

Progress toward hepatitis C virus elimination among people living with HIV–hepatitis C virus coinfection in Canada

Mariam Z El Sheikh MSc, MScPH^{1,2}, Jim Young PhD¹, Dimitra Panagiotoglou PhD¹, Curtis Cooper MD, FRCPC^{3,4}, Joseph Cox MD, MSc^{1,2}, Valérie Martel-Laferrrière MD, MSc, FRCPC⁵, Sharon Walmsley MSc, MD, FRCPC^{6,7}, Marina B Klein MD, MSc, FRCP(C)^{1,2,*}

ABSTRACT

BACKGROUND: Direct-acting antivirals (DAAs) for hepatitis C virus (HCV) were approved in Canada in 2013. By 2018, treatment restrictions had been lifted in all provinces, making DAAs universally accessible. Here, we aim to assess progress toward HCV elimination in the DAA era (2014–2022) within the Canadian Co-infection Cohort. **METHODS:** The CCC is a multisite open cohort of people living with HIV-HCV coinfection with cohort visits scheduled biannually. We calculated annual cure rates overall by province and key population: gay bisexual and other men who have sex with men, people who inject drugs, and Indigenous peoples. **RESULTS:** Among the 952 participants eligible for DAAs, 65% (n = 623) were cured and 3% (n = 26) achieved late clearance without treatment by the end of the study period. Of the 35% (n = 303) who were not cured, 46% (n = 138) were lost to follow-up, 31% (n = 95) died, and 23% (n = 70) had insufficient data to determine their cure status. Annual cure rates increased from 2014 to 2019 and then decreased across the cohort and in all key populations. From 2015 to 2018, gay bisexual and other men who have sex with men had the highest cure rates, but by 2019 people who inject drugs and Indigenous peoples caught up. Annual cure rates dropped in all provinces with the onset of the COVID-19 pandemic (after 2019). **CONCLUSIONS:** Universal accessibility of DAAs was an important step toward HCV elimination among people living with HIV-HCV coinfection, but this is not

*Canadian Co-infection Cohort

Author Affiliation

¹Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada; ²Centre for Outcomes Research and Evaluation, McGill University Health Center-Research Institute, Montreal, Quebec, Canada; ³Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada; ⁴Ottawa Hospital Research Institute, Ottawa, Ontario, Canada; ⁵Department of Microbiology, Infectiology and Immunology, Université de Montréal, Montreal, Quebec, Canada; ⁶Division of Infectious Diseases, Department of Medicine, University of Toronto, Toronto, Ontario, Canada; ⁷Toronto General Hospital Research Institute, University Health Network, Toronto, Ontario, Canada

Correspondence: Marina B Klein, Centre for Outcomes Research and Evaluation, RI-MUHC, 5252 Blvd. De Maisonneuve Ouest, Montreal, Quebec H4A 3S9 Canada. Telephone: 514-843-2090/514-934-1934, ext 32306. E-mail: marina.klein@mcgill.ca

© Canadian Association for the Study of the Liver, 2025. This article is free to read to all interested readers, immediately upon publication. For their own personal use, users may read, download, print, search, or link to the full text. Manuscripts published in the *Canadian Liver Journal* are copyrighted to the Canadian Association for the Study of the Liver. Requests for permission to reproduce this article should be made to the University of Toronto Press using the Permission Request Form: https://canlivj.utpjournals.press/policies#_copyright or by email: journal.permissions@utpress.utoronto.ca.

sufficient alone. Efforts are needed to re-engage those who remain uncured and reduce mortality in people living with HIV-HCV coinfection.

KEYWORDS: direct-acting antivirals; elimination; gbMSM; HIV-HCV coinfection; hepatitis C; Indigenous; priority populations; people who inject drugs

LAY SUMMARY

The World Health Organization set targets to eliminate hepatitis C virus infection (HCV) globally by 2030. In late 2013 oral direct-acting antiviral (DAA) medications for HCV were approved in Canada. DAAs can treat HCV within 8–12 weeks with minimal side effects and result in over 95% cure rates. DAA reimbursement eligibility in Canada was initially restricted to people with advanced fibrosis because of cost (\$45,000 to over \$100,000 per patient). These restrictions were lifted in different provinces at different times, but by 2018 all restrictions were removed, making DAAs universally accessible in Canada. In this study we assessed the progress toward HCV elimination, defined as being successfully treated, by calculating annual cure rates (2014–2022) overall by province and by key populations: gay bisexual and other men who have sex with men, people who inject drugs, and Indigenous peoples. We used data from the Canadian Co-Infection Cohort (CCC), which is a cohort of people living with HIV-HCV coinfection recruited from clinic sites across six provinces. We found that we have made progress toward eliminating HCV (65% of participants were successfully treated by the end of 2022); however, we are still short of the World Health Organization target, which requires that 80% of those diagnosed with HCV are treated by 2030. Annual cure rates increased from 2014 to 2019 and then dropped. We found most of those who were not cured were disengaged from care, and 1 in 10 had died, with many deaths due to drug poisoning before treatment for HCV was initiated. Removing a major structural barrier to treatment by making DAAs universally accessible was important, but this was not sufficient alone. Therefore, new tailored interventions are needed for people living with HIV-HCV coinfection to re-engage people into care and reduce premature death.

INTRODUCTION

Hepatitis C virus (HCV) infection is one of the most burdensome infectious diseases in Canada (1,2). In 2019, an estimated 204,000 Canadians

were living with chronic HCV and the infection rate was 30.4 cases/100,000 (3,4). HCV infection has historically been one of the leading causes of liver damage, liver cancer, liver transplant, and liver-related mortality (1,5). Progress in HCV treatment has been remarkable. In late 2013, sofosbuvir, the first second-generation direct-acting antiviral (DAA) medication, was approved in Canada to be used without interferon. Treatment with interferon was highly toxic, of long duration, and had low efficacy (6,7). In contrast, DAAs can treat patients within 8–12 weeks with minimal side effects and result in over 95% sustained virologic response (SVR), which equates to cure (8–10). There is evidence that successful treatment improves quality of life and decreases liver-related morbidity and mortality (11–16). After this significant improvement in HCV treatment, the World Health Organization (WHO) set targets to eliminate HCV globally by 2030. These targets include the treatment of 80% of those diagnosed in order to reduce HCV incidence by 85% and mortality by 65% (5).

People living with HIV, gay bisexual and other men who have sex with men (gbMSM), people who inject drugs (PWID), Indigenous peoples, immigrants from countries where HCV is endemic, and prisoners are disproportionately affected by HCV and face complex barriers to treatment and care (1). These populations have therefore been prioritized for HCV elimination efforts.

