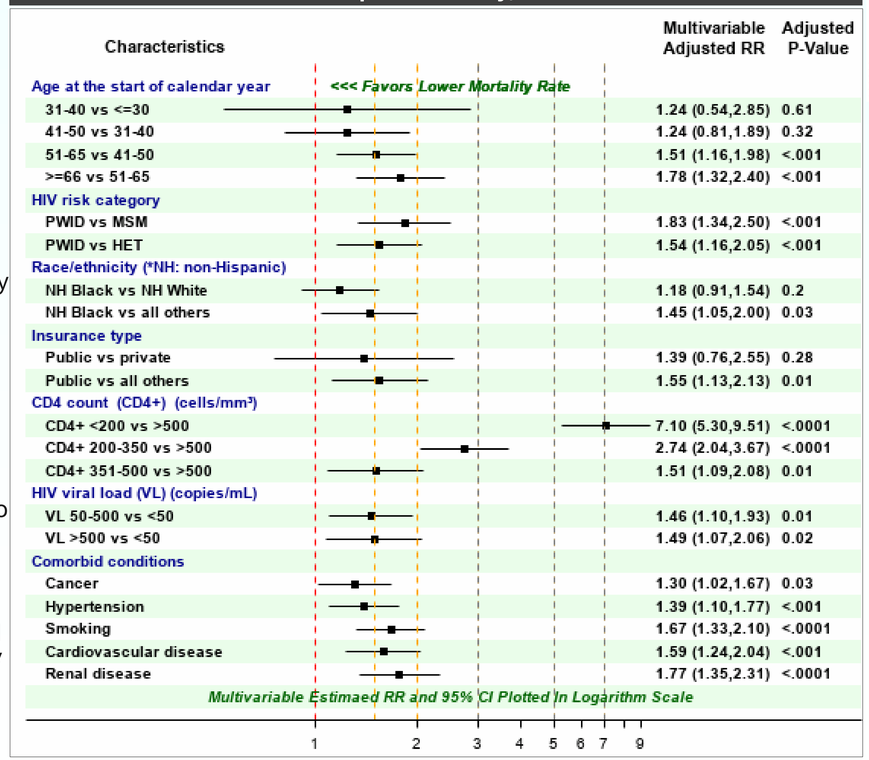
- Included were HOPS participants with ≥2 visits between 1/1/2007and 12/31/2022 who received ART continuously for ≥6 months and at least 75% of time under observation.
- PWH were followed from baseline (1/1/2007, or date of first HOPS visit thereafter) until death, or last contact date plus 6 months, or 12/31/2022. Deaths that occurred within 6 months of last contact were included.
- Univariable Poisson regression was used to generate overall and non-HIV/AIDS-related mortality rates by demographics and select risk factors. Multivariable Poisson regression with generalized estimating equation (GEE) was used for estimating adjusted mortality rates and rate ratio (RR). GEE model updated age in years and other death risks annually.

RESULTS:

- Of 4,859 participants, median age (interquartile range (IQR)) was 43 (33,49) years (yrs), 20% were women, 396 died, most from non-HIV/AIDS causes (n=307) during a median (IQR) of 7.0 (3.4,12) yrs. Median age (IQR) at death was 56 (49,63).
- Mortality rate (95% CI) were 1.3 (0.9,1.9) and 1.1 (0.7,1.8) per 100 person-years in 2007 and 2022, respectively.
- In multivariable models, having public insurance versus all other type of insurance (excluding private), was associated with greater all-cause mortality with RR (95% CI) of 1.55 (1.13,2.13).
- Non-Hispanic Black people, compared with White people, had higher non-HIV/AIDS related mortality rates (P<0.05), but not all-cause mortality.
- Other factors positively associated with overall mortality (P<0.05) were a history of injection drug use, and any of cardiovascular disease, renal disease, hypertension, smoking or cancer (Figure 1).
- The estimated increase in mortality when comparing PWH aged ≤30 years to those aged 31-40 years was not significant, while the risk increased exponentially when comparing PWH aged 41-50 years to those aged 65+ years.
- The magnitude of association with mortality risk was greatest for HIV related clinical factors (Figure 1), particularly low CD4 cell count, and including HIV viral non-suppression.
- Compared to PWH with CD4 cell count >500 cells/uL, lower CD4 count was associated with a higher mortality rate, especially below <200 cells/ul.
- Having VL>50 copies/mL was significantly associated with increased mortality risk (P<0.02) compared to having VL<50 copies/mL.
- Sex was not associated with mortality rate in adjusted analyses.

