Supervised Injection Facilities and Other Supervised Consumption Sites: Effectiveness and Value

Evidence Report

Posted November 13, 2020

Prepared for

NEW ENGLAND CEPAC
COMPARATIVE EFFECTIVENESS PUBLIC ADVISORY COUNCIL
AN ICER PROGRAM

ICER Staff	University of Washington Modeling Group
Eric Armbrecht, PhD, MS Professor Saint Louis University School of Medicine Health Outcomes and Clinical Research **Rajshree Pandey, PhD, MPH** Research Lead ICER **Katherine Fazioli, BS** Research Lead ICER **Rick Chapman, PhD, MS** Director of Health Economics ICER **Steven D. Pearson, MD, MSc** President ICER **David M. Rind, MD, MSc** Chief Medical Officer ICER	**Greg Guzauskas, MSPH, PhD** Senior Research Scientist University of Washington, CHOICE Institute **Ryan Hansen, PharmD, PhD** Associate Professor University of Washington, CHOICE Institute *The role of the University of Washington is limited to the development of the cost-effectiveness model, and the resulting ICER reports do not necessarily represent the views of the University of Washington.*

DATE OF PUBLICATION: November 13, 2020

How to cite this document: Armbrecht E, Guzauskas G, Hansen R, Pandey R, Fazioli K, Chapman R, Pearson SD, Rind DM. Supervised Injection Facilities and Other Supervised Consumption Sites: Effectiveness and Value; Evidence Report. Institute for Clinical and Economic Review, November 13, 2020. https://icer-review.org/material/supervised-injection-facilities-evidence-report/

Eric Armbrecht served as the lead author for the report and wrote the background, client perspectives, other benefits, and contextual considerations sections of the report. Rajshree Pandey and Katherine Fazioli were responsible for the oversight of the systematic review and authorship of the comparative clinical effectiveness section with the support of Serina Herron-Smith and Eric Borrelli. Rick Chapman was responsible for the oversight of the cost-effectiveness analyses. Azanta Thakur authored the section on operational guidelines. Greg Guzauskas and Ryan Hansen developed the cost-effectiveness model and authored the corresponding sections of the report. David Rind and Steven Pearson provided methodologic guidance on the clinical and economic evaluations. We would also like to thank Catherine Koola for her contributions to this report.

About ICER

The Institute for Clinical and Economic Review (ICER) is an independent non-profit research organization that evaluates medical evidence and convenes public deliberative bodies to help stakeholders interpret and apply evidence to improve patient outcomes and control costs. Through all its work, ICER seeks to help create a future in which collaborative efforts to move evidence into action provide the foundation for a more effective, efficient, and just health care system. More information about ICER is available at http://www.icer-review.org.

The funding for this report comes from government grants and non-profit foundations, with the largest single funder being Arnold Ventures. No funding for this work comes from health insurers, pharmacy benefit managers, or life science companies. ICER receives approximately 19% of its overall revenue from these health industry organizations to run a separate Policy Summit program, with funding approximately equally split between insurers/PBMs and life science companies. No life science companies who participate in this program are relevant to this review. For a complete list of funders and for more information on ICER's support, please visit http://www.icer-review.org/about/support/.

For drug topics, in addition to receiving recommendations from the public, ICER scans publicly available information and also benefits from a collaboration with IPD Analytics, an independent organization that performs analyses of the emerging drug pipeline for a diverse group of industry stakeholders, including payers, pharmaceutical manufacturers, providers, and wholesalers. IPD provides a tailored report on the drug pipeline on a courtesy basis to ICER but does not prioritize topics for specific ICER assessments.

About the New England CEPAC

The New England Comparative Effectiveness Public Advisory Council (New England CEPAC) – a core program of ICER – provides a public venue in which the evidence on the effectiveness and value of health care services can be discussed with the input of all stakeholders. The New England CEPAC seeks to help patients, clinicians, insurers, and policymakers interpret and use evidence to improve the quality and value of health care. The New England CEPAC Council is an independent committee of medical evidence experts from across New England, with a mix of practicing clinicians, methodologists, and leaders in patient engagement and advocacy. All Council members meet strict conflict of interest guidelines and are convened to discuss the evidence summarized in ICER reports and vote on the comparative clinical effectiveness and value of medical interventions. More information about the New England CEPAC is available at https://icer-review.org/programs/new-england-cepac/.

The findings contained within this report are current as of the date of publication. Readers should be aware that new evidence may emerge following the publication of this report that could potentially influence the results. ICER may revisit its analyses in a formal update to this report in the future.

The economic models used in ICER reports are intended to compare the clinical outcomes, expected costs, and cost-effectiveness of different care pathways for broad groups of patients. Model results therefore represent average findings across patients and should not be presumed to represent the clinical or cost outcomes for any specific patient. In addition, data inputs to ICER models often come from clinical trials; patients in these trials and provider prescribing patterns may differ in real-world practice settings.

In the development of this report, ICER's researchers consulted with several clinical experts, patients, manufacturers, and other stakeholders. The following clinical experts provided input that helped guide the ICER team as we shaped our scope and report. None of these individuals is responsible for the final contents of this report or should be assumed to support any part of this report, which is solely the work of the ICER team and its affiliated researchers.

For a complete list of stakeholders from whom we requested input, please visit: https://icer-review.org/material/supervised-injection-facilities-stakeholder-list/

Expert Reviewers

Brandon DL Marshall, PhD
Associate Professor of Epidemiology
Brown University School of Public Health
No relevant conflicts of interest to disclose, defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.

Amos Irwin
Program Director
Law Enforcement Action Partnership (LEAP)
No relevant conflicts of interest to disclose, defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.

Matt Bonn
Program Coordinator
Canadian Association of People who Use Drugs (CAPUD)
No relevant conflicts of interest to disclose, defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.

Table of Contents

List of Acronyms Used in this Report

ACCESS	**AIDS Care Cohort to Evaluate Access to Survival Services**
aHR	**Adjusted Hazard Ratio**
AIDS	**Acquired Immunodeficiency Syndrome**
aOR	**Adjusted Odds Ratio**
ASTHO	**Associate of State and Territorial Health Organizations**
BC	**British Columbia**
CDC	**Centers for Disease Control**
CIRI	**Cutaneous Injection-Relation Infection**
DCR	**Drug Consumption Rooms**
ED	**Emergency Department**
EMS	**Emergency Medical Services**
EMT	**Emergency Medical Technician**
evLYG	**Equal Value Life Years Gained**
HCV	**Hepatitis C Virus**
HIV	**Human Immunodeficiency Virus**
IDU	**Injection Drug User**
IRB	**Injection Risk Behavior**
MAT	**Medically Assisted Treatment**
MeSH	**Medical Subject Headings**
MSIC	**Medically Supervised Injecting Center**
MSIR	**Medically Supervised Injection Room**
NHBLI	**National Heart, Blood, and Lung Institute**
NSW	**New South Wales**
QALY	**Quality-Adjusted Life Years**
OPS	**Overdose Prevention Sites**
OST	**Opioid Substitution Treatment**
OUD	**Opioid Use Disorder**
PHS	**Portland Hotel Society**
PRISMA	**Preferred Reporting Items for Systematic Reviews and Meta-Analyses**
PWID	**People Who Inject Drugs**
PWUD	**People Who Use Drugs**
RCT	**Randomized Controlled Trial**
RR	**Risk Ratio**
SCS	**Supervised Consumption Sites**
SEOSI	**Scientific Evaluation of Supervised Injecting**
SIF	**Supervised Injection Facility**
SSP	**Syringe Service Program**
SUD	**Substance Use Disorder**
US	**United States**
VIDUS	**Vancouver Injection Drug Users Study**

Executive Summary

Background

The opioid overdose epidemic is devastating families and communities across the United States (US). Epidemiological studies from the US Centers for Disease Control and Prevention (CDC) have found that overall life expectancy of Americans has declined, and this decline was largely attributed to drug-related overdose deaths.[1-3] Today in the US, overdoses are classified as the leading cause of injury-related death.

The public health approach to addressing the overdose epidemic is multi-faceted, involving a combination of policy, education, and community interventions. A framework developed by the Association of State and Territorial Health Organizations (ASTHO) describes a cross-sectoral response with four key strategy areas: (1) training and education; (2) monitoring and surveillance; (3) primary and overdose prevention; and (4) treatment, and harm reduction.

Harm reduction strategies seek to mitigate the harms of behaviors.[4] Harm reduction strategies include improved access to the antidote naloxone, syringe service programs (SSPs) that allow people who inject drugs (PWID) to obtain or exchange equipment for injections, and drug checking services that screen for risky drugs such as fentanyl. These implement an alternative to the criminalization and disease treatment models of drug use and addiction. Supervised injection facilities (SIFs) are an additional method of harm reduction. While proponents of harm reduction theory recognize abstinence may be the ideal goal for some people, they accept alternatives which reduce the risk for death and disability even if they do not promote abstinence.[5] Opponents of such strategies often focus on their potential to enable activities that are criminal or perceived as immoral.[6]

Supervised Injection Facilities (or Supervised Consumption Sites)

A SIF is a permanent or mobile place where people can inject drugs they have obtained elsewhere.[7] If it permits use of drugs by routes other than injection (such as smoking or snorting), "supervised consumption site" (SCS) is a more appropriate term. SIFs typically provide equipment to allow users to perform safe and sterile injections while being monitored by trained medical staff who can treat overdoses with oxygen, naloxone, and/or other first-responder care.[7] While SIF model implementation seems to vary based on community needs, resources, and funding, interviews with stakeholders suggest that there are three core features: sterile equipment, trained personnel for supervision, and naloxone administration (along with other first-responder medical care). Additional services may be added to the core features, such as health screening, treatment for substance use disorders (SUDs), referral coordination for social support (e.g., housing), health care and mental health services.[7-10]

In 2003, Insite, the first legally-sanctioned SIF in North America, opened in Vancouver, British Columbia's Downtown Eastside, a neighborhood with high rates of drug use, homelessness, and poverty.[11] Vancouver has become an exemplar setting for researchers and policy advocates to understand the impact of the SIF model on a variety of outcomes, including the ones addressed in this ICER report.

The clients of SIFs are impacted by many social determinants of health. They are homeless, live alone, or have significant housing insecurity. Mental illness and unemployment are common. We spoke with a SIF client who described the people served by SIFs as "poor, homeless, marginalized…a beat-down people".

Although SIFs are considered a type of public health intervention, their population-level reach is measured in city blocks – not miles.[12,13] The location is an important attribute that determines whom a SIF serves as well as its potential public health impact.

There are no legally sanctioned SIFs operating in the United States. Per a report in the New England Journal of Medicine, one unsanctioned site has been operating in the US for six years.[14] There are news reports of elected officials or groups in New York City, Ithaca, Seattle, Denver, Washington DC, Chicago, Baltimore, Burlington, Oakland and San Francisco exploring feasibility, organizing coalitions, or preparing legislation for SIFs.[15-23]

Objectives

The purpose of this assessment is to evaluate the health and economic outcomes of a SIF. This review seeks to answer the question: *What is the net health benefit of implementing a SIF (which includes an SSP) versus an SSP alone?* The CDC recommends SSPs as an evidence-based program noting they are "safe, effective, and cost saving, do not increase illegal drug use or crime, and play an important role in reducing the transmission of viral hepatitis, HIV, and other infections."[24] The ICER value framework includes both quantitative and qualitative comparisons to ensure that the full range of benefits and harms are considered in the judgments about the clinical and economic value. The assessment of effectiveness and value is made in comparison to an SSP as we believe it unlikely that communities without SSPs would be willing to consider a SIF. A SIF implemented in a community without good SSP coverage may experience more than the incremental benefit.

Perspective of the Client and Impact on Persons Who Use Drugs

Section 2 of this report has an extensive description of what we heard from 48 stakeholders including those who are clients of SIFs/SSPs, staff members of SIFs/SSPs, researchers, clinical experts, legislative experts, and a law enforcement officer, and includes direct quotes from many stakeholders.

In brief, some of the major themes we heard include the following:

- **Social Isolation and Community**: SIFs serve the most vulnerable and marginalized people in a community, with many PWUD live in social isolation due to housing insecurity, mental illness, and poverty. SIFs can provide a place where PWUD will be welcomed and can build relationships with other clients and with staff. In contrast to client interactions with SSPs that were described as "transactional and hurried", SIFs have the potential to be more effective at introducing counseling interventions through a community built on camaraderie.
- **Integrated Services**: Providing on-site access to social workers, frontline workers, or counselors was widely considered essential. Their experience suggested that most clients could not be easily referred to external counseling as they often would not accept another counselling center for reasons such as distance, fears, and stigma.
- **Learning from Lived Experience**: Most people commented on how the best SIFs respect the expertise of PWUD and include them in setting policies and operating the facility.
- **Inhalation of Drugs and Safely Testing Drugs**: We heard from multiple stakeholders that changes in the drug supply and client preferences mean that SIFs must adapt and provide for the use of inhaled substances (not limited to opioids), becoming more comprehensive SCSs. Several PWUD described how they use the SIF to check the potency of a new batch under the protection of supervision and resuscitation, if needed.
- **Health Care System Bias**: PWUD noted "shaming and blaming" and "accusations of drug-seeking" from health care system (e.g., hospitals, doctors, and EMTs). SIFs offered a more compassionate way to access education, resources, and medical care.
- **Honeypot Effect**: Most PWUD and many stakeholders dismissed the possibility of a honeypot effect in which a SIF attracted PWUD or crime to a neighborhood, noting the long-established poor conditions of neighborhoods where SIFs are generally located. However, PWUD and stakeholders acknowledged that opposition to SIFs, SSPs, and other forms of harm reduction can exist in a community. We heard from PWUD and stakeholders that drug use still happens just outside of SIFs and SSPs, and at least some community members do complain about syringe/needle debris.
- **Public Drug Use**: There is a community-level trauma caused by public use as well as overdose. SIFs provide the possibility of reducing this trauma to the public.

Clinical Effectiveness

Overview of Studies

Our literature search identified a total of 1188 potentially relevant references for SIFs (see Appendix D2), and we included 48 studies that evaluated individual or community level outcomes for SIFs. The majority of studies evaluated SIFs from Canada (n=33), and the remaining studies evaluated

SIFs in Australia (n=8) and European countries (n=7, including, two from Germany, three from Denmark, and two from Spain). Eighteen studies used a cohort study design, while others employed a pre-post ecological or time series (n=11), and cross-sectional study design (n=10). Nine studies used a qualitative, exploratory, or descriptive study design. We also included government sanctioned evaluation reports from MSIC in Sydney, Australia, the MSIR in North Richmond Australia, and the SCSs in Alberta, Canada. To summarize the effectiveness of SSPs, we included one review of reviews[25] that summarized results from 13 prior systematic reviews as well as three additional systematic reviews.[26-28] These selections were drawn from a search of systematic reviews of SSPs which identified a total of 72 potentially relevant references.

We are assuming that PWID had access to SSPs during the study period, and the outcomes associated with SIFs are informing the added benefits of SIFs over baseline SSP access. Much of the evidence regarding SIFs arises from ongoing prospective cohort studies in Vancouver, Canada, including studies of Insite.

Mortality

Published evidence and unpublished reports from stakeholders suggest that no client of a SIF has ever experienced death from overdose within a facility.[14,29,30] However, PWUD are at high risk of death from overdose, and reduction of mortality inside SIFs does not necessarily demonstrate reduction in mortality in SIF clients.

A Canadian prospective cohort study found that frequent use of SIFs was associated with a lower risk of all-cause mortality (adjusted HR[aHR]: 0.46; 95% CI: 0.26-0.80).[31] However, it is hard to assess causality from such studies as PWUD who are frequent clients of SIFs are likely different from those who are not.

Higher quality evidence on the effect of SIF on mortality probably comes from a population-based study in Vancouver, Canada that evaluated the effects of Insite on overdose mortality by measuring overdose mortality pre-and post-SIF within and beyond the 500 m area around the facility.[12] The SIF opening was associated with a significant reduction of 35% in overdose mortality within 500 m of the facility, compared to a 9.3% decline in the rest of the city. Refer to Table ES1.[12]

Table ES1. Overdose Rates in the Vicinity of a SIF and Beyond (table adapted from Marshall et al. 2011)[12]

	Overdoses within 500 m of SIF		Overdoses farther than 500 m of SIF	
	Pre-SIF	Post-SIF	Pre-SIF	Post-SIF
Number of overdoses	56	33	113	88
Overdose rate (95% CI)*	254 (187 to 320)	165 (108 to 221)	7.6 (6.2 to 9.0)	6.9 (5.5 to 8.4)
Rate difference (95% CI)*; p value	-	88.7 (1.6-176); p=0.048	-	0.7 (-1.3-2.7); p=0.490
Percentage reduction (95% CI)	-	35.0% (0.0 to 57.7)	-	9.3% (-19.8 to 31.4)

SIF: supervised injection facility, CI: confidence interval; Pre-SIF period= January 1, 2001 to September 20, 2003. Post-SIF period= September 21, 2003 to December 31, 2005

*Expressed in units of per 100,000 person-years

Non-Fatal Overdose and Health Care Utilization for Overdose

We identified three studies that evaluated the effect of SIF use on non-fatal overdose and overdose requiring EMS, ambulance, or hospital care.[32,33] A study from Insite from March 2004 to August 2005 found 285 unique users who experienced 336 non-fatal overdose events. Of these overdose events, 28% resulted in a transfer to hospital.[32] A recent time-series analysis of SIF users at Insite reported that the overdose rate per 1000 visits increased from 2010 to 2017 (1.5 vs 9.5, p<0.001) with an increase in overdose events requiring naloxone administration (48.4% to 57.1%, p<0.001) but no overdose deaths were reported within the facility.[33]

In a 2007 study by the New South Wales (NSW) Health Department in Sydney, Australia, opioid overdose-related ambulance calls were analyzed in Sydney over 36 months pre-SIF and 60 months post-SIF. The SIF opening was associated with a greater reduction in ambulance calls for opioid-related overdose events in the vicinity of the SIF compared to the rest of NSW (68% vs 61% decline, p=0.002).[34] This effect was even higher during operating hours of the SIF (80% vs 60% decline, p<0.001).

Injection Risk Behaviors

Reducing injection risk behaviors (IRBs) is important in reducing the risk of infectious disease transmission.[35 1101] We identified seven studies that evaluated the effect of SIFs on reducing IRBs, including four studies from Vancouver and three studies from European countries (Denmark, Germany, and Spain). Most studies reported SIF use was associated with a reduction in IRBs. For example, a cross-sectional analysis of 431 PWID in Vancouver found that SIF use was associated with reduced syringe sharing (adjusted OR [aOR]: 0.30; 95% CI: 0.11 to 0.82; p=0.02).[36] Another cross-sectional study of 1082 PWID explored reasons for changes in changes in IRBs, noting 80% reported reductions in rushed injections, 71% reported less outdoor injections, 56% reported less

unsafe syringe disposal, and 37% reported using used syringes less often.[13] A meta-analysis combined results from three European studies (Wood 2005, Kerr 2005, and Bravo 2009) and found SIF use was associated with a 69% reduction in the likelihood of syringe sharing (pooled effect: 0.31; 95% CI: 0.17 to 0.55).[37]

Infection Prevalence/Incidence and Health Care Utilization

We identified studies that provided evidence on the effect of SIFs on infection incidence and prevalence, most of which were not designed to detect differences, specifically in rates of HIV or HCV.

A cross-sectional study of 510 PWID who attended a SIF in Catalonia, Spain found that there were no significant differences in the prevalence of HIV or HCV among those who had frequent SIF attendance (i.e., daily), medium SIF attendance (i.e., > half of days), and low SIF attendance (i.e., ≤ half of the days).[38]

More extensive evidence exists for the effects of SSPs on viral infections and the results are mixed. A meta-analysis pooled results from 10 studies and found a trend towards a reduced risk of HIV transmission with SSPs (effect size: 0.66; 95% CI: 0.43 to 1.01).[39] When the analysis looked only at six higher-quality studies, a significant reduction was observed (effect size: 0.42; 95% CI 0.22 to 0.81). One meta-analysis pooled results from seven studies and found an increased risk of acquiring HCV with SSPs (RR: 1.62; 95% CI: 1.04 to 2.52)[40], but the authors noted that studies included in their analysis may have been affected by volunteer bias as SSPs may attract higher-risk PWID. Other meta-analyses suggested SSPs may reduce the risk of acquiring HCV.[28,41]

A prospective cohort of 1065 PWID attending Insite (SEOSI cohort) found the use of SIF for all injections versus some injections was associated with a statistically non-significant decreased likelihood of developing a cutaneous injection-related infection in multivariate analysis (aOR 0.58; 95% CI: 0.29 to 1.19).[42] A prospective cohort study of 129 PWID attending a DCF in Essen, Germany found no statistically significant reduction in injection-related abscesses.[43]

Health-Related Quality of Life

No quantitative evidence directly measuring improvements in the health-related quality of life was identified. One qualitative study on people living with HIV who use drugs at Dr. Peter Center in Vancouver, Canada described the positive impacts on quality of life, noting the contributions of increased access to social, health, and broader environmental support services that led to improvement in their overall health.[44]

Other Outcomes

Use and/or more frequent use of SIFs is generally associated with a higher uptake or more rapid entry into treatment and recovery services.[45,38,46-49]

Frequent SIF use is also associated with facilitating access to health and other social services. A multi-country study in Europe reported an association between frequent supervised drug consumption facility use and a greater likelihood of accessing counseling services, medical services, syringe exchange services, and education on safer use.[50] A cross-sectional analysis in Denmark aligned with these results.[51]

One study that assessed changes in drug consumption associated with the use of SIFs reported no substantial differences in relapse rates for injection drug use or stopping drug use pre- and post-SIF opening.[52]

Community and Environmental Outcomes

Among the five studies that assessed the role of SIFs in addressing public drug use and syringe and paraphernalia disposal was an ecological study post-SIF opening in Vancouver Canada where statistically significant reductions in public injection drug use were observed. At the same facility, publicly discarded syringes and injection-related litter also reduced after SIF opening.[53] A retrospective cohort study among 714 PWID attending a SIF reported that increased waiting time at the SIF resulted in an increased likelihood of public injecting.[54] In Sydney, Australia, a time-series study reported that after a SIF opened there was a perceived decline in the proportion of residents and business owners witnessing public injections (19% vs 33%, $p<0.001$) and discarded syringes (40% vs 67%, $p<0.001$).[55] A study of a SIF opening in Copenhagen (Denmark) reported a 56% reduction in public injections as well as a significant improvement in safe syringe disposal.[56] In contrast, over a three-month period a prospective cohort study from Essen (Germany) reported no significant effect of a SIF on public drug use.[43] In a study of DCRs in Denmark, 71% of users also noted that they chose the SIF for drug-use as they were conscious of public drug use bothering people in the neighborhood.[51]

We also identified six studies that assessed the association of the SIF opening on drug-related crime and/or neighborhood safety. Three studies conducted in Sydney, Australia concluded that the opening of the SIF did not result in a significant increase or decrease in crime (i.e., theft, drug-related loitering, or robbery)[57-59], but a slight increase in loitering around the SIF was observed.[57] Similar observations were reported from Vancouver, Canada in an ecological (pre-post) study with no significant changes in robbery or drug trafficking[60] and a decline in vehicle break-ins post-SIF opening. Two studies reported that among SIF users, frequent use of SIFs was not associated with crime or recent incarceration.[61,62]

Uncertainty and Controversies

The available evidence about SIFs comes from studies with cohort and cross-sectional design. It is difficult to establish temporality in some cases and make inferences about the causal association without a reference population or control group.

Many community factors vary considerably across cities in the world (e.g., background risk of bloodborne infection, community support, policing practices, access to primary medical care, treatment capacity and effectiveness), and the variance could impact the generalizability of findings. Some of the risks to generalizability are may be lessened by a real-world experience in Canada and Australia where SIFs have expanded to other cities. For example, a new SIF in North Richmond (Melbourne, Australia) replicated overdose mortality protection observed in Sydney. The recently published review report by the Victorian Government also notes reductions in public injecting and ambulance calls due to overdoses, but no improvement in perceived safety and drug-related nuisances.

Our assessment of SIF effectiveness relies on many studies that are at least 10 years old. It is known that important community factors have changed since then, including global drug supply chains and user preferences. In some parts of the world, drugs typically injected are now being smoked; methamphetamines, for example, are replacing opioids. The increase in fentanyl additives to heroin and/or cocaine has changed the mortality risk of an overdose during the past decade. The estimated mortality reduction of the SIF model studied a decade ago is based on the types and forms of drugs consumed at that time. Naloxone is more widespread today, with police officers, paramedics, community members, and PWID and their allies all having it on hand in a variety of settings. It is unknown how much of a community's overdose mortality can be reduced by a SIF versus expanded naloxone distribution to high-risk people and their social networks.

Experts described the importance of local community support, including law enforcement, to open and maintain a SIF, noting that support for a SIF can erode when proposals and implementation plans with specific locations are presented to community stakeholders.

Summary and Comment

The review and synthesis of included evidence have been organized to demonstrate the contribution of a SIF to individual and population-level outcomes. We did not identify any RCTs and as such, have based comparisons of SIF vs SSP on evidence from the cohort, time-series, pre-post, and other observational studies. Given the available study designs from only a few communities, we recognize that differences between communities could impact generalizability. Moreover, our rating of the effectiveness of a SIF considers its operations in the context of other harm reduction strategies, such as SSPs, which were available to clients in the included studies. We believe that our

focus on the incremental value of a SIF is appropriate since many communities today are exploring if a SIF fits within a broader portfolio of harm reduction and overdose prevention framework.

We recognize that comparisons of SIF use versus no SIF, for which we have relevant data, have shown incremental benefits. Evidence from both Vancouver and Sydney found a significant reduction in occurrences of nonfatal overdose and mortality from overdose in the SIF neighborhood and beyond. Furthermore, our research team has not uncovered any report of an overdose death at a SIF, bolstering our confidence in this outcome. SIFs have demonstrated an ability to assist clients with accessing medical, mental health, and social support services, including the use of addiction treatment services.

The contribution of a SIF to bloodborne infection control is less certain in terms of direct measurement of disease incidence, both due to variation in the baseline infection rates and the lack of incremental data compared with SSPs. We believe that unsafe injecting behaviors are an important and reasonable proxy for infection control since syringe sharing is implicated as primary infection source of new cases of HCV in the US.

