

Health care costs associated with hepatitis C virus infection in First Nations populations in Ontario: a retrospective matched cohort study

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Abstract

Background: Colonization and marginalization have affected the risk for and experience of hepatitis C virus (HCV) infection for First Nations people in Canada. In partnership with the Ontario First Nations HIV/AIDS Education Circle, we estimated the publicly borne health care costs associated with HCV infection among Status First Nations people in Ontario.

Methods: In this retrospective matched cohort study, we used linked health administrative databases to identify Status First Nations people in Ontario who tested positive for HCV antibodies or RNA between 2004 and 2014, and Status First Nations people who had no HCV testing records or only a negative test result (control group, matched 2:1 to case participants). We estimated total and net costs (difference between case and control participants) for 4 phases of care: prediagnosis (6 mo before HCV infection diagnosis), initial (after diagnosis), late (liver disease) and terminal (6 mo before death), until death or Dec. 31, 2017, whichever occurred first. We stratified costs by sex and residence within or outside of First Nations communities. All costs were measured in 2018 Canadian dollars.

Results: From 2004 to 2014, 2197 people were diagnosed with HCV infection. The mean net total costs per 30 days of HCV infection were \$348 (95% confidence interval [CI] \$277 to \$427) for the prediagnosis phase, \$377 (95% CI \$288 to \$470) for the initial phase, \$1768 (95% CI \$1153 to \$2427) for the late phase and \$893 (95% CI -\$1114 to \$3149) for the terminal phase. After diagnosis of HCV infection, net costs varied considerably among those who resided within compared to outside of First Nations communities. Net costs were higher for females than for males except in the terminal phase.

Interpretation: The costs per 30 days of HCV infection among Status First Nations people in Ontario increased substantially with progression to advanced liver disease and finally to death. These estimates will allow for planning and evaluation of provincial and territorial population-specific hepatitis C control efforts.

About 220 000–246 000 Canadians are infected with hepatitis C virus (HCV).¹ Nearly half are unaware of their infection.¹ Infection with HCV can lead to chronic hepatic inflammation, cirrhosis, hepatocellular carcinoma and death.² In Ontario, HCV infection has a greater health burden than HIV infection.³

Hepatitis C virus infection places economic strain on the health care system, driven by expensive antiviral drugs and treatment of advanced liver disease.^{4,5} In 2013, the estimated cost of chronic HCV infection in Canada was \$161 million; this was expected to increase by 60% by 2032.⁶

Canada's sociopolitical history with First Nations people, one of the 3 major Indigenous populations, underlies the health disparities that continue to affect the population today.⁷ Among these disparities, higher incidence rates of HCV infection have been observed among certain First Nations popula-

tions than among non-First Nations populations in Canada.⁸ In its commitment to the World Health Organization strategy for eliminating viral hepatitis by 2030, Canada has prioritized partnerships with First Nations populations.⁹ The objective of

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this study was to estimate the health care costs and resource use associated with HCV infection, by phase of care, among Status First Nations populations in Ontario, stratified by sex and by residence within or outside of First Nations communities. An understanding of these measures is essential to planning and evaluating effective, culturally safe approaches to prevention and treatment of HCV infection.

Methods

Partnership

This study was conducted in partnership with the Ontario First Nations HIV/AIDS Education Circle and included First Nations community partners, ICES and academic researchers. Similar collaborations between First Nations organizations and researchers using ICES administrative data sets are described elsewhere.¹⁰⁻¹⁴ Access to the Indian Register was granted by the Chiefs of Ontario First Nations Data Governance Committee after the study was reviewed for compliance with the First Nations principles of ownership, control, access and possession (OCAP) and by Grand Council Treaty #3. Permission to access data for members of communities in the Kenora Chiefs Advisory was not granted; thus, they were excluded from the analysis.

Study design and population

We conducted a retrospective matched cohort study to evaluate health care costs from the provincial public payer perspective. We identified First Nations people in Ontario registered under the *Indian Act*¹⁵ using the Indian Register. The Indian Register includes demographic and administrative information for all First Nations people who have successfully applied for Indian status under the *Indian Act* (i.e., “Status First Nations”). We obtained HCV testing records from Public Health Ontario.

We identified Status First Nations people who had tested positive for HCV antibodies or RNA between Jan. 1, 2004, and Dec. 31, 2014, at age 18–105 years, and followed them until death or Dec. 31, 2017, whichever occurred first. Participants were linked to administrative data sets held at ICES (Appendix 1, available at www.cmajopen.ca/content/9/3/E897/suppl/DC1) by means of unique encoded identifiers and analyzed at ICES. People who had a valid Ontario Health Insurance Plan number at cohort entry and end of follow-up were included. People were excluded if they were potentially coinfecting with HIV or hepatitis B virus, or if their HCV infection was presumed to be spontaneously cleared or acute resolved (Table 1).

