Research

Characterizing the cascade of care for hepatitis C virus infection among Status First Nations peoples in Ontario: a retrospective cohort study

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Abstract

Background: As First Nations Peoples are a priority focus of Canada's commitment to eliminating hepatitis C virus (HCV) as a public health threat, understanding individuals' progression from diagnosis to cure can guide prioritization of elimination efforts. We sought to characterize and identify gaps in the HCV care cascade for Status First Nations peoples in Ontario.

Methods: In this retrospective cohort study, a partnership between the Ontario First Nations HIV/AIDS Education Circle and academic researchers, HCV testing records (1999–2018) for Status First Nations peoples in Ontario were linked to health administrative data. We defined the cascade of care as 6 stages, as follows: tested positive for HCV antibody, tested for HCV RNA, tested positive for HCV RNA, HCV genotyped, initiated treatment and achieved sustained viral response (SVR). We mapped the care cascade from 1999 to 2018, and estimated the number and proportion of people at each stage. We stratified analyses by sex, diagnosis date and location of residence. We used Cox regression to analyze the secondary outcomes, namely the associations between undergoing HCV RNA testing and initiating treatment, and demographic and clinical predictors.

Results: By Dec. 31, 2018, 4962 people tested positive for HCV antibody. Of those testing positive, 4118 (83.0%) were tested for HCV RNA, with 2480 (60.2%) testing positive. Genotyping was completed in 2374 (95.7%) of those who tested positive for HCV RNA, with 1002 (42.2%) initiating treatment. Nearly 80% (n = 801, 79.9%) of treated people achieved SVR, with 34 (4.2%) experiencing reinfection or relapse. Undergoing testing for HCV RNA was more likely among people in older age categories (within 1 yr of antibody test; adjusted hazard ratio [HR] 1.30, 95% confidence interval [CI] 1.19–1.41, among people aged 41–60 yr; adjusted HR 1.47, 95% CI 1.18–1.81, among people aged > 60 yr), those living in rural areas (adjusted HR 1.20, 95% CI 1.10–1.30), those with an index date after Dec. 31, 2013 (era of treatment with direct-acting antiviral regimens) (adjusted HR 1.99, 95% CI 1.85–2.15) and those with a record of substance use or addictive disorders (> 1 yr after antibody test; adjusted HR 1.38, 95% CI 1.18–1.60). Treatment initiation was more likely among people in older age categories at index date (adjusted HR 1.32, 95% CI 1.15–1.50, among people aged 41–60 yr; adjusted HR 2.62, 95% CI 1.80–3.82, among people aged > 60 yr) and those with a later diagnosis year (adjusted HR 2.71, 95% CI 2.29–3.22).

Interpretation: In comparison with HCV testing and diagnosis, a substantial gap in treatment initiation remains among Status First Nations populations in Ontario. Elimination efforts that prioritize linkage to care and integration with harm reduction and substance use services are needed to close gaps in HCV care among First Nations populations in Ontario.

Hepatitis C virus (HCV) infection remains an important public health problem in Canada, causing more years of life lost than any other infectious disease.[1] Direct-acting antiviral (DAA) regimens have revolutionized the treatment of HCV infection, offering the opportunity for cure before advanced liver disease develops.[2]

The historical and ongoing effects of colonialism and consequent intergenerational trauma have led to high rates of mental illness and substance use among First Nations peoples, one of the 3 main Indigenous groups in Canada (along with Inuit and Métis peoples), resulting in a disproportionate impact of HCV.[3] Both the prevalence and incidence of diagnosed HCV infection roughly doubled from 2006 to 2014 among Status First Nations peoples in Ontario.[4,5]

The cascade of care framework describes population-level engagement in progressive stages of care, allowing for the evaluation and monitoring of health care delivery and engagement

across various settings and populations.[6–8] In addition, attrition and gaps in engagement across various stages of the continuum of care can be measured.[9] First used for HIV, the cascade of care framework has been applied to HCV to identify care services, access and program effectiveness at a population level.[7]

Canada has committed to the World Health Organization's goal to eliminate viral hepatitis as a public health threat by the year 2030, and First Nations and other Indigenous Peoples are a priority focus.[10,11] Understanding where to prioritize elimination efforts requires a benchmark of how First Nations peoples progress from HCV testing, to diagnosis and, ultimately, to treatment, and of where heterogeneity and inequalities exist.[12] Using provincial health administrative data, the study objective was to characterize and map the HCV cascade of care among Status First Nations peoples in Ontario and to identify gaps in engagement and service delivery.

Methods

Study design

We conducted a population-based retrospective cohort study of Status First Nations peoples in Ontario with a confirmed positive test result for HCV antibody or RNA from Jan. 1, 1999, to Dec. 31, 2018. This study is part of an ongoing collaboration between the Ontario First Nations HIV/AIDS Education Circle (OFNHAEC), ICES (an independent, nonprofit research institute) and academic researchers, described elsewhere.[4,5,13]

Guided by Tri-Council Policy Statement chapter 9: Research Involving Indigenous Peoples in Canada,[14] collaboration with OFNHAEC throughout this research ensured the inclusion of First Nations representatives from different Provincial Territorial Organizations and Independent First Nations, patient representatives, Elders, and sexually transmitted and blood-borne infection coordinators and educators across the province.[13] The study was reviewed for compliance with the principles of ownership, control, access and possession (OCAP),[15,16] and approved by the Chiefs of Ontario First Nations Data Governance Committee and 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.

We reported this study in accordance with RECORD (Reporting of Studies Conducted Using Observational Routinely Collected Health Data).[17]

Setting

The Indian Register includes all people who are registered with the Canadian federal government and recognized under the *Indian Act* as members of a First Nation (i.e., Status First Nations).[18–20] Status First Nations peoples in Ontario were identified through previous linkage of the Indian Register to the Registered Persons Database (RPDB) at ICES.[18,20] First Nations communities (formerly referred to as reserves) are areas of land that are legally affiliated with First Nations bands in Canada.

In addition to provincial health insurance and third-party coverage, Status First Nations peoples are eligible for a wide range of federally funded benefits for health care. For example, they can seek primary care from community health centres, Aboriginal Health Access Centres or federally funded nursing stations or health centres; they can also seek care out of province (depending on proximity).[21,22] Status First Nations peoples are eligible for the federal noninsured health benefits (NIHB) program, which provides additional coverage for medical services and prescription drugs (including HCV treatments, as indicated on the NIHB drug benefits list)[23] that are not accessible through other programs.[24] However, the NIHB program is a payer of last resort, after all other provincial or third-party coverage is exhausted.[25,26] Those who are covered by another public or private health care plan are required to submit their claims to the other plans first.[25]

Second-generation DAA treatments were launched in Canada in 2014,[27] followed by changes in reimbursement criteria in Ontario after 2015.[28] To identify potential improvements in care from wider availability and use of DAA treatments, we examined the cascade of care for people alive and in the province on Dec. 31, 2013 (hereby referred to as the "pre-DAA era").

