

Health impacts of a scale-up of supervised injection services in a Canadian setting: an interrupted time series analysis

Mary Clare Kennedy^{1,2}  | Kanna Hayashi^{1,3}  | M-J Milloy^{1,2}  |
Miranda Compton⁴ | Thomas Kerr^{1,2}

¹British Columbia Centre on Substance Use, Vancouver, BC, Canada

²Department of Medicine, University of British Columbia, St Paul's Hospital, Vancouver, BC, Canada

³Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada

⁴Vancouver Coastal Health, Vancouver, BC, Canada

Correspondence

Mary Clare Kennedy PhD, Research Scientist, British Columbia Centre on Substance Use, Postdoctoral Research Fellow, Department of Medicine, University of British Columbia, 400-1045 Howe Street, Vancouver, BC, Canada V6Z 2A9.

Email: bccsu-mck@bccsu.ubc.ca

Funding information

Canadian Institutes of Health Research, Grant/Award Numbers: 20R74326, MSH-141971; Canopy Growth; Michael Smith Foundation for Health Research; National Institute on Drug Abuse, Grant/Award Number: U01DA021525; National Institutes of Health, Grant/Award Number: U01DA038886; NG Biomed Ltd; St. Paul's Foundation

Abstract

Background and Aims: In response to a dramatic rise in overdose deaths due to injection drug use, there was a rapid scale-up of low-threshold supervised injection services (SIS), termed 'overdose prevention sites' (OPS), in Vancouver, Canada in December 2016. We measured the potential impact of this intervention on SIS use and related health outcomes among people who inject drugs (PWID).

Design: Segmented regression analyses of interrupted time series data from two community-recruited prospective cohorts of PWID from January 2015 to November 2018 were used to measure the impact of the OPS scale-up on changes in SIS use, public injection, syringe sharing and addiction treatment participation, controlling for pre-existing secular trends.

Setting: Vancouver, Canada.

Participants: Of 745 PWID, 292 (39.7%) were women, 441 (59.6%) self-reported white ancestry and the median age was 47 years (interquartile range = 38, 53) at baseline.

Measurements: Immediate (i.e. step level) and gradual (i.e. slope) changes in the monthly proportion of participants who self-reported past 6-month SIS use, public injection, syringe sharing and participation in any form of addiction treatment.

Findings: PostOPS expansion, the monthly prevalence of SIS use immediately increased by an estimated 6.4% [95% confidence interval (CI) = 1.7, 11.2] and subsequently further increased by an estimated 0.7% (95% CI = 0.3, 1.1) per month. The monthly prevalence of addiction treatment participation immediately increased by an estimated 4.5% (95% CI = 0.5, 8.5) following the OPS expansion, while public injection and syringe sharing were estimated to immediately decrease by 5.5% (95% CI = 0.9, 10.0) and 2.5% (95% CI = 0.5, 4.6), respectively. Findings were inconclusive as to whether or not an association was present between the intervention and subsequent gradual changes in public injection, syringe sharing and addiction treatment participation.

Conclusions: Scaling-up overdose prevention sites in Vancouver, Canada in December 2016 was associated with immediate and continued gradual increases in supervised injection service engagement and immediate increases in related health benefits.

KEYWORDS

Canada, harm reduction, health policy, injection drug use, interrupted time series, overdose prevention, quasi-experimental, supervised consumption services, supervised injection services

INTRODUCTION

Driven largely by the increased presence of illicitly-manufactured fentanyl and its analogues in unregulated drug supplies, Canada and the United States continue to experience an unprecedented overdose crisis [1,2]. The Canadian province of British Columbia (BC) is among the jurisdictions that have been particularly impacted [3]. In 2016, the annual overdose death rate in BC was 20.4 per 100 000 population, a rate 84% higher than 2015 [3]. This marked increase in overdose deaths prompted the provincial government to declare a public health emergency in April 2016 [4].

In response, a number of overdose prevention and response interventions have since been implemented in BC [5]. Of note, the BC Minister of Health enacted a ministerial order on 8 December 2016 that directed regional health authorities to immediately implement low-threshold supervised injection services (SIS), known as overdose prevention sites (OPS), which provide spaces in which individuals can consume illicit drugs with sterile equipment while being monitored by trained staff [6,7]. Within 2 weeks, approximately 20 OPS were implemented into existing community services or temporary sites across the province [7,8]. Of these, five OPS opened in Vancouver's Downtown Eastside neighbourhood, a North American epicentre of the overdose crisis where approximately 5000 people who inject drugs (PWID) reside [8,9]. In addition to these community-based OPS, approximately 25 housing-based OPS were rapidly integrated into non-profit organization-operated housing buildings in Vancouver, beginning in December 2016 [10–12]. There have been no overdose deaths within any OPS to date [11].

OPS were intended to complement Vancouver's well-developed system of harm reduction programming, including Insite, North America's first government-sanctioned SIS [13]. Since 2003, Insite has been operating in the Downtown Eastside under an exemption from federal drug laws [13], and accommodated an average of 722 daily client visits in 2015 [14]. Insite was the only government-sanctioned SIS in Vancouver until January 2016, when a small injection room within an HIV-focused care facility (the Dr Peter Centre) was granted a legal exemption to operate after operating for approximately 14 years without such an exemption [13,15]. The Dr Peter Centre SIS exclusively provides services to people with HIV/AIDS and accommodates approximately 200 client visits per month [16].

In contrast with Insite and the Dr Peter Centre, OPS operate outside federal approval processes and regulations [7,13]. As such, OPS are often simpler in physical layout and also tend to be less medicalized in that these are typically staffed by trained peers [i.e. people who use(d) drugs] rather than health professionals and offer few to no clinical services [13,17,18]. Moreover, OPS are generally considered to be lower-barrier services because these are less regimented and often accommodate drug use practices (e.g. assisted injection, drug sharing/splitting) that traditionally have not been permitted under regulations that govern federally sanctioned SIS [7,19].

To date, scientific evaluations of SIS operating in Canada and international settings have provided consistent evidence to suggest that SIS are effective in meeting their primary objectives [20–22].

For example, past studies have identified associations between the establishment of SIS and reductions in local rates of overdose-related deaths, ambulance attendances and emergency department presentations [23–26]. Additionally, the establishment of SIS has been associated with neighbourhood-level declines in public injection [23,27–29], an injection practice that has been found to increase risk of harms such as overdose and infectious disease transmission [30–33]. SIS use has also been associated with reduced likelihood of engaging in injection-related risk behaviours among PWID, including used syringe sharing [34–36], a practice that remains a major driver of infectious disease transmission among PWID [37,38]. Further, several studies have found that SIS use is associated with increased engagement with addiction treatment among PWID [39–43].

However, most existing studies evaluating SIS have relied upon non-experimental study designs [20–22]. Quasi-experimental evaluations of the health impacts of SIS are scarce to date, despite calls for more of such studies to strengthen the causal evidence base for SIS given that randomized controlled trials have been deemed unethical and ill-suited for evaluating SIS [44,45]. Further, most existing studies of SIS have focused on highly-regulated, medicalized SIS staffed by health professionals, and rigorous quantitative evaluations of lower-threshold, peer-run SIS such as OPS are lacking [20]. We therefore employed an interrupted time series (ITS) approach to evaluate the potential impact of the rapid expansion of OPS in Vancouver on patterns of SIS use, public injection, syringe sharing and participation in addiction treatment using data from two linked prospective cohorts of PWID. Given that SIS are currently being scaled-up or considered in a number of settings in Canada and internationally [46–48], this study may provide useful information to support evidence-informed decision-making concerning the implementation and ongoing operation of such services.