Control participants were Status First Nations people with no HCV testing record or only negative results of HCV testing. For the terminal phase of care (6 mo before death from any cause), control participants who died during the observation period were matched 2:1 at 6 months before death to case participants who had died. All remaining unmatched control participants were censored 6 months before death or on Dec. 31, 2017, whichever occurred first, and were randomly assigned pseudo diagnosis dates based on the month and year distribution of the case participants’ HCV infection diagnosis

Table 1: Exclusion criteria

Exclusion criterion	Definition
Spontaneous clearance	<ul style="list-style-type: none"> Negative HCV RNA test result 12 mo after positive HCV antibody test result and no record of positive HCV RNA test result within 12 mo after first positive test result
Acute resolved	<ul style="list-style-type: none"> Negative HCV RNA test result within 12 mo after positive HCV RNA test result and no record of HCV-related treatment between testing dates (Appendix 2, Supplemental Table S3, available at www.cmajopen.ca/content/9/3/E897/suppl/DC1) The person never reverted to HCV RNA positive
HIV infection	<ul style="list-style-type: none"> Record in Ontario HIV database HIV diagnostic code in administrative data (Appendix 2, Supplemental Table S1)
HBV infection	<ul style="list-style-type: none"> Positive HBV test result in Public Health Ontario testing records HBV diagnostic code in administrative data (Appendix 2, Supplemental Table S1)

Note: HBV = hepatitis B virus, HCV = hepatitis C virus.

dates. Control participants with at least 6 months of observation time between their pseudo diagnosis date and censor date were matched 2:1 to case participants at the start of the pre-diagnosis phase (6 mo before HCV infection diagnosis date), initial phase (period following diagnosis with no liver disease) and late phase (liver disease). Each control participant was matched only once. Case and control participants for whom First Nations community residence was not known during the year of each match were excluded.

Control and case participants were greedy matched by hard-matching on sex and age within 2 years. They were then matched within a caliper width of 0.2 standardized difference of the logit of the propensity score based on Johns Hopkins ACG System, Aggregated Diagnosis Groups (ADGs) category¹⁶ (excluding ADG 32 – Malignancy for late phase), and records of mental health or substance abuse conditions during the year before matching date, age at HCV infection diagnosis, community residence status and rurality.¹⁷ We evaluated the quality of each match using descriptive statistics and the weighted standardized differences of matching variables between case and control participants.¹⁸

Cohort characteristics

We identified residence within or outside of a First Nations community at the year of phase entry using postal and residence codes from the Registered Persons Database, Discharge Abstract Database and National Ambulatory Care Reporting System.¹³ We used validated algorithms within the administrative data sets to detect complications related to liver disease, and HCV-specific drug prescription claims were captured (Appendix 2).¹⁹ We scored multimorbidity using ADGs.

Severe mental illnesses may be overrepresented in people at high risk for HCV infection.²⁰ Depression, bipolar mood

disorder, anxiety and stress-related disorders are prevalent and may be complicated by infection.^{21–23} We identified flags for mental health and substance abuse disorders using methods developed by ICES (Appendix 2), supplemented with Ontario Health Insurance Plan service codes.²⁴ As alcohol use can have a compounded effect with HCV infection, further affecting deterioration of the liver, we identified alcohol use disorder separately using related diagnostic codes (Appendix 2).²⁵

Outcomes

We used a phase-based approach to estimate costs over the natural history of disease.^{4,26–28} Patients who had a record of decompensated cirrhosis, hepatocellular carcinoma or liver transplantation (Appendix 2) were allocated to the late phase 3 months before the date of the first record. If that date was before their HCV infection diagnosis, they entered the late phase on their diagnosis date. The phase lengths were defined by means of joinpoint analyses and expert opinion from physicians with in-depth knowledge of HCV infection (J.J.F., M.K.) (Appendix 3, available at www.cmajopen.ca/content/9/3/E897/suppl/DC1).

We estimated provincial total and resource-specific costs for inpatient and ambulatory care, physician and diagnostic services, drugs for those aged 65 years or more, complex continuing care, home care and long-term care for case and control participants using standard person-level costing methods for administrative data (Table 2).²⁹ We adjusted costs to

2018 Canadian dollars using health-sector-specific consumer price indices^{29,30} and standardized them to per 30 days within each phase by dividing each patient-level cost by each person's time in phase.

Statistical analysis

We used clustered analyses by matched set using generalized estimating equations (γ family and log link) to estimate net costs (difference between case and control participants) with each cost category as the dependent variable and HCV infection status as the independent variable.³¹ We used clustered bootstrap sampling, where matched sets were resampled, with 1000 replications and the percentile method to estimate 95% confidence intervals (CIs). Results were stratified by sex and by case participant residence within or outside of a First Nations community at matching date. All analyses were done with R version 3.6.3 (R Foundation for Statistical Computing), SAS version 9.2 (SAS Institute) and Stata version 15.1 (StataCorp).

Ethics approval

This study was approved by the University of Toronto Health Sciences Research Ethics Board.

Results

From 2004 to 2014, 2197 First Nations people were diagnosed with HCV infection (Figure 1). Most (1848 [84.1%]) contributed time to a single phase after diagnosis (Appendix 4, available at www.cmajopen.ca/content/9/3/E897/suppl/DC1). After matching, 2096, 2077, 130 and 297 people with HCV infection contributed observation time to the prediagnosis, initial, late and terminal phases, respectively (Appendix 4).

