ASSISTED INJECTION WITHIN SUPERVISED INJECTION SERVICES: UPTAKE AND CLIENT CHARACTERISTICS AMONG PEOPLE WHO REQUIRE HELP INJECTING IN A CANADIAN SETTING

Mary Clare KENNEDY [1,2], M-J MILLOY [1,2], Kanna HAYASHI [1,3], Elizabeth HOLLIDAY[4], Evan WOOD[1,2], Thomas KERR[1,2]

1. British Columbia Centre on Substance Use, 400-1045 Howe Street, Vancouver, BC, CANADA, V6Z 2A9
2. Department of Medicine, University of British Columbia, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC, CANADA, V6Z 1Y6
3. Faculty of Health Sciences, Simon Fraser University, Blusson Hall, Room 11300, 8888 University Drive, Burnaby, BC, CANADA, V5A 1S6
4. Vancouver Coastal Health, 2775 Laurel Street, Vancouver, BC, CANADA V5Z 1M9

Send correspondence to:

Mary Clare Kennedy, PhD
Postdoctoral Fellow,
British Columbia Centre on Substance Use
Department of Medicine
University of British Columbia
400-1045 Howe St., Vancouver, BC, Canada V6Z 2A9
Tel: (250) 415-8187
Fax: (604) 806-9044
Email: bccsu-mck@bccsu.ubc.ca

Word Count: 5308
Figures: 1
Tables: 2
Revised: September 18, 2020

ABSTRACT

Background: People who require help injecting illicit drugs experience elevated rates of a range of health-related harms, including overdose and acquisition of blood-borne pathogens. In response, some supervised injection services (SIS) in Canada have begun to permit clients to be physically injected by fellow clients or staff members. However, little is known about uptake and characteristics of clients who engage in this practice. We therefore sought to examine factors associated with receiving injection assistance at SIS among people who require help injecting drugs in Vancouver, Canada.

Methods: Data were drawn from two community-recruited prospective cohort studies of people who inject drugs (PWID). We used multivariable generalized estimating equation (GEE) analyses with time-updated covariates to identify factors associated with self-reported receipt of injection assistance at SIS.

Results: Between June 2017 and December 2018, 319 individuals who reported having recently required help injecting were included in the study. Of these, 160 (51.0%) were women and the median age was 42 years at baseline. In total, 54 (16.9%) participants reported receiving injection assistance at a SIS at least once over an average of 3.3 months of follow-up. In multivariable GEE analyses, recent homelessness (Adjusted Odds Ratio [AOR] = 2.04; 95% confidence interval [CI]: 1.13 – 3.66), fentanyl injection (AOR = 3.45; 95% CI: 1.42 – 8.41), non-fatal overdose (AOR = 1.86; 95% CI: 1.02 – 3.38) and enrolment in methadone maintenance therapy (AOR = 1.89; 95% CI: 1.03 – 3.47) were associated with increased odds of receiving injection assistance at SIS.

Conclusion: Although **uptake** of assisted injection at SIS was relatively low among this sample of people who require help injecting, this practice was associated with several indicators of structural vulnerability and drug-related risk. These findings suggest that accommodating assisted injection within SIS may be providing opportunities to engage and reduce harms among higher-risk subpopulations of PWID in this setting.

Word Count: 299

Keywords: supervised injection services; injection drug use; assisted injection; harm reduction; Canada; generalized estimating equations

INTRODUCTION

In Canada and internationally, supervised injection services (SIS) are increasingly recognized as a standard intervention to mitigate harms associated with injection drug use, including fatal overdose and infectious disease transmission, and improve the health of people who inject drugs (PWID) (European Monitoring Centre for Drugs and Drug Addiction, 2018; Kerr et al., 2017; Stone & Shirley-Beavan, 2018). SIS provide regulated spaces in which people can inject illicit drugs in hygienic conditions under the supervision of health professionals or other trained staff (European Monitoring Centre for Drugs and Drug Addiction, 2018; Kerr et al., 2017). Within SIS, clients can typically obtain sterile injection supplies, education on safer injecting practices, and emergency care in the event of overdose (European Monitoring Centre for Drugs and Drug Addiction, 2018; Kerr et al., 2017). SIS also often provide direct access or referrals to other co-located and/or external health and social services (European Monitoring Centre for Drugs and Drug Addiction, 2018; Kerr et al., 2017). There are now an estimated 170 SIS operating worldwide, including in Canada, Australia and eleven countries in Europe (Correlation Network et al., 2018; Harm Reduction International, 2019; Health Canada, 2020a; Stone & Shirley-Beavan, 2018).

Scientific evaluations of SIS have identified a number of important health and social benefits associated with the establishment and use of these services, including reductions in fatal overdose and high-risk drug use practices such as used syringe sharing, as well as increased uptake of other health services, including addiction treatment, among PWID (Kennedy et al., 2017; McNeil & Small, 2014; Potier et al., 2014). Unfortunately, some subpopulations of PWID continue to encounter barriers in accessing SIS. In particular, people who cannot self-inject are

prohibited from receiving manual assistance with injections at SIS in many settings worldwide (Bayoumi et al., 2012; Gagnon, 2017; Kimber et al., 2005). For example, in Canada, federally-sanctioned SIS are governed by regulations under section 56 of the Controlled Drugs and Substances Act that have traditionally stipulated that all clients must self-administer injections, primarily due to criminal and civil liability concerns surrounding assisted injection (Gagnon, 2017; McNeil et al., 2014). Thus, at Insite (Canada's first government-sanctioned SIS that has been operating in Vancouver, British Columbia since 2003), nursing staff have been able to provide clients who require help injecting with education regarding how to safely self-inject and guidance with injecting (e.g., assistance with vein finding and stabilizing, lining up shots) since the facility was established (Wood, Tyndall, Stoltz, et al., 2005; Wood et al., 2008). However, clients have never been allowed to be physically injected by staff or service users under the parameters of the facility's exemption to federal drug laws (Gagnon, 2017; Wood, Tyndall, Stoltz, et al., 2005; Wood et al., 2008).