An estimated 12,500–18,800 Canadians are living with HIV-HCV coinfection (1,17,18). Modelling studies show that efforts to cure people living with HIV-HCV coinfection are essential to achieving WHO treatment targets in Canada (19). This population is ideal for micro-elimination—the pragmatic approach of focusing on priority populations to achieve elimination targets—because most patients with coinfection are already linked to HIV care, and this population intersects other priority populations, in particular gbMSM, PWID, and Indigenous peoples (1). For example, the majority of new HCV infections (about 85%) are among PWID, who also have the highest rates of coinfection (1). Furthermore, the benefits of HCV treatment for people living with HIV are greater because this popula-

tion experiences faster liver disease progression owing in part to HIV's immunocompromizing effects (20,21). Finally, focusing on this population could provide opportunities to reduce transmission of both HIV and HCV in the community.

When DAAs were first introduced in Canada, only people with advanced liver fibrosis were eligible for reimbursement owing to their cost [\$45,000 to over \$100,000 per patient (22)]. Over time, this treatment restriction was removed across the provinces and territories, in theory making it possible to achieve wide access to treatment. Quebec first removed this restriction for people living with HIV-HCV coinfection in June 2014 for a year, and then permanently in July 2016. The other provinces followed suit, with Ontario and British Columbia removing this restriction in March 2017, and the remaining provinces and territories removing it by the end of 2018 (23–25). The federal Non-Insured Health Benefits program for First Nations and Inuit persons removed the restriction for people living with HIV-HCV coinfection in 2017. While the introduction of DAAs has led to an increase in treatment uptake overall (19), many patient-, provider-, and system-level barriers to accessing care and treatment remain, particularly for priority populations (10,26–31).

Recent work has examined the progress of provinces and territories toward achieving WHO targets (32,33). However, these studies did not examine elimination progress within specific key populations, which is crucial for informing micro-elimination interventions and strategies in the short time left to reach WHO elimination targets by 2030. In this study, we assessed progress toward HCV elimination among key populations of people living with HIV-HCV coinfection who are linked to care. Given the importance of curing HCV in reducing both incident infections and liver-related mortality, we assessed cure rates over time.

METHODS

Data collection

We used the Canadian Co-infection Cohort (CCC) to examine progress toward the WHO HCV elimination treatment target of 80% treated during the DAA era. Given the high rates of SVR expected with treatment (95%), this treatment target should translate into an overall cure rate of at least 76%. CCC is an open prospective cohort following participants living with HIV-HCV coinfection recruited at 16 clinic sites from five provinces—Quebec, Ontario, Alberta, British Columbia, and Nova Scotia—since

2003, expanding to two sites in Saskatchewan in 2013 and 2014 (Figure S1) (34). The cohort includes adults (aged 16 years or older) who have an HIV infection and evidence of either a past or current HCV infection. Cohort visits are scheduled every 6 months when behavioural, treatment, and laboratory data are collected. This cohort is representative of the population of people living with HIV-HCV coinfection who are linked to care in large and small urban centres across Canada (34,35). Members of the community were engaged in the development of CCC questionnaires and the interpretation of data.

Study population

CCC participants who were HCV RNA positive on or after January 1, 2014 and eligible for DAA coverage were included in the analytic sample and could contribute person-time until December 31, 2022, or censoring (see later). Important definitions used to characterize the study population can be found in Figure 1. Before the removal of fibrosis stage restrictions, only HCV RNA positive participants with fibrosis were considered eligible for DAA coverage. After the restrictions were lifted, all HCV RNA participants were considered eligible. The date on which they were considered eligible was their follow-up start date. Participants were excluded if they: spontaneously cleared HCV within a year of their follow-up start date, or did not have enough time to achieve SVR before the study end date (December 31, 2022). For each calendar year from 2014 to 2022 inclusive, DAA-eligible participants were included in the population for that year (Figure S3). Each participant contributed person-time until they either: achieved SVR, achieved late spontaneous clearance, died, withdrew from the cohort, were lost to follow-up (LTFU), or were administratively censored (December 31 of the year of interest).

Statistical analysis

Annual cure rates (2014 to 2022, inclusive) were calculated and reported per 100 person-years for the cohort overall, by province and by key populations: gbMSM, PWID, and Indigenous. Poisson distributions were used to calculate 95% confidence intervals for the rates and to make inferences about the populations living with coinfection linked to care across Canada, assuming the CCC is representative of the Canadian coinfection population in care (36). We then described the characteristics of those who were not cured.

Important definitions:

Sustained virologic response (SVR): presence of a negative HCV RNA result at least 10 weeks from treatment completion date (50).

Spontaneous clearance: presence of a negative HCV RNA result within a year of follow-up start date without evidence of initiating treatment.

Late spontaneous clearance: presence of a negative HCV RNA result more than a year of follow-up start date without evidence of treatment.

Lost to follow-up (LTFU): a period of 18 months or more since the last collection of HCV data (i.e., HCV RNA lab result or HCV treatment information or cohort visit) (11). There are 2 types of LTFU: 1) Temporary LTFU: patient re-engaged in care after a gap of 18 months or more; and 2)

Permanent LTFU: patient never re-engaged in care until the end of the study period. Patients stop contributing person-time at the onset of LTFU, and in the case of temporary LTFU, reinitiate contributing person-time upon their return.

Active PWID: reported to have injected drugs at least once during the period of interest.

gbMSM: self-identified as male and as either homosexual or bisexual at baseline.

Figure 1: Important definitions

RESULTS

CCC overall

During the study period, 952 participants were eligible for DAA treatment (Figure S2). Of the DAA-eligible participants, 72% (n = 684) initiated treatment, of whom 91% (n = 623) achieved SVR (representing 65% of DAA-eligible participants overall); 3% (n = 26) achieved late spontaneous clearance (i.e. more than 1 year after follow-up start date). Most participants had only one HCV infection, although 4% experienced at least one re-infection following cure during the study period. Annual cure rates increased across the cohort from 2014 to 2019, then dropped substantially in 2020 and failed to recover thereafter (Figure 2).

Reflecting increased treatment rates, the total number of individuals in the DAA-eligible population decreased beginning in 2018 (Table 1). Furthermore, as the CCC expanded in Saskatchewan, the demographic composition of the DAA-eligible population changed over time. The proportion of Indigenous participants who were eligible for treatment increased from 15% in 2014 to 44% in 2021, peaking at 48% in 2019. Similarly, the percentage of female participants increased from 26% in 2014 to 40% in 2021 with a peak of 43% in 2020. The percentage of active PWID participants also increased from 28% in 2014 to 41% in 2021, peaking at 42% in 2019. Conversely, the percentage of gbMSM declined from 24% in 2014 to 19% in 2021, reaching its lowest point at 11% in 2019.