In at least some locations, SIFs appear to reduce public injection and, sometimes, syringe and injection litter. Finally, SIFs do not appear to be associated with changes in crime.

Unlike a medication that can be manufactured reliably and administered consistently to deliver benefits to similar patients across the world, how a SIF is implemented can impact individual and community outcomes. The intervention development, including stakeholder engagement, contributes to results. Our overall assessment of the evidence does not consider the ease or difficulty another organization may have in setting up and running a SIF. We assume that planning, stakeholder engagement, and daily management can be executed similarly to that of organizations in Vancouver and Sydney to produce the reported results.

On balance, we believe we have high certainty that, compared with SSPs, SIFs prevent overdose deaths. The degree to which overdose prevention translates to substantially lengthening the life of the individual is uncertain. The evidence on community overdose mortality from Marshall et al. 2011[12], provides moderate-quality evidence given the drop-off in effect over distance from the SIF, which is akin to a dose-response effect. This, too, provides moderate certainty of a substantial benefit. We do not believe that possible harms which have been reported – some communities report increases in needle litter near a SIF – could reduce the net benefit below incremental. There is good reason to believe the net benefit is substantial.

Thus, we have concluded that there is high certainty that SIFs, compared with SSPs provide a small, or substantial net health benefit , and moderate certainty that SIFs provide a substantial net health benefit, leading to a rating of “incremental or better” (**B+**).

Cost Effectiveness

Overview

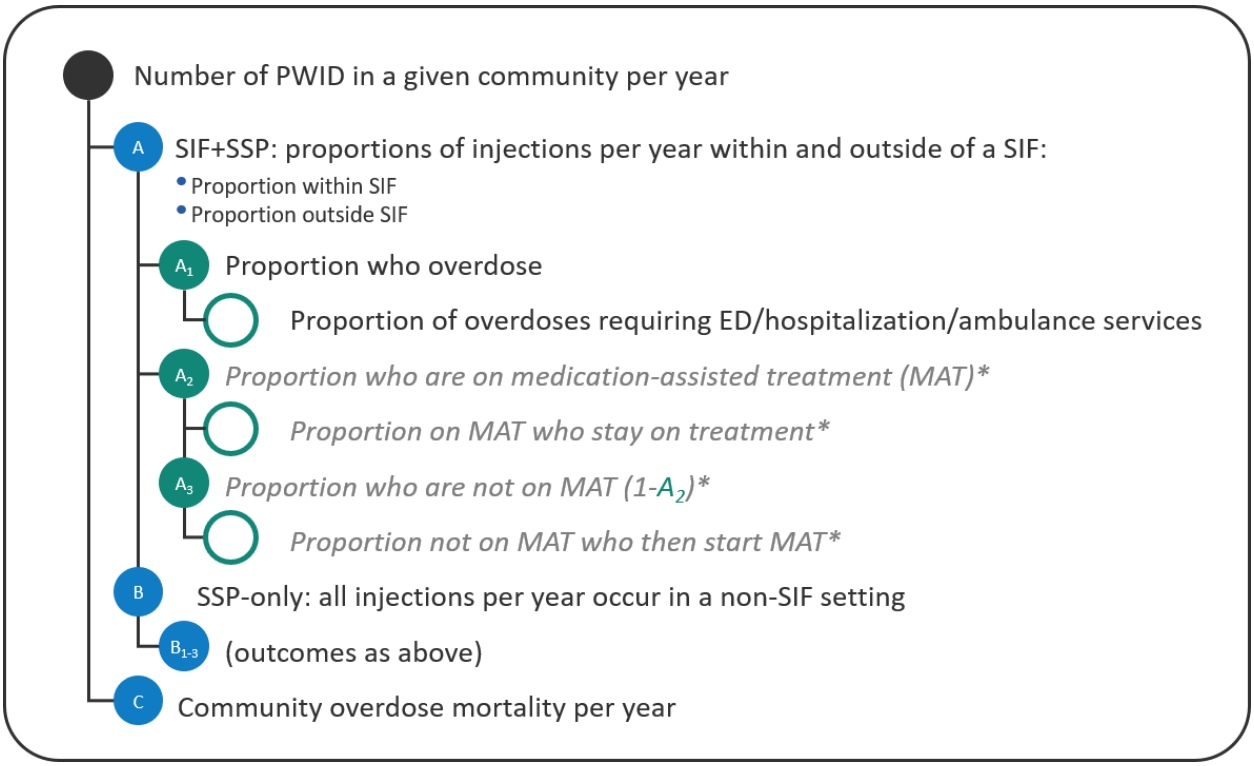
The primary aim of this analysis was to estimate the cost effectiveness of SIFs for IDU among PWID using a cost-effectiveness analysis. The model compared SIFs to SSPs, i.e., SIF+SSP, vs. SSP-only. Because SIFs are not funded by the health care system or payers of health care, the base-case analysis was a modified societal perspective and a one-year time horizon.

Methods and Model Structure

We developed a decision analytic model for this evaluation, with outcome calculations adapted from prior relevant economic models of harm reduction for PWID[63-69] and informed by interviews among key staff and researchers of SIFs.

The model focused on communities of PWID, specified by parameters for individual US cities, who could potentially utilize SIFs in locations where SSPs already exist. We modeled costs and outcomes for Boston, Philadelphia, San Francisco, Atlanta, Baltimore, and Seattle, based on the prior existence of an SSP,[70] US geographic location, and the availability of broad city-level estimates.

Figure ES1. Model Framework



ED: emergency department, MAT: medication-assisted treatment, PWID: people who inject drugs, SIF: supervised injection facilities, SSP: syringe service program

Key Model Characteristics, Assumptions, and Inputs

Table ES2. Key Model Assumptions

Assumption	Rationale
Hypothetical legally-sanctioned SIFs in US cities are comparable to Insite (Vancouver, BC, Canada) in terms of effectiveness, services offered, and cost of living-adjusted operating costs.	Insite is the first and most well-documented SIF in North America.
The US cities modeled have a 0.25-mile radius area within the city that could have 2100 PWID clients for a SIF.	The Insite client-service rate is the basis for the healthcare resource use effectiveness estimates for SIFs in all modeled cities.
Rates of HIV/hepatitis C/other infections are equivalent between SIF+SSP and SSP-only.	We recognize there is some evidence that SIFs may reduce needle sharing, leading to a reduction in infections. However, due to the short time horizon of our model (1 year) and the complexity of estimating the timing of infections and attributing costs to these conditions, we chose to take a conservative approach and not include these additional cost off-sets. We explored a difference in infection rates driven by a reduction in needle sharing conferred by the SIF setting in a scenario analysis.
We assumed that the rates of initiation and continuation of MAT are equivalent between clients using SIFs and SSPs.	There is a lack of comparative data between these two services; however, stakeholders have indicated that increased face-to-face time spent with PWID may lead to increased uptake of MAT. Therefore, we explored the impacts of marginal increases in MAT initiation due to SIFs in a scenario analysis.

BC: British Columbia, HIV: human immunodeficiency virus, MAT: medication-assisted treatment, PWID: people who inject drugs, SIF: supervised injection facility, SSP: syringe service program

Table ES3. Overdose Mortality Inputs

Parameter	Estimate (sensitivity analysis range)
Fatal OD reduction within 0.25 mi of SIF[12]	35.0% (±20%)
Fatal OD reduction beyond 0.25 mi of SIF[12]	9.3% (±20%)
Proportion of total overdose deaths occurring within 0.25 mi^2 of SIF[67]	5% (±20%)

OD: overdose, SIF: supervised injection facility

Utilizing estimates from Insite, we assumed that 0.95% of overall injections result in an overdose (Table ES3).[33] Emergency services included both ambulance services as well as hospital ED access, and were conditional on the occurrence of an overdose.

Table ES4. Overdose and Emergency Services Inputs

Parameter	Estimate (sensitivity analysis range)
Overdose (OD) Inputs	
Total annual injections [71]	180,000 (±20%)
Number of unique clients/month[71]	2,100 (±20%)
Percent of injections resulting in OD[33]	0.95% (±20%)
Emergency Services Inputs	
Proportion of ODs at SIF+SSP resulting in ambulance ride[67,72]	0.79% (±20%)
Proportion of ODs at SIF+SSP resulting in ED visit[67,72]	0.79% (±20%)
Proportion of SSP-only ODs resulting in ambulance ride[67,73]	46% (±20%)
Proportion of SSP-only ODs resulting in ED visit[67,73]	33% (±20%)
Proportion of ED visits resulting in hospitalization[74]	48% (±20%)

ED: emergency department, OD: overdose, SIF: supervised injection facility, SSP: syringe service program

We assumed that SIFs provide equivalent benefit to SSPs in terms of initiation of MAT. Therefore, we used the same estimate of 5.78% of PWID accessing MAT due to a referral from the SIF and/or SSP (Table ES5).[75] We assumed 50% of PWID who begin MAT stay on treatment each year.

Table ES5. Medication-Assisted Treatment Inputs

Parameter	Estimate (sensitivity analysis range)
Proportion of PWID who access MAT[75]	5.78% (±20%)
MAT continuation rate[67]	50% (±20%)

MAT: medication-assisted treatment, PWID: people who inject drugs

SIF facility and operation costs were estimated based on the Irwin et al. approach, adapting each community's estimate according to their individual characteristics.[66,67] Start-up and operating costs are shown in Table ES6. Downstream costs of ambulance rides, ED visit and hospitalization are presented in Table ES7.

Table ES6. Operating and Facility Cost Inputs

Parameter	Estimate (sensitivity analysis range)
Insite Annual Operating Cost[76,77]	**$1,687,286 (±20%)**
Term of Commercial Loan*	**15 years**
SIF Square Footage[67]	**1000**
Adjusted SSP Annual Operating Cost[77,78]	**$1,533,279 (±20%)**

*Assumption
SIF: supervised injection facility, SSP: syringe service program

Table ES7. Emergency Services Cost Inputs

Parameter	Estimate (sensitivity analysis range)
Ambulance Ride Costs[79]	
Boston	$523.06 (±20%)
Philadelphia	$487.41 (±20%)
San Francisco	$566.34 (±20%)
Atlanta	$461.63 (±20%)
Baltimore	$492.50 (±20%)
Seattle	$516.37 (±20%)
Overdose-related ED Visit Cost (All Cities)[74]	$3,451 (±20%)
Overdose-related Hospitalization Cost[80]	
Boston	$8,379 (±20%)
Philadelphia	$7,502 (±20%)
San Francisco	$8,683 (±20%)
Atlanta	$5,890 (±20%)
Baltimore	$7,502 (±20%)
Seattle	$8,683 (±20%)

ED: emergency department

Model Outcomes

Model outcomes included total overdose deaths prevented and total costs for each intervention. The model outcomes also include total emergency services avoided, and total increase in MAT initiation. Due to the one-year time horizon, all results are reported as undiscounted values.

Results

Base-Case Results

The annual cost of operating a SIF+SSP ranged from $1.6 million to $2.5 million, while the cost of operating an SSP-only ranged from $1.4 million to $1.7 million, depending on the location. A hypothetical SIF+SSP was found to result in the prevention of three (Boston) to 15 (Philadelphia) overdose deaths per year, as well as 773 fewer overdose-related ambulance rides, 551 fewer overdose-related ED visits, and 264 fewer hospitalizations (all based on 180,000 injections/year/comparator). This resulting in cost-savings by city are shown in Table ES8, ES9 and ES10.

Table ES8. Base-Case Results for Boston and Philadelphia

Outcome	Boston			Philadelphia		
	SIF+SSP	SSP-Only	Incremental	SIF+SSP	SSP-Only	Incremental
Total Cost	$2,261,000	$6,270,000	-$4,009,000	$1,896,000	$5,796,000	-$3,899,000
Annual Cost of Facility	$2,153,000	$1,641,000	$511,300	$1,794,000	$1,433,000	$361,500
Ambulance Costs	$7,100	$411,400	-$404,400	$6,600	$383,400	-$376,800
ED Visit Costs	$46,600	$1,947,000	-$1,901,000	$46,600	$1,947,000	-$1,901,000
Hospitalization Costs	$54,300	$2,270,000	-$2,215,000	$48,600	$2,032,000	-$1,983,000
Overdose Deaths	9	13	-3	43	58	-15
Ambulance Rides	14	787	-773	14	787	-773
ED Visits	14	564	-551	14	564	-551
Hospitalizations	6	271	-264	6	271	-264

ED: emergency department, SIF: supervised injection facility, SSP: syringe service program

Table ES9. Base-Case Results for San Francisco and Atlanta

Outcome	San Francisco			Atlanta		
	SIF+SSP	SSP-Only	Incremental	SIF+SSP	SSP-Only	Incremental
Total Cost	$2,624,000	$6,457,000	-$3,833,000	$1,687,000	$5,310,000	-$3,623,000
Annual Cost of Facility	$2,513,000	$1,712,000	$800,900	$1,596,000	$1,404,000	$191,500
Ambulance Costs	$7,700	$445,500	-$437,800	$6,200	$363,100	-$356,900
ED Visit Costs	$46,600	$1,947,000	-$1,901,000	$46,600	$1,947,000	-$1,901,000
Hospitalization Costs	$56,300	$2,352,000	-$2,296,000	$38,200	$1,595,000	-$1,557,000
Overdose Deaths	12	17	-4	18	24	-6
Ambulance Rides	14	787	-773	14	787	-773
ED Visits	14	564	-551	14	564	-551
Hospitalizations	6	271	-264	6	271	-264

ED: emergency department, OD: overdose, SIF: supervised injection facility, SSP: syringe service program

Table ES10. Base-Case Results for Baltimore and Seattle

Outcome	Baltimore			Seattle		
	SIF+SSP	SSP-Only	Incremental	SIF+SSP	SSP-Only	Incremental
Total Cost	$1,727,000	$5,750,000	-$4,023,000	$2,146,000	$6,346,000	-$4,199,000
Annual Cost of Facility	$1,625,000	$1,383,000	$241,900	$2,036,000	$1,640,000	$396,100
Ambulance Costs	$6,700	$387,400	-$380,700	$7,000	$406,200	-$399,200
ED Visit Costs	$46,600	$1,947,000	-$1,901,000	$46,600	$1,947,000	-$1,901,000
Hospitalization Costs	$48,600	$2,032,000	-$1,983,000	$56,300	$2,352,000	-$2,296,000
Overdose Deaths	26	35	-9	8	11	-3
Ambulance Rides	14	787	-773	14	787	-773
ED Visits	14	564	-551	14	564	-551
Hospitalizations	6	271	-264	6	271	-264

ED: emergency department, OD: overdose, SIF: supervised injection facility, SSP: syringe service program

Sensitivity & Scenario Analysis Results

To demonstrate effects of uncertainty on both costs and health outcomes, we varied input parameters using reasonable ranges to evaluate changes in costs and health services utilization. We also performed four scenario analyses to evaluate the base case assumptions around infection reduction, overdose rates, MAT uptake, and the perspective of the analysis. The results of these analyses are featured on pages 52-56 of the full report.

Summary and Comment

The costs of operating a SIF were estimated to be higher than operating an SSP across all six cities. However, those costs were offset by cost savings attributed to SIFs through the avoidance of ED visits and subsequent hospitalizations. Furthermore, in all six cities, SIFs were estimated to reduce mortality by avoiding overdose deaths.

The model results were sensitive to several input parameters, which varied slightly across the six cities. The underlying community-level risk parameters of overdose and overdose mortality, along with the mortality risk reduction attributed to SIFs, were the most influential model parameters. Additionally, parameters that determined the number of injections occurring in SIFs within each city also influenced the model estimates.

Potential Other Benefits and Contextual Considerations

For some communities, the opening of a SIF reflects a philosophical shift in addressing substance use disorders as a health issue, rather than a criminal issue. SIFs serve marginalized, vulnerable

populations that are disadvantaged or underserved. There are some potential other benefits offered by a SIF to the individual PWID, caregivers, the delivery system, other PWUD, or the public beyond what is described by the evidence on comparative clinical effectiveness. A summary of these potential other benefits is shown in the table below.

Table ES11. Potential Other Benefits or Contextual Considerations

Potential Other Benefit or Contextual Consideration	Relevant Information
Assumptions made in the base-case cost-effectiveness estimates rendering results overly optimistic or pessimistic.	Most quantitative data that informed the economic model are derived from SIFs operating in only two communities. Uncertainty exists about local factors (unmeasured or unmeasurable attributes unique to the people and place) that contributed to favorable outcomes at the time of the study.
Whether the intervention differentially benefits a historically disadvantaged or underserved community.	Persons served by SIFs are among the most vulnerable and marginalized in a community. Given the disparities in SUD by socio-economic class, SIFs differentially benefit groups with lower life expectancy and higher disability.
Whether the intervention will significantly reduce the negative impact of the condition on family and caregivers vs. the comparator.	In comparison to SSPs which have been described in interviews as "transactional", SIFs are more likely to engage clients in longer and more frequent interactions with staff and other clients. A trust-based relationship can be instrumental in helping clients improve injection behavior and link to medical, mental/behavioral health and social services.
Whether the intervention will have a significant impact on improving return to work and/or overall productivity vs. the comparator.	If SIFs increase the likelihood that clients will initiate and continue MAT, it is possible they could increase return to work and/or productivity.

Health-Benefit Price Benchmarks

As the assessment for this non-drug topic does not include estimates of incremental quality-adjusted life years (QALYs) or equal value life years gained (evLYG), ICER did not produce health-benefit price benchmarks as part of this report.

Potential Budget Impact

As the assessment for this non-drug topic does not include price per treatment or estimates of cost-effectiveness threshold prices, ICER did not produce potential budget impact analyses as part of this report.

1. Introduction

1.1 Background

National and Regional Epidemic

The opioid overdose epidemic is devastating families and communities across the United States (US). Epidemiological studies from the US Centers for Disease Control and Prevention (CDC) have found that overall life expectancy of Americans has declined, and this decline was largely attributed to drug-related overdose deaths.[1-3] Today in the US, overdoses are classified as the leading cause of injury-related death. Overall, drug overdose fatalities decreased 4.1% to 67,367 deaths between 2017 and 2018, and 69.5% involved an opioid [81] and the rest from cocaine or psychostimulants with abuse potential.[2] However, opioid-involved death rates during this period increased in a number of groups (those ages 65 and older, Hispanics, non-Hispanic Blacks) and regions (West, Northeast). In the Northeast region, synthetic opioids other than methadone drove the annual increase, at 17.9%.[81]

The CDC viewed the epidemic of opioid fatalities as having happened in three distinct episodes.[82] The first, which began in the 1990s, involved prescription opioids. Beginning in 2010, the second was marked by heroin-involved deaths. The current drivers of the epidemic are synthetic opioids such as fentanyl and fentanyl analogues, which are pushing mortality even higher. Opioid deaths attributable to synthetic opioids increased by 45.2% from 2016 to 2017.[83] Other sources of drug overdose deaths may be emerging: from 2012 to 2018, the age-adjusted death rate involving cocaine more than tripled, and overdose deaths involving psychostimulants (e.g., methamphetamine, amphetamine, and methylphenidate) increased nearly 5-fold over the same period.[2]

A Public Health Approach

The public health approach to addressing the overdose epidemic is multi-faceted, involving a combination of policy, education, and community interventions. A framework developed by the Association of State and Territorial Health Organizations (ASTHO) describes a cross-sectoral response with four key strategy areas: (1) training and education; (2) monitoring and surveillance; (3) primary and overdose prevention; and (4) treatment, and harm reduction. For example, training and education of physicians and pharmacists can improve adherence to clinical practice guidelines for pain management and reduce the number of patients at risk for addiction and dependence.[84] Expanding distribution channels of naloxone, an antidote for opioid overdose, can reduce rates of fatal overdose.[81,85,86] For people who seek treatment or want to reduce frequency of opioid use, a variety of medication-assisted treatments (MATs) are effective, a topic addressed by ICER assessments in 2014 and 2018. The ASTHO framework recommends funding and implementing

supervised injection facilities — also known as safer injection facilities, supervised consumption sites, or overdose prevention centers—as a harm reduction strategy, noting the program is evidence-based for reducing fatal opioid overdose and enhancing access to primary health care.[84]

Harm Reduction Theory

Harm reduction strategies seek to mitigate the harms of behaviors.[4] Injury prevention policies (e.g., mandating seat belts, bicycle helmets, and child safety seats) are forms of harm reduction that are typically widely accepted.[87] When harm reduction has been applied to substance use disorders, controversy has sometimes arisen because such strategies do not focus on preventing the use of drugs but rather on reducing the risk of such use.[88] Harm reduction strategies (including improved access to naloxone, syringe service programs, drug checking services and supervised injection facilities) implement an alternative to the criminalization and disease treatment models of drug use and addiction. While proponents of harm reduction theory recognize abstinence may be the ideal goal for some people, they accept alternatives which reduce the risk for death and disability even if they do not promote abstinence.[5] Opponents of such strategies often focus on their potential to enable activities that are criminal or perceived as immoral.[6]

Naloxone Access

Naloxone is an essential tool in responding to the overdose crisis as it reverses an opioid overdose when given intranasally or intramuscularly. Naloxone is an opioid antagonist that is used as an antidote to opioids when an overdose occurs. To be effective, it must be available at the time of overdose.[89] When naloxone is distributed widely in a community, it safely reduces overdose deaths in a cost-effective manner. We have not discovered objection to its administration in response to an overdose, although there have been concerns about costs[90] and encouragement of riskier behaviors.[91,92]

Syringe Service Programs

Syringe service programs (SSPs) reduce harm by providing access to safer materials for drug injection (sterile syringes and needles; clean water and other equipment), and also safer disposal of contaminated equipment, and referrals to addiction treatment services; some also offer screening for bloodborne pathogens such as HIV and hepatitis C, distribution of naloxone, safer sex products, and access to medical, mental health, and social support services.[24] As with expanded naloxone distribution, an SSP acknowledges injected drug use is occurring in a community and seeks to reduce harms associated with injecting behaviors. Using sterile equipment for every injection reduces risk for acquiring and transmitting bloodborne viral infections such as HIV, hepatitis B, and hepatitis C.[24] Because SSPs provide for disposal of contaminated equipment, they have the potential to enhance the safety of the public and also first responders. Historically, SSPs have raised concerns among those who feel that harm reduction strategies expend resources that encourage

immoral or illegal behaviors.[93] Thirty-eight states plus the District of Columbia have laws that enable and/or regulate SSPs, as of August 2019.[94] According to National Association of Syringe Exchange Network's provider database, there are 444 SSPs operating in the United States today employing a variety of models, such as mobile, mail-order, and needle exchange.[95] There are also unsanctioned SSPs that have been informally started by people who use drugs (PWUD) outside the restrictions imposed by some governments.[93]

The CDC recommends SSPs as an evidence-based program, summarizing the effectiveness in this way:

> "Nearly 30 years of research has shown that comprehensive SSPs are safe, effective, and cost saving, do not increase illegal drug use or crime, and play an important role in reducing the transmission of viral hepatitis, HIV, and other infections. Research shows that new users of SSPs are five times more likely to enter drug treatment and about three times more likely to stop using drugs than those who don't use the programs. SSPs that provide naloxone also help decrease opioid overdose deaths. SSPs protect the public and first responders by facilitating the safe disposal of used needles and syringes."[24]

Drug Checking Services

Drug checking services are another tool used to combat the overdose crisis. As the rate of illicit drugs containing highly potent opioids such as fentanyl and fentanyl analogues has increased, informing people about chemical composition can modify use behaviors, such as dose consumed, and reduce overdose risk.[96] A variety of technologies exists for analyzing chemical composition, but little is known about optimal process and setting to impact outcomes.[97] The public health impact of a drug checking service depends on the willingness of PWIDs to use it, and a wide range of willingness has been reported.[98,99]

Supervised Injection Facilities

Supervised injection facilities (SIFs) are permanent or mobile facilities where people can inject drugs they have obtained elsewhere.[7] If they permit use of drugs by routes other than injection (such as smoking or snorting), the more comprehensive term is "supervised consumption sites" (SCS). These facilities typically provide equipment to allow users to perform safe and sterile injections while being monitored by trained medical staff who can treat overdoses with oxygen, naloxone, and/or other first-responder care.[7] The sites may also have resources and information available for individuals seeking addiction treatment, primary health care, or social services. While SIF model implementation seems to vary based on community needs, resources, and funding, interviews with stakeholders suggest that there are three core features: sterile equipment, trained personnel for supervision, and naloxone administration (along with other first-responder medical care).

The following services may augment the core features: (1) self-management education for safer injecting practices, (2) screening for soft tissue infections, (3) hepatitis C screening/treatment, (4) drug toxicity screening (e.g., fentanyl), (5) on-site detoxification, (6) access to MAT, (7) referral coordination for social support (e.g., housing), health care and mental health services, (8) psychological/behavioral health counseling, (9) space for client relaxation and socialization, (10) personal hygiene supports (e.g., shower, laundry), (11) syringe service program (SSP) (e.g., needle exchange), (12) naloxone distribution, (13) space for consuming drugs by smoking, and (14) mobile unit to reach neighborhoods with high need.[7-10]

In the 1970s, The Netherlands established the first SIF model in Europe as part of a response to psychosocial needs of youth and their use of illegal drugs.[100] The model adapted to the needs of people using drugs problematically by combining a drop-in meeting space for drug consumption with basic health (e.g., counseling, medical care) hygiene, (e.g., shower, laundry) and food resources. In the 1980s, SIFs were promoted across Europe with a goal of reducing both the harms of injecting drugs and the community effects of public injecting. Around the same time, the model was adopted in Switzerland for similar reasons and SIFs were implemented in Germany in the 1990s and in Sydney, Australia in 2001.[101]

In 2003, Insite, the first legally-sanctioned SIF in North America, opened in Vancouver, British Columbia's Downtown Eastside, a neighborhood with high rates of drug use, homelessness, and poverty.[11] After 17 years of continuous operation, Vancouver has become an exemplar setting for researchers and policy advocates to understand the impact of the SIF model on a variety of outcomes, including the ones addressed in this ICER report. Currently, SIFs are available in 19 cities across Canada.[102]

Currently in the US, there are no legally sanctioned SIFs. Plans to open a SIF or initiate a multi-stakeholder planning process for a SIF have been announced by some cities. For example, the non-profit agency Safehouse has been engaged with the development of a SIF since January 2018 in Philadelphia, navigating through legal, policy and community support issues.[103] In 2019, the mayor of Somerville, a city in the Boston metropolitan area, stated plans to open a SIF in response to overdose deaths.[104] There are news reports of elected officials or groups in New York City, Ithaca, Seattle, Denver, Washington DC, Chicago, Baltimore, Burlington, Oakland and San Francisco exploring feasibility, organizing coalitions, or preparing legislation for SIFs.[15-23] A recent letter published in the New England Journal of Medicine described the experiences of an unsanctioned SIF that has been operating in the US for six years.[14]

The clients of SIFs are usually homeless, live alone, or have significant housing insecurity. Unemployment is common. SIF clients are impacted by many social determinants of health. We spoke with a SIF client who described the people served by SIFs as "poor, homeless, marginalized…a beat-down people" noting that he "had given up on himself" when he found harm reduction services. The prevalence of mental and behavioral health conditions is high among people who

inject drugs (PWID). Although SIFs are considered a type of public health intervention, their population-level reach is measured in city blocks – not miles.[12,13] It seems that a standalone SIF is generally able to address the needs of one neighborhood, as experts explained that PWIDs are unable or unwilling to travel far for SIF services. Thus, location is an important attribute that determines whom a SIF serves as well as its potential public health impact.

