Working Paper

Assessing the Evidence on Supervised Drug Consumption Sites

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Preface

Current levels of opioid-related morbidity and mortality in the United States are staggering. Data for 2017 indicate that there were more than 47,000 opioid-involved overdose deaths (roughly similar to deaths from AIDS at its peak in 1995), and 1 in 8 adults now report having had a family member or close friend die from opioids. There has been a near universal call from blue-ribbon commissions and expert panels for increasing access to Food and Drug Administration-approved medications for those with an opioid use disorder; however, jurisdictions addressing opioid use disorder and overdose may wish to consider additional interventions beyond increasing access to these medications. Two interventions that are implemented in some other countries but not in the United States are heroin-assisted treatment (HAT) and supervised consumption sites (SCSs). Given the severity of the opioid crisis, there is urgency to evaluate tools that might reduce its impact and save lives.

This working paper is part of a series of reports assessing the evidence on and arguments made about HAT and SCSs and examining some of the issues associated with implementing them in the United States. The target audiences include decision makers in rural and urban areas grappling with opioids as well as researchers and journalists. This working paper assesses evidence on and arguments made about SCSs. It also offers a descriptive assessment of SCSs and the logic model behind their implementation. The other parts of this series of reports include: (1) a summary report of all the components of the research study; (2) a review of the HAT literature; (3) a report on key informant views on the acceptability and feasibility of implementing HAT and SCSs in selected U.S. jurisdictions heavily affected by the opioid crisis and (4) a report on international experience with the implementation of HAT and SCSs.

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Table of Contents

Figures

Tables

Summary

The drug overdose crisis in the United States is unprecedented. The number of deaths continues to rise each year, now surpassing public health epidemics of prior generations, such as the HIV/AIDS crisis. Outside of the U.S., some jurisdictions have implemented supervised consumption sites (SCSs) in an attempt to reduce overdose deaths, disease transmission, unsafe injection practices, and issues surrounding public drug use. This report assesses the evidence base for SCSs.

We searched the databases PubMed, Embase, Scopus, Web of Science, and WorldCat for peer-reviewed articles and "grey literature" reports published between January 1990 and January 17, 2018. We used the following search terms with wildcard functions: supervised or safe* and injection or injecting or shooting or consumption and facil* or room or gallery or cent* or site or services or space*. We also screened reference lists of systematic reviews and narrative reviews identified during the study selection process to expand our search criteria. (Studies using less rigorous methods are discussed in the Appendix.) Our review of the studies employing "mathematical simulation" methods to evaluate SCSs is based on the articles identified by Kennedy et al. (2017).

Key insights from the review:

1) **Overall, the scientific evidence on the effectiveness of SCSs is limited in quality and number of locations evaluated.** There are no published RCTs evaluating an SCS's impact on individual and population-level outcomes. That is understandable as SCSs are often opened in response to crises, not as part of a research program. It is nonetheless problematic since some estimates of the cost-effectiveness of SCSs presume spillover effects on behavior outside of the SCS, and the extent of those indirect effects is hard to know without a controlled trial. Our review identified nine studies that evaluate the opening of an SCS as natural experiments with comparison cases, but these nine were based on just four SCSs in three cities: Sydney (5), Vancouver (2), and Barcelona (2). Furthermore, there was considerable overlap in the design, methods, authorship, and data employed across various studies, so that four of the nine are arguably superseded by later studies using better methods and/or longer time series, in some sense reducing the effective number of evaluations to five. These studies only covered three outcomes: overdose, disposal of injection material, and crime. We are not aware of any quasi-experimental studies examining the effect of SCSs on treatment uptake or other health outcomes.

   Most reviews of the SCS literature include studies which employ research methodologies that inadequately control for unobserved factors that may bias results. For example, the reviews often include studies that lack comparison groups or only compare frequent SCS users with those who use SCSs less frequently, making them vulnerable to selection bias.

Cross-sectional or simple pre-post studies can provide useful background information about client characteristics, but they are not well-suited for drawing causal inferences regarding the net effects of SCSs.

2) **Estimating the overall effect of SCSs on fatal and non-fatal overdoses is difficult.** Over the past 30 years, thousands of overdoses occurring at SCSs have been reversed; the number in Vancouver's Insite alone exceeded 2,000 in 2017. These figures do not equate to the net population-level effect of operating an SCS since it is impossible to know what would have happened had the SCS never been opened; however, PWUO who overdose in the presence of trained staff equipped with naloxone are much more likely to have it reversed than if they overdosed on the same product without supervision. One method that has been used to address this question compares the trends in overdoses in neighborhoods with and without an SCS, before and after the SCS opened. Our review identified two studies with comparison groups examining fatal population-level overdoses: one based on Vancouver, Canada from 2001-2005 and another focused on New South Wales, Australia (NSW) from 1998-2006. The former reported a significant reduction in fatal drug overdoses in the area surrounding the SCS, the latter did not; however, the latter did identify a significant decrease in opioid-involved emergency service calls in designated treatment areas relative to the rest of the state. Since the SCS in NSW opened during the Australian heroin drought, one must be careful about drawing strong conclusions about quasi-experimental studies conducted during this period.

3) **For drug consumption that is supervised, SCSs reduce the risk of disease transmission and other harms associated with unhygienic drug use practices; however, there is uncertainty about the size of the overall effect**. Cross-sectional studies show that those who visit SCSs frequently also adopt safer injection practices outside the facility than those who come to the SCS less frequently. Some studies presume this difference is caused by the SCS and find that these outside-the-building effects account for most of the SCS's effect on disease transmission. However, the correlation could merely reflect heterogeneity across individuals, with more risk averse users both frequenting SCSs and adopting safer practices outside the SCSs. Furthermore, the mathematical simulation studies of SCSs' effects on disease transmission in a review by Kennedy et al. (2017) were almost all based on one location (Insite in Vancouver), which like many SCSs, offers services beyond supervising consumption and providing sterile equipment for those consumption sessions. For example, Pinkerton (2010, 2011) credits Insite's syringe exchange program (SEP) that provided sterile equipment for use outside of Insite with preventing about 95% of the infections that were prevented by the SEP and SCS functions collectively.

This research on SCSs was mostly conducted in places and times when heroin was not often adulterated with potent synthetic opioids. Fentanyl and its various analogues increase the risk of overdose, which might make supervision more beneficial in places where it has penetrated the market. Another factor to consider is that since fentanyl has a shorter duration of effect compared to traditional illicit opioids, individuals with opioid use disorder may be injecting more

often (Peng & Sandler, 1999; Ciccarone et al., 2017), thus, increasing the number of times each day they put themselves at risk of overdose.

While there is a strong need for rigorous research on the advantages and disadvantages of SCSs, it should be noted that many SCSs have been around for 15 to 30 years and have survived multiple changes in local and national governments. Of course, persistence doesn't imply effectiveness; yet, it seems unlikely that these programs—which were initially controversial in many places—would have such longevity if they had serious adverse consequences for their clients or for their communities. During an emergency such as the present opioid crisis in the U.S., the absence of a large down-side risk for a program that has strong face validity may be sufficient for some decision makers to proceed, rather than waiting for high-quality evidence of the net effects from multiple sites demonstrating positive effects. Indeed, the American Medical Association has recently called for SCS pilot studies. If attempts to implement SCSs in the U.S. are not blocked, we hope a strong research component is incorporated into these efforts.

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Abbreviations

AIDS	acquired immunodeficiency syndrome
ARIMA	Autoregressive Integrated Moving Average
CSA	Controlled Substances Act
DTES	Downtown Eastside Vancouver, Canada
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
HAT	heroin-assisted treatment
HCV	hepatitis C Virus
HIV	human immunodeficiency virus
LAC	Local Area Command
MT	medication treatment
MSIC	Medically Supervised Injecting Centre
NCHECR	National Centre in HIV Epidemiology and Clinical Research
OD	overdose
OPS	overdose prevention site
OUD	opioid use disorder
PWID	people who inject drugs
PWUO	people who use opioids
PWUD	people who use drugs
QALY	quality-adjusted life year
RCT	randomized controlled trial
SCF	supervised consumption facility
SCS	supervised drug consumption site
SEP	syringe or needle exchange program
SEOSI	Scientific Evaluation of Supervised Injection
SIF	supervised injection facility

1. Introduction

Supervised drug consumption sites (SCSs), sometimes known as safe injection facilities or drug consumption rooms) are facilities that aim to reduce the acute and chronic harms from drug use. They are characterized as a low-threshold[1] intervention and aim to attract persons who use drugs in high-risk settings (e.g., chronic heroin, methamphetamine, or cocaine users who typically inject, drug-using sex workers, homeless individuals). They originally focused on reducing the spread of HIV/AIDS, hepatitis C (HCV), and other health and social consequences of unhygienic injection drug use and public consumption (Hedrich, 2004). Indeed, most SCSs still focus on injection drug use, though some allow or include space for drug smoking. SCSs also can be integrated with broader public health and treatment services, by offering treatment referrals, psychosocial services, or basic care of injection-related infections.

With overdose deaths rising sharply—driven in large part by the spread of fentanyl and other synthetic opioids—there is now greater emphasis on preventing overdose. Indeed, some jurisdictions, such as British Columbia, are rapidly deploying Overdose Prevention Sites (OPS) which also supervise drug consumption for purposes of overdose prevention but offer a smaller range of more targeted services compared to traditional SCSs.[2] OPS have not been formally evaluated, so the focus here is on traditional SCSs but some considerations may also apply to OPS.

Officially approved SCSs, either through a waiver or some other agreement with local and/or national authorities, allow people who use drugs to consume illicitly-obtained substances under trained supervision. Like needle or syringe exchange programs (SEP), SCSs are aimed at reducing risks of disease transmission via use of unhygienic needles and at connecting high-risk populations with social services (EMCDDA, 2017). However, they go beyond SEPs in allowing drug use on site so staff can intervene during drug overdoses and to reduce problems associated with public drug consumption.

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[1] The European Centre for Disease Prevention and Control and the European Monitoring Centre for Drugs and Drug Addiction describe low-threshold services as social and health services that aim to reach as many problematic drug users as early as possible in their drug-using careers, and to remain in contact with such individuals to prevent health damage while they continue to use drugs (European Centre for Disease Prevention and Control and European Monitoring Centre for Drugs and Drug Addiction 2011).

[2] Overdose Prevention Sites (OPS) focus on supervision of injections, naloxone and oxygen administration, and calls to 911 services (British Columbia Ministry of Health, 2017),) sometimes in standalone tents on the street or space co-located in public housing facilities. Though these services lack the same legal waivers under federal law that have been granted to many SCS, Ottawa has recognized the provincial power to regulate them when there is a public health emergency.

According to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), SCSs traditionally "represent a local response, closely linked to policy choices made by local stakeholders, based on an evaluation of local need and determined by municipal or regional options" (EMCDDA, 2017). They typically employ a client-oriented service model, sometimes offering a wide array of services beyond sterile needles and a hygienic environment to consume substances, including harm reduction education, access to basic health care, and psychosocial counselling.

Table 1 shows the number of cities and approved SCSs reported to be in operation by country. There are some 90 SCSs facilities in nine countries in Europe, and policymakers in Ireland and Scotland are considering opening facilities in Dublin and Glasgow (EMCDDA, 2017). Outside of Europe there are a growing number of facilities in Canada and Australia, but the number of SCSs worldwide still falls well short of other programs aimed at treating opioid use disorder. For example, there were an estimated 1,500 opioid treatment programs in the U.S. in 2016 (Alderks, 2017).

Discussions of opening SCSs are underway in major U.S. cities, including San Francisco, Seattle, and Philadelphia (Lopez, 2018). Until 2016, Vancouver, Canada was the only site in North America allowed to operate an SCS, but the federal government in Canada has now permitted additional fixed and mobile sites to operate (Wherry, 2017) and others are reported to have operated without official approval for some time (Kral & Davidson, 2017).

Table 1. Supervised Consumption Sites around the world

Country	Cities with SCSs	SCSs operating
Netherlands	25	31
Germany	15	24
Canada*	11 (5 more planned)	20** (11 more planned)
Switzerland	8	12
Spain	7	13
Denmark	4	5
Norway	2	2
France	2	2
Australia	2	2
Luxembourg	1	1 (1 more planned)
Ireland	1 planned	1 planned
Scotland	1 planned	1 planned

*Until 2017, there was only two operational SCSs in Canada.
**British Columbia has also deployed low threshold SCSs in the form of "Overdose Prevention Sites". This count does not include such sites which aim to reduce overdoses by allowing social workers and other injection drug users to set up facilities on the street to monitor injection drug use and distribute/administer naloxone.
Source: EMCDDA (2017); Health Canada (2018)

The arrival of HIV in the 1980s drove the creation of policies aimed at reducing the risk of disease transmission among people who use drugs (PWUD), particularly people who inject drugs (PWID). Though countries expanded medication therapies and outreach services, strict program requirements (abstaining from illicit drug use) or limited availability failed to attract at-risk populations in urban areas like Berne, Zurich, and Hamburg in Europe (Hedrich, 2004). At the same time, some countries began providing sterile syringes to reduce transmission of blood-borne diseases, but that did little to improve the unhygienic environment in which drugs were used or reduce the number of drug overdoses (Hedrich, 2004).

The first recognized SCS opened in Bern, Switzerland in 1986 (Hedrich, 2004). The policy shift emphasized survival and provision of services intended to attract the most at-risk injection drug users (Hedrich, 2004). The objectives were two-fold: to reduce the nuisance generated by public drug use and to reduce the health harms, including number of overdoses and the incidence of new HIV infections. Shortly thereafter, SCSs slowly expanded to other cities in Switzerland. By the mid-1990s cities in Germany and the Netherlands started to incorporate SCSs into local drug policy.

The EMCDDA classifies European SCSs into three models: integrated, specialized, and mobile (EMCDDA, 2017). The majority of SCSs are integrated and offer many other outreach services, such as food, clothing, sterile equipment, counseling, and referrals to drug treatment. Specialized SCSs offer a limited set of services related directly to supervised drug use, including sterile equipment, drug use education, observation, and emergency overdose intervention. Mobile services currently exist in Berlin, Barcelona, and Canada where mobile facilities (such as vans) deploy services to where they are needed. To date, systematic reviews note that studies generally do not account for any design differences between integrated and specialized models (Kennedy et al., 2017). For example, integrated models that offer drug counseling services may have a stronger association with outcomes related to access to treatment than specialized facilities, which limit services to drug use supervision. There is no research on the impact of mobile facilities, though some assessments note that they serve fewer clients (Dietze et al., 2012).

In Europe, access is often limited to registered clients that meet certain age and residency requirements. First time or occasional injection drug users are supposed to be excluded (Hedrich, 2004; Schäffer, Stöver and Weichert, 2014). This is to ensure that SCSs serve the most vulnerable members of drug using populations and do not attract non-injection drug users or minors given public concerns that such policies may be appealing to at-risk non-drug using populations.

Description of supervised consumption sites

Although there are over 100 SCSs operating around the world, two have received the most attention: Vancouver's Insite in Canada and Sydney's Uniting Medically Supervised Injecting

Centre (MSIC) in Australia. Insite is in Vancouver's Downtown East Side—an older and centrally located neighborhood known for high rates of homelessness and injection drug use. Similarly, the MSIC is in Sydney's Kings Cross neighborhood, which has been known for high rates of poverty and drug use.

At both facilities, clients are guided through several stages of service including reception, injection, and after-care that are physically segregated.[3] See Figure A.1 in the Appendix for a schematic of the layout of Sydney's MSIC.

Clients are checked-in, sometimes using a fictitious name or registration number, and health needs may be assessed by staff at reception before they are permitted to enter the injecting stage. Facilities track attendance and ensure that only registered clients are using the facility. During the first stage staff may assess client health needs and eligibility. Insite permits registered clients over the age of 19. At MSIC, clients must be over 18, not pregnant, and not intoxicated before being allowed to inject onsite. Some PWID may enter these facilities to obtain sterile injection equipment or other basic services without proceeding on to the injection room. In this case, the facilities operate like a syringe exchange program.

After reception, clients proceed to the injection part of the facility. Trained staff (sometimes nurses or other medical professionals) monitor clients while they self-administer their own drugs with sterile injection equipment, such as syringes, cookers, filters, water, and tourniquets, which is provided by the SCSs. Staff may also advise on less risky injection practices. Clients and staff are prohibited from administering injections on others. The MSIC maintains a resuscitation room adjacent to the injection area which is used to provide first aid and manage clients experiencing overdose.

The number of injection booths varies across SCSs. Insite has 12, and the MSIC reports eight that can seat two people each. According to a survey of SCSs in Europe, the number of booths range from one to 13, with an average of seven (EMCDDA, 2017). The injection area is designed with safety, sterility, and supervision in mind. In the case of Insite and the MSIC, each booth is separated by a vertical partition. Surfaces in the room are similar to those commonly found in a doctor's office, such as white tile, stainless steel, and vinyl flooring. There is ample lighting, including individual overhead lighting in each booth, as well as a sharps box for proper disposal of injection equipment. Booths are equipped with stainless steel tables anchored to the wall and a chair and are positioned facing outward around a central observation desk, allowing staff to monitor multiple clients simultaneously. Mirrors are positioned facing the client, allowing staff to observe drug consumption from multiple angles. For facilities that allow onsite smoking, segregated smoking areas are equipped with an exhaust vent.

[3] See http://www.communityinsite.ca/what-is-insite.html and https://uniting.org/who-we-help/for-adults/sydney-medically-supervised-injecting-centre/inside-the-medically-supervised-injecting-centre

After injection, clients often spend time in a post-injection after care room where they can rest until they are comfortable leaving. Staff may engage clients, providing outreach and information on social services, drug treatment, detoxification, and counselling. In some cases, staff may also offer basic primary care to treat wounds, abscesses, and other injection-related infections. Clients then leave through a separate exit. Table 2 provides some additional details on each facility.

Table 2. Characteristics of Supervised Consumption Sites in Vancouver and Sydney

	Medically Supervised Injecting Centre	Insite
Location	Kings Cross Neighborhood, Sydney	Downtown Eastside, Vancouver
Year opened	2001	2003
Hours of operation	12 hours a day Monday-Friday and eight hours on the weekends	18 hours, 7 days a week and 24 hours Wednesday to Friday when social assistance is disbursed
Number of booths	8	12
Injection room capacity	16 clients	12 clients
Registered clients (cumulative)	16,142	12,000+
Cumulative supervised injections	More than 1 million	More than 3.6 million
Cumulative overdoses managed	7,428	6,440
Estimated supervised injections per day	180	415
Referrals to health and rehabilitation services (cumulative)	13,000 (Cumulative)	443 (2017 only)
Annual operating cost	$2.77 million Australian in 2008	$3 million Canadian in 2008

Sources: Vancouver Coastal Health (2018); Insite (undated); Uniting (2018); Uniting (2015); Pinkerton (2010); SAHA (2008)

Logic model behind supervised consumption sites

Injection drug use in unhygienic and/or public settings poses risk to the health and wellbeing of people who use drugs and sometimes others. Individual and population-level harms, such as overdose, spread of blood-borne disease among PWID and their sex partners, and social disorder due to public drug consumption generate health, social, and economic costs.

SCSs aim to reduce these harms by engaging high-risk and hard-to-reach drug using populations. Figure 1, adapted from the EMCDDA (2017), shows a basic theoretical logic model regarding SCS objectives and intended outcomes. Taking into account some of the criticisms of SCSs, we have also included a set of hypothesized risks of negative consequences sometimes mentioned by opponents.

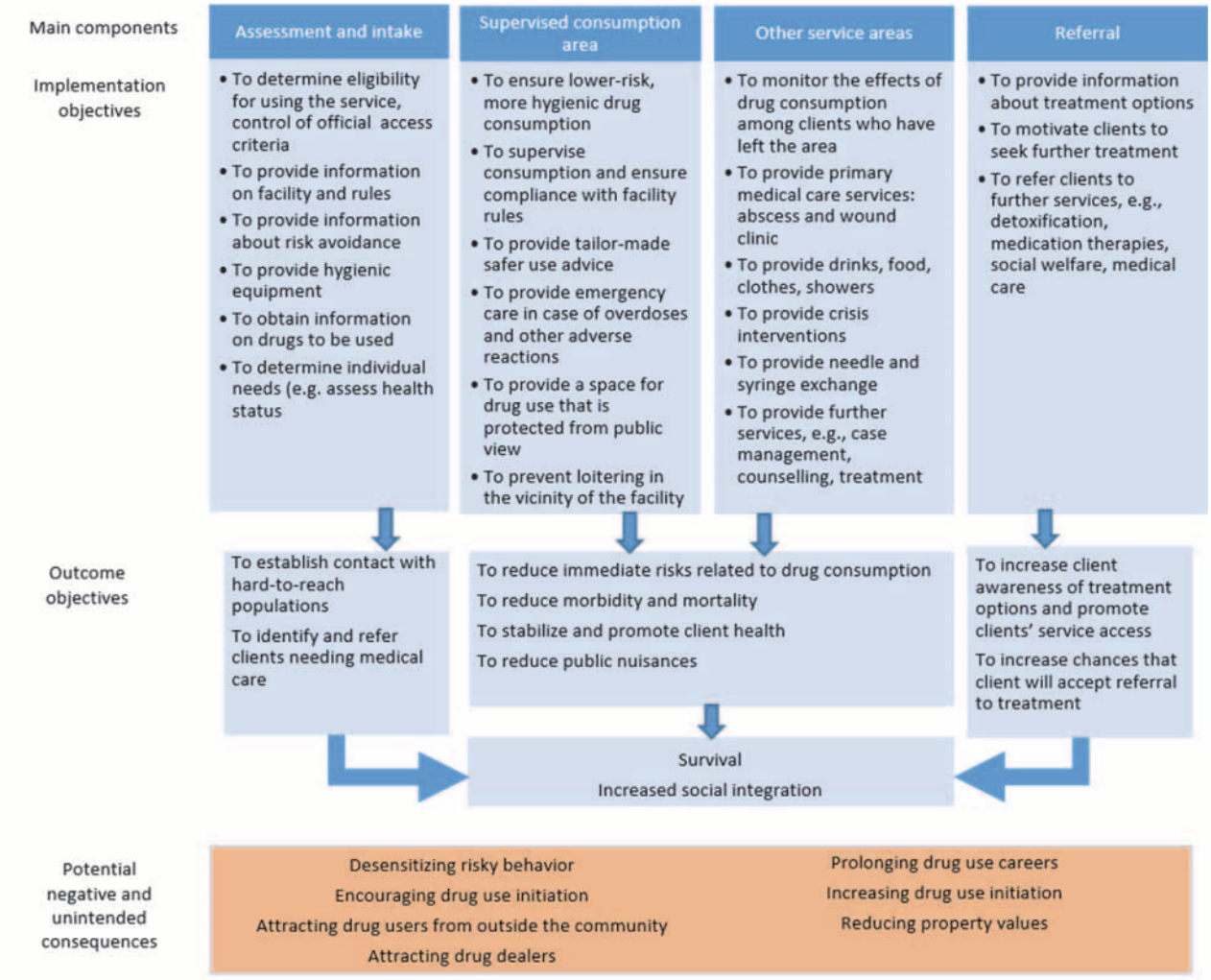
The theoretical model of expected public health outcomes has prima facie validity. Indeed, one can even draw certain parallels with familiar interventions such as chemotherapy and kidney dialysis. In each case, patients visit outpatient facilities designed for the purposes of transfusing medicines and fluids under staff supervision in a sterile setting rather than risk error or harm by letting patients attempt such procedures at home on their own. Individuals injecting street-sourced drugs, who may be homeless, can likewise benefit from such a sterile and safe environment. Further, the increased risk of fatal overdose from the proliferation of potent synthetic opioids may make supervised drug consumption even more relevant to current policy discussions.

However, questions remain surrounding the feasibility and cost-effectiveness of supervised drug consumption under an SCS model. Would the money spent on SCSs be better invested in drug treatment? Are the population-level effects merely the sum of the individual benefits of the SCS intervention? Are they amplified? Do they generate unwanted harms, as feared by some, by prolonging drug using careers, normalizing drug use, or concentrating criminal activity – including the SCS clients' drug suppliers – in one place, with adverse effects on property values and quality of life in the surrounding community?

After more than 30 years of operation, SCS research has generated scores of studies, evaluations, and even some systematic reviews that assess impacts at both the individual and population levels. However, the literature has limitations in terms of methods (making it sometimes difficult to reliably distinguish associations from causal effects), outcomes (e.g., apart from opinion surveys, we did not uncover any systematic assessment of effects on local property values), and limited number of sites studied (the majority of research articles focus on Vancouver's Insite and Sydney's MSIC).

These and other considerations, such as the variation in the quality and potency of drugs in today's markets, may increase the demand for supervision, putting additional strains on SCS capacity and quality of service, and alter its cost-effectiveness relative to other interventions such as treatment and SEP. At the same time, given the augmented risks from potent synthetic opioids, drug supervision and overdose management are likely to benefit at-risk PWID. Therefore, earlier findings may not apply similarly to today's situation.

