

# Excess Mortality among PLWH with Multimorbidity Compared To HIV-Negative Controls: A Population-Based Cohort Study in British Columbia, Canada

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Life Expectancy and Mortality

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## Introduction

Antiretroviral therapy (ART) related gains in life expectancy have increased the likelihood of people living with HIV (PLWH) developing multimorbidity (i.e., the coexistence of multiple chronic comorbidities).

**Objective:** (i) To compare the prevalence of multimorbidity and all-cause mortality rates among PLWH and HIV-negative individuals, stratified by neighborhood-level income; (ii) To assess the impact of multimorbidity on all-cause mortality among PLWH; (iii) To examine which chronic comorbidities, experienced in isolation or in combination, led to higher mortality among PLWH.

## Methods

**Population-based cohort** study using longitudinal individual-level data on all treated PLWH and 1:4 age-sex-matched HIV-negative controls in British Columbia (BC), Canada.

**Eligible participants** were  $\geq 19$  years old and enrolled in the Comparative Outcomes and Service Utilization Trends (COAST) cohort Study between 2001 and 2012 for  $\geq 1$  year.

**Selected comorbidities** included liver, cardiovascular (CVD), renal, non-AIDS-defining cancers (cancers), hypertension (HTN), diabetes, and chronic obstructive pulmonary disease (COPD); identified from provincial administrative health databases (i.e., hospitalizations, outpatient physician, and pharmacy records).

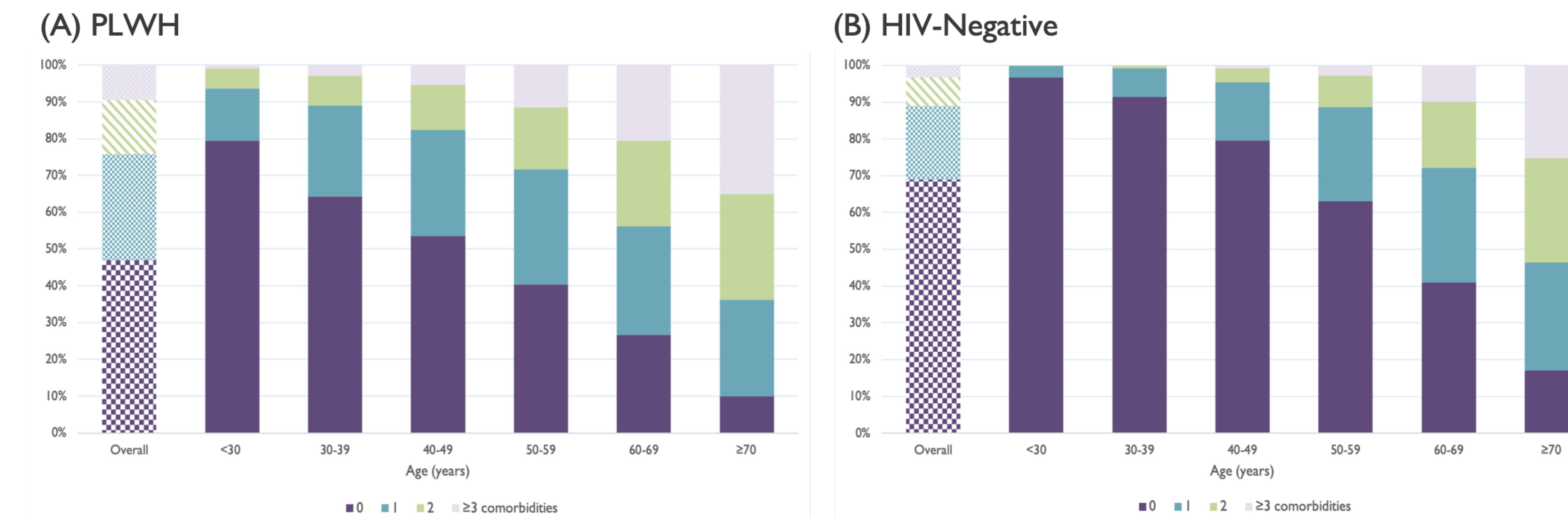
**Marginal structural models** estimated the risk of all-cause mortality among PLWH with 1, 2 and  $\geq 3$  comorbidities (versus none), adjusting for key time-varying confounders.