The sociodemographic characteristics, mental health conditions and comorbidity data of the case and control participants in each phase at matching dates are presented in Table 3. For the prediagnosis and initial phases, the weighted standardized differences were 0.1 or less for all matching variables. Despite efforts to improve matching, case and control participants were less well matched on some ADGs for the late and terminal phases (Appendix 5, Supplemental Table S7, available at www.cmajopen.ca/content/9/3/E897/suppl/DC1), likely owing to the small number of people with these conditions.

People with HCV infection spent, on average, 179, 2714, 1281 and 168 days in the prediagnosis, initial, late and terminal phases, respectively. They were older in the late and terminal phases (about 50 yr) than in the initial and prediagnosis phases (about 37 yr). In all phases, the majority were male and lived outside of First Nations communities. Substance abuse and addiction disorders were the most common comorbid conditions.

During the initial and late phases, 195 case participants (9.4%) and 23 case participants (17.7%), respectively, had records of an HCV-related prescription, and 155 (7.5%) and 21 (16.2%), respectively, received direct-acting antiviral treatment.

Table 2: Resource categories included in the cost estimates

Resource category	Included services*
Outpatient visits	Hospital outpatient clinic services, NACRS visits to dialysis clinics, NACRS visits to cancer clinics
Physician services	OHIP physician billings (including fee-for-service and most of the shadow billings†)
Emergency department visits	NACRS emergency department visits
Same-day surgery	Same-day surgery procedures
Inpatient care	Inpatient hospital admissions and OMHRS admissions to designated mental health beds
Outpatient prescription	Ontario Drug Benefit prescription claims
Laboratory tests/services	OHIP laboratory tests
Other services	OHIP nonphysician services, Assistive Devices Program, rehabilitation services, home care, complex continuing care and long-term care

Note: NACRS = National Ambulatory Care Reporting System, OHIP = Ontario Health Insurance Plan, OMHRS = Ontario Mental Health Reporting System.
 *Explanations of each administrative database can be found in Appendix 1. Additional details can be found in Appendix 2.
 †Refers to submitting a claim for services provided for which physicians are paid a small percentage of the usual fee.

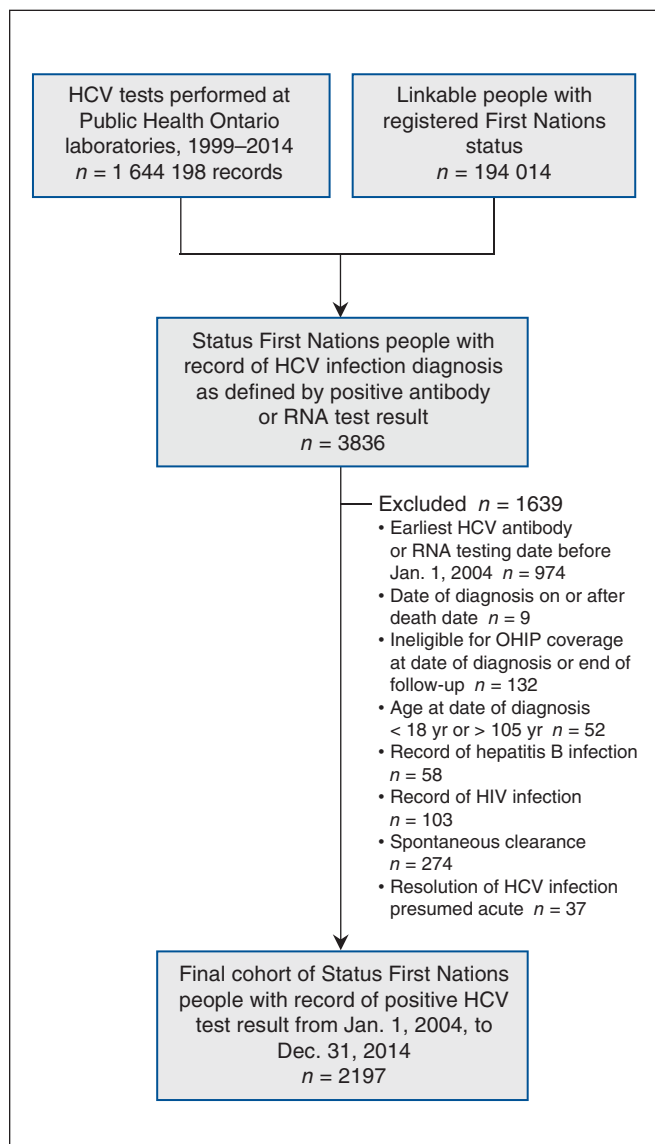


Figure 1: Flow diagram showing case selection. Note: HCV = hepatitis C virus, OHIP = Ontario Health Insurance Plan.

Total costs

Table 4 summarizes the mean total health care costs per 30 days by phase of care for the case and control participants. Among case participants, total costs were lowest in the prediagnosis phase (\$637), increased after HCV diagnosis (\$875) and increased substantially during the late phase (\$2786). Total costs were highest in the terminal phase for both case (\$8896) and control (\$8050) participants.