Although the provision of nurse-delivered safer injection education and guidance at SIS has been found to increase capacity for self-injection among people who require help injecting (Wood et al., 2008), the prohibition of on-site assisted injection has been found to hinder SIS access among this population (Fairbairn et al., 2010; McNeil et al., 2014; Wood, Tyndall, Qui, et al., 2006). This is a particularly concerning gap in service coverage given that studies conducted in Canada have found that people who require help injecting account for an estimated 14 to 49% of PWID (Cheng et al., 2016; O'Connell et al., 2005; Pedersen et al., 2016), and that women, youth and people with disabilities are disproportionately represented among this subpopulation (Cheng et al., 2016; Pedersen et al., 2016; Wood et al., 2003). Moreover, people who require help injecting are known to be at heightened risk of a range of serious health-related harms

including overdose, violence, skin and soft tissue infections, and infectious disease acquisition (Fairbairn et al., 2010; Kerr, Fairbairn, et al., 2007; Kral et al., 1999; Lamb et al., 2018; McNeil et al., 2014; O'Connell et al., 2005; Pedersen et al., 2016; Robertson et al., 2010), and rules prohibiting physical injection assistance at SIS have been found to exacerbate vulnerability to such harms by driving these individuals to inject in unsafe social and physical contexts (Fairbairn et al., 2010; McNeil et al., 2014; Wood, Tyndall, Qui, et al., 2006).

In recent years, the proliferation of illegally-manufactured fentanyl and other powerful synthetic opioids in illicit drug markets has contributed to rapid increases in accidental overdose death rates in Canada and the United States (Health Canada, 2020b; National Institute on Drug Abuse, 2018). Although unprecedented numbers of overdose deaths have become a pressing concern in many jurisdictions across Canada, the province of British Columbia has been among the most affected, with the annual fatal overdose rate increasing from 7.8 to 30.9 per 100,000 population between 2014 and 2018, leading the province to declare a public health emergency in April 2016 (BC Coroners Service, 2020). As part of the response, there has been an escalation of efforts to extend the coverage of SIS in Canada, and to increase the responsiveness of these services to the needs of underserved and marginalized populations, including people who require help injecting (Boyd et al., 2018; Health Canada, 2020a; Kerr et al., 2017; Kolla et al., 2020; Lupick, 2018). Indeed, although Insite was the only government-sanctioned SIS in Canada until 2016, 41 additional SIS have since been federally authorized to operate in municipalities across the country, including two SIS to complement Insite in Vancouver (Health Canada, 2020a; Kerr et al., 2017). Beginning in July 2018, Health Canada (the federal health agency responsible for approving and regulating SIS) initiated a pilot program that permitted peers (i.e., people who inject(ed) drugs) to manually assist clients with injections on a trial basis at twenty SIS operating

in three provinces (Alberta, Ontario and Quebec) (Kolla et al., 2020; Kuwabara Blanchard, 2020; Lupick, 2018). Then, in March 2020, the agency revised federal SIS guidelines to allow all new and existing SIS to apply for exemptions to accommodate this practice (Health Canada, 2020a; Kuwabara Blanchard, 2020). **As of September 2020, 24 federally-sanctioned SIS in Canada have received exemptions to accommodate peer-assisted injection** (Health Canada, 2020a)**. However, none of the three federally-sanctioned SIS presently operating in Vancouver have received such exemptions to date** (Health Canada, 2020a)**.**

In addition to the expansion of federally-sanctioned SIS in Canada, approximately 40 low-threshold SIS, typically referred to as overdose prevention sites (OPS), have been established across the country since 2016, eight of which are located in the city of Vancouver (Irvine et al., 2019; Perkel, 2019; Vancouver Coastal Health, 2020). OPS differ from federally-authorized SIS in that these were first sanctioned as a temporary measure in response to the overdose crisis upon the enactment of an emergency provincial ministerial order in British Columbia in December 2016 (Kerr et al., 2017; Wallace et al., 2019). In contrast with federally-sanctioned SIS, this **order** allowed OPS to be immediately implemented without first having to obtain individual exemptions to federal drug laws (Kerr et al., 2017; Wallace et al., 2019). OPS also differ from federally-sanctioned SIS in that these are often simpler in physical design as a result of being rapidly implemented into existing organizations or temporary sites rather than purpose-built facilities, and do not usually provide the same level of clinical services (e.g., formal health service referrals, treatment of skin and soft tissue infections) as federally-sanctioned SIS (Boyd et al., 2018; Kerr et al., 2017; Wallace et al., 2019). Another important distinction is that OPS are not governed by federal SIS regulations and guidelines (Boyd et al., 2018; Kerr et al., 2017; Wallace et al., 2019). Thus, these services are often primarily staffed by

peers given that health professional supervision of injections is not required and, of particular relevance to the present study, are able to accommodate drug use practices that have not traditionally been permitted at federally-sanctioned SIS, including physical injection assistance by staff members or service users (Boyd et al., 2018; Kerr et al., 2017; Wallace et al., 2019).

Although there is a dearth of evaluations of assisted injection at SIS in the scientific literature, several studies undertaken in Canada have provided evidence to suggest the acceptability and health benefits of permitting this practice within regulated settings (Boyd et al., 2018; Kolla et al., 2020; McNeil et al., 2014; Pijl et al., Under review). For example, ethnographic studies of unsanctioned SIS (i.e., sites operating without formal approval by any level of government) and OPS in Vancouver have found that the accommodation of assisted injection within these services has helped to foster service engagement among people who require help injecting, as well as helped enable these individuals to exercise greater agency over their drug use practices and avoid risks and harms associated with receiving help injecting within the street-based drug scene (Boyd et al., 2018; McNeil et al., 2014). In addition, a recent cross-sectional study found that approximately 8% of visits to an OPS in Toronto involved service users receiving injection assistance, and that this practice was independently and positively associated with overdosing at the OPS among women but not men (Kolla et al., 2020). The authors described the observed association among women as a favourable finding given that rapid overdose response by trained professionals is immediately available within OPS but is not usually available in community settings, where individuals receiving injection assistance are also at elevated risk of overdose (Kolla et al., 2020). However, it is noteworthy that **the study sample for that study was all OPS clients.** We know of no existing studies that have quantitatively characterized receipt of injection assistance at SIS among people who require help injecting.