**Potential time-varying confounders** measured every year included age, lowest CD4 cell count, viral suppression, ART naïve status and ART adherence. Time-fixed confounders included sex at birth, risk group and ART initiation era.

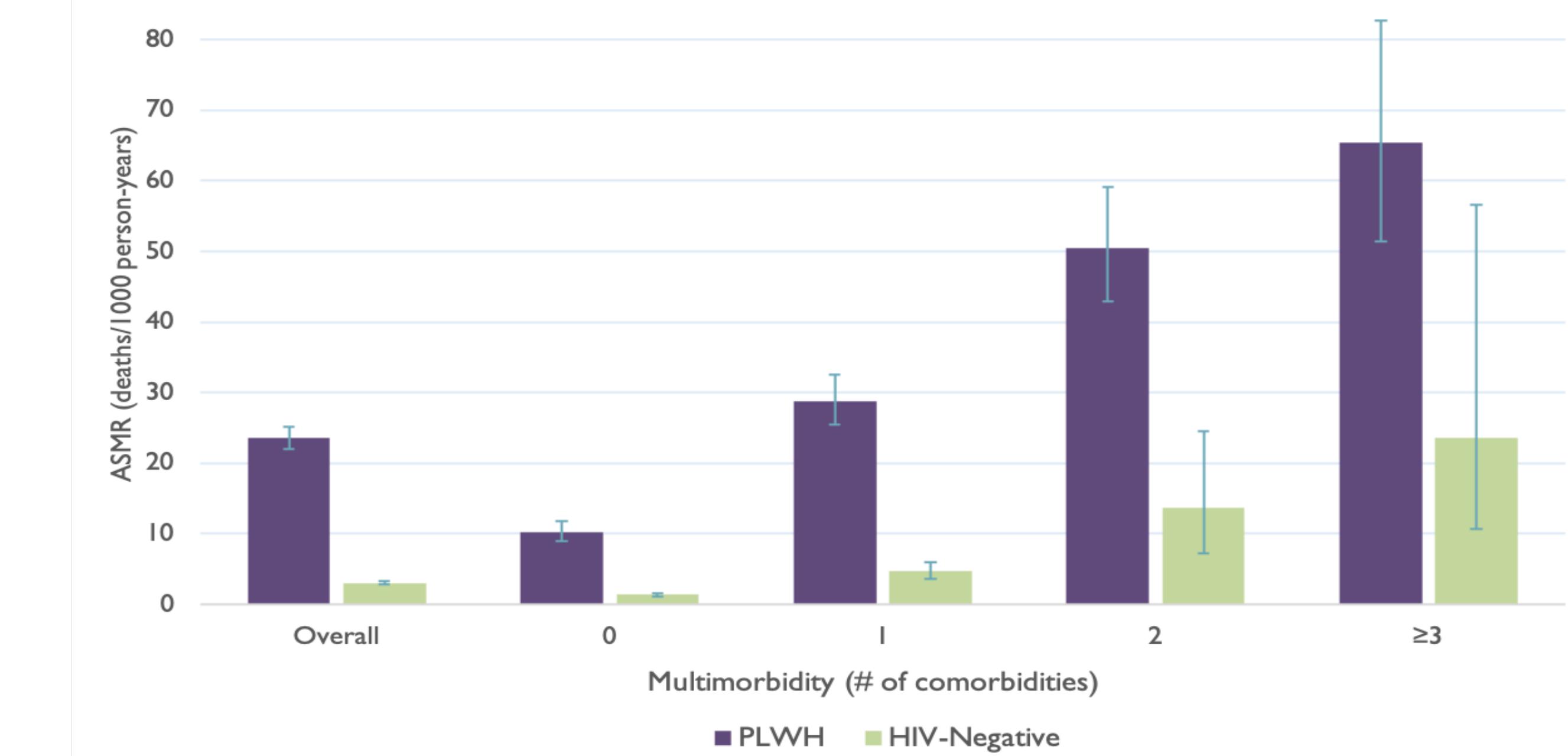
## Results

Analysis included 8,031 PLWH and 32,124 HIV-negative individuals (median age at baseline 40 years, 82% men, median follow-up 9 vs. 11 years).

