Rapid hepatitis C virus point-of-care RNA testing and treatment at an integrated supervised consumption service in Toronto, Canada: a prospective, observational cohort study

Bernadette Lettner,[a] Kate Mason,[a] Zoë R. Greenwald,[b,c] Jennifer Broad,[a] Erin Mandel,[d] Jordan J. Feld,[d] and Jeff Powis[e,*]

[a]South Riverdale Community Health Centre, 955 Queen St E, Toronto, ON, M4M 3P3, Canada
[b]Division of Epidemiology, Dalla Lana School of Public Health, University of Toronto, 155 College St, Toronto, ON M5T 3M7, Canada
[c]Centre on Drug Policy Evaluation, MAP Centre for Urban Health Solutions, St. Michael's Hospital, 30 Bond Street, Toronto, ON M5B 1X1, Canada
[d]Toronto Centre for Liver Disease, Toronto General Hospital, 200 Elizabeth St, Toronto, ON, M5G 2C4, Canada
[e]Michael Garron Hospital, 825 Coxwell Ave, Toronto, ON, M4C 3E7, Canada

The Lancet Regional Health - Americas 2023;■: 100490

Published Online XXX
https://doi.org/10.1016/j.lana.2023.100490

Summary

Background Despite high burden of Hepatitis C (HCV) among people who inject drugs, significant barriers to care persist. The aim of this study was to evaluate the provision of rapid, low-barrier point-of-care (POC) HCV RNA testing and linkage to care among clients of a supervised consumption service (SCS) located within a community health centre in Toronto, Canada. Secondary aims included measuring HCV RNA prevalence at baseline, HCV incidence during follow-up and exploring factors associated with HCV RNA positivity and treatment uptake.

Methods Participants were enrolled in a prospective, observational cohort from August 13, 2018 to September 30, 2021. Those with positive HCV RNA tests were offered immediate referral to onsite treatment. Those with negative results were offered repeat testing every three months for up to four visits. HCV incidence was estimated as the number of incident HCV infections per 100 person-years at risk, among those HCV RNA negative at baseline who returned for ≥1 follow-up visit. Missing data were reported when present.

Findings 128 participants were enrolled with four later removed due to ineligibility. At baseline, 54 of 124 eligible participants (43.5%) tested HCV RNA positive. HCV incidence was 35.1 cases per 100 person-years (95% CI: 18.9–65.3) with a cumulative incidence of 38.3% at 15 months of follow-up. Among participants HCV RNA positive at baseline or follow-up (n = 64), 67.2% (n = 43) were linked to HCV care and treatment was initiated among 67.4% (n = 29/43).

Interpretation High HCV RNA prevalence and incidence demonstrate that the SCS serves a high-risk population for HCV. Testing acceptance was high, as was treatment engagement. POC HCV RNA testing positions SCSs as an important point of HCV care access.

Funding HCV Micro-Elimination Grant, Gilead Sciences Canada; in-kind support from Cepheid.

Keywords: Hepatitis C; Injection drug use; Testing; Treatment; Primary care; Incidence

Introduction

Hepatitis C (HCV) is one of the world's most common chronic viral infections, with an estimated 58 million persons infected worldwide.[1] In Canada, while HCV seroprevalence is low in the general population (0.64%-0.71%), there is high burden of HCV among people who inject drugs with 64% HCV seroprevalence (HCV antibody positive) and 37% prevalence of current HCV infection (HCV RNA positive).[2,3] Advances in HCV treatments have both improved outcomes and reduced the burden of treatment.[4] Although up to 85% of incident HCV infections occur among people who inject drugs in Canada, treatment uptake for this group remains low.[3,5–7] Significant barriers to care persist for people who inject drugs at the individual and system level, along the cascade of care from testing to

*Corresponding author. Michael Garron Hospital, 825 Coxwell Ave, Toronto, ON, M4C 3E7, Canada.
E-mail address: Jeff.Powis@tehn.ca (J. Powis).

Research in context

Evidence before this study

Although people who inject drugs have long been recognized as a population at high risk of HCV infection, studies of testing and treatment engagement in harm reduction settings have been limited. In 2017 the results of a survey by the International Network of Drug Consumption Rooms (DCRs), completed by 49 DCRs worldwide on current practice and future capacity to address HCV in supervised consumption settings was presented. The study found that 65% were offered onsite HCV testing, however, the majority of DCRs referred offsite for treatment (86%). An evidence review took place between Dec 1, 2017 and March 8, 2018. Databases searched included PubMed/Medline, EMbase, Sage Publications, Sociological Abstracts, Social Work Abstracts, Psychinfo, Social Sciences Citations Index, and Google Scholar. The search terms used were combinations of HCV, Hepatitis C, testing, community, POC, "point-of-care", "supervised consumption", "people who use drugs", "addiction". This search of both grey and academic literature uncovered few studies of point-of-care (POC) HCV testing with people who use drugs generally, and only one study of POC HCV testing in a supervised consumption service. No studies reported on on-site referral and treatment initiation for clients of the DCRs who tested positive for HCV infection.

Added value of this study

This study demonstrates that offering HCV testing and treatment in supervised drug consumption services is possible. The very high prevalence of HCV infection justified the use of POC HCV RNA as the initial testing strategy. Importantly, serial testing identified a very high incidence of new HCV infections, much higher than documented in lower risk populations of people who use drugs. Despite the challenges faced by the population, progression through the continuum of care was good for those diagnosed at baseline or throughout the study.

Implications of all the available evidence

HCV elimination will require reaching those at highest risk of new infections. On-site HCV RNA testing and treatment in supervised drug consumption services is an effective strategy to reach a population with a high burden of HCV who may not otherwise engage with the health care system. Future studies should evaluate whether treatment in this high incidence setting has a benefit in terms of prevention. Access to POC HCV RNA testing will facilitate diagnosis and linkage to care in high risk populations.

treatment, and include: stigma/discrimination, complicated venous access, misinformation about HCV status and treatment options, and loss to follow-up during the typical two-step HCV antibody and subsequent HCV RNA confirmatory testing process.[7–10]

Recent developments in point-of-care (POC) HCV RNA testing using finger-prick blood samples hold promise for reducing barriers to HCV care by eliminating the need for diagnostic venipuncture, providing one-step rapid results (viral load quantification within an hour), and expanding testing access to non-clinical settings.[11,12] Studies have documented successful uptake of POC HCV antibody and HCV RNA testing in a variety of settings with people who inject drugs, such as pop-up community clinics, needle distribution programs and informal outreach locations.[13–17] The use of POC HCV RNA testing to facilitate engagement of individuals who use supervised consumption services (SCS) in HCV care, has not been well evaluated.