Therefore, in an effort to gain a better understanding of this practice and thereby inform the optimization of SIS programming, we undertook the present study to examine uptake and factors associated with receiving injection assistance at SIS among a community-recruited cohort of people who require help injecting in Vancouver.

METHODS

Data were drawn from two community-recruited open prospective cohort **studies** of people who use illicit drugs in Vancouver: the Vancouver Injection Drug Users Study (VIDUS) and the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS). These cohorts have been described in detail previously (Strathdee et al., 1998; Wood et al., 2001). In brief, participants have been recruited through community-based methods, including self-referral and street outreach, since May 1996. VIDUS is a cohort of HIV-negative adult PWID who have injected illicit drugs at least once in the month prior to study enrolment. ACCESS is a cohort of HIV-positive adults who have used illicit drugs other than or in addition to cannabis (which was a controlled substance in Canada for all but the final six weeks of the study period) in the month prior to enrolment. VIDUS and ACCESS employ harmonized data collection and follow-up procedures to allow for combined analyses. Specifically, at their baseline study visit and semi-annually thereafter, participants complete an interviewer-administered questionnaire and provide blood samples for serological analyses. The questionnaire collects information regarding socio-demographic characteristics, drug use and other behavioural patterns, social-structural exposures and use of health and social services. At each study visit, participants receive an honorarium ($40 CAD). VIDUS and ACCESS have received approval from the University of British Columbia/Providence Health Care Research Ethics Board.

As questionnaire items related to assisted injection at SIS were first added to the study questionnaire in June 2017, the present analyses were restricted to participants who completed at least one study visit between June 1, 2017 and November 30, 2018**. During that time period, a total of six SIS that accommodated assisted injection were operating in Vancouver, all of which were OPS (Kennedy, Boyd, et al., 2019).** We further restricted to observations in which participants reported having required help injecting drugs in the previous six months. The primary outcome for this analysis was recent receipt of assisted injection at SIS. This variable was defined as responding "overdose prevention sites/supervised injection facilities" (yes vs. no) to the question, '*Where or who did you get help from?',* which was a follow-up question asked of all participants who reported having received injection assistance in the previous six months. We considered a range of individual and contextual factors as explanatory variables, which were selected on the basis of previous research examining assisted injection and/or use of harm reduction services among PWID (Cheng et al., 2016; Kennedy, Klassen, et al., 2019; Kimber et al., 2003; Kolla et al., 2020; Lamb et al., 2018; Lee et al., 2013; McNeil et al., 2014; O'Connell et al., 2005; Pedersen et al., 2016; Wood et al., 2003; Wood, Tyndall, Qui, et al., 2006; Wood et al., 2008). These variables included age (per year older), years injecting drugs at baseline (per year increase), current gender identity (men [trans-inclusive] vs. women [trans-inclusive] and other genders), ancestry (white vs. non-white), and use of injection heroin/down, cocaine, and crystal methamphetamine (≥all daily vs. <daily). Additionally, we assessed the following as explanatory variables: residence in the Downtown Eastside (the neighbourhood in which most SIS in Vancouver are located), employment, homelessness, HIV seropositivity (measured based on serology at each study visit), hepatitis C seropositivity (measured based on serology at each study visit), public injection, fentanyl injection, non-fatal overdose, syringe sharing, enrolment in

methadone maintenance therapy (MMT), sex work involvement, exposure to violence, and incarceration (all yes vs. no). All explanatory variable definitions were consistent with those used in our previous work (Kennedy et al., 2020; Kerr et al., 2007; Pedersen et al., 2016; Wood, Tyndall, Qui, et al., 2006). Unless otherwise indicated, all variables were measured based on self-reported information, refer to activities or experiences that occurred in the six-month period prior to a study visit and were treated as time-updated based on each semi-annual follow-up visit.

As a first step, we used Pearson's chi-squared test for categorical variables and the Wilcoxon rank sum test for continuous variables to compare the baseline characteristics of those who did and did not report receiving assistance with injecting at SIS in the previous six months at baseline. Next, we descriptively examined the proportion of participants who reported past-six-month SIS use and past-six-month receipt of injection assistance within SIS, respectively, in at least one study visit during the study period as well as the proportion of participants who exclusively used federally-sanctioned SIS, exclusively used OPS, or used both federally-sanctioned SIS and OPS during the study period. We also descriptively examined the proportion of participants who reported at least one six-month period during the study period in which they mostly received injection assistance within SIS (as opposed to other settings). We then used generalized estimating equations (GEE) for binary outcomes with a logit link function and exchangeable correlation structure to estimate unadjusted odds ratios (OR) for the association between past-six-month receipt of injection assistance at SIS and each of the explanatory variables. We used GEE for the analysis of correlated data given that the factors potentially associated with the outcome were time-dependent measures. By using data from every participant study visit, these methods allowed for consideration of factors associated with receiving injection assistance at SIS over the full duration of the study period, with standard

errors calculated using an exchangeable correlation structure adjusted for multiple observations per individual (Lee et al., 2007). Bivariable GEE analyses were conducted to obtain unadjusted odds ratios and associated 95% confidence intervals (CI) for the associations between the outcome and each explanatory variable of interest. A multivariable model was then fit using an *a priori*-defined statistical protocol based on examined of the quasi-likelihood under the independence model criterion (QIC) for GEE and *p*-values. First, we fit a preliminary model that included all variables significant at $p < 0.20$ in bivariable GEE analyses. Each variable with the highest *p*-value was then removed sequentially, with the final model including the set of variables associated with the lowest QIC. We have successfully used this modelling approach in our past work (Gaddis et al., 2017).

