SYNDEMIC OF VIRAL CO-INFECTIONS AND INCIDENT END-STAGE RENAL DISEASE

Dahn Jeong[1,2], Carmine Rossi[1,2], Stanley Wong[2], Zahid A. Butt[2,3], Geoffrey McKee[2,4], Jason Wong[1,2], Amanda Yu[2], Mawuena Binka[2], Maria Alvarez[2], Prince Adu[1,2], Mel Krajden[1,2], Naveed Janjua[1,2]; The BC Hepatitis Testers Cohort Team

[1]UBC Faculty of Medicine, Vancouver, Canada; [2]BC Centre for Disease Control, Vancouver, Canada; [3]UWaterloo Faculty of Applied Health Sciences, Waterloo, Canada; [4]Vancouver Coastal Health

BC Centre for Disease Control
Provincial Health Services Authority

British Columbia Ministry of Health

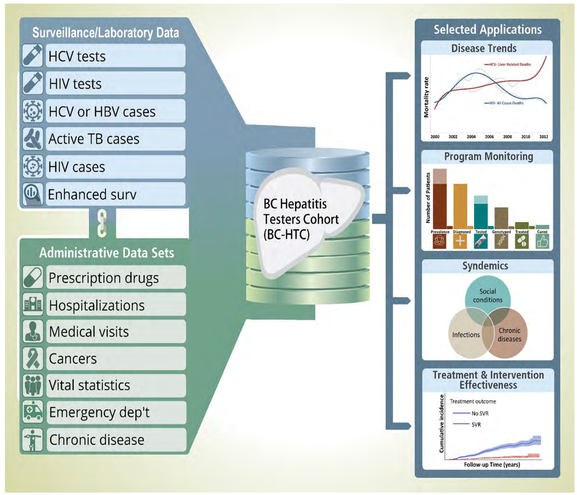
BC HTC British Columbia Hepatitis Testers Cohort

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]
- Additionally, it has been suggested that syndemic infections with hepatitis B virus (HBV) and human immunodeficiency virus (HIV) increased the risk of kidney disease in individuals with HCV infection.[3,4]
- Population-based estimates of the impact of syndemic co-infections are lacking. We assessed the effect of HBV, HCV and HIV co-infections on incident ESRD 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 since 1990, 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 case of ESRD, ii) death, iii) end of the study, December 31st, 2015.
- 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 age, sex, ethnicity, alcohol and injection drug use, social/material deprivation quintiles, and history of diabetes and hypertension.
- Stratified analyses were performed accounting for history of diabetes, or hypertension.

References
1. Fabrizi F, Messa P. The epidemiology of HCV infection in patients with advanced CKD/ESRD: A global perspective. Semin Dial. 2019;32(2):93–8.
2. Pagan J, Ladino M, Roth D. Treating hepatitis C virus in dialysis patients: How, when, and why? Semin Dial. 2019;32(2):152–8.
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=464001)	HBV mono (n=14129)	HCV mono (n=33855)	HIV mono (n=4657)	HBV/HCV (n=3285)	HBV/HIV (n=628)	HCV/HIV (n=2559)	HBV/HCV/HIV (n=1072)
Male sex (%)	204393 (44.1)	7088 (50.2)	21742 (64.2)	3951 (84.8)	2178 (66.3)	572 (91.1)	1843 (72.0)	738 (68.8)
Median age at last diagnosis (IQR), years	36 (29-47)	35 (28-46)	40 (32-48)	37 (30-46)	42 (34-51)	43 (35-50)	39 (32-46)	41 (34-47)
Urban density (%)								
Rural	39490 (8.5)	391 (2.8)	3449 (10.3)	200 (4.3)	280 (8.7)	27 (4.4)	112 (4.4)	32 (3.0)
Urban	423515 (91.5)	13572 (97.2)	29909 (89.7)	4411 (95.7)	2927 (91.3)	592 (95.6)	2429 (95.6)	1027 (97.0)
Injection drug use (%)	18348 (4.0)	306 (2.2)	6837 (20.2)	193 (4.1)	1227 (37.4)	67 (10.7)	1132 (44.2)	726 (67.7)
Drug use disorder (%)	34613 (7.5)	498 (3.5)	11884 (35.1)	360 (7.7)	1727 (52.6)	108 (17.2)	1538 (60.1)	846 (78.9)
Alcohol use disorder (%)	24533 (5.3)	342 (2.4)	6083 (18.0)	253 (5.4)	958 (29.2)	66 (10.5)	768 (30.0)	450 (42.0)
Hypertension (%)	55910 (12.1)	1154 (8.2)	2347 (6.9)	264 (5.7)	332 (10.1)	68 (10.8)	115 (4.5)	71 (6.6)
Diabetes (%)	28305 (6.1)	671 (4.8)	1329 (3.9)	139 (3.0)	266 (8.1)	49 (7.8)	73 (2.9)	50 (4.7)
Material deprivation								
Q1 (most privileged)	112856 (24.4)	2452 (17.5)	4350 (13.0)	1646 (35.6)	413 (12.8)	213 (34.4)	426 (16.8)	176 (16.7)
Q5 (most deprived)	78011 (16.9)	4003 (28.6)	10248 (30.5)	853 (18.4)	1060 (32.9)	117 (18.9)	924 (36.5)	437 (41.4)
Social deprivation								
Q1 (most privileged)	81517 (17.6)	3030 (21.6)	3404 (10.1)	382 (8.3)	287 (8.9)	53 (8.6)	127 (5.0)	41 (3.9)
Q5 (most deprived)	123022 (26.6)	3278 (23.4)	13572 (40.5)	2358 (51.0)	1493 (46.3)	358 (57.8)	1471 (58.1)	626 (59.3)

