Increased mortality among Indigenous persons in a multisite cohort of people living with HIV in Canada

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***Building Bridges research team**

Building Bridges consists of a research team in Toronto, Ontario and Vancouver, British Columbia. The nominated principal investigator was Mark Hull, located in Vancouver, and the Vancouver research team consisted of co-investigators Robert Hogg, Denise Jaworsky, Janet Raboud and Elizabeth Benson; additional research team members were Susan Giles, Evanna Brennan and Hasina Samji. Denise Jaworsky coordinated the project in Vancouver under the guidance of the Vancouver research team along with the Indigenous community advisory committee: Carol Kellman, Valerie Nicholson, Elder Doris Xele'milh Paul, Elder Roberta Price, and Flo Ranville. Mona Loutfy was the principal investigator in Toronto and the principal community investigator was Renée Masching. The Toronto research team consisted of co-investigators Anita C. Benoit, Doe O'Brien-Teengs and Janet Raboud. Jaime Younger conducted the data analyses for the Toronto Research team. Anita Benoit assumed direction of the project in Toronto under the guidance and expertise of the Toronto research team and assistance from Kerrigan Beaver, which includes the Indigenous community advisory committee, some of whom have requested to be listed: Kerrigan Beaver, Randy Jackson, Michael Keshane, Tony Nobis, Earl Nowgesic, Tera Tynes, Tonie Walsh, Spiritual Leader Wanda Whitebird and Art Zoccole. Toronto research team members substantially contributed to the conception and design, or acquisition of data, or analysis and interpretation of data.

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The CANOC principal investigators consist of Centre investigator Robert Hogg and Centre site investigators Ann N. Burchell, Curtis Cooper, Deborah Kelly, Marina Klein, Mona Loutfy, Nima Machouf, Julio Montaner, Janet Raboud, Chris Tsoukas, Stephen Sanche, Alexander Wong, Ahmed Bayoumi, Tony Antoniou, Bohdan Nosyk and Mark Hull. CANOC co-investigators include Angela Cescon, Michelle Cotterchio, Charlie Goldsmith, Silvia Guillemi, P. Richard Harrigan, Marianne Harris, Sean Hosein, Sharon Johnston, Claire Kendall, Clare Liddy, Viviane Lima, David Marsh, David Moore, Alexis Palmer, Sophie Patterson, Peter Phillips, Anita Rachlis, Sean B. Rourke, Hasina Samji, Marek Smieja, Benoit Trottier, Mark Wainberg [Dr. Mark Wainberg passed away after the manuscript was accepted for publication] and Sharon Walmsley.

ABSTRACT

OBJECTIVE: Compare all-cause mortality between Indigenous participants and participants of other ethnicities living with HIV initiating combination antiretroviral therapy (cART) in an interprovincial multi-site cohort.

METHODS: The Canadian Observational Cohort is a collaboration of 8 cohorts of treatment-naïve persons with HIV initiating cART after January 1, 2000. Participants were followed from the cART initiation date until death or last viral load (VL) test date on or before December 31, 2012. Cox proportional hazard models were used to estimate the effect of ethnicity on time until death after adjusting for age, gender, injection drug use, being a man who has sex with men, hepatitis C, province of origin, baseline VL and CD4 count, year of cART initiation and class of antiretroviral medication.

RESULTS: The study sample consisted of 7080 participants (497 Indigenous, 2471 Caucasian, 787 African/Caribbean/Black (ACB), 629 other, and 2696 unknown ethnicity). Most Indigenous persons were from British Columbia (BC) (83%), with smaller numbers from Ontario (13%) and Québec (4%). During the study period, 714 (10%) participants died. The five-year survival probability was lower for Indigenous persons (0.77) than for Caucasian (0.94), ACB (0.98), other ethnicities (0.96) and unknown ethnicities (0.85) ($p < 0.0001$). In an adjusted proportional hazard model for which missing data were imputed, Indigenous persons were more likely to die than Caucasian participants (hazard ratio = 2.69, $p < 0.0001$).

CONCLUSION: The mortality rate for Indigenous persons was higher than for other ethnicities and is largely reflective of the BC population. Addressing treatment challenges and identifying HIV- and non-HIV-related causes for mortality among Indigenous persons is required to optimize their clinical management.