We also recognized that our estimates of association could have been biased if the likelihood of loss to follow-up among study participants was related to both outcome and exposure status. We therefore conducted a sub-analysis to assess the potential for such selection-attrition bias. As study participants typically complete follow-up study visits on a semi-annual basis, we considered participants to be lost to follow-up for the purposes of this analysis if the duration of time between the end of the study period (November 30, 2018) and the date of their latest study visit during the study period exceeded 12 months. We then used Pearson's chi-squared test for categorical variables and the Wilcoxon rank sum test for continuous variables to compare the characteristics (including all explanatory variables and the outcome of interest, measured at the latest study visit) of this group to those retained in the study. We conducted all analyses with SAS version 9.4 (SAS Institute, Cary, NC). All *p*-values are two-sided.

RESULTS

As shown in Figure 1, 1309 VIDUS and ACCESS participants completed at least one study visit **between June 2017 and December 2018**, 919 of whom reported having injected drugs in the past six months in at least one study visit during this time period. Of these, 319 people reported having required help injecting in the past six months in at least one study visit and were included in the present study. These participants contributed a total of 475 observations during the study period with a median of 1 study visit (interquartile range [IQR]: 1 – 3) per participant. The median age of the study sample at baseline was 42 years (IQR: 34 – 52), 160 (51.0%) were women, and 172 (54.3%) self-reported white ancestry. Overall, participants contributed a total of 88.4 person-years of follow-up after their baseline interview (mean follow-up duration = 3.3 months; standard deviation = 4.7 months). Of the total 475 observations included in the study, 289 (60.8%) included at least one reported incident of SIS use in the previous six-month period, and 57 (12.0%) included at least one reported incident of receiving injection assistance at SIS in the previous six-month period.

As shown in Figure 1, a total of 214 (67.1%) participants reported past-six-month use of SIS in at least one study visit during the study period. Of these 214 participants, 59 (27.6%) reported exclusively using federally-sanctioned SIS, 19 (8.9%) reported exclusively using OPS, and the remaining 136 (63.6%) reported using both federally-sanctioned SIS and OPS during the study period. **Of the 155 participants who reported past-six-month use of SIS that accommodated assisted injection (i.e., OPS) in at least one study visit**, 54 **(34.8%)** reported past-six-month receipt of assistance with injecting at SIS in at least one study visit, accounting for **25.2% (54/214) of all SIS users (i.e., users of OPS and/or federally-sanctioned SIS) and** 16.9% (54/319) of the study sample. Of these 54 participants, 37 (68.5%) reported in at least one

study visit having mostly received injection assistance at SIS (as opposed to other settings) in the past six months, accounting for **23.8% (37/155) of users of SIS that accommodated assisted injection (i.e., OPS),** 17.3% (37/214) of **all** SIS users and 11.6% (37/319) of the study sample. Table 1 presents the baseline characteristics of the study sample, stratified by reporting having received injection assistance at SIS in the previous six months **at baseline.**

Table 2 presents the results of the crude and adjusted longitudinal estimates of the odds of recent receipt of injection assistance at SIS. As shown, in multivariable analyses, homelessness (Adjusted Odds Ratio [AOR] = 2.04; 95% CI: 1.13 – 3.66), fentanyl injection (AOR = 3.45; 95% CI: 1.42 – 8.41), non-fatal overdose (AOR = 1.86; 95% CI: 1.02 – 3.38) and enrolment in MMT (AOR = 1.89; 95% CI: 1.03 – 3.47) were associated with increased odds of receiving injection assistance at SIS in the previous six months.

In a sub-analysis, we found that 52 (16.3%) of participants had >12 months between the date of their latest study visit and the end of the study period. These individuals were more likely to inject cocaine ≥daily and to be enrolled in MMT compared to those retained in the study (all $p < 0.05$, data not shown). However, these two groups did not significantly differ in terms of receipt of assisted injection at SIS or any other variables examined (all $p > 0.05$, data not shown).

DISCUSSION

In this study of 319 people who require help injecting participating in a community-recruited cohort of PWID in Vancouver, Canada, we found that two-thirds of participants reported past-six-month SIS use at least once over an average follow-up duration of three months, the majority of whom (72%) reported using a SIS that was not governed by federal

regulations that prohibit assisted injection (i.e., an OPS) at least once. However, the prevalence of receiving assistance with injecting at SIS was relatively low, with approximately 17% of participants (25% of **all** SIS users **and 35% of OPS users**) reporting past-six-month receipt of injection assistance at SIS in at least one study visit **during follow-up**. Among participants who reported past-six-month receipt of injection assistance at SIS in at least one study visit, 69% reported at least one six-month period in which they mostly received assistance with injecting at SIS (as opposed to other settings). In multivariable GEE analyses, past-six-month receipt of injection assistance at SIS was positively associated with enrolment in MMT and several indicators of structural vulnerability and drug-related risk, including recent homelessness, fentanyl injection, and non-fatal overdose.

