

Research Paper

Gaps in hepatitis C virus prevention and care for HIV-hepatitis C virus co-infected people who inject drugs in Canada



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ABSTRACT

Background: People who inject drugs (PWID) living with HIV are a priority population for eliminating hepatitis C virus (HCV) as a public health threat. Maximizing access to HCV prevention and treatment strategies are key steps towards elimination. We aimed to evaluate engagement in harm reduction programs and HCV treatment, and to describe injection practices among HIV-HCV co-infected PWID in Canada from 2003 to 2019.

Methods: We included *Canadian Coinfection Cohort* study participants who reported injecting drugs between 2003 and 2019 in Quebec, Ontario, Saskatchewan, and British Columbia, Canada. We investigated temporal trends in HCV treatment uptake, efficacy, and effectiveness; injection practices; and engagement in harm reduction programs in three time periods based on HCV treatment availability: 1) interferon/ribavirin (2003–2010); 2) first-generation direct acting antivirals (DAAs) (2011–2013); 3) second-generation DAAs (2014–2019). Harm reduction services assessed included needle and syringe programs (NSP), opioid agonist therapy (OAT), and supervised injection sites (SIS).

Results: Median age of participants ($N = 1,077$) at cohort entry was 44 years; 69% were males. Province-specific HCV treatment rates increased among HCV RNA-positive PWID, reaching 16 to 31 per 100 person-years in 2014–2019. Treatment efficacy improved from a 50 to 70% range in 2003–2010 to >90% across provinces in 2014–2019. Drug injecting patterns among active PWID varied by province, with an overall decrease in cocaine injection frequency and increasing opioid injections. In the most recent time period (2014–2019), needle/syringe sharing was reported at 8–22% of visits. Gaps remained in engagement in harm reduction programs: NSP use decreased (58–70% of visits), OAT engagement among opioid users was low (8–26% of visits), and participants rarely used SIS (1–15% of visits).

Conclusion: HCV treatment uptake and outcomes have improved among HIV-HCV coinfecting PWID. Yet, this population remains exposed to drug-related harms, highlighting the need to tie HCV elimination strategies with enhanced harm reduction programs to improve overall health for this population.

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Introduction

In Canada, two out of three people who inject drugs (PWID) have evidence of current or past hepatitis C virus (HCV) infection and 85% of new HCV infections occur in this population (Canadian Network on Hepatitis C, 2019; Janjua et al., 2016; Krajden, Cook, & Janjua, 2018; Public Health Agency of Canada, 2011; Trubnikov, Yan, & Archibald, 2014; Wu et al., 2006). PWID have been identified as a priority population for the elimination of HCV as a public health threat by 2030 as defined by the World Health Organization's targets (World Health Organization, 2016). Coinfection with HIV can exacerbate the seriousness of HCV infection due to reduced spontaneous clearance, faster liver disease progression, and higher mortality (Chen & Morgan, 2006; Shepard, Finelli, & Alter, 2005; Valle Tovo et al., 2007). In Canada, it is estimated that approximately 10% of PWID are seropositive for both HIV and HCV (Public Health Agency of Canada, 2018). Although particularly vulnerable to the consequences of HCV infection, people living with HIV are more likely to be engaged in care through the HIV treatment and care continuum and can therefore be reached by interventions (Bartlett et al., 2019; Sacks-Davis et al., 2018).

Several public health interventions can contribute to reducing HCV incidence and mortality among PWID. The advent of second-generation direct acting antiviral (DAA) treatments in 2013 has provided a crucial tool for HCV treatment-as-prevention (Lim et al., 2021; Olafsson et al., 2021). These oral, well-tolerated regimens can achieve cure rates of more than 90%, even among previously difficult-to-treat HIV-HCV coinfecting individuals (Naggie et al., 2015; Sulkowski et al., 2015; Wyles et al., 2015). DAA uptake has been slower among PWID than in other population groups (Saeed et al., 2017; Socías et al., 2019; Tsui et al., 2019), yet empirical evidence shows high rates of treatment completion and sustained virologic response (SVR) among PWID engaged in treatment (Hajarizadeh et al., 2018).

Harm reduction programs also play a key role in preventing HCV transmission among PWID. Needle and syringe programs (NSP) and opioid agonist therapy (OAT) can reduce the risk of acquiring HCV by 20% and 50%, respectively (Platt et al., 2017). These programs were first introduced in Canada in the late 1980s and early 1990s (Canadian Public Health Association, 1994). NSP have evolved since their introduction, from exchange programs for used syringes to models providing unlimited access to various consumption materials (e.g., syringes, cookers, filters, sterile water) (Harm Reduction International, 2020; Høj, Minoyan, Artenie, Grebely, & Bruneau, 2018; Platt et al., 2017). The first supervised injection site (SIS) opened in Vancouver, British Columbia in 2003, and since 2017 other sites have emerged across provinces (Kerr, Mitra, Kennedy, & McNeil, 2017; Ziegler, Wray, & Luginaah, 2019). Although further empirical evidence is needed to quantify the impact of SIS on the risk of HCV acquisition, modeling findings suggest that these interventions can be cost-effective with regards to the potential number of HCV and HIV infections averted (Jozaghi, Reid, & Andresen, 2013, 2014).

According to Canadian harm reduction targets, by 2030 each person who injects drugs should receive 750 sterile needles and syringes per year, and 40% of PWID should be engaged in OAT (Canadian Network on Hepatitis C, 2019). The design and implementation of harm reduction programs must be informed by local injection patterns (Roy et al., 2017). Quantifying the public health efforts required to eliminate HCV among PWID living with HIV requires assessing gaps in access to HCV prevention and care for this population. Although engagement in HCV treatment and harm reduction practices has been studied among PWID in different Canadian settings, recent, comprehensive, longitudinal data are lacking to evaluate the coverage of these interventions among those living with HIV (Larney et al., 2017; Saeed et al., 2017; Socías et al., 2019; Young et al., 2018). This study aimed to investigate temporal trends in 1) HCV treatment uptake, efficacy, and effectiveness; 2) injection practices; and 3) engagement in harm reduction programs, among HIV-HCV coinfecting PWID in the Canadian provinces of Quebec, Ontario, Saskatchewan, and British Columbia, from 2003 to 2019.