SCS have demonstrated success at both reducing overdose and connecting people who use drugs to health and social services.[18,19] A 2018 global survey of 49 SCS, however, found that although most (65%) offer some type of onsite HCV testing, the majority refer offsite for treatment (86%).[20] The recent expansion of a variety of SCS models worldwide, including integrated care models, offer a unique opportunity to engage people who inject drugs in HCV care. Our primary aim was to evaluate the provision of POC HCV RNA testing and linkage to HCV care among service users of a small-scale integrated SCS co-located within a primary care community health centre. Secondary aims include measuring HCV RNA prevalence at baseline, HCV incidence during follow-up and exploring factors associated with HCV RNA positivity and HCV treatment uptake.

Methods

Study design

This prospective, cohort study was conducted from August 13, 2018 to September 30, 2021. SCS and Hep C program staff and clients were involved in the study design and analysis (author BL was the study nurse and JB was a Hep C program staff at the time of the study). Study participants were recruited and completed baseline POC HCV RNA testing study visits from August 13, 2018 to June 24, 2019. Study follow-up visits to assess incident HCV and/or linkage to care and HCV treatment outcomes occurred up to September 30, 2021. The follow-up period was extended to account for interrupted study visits due to a suspension of all non-COVID-19 related research activities across Toronto from March 26, 2020 to September 11, 2020 and redeployment of study staff until July 31, 2021. Although HCV care continued at the health centre during the

pandemic, many of the study follow-up visits could not be completed as planned. Research ethics approval was granted by Michael Garron Hospital, Toronto.

Study setting

The SCS (known as 'keepSIX') opened in November 2017 and is integrated within South Riverdale Community Health Centre in Toronto, Canada, a non-profit organization that provides primary health care and health promotion programs to a range of individuals across the life span, who may or may not use drugs. The SCS is staffed by nurses, health promoters, and harm reduction workers with lived/living experience of injection drug use.[21] The SCS accommodates up to five injections/consumptions at a time and had an average of 17 visits per day over the enrollment period. Service users are registered using a unique identifier code but can choose to access the SCS anonymously (unique identifier not required). The SCS is part of a diverse range of primary care and social service programs provided by the health centre, which includes HCV treatment and support from the Toronto Community Hep C Program (TCHCP).

Model of care

The TCHCP is an embedded program which operates as a partnership between four community-based health centres (including the study site) and provides care to people who use drugs and/or alcohol through the provision of multidisciplinary, holistic, and low barrier supports, leading to successful HCV treatment outcomes.[22] HCV care is coordinated by the HCV treatment nurse. Primary care physicians or nurse practitioners with experience treating HCV conduct the pre-treatment assessments and prescribe treatment. Study participants were required to meet with the clinical team on a different day/time from testing in order to initiate treatment. Clinical offices are located on a different floor in the same building as the SCS. Follow-up care (wellness checks, medication delivery) occasionally took place within SCS. During the enrollment period, the treatment nurse was available to provide HCV assessments and treatment monitoring three days per week. From March 26, 2020 to July 31, 2021, the HCV treatment nurse was redeployed for the COVID-19 response and was available only 1–2 days per week for HCV care. Prior to the study, the HCV treatment nurse had been in the role for two years and had worked on the development of the SCS including providing training to SCS staff and covering shifts at the service. They had no prior experience using the study testing platform which required approximately 2 h of training. HCV treatment at the health centre required baseline blood work to confirm diagnosis (since HCV POC testing platform is not accepted as a diagnostic tool in Canada) and for the following assessments: liver enzymes, liver function, Hep A/B, HIV, VDRL, CBC, fibrosis assessment, kidney function. Results were reviewed by the prescribing clinician. At the time of the study, publicly-funded treatment coverage required evidence of HCV chronicity with two HCV viral loads at least six months apart. Ultrasounds were required only if clinically indicated (i.e. cirrhosis) and took place off-site. Medication dispense was determined by participant preference with weekly dispense at the health centre, daily dispense from a pharmacy and, occasionally, monthly dispense at either of the above. For study participants a daily dispense option through the SCS was provided, with weekend carries. Blood work while on treatment took place only if there was a clinical indication to do so.

Procedures

Testing was conducted within the consumption area of the SCS by the study nurse who also worked at the co-located HCV treatment program as the treatment nurse. POC HCV RNA testing was conducted using 100 μL capillary blood samples and the Xpert HCV VL fingerstick test on the Cepheid GeneXpert© platform, which provides a quantitative viral load result within 60 min.[23] Dried blood spots (DBS) were obtained at baseline for HCV antibody testing and confirmatory PCR, with results reported back for research purposes. All participants received HCV pre/post-test counselling. A baseline questionnaire was administered to capture self-reported socio-demographics, substance use, SCS use and history of HCV care. Those with negative baseline HCV RNA test results were followed and offered repeat testing every three months for up to four visits. Participants were asked how they would like to be followed up with (phone, email, text, message board at health centre, message with SCS staff) at their baseline visit. Contact information and preferences were updated throughout the study at each successful visit/connection. Once contact was made, there was no repeat/assertive outreach made in order to respect people's agency in determining how and when to engage. Those who tested positive at baseline or follow-up visits were offered immediate in-person referral to the co-located HCV treatment program. Participants were offered an immediate intake, could book an appointment, or attend weekly drop-in hours within the week. Post-intake with the HCV treatment nurse, an appointment with one of the program prescribers (primary care physician or nurse practitioner) was required and offered during weekly drop-in hours. At the final study visit, a survey was administered to collect data on motivators for HCV testing and treatment. Short surveys consisting of closed and open-ended questions were also conducted with SCS and Hep C program staff six-months after enrollment completion to evaluate model of care acceptability, provider comfort and gather suggestions for sustainability and generalizability to other SCS settings.

Participants

Eligibility criteria included age ≥18 years and accessing the SCS for injection on the day of the study enrollment (i.e. current injection drug use). Exclusion criteria included current or recent (past six months) HCV treatment. Service users were recruited via posters in the SCS, SCS staff referrals and word-of-mouth. Potential participants were approached by SCS staff during intake and post-injection to determine potential interest in the study. Interested individuals were referred to the study nurse in-person or by phone. Service users could also self-refer directly to the study nurse. The study nurse obtained written informed consent. Participants were compensated for their time with $30 CAD for baseline and final visits and $10 CAD for follow-up POC testing-only visits.

Measures

Outcomes included HCV RNA prevalence at baseline, HCV incidence during follow-up, and HCV treatment initiation. Baseline HCV RNA prevalence was measured by POC HCV RNA testing (lower limit of quantification [LLQ] >100 IU/mL), or via DBS (LLQ >1000 IU/mL) or venous bloodwork (LLQ >15 IU/mL) if POC test results were invalid. Incident HCV was defined as an HCV RNA positive result at a follow-up testing visit among participants who were HCV RNA negative at baseline. Linkage to care and treatment initiation were defined as an intake visit with the HCV treatment nurse and direct-acting antiviral HCV treatment prescription with clinical follow-up at the co-located HCV program by the end of the study period (September 30, 2021) respectively. Sustained virologic response (SVR) was measured at 12 weeks or more post-treatment completion.