To our knowledge, this study is the first to quantitatively characterize receipt of injection assistance at SIS among a community-recruited cohort of people who require help injecting. There are a number of possible explanations for our finding of a relatively low uptake of this practice among this cohort despite SIS use being quite common. First, this could reflect the fact that some PWID only occasionally require physical injection assistance, such as on occasions when experiencing withdrawal symptoms (Pedersen et al., 2016; Small et al., 2012; Wood et al., 2003), **experiences of which might also make individuals less likely to seek assistance at SIS due to increased urgency to inject so as to alleviate such symptoms** (Fairbairn et al., 2010; Lloyd-Smith et al., 2010; McNeil et al., 2014). Second, the capacity of people to self-inject may be improved by injecting within SIS as opposed to community settings (McNeil et al., 2014; Small et al., 2012; Wood et al., 2003; Wood et al., 2008). For example, although PWID commonly report anxiousness and shakiness as reasons for experiencing difficulty injecting (Pedersen et al., 2016; Wood et al., 2003), such concerns may be alleviated by injecting within

the secure environments of SIS, where clients can avoid stressors related to injecting within the street-based drug scene, including fear of unwanted interference by police or other PWID (McNeil et al., 2014; Wood et al., 2003). **SIS may also provide other conditions that improve individual capacity for self-injection (e.g., adequate lighting, access to clean drinking water, secure environments to support ease of garment removal to facilitate vein access) (Small, Moore, et al., 2012).** Further, the provision of verbal assistance and guidance rather than physical injection by SIS staff or peers may be sufficient to enable some PWID to overcome self-injection challenges (Small et al., 2012; Wood et al., 2008). Indeed, although difficulties finding and hitting veins are often cited by PWID as key reasons for being unable to self-administer injections, these difficulties are **sometimes** related to gaps in knowledge concerning injection techniques (Fairbairn et al., 2010; Wood et al., 2003), and previous studies have found that individual ability to identify viable veins and preserve vein integrity are often increased after receiving nurse- or peer-delivered injection education and guidance (Small et al., 2012; Wood et al., 2008).

The relatively low uptake of assisted injection at SIS observed in the present study might also reflect a lack of awareness among PWID that this practice was accommodated at SIS, particularly given that assisted injection has never been permitted at Insite, Vancouver's longest-running and largest SIS, and that this practice was condoned by staff at OPS but not explicitly permitted by the local health authority for part of the study period (BC Centre for Disease Control, 2019; Boyd et al., 2018; Kerr et al., 2017; Vancouver Coastal Health, 2017). Further, no OPS in Vancouver have required staff or peers to provide injection assistance and therefore this service may not have always been readily available to OPS clients (BC Centre for Disease Control, 2019). Additionally, as 28% of participants who reported using SIS during follow-up

exclusively used Insite and/or other federally-sanctioned SIS that did not permit assisted injection, some of these participants may have not received injection assistance simply because it was not accommodated at the SIS they accessed. Other individual and social-structural barriers to receiving injection assistance at SIS that were not thoroughly examined in the present study, such as issues related to lack of privacy when receiving injection assistance in SIS or dynamics of established injecting routines and injection partnerships, may have also played a role in impeding uptake of this practice (Bardwell et al., 2019; Boyd et al., 2018; Fairbairn et al., 2010; Reddon et al., 2011; Small et al., 2011). However, these interpretations cannot be confirmed based on the current study. Further research, particularly ethnographic research, is needed to gain a better understanding of potential reasons why people who require help injecting might avoid or encounter barriers in receiving injection assistance at SIS.

Although overall uptake of assisted injection at SIS among the study sample was quite low, it is noteworthy that 69% of participants who engaged in this practice during follow-up reported at least one six-month period in which they mostly received injection assistance at SIS (as opposed to other settings). Further, similar to past studies demonstrating that SIS effectively engage higher-risk and socially marginalized subpopulations of PWID (Kennedy, Klassen, et al., 2019; Kimber et al., 2003; Wood, Tyndall, Li, et al., 2005; Wood, Tyndall, Qui, et al., 2006; Zurhold et al., 2003), we found that receipt of injection assistance at SIS among people who require help injecting was associated with several notable markers of structural vulnerability and drug-related risk, including homelessness, fentanyl injection, and non-fatal overdose. These findings are encouraging in light of past studies demonstrating the various positive health impacts associated with both SIS use in general (Kennedy et al., 2017; McNeil & Small, 2014;

Potier et al., 2014) and receipt of injection assistance within SIS specifically (Boyd et al., 2018; Kolla et al., 2020; McNeil et al., 2014; Wood et al., 2008).

In the context of the ongoing overdose crisis, it is particularly notable that we found that recent non-fatal overdose was positively associated with receiving injection assistance at SIS. As the design of the present study impedes our ability to determine temporality of associations, it could be argued that this finding is explained by assisted injection within SIS promoting drug use practices that increase overdose risk (e.g., injection of higher doses). This explanation may appear to align with a recent study documenting an association between receipt of injection assistance at an OPS in Toronto and increased odds of overdosing within the OPS among women (Kolla et al., 2020). However, given that the **study sample for that study was OPS clients rather than people who required help injecting,** this finding likely largely reflected the elevated overdose risk associated with receiving injection assistance in general rather than within OPS specifically (Fairbairn et al., 2010; Kerr, Fairbairn, et al., 2007; Kolla et al., 2020). Thus, rather than assisted injection at SIS promoting drug use practices that increase overdose risk, we instead suspect that our finding of a positive association between non-fatal overdose and receipt of injection assistance at SIS is more likely to be due to the accommodation of this practice attracting individuals to SIS who are at heightened risk of experiencing overdose. **For example, some individuals may seek assistance with injections at a SIS as a protective strategy against overdose-related harm if they are injecting drugs of unknown purity or composition (Kerr, Small, et al., 2007). Additionally, individuals who seek assistance at SIS may be more likely to contend with exposures and engage in behaviours that increase their risk of experiencing overdose in general, including outside of SIS**. This explanation is consistent with previous studies demonstrating that recent non-fatal overdose is associated with

subsequent uptake of and retention in SIS among PWID in this setting (Kennedy, Klassen, et al., 2019; Wood, Tyndall, Li, et al., 2005). Moreover, rather than increasing overdose risk, SIS have previously been found to modify the contexts of assisted injection practices in ways that mitigate risk of overdose-related morbidity and mortality (Boyd et al., 2018; McNeil et al., 2014). Specifically, past ethnographic studies have described how the provision of injection assistance within SIS may prevent overdose events by, for example, decreasing reliance on strangers and acquaintances for injection assistance, and promoting the adoption of harm reduction strategies such as the reduction of doses (Boyd et al., 2018; McNeil et al., 2014). The availability of prompt overdose response by trained personnel within SIS has also been found to reduce the risk of fatal overdose among PWID (Irvine et al., 2019; Marshall et al., 2011; McNeil et al., 2014), and no overdose deaths have ever occurred in any SIS in Canada or elsewhere (Kennedy et al., 2017).