Methods

Study procedures

We used longitudinal data from the *Canadian Co-infection Cohort* (CCC), which has been previously described (Klein et al., 2009). Briefly, the CCC is an ongoing, publicly funded, prospective cohort study of HIV-HCV co-infected participants ($N = 2018$ as of May 2020) recruited from 18 HIV treatment centres across six Canadian provinces. To be eligible, participants must be at least 16 years of age, have a documented HIV infection, and be chronically infected with HCV or have evidence of previous HCV exposure. Recruitment started in 2003 and is ongoing continuously: all eligible persons engaged in care at the recruitment sites are invited to participate in the CCC. Recruitment was designed to reach priority populations (e.g., PWID, Indigenous people, gay, bisexual, and other men who have sex with men). People who have cleared HCV either spontaneously or following antiviral treatment continue to be followed until they die or are lost to follow-up (18 months without a study visit). Study visits are scheduled every six months. Socio-demographic, behavioural data, including detailed information on drug use and engagement in harm reduction programs, are collected through questionnaires. Participants can choose to complete the questionnaires alone or with the assistance of a research nurse. Research personnel from the recruitment sites extract additional information, including HIV and HCV treatment data, from chart reviews. Blood tests are performed at baseline and every six months and include plasma HIV and HCV RNA. Information on deaths, including causes, is collected and cross-validated with provincial vital statistics bureaus.

We included participants who were recruited in the provinces of Quebec, Ontario, Saskatchewan, and British Columbia (as these provinces followed at least 100 participants in the second-generation DAA era), and who reported injecting drugs at least once between 2003 and 2019.

Measures

HCV treatment initiation was defined as the prescription of any drug regimen for HCV treatment. HCV treatment response was evaluated as the proportion of treatments leading to sustained virologic response 1) among all initiated treatments (effectiveness); and 2) among initiated treatments for which we had treatment response data (efficacy). Pre-2011, sustained virologic response was defined as HCV RNA negativity at least 24 weeks after completion of antiviral therapy (Ghany, Strader, Thomas, & Seeff, 2009; Lindsay, 2002). This was reduced to 12 weeks after 2011 (Burgess, Hussaini, & Yoshida, 2016; Martinot-Peignoux et al., 2010).

Other study outcomes were self-reported. Drug injection was defined as the self-reported injection of a specific substance at least once in the past six months. The study questionnaire allowed us to investigate the following drugs: cocaine; amphetamines; methamphetamine; benzodiazepines; barbiturates; and different types of opioids (i.e., heroin, morphine, methadone, hydromorphone, oxycodone, combination of buprenorphine and naloxone, fentanyl, carfentanyl, meperidine, pentazocine). Sharing of needles/syringes was defined as any self-reported episode of receptive or distributive sharing of needles or syringes in the past six months. Engagement in NSP was measured as the reported use of services where one can obtain sterile syringes and/or clean needles in the past six months. Engagement in OAT was defined as reported participation in an opioid substitution program in the past six months. Finally, use of SIS was measured as reporting having been to a supervised injection use site in the past six months.

Analyses

All analyses were conducted at the provincial level due to expected variability in participants' sociodemographic characteristics and access

Table 1
Study denominators for outcome estimation.

Outcome(s)	Denominator	Number of person-years, treatments initiated, or visits											
		Quebec			Ontario			Saskatchewan			British Columbia		
		2003–2010	2011–2013	2014–2019	2003–2010	2011–2013	2014–2019	2003–2010	2011–2013	2014–2019	2003–2010	2011–2013	2014–2019
HCV treatment initiation rate	Dynamic population of HCV RNA-positive participants (in person-years)	472	274	430	121	177	369	0	0	336	55	242	602
HCV treatment efficacy and effectiveness	Number of treatments initiated	28	18	135	10	10	61	0	0	60	5	10	94
Proportion of visits at which there was any: - needle and/or syringe sharing - drug-specific injections - use of needle and syringe programs - use of supervised injection sites	Number of visits at which injection drug use was reported in the past 6 months	726	408	729	136	116	300	0	0	492	320	489	949
Proportion of visits at which there was any opioid agonist therapy engagement	Number of visits at which opioid injection was reported in the past 6 months	172	149	306	54	34	115	0	0	210	211	297	518

to interventions and treatments according to provincial regulations. We defined three time periods of interest based on HCV treatment guidelines in Canada: 2003–2010 for interferon-based treatments, 2011–2013 for first-generation DAAs, and 2014–2019 for second-generation DAAs (Shah et al., 2018). For each period, we selected participants who reported actively injecting at least one visit during the period considered. Study outcomes were estimated using the denominators described in Table 1.

HCV treatment initiation rates were estimated among HCV RNA positive participants who formed an open, dynamic population that could contribute to person-time through multiple observation periods. A given observation period would start when the participant received an HCV RNA positive test result (at cohort entry or reinfection) and stop when the participant either initiated HCV treatment, had an HCV RNA negative test result, was lost to follow-up, withdrew from the study, or died, whichever happened first. Confidence intervals (CIs) for treatment initiation rates per 100 person-years were calculated assuming they followed a Poisson distribution.