Outpatient prescriptions, physician services and inpatient care accounted for the highest proportions of costs (Table 4). Inpatient care accounted for 30%–50% of the health care costs in the prediagnosis, initial and late care phases, and 60%–70% of total costs in the terminal phase. For the prediagnosis, initial and late phases, costs were higher among case participants than control participants for nearly all resource categories. In the terminal phase, control partici-

pants had higher costs for outpatient services (\$738 v. \$667), same-day surgery (\$31 v. \$17) and emergency department visits (\$271 v. \$249).

Other cost outcomes are described in Appendix 5, Supplemental Tables S8 to S11, and below.

Net costs

The mean net cost per 30 days increased from \$348 (95% CI \$277 to \$427) in the prediagnosis phase to \$893 (95% CI –\$1114 to \$3149) in the terminal phase (Table 5).

Figure 2 summarizes the net costs per 30 days for case participants who resided within and outside of First Nations communities in the year of matching date. Total net costs were higher in the initial, late and terminal phases for those who resided outside of versus within First Nations communities. Negative net costs indicate that the costs were higher for the control participants than for the case participants. In the terminal phase, the mean net total costs per 30 days were –\$1844 (95% CI –\$5182 to \$1419) and \$1289 (95% CI –\$892 to \$3515) for those who resided within and outside of First Nations communities, respectively.

Net total costs per 30 days were higher for females than males in the prediagnosis, initial and late phases (Figure 3). In particular, females had consistently higher net costs for physician services, inpatient care and outpatient prescription drugs. In the terminal phase, net costs were higher for males than for females (\$1745 [95% CI –\$639 to \$4460] v. –\$498 [95% CI –\$3563 to \$2832]).

Interpretation

Using administrative data to estimate the phase-specific provincial health care costs attributable to HCV infection among Status First Nations people in Ontario, we found that costs per 30 days increased with disease progression. Inpatient services, outpatient prescription drugs and physician services were the most costly resources. Female participants had higher net costs than male participants in the prediagnosis, initial and late phases of care, but males had higher net costs in the terminal phase. Net costs were consistently higher among those who resided outside of versus within First Nations communities, with the largest difference in the terminal phase. However, the large CIs around the net cost estimates indicate wide variations, and, therefore, definitive conclusions should be made with caution.

In our study, the average annual cost for Status First Nations people with HCV infection, before late-stage liver disease, was \$10 500, 1.5 times the average Canadian health care cost of \$6867 in 2018.³² Our annual net costs were considerably higher than those estimated in 2005 in British Columbia, \$1850 (\$2230 in 2018 Canadian dollars³⁰) for early infection and \$6000 (\$7234 in 2018 Canadian dollars³⁰) for infection with advanced liver disease.⁴ Our mean annual late-phase net cost of \$21 216 is similar to the cost of liver cancer care in the Ontario population (about \$20 000).²⁷ These estimates would be considerably higher if a broader societal perspective including patient-borne and productivity costs were considered.³³

Table 3: Characteristics of Status First Nations people in Ontario with HCV infection and matched control participants by phase of care