Key populations

At baseline, 22% (n = 208) of participants self-identified as gbMSM, 29% (n = 278) as women,

48% (n = 455) as heterosexual men, and 27% (n = 255) as Indigenous. Meanwhile, 43% (n = 406) reported having injected drugs during the study period—that is, they were active PWID (Table 1). As these groups were not mutually exclusive, we examined the intersectional identities of participants who belonged to several key populations. We found that 19% of participants identified as Indigenous and active PWID, 2% identified as gbMSM and Indigenous, 6% identified as active PWID and gbMSM, and 1% identified as Indigenous, active PWID, and gbMSM (Figure 3). Quebec and British Columbia had a large proportion of participants who identified as active PWID as the only priority group classification (58% and 40%, respectively), while Saskatchewan had the highest proportion of Indigenous peoples who were active PWID (51%). Ontario had the highest proportion of gbMSM (50%), and Saskatchewan had the lowest proportion of gbMSM (3%). Cure rates while taking intersectionality into account were not examined due to small sample sizes, except for people identifying as both Indigenous and active PWID. Cure rates for these participants were lower than rates for those who identified as either Indigenous or active PWID, except in 2019 when they all converged (Figure S4).

The percentage of participants who were HCV RNA negative (those achieving SVR/late spontaneous clearance combined) by the end of follow-up was highest among gbMSM (77%), followed by women (71%), and was lower among active PWID (66%), heterosexual men (65%), and Indigenous peoples (64%) (Figure S5).

Key populations had different trends in annual cure rates, suggesting differences in access to

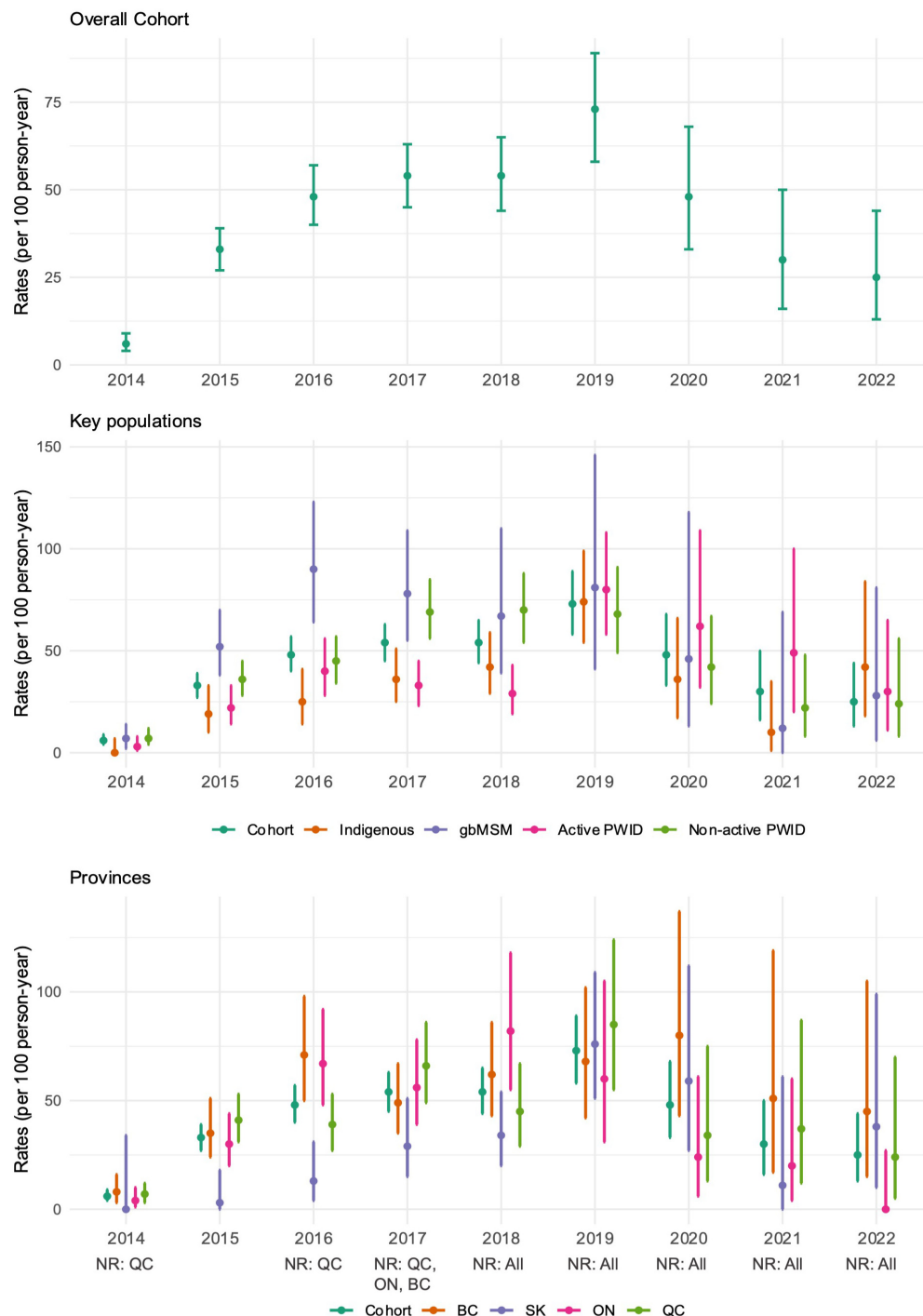


Figure 2: Annual cure rates for 2014–2022

treatment, particularly before the lifting of DAA restrictions. GbMSM had appreciably higher rates than the cohort overall and other key populations initially. Women and heterosexual men reached similar rates to gbMSM by 2018 (Figure S6). Indigenous peoples and active PWID had relatively lower cure rates than the cohort overall until 2019, when all cure rates converged. In 2020, cure rates dropped

notably in all populations, including gbMSM, with rates among Indigenous peoples dropping more sharply than those among active PWID (Figure 2B).

Differences in treatment access across key populations were present, even within the same province, and affected overall cure rates for certain key populations. For example, 36% of gbMSM were from Quebec, where fibrosis stage restrictions were

Table 1: Summary of direct-acting antiviral-eligible participants for the entire period and year of interest

