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Early retention does not mediate/moderate the effect of sex/sexual behavior on survival

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BACKGROUND

- Early retention in care has been associated with decreased mortality among persons living with HIV (PLWH)[1,2]
- Sex at birth and sexual mode of HIV acquisition have also been shown to correlate with mortality[3,4]
- Retention in care may mediate, or else act as an effect modifier of, the observed relationship between sex/sexual mode of HIV acquisition and mortality
- We therefore assessed whether early retention in care mediates or modifies the association between sex/sexual mode of HIV acquisition and risk of mortality among PLWH using ART in the Americas

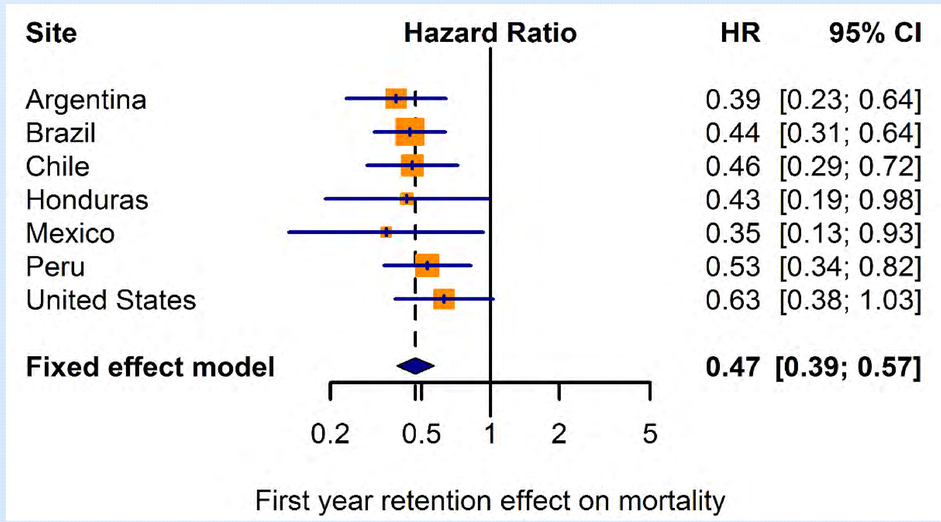
METHODS

- Population: ART-naïve, PLWH ≥18 years of age who enrolled after 2000, started ART after or ≤30 days prior to enrolment, and were in care ≥1 year after ART start at sites in North, Central and South America (the CCASAnet and the Vanderbilt Comprehensive Care Clinic cohorts)
- Definitions:
  - Early retention in care: ≥2 HIV care visits/labs ≥90 days apart in the first year after ART start
  - Sex/sexual mode of HIV acquisition, by self-report, categorized: women, heterosexual men, and men who have sex with men (MSM)
- Follow-up: one year after ART start date until date of death, last clinic visit, or study closure
- Analysis: Cox regression to assess associations between early retention and sex/sexual mode of HIV acquisition and mortality; interactions were also tested. Site-specific estimates were pooled using a Mantel-Haenszel fixed-effects model. Modified Poisson regression models were fit to assess whether sex/sexual mode of HIV acquisition was associated with early retention.

RESULTS

- Among 11,721 individuals included, 647 died and 1,985 were lost to follow-up, yielding mortality and lost to follow-up rates of 10.9/1000 and 33.6/1000 person-years beyond the first year after ART initiation
- Early retention in care decreased the risk of mortality one year after ART initiation across all sites (Figure 1)

Figure 1. Site-specific and pooled associations of early retention & mortality



Hazard Ratios adjusted for age, sex/sexual mode of HIV acquisition, nadir CD4, pre-ART AIDS defining illnesses, pre-ART HIV viral load, injection drug use and ART start year

- Sex/sexual mode of HIV acquisition was not associated with early retention (p>0.05); however, it was associated with mortality (aHR=0.75 for MSM [95%CI 0.61-0.92] and 0.92 for heterosexual men [95%CI 0.74-1.13] vs. women)