It is also noteworthy SIS have previously been found to facilitate access to health and social services among PWID, including addiction treatment (DeBeck et al., 2011; Gaddis et al., 2017; Kimber et al., 2008; Wood et al., 2007; Wood, Tyndall, Zhang, et al., 2006), which might explain the association we observed between receiving injection assistance at SIS and enrolment in MMT. However, given that the temporal direction of associations cannot be determined based on the results presented herein, it is possible that individuals enrolled in MMT were more likely to receive assistance with injecting at SIS due to, for example, having lower levels of illicit drug use that promoted greater overall stability and engagement with health services (Gowing et al., 2011; Lappalainen et al., 2015; Mattick et al., 2009). Additional studies may help to elucidate the underlying mechanisms that account for the observed association between receipt of injection assistance at SIS and enrolment in MMT.

Together with past studies demonstrating the health benefits of assisted injection within regulated settings (Boyd et al., 2018; Kolla et al., 2020; McNeil et al., 2014; Pijl et al., Under review), our findings underscore the importance of accommodating assisted injection within SIS as a strategy to engage and reduce the potential for health-related harms among highly-vulnerable subpopulations of PWID. Thus, it is reassuring that many of the recently-established OPS in Canada permit on-site assisted injection and that Health Canada recently revised federal guidelines to allow for the broader accommodation of peer-assisted injection within federally-authorized SIS (Boyd et al., 2018; Health Canada, 2020a; Kuwabara Blanchard, 2020). However, further research should be conducted to examine how various factors may shape the uptake and effectiveness of injection assistance provided within different SIS operational contexts. In particular, given that policies and procedures concerning assisted injection may differ across SIS (e.g., rules regarding drug sharing and the involvement of clients, peer staff and/or non-peer staff in injection assistance), investigations of the impacts of such programmatic factors would provide important information to inform the optimization of this emerging service feature.

This study has several limitations. First, the VIDUS and ACCESS cohorts are not random samples of the underlying population of people who use illicit drugs in our study setting. Therefore, the findings from this study may not be generalizable to people who require help injecting in local or other settings. **We should also note that the average follow-up duration per participant in the present study was relatively short and that this study was undertaken during a time when SIS in Vancouver had only recently begun to accommodate assisted injection. As such, our estimates of the prevalence of receiving assisted injection at SIS may not apply to the current context in which SIS in this setting have been accommodating this practice for several years. Further studies with longer study periods**

should be undertaken to assess individual- and population-level patterns of engagement in this practice over the long term among people who require help injecting. A further limitation is that, with the exception of HIV and hepatitis C serology, this study relied on self-reported data and thus our findings could be subject to reporting biases including social desirability bias. **However, previous studies have suggested that self-reported data from PWID are reliable and valid (Darke, 1998).** Another limitation mentioned previously is that our study design limits our ability to determine the temporal direction of the associations observed herein **given that measurements of self-reported exposures and the outcome all refer to the six months preceding the date of a study interview. Further, the ORs observed in this study may be overestimates of prevalence ratios and incidence rate ratios given that the outcome of interest was relatively common (Tamhane et al., 2016). To provide stronger evidence of temporality and causal relationships, future studies should seek to assess the incidence rate of receiving assisted injection at SIS and its association with lagged exposures among people who require help injecting. A final limitation is that approximately 16% of participants in this study could be considered lost to follow-up given that they had more than 12 months between the date of their latest interview and the end of the study period. This could have biased our observed estimates of association if the likelihood of loss to follow-up was related to both outcome and exposure status. However, we found that individuals who were lost to follow-up did not differ significantly from retained study participants on the basis of receipt of assisted injection at SIS status at the time of their latest study interview. Thus, it is unlikely that selection-attrition biases affected estimates of association.**

In summary, we found that uptake of assisted injection at SIS was relatively low among a cohort of people who require help injecting in Vancouver despite a high prevalence of SIS use. However, the majority of individuals who received injection assistance at SIS reported **having** regularly **engaged** in this practice **at least once during follow-up**. Receipt of injection assistance at SIS was associated with enrolment in MMT and several markers of structural disadvantage and drug-related risk. These findings suggest that accommodating assisted injection within SIS is affording unique opportunities to engage and reduce harms among marginalized and higher-risk subpopulations of PWID in this setting.

Acknowledgments:

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, Vivian Masigan, Ana Prado, Marina Abramishvili, Janet Mok, Carly Hoy, Peter Vann, Jennifer Matthews, and Steve Kain for their research and administrative support. The authors also gratefully acknowledge that this research took place on the unceded traditional territories of the xʷməθkwəy̓əm (Musqueam), Skwxwú7mesh (Squamish), and sel̓íl̓witulh (Tsleil-waututh) Nations. This study was supported by the US National Institutes of Health (U01DA038886, U01DA021525). This research was undertaken, in part, thanks to funding from the Canada Research Chairs program through a Tier 1 Canada Research Chair in Addiction Medicine, which

supports Evan Wood. Mary Clare Kennedy is supported by a Canadian Institutes of Health Research (CIHR) Fellowship Award. Thomas Kerr is supported by a CIHR Foundation grant (20R74326). Kanna Hayashi holds the St. Paul's Hospital Chair in Substance Use Research and is supported by the National Institutes of Drug Abuse (U01DA038886), a CIHR New Investigator Award (MSH-141971), and a Michael Smith Foundation for Health Research (MSFHR) Scholar Award. M-J Milloy 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 license 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 licensed producer of cannabis, and the Government of British Columbia's Ministry of Mental Health and Addictions.