	Overall	2014	2015	2016	2017	2018	2019	2020	2021	2022
Participants	952	490	512	384	405	301	219	105	79	73
Infection rounds*	994	491	514	386	407	303	222	105	80	73
Treatment initiation rounds†	730 (73%)‡	58 (12%)	140 (27%)	100 (26%)	139 (34%)	98 (13%)	72 (32%)	25 (24%)	12 (15%)	21 (29%)
Rounds with SVR§	663 (67%)	22 (4%)	121 (24%)	122 (32%)	143 (35%)	106 (35%)	91 (41%)	32 (30%)	14 (18%)	12 (16%)
Median uninterrupted follow-up time (months)	15.6	11.5	9.9	8.2	9.4	9.0	6.7	9.7	6.4	7.7
Key populations (n, percentage of total infection rounds*)										
Indigenous	255 (27%)	72 (15%)	99 (19%)	85 (22%)	128 (32%)	123 (41%)	104 (48%)	39 (37%)	32 (40%)	32 (44%)
gbMSM (self-identified at baseline)	208 (22%)	116 (24%)	116 (23%)	80 (21%)	75 (18%)	40 (13%)	25 (11%)	14 (13%)	11 (14%)	14 (19%)
Women	278 (29%)	126 (26%)	141 (28%)	110 (29%)	128 (32%)	109 (36%)	83 (38%)	45 (43%)	33 (42%)	29 (40%)
Heterosexual men	455 (48%)	245 (50%)	252 (49%)	191 (50%)	198 (49%)	149 (50%)	109 (50%)	45 (43%)	35 (44%)	27 (37%)
PWID (ever)	809 (85%)	403 (82%)	433 (85%)	330 (86%)	368 (91%)	276 (92%)	205 (94%)	95 (90%)	69 (87%)	61 (84%)
Active PWID	406 (43%)	135 (28%)	143 (28%)	123 (32%)	160 (40%)	112 (37%)	92 (42%)	33 (31%)	23 (29%)	30 (41%)
Provinces (n, percentage of total individuals)										
Quebec	300 (32%)	217 (44%)	218 (43%)	147 (38%)	124 (31%)	75 (25%)	53 (24%)	28 (27%)	19 (24%)	18 (25%)
Ontario	236 (25%)	117 (24%)	120 (23%)	90 (23%)	98 (24%)	63 (21%)	35 (16%)	24 (23%)	23 (29%)	17 (23%)
British Columbia	261 (27%)	113 (23%)	115 (22%)	85 (22%)	120 (30%)	84 (28%)	53 (24%)	26 (25%)	18 (23%)	20 (27%)
Saskatchewan	134 (14%)	29 (6%)	45 (9%)	53 (14%)	57 (14%)	76 (25%)	73 (33%)	25 (24%)	18 (23%)	18 (25%)
Alberta	14 (2%)	11 (2%)	11 (2%)	8 (2%)	6 (2%)	2 (1%)	1 (1%)	1 (1%)	1 (1%)	0 (0%)
Nova Scotia	7 (1%)	3 (1%)	3 (1%)	1 (0%)	0 (0%)	1 (0%)	4 (2%)	1 (1%)	0 (0%)	0 (0%)

*As some participants were infected more than once, this represents the number of infection rounds rather than number of individuals; for example, some participants would be counted two times if they got reinfected

†The number of participants who initiated treatment in a given year. It is important to note that usually when someone initiates treatment in a specific year, that does not mean that their SVR will be observed in that year

‡72% of participants who initiated treatment (as multiple participants were infected more than once and did not initiate treatment in all their infection rounds)

§The number of participants who achieved SVR in a given year

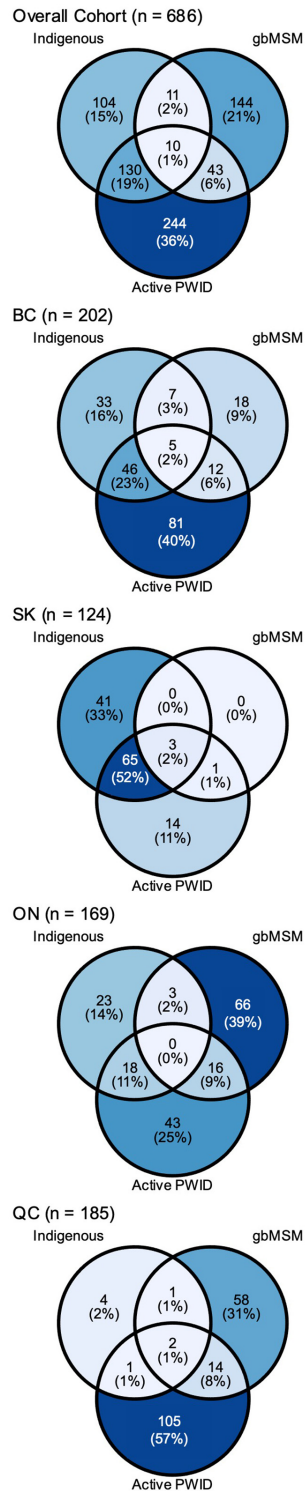
gbMSM = gay bisexual and other men who have sex with men; PWID = people who inject drugs; SVR = sustained virological response

removed earliest (briefly in 2014 for a year, then permanently in 2016), potentially explaining earlier treatment access for this group. However, while 30% of the active PWID population also lived in Quebec, they did not experience commensurate uptake of treatment with the removal of fibrosis-based restrictions, suggesting that gbMSM may have accessed treatment earlier for other reasons. There were no notable differences between gbMSM and other key populations in terms of fibrosis or advanced liver disease (Table S1). However, gbMSM were older, more educated, and had higher income on average than PWID and Indigenous peoples linked to care.

Provinces

Among 952 eligible participants, 32% (n = 300) were in Quebec, 27% (n = 261) were in British Columbia, 25% (n = 236) were in Ontario, and 14% (n = 134) were in Saskatchewan (Table 1). Alberta and Nova Scotia were excluded from this comparison due to their small sample size (n = 14 and 7, respectively). At the end of follow-up, British Columbia and Quebec had the highest percentage of participants who were HCV RNA negative (75% and 73%, respectively), followed by Ontario (65%) and, last, Saskatchewan (59%) (Figure S5). Although Saskatchewan had the lowest cure rates owing to lower initial treatment uptake rates, by

Total Key populations



B) Cured Key populations

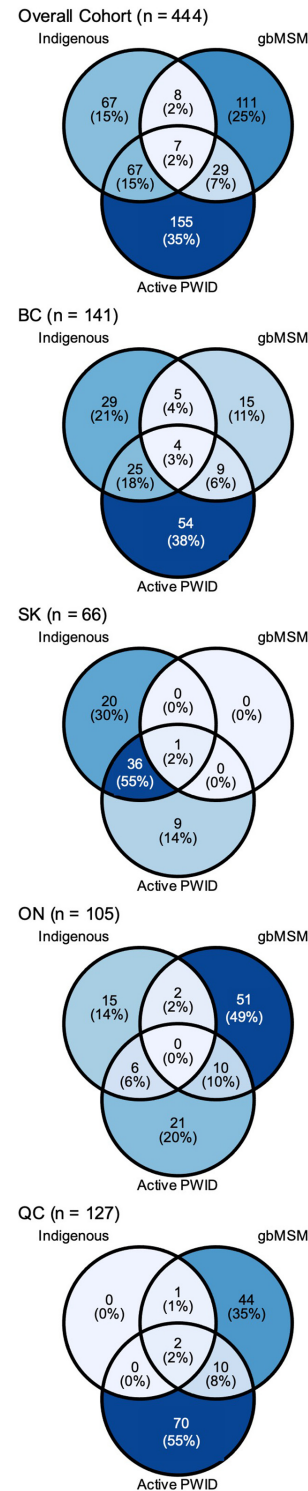


Figure 3: Overlap between key populations for cohort overall and by province

2019 its cure rates matched those observed in other provinces.

Participants who were not cured

Of those who were not cured (n = 303), 46% (n = 138) were LTFU (14% overall), 31% (n = 95) died

(10% overall), 19% (n = 58) were administratively censored, and 4% (n = 12) withdrew from the cohort.