KEY WORDS: Indigenous; mortality; HIV; cohort study; combination antiretroviral therapy

La traduction du résumé se trouve à la fin de l'article.

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Higher rates of mortality among Indigenous (as compared with non-Indigenous) persons have been attributed to circulatory and digestive system diseases, cancers, motor vehicle collisions, substance use, and HIV.[1–8] Data between 1991 and 2001 show that life expectancy at age 25 years was 4.7 and 6.5 years shorter for Indigenous men and women respectively, compared to their non-Indigenous counterparts.[1] Also, the probability of survival to 75 years was lower for Indigenous men (0.52 versus 0.65) and women (0.63 versus 0.80) compared to non-Indigenous men and women.[1] From 1995 through 1999, all-cause mortality among First Nations persons living in Manitoba was greater than that of all other Manitobans.[4] Inuit persons had lower life expectancy relative to the general Canadian population between 1989 and 2003.[7]

In Canada, the spread of HIV has disproportionately affected certain populations, including Indigenous persons.[9] Despite mortality having significantly declined due to advancements in antiretroviral (ARV) medications,[10] Indigenous persons living with HIV in Canada have elevated rates of mortality relative to Caucasians.[11–14] An international study of individuals with HIV on ARV therapy (ART), including sites in Europe, the United States, and the Canadian provinces of Alberta (AB) and British Columbia (BC), reported a trend towards elevated all-cause and HIV-related mortality for First Nations persons in Canada compared to white persons between 1998 and 2009.[11] Also of concern was that mortality among First Nations persons may have been underestimated due to their higher loss to follow-up at lower CD4 counts.[11] A separate study in AB revealed that HIV-positive Indigenous persons on their first ART regimen had higher all-cause and HIV-related mortality than persons of other ethnicities after adjusting for injection drug use (IDU).[12] Two cohort studies in BC showed that among participants initiating treatment between 1996 and 1999[13] and on or after January 1, 2000,[14] Indigenous persons had lower survival than non-Indigenous persons with HIV.

Studies to date that have evaluated all-cause and HIV-related mortality among Indigenous persons have included modest numbers of Indigenous persons with HIV, ranging from 90 to 200.[11–14] In addition, only one multi-provincial study evaluated mortality among Indigenous persons with HIV in Canada.[11] Furthermore, limited data are available on more recent experiences of Indigenous persons with HIV initiating cART in Canada, Australia, New Zealand, and the US.[15]

The purpose of this study was to include community-based research principles and Indigenous methodology to address an epidemiological question identified by Indigenous community members. This article presents the results of this process: a comparison of all-cause mortality between First Nations, Métis and Inuit people – collectively known as Indigenous persons – and persons of other ethnicities among individuals with HIV initiating cART since 2000, an era with substantial reductions in mortality due to improved ARVs; and an examination of trends over calendar time.

METHODS

Study methodology

"Building Bridges" was a collaborative project between Indigenous and allied stakeholders and the Canadian Observational Cohort (CANOC) Collaboration which used an Indigenous methodology and followed community-based research principles to conduct epidemiological health research. This collaborative process led to the establishment of an "Indigenous Health Epidemiology Model" which was used in our study.[16]

The Indigenous Health Epidemiology Model brings together Aboriginal or Indigenous perspectives and an epidemiological perspective.[17] The Indigenous perspectives resist methodologies

of Western science which validate colonized knowledge about Indigenous peoples.[18] An Indigenous methodology, characterized by recognizing Indigenous worldviews, knowledge, histories and realities as well as privileging Indigenous voices, peoples and lands, was used in this study.[17] This methodology enabled us to focus on Indigenous Peoples' priority health issues. Our research team also included an Indigenous advisory committee with diverse expertise in HIV and Indigenous health, clinical and social epidemiology, Indigenous methodology and ceremony, and lived experiences.[16] The Indigenous advisors guided the selection of the research questions, and informed the analysis plan as well as the reporting, interpretation and dissemination of the findings. Enhancing and building capacity also occurred during meetings to facilitate the interpretation of statistical data and to better understand the complex language used in biostatistics and/or epidemiology. Ceremony was present throughout the research process and steps to create an ethical space were taken.