METHODS

Data were drawn from two ongoing prospective cohort studies in Vancouver: the Vancouver Injection Drug Users Study (VIDUS) and the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS). Detailed descriptions of the cohorts have been published previously [49,50]. In brief, participants have been recruited through community-based methods since May 1996. VIDUS enrolls HIV-seronegative adults (aged ≥ 18 years) who have injected illicit drugs in the month preceding enrolment. ACCESS enrolls HIV-seropositive adults who have used illicit drugs other than or in addition to cannabis in the month preceding enrolment. The studies employ harmonized data collection and follow-up procedures to allow for combined analyses. Specifically, at baseline and semi-annually thereafter, participants complete an interviewer-administered questionnaire and provide blood samples for serological testing. The questionnaire elicits information regarding socio-demographic characteristics, behavioural patterns and social-structural exposures. Participants receive a CAD \$40 honorarium at each study visit. The cohorts have received

approval from the University of British Columbia/Providence Health Care Research Ethics Board.

For the present study, we included participants with at least one study visit in both the pre- (1 January 2015 to 30 November 2016) and post-intervention periods (1 January 2017 to 30 November 2018) in which they reported past 6-month injection drug use.

We examined four outcomes in the present study, each of which was assessed as a proportion of study participants in a given calendar month who reported having engaged in the activity of interest during the previous 6 months (yes versus no). These outcomes included SIS use, syringe sharing, participation in addiction treatment and public injection. These outcomes were selected to align with the primary objectives of SIS of attracting higher-risk subpopulations of PWID, reducing risk of drug-related harms, facilitating connections to addiction treatment and other services and reducing public order concerns associated with injection drug use [20,51]. Variable definitions were consistent with those used in our previous work [35,42,52] and are described in detail in Figs 1–4.

To examine the impact of the OPS expansion on each of the four outcomes of interest we used ITS analysis, which allows for control of pre-existing secular trends in time series data by comparing observed outcomes during a period after a given intervention with those

expected had the intervention not occurred [53–55]. The study period was divided into pre- and post-intervention segments, both of which were 23 months in duration. The month in which the OPS expansion primarily occurred (December 2016) was considered a transition period and was therefore excluded from the analyses. Thus, the final data set included a total of 46 time points (i.e. months of data), with an average of 92 (range = 63, 125) observations per month.

We conducted segmented regression analyses of these time series data to assess the impact of the OPS expansion on immediate (i.e. level) and gradual (i.e. slope) changes in the monthly prevalence of the four respective outcomes of interest in the post-intervention period compared to the pre-intervention period, controlling for pre-existing secular trends. The models included terms for the baseline level of the outcome at the beginning of the study period, trend in the outcome in the pre-intervention period (coded as 1... 47), level change in the outcome immediately after the intervention (coded as 1 after versus 0 before) and trend in the outcome in the post-intervention period (coded as 0 pre-intervention and 1... 23 in the months post-intervention). We used generalized least squares (GLS) models including autocorrelation terms for moving average or autoregressive processes, where appropriate, that were assessed independently for each outcome. Lag terms were determined using

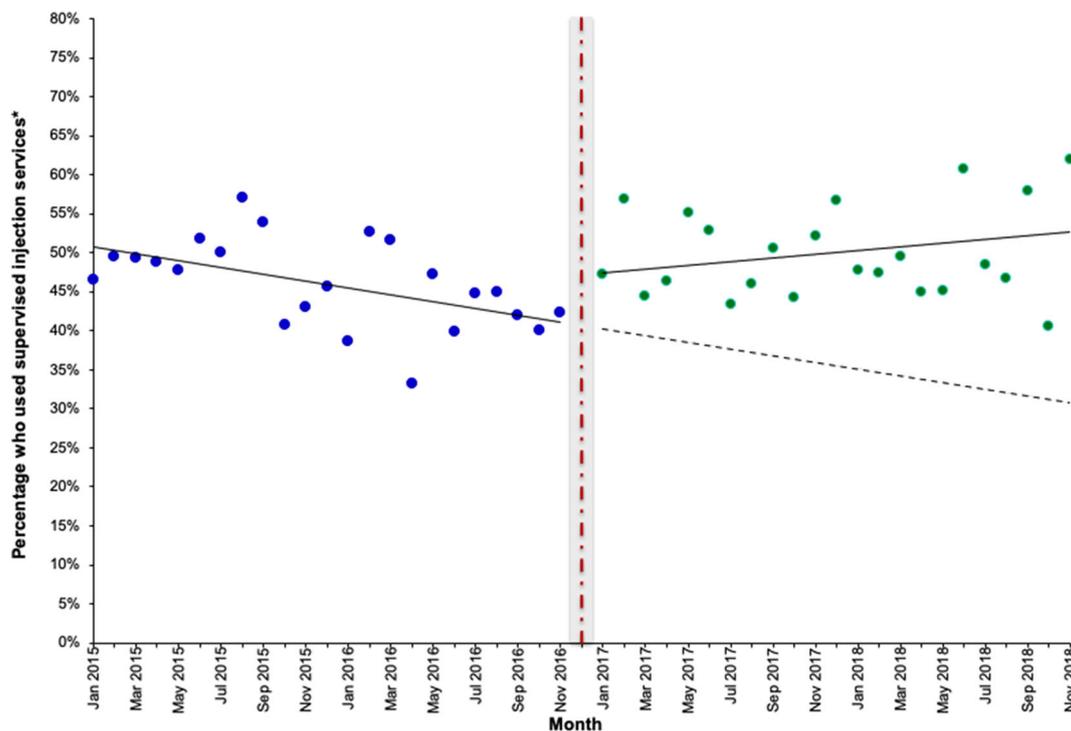


FIGURE 1 Supervised injection service use* among people who inject drugs in Vancouver, Canada, January 2015–December 2018 (*refers to past 6 months). Dashed red line indicates the month when the overdose prevention site (OPS) expansion primarily occurred (December 2016). Blue and green dots indicate the observed monthly prevalence of recent supervised injection services (SIS) use before and after the OPS expansion, respectively. Recent SIS use was defined in response to the questionnaire item: ‘In the last 6 months, have you fixed at any of the following supervised injection facilities?’. Response options included a list of currently operating federally sanctioned SIS and OPS, as well as other (specify). Participants could select more than one response. SIS use was defined as responding ‘yes’ to any response option. Solid black lines indicate the estimated monthly prevalence of recent SIS use in the pre- and post-OPS expansion periods. Dashed black line indicates the estimated monthly prevalence of recent SIS use if the OPS expansion did not occur and pre-existing trends in SIS use had continued unchanged