Characteristic	Cohort; no. (%) of people*							
	Prediagnosis phase		Initial phase		Late phase		Terminal phase	
	Case n = 2096	Control n = 3916	Case n = 2077	Control n = 3875	Case n = 130	Control n = 249	Case n = 297	Control n = 545
Length of phase, mean ± SD, d	179 ± 0	179 ± 0	2714.5 ± 1248.5	2098.2 ± 966.0	1280.9 ± 1086.1	1092.2 ± 826.5	168.5 ± 40.2	168.3 ± 40.7
Demographic characteristics								
Age, yr								
Mean ± SD	36.7 ± 11.4	36.9 ± 11.5	36.7 ± 11.1	36.8 ± 11.2	50.1 ± 9.4	50.1 ± 9.3	48.8 ± 12.3	49.5 ± 12.2
Median (IQR)	36 (27–45)	36 (27–46)	36 (28–45)	36 (28–45)	50 (46–57)	51 (45–57)	50 (40–57)	51 (41–58)
Age group, yr								
≤ 29	665 (31.7)	1227 (31.3)	645 (31.1)	1221 (31.5)	6 (4.6)	10 (4.0)	25 (8.4)	35 (6.4)
30–39	579 (27.6)	1080 (27.6)	594 (28.6)	1087 (28.1)	9 (6.9)	19 (7.6)	49 (16.5)	78 (14.3)
40–49	545 (26.0)	1018 (26.0)	550 (26.5)	1005 (25.9)	45 (34.6)	82 (32.9)	68 (22.9)	134 (24.6)
≥ 50	307 (14.6)	591 (15.1)	288 (13.9)	562 (14.5)	70 (53.8)	138 (55.4)	155 (52.2)	298 (54.7)
Rural mail delivery area								
No	2088 (99.6)	3897 (99.5)	2070 (99.7)	3863 (99.7)	130 (100.0)	249 (100.0)	–**	539 (98.9)
Yes	8 (0.4)	19 (0.5)	7 (0.3)	12 (0.3)	0 (0.0)	0 (0.0)	–**	6 (1.1)
Sex								
Female	944 (45.0)	1728 (44.1)	945 (45.5)	1762 (45.5)	42 (32.3)	80 (32.1)	116 (39.1)	205 (37.6)
Male	1152 (55.0)	2188 (55.9)	1132 (54.5)	2113 (54.5)	88 (67.7)	169 (67.9)	181 (60.9)	340 (62.4)
First Nations community status								
Outside of community†	1714 (81.8)	3142 (80.2)	1695 (81.6)	3075 (79.4)	112 (86.2)	216 (86.7)	259 (87.2)	477 (87.5)
Within community	382 (18.2)	774 (19.8)	382 (18.4)	800 (20.6)	18 (13.8)	33 (13.3)	38 (12.8)	68 (12.5)
Mental health conditions‡								
Alcohol use disorder	241 (11.5)	377 (9.6)	318 (15.3)	511 (13.2)	28 (21.5)	47 (18.9)	62 (20.9)	117 (21.5)
Substance-related/addictive disorders§	657 (31.3)	1136 (29.0)	997 (48.0)	1787 (46.1)	43 (33.1)	82 (32.9)	113 (38.0)	197 (36.1)
Depression	61 (2.9)	101 (2.6)	96 (4.6)	175 (4.5)	–**	9 (3.6)	11 (3.7)	19 (3.5)
Anxiety	165 (7.9)	284 (7.3)	187 (9.0)	320 (8.3)	–**	7 (2.8)	22 (7.4)	44 (8.1)
Bipolar	10 (0.5)	16 (0.4)	13 (0.6)	23 (0.6)	–**	–**	–**	–**
Schizophrenia spectrum disorder	35 (1.7)	46 (1.2)	45 (2.2)	89 (2.3)	–**	–**	7 (2.4)	7 (1.3)
Trauma-/stressor-related disorders	38 (1.8)	60 (1.5)	49 (2.4)	94 (2.4)	–**	–**	6 (2.0)	8 (1.5)
Comorbidity‡								
ADGs total score, mean ± SD	4.3 ± 3.6	3.9 ± 3.4	5.3 ± 3.7	5.0 ± 3.6	6.7 ± 4.4	6.5 ± 4.1	7.5 ± 4.8	7.6 ± 4.7
ADGs total score, median (IQR)	4 (1–7)	3 (1–6)	5 (2–8)	4 (2–7)	7 (3–10)	6 (3–9)	7 (4–11)	7 (4–11)
No. of ADGs categories¶								
≤ 3	668 (31.9)	1375 (35.1)	628 (30.2)	1284 (33.1)	–**	54 (21.7)	62 (20.9)	95 (17.4)
4–7	702 (33.5)	1280 (32.7)	762 (36.7)	1440 (37.2)	41 (31.5)	97 (39.0)	85 (28.6)	164 (30.1)
8–10	251 (12.0)	392 (10.0)	350 (16.9)	578 (14.9)	23 (17.7)	40 (16.1)	52 (17.5)	97 (17.8)
≥ 11	132 (6.3)	193 (4.9)	203 (9.8)	310 (8.0)	29 (22.3)	47 (18.9)	87 (29.3)	163 (29.9)
Nonuser/missing	343 (16.4)	676 (17.3)	134 (6.5)	263 (6.8)	–**	11 (4.4)	11 (3.7)	26 (4.8)

Note: ADGs = Aggregated Diagnosis Groups, HCV = hepatitis C virus, IQR = interquartile range, SD = standard deviation.

*Except where noted otherwise.

†Also included people who had an out-of-province residence code for the year of matching date.

‡During the year before matching date.

§Also contains records pertaining to alcohol use disorder.

¶The frequencies associated with each specific ADGs category can be found in Appendix 5, Supplemental Table S7.

**Suppressed to remove risk of reidentification as per ICES privacy rules.

Table 4: Mean total health care costs per 30 days for case and control participants, by cost category and phase of care

Resource category	Cohort; mean cost per 30 d, \$* (% of total)							
	Prediagnosis phase		Initial phase		Late phase		Terminal phase	
	Case	Control	Case	Control	Case	Control	Case	Control
Outpatient visits	62 (9.7)	31 (10.8)	89 (10.2)	70 (14.1)	227 (8.1)	240 (23.7)	667 (7.5)	738 (9.2)
Physician services	130 (20.3)	76 (26.5)	168 (19.2)	110 (22.1)	405 (14.5)	151 (14.8)	1056 (11.9)	875 (10.9)
Emergency department visits	77 (12.0)	27 (9.3)	55 (6.3)	40 (8.0)	173 (6.2)	57 (5.6)	249 (2.8)	271 (3.4)
Same-day surgery	8 (1.3)	9 (3.1)	9 (1.0)	10 (2.0)	33 (1.2)	16 (1.6)	17 (0.2)	31 (0.4)
Inpatient care	252 (39.6)	103 (35.5)	325 (37.2)	172 (34.7)	1307 (46.9)	332 (32.7)	5929 (66.6)	5261 (65.3)
Outpatient prescription	33 (5.2)	18 (6.3)	150 (17.1)	47 (9.5)	405 (14.5)	105 (10.4)	215 (2.4)	201 (2.5)
Laboratory tests/ services	28 (4.4)	11 (3.7)	17 (1.9)	9 (1.9)	21 (0.8)	10 (1.0)	17 (0.2)	12 (0.1)
Other services†	48 (7.5)	14 (4.9)	62 (7.1)	39 (7.8)	214 (7.7)	104 (10.3)	747 (8.4)	662 (8.2)
Total	637 (100.0)	289 (100.0)	875 (100.0)	497 (100.0)	2786 (100.0)	1016 (100.0)	8896 (100.0)	8050 (100.0)

*Costs are rounded to the nearest dollar and expressed in 2018 Canadian dollars.