Community-based research principles were applied in this study. The research team largely consisted of Indigenous persons, who selected the research questions, shaped the research process and determined how to implement Indigenous methodologies in the research process, all while being cognizant of the limitations associated with research conducted using a database.

Study design and population

This retrospective study was conducted using data from the CANOC collaboration, an interprovincial collaboration of 8 cohorts of people with HIV (as previously described; see ref.19). Participating provinces include BC (1 population-based site), Ontario (3 clinic-based sites and a multicentre cohort study) and Québec (3 clinic-based sites).

Participating sites submitted de-identified electronic demographic and clinical data to the BC data coordinating site. Eligible participants were 18 years and over, initiated cART on or after January 1, 2000, started a cART regimen consisting of at least three ARVs and had at least one measure of HIV plasma viral load (VL) and CD4 count within 1 year prior to or 15 days following the date of cART initiation. For this analysis, we excluded two clinics (one from Ontario and one from Québec) which did not collect ethnicity data.

Clinical variables included cART initiation date, baseline CD4 count and VL, baseline AIDS-defining illness (ADI), hepatitis B and C status (HBV and HCV), and class of cART regimen. Demographic variables included age, gender, ethnicity, province of residence and HIV risk factors, including a history of IDU and being a man who has sex with men (MSM).

Outcome

The primary outcome was time to death from any cause, defined as the time from initiation of cART until death, if it occurred. Persons who did not die during the study period were censored at the date of their last VL test. Loss to follow-up was defined as a last visit 18 months or more before death or the administrative censoring date.

Statistical analysis

Demographic and clinical characteristics were summarized by the following cultural and racial backgrounds that we will refer to as ethnicity: 1) Indigenous (i.e., First Nations, Métis and Inuit), 2) African, Caribbean or Black (ACB), 3) Caucasian, 4) other and 5) unknown. Frequencies and proportions were used to compare categorical variables and medians and interquartile ranges (IQR) for continuous variables. Characteristics were compared among ethnicities using the Pearson's χ^2 test or Kruskal–Wallis test for categorical and continuous variables respectively.

Kaplan–Meier curves were used to compare time to death by ethnicity. The association of Indigenous ethnicity with all-cause mortality was estimated with proportional hazard models after adjusting for confounding variables, including age, gender, IDU, MSM, HCV, province of origin, class of cART regimen, baseline CD4 count and VL, and year of cART initiation. In BC, death dates were collected via linkage to a population-based vital statistics database. In Ontario and Québec, death information was obtained from participating clinics. The consistency of the association of Indigenous ethnicity with death across provinces and calendar year was examined by fitting two proportional hazard models, one with an interaction term between province and ethnicity, where province was dichotomized to BC vs. Ontario and Québec, due to small numbers, and the other with an interaction term between calendar year of cART initiation (treated as a continuous variable) and ethnicity.

Models with inverse probability weights for censoring due to loss to follow-up were used to investigate potential bias in results due to differential loss to follow-up by ethnicity.[20] Missing values of ethnicity, MSM, IDU and HCV status were imputed with a substantive model compatible version of the fully conditional specification model.[21] A discriminant function was used to impute missing values of the categorical ethnicity variable and logistic regression models were used to impute missing values of binary variables IDU, MSM and HCV. All variables contained in the substantive model were used in the imputation models, as well as a specification of the survival distribution of time to death. Analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC) and R 3.3.1 (R Development Core Team, Vienna, Austria).

RESULTS

Study population

A total of 7080 participants were included in the analysis, of whom 497 were Indigenous, 2471 were Caucasian, 787 were ACB, 629 were other (ethnicities) and 2696 were of unknown ethnicity. Among participants, 5566 (79%) were male, the median age was 40 (IQR: 33–47), and 27% had a history of IDU. The median (IQR) duration of follow-up was 4.2 (1.9–7.4) years. Table 1 details demographics, risk factors and baseline clinical characteristics by ethnicity.