We measured baseline self-reported characteristics representing potential correlates of HCV infection or HCV treatment uptake, including: age (years); duration of injection drug use (approximate cumulative years since first injection); self-reported gender (male, female, or prefer to self-identify – see Supplementary Table S2 for full gender responses); self-reported race or ethnicity (categorized as white, Indigenous, or racialized non-Indigenous – see Supplementary Table S2 for full ethnicity responses); current (i.e. past 30 days) housing status (stable: one's own apartment/house versus unstable: rooming/boarding home, friend/relative's place, hotel/motel, shelter/hostel/transitional housing, public place, or in an institution); current primary income source (social assistance versus employment/other [full-time or part-time work, money from family/friends, asking for money on the street, sex work, or other income sources]); current drug injected most often (heroin or prescription opioids, fentanyl, or stimulants/stimulant-containing substances including crack, cocaine, crystal meth, or speedballs); current frequency of injection drug use (daily versus less than daily injecting), current frequency of SCS use at the study site (keepSIX) or other SCS (daily, weekly, or a few times per month versus less than monthly or first-time use); and self-reported HCV infection status prior to testing (categorized as "don't know" among participants reporting never receiving HCV testing or not aware of prior test results versus never infected, current HCV infection, or prior HCV infection [cleared spontaneously or via treatment] among participants aware of prior HCV test results). Risk behaviours and opiate substitution therapy use were not included to mitigate concerns of self-incrimination and possible impact on future access to the newly opened SCS.

Enrollment target

The study had an enrollment target of 125 to assess outcomes of offering POC HCV RNA testing within the SCS. This was based on our goal to recruit over a one-year period and estimates of the number of unique service users per year. No formal sample size calculation was performed as the goal of the study was exploratory and not to estimate the absolute effect of the intervention.

Statistical methods

Among all participants, we calculated baseline HCV RNA prevalence and summarized baseline characteristics. HCV incidence was estimated as the number of incident HCV infections per 100 person-years at risk, among all individuals HCV RNA negative at baseline who returned for ≥1 follow-up visit. Person-time at risk was measured from the date of the baseline HCV RNA negative test up to the earliest date of an HCV RNA positive test (i.e. left censoring, given the date of infection is unlikely to be directly observed), the latest date of follow-up with an HCV RNA negative test on record, or right-censored as HCV RNA negative up to 15 months for those with prolonged follow-up due to the COVID-related study suspension. HCV treatment initiation was calculated among all participants who tested HCV RNA positive at baseline or follow-up, excluding anyone ineligible for treatment due to spontaneous clearance and those who died prior to treatment initiation.

To identify factors associated with baseline HCV RNA prevalence or treatment initiation, we used modified Poisson regression models to estimate unadjusted prevalence ratios (PR) with 95% confidence intervals (CI) for each covariate and outcome of interest. Covariate-adjusted models to control for confounding were not performed given our objectives were to explore potential correlates of HCV prevalence and treatment, rather than to isolate a single causal effect of interest.

Due to a small sample size precluding an analysis of factors associated with incident HCV, we explored factors associated with recent HCV infection. Our definition for recent HCV infection pooled together incident HCV cases observed over follow-up with probable acute HCV cases at baseline (RNA positive, antibody negative

results). Recent infections were compared to those without HCV infection, and the analysis was restricted to individuals returning for ≥1 follow-up to reduce the potential of bias due to missing data among those lost to follow-up. Characteristics between those with and without recent HCV infection were compared descriptively using t-tests for continuous variables and chi-square tests for categorical variables. Where present, missing data were reported in tables and a complete case analysis was performed. Analysis was completed using Stata SE version 14.2.

Role of funding the source

Our investigator-initiated study was supported by an HCV Micro-Elimination Grant from Gilead Sciences Canada and in-kind support from Cepheid. These companies had no role in the study design, data collection, analysis, interpretation or writing of this manuscript or in the decision to publish.

Results

128 participants were enrolled in the study. Two were later removed for ineligibility (due to being currently on treatment and not someone who injects drugs) and two were removed as duplicates (first enrollment data set was maintained). Ultimately, 124 eligible participants were included in the study among at least 427 unique service users who accessed the SCS during the enrollment period (August 13, 2018–June 24, 2019). All individuals who met with the study nurse to learn more about the study agreed to participate. It was not possible to estimate an overall participation rate because some service users access SCS anonymously, and some may have used the SCS outside of the hours when the study nurse was available. All of the study participants received their results. All but one received results within the hour following testing.

The mean age of participants (n = 124) was 40.9 (SD:11.8) years and the majority were male (n = 81, 65.3%) and white (n = 71, 57.2%), see Table 1. At baseline, most reported unstable housing (n = 91, 73.4%) and social assistance as their primary income source (n = 106; 85.5%). Over two-thirds of participants reported daily injecting (n = 85, 68.5%) and three-quarters reported using SCS daily, weekly, or a few times per month (n = 94, 75.8%). Most participants (n = 86, 69.4%) had a history of HCV testing, however over half (n = 66, 53.2%) were unaware of their current HCV status prior to the study (either due to lack of HCV RNA testing or not receiving test results). Additionally, 17 (13.7%) participants reported current/untreated HCV and 11 reported prior HCV (2 spontaneous clearances, 9 SVR to treatment).

At baseline, 54 (43.5%) participants tested HCV RNA positive (47 via POC HCV RNA testing, 6 via DBS and 1 via venipuncture). Of the 124 baseline POC HCV RNA tests, there were 15 invalid results (12%) due to inadequate blood sample size or cartridge error (see Fig. 1). Of the 113 valid POC HCV RNA tests (original and repeat testing), 47 were positive. Three of these results were positive below the lower limit of quantification but meeting threshold for detection (>40 IU/mL). Baseline HCV antibody prevalence as determined by DBS was 50.4% (62/123). Among those with negative HCV antibody results, 9 were HCV RNA positive, indicating likely acute HCV infection.

Among those HCV RNA positive at baseline (n = 54), 39 (72.2%) were first-time diagnoses/previously unaware of their HCV infection (Table 1). HCV RNA prevalence at baseline was over two-fold higher among those experiencing unstable housing compared to those stably housed (PR: 2.09, 95% CI: 1.10–3.95) and nearly three-fold higher among people with daily relative to less than daily injection drug use (PR: 2.92, 95% CI: 1.46–5.86).

Of the 70 participants who were HCV RNA negative at baseline, 37 returned for follow-up testing visits among whom ten incident HCV infections were observed over 28.5 person-years of follow-up (mean of 9.2 months of follow-up per participant). The HCV incidence was 35.1 cases per 100 person-years (95% CI: 18.9–65.3) and the cumulative incidence of HCV was 38.3% (95% CI: 22.8–59.5%) at 15 months of follow-up (Fig. 2). Participants with recent (incident or acute) HCV infection were on average younger and more likely to report daily injecting relative to participants remaining HCV negative over follow-up (Supplementary Table S1).