Data sources

The Indian Register data set at ICES includes all Status First Nations peoples registered as of 2014.[20] We linked these records to administrative health services data held at ICES (Appendix 1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220717/tab-related-content) and to HCV testing records spanning Jan. 1, 1999, to Dec. 31, 2018, acquired from Public Health Ontario laboratories. Public Health Ontario is responsible for public health surveillance, including centralized processing of viral hepatitis testing across Ontario.[29] These data sets were linked using unique encoded identifiers and analyzed at ICES.

Participants

We identified Status First Nations peoples recorded in the Indian Register and with a conclusive HCV test record in the Public Health Ontario data from Jan. 1, 1999, to Dec. 31, 2018. Of these, we included people who were alive and in the province on Dec. 31, 2018, in the HCV cascade of care analysis. For comparison, and to represent the pre-DAA era, we also examined the cascade of care for people who were alive and in the province on Dec. 31, 2013.

Cascade of care

We defined the HCV cascade of care in 6 stages, as follows: tested positive for HCV antibody, tested for HCV RNA, tested positive for HCV RNA, HCV genotyped, initiated treatment and achieved sustained virologic response (SVR) (Table 1).[30] We defined relapse or reinfection as testing positive for HCV RNA after achieving SVR.[31] For each individual, we assigned an index date as the earliest date of a positive HCV antibody or HCV RNA test result, genotype test or treatment initiation record.

We separated people who ever spontaneously cleared infection from those who tested positive for HCV RNA and from subsequent stages of the care cascade (Table 1). For the treatment initiation stage, we identified outpatient prescription drugs for HCV infection from the Ontario Drug Benefit (ODB) database

Table 1: Definitions of stages in cascade of care for hepatitis C virus (HCV) infection*

Care stage	Definition
Positive for HCV antibody	• Positive result for HCV antibody • Backfilled with people who had a result from an HCV RNA test and no previous result from an HCV antibody test
Tested for HCV RNA	• Tested for HCV RNA

Positive for HCV RNA	• Positive result for HCV RNA
	• Excluded people who spontaneously cleared infection, identified by
	  • Negative result for HCV RNA test after testing positive for HCV antibody, with no record of treatment or positive test result for HCV RNA in between
	  • Negative result for HCV RNA within a year after testing positive for HCV RNA, with no record of treatment in between

HCV genotyped	• HCV genotype result • Backfilled with people who were backfilled into the treatment initiated stage with no genotype record
HCV treatment initiated	• HCV treatment initiated • Backfilled with people who were backfilled into the achieved SVR stage†

Achieved SVR‡	• For people with a record of an HCV treatment
	  • If first dispensation record was for an IFN-based treatment, negative result for HCV RNA at least 40 weeks¶ after first date of treatment
	  • If first dispensation record was for a DAA treatment, negative result from HCV RNA test at least 18 weeks** after first date of treatment
	• Backfilled with people who subsequently tested negative for HCV RNA more than a year after the date of their first positive result for HCV RNA, with no record of treatment

Note: DAA = direct-acting antiviral, IFN = interferon, SVR = sustained virologic response.
*At each stage, the individual must have achieved the stage on or before Dec. 31, 2018 (for main analysis), or Dec. 31, 2013 (for comparison analysis). Additional details regarding backfilled individuals and definition of spontaneous clearance can be found in Appendix 2, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220717/tab-related-content.
†For backfilled people, treatment date was assumed to be 6 months before SVR date.
‡SVR date was assumed to be the date of the corresponding negative test result for HCV RNA.
¶Interferon treatment duration was assumed to be an average of 24 weeks, with SVR measured 16 weeks after treatment completion.
**DAA treatment duration was assumed to be an average of 8 weeks, with SVR measured 10 weeks after treatment completion.

(Appendix 3, Table S2, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220717/tab-related-content). We inferred SVR for people with a negative result for HCV RNA more than 40 weeks or 18 weeks after first interferon[32] or DAA[33] treatment dispensation, respectively.

In the absence of testing and treatment records, we backfilled or assigned people to an earlier care stage based on assumptions around HCV RNA testing trends within the Public Health Ontario data. We backfilled people into the antibody-positive stage if they had a record of an HCV RNA test without a corresponding record of testing positive for HCV antibody. We added people to the genotyped stage if they had a record of initiating treatment or achieving SVR. In the absence of treatment records, we backfilled people into the treatment and SVR stages if they had a negative result for HCV RNA more than a year after their positive HCV RNA test. More details regarding backfilling can be found in Appendix 2, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220717/tab-related-content.

Engagement in each stage of the HCV cascade of care was reported among those alive and in the province at Dec. 31, 2018. Primary outcome measures were the number and proportion of people who had initially tested positive for HCV antibody in each stage of the cascade of care, and the percentage of people who progressed from the previous care stage. We also stratified measures by sex and residence within or outside of First Nations community at year of index. Secondary outcomes included time to subsequent RNA testing from testing positive for HCV antibody, and time to initiating treatment from testing positive for HCV RNA. For these analyses, we included all individuals, and censored those who did not have the event of interest at the end of the study period, date of death or when they left the province.

Variables

We assessed demographic and clinical characteristics at index date and date of treatment initiation. In addition to age at index, we characterized birth cohort because previous studies have cited a higher prevalence of HCV among people in certain birth cohorts (1945–1975).[34] We classified location of residence by health service region (i.e., Local Health Integration Network) and urbanicity. As health care service delivery and access can differ within First Nations communities,[22] we also characterized people as residing within or outside of a First Nations community during the year of reference, using mapped postal and residence codes at ICES.

Mental illness is overrepresented among people with HCV infection and is complicated by infection.[35] In particular, substance use has been identified as an important risk factor for infection and barrier to care.[36] Therefore, we characterized mental health conditions using diagnostic categories,[37] supplemented

with billing codes from the Ontario Health Insurance Plan (OHIP) (Appendix 3, Table S3). We identified records of hepatitis B virus (HBV) and HIV coinfections, given that these have been shown to affect progression through the HCV testing continuum and whether people seek care (Appendix 3, Table S4).[7] As chronic infection leads to accelerated progression of liver disease, we used validated algorithms of diagnostic and OHIP billing codes to identify records of advanced liver disease (e.g., cirrhosis, decompensated cirrhosis, hepatocellular carcinoma) and liver transplant within the cohort (Appendix 3, Table S5 to S8).[38] We categorized multimorbidity using the Johns Hopkins ACG System's (version 10) Aggregated Diagnosis Groups (ADG) up to 1 year before index date and up to 1 year before treatment initiation.[39]

Statistical analysis

For cohort characteristics, we described continuous variables using means and standard deviations, and medians and interquartile ranges. We reported counts of people with conditions before the index date, treatment start date and study end date.

We used Cox regression models to identify associations between characteristics and time to subsequent RNA testing for people whose index date corresponded to a record of a positive antibody test, and time to initiating treatment (including those who were backfilled) from first record of a positive result for HCV RNA. We censored those without the event of interest at date of death, 10 years after date of last contact with the health care system or Dec. 31, 2018 (end of study period), whichever occurred first. We generated and fitted time-to-event curves using the Kaplan–Meier method.[40] We performed multivariable analyses with covariates identified a priori and defined at index date. Covariates included age category; sex; urbanicity; residence within or outside of a First Nations community; ADG score; coinfection with HBV, HIV or both; substance use or addictive disorder; and treatment era.