Rates of mortality

During the study period, 714 (10%) participants died. A log rank test indicated that there was a significant difference in time to death by ethnicity ($p < 0.0001$) (Figure 1A). The five-year survival probability was lower for Indigenous persons (0.77) than for Caucasian individuals (0.94), ACB persons (0.98), people of other ethnicity (0.96) and persons of unknown ethnicity (0.85) (Figure 1). Since the proportion of Indigenous participants for whom IDU was an HIV risk factor was substantially higher than for

Table 1. Demographic, risk factor, and baseline clinical characteristics by ethnicity

	Total (*N* = 7080)	Indigenous (*n* = 497)	ACB (*n* = 787)	Caucasian (*n* = 2471)	Other (*n* = 629)	Unknown (*n* = 2696)	*p*
Demographics							
Age (years)	40 (33–47)	39 (32–44)	37 (32–43)	41 (34–48)	37 (31–44)	41 (34–48)	<0.0001
Male	5566 (79%)	294 (59%)	367 (47%)	2154 (87%)	552 (88%)	2199 (82%)	<0.0001
Province							<0.0001
BC	4395 (62%)	413 (83%)	85 (11%)	1160 (47%)	252 (40%)	2485 (92%)	
ON	2035 (29%)	66 (13%)	460 (58%)	1113 (45%)	303 (48%)	93 (3%)	
QC	650 (9%)	18 (4%)	242 (31%)	198 (8%)	74 (12%)	118 (4%)	
Risk factors*							
MSM	2376 (34%)	98 (20%)	65 (8%)	1486 (60%)	403 (64%)	324 (12%)	<0.0001
IDU	1896 (27%)	357 (72%)	26 (3%)	724 (29%)	64 (10%)	725 (27%)	<0.0001
Heterosexual	2229 (31%)	262 (53%)	548 (70%)	1010 (41%)	228 (36%)	181 (7%)	<0.0001
Clinical							
Year of cART initiation	2007 (2003–2009)	2005 (2002–2008)	2006 (2003–2009)	2006 (2003–2009)	2007 (2003–2009)	2008 (2005–2010)	<0.0001
Regimen							0.42
PI based	3517 (50%)	246 (49%)	374 (48%)	1241 (50%)	299 (48%)	1357 (50%)	
NNRTI based	3302 (47%)	231 (46%)	376 (48%)	1133 (46%)	311 (49%)	1251 (46%)	
Baseline CD4 (cells/mm^3)	210 (106–316)	160 (80–270)	189 (102–277)	210 (105–313)	204 (90–290)	230 (120–350)	<0.0001
Baseline VL (log_{10} c/mL)	4.89 (4.39–5.10)	4.85 (4.38–5.00)	4.51 (3.97–4.96)	4.98 (4.53–5.23)	4.86 (4.34–5.18)	4.90 (4.40–5.03)	<0.0001
Baseline ADI	1120 (16%)	83 (17%)	119 (15%)	479 (19%)	124 (20%)	315 (12%)	<0.0001
Hepatitis B	391 (6%)	16 (3%)	70 (9%)	160 (6%)	62 (10%)	83 (3%)	<0.0001
Hepatitis C	2014 (28%)	351 (70%)	44 (6%)	750 (30%)	82 (13%)	787 (29%)	<0.0001

Note: Results are reported as frequency and percent, or median and interquartile range. ACB = African, Caribbean or Black; ADI = AIDS-defining illness; BC = British Columbia; cART = combination antiretroviral therapy; IDU = injection drug use; MSM = men having sex with men; NNRTI = non nucleoside reverse transcriptase inhibitor; ON = Ontario; PI = protease inhibitor; QC = Québec; VL = viral load.
* Risk factors are not mutually exclusive.