For injection practices and engagement in harm reduction programs, we used the total number of visits with reported injection drug use in the past six months as the denominator. We calculated the proportion of these visits at which the following outcomes were reported in the past six months: (1) injection of specific drugs; (2) any sharing of needles/syringes; (3) any use of NSP; (4) any use of SIS. Because OAT does not apply to people who exclusively inject stimulants, we used the total number of visits with reported opioid injection in the past six months to estimate the proportion of visits at which any OAT engagement was reported in the past six months. CIs for proportions were estimated using the Wilson score interval for clustered binary data (Saha, Miller, & Wang, 2016).

Because HCV RNA tests were not always performed at each study visit, we carried forward the last HCV RNA test result available for a given participant when the test was not performed at a specific visit, with 23% of HCV RNA status values imputed this way.

Ethical considerations

All participants provided written informed consent and received \$15 CAD per visit to compensate for out-of-pocket expenses. The study has been approved by all the research ethics boards of all participating in-

stitutions and the community advisory committee of the *Canadian HIV Trials Network*.

Results

Selection of participants and visits

A total of 1077 participants in the CCC injected at least once between 2003 and 2019: 344 in Quebec, 176 in Ontario, 187 in Saskatchewan, and 370 in British Columbia (Table 2). Because recruitment started in 2014 in Saskatchewan, we only provide estimates for the second-generation DAA era for this province.

Baseline characteristics of participants

Table 2 displays the participants' characteristics at cohort entry for each province. Participants recruited in the eastern provinces of Quebec and Ontario had a high proportion of males (approximately 80%), a median age of 45 years, a relatively high percentage of gay, bisexual, and other men who have sex with men (35%), and fewer people self-identifying as Indigenous (3% in Quebec and 25% in Ontario). Comparatively, males represented a smaller proportion of participants in Saskatchewan (57%) and British Columbia (59%). The percentage of Indigenous participants was also higher in western provinces, particularly in Saskatchewan (82%), with fewer gay, bisexual, and other men who have sex with men (5% in Saskatchewan and 20% in British Columbia). Saskatchewan participants were also younger (median age, 38 years) than in other provinces. Across provinces, several indicators reflected a socio-economically deprived population: the proportion of participants living under the poverty line (<18,000 CAD) varied from 72% to 88%, only 6% to 25% of participants achieved post-secondary education, and between 53% and 71% had previously been incarcerated.

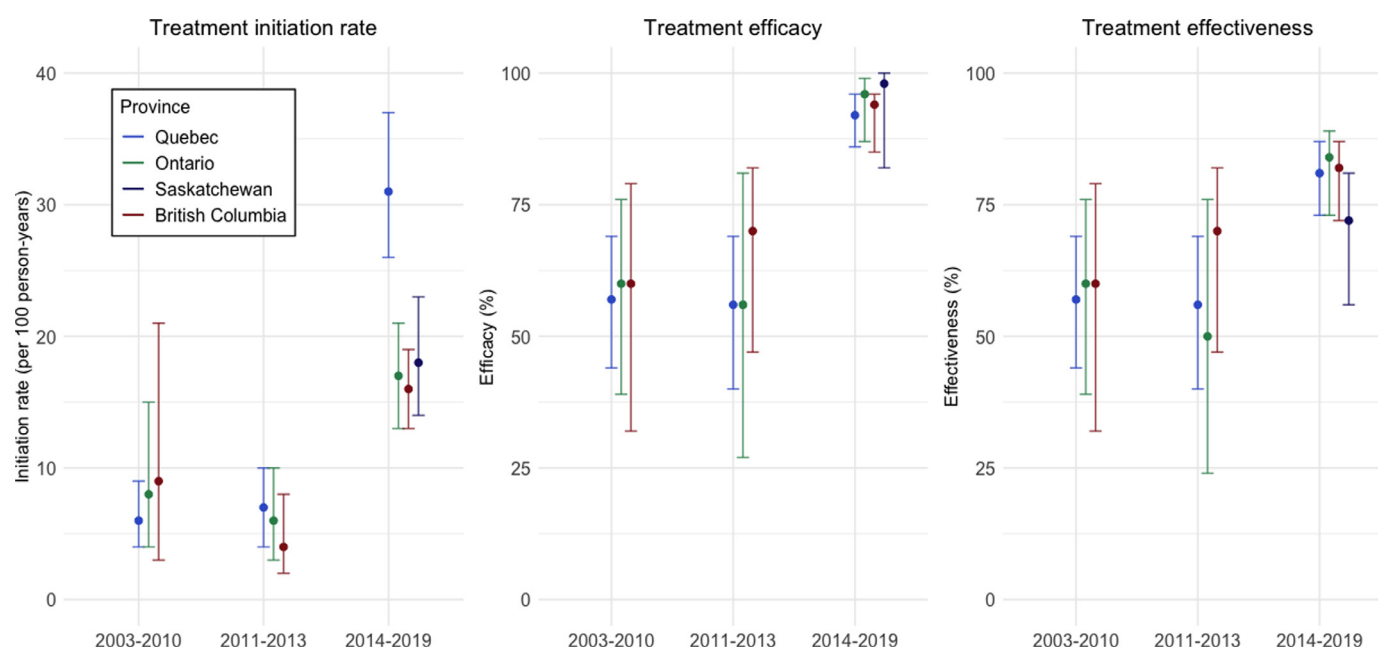
HCV treatment initiation, efficacy, and effectiveness

Province-specific HCV treatment initiation rates, efficacy, and effectiveness are presented in Fig. 1. Treatment uptake remained relatively stable from 2003–2010 to 2011–2013, with rates ranging from 4 to 9 per 100 person-years. Treatment uptake increased substantially in the second-generation DAA era in all provinces but particularly in Quebec (31 per 100 person-years, 95% CI: 26–37). Despite these increases, 46%

Table 2

Participants' characteristics at cohort entry among those who injected at least once between 2003 and 2019.