We estimated model parameters, and unadjusted and adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). We assessed the proportional hazards assumption for both models by examining time-to-event curves and scaled Schoenfeld residuals for all covariates. In the case of violation, we used piecewise regression to calculate period-specific HRs for the affected covariates at 1 year or less and greater than 1 year from the start date.[41] We used complete case analysis to handle missing variables.

Sensitivity analyses

We tested backfilling assumptions in sensitivity analyses of HCV RNA testing trends and testing frequencies. Post hoc analyses assessed the effects of potential misclassification of people backfilled into the treatment initiation and SVR stages (including those identified as treatment nonresponders, defined in Appendix 4, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220717/tab-related-content), as having spontaneous clearance (defined in Appendix 2), or relapse or reinfection (defined in Appendix 4).

To balance concerns regarding changes in treatment eligibility over the study period and after 2018, we performed post hoc analyses of annual ODB records of treatment from the earliest date available to Dec. 31, 2020. For the regression analysis of time to treatment, we ran a version of the model considering only those with an actual ODB treatment record (not backfilled).

We conducted all analyses using SAS version 9.4 (SAS Institute) and R version 3.6 (R Core Team).

Ethics approval

This study was approved by the University Health Network and University of Toronto Health Sciences Research Ethics Boards. ICES' legal status under Ontario's health information privacy law (Section 45) allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement.

Results

From Jan. 1, 1999, to Dec. 31, 2018, 40 533 Status First Nations peoples in Ontario had HCV testing records (Figure 1). Of these, 35 775 were alive and resided in the province on Dec. 31, 2018. Overall, 4962 people ever tested positive for HCV antibody and were alive and in the province at Dec. 31, 2018 (Table 2). Before their index date, 52 (1.0%) and 94 (1.9%) people had diagnoses of HBV and HIV infection (or both), respectively, which increased to 119 (2.4%) and 187 (3.8%) by the end of 2018. Cirrhosis and decompensated cirrhosis were recorded for 89 (1.8%) and 65 (1.3%) people before their index date and for 240 (4.8%) and 139 (2.8%) people, respectively, by the end of 2018. Mental health conditions before index dates were common, particularly substance use and addictive disorders (n = 3728, 75.1%) or anxiety disorders (n = 3731, 75.2%).

Care cascade by Dec. 31, 2018

Figure 2 describes the cascade of care by Dec. 31, 2018. Among the 4962 people who ever tested positive for HCV antibody, 4118 (83.0%) had a record of HCV RNA testing; 442 had no record of an antibody test ever being performed and were therefore backfilled into this population. Of those people tested for HCV RNA, 2480 (60.2%) were positive for HCV RNA, for whom 2374 (95.7%) samples were genotyped (incorporating 32 people who were backfilled because treatment was initiated without having a genotype record). The most common genotype was 1, identified in 1592 of those whose samples were genotyped (67.1%).

Treatment was initiated for 1002 people (42.2% of those whose samples were genotyped), of whom 801 (79.9%) achieved SVR. There were 509 people (50.8% and 63.5% of those who initiated treatment and achieved SVR, respectively) with no treatment record who were backfilled based on HCV RNA testing trends. Among the 493 people with an ODB record of treatment initiation (not backfilled), 56 (11.4%) could not be evaluated for SVR because not enough time had passed between treatment initiation and the study end date. Of those who achieved SVR, 34 (4.2%) subsequently tested positive for HCV RNA, indicating reinfection or relapse. Of these, 22 (64.7%) tested positive within a year (likely indicating relapse), and 12 (35.3%) tested positive more than a year after SVR (likely indicating reinfection).

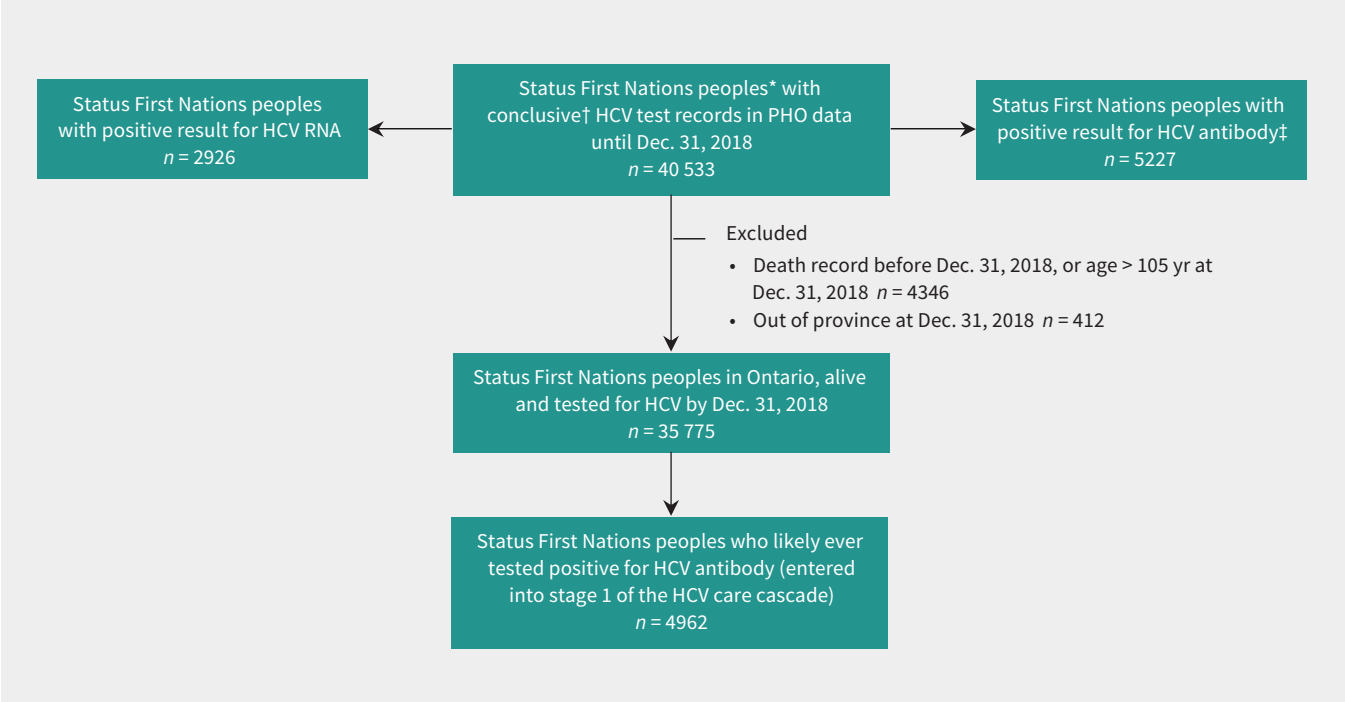

Figure 1: Flow diagram showing cohort selection for analysis of cascade of care on Dec. 31, 2018. *Members of the Kenora Chiefs Advisory were excluded from the analyses. †166 people had only inconclusive results from an HCV antibody test and no record of an HCV RNA test. ‡After complete case analysis, multivariable analysis (time from testing positive for HCV antibody to RNA test) was performed with 4771 people who underwent testing for HCV RNA after a positive result for HCV antibody. §After complete case analysis, multivariable analysis (time from testing positive for HCV RNA to treatment initiation) was performed with 2675 people who had a record of first HCV treatment after a positive result for HCV RNA. Note: HCV = hepatitis C virus, PHO = Public Health Ontario.