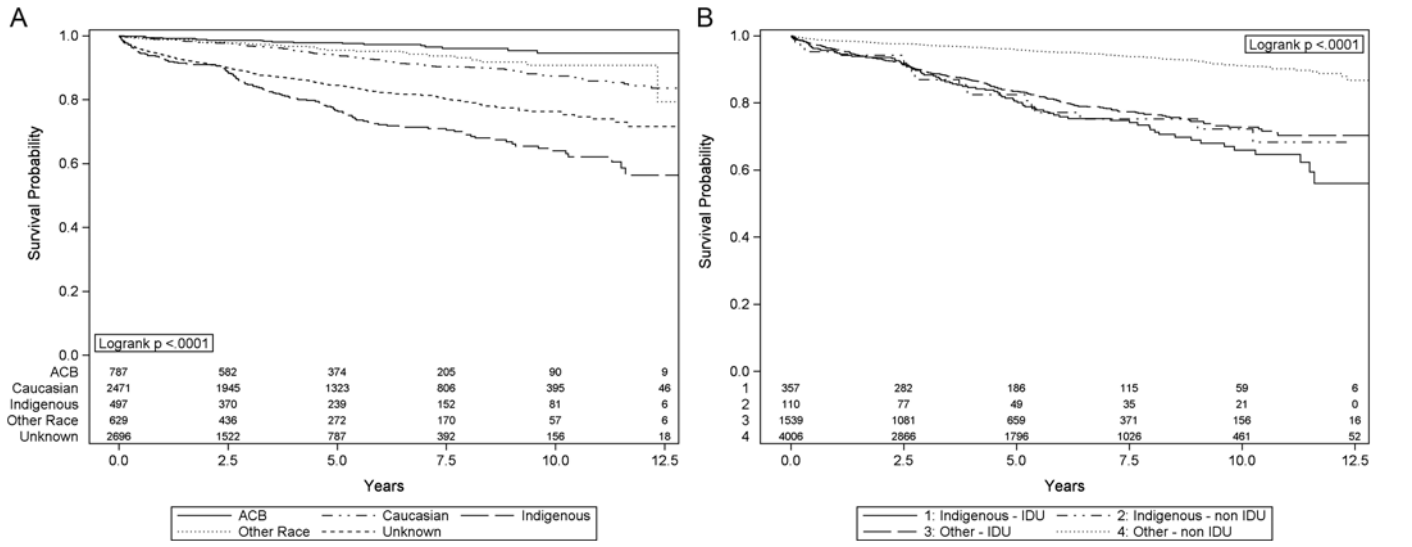

Figure 1. Probability of all-cause mortality by years since initiating cART (A) comparing persons living with HIV by ethnicity and (B) comparing persons living with HIV by Indigenous/non-Indigenous ethnicity and IDU/non-IDU status

other ethnicities, Kaplan–Meier estimates were calculated by IDU status and ethnicity to investigate the contributions of these two factors on mortality. Participants were classified as either Indigenous or non-Indigenous and IDU or non-IDU; those with an unknown IDU status were excluded (Figure 1B). Mortality rates were similar for Indigenous persons regardless of IDU status.

In a univariable proportional hazard model for which missing values of ethnicity were imputed, Indigenous persons were at increased risk of death (HR [hazard ratio] = 3.73, 95% CI: 2.95–4.71; $p < 0.0001$) compared to Caucasian persons. After adjusting for age, gender, IDU, MSM, HCV, province of origin, cART regimen, baseline CD4 count and VL, and year of cART initiation, the hazard ratio of mortality associated with Indigenous ethnicity was 2.69 (95% CI: 2.05–3.52; $p < 0.0001$) compared to Caucasian persons (Table 2). Mortality was not statistically significantly different between individuals identifying as ACB (HR = 0.73, 95% CI: 0.42–1.24;

Table 2. Univariable and multivariable time to death using proportional hazard models (n = 7080)