Characteristic	Quebec (N = 344) N (%)	Ontario (N = 176) N (%)	Saskatchewan (N = 187) N (%)	British Columbia (N = 370) N (%)
Age ¹	45 (39–49)	45 (38–50)	38 (32–46)	45 (39–52)
Missing	1 (<1%)	0	0	1 (<1%)
Male (sex at birth)	274 (80%)	134 (76%)	106 (57%)	220 (59%)
Missing	1 (<1%)	0	4 (2%)	2 (1%)
Transgender	3 (<1%)	0	0	4 (1%)
Missing	1 (<1%)	0	4 (2%)	2 (1%)
Self-reported Indigenous ethnicity	10 (3%)	44 (25%)	153 (82%)	146 (39%)
Missing	23 (7%)	5 (3%)	5 (3%)	18 (5%)
Gay, bisexual, and other men who have sex with men (sexual orientation)	119 (35%)	61 (35%)	9 (5%)	74 (20%)
Missing	7 (2%)	2 (1%)	3 (2%)	5 (1%)
Annual income <18,000 CAD ²	303 (88%)	126 (72%)	154 (82%)	316 (85%)
Missing	4 (1%)	4 (2%)	15 (8%)	10 (3%)
Received post-secondary education	56 (16%)	44 (25%)	12 (6%)	77 (21%)
Missing	2 (1%)	0	1 (1%)	10 (3%)
No fixed address	48 (14%)	12 (7%)	21 (11%)	53 (14%)
Missing	3 (1%)	3 (2%)	6 (3%)	11 (3%)
Ever incarcerated	183 (53%)	106 (60%)	133 (71%)	232 (63%)
Missing	30 (9%)	17 (10%)	15 (8%)	56 (15%)
HCV RNA positive	188 (55%)	134 (76%)	127 (68%)	120 (32%)
Missing	139 (40%)	20 (11%)	18 (10%)	226 (61%)
HCV genotype among HCV RNA positive participants				
1	113 (60%)	89 (66%)	63 (50%)	79 (66%)
3	43 (23%)	22 (16%)	30 (24%)	25 (15%)
Other	4 (2%)	5 (4%)	3 (2%)	3 (2%)
Missing	28 (15%)	18 (13%)	31 (24%)	13 (11%)
History of prior HCV treatment	33 (10%)	20 (11%)	9 (5%)	41 (11%)
Missing	22 (6%)	28 (16%)	46 (25%)	45 (12%)
Significant fibrosis ³	62 (18%)	29 (16%)	19 (10%)	48 (13%)
Missing	42 (12%)	11 (6%)	29 (16%)	21 (6%)
On anti-retroviral treatment	262 (76%)	143 (81%)	152 (81%)	301 (81%)
Missing	3 (<1%)	0	0	0
CD4 cell count / uL ¹	398 (250–550)	403 (259–610)	360 (226–573)	400 (250–610)
Missing	6 (2%)	13 (7%)	15 (8%)	17 (5%)
Suppressed HIV RNA viral load (<200 copies/mL)				
Among those on anti-retroviral treatment	199 (78%)	105 (73%)	88 (58%)	234 (78%)
Missing	18 (4%)	21 (15%)	25 (16%)	13 (4%)
Among those not on treatment	5 (6%)	4 (12%)	5 (14%)	25 (36%)
Missing	6 (7%)	3 (9%)	3 (9%)	6 (9%)

¹ Median (interquartile range).² Canadian dollars.³ Defined as an AST to platelet ratio index (APRI) >1.5.**Fig. 1.** Hepatitis C treatment uptake, efficacy, and effectiveness among RNA-positive participants of the Canadian Co-infection Cohort (2003–2019).

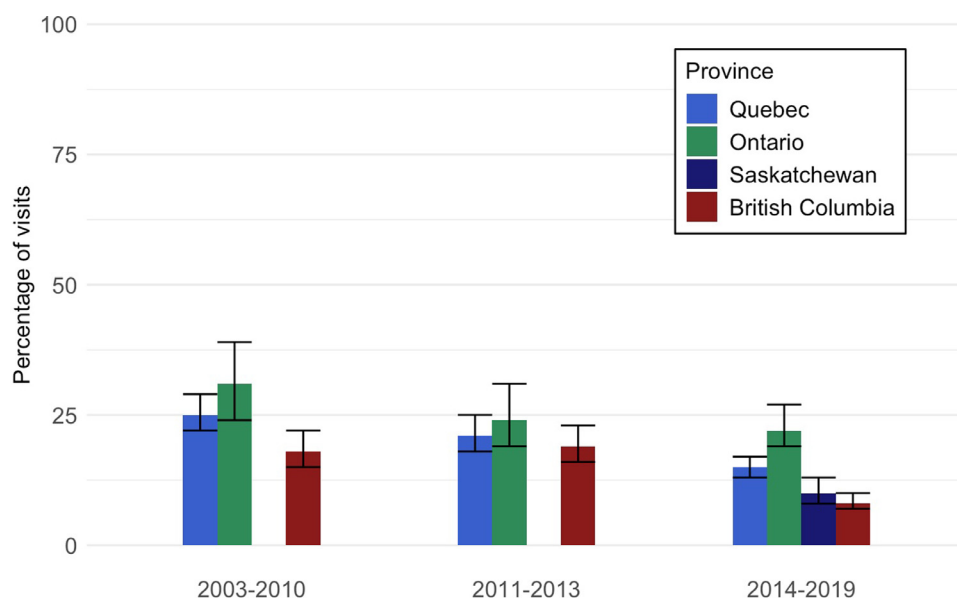


Fig. 2. Percentage of visits where needles or syringe sharing was reported in the past six months among people who currently inject drugs in the Canadian Co-infection Cohort (2003–2019).

of participants who reported injecting at least once during 2014–2019 were still HCV RNA positive at their last study visit.