We excluded 1122 people who spontaneously cleared their infection (22.6% of those who ever tested positive for HCV antibody) from the stage of testing positive for HCV RNA, of whom 111 (9.9%) tested positive for HCV RNA at a later date. We estimated that 26 (23.4%) of these 111 cleared their infection through treatment and 17 (15.3%) spontaneously cleared their infection by Dec. 31, 2018.

Results of sensitivity analyses around backfilling assumptions can be found in Appendix 4. When considering the changing treatment landscape beyond 2018, the largest increases in ODB claimants of prescriptions for HCV treatment were observed in 2015 and 2017, with minimal year-to-year changes thereafter (Appendix 5, Table S9, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220717/tab-related-content).

Care cascade by sex and First Nations community residence

By Dec. 31, 2018, 2348 females ever tested positive for HCV antibody and 997 were genotyped. Treatment was initiated for 444 females (44.5% of those genotyped), of whom 370 (83.3%) achieved SVR (Appendix 6, Figure S1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220717/tab-related-content). Among the 2614 males who ever tested positive for HCV antibody, treatment was initiated for 558 (40.5% of genotyped) of them, and 431 (77.2% of those who initiated treatment) achieved SVR.

By Dec. 31, 2018, 3583 HCV antibody–positive people resided outside of First Nations communities at index date, of whom 2920 (81.5%) ever underwent HCV RNA testing (Appendix 6, Figure S2). Among those who resided outside of First Nations communities during their index year, 750 (43.7% of genotyped) ever initiated treatment, 586 (78.1% of those who initiated treatment) achieved SVR and 21 (3.6% of those who achieved SVR) had reinfection or relapse. Among the 1098 antibody-positive people who resided within First Nations communities during their index year, 971 (88.4%) ever underwent HCV RNA testing. Of the 169 (33.7% of genotyped) people who initiated treatment, 150 (88.8%) achieved SVR and 10 (6.7% of those who achieved SVR) had reinfection or relapse.

Comparison of 2013 and 2018 care cascades

By Dec. 31, 2013, 3146 people ever tested positive for HCV antibody (Appendix 6, Figure S3). Appendix 6, Table S10 describes patients who initiated treatment by Dec. 31, 2013 (pre-DAA era, n = 207) and for the entire cohort who initiated treatment by Dec. 31, 2018 (n = 1002). Their mean ages at date of treatment initiation were 44.0 and 43.7 years, respectively. In both groups, those who initiated treatment had higher proportions of cirrhosis and decompensated cirrhosis than those in earlier stages of the cascade (Table 2 and Appendix 6, Table S11).

Comparing the cascades of care in the pre-DAA era to 2018, we observed increases in the proportion of people who underwent HCV RNA testing after a positive antibody test (69.8% to 83.0%), and in treatment initiation after genotype testing (15.4% to 42.2%). Of those who were treated, 78.3% achieved SVR in the pre-DAA era, increasing to 79.9% by 2018 (Appendix 6, Figure S4).

Table 2 (part 1 of 3): Demographic and clinical characteristics of Status First Nations peoples in Ontario for each stage of the cascade of care for hepatitis C virus (HCV) infection on Dec. 31, 2018

Characteristic†	No. (%) of participants*					
	Positive for HCV antibody *n* = 4962	Tested for HCV RNA *n* = 4118	Positive for HCV RNA *n* = 2480	Genotyped *n* = 2374	Initiated treatment *n* = 1002	Achieved SVR‡ *n* = 801
Backfilled	442 (8.9)	0	0	32 (1.3)	509 (50.8)	509 (63.5)
Age at index date, yr, mean ± SD	35.3 ± 11.8	35.6 ± 11.9	35.5 ± 10.8	35.6 ± 10.8	37.5 ± 11.3	37.7 ± 11.2
Age at index date, yr, median (IQR)	34 (27–43)	34 (27–44)	34 (27–43)	35 (27–43)	37 (28–46)	38 (28–46)
Age at index date, yr						
0–24	926 (18.7)	777 (18.9)	427 (17.2)	404 (17.0)	139 (13.9)	104 (13.0)
25–29	828 (16.7)	669 (16.2)	429 (17.3)	413 (17.4)	149 (14.9)	124 (15.5)
30–34	766 (15.4)	623 (15.1)	395 (15.9)	370 (15.6)	141 (14.1)	109 (13.6)
35–39	720 (14.5)	566 (13.7)	348 (14.0)	331 (13.9)	136 (13.6)	102 (12.7)
40–44	640 (12.9)	533 (12.9)	350 (14.1)	339 (14.3)	153 (15.3)	121 (15.1)
45–49	464 (9.4)	407 (9.9)	250 (10.1)	246 (10.4)	129 (12.9)	114 (14.2)
50–54	305 (6.1)	265 (6.4)	154 (6.2)	148 (6.2)	76 (7.6)	66 (8.2)
≥ 55	313 (6.3)	278 (6.8)	127 (5.1)	123 (5.2)	79 (7.9)	61 (7.6)
Birth cohort						
< 1945	34 (0.7)	28 (0.7)	15 (0.6)	14 (0.6)	9 (0.9)	6 (0.7)
1945–1964	1157 (23.3)	1002 (24.3)	611 (24.6)	600 (25.3)	347 (34.6)	289 (36.1)
1965–1975	1213 (24.4)	1004 (24.4)	632 (25.5)	612 (25.8)	260 (25.9)	208 (26.0)
> 1975	2558 (51.6)	2084 (50.6)	1222 (49.3)	1148 (48.4)	386 (38.5)	298 (37.2)
Sex						
Female	2348 (47.3)	1974 (47.9)	1054 (42.5)	997 (42.0)	444 (44.3)	370 (46.2)
Male	2614 (52.7)	2144 (52.1)	1426 (57.5)	1377 (58.0)	558 (55.7)	431 (53.8)
Urbanicity at index date						
Missing or unknown	53 (1.1)	32 (0.8)	19 (0.8)	18 (0.8)	6 (0.6)	≤ 5
Urban	3244 (65.4)	2632 (63.9)	1662 (67.0)	1598 (67.3)	734 (73.3)	579 (72.3)
Rural	1665 (33.6)	1454 (35.3)	799 (32.2)	758 (31.9)	262 (26.1)	≤ 221
Community status at index date§						
Missing or unknown	281 (5.7)	227 (5.5)	157 (6.3)	155 (6.5)	83 (8.3)	65 (8.1)
Outside of First Nations community	3583 (72.2)	2920 (70.9)	1795 (72.4)	1718 (72.4)	750 (74.9)	586 (73.2)
Within First Nations community	1098 (22.1)	971 (23.6)	528 (21.3)	501 (21.1)	169 (16.9)	150 (18.7)
LHIN at index date						
Missing or unknown	30 (0.6)	16 (0.4)	11 (0.4)	11 (0.5)	≤ 5	≤ 5
1. Erie St. Clair	328 (6.6)	249 (6.0)	148 (6.0)	139 (5.9)	≤ 5	35 (4.4)
2. South West	376 (7.6)	310 (7.5)	185 (7.5)	174 (7.3)	80 (8.0)	65 (8.1)
3. Waterloo Wellington	56 (1.1)	50 (1.2)	29 (1.2)	27 (1.1)	15 (1.5)	12 (1.5)
4. Hamilton Niagara Haldimand Brant	474 (9.6)	387 (9.4)	238 (9.6)	229 (9.6)	98 (9.8)	81 (10.1)
5. Central West	33 (0.7)	28 (0.7)	15 (0.6)	14 (0.6)	9 (0.9)	7 (0.9)
6. Mississauga Halton	28 (0.6)	22 (0.5)	12 (0.5)	10 (0.4)	≤ 5	≤ 5
7. Toronto Central	335 (6.8)	271 (6.6)	167 (6.7)	163 (6.9)	88 (8.8)	66 (8.2)
8. Central	55 (1.1)	50 (1.2)	27 (1.1)	27 (1.1)	13 (1.3)	11 (1.4)
9. Central East	138 (2.8)	110 (2.7)	69 (2.8)	68 (2.9)	40 (4.0)	32 (4.0)
10. South East	108 (2.2)	88 (2.1)	57 (2.3)	56 (2.4)	31 (3.1)	25 (3.1)
11. Champlain	184 (3.7)	142 (3.4)	95 (3.8)	91 (3.8)	32 (3.2)	23 (2.9)
12. North Simcoe Muskoka	106 (2.1)	82 (2.0)	52 (2.1)	48 (2.0)	29 (2.9)	23 (2.9)
13. North East	1023 (20.6)	845 (20.5)	530 (21.4)	509 (21.4)	202 (20.2)	151 (18.9)
14. North West	1688 (34.0)	1468 (35.6)	845 (34.1)	808 (34.0)	310 (30.9)	267 (33.3)