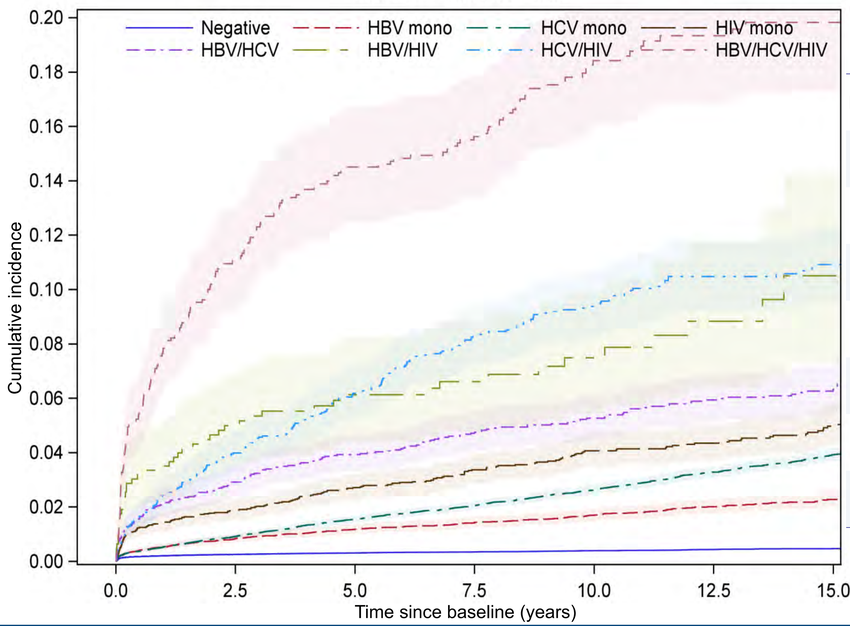
Table 2. Adjusted hazard ratios (95% CI) for the effect of syndemic infections on incident ESRD, overall, stratified by baseline diabetes/hypertension status

	Overall	No baseline diabetes	Baseline diabetes	No baseline hypertension	Baseline hypertension
Negative	1	1	2.96 (2.60-3.37)	1	4.55 (3.98-5.20)
HBV mono	4.61 (3.98-5.33)	4.33 (3.64-5.16)	16.25 (12.69-20.80)	5.57 (4.62-6.71)	17.69 (13.86-22.58)
HCV mono	6.14 (5.57-6.77)	6.11 (5.47-6.82)	20.06 (16.94-23.75)	7.87 (6.94-8.92)	18.86 (15.80-22.50)
HIV mono	9.21 (7.81-10.85)	10.13 (8.53-12.05)	14.05 (8.16-24.18)	12.57 (10.45-15.12)	19.11 (12.46-29.31)
HBV/HCV	8.29 (7.02-9.81)	9.02 (7.47-10.89)	19.33 (13.90-26.90)	12.38 (10.19-15.04)	21.46 (15.16-30.37)
HBV/HIV	16.78 (12.44-22.62)	17.78 (12.70-24.88)	41.80 (22.12-79.00)	23.11 (16.53-32.32)	46.44 (23.62-91.31)
HCV/HIV	18.72 (15.97-21.95)	20.39 (17.29-24.05)	18.60 (9.28-37.27)	25.13 (21.10-29.93)	19.69 (10.50-36.93)
HBV/HCV/HIV	34.18 (28.51-40.98)	37.80 (31.38-45.54)	45.90 (25.10-83.93)	46.98 (38.63-57.14)	52.79 (30.97-89.98)

Key Messages

- Persons living with **HIV/HBV/HCV triple infection** were at **the highest risk of ESRD**, and the risk was even higher in individuals with pre-existing diabetes and hypertension.
- Prevention and screening for ESRD in people with HIV/HBV/HCV **infections** and **coinfections** should be considered as an important part of the clinical care and management.
- Scaling up treatment of infections may reduce the risk of ESRD, further assessment is needed to evaluate the effect of treatment.

Figure 1. The cumulative incidence curves of incident ESRD among individuals with viral infections/coinfections, incidence rates (95% CI) per 1,000 person-years of follow-up



Negative	0.59 (0.56-0.62)
HBV mono	1.75 (1.55-1.97)
HCV mono	2.96 (2.80-3.13)
HIV mono	3.76 (3.27-4.33)
HBV/HCV	5.84 (5.09-6.71)
HBV/HIV	9.99 (7.53-13.26)
HCV/HIV	10.17 (8.96-11.55)
HBV/HCV/HIV	26.7 (23.2-30.72)

Web: http://bchtc.med.ubc.ca Follow on Twitter: @BCHepCo For more information, please contact Dahn Jeong (Dahn.Jeong@bccdc.ca)