Treatment efficacy changed little between the interferon and first-generation DAA eras— 58% (95% CI: 47–68) in 2003–2010 and 59% (95% CI: 43–74) in 2011–2013. Efficacy improved dramatically across provinces with the introduction of second-generation DAAs, with all point estimates exceeding 90%. Although effectiveness also appeared to improve in the second-generation DAA era, ranging from 72% in Saskatchewan to 84% in Ontario, there was considerable uncertainty around these estimates.

Injection practices

Overall, the percentage of visits at which active PWID reported sharing needles or syringes in the past six months decreased over time (Fig. 2). The frequency of needle or syringe sharing based on this percentage of visits was highest in Ontario: 31% (95% CI: 24–39) in 2003–2010 and 22% (95% CI: 19–27) in 2014–2019. It was lowest in British Columbia: 18% (95% CI: 15–22) in 2003–2010 and 8% (95% CI: 7–10) in 2014–2019.

We observed different trends in past six months drug injecting patterns across provinces (Fig. 3). The percentage of visits at which active PWID reported injecting cocaine decreased overall. Cocaine still remained the most frequently injected drug in eastern provinces in 2014–2019 (Quebec, 76% of visits, 95% CI: 74–78; Ontario, 50%, 95% CI: 45–55). Among Saskatchewan participants, opioids (46%; 95% CI: 42–50%) and cocaine (43%; 95% CI: 39–47) were injected at similar frequencies in 2014–2019. Overall, the frequency of opioid injection increased among participants. In British Columbia, opioid injection was reported at 59% of visits (95% CI: 57–62) in 2014–2019, while cocaine injection was reported at 38% of visits (95% CI: 35–41) in the same time period. In Quebec, Ontario, and British Columbia we observed increases of varying magnitude in the frequency of reported methamphetamine injection. Methamphetamine injection was also reported frequently among Saskatchewan participants in 2014–2019 (19% of visits, 95% CI: 16–22). The frequency of injection of benzodiazepines also increased over time with the 2014–2019 province-level estimates ranging from 2% of visits (95% CI: 1–3) in Quebec to 17% (95% CI: 14–20) in Saskatchewan.

Engagement in harm reduction programs

Overall, recent engagement in NSP remained stable from 2003–2010 to 2011–2013 but decreased in subsequent years (Fig. 4). From 2011–

2013 to 2014–2019, the proportion of visits at which active PWID reported using NSP in the past six months decreased from 94% (95% CI: 92–96) to 70% (95% CI: 68–72) in Quebec, from 81% (95% CI: 73–87) to 58% (95% CI: 53–64) in Ontario, and from 90% (95% CI: 87–93) to 64% (95% CI: 62–66) in British Columbia. Use of SIS in the past six months was rare from 2014 to 2019, with participants from British Columbia reporting the most frequent access at 15% of visits (95% CI: 13–17). Finally, OAT engagement in the past six months among people currently injecting opioids was relatively low and stable over time. Over 2014–2019, engagement in OAT was reported more frequently in British Columbia at 26% of visits (95% CI: 23–30) compared with other provinces.

Discussion

Analysing longitudinal data collected among HIV-HCV coinfecting PWID over 16 years across four Canadian provinces, we observed a marked improvement in HCV treatment uptake and outcomes in the second-generation DAA era. Unfortunately, these successes were offset by inadequate coverage of harm reduction programs. Sharing of needles or syringes continues to be reported, and substantial gaps remain in engagement in harm reduction programs, with declining NSP engagement and low use of OAT and SIS. Drug injecting patterns varied with time and across geographical settings, with an overall decrease in the frequency of cocaine injection and opioid injections becoming dominant across the country. The frequency of methamphetamine and benzodiazepine injection also seems to be on the rise in all provinces, although to a lesser extent in Quebec.

Our study provides recent, contextualized estimates of HCV treatment uptake among HIV-HCV coinfecting PWID. This work builds on a study conducted by Saeed et al. (2017), where HCV treatment initiation rates among CCC participants were assessed between 2007 and 2015. Although treatment rates were consistently lower among active PWID compared with other risk groups, uptake had increased in this population, from 3 per 100 person-years in 2014 (95% CI: 1–8) to 16 per 100 person-years in 2015 (95% CI: 11–24). Our results suggest that this increase in HCV treatment, which followed the introduction of second-generation DAAs, has been sustained during the 2014–2019 period. Yet more than 50% of PWID living with HIV were chronically infected with HCV across Canada in 2017–2019 (Tarasuk et al., 2020), and approximately half of the CCC participants who reported injecting between 2014 and 2019 were still HCV RNA positive at their last visit, showing