The majority of those who were not cured were LTFU (46%) (Figure S5). The majority of LTFU events occurred in 2017 (18%), followed by 2016

and 2020 (15%) (Figure S7). Socio-demographic, clinical, risk, and behavioural factors were compared between those who achieved SVR and those who were LTFU (Table S3). The percentage of participants who were actively injecting drugs among those who were LTFU was greater than that among those who achieved SVR (51% versus 40% for actively injecting drugs ever during the study period, and 40% versus 24% for those reporting to have injected drugs in the 6 months prior to their last visit).

Among participants who died ($n = 95$; 31%), the most common causes were drug poisoning (overdose; 17%), infection (16%), and end-stage liver disease (15%); 22% of deaths were due to unknown causes (Table S2). Heterosexual men were over-represented among those who died without being cured compared with those who achieved SVR (61% versus 45%), while there were fewer gbMSM among those who died than were cured (12% versus 25%). Additionally, the proportion of recent injection drug use and those who were experiencing homelessness/living in a shelter was nearly twice as high among those who died compared with those who achieved SVR (43% versus 24%, 14% versus 6%, respectively). Low income was also more common among those who died than among those who achieved SVR (77% versus 62%). Finally, the percentage of those with uncontrolled HIV and cirrhosis was greater among those who died than among those who achieved SVR (23% versus 1%, 48% versus 20%, respectively).

DISCUSSION

We found that there has been considerable progress toward HCV elimination through treatment and cure of people living with HIV-HCV coinfection in Canada during the DAA era. Overall, 72% of those eligible for treatment started DAAs and 65% were cured by the end of 2022. Making DAAs universally accessible has helped to make this progress possible. However, during the COVID-19 pandemic years (2020–2022) cure rates dropped by 50% and have yet to recover. Reaching the WHO target of treating 80% of those diagnosed by 2030 will require maintaining or exceeding pre-pandemic treatment rates and addressing remaining gaps in care. In particular, 14% of participants were lost from care, representing 47% of those who were not cured in the cohort. Mortality was also very high, with 10% dying before being cured.

Cure rates peaked in 2019 in the cohort overall, across provinces and key populations. DAA coverage restrictions were lifted in different provinces at different times, but by 2018 all restrictions were removed, making DAAs universally accessible in Canada. The increase in treatment uptake and subsequent high cure rates in 2019 may be due to a warehousing effect, where the majority of those who were linked to care but could not yet be treated due to earlier restrictions were treated shortly after their removal (23). The steep decline in treatment uptake observed after 2019 may be explained by the successful treatment of most people in care, leaving behind the more vulnerable individuals who continued to encounter barriers to care and stigma, which may have been further accentuated during the pandemic (32,33). However, even with the pre-pandemic gains, only 65% of the cohort were cured, short of the elimination cure target of 76%. Our data tracks well with other available data sources. Trends in annual cure rates for Ontario are consistent with trends in reported DAA dispensation in the province up to 2018 (37). Similar trends have also been reported in Australia where, following the introduction of unrestricted access to DAAs in March 2016, treatment uptake rapidly increased and has then declined ever since (38,39). While the pandemic likely accelerated this decline, Australia has identified increased testing and linkage to care of populations not connected to, or alienated from, mainstream health services as being key to reaching elimination goals (40).

Cure rate trends differed between key populations. From 2015 to 2018, gbMSM had the highest cure rates, while active PWID and Indigenous populations had the lowest rates. However, by 2019 the rates among PWID and Indigenous peoples had caught up. Pre-2020 trends in cure rates suggest the presence of treatment access disparities according to key populations and even within the same province. For example, the results suggest that in Quebec, gbMSM accessed treatment earlier than PWID regardless of the presence of fibrosis. In our study, gbMSM were more educated and had higher income when compared with other key populations. Similarly, in the British Columbia Hepatitis Testers Cohort, gbMSM had increased odds of treatment uptake while PWID had lower odds of treatment uptake. The majority of prescribing physicians treating gbMSM were infectious disease specialists, suggesting they had different access to care and higher socioeconomic status (41). As with other infections, such as HIV, socioeconomic fac-

tors may contribute to differences in treatment rates observed across key populations (42).

Across provinces, there was a general increase in cure rates after changes in provincial policies. Variation in HCV-related provincial policies was likely a contributing factor to the differences in cure rates observed. For example, in Ontario cure rates increased in 2016, 2018, and 2019. This likely represents the effects of three policies implemented in the province over time: DAAs were added to the Exceptional Access Program in 2015, fibrosis stage restrictions were removed in 2017, and newer DAAs with fewer side effects and drug-drug interactions were added to the public drug formulary in 2018 (37). By the end of 2018, once policies were consistent across all provinces, cure rates converged despite demographic differences, suggesting that unrestricted access to DAA reduced geographic heterogeneity and thus democratized HCV treatment and consequently cure. These patterns emphasize the power of health policies and show their potential for an immediate impact on access to care and treatment for different patient populations. New policies and programs involving tailored holistic interventions are now needed to remove barriers to care for the patient populations left behind if Canada is to meet the WHO targets and to address the effects of the pandemic that we have not recovered from yet.

The majority of those who were not cured were LTFU, which underscores the importance of re-engaging this group in care. Our results show that more people were actively injecting drugs among those LTFU compared with those who achieved SVR. PWID have different experiences than those who do not use drugs due to stigma and other structural barriers, limiting their access to treatment (43). In Canada, PWID remain most at risk of acquiring HCV, accounting for 60%–85% of new HCV infections (1). Recent studies show that high treatment uptake by PWID is essential for HCV elimination and that harm-reduction interventions are critical to maintaining elimination successes (44–47). These initiatives prevent people from drug poisoning and reduce transmission of HCV in the community (24). Evidence also supports the diversification of models of care so that people are cared for where they can be found, such as integrating HCV care (including HCV diagnosis and treatment) within supervised consumption sites, harm-reduction programs, and prisons (37,48,49). An effective HCV elimination strategy will con-

sider initiatives that enhance HCV infection prevention while reducing the harms of injection drug use and the toxic drug supply. This will also allow us to have a positive impact on the health of people living with HIV-HCV coinfection beyond HCV.

Furthermore, a high percentage of those who were not cured died while in care before achieving SVR, with the leading cause of death for those who died with known causes being drug poisoning followed by infection and end-stage liver disease (all preventable deaths). Our findings show that those who died were more marginalized compared with those who achieved SVR. Similarly, a recent study reported that markers of vulnerability were associated with mortality among those living with HIV-HCV coinfection (50). This suggests the presence of systemic problems along the HCV care cascade that discriminates against marginalized populations. This underscores the importance of holistic systemic and structural interventions along different points of the HCV cascade.

