SYNDEMIC OF CHRONIC VIRAL INFECTIONS ON THE RISK OF END-STAGE RENAL DISEASE

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BC Centre for Disease Control
Provincial Health Services Authority

British Columbia Ministry of Health

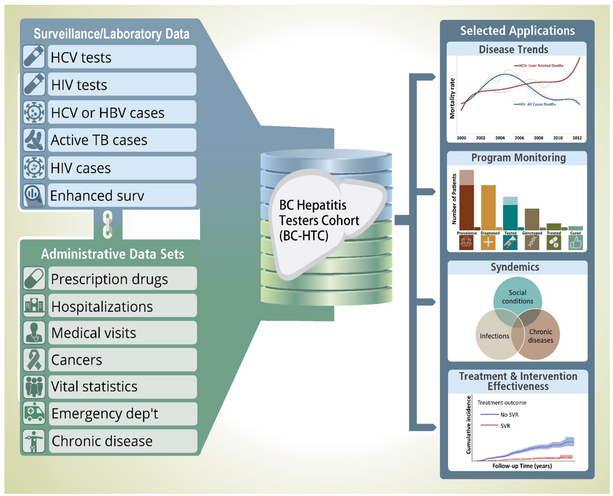
BC HTC British Columbia Hepatitis Testers Cohort

UBC

Background

- Untreated HCV infection is associated with increased morbidity and mortality due to hepatic and extrahepatic manifestations, including diabetes, chronic kidney diseases, and cardiovascular diseases. Previous studies showed evidence of the association between HCV infection and increased risk of chronic kidney disease (CKD) and end-stage renal disease (ESRD).[1,2]
- Syndemic of viral infections with hepatitis B virus (HBV) and human immunodeficiency virus (HIV) also increased the risk of kidney disease in individuals with HCV infection.[3,4] In addition, hypertension and diabetes are important risk factors of ESRD.
- We assessed the effect of HBV, HCV and HIV mono-, co-, and triple infections on incident ESRD, among people with and without hypertension or diabetes, in a large population-based cohort based in British Columbia (BC), Canada.

Methods



- This longitudinal cohort study used data from the BC Hepatitis Testers Cohort, which includes data on ~1.7 million individuals who are tested for HCV or HIV at the BC Centre for Disease Control (BCCDC), or reported as a case of HBV, HCV, or HIV in BC between 1990-2015, and integrated through a personal health number with administrative healthcare data.
- Individuals were followed from the date of their last diagnosis of HBV, HCV or HIV until the earliest of: i) incident ESRD, ii) death, iii) end of the study, **March 31st, 2021**.
- To assess the effect of each infection or multiple infections on incident ESRD, subdistributional hazard ratios (HR) and 95% confidence intervals were estimated by Fine-Gray competing risk models, with adjustment for sex, birth year, ethnicity, material/social deprivation, alcohol use, drug use disorder, major mental illness, opioid agonist therapy and injection drug use.
- We also examined the impact of infections on ESRD by baseline hypertension or diabetes status.

References

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3. Mocroft A, Neuhaus J, Peters L, Ryom L, Bickel M, Grint D, et al. Hepatitis B and C co-infection are independent predictors of progressive kidney disease in hiv-positive, antiretroviral-treated adults. PLoS One. 2012;7(7):1–10.
4. Rossi C, Cox J, Cooper C, Martel-Laferrière V, Walmsley S, Gill J, et al. Frequent injection cocaine use increases the risk of renal impairment among hepatitis C and HIV coinfected patients. Aids. 2016;30(9):1403–11.

Results

Table 1. Baseline characteristics of study population by HCV, HBV and HIV infection status

	Negative (n=627,273)	HBV mono (n=13,602)	HCV mono (n=38,067)	HIV mono (n=3,625)	HBV/HCV (n=3,657)	HBV/HIV (n=461)	HCV/HIV (n=2,982)	HBV/HCV/HIV (n=1,206)
Male sex (%)	266,174 (42.4)	6,678 (49.1)	24,320 (63.9)	2,896 (79.9)	2,424 (66.3)	411 (89.2)	2,153 (72.2)	832 (69.0)
Median age at last diagnosis (IQR), years	39 (31-51)	37 (29-49)	40 (32-48)	38 (30-48)	44 (35-53)	45 (36-54)	39 (32-46)	42 (35-49)
Ethnicity (%)								
East Asian	66,400 (10.6)	7,763 (57.1)	912 (2.4)	164 (4.5)	229 (6.3)	39 (8.5)	45 (1.5)	19 (1.6)
South Asian	50,514 (8.1)	619 (4.6)	1,181 (3.1)	178 (4.9)	87 (2.4)	11 (2.4)	32 (1.1)	9 (0.7)
Other	510,359 (81.4)	5,220 (38.4)	35,974 (94.5)	3,283 (90.6)	3,341 (91.4)	411 (89.2)	2,905 (97.4)	1,178 (97.7)
Injection drug use (%)	33,310 (5.3)	255 (1.9)	8,573 (22.5)	181 (5.0)	1,388 (38.0)	50 (10.8)	1374 (46.1)	826 (68.5)
Drug use disorder (%)	53,116 (8.5)	402 (3.0)	13,909 (36.5)	323 (8.9)	1,930 (52.8)	76 (16.5)	1832 (61.4)	957 (79.4)
Alcohol use disorder (%)	38,802 (6.2)	297 (2.2)	7,303 (19.2)	229 (6.3)	1,126 (30.8)	46 (10.0)	932 (31.3)	511 (42.4)
Hypertension (%)	95,616 (15.2)	1,366 (10.0)	2,832 (7.4)	296 (8.2)	478 (13.1)	68 (14.8)	170 (5.7)	96 (8.0)
Diabetes (%)	47,785 (7.6)	727 (5.3)	1,560 (4.1)	145 (4.0)	333 (9.1)	37 (8.0)	98 (3.3)	65 (5.4)
Material deprivation								
Q1 (most privileged)	144,482 (23.0)	2,521 (18.5)	5,496 (14.4)	1,140 (31.4)	476 (13.0)	155 (33.6)	536 (18.0)	201 (16.7)
Q5 (most deprived)	123,370 (19.7)	3,517 (25.9)	9,454 (24.8)	583 (16.1)	996 (27.2)	69 (15.0)	751 (25.2)	318 (26.4)
Social deprivation								
Q1 (most privileged)	106,167 (16.9)	2,776 (20.4)	4,763 (12.5)	388 (10.7)	419 (11.5)	41 (8.9)	193 (6.5)	56 (4.6)
Q5 (most deprived)	167,699 (26.7)	2,740 (20.1)	11,365 (29.9)	1,414 (39.0)	1,261 (34.5)	211 (45.8)	1,223 (41.0)	529 (43.9)
Major mental illness (%)	110,368 (17.6)	844 (6.2)	7,725 (20.3)	561 (15.5)	1,042 (28.5)	121 (26.2)	921 (30.9)	511 (42.4)