Figure 1. Logic Model for Supervised Consumption Sites



Source: Adapted from EMCDDA, 2017

Note: This theoretical logic model captures the intended survival and social integration objectives proposed by SCSs proponents as well as the potential negative and unintended consequences highlighted by opponents. Just because an outcome or consequence is listed does not mean there is evidence supporting a causal link.

2. Methods

Search strategy

We searched the research databases PubMed, Embase, Scopus, Web of Science, and WorldCat for peer-reviewed articles and "grey literature"[4] reports published between January 1990 and January 17, 2018. We used the following search terms with wildcard functions: supervised or safe* and injection or injecting or shooting or consumption and facil* or room or gallery or cent* or site or services or space*. We also screened reference lists of systematic reviews and narrative reviews identified during the study selection process to expand our search criteria.

Inclusion and exclusion criteria

Our synthesis aimed at collecting evidence concerning the effects of SCSs on patient- and community-level outcomes. We began by identifying systematic and literature reviews of SCSs, then assessed their individual studies.

To standardize our selection, we first established inclusion criteria. Systematic reviews had to 1) show some systematic search strategy, including key terms and extraction methods; 2) include SCSs (as defined by our search terms to capture their various design names) as an intervention; and 3) report on relevant patient- and community-level outcomes or model the costs associated with SCSs.

Studies that did not explicitly evaluate outcomes relevant to the health, safety, and wellbeing of SCS clients or the broader community were excluded from analysis. Articles that modeled projected cost and outcome measures (e.g., overdoses averted or reductions in HIV transmissions attributed to an SCS) included in systematic reviews depend on parameter estimates drawn from peer-reviewed literature analyzed here. Therefore, we evaluated them separately from outcome studies.

Results were not restricted by language. Nor did our search strategy focus only on systematic reviews. Individual articles assessing SCS-related outcomes not included or mentioned in systematic reviews were also evaluated. Some of these articles were published after systematic reviews and were therefore not captured by earlier publications.

[4] Grey literature refers to sources not published by a commercial publisher, such as government reports, civil society publications, etc. For a more detailed definition, see Grey Literature Report, New York Academy of Medicine, undated.

Study selection process

Search results were first screened by title and abstract by one researcher. Any article considered potentially relevant as a systematic review or individual study was retrieved in full text and reviewed to determine whether it met the selection criteria. Questions about the relevance of any particular reference were resolved through discussion with other research team members.

Data extraction and quality assessment

One reviewer extracted data from each study using an electronic template that was developed for this study prior to the literature search. The template for SCS data extraction was similar to that used for the literature review on prescription heroin (Smart, 2018). Separate templates were used for reviews and for individual studies. Extracted data for reviews included general article information (e.g., authors, year of publication, source of article); research question and/or objective of the review; details on review content (e.g., setting, years and databases searched, study eligibility criteria, number of studies, and number of participants); and information on outcome measures and study conclusions. Extracted data for single studies included similar information except details on study content were focused on study period, study design and analytic approach, definition of intervention, and control groups (where applicable).

Study inclusion

The above-defined search strategy resulted in 3,442 unique articles. A total of 3,292 articles were removed by screening out titles and abstracts that were not specific to supervised illicit drug consumption. The remaining 150 articles pertained to SCS history, outcomes, or focused on public or client opinion. Of those, 80 were commentaries or descriptive in nature (e.g., narratives of SCS adoption and design in different cities, legal descriptive analyses, etc.), and five were systematic reviews (Kerr, Kimber et al., 2007; McNeil and Small 2014; Potier et al. 2014; Garcia 2015; Kennedy et al. 2017), leaving 65 individual studies on SCSs that met our inclusion criteria.

In addition to the five systematic reviews captured in our search of electronic databases, we also evaluated one "grey" literature review from the EMCDDA (Hedrich, 2004). This review included many non-English assessments from preliminary reports in Europe that were not captured by our search (most were not peer-reviewed articles, but government or NGO assessments of SCSs implementation published in languages other than English) and provide some descriptive assessment of SCSs in Europe during the 1990s and early 2000s.

Lastly, one meta-analysis (May, Bennett, and Holloway, 2018) was published in September 2018 and was not captured by our search criteria. The article was shortly retracted by the editors with support from the authors due to "methodological weaknesses of pooling diverse outcomes into a single composite measure." We did not include this paper in our full analysis, though we discuss it briefly in the Appendix.

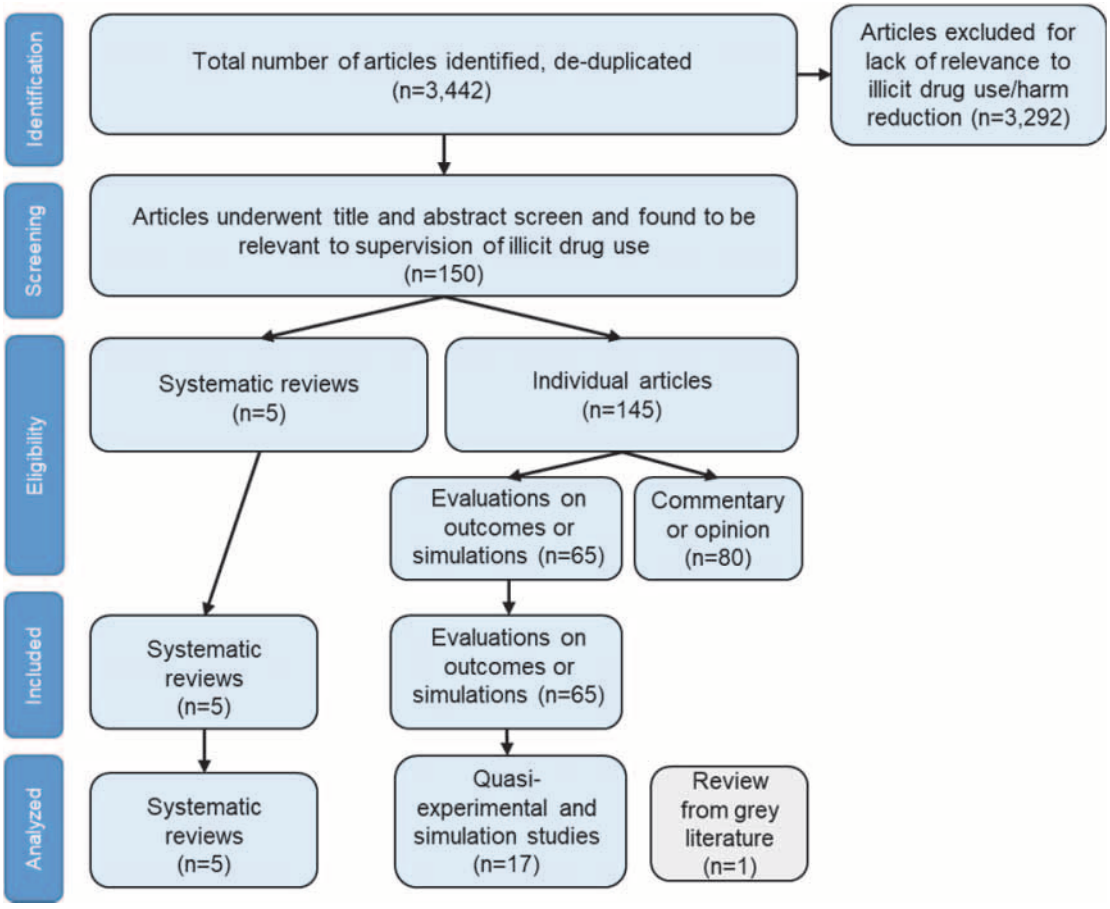
After identifying relevant reviews and individual articles from the peer-reviewed and grey literature, we narrowed our focus of the evidence further by outcomes of interest (e.g., overdose, drug-related crime, access or referral to treatment, changes in risky drug behavior, improperly discarded injection equipment, etc.). We identified 65 unique articles for in-depth analysis based on outcomes of interest and modeling costs (see Appendix for additional information on the studies identified in the literature). After reviewing study research design, we concluded that most studies did not allow for making strong inferences (i.e., those that were cross-sectional or did not include suitable comparison groups from which to draw a counterfactual).

Therefore, we further narrowed our focus to studies that were experimental, quasi-experimental (including natural experiments) studies, and mathematical and simulation models. Of the 65 studies we identified in the literature, none were based on an RCT; nine were natural experiments and nine were simulations or mathematical models assessing the costs and benefits of operational SCSs.[5]

This Working Paper focuses on the nine studies of natural experiments and the eight mathematical or simulation models of population-level outcomes that pertained to existing SCSs. The natural experiments are ecological studies that compare aggregate-level outcomes before and after the opening or operation of an SCS across spatial and temporal units. An overview of other studies is included in the Appendix.

[5] One modeling paper by Jozaghi et al. (2013) projected potential effectiveness of SCS operation in Montreal, which had not yet approved of a facility. We excluded it from analysis as it projected potential impacts in a city without an SCS though it employs similar estimates from other mathematical models evaluated here. There are other simulation studies that project what the benefits might be of opening SCSs in places where they do not exist, but these eight appear to be the primary instances of using such methods to draw inferences from existing SCS.

Figure 2. Flow diagram of study inclusion



Systematic reviews

We identified five systematic or literature reviews captured in our search of the literature level (McNeil and Small 2014; Potier et al. 2014; Garcia 2015; Kennedy et al. 2017; Kerr, Kimber et al., 2007). Readers are referred to the Appendix for more detail. In general, studies evaluated public and SCS client opinions, individual-level outcomes reported by SCS clients (e.g., access or referral to treatment, changes in drug use practices, risky drug use, and social and health outreach), and community-level outcomes (e.g., morbidity and mortality, crime, violence and public disorder). The majority of individual studies come from a handful of sites; almost 80% of the literature base evaluated in systematic reviews come from Insite in Vancouver or the MSIC in Sydney.

Limitations

Before assessing the natural experiments and simulation studies in the literature, we briefly discuss some limitations of research design of the broader SCS literature.

Research design

Generally, the best way to ascertain the causal impact of an intervention is to conduct a randomized control trial (RCT). An RCT randomly assigns participants to a treatment or control group and then compares outcomes across groups after the intervention. Randomization allows researchers to isolate the treatment effect, protecting against selection bias and confounding factors (i.e., unobservable elements correlated with the intervention and the outcome).

None of the studies from the SCS literature were RCTs, perhaps understandably given the nature of the facilities and their services offered. The logistical and ethical concerns of randomizing SCS participation or SCSs facility siting makes studies that employ randomization difficult (Christie et al., 2004), forcing greater reliance on natural experiments. We include an additional discussion of randomization in Chapter 5.

Natural experiments contrast outcomes for cases before and after the application of a treatment intervention (Shadish, Cook, and Campbell, 2002). For example, to isolate the effect of an SCS on overdoses in the community, one approach is to conduct a differences-in-differences analysis. Here researchers compare the trends in overdoses in neighborhoods with and without an SCS, before and after the SCS opened. The inclusion of an appropriate non-treatment case (e.g., a neighborhood without an SCS) attempts to produce a counterfactual trend that controls for other factors, such as seasonality, local cultural attitudes toward public drug use and disorder, or broader trends in the supply of illicit drugs.

Natural experiments can be highly informative but they are not perfect and do not allow for researchers to control all elements. For example, if the treatment and control regions are very different, then even if they are exposed to the same exogenous shocks (besides the treatment intervention itself), they might respond differently to those shocks, and that difference could then wrongly be attributed to the treatment intervention.

We identified nine articles from the SCS literature that met the criteria of a natural experiment. Articles evaluated community-level outcomes before and after the opening of an SCS. These studies compared a treatment area, typically an administrative district where the SCS was sited or a radius around it (500 meters), with a control case, usually the city as a whole or an adjacent neighborhood or district, then compared outcome measures before and after.

Thirty-four other cohort or time-series studies evaluate SCSs outcomes without suitable comparison cases. In eighteen, researchers attempted to fashion a comparison group by dividing SCS clients into low- and high-frequency groups. Sometimes that distinguished those that visit the SCS less than once a week versus those that utilize an SCS more than once a week. Other studies defined high-frequency as utilizing the SCS for more than three-quarters of self-reported injection events. The typical finding was that those who used the SCS more often had better outcomes (e.g., were more likely to be referred to treatment, less likely to share injection equipment, etc.) than those who used the SCS less often. Though these researchers attempted to control for additional observable factors (e.g., age, drug use history, housing status, etc.),

unobservable factors may remain even after such adjustment. For example, those who are more risk averse may be more likely to use the SCS and less likely to share injection equipment but not because of their utilization of an SCS per se. Authors discuss these limitations, noting that causal inferences cannot be drawn and urge caution when interpreting results.

Another 16 of the 34 studies lacked control groups but examined correlates related to self-reported individual behaviors (e.g., risky injection practices, needle sharing, etc.) or community-level outcomes (e.g., number of discarded needles, observed public injections, etc.) associated with use or implementation of an SCS. Though such cross-sectional or time-series evaluations suggest favorable changes or associations in outcomes related to an SCS, lack of a control group limits causal inference. Such changes could be attributed to market-wide phenomena (e.g., changes in the supply of heroin, changes in policing practices, seasonality, etc.) and not due to the SCS.

The remaining articles reported in systematic reviews and captured by our search strategy are descriptive or qualitative in nature. These studies provide insight into practices and attitudes surrounding SCSs, yet do not allow for strong inferences.

That said, it has been noted that no fatal overdose has occurred in an SCS (Hedrich, 2004; Potier et al., 2014). Though obviously an important outcome, it does not speak directly to population-level impacts, which could be larger or smaller, or even to SCS clients' overall risk of overdose since many clients shift only a portion of their drug use into the SCS. Nor does it shed light on whether the number of overdoses averted is large or small compared to the resources expended on the SCS. Hence, we focus here on the nine natural experiments assessing population-level outcomes. These studies each address population-level outcomes, although they vary in rigor, including control designation and estimation strategy, and there is considerable overlap in terms of authors, time periods, and study design.

We also assess eight simulation models that have been included in literature reviews (e.g., Kennedy, Karamouzian and Kerr, 2017; Potier et al., 2014). These models draw their parameter estimates from the literature examined in this working paper and try to address questions such as whether SCSs pass a benefit-cost test, meaning they generate more benefits (in the form of averted harms) than they cost to operate. Naturally these simulation studies inherit the limitations of the literature producing the parameter estimates. Further, all but one of these simulation studies are based on just one SCS: Insite in Vancouver.

Heterogeneity of intervention design

In addition to the varying quality of research design among articles analyzed, it is important to note the variation in SCSs service provision and design. Most studies draw from the experience of Insite in Vancouver and Sydney's MSIC. That can be problematic because not all SCSs are alike; there is no consensus definition of what qualifies as an SCS (Potier et al., 2014). There is considerable heterogeneity in terms of size, staffing, services offered, and patient exclusion criteria. As noted in Chapter 1, the EMCDDA groups SCSs in Europe into three

categories: integrated, specialized, and mobile (EMCDDA, 2017). British Columbia is now deploying Overdose Prevention Sites, a possible fourth and even lower-threshold category. Therefore, findings reported here may not be generalizable to all SCSs. Definitional ambiguity of SCSs and heterogeneity of services provided may help explain some of the mixed findings reported in the literature.

3. Natural experiments

The nine natural experiments that included a non-treatment comparison group examined community-level outcomes, such as overdose events, reported crime, and disposal of injection equipment. Of those, five focused on Sydney's MSIC, two evaluated outcomes related to the operation of Insite in Vancouver, and two evaluated SCSs facilities in Barcelona, Spain. Four studies examined outcomes related to crime, such as criminal incident reports for property or violent crime. Of those, there was considerable overlap among the three articles from Sydney (Donnelly and Mahoney, 2013; Fitzgerald, Burgess and Snowball, 2010; Freeman et al., 2005). Another three articles evaluated overdose outcomes, including fatal overdoses as well as emergency service calls or department episodes. Two examined public nuisance outcomes, such as improperly discarded injection material.

In terms of designating a control case, five evaluations from Sydney compared outcomes in the neighborhood where the SCS was located with aggregate citywide or statewide outcomes (Donnelly and Mahoney, 2013; Fitzgerald, Burgess and Snowball, 2010; Freeman et al., 2005; NCHECR, 2007; Salmon et al., 2010). This may fail to capture local trends or differentiate other factors (e.g., urban renewal programs in a part of the city, construction of new facilities to host the Olympic Games, changes in law enforcement activity, etc.). Three studies from Vancouver and Barcelona designate local control districts, allowing for a more granular analysis (Marshall et al., 2011; Espelt et al., 2017; Myer and Belisle, 2018).

That said, not all evaluations employ the same level of analytical rigor. Some visually inspect outcome trends between treatment and control cases (instead of relying on statistical hypothesis testing) while others use non-parametric hypothesis testing. Few employ more robust estimation techniques, such as a differences-in-differences approach, to calculate the treatment effect that SCSs might have on outcomes of interest.

Table 3 provides a synopsis of the nine natural experiments, including the outcomes of consideration, where the intervention occurred, the time period evaluated, the methods used, the control designation, and the reported findings. These studies only cover three outcomes: overdose, disposal of injection material, and crime. We are not aware of any quasi-experimental studies examining treatment uptake or other health outcomes (e.g., infections and other injuries). Apart from those mentioned below, we did not identify any causal studies that attempt to examine other negative community-level impacts. Though there have been studies evaluating community and public opinion before and after the opening of an SCS, we did not identify any that systematically examined changes in property values or fear of crime. The simulation literature largely focuses on disease transmission and we assess these studies in Chapter 4.

Table 3. Natural experiments of Supervised Consumption Sites

Study	Outcomes Measured	Period	Location	Analytical Method	Treatment designation	Control designation	SCSs association with outcome
Donnelly and Mahoney (2013)	Criminal incident reports and rates of robbery, theft, and drug-specific crime	Jan. 1999 – Dec. 2012	Sydney, Australia	Visual comparison across cases. Non-parametric hypothesis test (tau coefficient) to test within-case changes	Where SCS is located-- Kings Cross neighborhood called "Local Area Command"	Rest of Sydney	No visual difference in reported crime trends incidents between treatment and control case areas. Significant reductions of crime within cases over time
Espelt et al. (2017)	Discarded injection material	2004-2014	Barcelona, Spain	Interrupted time-series, Poisson regression	Districts B and C where SCSs opened	Non-treatment districts in city	Short-term increase in discarded syringes in treatment and control districts, then decrease and stabilization in number of improperly discarded syringes in public spaces across city.
Fitzgerald, Burgess and Snowball (2010)	Criminal incident reports of robbery, theft, and drug-specific crime	Jan. 1999 – Mar. 2010	Sydney, Australia	Visual comparison across cases. Non-parametric hypothesis test (tau coefficient) to test within-case changes	Where SCS is located-- Kings Cross neighborhood called "Local Area Command"	Rest of Sydney	No visual difference in reported theft and robbery incidents between treatment and control case areas. Drug-specific crime stable in treatment area, up in rest of Sydney. Significant reductions of robbery and crime within cases over time
Freeman et al. (2005)	Incidence of drug-related property and violent crime	Sep. 1999 – Oct. 2002	Sydney, Australia	Visual comparison across cases. Time series analysis with a segmented regression approach within treatment case	Where SCS is located-- Kings Cross neighborhood called "Local Area Command"	Rest of Sydney	No visual difference in reported crime trends in treatment and control areas. Regression coefficient indicating operation of SCS not statistically significant with incidence of crime reported in treatment area
Marshall et al. (2011)	Fatal drug overdoses	Jan. 2001 – Dec. 2005	Vancouver, Canada	Non-parametric hypothesis test (Wilcoxon test); non-linear modeling of rate difference pre/post	500 meter radius around SCS	Blocks outside of 500 meter radius of SCS	Significant reductions in the number of overdoses within treatment area compared with rest of city. Reductions in overdose rate in person-years exponentially declines farther from SCS.
Myer and Belisle (2018)	Reported incidence of violent and property crime	Jan. 2002 – Dec. 2004	Vancouver, Canada	Time series analysis using ARIMA to compare changes over time within cases	Police District 1, where SCS is located	Police Districts 2-4	Significant reductions in reported property and violent crime in treatment district after SCS opening. No reported reductions in crime in control districts.
NCHECR (2007)	Fatal overdoses and overdose-	May 1998 – Apr. 2006	Sydney, Australia	Poisson regression to test significance between	Postal zone where SCS is located in Kings Cross	Rest of State of New South Wales	No significant difference in number of fatal overdoses between treatment and control

	initiated emergency service calls			treatment and control cases	neighborhood		areas. Significant difference in decline of emergency service calls in designated treatment area relative to rest of state.
Salmon et al. (2010)	Emergency service calls for opioid-related overdoses	May 1998 to May 2006	Sydney, Australia	Poisson regression to test significance between treatment and control cases	Where SCS is located in Kings Cross neighborhood ; postal zone where SCS is located	Rest of State of New South Wales	Significant difference in decline of emergency service calls in designated treatment area relative to rest of state.
Vecino et al. (2013)	Discarded injection material	2004-2012	Barcelona, Spain	Non-parametric hypothesis test (Mann-Whitney)	Two Districts where SCSs opened	Rest of Barcelona	No significant change in number of improperly discarded syringes in treatment district. Statistically significant reduction of discarded injection equipment across city.

Overdose

One study of overdose-related outcomes cited in the literature comes from a report published in 2007 by the National Centre in HIV Epidemiology and Clinical Research (NCHECR) in Sydney, Australia. The NCHECR report examined the operation of Sydney's SCS, including three monthly overdose-related outcomes between May 1998 and April 2006: ambulance service calls for suspected opioid overdoses (i.e., when naloxone was administered), opioid poisonings presented to emergency departments, and opioid-related overdose deaths. Researchers compared fatal opioid overdoses and ambulance service calls for opioid overdose in the Kings Cross vicinity (broadly captured in two postal codes: one where the SCS was located and a neighboring area) and the rest of the state of New South Wales. The study did not include a control case for emergency department presentations for opioids overdose, though researchers evaluated this change before and after the opening of the SCS in Kings Cross.

Monthly counts for each case area were calculated and compared between the 36-month pre-treatment period and the 60-month post-treatment period after the opening of the SCS in Kings Cross. Researchers used a Poisson regression to test significance with interactions between time period and location for ambulance service calls and fatal overdoses before and after opening of the SCS. Authors further examined ambulance service calls by separate postal code, examining in closer detail the postal code that housed the SCS.

The report found substantial declines in all three outcomes over time. Authors note that the declining availability of heroin in Australia coincided with the opening of the SCS in Kings Cross. Nevertheless, there was a statistically significantly different rate of decline in ambulance service calls in the treatment-designated areas compared with the rest of New South Wales. The monthly rate of service calls declined by two-thirds in the treatment area and by about 60 percent

in the rest of New South Wales. Both of these declines were significant within each case. The results from the Poisson regression with locality and period interactions shows that these differences are statistically significant between treatment and control cases ($p=0.002$).

Researchers then compared outcomes specific to each postal code. They found that the magnitude of decline was greatest in the postal code that included all of the Kings Cross neighborhood (i.e., where the SCS was sited). When comparing ambulance service calls from just the postal code where the SCS was located to the rest of New South Wales (including the other postal code originally designated as treatment) they report a much larger effect size. After the SCS opened, average monthly service calls dropped 80 percent in the postal code with the SCS compared to 60 percent in the rest of New South Wales. The difference between the two was tested with Poisson regression and found to be statistically significant ($p<0.001$).

When looking at overdose-related deaths, the NCHECR report found similar reductions in both the treatment and control areas. After the opening of the SCS, monthly overdose deaths declined by about 70 percent in both areas. Researchers report that there was no statistically significant difference in rates of decline in overdose deaths between treatment and control cases ($p=0.88$). They note that the declining availability of heroin across the region is likely to have disproportionately impacted outcomes evaluated and may have hampered their assessment (NCHECR, 2007).

Lastly, authors evaluated the changes in opioid poisoning presentations at emergency departments in two hospitals near Kings Cross in Sydney. They did not evaluate outcome measures in a control case, but noted that opioid emergency department episodes declined by 35 percent after opening of the SCS. Yet, these changes could be attributed to declining heroin availability throughout the region.

Compared to visual inspection, the NCHECR report is more analytically robust. The specification of time and location interaction terms in their Poisson regression allows for measuring the difference before and after as well as across treatment and control cases, allowing for stronger inferences. Though the evaluation is complicated by the Australian heroin drought, the NCHECR report showed significantly greater declines in ambulance service calls for opioid-suspected overdoses in the postal code where the SCS is located compared with the rest of the state. Changes in the monthly average of fatal overdoses were similar across both cases and not significantly different.