Role of the funding source:

The aforementioned funders had no role in the study design, collection analysis or interpretation of data, writing of the report or decision to submit the article for publication.

Declarations of interest:

M-J Milloy's institution has received an unstructured gift to support his research from NG Biomed, Ltd, an applicant to the Canadian federal government for a license 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 licensed producer of cannabis, and the Government of British Columbia's Ministry of Mental Health and Addictions. Kanna Hayashi 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 Authority, which runs supervised injection services examined in the present study. 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.

Contributors:

MCK conceptualized and designed the statistical analyses with input from TK, conducted the analyses, prepared the original draft of the manuscript, and incorporated edits from all co-authors. MJM, KH, and TK designed and oversee the cohort studies. TK, MJM, KH, EH and EW critically revised the manuscript and contributed important intellectual content. All authors reviewed and approved the final version of the manuscript.

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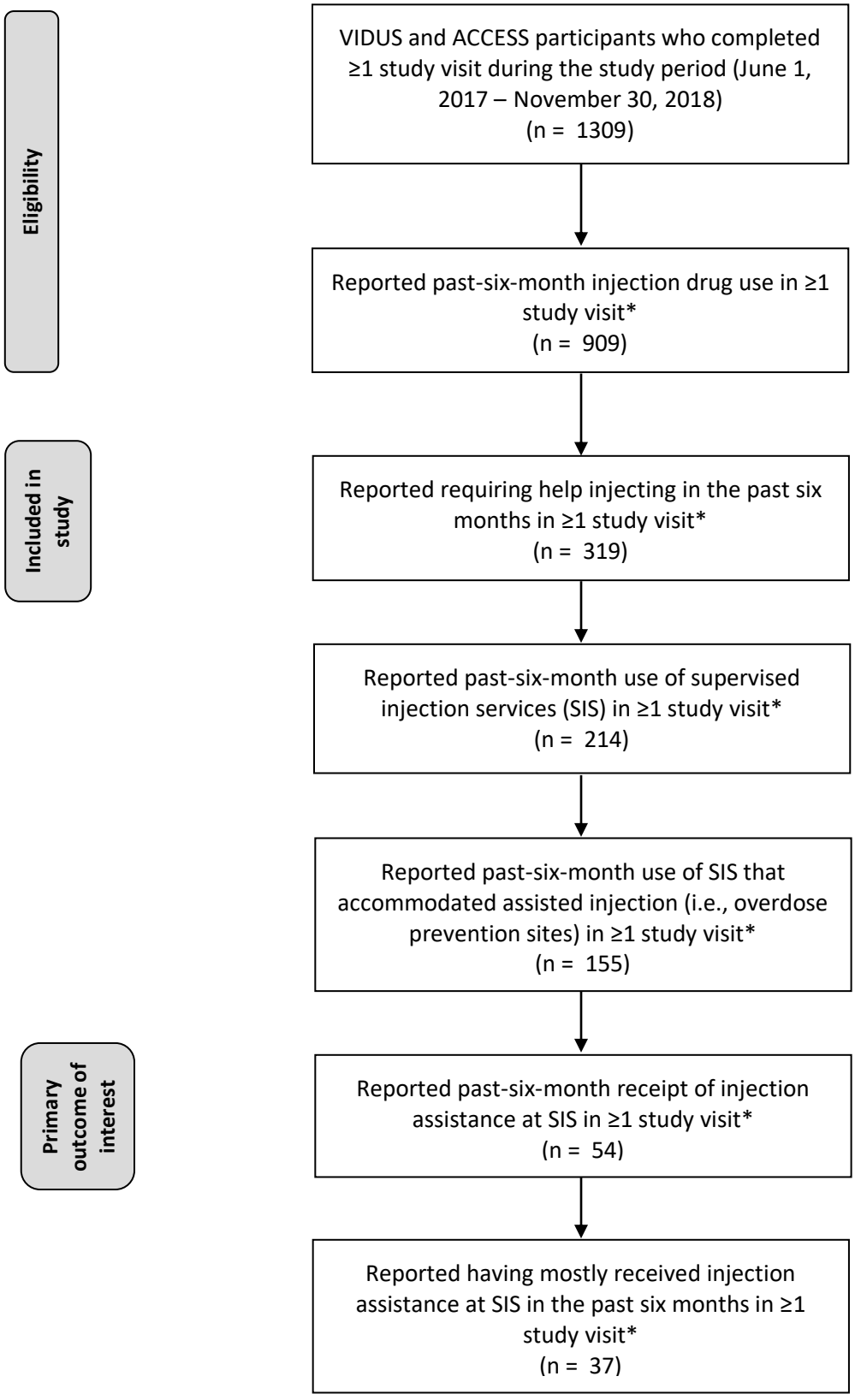
Figure 1: Flow diagram showing the numbers of participants who were included in the study and experienced the outcomes of interest.



*Refers to at least one study visit during the study period (June 1, 2017 – November 30, 2018).

Table 1: Baseline characteristics of 319 people who require help injecting drugs in Vancouver, Canada, stratified by having recently received injection assistance at supervised injection services* (2017-2018).