†Costs related to the Assistive Devices Program, nonphysician health care professional services, rehabilitation, home care, complex continuing care and long-term care services.

Table 5: Mean net costs of care per 30 days, by cost category and phase of care

Resource category	Phase of care; mean net cost (95% CI) per 30 days, \$*			
	Prediagnosis phase	Initial phase	Late	Terminal
Outpatient visits	31 (12 to 54)	19 (−9 to 47)	−14 (−190 to 166)	−66 (−312 to 193)
Physician services	53 (41 to 65)	58 (47 to 69)	255 (181 to 338)	182 (−34 to 448)
Emergency department visits	50 (43 to 56)	15 (10 to 20)	116 (66 to 170)	−22 (−77 to 30)
Same-day surgery	−1 (−4 to 3)	−1 (−2 to 0)	17 (3 to 34)	−14 (−31 to 1)
Inpatient care	150 (106 to 202)	153 (97 to 219)	975 (621 to 1378)	696 (−975 to 2487)
Outpatient prescription	15 (9 to 20)	102 (89 to 115)	300 (171 to 443)	14 (−73 to 120)
Laboratory tests/ services	17 (14 to 20)	8 (6 to 9)	11 (4 to 21)	5 (0 to 10)
Other services	34 (7 to 65)	23 (−4 to 54)	109 (10 to 205)	85 (−198 to 389)
Total	348 (277 to 427)	377 (288 to 470)	1768 (1153 to 2427)	893 (−1114 to 3149)

Note: CI = confidence interval.
*Costs are rounded to the nearest dollar and expressed in 2018 Canadian dollars.

The mean end-of-life costs for case and control participants in our study were higher than costs in the last year of life for patients with heart failure, renal disease or mental health disorders.³⁴ An Ontario study showed that patients with end-stage liver disease incurred an additional \$4201 in the last 90 days of life compared to other decedents.³⁴ Extrapolating 30-day costs from our study shows that Status First Nations people with HCV infection incurred \$2679 more in their last 90 days of life than other Status First Nations people.

Differences in costs between people with HCV infection who lived within and outside of First Nations communities may indicate unique patterns of use of health care resources and health care policy by the 2 populations.³⁵ A history of government mistrust, marginalization and alienation has created hesitancy among First Nations people to seek mainstream medical care, especially in rurally isolated communities with barriers to access to care.³⁶ The largest difference in net costs was in the terminal phase, which may indicate that