Table 2 (part 2 of 3): Demographic and clinical characteristics of Status First Nations peoples in Ontario for each stage of the cascade of care for hepatitis C virus (HCV) infection on Dec. 31, 2018

Characteristic†	No. (%) of participants*					
	Positive for HCV antibody *n* = 4962	Tested for HCV RNA *n* = 4118	Positive for HCV RNA *n* = 2480	Genotyped *n* = 2374	Initiated treatment *n* = 1002	Achieved SVR‡ *n* = 801
Comorbidities¶						
ADG score 1 year before index date, mean ± SD	5.1 ± 3.8	5.1 ± 3.7	5.1 ± 3.7	5.1 ± 3.7	5.2 ± 3.7	5.1 ± 3.6
ADG score 1 year before index date, median (IQR)	4 (2–8)	4 (2–8)	5 (2–8)	5 (2–8)	5 (2–8)	5 (2–7)
Number of ADG categories 1 year before index date						
0	387 (7.7)	323 (7.8)	200 (8.1)	193 (8.1)	81 (8.1)	65 (8.1)
1–4	2100 (42.3)	1759 (42.7)	1023 (41.3)	974 (41.0)	393 (39.2)	314 (39.2)
5–9	1806 (36.4)	1500 (36.4)	945 (38.1)	908 (38.2)	399 (39.8)	325 (40.6)
≥ 10	674 (13.6)	536 (13.0)	312 (12.6)	299 (12.5)	129 (12.9)	97 (12.1)
Mental health records						
Substance use and addictive disorders						
Before index date	3728 (75.1)	3069 (74.5)	1918 (77.3)	1825 (76.9)	743 (74.2)	567 (70.8)
Before Dec. 31, 2018	4233 (85.3)	3500 (85.0)	2189 (88.3)	2094 (88.2)	858 (85.6)	667 (83.3)
Mood disorders						
Before index date	1890 (38.1)	1559 (37.9)	931 (37.5)	891 (37.5)	365 (36.4)	281 (35.1)
Before Dec. 31, 2018	2566 (51.7)	2138 (51.9)	1303 (52.5)	1254 (52.8)	539 (53.8)	425 (53.1)
Personality disorders						
Before index date	821 (16.5)	663 (16.1)	428 (17.3)	408 (17.2)	163 (16.3)	121 (15.1)
Before Dec. 31, 2018	1099 (22.1)	897 (21.8)	599 (24.2)	574 (24.2)	232 (23.2)	181 (22.6)
Schizophrenia spectrum and other psychotic disorders						
Before index date	619 (12.5)	494 (12.0)	331 (13.3)	314 (13.2)	123 (12.3)	83 (10.4)
Before Dec. 31, 2018	992 (20.0)	809 (19.6)	551 (22.2)	531 (22.4)	213 (21.3)	152 (19.0)
Anxiety disorders						
Before index date	3731 (75.2)	3107 (75.4)	1914 (77.2)	1833 (77.2)	796 (79.4)	621 (77.5)
Before Dec. 31, 2018	4144 (83.5)	3447 (83.7)	2121 (85.5)	2035 (85.7)	875 (87.3)	691 (86.3)
Trauma or stressor-related disorders						
Before index date	1343 (27.1)	1122 (27.2)	712 (28.7)	685 (28.9)	257 (25.6)	198 (24.7)
Before Dec. 31, 2018	1849 (37.3)	1545 (37.5)	1000 (40.3)	969 (40.8)	379 (37.8)	297 (37.1)
Deliberate self harm						
Before index date	836 (16.8)	675 (16.4)	436 (17.6)	411 (17.3)	152 (15.2)	113 (14.1)
Before Dec. 31, 2018	1245 (25.1)	1025 (24.9)	677 (27.3)	644 (27.1)	236 (23.6)	179 (22.3)
Disease-specific records						
Genotype of HCV infection						
Genotype 1	1711 (34.5)	1711 (41.5)	1592 (64.2)	1592 (67.1)	665 (66.4)	533 (66.5)
Genotype 2	162 (3.3)	162 (3.9)	149 (6.0)	149 (6.3)	70 (7.0)	62 (7.7)
Genotype 3	600 (12.1)	600 (14.6)	559 (22.5)	559 (23.5)	217 (21.7)	164 (20.5)
Genotype 4	≤ 5	≤ 5	≤ 5	≤ 5	≤ 5	≤ 5
Multiple genotypes	≤ 19	≤ 19	≤ 16	≤ 16	≤ 6	≤ 5
Missing or unknown**	2469 (49.8)	1625 (39.5)	163 (6.6)	57 (2.4)	43 (4.3)	36 (4.5)
HBV						
Before index date	52 (1.0)	42 (1.0)	26 (1.0)	26 (1.1)	14 (1.4)	13 (1.6)
Before Dec. 31, 2018	119 (2.4)	103 (2.5)	64 (2.6)	64 (2.7)	32 (3.2)	27 (3.4)

Table 2 (part 3 of 3): Demographic and clinical characteristics of Status First Nations peoples in Ontario for each stage of the cascade of care for hepatitis C virus (HCV) infection on Dec. 31, 2018