	Unadjusted model		Adjusted model	
	HR (95% CI)	***p***	**HR (95% CI)**	***p***
Ethnicity				
Caucasian	1.00		1.00	
Indigenous	3.73 (2.95–4.71)	<0.0001	2.69 (2.05–3.52)	<0.0001
ACB	0.35 (0.22–0.57)	<0.0001	0.73 (0.42–1.24)	0.24
Other	0.70 (0.49–0.98)	0.04	1.02 (0.72–1.46)	0.89
Age (per 10 years)	1.41 (1.31–1.51)	<0.0001	1.52 (1.41–1.65)	<0.0001
Gender				
Male	1.00		1.00	
Female	1.14 (0.96–1.36)	0.14	0.96 (0.78–1.18)	0.69
Transgender	1.84 (0.91–3.69)	0.09	1.03 (0.50–2.11)	0.94
Province				
ON	1.00		1.00	
BC	4.11 (3.23–5.22)	<0.0001	2.06 (1.59–2.68)	<0.0001
QC	1.29 (0.85–1.96)	0.23	1.47 (0.96–2.25)	0.08
MSM				
No	1.00		1.00	
Yes	0.47 (0.40–0.56)	<0.0001	0.91 (0.73–1.15)	0.44
IDU				
No	1.00		1.00	
Yes	3.64 (3.10–4.27)	<0.0001	1.34 (1.01–1.76)	0.04
Hepatitis C (ever/never)				
No	1.00		1.00	
Yes	3.82 (3.27–4.47)	<0.0001	1.86 (1.44–2.40)	<0.0001
Year of cART initiation	0.92 (0.90–0.95)	<0.0001	0.93 (0.91–0.96)	<0.0001
cART regimen				
Boosted PI	1.00		1.00	
II	0.78 (0.19–3.12)	0.72	1.11 (0.27–4.53)	0.88
NNRTI	0.81 (0.69–0.95)	<0.01	0.87 (0.74–1.02)	0.09
PI	0.83 (0.63–1.11)	0.21	1.07 (0.78–1.45)	0.68
Other	0.94 (0.62–1.41)	0.76	0.96 (0.63–1.45)	0.83
Baseline CD4				
<200 cells/mm^3	1.00		1.00	
≥200 cells/mm^3	0.53 (0.45–0.61)	<0.0001	0.70 (0.59–0.83)	<0.0001
Baseline VL				
<100 000 copies/mL	1.00		1.00	
≥100 000 copies/mL	1.56 (1.35–1.81)	<0.0001	1.32 (1.13–1.55)	<0.001

Note: ACB = African, Caribbean or Black; ADI = AIDS-defining illness; cART = combination antiretroviral therapy; HR = hazard ratio; IDU = injection drug use; II = integrase inhibitor; MSM = men having sex with men; ON = Ontario; NNRTI = non nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; QC = Québec; VL = viral load.

p = 0.24) and other ethnicities (HR = 1.02, 95% CI: 0.72–1.46; p = 0.89) relative to Caucasian participants. We also conducted analyses after incorporating inverse probability weights due to loss to follow-up. Results were very similar to the primary analyses (data not shown).

In order to investigate whether the increased risk of mortality among Indigenous persons relative to other ethnicities differed by geographic region, we fit an interaction term between ethnicity and province of origin, combining Ontario and Québec due to the small numbers of Indigenous persons in those provinces. The HR of death for Indigenous persons compared to Caucasian individuals in Ontario/Québec (HR = 1.80, 95% CI: 0.75–4.32) was not statistically significantly different from that in BC (HR = 2.64, 95% CI: 1.87–3.72) (p = 0.36).

We also evaluated a model with an interaction between ethnicity and calendar year of cART initiation. The HR of death for Indigenous persons compared to Caucasian individuals who initiated cART in 2000 was 1.96 (95% CI: 1.27–3.00). For each year past 2000, the HR of death for Indigenous persons compared to Caucasian persons was increased multiplicatively by 1.07 (95% CI: 1.00–1.15). Results were similar when the analysis was restricted to participants from BC: the HR of death for Indigenous persons compared to Caucasian individuals who initiated cART in 2000 was 1.97 (95% CI: 1.25–3.12), increasing multiplicatively by 1.08 (95% CI: 1.00–1.16) for each year past 2000.

DISCUSSION

In our study, Indigenous persons had a more than twofold higher mortality rate than Caucasian persons after adjusting for confounders, and the gap appears to be widening over time. Our finding is consistent with the literature, noting that there is some overlap between the population in our study and that of the ART Cohort Collaboration study.[11–13]

In other studies, factors shown to impact all-cause mortality among Indigenous persons with HIV included being on PI-based regimens in the first regimen, and having a less experienced HIV clinician, a history of IDU, lower educational attainment, and an income less than $10,000.[13] Also, comparison of HIV-related mortality between persons not on treatment and those having received treatment showed that Indigenous ethnicity, female sex, and low income were negatively associated with receiving treatment before death.[22] Since Indigenous persons experience elevated rates of all-cause mortality,[1,3–7,12] differences in mortality in our study may reflect these trends rather than differences due to living with HIV and cART use. A reported twofold increase in avoidable mortality in First Nations adults in Canada was explained in part by differences in education and income adequacy.[8] Risk ratios by specific causes of death were highest for alcohol and drug use (RR = 5.43 for men, RR = 10.11 for women), unintentional injuries (RR = 4.71 for men, RR = 4.91 for women) and diabetes mellitus (RR = 4.31 for men, RR = 7.97 for women). The gap in mortality between First Nations peoples and non-Indigenous people increased over the study period (1991–2006), although changes in relative risk for specific causes of death were not described.[8]