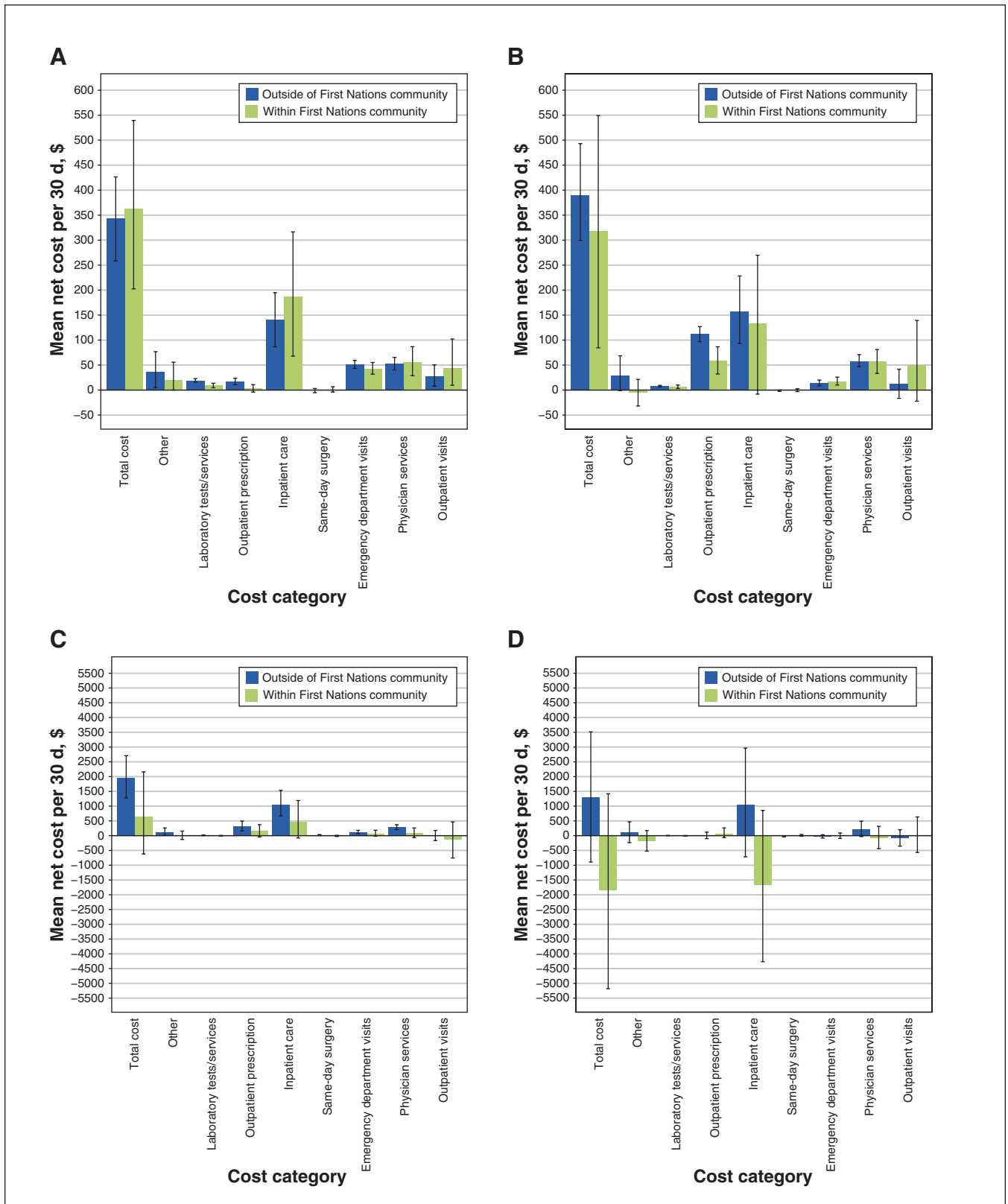


Figure 2: Net costs of care per 30 days by cost category for the prediagnosis (A), initial (B), late (C) and terminal (D) phases of care, stratified by residence within or outside of a First Nations community at matching date. Each cost is rounded to the nearest dollar and expressed in 2018 Canadian dollars. “Other” includes Ontario Health Insurance Plan nonphysician services, Assistive Devices Program, rehabilitation services, home care, complex continuing care and long-term care. Error bars represent 95% confidence intervals. Mean cost and net cost results stratified by community status can be found in Appendix 5, Supplemental Tables S8 and S9.