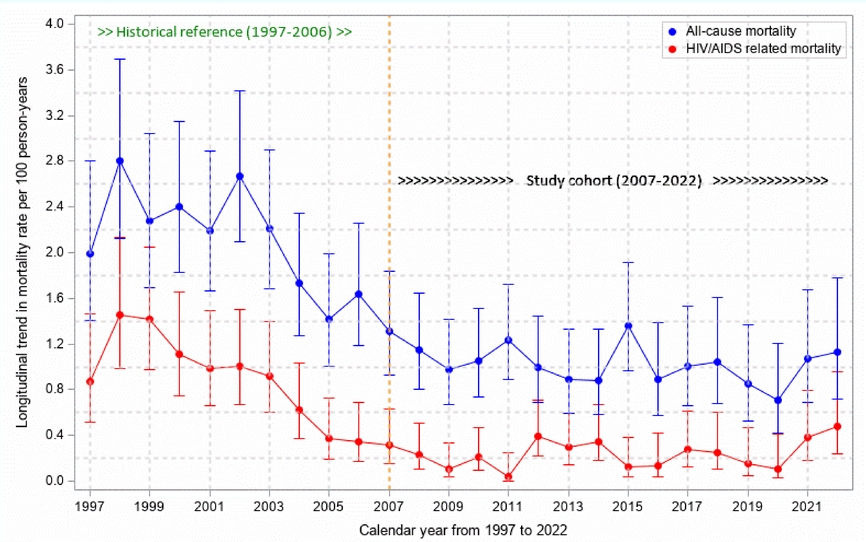
Among PWH receiving ART and mostly virally suppressed, mortality rates have remained low since 2007, and non-HIV/AIDS related causes of death have predominated. Nevertheless, HIV-related factors, particularly having lower CD4 counts, remain important determinants of mortality risk in this group.

Figure 1: Adjusted rate ratio of all-cause mortality using GEE analyses, the HIV Outpatient Study, 2007-2022.



Abbreviations: HET: heterosexual; MSM: men who have sex with men; PWID: people who inject drugs; NH; Non-Hispanic; RR: rate ratio. Notes: Overall mortality include HIV/AIDS related, non-HIV/AIDS related, and death without reason (lack of annotation). Poisson regression with GEE approach was used to model rate of mortality on a per 100 person-year basis. Three-year intervals were used to aggregate count of death for longitudinal analyses. Participants' age, comorbid condition, HIV viral load, and CD4 counts were continuously updated at the beginning of each three-year period. Categories in age, HIV viral load and CD4 counts were determined based on respective distribution.

Figure 2: Mortality rates per 100 PY among HOPS participants with ≥2 visits and consistent ART treatment from 2007-2022.



Notes: HIV/AIDS related mortality refers to cases with HIV/AIDS as at least one of the reasons for death in diagnosis annotation. Overall mortality include death of HIV-AIDS related, Non-HIV/AIDS related, and cases without documented reason of death. Mortality rate estimates from 1997-2006 were included for comparison with the study cohort from 2007-2022.

LIMITATIONS:

- Medical record data from HOPS-participating clinical care facilities may not be fully captured over time.
- Misclassifications may exist when assigning deaths as being HIV/AIDS-related and non-HIV/AIDS related.
- Assessment of mortality using the national death index did not occur from years 2020 to 2022.

CONCLUSIONS:

- **Among PWH with a high prevalence of ART use and viral suppression, mortality rates have remained very low (approaching 1%) since 2007, and non-HIV/AIDS related causes of death have predominated (Figure 2).**
- **Despite consistent high rates of ART use and virologic suppression, the greatest risks for death have remained HIV-related factors particularly having a lower CD4 cell count.**
- **Likewise, even low-level viremia has remained a significant risk factor for death**
- **Interventions to further optimize lifespan among aging PWH will require improvement in prevention and management of common non-HIV/AIDS related comorbidities as well as tight maintenance of virologic suppression to optimize immune health.**

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