Only a moderate effect of IDU on mortality was seen in our study, after adjusting for confounders, possibly due to several reasons. First, there was a high correlation between Indigenous ethnicity and IDU. Seventy-two percent of Indigenous persons reported IDU as the likely mode of HIV transmission. Second, our IDU variable measured whether or not IDU was the likely source of HIV infection, was not time-updated during the study period and may not have reflected a participant's current status. Third, IDU status was unknown for 27% of participants, limiting precision of estimates associated with this covariate.

Persons with HIV who inject drugs have previously been shown to have higher mortality rates compared to MSM with HIV.[23,24] Higher mortality rates were reportedly due to lower ARV uptake and were attributed to ADIs.[24] In other studies, IDUs had similar responses to ARVs as non-IDUs and increased mortality was associated with non-HIV-related causes such as suicide, chronic liver disease and drug overdoses.[23] Suboptimal adherence has been associated with injection behaviours among current IDUs and social instability among former IDUs.[25] Social instability and differentiation between former and current IDU status was not

captured in CANOC. Both may inform the cause behind the comparable mortality rates among Indigenous persons with HIV with and without IDU as an HIV risk factor.

Strengths and limitations

Strengths of this study include its large sample size and large number of Indigenous persons. It is the largest study to date of Indigenous people with HIV in Canada.[11–13] Inclusion of only individuals who have initiated cART since 2000 allowed us to examine differences due to ethnicity in the modern cART era, when mortality rates were lower than in the era of dual therapy and monotherapy.[11–13] The interprovincial strength of CANOC also distinguishes our study from other publications evaluating mortality for Indigenous persons with HIV.[11–13]

There are a number of limitations to our study. First, since approximately 80% of Indigenous persons in CANOC are from BC, the findings may not be generalizable to Indigenous persons outside the province. We were unable to conduct separate data analyses for each province due to small numbers of Indigenous participants in Ontario and Québec, and our ability to detect an interaction between ethnicity and province was limited by low statistical power due to small numbers of Indigenous Peoples in Ontario and Québec. Second, data on cause of death were not available, preventing us from examining trends in HIV-related and all-cause mortality. Third, mortality data were collected differently by province. Deaths were ascertained in BC via linkage to a provincial vital statistics database, but were passively reported to clinics in Ontario and Québec. Nonetheless, sensitivity analyses using only the participants from BC found similar results. Fourth, data from BC were population-based and included all individuals on cART in BC, with a greater diversity of health care settings.[19] In contrast, CANOC cohorts from Ontario and Québec were clinic-based and under-represent individuals receiving HIV care outside of specialized primary and tertiary HIV health care sites and infectious diseases clinics, such as community health centres.[19] Fifth, the provincial health care systems differ in that antiretroviral medications are covered free of charge for residents of BC, but are only free of charge in the province of Ontario for individuals on disability, those over the age of 65 or those who meet income criteria. In the province of Québec, coverage of antiretroviral therapy varies by age, income and student status, with total out-of-pocket expenses for medications for HIV and other illnesses capped at CDN$1046 per year. Sixth, the large amount of missing data on ethnicity and IDU may have reduced the precision of estimated HRs of death associated with Indigenous ethnicity. The missing data in BC were due to missing ethnicity on enrolment forms for the Drug Treatment Program, largely from two high-volume clinics. Seventh, data were not available on dates of HCV infection and clearance. Indigenous people are reportedly more likely to spontaneously clear HCV infection than Caucasian peoples;[26,27] not accounting for HCV clearance may have overestimated the time Indigenous participants were co-infected with HCV. HCV seropositivity is associated with higher mortality, particularly HIV-related mortality,[28] so this may have diminished our estimates of the association of Indigenous ethnicity with mortality. Eighth, data were not available for current use of alcohol and injection drugs, cART adherence, and determinants of health such as socio-economic insecurity, adverse social and physical environments, culture loss and intergenerational trauma, adverse child development, discrimination and inequitable health care use and access, which have been described as contributing to the development and progression of health concerns, including death.[1–7,15,17,29,30] Last, in addition to the limitations associated with the use of a clinical database, we encountered limitations relevant to our Indigenous community advisory committee. We were unable to identify whether Indigenous-grounded health and wellness approaches were accessed by Indigenous people because CANOC does not collect such data.[17]