Finally, it is important to acknowledge that membership in key populations is not exclusive and recognize the role intersectional realities play in facilitating or keeping people from initiating HCV treatment (19). As discussed earlier, PWID face stigma and structural barriers, and Indigenous peoples contend with persisting systemic and structural racism. Given the disproportionate burden of substance use within the Indigenous population stemming from the legacy of residential schools and ongoing colonization, these intersecting challenges exacerbate the barriers these populations encounter (24). Furthermore, PWID, for example, intersect differently with other populations across provinces. PWID in Saskatchewan largely intersect with the Indigenous population, while PWID in Quebec do not (Figure 3A). This underscores the inherent heterogeneity of PWID populations and the need for interventions to be tailored differently, as each population faces different barriers to care.

A key strength of our study was using one of the world's largest and most diverse longitudinal cohorts of people living with HIV-HCV coinfection linked to care to describe progress toward HCV elimination in Canada across provinces and key population groups. Our approach examined elimination progress using rich patient-level data. These data enabled us to explore the intersectional identities in our cohort and illustrated that the compounding effects of belonging to more than one population can amplify the barriers faced by pa-

tients. However, we could not fully explore the impact of intersectionality on cure rates due to the limited sample size of subgroups. Future studies should aim to examine the role of intersectionality in treatment initiation and cure to better identify barriers along the HCV cascade of care. Cure rates could be underestimated as 7% of participants ($n = 70$) had insufficient data to determine their cure status due to administrative censoring or withdrawal from the cohort. A limitation of our study is that it did not capture patients not linked to care, estimated to be up to 15% of those diagnosed with HIV-HCV coinfection (23), who likely have much lower cure rates and likely face even more barriers requiring different approaches.

Over the past 8 years, we have made significant strides in democratizing access to HCV treatment by making DAAs universally accessible in Canada, moving into a 'treat all' era. Despite remarkable progress, universal access to DAAs does not appear to be sufficient to reach HCV elimination for people living with HIV-HCV coinfection. The COVID-19 pandemic has further impacted treatment efforts. Tailored holistic interventions are needed to reach people left behind, engage, and retain in care different patient populations, and reduce premature deaths in people living with HIV-HCV coinfection.

ACKNOWLEDGEMENTS: The authors acknowledge participants of the Canadian Coinfection Cohort (CTN222), the study co-ordinators, and nurses for their assistance with study coordination, participant recruitment, and care, and the CTN222 co-investigators. This work was submitted as a poster abstract at the Annual Meeting of the Canadian Association for the Study of the Liver (CASL), the Canadian Network on Hepatitis C (CANHEPC), and the Canadian Association of Hepatology Nurses (CAHN) 2024.

CONTRIBUTIONS: Conceptualization: MZ El Sheikh, J Young, MB Klein; Methodology: MZ El Sheikh, J Young, MB Klein; Validation: MZ El Sheikh, J Young, D Panagiotoglou, MB Klein; Formal Analysis: MZ El Sheikh; Investigation: MZ El Sheikh, J Young, D Panagiotoglou, MB Klein; Data Curation: J Cox, C Cooper, V Martel-Laferrrière, S Walmsley, MB Klein; Writing - Original Draft: MZ El Sheikh, J Young, D Panagiotoglou, MB Klein; Writing - Review & Editing: MZ El Sheikh, J Young, D Panagiotoglou, J Cox, C Cooper, V Martel-Laferrrière, S Walmsley, MB Klein; Visualization: MZ El Sheikh; Supervision: J Young, D Panagiotoglou, MB Klein.

ETHICS APPROVAL: The CCC was approved by a community advisory committee of the Canadian Institutes of

Health Research (CIHR)–Canadian HIV Trials Network and by all institutional ethics boards of the participating centres.

INFORMED CONSENT: Participants in the CCC signed consent forms permitting use of their data for secondary analyses.

REGISTRY AND THE REGISTRATION NO. OF THE STUDY/TRIAL: N/A

DATA ACCESSIBILITY: The data used in this study are not publicly available. However, they may be shared after being de-identified with researchers provided that a data-sharing agreement is acquired which includes a project proposal, an analysis plan and a data management plan.

FUNDING: This study was supported by the Canadian Institutes of Health Research (CIHR; FDN-143270 and PJT-185954), Fonds de recherche du Québec-Santé (FRQS), Réseau sida/maladies infectieuses, and the CIHR Canadian HIV Trials Networks (CTN222). ME was supported by the McGill Centre for Viral Diseases and McGill Interdisciplinary Initiative in Infection and Immunity Studentship Award. MB Klein is supported by a Tier I Canada Research Chair.

DISCLOSURES: ME, DP, JY: No conflicts of interest to disclose. VML: 1) Grant or contract from Gilead Sciences and Merck (Outside the submitted work), 2) Participation on a Data Safety Monitoring Board or Advisory Board: Gilead Sciences and AbbVie (Outside the submitted work), 3) Supported by Clinical Research Scholar - Junior 2 program (FRQ-S). JC: 1) Grant or contract from Gilead and ViiV Healthcare, 2) Support for attending meetings and/or travel from Gilead and ViiV Healthcare, 3) Participation on a Data Safety Monitoring Board or Advisory Board: Gilead and ViiV Healthcare. CC: 1) Grants or contract from AbbVie, Gilead and ViiV Healthcare, 2) Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from AbbVie, Gilead and ViiV Healthcare, 3) Participation on a Data Safety Monitoring Board or Advisory Board: AbbVie, Gilead and ViiV Healthcare. SW: 1) Grant or contract from Gilead Sciences, Merck, ViiV Healthcare and Janssen, 2) Consulting fees from Gilead Sciences, Merck, and ViiV Healthcare, 3) Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Merck, ViiV Healthcare. MK: 1) Grants or contract from AbbVie, Gilead and ViiV Healthcare, 2) Consulting fees from ViiV Healthcare, AbbVie and Gilead, 3) Participation on a Data Safety Monitoring Board or Advisory Board: AbbVie, Gilead and ViiV Healthcare.

PEER REVIEW: This manuscript was peer reviewed.