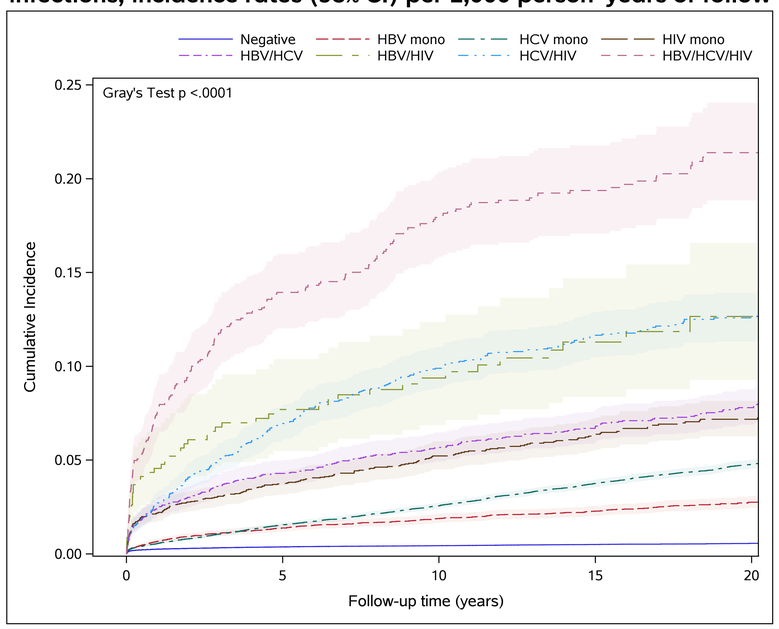
Table 2. Adjusted hazard ratios (95% CI) for the effect of viral infections on incident ESRD, overall, stratified by baseline diabetes/hypertension status

	Overall	No baseline diabetes	Baseline diabetes	No baseline hypertension	Baseline hypertension
Negative	Ref	Ref	3.72 (3.38-4.08)	Ref	4.07 (3.69-4.49)
HBV mono	3.54 (3.11-4.03)	3.87 (3.33-4.50)	17.61 (14.09-22.00)	4.83 (4.10-5.69)	16.65 (13.58-20.43)
HCV mono	4.27 (3.98-4.58)	5.15 (4.74-5.59)	18.42 (15.92-21.32)	7.16 (6.51-7.88)	14.77 (12.71-17.16)
HIV mono	7.91 (6.86-9.11)	10.37 (8.91-12.06)	19.55 (12.51-30.54)	13.39 (11.37-15.76)	25.40 (18.24-35.39)
HBV/HCV	6.07 (5.30-6.95)	7.32 (6.28-8.53)	18.40 (13.89-24.36)	10.78 (9.19-12.65)	15.69 (11.65-21.14)
HBV/HIV	12.75 (9.53-17.07)	15.90 (11.51-21.95)	39.97 (20.78-76.89)	21.39 (15.28-29.94)	41.29 (22.89-74.48)
HCV/HIV	11.25 (9.88-12.80)	14.52 (12.67-16.64)	24.33 (15.28-38.72)	20.03 (17.32-23.15)	19.72 (12.64-30.77)
HBV/HCV/HIV	16.94 (14.45-19.87)	22.45 (19.02-26.50)	27.73 (16.05-47.91)	30.46 (25.55-36.31)	36.78 (23.91-56.59)

Key Messages

- Persons living with **HBV/HCV/HIV triple infection** had **the highest risk of ESRD** and the risk increased with baseline diabetes and hypertension.
- Prevention and surveillance for ESRD is crucial for the aging population with viral infections, especially among those with other chronic comorbidities.
- Scaling up treatment of HBV, HCV and HIV infections may reduce the risk of ESRD. Further assessment is needed to evaluate the effect of treatment.

Figure 1. Cumulative incidence curves for incident ESRD among individuals with chronic viral infections, incidence rates (95% CI) per 1,000 person-years of follow-up (Table)



Negative	0.55 (0.53-0.57)
HBV mono	1.58 (1.42-1.76)
HCV mono	2.83 (2.7-2.97)
HIV mono	4.75 (4.18-5.41)
HBV/HCV	5.8 (5.14-6.54)
HBV/HIV	11.39 (8.59-15.12)
HCV/HIV	10.32 (9.28-11.47)
HBV/ HCV/HIV	23.23 (20.4-26.46)

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