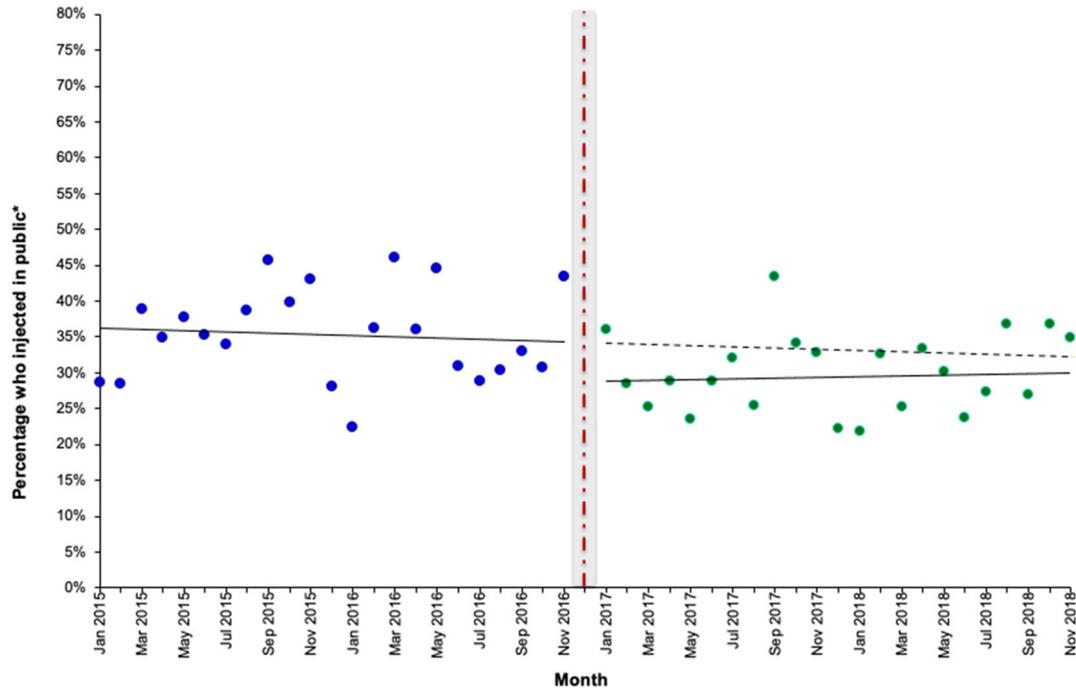


FIGURE 2 Public injection* among people who inject drugs in Vancouver, Canada, January 2015–December 2018 (*refers to past 6 months). Dashed red line indicates the month when the overdose prevention site (OPS) expansion primarily occurred (December 2016). Blue and green dots indicate the observed monthly prevalence of recent public injection before and after the OPS expansion, respectively. Public injection was defined in response to the questionnaire item: ‘In the last 6 months, how often did you inject in public places?’ (always, usually, sometimes, occasionally versus never). Solid black lines indicate the estimated monthly prevalence of recent public injection in the pre- and post-OPS expansion periods. Dashed black line indicates the estimated monthly prevalence of recent public injection if the OPS expansion did not occur and pre-existing trends in public injection had continued unchanged

autocorrelation function (ACF) and partial autocorrelation function (PACF) plots [56]. We assessed seasonality by including a season variable (January–March; April–June; July–September; and October–December) in models for the respective outcomes [55,57], but observed no statistically significant associations; therefore, we did not include the season variable in any of the final models. The linear pre-intervention trends assumption was assessed and confirmed using residuals plots [53]. We calculated absolute and relative differences to compare the estimated prevalence of each outcome 6 months after the OPS expansion with the estimated prevalence if the intervention had not occurred and pre-existing trends had continued unchanged [58].

As a sensitivity analysis, we re-ran the ITS analyses with the intervention transition month (i.e. December 2016) included and considered as the first month of the post-intervention period. All analyses were performed using SAS version 9.4 (SAS, Cary, NC, USA). All *P*-values are two-sided. This analysis plan was not pre-registered and therefore the results should be considered exploratory.

RESULTS

Of 745 PWID included in the study, 292 (39.7%) were women and the median age was 47 years [interquartile range (IQR) = 38, 53] at

baseline. Participants contributed a median of six study visits (IQR = 4, 7) each. Table 1 presents baseline characteristics of study participants. Table 2 presents the results of the segmented regression analyses assessing the impact of the OPS expansion on immediate and gradual changes in the monthly prevalence of the four respective outcomes of interest.

Supervised injection service use

Figure 1 presents the monthly proportion of PWID who reported recent SIS use during the study period. As shown, the estimated prevalence of SIS use at the beginning of the study period was 50.8% [95% confidence interval (CI) = 46.6, 55.0%], which subsequently decreased to 41.4% (95% CI = 37.3, 45.5%) in the month prior to the OPS expansion. Post OPS expansion, the monthly prevalence immediately increased by an estimated 6.4% (95% CI = 1.7, 11.2) and subsequently further increased by an estimated 0.7% per month (95% CI = 0.3, 1.1%). In June 2017, 6 months after the OPS expansion, the estimated prevalence of SIS use was 49.0% (95% CI = 46.3, 51.8%), 10.6% (95% CI = 3.8, 17.3%) higher than the estimated prevalence if the OPS expansion had not occurred and pre-existing trends in SIS use had continued unchanged, corresponding to a relative intervention effect of 27.5% (95% CI = 5.9, 49.1%).

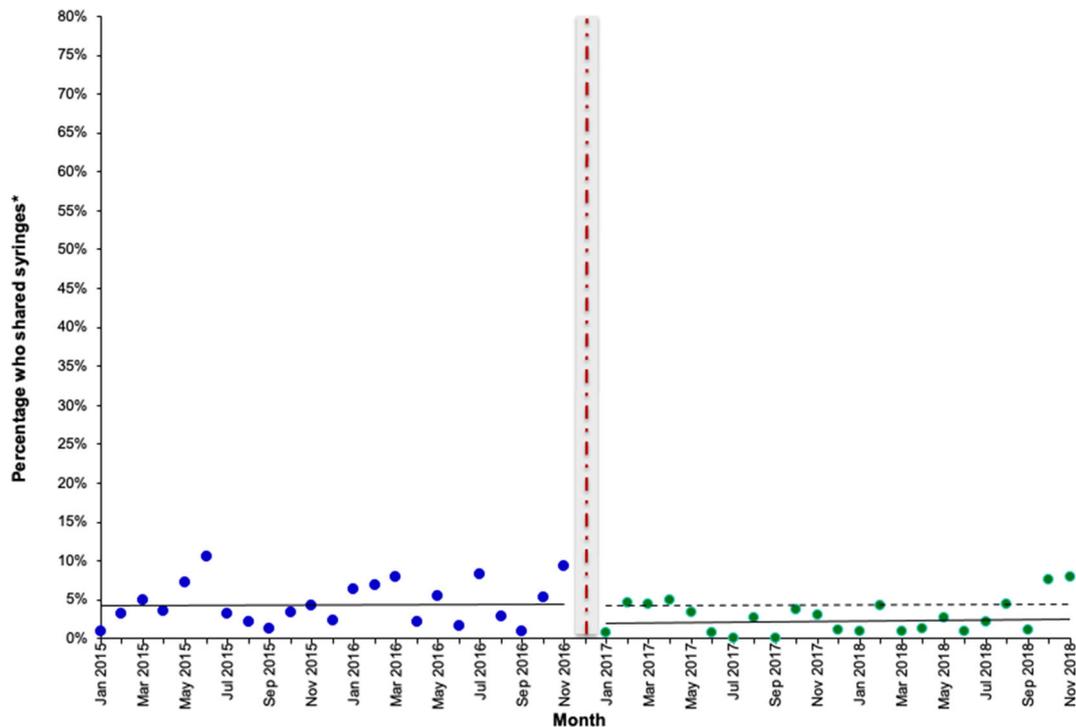


FIGURE 3 Syringe sharing* among people who inject drugs in Vancouver, Canada, January 2015–December 2018 (*refers to past 6 months). Dashed red line indicates the month when the overdose prevention site (OPS) expansion primarily occurred (December 2016). Blue and green dots indicate the observed monthly prevalence of recent syringe sharing before and after the OPS expansion, respectively. Syringe sharing was defined as responding ‘yes’ to either of the following questionnaire items: ‘In the last 6 months, have you lent your used rig to someone else?’ or ‘In the last 6 months, have you fixed with a rig that had already been used by someone else?’. Solid black lines indicate the estimated monthly prevalence of recent syringe sharing in the pre- and post-OPS expansion periods. Dashed black line indicates the estimated monthly prevalence of recent syringe sharing if the OPS expansion did not occur and pre-existing trends in syringe sharing had continued unchanged

Public injection

Figure 2 presents the monthly proportion of PWID who reported recent public injection during the study period. As shown, the estimated prevalence of public injection at the beginning of the study period was 36.2% (95% CI = 32.1, 40.3%). The findings were inconclusive as to whether or not there was a subsequent change in trend before the OPS expansion. Post OPS expansion, the monthly prevalence immediately decreased by 5.5% (95% CI = -10.0, -0.9%). The findings were inconclusive as to whether or not there was a subsequent change in trend thereafter. Six months after the OPS expansion, the estimated prevalence of public injection was 29.4% (95% CI = 26.8, 31.9%), 5.9% (95% CI = -11.7, -0.1%) lower than the estimated prevalence if the OPS expansion had not occurred and pre-existing trends in public injection had continued unchanged, corresponding to a relative intervention effect of -16.8% (95% CI = -32.2, -1.4%).