Among participants who were HCV RNA positive at baseline or follow-up (n = 64), 67.2% (n = 43) were linked to co-located HCV care (intake with the health centre's HCV Treatment Nurse). The median time from first positive HCV RNA test to linkage to care was 63 days (IQR: 6–230 days). The proportion of participants linked to care varied based on the timing of diagnosis: 62.9% (34/54) of cases diagnosed at baseline versus 90% (9/10) of incident cases diagnosed during follow up were linked to care. Among the 64 HCV RNA positive participants, 57 were eligible for treatment (3 spontaneously cleared and 4 died) and 43 were linked to care. Of those linked to care, 67.4% (29/43) initiated treatment at the health centre (Fig. 3). The median time between first positive HCV RNA test and treatment initiation was 265 days (IQR: 177–503 days). Factors positively associated with treatment uptake included older age, a longer duration of injection drug use, and identifying as racialized/Indigenous relative to white (Table 2). Participants who most frequently inject fentanyl had lower treatment uptake relative to those injecting heroin/prescription opioids. Among those who initiated treatment, there was an SVR rate of 86.2% (25/29). There was one treatment failure with subsequent re-treatment and SVR (outside of the study

Baseline characteristic	Overall	Baseline HCV RNA result		Prevalence ratio (95% CI)
		Negative	Positive	
	N (% column)	N (% row)	N (% row)	
Age, mean (SD)	40.9 (11.8)	42.5 (11.5)	38.8 (11.3)	0.92 (0.84–1.01)[a]
Years of injection drug use, mean (SD)	10.8 (11.9)	9.4 (11.2)	12.7 (12.5)	1.06 (0.99–1.14)[a]
Self-reported gender identity				
Male	81 (65.3)	43 (53.1)	38 (46.9)	(Ref)
Female	42 (33.9)	27 (64.3)	15 (35.7)	0.76 (0.48–1.22)
Prefer to self-identify	1 (0.8)	0 (0)	1 (100)	
Race/ethnicity				
White	71 (57.3)	40 (56.3)	31 (43.7)	(Ref)
Indigenous	41 (33.1)	22 (53.7)	19 (46.3)	1.06 (0.69–1.62)
Racialized, non-Indigenous	12 (9.7)	8 (66.7)	4 (33.3)	0.76 (0.33–1.78)
Housing status				
Stable housing	33 (26.6)	25 (75.8)	8 (24.2)	(Ref)
Unstable housing	91 (73.4)	45 (49.5)	46 (50.5)	**2.09 (1.10–3.95)**
Income source				
Social assistance	106 (85.5)	61 (57.5)	45 (42.5)	(Ref)
Employment/other	17 (13.7)	9 (52.9)	8 (47.1)	1.11 (0.64–1.93)
Unknown/missing	1 (0.8)	0 (0)	1 (100)	
Drug injected most often[b]				
Heroin or prescription opioids	29 (23.6)	20 (69)	9 (31)	(Ref)
Fentanyl	61 (49.6)	27 (44.3)	34 (55.7)	1.80 (1.00–3.24)
Crack, cocaine, crystal meth, speedball	33 (26.8)	22 (66.7)	11 (33.3)	1.07 (0.52–2.23)
Frequency of injection drug use[b]				
Less than daily injecting	37 (29.8)	30 (81.1)	7 (18.9)	(Ref)
Daily injecting	85 (68.5)	38 (44.7)	47 (55.3)	**2.92 (1.46–5.86)**
Unknown/missing	2 (1.6)	2 (100)	0 (0)	
Frequency of SCS use (keepSIX or other)[b]				
Less than monthly/new SCS user	30 (24.2)	21 (70)	9 (30)	(Ref)
Daily/weekly/few times per month	94 (75.8)	49 (52.1)	45 (47.9)	1.60 (0.89–2.87)
Self-reported HCV status				
Don't know/never tested	66 (53.2)	33 (50)	33 (50)	Not evaluated[c]
Never infected	30 (24.2)	24 (80)	6 (20)	
Current HCV infection	17 (13.7)	2 (11.8)	15 (88.2)	
Prior HCV infection	11 (8.9)	11 (100)	0 (0)	
Total	**124 (100)**	**70 (56.5)**	**54 (43.5)**	

Notes: CI: confidence interval; SD: standard deviation; HCV: hepatitis C virus; SCS: supervised consumption service. Missing data is reported where present. Results in bold indicate statistical significance at $p < 0.05$. [a]Reported per 5-year increase. [b]Measured in 30 days prior to baseline. [c]By definition, self-reported current HCV infection is correlated with HCV RNA prevalence, therefore this variable was not evaluated.

Table 1: **Distribution of baseline characteristics and estimated associations for correlates of Hepatitis C (HCV) infection at baseline among 124 supervised consumption service users (SCS) accessing point-of-care HCV RNA testing – August 2018 to June 2019.**

period) and three others missing SVR assessments (two deaths; one while on treatment, one post-treatment completion and one not yet returned for SVR testing (both unrelated to HCV medication). In total, there were ten known study participant deaths (seven due to overdose).

In total, 52 participants completed a final questionnaire and were asked what motived them to participate in testing (could select more than one reason). The top motivations were: honoraria received (n = 18), testing was offered by someone participants trusted (n = 17), ease/convenience of testing location (n = 17) and more generally, the open offer of testing (n = 17). Of those who initiated treatment (n = 18), the main reason for doing so was "wanting to get rid of HCV" (n = 11), followed by trust in the team who offered it (n = 4).

Eight health centre staff and managers were interviewed six months post completion of study enrollment. All reported that overall, they were 'satisfied or very satisfied' with the integration of POC RNA HCV testing within the SCS. Everyone interviewed felt that this model of testing/treatment could be adapted to other supervised consumption services, both integrated services and stand-alone sites.