Characteristic†	No. (%) of participants*					
	Positive for HCV antibody *n* = 4962	Tested for HCV RNA *n* = 4118	Positive for HCV RNA *n* = 2480	Genotyped *n* = 2374	Initiated treatment *n* = 1002	Achieved SVR‡ *n* = 801
HIV						
Before index date	94 (1.9)	89 (2.2)	45 (1.8)	45 (1.9)	29 (2.9)	22 (2.7)
Before Dec. 31, 2018	187 (3.8)	178 (4.3)	110 (4.4)	109 (4.6)	47 (4.7)	32 (4.0)
Cirrhosis						
Before index date	89 (1.8)	79 (1.9)	50 (2.0)	50 (2.1)	33 (3.3)	31 (3.9)
Before Dec. 31, 2018	240 (4.8)	224 (5.4)	173 (7.0)	173 (7.3)	119 (11.9)	105 (13.1)
Decompensated cirrhosis						
Before index date	65 (1.3)	58 (1.4)	36 (1.5)	36 (1.5)	24 (2.4)	22 (2.7)
Before Dec. 31, 2018	139 (2.8)	130 (3.2)	96 (3.9)	96 (4.0)	67 (6.7)	59 (7.4)
Hepatocellular carcinoma						
Before index date	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Before Dec. 31, 2018	15 (0.3)	14 (0.3)	14 (0.6)	14 (0.6)	9 (0.9)	9 (1.1)
Liver transplant						
Before index date	≤ 5	≤ 5	≤ 5	≤ 5	0 (0.0)	0 (0.0)
Before Dec. 31, 2018	18 (0.4)	18 (0.4)	12 (0.5)	12 (0.5)	10 (1.0)	9 (1.1)

Note: ADG = aggregated diagnosis groups, HBV = hepatitis B virus, IQR = interquartile range, LHIN = Local Health Integration Network, SD = standard deviation, SVR = sustained virologic response.
*Unless indicated otherwise.
†Index date corresponded to the earliest positive record date (positive for HCV antibody, positive for HCV RNA, genotype or treatment dispensation record). For people with only RNA tests on record, index date was assigned as earliest RNA test date. Cell sizes ≤ 5 cannot be reported or able to be recalculated to comply with ICES privacy rules.
‡For certain people, we were unable to check for SVR owing to minimal post-treatment follow-up time.
§Includes people for whom this variable indicated residence outside of Ontario during the year of assessment. Ontario residence for the initial exclusion criteria was determined using the Registered Persons Database rather than the residence within or outside of the First Nations community database.
¶ADG score was derived using the John Hopkins ACG system.
**Includes people with an indeterminate genotype result.

Time to RNA test and treatment initiation

Among the 40 533 Status First Nations peoples with HCV test records (Figure 1), 5227 (12.9%) had a record of a positive HCV antibody test as their index (earliest positive test) date, of whom 4052 had a subsequent record of an HCV RNA test. After censoring those who did not undergo RNA testing (*n* = 1175, 22.5%), the overall median time to subsequent RNA test was 0.64 (95% CI 0.56–0.74) years or about 233 days (Appendix 7, Figure S5, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220717/tab-related-content). For people who resided within First Nations communities, the median time to RNA testing was 0.19 (95% CI 0.16–0.22) years or about 68 days, compared with 0.79 (95% CI 0.66–0.94) years or about 288 days among those who resided outside First Nations communities. When stratified by index date, the median time to RNA test was 1.74 (95% CI 1.49–2.08) years or about 636 days among those with an index date before Dec. 31, 2013, and 0.17 (95% CI 0.15–0.19) years or about 61 days among those with an index date after Dec. 31, 2013.

The overall median time from first positive RNA test to first record of treatment dispensation among all people with a positive RNA test (*n* = 2926, of whom 1071 had a treatment record or were backfilled, and the remaining were censored) was 10.50 (95% CI 9.71–11.14) years (Appendix 7, Figure S6). Stratifying by community status, median time to treatment was 7.60 (95% CI 6.60–9.73) years and 9.75 (95% CI 9.04–10.70) years for people who resided within and outside of First Nations communities, respectively. When stratifying by treatment era, after 2013, the time-to-event curve did not reach a point where 50% of people were treated. When comparing the 25% quartiles, we observed a time to treatment of 5.20 (95% CI 4.80–5.63) years and 1.74 (95% CI 1.50–2.05) years for those with an index date before and after Dec. 31, 2013, respectively.

HCV RNA testing and treatment initiation

In the multivariable analysis of HCV RNA testing, complete case analyses resulted in loss of 8.7% of observations (4771 of 5227 antibody-positive people included). Age category at index date and record of substance use or addictive disorders before the index date were the only covariates that violated the proportional hazards assumption. Therefore, we used piecewise regression to model their effects for up to 1 year and more than 1 year after testing positive for HCV antibody.

Age categories of 41 years and older were positively associated with undergoing an HCV RNA test up to 1 year after testing