Syringe sharing

Figure 3 presents the monthly proportion of PWID who reported recent syringe sharing during the study period. As shown, the

estimated prevalence of syringe sharing was 4.4% (95% CI = 2.8, 6.0%) at the beginning of the study period. The findings were inconclusive as to whether or not there was a subsequent change in trend before the OPS expansion. Post OPS expansion, the monthly prevalence immediately decreased by 2.5% (95% CI = -4.6, -0.5%). The findings were inconclusive as to whether or not there was a subsequent change in trend thereafter. Six months after the OPS expansion, the estimated prevalence of syringe sharing was 2.2% (95% CI = 1.2, 3.3%), 3.1% (95% CI = -5.6, -0.7%) lower than the estimated prevalence if the OPS expansion had not occurred and pre-existing trends in syringe sharing had continued unchanged, corresponding to a relative intervention effect of -58.1% (95% CI = -83.8, -32.3%).

Participation in addiction treatment

Figure 4 presents the monthly proportion of PWID who reported recent participation in addiction treatment during the study period. As shown, the estimated prevalence of addiction treatment participation was 64.6% (95% CI = 60.3, 68.8%) at the beginning of the study period. The findings were inconclusive as to whether or not there was a subsequent change in trend before the OPS expansion. Post OPS expansion, the monthly prevalence immediately increased by 4.5%

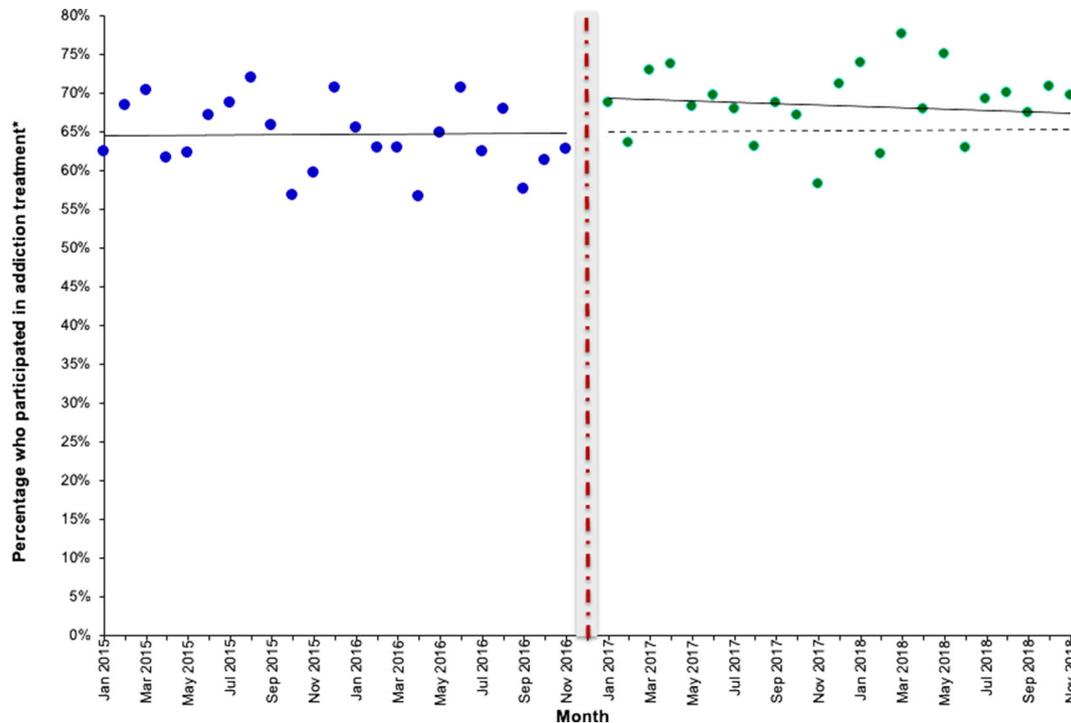


FIGURE 4 Participation in addiction treatment* among people who inject drugs in Vancouver, Canada, January 2015–December 2018 (*refers to past 6 months). Dashed red line indicates the month when the overdose prevention site (OPS) expansion primarily occurred (December 2016). Blue and green dots indicate the observed monthly prevalence of recent participation in addiction treatment before and after the OPS expansion, respectively. Participation in addiction treatment was defined as responding ‘yes’ to any of the following questionnaire items: (1) ‘In the last 6 months, have you accessed detox or daytox services for your alcohol or drug use?’; (2) ‘In the last 6 months, have you received any treatment for your alcohol or drug use in a residential programme (i.e. where you lived inside a treatment facility or residence, such as a residential treatment centre or recovery house, while receiving treatment)?’; (3) ‘In the last 6 months, did you receive any kind of treatment (not including medications) in a community setting?’; or (4) ‘In the last 6 months, have you received any medications (such as Methadose or Suboxone) for the treatment of your drug use?’. Solid black lines indicate the estimated monthly prevalence of recent participation in addiction treatment in the pre- and post-OPS expansion periods. Dashed black line indicates the estimated monthly prevalence of recent participation in addiction treatment if the OPS expansion did not occur and pre-existing trends in participation in addiction treatment had continued unchanged

(95% CI = 0.5, 8.5%). The findings were inconclusive as to whether or not there was a subsequent change in trend thereafter. Six months after the OPS expansion, the estimated prevalence of addiction treatment participation was 68.6% (95% CI = 66.0, 71.2%), 7.1% (95% CI = 0.1, 13.4%) higher than the estimated prevalence if the OPS expansion had not occurred and pre-existing trends in treatment participation had continued unchanged, corresponding to a relative intervention effect of 11.5% (95% CI = 0.2, 22.7%).

Our sensitivity analysis with the transition month of December 2016 included yielded similar results for all outcomes examined (data not shown).

DISCUSSION

In this ITS study of data from a community-recruited cohort of PWID in Vancouver, we found that the monthly prevalence of recent SIS use increased immediately after a rapid expansion of OPS in December 2016 and continued to gradually increase in the 22 months thereafter. The monthly prevalence of recent participation in addiction treatment

immediately increased after the OPS expansion, while the monthly prevalence of recent public injection and syringe sharing immediately decreased after this intervention. Our findings were inconclusive as to whether or not there were subsequent gradual changes in addiction treatment participation, public injection or syringe sharing thereafter.

To our knowledge, this study is the first to employ a rigorous quasi-experimental design to estimate the impacts of a rapid low-threshold SIS expansion on SIS engagement, injection-related risk behaviours and addiction treatment participation among PWID. Our finding that SIS use increased immediately after the OPS expansion and continued to increase in the months thereafter suggests that this intervention helped to address gaps in the coverage of existing SIS programming in this setting. Specifically, scaling-up OPS may have helped to address the unmet need for SIS among local PWID that has been documented previously [59–61]. Additionally, the opening of OPS in various locations may have helped to mitigate geospatial barriers to SIS engagement [59,62]. The low-threshold models of OPS may also be more responsive to the service needs and preferences of some PWID, particularly given that OPS accommodate some drug use practices that are not permitted at Insite (e.g. assisted injection)

TABLE 1 Baseline characteristics of 745 people who inject drugs in Vancouver, Canada

Characteristic	Frequency	Proportion (%)
Gender (trans inclusive)		
Men	440	59.8%
Women	292	39.7%
Other (e.g. non-binary, two-spirit)	4	0.5%
Ancestry		
White	441	59.6%
Non-white	299	40.4%
Downtown Eastside residence ^a		
Yes	479	64.3%
No	266	35.7%
Employment ^a		
Yes	182	24.5%
No	562	75.5%
Homeless ^a		
Yes	145	19.5%
No	600	80.5%
HIV seropositive		
Yes	289	38.8%
No	456	61.2%
Heroin injection ^a		
≥ Daily	212	28.5%
< Daily	533	71.5%
Cocaine injection ^a		
≥ Daily	47	6.3%
< Daily	698	93.7%
Crystal methamphetamine injection ^a		
≥ Daily	103	13.8%
< Daily	642	86.2%
Require help injecting ^a		
Yes	187	25.1%
No	558	74.9%
Non-fatal overdose ^a		
Yes	79	10.6%
No	665	89.4%
Sex work involvement ^a		
Yes	126	16.9%
No	619	83.1%
Incarceration ^a		
Yes	44	5.9%
No	699	94.1%
Characteristic	Median	IQR
Age (years)	47	38–53

Note: not all cells add up to 745 due to missing values.