That said, the use of statewide outcomes as a control may have complicated the analysis. It is unlikely that the state as a whole was reasonably similar to the Kings Cross area. Shifting drug consumption patterns or attitudes toward drug use elsewhere in the state (outside of Sydney) may have resulted in a greater rate of ambulance service calls for suspected drug overdoses. It is conceivable that those unaccustomed to witnessing a suspected drug overdose in suburban parts of the state may be more inclined to call emergency services. Further, the study cannot account for any possible changes in ambulance service protocols in either the treatment area or the rest of the state. In addition to this limitation, authors noted that treatment designated areas are

approximations at best, as they cover large and diverse areas around where the SCS is sited. Therefore, a stronger analysis would employ more precise treatment and control case designations.

In a peer-reviewed article, Salmon et al. (2010) build from the NCHECR report. In fact, authors of the NCHECR report were also co-authors of this study. Here authors narrowed their scope to ambulance service calls for suspected opioid overdoses in the vicinity of the SCS in Kings Cross (the same two postal codes) and the rest of the state of New South Wales from May 1998 to May 2006 (the same time period covered by NCHECR, 2007). Opioid-related overdoses were defined as those that required naloxone.

The authors employed the same empirical specification. First, they calculated the average monthly rate of calls in both the treatment and control areas before and after the opening of the SCS, then tested if the changes in rates were significantly different using Poisson regression with an interaction term for time period and location. They broke down outcome events by time (during or outside the SCS's operating hours) for further analysis.

Their results were the same as those found in the NCHECR report: ambulance service calls decreased by 68 percent in the vicinity of the two postal codes around the SCS compared to a 61 percent decline in the rest of the state. These differences are statistically significant from each other ($p=0.002$) (Salmon et al., 2010). These results were greater when comparing the immediate postal code (where the SCS was sited) to the rest of the state (80 percent decline versus a 60 percent decline; $p <0.001$). The effect size varied when examining outcomes during hours of operation. The greatest decline in ambulance calls for suspected opioid overdoses occurred in the postal code where the SCS was located and during the SCS hours of operation (80 percent). Outside of hours of operation, overdoses declined slightly less (70 percent). This difference was statistically significant ($p <0.001$). The magnitude in decline in calls for non-treatment areas (either the neighboring postal code or the rest of the state) was also significantly greater during hours of operation.

Though authors reported a significant decline in ambulance service calls for opioid overdose, the analysis is confounded by much of the same limitations and threats to validity found in the NCHECR report—namely, the designation of treatment and control cases as well as the confounding effect of the Australian heroin drought, which the authors mention.

One study published in *The Lancet* evaluated the spatial-temporal nature of drug overdose deaths (not limited to opioids) in Vancouver, Canada after the city opened its first SCS in September 2003. Authors examined population-based fatal overdose rates and the location (address, postal code, or descriptive geographic identifier) of death reported in British Columbia Coroners Services records from January 2001 to December 2005. Authors state that location data is accurate down to the one-block level, allowing for reasonable spatial analysis.

Researchers first calculated person-years at risk of overdose at the smallest geographic unit for which population data was available from Statistics Canada, in this case a city block. Authors summed each year's population for each of the geographical units for one period before the

opening of the SCS and another period after the SCS (from 1 January 2001 to 20 September 2003; 21 September 2003 to 31 December 2005). Intercensal population counts between 2001 and 2006 were linearly interpolated. In doing so, authors assume that individuals are facing a constant risk of overdose throughout each period.[6]

Authors determined that approximately 70 percent of registered SCS clients live within four blocks (i.e., 500 meters) of the facility. Therefore a 500-meter radius around the SCS was designated as the treatment area. Authors compared the socio-demographic characteristics of the 290 decedents who succumbed to a fatal drug overdose within and outside the 500-meter radius. Decedents farther away from the facility during the post-treatment period were more likely to be female ($p = 0.005$) and of First Nations ancestry ($p = 0.04$), but otherwise did not differ significantly from those that died within 500 meters of the facility after the SCS opened.

Authors evaluated seasonality via ANOVA and report that overdoses did not vary significantly when collapsed into three-month periods ($p=0.78$). To account for changes in methadone provision around the SCS, authors randomly sampled SCS participants enrolled in the Scientific Evaluation of Supervised Injection (SEOSI) study to evaluate any differences in methadone expansion between those living in treatment or control-designated areas. Baseline rates of methadone enrollment were similar (23.4 vs 23.9 percent; $p = 0.84$) for those living within 500 meters of the SCS compared to those outside that radius. Upon follow-up, authors report that trends in proportion of methadone participants did not vary significantly between the two areas over time ($p=0.833$).

Authors report that the overdose rate within 500 meters of the facility significantly declined by about 35 percent (from 253.8 to 165.1 overdoses per 100,000 person-years, $p<0.05$). Beyond 500 meters, drug overdoses dropped by 9.3 percent (from 7.6 to 6.9 overdoses per 100,000 person-years, $p=0.49$), but this decline was not significant. Authors conducted a spatial assessment of the rate difference in overdose deaths at the census tract level before and after the opening of the SCS. Distance was measured as the Euclidian shortest path between the SCS and the centroid of the census tract where the fatal overdose occurred. The rate difference in overdose mortality, calculated as the difference in fatal overdose rate before and after the opening of the SCS, was modeled with an exponential fit. Authors report that the model of best fit (R^2 of 0.58) shows that the observed rate difference is minimal further than 500 meters and negligible beyond 1000 meters (Marshall et al., 2011).

Unlike the studies from Australia, heroin supply in Vancouver did not abruptly change. This helps to isolate the relationship that SCS had on population-level mortality. Nevertheless, authors assume that overdose risk is constant for all individuals in the same census tract over time and that population counts of hard-to-reach, drug-using populations are accurate. Likewise, shifts in

[6] This may be less of a concern when there is little variation in the supply of illicit opioids. However, given the variability of consistency and potency in today's illicit markets, such an assumption may not hold.

overdose rates may be attributable to neighborhood-level changes not accounted for, such as changes in police activity, introduction of a potent batch of drugs in one locality, or migration into and out of the indigent community in the Downtown Eastside. Though authors recognize these limitations, they suggest that neither factor is likely to have occurred though emphasize caution in interpretation.[7]

Disposal of injection material

One study from Barcelona, Spain examined improper disposal of injection material using a quasi-experimental design, comparing outcomes before and after the opening of the city's SCSs across various districts in the city. Vecino et al. (2013) examined the number of improperly disposed injection material remitted to public health authorities by municipal cleaning crews, parks and service employees, community educators, and the general public in five districts in the city. The monthly series ran from July 2004 to June 2012 for three districts (Ciutat Vella, Sants-Montjuïc, and Nou Barris); the program was expanded to the Sant Andreu district in March 2007 and to Sant Marti in March 2008 through until June 2012.

During this period two SCSs were opened or expanded, in Ciutat Vella in December 2004 and in Sant Marti in December 2011. Throughout various periods, police sweeps were carried out to reduce open-air drug use and distribution: Nou Barris and Ciutat Vella from November 2005 to February 2006; Sants-Montjuic in June 2008; Ciutat Vella from August to October 2008 and again in February 2009; and Sant Andreu in December 2011. Except for the last police operation in December 2011, none of the police operations overlapped with the expansion or opening of an SCS.

Authors compared the monthly count of improperly disposed syringes delivered to public officials six months before each intervention in each district with the count from the following six months using non-parametric hypothesis tests. The staggered nature of the opening or expansion of SCSs facilities in Barcelona allows for multiple treatment cases (in this case in Ciutat Vella and Sant Marti).

They reported that the number of improperly disposed syringes in the Ciutat Vella district did not significantly change after versus before its SCS facility expanded in December 2004. However, the number of improperly disposed needles declined by 20 percent across the city ($p< 0.01$) and the district's share of all improperly disposed needles collected in Barcelona increased by a third ($p<0.001$). When examining the other case of opening an SCS in Sant Marti in December 2011, authors reported that the number of improperly disposed syringes did not significantly change (counts were small). During this period, police undertook a counterdrug

[7] Authors state, "Regarding the potential for the ecological fallacy (i.e., the primary unit of analysis was an aggregated measure as opposed to an individual-level estimate of risk), we emphasize that the nature of our results requires caution in interpretation" (Marshall et al., 2011, p. 1435).

operation in the neighboring Sant Andreu district, which may confound results. However, the number of improperly disposed needles declined by 10 percent across the city ($p<0.001$) and the district's share of all publicly disposed needles collected in the city doubled from 10 to 22 percent ($p<0.001$) (Vecino et al., 2013).The results are counterintuitive as one might have expected that individuals would be more inclined to properly dispose their injection equipment in an SCS.

According to public health data, authors note that the number of injection drug users remained stable throughout the evaluation period. They conclude that changes in the number of improperly disposed syringes in the city, which declined from over 13,000 to 3,200 over eight years, may be due to successive police sweeps and the opening and expansion of SCSs.

Nevertheless, several limitations remain. Authors were unable to control for the effect that police sweeps had, especially when Sant Marti opened its SCS while Sant Andreu experienced police activity. These operations may have had a confounding effect in that time period as well as a run-up effect by changing user habits and practices with regard to public drug use and possession of injection equipment. Likewise, the citywide control case ignores any developments at the district level (e.g., district-level public events/festivals that may displace drug users from public spaces, etc.). Though pre-and post-treatment periods were six months long, authors did not control for short-term seasonality that might impact public drug use, such as changes in weather or tourist season.

Another natural experiment from Barcelona expanded on Vecino et al. (2013) and found very different results. Espelt et al. (2017) examined the monthly counts of publicly discarded syringes across the same five districts from June 2004 to December 2014. Authors examined the impact of various policy interventions, including the opening or expansion of SCS facilities as well as police sweeps. Unlike Vecino et al. (2013), this study included additional covariates to control for underlying drug use trends (e.g., number of individuals in opioid outpatient treatment, monthly percentage of distributed syringes not returned, and number of overdose deaths). Authors employed an interrupted time-series analysis with Poisson regression, allowing them to control for underlying trends and seasonal patterns.

Results from Espelt et al. (2017) show that after opening an SCS in District B in December 2004, the number of improperly disposed injection materials significantly declined (RR = 0.96; 95%CI = 0.94-0.98) in that District, but remained the same in Districts A and E. After an additional SCSs opening in District C in December 2010, the number of improperly discarded injection equipment sharply and significantly rose in that district (RR = 2.72; 95%CI = 1.57–4.71), but stabilized shortly thereafter (RR = 0.97; 95%CI = 0.91–1.03); the trend in publicly disposed injection equipment across other districts was stable, with the exception of neighboring District D, which saw a significant decline (RR = 0.95; 95%CI = 0.90–0.99).

The authors stated that results vary by intervention, with police sweeps likely to displace the number of publicly discarded injection materials to neighboring districts, but that opening of harm reduction centers may be followed by a short-term increase in discarded needles in the

treatment district and a citywide decline (Espelt et al., 2017). However, authors note that short-term increases in the number of discarded injection equipment in districts that opened SCSs could be due to the attraction of injection drug users who seek to use these or other harm reduction services located at the SCS. It remains unclear given the mixed effects reported in Districts B and C, with one seeing a modest decline in improperly disposed injection material while another seeing a large increase.

We note that there is a discrepancy between Vecino et al. (2013) and Espelt et al. (2017) with regard to the opening of an SCS in Sant Marti (District C). Vecino et al. (2013) notes that the SCS opened in December 2011, at the same time as a police operation in neighboring Sant Andreau (District D). However, Espelt et al. (2017) reports that the SCS opened in District C (Sant Marti) in December 2010, but the police operation in District D (Sant Andreau) occurred in December 2011. We were unable to determine the reason behind this discrepancy.

Though Espelt et al. (2017) build from Vecino et al. (2013) and control for seasonality and underlying trends, the study has limitations. Authors are unable to make strong inferences given the design of their analysis. Though overall numbers of publicly discarded syringes declined over the period, police operations aimed at public drug use and distribution may, in part, be driving this finding.

Crime

In addition to outcomes related to overdose and disposal of injection equipment, the literature evaluates several natural experiments related to the opening of an SCS for impacts on crime. We explore their findings here.

Freeman et al. (2005) examined trends in theft and robbery incidents reported to police before and after the opening of Sydney's SCS in May 2001 in the Kings Cross neighborhood. Authors used monthly administrative police data on reported thefts and robberies as a proxy for acquisitive drug crime, yet recognized that there was no way of confirming if an incident was related to drug use. The monthly series ran from January 1999 to September 2002.

Authors used a segmented regression approach, with ordinary least squares, to estimate the changes in drug acquisition crimes within the Kings Cross police-designated Local Area Command (LAC) after the opening of the SCS. Given that the Australian heroin drought started in January 2001 (Weatherburn et al., 2002), authors attempt to control for these market-wide effects by including terms to capture when the drought was ongoing. Counts of robberies and thefts for the rest of Sydney were used to visually compare trends across treatment and control cases. Authors did not employ a differences-in-differences approach to isolate the treatment effect, but rather a time series analysis of before and after trends within Kings Cross LAC, visually comparing those trends against the incidents of reported crime elsewhere in the city.

They observed an immediate increase in the number of acquisitive drug crime in both the Kings Cross LAC and the rest of Sydney after the heroin drought started, followed by an overall

downward trend throughout the rest of the series. Authors reported no significant change in the number of reported thefts or robberies in the Kings Cross LAC after opening the SCS. A visual comparison of trends in the LAC and the rest of Sydney showed that crime trends were broadly similar, leading authors to conclude that crime trends are neither positively or negatively related with the opening and operation of the SCS in Kings Cross (Freeman et al., 2005).

This early evaluation included a non-treatment comparison case. Yet authors visually compared trends in the treatment and comparison case instead of estimating the relationship using a traditional difference-in-differences statistical approach. Also, the Australian heroin drought remains a major potential confounder since it started several months before the SCS opened in Sydney. The drought brought overall declines in crime and drug trends across the entire country, but can be expected to affect different areas differently depending on their relative concentrations of heroin users, which may complicate interpretation.

Building off Freeman et al. (2005), Fitzgerald, Burgess, and Snowball (2010) obtained monthly incident counts for robberies, thefts, and illicit drug-specific crime (offenses related to supply or possession of amphetamines, cocaine, or narcotics) for the Kings Cross LAC as well as all of Sydney from January 1999 to March 2010, giving them a longer follow up period. Theft and robbery offenses were further broken down by category: robbery with a firearm, robbery without a weapon, breaking and entering, motor vehicle theft, theft from store, etc.

Similar to Freeman et al. (2005), Fitzgerald et al. visually compared the monthly incident counts, and they also calculated the within-case difference in the number of recorded robbery, theft, and illicit drug offenses between when the SCS opened in May 2001 and March 2010 across both cases. They then used a non-parametric test (Kendall's rank correlation) to determine if changes within each case area were statistically significant. It should be noted that authors only tested whether the change in crimes *within* an area changed over time and not the difference *between* treatment and control cases.

Fitzgerald, Burgess, and Snowball (2010) showed that trends in robbery and theft offenses were quite similar between the Kings Cross LAC and the rest of Sydney. Since the beginning of the heroin drought in 2001, robbery and theft offenses had declined.

However, when examining offense categories in finer detail, robbery with a firearm was stable in Kings Cross LAC but declined in the rest of Sydney and the number of retail thefts was up in Kings Cross LAC but stable in the rest of Sydney. Of the drug-specific offenses, five of six were stable between May 2001 and March 2010 in Kings Cross LAC. Offenses for possession or use of cocaine was up for both Kings Cross LAC and the rest of Sydney. Drug-specific crimes in the rest of Sydney went up overall between May 2001 and March 2010.

Fitzgerald et al. (2010) concluded the operation of the SCS has not had an undesirable impact on robbery, theft, or drug-specific offenses in Kings Cross LAC. Yet authors urge caution when interpreting some findings, especially counts of drug-specific offenses, which may have resulted from changes in law enforcement activity rather than changes in the underlying criminal activity.

Donnelly and Mahoney (2013) extend the data series and analysis through 2012 for both the Kings Cross LAC and the rest of Sydney. Researchers visually compared monthly incident counts for three offenses (robbery, theft, and drug-specific violations). Total numbers of offenses were assessed using a non-parametric test (Kendall's rank correlation) to determine if there was a statistically significant change in offense counts within an area between May 2001 and December 2012. Given the long-time series, authors also compared rates of incidents per 100,000 residents to account for any diverging changes in population density between Kings Cross and the rest of Sydney.

For robberies and thefts, authors report that incidents declined in both Kings Cross LAC and the rest of Sydney. When breaking out theft offenses by category, authors show that thefts from retail stores increased in Kings Cross LAC but remained stable in the rest of Sydney. The reported incidents of drug-specific offenses in Kings Cross and the rest of Sydney moved in tandem. Between January 1999 and January 2001 reported drug offenses declined in both Kings Cross LAC and the rest of Sydney, then remained flat from 2002 to 2009, after which they started to increase.

Analysis over longer time periods suggests slightly diverging trends. Drug-specific crime incidents significantly declined in Kings Cross LAC until December 2004 and remained flat from January 2005 until December 2008, significantly rising from January 2009 until December 2012. In contrast, drug-specific crime in the rest of Sydney was flat from January 1999 until December 2004, significantly rising slightly from January 2005 until December 2008. From January 2009 to December 2012 drug-specific offenses rose faster than in the previous period. These trends held for per capita rates in both Kings Cross LAC and the rest of Sydney (Donnelly and Mahoney, 2013). Drug-specific crime trends varied by type of drug, with possession of narcotics significantly up in Kings Cross LAC but stable in the rest of Sydney. Arrests for dealing cocaine was significantly down in Kings Cross LAC but significantly up in the rest of the city. Arrests for dealing in narcotics or amphetamines was stable in Kings Cross LAC but down or up, respectively, in the rest of Sydney. Again, authors caution that police activity may have had more to do with the diverging trends than the SCS.

Authors concluded that Sydney's SCS had no unwanted impact on acquisitive drug crime and little evidence that it had an adverse impact on drug-specific crime. Drug-specific crimes did start rising in 2009 in Kings Cross LAC, but they also did in the rest of the city, suggesting other factors. Much like the previous two crime analyses from Sydney, Donnelly and Mahoney (2013) did not apply a more rigorous statistical methodology that would allow for stronger inference. Like earlier papers, they do not control for law enforcement activity or other potential confounding factors. Similarly, the non-parametric hypothesis test, Kendall's tau, did not account for seasonal variation or auto-correlated nature of time series data.

As far as the Australian evaluations, all three reported similar trends in crime between Kings Cross LAC and the rest of Sydney. Only Freeman et al. (2005) report no changes in reported crime trends over time in either case, but this is in part due to the short period of analysis (1999

to 2002). Fitzgerald, Burgess, and Snowball (2010) and Donnelly and Mahoney (2013) report that incidents of crime decline over time for both the Kings Cross LAC and the rest of Sydney.

In a more recent analysis of crime trends in Vancouver, Myer and Belisle (2018) assessed weekly counts of reported violent and property crimes in four police districts (one of which housed the SCS) between the first week in January 2002 and the last week in December 2004. The city's SCS opened in September 2003, allowing for a before and after assessment across smaller units of analysis. In total, there were 178 time periods (89 pre-treatment and 89 post-treatment) across four districts and the city as a whole. Authors suggested that examining outcomes across police districts rather than the city as a whole avoids overlooking underlying or local processes that are not captured when looking at trends at the citywide level (Myer and Belisle, 2018).

Myer and Belisle used an Autoregressive Integrated Moving Average (ARIMA) technique to account for the autoregressive and non-stationary nature of time series data. In short, previous counts of reported crime are likely to predict current counts and elements of seasonality introduce fluctuations over time. ARIMA can help to reduce the influence of these factors to improve estimation. Aggregating reported crime incidents by police district allows researchers to evaluate the changes over time within a treatment district as well as three control districts. In police district 1, where the SCS was sited, reported incidents of both property and violent crime significantly declined between the pre-treatment and post-treatment periods; all crimes declined by 42 incidents a week, violent crimes (robbery and assault) declined by 6 incidents a week, and property crimes (breaking and entering, theft from vehicle, and mischief) declined by 35 incidents a week. Authors reported that these changes were abrupt and permanent. No statistically significant change in reported crime was found in any of the other police districts designated as controls or the city as a whole (Myer and Belisle, 2018).

Authors reported these statistically significant trends for the treatment case, suggesting two plausible mechanisms of action: that the SCS reduced predatory crime of drug users by providing protection to vulnerable individuals and that perhaps the SCS increased provision of services, reducing acquisitive crime. Unlike Donnelly and Mahoney (2013) or Fitzgerald, Burgess, and Snowball (2010), Myer and Belisle (2018) did not assess the counts of drug-specific crime (e.g., drug possession and distribution crime), though they evaluated changes in total crime (which includes drug-specific crimes).

Overall, three of the four studies suggest that there was no association between the opening of Sydney's SCS and trends in incidents of robbery or theft, but they do not employ more rigorous estimation strategies (Freeman et al. 2005; Fitzgerald, Burgess, and Snowball 2010; Donnelly and Mahoney 2013). Myer and Belisle (2018) compare trends across police districts in Vancouver rather than aggregating a control case to the citywide level. Further, their use of ARIMA is a more appropriate specification for the time series nature of their data. This last study reported that property, violent, and total crime significantly declined in the police district where the SCS was located whereas no change was reported in other police districts in

Vancouver over the same period. Authors suggested that this may indicate a negative relationship between SCS operation and reported crimes.

4. Mathematical and simulation studies

Kennedy et al.'s (2017) review of the SCS literature discusses eight studies they describe as "mathematical simulations" and whose results make statements about outcomes such as overdose deaths and/or HIV infections averted by SCSs for injection drug use, plus one that looks at a safe smoking facility in Vancouver. These papers vary substantially in the type of analysis and conclusions drawn, so we describe them in some detail.

The oldest (Hedrich, 2004) is a literature review that contains a simple estimate of overdoses averted in Germany, which Kennedy et al. (2017, p.164) describe as finding that "An estimated > 10 [overdose] deaths are prevented by SCFs [supervised consumption facilities] in Germany each year." The analysis underpinning that conclusion is just that (Hedrich, 2004, p.53) "at least 500,000 drug consumptions are supervised per year. … Assuming that one 'person-year of active use' are 1000 consumptions (= two to three per day), these are 500 person years. Applying a mortality rate of 2% … at least 10 deaths per year could be prevented." In other words, the "model" consists of assuming the mortality rate is 2% per 1,000 drug use episodes outside the SCS and 0% in the SCS.

At the other end of the spectrum, Bayoumi and Zaric (2008) is truly a simulation in the sense of projecting the state of a "system" (the HIV epidemic) as it progresses over time (10-year horizon) both with and without an SCS (specifically Vancouver's Insite). They use a "compartment model" to track how many people are in various states defined by their HIV status (present or absent), HCV status (present or absent), and drug use status (non-user, user in methadone treatment, user not in treatment).

Bayoumi and Zaric's (2008) base assumption is that 21% of the 7,000 injection drug users in Vancouver use Insite regularly (self-report "all, most or some injection" were at the facility) and this reduced their needle sharing outside of the facility by 70%. (In extensions they also considered what would happen if Insite increased referrals to treatment and safe injection practices when syringes were shared.) Their base case result was the prevention of 1,191 new HIV cases over 10 years or 119 per year, on average. They report the operating cost for safe injection as $2.95 million, so the cost per case of HIV averted is about $25,000, making the operation highly cost-beneficial.

The literature has been sharply critical of this model's projections. Des Jarlais et al. (2008) note that "the model generates an incidence rate of HIV infection of 5-6 per 100 person-years" whereas the actual rate in Vancouver before Insite opened was only 1-2 per 100 person-years (or as much as 2-3 per 100 person-years allowing for cohort effects). Des Jarlais et al. (2008) do not question that Insite is cost-effective; they just believe that Bayoumi and Zaric's model is unduly optimistic and suggest that 20-30 HIV cases averted per year may be more realistic.

Pinkerton (2010) likewise observes that Bayoumi and Zaric's (2008) model projected an increase in HIV prevalence even with Insite in operation (from about 18% to 40% over 10 years), whereas there was in fact "no evidence of rapid growth in the epidemic among Vancouver IDUs (injection drug users) in recent years" (p. 1430). Andresen and Jozaghi (2012, p.3533) call Bayoumi and Zaric's numbers "quite simply too good to be true", observing that in "the five years before Insite opened, there were [only] approximately 140 new cases of HIV related to IDUs" in all of British Columbia. So the model predicted that Insite eliminated 80% of HIV infections in the province even though it only hosted 5% of the injections.

Studies that use simulation only to surround point estimates with ranges

The remaining six models reviewed by Kennedy et al. (2017) use simulation in a narrower sense just to describe how uncertainty in parameter values translates into uncertainty about bottom line results. The next article chronologically was Milloy et al. (2008). Describing it gives a concrete sense of the general character of the modeling in the remaining six papers.