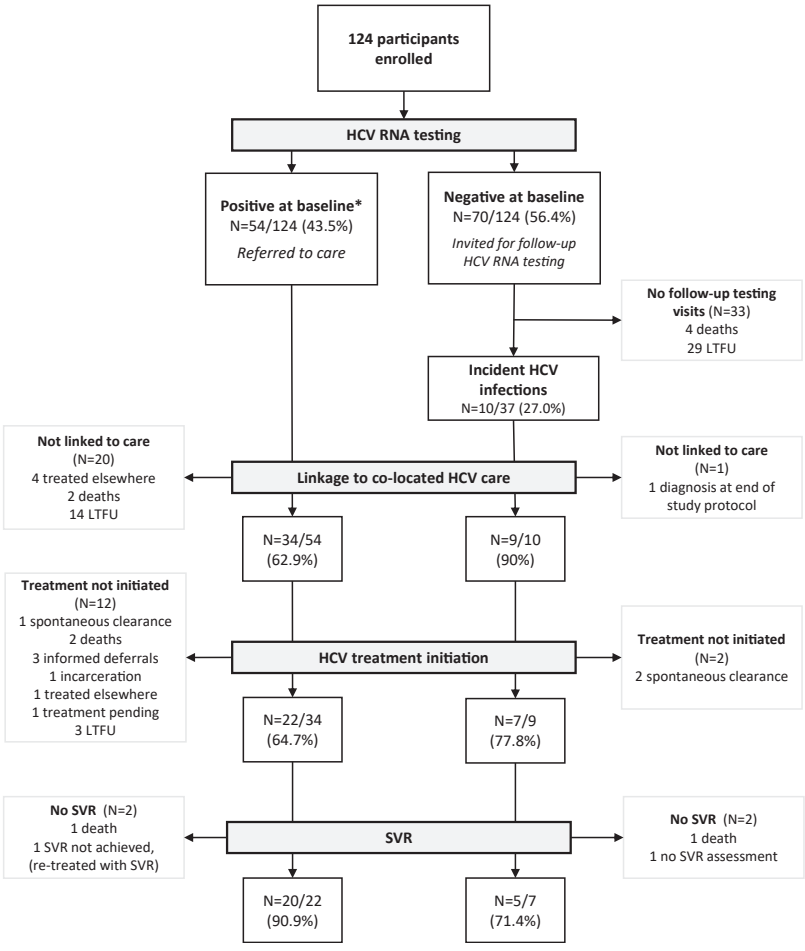


***Fig. 1:* Study participant disposition**. *47 detected via Cepheid +6 via dried blood spot HCV RNA testing and 1 via bloodwork where Cepheid results were invalid. BL valid POC test results = 109/124 [87.9%]. Five participants agreed to immediate repeat testing. Pattern of likely acute HCV infection (POC HCV RNA-/DBS HCV Ab + for N = 9 participants at baseline). Known participant deaths leading to exclusions have been reported, however among those labelled as LTFU (lost to follow-up), unreported deaths may be an underlying cause of LTFU.

Discussion

We demonstrated that offering rapid, low-barrier POC HCV RNA testing in a small-scale SCS allowed us to diagnose HCV in a population with high prevalence and to link a majority to HCV care and treatment. By offering POC HCV RNA testing in a place where people who use drugs already go, our model succeeded in expanding access to HCV RNA testing to a highly marginalized group of individuals at high risk of HCV acquisition. Our findings of high HCV RNA prevalence and incidence among SCS clients demonstrate the value of adding POC HCV RNA testing within SCS to support diagnosis and linkage to care/treatment among populations with the greatest HCV burden.

We observed a baseline HCV RNA prevalence of 44% (54/124) which is similar to the 37% HCV RNA prevalence in I-Track 2017–2019 a Canadian bio-behavioral surveillance study of people who inject drugs.[3] Notably, we observed a high HCV incidence rate of 35 per 100 person-years, albeit with a wide confidence interval due to small sample size. As daily vs less than daily injecting was associated with loss to follow-up, our reported HCV incidence may be an underestimate. Our estimated HCV incidence rate is high relative to other studies among people who inject drugs. Minoyan et al. found an HCV incidence of 13.76 (95% CI: 11.08–16.91) among people who inject drugs reporting partial harm reduction coverage (i.e. ≤100% needle syringe program or high-dose opioid agonist therapy) in Montreal from 2010 to 2017 although only a minority were underhoused and the median days injecting was only 10 per month.[24] A systematic review and meta-analysis including 28 studies world-wide estimated a pooled HCV incidence rates of 20.36 (95% CI: 13.86–29.90) and 15.20 (95% CI: 10.52–21.97) per 100 person-years in female and males who inject drugs,

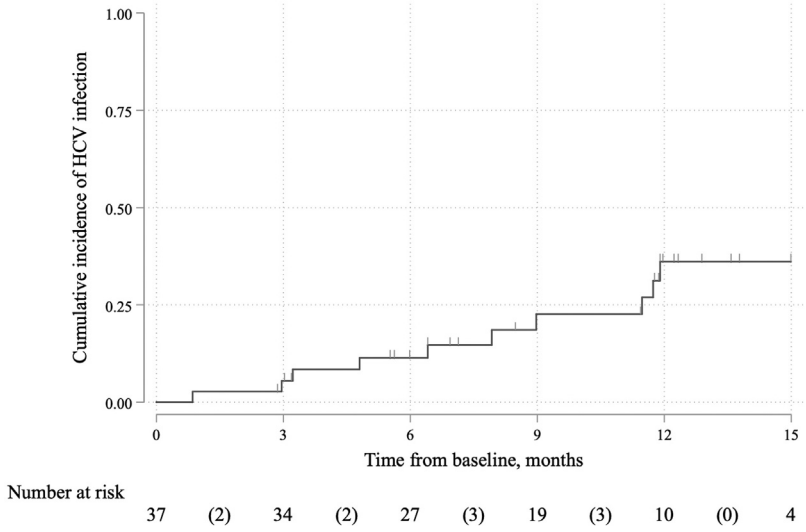
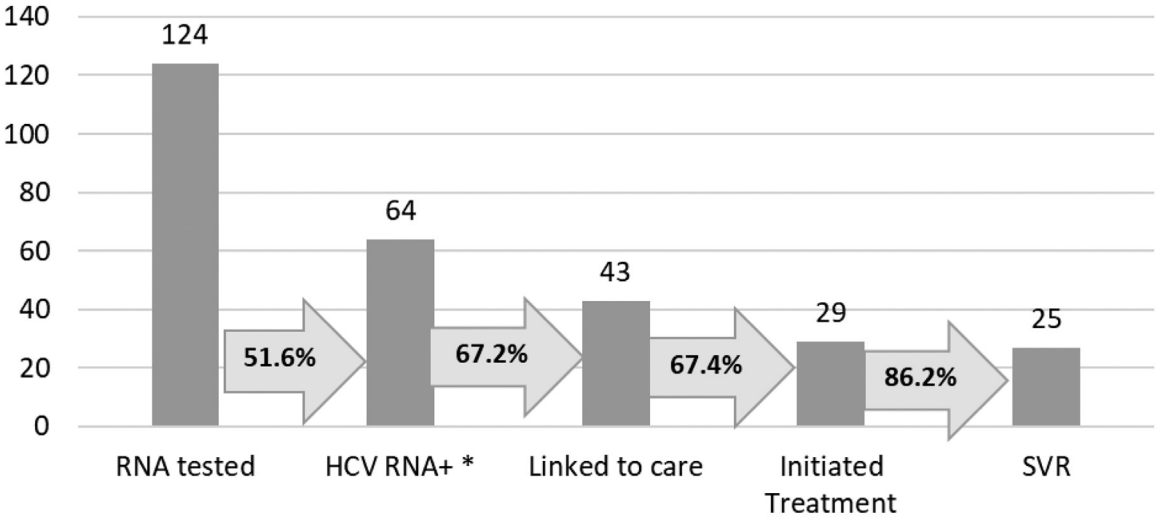