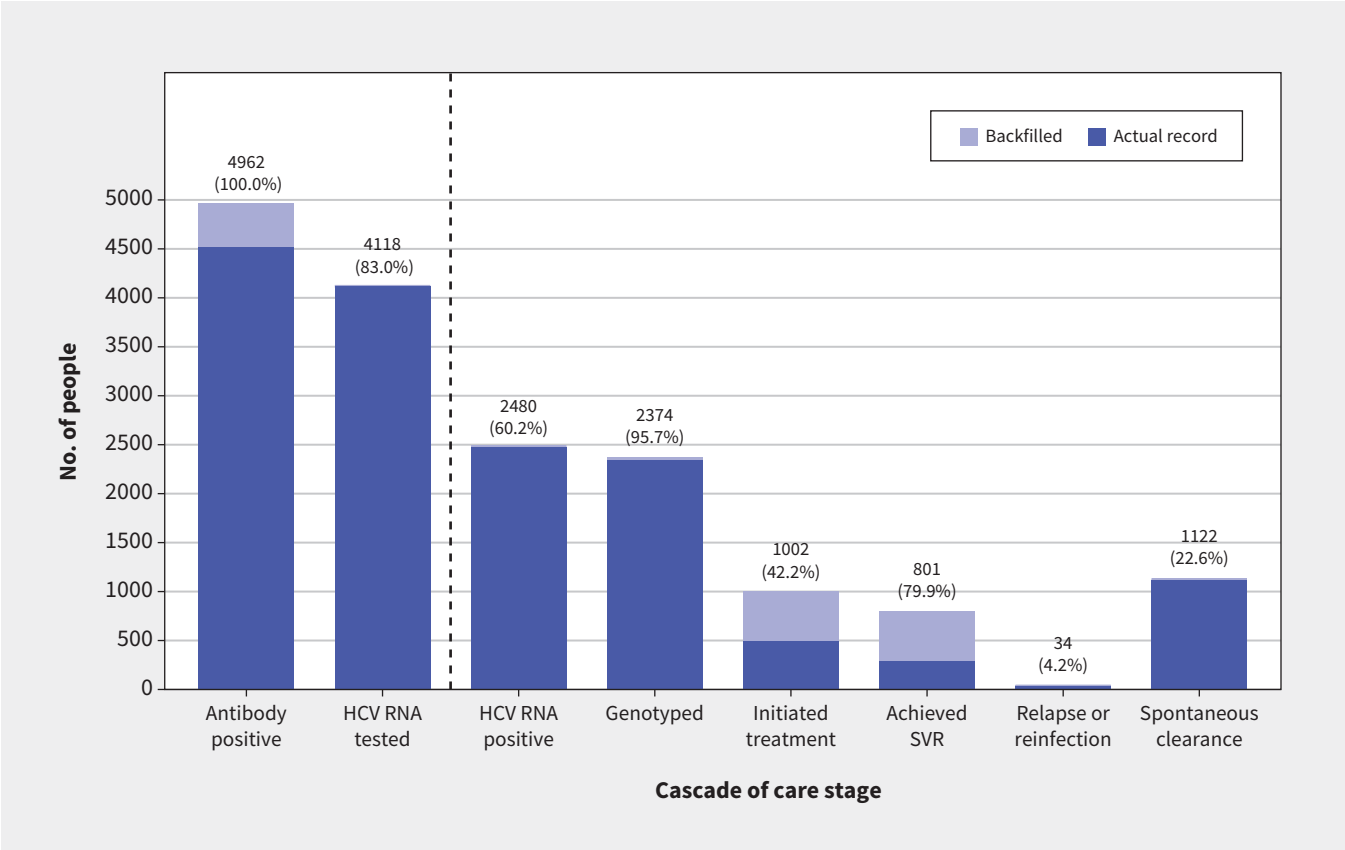

Figure 2: Cascade of care for hepatitis C virus (HCV) infection among Status First Nations peoples in Ontario on Dec. 31, 2018. The annotation above each bar describes the number of individuals and percentages relative to the previous stage. For the spontaneous clearance stage, the annotation above the bar describes the percentage of those who tested positive for HCV antibody. Note: SVR = sustained virologic response.

positive for HCV antibody (Table 3). Female sex, rural residence, residing within a First Nations community and index date in the post-DAA era were significantly positively associated with undergoing an RNA test. Record of substance use or addictive disorders before index date was significantly negatively associated with undergoing RNA testing up to 1 year after testing positive for HCV antibody, but positively associated with being tested for HCV RNA in the later period (Table 3).

In multivariable analysis of initiating treatment after a positive HCV RNA test, complete case analysis resulted in a loss of 8.6% of observations (2675 of 2926 included). Older age category, female sex and index date in the post-DAA era were significantly positively associated with initiating treatment after a positive HCV RNA test (Table 4).

As a sensitivity analysis, when the model was run only considering people with an ODB treatment record (i.e., not backfilled), older age category, previous record of substance use or addictive disorders and index date in the post-DAA era were positively associated with treatment (Appendix 7, Table S12).

Interpretation

We used administrative data to describe the cascade of care for Status First Nations peoples with HCV infection in Ontario. Overall, 17.0% of those who tested positive for HCV antibody did not receive follow-up testing for HCV RNA; 60.0% of those with a reactive HCV RNA test did not initiate treatment, and we were unable to confirm SVR for 20.1% of those who initiated treatment.

From 2013 to 2018, we observed improvements of 13.2% in testing for HCV RNA among antibody-positive people, and of 26.8% in treatment initiation among those genotyped, likely related to the wider availability of DAAs and broader eligibility criteria after 2014.[27] Previous research showed increases in testing and diagnosis of HCV infection among First Nations peoples in Ontario by 2014.[5] Despite these improvements, our results showed a major gap in the treatment initiation stage of the cascade of care for First Nations peoples.

Our time-to-event estimates and uptake rates also likely reflect changes in treatment availability over the study period, including the expanded eligibility for public funding of DAAs for HCV in 2017 in Ontario.[28] The long time from testing positive for HCV RNA to treatment in some individuals may have reflected the documented warehousing effect, with a backlog of treatment-eligible individuals who deferred treatment in anticipation of the wider availability of DAAs.[42] However, crude analyses of ODB records up to 2020 were not indicative of higher prescribing trends after 2017 (Appendix 5).

Barriers such as poor access to health services, and systemic oppression and discrimination, may discourage Indigenous Peoples

Table 3: Factors associated with Status First Nations peoples who underwent testing for hepatitis C virus (HCV) RNA after a positive HCV antibody test (*n* = 4771)*

Variable	Unadjusted* hazard ratio (95% CI)	Adjusted hazard ratio (95% CI)
Sex		
Male	Ref.	Ref.
Female	1.07 (1.01–1.15)	1.12 (1.05–1.19)
Age category (RNA testing ≤ 1 yr after testing positive for antibody)*, yr		
0–20	0.93 (0.78–1.11)	0.94 (0.79–1.13)
21–40	Ref.	Ref.
41–60	1.15 (1.06–1.25)	1.30 (1.19–1.41)
≥ 61	1.68 (1.36–2.06)	1.47 (1.18–1.81)
Age category (RNA testing > 1 yr after testing positive for antibody)*, yr		
0–20	1.05 (0.82–1.34)	1.11 (0.86–1.42)
21–40	Ref.	Ref.
41–60	0.96 (0.84–1.09)	1.03 (0.90–1.17)
≥ 61	0.97 (0.55–1.72)	1.06 (0.60–1.88)
Urbanicity of residence		
Urban	Ref.	Ref.
Rural	1.43 (1.34–1.53)	1.20 (1.10–1.30)
Community residence		
Outside of First Nations community	Ref.	Ref.
Within First Nations community	1.54 (1.42–1.66)	1.19 (1.08–1.31)
Comorbidities†		
ADG score, 1 year before index date	0.98 (0.97–0.99)	0.99 (0.98–0.99)
Coinfection with HBV or HIV		
No record	Ref.	Ref.
Record before index date	0.96 (0.79–1.17)	1.09 (0.89–1.33)
Substance use or addictive disorders (RNA testing ≤ 1 yr after testing positive for antibody)*		
No record	Ref.	Ref.
Record before index date	0.91 (0.84–1.00)	0.88 (0.80–0.96)
Substance use or addictive disorders (RNA testing > 1 yr after testing positive for antibody)*		
No record	Ref.	Ref.
Record before index date	1.36 (1.18–1.58)	1.38 (1.18–1.60)
Treatment era		
Index date before Dec. 31, 2013 (pre-DAA era)	Ref.	Ref.
Index date after Dec. 31, 2013 (post-DAA era)	2.06 (1.92–2.21)	1.99 (1.85–2.15)

Note: ADG = aggregated diagnosis groups, CI = confidence interval, DAA = direct-acting antiviral, HBV = hepatitis B virus, Ref. = reference.
*Model was run with people who had an index date that corresponded to their positive antibody test. Those who did not have an HCV RNA test were censored at date of death, 10 years after date of last contact with the health care system or on Dec. 31, 2018, whichever occurred first. The model was run with 4771 people and consisted of 3753 events and 1018 individuals censored. In total, the model had 14 degrees of freedom. The proportional hazards assumption was checked for each model covariate using time-to-event curves and weighted Schoenfeld residuals (at a threshold of $p < 0.05$). For covariates that violated the assumption, piecewise regression was used where the time interval was split into ≤ 1 year and > 1 year after testing positive for HCV antibody. For covariates that violated the proportional hazards assumption, univariate analyses consisted of the covariate run piecewise over both time intervals.
†ADG score was derived using the John Hopkins ACG System.

from engaging in care and initiating treatment.[3,43,44] We observed a substantial gap in the proportion of people who initiated treatment among those who resided within First Nations communities (33.7% of those genotyped) compared with those who resided outside (43.7% of those genotyped), likely reflecting broader inequalities within communities.[45] Despite this observed gap, we did not observe an association between community residence and treatment initiation in the multivariable analysis.