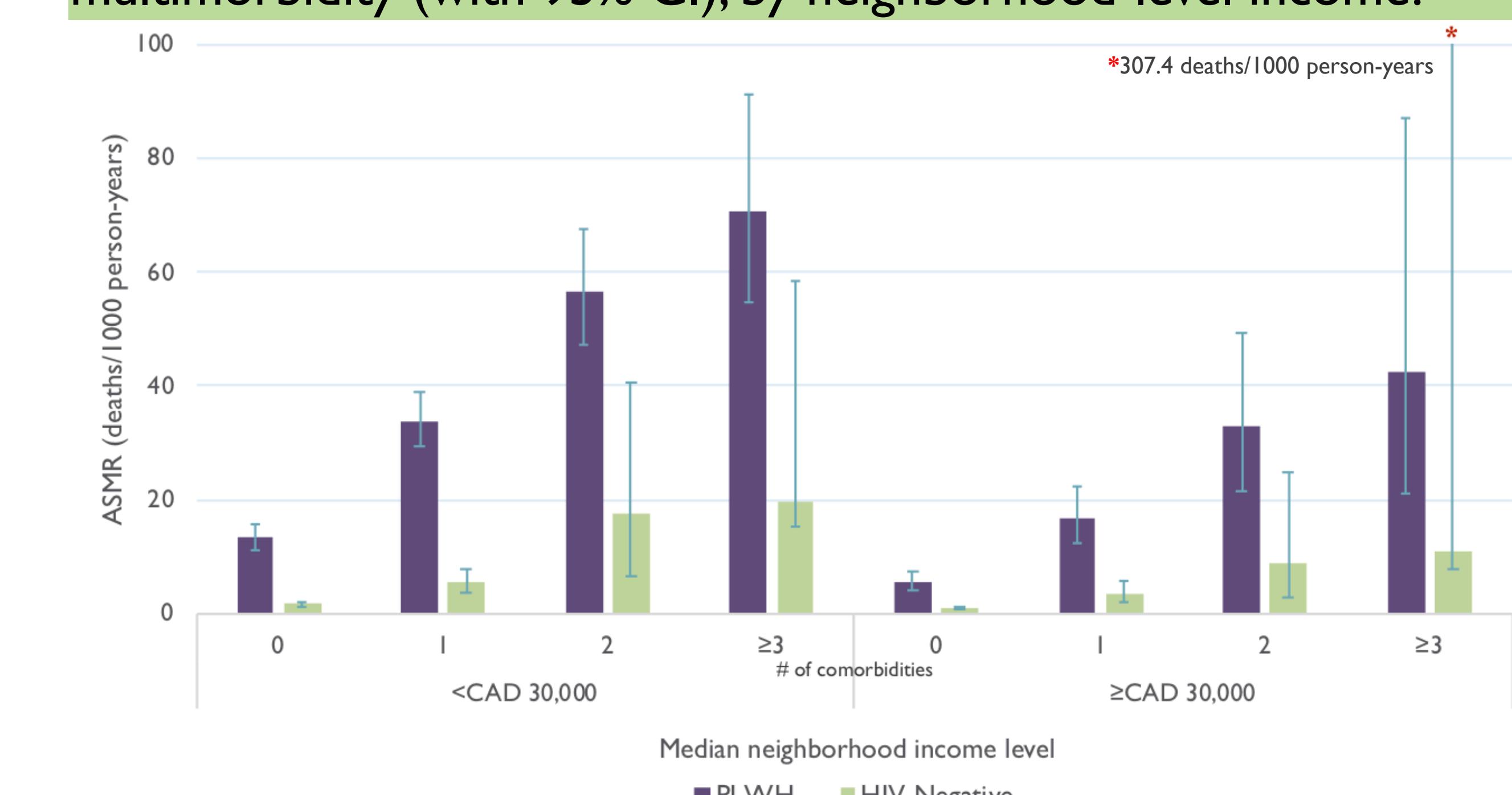
**Figure 1. Prevalence of multimorbidity, overall and across age groups.**