^aRefers to activities or experiences in the 6-month period prior to a baseline interview.

IQR = interquartile range.

[7,19,63–66]. Additionally, some PWID may be more receptive to OPS given that these are less medicalized services [7,17,18,63,64]. For example, recent ethnographic research has described how peer involvement as staff in OPS may foster service engagement among PWID by enhancing client feelings of comfort and safety [17].

We should note that SIS use was observed to trend downwards before the OPS scale-up. The underlying explanations for this finding are unclear. However, this could be partly explained by some PWID transitioning to using newly established unsanctioned SIS near the end of the pre-intervention period [13,67], but not regarding or reporting this as official SIS use. Although it is unlikely that this would fully account for the observed declining trend, it is possible that this contributed to an overestimate of the level change in the prevalence of SIS use immediately after the OPS expansion.

We also observed that the proportion of PWID reporting recent public injection immediately decreased after the OPS scale-up. This finding is consistent with past research demonstrating that SIS effectively attract PWID who would otherwise inject in public [34,52,68–70], as well as studies documenting declines in public injection after the establishment of SIS [23,27–29]. For example, a previous study reported a significant reduction in the number of PWID injecting in public and publicly discarded syringes in the area surrounding Insite after the facility opened [27]. However, a subsequent study found that PWID who reported waiting times as a barrier to accessing Insite had greater odds of injecting in public [61]. Thus, by addressing an unmet demand for SIS, while also reducing geographic and programmatic barriers to engagement with such services, the OPS expansion likely helped to reduce reliance on public settings for injections among PWID. In the context of current overdose crisis, these findings are notable given that public injection has been associated with an elevated risk of overdose-related harms [30,33] and that SIS have previously been found to mitigate such harms [23–26].

Our finding that the prevalence of syringe sharing immediately decreased after the OPS expansion builds upon past non-experimental studies identifying associations between SIS use and decreased syringe sharing [34–36]. This includes a previous meta-analysis of three studies undertaken in Vancouver and Spain, which estimated that SIS use was associated with a 69% reduction in the odds of sharing syringes among PWID [71]. The OPS expansion likely primarily contributed to decreased syringe sharing by increasing the distribution of sterile injection equipment to PWID for both on- and off-site use and by providing social and environmental conditions that foster the adoption of harm reduction practices [72,73].

Previous studies have documented associations between SIS use and enrolment in addiction treatment [39–43]. The present study extends this work in finding that the proportion of PWID enrolled in addiction treatment in this setting immediately increased following the OPS expansion. The mechanisms through which these newly established services may have promoted treatment uptake are somewhat difficult to discern with certainty, particularly given that OPS often do not employ health professionals who can provide formal referrals to treatment [7,13]. Further, although some OPS have

TABLE 2 Segmented regression analyses assessing the impact of the OPS scale-up on immediate and gradual changes in supervised injection service use, public injection, syringe sharing and participation in addiction treatment

Supervised injection service (SIS) use ^a			
	Coefficient	95% CI	P-value
Intercept (β_0)	51.1	46.4, 55.8	< 0.001
Time (month) (β_1)	-0.4	-0.7, -0.2	0.001
Level change after OPS scale-up (β_2)	6.4	1.7, 11.2	0.008
Time (month) after OPS scale-up (β_3)	0.7	0.3, 1.1	0.001
Public injection ^b			
	Coefficient	95% CI	P-value
Intercept (β_0)	36.3	32.0, 40.6	< 0.001
Time (month) (β_1)	-0.1	-0.3, 0.2	0.515
Level change after OPS scale-up (β_2)	-5.5	-10.0, -0.9	0.018
Time (month) after OPS scale-up (β_3)	0.1	-0.3, 0.5	0.489
Syringe sharing ^b			
	Coefficient	95% CI	P-value
Intercept (β_0)	4.4	2.7, 6.0	< 0.001
Time (month) (β_1)	0.1	-0.0, 0.2	0.851
Level change after OPS scale-up (β_2)	-2.5	-4.6, -0.5	0.015
Time (month) after OPS scale-up (β_3)	0.0	-0.1, 0.2	0.777
Addiction treatment participation ^b			
	Coefficient	95% CI	P-value
Intercept (β_0)	64.6	60.2, 68.9	< 0.001
Time (month) (β_1)	0.0	-0.2, 0.2	0.885
Level change after OPS scale-up (β_2)	4.5	0.5, 8.5	0.028
Time (month) after OPS scale-up (β_3)	-0.1	-0.5, 0.3	0.568

^aWe used a generalized least squares model with an autoregressive lag term of 3 to assess trends in supervised injection service (SIS) use.

^bWe used a generalized least squares model with an autoregressive lag term of 2 to assess trends in public injection, syringe sharing and addiction treatment participation, respectively. OPS = overdose prevention site; CI = confidence interval.

recently begun providing co-located treatment services, these services were not offered in the early stages of implementation [63]. However, recent ethnographic research has described how peer workers at OPS often have expertise and experiential knowledge that uniquely positions these individuals to promote client awareness and uptake of addiction treatment services [17]. The low-barrier service models of OPS may have further increased opportunities to enhance linkages to treatment by engaging subpopulations of PWID who are difficult to reach with conventional health services [63].

Collectively, our findings suggest that the rapid scale-up of OPS was an effective strategy to extend the reach and benefits of existing SIS programming in this setting. We employed an ITS approach, which is among the strongest quasi-experimental research designs for causal inference, particularly due to its ability to control for pre-existing secular trends [53,54,74]. Moreover, this design addresses other important threats to validity, including selection bias and unmeasured confounding due to between-group differences [75]. However, because we did not use an external control group, we cannot exclude the possibility that the observed intervention effects were due to other events that co-occurred with the OPS scale-up [54,75]. In

particular, since the declaration of the public health emergency in April 2016, there have been a number of efforts to expand access to addiction treatment in BC, which could have contributed to the observed increase in addiction treatment participation and potentially the other observed changes in evaluated outcomes [5,26,76]. However, these efforts were not concentrated around the time of the OPS scale-up, and thus we would have expected such efforts to translate into gradual changes rather than the abrupt, sharp post-intervention changes that we observed for all outcomes examined. We can think of no other alternative competing events that could potentially explain our findings.

Given our robust study design and our finding that the OPS expansion was associated with changes in drug use practices and service engagement that may mitigate risk of overdose-related harms and other adverse health outcomes among PWID, we believe that our study provides strong evidence to support the scale-up of SIS as part of responses to the overdose crisis and other health concerns related to illicit drug use. The wider adoption of low-threshold, less medicalized, peer-run service models in particular should be considered in light of compelling scientific evidence presented herein and elsewhere

demonstrating the acceptability and effectiveness of this novel service delivery approach [7,17–19,26,63,64,77]. Our findings also reinforce calls for enhanced resources for peer staff to support the sustainability of such programming [17,78].

This study has several limitations. First, data were drawn from non-random cohorts and therefore our findings might not be generalizable to PWID in Vancouver or elsewhere. This study also relied upon self-reported data, and therefore our findings are susceptible to reporting biases. Another limitation is that an average of only 92 observations per month were collected, which might account for the large variability over time in the outcome measures. A further limitation is that we were unable to account for individual-level clustering of observations in our analyses. Additionally, as mentioned above, we did not use an external control group, and thus it is possible that our findings are explained by confounding due to co-occurring events [54,75]. We were also unable to assess the direct impact of the OPS expansion on overdose-related harms due to the potential for time-varying confounding if the concentration of synthetic opioids in the unregulated drug supply had changed around the time of the intervention [75,79]. Further, we did not have sufficient statistical power to examine overdose deaths due to low monthly counts [80]. However, it is notable that we found that the OPS expansion was linked to decreased prevalence of risk factors (i.e. public injection) and increased prevalence of protective factors (i.e. utilization of SIS and addiction treatment) for overdose-related harms [24,30,32,33,81].