Characteristic	Yes n (%) *n* = 46	No n (%) *n* = 273	Odds Ratio (95% CI)[‡]	*p* - value
Age (per year older)				
Median (IQR)[†]	41 (32–48)	42 (35–52)	0.98 (0.96 – 1.02)	0.315
Years injecting (per year increase)				
Median (IQR)[†]	14 (5–19)	11 (4–21)	1.00 (0.97 – 1.03)	0.802
Gender				
Men	22 (47.8)	128 (47.9)	1.01 (0.54 – 1.88)	0.989
Women/non-binary genders[#]	24 (52.2)	139 (52.1)		
Ancestry				
White	28 (62.2)	143 (52.8)	1.47 (0.77 – 2.82)	0.241
Non-white	17 (37.8)	128 (47.2)		
Downtown Eastside residence*				
Yes	35 (76.1)	212 (77.7)	0.92 (0.44 – 1.91)	0.814
No	11 (23.9)	61 (22.3)		
Employment*				
Yes	12 (26.1)	44 (16.2)	1.83 (0.88 – 3.81)	0.107
No	34 (73.9)	228 (83.8)		
Homelessness*				
Yes	22 (47.8)	71 (26.2)	2.59 (1.36 – 4.89)	0.004
No	24 (52.2)	200 (73.8)		
HIV seropositivity				
Yes	13 (28.3)	102 (37.4)	0.66 (0.33 – 1.31)	0.237
No	33 (71.7)	171 (62.6)		
HCV seropositivity				
Yes	35 (77.8)	215 (79.3)	0.91 (0.43 – 1.95)	0.812
No	10 (22.2)	56 (20.7)		
Heroin/down injection*				
≥Daily	19 (41.3)	111 (40.7)	1.03 (0.54 – 1.94)	0.934
<Daily	27 (58.7)	162 (59.3)		
Cocaine injection*				
≥Daily	2 (4.4)	12 (4.4)	0.99 (0.21 – 4.57)	1.000
<Daily	44 (95.7)	261 (95.6)		
Crystal methamphetamine injection*				
≥Daily	11 (23.9)	70 (25.6)	0.91 (0.44 – 1.89)	0.803
<Daily	35 (76.1)	203 (74.4)		

Fentanyl injection*				
Yes	9 (19.6)	11 (4.0)	5.80 (2.25 – 14.9)	<0.001
No	37 (80.4)	262 (96.0)		
Public injection*				
Yes	28 (60.9)	128 (46.9)	1.76 (0.93 – 3.34)	0.082
No	18 (39.1)	145 (53.1)		
Non-fatal overdose*				
Yes	19 (41.3)	69 (25.4)	2.07 (1.08 – 3.96)	0.028
No	27 (58.7)	203 (74.6)		
Syringe sharing*				
Yes	41 (89.1)	18 (6.6)	1.73 (0.61 – 4.91)	0.305
No	5 (10.9)	255 (93.4)		
Enrolment in MMT*^				
Yes	26 (56.5)	121 (44.3)	1.63 (0.87 – 3.07)	0.127
No	20 (43.5)	152 (55.7)		
Sex work involvement*				
Yes	7 (15.2)	61 (22.3)	0.62 (0.27 – 1.46)	0.278
No	39 (84.8)	212 (77.7)		
Exposure to violence*				
Yes	14 (30.4)	55 (20.2)	1.73 (0.87 – 3.47)	0.120
No	32 (69.6)	218 (79.9)		
Incarceration*				
Yes	5 (10.9)	25 (9.2)	1.21 (0.44 – 3.34)	0.784
No	41 (89.1)	248 (90.8)		

‡ = confidence interval.
* Refers to activities or experiences in the 6-month period prior to a baseline interview.
† IQR = interquartile range.
# A total of 160 participants were women and 3 had non-binary gender identities.
^ MMT = Methadone maintenance therapy.
Note: not all cells add up to *n* = 319 due to missing values.

Table 2. Bivariable and multivariable generalized estimating equation analyses of factors associated with receiving injection assistance at supervised injection services* among 319 people who require help injecting drugs in Vancouver, Canada (2017-2018).

Characteristic	Unadjusted		Adjusted	
	Odds Ratio (95% CI)	*p* - value	Odds Ratio (95% CI)	*p* - value
Age (per year older)	0.98 (0.95 – 1.01)	0.227		
Years injecting at baseline (per year increase)	0.99 (0.97 – 1.02)	0.677		
Gender (men vs. women/non-binary)	0.81 (0.45 – 1.44)	0.464		
Ancestry (white vs. non-white)	1.66 (0.91 – 3.04)	0.097	1.74 (0.94 – 3.24)	0.080
Downtown Eastside residence* (yes vs. no)	0.88 (0.47 – 1.66)	0.695		
Employment* (yes vs. no)	1.55 (0.79 – 3.03)	0.201		
Homelessness* (yes vs. no)	2.53 (1.43 – 4.49)	0.002	2.04 (1.13 – 3.66)	0.018
HIV seropositivity (yes vs. no)	0.73 (0.39 – 1.35)	0.311		
HCV seropositivity (yes vs. no)	0.78 (0.39 – 1.53)	0.462		
Heroin/down injection* (≥daily vs. <daily)	0.94 (0.53 – 1.67)	0.826		
Cocaine injection* (≥daily vs. <daily)	0.91 (0.24 – 3.49)	0.890		
Crystal methamphetamine injection* (≥daily vs. <daily)	1.24 (0.65 – 2.35)	0.519		
Fentanyl injection* (yes vs. no)	4.23 (1.79 – 10.00)	0.001	3.45 (1.42 – 8.41)	0.006
Public injection* (yes vs. no)	1.77 (1.02 – 3.06)	0.041		
Non-fatal overdose* (yes vs. no)	2.05 (1.17 – 3.59)	0.012	1.86 (1.02 – 3.38)	0.044
Syringe sharing* (yes vs. no)	1.56 (0.57 – 4.27)	0.381		
Enrolment in MMT* (yes vs. no)	1.79 (1.00 – 3.20)	0.049	1.89 (1.03 – 3.47)	0.038
Sex work involvement* (yes vs. no)	0.76 (0.38 – 1.52)	0.436		

Exposure to violence*		
(yes vs. no)	1.74 (0.95 – 3.19)	0.071
Incarceration*		
(yes vs. no)	1.50 (0.60 – 3.70)	0.384

*Refers to the 6-month period prior to a study interview.