Even more than SSPs, the potential implementation of SIFs has raised objections from those who do not feel that facilitation (or direct observation) of drug consumption is appropriate for a health care or public health worker. Even among those who support harm reduction strategies, concerns may be raised about the effects on a neighborhood if PWIDs are attracted and congregate. In 2000, a survey of 515 residents and 209 businesses near a planned SIF location in Sydney showed that 26% and 37% of respondents, respectively, disagreed with the establishment of the SIF. Disagreement waned two years after the SIF opened.[105]

Objectives

The purpose of this assessment is to evaluate the health and economic outcomes of a SIF. This review seeks to answer the question: *What is the net health benefit of implementing a SIF (which includes an SSP) versus an SSP alone?* The ICER value framework includes both quantitative and qualitative comparisons across treatments to ensure that the full range of benefits and harms are considered in the judgments about the clinical and economic value. The assessment of effectiveness and value is made in comparison to an SSP as we believe it unlikely that communities that have not been willing to implement SSPs would be willing to consider a SIF. A SIF implemented in a community without good SSP coverage may experience more than the incremental benefit.

1.2 Scope of the Assessment

Populations

The population of focus for the review included all PWID living in an area with access to an SSP and where a SIF could potentially be placed within a few blocks of where they reside.

We also sought evidence on subpopulations suggested by the stakeholders, looking for evidence on the following subgroup effects:

- Housing status, comparing effects in people living with homelessness or unstable housing and those with stable housing
- Injected drug class, comparing effects in people who inject opioids with effects in people who inject stimulants such as cocaine or methamphetamine

Interventions

The intervention of interest is the implementation of SIFs including sites that permit other forms of drug consumption. We assume that SIFs will include, at a minimum, three core features: sterile equipment, trained personnel for supervision, and naloxone administration (along with other first-responder medical care). We recognize that published data come from SIFs that offer additional resources and services to clients which may impact some of the individual and community outcomes of interest.

Comparators

We compared SIFs to SSPs.

Outcomes

The outcomes of interest are described in the list below.

- Individual outcomes
    - Overdose
        - Requiring EMS/ambulance or hospital care
        - Mortality (occurring in or out of the facility)
    - All-cause mortality
    - Infection
        - Chronic viral infection (hepatitis C and HIV)
        - Bacterial infection requiring hospitalization (e.g., antibiotics, surgery, endocarditis)
        - Skin and soft tissue infection not requiring hospitalization
    - Health-related quality of life
    - Intermediate outcomes
        - Use of treatment and recovery support services
        - Receipt of social (e.g., housing), primary medical care, dental and mental health services
        - Injection behaviors (e.g., needle and syringe sharing)
    - Drug consumption (e.g., frequency, amount)
- Community and environmental outcomes
    - Syringe and paraphernalia disposal
    - Public drug use
    - Drug-related crime
    - Drug use prevalence
- Health system utilization
    - Hospitalizations

- Emergency department visits
- EMT/paramedic calls/responses

Timing

Evidence on intervention effectiveness and safety has been collected from studies of any duration.

Settings

The setting of interest is community SIFs, whether they are affiliated with health centers and hospitals, and mobile SIFs, or not. Inpatient SIFs (i.e., located within hospital settings) are not part of the scope of this review.

1.3 Definitions

Supervised Injection Facility (SIF) – The Drug Policy Alliance defines SIFs as "Legally sanctioned facilities that allow people to consume pre-obtained drugs under the supervision of trained staff and are designed to reduce the health and public order issues often associated with public drug consumption. They are also called overdose prevention sites (OPS), safe or supervised consumption services (SCS), and drug consumption rooms (DCR)."[8]

Syringe Service Programs (SSPs) – The CDC defines SSPs as "Community-based prevention programs that provide access to or disposal of sterile syringes and injection equipment, access to substance use or addiction treatments/services, health care and social services, vaccination, and testing services."[24]

Medication Assisted Treatments (MAT) – The Substance Abuse and Mental Health Services Administration defines MAT as "Use of medications, in combination with counseling and behavioral therapies, to provide a "whole-patient" approach to the treatment of substance use disorder."[106]

1.4 Potential Cost-Saving Measures in Opioid Use Disorder

ICER now includes in its reports information on wasteful or lower-value services in the same clinical area that could be reduced or eliminated to create headroom in health care budgets for higher-value innovative services (for more information, see https://icer-review.org/final-vaf-2017-2019/). These services are ones that would not be directly affected by therapies for opioid use disorder (OUD) (e.g., reduction in disability), as these services will be captured in the economic model. Rather, we are seeking services used in the current management of OUD beyond the potential offsets that arise from a new intervention. During stakeholder engagement and public comment periods, ICER encouraged all stakeholders to suggest services (including treatments and mechanisms of care) currently used for patients with OUD that could be reduced, eliminated, or

made more efficient. We received a suggestion that advertising (e.g., billboards) which promotes OUD treatment and other services for PWID may be a low value use of resources.

2. Perspective of People Who Use Drugs

2.1 Methods

During ICER's scoping and open input periods, we received public comment submissions from 4 stakeholders (1 SIF, 2 advocacy groups, and 1 clinical researcher) and participated in conversations with 37 key informants and/or organizations (4 advocacy organizations, 6 SIF/SSP staff members, 23 researchers, 5 clinical experts, 1 law enforcement officer, 8 legislative/policy experts). These comments and conversations helped us to discuss the impact on PWUD as described below.

The ICER team also interviewed 11 clients/staff members of SIFs or SSPs that operate in Canada as government-approved safe consumption sites (SCS) or overdose prevention sites (OPS); they were also affiliated with the Canadian Association of People Who Use Drugs (CAPUD), the non-profit organization that assisted ICER with interviews. The quotations that are integrated into the text below came directly from these interviews.

2.2 Impact on People Who Use Drugs

Social Isolation

"Lots of people are dead because they overdosed in public alone with no help around them…I can think of 13 people who are still alive today because I was there to call 911 or seek help." – SCS Client

The PWUD we interviewed affirmed that SIFs serve the most vulnerable and marginalized people in a community, noting that many PWUD live in social isolation due to housing insecurity, mental illness, and poverty. Through supervisory services, SIFs mitigate overdose risks associated with injecting alone, a common behavior among PWUD who do not have access to a SIF. One stakeholder described the main task of a SIF as "provid[ing] a place where people will be attracted to come and feel welcomed" so they are not alone. In addition to time-critical first-responder care, SIFs serve as an access point for people who are socially isolated to learn about community resources and be linked to health and social services.

"To me, a lot of drug use is very rational…very rationale response to a society where mental health care is difficult to access." – OPS Staff Member and Client

Camaraderie and Community

"PWUD don't have a lot of places they can go without being stigmatized, so it's so important to have a place you can go and be welcomed and use safely." – OPS Staff Member and Client

Many PWUD and stakeholders described how the SIF had enabled building of relationships with staff and other regular clients. The SIF provides a comfortable, safe space for people to be their true selves and forge trust with others. The SIF was one of the only judgement-free zones available to PWUD whose lives are filled with discrimination, criminalization, and trauma. They felt that SIFs contribute to positive changes in the community that stem from relationship-building among clients, harm reduction workers (e.g., nurses, technicians), police, and even drug dealers. SIFs provide an "opportunity to meet people in a positive way...and that is an immeasurable kind of benefit, in my opinion," noted one former SIF client. One SIF administrator described the purpose of a SIF as "being community space first, that happens to have clinical supports." Another one described the "living room effect" of a SIF – providing a comfortable environment that can help reduce stress and reduce the need to self-soothe with drugs. One stakeholder pointed out that experience and research has demonstrated that PWIDs use SIFs when they are available.

"Needle exchange programs, yeah, it's great, but it's a momentary interaction; they're not going to be there to save your life." – SCS Client

Health Care System Bias

We heard from some stakeholders that SIFs provide a way for PWUD to reduce interactions with hospitals, doctors, and EMTs, during which they often felt there was frequent "shaming and blaming" and "accusations of drug-seeking". Many PWUD relayed stories of stigmatization that compromised their physical and mental health, such as refusal of primary medical care for hepatitis treatment follow-up. Multiple people noted a lack of respect by the health care system for those who work in harm reduction (and their clients). A participant – who was a SIF client and worked for an SSP – found the health care system to be "scary" and distrusted doctors because of poor treatment in a hospital setting. Nurses and doctors at SCSs, however, were stated to be much more compassionate to the problems faced by clients.

"Most interactions with pharmacists, doctors, lawyers…are all so stigmatizing. They make you feel kind of like a moral failure." – OPS Staff Member and Client

Another client noted that electronic health records assured PWUD are labeled "junkie" across the health care system, even before meeting a health care provider. He and others felt that SIFs can offer a counterbalance to the bias of the health care system while providing health-related services valued by PWUD.

Inhalation

We heard from multiple stakeholders that changes in the drug supply and client preferences mean that SIFs must adapt and provide for the use of inhaled substances (not limited to opioids), becoming more comprehensive SCSs. One person noted that smoking is on the rise now since people have learned how to get the same high with less need for the complexities of injecting. We heard that provision of supplies for smoking by one harm reduction program had quadrupled over the prior 18 months. One interviewee believed that technology (e.g., rapid negative pressure decontamination) could protect the staff if government leaders allowed the spending. Nearly every person we interviewed recommended that a space for smoking be included in a SIF because the strategy should focus on the person, not the drug. One stakeholder highlighted the racial disparities in incarceration related to crack cocaine, which is primarily smoked, and recommended the provision of smoking facilities not only as a harm reduction practice, but also as a component of addressing structural racism in the United States.

> *"We heard loud and clear from PWUD; they did not want the SIF to be just for injection."* – Public health agency professional

Testing New Batches or New Suppliers

SIFs are used by some PWUD to test out new batches or drugs obtained from new suppliers. Several PWUD described how they use the SIF to check the potency of a new batch under the protection of supervision and resuscitation, if needed. Depending on the degree of this practice in a community, there may be unmeasured value of a SIF related to particularly volatile periods of changes in the toxicity and potency of the drug supply chain.

Pain Management

> *"Lot of this community with lived experience have been through some hard stuff that have gone unaddressed."* – OPS/SCS Staff Member

We heard that PWUD are frequently dismissed as "drug seeking addicts". Classism, racism, sexism, and homophobia can add to oppression and discrimination that PWUD already experience. However, one person noted that most people who inject or smoke drugs are managing significant physical and emotional pain caused by injury, occupation, sexual assault, or trauma. As opioid prescribing patterns of physicians have changed in recent years, many people have turned to heroin or crack for pain management. One woman noted that "[her] doctor was more concerned about getting [her] off opiates than worrying about [her] pain." We even heard suggestions that SIFs are a safer option for people with "legitimate pain, legitimate anxiety" to self-manage, especially for the poor and marginalized "who cannot even ask a hospital for the medications they actually need."

Access to Treatment

> *"First of all, reach people…and look at what their individual goals are. You cannot treat everyone the same."* – SIF Manager

Multiple stakeholders described differences in the time and frequency of interactions with SIFs versus SSPs. In contrast to client interactions with SSPs that were described as "transactional and hurried", SIFs have the potential to be more effective at introducing counseling interventions through a community built on camaraderie. Frequency of engagement was noted as a good predictor for the degree to which people can transition into an engagement process for referral to treatment. A setting like a SIF where people may expect to use it more frequently will allow for more points of contact to accelerate trust-building with the program. We also heard, though, that there are many users of SSPs who have no interest in making use of SIF services. Relationships and counseling enable access to a variety of services, including MAT, when clients are ready. One SIF manager noted the staff are not curing people nor pretending to; rather, they work to motivate people to find their way into wellness, which may or may not be abstinence-based treatment. A recovery specialist noted that SIFs are merely another interconnected pathway to recovery (among many in a community), and far "better than a shooting gallery in an abandoned building where there is no opportunity for recovery." Several stakeholders noted that SIFs do not address the health care system capacity constraints for treatment (e.g., new patients for MAT), adding that referrals must be picked up in timely manner by compassionate, culturally-competent professionals who respect the client's goals. One person called out a paradox in the evidence, observing that harm reduction programs must demonstrate an ability to get people into treatment, but treatment programs do not have to demonstrate ability to accept referrals from harm reduction programs.

2.3 Other Considerations

Learning from Lived Experience

Most people commented on how the best SIFs respect the expertise of PWUD and include them in setting policies and operating the facility. One example involved how client input has adjusted the use of naloxone. Rapid, full-dose administration of naloxone eliminates the pain relief benefit and sends a client who is opioid-tolerant into withdrawal. While one SIF was "too trigger happy with naloxone a few years back", it now favors oxygen and micro-dosing of naloxone because it respected the expertise of PWUD.

> *"I can attest that bedside care is really lacking from health care professionals, especially in emergency situations. People with lived experience are the experts."* – OPS Staff Member, Former Paramedic

Honeypot Effect

PWUD dismissed the possibility of a honeypot effect in which a SIF attracted PWUD or crime to a neighborhood, noting the long-established poor conditions of neighborhoods where SIFs are generally located, and that SIFs serve people who live nearby. Many stakeholders agreed. One person from Vancouver who had feared Insite would become a drug destination for people from other Canadian cities noted this has not happened and that "people won't travel more than a few blocks" to visit the SIF. However, PWUD and stakeholders acknowledged that opposition to SIFs, SSPs, and other forms of harm reduction can exist in a community due to fear, classism, moral objection to drug use, and societal failures to view addiction as a health care issue. We heard from PWUD and stakeholders that drug use still happens just outside of SIFs and SSPs, and at least some community members do complain about syringe/needle debris.

Medical versus Community Model

For a long time, the "nurse-centric Insite model" was the only SIF model in practice, but a variety of models are now available across Canada. A few participants described how a simple first-aid model can be effective in preventing overdose mortality and suggest that the more expensive nurse-centric model may not always be needed. However, there was appreciation for the Insite model; one participant recommended that a city opening a SIF start with the Insite model and "then work your way from there", moving toward a less medical model over time.

Integrated Services

Providing on-site access to social workers, frontline workers, or counselors was widely considered essential. Their experience suggested that most clients could not be easily referred to external

counseling as they often would not accept another counselling center for reasons such as distance, fears, and stigma. "A simple consumption room is better than nothing but having a little bit of social support on-site is fantastic," explained a manager. The medical director of a new SIF that opened in 2019 explained how it was co-designed with PWUD as a mixed service model and included a consulting area space (three private rooms) to offer low threshold, non-appointment-based support for health and social services. Experience there suggests integration boosts service uptake in a PWUD population where referrals to external services are less effective.

Housing Security

SIF clients are impacted by many social determinants of health, including housing security. A few stakeholders noted the clear limitations of a SIF to impact outcomes when the basic need for housing remained unaddressed. One stakeholder who worked in San Francisco described how the housing crisis there was linked to substance use. Any harm reduction strategy, including a SIF, is affected by the housing policy and resources in the surrounding community. As one stakeholder said, "mortality is important, but mortality is connected to lack of housing and other issues — and SIFs cannot solve for that…until housing is solved, a SIF can keep people alive and connect them to treatment, which has a dramatic impact on mortality." Another stakeholder stated that stable housing is required for a PWID to ever improve quality of life.

Traumatized by Public Drug Use

There is a community-level trauma caused by public use as well as overdose. In many communities, PWUD inject in public spaces (e.g., parks, alleys) but in a location that is discreet and hidden. They prefer to choose bathrooms of businesses because they have privacy (i.e., doors that close), soap, running water, and low chance of being caught by the police. Both locations can lead to trauma among people who witness the drug use or discover an overdose. SIFs offer a means to prevent this form of community-level trauma if the SIF can operate at scale. An advocate for people with substance use disorder noted that harm reduction strategies are making drug use invisible in communities where there are enough services available by normalizing substance use and allowing people to access health and social services. Quality of life increased for the community due to decreased public drug use.

3. Operational Guidelines

3.1 About Insite

Insite: Supervised Consumption Site – Vancouver Coastal Health[107]

Insite was opened in 2003 in Vancouver, Canada as the first legal SIF in North America. The facility was founded in response to a large number of drug-related deaths occurring in Vancouver's Downtown Eastside neighborhood. Insite is co-managed by Vancouver Coastal Health, a regional health authority providing health services, and the Portland Hotel Society (PHS) Community Services Society, a social services non-profit. Operating on a harm-reduction model, Insite works to mitigate the health and socioeconomic consequences of drug use; abstinence from drugs is not required to be connected to care. The model also provides care for those who use substances and have medical or psychological needs including Hepatitis C, HIV/AIDs, and psychiatric disorders.

As a SIF, the site is accessible to anyone 16 years or older who injects drugs and wants a sterile and safe facility to do so; it is open 7 days a week, 9AM to 3AM. Insite has a 12-booth injection room where PWUD can inject drugs they bring with them and where they can be supervised by nurses and other health care staff. They have access to injection equipment including sterile syringes and clean cookers, filters, and water. In the event of an overdose, teams are available to intervene immediately providing medical support including naloxone when indicated. After injecting, clients move to a post-injection room where they are provided with drinks such as juice or coffee and space to spend time with staff in a comfortable environment. Wound care and immunizations are available from the medical staff which also coordinates referrals for medical, mental health, and social support services.

Insite also has onsite services for withdrawal management (i.e., detoxification) on the second floor of the building, known as Onsite. Onsite has twelve detoxification rooms with private bathrooms and has health care teams, doctors, nurses, counselors, and mental health workers. After clients are stabilized, they can move to transitional recovery housing located on the third floor of the same building. There they can be connected to additional resources for housing, treatment programs, and community support.

According to Insite's website, the facility sees an average of 415 visits a day and over 175,464 visits annually – as of 2017. By March 2010, 7 years after their opening, there had been over 1.5 million visits. Many clients visit Insite multiple times; clients average 11 visits per month. There have been no fatal overdoses at Insite and, compared with non-Insite-users, Insite users are more likely to engage in addiction treatment.[107]

3.2 About Uniting Medically Supervised Injecting Centre

Uniting Medically Supervised Injecting Centre[108-112]

Uniting Medically Supervised Injecting Centre (MSIC) opened in Kings Cross, Sydney, Australia in May of 2001 and was the only SIF in Australia for 17 years before a second SIF opened in North Richmond, Melbourne in June 2018. The facility was founded following suit of the opening of the Switzerland SIF in 1986 and was placed in Kings Cross due to the area having the highest concentration of people dying from drug overdose in Australia. Uniting MSIC remains the only SIF in the Southern hemisphere. Like the Insite SIF, Uniting MSIC work to minimize the harm associated with injecting drugs through their team of nurses, counselors, and health education professions. In their mission, they emphasize that they act to prevent injury and death by being present while someone injects rather than supporting and/or promoting drug use to provide immediate medical assistance if and when needed.

Uniting MSIC is open Mondays and Wednesdays-Fridays from 9:30 AM-9:30 PM and Tuesdays from 9:30 AM-3:45 PM and 6:00 PM-9:30 PM. On weekends and public holidays, they are open from 9:30 AM to 5:30 PM. When visiting the SIF, clients first have access to the waiting room and assessment area. Once staff have a clear idea of their current situations and medical histories, they are invited into the injecting room that houses eight open booths fitting two people each. Those who visit must be 18 years or older, not intoxicated in the moment, and they cannot be pregnant or accompanied by a child. A registered nurse is always on duty and present.

Uniting MSIC also functions as an SSP, provides advice on safer injecting practices, and also provides first aid and other health services. The facility does have a resuscitation room in the event of a drug overdose or another health care emergency. After injecting, clients move into an after-care area until they are ready to leave. In this space, they can connect and talk with the health care team in an informal environment. Coffee and tea are available as well as health promoting activities and the ability to connect with medical, psychosocial, housing, rehabilitation, and legal services.

Since opening in 2001, Uniting MSIC has supported over 16,500 clients, managed over 8,500 overdoses, and referred over 14,500 to further care and support – with 0 fatalities. Studies have shown that 70% of local businesses and 78% of local residents support the center. Uniting MSIC does not have an integrated detoxification program but rather refers clients who desire treatment for addiction, medical and mental health care, or social services support. Around 80% of Uniting MSIC's frequent clients ultimately accept referrals for these forms of treatment.

4. Comparative Clinical Effectiveness

4.1 Overview

In this review of the comparative clinical effectiveness of SIFs and other SCS, we systematically reviewed and synthesized existing evidence from available studies. Full PICOTS criteria are described in Chapter 1.2.

Our review focused on the effectiveness of the implementation of SIFs and other SCS in comparison to SSPs. We reviewed the benefits of SIFs important to PWID and sought evidence on all outcomes listed in Chapter 1. The methods and findings of our review of the evidence are described in the sections that follow.

4.2 Methods

Data Sources and Searches

Procedures for the systematic literature review assessing the evidence on SIFs for PWID followed established best research methods.[113,114] The review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[115] These guidelines include a checklist of 27 items, which are described further in Appendix Table A1.

We searched MEDLINE, PsycINFO, Web of Science, and EMBASE for relevant studies of SIFs through July 2020. Each search was limited to English-language studies of human subjects and excluded articles indexed as guidelines, letters, editorials, narrative reviews, case reports, or news items. We also searched for systematic reviews of SSPs in MEDLINE and PsycINFO through July 2020. All search strategies were generated utilizing the Population, Intervention, Comparator, and Study Design elements described previously. The proposed search strategies included a combination of indexing terms (MeSH terms in MEDLINE and EMTREE terms in EMBASE) as well as free-text terms.

To supplement the database searches, we performed manual checks of the reference lists of included studies and systematic reviews and invited key stakeholders to share references germane to the scope of this project. We also supplemented our review with information submitted by stakeholders, SIF/SCS evaluations or reports, and other grey literature when the evidence met ICER standards (for more information, see https://icer-review.org/methodology/icers-methods/icer-value-assessment-framework-2/grey-literature-policy/).

Study Selection

After the removal of duplicate citations, references went through two levels of screening at both the abstract and full-text levels. Four reviewers independently screened the titles and abstracts of all publications identified using DistillerSR (Evidence Partners, Ottawa, Canada) and disagreements were resolved through consensus. Studies that did not meet PICOTS criteria were excluded.

No evidence from randomized controlled trials (RCTs) was identified. Relevant published high-quality cohort and other observational studies of any sample size or duration were included (see below for details on quality assessment). Only studies that evaluated SIF use in association with the relevant outcomes of interest were included in this review. Further, we recognize that a variety of SIF intervention models exist. We looked for studies of different forms of consumption (e.g., smoking) that expand on the SIF model. However, we did not identify any studies that compared different SIF models and forms of consumption (e.g., injecting vs smoking) in terms of outcomes of interest. A detailed protocol of the methods was registered on Prospero (CRD42020199977).

Data Extraction and Quality Assessment

Four reviewers extracted data into evidence tables. Extracted data were verified by another researcher. Elements included study name, study year, study design, location of the SIF, study inclusion and exclusion criteria, description of study populations, sample size, duration of follow-up, exposure, outcome assessments, findings, and quality assessment for each study. The report utilized the 12-item and 14-item study quality assessment criteria published by NHBLI for cohort, cross-sectional, and before-and-after (pre-post) studies, using the categories "good," "fair," or "poor."[116] For more information on data extraction and quality assessment, refer to Appendix D.

Assessment of Level of Certainty in Evidence

We used the ICER Evidence Rating Matrix to evaluate the level of certainty in the available evidence of a net health benefit among each of the interventions of focus (see Appendix D1).[117,118]

Assessment of Bias

It is customary at ICER to assess for publication bias as part of a review. We have no systematic way to conduct such an assessment on this topic. Many published reports about SIFs are linked to those who provide the services. As such, apart from the greater perceived difficulty in publishing reports showing negative results, there may be an additional preference to report favorable results.

Data Synthesis and Statistical Analyses

Data for the available evidence on outcomes of interest are summarized in evidence tables (see Appendix D2) and are synthesized in the text on the following pages. Relevant data include those listed in the data extraction section. Studies that were deemed sufficiently similar in terms of population, intervention type, and outcome definitions were included in the synthesis.

Due to the unavailability of RCTs among PWID to assess the implementation of SIFs, we have summarized the best available evidence from a comparative cohort, experimental or pre-post, and other observational studies. Due to differences between the studies in terms of the study design, population characteristics, and outcomes (including definitions and methods of assessments), we were unable to conduct a quantitative assessment. Hence, our review provides a narrative description of the outcomes of interest.

4.3 Results

Study Selection

Our literature search identified a total of 1188 potentially relevant references for SIFs (see Appendix D2), and we included 48 studies that evaluated individual or community level outcomes for SIFs. The majority of studies evaluated SIFs from Canada (n=33), and the remaining studies evaluated SIFs in Australia (n=8) and European countries (n=7, including, two from Germany, three from Denmark, and two from Spain). Eighteen studies used a cohort study design, while others employed a pre-post ecological or time series (n=11), and cross-sectional study design (n=10). Nine studies used a qualitative, exploratory, or descriptive study design. We also included government sanctioned evaluation reports from MSIC in Sydney, Australia, the MSIR in North Richmond Australia, and the SCSs in Alberta, Canada.