Milloy et al. (2008) estimate overdose deaths averted by Vancouver's Insite as the number of potentially fatal overdoses that occurred within the facility (453 over approximately four years) divided by the ratio of non-fatal to fatal overdose observed in the area generally. They conclude that in Vancouver there were 5.6 fatal overdoses per 1,000 person-years of injection drug use, apparently by starting with counts of drug-induced deaths and making assumptions about the proportion that were from overdose and the number of PWID. They cite "various official and peer-reviewed sources" as placing the non-fatal overdose rate at between 50 and 300 non-fatal overdoses per 1,000 person-years, implying that there are about 50 / 5.6 = 9 to 300 / 5.6 = 54 nonfatal overdoses for every fatal OD. Dividing the 453 potentially fatal OD events at Insite by these ratios, they reason that Insite saved between 453 / 54 = 8 and 453 / 9 = 51 overdose deaths over those years (so 1.9 – 11.7 per year).

This is a sensible back of the envelope calculation, but the only way that simulation entered was for exploring how uncertainty about parameter values translates into uncertainty about conclusions. For example, the lower estimate of 1.9 overdose deaths prevented per year comes with a range of 1.5 – 2.4 OD deaths averted per year, and the higher estimates of 11.7 deaths averted per year has a corresponding range of 5.4 – 18.0.

Four of the remaining five papers Kennedy et al. (2017) label as mathematical simulations also analyze Vancouver's Insite. They fall into two groups of two. The two written by Andresen (and co-authors) assume that Insite favorably changes risky injection practices outside of Insite's walls, whereas Pinkerton (2010 & 2011) more conservatively assumes that the SCS aspect of Insite only affects the injections that occur within Insite.

Naturally, the Andresen papers conclude that Insite averts more HIV cases per year (35 per year in Andresen and Boyd (2010); 22 in Andresen and Jozaghi (2012)) than does Pinkerton (2.8 in his 2010 paper, revised upward to 5.2 per year in his 2011 paper). On the other hand,

Pinkerton (2010 and 2011) estimates that a separate program run by Insite, its needle/syringe exchange program (NEP), averts 80+ HIV infections per year. Thus, Pinkerton also concludes that Insite as a whole is extremely cost-effective, but the SCS component of Insite much less so.

We return below to this crucial question of whether to credit Insite's SCS function with changing risky injection behavior outside of its walls, after first describing these studies and some of their potential limitations in detail.

Andresen and Boyd (2010) estimate the benefit of Insite as:

$$(overdose\ deaths\ averted \times\ social\ cost\ per\ overdose\ death) + (HIV\ deaths\ averted \times\ social\ cost\ per\ HIV\ death)$$

OD deaths averted is computed in a manner reminiscent of Hedrich (2004). The authors note that there were 50 OD deaths in Vancouver and the Downtown Eastside (DTES) has 42% of Vancouver's IDUs, so they assume the DTES had 50 * 42% = 21 of those deaths. Concluding that the DTES had 4,565,000 injections, they reason the OD death risk is 21 / 4,565,000 = 4.6 per million injections or about one-quarter Hedrich's (2004) assumption of 20 per million consumption episodes. Andresen and Boyd (2010) reason that if the 236,520 injections that took place at Insite had been unsupervised, there would have been 4.6 * 0.2365 = 1.088 additional deaths.

Reasoning based on averages can generate incorrect inferences if there is heterogeneity across users. Perhaps some DTES PWID are at lower and some are at higher risk of fatal OD. If it was the lower [higher] risk PWID who were in sufficient control of their actions to make use of Insite's services then applying the average risk of 4.6 per million injections might overstate [understate] Insite's benefits. Nonetheless this seems like a sensible calculation, and is perhaps conservative in excluding (as does much of the literature) potential effects on non-fatal overdoses.

By contrast, Andresen and Boyd's (2010, p.72) calculation of "prevention of deaths attributable to new HIV infections" is harder to follow. The authors observe that "In 2002, 5.1 percent of illicit drug related deaths [in Canada overall] were attributable to HIV infections." They then estimate the number of HIV infections averted and assume that "number of deaths prevented is simply 5.1 percent of the number of new HIV infections prevented." This seems problematic since the first sentence implies that 5.1% = P{ attributable to HIV | illicit drug related death }, not that P{ death | HIV due to drug use }.[8]

[8] Andresen and Boyd (2010) also appear to have a small error in their calculation of the cost per death. They compute the social cost per death based on lost earnings. Specifically, they multiply the average annual income in the province ($33,640) by the number of years of life lost before retirement age (65), discounting at 3% per year and recognizing that the average age of Insite users is 35. For OD deaths this simply sums the 30 (discounted) years

Furthermore, Andresen and Boyd's estimate that Insite prevents 35 HIV infections per year (based on an average of four mathematical models) is sharply criticized by Pinkerton (2011), who argues that several of those models and calculations were inappropriate and/or not replicable.

Pinkerton (2010) introduces another approach, which he revised the next year (Pinkerton, 2011). It uses a simplified version of Kaplan's (1994) 'needle circulation theory' model to separately estimate the effects of Insite's SCS and its syringe exchange program (SEP). He argues that closing Insite would increase the number of HIV infections 83.5 per year but credits supervising consumptions with averting only 2.8 of those infections per year. He says the discounted total cost of medical care per new HIV infection is $210,555 (CA$ in 2008), so that savings of 2.8 * $210,555 = $589,554 is well short of Insite's annual budget. But Insite overall is cost saving since 83.5 * $210,555 = $17.6M greatly exceeds the cost of operating Insite.[9]

Pinkerton (2011, p.183) increases from 2.8 to 5.2 the estimated number of HIV infections averted per year through Insite's supervision of injection because "the previous [2010] analysis did not take into account the reduction in the contamination rate amongst circulating syringes due to the reduced number of 'street' injections. Otherwise the two models are formally equivalent."

Andresen and Jozaghi (2012) reprise one of the four models used by Andresen and Boyd (2010) with revised parameter values. They note that with Andresen and Boyd's (2010) parameters, that model made the unrealistic prediction of 165 new HIV cases per year in the DTES, whereas there were actually only 108 per year in all of British Columbia. After Andresen and Jozaghi (2012) changed the parameter values to get more plausible results, the model credits Insite with averting 22 new HIV cases per year.

Finally, the eighth simulation study reviewed by Kennedy et al. (2017) was a very similar analysis but of Vancouver's unsanctioned safe *smoking* facility (SSF) for crack users, which supervised 23,120 crack smoking sessions per year, out of an estimated 15.8 million such sessions (Jozaghi, 2014). It concluded that the SSF was highly cost-beneficial at preventing HCV infection, in part because it was run informally by volunteers and so had very low operating costs.

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from age 35 to 65, producing a total of 19.6 discounted years times $33,640 or about $660,000. For HIV deaths, they note that people survive for 10 years, so they only sum 20 years, but instead of summing the (discounted) years 11-30 they sum years 1-20. So they (incorrectly) count that death as losing 14.9 (discounted) years at $33,640 per year or about $500,000.

[9] The focus here is on SCS, not NEP, but we note Pinkerton (2010) assumes that PWID who are not using the SEP only acquire 15 syringes per year. If, as assumed, they are injecting three times per day, then those syringes are used an average of 73 times before being discarded, which may be high. If Pinkerton underestimates how many syringes PWID acquire outside of NEP, then his model over-estimates the number of infections averted by Insite's NEP.

The evidence for SCSs inducing behavioral change outside of the facility

To summarize, there is a sharp disagreement among the simulation studies as to how many HIV infections Insite prevents by supervising drug consumption (as opposed to its SEP-like function of providing sterile equipment for use outside of the facility). Andresen's two papers conclude it is many: 35 per year in Andresen & Boyd (2010) and 22 per year in Andresen & Jozaghi (2012). Pinkerton concludes it is few: 2.8 per year in Pinkerton (2010) and 5.2 per year by Pinkerton (2011). If the discounted total cost of medical care per new HIV infection is in fact on the order of $200,000, then who is right matters for whether Insite is cost-effective through this effect.

The papers use different models, but a primary driver of the differences is disagreement about the strength of the empirical evidence for what effect, if any, Insite's SCS has on the number of risky injections *outside of* the SCS facility.

The authors of these studies understand this. Andresen and Jozaghi (2012, p.3540) summarize: "if one accepts the scientific research regarding behavioural changes (decreased risky behavior such as needle sharing) in the IDU [injection drug using] population, there is a strong case for maintaining Insite" but "All expansions of Insite that do not consider additional behavioural changes in the IDU population only averted one or two new HIV infections per year, [yielding] 0.11 and 0.21 benefit-cost ratios, respectively. These latter numbers are more in line with those of Pinkerton (2010, 2011)."

In defending the presumption that Insite changes drug use behavior that it does not supervise, Andresen and Boyd (2010) note that Kerr et al. (2005) "found attendance at Insite significantly reduced needle sharing: Insite PWID share needles at 0.30 the frequency of non-Insite PWIDs. The [Sydney] MSIC Evaluation Committee (2003) also found a reduction in injecting risk behaviour after the establishment of a supervised injection facility (Sydney, Australia), but no significant changes in needle sharing. Despite the goodness of fit reported by Kerr et al. (2005) we wished to be conservative and so considered 50 percent of their reported effect on needle sharing as our benchmark, an odds-ratio of 0.60." Andresen and Jozaghi (2012) also cite Kerr et al. (2005), among other studies, but dispense with the conservativism and set that parameter at 0.30, not 0.60.

Pinkerton (2011) argues that: "no empirical data are available to quantify the magnitude of this reduction (if any). Kerr, Tyndall, Li, Montaner and Wood (2005) found that Vancouver IDUs who reported that "some, most, or all" of their injections took place at the Insite SIF were 70% less likely than other injection drug users to have borrowed or lent a syringe in the past 6 months. However, a 70% reduction in the prevalence of borrowing or lending does not imply an equivalent reduction in the borrowing rate." That is, Pinkerton notes the distinction between the proportion of people who borrow or lend and the change in the number of instances in which a syringe was borrowed or lent.

Since much hinges on this parameter, it is worth recapping Kerr et al.'s (2005) methods. Kerr et al. obtained data on a cohort study of 431 active injection drug users in Vancouver, 90 of whom (20.9%) "reported that all, most, or some of their injections were at the safer injection facility" and 49 of whom reported sharing syringes at some point during the six-month period from December 1, 2003 to June 1, 2004. A logistic regression predicting whether the individual shared syringes at any point over that six months found that those 90 had an adjusted odds ratio of 0.30 (CI 0.11 – 0.82, p = 0.02) of being as likely to have shared, i.e., a 70% reduction relative to the referent group.

Thus, the critical 0.3 odds-ratio is not very precisely measured. Nor does it come from comparing SCS clients with non-clients, but rather those that report frequently injecting at Insite versus those that report infrequent or no injection at Insite.

Kerr et al. (2005) "realise that despite multivariate adjustment, our findings could be due to residual confounding if the safer injection facility had selected injection drug users who were inherently at a lower risk of syringe sharing." They argue that this may not be a major concern because in September (2003), just *before* Insite opened, "the rates of syringe sharing were similar in these populations" so "the differences only emerged during follow-up after the facility had opened". Still, Kerr et al. (2005) admit that "our study is limited by its cross-sectional design and hence we caution against inferring such a causal relation" while at the same time observing that "ethical issues will probably prevent interventional study designs." Furthermore, other cross-sectional studies conducted in other places have reached similar conclusions (e.g., Bravo et al., 2009).

The difference between Pinkerton's pessimistic conclusions about Insite's SCS and Andresen and others' optimistic conclusions hinges importantly on whether one interprets that odds ratio as capturing a causal effect of Insite on behavior outside of the facility.

That Kerr et al. say the differences across groups were not apparent in September 2003 is important evidence supporting a causal interpretation, but it is not dispositive for at least two reasons. First, it has long been understood that drug using careers are chaotic, and even dependent heroin users go through phases of greater and lesser use, and greater and lesser stability in their lives (Preble & Casey, 1969; Johnson, 1978; Kaplan, 1983; Hser et al., 2007). Some PWID who were stable and not sharing in September 2003 may have started sharing by December 2003 and vice versa. If so, then there could still be a selection bias, with the more stable users both refraining from sharing and having the wherewithal to take their drugs to Insite before using them.

Second, even if Insite did cause changes in behavior outside of its walls, that does not necessarily mean it was the supervision of consumption that effected that change. Insite offered a range of services, and it is hard to know whether the supervision of consumption should get credit. Perhaps those who visited Insite often shared less when they used outside of Insite because frequent visits gave them convenient access to Insite's NEP, and their reduced sharing should be credited to Insite's distribution of sterile injection equipment, not its supervision of

drug consumption. (Pinkerton [2010] reports that Insite distributed about 1.3 million syringes for use outside its walls, vs. just 0.2 million for drug consumption that was supervised on site.)

There is no way to resolve this issue, but it is worth remembering when interpreting Kennedy et al.'s (2017, p.177) summary of cost-effectiveness results: "A total of six studies have evaluated the cost-effectiveness of SCFs, all of which were conducted in Vancouver". One was Jozaghi's (2014) study of an unsanctioned SCF for smoking, but the other "Five studies examined the impacts of Insite and found it to be cost-effective". Of the five, one (Bayoumi and Zaric) has been rejected by subsequent authors, two (those by Andresen) depend on a causal interpretation of Kerr et al.'s (2005) 0.30 odds ratio, and two (those by Pinkerton) conclude that Insite was cost-effective primarily because of its SEP, and not because of its supervision of consumption. Hence, the actual strength of the evidence may be slightly less compelling than one could infer from a quick reading of Kennedy et al. (2017).

5. Conclusions from a limited evidence base

We identified 65 articles for inclusion. Of those, eight were simulation or mathematical models of existing SCSs and 57 were outcome-related articles relevant to SCSs, but none involved a randomized controlled trial and just nine employed a quasi-experimental design (or natural experiment) with control groups. We examined in detail the nine quasi-experimental articles and the eight mathematical/simulation modeling studies, noting problems or limitations with them.

The nine studies of natural experiments came from just three cities. Specifically, five were from Sydney, two from Vancouver, and two from Barcelona. They examined community-level outcomes related to overdose, discarded injection equipment, or crime using varying analytical approaches. Some earlier studies merely visually compared outcomes between treatment and control cases; later studies applied more formal statistical methods.

Furthermore, not all these studies were independent. In some cases, subsequent studies examined the same intervention and outcome variables, just with a longer time series and (sometimes) more sophisticated methods. For example, the three studies examining crime outcomes of the MSIC in Sydney were very similar. In particular, they report that changes in thefts, robberies, and drug-law violations where the SCS was located were similar to changes in the rest of the city, suggesting a null effect.

By contrast, the one study from Vancouver of SCS's effect on crime used a more rigorous analytical design that accounted for underlying trends and seasonality. It found that there was an abrupt and permanent decline in property and violent crime in the police district where the SCS was located vis-à-vis elsewhere in the city.

Two (overlapping) studies from Sydney that examine overdose-involved outcomes did not find a statistically significant effect on fatal overdoses, but did find a statistically significant negative relationship with ambulance service calls for suspected opioid-involved overdoses. That SCS opened around the same time there was a severe shortage of heroin in Australia's drug markets, so overdose-involved outcomes fell precipitously in the control areas and even more precipitously near the SCS. The analysis did employ a control group area, but the control (the state of New South Wales as a whole) is not a perfect comparator to the treatment area, so it is not inconceivable that an exogenous shock as dramatic as the Australian heroin drought might have affected the SCS site's neighborhood differently than it affected other parts of the state, though the effect was strongest during the facility's hours of operation.

The Vancouver study of overdose outcomes was even more positive about SCS's effects. Although overdose fell somewhat in the control areas, declines around the time and place the SCS opened were much greater, with the rate of decline in fatal overdoses falling exponentially

the farther from the facility. Yet as of this writing, Marshall et al. (2011) appears to be the only study that shows a favorable finding of an SCS reducing fatal overdoses at the population-level.

The last two studies analyzed SCSs in Barcelona. They produced somewhat inconsistent results despite being very similar. Vecino et al. (2013) found no significant change in the number of improperly discarded syringes in the treatment district, but they did report a statistically significant reduction of discarded injection equipment across the city. Espelt et al. (2017) used a more rigorous research design, specifically an uninterrupted time series with Poisson regression and additional control covariates. The results for the two locations evaluated were different than in Vecino et al. and different from each other. After an SCS opened in Ciutat Vella, authors report a significant but modest reduction in the number of publicly disposed injection materials in that district, with no changes in neighboring districts. Yet, after the opening of an SCS in Sant Marti, they find a significant and substantial *increase* in publicly disposed injection material. Authors note that simultaneous police sweeps focused on public drug use may have confounded their analysis.

Selection of control cases is also limited in these studies. Six of the nine studies use either the rest of the city or the state as a control case when comparing outcomes in the treatment area. Three evaluate outcomes in other districts within the city or in one case outside a 500-meter radius from the SCS. Greater precision in control case designation (i.e., one that ensures controls are reasonably similar to the treatment case) can reduce the potential for confounding effects. Using a large control case, such as a city or state, makes it harder to rule out alternative explanations for any observed differences.

We urge caution when interpreting this literature evaluating the opening of SCSs as natural experiments and similarly urge caution with regard to the eight studies labelled as mathematical simulations in Kennedy et al.'s (2017) review. Only one was really a simulation in the sense of simulating the evolution of the state of some system (such as the HIV epidemic) over time both with and without the SCS, and that study has been challenged as producing implausible results. The others used simulation primarily to explore the implications of uncertainty about parameters.

With the exception of Hedrich (2004), which assumed that using drugs in an SCS cut the mortality risk from 2% per 1,000 use sessions to zero, and Jozaghi (2014), which examined a small, unsanctioned supervised *smoking* facility for crack users, all of these papers pertain to just one SCS, the Insite facility in Vancouver.

Milloy et al. (2008) estimate the number of fatal overdoses averted by dividing the number of near fatal overdoses within the SCS by the ratio of near fatal to fatal overdoses, but that ratio is unknown, with plausible values differing by a factor of six, so the resulting point estimates vary dramatically (from 1.9 to 11.7 deaths averted per year), and uncertainty about other parameters renders those point estimates into ranges, e.g., the 11.7 comes with a plausible range from 5.4 to 18.0.

The four modeling studies of Insite's effects on HIV transmission split into two camps that disagree. Andresen and Boyd (2010) and Andresen & Jozaghi (2012) assume that people who

perform all, most, or some of their injections at Insite also behave much more safely when they inject outside the SCS, and their papers credit Insite's SCS with averting 35 and 22 new HIV infections per year, respectively.

Pinkerton (2010, 2011) is sharply critical of Andresen and Boyd in particular, criticizing the models (which indeed seem to have some errors) and the assumption of behavioral effects extending beyond Insite's walls. Pinkerton's 2010 and 2011 papers take a more conservative approach and credit Insite's supervision of consumption with averting only 2.8 and 5.2 new HIV infections per year, respectively, probably not enough to make Insite cost-effective on those grounds. However, Pinkerton believes that Insite's SEP program is much more successful at preventing HIV infection.

This crucial division about whether SCSs induce behavioral effects that manifest outside the SCSs boils down to how one interprets findings such as those reported by Kerr et al. (2005). Indeed, Kerr et al. caution that "our study is limited by its cross-sectional design and hence we caution against inferring such a causal relation." Kerr et al. (2005) estimate that those who report using the SCS for all, most, or some of their injections are 70% less likely to report having shared injection equipment, but Pinkerton (2011) notes there is a difference between the proportion of people who have shared and the number of instances of sharing. Furthermore, even if Insite caused the behavioral change, it is not clear how one could know that Insite's SCS should get the credit, as opposed to its SEP or some other component of its multi-faceted operation.

In sum, even though reviews such as Kennedy et al. (2017) report that "high-quality scientific evidence derived from the observational and simulation studies included in this review demonstrates the effectiveness of SCFs in meeting their primary public health and order objectives" and "Five [modeling] studies examined the impacts of Insite and found it to be cost-effective," the modeling studies are perhaps somewhat less persuasive when one examines closely their methods and assumptions regarding key parameters.

Our search also identified eighteen studies that compared outcomes across non-suitable comparison groups (e.g., dividing clients based on SCS utilization frequency rather than comparing SCS clients to non-clients). This bifurcation allows for comparisons across high- and low-frequency SCS clients, but it could introduce a substantial amount of selection bias, complicating interpretation. Alternatives could explain what researchers observed in these studies that report favorable findings. For example, it is possible that drug users that utilize an SCS more frequently are inherently risk averse or reasonably stable in their drug using career and thus avoid risky practices, like needle sharing. Another sixteen studies were cross-sectional, precluding any causal inferences, or evaluated community-level outcomes without any control case. The remainder of the fifty-seven individual studies identified were descriptive or qualitative in nature. Further, there is no standard definition of what comprises an SCS and there may be considerable heterogeneity of services provided at facilities. This may limit the generalizability of the studies of such interventions.

Overall, the scientific evidence about the effectiveness of SCSs is limited in quality and number of locations evaluated. This is an important factor when considering allocation of resources. Given the magnitude of today's overdose crisis, public resources, including scarce municipal funds, are best allocated to interventions that produce the greatest reduction in harm (e.g., fatal overdoses) per dollar spent. As an illustration, suppose a city decides to spend $3 million to address opioid problems. That is roughly the annual operating cost of Insite and MSIC. Its leaders may wonder how those dollars should be allocated to maximize the social benefit: Set up an SCS? Fund methadone treatment? Expand EMS services? Purchase and distribute more naloxone in the community? A combination of these activities? Something else? The same question can be asked, albeit less precisely, in terms of political energy and capital. The existing literature cannot answer these questions.

There is debate about the level of proof policy makers should demand concerning the effectiveness of SCSs. One view is that SCSs should be subject to the same evidentiary standards as any other health intervention. To simplify, that means RCTs are the gold standard and quasi-experiments can be informative, but associations (e.g., in cross-sectional analyses) are not taken as strong evidence of causality. Another view argues for lower standards of proof given a) the urgency of the present crisis, b) the fact that SCSs were created in response to health crises, not as part of research studies, c) it can be difficult to research controversial interventions focused on stigmatized populations,[10] and d) the logic model underpinning the direct effects of SCSs is clear. When consumption leads to overdose in an SCS, prompt intervention is undertaken to manage the patient; indeed, there are no known overdose deaths from consumption inside an SCS (Hedrich, 2004; Potier et al., 2014). Likewise, injections within the SCS are done with sterile equipment, effectively eliminating the spread of blood-borne diseases and other harms from unhygienic injection – from those supervised use sessions. (Many SCS clients also continue to inject drugs outside of the SCS; see e.g., Kimber et al., 2003)

Scores of RCTs have been conducted on methadone, and our literature review identified 10 RCTs for HAT. Given that an increasing number of jurisdictions are considering SCS pilots, one or more may want to consider launching that pilot in a way that supports an RCT or strong quasi-experimental evaluation. As with syringe exchange programs, discussions of using randomization to evaluate SCSs raise questions about whether this would be ethical. While it is common in studies of medication to randomly assign participants to the promising drug or another medication (or placebo), those who believe that SCSs reduce overdose deaths could argue that it is unethical to deny access to this intervention, including to members of a study's control group. There may be ways to address this problem, and we sketch a few possibilities here.

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[10] One of our reviewers offered an insightful reminder: "It is important to recall that the US federal government for most of the past 30 years has prohibited funding to SEPs and prohibited funding of research on SEPs for much of this time as well. Developing evidence in support of these programs has been challenging as a consequence."

In places where resource constraints imply that an SCS will not be able to serve everyone interested in using the service, researchers may be able to leverage this scarcity. One approach, which can be controversial, is a wait-list study. In such a study design, those who express interest in using an SCS are randomly assigned to immediate access or to a wait list; those in the wait list group will eventually receive SCS services, just not immediately. This approach has been used in the drug treatment literature and can be useful for measuring the individual-level effects of an intervention (see e.g., Mattick et al., 2002; Magill & Ray, 2009).

A less controversial approach would be a multi-site stepped-wedge cluster randomized trial which is sometimes used to evaluate service delivery interventions (Hemming et al., 2015).[11] With this approach, all sites will eventually get the treatment—in this case an SCS—but the treatment is phased in over time. In some ways this is similar to a wait-list design, but it is neighborhoods or communities, not individuals, that wait for a facility to be available. Even if randomization is not possible, much can be learned from rigorous quasi-experimental studies that compare neighborhood-level outcomes in places with and without an SCS.