ANIMAL STUDIES: N/A

REFERENCES

1. The Canadian network on hepatitis C blueprint writing committee and working groups. Blueprint to inform hepatitis C elimination efforts in Canada. Montreal, QC. 2019. https://canhepc.ca/sites/default/files/media/documents/blueprint_hcv_2019_05.pdf (Accessed January 13, 2022).
2. Global health sector strategy on viral hepatitis 2016–2021. Towards ending viral hepatitis. World Health Organization. 2016. https://apps.who.int/iris/bitstream/handle/10665/246177/WHO-HIV-2016_06-eng.pdf?sequence=1 (Accessed January 13, 2022).
3. Canada PHA of hepatitis C in Canada: 2019 surveillance data. 2021. <https://www.canada.ca/en/public-health/services/publications/diseases-conditions/hepatitis-c-2019-surveillance-data.html> (Accessed August 8, 2022).
4. Canada PHA of people living with hepatitis C (HCV) in Canada. 2022. <https://www.canada.ca/en/public-health/services/publications/diseases-conditions/infographic-people-living-with-hepatitis-c.html> (Accessed September 27, 2022).
5. Stanaway JD, Flaxman AD, Naghavi M, et al. The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. *The Lancet*. 2016;388(10049):1081–8. [http://doi.org/10.1016/S0140-6736\(16\)30579-7](http://doi.org/10.1016/S0140-6736(16)30579-7). Medline: 27394647
6. Kish T, Aziz A, Sorio M. Hepatitis C in a new era: A review of current therapies. *Pharm Ther*. 2017;42(5):316–29.
7. Gane E. Future perspectives: towards interferon-free regimens for HCV. *Antivir Ther*. 2012;17(6):1201–10. <http://doi.org/10.3851/IMP2431>. Medline: 23186654
8. Zoratti MJ, Siddiqua A, Morassut RE, et al. Pangenotypic direct acting antivirals for the treatment of chronic hepatitis C virus infection: A systematic literature review and meta-analysis. *EClinicalMedicine*. 2020;18:100237. <http://doi.org/10.1016/j.eclinm.2019.12.007>. Medline: 31922124
9. Afdhal N, Zeuzem S, Kwo P, et al. Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. *N Engl J Med*. 2014;370(20):1889–98. <http://doi.org/10.1056/NEJMoa1402454>. Medline: 24725239
10. Saeed S, Strumpf EC, Moodie EE, et al. Disparities in direct acting antivirals uptake in HIV-hepatitis C co-infected populations in Canada. *J Int AIDS Soc*. 2017;20(3):e25013. <http://doi.org/10.1002/jia2.25013>. Medline: 29116684
11. Mohanty A, Salameh S, Butt AA. Impact of direct acting antiviral agent therapy upon extrahepatic manifestations of hepatitis C virus infection. *Curr HIV/AIDS Rep*. 2019;16(5):389–94. <http://doi.org/10.1007/s11904-019-00466-1>. Medline: 31482299
12. Saeed S, Moodie EEM, Strumpf E, et al. Real-world impact of direct acting antiviral therapy on health-related quality of life in HIV/hepatitis C co-infected individuals. *J Viral Hepat*. 2018;25(12):1507–14. <http://doi.org/10.1111/jvh.12985>. Medline: 30141236
13. Backus LI, Belperio PS, Shahoumian TA, Mole LA. Direct-acting antiviral sustained virologic response: Impact on mortality in patients without advanced liver disease. *Hepatology*. 2018;68(3):827–38. <http://doi.org/10.1002/hep.29811>. Medline: 29377196
14. Singal AG, Rich NE, Mehta N, et al. Direct-acting antiviral therapy for hepatitis C virus infection is associated with increased survival in patients with a history of hepatocellular carcinoma. *Gastroenterology*. 2019;157(5):1253–1263.e2. <http://doi.org/10.1053/j.gastro.2019.07.040>. Medline: 31374215
15. Butt AA, Yan P, Shuaib A, Abou-Samra AB, Shaikh OS, Freiberg MS. Direct-acting antiviral therapy for HCV infection is associated with a reduced risk of cardiovascular disease events. *Gastroenterology*. 2019;156(4):987–996.e8. <http://doi.org/10.1053/j.gastro.2018.11.022>. Medline: 30445009
16. Butt AA, Yan P, Aslam S, Shaikh OS, Abou-Samra AB. Hepatitis C virus (HCV) treatment with directly acting agents reduces the risk of incident diabetes: Results from electronically retrieved cohort of HCV infected veterans (ERCHIVES). *Clin Infect Dis*. 2020;70(6):1153–60. <http://doi.org/10.1093/cid/ciz304>. Medline: 30977808
17. Hull M, Shafran S, Wong A, et al. CIHR Canadian HIV trials network coinfection and concurrent diseases core research group: 2016 updated Canadian HIV/Hepatitis

- C adult guidelines for management and treatment. *Can J Infect Dis Med Microbiol*. 2016;2016:e4385643. <http://doi.org/10.1155/2016/4385643>. Medline: 27471521
18. Canada PHA of estimates of HIV incidence, prevalence and Canada's progress on meeting the 90-90-90 HIV targets, 2020. 2022. <https://www.canada.ca/en/public-health/services/publications/diseases-conditions/estimates-hiv-incidence-prevalence-canada-meeting-90-90-90-targets-2020.html> (Accessed October 7, 2023).
19. Binka M, Janjua NZ, Grebely J, et al. Assessment of treatment strategies to achieve hepatitis C elimination in Canada using a validated model. *JAMA Netw Open*. 2020;3(5):e204192. <http://doi.org/10.1001/jamanetworkopen.2020.4192>. Medline: 32374397
20. Gobran ST, Ancuta P, Shoukry NH. A tale of two viruses: Immunological insights into HCV/HIV coinfection. *Front Immunol*. 2021; 12:726419. <http://doi.org/10.3389/fimmu.2021.726419>. Medline: 34456931
21. Chen JY, Feeney ER, Chung RT. HCV and HIV co-infection: mechanisms and management. *Nat Rev Gastroenterol Hepatol*. 2014;11(6):362–71. <http://doi.org/10.1038/nrgastro.2014.17>. Medline: 24535328
22. Alliance PCP. A statement from the pan-Canadian pharmaceutical alliance. 2017. <https://www.newswire.ca/news-releases/a-statement-from-the-pan-canadian-pharmaceutical-alliance-614373463.html> (Accessed August 23, 2024).
23. Saeed S, Strumpf E, Moodie EEM, et al. Eliminating structural barriers: The impact of unrestricted access on hepatitis C treatment uptake among people living with human immunodeficiency virus. *Clin Infect Dis*. 2019; ciz833.
24. Lourenço L, Kelly M, Tarasuk J, et al. The hepatitis C epidemic in Canada: An overview of recent trends in surveillance, injection drug use, harm reduction and treatment. *Can Commun Dis Rep*. 2021;47(12):505–14. <http://doi.org/10.14745/ccdr.v47i12a01>. Medline: 35692566
25. CATIE - Canada's source for HIV and hepatitis C information. A brief history of hepatitis C: 1989–2022. 2022. <https://www.catie.ca/hepatitis-c-an-in-depth-guide/a-brief-history-of-hepatitis-c-1989-2022> (Accessed October 8, 2022).
26. Ortiz-Paredes D, Amoako A, Lessard D, Engler K, Lebouché B, Klein MB. Barriers and facilitators related to HCV treatment uptake among HIV coinfecting populations in Canada: Patients and treatment provider perceptions. *Can Liver J*. 2021;5(2):124–43. <http://doi.org/10.3138/canlivj-2021-0020>. Medline: 35991485
27. Grebely J, Oser M, Taylor LE, Dore GJ. Breaking down the barriers to hepatitis C virus (HCV) treatment among individuals with HCV/HIV coinfection: Action required at the system, provider, and patient levels. *J Infect Dis*. 2013;207(Suppl. 1):S19–25. <http://doi.org/10.1093/infdis/jis928>. Medline: 23390301
28. McGowan CE, Fried MW. Barriers to hepatitis C treatment. *Liver Int*. 2012;32:151–6. <http://doi.org/10.1111/j.1478-3231.2011.02706.x>. Medline: 22212587
29. Amoako A, Ortiz-Paredes D, Engler K, Lebouché B, Klein MB. Patient and provider perceived barriers and facilitators to direct acting antiviral hepatitis C treatment among priority populations in high income countries: A knowledge synthesis. *Int J Drug Policy* 2021;96:103247. <http://doi.org/10.1016/j.drugpo.2021.103247>. Medline: 33853727
30. Chan J, Young J, Cox J, Nitulescu R, Klein MB. Patterns of practice and barriers to care for hepatitis C in the direct-acting antiviral (DAA) era: A national survey of Canadian infectious diseases physicians. *Can Liver J*. 2018;1(4):231–9. <http://doi.org/10.3138/canlivj.2018-0012>. Medline: 35992622
31. Snell G, Marshall AD, van Gennip J, et al. Public reimbursement policies in Canada for direct-acting antiviral treatment of hepatitis C virus infection: A descriptive study. *Can Liver J*. 6(2):190–200. <http://doi.org/10.3138/canlivj-2022-0040>. Medline: 37503523
32. Feld JJ, Klein MB, Rahal Y, et al. Timing of elimination of hepatitis C virus in Canada's provinces. *Can Liver J*. 2022;5(4):493–506. <http://doi.org/10.3138/canlivj-2022-0003>. Medline: 38144411
33. Action Hepatitis Canada. Progress towards viral hepatitis elimination by 2030 in Canada: 2021 Report. Toronto, ON, Canada. 2021. <https://www.actionhepatitiscanada.ca/> (Accessed September 23, 2022).
34. Klein MB, Saeed S, Yang H, et al. Cohort profile: The Canadian HIV-hepatitis C co-infection cohort study. *Int J Epidemiol*. 2010;39(5):1162–9.