The primary reasons for study exclusion included outcomes that were outside the scope of this review, different study populations of interest, feasibility or mathematical simulation studies, or conference abstracts that reported duplicative data to the full publications. In the results that follow, we focus on the effectiveness and implementation of SIFs on individual-level outcomes, community and environmental outcomes, and health system utilization outcomes.

We also searched for systematic reviews of SSPs and identified a total of 72 potentially relevant references. We included one review of reviews[25] that summarized results from 13 prior systematic reviews as well as three recent systematic reviews not included in the review of reviews.[26-28]

Overview of Studies

As mentioned previously, evidence for SIFs arises primarily from ongoing prospective cohort studies in Vancouver, Canada. The Vancouver Injection Drug Users Study (VIDUS), AIDS Care Cohort to Evaluate Access to Survival Services (ACCESS), and Scientific Evaluation of Supervised Injecting (SEOSI) are among the longest-running community recruited prospective cohorts of PWUD (recruitment since May 1996). In addition, data from cohorts enrolled from MSIC in Sydney and MSIR in North Richmond in Australia (SUPERMix cohort) have also been included in this assessment.

Overall, the included studies for SIFs were comparable with respect to age (median: 30 years, range: 25-60) and gender (males >50%). However, there was some variation in the exposure assessment based of the frequency of SIF use ranging from PWID who use a SIF versus do not use a SIF, frequent versus rare/occasional use, PWID administering ≥75% versus <75% of their injections in the SIF, or used the SIF at least once versus never during the study period. PWID experiencing unstable housing or homelessness also varied from country to country. Further, unstable housing or homelessness was not reported consistently and ranged between 17%-82% across the studies. Additional details of included references, their key characteristics, and main findings are summarized in Appendix D2.

To determine the incremental benefit of implementing a SIF versus an SSP alone, we included systematic reviews of SSPs as noted above to understand the effects of SSPs. The included systematic reviews evaluated the effect of SSPs on injection risk behaviors (IRBs), HIV, or HCV. We did not find evidence from systematic reviews on the effects of SSPs for other outcomes included in our scope (e.g., access to MAT, overdose mortality); therefore, we have limited our review of the evidence of SSPs to infection prevention. We acknowledge, however, SSPs have benefits beyond infection prevention, as noted in the CDC summary in the background section, such as increasing the likelihood of entering treatment.[119]

However, the primary basis of our assessment of the incremental benefit of SIFs over pre-existing SSPs is derived from the studies evaluating the effects of SIFs as described above. We are assuming that PWID had access to SSPs during the study period, and the outcomes associated with SIFs are informing the added benefits of SIFs over baseline SSP access. We acknowledge, however, that the proportion who utilized services from SSPs is unclear, although the literature has suggested a considerable proportion of PWID access SSPs.[120]

Quality of Individual Studies

We used the National Heart, Blood and Lung Institute (NHBLI) criteria to rate the quality of the included evidence (see Appendix D).[116] For the cohort, and cross-sectional study designs, we used a 14-item NHBLI quality assessment inventory. For the pre-post and time series studies, we used the 12-item NHBLI quality assessment inventory. The studies were rated “good”, “fair”, or “poor.”

These tools included items for evaluating potential flaws in study methods or implementation, including sources of bias (e.g., population selection, performance, attrition, and detection), confounding, study power, the strength of causality in the association between interventions and outcomes, and other factors.

We only rated the studies that were published in peer-reviewed journals. We did not assign a quality rating to qualitative, exploratory, or descriptive studies. In addition, we did not assign quality ratings to references obtained from the grey literature (e.g., evaluation reports). Overall, the cohort and pre-post studies included in this review were rated good to fair; these studies had the least or some risk of bias but deemed not sufficient to invalidate its results. These studies considered some, but not all-important outcomes and used acceptable measures that were generally applied equally. On the other hand, all the cross-sectional studies were rated to be of fair to poor quality.

Health-Related Quality of Life

SIFs contribute towards a reduction in overdose-related events, infections, and other individual-level outcomes as discussed before. While we did not identify any quantitative evidence directly assessing these improvements in the health-related quality of life of PWID, these potentials for a SIF have been regarded to improve the quality of life of PWID. We identified one qualitative study on people living with HIV who use drugs at Dr. Peter Center in Vancouver, Canada. The study participants described the positive impacts of this harm reduction policy on their quality of life. The participants also mentioned increased access to social, health, and broader environmental support services that led to an improvement in their overall health.[44]

Clinical Benefits

All-Cause Mortality

There is an increased risk of premature mortality leading to a decrease in the life expectancy of PWID in the US.[1,121] Beyond age 15, life expectancy in the US (1999-2016) due to drug use was estimated to cost men 1.4 years and women 0.7 years, on average.[122] In Canada, premature mortality was 13 and 54 times higher among young men and women who inject drugs as compared to the general population.[123] However, there is very limited evidence on the effect of SIFs on all-cause mortality. One study conducted using data from two Canadian prospective cohorts reported that frequent use of SIFs was significantly associated with a lower risk of all-cause mortality (adjusted HR[aHR]: 0.46; 95% CI: 0.26-0.80, p=0.006). The crude mortality rate of the 811 SIF clients in the study was 22.7 deaths per 1000 person-years, which translates to 34 years (median, IQR 27–42) of potential life-years lost for the 13.8% who died during the study period.[31]

Overdose Mortality within SIFs

The published evidence on overdose mortality within the SIFs suggests that no client has ever experienced overdose death within the facility.[29,30]

In a qualitative study from Vancouver, clients reported that staff was available to rapidly respond to an overdose event, and injecting at a SIF in the presence of a nurse saved many lives that would have otherwise been lost.[124]

We also heard from multiple people who work at SIFs that they know of no episodes of a client dying at a SIF from an overdose. One stakeholder cited data from an unsanctioned SIF that operates at an undisclosed location in the United States.[14] Many interviewees pointed to the increased risk of mortality associated with clients who live in isolation and therefore inject alone. Without a partner or observer, overdoses that occur when injecting alone can have fatal consequences. Experts highlighted how SIFs address a specific and large group of PWUD whose risk for overdose mortality is elevated due to social isolation.

Overdose Mortality within Communities

A population-based study in Vancouver, Canada evaluated the effects of Insite on overdose mortality.[12] Researchers assessed overdose mortality stratified by pre-and post-SIF within and beyond the 500 m area around the facility. The data were obtained from the British Columbia Coroners Service's registry for deaths caused by overdose, before the opening of the SIF (January 2001 to September 2003) and after the opening of the SIF (September 21, 2003, to December 2005). The SIF opening was associated with a significant reduction of 35% in overdose mortality within 500 m of the facility (absolute reduction in overdose mortality rates from 254 to 165 per 100,000-PYs, rate difference (RD): 89 per 100,000-PYs; 95% CI: 1.6 to 175.8, p=0.048), compared to a 9.3% decline in the rest of the city (Table 4.1; RD: 0.7, 95% CI: -1.3 to 2.7, p=0.49). The authors noted that most SIF users (70%) lived within four blocks of the facility.[12]

Table 4.1 Overdose Rates in the Vicinity of a SIF and Beyond (table adapted from Marshall et al. 2011)[12]

	Overdoses within 500 m of SIF		Overdoses farther than 500 m of SIF	
	Pre-SIF	Post-SIF	Pre-SIF	Post-SIF
Number of overdoses	56	33	113	88
Overdose rate (95% CI)*	254 (187 to 320)	165 (108 to 221)	7.6 (6.2 to 9.0)	6.9 (5.5 to 8.4)
Rate difference (95% CI)*; p value	-	88.7 (1.6-176); p=0.048	-	0.7 (-1.3-2.7); p=0.490
Percentage reduction (95% CI)	-	35.0% (0.0 to 57.7)	-	9.3% (-19.8 to 31.4)

SIF: supervised injection facility, CI: confidence interval; Pre-SIF period= January 1, 2001 to September 20, 2003. Post-SIF period= September 21, 2003 to December 31, 2005

*Expressed in units of per 100,000 person-years

Non-Fatal Overdose and Health Care Utilization for Overdose

Non-fatal overdose events within a SIF have been captured by looking at events where SIF staff intervened by administering naloxone and/or oxygen or by calling EMS.[32,33] We identified three studies that evaluated the effect of SIF use on non-fatal overdose and overdose requiring EMS, ambulance, or hospital care.

A study from Insite from March 2004 to August 2005 found 285 unique users who experienced 336 non-fatal overdose events. Of these overdose events, 28% resulted in a transfer to hospital, and 27% resulted in the administration of naloxone.[32] A recent time-series analysis of SIF users at Insite reported that the overdose rate per 1000 visits increased from 2010 to 2017 (1.5 vs 9.5, $p<0.001$) with an increase in overdose events requiring naloxone administration (48.4% to 57.1%, $p<0.001$) but no overdose deaths were reported within the facility.[33]

In a 2007 study by the New South Wales (NSW) Health Department in Sydney, Australia, opioid overdose-related ambulance calls were analyzed in Sydney over 36 months pre-SIF and 60 months post-SIF. The SIF opening was associated with a greater reduction in ambulance calls for opioid-related overdose events in the vicinity of the SIF compared to the rest of NSW (68% vs 61% decline, $p=0.002$).[34] This effect was even higher during operating hours of the SIF (80% vs 60% decline, $p<0.001$).

Changes in the Drug Supply and Injected Drug Class

Changes in drug class and composition over time, especially a recent increase in the presence of fentanyl or its analogs, have caused a huge public health burden by adding to the toll of overdose mortality.[125] The latest reports from Insite suggest that atypical overdose presentations (muscle rigidity, dyskinesia, or confusion) increased from 23% of overdoses in 2015 to 41% in 2017; 15% of atypical overdoses required transportation to a hospital via ambulance.[126] The authors felt that this increase might be caused by fentanyl contamination in the illicit drug supply. As noted previously, a recent time series analysis from Insite reported that overdose rates increased significantly for all drug categories. Also, the overdose rate associated with heroin increased from 2.7 per 1000 visits to 13 per 1000 visits over the study period. Compared to the baseline period, SIF users in the most recent period had 10.4 times the risk of overdose following cocaine consumption, 4.8 times the risk of overdose following heroin consumption, and 2.5 times the risk of overdose following consumption of other opioids.[33]

Likewise, in Sydney, Australia, a retrospective clinical audit of MSIC (2012-2015) reported that about 44 of 1000 injections contained fentanyl and with 4.4% of injections containing fentanyl resulted in an overdose. Further, fentanyl users were 2.2 to 8.0 times more likely to experience an

overdose than heroin and other prescription opioid users (p<0.001).[127] In Denmark during 2007-2014 a prospective analysis reported that there were 12.7 heroin overdoses per 1000 injections compared to 4.1 oxycodone overdoses per 1000 injections.[128]

A stakeholder pointed to a 5-year study of an unsanctioned SIF in the United States that documented a shift in types of drugs injected -- from about 85% of injections being opioid only in 2014 to just 30% in 2019 when using a combination of opioid and stimulants (e.g., cocaine, methamphetamine) became common.[14] Other experts described substantial variation and changes in the drug supply chain by region (e.g., black tar, white powder, fentanyl), polydrug use, and smoked products as major issues when studying harm reduction strategies. In pursuit of identifying changes in drug supply that increase risk for overdose, SIFs have responded to changes in the drug supply chain by analyzing drug composition (e.g., fentanyl), using fentanyl testing strips and other devices such as mass spectrometers.

Injection Risk Behaviors

As noted earlier, injection drug use increases the risk of transmission of viral and bacterial infections. Reducing injection risk behaviors (IRBs) is important in reducing the risk of infectious disease transmission.[35 1101] The evidence on the effect of SIFs on the incidence of infections over time is limited given the methodological challenges described previously.[129,130] However, the effect of SIFs on reducing IRBs as well as increasing uptake of safer injection education is well-established and serves as the primary basis of our evaluation of the effect of SIFs on infections.

We identified seven studies that evaluated the effect of SIFs on reducing IRBs, including four studies from Vancouver and three studies from European countries (Denmark, Germany, and Spain). Most studies reported SIF use was associated with a reduction in IRBs.

A cross-sectional analysis of 431 PWID in Vancouver (data derived from VIDUS cohort) found that use of a SIF for all, most, or some injections compared to SIF use for no or few injections was independently associated with reduced syringe sharing (adjusted OR [aOR]: 0.30; 95% CI: 0.11 to 0.82; p=0.02).[36] The authors found that the rates of syringe sharing were similar in the two groups before the SIF opened, and differences only emerged after the SIF opened; this finding suggests that the observed association was not confounded by an inherently lower risk of syringe sharing among those who used the SIF.

Two cross-sectional studies among PWID attending Insite (SEOSI cohort) reported that more frequent SIF use was associated with reductions in IRBs. A study of 760 PWID found consistent SIF use (≥25% of injections) compared to inconsistent SIF use (<25%) was positively associated with reductions in many IRBs, including less reuse of syringes (aOR: 2.04; 95% CI: 1.38 to 3.01), less rushed injection (aOR: 2.79; 95% CI: 2.03 to 3.85), less outdoor injection (aOR: 2.70; 95% CI: 1.98 to 3.87), using clean water (aOR: 2.99; 95% CI: 2.13 to 4.18), cooking/filtering drugs prior to injection

(aOR: 2.76; 95% CI: 1.84 to 4.15), safer syringe disposal (aOR: 2.13; 95% CI: 1.47-3.09), injecting in a clean place (aOR: 2.85; 95% CI: 1.83 to 3.86), and others.[131] Another study of 582 PWID found exclusive SIF use (i.e., use of SIF for 100% of injections) compared to some SIF use was associated with reduced syringe sharing among HIV-negative individuals (OR: 0.14; 95% CI 0.00 to 0.78) but was not significantly associated with reduced syringe lending among HIV-positive individuals (OR: 0.94; 95% CI 0.00 to 7.90).[132] Lastly, another cross-sectional study of 1082 PWID found 75% of participants had perceived reductions in IRBs since the opening of the SIF. Among those who reported perceived changes in IRBs, 80% reported reductions in rushed injections, 71% reported less outdoor injections, 56% reported less unsafe syringe disposal, and 37% reported using syringes less often.[13] Of note, these three cross-sectional studies among PWID in the SEOSI cohort had overlapping study periods (Stolz: March '04 to October '04; Wood: July '04 to June '05; Petrar: December '03 to September '05).

We also identified three studies from European countries including Denmark, Germany, and Spain. A cross-sectional study of 41 PWID in Denmark found 76% of participants reported perceived reductions in IRBs since the opening of the SIF, including less rushed injections (63%), fewer outdoor injections (56%), ceasing to share syringes (54%), and cleaning injection site more often (44%).[56] A prospective cohort study of 129 PWID in Germany found no changes in IRBs after three months of SIF use.[43] A cross-sectional study of 249 young heroin users in Spain found SIF use was significantly associated with not borrowing used syringes (OR: 3.3, 95% CI: 1.4 to 7.7); of note, 96% of participants reported using an SSP during the reference period.[133]

A meta-analysis combined results from three of the studies described above (Wood 2005, Kerr 2005, and Bravo 2009) and found SIF use was associated with a 69% reduction in the likelihood of syringe sharing (pooled effect: 0.31; 95% CI: 0.17 to 0.55).[37]

Stakeholders noted SIFs are effective in reducing IRBs by providing a clean, safe space to inject in a less rushed manner. They described an advantage SIFs have in education and supporting safer IRBs, attributable to the SIF's ability to build trust and relationships with clients over time.

In our review of SSPs, six of the thirteen systematic reviews included in the review of reviews examined IRBs, two of which performed meta-analyses. An earlier meta-analysis pooled results from 10 studies and found SSPs reduced HIV risk behaviors (weighted group mean effect size: 0.28; 95% CI: 0.21 to 0.35).[134] The other meta-analysis examined the effect of high SSP coverage plus opioid substitution treatment (OST) and found a reduced likelihood of syringe sharing (aOR: 0.52, 95% CI: 0.32 to 0.83)[41]; of note, this review only included studies conducted in the UK and reported the effect of full harm reduction (i.e., high SSP coverage and OST) on IRBs as opposed to the effect of just SSPs. The other reviews provided a qualitative synthesis that generally supported SSPs' reduction in IRBs.

Safer Injection Education

We identified three studies that reported the uptake of safer injection education (SIE) at SIFs. All studies were among PWID attending Insite (SEOSI cohort). One prospective study of 1087 PWID found frequent SIF use (≥75% of injections) compared to less frequent use (<75% of injections) was associated with an increased likelihood of receiving SIE in multivariate analyses (aOR: 1.47, 95% CI: 1.22, 1.77),[135] and one cross-sectional study of 874 PWID found daily SIF use was marginally associated with receiving SIE in univariate analyses (p=0.085).[136] Lastly, in one qualitative study, narratives from 50 participants showed the SIF allows participants to identify gaps in safer injection knowledge by providing targeted educational messages and demonstrations of safer techniques as well as by promoting meaningful relationships with health care professionals. In addition, participants said the environment of the SIF incites safer injecting practices over time, including within and outside of the SIF.[137]

Infection Prevalence/Incidence

We identified four studies that provided evidence on the effect of SIFs on infection incidence and prevalence, most of which were not designed to detect differences, specifically in rates of HIV or HCV.

Viral Infections

A cross-sectional study of 510 PWID who attended a SIF in Catalonia, Spain found that there were no significant differences in the prevalence of HIV or HCV among those who had frequent SIF attendance (i.e., daily), medium SIF attendance (i.e., > half of days), and low SIF attendance (i.e., ≤ half of the days).[38] In a qualitative study among 22 PWID and seven staff members at the Harm Reduction Room in the Dr. Peter Centre in Vancouver, staff members perceived that there was a reduction in infections that could be potentially attributed to having a safer place to inject and safer injection education.[138]

Much more extensive evidence exists for the effects of SSPs on viral infections. Nine of the thirteen systematic reviews included in reviews of reviews examined the incidence of HIV, including one meta-analysis. The meta-analysis pooled results from 10 studies and found a trend towards a reduced risk of HIV transmission with SSPs, although the results were not significant (effect size: 0.66; 95% CI: 0.43 to 1.01).[39] However, when pooling results from six higher-quality studies, a significant reduction was observed (effect size: 0.42; 95% CI 0.22 to 0.81). Other reviews provided a qualitative synthesis, and their conclusions generally supported the findings of the meta-analysis. However, a more recent meta-analysis not included in the review of reviews found SSP use was associated with an increased risk of HIV seroconversion when pooling results from two studies (HR: 1.59; 95% CI: 1.2 to 2.1).[27]

Eight of the thirteen systematic reviews included in reviews of reviews examined the incidence of HCV, including two meta-analyses. One meta-analysis pooled results from seven studies and found an increased risk of acquiring HCV with SSPs (RR: 1.62; 95% CI: 1.04 to 2.52).[40] There was substantial heterogeneity (I^2=81%), and the authors did not conduct any sensitivity or subgroup analyses. The authors noted that studies included in their analysis may have been affected by volunteer bias as SSPs may attract higher-risk PWID. The other meta-analysis included three studies conducted in the UK and found high SSP coverage was associated with a reduced risk of HCV transmission (aOR: 0.48, 95% CI: 0.25 to 0.93).[41] The other systematic reviews provided a qualitative synthesis and results were mixed; these reviews also included many earlier studies that were not included in the meta-analyses.

We identified two meta-analyses published after the reviews of reviews that provide additional, recent context. A meta-analysis by Cochrane found a trend towards reduced risk of HCV with high SSP coverage, although the results were not significant (RR: 0.79; 95% CI: 0.39 to 1.61); this analysis combined studies from North America and Europe, and there was high heterogeneity (I^2=77%).[28] When stratified by region, high SSP coverage in Europe was associated with a significant reduction in risk of HCV acquisition (RR: 0.24; 95% CI 0.09 to 0.62). Another meta-analysis analyzed results from studies reporting ORs and HRs separately and found no association when analyzing ORs (OR 0.51, 95% CI 0.05 to 5.15) but an increased risk when analyzing HRs (HR 2.05, 95% CI 1.39 to 3.03).[26] There is continued uncertainty from published research around SSPs' effects on viral infections although results are likely affected by selection biases, and we urge caution when interpreting these results.

Expert stakeholders we interviewed felt that the infection control benefits of SSPs are obvious and HIV and HCV incidence rates would rise quickly if the service were removed from a community given the high-risk profiles of clients of SSPs. Experts pointed out that SIFs serve clients at even higher risk than SSPs. Stakeholders believed that SIFs play an important role in reducing the transmission of infections, but it is difficult to measure the impact due to variable baseline rates of HCV and HIV among PWID in different communities. Additionally, stakeholders noted that SIFs have been effective in referring clients to HCV treatment.

Bacterial Infections

A prospective cohort of 1065 PWID attending Insite (SEOSI cohort) found the use of SIF for all injections versus some injections was associated with a decreased likelihood of developing a cutaneous injection-related infection (CIRI) (OR: 0.47; 95% CI: 0.23 to 0.94) in univariate analyses; in multivariate analyses, the aOR was 0.58 and was no longer statistically significant (95% CI: 0.29 to 1.19).[42] A prospective cohort study of 129 PWID attending a DCF in Essen, Germany found no statistically significant reduction in injection-related abscesses.[43]

Stakeholders noted that SIFs can be effective in preventing bacterial infections such as endocarditis and can provide or encourage wound care. One expert noted that SIFs have an advantage over other harm reduction strategies in detecting and intervening early on common soft tissue disease. This advantage was attributed to the frequency that clients visit SIFs and how staff build relationships with clients that permit discussion and intervention to prevent serious wound infections.

Health Care Utilization for Infections

We identified two studies that provided evidence on the effect of SIFs on health care utilization for infections among PWID attending Insite (SEOSI).

A prospective cohort study of 1083 PWID found that over a median follow-up of 21.4 months, 9% of participants were admitted to the hospital of whom 49% were admitted for CIRI or complications.[139] In multivariate analysis, referral to the hospital by a SIF nurse was significantly associated with an increased likelihood of hospitalization for CIRI (aOR: 5.38; 95% CI: 3.39, 8.55). Participants referred to the hospital by a SIF nurse had shorter hospital stays compared to those who were not referred by a SIF nurse (4 days [IQR: 2-7] vs 12 days [IQR: 5-33], p=0.001 after adjustment). A similar analysis of 1083 PWID found that over a median follow-up of 18.6 months, 27% of participants visited the ED for a CIRI. Referral by a SIF nurse was significantly associated with ED use for CIRI among females (aHR: 4.48; 95% CI: 2.76 to 7.30) and males (aHR: 2.97; 95%CI: 1.93 to 4.57).[140]

Hospitalization for bacterial infections including endocarditis have not been reported directly in studies that assessed the effect of SIF use on health care utilization for infections. However, a comment received during the public review period noted the large scale of infections and the burden placed on the healthcare system. It is estimated that anywhere between 5% and 20% of people who inject drugs (PWID) have had infective endocarditis and related hospitalizations increased between 2000 and 2013, especially for young adults.[141]

Intermediate Outcomes

Uptake of Services

SIFs may facilitate access to various services programs for PWID and in turn enable them to access and utilize services like treatment and recovery, health, and social services.

Treatment and Recovery Support Services

We identified six studies that assessed the impact of SIFs on treatment and recovery support services. Across studies, the use of SIFs was associated with a higher uptake of treatment and recovery services.

A recent two-year prospective assessment of Insite reported that 11.2% of clients were enrolled in the co-located detoxification services at least once and frequent SIF users were more likely to enroll and use this service compared to non-frequent (less than once per week) users (aOR:8.15, 95% CI: 5.38-12.34, p<0.001).[45]

Three prospective studies from the SEOSI cohort reported associations between SIF use and rate of rapid entry into the detoxification treatment or service. In these overlapping analyses, SIF use and contact with an addiction counselor led to a significant increase in detoxification uptake, resulting in rapid entry into methadone maintenance treatment.[46-48] A prospective study found that weekly SIF use was positively associated with enrollment in addiction treatment and increased likelihood of injection cessation.[47]

In Sydney Australia, a prospective study from 2001-2002 reported that frequent use of an SCS was positively associated with receiving a referral to a detoxification program (aOR:1.6, 95% CI: 1.2-2.2).[49] Similar findings were reported from Catalonia (Spain), with PWID who utilized a SIF having a significantly higher likelihood of accessing drug dependence services (aOR: 2.12, 95% CI: 1.18-3.81).[38]

Health and Social Services

We identified seven studies that assessed the impact of SIFs on health and social services. Broadly, across studies, the use of SIF was associated with increased access to health and social services.

As described previously, PWID in Vancouver with cutaneous injection-related infections when referred by SIF nurse to the hospital was associated with an increased likelihood of admission resulting in a decrease in the average length of stay by 8 days.[139] Across studies, higher use of ancillary services has also been reported for PWID who utilized SIF frequently compared to those who used them occasionally or rarely.

A multi-country study in Europe reported an association between frequent supervised drug consumption facility use (compared with occasional or rare use) and a greater likelihood of accessing counseling services (46% vs 35% and 25%; p<0.01), medical services (37% vs 29% and 17%, p<0.01), syringe exchange services (59% vs 54% and 44%, p<0.05), and education on safer use (9% vs 3% and 3%, p<0.05).[50] A cross-sectional analysis in Denmark also reported that clients who used the facility frequently were more than twice as likely to receive treatment for an acute health condition compared to non-users.[51]

These observations are in line with the qualitative and exploratory evidence where SIF users have reported greater access to care and treatment with fewer structural and social barriers as a result of services being provided at one accessible location.[50,51,142] In a study from Dr. Peters Centre, Vancouver, PWID who were HIV positive highlighted that they felt comfortable discussing their drug use and health needs with the staff. They also noted that the harm reduction approach used at DPC

led to an increase in access to health care services including palliative and supportive care.[44] Likewise, qualitative evidence collected from 50 in-depth interviews indicated that SIF use facilitates access to care, although a minority of participants expressed otherwise. The PWID described that having on-site nurses at a SIF helped in providing assessment and care for injection-related infections as well as facilitating access to off-site health care services.[143,144]

Expert stakeholders felt that access to treatment, social services, recovery services, and referrals is important to SIF users. They also felt that allowing people an opportunity to enroll in treatment services reduces mortality. However, agreeing to enroll in MAT or other addiction treatment services can take time and may depend on the client's comfort and trust in the facility. In cases where people visit SIFs frequently, the relationship can be fostered by providing more points of contact and a stress-free and safe environment for clients.