In this study, we observed both immediate and continued gradual increases in SIS use among PWID after a rapid scale-up of OPS in Vancouver, as well as immediate increases in addiction treatment participation and immediate decreases in public injection and syringe sharing.

DECLARATION OF INTERESTS

M.-J.M.'s institution has received an unstructured gift to support his research from NG Biomed Ltd, an applicant to the Canadian federal government for a licence to produce medical cannabis. He is the Canopy Growth Professor of cannabis science at the University of British Columbia, a position created by an unstructured gift to the university from Canopy Growth, a licenced producer of cannabis and the Government of British Columbia's Ministry of Mental Health and Addictions. K.H. has an unpaid appointment as a member of the Scientific and Research Staff at the Department of Family and Community Practice of the Vancouver Coastal Health (VCH) Authority, which runs supervised injection services that were examined in the present study. M.C. is Executive Director of Prevention Services and Public Health at VCH and Regional Program Director of the Regional Addictions Program at VCH. However, neither the health authority nor the aforementioned funders had a role in the study design; collection, analysis and interpretation of data; writing of the paper; or decision to submit for publication. All other authors have declared that they have no competing interests.

ACKNOWLEDGEMENTS

The authors thank the study participants for their contribution to the research, as well as current and past researchers and staff. We

would specifically like to thank Julie Sagram, Ana Prado, Peter Vann, Jennifer Matthews, Cristy Zonneveld and Steve Kain for their research and administrative assistance. The authors also gratefully acknowledge that this research took place on the unceded territories of the *xməθkwəy̓əm* (Musqueam), *Skwxwú7mesh* (Squamish) and *sel̓ilwítulh* (Tsleil-waututh) Nations. We thank Evan Wood for his input on an earlier version of this paper. This study was supported by the US National Institutes of Health (U01DA038886, U01DA021525). M.C.K. is supported by a Canadian Institutes of Health Research (CIHR) Fellowship Award. T.K. is supported by a CIHR Foundation grant (20R74326). K.H. is supported by a CIHR New Investigator Award (MSH-141971), a Michael Smith Foundation for Health Research (MSFHR) Scholar Award and the St Paul's Foundation. M.-J.M. is supported by a CIHR New Investigator Award, a MSFHR Scholar Award and the National Institutes of Drug Abuse (U01DA0251525). His institution has received an unstructured gift to support his research from NG Biomed Ltd, an applicant to the Canadian federal government for a licence to produce medical cannabis. He is the Canopy Growth Professor of cannabis science at the University of British Columbia, a position created by an unstructured gift to the university from Canopy Growth, a licenced producer of cannabis and the Government of British Columbia's Ministry of Mental Health and Addictions.

AUTHOR CONTRIBUTIONS

Mary Clare Kennedy: Conceptualization; formal analysis; methodology; writing-original draft preparation; writing-review & editing. **Kanna Hayashi:** Funding acquisition; investigation; project administration; writing-review & editing. **M-J Milloy:** Funding acquisition; investigation; project administration; writing-review & editing. **Miranda Compton:** writing-review & editing. **Thomas Kerr:** Funding acquisition; investigation; project administration; supervision; writing-review & editing.

ORCID

Mary Clare Kennedy  <https://orcid.org/0000-0003-1186-2151>

Kanna Hayashi  <https://orcid.org/0000-0003-3843-2928>

M-J Milloy  <https://orcid.org/0000-0003-3821-6221>

REFERENCES

1. Special Advisory Committee on the Epidemic of Opioid Overdoses. Opioid-related Harms in Canada [internet]. Ottawa: Public Health Agency of Canada; 2021 Jul [cited 2020, 14 Sep]. Available at: <https://health-infobase.canada.ca/substance-related-harms/opioids>. Accessed 14 Sep 2020.
2. National Institute on Drug Abuse. Overdose Death Rates [internet]. 2020 [cited 2020, 14 Sep]. Available at: <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>. Accessed 14 Sep 2020.
3. BC Coroners Service. Illicit drug overdose deaths in BC (1 January 2010–31 July 2020) [internet]. Burnaby, BC: Office of the Chief Coroner; 2020 [cited 2020, 14 Sep]. Available at: <https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/statistical/illicit-drug.pdf>
4. BC Ministry of Health. Provincial health officer declares public health emergency [internet]. 2016 [cited 2020, 14 Sep]. Available at:

