The Compounding Impact of Comorbidities on Mortality among People Living with HIV: A Marginal Structural Model Analysis in the COAST Study

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Background

- Due to the widespread use of modern combination antiretroviral therapy (ART) in high-income countries like Canada, HIV infection has become a chronic manageable disease.
- Extended time on antiretroviral therapy as well as aging increases the likelihood of developing other comorbid conditions in people living with HIV (PLWH). As a result, premature mortality from non-AIDS related causes are on the rise among PLWH.
- In this study, we examined the impact of comorbidities on all-cause mortality among PLWH in British Columbia, Canada, from 2000 until 2013.

Methods

- This retrospective cohort study was based on data from the Comparative Outcomes and Service Utilization Trends (COAST) study.
  - Which contains longitudinal, population-based data on PLWH in British Columbia, Canada.
- Eligible individuals ART-naïve, ≥19 years old, and initiated ART between January 2000 and March 2013, and were followed until the earliest of death date, 31/03/2013, or the last contact date.
- The main outcome was all-cause mortality occurring within the follow-up period.
- The main exposure was the presence of comorbidities identified using a validated case-finding algorithm (Charlson Comorbidity Index) and was categorized into i) Cardiovascular ii) Pulmonary iii) Liver iv) Diabetes v) Renal vi) Cancer and vii) Other diseases including dementia, peptic ulcer, para/ hemiplegia, connective tissue/rheumatic disease.
- Marginal structural modeling was used to estimate the longitudinal effect of having 1, 2, and ≥3 comorbidities versus none on mortality risk and to address the potential confounding between the main exposure and time-dependent confounders.
  - All models were adjusted for sex, age, cohort effect, HIV risk group, and treatment related factors.

Results

- Of the 5195 PLWH included in the analysis,
  - 58% had ≥1 comorbidity at baseline. The top three comorbidities were liver disease, pulmonary disease and cancer. (Figure 1)
  - 72% had ≥1 comorbidity by the end of the follow-up period. Figure 2 shows the distribution of deaths by comorbidity type at end of follow up.
- Those with ≥1 comorbidity were more likely to be female, older than 50 years, to have lower CD4 cell count at ART initiation, to have history of injection drug use, and to have started ART prior to 2008.

Results (cont.)

- The age-sex standardized mortality rates were 8.13/1000 person-years (PY) (95% Confidence Interval (CI): 3.92-18.11) for individuals without comorbidities, 25.53/1000PY (95% CI: 17.68-48.87) for individuals with 1 comorbidity, 32.48/1000PY (95% CI: 26.56-40.72) for individuals with 2 comorbidities and 51.22/1000PY (95% CI: 43.28-60.73) for individuals with 3 or more comorbidities.
- Marginal structural modeling showed that, compared to individuals with no comorbidity, those with 1, 2 or ≥3 comorbidities had significantly increased risk of mortality. (Figure 3)

Figure 1. Pattern of co-occurring comorbidities at baseline (showing only up to two conditions)

		Liver	Pulmonary	Cancer	Cardiovascular	Renal	Diabetes	Other: Dementia	Other: Peptic ulcer disease	Other: Paraplegia and hemiplegia	Other: Connective tissue/Rheumatic disease
	Liver	865									
	Pulmonary	328	728								
	Cancer	93	82	306							
	Cardiovascular	37	42	28	48						
	Renal	22	9	2	8	74					
	Diabetes	27	27	13	8	5	14				
Other	Dementia	26	10	6	8	2	5	73			
Other	Peptic ulcer disease	21	-	9	3	4	26	1	1		
Other	Paraplegia and hemiplegia	4	-	3	7	-	5	1	1	19	
Other	Connective tissue/rheumatic disease	31	40	4	3	3	4	-	1	1	87

Figure 2. The percentage of deaths by comorbidity type at end of follow-up

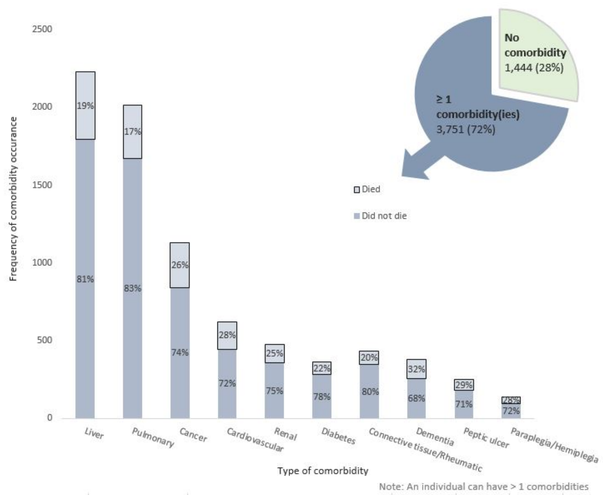
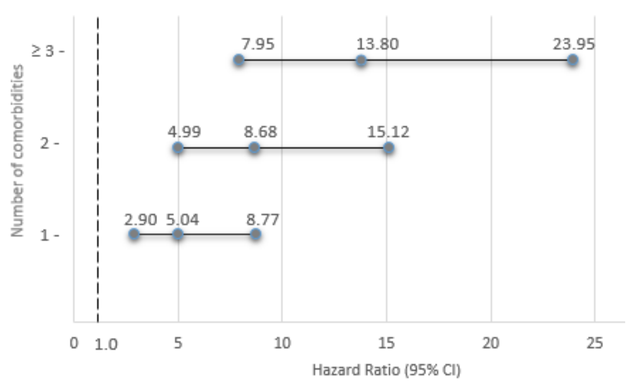


Figure 3. Hazard ratios* (95%CI) for mortality among PLWH who have comorbidity(ies)



*Estimated using marginal structural model adjusting for sex, age, cohort effect, HIV risk group, and treatment related factors. PLWH with no comorbidity are the reference group; their risk (1.0) is indicated by the dotted line.

Discussion

- There is a strong positive dose-response association between the number of comorbidities and mortality risk among PLWH.
- Further analyses are underway to investigate which comorbidities have the highest impact on the risk of mortality.
- Understanding this will help to inform and potentially redesign delivery of care for PLWH with specific comorbidity(ies).

CONFERENCE CAHR 2018

All inferences, opinions, and conclusions drawn in this poster are those of the authors, and do not reflect the opinions or policies of the Data Steward(s).