Drug Consumption (e.g., frequency and amount)

We only identified one study that assessed changes in drug consumption associated with the use of SIFs. A pre-post study from Vancouver reported no substantial differences in relapse rates for injection drug use or stopping drug use pre- and post-SIF opening. The authors acknowledged that there was an increase in smoking crack after SIF opening but it is unlikely that the facility which does not allow smoking could have prompted this change.[52]

Community and Environmental Outcomes

Some of the key concerns regarding the implementation of SIFs relate to community and environmental issues including public drug use, syringe and paraphernalia disposal, and drug-related crime.

Public Drug Use and Syringe or Paraphernalia Disposal

Five studies assessed the role of SIFs in addressing public drug use and syringe and paraphernalia disposal associated with injection drug use.

An ecological study post-SIF opening in Vancouver Canada reported statistically significant reductions in public injection drug use (measured by researcher counts), compared to pre-SIF opening (daily mean: 4.3 vs 2.4, $p<0.001$). At the same facility, publicly discarded syringes (daily mean: 11.5 vs 5.4, $p<0.05$) and injection-related litter (daily mean: 601.7 vs 305.3, $p=0.01$) also reduced after SIF opening. These declines were independent of police presence and weather conditions.[53] A retrospective cohort study among 714 PWID attending a SIF reported that increased waiting time at the SIF resulted in an increased likelihood of public injecting (aOR: 3.26, 95% CI: 2.11-5.6, $p<0.001$).[54]

In Sydney, Australia, a time-series study reported that after a SIF opened there was a perceived decline in the proportion of residents and business owners witnessing public injections (19% vs 33%, p<0.001) and discarded syringes (40% vs 67%, p<0.001).[55] A study of a SIF opening in Copenhagen (Denmark) reported a 56% reduction in public injections as well as a significant improvement in safe syringe disposal (59%, p <0.001).[56] In contrast, over a three-month period a prospective cohort study from Essen (Germany) reported no significant effect of a SIF on public drug use.[43]

In a study of DCRs in Denmark, 71% of users also noted that they chose the SIF for drug-use as they were conscious of public drug use bothering people in the neighborhood.[51]

Drug-Related Crime

An important aspect of harm reduction with SIFs is promoting (or at least not worsening) neighborhood safety. We identified six studies that assessed the association of the SIF opening on drug-related crime and/or neighborhood safety.

Three studies conducted in Sydney, Australia reported that opening of the SIF did not result in a significant increase or decrease in crime (i.e., theft, drug-related loitering, or robbery).[57-59] After the opening of the SIF, a slight increase was reported for overall loitering at the front and back of the SIF.[57] Additionally, a prospective study conducted from 1999 to 2010 reported a significant decline in robbery and property offenses both in the vicinity of the SIF and across the city. Of note, the rates of drug-related crimes declined between 1999 to 2003 and then remained constant until the end of the study period. However, the authors found no association of the SIF (Sydney MSIC) with robbery, property crime, or drug offenses.[58] In contrast, a separate pre-post study in 2013 reported a decline in robbery or thefts in the neighborhood after the SIF was opened.[59] This study also found that between 2001-2008, possession of illicit substances remained stable while increases were reported both in the SIF neighborhood and citywide from 2009 onwards.

Similar observations were reported from Vancouver, Canada in an ecological (pre-post) study with no significant changes in robbery or drug trafficking.[60] However, compared to the pre-SIF opening, a decline in vehicle break-ins (302 vs 227, p<0.001) was observed post-SIF opening. Two studies—one prospective cohort and another a time-series analysis—also reported that among SIF users, frequent use of SIFs was not associated with crime or recent incarceration.[61,62]

The presence of and interactions with law enforcement may have affected the estimates but were not accounted for in these studies. However, studies do not appear to show an increase in crime when a SIF is opened. Furthermore, the evidence on drug-related crime is in line with observations shared by the experts during interviews.

Government Sanctioned Evaluation Reports for SIFs

Uniting Medically Supervised Injecting Centre (MSIC) Sydney, Australia

In May 2001, Uniting MSIC was established in Kings Cross, Sydney under a license issued by the government of New South Wales (NSW). A first evaluation report was published in 2003 to cover the first 18 months of operation.[145] In response to the evaluation results, the operation license was then extended. A second set of evaluation reports was then commissioned by the NSW government[146-149] that assessed the impact of Uniting MSIC on a range of individual outcomes (e.g., overdose) and community outcomes (e.g., syringe and needle disposal). A total of 9778 PWID used this SIF from May 2001 to April 2007, a majority of whom were male (70%) with a mean age of 33 years. About 40% of SIF users injected daily, and 24% were living in unstable housing. The most injected drugs on-site were heroin (62%), other opioids (12%), cocaine (14%), and meth/amphetamines (6%).

During these years of operation, the SIF managed 2,106 overdose-related events on-site, without a single death within the facility. Between May 1998 (pre-SIF) and April 2006 (post-SIF), a significant decline in overdose mortality was reported both in proximity to the SIF (mean: 4 vs 1 death per month, $p<0.001$) as well as in the rest of the city (mean: 27 vs 8 deaths per month, $p<0.001$). A decline in mean monthly ambulance attendances was reported near the SIF, compared to the rest of the city (mean: 61% vs 68% monthly ambulance attendances, $p=0.002$); the percentage decline was reported to be higher during operational hours of the SIF. After the SIF opening, a 35% reduction was reported for average monthly opioid poisoning presentation at the ED compared to before the SIF opening (11 vs 7, $p<0.01$).

In addition, there was a downward trend in reporting public injecting among SIF users between 2001-2004 as well as in witnessing public injecting among residents and business operators between 2000-2005. In addition, residents and business operators also reported seeing less discarded syringe in the past month between 2000-2005. The monthly totals of discarded needles and syringes collected locally signaled about a 50% decrease in syringe litter following the establishment of the SIF; this was sustained between May 2001- April 2007.

Medically Supervised Injection Room in North Richmond, Australia

In October 2017, the Victorian government announced a two-year trial (June 2018 to June 2020) of a Medically Supervised Injection Room (MSIR) in North Richmond, Australia, with the possibility of a trial extension. An independent review panel evaluated the impact of the SIF during the first 18 months of the trial, and a report was published in June 2020.[150] During the first 18 months, almost 4,000 people visited the SIF; the average age of the clients was 41 years and 35% were living with homelessness or insecure accommodation. There were 116,802 supervised injections (96.6% involving heroin), 2,657 overdoses, and no deaths within the facility.

Ambulance calls involving naloxone reduced by 25% within 1 kilometer after the SIF opened; the decline was even greater during hours of SIF operation, with a reduction of 36%.[150]

There was a decrease in the proportion of residents and business respondents reporting they had seen public injections since the SIF opened ($p<0.05$ for both groups). There was no change in the proportions of residents reporting they had seen discarded syringes or needles, but there was an increase among business respondents). There was an increase in the number of syringes and needles collected after the SIF opened, but there were also increased collection efforts during the last eight months of the trial.[150]

The number and types of offenses within 1 kilometer of the SIF generally remained stable between 2014 to 2019, except for drug use and drug possession offenses. Victoria police members reported seeing more buying and selling of drugs and people who appeared to be under the influence. Victoria police also reported that crime near the facility was largely attributable to local crime trends that were not connected to the MSIR trial.[150]

Supervised Consumptions Services in Alberta, Canada

In 2019, the Alberta government froze the funding for new SCSs and reviewed the socioeconomic impacts of existing and proposed SCSs. A review committee conducted public consultations and a review of qualitative and quantitative data and a report was published in March 2020.[151]

There were seven established SCSs in Alberta at the time of the review– four in Edmonton, one in Calgary, one in Lethbridge, and one in Grande Prairie. Most sites had been operating for more than 12 months. The impact of the SCSs was generally assessed within 250 to 500 meters of the SCSs in this review.

The report found there was a 64% increase in all drug and alcohol poisoning deaths within 500 meters of the SCSs compared to a 30% increase in the 501 to 2000 meter zone outside the SCSs; the committee noted these deaths were predominantly related to opioids. However, the review committee acknowledged the role of SIFs and other SCSs in saving lives. In addition, there was a 74% increase in total opioid-related EMS responses within 500 meters of the SCSs. In the comparison zone beyond 500 meters, an average 11% decline was reported. Additionally, police calls for service (a proxy for crime in their review) had generally increased in the immediate vicinities around the Calgary, Lethbridge, and Grande Prairie sites but not around the four Edmonton sites.[151]

More than 16,000 Alberta residents completed an online survey about their perceptions of the SCSs in their communities. The primary complaint by residents was around needle debris. Residents noted an increase in seeing needles and other drug-related paraphernalia discarded in the vicinity of the SCSs. In addition, residents noted concerns around public safety, seeing people who

appeared under the influence, and general social disorder.[151] Of note, the report did not specifically include feedback from clients of these SCSs or the personnel who worked there.

At least some experts and researchers have expressed serious concerns with the methods used in this report, including but not limited to the lack of statistical significance testing and adjustment for potential confounders, and have called for it to be retracted.[152]

Heterogeneity and Subgroups

Unstable Housing

The rates of people living with homelessness or unstable housing in the included studies varies by region with ranges from 17% to 82%, that causes an increased public health burden.[53,55] People living with homelessness or in unstable housing experience multiple barriers in accessing health and social services especially a safe place to inject.[153] Although a considerable proportion of SIF users in studies were experiencing homelessness or living in an unstable housing, we identified few studies that reported results for outcomes of interest stratified by this sub-group.

In a prospective study from Insite, SIF users experiencing homelessness had a higher likelihood of entry into detoxification program (aHR: 1.42, 95% CI: 1.06-1.90, p=0.019), compared to those who were not.[48] However, another prospective study from Insite Vancouver, Canada reported that SIF users experiencing homelessness had a higher likelihood of not being able to access addiction treatment (aOR: 1.47, 95% CI: 1.09-1.98, p=0.011).[154] SIF users living in unstable housing were more likely to receive CIRI care (aHR = 1.39, 95% CI = 1.02–1.88, compared to those with stable housing.[155]

A study from Insite suggests that homelessness increases the likelihood of injecting in public even among SIF users (aOR: 3.10, 95% CI: 1.46-6.58, p<0.001).[54]

Uncertainty and Controversies

Research Methods

The available evidence about SIFs comes from studies with cohort and cross-sectional design. It is difficult to establish temporality in some cases and make inferences about the causal association without a reference population or control group.

Generalizability

Many community factors vary considerably across cities in the world (e.g., background risk of bloodborne infection, community support, policing practices, access to primary medical care, treatment capacity and effectiveness), and the variance could impact the generalizability of

findings. Some of the risks to generalizability are may be lessened by a real-world experience in Canada and Australia where SIFs have expanded to other cities. For example, a new SIF in North Richmond (Melbourne, Australia) replicated overdose mortality protection observed in Sydney. The recently published review report by the Victorian Government also notes reductions in public injecting and ambulance calls due to overdoses, but no improvement in perceived safety and drug-related nuisances.

Changes in Drug Supply

Our assessment of SIF effectiveness relies on many studies that are at least 10 years old. It is known that important community factors have changed since then, including global drug supply chains and user preferences. In some parts of the world, drugs typically injected are now being smoked; methamphetamines, for example, are replacing opioids. The increase in fentanyl additives to heroin and/or cocaine has changed the mortality risk of an overdose during the past decade. The estimated mortality reduction of the SIF model studied a decade ago is based on the types and forms of drugs consumed at that time.

Frequency of SIF Use

Although published studies report a range of utilization statistics (e.g., percentage of injections per month occurring at a SIF), uncertainty remains about the relationship between SIF visit frequency and effectiveness. It is reasonable to assume that a dose-response curve exists, especially for overdose mortality reduction. It is unknown what level of SIF utilization is required to achieve results for infection control, all-cause mortality, and overdose mortality.

Widespread Access to Naloxone

Naloxone is more widespread today, with police officers, paramedics, community members, and PWID and their allies all having it on hand in a variety of settings. It is unknown how much of a community's overdose mortality can be reduced by a SIF versus expanded naloxone distribution to high-risk people and their social networks.

Community Support

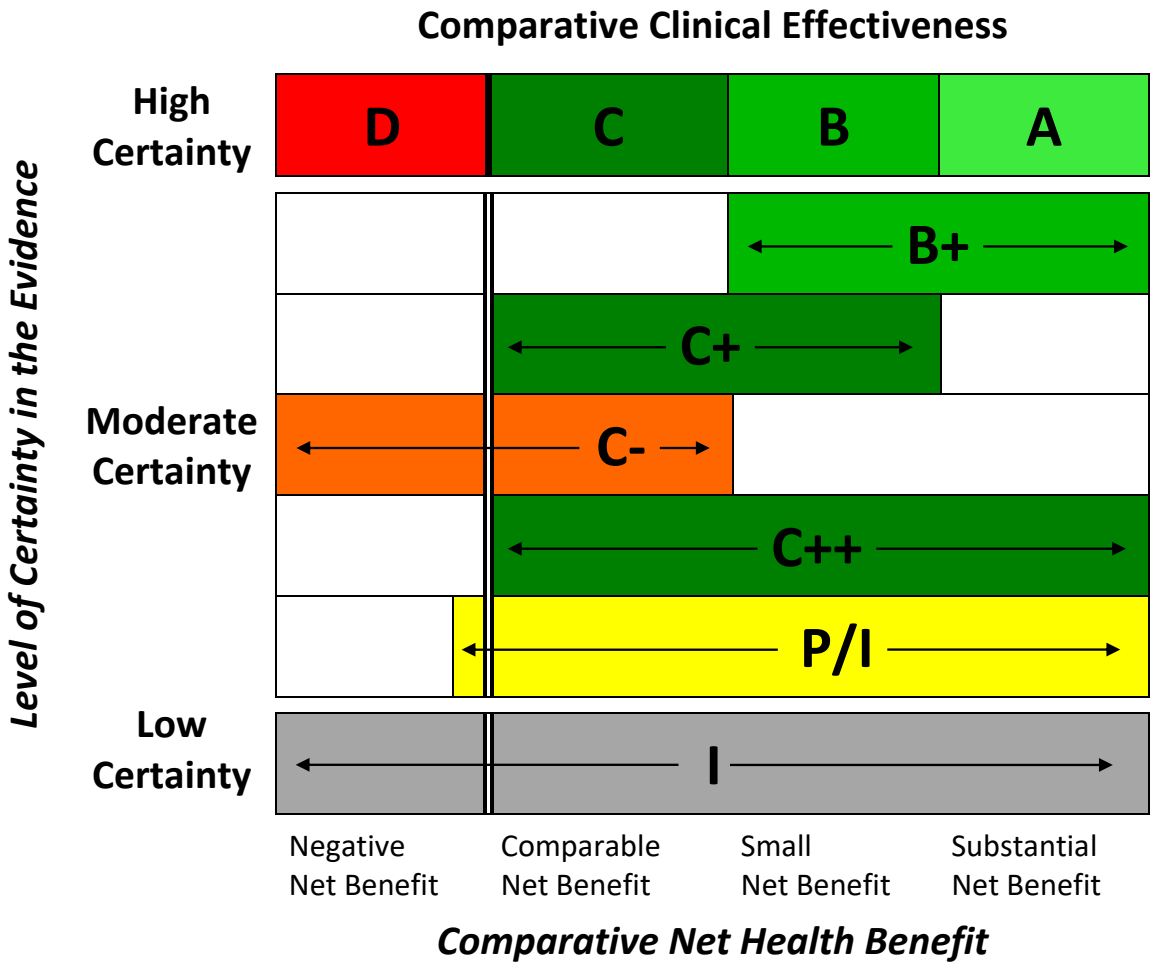
Experts described the importance of local community support, including law enforcement, to open and maintain a SIF, noting that support for a SIF can erode when proposals and implementation plans with specific locations are presented to community stakeholders. While there is no apparent evidence that SIFs attract more PWID or drug-related activity to a neighborhood, uncertainty remains, and concerns over local health and safety might diminish support which could, in turn, decrease the effectiveness of a given SIF.

Law Enforcement

The contribution of law enforcement to a SIF's effectiveness is unknown. Interviews with experts pointed to the importance of collaboration with local law enforcement to assure clients could enter and exit the SIF without being intimidated or arrested by police officers. The data from Vancouver originated from a pilot study that was supported by the police department as well as city government officials.[156] One ethnographic study described the how the increased police presence in the neighborhood of a SIF intimidated clients – forcing some to continuously navigate the risks of arrest or overdosing alone, especially clients who have outstanding warrants.[157] The ability of a SIF to reach PWID, cultivate support from the broader community, and deliver results (individual and community-level outcomes) may depend on its level of collaboration with the police. Notwithstanding state and federal legal issues, the controversy with and for law enforcement involves a concern that SIFs give people the green light to use drugs illegally.

4.4 Summary and Comment

Figure 4.1. ICER Evidence Rating Matrix



A = "Superior" - *High certainty of a substantial (moderate-large) net health benefit*
B = "Incremental" - *High certainty of a small net health benefit*
C = "Comparable"- *High certainty of a comparable net health benefit*
D= "Negative"- *High certainty of an inferior net health benefit*
B+= "Incremental or Better" – *Moderate certainty of a small or substantial net health benefit, with high certainty of at least a small net health benefit*
C+ = "Comparable or Incremental" - *Moderate certainty of a comparable or small net health benefit, with high certainty of at least a comparable net health benefit*
C- = "Comparable or Inferior" *– Moderate certainty that the net health benefit is either comparable or inferior with high certainty of at best a comparable net health benefit*
C++ = "Comparable or Better" - *Moderate certainty of a comparable, small, or substantial net health benefit, with high certainty of at least a comparable net health benefit*
P/I = "Promising but Inconclusive" *- Moderate certainty of a small or substantial net health benefit, small likelihood of a negative net health benefit*
I = "Insufficient" – *Any situation in which the level of certainty in the evidence is low*

The review and synthesis of included evidence have been organized to demonstrate the contribution of a SIF to individual and population-level outcomes. We did not identify any RCTs and as such, have based comparisons of SIF vs SSP on evidence from the cohort, time-series, pre-post, and other observational studies. Our research process also included interviews with 37 experts, including 11 PWID, who provided anecdotes and helped build the framework of outcomes to investigate. Given the available study designs from only a few communities, we recognize that differences between communities could impact generalizability. Moreover, our rating of the effectiveness of a SIF considers its operations in the context of other harm reduction strategies, such as SSPs, which were available to clients in the included studies. We believe that our focus on the incremental value of a SIF is appropriate since many communities today are exploring if a SIF fits within a broader portfolio of harm reduction and overdose prevention framework.

We produced a single evidence rating using the ICER Evidence Rating Matrix (Figure 4.1), considering the effectiveness of a SIF in addressing the public health challenges of injection drug use. We recognize that comparisons of SIF use versus no SIF, for which we have relevant data, have shown incremental benefits. Evidence from both Vancouver and Sydney found a significant reduction in occurrences of nonfatal overdose and mortality from overdose in the SIF neighborhood and beyond. Furthermore, our research team has not uncovered any report of an overdose death at a SIF, bolstering our confidence in this outcome. SIFs have demonstrated an ability to assist clients with accessing medical, mental health, and social support services, including the use of addiction treatment services.

The contribution of a SIF to bloodborne infection control is less certain in terms of direct measurement of disease incidence, both due to variation in the baseline infection rates and the lack of incremental data compared with SSPs. SIFs do reach a population that is known to be at high risk for transmission of serious infectious diseases such as HIV and HCV, and the available evidence demonstrates improvements in injection behaviors; these improvements would be expected to reduce disease transmission. We believe that unsafe injecting behaviors are an important and reasonable proxy for infection control since syringe sharing is implicated as primary infection source of new cases of HCV in the US. In at least some locations, SIFs appear to reduce public injection and, sometimes, syringe and injection litter. Finally, SIFs do not appear to be associated with changes in crime.

Unlike a medication that can be manufactured reliably and administered consistently to deliver benefits to similar patients across the world, how a SIF is implemented can impact individual and community outcomes. The intervention development, including stakeholder engagement, contributes to results. Our overall assessment of the evidence does not consider the ease or difficulty another organization may have in setting up and running a SIF. We assume that planning, stakeholder engagement, and daily management can be executed similarly to that of organizations in Vancouver and Sydney to produce the reported results.

On balance, we believe we have high certainty that, compared with SSPs, SIFs prevent overdose deaths. The degree to which overdose prevention translates to substantially lengthening the life of the individual is uncertain. The evidence on community overdose mortality from Marshall et al. 2011[12], provides moderate-quality evidence given the drop-off in effect over distance from the SIF, which is akin to a dose-response effect. This, too, provides moderate certainty of a substantial benefit. We do not believe that possible harms which have been reported – some communities report increases in needle litter near a SIF – could reduce the net benefit below incremental. There is good reason to believe the net benefit is substantial.

Thus, we have concluded that there is high certainty that SIFs, compared with SSPs provide a small, or substantial net health benefit , and moderate certainty that SIFs provide a substantial net health benefit, leading to a rating of "incremental or better" (**B+**).

5. Cost Effectiveness

5.1 Overview

The primary aim of this analysis was to estimate the cost effectiveness of SIFs for IDU among PWID using a cost-effectiveness analysis. The model compared SIFs to SSPs, which may provide a multi-day or multi-week supply of clean needles and syringes to PWID or provide one-to-one exchanges for contaminated products.[158] Because SIFs are not funded by the health care system or payers of health care, the base-case analysis was a modified societal perspective and a one-year time horizon. We also considered a health care payer perspective as a scenario analysis. The model was developed in Microsoft® Excel® for Office 365 (Version 2005).

5.2 Methods

We developed a decision analytic model for this evaluation, with outcome calculations adapted from prior relevant economic models of harm reduction for PWID[63-69] and informed by interviews among key staff and researchers of SIFs.

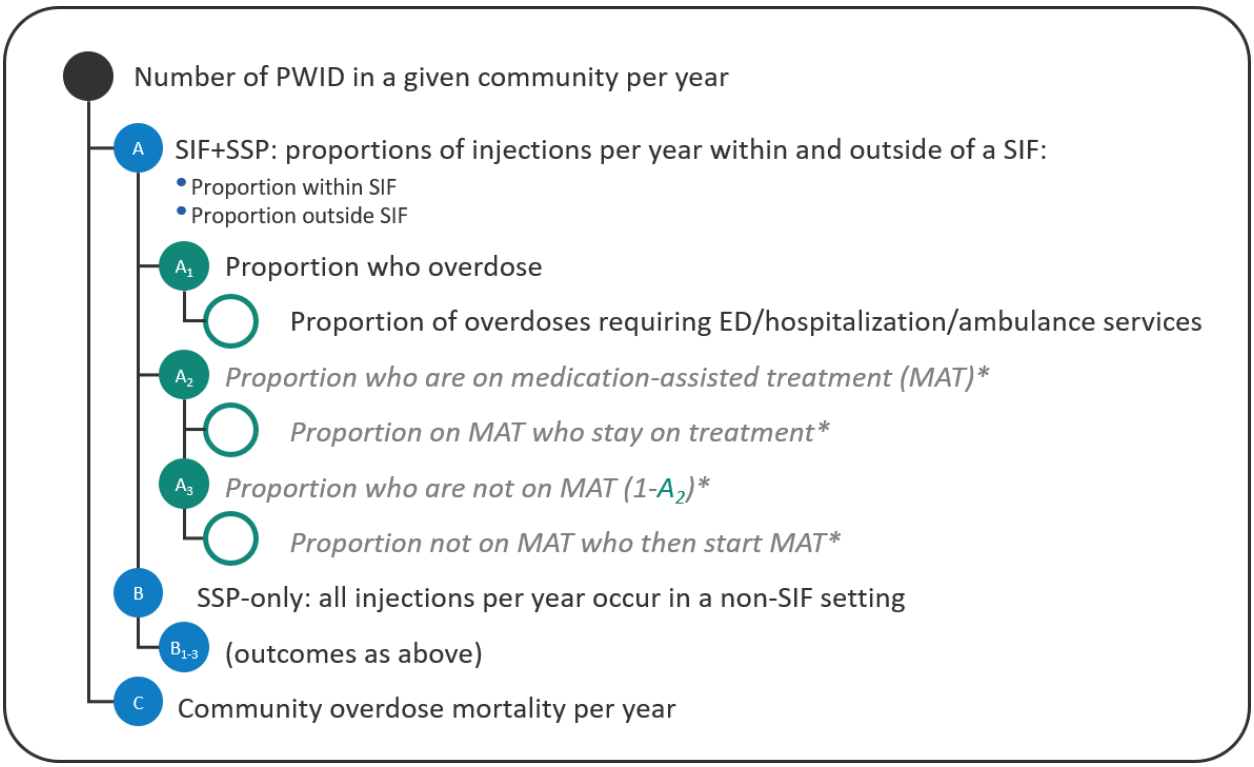
The model focused on communities of PWID, specified by parameters for individual US cities, who could potentially utilize SIFs in locations where SSPs already exist, i.e., SIF+SSP, vs. SSP-only. We calculated each setting's outcomes over one year, based on published data and observations in prior published economic models. The model did not track a single PWID cohort over time; rather, a population of PWID within a given community was estimated based on available data for each location and then outcomes for each community were calculated per year. The costs and outcomes were then summed over the one-year time horizon. We modeled six different US cities, based on local parameters, in order to develop a tool that may be customized to provide cost-effectiveness estimates for any US city given the appropriate data.

Model Structure

PWID within a given community entered the model in either the SIF+SSP (i.e., post-SIF) or SSP-only (i.e., pre-SIF) arm (Figure 5.1). Among the total population of PWID, the number of post-SIF injections/month was calculated (A); all pre-SIF injections were assumed to occur without availability of a SIF (B). For PWID who overdose (A_1), we calculated the proportions that require ambulance utilization and emergency department (ED) visits. We also calculated PWID who are on (A_2) or not on (A_3) medication-assisted treatment (MAT); among PWID who are already on MAT, we calculated the proportion per year who successfully stay on treatment. Among PWID who are not on MAT, we calculated the proportion per year who start it. MAT uptake and success rates were assumed to be equivalent between comparators in the base case, but increased MAT uptake and

success rates due to a SIF were explored in a scenario analysis. These same outcomes were calculated for B_{1-3} and totals for a given community were estimated and compared. Community overdose mortality (C) was estimated based on the proportion of injections in the SIF, applying a risk reduction estimate described below.