**Figure 2. Age-standardized mortality rates in deaths/1000 person-years (with 95% CI), stratified by multimorbidity groups.**



**Figure 3. Age-standardized mortality rates associated with multimorbidity (with 95% CI), by neighborhood-level income.**



- PLWH experience **higher multimorbidity**, which was comparable to HIV-negative controls who are 10-20 years older (Figure 1).
- PLWH also experience **higher age-standardized all-cause mortality rates** compared to HIV-negative individuals with the same number of comorbidities (Figure 2) and neighborhood-level income (Figure 3).
- Adjusting for time-varying confounders in PLWH, an increase in number of comorbidities was associated with increased **odds of mortality** (Table 1).
- A combination of **cancer-liver, cancer-COPD, and cancer-renal**, were associated with the three highest mortality rates among PLWH (Figure 4)

**Figure 4. Crude mortality rates in deaths/1000 person-years associated with chronic comorbidities, experienced in isolation or in combination, among PLWH.**

PLWH	Liver	Cancer	HTN	CVD	Renal	Diabetes	COPD
Liver	937 26.77 (23.13-30.42)						
Cancer	52 106.31 (72.06-140.57)	145 52.46 (39.08-65.85)					
HTN	102 20.13 (10.83-29.43)	26 37.07 (12.85-61.29)	463 7.33 (4.75-9.91)				
CVD	58 62.82 (39.55-86.08)	10 21.56 (-8.32-51.44)	82 10.41 (3.2-17.63)	109 36.02 (23.13-48.91)			
Renal	252 56.45 (46.04-66.86)	23 89.48 (44.2-134.76)	71 27.61 (14.86-40.37)	253 50.28 (23.94-76.62)	37 45.35 (35.65-55.05)		
Diabetes	50 14.64 (3.79-25.48)	9 40.78 (-5.37-86.93)	124 4.22 (0.52-7.91)	16 72.95 (22.4-123.51)	43 31.77 (13.50-55)	240 6.32 (3.01-9.63)	
COPD	104 28.78 (17.72-39.85)	18 104.57 (47.73-161.42)	36 16.32 (2.02-30.63)	23 34.83 (9.03-60.64)	25 65.69 (28.52-102.86)	20 11.18 (-4.31-26.67)	147 23.31 (14.83-31.79)

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**Table 1. Results of marginal structural model of the effect of multimorbidity on mortality among PLWH, adjusted for time-varying sociodemographic and HIV-related clinical confounders.**

Number of Comorbidities (0 = reference)	Overall aOR (95%CI)	Neighborhood-Level Income	
		<\$30000	≥\$30000
1	2.81 (2.29-3.45)	2.44 (1.87-3.19)	3.29 (2.31-4.70)
2	5.46 (4.3-6.94)	4.86 (3.62-6.52)	5.69 (3.74-8.65)
≥3	10.48 (7.88-13.93)	8.22 (5.67-11.9)	12.22 (7.68-19.45)

## Conclusions

Compared to HIV-negative controls with similar socioeconomic status, PLWH experienced substantial excess in multimorbidity and associated mortality. Among PLWH, we observed a positive dose-response between the number of comorbidities and the odds of mortality. These results highlight the critical role that additional comorbidities pose as drivers of morbidity and mortality among PLWH within a publicly funded ART program.

**Limitations:** administrative data is prone to coding errors; large confidence intervals; unable to adjust for lifestyle differences.