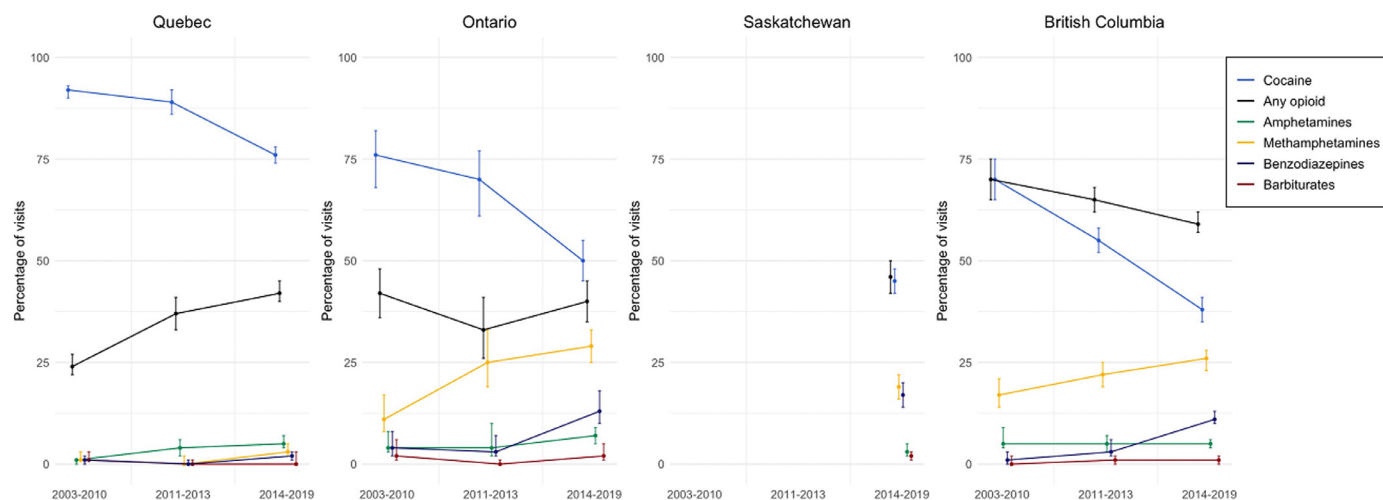


Fig. 3. Percentage of visits where specific injection drugs were reported being used in the past six months among people who currently inject drugs in the Canadian Co-infection Cohort (2003–2019).

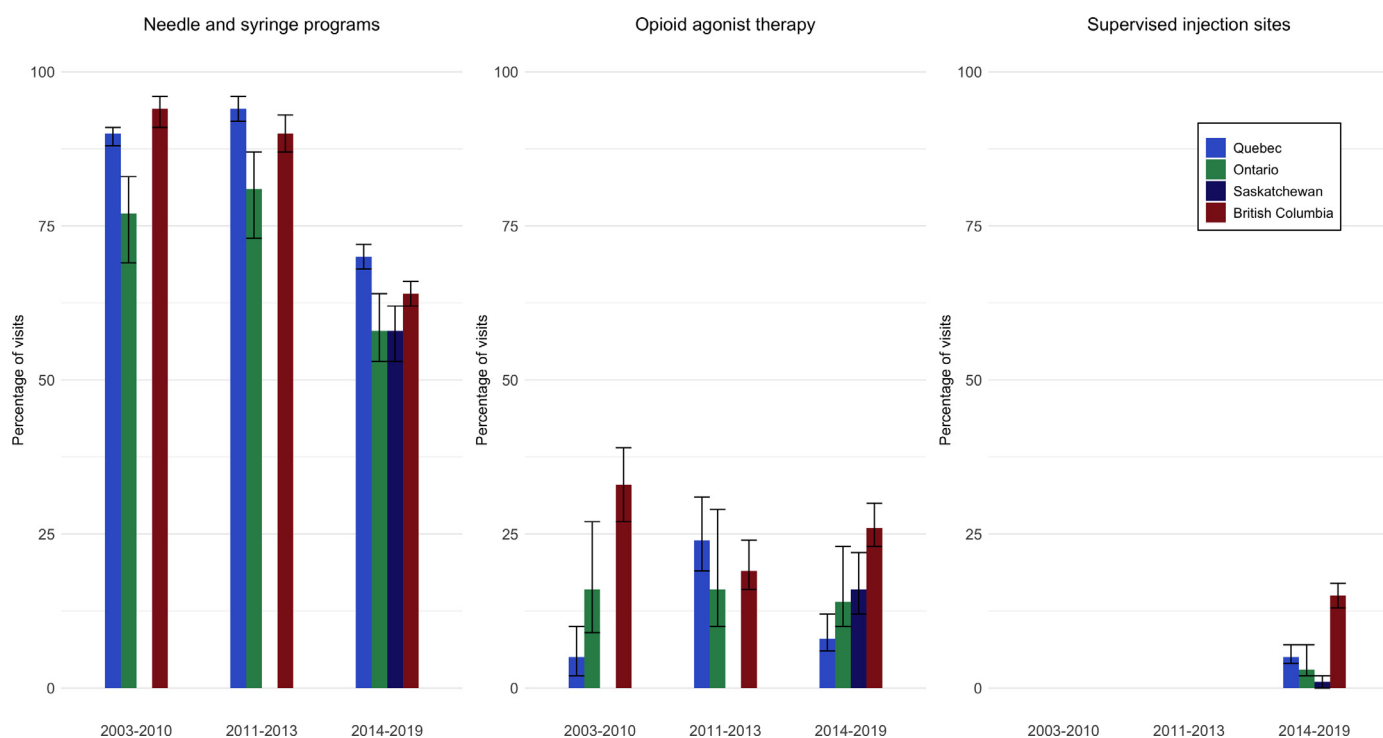


Fig. 4. Percentage of visits where engagement in harm reduction programs was reported in the past six months among people who currently inject drugs in the Canadian Co-infection Cohort (2003–2019).

that continued efforts to scale-up treatment are needed. In Canada, reimbursement of DAA treatments was previously conditional on diagnosis of significant fibrosis (Marshall et al., 2016). This restriction, a major barrier to care, was lifted earlier in Quebec for people living with HIV (July 2016) than in other provinces (March 2017 in Ontario and British Columbia; April 2018 in Saskatchewan). This likely explains why participants recruited in Quebec were more likely to initiate treatment during 2014–2019 (Action Hepatitis Canada, 2018; Saeed et al., 2020). In three cohorts of PWID recruited in Vancouver, HCV treatment was initiated at a rate of 5 per 100 person-years (95% CI: 4–6) between 2015 and 2017, and coinfecting PWID had twice the odds of starting treatment as mono-

infected PWID (Socías et al., 2019). The higher treatment rate observed among coinfecting PWID is in line with our findings. PWID are at high risk of acquiring and transmitting HCV, and although those living with HIV can be more vulnerable to HCV infection, they are also more likely to be engaged in care with health care providers experienced in treating HCV (Bartlett et al., 2019; Sacks-Davis et al., 2018; Socías et al., 2019). In addition, high treatment efficacy has been demonstrated in this population, in our study and elsewhere (Hajarizadeh et al., 2018). Taken together, these findings send an encouraging message: that it is both feasible and effective to prioritize HCV treatment in HIV-HCV co-infected PWID and that doing so will help progress towards elimi-

nation (Lanièce Delaunay et al., 2021). Challenges to obtain follow-up HCV RNA measures post treatment completion account for the observed gap between treatment efficacy and effectiveness. We must consider this source of uncertainty when estimating progress towards the HCV elimination targets and rates of HCV reinfection.