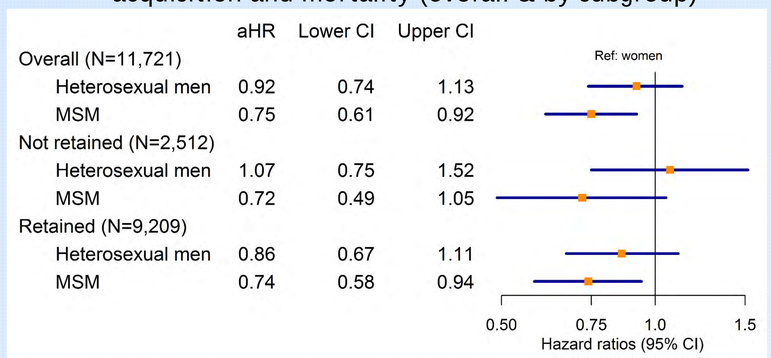
Table 1. Sex/sexual mode of HIV acquisition effect on mortality by site and pooled across sites (adjusted hazard ratios and Mantel-Haenszel fixed effects)

	Argentina	Brazil	Chile	Honduras	Mexico	Peru	United States	Pooled Effects
N	1896	2539	1567	595	1001	2512	1611	
Deaths	64	169	82	43	36	96	157	
Models with sex/sexual mode of HIV acquisition*								
Sex/sexual mode of HIV acquisition								
Women	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Het. men	0.9 (0.5,1.7)	1.1 (0.8,1.6)	0. 9 (0.4,1.8)	1.3 (0.6,2.7)	1.8 (0.6,5.4)	0.6 (0.4,1.0)	0.8 (0.5,1.2)	0.9 (0.7,1.1)
MSM	0.7 (0.4,1.2)	0.8 (0.6,1.2)	0.5 (0.3,0.9)	2.1 (0.8,5.5)	1.1 (0.4,3.3)	0.7 (0.4,1.1)	0.7 (0.5,1.0)	0.8 (0.6,0.9)
Models with sex/sexual mode of HIV acquisition and early retention*								
Sex/sexual mode of HIV acquisition								
Women	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Het. men	0.9 (0.5,1.7)	1.1 (0.8,1.6)	0.9 (0.5,2.0)	1.2 (0.6,2.6)	1.6 (0.5,4.9)	0.6 (0.4,1.0)	0.8 (0.5,1.2)	0.9 (0.7,1.1)
MSM	0.7 (0.4,1.3)	0.8 (0.6,1.2)	0.6 (0.3,1.1)	2.5 (0.9,7.4)	1.0 (0.3,3.1)	0.7 (0.4,1.1)	0.7 (0.5,1.1)	0.8 (0.6,0.9)
Retention	0.4 (0.2,0.6)	0.4 (0.3,0.6)	0.5 (0.3,0.7)	0.4 (0.2,0.9)	0.4 (0.1,0.9)	0.5 (0.3,0.8)	0.6 (0.4,1.0)	0.5 (0.4,0.6)

RESULTS (cont'd.)

- Results were similar in the model including retention (Table 1) suggesting early retention is not a mediator
- No interaction was found between sex/sexual mode of HIV acquisition and early retention (p-values all >0.05), suggesting it early retention is not an effect modifier
- Among those not retained, mortality risks were similar by sex/sexual mode of HIV acquisition: aHR=1.07 for heterosexual men vs. women, 95%CI: 0.75-1.52; aHR=0.72 for MSM vs. women, 95%CI: 0.49-1.05.
- Among those retained, mortality risks were similar to the aforementioned: nonsignificant for heterosexual men (aHR=0.86, 95%CI: 0.67-1.11), though significantly lower for MSM (aHR=0.74, 95%CI: 0.58-0.94) (Figure 2)

Figure 2. Pooled associations between sex/sexual mode of HIV acquisition and mortality (overall & by subgroup)



- These results again suggest that early retention is not an effect modifier of the association between sex/sexual mode of HIV acquisition and mortality.

CONCLUSIONS

Early retention in care was associated with a substantially decreased mortality risk after one year on ART. Additionally, MSM tended to have lower mortality risk than women. We found no evidence of early retention mediating or modifying the association between sex/sexual mode of HIV acquisition and mortality.

1 Beckham SW et al. Marked sex differences in all-cause mortality on antiretroviral therapy in low- and middle-income countries: a systematic review and meta-analysis. J Int AIDS Soc. 2016 Nov 8;19(1):21106.
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