Regardless of whether an RCT or quasi-experimental approach is employed, it would be extremely useful to collect individual-level data on PWUO in the treatment and control regions before and after the SCS opens. One approach could use respondent driven sampling (RDS) to approximate a random sample of PWUO in each area (Heckathorn, 1997; Heckathorn & Cameron, 2017) and then follow them over time.[12]

One important caveat should be made regarding any analysis of the historical literature: Times have changed. Most research has evaluated SCSs prior to the spread of potent synthetic opioids. Fentanyl and its various analogues may change the profile of individuals at risk of overdose (i.e., opioid naïve drug users or recent initiates without a substance use disorder) as well as the way individuals respond to developments in the supply of drugs in illicit markets. For one, the potency of these substances increases the risk of overdose during any given use event, increasing the number of overdoses prevented per use session supervised. Another factor to consider is that since fentanyl has a shorter duration of effect compared to traditional illicit

[11] From Hemming et al.: "The stepped wedge cluster randomised controlled trial is a relatively new study design that is increasing in popularity. It is an alternative to parallel cluster trial designs, which are commonly used for the evaluation of service delivery or policy interventions delivered at the level of the cluster. The design includes an initial period in which no clusters are exposed to the intervention. Subsequently, at regular intervals (the "steps") one cluster (or a group of clusters) is randomised to cross from the control to the intervention under evaluation. This process continues until all clusters have crossed over to be exposed to the intervention. At the end of the study there will be a period when all clusters are exposed. Data collection continues throughout the study, so that each cluster contributes observations under both control and intervention observation periods. It is a pragmatic study design, giving great potential for robust scientific evaluations that might otherwise not be possible."

[12] A number of studies have used RDS to obtain information from PWUO (e.g., Paquette et al. 2016; Ober et al., 2016). These individuals are typically compensated for their interviews as well as for recruiting other PWUO to join the study.

opioids, individuals with opioid use disorder may be injecting more often (Peng & Sandler, 1999; Ciccarone et al., 2017).

Finally, we note that although the research on SCSs is largely limited in its type and design, many SCSs have been around for 15 to 30 years and have survived multiple changes in local and national governments. Of course, persistence doesn't imply effectiveness; however, it seems relatively unlikely that these programs—which were initially controversial in many places—would have achieved such longevity if they had serious adverse consequences for their clients or for their communities. There are researchers and advocates who believe that during an emergency such as the present opioid crisis in the U.S., the absence of a large down-side risk for a program that has strong face validity may be sufficient for some policy makers to proceed, rather than waiting for high-quality evidence demonstrating positive effects. Nevertheless, if SCSs are implemented in the U.S., we hope a strong research component is incorporated into these efforts.

References

Alderks, C., “Trends in the Use of methadone, buprenorphine, and extended-release naltrexone at substance abuse treatment facilities: 2003-2015 (update).” *National Survey of Substance Abuse Treatment Services.* Substance Abuse and Mental Health Services Administration. August 2017.

Andreo, L., J. Roges, C. Marco, M. Bua, M. Segador, S. Gomez-Heredia, and E. Henar, "Síndrome postconsumo en consumidores de cocaína inyectada a partir de las observaciones realizadas en salas de consumo de diferentes ciudades españolas," *Low Threshold Journal,* Vol. 1, No. 1, 2013, pp. 13-16.

Andresen, M.A., and E. Jozaghi. "The point of diminishing returns: an examination of expanding Vancouver’s Insite." *Urban Studies* 49, no. 16 (2012): 3531-3544.

Andresen, M.A., and N. Boyd. "A cost-benefit and cost-effectiveness analysis of Vancouver's supervised injection facility." *International Journal of Drug Policy* 21, no. 1 (2010): 70-76.

Anoro, M., E. Ilundain, and O. Santisteban, "Barcelona's safer injection facility-EVA: A harm reduction program lacking official support," *Journal of Drug Issues,* Vol. 33, No. 3, 2003, pp. 689-711.

Anoro, M., E. Ilundain, R. Rodriguez, L. Rossell, B. Iglesias, C. Guinovart, and M. Gabari, "Factores asociados a presentar parada respiratoria en las sobredosis por opiáceos atendidas en un escenario abierto de consumo de drogas en Barcelona," *Revista Española de Salud Pública,* Vol. 78, No. 5, 2004, pp. 601-608. As of 30 March 2018: http://scielo.isciii.es/scielo.php?script=sci_abstract&pid=S1135-57272004000500005&lng=es&nrm=iso&tlng=es

Baars, J.E., B.J. F. Boon, H.F. L. Garretsen, and D. van de Mheen, "The reach of a free hepatitis B vaccination programme: results of a Dutch study among drug users," *Int J Drug Policy,* Vol. 21, No. 3, 2010, pp. 247-250.

Bayoumi, A.M., and G.S. Zaric. "The cost-effectiveness of Vancouver's supervised injection facility." *Canadian Medical Association Journal* 179, no. 11 (2008): 1143-1151.

Benninghoff, F., and F. Dubois-Arber, "Résultats de l’étude de la clientèle du Cactus BIEL/BIENNE 2001," Institut universitaire de médecine sociale et préventive, 2002.

Benninghoff, F., R. Geense, and F. Dubois-Arber, "Resultats de l’étude ‘La clientèle des structures à bas seuil d’accessibilité en Suisse’ 2000 Bienne," Institut universitaire de médecine sociale et préventive, 2001.

Benninghoff, F., S. Solai, T. Huissoud, and F. Dubois-Arber, "Evaluation de Quai 9 ‘Espace d’acceuil et d’injection’ à Genéve: période 12/2001–12/2000," Institut universitaire de médecine sociale et préventive, 2003.

Biesma, S., and B. Bieleman, "De Daeke in gebruik. Evaluatie Opvang en Adviescentrum en gebruiksruimte De Daeke in Venlo," 1998.

Bravo, M.J., L. Royuela, L. De la Fuente, M.T. Brugal, G. Barrio, A. Domingo□Salvany, and Itínere Project Group. "Use of supervised injection facilities and injection risk behaviours among young drug injectors." *Addiction* 104, no. 4 (2009): 614-619.

British Columbia Ministry of Health. Progress update on B.C.’s response to the opioid overdose public health emergency. 2017 May. As of 7 September 2018: http://www2.gov.bc.ca/assets/gov/health/about-bc-s-health-care-system/office-of-the-provincial-health-officer/overdose-response-progress-update-march2017.pdf

Burrows, D., "Starting and Managing Needle and Syringe Programs. A guide for Central and Eastern Europe and the newly independent states of the former Soviet Union," International Harm Reduction Development, 2000.

Christie, T., E. Wood, M.T. Schechter, and M.V. O’Shaughnessy, "A comparison of the new Federal Guidelines regulating supervised injection site research in Canada and the Tri-Council Policy Statement on Ethical Conduct for Research Involving Human Subjects," *International Journal of Drug Policy,* Vol. 15, No. 1, 2004, pp. 66-73. As of 25 July 2018: http://www.sciencedirect.com/science/article/pii/S0955395903001300

Ciccarone, D., Ondocsin, J. and Mars, S.G., 2017. Heroin uncertainties: Exploring users’ perceptions of fentanyl-adulterated and-substituted ‘heroin’. *International Journal of Drug Policy*, 46, pp.146-155.

Clua García, R. "A ritmo de bombeo: etnografía en un espacio de venopunción asistida," *Clua García, Rafael. A ritmo de bombeo: etnografía en un espacio de venopunción asistida. En: Revista Española de Drogodependencias,* Vol. 36, No. 4: 463, 2011. As of 30 March 2018: http://roderic.uv.es/handle/10550/47555

Daigre, C., M. Comin, L. Rodriguez-Cintas, N. Voltes, A. Alvarez, C. Roncero, B. Gonzalvo, and M. Casas, "[Users' perception of a harm reduction program in an outpatient drug dependency treatment center]," *Gac Sanit,* Vol. 24, No. 6, 2010/11//undefined, 2010, pp. 446-452.

DeBeck, K., T. Kerr, L. Bird, R. Zhang, D. Marsh, M. Tyndall, J. Montaner, and E. Wood, "Injection drug use cessation and use of North America's first medically supervised safer injecting facility," *Drug Alcohol Depend,* Vol. 113, No. 2-3, 2011, pp. 172-176.

Delás, J., A. G. Priore, A. Pigem, and M. Aguas, "Síndrome posconsumo de cocaína inyectada a partir de las observaciones en una sala de consumo supervisada," *Medicina Clinica,* Vol. 130, No. 1, 2008, p. 35.

Delas, J., E. Adan, O. Diaz, M. Aguas, M. Pons, and R. Fuertes, "Smoked cocaine in socially-depressed areas," *Harm Reduction Journal,* Vol. 7, 2010.

Des Jarlais, D.C., K. Arasteh, and H. Hagan. "Evaluating Vancouver's supervised injection facility: data and dollars, symbols and ethics." *Canadian Medical Association Journal* 179, no. 11 (2008): 1105-1106.

Dietze, P., Winter, R., Pedrana, A., Leicht, A., i Roca, X.M. and Brugal, M.T., 2012. Mobile safe injecting facilities in Barcelona and Berlin. *International Journal of Drug Policy*, 23(4), pp.257-260.

Donnelly, N., and N. Mahoney, "Trends in property and illicit drug crime around the medically supervised injecting centre in Kings Cross: 2012 update," 2013, p. 10.

Dubois-Arber, F., A. Jeannin, and B. Spencer, "Evaluation of the AIDS Prevention Strategy in Switzerland (6th synthesis report 1996–1998)," Lausanne: Institut universitaire de medicine sociale e preventive, 1999.

Dubois-Arber, F., F. Benninghoff, and A. Jeannin, "Typology of injection profiles of clients of a supervised drug consumption facility in Geneva, Switzerland," *Eur Addict Res,* Vol. 14, No. 1, 2008, pp. 1-10.

EMCDDA, *Drug consumption rooms: an overview of provision and evidence*, Lisbon, Portugal, 2017.

Espelt, A., J. R. Villalbi, M. Bosque-Prous, O. Pares-Badell, M. Mari-Dell'Olmo, and M. T. Brugal, "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," *International Journal of Drug Policy,* Vol. 50, 2017, pp. 11-18.

European Centre for Disease, Prevention, Control, Drugs European Monitoring Centre for, and Addiction Drug, "Prevention and control of infectious diseases among people who inject drugs," 2011. https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/111012_Guidance_ECDC-EMCDDA.pdf

Fairbairn, N., W. Small, N. Van Borek, E. Wood, and T. Kerr, "Social structural factors that shape assisted injecting practices among injection drug users in Vancouver, Canada: a qualitative study," *Harm Reduct J,* Vol. 7, 2010, p. 20.

Fast, D., W. Small, E. Wood, and T. Kerr, "The perspectives of injection drug users regarding safer injecting education delivered through a supervised injecting facility," *Harm Reduct J,* Vol. 5, 2008, p. 32.

Fisher, D.G., Fenaughty, A.M., Cagle, H.H. and Wells, R.S., 2003. Needle exchange and injection drug use frequency: a randomized clinical trial. JAIDS-HAGERSTOWN MD-, 33(2), pp.199-205.

Fitzgerald, J., M. Burgess, and L. Snowball, *Trends in property and illicit drug crime around the Medically Supervised Injecting Centre in Kings Cross: An update*, Sydney: NSW Bureau of Crime Statistics and Research, As of 30 March 2018: http://apo.org.au/system/files/22857/apo-nid22857-27411.pdf

Freeman, K., C. G. Jones, D. J. Weatherburn, S. Rutter, C. J. Spooner, and N. Donnelly, "The impact of the Sydney Medically Supervised Injecting Centre (MSIC) on crime," *Drug Alcohol Rev,* Vol. 24, No. 2, 2005, pp. 173-184.

Garcia, R. C., "Drug consumption rooms in Spain (2000-2013)," *Salud Colectiva,* Vol. 11, No. 2, 2015, pp. 261-282.

Geense, R., "Evaluation of the Federal Measures to Reduce Problems Related to Drug Use. To Have or Have Not: That's the Question. A Qualitative Study on Four Low-threshold Needle Exchange Services for Drug Users in 92 Switzerland," University of Social and Preventive Medicine, Prevention Programmes Evaluation Unit, 1997.

Grey Literature Report, New York Academy of Medicine, "What Is Grey Literature?" webpage, undated. As of September 26, 2018: http://www.greylit.org/about

Hadland, S. E., K. DeBeck, T. Kerr, P. Nguyen, A. Simo, J. S. Montaner, and E. Wood, "Use of a medically supervised injection facility among street youth," *J Adolesc Health,* Vol. 55, No. 5, 2014, pp. 684-689.

Happel, V., "Erfahrungen in und mit Konsumräumen," *Drogenvisionen – Zukunftswerkstatt für eine innovative Drogenpolitik und Drogenhilfe. Dokumentationsband zum 2. intern. Drogenkongress*, Berlin: Akzept, 1997.

Happel, V., and J. Steinmetz, "Überdosierungen im Konsumraum. Ergebnisse und Erfahrungen nach fünfjähriger Begleitung des grössten Frankfurter Konsumraums," Akzept, 2001.

Health Canada, "Supervised consumption sites: status of applications," *aem*, 2018. As of 21 February 2018: https://www.canada.ca/en/health-canada/services/substance-abuse/supervised-consumption-sites/status-application.html

Heckathorn, D.D., 1997. Respondent-driven sampling: a new approach to the study of hidden populations. *Social problems*, 44(2), pp.174-199.

Heckathorn, D.D. and Cameron, C.J., 2017. Network sampling: From snowball and multiplicity to respondent-driven sampling. *Annual review of sociology*, 43, pp.101-119.

Hedrich, D. *European report on drug consumption rooms*, European Monitoring Centre for Drugs and Drug Addiction, 2004.

Hemming, K., Haines, T.P., Chilton, P.J., Girling, A.J. and Lilford, R.J., 2015. The stepped wedge cluster randomised trial: rationale, design, analysis, and reporting. *BMJ*, 350, p.h391.

Holder, H.D., and J.O. Blose, "Impact of Changes in Distilled Spirits Availability on Apparent Consumption: a time series analysis of liquor-by-the-drink," British Journal of Addiction, Vol. 82, No. 6, 1987, pp. 623-631. As of 3 August 2018: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1360-0443.1987.tb01524.x

Hser, Y.I., Huang, D., Chou, C.P., & Anglin, M.D. (2007). Trajectories of heroin addiction: growth mixture modeling results based on a 33-year follow-up study. *Eval Rev*, 31(6), 548-563. doi:31/6/548 [pii]10.1177/0193841X07307315

Insite. "Insite by the numbers," undated. As of 1 December 2018: http://www.communityinsite.ca/numbers.html

Irwin, A., E. Jozaghi, R.N. Bluthenthal, and A.H. Kral. "A cost-benefit analysis of a potential supervised injection facility in San Francisco, California, USA." Journal of Drug Issues 47, no. 2 (2017): 164-184.

Jacobs, P., P. Calder, M. Taylor, S. Houston, L.D. Saunders, and T. Albert. "Cost effectiveness of Streetworks' needle exchange program of Edmonton." *Can J Public Health* 90, no. 3 (1999): 168-71.

Johnson, B.D. "Once an addict, seldom an addict." *Contemp. Drug Probs.* 7 (1978): 35.

Jozaghi, E., Reid, A.A., Andresen, M.A. A cost-benefit/cost-effectiveness analysis of proposed supervised injection facilities in Montreal, *Canada. Subst. Abuse Treat. Prev. Policy.* (2013) 8, 25

Jozaghi, E. "A cost-benefit/cost-effectiveness analysis of an unsanctioned supervised smoking facility in the Downtown Eastside of Vancouver, Canada." *Harm reduction journal* 11, no. 1 (2014): 30.

Kaplan, E.H., and E. O'Keefe. "Let the needles do the talking! Evaluating the New Haven needle exchange." *Interfaces* 23, no. 1 (1993): 7-26.

Kaplan, J. *The hardest drug: Heroin and public policy*. Chicago: University of Chicago Press, 1983.

Kennedy, M. C., M. Karamouzian, and T. Kerr, "Public Health and Public Order Outcomes Associated with Supervised Drug Consumption Facilities: a Systematic Review," *Curr HIV/AIDS Rep,* Vol. 14, No. 5, 2017, pp. 161-183.

Kerr, T., J. A. Stoltz, M. Tyndall, K. Li, R. Zhang, J. Montaner, and E. Wood, "Impact of a medically supervised safer injection facility on community drug use patterns: a before and after study," *Bmj,* Vol. 332, No. 7535, 2006a, pp. 220-222.

Kerr, T., J. Kimber, K. Debeck, and E. Wood, "The role of safer injection facilities in the response to HIV/AIDS among injection drug users," *Curr HIV/AIDS Rep,* Vol. 4, No. 4, 2007a, pp. 158-164.

Kerr, T., M. Tyndall, K. Li, J. Montaner, and E. Wood, "Safer injection facility use and syringe sharing in injection drug users," *Lancet,* Vol. 366, No. 9482, 2005, pp. 316-318.

Kerr, T., M. W. Tyndall, C. Lai, J. S. G. Montaner, and E. Wood, "Drug-related overdoses within a medically supervised safer injection facility," *International Journal of Drug Policy,* Vol. 17, No. 5, 2006b, pp. 436-441.

Kerr, T., M. W. Tyndall, R. Zhang, C. Lai, J. S. Montaner, and E. Wood, "Circumstances of first injection among illicit drug users accessing a medically supervised safer injection facility," *Am J Public Health,* Vol. 97, No. 7, 2007c, pp. 1228-1230.

Kerr, T., W. Small, D. Moore, and E. Wood, "A micro-environmental intervention to reduce the harms associated with drug-related overdose: evidence from the evaluation of Vancouver's safer injection facility," *Int J Drug Policy,* Vol. 18, No. 1, 2007b, pp. 37-45.

Kerr, Thomas, Mark Tyndall, Kathy Li, Julio Montaner, and Evan Wood. "Safer injection facility use and syringe sharing in injection drug users." *The Lancet* 366, no. 9482 (2005): 316-318.

Kimber, J., K. Dolan, and A. Wodak, *International Survey of Supervised Injecting Centres (1999–2000)*, Sydney: National Drug and Alcohol Research Centre, 2001.

Kimber, J., M. MacDonald, I. van Beek, J. Kaldor, D. Weatherburn, H. Lapsley, and R. P. Mattick, "The Sydney Medically Supervised Injecting Centre: Client characteristics and predictors of frequent attendance during the first 12 months of operation," *Journal of Drug Issues,* Vol. 33, No. 3, 2003, pp. 639-648.

Kinnard, E. N., C. J. Howe, T. Kerr, V. Skjodt Hass, and B. D. Marshall, "Self-reported changes in drug use behaviors and syringe disposal methods following the opening of a supervised injecting facility in Copenhagen, Denmark," *Harm Reduct J,* Vol. 11, No. 1, 2014, p. 29.

Kral, A.H. and Davidson, P.J., 2017. Addressing the Nation's opioid epidemic: lessons from an unsanctioned supervised injection site in the US. *American journal of preventive medicine*, 53(6), pp.919-922.

Krusi, A., W. Small, E. Wood, and T. Kerr, "An integrated supervised injecting program within a care facility for HIV-positive individuals: a qualitative evaluation," *AIDS Care,* Vol. 21, No. 5, 2009, pp. 638-644.

Linssen, L., W. de Jong, and J. Wolf, *Gebruiksruimten. Een systematisch overzicht van de voorziening en de effecten ervan*, Trimbos Instituut, 2001.

Lloyd-Smith, E., E. Wood, R. Zhang, M. W. Tyndall, J. S. G. Montaner, and T. Kerr, "Risk factors for developing a cutaneous injection-related infection among injection drug users: a cohort study," *BMC Public Health,* Vol. 8, 2008.

Lloyd-Smith, E., E. Wood, R. Zhang, M. W. Tyndall, J. S. Montaner, and T. Kerr, "Determinants of cutaneous injection-related infection care at a supervised injecting facility," *Ann Epidemiol,* Vol. 19, No. 6, 2009, pp. 404-409.

Lloyd-Smith, E., M. Tyndall, R. Zhang, E. Grafstein, S. Sheps, E. Wood, J. Montaner, and T. Kerr, "Determinants of Cutaneous Injection-Related Infections Among Injecting Drug Users at an Emergency Department," *Open Infect Dis J,* Vol. 6, 2012.

Lloyd-Smith, E., M. W. Hull, M. W. Tyndall, R. Zhang, E. Wood, J. S. Montaner, T. Kerr, and M. G. Romney, "Community-associated methicillin-resistant Staphylococcus aureus is prevalent in wounds of community-based injection drug users," *Epidemiol Infect,* Vol. 138, No. 5, 2010, pp. 713-720.

Lopez, G. "Why some US cities are opening safe spaces for injecting heroin," *Vox*, 2018. As of 29 January 2018: https://www.vox.com/science-and-health/2018/1/25/16928144/safe-injection-sites-heroin-opioid-epidemic

Lysyshyn, M., C. Dohoo, S. Forsting, T. Kerr, and R. McNeil, "Evaluation of a fentanyl drug checking program for clients of a supervised injection site, Vancouver, Canada," 2017. As of 30 March 2018: https://www.hri.global/abstracts/abstrct/188/print

Magill, M. and L.A. Ray, "Cognitive-Behavioral Treatment With Adult Alcohol and Illicit Drug Users: A Meta-Analysis of Randomized Controlled Trials," Journal of Studies on Alcohol and Drugs, Vol. 70, No. 4, 2009, pp. 516-527. As of 3 August 2018: https://www.jsad.com/doi/abs/10.15288/jsad.2009.70.516

Marshall, B., E. Wood, R. Zhang, M.W. Tyndall, J.S. Montaner, and T. Kerr, "Condom use among injection drug users accessing a supervised injecting facility," *Sex Transm Infect,* Vol. 85, No. 2, 2009, pp. 121-126.

Marshall, B., M.J. Milloy, E. Wood, J.S. Montaner, and T. Kerr, "Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study," Lancet, Vol. 377, No. 9775, 2011, pp. 1429-1437.

Masson, C.L., J.L. Sorensen, D.C. Perlman, M.S. Shopshire, K.L. Delucchi, T. Chen, K. Sporer, D. Des Jarlais, and S.M. Hall, "Hospital- Versus Community–Based Syringe Exchange: A Randomized Controlled Trial," AIDS Education and Prevention, Vol. 19, No. 2, 2007, pp. 97-110. As of 3 August 2018: https://guilfordjournals.com/doi/abs/10.1521/aeap.2007.19.2.97

Mattick, R. P., C. Breen, J. Kimber, and M. Davoli, "Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence," Cochrane Database Syst Rev, Vol. 4, 2002, p. CD002209. As of 3 August 2018: http://researchonline.lshtm.ac.uk/61131/

May, T., T. Bennett, and K. Holloway, "The impact of medically supervised injection centres on drug-related harms: A meta-analysis," *International Journal of Drug Policy,* Vol. 59, 2018, pp. 98-107. As of 6 August 2018: http://www.sciencedirect.com/science/article/pii/S0955395918301804

McKnight, I., B. Maas, E. Wood, M.W. Tyndall, W. Small, C. Lai, J. S. Montaner, and T. Kerr, "Factors associated with public injecting among users of Vancouver's supervised injection facility," *Am J Drug Alcohol Abuse,* Vol. 33, No. 2, 2007, pp. 319-325.

McNeil, R., L. B. Dilley, M. Guirguis-Younger, S. W. Hwang, and W. Small, "Impact of supervised drug consumption services on access to and engagement with care at a palliative and supportive care facility for people living with HIV/AIDS: a qualitative study," *J Int AIDS Soc,* Vol. 17, 2014, p. 18855.

Meijer, G., A. de Jong, M. Koeter, and B. Bieleman, "Gebruik van de straat. Evaluatie gebruiksruimnte Binnenstad-Zuid Groningen," Amsterdam/Groningen: Amsterdam Institute for Addiction Research (AIAR)/Intraval, 2001.

Milloy, M.J., and E. Wood, "Emerging role of supervised injecting facilities in human immunodeficiency virus prevention," *Addiction,* Vol. 104, No. 4, 2009, pp. 620-621.

Milloy, M.J., E. Wood, M. Tyndall, C. Lai, J. Montaner, and T. Kerr, "Recent incarceration and use of a supervised injection facility in Vancouver, Canada," *Addiction Research & Theory,* Vol. 17, No. 5, 2009, pp. 538-545.

Milloy, M.J., T. Kerr, R. Mathias, R. Zhang, J.S. Montaner, M. Tyndall, and E. Wood, "Non-fatal overdose among a cohort of active injection drug users recruited from a supervised injection facility," *Am J Drug Alcohol Abuse,* Vol. 34, No. 4, 2008, pp. 499-509.

Milloy, M.J., T. Kerr, R. Zhang, M. Tyndall, J. Montaner, and E. Wood, "Inability to access addiction treatment and risk of HIV infection among injection drug users recruited from a supervised injection facility," *J Public Health (Oxf),* Vol. 32, No. 3, 2010, pp. 342-349.

Milloy, M.J., T. Kerr, M. Tyndall, J. Montaner, and E. Wood. "Estimated drug overdose deaths averted by North America's first medically-supervised safer injection facility." *PLoS One* 3, no. 10 (2008): e3351.

Myer, A.J., and L. Belisle, "Highs and Lows: An Interrupted Time-Series Evaluation of the Impact of North America's Only Supervised Injection Facility on Crime," *Journal of Drug Issues*, Vol. 48, No. 1, 2018, pp. 36-49.