- <https://news.gov.bc.ca/releases/2016HLTH0026-000568>. Accessed 14 Sep 2020.
5. British Columbia Ministry of Mental Health and Addictions. Escalating BC's response to the overdose emergency [internet]. Victoria; 2019 [cited 2020, 14 Sep]. Available at: https://www2.gov.bc.ca/assets/gov/overdose-awareness/mhha_escalating_bcs_response_report_final_26feb.pdf. Accessed 14 Sep 2020.
 6. BC Ministry of Health. Ministerial order supports urgent overdose response action [internet]. 2016 [cited 2020, 14 Sep]. Available at: <https://news.gov.bc.ca/releases/2016HLTH0094-002737>. Accessed 14 Sep 2020.
 7. Wallace B, Pagan F, Bernie PB. The implementation of overdose prevention sites as a novel and nimble response during an illegal drug overdose public health emergency. *Int J Drug Policy*. 2019;66:64–72.
 8. Lupick T. After a spike in deaths, B.C. opens 18 overdose-prevention sites in less than two weeks. In: *The Georgia Straight* [internet]; 2016 20 Dec [cited 2020, 14 Sep]. Available at: <https://www.straight.com/news/847056/after-spike-deaths-bc-opens-18-overdose-prevention-sites-less-two-weeks>. Accessed 14 Sep 2020.
 9. Maas B, Fairbairn N, Kerr T, Li K, Montaner JSG, Wood E. Neighborhood and HIV infection among IDU: place of residence independently predicts HIV infection among a cohort of injection drug users. *Health Place*. 2007;13:432–9.
 10. Collins AB, Boyd J, Hayashi K, Cooper HLF, Goldenberg S, McNeil R. Women's utilization of housing-based overdose prevention sites in Vancouver, Canada, an ethnographic study. *Int J Drug Policy*. 2020;76:102641.
 11. Vancouver Coastal Health. Response to the opioid overdose crisis in Vancouver Coastal Health [internet]. Vancouver: Vancouver Coastal Health; 2018 [cited 2020 Sep 14]. Available at: <http://www.vch.ca/Documents/CMHO-report.pdf>. Accessed 9 Sep 2020.
 12. Vancouver Coastal Health. Housing overdose prevention site manual [internet]. Vancouver: Vancouver Coastal Health; 2018 [cited 2020, 14 Sep]. Available at: <http://www.vch.ca/Documents/Housing-overdose-revention-site-HOPS-Manual.pdf>. Accessed 14 Sep 2020.
 13. Kerr T, Mitra S, Kennedy MC, McNeil R. Supervised injection facilities in Canada: past, present, and future. *Harm Reduct J*. 2017;14:28.
 14. Vancouver Coastal Health. Insite expands hours to combat overdose crisis [internet]. 2016 [cited 2021, 11 Jan]. Available at: <http://www.vch.ca/about-us/news/insite-expands-hours-to-combat-overdose-crisis>. Accessed 11 Jun 2021.
 15. Krüsi A, Small W, Wood E, Kerr T. An integrated supervised injecting program within a care facility for HIV-positive individuals: a qualitative evaluation. *AIDS Care*. 2009;21:638–44.
 16. BC Centre on Substance Use. Supervised consumption services operational guidance [internet]. Vancouver, BC; 2018 [cited 2018, 25 Aug]. Available at: <http://www.bccsu.ca/wp-content/uploads/2017/07/BC-SCS-Operational-Guidance.pdf>. Accessed 11 Jun 2020.
 17. Kennedy MC, Boyd J, Mayer S, Collins A, Kerr T, McNeil R. Peer worker involvement in low-threshold supervised consumption facilities in the context of an overdose epidemic in Vancouver, Canada. *Soc Sci Med*. 2019;225:60–8.
 18. Pauly B, Wallace B, Pagan F, Phillips J, Wilson M, Hobbs H, et al. Impact of overdose prevention sites during a public health emergency in Victoria, Canada. *PLoS ONE*. 2020;15:e0229208.
 19. Boyd J, Collins AB, Mayer S, Maher L, Kerr T, McNeil R. Gendered violence and overdose prevention sites: a rapid ethnographic study during an overdose epidemic in Vancouver, Canada. *Addiction*. 2018;113:2261–70.
 20. Kennedy MC, Karamouzian M, Kerr T. Public health and public order outcomes associated with supervised drug consumption facilities: a systematic review. *Curr HIV/AIDS Rep*. 2017;14:161–83.
 21. Potier C, Laprévote 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.
 22. McNeil R, Small W. 'Safer environment interventions': a qualitative synthesis of the experiences and perceptions of people who inject drugs. *Soc Sci Med*. 2014;106:151–8.
 23. National Centre in HIV Epidemiology and Clinical Research (NCHECR). Sydney Medically Supervised Injecting Centre evaluation report no. 4: evaluation of service operation and overdose-related events [internet]. Sydney: National Centre in HIV Epidemiology and Clinical Research, University of New South Wales; 2007 [cited 2017, 7 Jun]. Available at: <https://kirby.unsw.edu.au/report/sydney-medically-supervised-injecting-centre-msic-evaluation-report-4>. Accessed 14 Sep 2020.
 24. Marshall BDL, Milloy M-J, Wood E, Montaner JS, Kerr T. Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study. *Lancet*. 2011;377:1429–37.
 25. Salmon AM, Van Beek I, Amin J, Kaldor J, Maher L. The impact of a supervised injecting facility on ambulance call-outs in Sydney, Australia. *Addiction*. 2010;105:676–83.
 26. Irvine MA, Kuo M, Buxton J, Balshaw R, Otterstatter M, Macdougall L, et al. Modelling the combined impact of interventions in averting deaths during a synthetic-opioid overdose epidemic. In: *Addiction* [internet]; 2019 [cited 2019, 5 Jun]. Available at: <https://www.onlinelibrary.wiley.com/doi/abs/10.1111/add.14664>
 27. Wood E, Kerr T, Small W, Li K, Marsh DC, Montaner JSG, et al. Changes in public order after the opening of a medically supervised safer injecting facility for illicit injection drug users. *Can Med Assoc J*. 2004;171:731–4.
 28. Salmon AM, Thein HH, Kimber J, Kaldor JM, Maher L. Five years on: what are the community perceptions of drug-related public amenity following the establishment of the Sydney medically supervised injecting centre? *Int J Drug Policy*. 2007;18:46–53.
 29. Espelt A, Villalbí JR, Bosque-Prous M, Parés-Badell O, Mari-Dell'Olmo M, Brugal MT. The impact of harm reduction programs and police interventions on the number of syringes collected from public spaces. A time series analysis in Barcelona, 2004–2014. *Int J Drug Policy*. 2017;50:11–8.
 30. Hunter K, Park JN, Allen ST, Chaulk P, Frost T, Weir BW, et al. Safe and unsafe spaces: non-fatal overdose, arrest, and receptive syringe sharing among people who inject drugs in public and semi-public spaces in Baltimore City. *Int J Drug Policy*. 2018;57:25–31.
 31. Rhodes T. Risk environments and drug harms: a social science for harm reduction approach. *Int J Drug Policy*. 2009;20:193–201.
 32. Small W, Rhodes T, Wood E, Kerr T. Public injection settings in Vancouver: physical environment, social context and risk. *Int J Drug Policy*. 2007;18:27–36.
 33. Wallace B, Kennedy MC, Kerr T, Pauly B. Factors associated with nonfatal overdose during a public health emergency. *Subst Use Misuse*. 2019;54:39–45.
 34. Bravo MJ, Royuela L, De la Fuente L, Brugal MT, Barrio G, Domingo-Salvany A, et al. Use of supervised injection facilities and injection risk behaviours among young drug injectors. *Addiction*. 2009;104:614–9.
 35. Kerr T, Tyndall M, Li K, Montaner J, Wood E. Safer injection facility use and syringe sharing in injection drug users. *Lancet*. 2005;366:316–8.
 36. Wood E, Tyndall MW, Stoltz J, Small W, Lloyd-Smith E, Zhang R, et al. Factors associated with syringe sharing among users of a medically supervised safer injecting facility. *Am J Infect Dis*. 2005;1(1):50–54.
 37. Joint United Nations Programme on HIV/AIDS (UNAIDS). Harm reduction saves lives [internet]. Geneva, Switzerland; 2017 [cited 2018, 10 Nov]. Available at: http://www.unaids.org/sites/default/files/media_asset/harm-reduction-saves-lives_en.pdf. Accessed 20 Sep 2020.