CONCLUSION

There were several questions raised during our study. It would be important to assess how Indigenous participants in CANOC differ from all other Indigenous persons with HIV in BC, Ontario and Québec since they may have different levels of engagement in care, including reduced access to HIV speciality care or greater access to community health centres. Future work may include linkage with provincial administrative health databases to capture information on cause of death, and accessing of databases possessing some description of socio-economic status or neighbourhood income. There is an urgent need to address gaps in survival rates in the era of effective cART for Indigenous persons with HIV. Greater recognition of the diversity of Indigenous persons with HIV and its differential impact on First Nations, Métis and Inuit people in each of the three provinces is needed to better describe their gaps in survival rates. Another important consideration for future studies is to separately elucidate challenges for urban and rural Indigenous persons with HIV. There may be factors disrupting access to and use of health care and support services, including quality and knowledge of HIV care and cultural awareness by service providers to sustain engagement and continuity of care. Also, for Indigenous persons with HIV, challenges in achieving positive HIV health outcomes may be compounded by other health concerns. Finally, our findings of increased mortality among Indigenous persons with HIV require immediate action to discern causes of death, to identify structural barriers and challenges to self-determination in health and wellness and to identify initiatives exemplifying the success of Indigenous strengths for improving and maintaining health and wellness.

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RÉSUMÉ

OBJECTIF : Comparer la mortalité toutes causes confondues de participants autochtones et de participants d'autres origines ethniques vivant avec le VIH ayant entrepris un traitement antirétroviral d'association (TARa) dans une cohorte interprovinciale multi-sites.

MÉTHODE : Le centre de recherche collaborative CANOC (Canadian HIV Observational Cohort Collaboration) est une collaboration impliquant 8 cohortes de patients atteints du VIH n'ayant jamais reçu de traitement qui ont amorcé un TARa après le 1er janvier 2000. Ces patients ont été suivis depuis la date de début de leur TARa jusqu'à leur décès ou à la date de la dernière mesure de leur charge virale, soit au plus tard le 31 décembre 2012. À l'aide de modèles à risques proportionnels de Cox, nous avons estimé l'effet de l'ethnicité sur la longévité après avoir tenu compte de l'âge, du sexe, de l'utilisation de drogues par injection, du fait d'être un homme ayant des relations sexuelles avec des hommes, de l'hépatite C, de la province d'origine, de la charge virale et de la numération des lymphocytes CD4 de référence, de l'année de début du TARa et de la classe d'antirétroviraux.

RÉSULTATS : L'échantillon de l'étude comprenait 7 080 participants (497 Autochtones, 2 471 Blancs, 787 personnes des communautés africaine, caribéenne et noire [ACN], 629 personnes d'autres origines ethniques, et 2 696 personnes d'ethnicité inconnue). La plupart des Autochtones venaient de la Colombie-Britannique (C.-B.) (83 %) et dans de moindres proportions de l'Ontario (13 %) et du Québec (4 %). Durant la période de l'étude, 714 participants (10 %) sont décédés. La probabilité de survie après cinq ans a été plus faible chez les Autochtones (0,77) que chez les Blancs (0,94), les participants des communautés ACN (0,98), les participants d'autres origines ethniques (0,96) et les participants d'ethnicité inconnue (0,85) ($p < 0{,}0001$). Avec un modèle à risques proportionnels ajusté pour lequel les données manquantes ont été imputées, les Autochtones ont été plus susceptibles de mourir que les Blancs (coefficient de danger = 2,69, $p < 0{,}0001$).

CONCLUSION : Le taux de mortalité des Autochtones était plus élevé que celui des participants d'autres origines ethniques et reflète dans une large mesure la population de la C.-B. Il est nécessaire d'aborder les défis thérapeutiques et de déterminer les causes de mortalité liées et non liées au VIH chez les Autochtones pour optimiser leur prise en charge clinique.

MOTS CLÉS : Autochtones; mortalité; VIH; étude de cohorte; traitement antirétroviral d'association