Figure 5.1. Model Framework



ED: emergency department, MAT: medication-assisted treatment, PWID: people who inject drugs, SIF: supervised injection facilities, SSP: syringe service program

Locations

The populations of focus for the economic evaluation included PWID at various locations in the US. We modeled costs and outcomes for Boston, Philadelphia, San Francisco, Atlanta, Baltimore, and Seattle, based on the prior existence of an SSP,[70] US geographic location, and the availability of broad city-level estimates (Table 5.1).

Table 5.1. Baseline Community Characteristics

City Characteristics	Boston	Philadelphia	San Francisco	Atlanta	Baltimore	Seattle
Population Density (people/square mile)[159,160]	13,943	11,692	18,581	3,858	7,594	8,391
Commercial Property Value(Cost per square foot)[161-163]	$550	$207	$300	$244	$202	$414
Commercial Mortgage Loan Rates[164,165]	7%	7%	7%	7%	7%	7%
Cost of Living Ratio vs. Vancouver, BC[166]	1.24	1.05	1.47	0.93	0.95	1.18
Number of PWID within city limits[167-172]	29,500*	68,800*	22,500	23,100*	42,200	26,000
Number of Overdose Deaths per Year[173-178]	250	1,150	330	482	692	227

*Estimated based on city population size and average proportion of known PWID in San Francisco, Baltimore, and Seattle

BC: British Columbia, PWID: people who inject drugs

Interventions

The list of interventions was developed with input from community organizations, clinicians, researchers, and government agencies on which interventions to include. The full list of interventions is as follows:

- Intervention of interest: SIF+SSP (i.e., Post-SIF)
- Comparator intervention: SSP-Only (i.e., Pre-SIF)

Key Model Characteristics and Assumptions

Table 5.2. Key Model Assumptions

Assumption	Rationale
Hypothetical legally-sanctioned SIFs in US cities are comparable to Insite (Vancouver, BC, Canada) in terms of effectiveness, services offered, and cost of living-adjusted operating costs.	Insite is the first and most well-documented SIF in North America.
The US cities modeled have a 0.25-mile radius area within the city that could have 2100 PWID clients for a SIF.	The Insite client-service rate is the basis for the healthcare resource use effectiveness estimates for SIFs in all modeled cities.
Rates of HIV/hepatitis C/other infections are equivalent between SIF+SSP and SSP-only.	We recognize there is some evidence that SIFs may reduce needle sharing, leading to a reduction in infections. However, due to the short time horizon of our model (1 year) and the complexity of estimating the timing of infections and attributing costs to these conditions, we chose to take a conservative approach and not include these additional cost off-sets. We explored a difference in infection rates driven by a reduction in needle sharing conferred by the SIF setting in a scenario analysis.
We assumed that the rates of initiation and continuation of MAT are equivalent between clients using SIFs and SSPs.	There is a lack of comparative data between these two services; however, stakeholders have indicated that increased face-to-face time spent with PWID may lead to increased uptake of MAT. Therefore, we explored the impacts of marginal increases in MAT initiation due to SIFs in a scenario analysis.

BC: British Columbia, HIV: human immunodeficiency virus, MAT: medication-assisted treatment, PWID: people who inject drugs, SIF: supervised injection facility, SSP: syringe service program

Model Inputs

Overdose Mortality

We utilized estimates from Marshall et al.[12] to calculate the overdose mortality risk reduction associated with SIFs (Table 5.3). We calculated the mortality reduction attributable to the SIF as the absolute difference between: (a) fatal overdose reduction within a 0.25 mile radius around the SIF and (b) fatal overdose reduction beyond a 0.25 mile radius around the SIF; this was then applied to pre-SIF overdose fatalities per city to derive expected fatalities within and outside the effective range of the SIF. Of note, the Marshall et al. estimate for overdose reduction near the SIF is a weighted average of two Vancouver, BC census tracts within a 500-meter radius of the SIF. As these two census tract distances were within 0.25 mile, we employed this distance instead of 500 meters in this US-based analysis. As in Irwin et al.,[66,67] we assumed that 5% of overall overdose deaths in each city occurred within the 0.25 mi radius of the SIF. Thus, the equation for calculating post-SIF OD deaths was:

*Pre-SIF_OD_deaths_(City)–(OD_reduction_<0.25_mi – OD_reduction_>0.25_mi)*ppn_OD_death_<0.25_mi*OD_deaths_(City)*

Table 5.3. Overdose Mortality Inputs

Parameter	Estimate (sensitivity analysis range)
Fatal OD reduction within 0.25 mi of SIF[12]	35.0% (±20%)
Fatal OD reduction beyond 0.25 mi of SIF[12]	9.3% (±20%)
Proportion of total overdose deaths occurring within 0.25 mi^2 of SIF[67]	5% (±20%)

OD: overdose, SIF: supervised injection facility

Overdoses and Emergency Services

Utilizing estimates from Insite, we assumed that 0.95% of overall injections result in an overdose (Table 5.4).[33] Emergency services included both ambulance services as well as hospital ED access, and were conditional on the occurrence of an overdose. We utilized estimates from Irwin et al. to parameterize these services, with 0.79% of overdoses at a SIF versus 46% of overdoses outside a SIF resulting in an ambulance call, and 0.79% of overdoses at a SIF versus 33% of overdoses outside a SIF resulting in an ED visit.[67] We note that the estimates for emergency services utilization for overdoses at a SIF are lower than some published estimates,[32-33] but are in line with current protocols based on stakeholder feedback. Based on an analysis of the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project (HCUP) National Emergency Department Sample, we assumed that 48% of ED visits for overdoses resulted in an inpatient admission.[74]

Table 5.4. Overdose and Emergency Services Inputs

Parameter	Estimate (sensitivity analysis range)
Overdose (OD) Inputs	
Total annual injections [71]	180,000 (±20%)
Number of unique clients/month[71]	2,100 (±20%)
Percent of injections resulting in OD[33]	0.95% (±20%)
Emergency Services Inputs	
Proportion of ODs at SIF+SSP resulting in ambulance ride[67,72]	0.79% (±20%)
Proportion of ODs at SIF+SSP resulting in ED visit[67,72]	0.79% (±20%)
Proportion of SSP-only ODs resulting in ambulance ride[67,73]	46% (±20%)
Proportion of SSP-only ODs resulting in ED visit[67,73]	33% (±20%)
Proportion of ED visits resulting in hospitalization[74]	48% (±20%)

ED: emergency department, OD: overdose, SIF: supervised injection facility, SSP: syringe service program

Medication-Assisted Treatment

We assumed that SIFs provide equivalent benefit to SSPs in terms of initiation of MAT. Therefore, we used the same estimate of 5.78% of PWID accessing MAT due to a referral from the SIF and/or SSP (Table 5.5).[75] We explored differences in uptake in MAT in a scenario analysis. We assumed 50% of PWID who begin MAT stay on treatment each year.

Table 5.5. Medication-Assisted Treatment Inputs

Parameter	Estimate (sensitivity analysis range)
Proportion of PWID who access MAT[75]	5.78% (±20%)
MAT continuation rate[67]	50% (±20%)

MAT: medication-assisted treatment, PWID: people who inject drugs

SIF and SSP Operations and Facilities Costs

SIF facility and operation costs were estimated based on the Irwin et al. approach, adapting each community's estimate according to their individual characteristics.[66,67] We applied start-up costs as well as marginal operating costs, adjusting prior 2013 estimates to 2020 US dollars using the Consumer Price Index (Table 5.6, below).[77] Start-up costs were calculated by multiplying the size of

the Insite SIF (1000 ft^2) by the commercial real estate cost per ft^2 per city (Table 5.1, above); this cost was then amortized over the length of the loan period to calculate an annual loan payment. The Insite annual operating cost was multiplied by the cost-of-living ratio per city compared to Vancouver, BC (Table 5.1, above). Each city's annual SIF cost thus equaled the annual loan payment plus the annual operating cost. We assumed that the SIF's service offerings match those of Insite, as that site is also the source for the effectiveness parameters.

SSP facility and operation costs were estimated from Teshale et al., who reported on the costs of operating these facilities in a variety of settings in the US.[78] We adopted the large (serving 2500 clients), urban SSP setting from Teshale, and then adjusted the budget items based on the SSP offerings that were available at the time of the launch of Insite, in order to align the differences in costs with the services that were added with Insite and the measured mortality impact. This included removing naloxone distribution and medical/testing services, and their associated personnel costs (including benefits). We then adjusted the costs to 2020 US dollars using the Consumer Price Index from 2016 to 2020 dollars.[77] In order to estimate SSP operation and facility costs in each modeled city, we applied US cost-of-living city-level weights, with Teshale's estimate assumed to be the overall mean.

Table 5.6. Operating and Facility Cost Inputs

Parameter	Estimate (sensitivity analysis range)
Insite Annual Operating Cost[76,77]	$1,687,286 (±20%)
Term of Commercial Loan*	15 years
SIF Square Footage[67]	1000
Adjusted SSP Annual Operating Cost[77,78]	$1,533,279 (±20%)

*Assumption

SIF: supervised injection facility, SSP: syringe service program

Emergency Services Costs

We used Centers for Medicare and Medicaid Services (CMS) fee schedules with location-specific adjustments to calculate the costs of ambulance rides (Table 5.7).[79] Overdose-related ED visit costs were estimated from the Nationwide Emergency Department Sample, assuming a 30% cost-to-charge ratio.[74] Overdose-related hospitalization costs were adapted from an analysis of Vizient hospital data that were summarized at the regional level, using the average amount that the hospital was paid for opioid-related admissions.[80]

Table 5.7. Emergency Services Cost Inputs

Parameter	Estimate (sensitivity analysis range)
Ambulance Ride Costs[79]	
Boston	$523.06 (±20%)
Philadelphia	$487.41 (±20%)
San Francisco	$566.34 (±20%)
Atlanta	$461.63 (±20%)
Baltimore	$492.50 (±20%)
Seattle	$516.37 (±20%)
Overdose-related ED Visit Cost (All Cities)[74]	$3,451 (±20%)
Overdose-related Hospitalization Cost[80]	
Boston	$8,379 (±20%)
Philadelphia	$7,502 (±20%)
San Francisco	$8,683 (±20%)
Atlanta	$5,890 (±20%)
Baltimore	$7,502 (±20%)
Seattle	$8,683 (±20%)

ED: emergency department

Model Outcomes

Model outcomes included total overdose deaths prevented and total costs for each intervention. The model outcomes will also include total emergency services avoided, and total increase in MAT initiation. Due to the one-year time horizon, all results are reported as undiscounted values.

Base-Case Analysis

Costs and cost effectiveness were estimated using the incremental cost-effectiveness ratios, with incremental analyses comparing SIF+SSP to SSP-only. Because the health care system does not hold financial responsibility for funding SIFs, the base-case analysis used a modified societal perspective.

Sensitivity Analyses

We performed one-way sensitivity analyses to identify the key drivers of model outcomes, using available measures of parameter uncertainty (i.e., confidence intervals) or reasonable ranges for each input described in the model inputs section above.

Scenario Analyses

In addition, we also performed the following scenario analyses to test the impacts of our model assumptions:

- SIF-associated reduction in HIV and HCV infections. We employed the approach used by Irwin et al. to estimate the reduction in infections among PWID. This approach was driven by a 70% reduction in needle sharing among SIF clients compared to the non-SIF PWID (Table 5.8). Given the 1-year time horizon and the decision to exclude health benefits in terms of utility weights, we did not include costs associated with HIV/HCV treatment in this scenario.

Table 5.8. SIF-Associated HIV and HCV Reduction Inputs for Scenario Analysis[66,67]

Parameter	Estimate (sensitivity analysis range)
Odds Ratio: SIF reduction in needle sharing	0.30 (95% CI: 0.11 to 0.82)
Probability of HIV infection from single injection	0.0067 (±20%)
Probability of HCV infection from single injection	0.030 (±20%)
Needle sharing rate among PWID	0.011 (±20%)
Proportion of unbleached needles	100% (±20%)
Number of needle sharing partners among PWID	1.69 (±20%)
Proportion of PWID who are HIV Positive (all cities)	0.17 (±20%)
Proportion of PWID who are HCV Positive (all cities)	0.25 (±20%)

HCV: hepatitis C virus, HIV: human immunodeficiency virus, PWID: people who inject drugs, SIF: supervised injection facilities

- Threshold analysis of overdose rate needed for cost parity. We lowered the overdose rate per city until the overall costs of a SIF+SSP and an SSP-only were equivalent.

- SIF-associated increase in MAT uptake and MAT retention. Assuming that MAT uptake at an SSP-only would be lower than the proportion of SIF+SSP clients who access MAT (5.78%), we estimated the incremental number of MAT clients at a SIF+SSP by decreasing (over a range of 0%-100%) the relative proportion of SSP-only clients who access it. In addition, we did a two-way sensitivity analysis of the differences in (a) MAT uptake and (b) MAT retention rates between SIF+SSP and SSP-only. Given the 1-year time horizon and the decision to exclude health benefits in terms of utility weights, we did not include costs associated with MAT in this scenario.

- Health care payer perspective analysis. In this scenario we focused on direct health care costs by excluding SIF and SSP costs and utilizing health care reimbursements instead of

total cost for hospitalizations. Reimbursements represent what the health care payer paid to the hospital for the provision of care rather than the net cost of care to the hospital.

Table 5.9. Hospitalization Costs for Health Care Payer Scenario Analysis

City	Health Care Payer Reimbursement[80]
Boston	$5,290
Philadelphia	$6,318
San Francisco	$7,224
Atlanta	$4,309
Baltimore	$6,318
Seattle	$7,224

Model Validation

We used several approaches to validate the model. First, we provided preliminary methods and results to multiple SIF stakeholders, including researchers and SIF staff from various locations. Based on feedback from these groups, we refined data inputs used in the model. Second, we varied model input parameters to evaluate face validity of changes in results. We performed model verification for model calculations using internal reviewers. Finally, we compared results to other cost-effectiveness models in this therapy area.

5.3 Results

Base-Case Results

The annual cost of operating a SIF+SSP ranged from $1.6 million to $2.5 million, while the cost of operating an SSP-only ranged from $1.4 million to $1.7 million, depending on the location. A hypothetical SIF+SSP was found to result in the prevention of three (Boston) to 15 (Philadelphia) overdose deaths per year, as well as 773 fewer overdose-related ambulance rides, 551 fewer overdose-related ED visits, and 264 fewer hospitalizations (all based on 180,000 injections/year/comparator). This resulted in cost-savings for: (a) ambulance rides avoided, from -$437,800 (San Francisco) to -$356,900 (Atlanta); (b) ED visits avoided (-$1.9 million); and (c) hospitalizations avoided, from -$2.3 million (San Francisco and Seattle) to -$1.6 million (Atlanta). For each of the six cities, a SIF+SSP saved money compared to an SSP-only, driven primarily by reductions in ED visit and hospitalization costs (of note, OD deaths avoided is not included in the costs per comparator). The overall cost-savings for a SIF+SSP versus SSP-only ranged from -$4.2 million (Seattle) to -$3.6 million (Atlanta).

Table 5.10. Base-Case Results for Boston and Philadelphia

Outcome	Boston			Philadelphia		
	SIF+SSP	SSP-Only	Incremental	SIF+SSP	SSP-Only	Incremental
Total Cost	$2,261,000	$6,270,000	-$4,009,000	$1,896,000	$5,796,000	-$3,899,000
Annual Cost of Facility	$2,153,000	$1,641,000	$511,300	$1,794,000	$1,433,000	$361,500
Ambulance Costs	$7,100	$411,400	-$404,400	$6,600	$383,400	-$376,800
ED Visit Costs	$46,600	$1,947,000	-$1,901,000	$46,600	$1,947,000	-$1,901,000
Hospitalization Costs	$54,300	$2,270,000	-$2,215,000	$48,600	$2,032,000	-$1,983,000
Overdose Deaths	9	13	-3	43	58	-15
Ambulance Rides	14	787	-773	14	787	-773
ED Visits	14	564	-551	14	564	-551
Hospitalizations	6	271	-264	6	271	-264

ED: emergency department, SIF: supervised injection facility, SSP: syringe service program

Table 5.11. Base-Case Results for San Francisco and Atlanta

Outcome	San Francisco			Atlanta		
	SIF+SSP	SSP-Only	Incremental	SIF+SSP	SSP-Only	Incremental
Total Cost	$2,624,000	$6,457,000	-$3,833,000	$1,687,000	$5,310,000	-$3,623,000
Annual Cost of Facility	$2,513,000	$1,712,000	$800,900	$1,596,000	$1,404,000	$191,500
Ambulance Costs	$7,700	$445,500	-$437,800	$6,200	$363,100	-$356,900
ED Visit Costs	$46,600	$1,947,000	-$1,901,000	$46,600	$1,947,000	-$1,901,000
Hospitalization Costs	$56,300	$2,352,000	-$2,296,000	$38,200	$1,595,000	-$1,557,000
Overdose Deaths	12	17	-4	18	24	-6
Ambulance Rides	14	787	-773	14	787	-773
ED Visits	14	564	-551	14	564	-551
Hospitalizations	6	271	-264	6	271	-264

ED: emergency department, SIF: supervised injection facility, SSP: syringe service program

Table 5.12. Base-Case Results for Baltimore and Seattle

Outcome	Baltimore			Seattle		
	SIF+SSP	SSP-Only	Incremental	SIF+SSP	SSP-Only	Incremental
Total Cost	$1,727,000	$5,750,000	-$4,023,000	$2,146,000	$6,346,000	-$4,199,000
Annual Cost of Facility	$1,625,000	$1,383,000	$241,900	$2,036,000	$1,640,000	$396,100
Ambulance Costs	$6,700	$387,400	-$380,700	$7,000	$406,200	-$399,200
ED Visit Costs	$46,600	$1,947,000	-$1,901,000	$46,600	$1,947,000	-$1,901,000
Hospitalization Costs	$48,600	$2,032,000	-$1,983,000	$56,300	$2,352,000	-$2,296,000
Overdose Deaths	26	35	-9	8	11	-3
Ambulance Rides	14	787	-773	14	787	-773
ED Visits	14	564	-551	14	564	-551
Hospitalizations	6	271	-264	6	271	-264

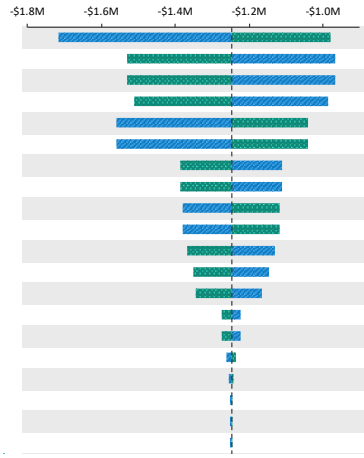
ED: emergency department, SIF: supervised injection facility, SSP: syringe service program

Sensitivity Analysis Results

To demonstrate effects of uncertainty on both costs and health outcomes, we varied input parameters using reasonable ranges to evaluate changes in costs saved per overdose death avoided (Figure 5.2), cost per ambulance ride avoided (Appendix Figure E1), cost per ED visit avoided (Appendix Figure E2), and cost per hospitalization avoided (Appendix Figure E3). The parameter with the largest impact on the cost per OD death avoided was the overdose mortality reduction within 0.25 mi^2 of the SIF.[12] Other parameters with notable impact included the number of injections/year/clientele, the proportion of injections that result in overdoses, the proportion of overall overdose deaths/year/city that occur within 0.25 mi^2 of a SIF, and overdose deaths per city.

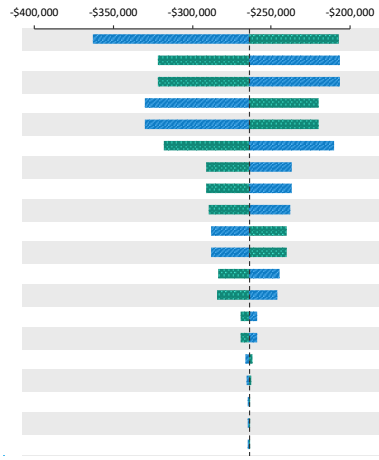
Figure 5.2. One-Way Sensitivity Analysis Results

Costs Saved per OD Death Avoided, Boston



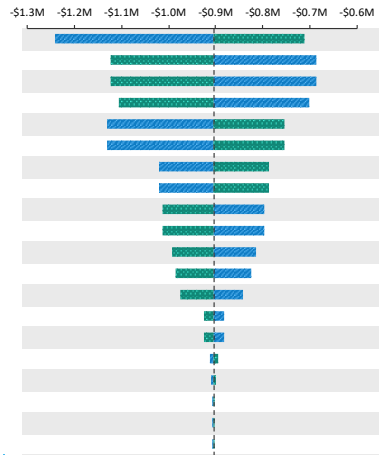
Parameter	Low Value	High Value	Low Result	High Result	Spread
Overdose Mortality: Reduction Within 0.25 mi of SIF	0.280	0.420	-$1,715,144	-$980,831	$734,312
Total annual injections in the SIF	144,000	216,000	-$966,552	-$1,529,415	$562,863
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$966,552	-$1,529,415	$562,863
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$985,442	-$1,510,526	$525,083
Overdose Mortality: Ppn. of City OD Deaths Within 0.25 mi of SIF	0.040	0.060	-$1,559,980	-$1,039,987	$519,993
Overdose Deaths/Year: Boston	200	300	-$1,559,980	-$1,039,987	$519,993
Hospitalization Cost: Boston	$6,704	$10,055	-$1,110,064	-$1,385,904	$275,840
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$1,110,064	-$1,385,904	$275,840
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$1,378,240	-$1,117,728	$260,512
Cost of Living Ratio vs. Vancouver: Boston	0.99	1.49	-$1,378,240	-$1,117,728	$260,512
Cost of ED VIsit: Boston	$2,761	$4,141	-$1,129,647	-$1,366,320	$236,673
First Year SSP Cost	$1,226,623	$1,839,934	-$1,145,803	-$1,350,165	$204,361
Overdose Mortality: Reduction Outside 0.25 mi of SIF	0.074	0.112	-$1,163,759	-$1,345,352	$181,593
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$1,222,369	-$1,273,599	$51,230
Cost of Ambulance Ride: Boston	$418	$628	-$1,222,809	-$1,273,159	$50,350
Number of Unique SIF Clients/Month	1,680	2,520	-$1,259,937	-$1,236,031	$23,907
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$1,254,269	-$1,241,699	$12,570
Cost/sqft Commercial Property: Boston	$440	$660	-$1,251,743	-$1,244,224	$7,519
Commercial Mortgage Loan Interest: Boston	5%	9%	-$1,250,287	-$1,245,542	$4,745
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$1,248,424	-$1,247,544	$880

Costs Saved per OD Death Avoided, Philadelphia



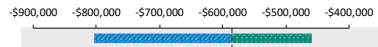
Parameter	Low Value	High Value	Low Result	High Result	Spread
Overdose Mortality: Reduction Within 0.25 mi of SIF	0.280	0.420	-$362,657	-$207,391	$155,266
Total annual injections in the SIF	144,000	216,000	-$206,211	-$321,547	$115,336
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$206,211	-$321,547	$115,336
Overdose Mortality: Ppn. of City OD Deaths Within 0.25 mi of SIF	0.040	0.060	-$329,849	-$219,899	$109,950
Overdose Deaths/Year: Philadelphia	920	1380	-$329,849	-$219,899	$109,950
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$210,022	-$317,736	$107,715
Hospitalization Cost: Philadelphia	$6,001	$9,002	-$237,036	-$290,722	$53,685
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$237,036	-$290,722	$53,685
Cost of ED VIsit: Philadelphia	$2,761	$4,141	-$238,154	-$289,604	$51,451
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$287,857	-$239,901	$47,955
Cost of Living Ratio vs. Vancouver: Philadelphia	0.84	1.26	-$287,857	-$239,901	$47,955
First Year SSP Cost	$1,226,623	$1,839,934	-$244,486	-$283,272	$38,786
Overdose Mortality: Reduction Outside 0.25 mi of SIF	0.074	0.112	-$246,070	-$284,467	$38,397
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$258,690	-$269,068	$10,378
Cost of Ambulance Ride: Philadelphia	$390	$585	-$258,779	-$268,979	$10,200
Number of Unique SIF Clients/Month	1,680	2,520	-$266,148	-$261,610	$4,537
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$265,168	-$262,590	$2,579
Cost/sqft Commercial Property: Philadelphia	$166	$248	-$264,186	-$263,571	$615
Commercial Mortgage Loan Interest: Philadelphia	5%	9%	-$264,067	-$263,679	$388
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$263,968	-$263,790	$178

Costs Saved per OD Death Avoided, San Francisco



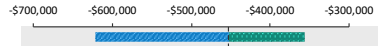
Parameter	Low Value	High Value	Low Result	High Result	Spread
Overdose Mortality: Reduction Within 0.25 mi of SIF	0.280	0.420	-$1,242,355	-$710,460	$531,895
Total annual injections in the SIF	144,000	216,000	-$685,403	-$1,122,538	$437,136
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$685,403	-$1,122,538	$437,136
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$701,199	-$1,106,743	$405,544
Overdose Mortality: Ppn. of City OD Deaths Within 0.25 mi of SIF	0.040	0.060	-$1,129,963	-$753,309	$376,654
Overdose Deaths/Year: San Francisco`	264	396	-$1,129,963	-$753,309	$376,654
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$1,020,953	-$786,989	$233,964
Cost of Living Ratio vs. Vancouver: San Francisco	1.18	1.76	-$1,020,953	-$786,989	$233,964
Hospitalization Cost: San Francisco	$6,946	$10,419	-$795,702	-$1,012,239	$216,538
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$795,702	-$1,012,239	$216,538
Cost of ED VIsit: San Francisco	$2,761	$4,141	-$814,322	-$993,619	$179,298
First Year SSP Cost	$1,226,623	$1,839,934	-$823,209	-$984,732	$161,524
Overdose Mortality: Reduction Outside 0.25 mi of SIF	0.074	0.112	-$842,962	-$974,498	$131,536
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$882,960	-$924,981	$42,022
Cost of Ambulance Ride: San Francisco	$453	$680	-$883,321	-$924,621	$41,300
Number of Unique SIF Clients/Month	1,680	2,520	-$913,418	-$894,523	$18,895
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$908,825	-$899,116	$9,708
Cost/sqft Commercial Property: San Francisco	$240	$360	-$905,524	-$902,417	$3,107
Commercial Mortgage Loan Interest: San Francisco	5%	9%	-$904,922	-$902,961	$1,961
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$904,331	-$903,610	$722