***Fig. 2:* Kaplan-Meier curve for the cumulative incidence of hepatitis C infection over follow-up.** Among 37 individuals with negative HCV RNA baseline results who returned for at least 1 follow-up visit, a total of 10 incident HCV infections were measured over 28.5 person-years of follow-up. The HCV incidence was 35.1 cases per 100 person-years (95% CI: 18.9–65.3) and the cumulative incidence of HCV was 38.3% (95% CI: 22.8–59.5%) at 15 months of follow-up. HCV: hepatitis C virus. Notes: The risk table below the figure presents the total number of participants at risk per 3-month interval, with the number of HCV infections measured per interval shown in brackets. Censoring events are indicated by ticks/number markers on the cumulative incidence curve.

respectively although noted high heterogeneity in the studies included.[25] Our incidence data should not be interpreted as a lack of efficacy of SCS as a harm reduction intervention for HCV as there is no comparable data for a group with similar IDU patterns. The high HCV incidence in our study was determined through frequent RNA testing and likely reflects that a high proportion of our cohort included individuals with factors associated with incident infection such as high frequency of daily injecting associated with fentanyl, and housing instability. HCV incidence rates are also likely increasing over time, according to national



* at any point during baseline/follow up

***Fig. 3:* HCV Care Cascade among supervised consumption service users accessing point-of-care HCV RNA testing.**

Baseline characteristics	Total participants HCV RNA + at baseline or follow-up (N = 57)	HCV treatment initiation via co-located HCV care		Prevalence ratio (95% CI)
		No (N = 28)	Yes (N = 29)	
	N (% column)	N (% row)	N (% row)	
Age, mean (SD)	38.0 (10.1)	34.6 (9.5)	41.2 (9.9)	**1.16 (1.03–1.31)** [a]
Years of injection drug use, mean (SD)	10.8 (11.5)	7.9 (9.9)	13.6 (12.5)	**1.10 (1.01–1.20)** [a]
Self-reported gender identity				
Male	39 (68.4)	19 (48.7)	20 (51.3)	(Ref)
Female	17 (29.8)	9 (52.9)	8 (47.1)	0.92 (0.51–1.66)
Prefer to self-identify	1 (1.8)	0 (0)	1 (100)	
Race/ethnicity				
White	29 (50.9)	19 (65.5)	10 (34.5)	(Ref)
Indigenous/Racialized	28 (49.1)	9 (32.1)	19 (67.9)	**1.97 (1.12–3.47)**
Housing status				
Stable housing	9 (15.8)	5 (55.6)	4 (44.4)	(Ref)
Unstable housing	48 (84.2)	23 (47.9)	25 (52.1)	1.17 (0.53–2.57)
Income source				
Social assistance	46 (80.7)	23 (50)	23 (50)	(Ref)
Employment/other	10 (17.5)	4 (40)	6 (60)	1.2 (0.67–2.16)
Unknown/missing	1 (1.8)	1 (100)	0 (0)	
Drug injected most often[b]				
Heroin or prescription opioids	10 (17.5)	2 (20)	8 (80)	(Ref)
Fentanyl	36 (63.2)	20 (55.6)	16 (44.4)	**0.56 (0.34–0.9)**
Crack, cocaine, crystal meth, speedball	11 (19.3)	6 (54.5)	5 (45.5)	0.57 (0.28–1.17)
Frequency of injection drug use[b]				
Less than daily injecting	8 (14)	4 (50)	4 (50)	(Ref)
Daily injecting	48 (84.2)	24 (50)	24 (50)	1 (0.47–2.13)
Unknown/missing	1 (1.8)	0 (0)	1 (100)	
Frequency of SCS use (keepSIX)[b]				
Less than monthly/new SCS user	26 (45.6)	13 (50)	13 (50)	(Ref)
Daily/weekly/few times per month	31 (54.4)	15 (48.4)	16 (51.6)	1.03 (0.61–1.73)
Self-reported HCV status				
Never infected/don't know	43 (75.4)	19 (44.2)	24 (55.8)	(Ref)
Current HCV infection	14 (24.6)	9 (64.3)	5 (35.7)	0.64 (0.3–1.37)
Total	**57 (100)**	**28 (49.1)**	**29 (50.9)**	

Notes: CI: confidence interval; SD: standard deviation; HCV: hepatitis C virus; SCS: supervised consumption service. Missing data is reported where present. Among total of 64 participants tested HCV RNA positive at baseline (N = 54) or follow-up visits (N = 10), this analysis excludes individuals who spontaneously cleared an acute HCV infection (N = 3) and those who died before treatment could be initiated (N = 4). Some variable categories have been collapsed: for the race/ethnicity variable, the Indigenous/racialized group includes a total of 22 Indigenous participants and 6 racialized, non-Indigenous participants; the baseline self-reported HCV status variable includes 33 participants unaware HCV status and 10 who reported not having HCV at baseline. Results in bold indicate statistical significance at $p < 0.05$. [a]Reported per 5-year increase. [b]Measured in 30 days prior to baseline.

***Table 2*: Distribution of baseline characteristics and estimated associations for correlates of HCV treatment initiation among 57 supervised consumption service users testing HCV RNA positive at baseline or follow-up visits.**

surveillance data indicating a rise in HCV infections from 2014 to 2018 in Canada.[26]

The 67% (29/43) HCV treatment initiation rate among SCS clients who were linked to care in our study is high relative to other Canadian studies of people who inject drugs. National survey data from 2017 to 2019 found only 14.4% of people who inject drugs and aware of their HCV infection had received treatment in 2017–2019.[3] In British Columbia, Canada among people who currently inject drugs (defined as past 24 months) with HCV RNA positive results, 40% had initiated treatment up to 2018.[5] There were several factors supporting high treatment initiation rates in our setting. Rapid HCV RNA testing allowed the vast majority of study participants to receive assessment of viremia within the visit/hour following testing and all HCV RNA positive individuals received same-day referrals to care. This is in stark contrast to the usual diagnostic pathway consisting of two-step antibody and subsequent RNA assessment through phlebotomy. Additionally, the detection of acute HCV cases in our study highlights the high HCV acquisition risk among people who inject drugs, and the importance of frequent HCV RNA testing to detect and treat acute HCV infections. The

program's previous work evaluating the impact of POC HCV antibody testing among people who inject drugs in a wide range of outreach locations found low uptake in HCV care (3% of those who were antibody positive followed up for additional testing), indicating that HCV antibody testing alone is less valuable as a tool to engage individuals in HCV care among a population with high seropositivity.[17] POC RNA testing offered simplified diagnostics and immediate linkage to trusted care.