NCHECR, *Sydney Medically Supervised Injecting Centre Evaluation Report No. 4: Evaluation of service operation and overdose-related events*, Sydney: NSW Department of Health, 2007.

Ober, A.J., Sussell, J., Kilmer, B., Saunders, J., & Heckathorn, D.D. (2016). Using respondent-driven sampling to recruit illegal drug purchasers to evaluate a drug market intervention. *Evaluation review*, 40(2), 87-121.

Paquette, D., Bryant, J., & De Wit, J. (2012). Respondent-driven sampling and the recruitment of people with small injecting networks. *AIDS and Behavior*, 16(4), 890-899.

Peng, P.W. and Sandler, A.N., 1999. A review of the use of fentanyl analgesia in the management of acute pain in adults. *The Journal of the American Society of Anesthesiologists*, 90(2), pp.576-599.

Pinkerton, S.D. "How many HIV infections are prevented by Vancouver Canada's supervised injection facility?." *International Journal of Drug Policy* 22, no. 3 (2011): 179-183.

Pinkerton, S.D. "Is Vancouver Canada's supervised injection facility cost□saving?." *Addiction* 105, no. 8 (2010): 1429-1436.

Preble, E., and J.J. Casey. "Taking care of business—the heroin user's life on the street." *International journal of the addictions* 4, no. 1 (1969): 1-24.

Poschadel, S., R. Hoeger, J. Schnitzler, and D. Schreckenberg, *Evaluation der Arbeit der Drogenkonsumräume in der Bundesrepublik Deutschland*, Bundesministerium für Gesundheit. Baden-Baden: Nomos Verlagsgesellschaft 2003.

Potier, C., V. Laprevote, F. Dubois-Arber, O. Cottencin, and B. Rolland, "Supervised injection services: what has been demonstrated? A systematic literature review," *Drug Alcohol Depend,* Vol. 145, 2014/12/01/, 2014, pp. 48-68.

Reddon, H., E. Wood, M. Tyndall, C. Lai, R. Hogg, J. Montaner, and T. Kerr, "Use of North America's first medically supervised safer injecting facility among HIV-positive injection drug users," *AIDS Educ Prev,* Vol. 23, No. 5, 2011, pp. 412-422.

Reyes Fuentes, V. C., *15 Jahre Fixerraum Bern. Auswirkungen auf soziale und medizinische Aspekte bei Drogenabhängigen*, University of Bern, 2003.

Richardson, L., E. Wood, R. Zhang, J. Montaner, M. Tyndall, and T. Kerr, "Employment among users of a medically supervised safer injection facility," *Am J Drug Alcohol Abuse,* Vol. 34, No. 5, 2008, pp. 519-525.

Rodriguez, E., U. Martin, and A. Bacigalupe, *Análisis de la actividad de la Sala de Consumo Supervisado de Munduko Medikuak: 2003-2009*, Bilbao, 2010.

Roncero, C., N. Martínez-Luna, C. Daigre, L. Grau-López, B. Gonzalvo, J. Pérez-Pazos, and M. Casas, "Psychotic symptoms of cocaine self-injectors in a harm reduction program," *Subst Abus,* Vol. 34, No. 2, 2013, pp. 118-121.

Ronco, C., and G. Spuhler, "Evaluation des mesures de la Confédération destinées à réduire les problèmes liéd à la toxicomanie: phase II," Institut universitaire de médicine sociale et préventive, 1994.

Ronco, C., G. Spuhler, P. Coda, and R. Schopfer, "Evaluation der Gassenzimmer I, II und III in Basel," Institut für Sozial- und Präventivmedizin der Universität Basel, 1994.

Rosenstein, R.J., 2018. Opinion | Fight Drug Abuse, Don't Subsidize It. *The New York Times*.

Roxburgh, A., S. Darke, A. M. Salmon, T. Dobbins, and M. Jauncey, "Frequency and severity of non-fatal opioid overdoses among clients attending the Sydney Medically Supervised Injecting Centre," *Drug Alcohol Depend,* Vol. 176, 2017, pp. 126-132.

SAHA. "Economic Evaluation of the Medically Supervised Injection Centre at Kings Cross (MSIC)." August 2008. As of 1 December 2018: https://uniting.org/__data/assets/pdf_file/0008/136439/MSIC-Final-Report-26-9-08-Saha.pdf

Salmon, A. M., I. van Beek, J. Amin, A. Grulich, and L. Maher, "High HIV testing and low HIV prevalence among injecting drug users attending the Sydney Medically Supervised Injecting Centre," *Aust N Z J Public Health,* Vol. 33, No. 3, 2009b, pp. 280-283.

Salmon, A. M., I. van Beek, J. Amin, J. Kaldor, and L. Maher, "The impact of a supervised injecting facility on ambulance call-outs in Sydney, Australia," *Addiction,* Vol. 105, No. 4, 2010, pp. 676-683.

Salmon, A. M., R. Dwyer, M. Jauncey, I. van Beek, L. Topp, and L. Maher, "Injecting-related injury and disease among clients of a supervised injecting facility," *Drug Alcohol Depend,* Vol. 101, No. 1-2, pp. 132-136.

Sampson, R.J., and S.W. Raudenbush, "Systematic Social Observation of Public Spaces: A New Look at Disorder in Urban Neighborhoods," American Journal of Sociology, Vol. 105, No. 3, 1999, pp. 603-651. As of 23 August 2018: https://www.journals.uchicago.edu/doi/abs/10.1086/210356

Schäffer, D., Stöver, H. and Weichert, L., 2014. Drug consumption rooms in Europe: Models, best practice and challenges. *Amsterdam: European Harm Reduction Network*.

Scherbaum, N., M. Specka, J. Bombeck, and B. Marrziniak, "Drug consumption facility as part of a primary health care centre for problem drug users-Which clients are attracted?," *International Journal of Drug Policy,* Vol. 20, No. 5, 2009, pp. 447-449.

Shadish, C. and Cook, T.D., 86. Campbell (2002): Experimental and Quasi-Experimental Designs for Generalized Causal Inference.

Skelton, E., B. Bonevski, F. Tzelepis, A. Shakeshaft, A. Guillaumier, W. Wood, M. Jauncey, and A. Salmon, "Addressing tobacco smoking in a medically supervised injecting center with an organizational change intervention: An acceptability study," *Asia-Pacific Journal of Clinical Oncology,* Vol. 12 Supplement 6, 2016, p. 13.

Small, W., E. Wood, E. Lloyd-Smith, M. Tyndall, and T. Kerr, "Accessing care for injection-related infections through a medically supervised injecting facility: a qualitative study," *Drug Alcohol Depend,* Vol. 98, No. 1-2, 2008, pp. 159-162.

Small, W., N. Van Borek, N. Fairbairn, E. Wood, and T. Kerr, "Access to health and social services for IDU: the impact of a medically supervised injection facility," *Drug Alcohol Rev,* Vol. 28, No. 4, 2009, pp. 341-346.

Spreyermann, C., and C. Willen, "Evaluationsbericht Pilotproject Cactus. Evaluation der Kontakt- und Anlaufstelle des Contact Netz Drop-in Biel," 2002.

Stoltz, J. A., E. Wood, C. Miller, W. Small, K. Li, M. Tyndall, J. Montaner, and T. Kerr, "Characteristics of young illicit drug injectors who use North America's first medically supervised safer injecting facility," *Addiction Research & Theory,* Vol. 15, No. 1, 2007a, pp. 63-69.

Stoltz, J. A., E. Wood, W. Small, K. Li, M. Tyndall, J. Montaner, and T. Kerr, "Changes in injecting practices associated with the use of a medically supervised safer injection facility," *J Public Health (Oxf),* Vol. 29, No. 1, 2007b, pp. 35-39.

Torrents, Oriol, "Perfil psicológico de sujetos toxicómanos en activo, usuarios de un programa de reducción de daños," *Revista de psiquiatría de la Facultad de Medicina de Barcelona,* Vol. 33, No. 1, 2006, pp. 24-33. As of 30 March 2018: https://dialnet.unirioja.es/servlet/articulo?codigo=2049749

Toth, E. C., J. Tegner, S. Lauridsen, and N. Kappel, "A cross-sectional national survey assessing self-reported drug intake behavior, contact with the primary sector and drug treatment among service users of Danish drug consumption rooms," *Harm Reduction Journal,* Vol. 13, 2016.

Tyndall, M. W., E. Wood, R. Zhang, C. Lai, J. S. Montaner, and T. Kerr, "HIV seroprevalence among participants at a Supervised Injection Facility in Vancouver, Canada: implications for prevention, care and treatment," *Harm Reduct J,* Vol. 3, 2006b, p. 36.

Tyndall, M. W., T. Kerr, R. Zhang, E. King, J. G. Montaner, and E. Wood, "Attendance, drug use patterns, and referrals made from North America's first supervised injection facility," *Drug Alcohol Depend,* Vol. 83, No. 3, 2006a, pp. 193-198.

Uniting. "What the Uniting MSIC does". May 2015. As of 1 December 2018: https://uniting.org/who-we-help/for-adults/sydney-medically-supervised-injecting-centre/what-the-uniting-sydney-msic-does

Uniting. "Get to know our story". Uniting Medically Supervised Injecting Centre. 2018. As of 1 December 2018: https://uniting.org/__data/assets/pdf_file/0005/139370/Get-to-know-our-story.pdf

van Beek, I., J. Kimber, A. Dakin, and S. Gilmour, "The Sydney Medically Supervised Injecting Centre: Reducing harm associated with heroin overdose," *Critical Public Health,* Vol. 14, No. 4, 2004, pp. 391-406.

van der Poel, A., C. Barendregt, and D. van de Mheen, "Drug consumption rooms in Rotterdam: an explorative description," *European Addiction Research,* Vol. 9, 2003.

Vancouver Coastal Health. "Insite user statistics". February 2018. As of 1 December 2018: http://www.vch.ca/public-health/harm-reduction/supervised-consumption-sites/insite-user-statistics

Vecino, C., J. R. Villalbi, A. Guitart, A. Espelt, M. Bartroli, Y. Castellano, and M. T. Brugal, "[Safe injection rooms and police crackdowns in areas with heavy drug dealing. Evaluation by counting discarded syringes collected from the public space]," *Adicciones,* Vol. 25, No. 4, 2013, pp. 333-338.

Weatherburn, D., C. Jones, K. Freeman, and T. Makkai, "Supply control and harm reduction: lessons from the Australian heroin 'drought'," *Addiction,* Vol. 98, No. 1, 2002, pp. 83-91. As of 29 June 2018: https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1360-0443.2003.00248.x

West, S. G., Duan, N., Pequegnat, W., Gaist, P., Des Jarlais, D. C., Holtgrave, D., Mullen, P. D. (2008). Alternatives to the Randomized Controlled Trial. *American Journal of Public Health*, 98(8), 1359-1366. doi:10.2105/AJPH.2007.124446

Wherry, Aaron, "Debate over drug consumption sites might be coming to end," *CBC News*, 2017. As of 21 February 2018: http://www.cbc.ca/news/politics/consumption-sites-heroin-opioid-analysis-wherry-1.4280612

Wood, E., M. W. Tyndall, C. Lai, J. S. Montaner, and T. Kerr, "Impact of a medically supervised safer injecting facility on drug dealing and other drug-related crime," *Subst Abuse Treat Prev Policy,* Vol. 1, 2006a, p. 13.

Wood, E., M. W. Tyndall, K. Li, E. Lloyd-Smith, W. Small, J. S. Montaner, and T. Kerr, "Do supervised injecting facilities attract higher-risk injection drug users?," *Am J Prev Med,* Vol. 29, No. 2, 2005b, pp. 126-130.

Wood, E., M. W. Tyndall, R. Zhang, J. A. Stoltz, C. Lai, J. S. Montaner, and T. Kerr, "Attendance at supervised injecting facilities and use of detoxification services," *N Engl J Med,* Vol. 354, No. 23, 2006c, pp. 2512-2514.

Wood, E., M. W. Tyndall, R. Zhang, J. S. Montaner, and T. Kerr, "Rate of detoxification service use and its impact among a cohort of supervised injecting facility users," *Addiction,* Vol. 102, No. 6, 2007, pp. 916-919.

Wood, E., M. W. Tyndall, Z. Qui, R. Zhang, J. S. Montaner, and T. Kerr, "Service uptake and characteristics of injection drug users utilizing North America's first medically supervised safer injecting facility," *Am J Public Health,* Vol. 96, No. 5, 2006b, pp. 770-773.

Wood, E., T. Kerr, J. S. Montaner, S. A. Strathdee, A. Wodak, C. A. Hankins, M. T. Schechter, and M. W. Tyndall, "Rationale for evaluating North America's first medically supervised safer-injecting facility," *Lancet Infect Dis,* Vol. 4, No. 5, 2004, pp. 301-306.

Wood, E., T. Kerr, J. Stoltz, Z. Qui, R. Zhang, J. S. Montaner, and M. W. Tyndall, "Prevalence and correlates of hepatitis C infection among users of North America's first medically supervised safer injection facility," *Public Health,* Vol. 119, No. 12, 2005a, pp. 1111-1115.

Wood, R. A., E. Wood, C. Lai, M. W. Tyndall, J. S. Montaner, and T. Kerr, "Nurse-delivered safer injection education among a cohort of injection drug users: evidence from the evaluation of Vancouver's supervised injection facility," *Int J Drug Policy,* Vol. 19, No. 3, 2008, pp. 183-188.

Zurhold, Heike, Peter Degkwitz, Uwe Verthein, and Christian Haasen, "Drug Consumption Rooms in Hamburg, Germany: Evaluation of the Effects on Harm Reduction and the Reduction of Public Nuisance," *Journal of Drug Issues,* Vol. 33, No. 3, 2003, pp. 663-688. As of 30 March 2018: https://doi.org/10.1177/002204260303300308

Appendix A: Other Studies

This appendix provides additional information about the SCS literature, with a focus on describing studies that did not have an experimental or quasi-experimental (including natural experiments) design. Much of the SCS literature is descriptive or lacks suitable controls that allow for making inferences about the impact facilities may have on outcomes of interest. Nevertheless, some provide useful insights.

We first assess the review articles before examining the various outcomes from the literature. We focus on the evaluations and descriptive studies that do not allow for making causal inferences, but do mention natural experiments that were assessed above. Much of the literature on SCSs focuses on individual-level outcomes not captured in natural experiments. We remind the reader that without suitable controls, these studies should be interpreted with caution.

Overview of review articles

Our literature search identified five systematic reviews, which are summarized in Table A.1. One (Kerr, Kimber, et al., 2007) was excluded from additional analysis as it did not report specific effect sizes for outcomes. These systematic reviews are often cited as supporting evidence in favor of implementing SCSs.

We determined the number of non-overlapping studies across the remaining four reviews, their design, and the locations of the interventions they assess. In total, the four reviews mention 139 articles, but 37 were overlapping, leaving 102 unique articles. We did nothing further with articles that only discussed user or public opinion, focusing instead on studies that examined the impact of SCSs on outcomes related to mortality, morbidity, crime, access to treatment, etc.

The systematic reviews report favorable findings across a broad range of outcomes at both the individual and community levels. Most of the articles evaluated in the systematic reviews assessed SCS client profiles (20), user opinions about SCS utilization (15), morbidity and mortality (13), risky drug use (12), access or referral to treatment (7), crime, violence and public disorder (8), social and health outreach (9), public opinions surrounding SCSs (7), and changes in drug use (2). The remaining 9 were simulation studies modeling cost-benefit of SCSs. Most articles included in systematic reviews report on outcomes come from a handful of sites: Vancouver, Canada (58); Sydney, Australia (16); Spain (12); Germany (4); Denmark (2); Netherlands (1); and Switzerland (1). See Table A.2 for a regional breakdown of studies included in systematic reviews. Of the 102 articles mentioned in systematic reviews, half (51) describe SCS client profiles and opinion, public opinion, or are modeling/simulation studies. The other half evaluate patient- or community-level outcomes that are of interest here (e.g., morbidity and mortality, access or referral to treatment, crime and violence, etc.).

In addition, we include one review from the grey literature. Hedrich (2004) does not detail selection criteria nor report study findings systematically. Rather, it is a literature review that "aims to provide a descriptive analysis of historical background, operational frameworks and outcomes" related to SCSs (Hedrich 2004). The review focuses largely on individual health outcomes as well as community-level outcomes such as crime and public drug use. In most cases Hedrich (2004) does not discuss study design of articles, though most appear to be descriptive survey-based studies targeted at SCS clients and staff. Findings reported by Hedrich (2004) provide an additional level of detail not captured elsewhere. We report these findings in the relevant Study Outcome subsections.

Subsequent to our search and original analysis, May, Bennett, and Holloway (2018) published the first meta-analysis of SCSs. (A meta-analysis uses formal statistical methods to synthesize data from a series of studies, such as those uncovered by a systematic review.) The desire to provide such a synthesis is understandable but in retrospect perhaps overly ambitious. Shortly after publication, the article was retracted by the editors with support from the authors due to "methodological weaknesses of pooling diverse outcomes into a single composite measure."

Note that the study was retracted because of how the authors pooled the studies, not because of their search criteria. May et al. (2018) searched public health databases and identified 40 published studies that were potentially suitable. Using a set of inclusion criteria similar to those employed in this Working Paper (prioritizing RCTs and natural experiments), they identified eight studies for further consideration. Excluded studies either did not include a suitable comparison group or did not report data allowing authors to calculate effect sizes.

Of these eight studies, five were also included in this Working Paper (Bravo et al., 2009; Donnelly and Snowball, 2006; Marshall et al., 2011; NCHECR, 2007; and Salmon et al., 2010). One was captured but excluded (Wood et al., 2005) in this Working Paper as it did not include a suitable comparison group (authors compared whether or not SCS clients utilized the facility in the last month instead of comparing clients and non-clients). Two were not captured in this analysis; one was a study of methadone treatment patients in Barcelona published in 2017[13] and another was an early evaluation of Sydney's MSIC that was superseded by later evaluations included in our analysis. Of the studies analyzed, three evaluated Insite in Vancouver, three evaluated the MSIC in Sydney, and two looked at SCSs in Barcelona.

[13] It is possible that our search strategy did not find the study given its recent publication in a specialized European psychiatric journal.

Table A.1. Peer-reviewed literature reviews focusing on safer drug using environments

Authors (year published)	Period	No. of articles	SCS sites	Outcomes measured (No. of articles)	Observations and quality of design of included studies	Findings and conclusions
McNeil and Small (2014)	1997 - 2012	29 (11 related to SCSs)	Vancouver (10) Sydney (1)	Mortality (1) Morbidity (1) Utilization (5) Health and social outcomes (3)	Included studies are qualitative semi-structured interviews using self-reported data. Many studies by same authors and appear to use same sample of interviewees across several studies.	SCSs allow users a safer environment, helping to avoid risky drug using behaviors. Safety and reducing risk were primary motivators for some clients. Positive interactions with outreach staff were also reported. SCS clients report that some facility-imposed restrictions and operational limitations may deter some. Long wait times and prohibitions on sharing drugs were some complaints.
Potier et al. (2014)	Up to January 2014	75 (70 studies related to SCSs)	Vancouver (51) Sydney (13) Europe (2) Elsewhere* (4)	Risky drug use (8) Mortality (7) Morbidity (6) Treatment access/referral (5) Public disorder (6) Drug-related crime (4) Changes in drug use (2) Public opinion (7)	Included studies vary in design. Overlap in authors from studies out of Vancouver. Four studies were quasi-experimental	SCSs fulfill many of their stated public health and public-order goals without any spillover effect as measured by increased drug use or trafficking. Studies report reductions in needle sharing, reversals of overdoses, reductions in public drug consumption and overdose, and increased treatment referrals and access to health care. Favorable community opinion of SCS facilities increased after implementation.
Garcia (2015)	2000 - 2013	21 (11 were studies)	Spain (21)	Risky drug use (1) Mortality or morbidity (7) Health and social outcomes (3) Public disorder (2) Treatment access/referral (4)	Included studies vary in design. Diverse set of authors.	Opening of SCSs associated with positive individual drug user benefits and public health outcomes. Fatal overdoses averted, reduction in dangerous drug using practices, reductions in transmission of blood-borne disease, and facilitating entry into treatment are reported. Reductions in reported public drug consumption and improperly disposed needles.
Kennedy, Karamouzian, and Kerr (2017)	2003 - 2017	47	Vancouver (28) Sydney (10) Germany (4)	Risky drug use (9) Mortality (8) Health and social outcomes	Included studies vary in design. Overlap in authors from studies out of Vancouver.	SCSs meet their primary public health and public order objectives while offering a range of services to injection drug users. Studies report that SCS clients

	Spain (2) Denmark (2) Netherlands (1)	(2) Treatment access/referral (4) Public disorder (5) Drug-related crime (6)	Seven studies were quasi-experimental**	adopt less risky injection practices; are associated with reductions in public drug use and discarded paraphernalia; and have reversed potentially fatal overdoses. SCS use associated with uptake of treatment services. SCSs openings were not associated with changes in drug-related crime (thefts/robbery, dealing) or public disorder complaints.

*Public/client opinion feasibility studies of prospective siting of SCSs in locations where an SCS was not present.

** Four of the seven were included in Potier et al. (2014).

Kerr, Kimber et al. (2007) did not meet our eligibility criteria and was thus excluded from this table as it did not provide systematic outcome measures.

Table A.2. Breakdown of articles included in four systematic reviews

Color Key	Vancouver (39)	Sydney (14)	Spain (12)	Germany (3)	Denmark (2)	Netherlands (1)	Switzerland (1)

	Drug user profile				Morbidity & mortality				Crime, violence and public disorder				Risky drug use				Access or referral to treatment				Social outreach & health				Changes in drug use			
	McNeill and Small (2014)	Kennedy, Karamouzian, and Kerr (2017)	Potier et al., (2014)	Garcia (2015)	McNeill and Small (2014)	Kennedy, Karamouzian, and Kerr (2017)	Potier et al., (2014)	Garcia (2015)	McNeill and Small (2014)	Kennedy, Karamouzian, and Kerr (2017)	Potier et al., (2014)	Garcia (2015)	McNeill and Small (2014)	Kennedy, Karamouzian, and Kerr (2017)	Potier et al., (2014)	Garcia (2015)	McNeill and Small (2014)	Kennedy, Karamouzian, and Kerr (2017)	Potier et al., (2014)	Garcia (2015)	McNeill and Small (2014)	Kennedy, Karamouzian, and Kerr (2017)	Potier et al., (2014)	Garcia (2015)	McNeill and Small (2014)	Kennedy, Karamouzian, and Kerr (2017)	Potier et al., (2014)	Garcia (2015)
Descriptive cross-sectional studies																												
Anoro, Ilundain, and Santisteban (2003)				X																								
Delas et al. (2008)								X																				
Delas et al. (2010)								X																				
Kerr, Tyndall, et al. (2006)							X																					
Roncero et al. (2013)				X																								
Torrents (2006)				X																								
Tyndall et al. (2006)			X																									
Wood, Tyndall, Qui, et al. (2006)			X																									
Observational retrospective & prospective studies																												
Andreo et al. (2013)				X																								
Anoro et al. (2004)								X																				
Baars et al. (2010)						X																						
Bravo et al. (2009)		X	X	X																								
DeBeck et al. (2011)																		X	X									
Dubois-Arber et al. (2008)			X																									
Hadland et al. (2014)			X																									
Kerr, Stoltz, et al. (2006)																										X	X	
Kerr et al. (2005)														X	X													
Kerr, Tyndall, et al. (2007)																										X	X	
Kimber, Mattick, et al. (2008)																		X	X									
Kimber et al. (2003)			X																									
Kimber, Hickman, et al. (2008)																			X									
Kinnard et al. (2014)														X														
Lloyd-Smith et al. (2012)						X																						
Lloyd-Smith et al. (2008)																						X	X					
Lloyd-Smith et al. (2009)																							X					
Lloyd-Smith et al. (2010)																						X	X					
Lysyshyn et al. (2017)														X														
Marshall et al. (2009)																						X	X					
McKnight et al. (2007)											X																	
Milloy and Wood (2009)															X													

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Milloy et al. (2008)					X	X															
Milloy et al. (2009)								X	X												
Milloy et al. (2010)														X	X						
Reddon et al. (2011)		X																			
Richardson et al. (2008)	X	X																			
Rodriguez, Martin, and Bacigalupe (2010)			X																		
Salmon, Dwyer, et al. (2009)												X									
Salmon, van Beek, et al. (2009)		X																			
Scherbaum et al. (2010)											X										
Skelton et al. (2016)														X							
Stoltz, Wood, Miller, et al. (2007)	X																				
Stoltz, Wood, Small, et al. (2007)											X	X									
Toth et al. (2016)																	X				
Tyndall, Wood, et al. (2006)		X																			
van Beek et al. (2004)					X	X															
Wood, Tyndall, Zhang, et al. (2006)														X	X						
Wood et al. (2007)														X	X						
Wood et al. (2008)											X	X									
Wood, Kerr, et al. (2005)		X																			
Wood, Tyndall, Stoltz, Small, Lloyd-Smith, et al. (2005)											X	X									
Wood, Tyndall, Li, et al. (2005)		X																			
Wood, Tyndall, Stoltz, Small, Zhang, et al. (2005)												X									
Zurhold et al. (2003)																	X				
Qualitative studies																					
Clua García (2011)			X																		
Daigre et al. (2010)			X																		
Fairbairn et al. (2010)										X											
Fast et al. (2008)										X		X									
Kerr, Small, et al. (2007)				X		X															
Krusi et al. (2009)																X					
Small et al. (2008)																X		X			
Small et al. (2009)																X		X			
Time series, pre-post ecological studies																					
Donnelly and Mahoney (2013)								X													
Fitzgerald, Burgess, and Snowball (2010)								X	X												
Freeman et al. (2005)								X	X												
Marshall et al. (2011)					X	X															
NCHECR (2007)					X																
Poschadel et al. (2003)					X																
Salmon et al. (2010)					X	X															
Vecino et al. (2013)								X													
Wood et al. (2004)								X	X												
Wood, Tyndall, Lai, et al. (2006)								X	X												

Color Key	Vancouver (39)	Sydney (14)	Spain (12)	Germany (3)	Denmark (2)	Netherlands (1)	Switzerland (1)

Study outcomes

After excluding the 51 articles that describe client profiles, opinions, and simulation or modeling studies from systematic reviews and adding six studies not discussed in review articles, we are left with 57 individual and community-level outcome studies. These articles focus on morbidity and mortality (16), followed by risky drug use (12), crime, violence and public disorder (10), social outreach and health (10), access or referral to treatment (7), and changes in drug use (2). Of these 57 studies, the majority (44) evaluated individual SCS facilities in either Vancouver, Canada or Sydney, Australia.