Costs Saved per OD Death Avoided, Atlanta



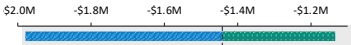
Parameter	Low Value	High Value	Low Result	High Result	Spread
Overdose Mortality: Reduction Within 0.25 mi of SIF	0.280	0.420	-$803,995	-$459,777	$344,218
Total annual injections in the SIF	144,000	216,000	-$461,822	-$708,194	$246,372
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$461,822	-$708,194	$246,372
Overdose Deaths/Year: Atlanta	386	578	-$731,260	-$487,507	$243,753
Overdose Mortality: Ppn. of City OD Deaths Within 0.25 mi of SIF	0.040	0.060	-$731,260	-$487,507	$243,753
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$470,608	-$699,409	$228,801
Cost of ED VIsit: Atlanta	$2,761	$4,141	-$523,630	-$646,386	$122,756
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$635,678	-$534,338	$101,340
Cost of Living Ratio vs. Vancouver: Atlanta	0.74	1.12	-$635,678	-$534,338	$101,340
Hospitalization Cost: Atlanta	$4,712	$7,068	-$534,724	-$635,292	$100,568
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$534,724	-$635,292	$100,568
First Year SSP Cost	$1,226,623	$1,839,934	-$539,656	-$630,360	$90,704
Overdose Mortality: Reduction Outside 0.25 mi of SIF	0.074	0.112	-$545,526	-$630,650	$85,124
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$573,283	-$596,733	$23,451
Cost of Ambulance Ride: Atlanta	$369	$554	-$573,484	-$596,532	$23,048
Number of Unique SIF Clients/Month	1,680	2,520	-$590,313	-$579,703	$10,611
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$587,747	-$582,269	$5,477
Cost/sqft Commercial Property: Atlanta	$195	$293	-$585,874	-$584,142	$1,732
Commercial Mortgage Loan Interest: Atlanta	5%	9%	-$585,539	-$584,445	$1,093
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$585,209	-$584,807	$403

Costs Saved per OD Death Avoided, Baltimore



Parameter	Low Value	High Value	Low Result	High Result	Spread
Overdose Mortality: Reduction Within 0.25 mi of SIF	0.280	0.420	-$621,763	-$355,565	$266,198
Total annual injections in the SIF	144,000	216,000	-$356,487	-$548,335	$191,848
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$356,487	-$548,335	$191,848
Overdose Deaths/Year: Baltimore	554	830	-$565,514	-$377,009	$188,505
Overdose Mortality: Ppn. of City OD Deaths Within 0.25 mi of SIF	0.040	0.060	-$565,514	-$377,009	$188,505
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$362,908	-$541,914	$179,006
Hospitalization Cost: Baltimore	$6,001	$9,002	-$407,803	-$497,020	$89,217
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$407,803	-$497,020	$89,217
Cost of ED VIsit: Baltimore	$2,761	$4,141	-$409,660	-$495,163	$85,503
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$488,463	-$416,359	$72,105
Cost of Living Ratio vs. Vancouver: Baltimore	0.76	1.14	-$488,463	-$416,359	$72,105
Overdose Mortality: Reduction Outside 0.25 mi of SIF	0.074	0.112	-$421,878	-$487,708	$65,830
First Year SSP Cost	$1,226,623	$1,839,934	-$421,302	-$483,521	$62,219
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$443,698	-$461,124	$17,427
Cost of Ambulance Ride: Baltimore	$394	$591	-$443,848	-$460,975	$17,127
Number of Unique SIF Clients/Month	1,680	2,520	-$456,050	-$448,772	$7,278
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$454,554	-$450,269	$4,285
Cost/sqft Commercial Property: Baltimore	$162	$242	-$452,910	-$451,912	$998
Commercial Mortgage Loan Interest: Baltimore	5%	9%	-$452,717	-$452,087	$630
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$452,561	-$452,262	$299

Costs Saved per OD Death Avoided, Seattle



Parameter	Low Value	High Value	Low Result	High Result	Spread
Overdose Mortality: Reduction Within 0.25 mi of SIF	0.280	0.420	-$1,980,327	-$1,132,481	$847,846
Total annual injections in the SIF	144,000	216,000	-$1,125,567	-$1,756,309	$630,742
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$1,125,567	-$1,756,309	$630,742
Overdose Mortality: Ppn. of City OD Deaths Within 0.25 mi of SIF	0.040	0.060	-$1,801,173	-$1,200,782	$600,391
Overdose Deaths/Year: Seattle	181	272	-$1,801,173	-$1,200,782	$600,391
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$1,145,900	-$1,735,977	$590,077
Hospitalization Cost: Seattle	$6,946	$10,419	-$1,283,404	-$1,598,472	$315,068
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$1,283,404	-$1,598,472	$315,068
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$1,577,571	-$1,304,306	$273,265
Cost of Living Ratio vs. Vancouver: Seattle	0.94	1.42	-$1,577,571	-$1,304,306	$273,265
Cost of ED VIsit: Seattle	$2,761	$4,141	-$1,310,497	-$1,571,380	$260,883
First Year SSP Cost	$1,226,623	$1,839,934	-$1,328,369	-$1,553,507	$225,138
Overdose Mortality: Reduction Outside 0.25 mi of SIF	0.074	0.112	-$1,343,691	-$1,553,360	$209,670
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$1,413,064	-$1,468,812	$55,748
Cost of Ambulance Ride: Seattle	$413	$620	-$1,413,543	-$1,468,334	$54,791
Number of Unique SIF Clients/Month	1,680	2,520	-$1,454,107	-$1,427,770	$26,337
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$1,448,001	-$1,433,875	$14,126
Cost/sqft Commercial Property: Seattle	$331	$497	-$1,444,058	-$1,437,819	$6,239
Commercial Mortgage Loan Interest: Seattle	5%	9%	-$1,442,849	-$1,438,912	$3,937
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$1,441,417	-$1,440,460	$957

Scenario Analyses Results

SIF-Associated Reduction in HIV and HCV Infections

In a model assuming that SIFs reduce needle sharing, and that this reduction in needle sharing reduces transmission of viral infection, a single SIF was found to decrease the number of new cases of HIV by between 1 (Baltimore) and 4 (San Francisco) cases per year, and to decrease the number of HCV infections per year by between 6 (Baltimore) and 23 (San Francisco) cases per year (Appendix Table E1).

Threshold Analysis of Overdose Rate Needed for Cost Parity Between SIF+SSP and SSP-Only

We performed a threshold analysis that estimated how low the OD rate would need to be in each city to reach parity between the costs of a SIF+SSP and SSP-only. These ranged between 0.05% (Atlanta and Baltimore) and 0.16% (San Francisco), all representing significantly lower OD rates than the base case (Table 5.13).

Table 5.13. Threshold Analysis of Overdose Rate

	Base Case OD Rate	Incremental Cost	Threshold OD Rate	Incremental Cost
Boston	0.95%	-$4,009,000	0.11%	$0
Philadelphia	0.95%	-$3,899,000	0.08%	$0
San Francisco	0.95%	-$3,833,000	0.16%	$0
Atlanta	0.95%	-$3,623,000	0.05%	$0
Baltimore	0.95%	-$4,023,000	0.05%	$0
Seattle	0.95%	-$4,199,000	0.08%	$0

OD: overdose

SIF-Associated Increase in MAT Uptake and MAT Retention

In the base-case analysis, the proportion of clients who accessed MAT was 5.78% in both comparator arms. This estimate was based on data collected from a SIF in Australia. If MAT uptake at an SSP-only is instead assumed to be 0% of the SIF+SSP, the SIF+SSP would result in 121 additional clients who access treatment. We modeled this increase in MAT uptake in increments of 10% in order to demonstrate the impact of these assumptions (Table 5.14). The two-way sensitivity analysis of MAT uptake and MAT retention is available in Appendix Table E2.

Table 5.14. Scenario Analysis of Differential MAT Uptake at SIF+SSP vs. SSP-only

Relative Difference in SSP-Only Clients who Access MAT Compared to SIF+SSP	0% (SIF+SSP=5.78%, SSP-Only=0%)	10%	20%	30%	40%	50% (SIF+SSP=5.78%, SSP-Only=2.89%)	60%	70%	80%	90%	100%* (SIF+SSP=5.78%, SSP-Only=5.78%)
Incremental MAT Uptake at SIF+SSP	121	109	97	85	73	61	49	36	24	12	0

*Base case

MAT: medication-assisted treatment, SIF: Supervised Injection Facilities, SSP: Syringe Service Program

Health Care Payer Perspective Analysis Focused on Direct Health Care Costs and the Potential Differences in Those Costs between the Interventions

When we focused on health care payer costs only by excluding SIF and SSP operating and facility costs, and by utilizing payer reimbursement costs instead of total (societal) cost, SIF+SSP was still cost-saving versus SSP-only due to savings from avoidance of ambulance rides, ED visits, and hospitalizations.

Table 5.15. Scenario Analysis of Health Care Payer Perspective

	Boston			Philadelphia		
	SIF+SSP	SSP-Only	Incremental	SIF+SSP	SSP-Only	Incremental
Total Cost	$88,000	$3,792,000	-$3,704,000	$94,200	$4,042,000	-$3,948,000
Annual Cost of Facility	$0	$0	$0	$0	$0	$0
Ambulance Costs	$7,100	$411,400	-$404,400	$6,600	$383,400	-$376,800
ED Visit Costs	$46,600	$1,947,000	-$1,901,000	$46,600	$1,947,000	-$1,901,000
Hospitalization Costs	$34,300	$1,433,000	-$1,398,000	$41,000	$1,711,000	-$1,670,000
	San Francisco			Atlanta		
	SIF+SSP	SSP-Only	Incremental	SIF+SSP	SSP-Only	Incremental
Total Cost	$101,100	$4,350,000	-$4,248,000	$80,800	$3,478,000	-$3,397,000
Annual Cost of Facility	$0	$0	$0	$0	$0	$0
Ambulance Costs	$7,700	$445,500	-$437,800	$6,200	$363,100	-$356,900
ED Visit Costs	$46,600	$1,947,000	-$1,901,000	$46,600	$1,947,000	-$1,901,000
Hospitalization Costs	$46,800	$1,957,000	-$1,910,000	$27,900	$1,167,000	-$1,139,000
	Baltimore			Seattle		
	SIF+SSP	SSP-Only	Incremental	SIF+SSP	SSP-Only	Incremental
Total Cost	$94,200	$4,046,000	-$3,952,000	$100,400	$4,310,000	-$4,210,000
Annual Cost of Facility	$0	$0	$0	$0	$0	$0
Ambulance Costs	$6,700	$387,400	-$380,700	$7,000	$406,200	-$399,200
ED Visit Costs	$46,600	$1,947,000	-$1,901,000	$46,600	$1,947,000	-$1,901,000
Hospitalization Costs	$41,000	$1,711,000	-$1,670,000	$46,800	$1,957,000	-$1,910,000

ED: emergency department, SIF: supervised injection facility, SSP: syringe service program

Model Validation

Model validation followed standard practices in the field. We tested all mathematical functions in the model to ensure they were consistent with the report (and supplemental Appendix materials). We also conducted sensitivity analyses with null input values to ensure the model was producing findings consistent with expectations. Further, independent modelers tested the mathematical functions in the model as well as the specific inputs and corresponding outputs.

Model validation was also conducted in terms of comparisons to other model findings. We searched the literature to identify models that were similar to our analysis, with comparable populations, settings, perspective, and treatments.

Prior Economic Models

We identified four prior published economic evaluations of SIFs in the US, along with published analyses of the Insite facility in Vancouver, BC. Our model was informed in large part by these models, though with some different assumptions. Unlike prior models, our approach focused on explicitly comparing SIF+SSP to an SSP operating alone in a city. Because of this decision, many of the outcomes highlighted by prior models, such as infection rates and MAT initiation, were assumed to be equivalent in our base case.

Our model also utilized the distance-based OD death risk reduction from Marshall et al. in a slightly different way than most previous models, by attributing the 25.7% incremental mortality risk reduction associated with the SIF to one quarter mile radius around the SIF.[12] Behrends et al. attributed this risk reduction more broadly to a half-mile radius, while other prior models have used a variety of other methods to attribute lives saved to SIFs.[63] Therefore, it is difficult to exactly reconcile the estimated mortality impact from our model with others, though they are all consistent in estimating that SIFs reduce mortality.

In terms of SIF operating costs, our model estimates aligned fairly closely with those taking the same costing approach but diverged slightly from those that used city- or county-specific wage estimates or different financing approaches. For example, our estimated cost of running the SIF in Seattle for one year was $2,036,000, compared to the Hood et al. estimate of $1,222,332 using wage rates for actual staff employed by the county to run their hypothetical SIF.[64] In that regard, our results for Seattle may be conservative, assuming their SIF operating model was to be executed.

Limitations

There are a number of important limitations to consider when evaluating our model estimates. First, the costs of operating a SIF in cities around the US are extrapolations from a single North American SIF in Vancouver, BC. The actual costs of operating a SIF in any of the cities we modeled will depend on many local factors and the actual funding mechanisms used. Furthermore, the operations of both SIFs and SSPs may vary widely from city to city. Second, the mortality risk reduction estimates we used also come from the estimated impact of that same single North American SIF at a single point in time. The long-term OD mortality risk reduction associated with SIFs is unknown. Lastly, we cannot account for rapidly evolving pandemic-associated factors.

5.4 Summary and Comment

We developed a decision analytic model to estimate the costs and outcomes associated with operating a SIF compared to an SSP only in six cities in the US over a one-year time horizon. The costs of operating a SIF were estimated to be higher than operating an SSP across all six cities. However, those costs were offset by cost savings attributed to SIFs through the avoidance of ED

visits and subsequent hospitalizations. Furthermore, in all six cities, SIFs were estimated to reduce mortality by avoiding overdose deaths.

The model results were sensitive to several input parameters, which varied slightly across the six cities. The underlying community-level risk parameters of overdose and overdose mortality, along with the mortality risk reduction attributed to SIFs, were the most influential model parameters. Additionally, parameters that determined the number of injections occurring in SIFs within each city also influenced the model estimates.

Conclusions

Operating a SIF was estimated to save lives and additionally to reduce medical care associated with overdoses in all six US cities modeled. We estimated that operating a SIF results in fewer lives lost to overdoses and lower costs overall after accounting for the incremental costs associated with operating a SIF compared to an SSP alone.

6. Potential Other Benefits and Contextual Considerations

Our reviews seek to provide information on potential other benefits offered by the intervention to the individual PWID, caregivers, the delivery system, other PWUD, or the public that would not have been considered as part of the evidence on comparative clinical effectiveness. We also recognize that there may be broader contextual issues related to the severity of the condition, whether other treatments are available, and ethical, legal, or other societal priorities that influence the relative value of illnesses and interventions. These general elements are listed in the table below, and the subsequent text provides detail about the elements that are applicable. We sought input from stakeholders, including individual clients, advocacy organizations, policy makers, clinicians, law enforcement agencies, researchers, and SIF managers, to inform the contents of this section.

Each ICER review culminates in a public meeting of an independent voting Council of clinicians, patients, and health services researchers. As part of their deliberations, Council members will judge whether a treatment may substantially impact the considerations listed in Table 6.1. The presence of substantial other benefits or contextual considerations may shift a council member's vote on an intervention's long-term value for money to a different category than would be indicated by the clinical evidence and economic modeling alone. A Council member may also determine that there are no other benefits or contextual considerations substantial enough to shift their vote. All factors that are considered in the voting process are outlined in ICER's value assessment framework. The content of these deliberations is described in the last chapter of ICER's Final Evidence Report, which is released after the public meeting.

This section, as well as the Council's deliberation, provides stakeholders with information to inform analysis on a range of issues related to SIFs, including public policy development.

Table 6.1. Potential Other Benefits or Contextual Considerations

Likert Scale of Potential Other Benefits and Contextual Considerations		
1 (Suggests Lower Value)	**2 (Intermediate)**	**3 (Suggests Higher Value)**
Uncertainty or overly favorable model assumptions creates significant risk that base-case cost-effectiveness estimates are too optimistic.		Uncertainty or overly unfavorable model assumptions creates significant risk that base-case cost-effectiveness estimates are too pessimistic.
This intervention will not differentially benefit a historically disadvantaged or underserved community.		This intervention will differentially benefit a historically disadvantaged or underserved community.
Will not significantly reduce the negative impact of the condition on family and caregivers vs. the comparator.		Will significantly reduce the negative impact of the condition on family and caregivers vs. the comparator.
Will not have a significant impact on improving return to work and/or overall productivity vs. the comparator.		Will have a significant impact on improving return to work and/or overall productivity vs. the comparator.
Other		Other

6.1 Potential Other Benefits and Contextual Considerations

Impact on PWID Care

The opening of a SIF represents a community's commitment to treat substance use disorders as a health issue, rather than a criminal issue. Its availability allows law enforcement and medical professionals to guide PWID to a SIF for immediate and long-term support of a substance use disorder, including screening and prevention of related health issues (e.g., HIV, hepatitis, soft tissue infections). It provides another access point for health and social support services, and referral coordination, especially for people with housing insecurity and mental illness. It is possible that a SIF makes a significant impact on the entire infrastructure of care for substance use disorders in the neighborhoods where it operates and/or for the clients it serves.

Serving the Marginalized

Persons served by SIFs are among the most vulnerable and marginalized in a community. Well-established social norms and public opinions regarding substance use disorders place PWID at a disadvantage for health and social support resources in many communities.

Addressing Health Disparities

Given the disparities in SUD by socio-economic class, SIFs differentially benefit groups with lower life expectancy and higher disability. For example, the average annual rate of heroin use was 5.5% for people in the lowest household income group (<$20,000), which was 3.4 times higher than the >$50,000 household income group.[179] The relationship between race-ethnicity and SUD is confounded by income with larger percentages of minority populations living in poverty. A SIF that

is able to engage clients and successfully refer them to treatment can contribute to improving health equity for recovery as well as overdose-related deaths.

Relationship-Building with Clients

Due to the personal histories of mental illness and substance abuse, some SIF clients have difficulty building and maintaining trust with others, especially health care professionals. In comparison to SSPs which have been described in interviews as "transactional", SIFs are more likely to engage clients in longer and more frequent interactions with staff and other clients. A trust-based relationship can be instrumental in helping clients improve injection behavior and link to medical, mental/behavioral health and social services.

Screening of Street Drug Toxicity

It was reported that some SIF clients use the facility when obtaining drugs from a new or different source. The SIF can provide direct protection for PWID in this case. Toxicity screening of drugs before injection and/or analysis of remnants allows for a SIF to be part of a community's surveillance system of the drug supply and contribute to timely public warnings about lethal substances in circulation.

Attribution of Benefits to the SIF versus Other Factors

Most quantitative data that informed the economic model are derived from SIFs operating in only two communities. Uncertainty exists about local factors (unmeasured or unmeasurable attributes unique to the people and place) that contributed to favorable outcomes at the time of the study. It is not possible to separate features of the intervention from local community factors, such as infection rates, resources for persons with housing insecurity, access to primary medical care, etc. that vary across communities that may be considering implementing a SIF. In communities where SIFs are introduced, they represent a new form of harm reduction that augments other strategies already in place, notably medication-assisted treatment, naloxone distribution, and syringe service programs.

7. Health-Benefit Price Benchmarks

As the assessment for this non-drug topic does not include estimates of incremental quality-adjusted life years (QALYs) or equal value life years gained (evLYG), ICER did not produce health-benefit price benchmarks as part of this report.

8. Potential Budget Impact

As the assessment for this non-drug topic does not include price per treatment or estimates of cost-effectiveness threshold prices, ICER did not produce potential budget impact analyses as part of this report.

****

This is the first ICER review of supervised injection facilities.

References

1. Dowell D AE, Kochanek K, et al. . Contribution of Opioid-Involved Poisoning to the Change in Life Expectancy in the United States, 2000-2015. *JAMA.* 2017;318(11):1065-1067.
2. Hedegaard H MA, Warner M. . *Drug overdose deaths in the United States, 1999–2018. NCHS Data Brief.* 2020.
3. Wakeman SE, Barnett ML. Primary Care and the Opioid-Overdose Crisis — Buprenorphine Myths and Realities. *New England Journal of Medicine.* 2018;379(1):1-4.
4. Jarlais DD, A N, A S, J F, J M, D H. Syringe service programs for persons who inject drugs in urban, suburban, and rural areas — United States. *MMWR Morb Mortal Wkly Rep.* 2013;64(48):1337-1341.
5. National Harm Reduction Coalition. Harm Reduction Principles: National Harm Reduction Coalition. 2020; https://harmreduction.org/about-us/principles-of-harm-reduction/. Accessed September 15, 2020.
6. Keane H. Critiques of harm reduction, morality and the promise of human rights. *International Journal of Drug Policy.* 2003;14(3):227-232.
7. Kerr T, Mitra, S., Kennedy, M.C. et al. Supervised injection facilities in Canada: past, present, and future. *Harm Reduct J.* 2017;14(28).
8. Drug Policy Alliance. Supervised Consumption Services. https://www.drugpolicy.org/issues/supervised-consumption-services. Accessed September 15, 2020.
9. Belackova V, Salmon, A. M., Schatz, E., Jauncey, M. *Online census of Drug Consumption Rooms (DCRs) as a setting to address HCV: current practice and future capacity, Amsterdam, Sydney.* International Network of Drug Consumption Rooms, Correlation Network, Uniting Medically Supervised Injecting Centre;2017.
10. Woods S. *Drug Consumption Rooms in Europe: Organizational Review.* 2014.
11. Dooling K RM. Vancouver's supervised injection facility challenges Canada's drug laws. *CMAJ.* 2010;182(3):1440-1444.
12. Marshall BD, Milloy MJ, Wood E, Montaner JS, Kerr T. Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study. *Lancet.* 2011;377(9775):1429-1437.
13. Petrar S, Kerr T, Tyndall MW, Zhang R, Montaner JSG, Wood E. Injection drug users' perceptions regarding use of a medically supervised safer injecting facility. *Addictive Behaviors.* 2007;32(5):1088-1093.
14. Kral A, Lambdin, BH, Wenger, LD, Davidson, PJ. Evaluation of an Unsanctioned Safe Consumption Site in the United States. *N Engl J Med.* 2020;383:589-590.
15. Gutman D. Seattle, King County move to open nation's first safe injection sites for drug users. *The Seattle Times*2017.
16. Miller B. Denver City Council approves supervised injection site pilot, which still needs legislative approval. *The Denver Channel*2018.
17. Ackland M. DC looking into proposal of setting up supervised injection sites for drug users. *Fox5*2017.
18. Chen E. Should Chicago open safe sites for drug users? There's already a makeshift network — and it's saving lives. *Chicago Tribune*2020.
19. Neuman W. To Curb Overdoses, New York Plans to Try Safe Injection Sites. *The New York Times*2018;A: 1.

20. CBS. San Francisco Safe Injection Bill Passes Calif. Legislature; DOJ Threatens Prosecution. *CBS SF BayArea*2018.
21. Cohn M. Supporters push safe injection sites to stem overdose deaths in Maryland, but legal questions unresolved. *Baltimore Sun.* September 25, 2019, 2019;Health.
22. Board CE. California is still stuck in a safe injection debate that should have ended years ago. *San Francisco Chronicle.* October 10, 2020, 2020.
23. Reynolds N. Local leaders meet to discuss future of safe injection facilities. *ithaca.com*2018.
24. CDC. Summary of Information on The Safety and Effectiveness of Syringe Services Programs (SSPs). 2019; https://www.cdc.gov/ssp/syringe-services-programs-summary.html. Accessed September 15, 2020.
25. Fernandes RM, Cary M, Duarte G, et al. Effectiveness of needle and syringe Programmes in people who inject drugs - An overview of systematic reviews. *BMC public health.* 2017;17(1):309.
26. Davis SM, Daily S, Kristjansson AL, et al. Needle exchange programs for the prevention of hepatitis C virus infection in people who inject drugs: a systematic review with meta-analysis. *Harm Reduct J.* 2017;14(1):25.
27. Mir MU, Akhtar F, Zhang M, Thomas NJ, Shao H. A Meta-analysis of the Association Between Needle Exchange Programs and HIV Seroconversion Among Injection Drug Users. *Cureus.* 2018;10(9):e3328.
28. Platt L, Minozzi S, Reed J, et al. Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs. *Cochrane Database of Systematic Reviews.* 2017(9).
29. Kennedy MC KM, Kerr T. Public Health and Public Order Outcomes Associated with Supervised Drug Consumption Facilities: a Systematic Review. *Curr HIV/AIDS Rep.* 2017;14(5):161-183.
30. Potier C, V L, F D-A, O C, B R. Supervised injection services: what has been demonstrated? A systematic literature review. *Drug Alcohol Depend.* 2014;145:48-68.
31. Kennedy MC, Hayashi K, Milloy M, Wood E, Kerr T. Supervised injection facility use and all-cause mortality among people who inject drugs in Vancouver, Canada: A cohort study. *PLoS Med.* 2019;16(11):e1002964.
32. Kerr T, Tyndall MW, Lai C, Montaner JSG, Wood E. Drug-related overdoses within a medically supervised safer injection facility. *International Journal of Drug Policy.* 2006;17(5):436-441.
33. Notta D, Black B, Chu T, Joe R, Lysyshyn M. Changing risk and presentation of overdose associated with consumption of street drugs at a supervised injection site in Vancouver, Canada. *Drug Alcohol Depend.* 2019;196:46-50.
34. Salmon AM, van Beek I, Amin J, Kaldor J, Maher L. The impact of a supervised injecting facility on ambulance call-outs in Sydney, Australia. *Addiction.* 2010;105(4):676-683.
35. Centers for Disease Control and Prevention. Injection Drug Use and HIV Risk. Last reviewed: February 6, 2020; https://www.cdc.gov/hiv/risk/idu.html. Accessed September 11, 2020.
36. Kerr T, Tyndall M, Li K, Montaner J, Wood E. Safer injection facility use and syringe sharing in injection drug users. *Lancet.* 2005;366(9482):316-318.
37. Milloy M-J, Wood E. [Commentary] Emerging Role of Supervised Injecting Facilities in Human Immunodeficiency Virus Prevention. *Addiction.* 2009;104(4):620-621.
38. Folch C, Lorente N, Majó X, et al. Drug consumption rooms in Catalonia: A comprehensive evaluation of social, health and harm reduction benefits. *The International journal of drug policy.* 2018;62:24-29.