The co-location of HCV care in spaces where people who inject drugs feel safe and can access low-threshold supports, such has harm reduction programs or primary care, has been identified as a facilitator to HCV treatment elsewhere.[27–30] Trust in the team offering testing or treatment was a commonly cited motivation for engagement in care in our study. The study nurse/health centre's HCV nurse was a regular presence in the SCS before and during the study period thereby offering a constant 'open door' for counselling and questions. In addition, SCS staff with lived experience of HCV often provided HCV information and treatment encouragement after the official 'post-test' conversation which likely helped to establish care engagement. The Indigenous Health Promoter who worked within the SCS may have supported the high treatment uptake we found among participants who identified as Indigenous and who were over-represented in our sample, likely a reflection of historical and ongoing impacts of colonization and oppression of Indigenous populations in Canada. This finding highlights the importance of culturally safe healthcare spaces and for the inclusion of Indigenous community members in HCV and harm reduction research and program design. The role of trusted care providers and people with lived experience in improving HCV care engagement has been supported by other research and policy recommendations.[9,31,32] Finally, we observed a pattern of high linkage to care among incident infections detected during follow-up testing, suggesting the value of frequent and ongoing POC testing within SCS to identify and treat service users soon after they become infected.

There were also likely some factors that may have impacted treatment initiation rates and time to treatment. Rapid HCV treatment initiation was not done in this study. Our treatment protocols required confirmation of chronic HCV viremia and pre-treatment evaluation at a public health reference laboratory. Additionally, publicly-funded treatment coverage in Ontario required evidence of HCV chronicity with two HCV viral loads at least six months apart. This resulted in treatment delays for individuals who had a novel HCV viral load result identified through the study testing. Ambivalence around chronic disease management in the context of a toxic drug supply and escalating overdose crisis, coupled with the disruptions caused by the COVID-19 pandemic, also presented challenges to engagement. The remuneration provided to individuals for their time to participate in the study intervention was the main reason cited for engaging in HCV testing. However, our study incentives were tied to testing time points only. Linkage to care and treatment initiation were not incentivized which may have contributed to a drop in retention. This finding supports research elsewhere which has demonstrated the value of incentives at multiple stages of the HCV care cascade and suggests they may be necessary to overcome initial barriers to care for people who are marginalized.[33] On an individual-level, we found characteristics associated with lower treatment uptake included younger age, primarily injecting fentanyl, and being previously aware of one's current hepatitis C.

Limitations

Our study was subject to limitations common to prospective cohorts among people who inject drugs, including selection bias in those opting to participate and those who were retained without loss to follow-up. Our participants are representative of the population of SCS clients in Toronto with respect to sociodemographic and drug use practices,[21] supporting the generalizability of our results within our setting. However, this model may not be transferrable to a larger SCS with more transient clients or to SCS without a co-located, comprehensive HCV program. Testing was remunerated as compensation for the study participation, as such, it is possible that testing uptake might have been lower without incentivization or that participants might not have waited to receive their test results (when the honorarium was received). However, given that the model of care offered testing in a place where participants are encouraged to spend time and could access other social and health care supports while waiting for their results, the time to receive test results was not a significant challenge in this setting. We observed high rates of loss-to-follow-up after the baseline POC HCV RNA testing visit, possibly exacerbated by the COVID-19 study interruption, which impacted the sample size and precision of our HCV incidence estimate. Additionally, our enrollment target was designed to assess our primary aim of the uptake of POC HCV RNA testing within an SCS, however we had low precision for analyzing factors associated with secondary outcomes, such as HCV prevalence, incidence, and treatment uptake. Our sample size did not allow us to assess the prevention impact of prompt treatment but in a high incidence setting, this is an important population level outcome related to SVR. Our study was also not designed to determine if participants had engaged in HCV care outside of the health centre's hepatitis C treatment program and additional treatment initiations may have occurred in those lost to follow up. Due to variations in drug use trends and harm reduction service availability across settings, our results may not be generalizable to other settings.

Conclusion

Point-of-care HCV RNA testing providing rapid determination of viremia within SCS, coupled with co-located HCV care is a promising model to increase HCV engagement among people who inject drugs. Among participants who were found to be HCV RNA positive there was substantial engagement in HCV care, particularly amongst those who tested positive during the follow-up period. As a trusted and low-barrier health care setting, SCSs offer an important opportunity for HCV-screening and linkage-to-care especially when co-located with health-care services and where POC RNA testing can be routinely offered.

Contributors

JF and JP conceived of the study. BL, KM, JB, JF, JP contributed to the study design. BL carried out the intervention as the study nurse conducting testing and treatment and completed the study activities with support from JB and KM. EM coordinated the confirmatory DBS testing component. JF and JP had study oversight. ZG conducted the data analysis. BL and KM verified the data. BL, KM and ZG drafted the manuscript. All coauthors critically revised the manuscript and approved the final version to be published.

Data sharing statement

De-identified study data and additional study documents (consent form, study protocol, survey tool) are available on request, after approval of a proposal with signed data access agreement.

Declaration of interests

JJF reports research support and honoraria for consulting from Abbvie and Gilead.

JP received the grant from Gilead Sciences Canada and the in-kind donation of the testing platform from Cepheid to conduct the study.

Acknowledgements

The authors would like to acknowledge the support of South Riverdale Community Health Centre and the Toronto Community Hep C Program Staff and Patient Advisory Board. Thanks also to the keepSIX Community Advisory Group. Special thanks to Jason Altenberg, Frank Crichlow, Georgia Dyer, Les Harper, Jennifer Ko, Sushi Rosborough, Paula Tookey and Dan Werb for their support of this project. The Toronto Community Hep C Program receives funding from the Ontario Ministry of Health, AIDS and Hepatitis C Funding Program. The views expressed in this paper are those solely of the authors.

Sources of funding: this investigator-initiated study was supported by an HCV Micro-Elimination Grant from Gilead Sciences Canada, Inc. and by in-kind support from Cepheid. ZRG is supported by a Canadian Institutes of Health Research Doctoral Award: Frederick Banting and Charles Best Canadian Graduate Scholarship [202011FBD-457278-253354] and a Doctoral Fellowship Award from the Canadian Network on Hepatitis C (CanHepC). CanHepC is funded by a joint initiative of the Canadian Institutes of Health Research (NPC-178912) and the Public Health Agency of Canada.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2023.100490.