We observed a decrease in the frequency of cocaine injection across provinces, although this drug remained the most frequently injected in Quebec, Ontario, and Saskatchewan (where it was comparable to that of opioids). These results are consistent with data collected through the *Track survey of people who inject drugs in Canada* (Public Health Agency of Canada, 2014; Tarasuk et al., 2020), and in cohorts in Montreal (Roy et al., 2017) and Vancouver (Urban Health Research Initiative, 2013). We also observed that opioid injection was frequent across provinces, with trends varying by province –increasing in Quebec, remaining relatively stable in Ontario, and decreasing in British Columbia. This observation mirrors the marked increase in non-medical use of prescription opioids reported across Canada since the early 2000s (Fischer & Argento, 2012; Fischer, Keates, Bühringer, Reimer, & Rehm, 2014; Ho et al., 2018; Puzhko et al., 2017; Roy et al., 2017; Urban Health Research Initiative, 2013). Injection of prescription opioids and their analogues has been associated with higher injection frequency (Roy et al., 2017), engaging in risky behaviours such as sharing needles and syringes (Bruneau, Roy, Arruda, Zang, & Jutras-Aswad, 2012), increased risk of HIV and HCV transmission (Bruneau, Roy, Arruda, Zang, & Jutras-Aswad, 2012; Conrad et al., 2015; Lankenau, Kecojevic, & Silva, 2015; Zibbell, Hart-Malloy, Barry, Fan, & Flanigan, 2014), and heightened exposure to non-fatal and fatal overdose (Fischer, Jones, & Rehm, 2013; Jones, Mack, & Paulozzi, 2013; Rudd, Aleshire, Zibbell, & Gladden, 2016). The frequency of methamphetamine injection also increased with time in our population, although the frequency of use was lower in Quebec than in other provinces. This finding correlates the increasing trend of methamphetamine injection observed in Vancouver (Urban Health Research Initiative, 2013). Methamphetamine use has been associated with binge drug use (Cheng et al., 2010) and sexual behaviours increasing the risk of exposure to HIV (Boddiger, 2005) and HCV (Pufall et al., 2018). Furthermore, polydrug use (e.g., consumption of opioids with stimulants or sedatives) is common and associated with severe adverse health and psychosocial effects (Puzhko et al., 2017). We did not examine concomitant injection of different drugs due to data limitations.

Overall, the observed trends in drug injecting patterns suggest that HIV-HCV coinfecting people are highly exposed to substances that amplify the risk of drug-related harms. These results emphasize the need for adequate coverage of harm reduction programs in this population group. Modeling studies also suggest that high engagement in harm reduction programs would help reaching and sustaining HCV elimination targets among PWID (Lanièce Delaunay et al., 2021; Pitcher, Borquez, Skaathun, & Martin, 2019). In many settings, the WHO elimination targets can be reached by increasing HCV treatment rates, yet scaling-up harm reduction access can reduce the number of treatments required by preventing primary infections and re-infections post-treatment.

While reported needle or syringe sharing declined over the study periods overall, it still remained frequent among actively injecting participants in recent years, indicating ongoing risk of acquiring and/or transmitting HCV. Paradoxically, engagement in NSP also decreased over time. Importantly, we measured the report of any needle/syringe sharing and use of NSP in the past six months, therefore these trends do not capture variations in frequency of drug use over that six-month period. Nevertheless, this finding is concerning given that NSP represent one of few interventions that can benefit all PWID regardless of the drug(s) they inject, and that we know to be cost-effective for HIV and HCV prevention (Wilson, Donald, Shattock, Wilson, & Fraser-Hurt, 2015). Compared to opiates, cocaine has a short half-life and is associated with more frequent injections in order to sustain a high (Korsmeyer & Kranzler, 2009). The observed decrease in NSP use might therefore reflect a reduction in the number of daily injections due to reduced cocaine use across provinces. An alternative hypothesis is that the material dis-

tributed through NSP was less appropriate for injection practices in recent years (e.g., for the injection of prescription opioids) (Bruneau et al., 2012; Roy, Arruda, & Bourgois, 2011). To the best of our knowledge, existing evidence does not suggest reduced use of NSP among PWID in Canada (Jacka et al., 2019). The comparison of harm reduction coverage among PWID across studies is difficult because estimates are generated from non-random, convenience samples of PWID. Nevertheless, it will be important to confirm this finding among HIV-HCV coinfecting PWID, and to understand the mechanisms at play in order to better tailor these programs and maximize their uptake.

Similarly, our results suggest that OAT engagement is lower among HIV-HCV coinfecting PWID who inject opioids than among the general PWID population (Jacka et al., 2019). With recent use of OAT reported at 8 to 27% of visits across provinces, the Canadian OAT coverage target of 40% was not met among our participants. Potential barriers to OAT engagement and adherence include polydrug use, high injection frequency, recent incarceration, injecting in public spaces, needles/syringes sharing, lack of social support, and mental health issues (Geddes, Iversen, Wand, & Maher, 2021; Makarenko et al., 2016; Strike, Millson, Hopkins, & Smith, 2013). Low threshold OAT, which focuses on removing barriers to treatment, can improve access to OAT (Jakubowski & Fox, 2020). Investigating potential barriers and facilitators to OAT uptake among co-infected people who inject opioids will be key to improve coverage among this priority population. Effective treatments for stimulant use are also needed to complement other harm reduction programs. The rare use of SIS was expected given that these interventions were implemented only recently in most Canadian provinces, with the exception of Vancouver which adopted SIS earlier than in other jurisdictions (Kerr et al., 2017). Scaling-up access to these sites is critical, especially in the current context of the opioid-related death crisis (Fischer, Pang, & Tyndall, 2019). Our results provide a benchmark to evaluate the uptake of these interventions in upcoming years.