Most articles evaluated individual-level health and drug use outcomes. The exceptions are the six studies that focused on outcomes related to crime, violence, and disorder in the community (e.g., improperly disposed injection material, incidents of reported crime, observed public drug use, etc.); three time-series ecological studies evaluating morbidity and mortality (e.g., number of fatal overdoses or emergency service calls for overdose); and one pre/post ecological study looking at injection drug use re-initiation in the local drug-using population (Kerr, Stoltz, et al. 2006).

The systematic reviews report positive findings across a broad range of outcomes at both the individual and community level, associated with the operation of an SCS (Garcia 2015; Kennedy, Karamouzian, and Kerr 2017; McNeil and Small 2014; Potier et al. 2014). Studies report that SCS utilization is associated with reductions in unsafe or unhygienic injection practices (such as sharing needles), that users are more likely to avoid fatal overdose (no fatal overdose has been reported in facilities), are more likely to access counseling and drug treatment services, and individuals avail themselves of primary health care, sterile injection equipment, prophylactics (e.g., condoms), and harm reduction information. Several studies report fewer overdose or emergency service calls in and around areas that have opened an SCS, compared to designated control sites that did not open a supervised facility. Table A.3 reports individual study outcomes. We summarize the findings relevant to individual- and community-level outcomes below, supplementing with findings from Hedrich (2004).

SCS client profiles

Observational and descriptive articles suggest that the typical SCS client is a male in his early- to mid-thirties. Only Hadland et al. (2014) reported the average age of SCS users was under thirty. This is by design as the study was focused on young drug users in Vancouver. Regular use of injection drugs, frequency of injection, public drug use, unstable housing, and seroprevalence of HIV or HCV are associated with SCS utilization. Bravo et al. (2009) surveyed local drug-using populations (as opposed to just SCS clients) in Madrid and Barcelona to evaluate SCS utilization among street-drug users. Authors reported that those injecting once or more a week were almost five times (OR = 4.9, 95%CI = [2.7–8.8]) more likely to utilize an SCS than those that report less frequent injection drug use.

Likewise, two studies from Vancouver examine SCS factors relevant to SCS utilization between samples of clients and non-clients. In one study of drug users under 29, authors report that individuals were more likely to begin utilizing the SCS if they had been to jail (OR = 2.88, [1.29-6.4]), experienced an overdose (OR = 2.55, [1.02−6.19]), used heroin daily (OR = 2.16, [1.07−4.37]), or injected in public (OR = 3.02, [1.29−7.04]) (Stoltz, Wood, Miller, et al. 2007). In another analysis comparing SCS initiates and non-initiates, authors report that public injection, recent overdose, and daily drug injection were associated with higher odds ratios of SCS initiation (Wood, Tyndall, Li, et al. 2005).

Others show that SCS clients that inject heroin are almost three and a half times more likely to use an SCS compared to clients that do not inject heroin (OR = 3.44, 95%CI = [2.5–4.73]) (Wood, Tyndall, Qui, et al. 2006). Another study from Sydney found similar increased odds of SCS utilization for drug users who reported frequent injection drug use as well as injecting in public (Kimber et al. 2003). Here, authors are not comparing clients with non-clients, but showing that higher-risk clients are more likely to utilize the SCS than others who use less in public or inject less frequently. However, there was a statistically significant positive relationship with SCS initiation among individuals currently receiving methadone, working in the sex trade, or being HIV positive.

Unstable housing or homelessness was also positively associated with SCS initiation in samples of street-drug users. Stoltz, Wood, Miller, et al. (2007) report that homeless drug users were more than five times (OR = 5.24, [1.99-13.71]) as likely to utilize an SCS than those with some stable form of housing. Three other studies report a near doubling in the likelihood of SCS utilization for drug users with unstable housing (Wood, Tyndall, Qui, et al. 2006; Reddon et al. 2011; Wood, Tyndall, Li, et al. 2005). Lack of housing correlates with public drug use. Two studies estimate that those that report previous public drug use are more than twice as likely to report utilizing an SCS as opposed to those that did not report public drug use (Hadland et al. 2014; Wood, Tyndall, Li, et al. 2005).

European studies evaluated by Hedrich (2004) report a similar demographic profile of SCS clients (e.g., male, older than 30 with at least a decade of drug use). Most are injection drug users with unstable housing situations. In the case of Spain, about 40% of SCS clients in Madrid and an estimated 60% in Barcelona are homeless (Anoro, Ilundain, and Santisteban 2003). About half of clients in Germany and Spain had been in drug treatment before and sizeable portions were concurrently receiving medication therapies—40% in one Germany study and between 70-80% in Switzerland (Hedrich 2004).

Morbidity and mortality

In terms of individual-level morbidity and mortality outcomes, articles reported the number of overdoses reversed onsite, and the likelihood of experiencing an overdose elsewhere. Several articles suggested that SCSs attracted or reached marginalized populations by offering injection equipment and/or education services (Kerr, Small, et al. 2007). A pair of studies evaluating

Sydney's SCS suggested that use of certain street opioids carried more risk than use of others. Roxburgh et al. (2017) reported that clients using heroin were three times more likely to overdose than oxycodone users (12.7 vs 4.1 overdoses per 1000 injections). Latimer et al. (2016) found that fentanyl injectors[14] in Sydney were four and a half times more likely to overdose than SCS clients that used heroin or prescription opioids. One study of SCS clients in Vancouver reported that regular SCS attendance, defined as more than three-quarters of self-reported injection episodes taking place in the facility, was not associated with an increased likelihood of experiencing an overdose (OR = 1.05, 0.81–1.36) compared with users who utilized the SCS less frequently (Milloy et al. 2008).

Studies from Europe, assessed by Hedrich (2004), show that overdoses do occur in facilities, but rates varied across sites and over time. They were typically rare, at around 1-3 overdoses per 1000 supervised injections and as little as one per 8000 inhalations in one Swiss study (Hedrich 2004). In two German studies, authors noted that overdoses occurring outside of the SCS but in its immediate vicinity were often more severe and required assistance from emergency responders, suggesting that overdoses taking place within an SCS are better managed (Hedrich 2004; Happel 1997; Happel and Steinmetz 2001). One time series analysis in Germany (without controls) reported that openings of SCSs in German cities were significantly associated with community-level reductions in reported overdoses (Poschadel et al. 2003).

Access or referral to treatment

Several studies evaluated access or referrals to drug rehabilitation and treatment services initiated by an SCS. Studies reported that the rate of entry into treatment or a detoxification service ranged from 11 to 57% of clients over a given period (DeBeck et al. 2011; Kimber, Mattick, et al. 2008; Gaddis et al. 2017; Poschadel et al. 2003). Again, most of these studies evaluate frequency of utilization across SCS clients instead of comparing SCS clients to non-client populations. This selection design may introduce considerable bias. Therefore, these odds ratios should be interpreted with extreme caution.

One study in Vancouver reported that about 20% of clients tried and were unable to access some form of drug or alcohol treatment, but that more frequent SCS attendance was not associated with failure to access treatment (OR = 1.08, [0.84-1.4]) (Milloy et al. 2010). According to Hedrich (2004), many SCSs in Europe (at the time) did not record the number of clients referred to treatment. However, according to one study, the Geneva SCS referred about 38% of its 736 clients to some treatment service (not identified by Hedrich (2004)) over a six-month period (Benninghoff et al. 2003). Though several studies reported number of referrals, a more important measure would be enrollment or completion of treatment. We report below, when possible, the share of referrals that went on to enroll or to complete treatment.

[14] Injection of fentanyl in Australia appears to be from diverted sources and not illicitly-manufactured fentanyl.

In one retrospective study that recruited SCS clients into a cohort study, authors merged administrative data from the facility with data from three residential detoxification facilities in Vancouver to determine client entry into detoxification before and after Insite's opening. The study reported a significant uptake of detoxification services by SCS clients in the first year after opening versus the year before (aOR = 1.32, [1.11-1.35]) (Wood et al. 2007). Authors went on to report that individual client SCS utilization significantly declined one month after discharge from detoxification (24 versus 19 visits per month; p = 0.002) (Wood et al. 2007). However, because substance use disorder is a chronic and relapsing condition, individuals will make several attempts at detoxification. Therefore, without a control group these increased rates of entry into detoxification may be a function of time and other factors not related to the SCS.

Other studies found that, among SCS clients, regular attendance at the SCS (generally defined as once a week or more) was associated with higher likelihood of entry into addiction treatment or detoxification, with odds ratios ranging from 1.33 to 8.15 (DeBeck et al. 2011; Kimber, Mattick, et al. 2008; Gaddis et al. 2017; Wood, Tyndall, Zhang, et al. 2006). DeBeck et al. (2011) reported a significant increase in self-reported entry in treatment (aOR = 1.33, [1.04 – 1.72]) for clients that use the facility more frequently. Kimber, Mattick, et al. (2008) tracked clients as they presented themselves to treatment services post-referral. Authors reported that though clients that use the SCS with greater frequency are more likely to be referred to treatment, there was no statistically significant difference in treatment enrollment post referral between low- and high-frequency clients (81 vs 79%, p = 0.8). Factors associated with enrollment post referral were daily injection (OR = 2.4, [1.1 – 4.9]) and public drug use (OR = 2.2, [1.1 – 4.3]). Gaddis et al. (2017) report that SCS clients who utilized Insite more than once a week were more than eight times as likely to enroll at the on-site detoxification service as compared to those that use less than once a week. In one longitudinal study from Germany, the median length of attendance at the SCS was five weeks; users' drug use behavior remained unchanged after three months, though 37% of clients were referred to methadone after engaging with SCS services (Scherbaum et al. 2010).

Crime, violence, and public disorder

Descriptive analyses of police data from three sites in Europe reviewed in Hedrich (2004) suggest no changes in the rate of acquisitive crime reported by police departments (e.g., theft, robbery and burglary) committed near an SCS (Hedrich 2004; Meijer et al. 2001; Spreyermann and Willen 2002; Benninghoff et al. 2003). However, the European review noted several studies that reported small-scale drug trafficking in the immediate vicinity of SCSs (Hedrich 2004; Geense 1997; Dubois-Arber, Jeannin, and Spencer 1999; Kimber, Dolan, and Wodak 2001; Heike Zurhold et al. 2003; Reyes Fuentes 2003). Yet Hedrich (2004) noted that the siting of SCSs near urban drug markets makes it difficult to claim a causal impact on rate of drug dealing.

At the individual level, one study from Vancouver evaluated SCS utilization and client incarceration to assess the link between facilities and crime. Researchers randomly selected 902

SCS clients to participate in a prospective cohort study. Participants were later interviewed between July 2004 and November 2005 to evaluate self-reported recent incarceration (defined as detention, prison, or jail lasting more than one night for any period in the previous six months) at any point during the study. Authors reported a high prevalence of incarceration with almost 60% of clients in the sample reporting incarceration since initiating injection drug use (Milloy et al. 2009). The study reported no significant difference in the association of SCS attendance (those that use an SCS for 75% or more injections versus those that use less frequently) with recent incarceration (aOR = 0.99, [0.79–1.23]) (Milloy et al. 2009). Factors independently associated with recent incarceration include unstable housing (aOR = 3.63, [2.70–4.88]), public injecting (aOR = 1.60, [1.11–2.31]), frequent heroin use (aOR = 1.38, [1.11–1.71]), and drug dealing (aOR = 1.51, [1.23–1.85]) (Milloy et al. 2009). Authors noted the correlational nature and limits of their study and that it lacked an assessment of what impact SCS utilization had on client incarceration in the future.

One study from Vancouver trained observers to count the number of improperly discarded pieces of injection equipment and number of visible episodes of public drug use in the 10 city blocks surrounding Insite over a period of six weeks before and twelve weeks after the SCS opened. There was no control area to compare results to, but authors report that the number of publicly discarded syringes decreased by as much as half after the opening of Vancouver's SCS (daily average of 11.5 to 5.4) (Wood et al. 2004).

Hedrich (2004) notes two community surveys relating to discarded injection materials. A study from Switzerland found a reported increase in improperly discarded injection equipment after the SCS opened, while a study in the Netherlands instead found a reduction in discarded injection material reported by residents near the SCS (Hedrich 2004; Burrows 2000; Biesma and Bieleman 1998; Linssen, de Jong, and Wolf 2001).

Public drug use and other associated nuisance behaviors are cited as one driver behind the adoption of SCSs in Europe (Hedrich 2004). When asked, clients welcome such facilities to avoid public use; Poschadel et al. (2003) report that a third of drug users considered SCSs useful to avoid using in public. Additionally, authors mentioned that half of clients that reported public use in the last 24 hours cited use outside of business hours and a third noted wait times as reasons for injecting in public (Poschadel et al. 2003). A sample of drug users in Geneva found that 61% had frequently injected at home, with 29% reporting an SCS as their most frequent location and the remainder reporting public use (Hedrich 2004). A study of clients in Rotterdam found that 80% of clients self-reported reducing their public drug use after registering with the SCS (van der Poel, Barendregt, and van de Mheen 2003). Likewise, Zurhold et al. (2001) find that of clients surveyed in Hamburg, 30% cited reductions in self-reported public use due to the availability of the local SCSs.

Two studies from Vancouver suggest that SCS availability was associated with reductions in reported public drug use by clients. Wood et al. (2004), in addition to examining discarded injection equipment, trained observers to count observed episodes of public drug use. There was

no control area to compare results to, but authors report that Insite's opening was associated with a reduction in the number of public drug use incidents from 4.3 events per day to 2.4 incidents in the immediate 10 blocks around the facility. However, authors did not control for seasonality. Insite opened on September 22, 2003, which may confound evaluations that gauge changes in public drug use three months into the winter. Another study evaluated self-reported public drug use in SCS clients in Vancouver. Authors reported that public injectors were four times more likely to report waiting to enter Insite to use their drugs (McKnight et al. 2007).

Changes in drug use

Our search identified two studies relevant to changes in drug use. Both evaluated Vancouver's Insite and reported no substantial difference in the relapse rate among its clients (Kerr, Stoltz, et al. 2006; Kerr, Tyndall, et al. 2007). Kerr, Stoltz, et al. (2006) evaluated 674 drug users recruited through self-referral and street outreach during a one-year period before Insite opened and asked participants about changes in their drug use behavior in the last 12 months. Authors then compared these self-reported changes in drug use behavior with a sample of 700 injection drug users from the same population after Insite opened who were also asked 12 months later about changes in their drug use behavior. Results showed that both samples had similar rates of self-reported relapse into injection use[15] (17% relapse rate for the pre- Insite sample, 20% for the post-Insite sample). Kerr, Tyndall, et al. (2007) estimated that between December 2003 and October 2005 some five individuals out of 5,000, or about 0.1%, may have initiated injection drug use inside the facility. Note: that estimate pertains only to initiation among registered SCS users. The authors are not evaluating any potential effect that Insite's opening may have had on other people's initiation or drug use, e.g., by normalizing injection use.

Descriptive analyses of studies in Europe report mixed results in terms of how SCSs impact frequency of drug use. In one Swiss study, two of 17 drug users interviewed attributed reductions in drug use to SCS utilization whereas three reported an increase in their use (Hedrich 2004; Benninghoff et al. 2003). In a study of 67 clients from the Netherlands, 8 (12%) self-reported reductions in drug use while 11 (16%) reported using more frequently after registering with the facility (Hedrich 2004; van der Poel, Barendregt, and van de Mheen 2003).

Social outreach and health

A handful of studies have reported the type and quality of social and health services available to SCS clients. Qualitative studies show that clients report reduced stigmatization and reduced barriers to medical and social services (Small et al. 2008, 2009; Kappel et al. 2016). Frequent SCS clients were more likely to avail themselves of syringe exchanges, counselling and medical services, and harm reduction information (Heike Zurhold et al. 2003; B. Marshall et al. 2009).

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[15] Reported as changing from self-reported non-injection throughout the first six months to self-reported injection.

Most studies suggest that clients sought basic medical attention related to acute injection-related injuries (such as infections at injection sites). To a lesser extent, clients reported seeking psychosocial care.

In one study, approximately 9% of SCS clients had been referred to hospitals for injection-related infections (Lloyd-Smith et al. 2010). One longitudinal study estimated that about 6-10% of SCS clients at Insite developed a cutaneous injection-related infection within two years while utilizing the facility, which is relatively lower than rates previously reported (10-30%) in populations that inject street-sourced drugs (Lloyd-Smith et al. 2008). In a sample of 1080 clients at Insite, researchers report that two-thirds sought medical attention for cutaneous injection-related infections and 7% sought psychosocial support (Lloyd-Smith et al. 2009).

One qualitative study of 22 users and staff reported that SCS staff integrated medical referrals, influencing drug users' decision to seek medical attention for injection-related infections and reduce use of non-sterile needles (Krusi et al. 2009). One cross-sectional study that surveyed SCS clients from Denmark also reported individuals are more than twice as likely ($p = 0.024$) to adopt hygienic injection practices and were twice as likely ($p = 0.003$) to receive treatment for an acute health condition compared to drug users that did not utilize SCS facilities (Toth et al. 2016).

Based on descriptive studies from Europe, Hedrich (2004) reported the rate of health or outreach service utilization range from 4.6% to 10.5% of visits over periods ranging 10-26 months. Most services delivered were for medical consultations related to basic medical care and treatment of injection-related infections or tissue damage, followed by psycho-social counselling (Hedrich 2004). In one sample of 168 SCS clients in Germany, 60% had received medical services, mostly for small wounds and abscesses, and two-thirds had participated in at least one general counselling session with staff (Poschadel et al. 2003). Studies of SCSs in Hamburg and Rotterdam report that about a third of surveyed clients reported regularly receiving medical care services offered at an SCS (Heike Zurhold et al. 2003; van der Poel, Barendregt, and van de Mheen 2003). When surveyed, clients reported improvements in their health after seeking basic outreach services from an SCS (Linssen, de Jong, and Wolf 2001; Ronco and Spuhler 1994; Ronco et al. 1994).

Risky drug use

Hedrich (2004) reported that SCSs clients in Germany, Spain, and Switzerland are attracted to the low-risk atmosphere in facilities where they are not pressured to rush injections for fear of being disturbed by other users, dealers, or law enforcement. Several studies have assessed shifts in client behavior, especially as it pertains to risky drug use, for users who utilize the SCS more frequently versus those who utilize it less frequently or not at all. These include self-reported reductions in syringe sharing (aOR = 0.30, [0.11–0.82]), adjusting for age and binge use of drugs (Kerr et al. 2005); reductions in rushed injections (63%), desistence from needle sharing (54%), improved drug administration hygiene (44%), reduced injection frequency (12%), and better

syringe disposal practices (59%) (Kinnard et al. 2014). Others reported similar outcomes, including decreased reuse of syringes (aOR = 2.04, [1.38–3.01]) and decreased injections in public places (aOR = 2.79, [1.93–3.87]) (Stoltz, Wood, Small, et al. 2007).

One qualitative study reported that injection drug users often lack the appropriate knowledge surrounding safe injection practices (Fast et al. 2008). Another qualitative survey of drug users from Vancouver reported that rules prohibiting assisted injections at facilities were a barrier to access (Fairbairn et al. 2010).

Of other studies from Europe reviewed by Hedrich (2004), several reported that clients' knowledge of safe injection practices increased after they utilized an SCS for a period of a few months. Several studies in Switzerland suggested that respondents in samples of later waves of clients reported lower rates of injecting-related high-risk behaviors, such as sharing spoons, filters, and water (Hedrich 2004; Dubois-Arber, Jeannin, and Spencer 1999; Benninghoff, Geense, and Dubois-Arber 2001; Benninghoff and Dubois-Arber 2002). In other self-reported qualitative interview studies from Germany and the Netherlands, 22% and 90% of clients, respectively, attributed positive changes in their injection practices to attending an SCS (Hedrich 2004; H Zurhold et al. 2001; van der Poel, Barendregt, and van de Mheen 2003).

Table A.3: Studies of Supervised Consumption Sites

Study	Design	Period	N	Control	Location	Findings
Access or Referral to Treatment						
DeBeck et al. (2011)	Prospective	December 2003 to June 2006	1090		Vancouver, Canada	The cumulative incidence of injection cessation was 23% (95%CI = [16.2–29.9]). Factors associated with the initiation of addiction treatment: regular attendance at the SCS (aHR = 1.33, 95%CI = [1.04–1.72]), interviews with an addiction counselor (aHR = 1.54, 95%CI = [1.13–2.08]) and the use of methadone treatment, (aHR = 1.57, 95%CI = [1.02–2.40]). The cumulative incidence of entry into addiction treatment was 57.21% (95%CI = [50.9–63.5])
Kimber, Mattick, et al. (2008)	Prospective	May 2001 - October 2002	3715		Sydney, Australia	Approximately 16% (577 clients) have received counseling, 12% (443) for addiction treatment. Entering into a detoxification program was confirmed for 20% of clients. Factors associated with receiving referral to detoxification program: frequent use of the SCS (aOR = 1.6, 95%CI = [1.2–2.2]), majority heroin injection (aOR = 1.9, 95%CI = [1.2–2.2]), and obtaining a high school diploma (aOR = 1.6, 95%CI = [1.2–2.2]). Factors associated with treatment entry: prostitution (aOR = 2.6, 95%CI = [1.1–5.8]) and daily injection (aOR = 2.3, 95%CI = [1.1–5.2]). A psychiatric history was negatively associated with entry into treatment (aOR = 0.2, 95%CI = [0.5–0.7]).
Milloy et al. (2010)	Prospective	June 2004 - June 3006	889		Vancouver, Canada	Approximately 20% of respondents reported trying but being unable to access any type of drug or alcohol treatment in the previous 6 months. Binary outcome regression, suggests SCS use was not significantly associated with trying but being unable to access addiction treatment (OR = 1.08; 95% CI 0.84–1.40).
Skelton et al. (2016)	Prospective	July-October 2014	506		Sydney, Australia	In the post intervention period, more SCS users reported receiving tobacco smoking cessation care ($p < 0.05$), and more SCS staff reported providing verbal advice regarding smoking cessation, offer of free nicotine replacement therapy, referral to a physician and follow up to check on smoking cessation progress (all $p < 0.01$)

Wood, Tyndall, Zhang, et al. (2006)	Prospective	December 2003 - March 2005	1031	Vancouver, Canada	Regular SCS use (AHR = 1.72; 95% CI 1.25–2.38) and contact with the SCS staff (AHR = 1.98; 95% CI 1.26–3.10) were associated with more rapid time to entry into a detoxification program.
Wood et al. (2007)	Retrospective	December 2003 - March 2005	1031	Vancouver, Canada	Logit regression shows there was a significant increase in uptake of detoxification services in the year after vs. the year before the SCS opened (AOR = 1.32; 95% CI 1.11–1.58). Detoxification service use was associated with more rapid entry into MMT (AHR = 1.56; 95% CI 1.04–2.34) and other forms of addiction treatment (AHR = 3.73; 95% CI 2.57–5.39). Among those who enrolled in detoxification, the rate of SCS use declined in the month after enrollment compared to the rate of SCS use in the month prior to enrolment (24 vs. 19 visits, p = 0.002).
Gaddis et al. (2017)	Prospective	November 2010 - December 2010	1316	Vancouver, Canada	Among clients, 147 (11.2%) reported enrolling in detoxification services co-located with the SCS at least once during the two-year study period. Factors independently and positively associated with use of this service included residence within 5 blocks from the SCS (Adjusted Odds Ratio [AOR] = 1.70), enrollment in methadone maintenance therapy (AOR = 1.90), public injection (AOR = 1.53), binge injection (AOR = 1.93), recent overdose (AOR = 1.90) and frequent SIF use (AOR = 8.15) (all p < 0.05)
			Crime, Violence and Public Disorder		
Donnelly and Mahoney (2013)	Time series	January 1999 - December 2012	Yes, non-treatment areas in city	Sydney, Australia	With a few minor exceptions there has been a decline in the incidence of robbery and theft incidents in treatment area since the SCS opened. This is consistent with what occurred in the rest of Sydney. The trend in possess/deal cocaine, narcotics or amphetamines was relatively stable from May 2001 through December 2008 but then increased from January 2009 in both Kings Cross and the rest of Sydney. There has been no noticeable trend in the percentage of illicit drug offences which occurred within 50 meters of the SCS.