- <http://doi.org/10.1093/ije/dyp297>. Medline: 19786463
35. Canadian Co-infection Cohort. Canadian co-infection cohort. About the cohort – cocostudy. <http://cocostudy.ca/the-study/about-the-cohort/> (Accessed February 11, 2022).
 36. Young J, Wang S, Lanièce Delaunay C, et al. The rate of hepatitis C reinfection in Canadians coinfecting with HIV and its implications for national elimination. *Int J Drug Policy*. 2023;114:103981. <http://doi.org/10.1016/j.drugpo.2023.103981>. Medline: 36893502
 37. Tadrous M, Mason K, Dodd Z, et al. Prescribing trends in direct-acting antivirals for the treatment of hepatitis C in Ontario, Canada. *Can Liver J*. 2021;4(1):51–8. <http://doi.org/10.3138/canlivj-2020-0025>. Medline: 35991476
 38. Kwon JA, Dore GJ, Hajarizadeh B, et al. Australia could miss the WHO hepatitis C virus elimination targets due to declining treatment uptake and ongoing burden of advanced liver disease complications. *PLoS ONE*. 2021;16(9):e0257369. <http://doi.org/10.1371/journal.pone.0257369>. Medline: 34529711
 39. The Kirby Institute. Monitoring hepatitis C treatment uptake in Australia issue 10. UNSW Sydney, NSW, Australia: The Kirby Institute. 2019; p. 1–12. https://www.kirby.unsw.edu.au/sites/default/files/documents/Monitoring-hep-C-treatment-uptake-in-Australia_Iss10-JUN19.pdf (Accessed August 13, 2022).
 40. Scott N, Sacks-Davis R, Wade AJ, et al. Australia needs to increase testing to achieve hepatitis C elimination. *Med J Aust*. 2020;212(8):365–70. <http://doi.org/10.5694/mja2.50544>. Medline: 32167586
 41. Clementi E. Classifying people living with hepatitis C virus using a population-level latent class analysis to understand association with treatment uptake and optimize integration of health services. Vancouver, BC, Canada: University of British Columbia; 2020. <https://open.library.ubc.ca/soa/cIRcle/collections/ubctheses/24/items/1.0390304>. (Accessed February 5, 2024)
 42. Public Health Agency of Canada. Chapter 4: Population-specific HIV/AIDS status report: People living with HIV/AIDS – Current evidence on social determinants of health. 2015. <https://www.canada.ca/en/public-health/services/hiv-aids/publications/population-specific-hiv-aids-status-reports/people-living-hiv-aids/chapter-4-current-evidence-social-determinants-health-affecting-people-living-hiv-aids.html> (Accessed January 17, 2022)
 43. Antoniou T, Pritlove C, Shearer D, Tadrous M, Shah H, Gomes T. Accessing hepatitis C direct acting antivirals among people living with hepatitis C: A qualitative study. *Int J Equity Health*. 2023;22(1):112. <http://doi.org/10.1186/s12939-023-01924-4>. Medline: 37280588
 44. Lanièce Delaunay C, Klein MB, Godin A, et al. Public health interventions, priority populations, and the impact of COVID-19 disruptions on hepatitis C elimination among people who have injected drugs in Montreal (Canada): A modeling study. *Int J Drug Policy*. 2023;116:104026. <http://doi.org/10.1016/j.drugpo.2023.104026>. Medline: 37075626
 45. Lanièce Delaunay C, Godin A, Kronfli N, et al. Can hepatitis C elimination targets be sustained among people who inject drugs post-2030? *Int J Drug Policy*. 2021;96:103343. <http://doi.org/10.1016/j.drugpo.2021.103343>. Medline: 34215459
 46. Lanièce Delaunay C, Maheu-Giroux M, Marathe G, et al. Gaps in hepatitis C virus prevention and care for HIV-hepatitis C virus co-infected people who inject drugs in Canada. *Int J Drug Policy*. 2022;103:103627. <http://doi.org/10.1016/j.drugpo.2022.103627>. Medline: 35218989
 47. Pitcher AB, Borquez A, Skaathun B, Martin NK. Mathematical modeling of hepatitis C virus (HCV) prevention among people who inject drugs: a review of the literature and insights for elimination strategies. *J Theor Biol*. 2019;481:194–201. <http://doi.org/10.1016/j.jtbi.2018.11.013>. Medline: 30452959
 48. Biondi MJ, Feld JJ. Hepatitis C models of care: approaches to elimination. *Can Liver J*. 2020;3(2):165–76. <http://doi.org/10.3138/canlivj.2019-0002>. Medline: 35991853
 49. Godin A, Kronfli N, Cox J, Alary M, Maheu-Giroux M. The role of prison-based interventions for hepatitis C virus (HCV) micro-elimination among people who inject

- drugs in Montréal, Canada. *Int J Drug Policy* 2021;88:102738. <http://doi.org/10.1016/j.drugpo.2020.102738>. Medline: 32278651
50. Saeed S, Thomas T, Dinh DA, et al. Frequent disengagement and subsequent mortality among people with HIV and Hepatitis C in Canada: A prospective cohort study. *Open Forum Infect Dis*. 2024;11(5):ofae239. <http://doi.org/10.1093/ofid/ofae239>. Medline: 38798898