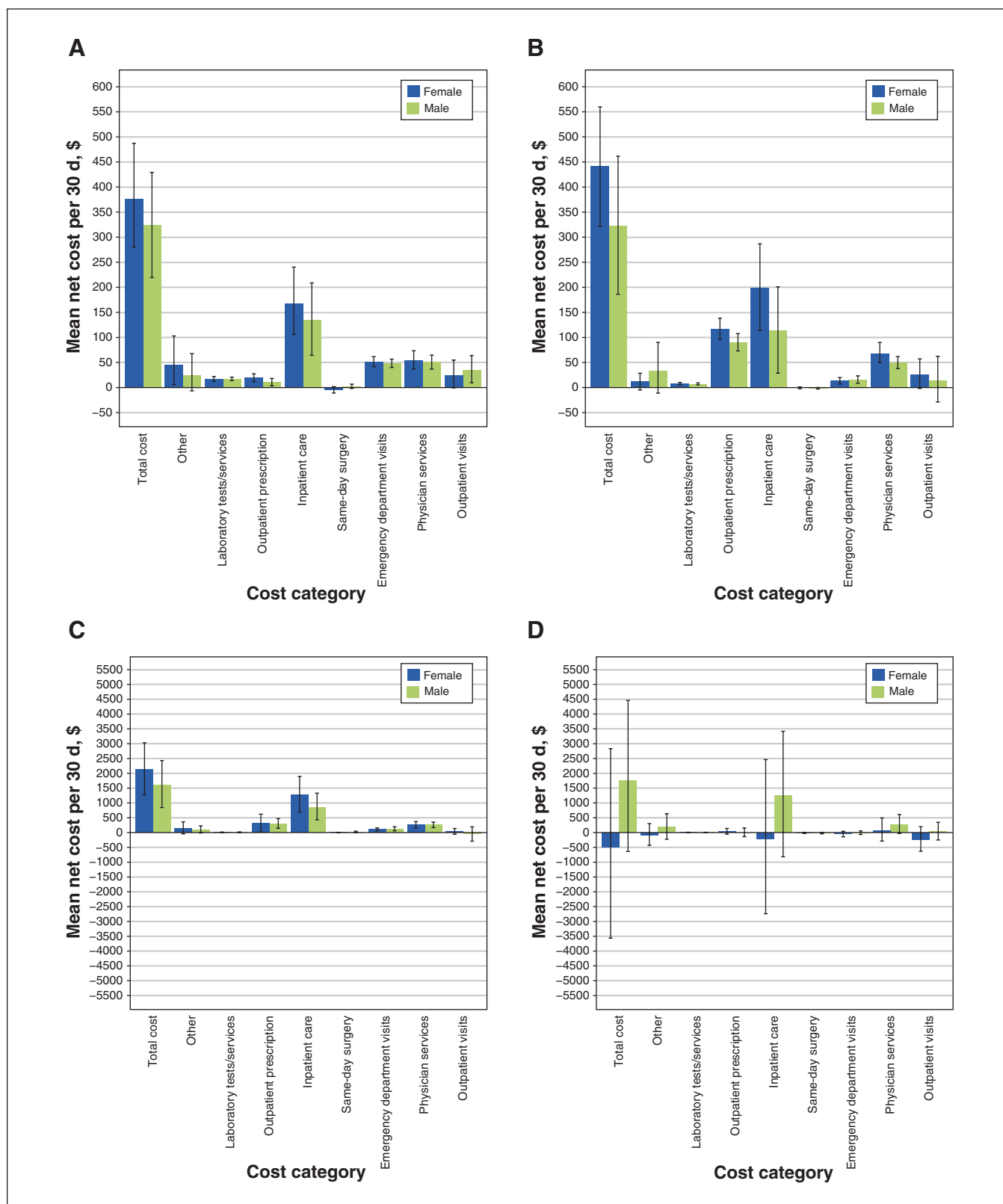


Figure 3: Net costs of care per 30 days by cost category for the prediagnosis (A), initial (B), late (C) and terminal (D) phases of care, stratified by sex. Each cost is rounded to the nearest dollar and expressed in 2018 Canadian dollars. “Other” includes Ontario Health Insurance Plan nonphysician services, Assistive Devices Program, rehabilitation services, home care, complex continuing care and long-term care. Error bars represent 95% confidence intervals. Mean cost and net cost results stratified by sex can be found in Appendix 5, Supplemental Tables S10 and S11.

end-of-life care within First Nations communities is associated with family support rather than hospital or hospice care.³⁶ The lower cost of end-of-life care within First Nations communities may also be attributable to funding constraints, resulting in unavailable or limited access to end-of-life health care services.³⁶ In addition, 1 in 4 First Nations communities in Ontario are in remote areas accessible only by air year round or by ice road in winter.³⁷ These barriers can translate to people having to leave their community to seek care or, in certain cases, receiving no end-of-life care at all.³⁶

In the prediagnosis, initial and late phases, female case participants exhibited higher costs of care than male case participants. Verde and Li³⁸ found that First Nations women were more likely to have a family physician and seek health care services than First Nations men, perhaps owing to cultural norms regarding male strength and perception of less severe physical symptoms. Similarly, using ICES data, Green and colleagues³⁹ studied the monitoring, treatment and control of blood glucose and lipids in Status First Nations people with diabetes in Ontario and observed that women were more likely than men to be engaged in diabetes-related care. The higher net cost for males during the terminal phase in our study may indicate that males seek health care only when disease progresses to a critical stage.³⁸ Also, females may choose traditional medicine and community supports rather than hospital or hospice care at the end of life (Evelynne Hill, Ontario First Nations HIV/AIDS Education Circle: personal communication, 2020).

Safe, effective and curative direct-acting antiviral treatments for HCV infection were introduced in Canada in 2012.⁴⁰ However, Indigenous people face barriers in access to treatment.⁴¹ Although progression to advanced liver disease can take decades,⁴² the higher net costs in the late and terminal phases compared to the prediagnosis and initial phases forecast the potential economic impact if HCV infection remains untreated or is diagnosed late. Understanding health care expenditures in First Nations people with HCV infection can stimulate research, planning and evaluation of culturally specific services for combatting hepatitis C in this population.⁴³

Limitations

Although matching minimized differences between case and control participants, residual confounding and differences in health care-seeking behaviour potentially existed and may have introduced bias. The Public Health Ontario laboratory data set does not include all private diagnostic laboratory results. The Indian Register includes only First Nations people who are registered with the Canadian government.¹³ Our study included those who could be linked to ICES databases but excluded data for those who are members of communities in the Kenora Chiefs' Advisory.

Costs may be underestimated because ICES data sets do not capture federally funded or out-of-province health care services, including those covered by the Non-Insured Health Benefit program (drug coverage and certain health care services). The Ontario Drug Benefit program, our source of

prescription information, covers only people aged 65 years or more, receiving social assistance or in long-term care homes.

We included all-cause mortality; thus, our terminal-phase net costs are not entirely attributable to HCV infection.⁴ Many mental health conditions could not be distinguished as being a cause or consequence of HCV infection. Because determination of residence in a given Local Health Integration Network and within a First Nations community relied on annual postal and residence codes updated at health card use or renewal, residence may have been misclassified.

As HCV infection can remain asymptomatic, control participants may have had undiagnosed infection. By excluding case participants with HIV and HBV infection, our study estimates reflect the cost of diagnosed mono-infection. Coinfection has been associated with potentially rapid fibrosis progression⁴⁴ and different treatment of infection. Coinfection with HIV in particular has been associated with increased health care costs.^{4,45}

Conclusion

Our results suggest that the costs of HCV infection in Status First Nations people vary by phase of care and increase as the disease progresses. Canada's commitment to partnership with First Nations people to eliminate hepatitis C will require measures that comprehensively depict its population-specific impact. Our population-specific health care costs can support research, planning and formulation of First Nations-specific prevention and treatment interventions for HCV infection.

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- Data sharing:** The data set from this study is held securely in coded form at ICES. Although data-sharing agreements prohibit ICES from making the data set publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at <https://www.ices.on.ca/DAS>. The full data set creation plan and underlying analytic code are available from the authors on request, with the understanding that the computer programs may rely on coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.
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