Espelt et al. (2017)	Time series	2004-2014		Yes, non-treatment areas in city	Barcelona, Spain	Following the opening of an SCS in one district, observed an initial increase in the number of spent syringes collected in this district [RR = 2.72 (95% CI: 1.57–4.71)] and stabilization of the trend thereafter [RR = 0.97 (95% CI: 0.91–1.03)]
Fitzgerald, Burgess, and Snowball (2010a)	Time series	January 1999 - March 2010		Yes, non-treatment areas in city	Sydney, Australia	Overall, there was no significant difference in the drug crimes in the vicinity of the SCS. Discordant trends with the rest of Sydney were as follows: theft with a firearm (stable at treatment site, vs. downward trend in the rest of Sydney) and retail theft (up at treatment site vs. steady in the rest of Sydney). Arrests for possession or trafficking of drugs remained stable at treatment site unlike the rest of Sydney (increase in amphetamine possession and cocaine trafficking; decreased traffic and possession of narcotics).
Freeman et al. (2005)	Time series	September 1999 - October 2002		Yes, non-treatment areas in city	Sydney, Australia	There was no evidence that the SCS trial led to either an increase or decrease in theft or robbery incidents. There was also no evidence that the SCS led to an increase in 'drug-related' loitering at the front of the facility after it opened, although there was a small increase in 'total' loitering (by 1.2 persons per occasion of observation). Trends in both 'drug-related' and 'total' loitering at the front of the facility steadily declined to baseline levels, or below, after it opened. There was a very small but sustained increase in 'drug-related' (0.09 persons per count) and 'total' loitering (0.37 persons per count) at the back of the facility after it opened.
McKnight et al. (2007)	Retrospective	June 2004 - July 2005	714		Vancouver, Canada	Factors associated with public injecting: homelessness (aOR = 3.1, 95%CI = [1.46–6.58], recent incarceration (aOR = 1.77, 95%CI = [1.15–2.73]), needle sharing (aOR = 5.39, 95%CI = [1.96–14.78]), the need for help injecting (aOR = 1.60, 95%CI = [1.01–2.54], daily heroin injection (aOR = 2.71, 95%CI = [1.84–3.98]) and waiting time at the SCS (aOR = 3.26, 95%CI = [2.11–5.6]).
Milloy et al. (2009)	Prospective	July 2004 - November 2005	902		Vancouver, Canada	The recent incarceration rate of clients remained stable between 25 and 33% throughout follow-up, and frequent use of the SCS was not associated with this rate (aOR = 0.99, 95%CI = [0.79–1.23]). Associated factors included the following: precarious housing (aOR = 3.63, 95%CI = [2.70–4.88]), public injection (aOR = 1.60, 95%CI = [1.11–2.31]) and frequent heroin injection (aOR = 1.38, 95%CI = [1.11–1.71])

Myer and Belisle (2018)	Time series	January 2002 - December 2004		Yes, non-treatment areas in city	Vancouver, Canada	District 1—where the supervised injection facility is located—observed an abrupt, permanent decrease in crime. Following the opening of the supervised injection facility in District 1, total crimes decreased by 42 crimes per week. When crimes were disaggregated into violent and property crimes, a similar pattern was observed. Property crimes decreased by nearly 35 crimes per week, while violent crimes decreased by six crimes per week.
Vecino et al. (2013)	Time series	2004-2012		Yes, non-treatment areas in city	Barcelona, Spain	Comparing indicators before and after health and police interventions, the opening of a facility with a supervised drug consumption room in the inner city was associated with a huge reduction in the number of abandoned syringes in the city, while its number did not rise in the district where the facility was located. The subsequent opening of another drug consumption room did not have a significant impact in collected syringes in the area.
Wood et al. (2004)	Time series	From 6 weeks before to 12 weeks after SIS opening			Vancouver, Canada	SCS opening was associated with reductions in the number of people injecting in public (mean daily 2.4 (95% confidence interval [CI] 1.9–3.0) after vs. 4.3 (95% CI 3.5–5.4) before opening), publicly discarded syringes (mean daily 5.4 (95% CI 4.7–6.3) after vs. 11.5 (95% CI 10.0–13.2) before), and injection-related litter (mean daily 310 (95% CI 305–317) after vs. 601 (95% CI 590–613) before) (all $p < 0.05$)
Wood, Tyndall, Lai, et al. (2006)	Time series	October 2003 - September 2005			Vancouver, Canada	No increases were seen with respect to drug trafficking (124 vs. 116) or assaults/robbery (174 vs. 180), although a decline in vehicle break-ins/vehicle theft was observed (302 vs. 227).
				Changes in drug use		
Kerr, Stoltz, et al. (2006)	Prospective	March 2002 - March 2004	871		Vancouver, Canada	There was no significant difference in the relapse rate in the community (17% vs. 20%), stopping injections (17% vs. 15%), or the introduction or discontinuation of methadone (11% vs. 7% and 13 vs. 11%, respectively)

Kerr, Tyndall, et al. (2007)	Prospective	December 2003 - October 2005	1065	Vancouver, Canada	One client reported performing his first injection within the safer injecting facility. On the basis of the difference between age at first injection and current age, we calculated that an additional 14 individuals had initiated injection drug use since the opening of the SCS, all of whom did not report performing their first injection within the facility. When these data were extrapolated to the entire population of SCS clients (i.e., approximately 5000 individuals), the estimated number of injection drug users who may have initiated injection drug use inside and outside the safer injecting facility were 5 (95% confidence interval [CI] = 2, 12) and 70 (95% CI = 55, 80), respectively.
				Morbidity/Mortality	
Anoro et al. (2004)	Retrospective	March 2001 - June 2002	222	Barcelona, Spain	Of 222 opiate overdose cases, 60.8% showed respiratory arrest. Of all risk factors tested, only prior abstinence heroin abstinence for 2 weeks or longer (OR= 1.893; p=0.04), and no previous consumption of benzodiazepines (OR: 0.462; p=0.017), proved to have a statistically significant association with suffering a respiratory arrest. Concomitant use of alcohol, cocaine or methadone was not associated with suffering respiratory arrest in opiate overdose.
Baars et al. (2010)	Retrospective	February-December 2005	309	Rotterdam, Utrecht and South Limburg, Netherlands	Of the sample, 63% were aware of the free hepatitis B vaccine, and 44% said they had been vaccinated. Clients who visited drug consumption rooms were more likely to be aware of the program than those who did not.
Delas et al. (2008)	Descriptive	2003	72	Barcelona, Spain	Descriptive health outcomes of cocaine use in SCS clients in Barcelona.
Delas et al. (2010)	Descriptive	January 2008	56	Barcelona, Spain	Descriptive health outcomes of cocaine use in SCS clients in Barcelona.

Kerr, Tyndall, et al. (2006)	Descriptive	March 2004 - February 2008	1046		Vancouver, Canada	There were 336 overdoses in 90 different individuals. There were no deaths. Administration of oxygen in 87% of cases, of naloxone in 27% of cases, and transfer to the hospital in 21% of cases
Kerr, Small, et al. (2007)	Qualitative	November 2005 - February 2006	50		Vancouver, Canada	The perspectives of participants suggest that the Vancouver SIF plays an important role in mediating various risks associated with overdose. In particular, the SIF addresses many of the unique contextual risks associated with injection in public spaces, including the need to rush injections due to fear of arrest. Further, SIF use appears to enable overdose prevention by simultaneously offsetting potential social risks associated with injecting alone and injecting in the presence of strangers.
Lloyd-Smith et al. (2012)	Prospective	January 2004 - January 2008	1083		Vancouver, Canada	In regression analyses, referral to hospital by SCS nurses was independently and positively associated with ED use for cutaneous injection-related infections among females (AOR = 4.48; 95% CI 2.76–7.30) and males (AOR = 2.97; 95% CI 1.93–4.57).
Marshall et al. (2011)	Time series	January 2001 - December 2005	290	Yes, non-treatment areas in city	Vancouver, Canada	Significant reductions in the number of overdoses within 500 m of the SCS (343434345%) were observed compared with the rest of Vancouver (9.3% reduction).
Milloy et al. (2008)	Prospective	December 2003 - December 2005	1090		Vancouver, Canada	Approximately 58.53% reported a history of overdose, and between 8 and 12% reported an overdose in the last six months. Factors associated with overdose: prostitution (aOR = 1.45, 95%CI = [1.07–1.99]) and public injection (aOR = 1.50, 95%CI = [1.09–2.06]). SCS attendance for more than 75% of injections was not associated with an increase in overdoses (OR = 1.05).

NCHECR (2007)	Time series	May 2001 - April 2007	1652	Yes, non-treatment areas in city	Sydney, Australia	There was a significant decrease from an average of 4 to 1 deaths per month in the immediate vicinity of the SIF after the SIF was established ($p < 0.001$), compared to a decrease from 27 to 8 deaths in the rest of the state ($p < 0.001$). This difference in rate changes was not statistically significant ($p = 0.877$). There was a significant decrease from an average of 11 to 7 opioid poisoning ED presentations (35% reduction) after the SIF establishment ($p < 0.001$) and a significant decline in ambulance service calls in the postal zone where the SCS was located (80% decline) relative to the neighboring postal zone (45% decline) ($p < 0.001$).
Poschadel et al. (2003)	Time series				Saarbrucken, Hannover, Hamburg and Frankfurt, Germany	After the establishment of the SCS, there were significant reductions in drug-related deaths in the four respective cities (all $p < 0.05$]
Salmon et al. (2010)	Time series	May 1998 to May 2006	20409	Yes, non-treatment areas in city	Sydney, Australia	After the opening of the SCS, the average monthly ambulance attendances at suspected opioid-related overdoses declined significantly in the immediate vicinity of the SCS (by 68%) compared to 61% in the rest of the state during SCS operating hours ($p = 0.002$). During the SCS operating hours, this difference was more pronounced with an 80% decline in the immediate vicinity of the SCS compared to a 60% decline in the rest of the state ($p < 0.001$).
van Beek et al. (2004)	Prospective	May 2001 - October 2002	3747		Sydney, Australia	Frequent SCS use was positively associated with experiencing a non-fatal overdose within the SCS (AOR = 6.1; 95% CI 4.3–8.6)
Latimer et al. (2016)	Retrospective	September 2012 - August 2015	189203		Sydney, Australia	The number of fentanyl injections increased by 1000% during time period. Crude relative risk estimates demonstrated that fentanyl injections had approximately four and a half times the risk of resulting in overdose than injections involving either heroin or other Rx opioids (RR = 4.6; 95%CI 3.8– 5.5). Specifically, fentanyl injections had two times the risk of overdose than heroin injections, and eight times the risk of overdose than other Rx opioid injections, to result in overdose (RR = 2.2; 95%CI 1.8–2.7; and RR = 7.9; 95%CI 6.7–9.5 respectively).

McNeil and Small (2014)	Qualitative	November 2010 - August 2011	13	Vancouver, Canada	Participant accounts highlight how the harm reduction policy altered the structural-environmental context of healthcare services and thus mediated access to palliative and supportive care services.
Roxburgh et al. (2017)	Prospective	January 2007 - April 2014	8382	Sydney, Australia	Heroin overdoses occurred at three times the rate of oxycodone overdoses (12.7 v 4.1 per 1000 injections). Heroin overdoses appeared to be more severe than oxycodone overdoses, with higher levels of compromised consciousness (31 v 18%) and severe respiratory depression (67 v 48%), but there were no differences in naloxone doses (20 v 17%).
			Social Outreach & Health		
Krusi et al. (2009)	Qualitative	May-June 2007	22	Vancouver, Canada	Participant and staff reports indicated that the integrated supervised injection program influenced client access to care by building more open and trusting relationships with staff, facilitating engagement in safer injection education and improving the management of injection-related infections. Participants and staff viewed the program as facilitating the delivery of care through mediating overdose risks, reducing the need to punitively manage drug use onsite and reducing the risks of encountering used syringes on the premises.
Lloyd-Smith et al. (2009)	Retrospective	December 2003 - January 2008	1080	Vancouver, Canada	Approximately 27% received care, 65% of whom attended the SCS for this purpose. Factors associated with receiving care included female gender (aOR = 1.87, 95%CI = [1.32–2.64]), unstable housing (aOR = 1.39, 95%CI = [1.02–1.88]), and daily heroin injection (aOR = 1.52, 95%CI = [1.13–2.4]).
Lloyd-Smith et al. (2010)	Prospective	January 2004 - December 2005	1083	Vancouver, Canada	Approximately 9% of participants were hospitalized, including 49% for cutaneous disorders caused by injection. Associated factors: HIV seropositivity (aOR = 1.79, 95%CI = [1.16–2.75]), orientation by an SIS nurse (aOR = 5.38, 95%CI = [3.39–8.55]). The hospital stay was significantly shorter among participants sent by an SIS nurse compared with those who were not sent by one (4 days (95%CI = [2–7]) vs. 12 days (95%CI = [5–33]))

Lloyd-Smith et al. (2008)	Prospective	January 2004 - February 2006	1065	Vancouver, Canada	Approximately 6–10% of participants reported cutaneous injection-related infections. Factors associated: female gender (aOR = 1.68, 95%CI = [1.16–2.43]), unstable housing (aOR = 1.49, 95%CI = [1.10–2.03]), borrowing used syringes (aOR = 1.60, 95%CI = [1.03–2.48]), requiring help to inject (aOR = 1.42, 95%CI = [1.03–1.94]) and daily cocaine injection (aOR = 1.41, 95%CI = [1.02–1.95])
Marshall et al. (2009)	Prospective	December 2003 - December 2005	794	Vancouver, Canada	The proportion of individuals using a condom during every act of intercourse increased by 8% over the two years of the study. The main predictive factor was HIV seropositivity (aOR = 2.23, 95%CI = [1.51–3.31]).
Small et al. (2008)	Qualitative	November 2005 - February 2006	50	Vancouver, Canada	Clients reported that the facility provided assessment and care of injection-related infections, as well as enhanced access to off-site medical services. The presence of professional nursing personnel within a sanctioned drug consumption setting serves to address social and structural barriers that often impede PWID access to health care.
Small et al. (2009)	Qualitative	November 2005 - February 2006	50	Vancouver, Canada	Client narratives indicate that the SCS serves to facilitate access to health care by providing much-needed care on-site and connects users to external services through referrals. Participants' perspectives suggest that the SIF has facilitated increased uptake of health and social services among IDU.
Zurhold et al. (2003)	Retrospective	2000	616	Hamburg, Germany	Frequent SCS users were more likely to use syringe exchange services compared to occasional or rare visitors (59 vs. 54 and 44%, respectively; $p < 0.05$). The same was true of counselling services (corresponding percentages = 46 vs. 35 and 25%; $p < 0.01$), medical services (37 vs. 29 and 17%; $p < 0.01$) and education on safer use (9 vs. 3 and 3%; $p < 0.05$)
Kappel et al. (2016)	Qualitative	March-June 2014	67	Denmark	Clients experienced a sense of social acceptance while inside facilities. Members of staff conveyed a welcoming, non-judgmental attitude, and clients were predominantly satisfied with the facilities. They prioritized forging relations with drug users so as to foster a sense of social acceptance within facilities.

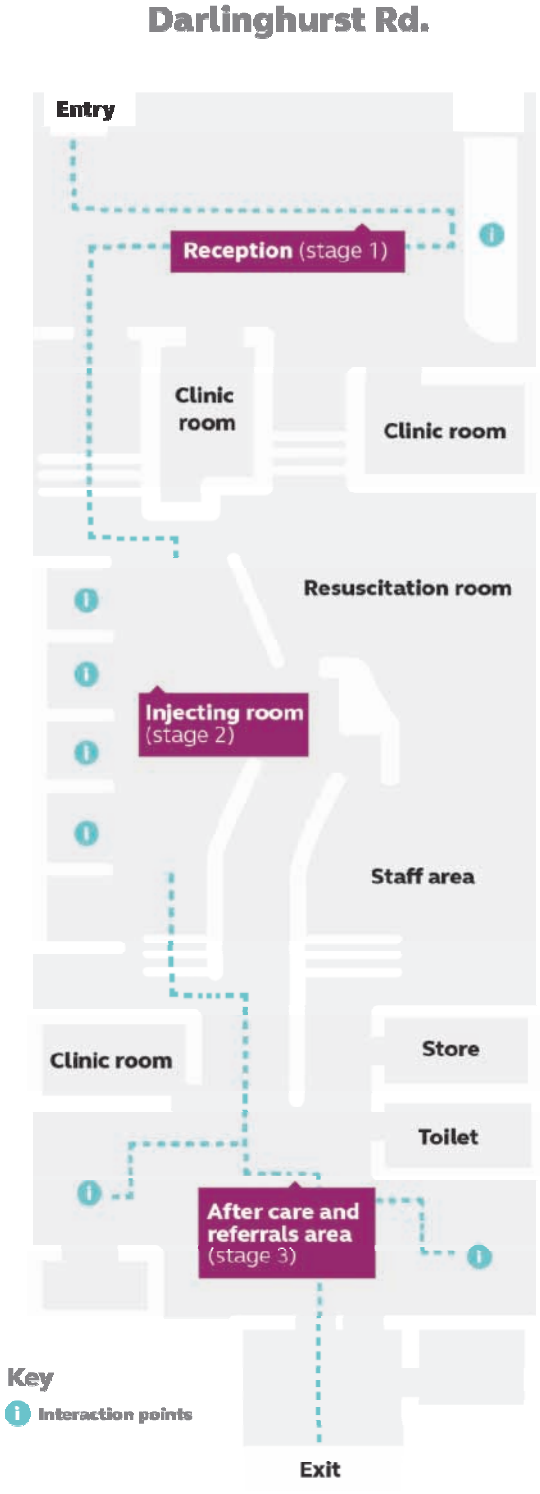
Toth et al. (2016)	Retrospective	January-February 2015	154	Copenhagen, Aarhus and Odense, Denmark	Those who had received education on hygienic injection practices at an SCS were more likely to access the service for clean injection equipment vs. those who had not received such education (68.8 vs. 25.9%, p = 0.024). Those advised to seek medical help by staff for a medical condition were more likely to receive treatment for the condition than who were not advised to seek treatment for a condition (51.3 vs. 25.7%, p = 0.003)
				Risky Drug Use	
Fairbairn et al. (2010)	Qualitative	June-July 2007	20	Vancouver, Canada	Participants reported that the rule prohibiting assisted injections at the SCS was a significant barrier to accessing that services.
Fast et al. (2008)	Qualitative	November 2005 - February 2006	50	Vancouver, Canada	Participant narratives indicate that significant gaps in knowledge regarding safer injecting practices exist among local injection drug users, and that these knowledge deficits result in unsafe injecting practices and negative health outcomes. However, users' perspectives reveal that the SCS allows clients to identify and address these gaps in knowledge through a number of mechanisms that are unique to this facility, including targeted educational messaging
Kerr et al. (2005)	Retrospective	December 2003 - June 2004	431	Vancouver, Canada	In logistic regression analyses, use of the SCS was independently associated with reduced syringe sharing (aOR = 0.30, 95%CI = [0.11–0.82], p = 0.02). In univariate analyses, significant factors associated with syringe sharing: need help to inject (aOR = 2.94, 95%CI = [1.59–5.42]), binge consumption (aOR = 2.04, 95%CI = [1.05–3.95], and regular injection of heroin (aOR = 1.72, 95%CI = [0.95–3.13]) or cocaine (aOR = 1.70, 95%CI = [0.93–3.06]).
Kinnard et al. (2014)	Retrospective	February-August 2013	41	Copenhagen, Denmark	Three-quarters (75.6%) of participants reported reductions in injection risk behaviors since the opening of the SCS, such as injecting in a less rushed manner (63.4%), fewer outdoor injections (56.1%), no longer sharing syringes (53.7%), and cleaning injecting site(s) more often (43.9%). Approximately two-thirds (65.9%) of participants did not feel that their frequency of injecting had changed; five participants (12.2%) reported a decrease in injecting frequency, and only two participants (4.9%) reported an increase in injecting frequency. Twenty-four (58.5%) individuals reported changing their syringe disposal practices since the opening of the SCS; of those, twenty-three (95.8%) reported changing from not always disposing safely to always disposing safely.

Lysyshyn et al. (2017)	Retrospective	July-September 2016	472		Vancouver, Canada	Using immunoassay testing strips, 472 drug samples were tested for fentanyl. Overall, 80% of drugs checked were positive for fentanyl (84% of heroin samples, 83% of other opioid samples, and 64% of non-opioid samples). Of substances checked pre-consumption, compared to receiving a negative result, receiving a positive result did result in more dose reductions (37% vs. 8%) but not in more disposals (9% vs. 8%).
Salmon, Dwyer, et al. (2009)	Prospective	May 2001 - April 2007	9552		Sydney, Australia	Approximately 29% had problems related to the injection. Approximately 10% had an injury or illness related to the injection. Main injection-related problems: difficulty finding a vein (18%), scarring or bruising (14%), and swelling of hands/feet (7%). Major diseases: abscess or cutaneous infection (6%), thrombosis (4%), sepsis (2%), and endocarditis (1%). Factors associated with disorders: female injecting the drug (except heroin), antecedent of dependence program, and history of overdose, prostitution, recent public injecting, and sharing needles.
Scherbaum et al. (2010)	Prospective	November 2002 - December 2003	129	Longitudinal	Essen, Germany	Median length of attendance was of 5 weeks; 22% of clients attended for less than 1 week. Although with respect to the period previous to recruitment at-risk behavior rates remained unchanged, by the 3-month follow-up; 13 (10%) clients out of those 129 who had initially enrolled had taken advantage of counseling opportunities. Some 37% of clients were referred to methadone treatment.
Stoltz, Wood, Small, et al. (2007)	Prospective	July 2004 - June 2005	760		Vancouver, Canada	SCS use is associated with positive changes in injecting practices: decreased the reuse of syringes (aOR = 2.04, 95%CI = [1.38–3.01]), decreased injections in public places (aOR = 2.79, 95%CI = [1.93–3.87]), taking the time needed (aOR = 2.7, 95%CI = [2.03–3.85]), use of clean water (aOR = 3, 95%CI = [2.13–4.18]), cooking/filtering drugs (aOR = 2.76, 95%CI = [1.84–4.15]), tie off prior to injection (aOR = 2.6, 95%CI = [1.58–4.37]), and safe disposal of syringes (aOR = 2.13, 95%CI = [1.47–3.09]).

Wood, Tyndall, Stoltz, Small, Lloyd-Smith, et al. (2005)	Prospective	March-October 2004	582	Vancouver, Canada	Exclusive SCS use was associated with decreased odds of syringe borrowing among HIV-negative participants (OR = 0.14; 95% CI 0.00–0.78) but was not significantly associated with syringe lending among HIV-positive participants (OR = 0.94; 95% CI 0.00–7.90)
Wood, Tyndall, Stoltz, Small, Zhang, et al. (2005)	Retrospective	March-October 2004	874	Vancouver, Canada	Approximately 33.5% were educated on safe injection practices. Factors associated: need help to inject (aOR = 2.20, 95%IC = [1.62–2.98]), prostitution (aOR = 1.54, 95%CI = [1.09–2.16]) and a few years of experience (aOR = 0.99, 95%CI = [0.97– 1.00]).
Wood et al. (2008)	Prospective	March 2004 - March 2005	1087	Vancouver, Canada	Frequent SCS use was associated with an increased likelihood of receiving safer injection education at the SIF (AOR = 1.47; 95% CI 1.22–1.77)
Axelsson et al. (2012)	Retrospective	September 2011 - February 2012	1139	Denmark	SCS reduced the risky behavior and bacterial infections and increased the rate of detoxification and access to health care.

Sources: Table adapted from Kennedy, Karamouzian, and Kerr (2017); Potier et al. (2014); Garcia (2015); McNeil and Small (2014)

Figure A.1. Schematic of Sydney's MSIC



Source: Uniting (2015)