References

1 World Health Organization. Global progress report on HIV, viral hepatitis and sexually transmitted infections. https://www.who.int/publications/i/item/9789241550345; 2021. Accessed June 20, 2022.
2 Trubnikov M, Yan P, Archibald C. Estimated prevalence of hepatitis C virus infection in Canada, 2011. *Can Commun Dis Rep*. 2014;40(19):429–436.
3 Tarasuk J, Zhang J, Lemyre A, Cholette F, Bryson M, Paquette D. National findings from the Tracks survey of people who inject drugs in Canada, Phase 4, 2017-2019. *Can Commun Dis Rep*. 2020;46(5):138–148.
4 Burstow NJ, Mohamed Z, Gomaa AI, et al. Hepatitis C treatment: where are we now? *Int J Gen Med*. 2017;10:39–52.
5 Bartlett SR, Yu A, Chapinal N, et al. The population level care cascade for hepatitis C in British Columbia, Canada as of 2018: impact of direct acting antivirals. *Liver Int*. 2019;39(12):2261–2272.
6 Socías ME, Ti L, Wood E, et al. Disparities in uptake of direct-acting antiviral therapy for hepatitis C among people who inject drugs in a Canadian setting. *Liver Int*. 2019;39(8):1400–1407.
7 Young S, Wood E, Milloy MJ, et al. Hepatitis C cascade of care among people who inject drugs in Vancouver, Canada. *Subst Abuse*. 2018;39(4):461–468.
8 Madden A, Hopwood M, Neale J, Treloar C. Beyond interferon side effects: what residual barriers exist to DAA hepatitis C treatment for people who inject drugs? *PLoS One*. 2018;13(11). https://doi.org/10.1371/journal.pone.0207226.
9 Treloar C, Rance J, Backmund M. Understanding barriers to hepatitis C virus care and stigmatization from a social perspective. *Clin Infect Dis*. 2013;57(Suppl 2):S51–S55.
10 Aleman S, Soderholm J, Busch K, Kovamees J, Duberg AS. Frequent loss to follow-up after diagnosis of hepatitis C virus infection: a barrier towards the elimination of hepatitis C virus. *Liver Int*. 2020;40(8):1832–1840.
11 Grebely J, Applegate TL, Cunningham P, Feld JJ. Hepatitis C point-of-care diagnostics: in search of a single visit diagnosis. *Expert Rev Mol Diagn*. 2017;17(12):1109–1115.
12 Bajis S, Maher L, Treloar C, et al. Acceptability and preferences of point-of-care finger-stick whole-blood and venepuncture hepatitis C virus testing among people who inject drugs in Australia. *Int J Drug Policy*. 2018;61:23–30.
13 Bottero J, Boyd A, Gozlan J, et al. Simultaneous human immunodeficiency virus-hepatitis B-hepatitis C point-of-care tests improve outcomes in linkage-to-care: results of a randomized control trial in persons without healthcare coverage. *Open Forum Infect Dis*. 2015;2(4). https://doi.org/10.1093/ofid/ofv162.
14 Jewett A, Al-Tayyib AA, Ginnett L, Smith BD. Successful integration of hepatitis C virus point-of-care tests into the Denver metro health clinic. *AIDS Res Treat*. 2013. https://doi.org/10.1155/2013/528904.
15 Latham NH, Pedrana A, Doyle JS, et al. Community-based, point-of-care hepatitis C testing: perspectives and preferences of people who inject drugs. *J Viral Hepat*. 2019;26(7):919–922.
16 Alimohammadi A, Holeksa J, Parsons R, et al. Diagnosis and treatment of hepatitis C virus infection: a tool for engagement with people who inject drugs in Vancouver's Downtown Eastside. *Can Liver J*. 2018;1(2):14–33.
17 Broad J, Mason K, Guyton M, Lettner B, Matelski J, Powis J. Peer outreach point-of-care testing as a bridge to hepatitis C care for people who inject drugs in Toronto, Canada. *Int J Drug Policy*. 2020;80. https://doi.org/10.1016/j.drugpo.2020.102755.
18 Potier C, Laprevote V, Dubois-Arber F, Cottencin O, Rolland B. Supervised injection services: what has been demonstrated? A systematic literature review. *Drug Alcohol Depend*. 2014;145:48–68.
19 Ontario HIV Treatment Network. Rapid Response Service. A review of structural, process, and outcome measures for supervised consumption services. https://www.ohtn.on.ca/wp-content/uploads/2021/07/RR157_SCS-measures.pdf; 2021. Accessed June 20, 2022.
20 Belackova V, Salmon AM, Schatz E, Jauncey M. Drug consumption rooms (DCRs) as a setting to address hepatitis C - findings from an international online survey. *Hepatol Med Policy*. 2018;3(9). https://doi.org/10.1186/s41124-018-0035-6.
21 Scheim AI, Sniderman R, Wang R, et al. The Ontario integrated supervised injection services cohort study of people who inject drugs in Toronto, Canada (OiSIS-Toronto): cohort profile. *J Urban Health*. 2021;98(4):538–550.
22 Mason K, Dodd Z, Guyton M, et al. Understanding real-world adherence in the directly acting antiviral era: a prospective evaluation of adherence among people with a history of drug use at a community-based program in Toronto, Canada. *Int J Drug Policy*. 2017;47:202–208.
23 Lamoury FMJ, Bajis S, Hajarizadeh B, et al. Evaluation of the Xpert HCV viral load finger-stick point-of-care assay. *J Infect Dis*. 2018;217(12):1889–1896.

24 Minoyan N, Artenie AA, Zang G, Jutras-Aswad D, Turcotte ME, Bruneau J. Harm reduction coverage and hepatitis C incidence: findings from a cohort of people who inject drugs. *Am J Prev Med*. 2020;58(6):845–853.
25 Esmaeili A, Mirzazadeh A, Carter GM, et al. Higher incidence of HCV in females compared to males who inject drugs: a systematic review and meta-analysis. *J Viral Hepat*. 2017;24(2):117–127.
26 Public Health Agency of Canada. Report on hepatitis B and C in Canada: 2019. https://www.canada.ca/en/public-health/services/publications/diseases-conditions/report-hepatitis-b-c-canada-2019.html; 2022. Accessed August 12, 2022.
27 Falade-Nwulia O, Irvin R, Merkow A, et al. Barriers and facilitators of hepatitis C treatment uptake among people who inject drugs enrolled in opioid treatment programs in Baltimore. *J Subst Abuse Treat*. 2019;100:45–51.
28 Howell J, Traeger MW, Williams B, et al. The impact of point-of-care hepatitis C testing in needle and syringe exchange programs on linkage to care and treatment uptake among people who inject drugs: an Australian pilot study. *J Viral Hepat*. 2022;29(5):375–384.
29 Greenwald ZR, Bouck Z, McLean E, et al. Integrated supervised consumption services and hepatitis C testing and treatment among people who inject drugs in Toronto, Canada: a cross-sectional analysis. *J Viral Hepat*. 2023;30(2):160–171.
30 Oru E, Trickey A, Shirali R, Kanters S, Easterbrook P. Decentralisation, integration, and task-shifting in hepatitis C virus infection testing and treatment: a global systematic review and meta-analysis. *Lancet Global Health*. 2021;9(4):e431–e445. https://doi.org/10.1016/S2214-109X(20)30505-2.
31 Crawford S, Bath N. Peer support models for people with a history of injecting drug use undertaking assessment and treatment for hepatitis C virus infection. *Clin Infect Dis*. 2013;57(Suppl 2):S75–S79.
32 Grebely J, Dore GJ, Morin S, Rockstroh JK, Klein MB. Elimination of HCV as a public health concern among people who inject drugs by 2030 - what will it take to get there? *J Int AIDS Soc*. 2017;20(1):22146.
33 Ontario HIV Treatment Network. Rapid Response Service. Effectiveness of and best practices for using contingency management and incentives in hepatitis C infection among people who use drugs. https://www.ohtn.on.ca/wp-content/uploads/2021/07/RR160_HCV-incentives.pdf; 2021. Accessed June 20, 2022.