Table 4: Factors associated with Status First Nations peoples who had a record of first treatment dispensation for hepatitis C virus (HCV) infection after a positive HCV RNA test (*n* = 2675)*

Variable	Unadjusted hazard ratio (95% CI)	Adjusted hazard ratio (95% CI)
Sex		
Male	Ref.	Ref.
Female	1.10 (0.97–1.25)	1.15 (1.01–1.31)
Age, yr		
0–20	1.11 (0.80–1.53)	1.08 (0.78–1.50)
21–40	Ref.	Ref.
41–60	1.18 (1.03–1.34)	1.32 (1.15–1.50)
≥ 61	2.58 (1.78–3.76)	2.62 (1.80–3.82)
Urbanicity of residence		
Urban	Ref.	Ref.
Rural	0.98 (0.85–1.13)	0.85 (0.72–1.01)
Community residence		
Outside of First Nations community	Ref.	Ref.
Within First Nations community	1.13 (0.96–1.33)	1.03 (0.85–1.25)
Comorbidities†		
ADG score, 1 year before index date	0.99 (0.97–1.01)	0.99 (0.97–1.01)
Coinfection with HBV or HIV		
No record	Ref.	Ref.
Record before index date	0.96 (0.69–1.33)	1.00 (0.72–1.40)
Substance use or addictive disorders		
No record	Ref.	Ref.
Record before index date	1.15 (0.99–1.33)	1.09 (0.94–1.28)
Treatment era		
Index date before Dec. 31, 2013 (pre-DAA era)	Ref.	Ref.
Index date after Dec. 31, 2013 (post-DAA era)	2.59 (2.20–3.05)	2.71 (2.29–3.22)

Note: ADG = aggregated diagnosis groups, CI = confidence interval, DAA = direct-acting antiviral, HBV = hepatitis B virus, Ref. = reference.
*Model was run only with people with a positive RNA test. Those who did not initiate treatment were censored at date of death, 10 years after date of last contact with the health care system or on Dec. 31, 2018, whichever occurred first. The model was run with 2675 people and consisted of 973 events (including backfilled treatment people) and 1702 people censored. In total, the model had 10 degrees of freedom. The proportional hazards assumption was checked for each model covariate using time-to-event curves and weighted Schoenfeld residuals (at a threshold of $p < 0.05$) and no variables violated the assumption.
†ADG score was derived using the John Hopkins ACG system.

Long wait times and provider shortages are common barriers to accessing health care services,[46] contributing to lower rates of specialist and family physician visits among First Nations peoples than among non–First Nations people.[47,48] Therefore, allowing other health care professionals such as nurse practitioners to prescribe DAA treatment may increase access.[28] In addition, as the efficacy of treatment relies on adherence, HCV elimination efforts will need to provide services that emphasize peer and community supports, as well as trust between provider and patient, which have been shown to increase adherence and treatment completion among Indigenous peoples.[49] Broader efforts to promote and implement anti-racism and cultural safety training for health care providers will be critical to fostering and restoring trust between Indigenous Peoples and the health care system to encourage them to seek HCV testing and care.[50]

A high prevalence of mental health disorders before the index date suggests that co-location of HCV screening and treatment with harm reduction or addiction treatment services may reach and engage at-risk people.[51,52] Such services, developed with First Nations leadership, have created meaningful relationships between health care providers and at-risk people, and are low-barrier, nonstigmatizing approaches to fast-tracking HCV screening and care within First Nations communities.[51]

It is important to highlight the inherent resilience and tenacity of Indigenous Peoples and the contributions of Indigenous culture and strength to their health today.[53] Cultural teachings and values have been shown to be protective buffers to

HCV infection and the historical and ongoing injustices faced by Indigenous Peoples.[53] The successful engagement in HCV RNA testing and shorter median time to treatment among those who resided within rather than outside of First Nations communities may demonstrate how community attachment, cultural continuity and social supports promote resilience and improve quality of life after HCV diagnosis.[3,13,54,55]

Limitations

Health administrative data have limitations in capturing sociocultural factors and the complex relationships between social determinants of health and HCV among First Nations peoples. The Indian Registry data set at ICES includes Status First Nations peoples who are registered with the Canadian federal government under the *Indian Act* as of 2014.[20] Therefore, it has incomplete enumeration after 2013 and includes no people who registered after 2014.[20] However, registration often occurs at birth[20] and clinically recognized HCV infection is rare in children.[56] Thus, we hypothesize that these missing records would not greatly change our findings. Census estimates show that 151 210 people in Ontario identified as First Nations with Registered or Treaty status in 2016.[57] In comparison, at the midpoint (July) of 2018, we observed 164 711 Status First Nations peoples alive and in the province. Census estimates are generally lower than actual numbers because of people who decline participation or communities being incompletely enumerated.[20]

The Indian Registry data set was linked to the RPDB at ICES, with a linkage rate by year of registration ranging from 63% to 95% and accuracy ranging from 77% to 83%.[20] In addition to people who were not included owing to imperfect data linkage, Ontario is home to 85 475 nonregistered First Nations peoples (as of Census 2016 estimates),[57] and Inuit and Métis peoples; thus, this research does not represent the impact of HCV on Indigenous Peoples overall. We did not obtain permission from Kenora Chiefs Advisory to include information about members of their communities, which represent 9 of the 133 First Nations communities in Ontario.[58]

We relied on annual postal and residence codes to determine LHIN and community residence, which may have led to some misclassification.[18,19] Dichotomizing residence as within or outside of First Nations communities does not express the vast diversity of these communities across Ontario.

Laboratory data from Public Health Ontario do not include results from commercial or private laboratories. ICES data holdings do not include records from the NIHB program, which provides drug coverage and federal or band-funded health services (Appendix 5).[59] To account for these data limitations, we used patterns of HCV RNA testing and other assumptions to backfill stages in the cascade of care.

Because HCV infection can remain asymptomatic until advanced liver disease develops, a limitation of starting our analysis with the stage of testing positive for HCV antibody in the continuum of care is that we are unable to comment on the true prevalence of infection and potential gaps in the reach of HCV antibody testing and screening among the population.

Conclusion

We identified progress and gaps in HCV care among Status First Nations peoples in Ontario. Although progress has been made with the availability of DAA treatments, substantial gaps remain in treatment initiation. Culturally relevant interpretations of the HCV cascade of care can provide data to guide community and policy action that is grounded in First Nations determinants of health and considers the impact of social and structural barriers to accessing health care services. These data provide the opportunity to partner with First Nations decision-makers and health leaders to co-create elimination efforts that include both clinical and nonclinical approaches to prioritize engaging people in HCV testing and care.

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