Taken together, multi-level efforts to maximize engagement of PWID in HCV treatment and care, harm reduction services and to prevent opioid overdose are needed. Interventions to improve treatment among PWID have been described as falling into four categories: 1) macro-level health policies requiring government investment and commitment (e.g., funding for HCV health services and research); 2) care models that provide alternatives to hospital-based specialized HCV care (e.g., multidisciplinary clinics where the needs of PWID can be addressed beyond HCV care); 3) adoption of strategies to facilitate patient and provider health services utilization (e.g., involving peers with relatable lived experience) and; 4) HCV education (e.g., awareness campaigns and patient education resources at community organizations) (Amoako, Ortiz-Paredes, Engler, Lebouché, & Klein, 2021; Ortiz-Paredes et al., 2021). Interventions to improve harm reduction coverage include sustained governmental funding of programs, co-location of HIV, HCV, and harm reduction services, as well as, involvement of peers to navigate these services (Feder et al., 2019; Rosenthal et al., 2020; Weeks et al., 2009). Finally, avenues to reduce opioid overdose and mortality include community distribution of naloxone (Clark, Wilder, & Winstanley, 2014; Mueller, Walley, Calcattera, Glanz, & Binswanger, 2015), drug decriminalization and safe supply provision (Bonn et al., 2020), and provider education related to pain management and addiction treatment (Alexandridis et al., 2018).

Our study has several limitations. First, we analysed data collected prior to the beginning of the severe acute respiratory syndrome coronavirus 2 pandemic. Pre-pandemic, the essential needs (i.e., decent and safe housing, food security, social support, access to healthcare) of many PWID were not met. The pandemic has further weakened already fragile support systems, aggravating the pre-existing overdose death crisis (Gomes, Kitchen, & Murray, 2021) and exacerbating pre-existing gaps in access to HCV care and prevention, with dramatic individual- and population-level implications for the transmission of blood-borne infections (Glick et al., 2020; Jacka et al., 2021; Vasylyeva, Smyrnov,

Strathdee, & Friedman, 2020). This reality only strengthens the need for intensified efforts towards HCV elimination among PWID.

The generalizability of our results to all HIV-HCV coinfecting PWID is also limited to people already engaged in care. Nevertheless, recruitment was designed to reach priority populations who access diverse models of care, including PWID in urban and semi-urban settings (e.g., through a mobile care clinic that serves homeless PWID in Montreal, and a community center that provides health services to PWID living in Vancouver's Downtown East Side) (Klein et al., 2009). Finally, our analyses are descriptive and preclude any causal exploration of the impact of changes in drug injecting patterns on access to HCV treatment and harm reduction programs. However, we capitalized on more than 15 years of longitudinal data collected among HIV-HCV coinfecting PWID to assess gaps in access to HCV treatment and harm reduction initiatives in this priority, understudied population. Our results show that despite improved HCV treatment initiation and outcomes, Canadian targets for the coverage of harm reduction programs are not met for HIV-HCV coinfecting PWID, which could compromise our ability to eliminate HCV in this population and preclude addressing other drug-related harms. These quantitative estimates can inform the scale of public health efforts needed to achieve elimination of HCV among HIV-HCV coinfecting PWID in Canada by 2030.

Conclusion

HCV treatment uptake and effectiveness have remarkably improved among HIV-HCV coinfecting PWID in the second-generation DAA era, indicating that we can and should continue to prioritize treatment among this group to reach HCV elimination. The observed drug injecting patterns suggest that this population is highly exposed to various drug-related harms, including through frequent opioid injection. Furthermore, important gaps remain in engagement in harm reduction programs, with province-level disparities. There is a need to tie HCV elimination strategies with enhanced harm reduction programs to prevent the transmission of blood-borne infections, HCV reinfection post-treatment, and overdose among HIV-HCV coinfecting PWID.

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Ethical approval

The *Canadian Co-infection Cohort* study has been approved by all the research ethics boards of all participating institutions and the community advisory committee of the *Canadian HIV Trials Network*.

Declarations of Interest

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CRediT authorship contribution statement

Charlotte Lanièce Delaunay: Conceptualization, Methodology, Software, Validation, Formal analysis, Data curation, Writing – original draft, Visualization. **Mathieu Maheu-Giroux:** Conceptualization, Methodology, Resources, Writing – review & editing, Visualization, Supervision. **Gayatri Marathe:** Methodology, Data curation, Writing – review & editing. **Sahar Saeed:** Methodology, Writing – review & editing, Investigation. **Valérie Martel-Laferrrière:** Investigation, Writing – review & editing, Project administration, Funding acquisition. **Curtis L. Cooper:** Investigation, Writing – review & editing, Project administration, Funding acquisition. **Sharon Walmsley:** Investigation, Writing – review & editing, Project administration, Funding acquisition. **Joseph Cox:** Conceptualization, Investigation, Writing – review & editing, Supervision, Project administration, Funding acquisition. **Alexander Wong:** Investigation, Writing – review & editing, Project administration, Funding acquisition. **Marina B Klein:** Conceptualization, Methodology, Investigation, Resources, Writing – review & editing, Visualization, Supervision, Project administration, Funding acquisition.

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