38. Hagan H, Pouget ER, Des Jarlais DC, Lelutiu-Weinberger C. Meta-regression of hepatitis C virus infection in relation to time since onset of illicit drug injection: the influence of time and place. *Am J Epidemiol*. 2008;168:1099–109.
39. Wood E, Tyndall MW, Zhang R, Stoltz J-A, Lai C, Montaner JSG, et al. Attendance at supervised injecting facilities and use of detoxification services. *N Engl J Med*. 2006;354:2512–4.
40. Wood E, Tyndall MW, Zhang R, Montaner JSG, Kerr T. Rate of detoxification service use and its impact among a cohort of supervised injecting facility users. *Addiction*. 2007;102:916–9.
41. Kimber J, Mattick RP, Kaldor J, van Beek I, Gilmour S, Rance JA. Process and predictors of drug treatment referral and referral uptake at the Sydney medically supervised injecting Centre. *Drug Alcohol Rev*. 2008;27:602–12.
42. DeBeck K, Kerr T, Bird L, Zhang R, Marsh D, Tyndall M, et al. Injection drug use cessation and use of North America's first medically supervised safer injecting facility. *Drug Alcohol Depend*. 2011;113:172–6.
43. Gaddis A, Kennedy MC, Nosova E, Milloy M-J, Hayashi K, Wood E, et al. Use of on-site detoxification services co-located with a supervised injection facility. *J Subst Abuse Treat*. 2017;82:1–6.
44. Caulkins JP, Pardo B, Kilmer B. Supervised consumption sites: a nuanced assessment of the causal evidence. *Addiction*. 2019;114:2109–15.
45. Reddon H, Kerr T, Milloy M-J. Ranking evidence in substance use and addiction. *Int J Drug Policy*. 2020;83:102840.
46. Newman M. Could drug consumption rooms save lives? *BMJ*. 2019;366:l4906.
47. Yang YT, Beletsky L. United States vs Safehouse: the implications of the Philadelphia supervised consumption facility ruling for law and social stigma. *Prev Med*. 2020;135:106070.
48. Health Canada. Supervised consumption sites: status of applications [internet]. 2021 [cited 2021, 30 Jul]. Available at: <https://www.canada.ca/en/health-canada/services/substance-use/supervised-consumption-sites/status-application.html>. Accessed 30 Jul 2021.
49. Wood E, Tyndall MW, Spittal PM, Li K, Kerr T, Hogg RS et al. Unsafe injection practices in a cohort of injection drug users in Vancouver: could safer injecting rooms help? *Can Med Assoc J* 2001;165:405–410.
50. Strathdee SA, Palepu A, Cornelisse PGA, Yip B, O'Shaughnessy MV, Montaner JSG, et al. Barriers to use of free antiretroviral therapy in injection drug users. *JAMA*. 1998;280:547–9.
51. Hedrich D, Kerr T, Dubois-Arber F. Drug consumption facilities in Europe and beyond. In: Rhodes T, Hedrich D, editors *Harm Reduction: Evidence, Impacts, and Challenges*. Lisbon, Portugal: European Monitoring Centre for Drugs and Drug Addiction; 2010. p. 306–31.
52. Kennedy MC, Klassen DC, Dong H, Milloy M-JS, Hayashi K, Kerr TH. Supervised injection facility utilization patterns: A prospective cohort Study in Vancouver, Canada. *Am J Prev Med*. 2019;57:330–7.
53. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. *J Clin Pharm Ther*. 2002;27:299–309.
54. Penfold RB, Zhang F. Use of interrupted time series analysis in evaluating health care quality improvements. *Acad Pediatr*. 2013;13: S38–44.
55. Beard E, Marsden J, Brown J, Tombor I, Stapleton J, Michie S, et al. Understanding and using time series analyses in addiction research. *Addiction*. 2019;114:1866–84.
56. Schaffer AL, Dobbins TA, Pearson S-A. Interrupted time series analysis using autoregressive integrated moving average (ARIMA) models: a guide for evaluating large-scale health interventions. *BMC Med Res Methodol*. 2021;21:58.
57. Iyer HS, Hirschhorn LR, Nisingizwe MP, Kamanzi E, Drobac PC, Rwabukwisi FC, et al. Impact of a district-wide health center strengthening intervention on healthcare utilization in rural Rwanda: use of interrupted time series analysis. *PLoS ONE*. 2017;12:e0182418.
58. Zhang F, Wagner AK, Soumerai SB, Ross-Degnan D. Methods for estimating confidence intervals in interrupted time series analyses of health interventions. *J Clin Epidemiol*. 2009;62:143–8.
59. Petrar S, Kerr T, Tyndall MW, Zhang R, Montaner JSG, Wood E. Injection drug users' perceptions regarding use of a medically supervised safer injecting facility. *Addict Behav*. 2007;32:1088–93.
60. Small W, Van Borek N, Fairbairn N, Wood E, Kerr T. Access to health and social services for IDU: the impact of a medically supervised injection facility. *Drug Alcohol Rev*. 2009;28:341–6.
61. McKnight I, Maas B, Wood E, Tyndall MW, Small W, Lai C, et al. Factors associated with public injecting among users of Vancouver's supervised injection facility. *Am J Drug Alcohol Abuse*. 2007;33:319–25.
62. McNeil R, Shannon K, Shaver L, Kerr T, Small W. Negotiating place and gendered violence in Canada's largest open drug scene. *Int J Drug Policy*. 2014;25:608–15.
63. Olding M, Ivsins A, Mayer S, Betsos A, Boyd J, Sutherland C, et al. A low-barrier and comprehensive community-based harm-reduction site in Vancouver, Canada. *Am J Public Health*. 2020;110:833–5.
64. Boyd J, Lavalley J, Czechaczek S, Mayer S, Kerr T, Maher L, et al. 'Bed bugs and beyond': an ethnographic analysis of North America's first women-only supervised drug consumption site. *Int J Drug Policy*. 2020;78:102733.
65. Kennedy MC, Milloy M-J, Hayashi K, Holliday E, Wood E, Kerr T. Assisted injection within supervised injection services: uptake and client characteristics among people who require help injecting in a Canadian setting. *Int J Drug Policy*. 2020;86:102967.
66. Kolla G, Kenny KS, Bannerman M, Boyce N, Chapman L, Dodd Z, et al. Help me fix: the provision of injection assistance at an unsanctioned overdose prevention site in Toronto, Canada. *Int J Drug Policy*. 2020;76:102617.
67. Brend Y. Activists bring more pop-up injections sites to Vancouver's overdose 'battle zone'. *CBC News* [internet]. 2016, 21 Nov [cited 2021, 5 Jul]. Available at: <https://www.cbc.ca/news/canada/british-columbia/drug-overdose-vancouver-bc-pop-up-battle-zone-insite-injection-blue-hue-1.3860193>. Accessed 5 Jul 2021.
68. Kimber J, MacDonald M, van Beek I, Kaldor J, Weatherburn D, Lapsley H, et al. The Sydney medically supervised injecting Centre: client characteristics and predictors of frequent attendance during the first 12 months of operation. *J Drug Issues*. 2003;33:639–48.
69. Wood E, Tyndall MW, Li K, Lloyd-Smith E, Small W, Montaner JSG, et al. Do supervised injecting facilities attract higher-risk injection drug users? *Am J Prev Med*. 2005;29:126–30.
70. Wood E, Tyndall MW, Qui Z, Zhang R, Montaner JSG, Kerr T. Service uptake and characteristics of injection drug users utilizing North America's first medically supervised safer injecting facility. *Am J Public Health*. 2006;96:770–3.
71. Milloy M-J, Wood E. Emerging role of supervised injecting facilities in human immunodeficiency virus prevention. *Addiction*. 2009;104:620–1.
72. Vancouver Coastal Health. Overdose prevention site manual 2017 [internet]. 2017 [cited 2020, 24 Jun]. Available at: <http://www.vch.ca/Documents/Overdose-Prevention-Site-OPS-Manual.pdf>. Accessed 24 Jun 2020.
73. BC Centre for Disease Control. BC overdose prevention services guide 2019 [i]. 2019 [cited 2020, 30 Apr]. Available at: http://www.bccdc.ca/resource-gallery/Documents/Guidelines%20and%20Forms/Guidelines%20and%20Manuals/Epid/Other/BC%20Overdose%20Prevention%20Services%20Guide_Jan2019.pdf. Accessed 30 Apr 2020.
74. Shadish W, Cook T, Campbell D. *Experimental and quasi-experimental designs for generalized causal inference*. Houghton Mifflin: Boston, MA; 2002.

75. Lopez Bernal J, Cummins S, Gasparrini A. The use of controls in interrupted time series studies of public health interventions. *Int J Epidemiol.* 2018;47:2082–93.
76. Joint Task Force on Overdose Prevention and Response. B.C.'s Opioid Overdose Response One-Year Update [internet]. 2017 Apr [cited 2020, 22 Oct]. Available at: <https://www2.gov.bc.ca/assets/gov/health/about-bc-s-health-care-system/office-of-the-provincial-health-officer/overdose-response-one-year-update-april2017.pdf>. Accessed 22 Oct 2020.
77. McNeil R, Small W, Lampkin H, Shannon K, Kerr T. 'People knew they could come here to get help': an ethnographic study of assisted injection practices at a peer-run 'unsanctioned' supervised drug consumption room in a Canadian setting. *AIDS Behav.* 2014;18:473–85.
78. Olding M, Boyd J, Kerr T, McNeil R. 'And we just have to keep going': task shifting and the production of burnout among overdose response workers with lived experience. *Soc Sci Med.* 2021;270:113631.
79. Campbell DT, Stanley JC. *Experimental and Quasi-Experimental Designs for Research.* In: Boston, MA: Ravenio Books; 2015.
80. Kennedy MC, Hayashi K, Milloy M-J, Wood E, Kerr T. Supervised injection facility use and all-cause mortality among people who inject drugs in Vancouver, Canada: a cohort study. *PLoS Med.* 2019;16:e1002964.
81. Ma J, Bao Y-P, Wang R-J, Su M-F, Liu M-X, Li J-Q, et al. Effects of medication-assisted treatment on mortality among opioids users: a systematic review and meta-analysis. *Mol Psychiatry.* 2019;24:1868–83.

How to cite this article: Kennedy MC, Hayashi K, Milloy M-J, Compton M, Kerr T. Health impacts of a scale-up of supervised injection services in a Canadian setting: an interrupted time series analysis. *Addiction.* 2021;1–12. <https://doi.org/10.1111/add.15717>