39. Aspinall EJ, Nambiar D, Goldberg DJ, et al. Are needle and syringe programmes associated with a reduction in HIV transmission among people who inject drugs: a systematic review and meta-analysis. *International journal of epidemiology.* 2014;43(1):235-248.
40. Hagan H, Pouget ER, Des Jarlais DC. A systematic review and meta-analysis of interventions to prevent hepatitis C virus infection in people who inject drugs. *The Journal of infectious diseases.* 2011;204(1):74-83.
41. Turner KM, Hutchinson S, Vickerman P, et al. The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. *Addiction.* 2011;106(11):1978-1988.
42. Lloyd-Smith E, Wood E, Zhang R, Tyndall MW, Montaner JS, Kerr T. Risk factors for developing a cutaneous injection-related infection among injection drug users: a cohort study. *BMC public health.* 2008;8:405.
43. Scherbaum N, Specka M, Schifano F, Bombeck J, Marrziniak B. Longitudinal observation of a sample of German drug consumption facility clients. *Substance use & misuse.* 2010;45(1-2):176-189.
44. McNeil R, Dilley LB, Guirguis-Younger M, Hwang SW, Small W. 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. *Journal of the International AIDS Society.* 2014;17(1):18855.
45. Gaddis A, Kennedy MC, Nosova E, et al. Use of on-site detoxification services co-located with a supervised injection facility. *Journal of Substance Abuse Treatment.* 2017;82:1-6.
46. Wood E, Tyndall MW, Zhang R, et al. Attendance at Supervised Injecting Facilities and Use of Detoxification Services. *New England Journal of Medicine.* 2006;354(23):2512-2514.
47. Debeck K, Kerr T, Bird L. Injection drug use cessation and use of North Americas first medically supervised safer injecting facility. *Drug and Alcohol Dependence.* 2011;113(2-3):172-176.
48. Wood E, Tyndall MW, Zhang R, Montaner JSG, Kerr T. Rate of detoxification service use and its impact among a cohort of supervised injecting facility users. *Addiction.* 2007;102(6):916-919.
49. Kimber J, Mattick RP, Kaldor J, van Beek I, Gilmour S, Rance JA. Process and predictors of drug treatment referral and referral uptake at the Sydney Medically Supervised Injecting Centre. *Drug Alcohol Rev.* 2008;27(6):602-612.
50. Zurhold H, Degkwitz P, Haasen C, Uwe V. Drug consumption rooms in Hamburg, Germany: evaluation of the effects on harm reduction and the reduction of public nuisance. *Journal of drug issues.* 2003;33(3):663-688.
51. Toth EC, Tegner J, Lauridsen S, Kappel N. 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.* 2016;13(1):27.
52. Kerr T, Stoltz J-A, Tyndall M, et al. Impact of a medically supervised safer injection facility on community drug use patterns: a before and after study. *BMJ.* 2006;332:220-222.
53. Wood E KT, Small W, Li K, Marsh DC, Montaner JSG, et al. Changes in public order after the opening of a medically supervised safer injecting facility for illicit injection drug users. *Canadian Medical Association Journal.* 2004;171(7):731-734.
54. McKnight I, Maas B, Wood E, et al. Factors Associated with Public Injecting Among Users of Vancouver's Supervised Injection Facility. *The American Journal of Drug and Alcohol Abuse.* 2007;33(2):319-325.
55. Salmon AM, Thein HH, Kimber J, Kaldor JM, Maher L. Five years on: what are the community perceptions of drug-related public amenity following the establishment of the Sydney Medically Supervised Injecting Centre? *Int J Drug Policy.* 2007;18(1):46-53.

56. Kinnard EN, Howe CJ, Kerr T, Skjødt Hass V, Marshall BDL. Self-reported changes in drug use behaviors and syringe disposal methods following the opening of a supervised injecting facility in Copenhagen, Denmark. *Harm Reduction Journal.* 2014;11(1):29.
57. Freeman K JC, Weatherburn DJ, Rutter S, Spooner CJ, Donnelly N. The impact of the Sydney Medically Supervised Injecting Centre (MSIC) on crime. *Drug Alcohol Rev.* 2005;24(2):173-184.
58. Fitzgerald J BM, Snowball L. Trends in property and illicit drug crime around the Medically Supervised Injecting Centre in Kings Cross: An update. *Crime and Justice Statistics - Bureau Brief.* 2010(51).
59. Donnelly N, Mahoney Nichole. Trends in property and illicit drug crime around the Medically Supervised Injecting Centre in Kings Cross: 2012 update. *NSW Bureau of Crime Statistics and Research.* 2013.
60. Wood E TM, Lai C, Montaner JS, Kerr T. Impact of a medically supervised safer injecting facility on drug dealing and other drug-related crime. *Substance Abuse Treatment, Prevention, and Policy.* 2006;1(13).
61. Milloy M-J, Wood E, Tyndall M, Lai C, Montaner J, Kerr T. Recent incarceration and use of a supervised injection facility in Vancouver, Canada. *Addiction Research & Theory.* 2009;17(5):538-545.
62. Myer AJ, Belisle L. 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.* 2018;48(1):36-49.
63. Behrends CN, Paone D, Nolan ML, et al. Estimated impact of supervised injection facilities on overdose fatalities and healthcare costs in New York City. *J Subst Abuse Treat.* 2019;106:79-88.
64. Hood JE, Behrends CN, Irwin A, et al. The projected costs and benefits of a supervised injection facility in Seattle, WA, USA. *Int J Drug Policy.* 2019;67:9-18.
65. Irvine MA, Kuo M, Buxton JA, et al. Modelling the combined impact of interventions in averting deaths during a synthetic-opioid overdose epidemic. *Addiction.* 2019;114(9):1602-1613.
66. Irwin A, Jozaghi E, Bluthenthal RN, Kral AH. A Cost-Benefit Analysis of a Potential Supervised Injection Facility in San Francisco, California, USA. *Journal of Drug Issues.* 2017;47(2):164-184.
67. Irwin A, Jozaghi E, Weir BW, Allen ST, Lindsay A, Sherman SG. Mitigating the heroin crisis in Baltimore, MD, USA: a cost-benefit analysis of a hypothetical supervised injection facility. *Harm Reduct J.* 2017;14(1):29.
68. Jozaghi E. A cost-benefit/cost-effectiveness analysis of an unsanctioned supervised smoking facility in the Downtown Eastside of Vancouver, Canada. *Harm Reduct J.* 2014;11(1):30.
69. Jozaghi E, Vancouver Area Network of Drug U. Exploring the role of an unsanctioned, supervised peer driven injection facility in reducing HIV and hepatitis C infections in people that require assistance during injection. *Health & Justice.* 2015;3(1):16.
70. The Foundation for Aids Research. Opioid & Health Indicators Database. 2020; https://opioid.amfar.org/indicator/num_SSPs#. Accessed 9/1/2020.
71. Milloy MJ, Kerr T, Tyndall M, Montaner J, Wood E. Estimated drug overdose deaths averted by North America's first medically-supervised safer injection facility. *PLoS One.* 2008;3(10):e3351.
72. KPMG. Further evaluation of the Medically Supervised Injecting Centre during its extended Trial period (2007-2011). 2020.
73. Pollini RA, McCall L, Mehta SH, Vlahov D, Strathdee SA. Non-fatal overdose and subsequent drug treatment among injection drug users. *Drug Alcohol Depend.* 2006;83(2):104-110.
74. HCUP Nationwide Emergency Department Sample (NEDS). Agency for Healthcare Research and Quality; 2017. https://www.hcup-us.ahrq.gov/nedsoverview.jsp. Accessed 9/11/2020.

75. MSIC Evaluation Committee. Final report of the evaluation of the Sydney Medically Supervised Injecting Centre. 2020; https://www.drugsandalcohol.ie/5706/1/MSIC_final_evaluation_report.pdf.
76. Jozaghi E, Hodgkinson T, Andresen MA. Is there a role for potential supervised injection facilities in Victoria, British Columbia, Canada? *Urban Geography.* 2015;36(8):1241-1255.
77. U. S. Bureau of Labor Statistics. CPI for All Urban Consumers (CPI-U); Series Id: CUUR0000SA0. 2020; https://data.bls.gov/cgi-bin/surveymost. Accessed 9/11/2020.
78. Teshale EH, Asher A, Aslam MV, et al. Estimated cost of comprehensive syringe service program in the United States. *PLoS One.* 2019;14(4):e0216205.
79. Centers for Medicare & Medicaid Services. Ambulance Fee Schedule Public Use Files. 2020; https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AmbulanceFeeSchedule/afspuf.
80. Mallow PJ, Belk KW, Topmiller M, Strassels SA. Geographic variation in hospital costs, payments, and length of stay for opioid-related hospital visits in the USA. *J Pain Res.* 2018;11:3079-3088.
81. Wilson N KM, Seth P, Smith H IV, Davis NL. Drug and Opioid-Involved Overdose Deaths — United States, 2017–2018. *MMWR Morb Mortal Wkly Rep.* 2020;69:290-297.
82. Centers for Disease Control aP. Understanding the Epidemic. 2020; https://www.cdc.gov/drugoverdose/epidemic/index.html.
83. Control CfD. Opioid Data Analysis and Resources. 2020; https://www.cdc.gov/drugoverdose/data/analysis.html. Accessed September 10, 2020.
84. ASTHO. Preventing Opioid Misuse and Overdose in the States and Territories: ASTHO. Opioids. https://my.astho.org/opioids/home. Accessed September 15, 2020.
85. Office of the Surgeon General ASfHA. U.S. Surgeon General's Advisory on Naloxone and Opioid Overdose. 2018; https://www.hhs.gov/surgeongeneral/priorities/opioids-and-addiction/naloxoneadvisory/index.html.
86. Kim D IK, Khoshnood K. . Expanded access to naloxone: options for critical response to the epidemic of opioid overdose mortality. *Am J Public Health.* 2009;99(3):402-407.
87. Harm Reduction DPA. Harm Reduction. 2020; https://www.drugpolicy.org/issues/harm-reduction. Accessed September 15, 2020.
88. McGinty EE, Barry CL, Stone EM, et al. Public support for safe consumption sites and syringe services programs to combat the opioid epidemic. *Prev Med.* 2018;111:73-77.
89. Wheeler E JS, Gilbert MK, Davidson PJ. *Opioid Overdose Prevention Pograms Providing Naloxone to Laypersons - United States, 2014.* Centers for Disease Control and Prevention2015.
90. Coffin PO SS. Cost-effectiveness of distributing naloxone to heroin users for lay overdose reversal. *Ann Intern Med.* 2017;158(1):1-9.
91. Gupta R, Shah, ND., Ross, J. The Rising Price of Naloxone — Risks to Efforts to Stem Overdose Deaths. *N Engl J Med.* 2016;375:2213-2215.
92. Doleac JLaM, Anita, . The Moral Hazard of Lifesaving Innovations: Naloxone Access, Opioid Abuse, and Crime. *SSRN.* 2019.
93. McLean K. Needle exchange and the geography of survival in the South Bronx. *Int J Drug Policy.* 2012;23(4):295-302.
94. Fernández-Viña MH PN, Herpolsheimer A, Waimberg J, Burris S. . State Laws Governing Syringe Services Programs and Participant Syringe Possession, 2014-2019. *Public Health Reports.* 2020;135(1).
95. NASEN. SEP Locations. https://www.nasen.org/map/. Accessed September 15, 2020.

96. Karamouzian M, Dohoo C, Forsting S, McNeil R, Kerr T, Lysyshyn M. Evaluation of a fentanyl drug checking service for clients of a supervised injection facility, Vancouver, Canada. *Harm Reduct J.* 2018;15(1):46.
97. Bardwell G, Kerr T. Drug checking: a potential solution to the opioid overdose epidemic? *Subst Abuse Treat Prev Policy.* 2018;13(1):20.
98. Kennedy MC, Scheim A, Rachlis B, et al. Willingness to use drug checking within future supervised injection services among people who inject drugs in a mid-sized Canadian city. *Drug Alcohol Depend.* 2018;185:248-252.
99. Krieger MS, Yedinak JL, Buxton JA, et al. High willingness to use rapid fentanyl test strips among young adults who use drugs. *Harm Reduct J.* 2018;15(1):7.
100. Dolan JK, Craig Fry, David McDonald, John Fitzgerald, Franz Trautmann, Kate. Drug consumption facilities in Europe and the establishment of supervised injecting centres in Australia. *Drug and alcohol review.* 2000;19(3):337-346.
101. Hedrich D. *European report on drug consumption rooms.* The European Monitoring Centre for Drugs and Drug Addiction;2004.
102. Canada CHGo. Supervised consumption sites: Guidance for Application Form - Canada. 2020; https://www.canada.ca/en/health-canada/services/substance-use/supervised-consumption-sites/status-application.html. Accessed September 15, 2020.
103. Yang T, Beletsky, L. United States vs Safehouse: The implications of the Philadelphia supervised consumption facility ruling for law and social stigma. *Preventive Medicine.* 2020;135.
104. Gavin C. Despite legal issues, Somerville plans to open a safe consumption site for drug users in 2020. 2019. https://www.boston.com/news/local-news/2019/08/14/somerville-safe-consumption-site.
105. Thein H-HK, Jo & Maher, Lisa & MacDonald, Margaret & Kaldor, John. Public opinion towards Supervised Injecting Centres and the community impact of Sydney Medically Supervised Injecting Centre. *International Journal of Drug Policy.* 2005;16:275-280.
106. SAMHSA. Medication-Assisted Treatment (MAT). https://www.samhsa.gov/medication-assisted-treatment. Accessed September 15, 2020.
107. Vancouver Coastal Health. Insite - Supervised Consumption Site. http://www.vch.ca/locations-services/result?res_id=964. Accessed August 27, 2020.
108. Uniting MSIC. Uniting Medically Supervised Injecting Centre. https://www.uniting.org/community-impact/uniting-medically-supervised-injecting-centre--msic. Accessed September 10, 2020.
109. Uniting MSIC. History of the Uniting Medically Supervised Injecting Centre. https://www.uniting.org/community-impact/uniting-medically-supervised-injecting-centre--msic/history-of-uniting-msic. Accessed September 10, 2020.
110. Uniting MSIC. Get to Know Our Story. In:2018.
111. Foundation AaD. Medically supervised injecting centres save lives. 2020; https://adf.org.au/insights/medically-supervised-injecting-centres/. Accessed September 10, 2020.
112. MSIC U. Accessing the service. https://www.uniting.org/community-impact/uniting-medically-supervised-injecting-centre--msic/accessing-the-service. Accessed September 10, 2020.
113. Cook DJ, Mulrow CD, Haynes RB. Systematic reviews: synthesis of best evidence for clinical decisions. *Ann Intern Med.* 1997;126(5):376-380.
114. Higgins JPT GSe. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011].* The Cochrane Collaboration. Available from http://handbook.cochrane.org.; 2011.

115. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg.* 2010;8(5):336-341.
116. National Institutes of Health (U.S.). National Heart Lung and Blood Institute. Study Quality Assessment Tools. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools. Accessed July 8, 2020.
117. Ollendorf DA PS. An integrated evidence rating to frame comparative effectiveness assessments for decision makers. *Medical care.* 2010;48(6 suppl):s145-152.
118. Ollendorf DA PS. ICER Evidence Rating Matrix: A User's Guide. 2020.
119. Hagan H, McGough JP, Thiede H, Hopkins S, Duchin J, Alexander ER. Reduced injection frequency and increased entry and retention in drug treatment associated with needle-exchange participation in Seattle drug injectors. *J Subst Abuse Treat.* 2000;19(3):247-252.
120. Kerr T, Small W, Buchner C, et al. Syringe sharing and HIV incidence among injection drug users and increased access to sterile syringes. *Am J Public Health.* 2010;100(8):1449-1453.
121. Abuse NIoD. Overdose Death Rates. 2020; https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates. Accessed August 10, 2020.
122. Glei DA PS. Estimating the impact of drug use on US mortality, 1999-2016. *PLOS ONE.* 2020;15(1):e0226732.
123. Miller CL KT, Strathdee SA, Li K, Wood E. . Factors associated with premature mortality among young injection drug users in Vancouver. *Harm Reduct J.* 2007;4(1).
124. Kerr T, Small W, Moore D, Wood E. 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.* 2007;18(1):37-45.
125. Frank RG PH. Addressing the Fentanyl Threat to Public Health. *N Engl J Med.* 2017;376(7):605-607.
126. Kinshella MW, Gauthier, T. & Lysyshyn, M. Rigidity, dyskinesia and other atypical overdose presentations observed at a supervised injection site, Vancouver, Canada. *Harm Reduct J.* 2018;15(64).
127. Latimer J, Ling S, Flaherty I, Jauncey M, Salmon AM. Risk of fentanyl overdose among clients of the Sydney Medically Supervised Injecting Centre. *Int J Drug Policy.* 2016;37:111-114.
128. Roxburgh A, Darke S, Salmon AM, Dobbins T, Jauncey M. Frequency and severity of non-fatal opioid overdoses among clients attending the Sydney Medically Supervised Injecting Centre. *Drug and Alcohol Dependence.* 2017;176:126-132.
129. Hedrich D, Kerr, T. and Dubois-Arber, F. . Drug consumption facilities in Europe and beyond', in Rhodes, T. and Hedrich, D. (eds), Harm reduction: evidence, impacts and challenges. *EMCDDA Scientific Monograph Series No 10, Publications Office of the European Union, Luxembourg.* 2010:305-331.
130. EMCDDA. *Drug consumption rooms: An overview of provision and evidence.* June 07, 2018 2018.
131. Stoltz JA, Wood E, Small W, et al. Changes in injecting practices associated with the use of a medically supervised safer injection facility. *Journal of public health (Oxford, England).* 2007;29(1):35-39.
132. Wood E, Tyndall M, Stoltz J, et al. Factors Associated with Syringe Sharing Among Users of a Medically Supervised Safer Injecting Facility. *American Journal of Infectious Diseases.* 2005.
133. Bravo M, Royuela L, De la Fuente L, Brugal M, Barrio G, Domingo-Salvany A. Use of supervised injection facilities and injection risk behaviours among young drug injectors. *Addiction.* 2009;104(4):614-619.

134. Cross JE, Saunders CM, Bartelli D. The Effectiveness of Educational and Needle Exchange Programs: A Meta-analysis of HIV Prevention Strategies for Injecting Drug Users. *Quality and Quantity.* 1998;32(2):165-180.
135. Wood RA, Wood E, Lai C, Tyndall MW, Montaner JS, Kerr T. 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.* 2008;19(3):183-188.
136. Wood E, Tyndall MW, Stoltz J-A, et al. Safer injecting education for HIV prevention within a medically supervised safer injecting facility. *International Journal of Drug Policy.* 2005;16(4):281-284.
137. Fast D, Small W, Wood E, Kerr T. The perspectives of injection drug users regarding safer injecting education delivered through a supervised injecting facility. *Harm reduction journal.* 2008;5:32-32.
138. Krüsi A, Small W, Wood E, Kerr T. An integrated supervised injecting program within a care facility for HIV-positive individuals: a qualitative evaluation. *AIDS Care.* 2009;21(5):638-644.
139. Lloyd-Smith E, Wood E, Zhang R, et al. Determinants of hospitalization for a cutaneous injection-related infection among injection drug users: a cohort study. *BMC public health.* 2010;10:327.
140. Lloyd-Smith E, Tyndall M, Zhang R, et al. Determinants of Cutaneous Injection-Related Infections Among Injection Drug Users at an Emergency Department. *The open infectious diseases journal.* 2012;6.
141. Alysse G. Wurcel JEA, Kenneth K. H. Chui, Sally Skinner, Tamsin A. Knox, David R. Snydman, Thomas J. Stopka. Increasing Infectious Endocarditis Admissions Among Young People Who Inject Drugs. *Open Forum Infectious Diseases.* 2016;3(3).
142. van der Poel A, Barendregt C, van de Mheen D. Drug consumption rooms in rotterdam: an explorative description. *Eur Addict Res.* 2003;9(2):94-100.
143. Small W, Van Borek N, Fairbairn N, Wood E, Kerr T. Access to health and social services for IDU: the impact of a medically supervised injection facility. *Drug Alcohol Rev.* 2009;28(4):341-346.
144. Small W, Wood E, Lloyd-Smith E, Tyndall M, Kerr T. Accessing care for injection-related infections through a medically supervised injecting facility: a qualitative study. *Drug Alcohol Depend.* 2008;98(1-2):159-162.
145. MSIC Evaluation Committee. *Final report on the evaluation of the Sydney Medically Supervised Injection Centre.* Sydney2003.
146. NCHECR. *Sydney Medically Supervised Injecting Centre Interim Evaluation Report No. 4. Evaluation of service operation and overdose-related events.* Sydney, UNSW2007.
147. NCHECR. *Sydney Medically Supervised Injecting Centre Interim Evaluation Report No. 3. Evaluation of Client Referral and Health Issues.* Sydney, UNSW2007.
148. NCHECR. *Sydney Medically Supervised Injecting Centre Interim Evaluation Report No. 2. Evaluation of Community Attitudes towards the Sydney MSIC.* Sydney, UNSW2006.
149. NCHECR. *Sydney Medically Supervised Injecting Centre Interim Evaluation Report No. 1. Operation & Service Delivery.* Sydney, UNSW2005.
150. Medically Supervised Injecting Review Panel. *Review of the Medically Supervised Injecting Room.* State of Victoria2020.
151. Supervised Consumption Services Review Committee. *A socio-economic review of supervised consumption sites in Alberta.* Alberta Health, Government of Alberta2020.
152. Coalition. CDP. Call for Retraction of Alberta's Supervised Consumption Sites (SCS) Report. 2020; An Open Letter from Concerned Scientists and Scholars to Premier Jason Kenny of Alberta. Available at: https://www.drugpolicy.ca/wp-content/uploads/2020/03/Open-Letter-RE-SCS_Final.pdf, 2020.

153. KPMG. *Further evaluation of the medically supervised injecting centre during its extended trial period (2001-2011): final report.* KPMG Sydney2010.
154. Milloy MJ, Kerr T, Zhang R, Tyndall M, Montaner J, Wood E. Inability to access addiction treatment and risk of HIV infection among injection drug users recruited from a supervised injection facility. *Journal of public health (Oxford, England).* 2010;32(3):342-349.
155. Lloyd-Smith E WE, Zhang R, Tyndall MW, Montaner JS, Kerr T. Determinants of cutaneous injection-related infection care at a supervised injecting facility. *Ann Epidemiol.* 2009;19(6):404-409.
156. DeBeck K, Wood, E., Zhang, R. et al. Police and public health partnerships: Evidence from the evaluation of Vancouver's supervised injection facility. *Substance Abuse Treatment Prevention Policy.* 2008;3(11).
157. Collins AB, Jade Boyd, Samara Mayer, Al Fowler, Mary Clare Kennedy, Ricky N. Bluthenthal, Thomas Kerr, Ryan McNeil,. Policing space in the overdose crisis: A rapid ethnographic study of the impact of law enforcement practices on the effectiveness of overdose prevention sites. *International Journal of Drug Policy.* 2019;73:199-207.
158. Des Jarlais DC, Nugent A, Solberg A, Feelemyer J, Mermin J, Holtzman D. Syringe Service Programs for Persons Who Inject Drugs in Urban, Suburban, and Rural Areas - United States, 2013. *MMWR Morb Mortal Wkly Rep.* 2015;64(48):1337-1341.
159. Population Density for U.S. Cities Statistics. 2020; https://www.governing.com/gov-data/population-density-land-area-cities-map.html. Accessed 8/5/2020.
160. Canada S. Focus on Geography Series, 2011 Census: Census subdivision of Vancouver, CY - British Columbia. 2011; https://www12.statcan.gc.ca/census-recensement/2011/as-sa/fogs-spg/Facts-csd-eng.cfm?LANG=Eng&GK=CSD&GC=5915022. Accessed 8/5/2020.
161. Office prices per square foot in major U.S. cities 2017 | Statista. 2020; https://www.statista.com/statistics/789935/cost-of-office-space-in-selected-major-cities-usa/. Accessed 8/5/2020.
162. Top 100 Most Expensive U.S. Office Submarkets in 2019. 2020; https://www.commercialcafe.com/blog/top-100-expensive-office-submarkets-2019/. Accessed 8/5/2020.
163. Vancouver Commercial Real Estate Market 2019 | Marcus & Millichap. 2020; https://marcusmillichap.ca/newsroom/2019/04/vancouver-commercial-real-estate-market-2019/. Accessed 8/5/2020.
164. Average Commercial Real Estate Loan Rates for 2020. 2020; https://www.valuepenguin.com/average-commercial-real-estate-loan-rates. Accessed 8/5/2020.
165. British Columbia. 2016; https://www.lowestrates.ca/mortgage/british-columbia. Accessed 8/5/2020.
166. Cost of Living Comparisons, 2020 data. 2020; https://www.expatistan.com. Accessed 8/5/2020.
167. Safe Consumption Spaces: A Strategy for Baltimore. 2020; https://www.abell.org/publications/safe-consumption-spaces-strategy-baltimore. Accessed 8/5/2020.
168. King County Washington. HIV/AIDS Fact Sheet: People Who Inject Drugs (PWID). 2020; https://www.kingcounty.gov/depts/health/~/media/depts/health/overdose/documents/people-who-inject-drugs-facts.ashx. Accessed 8/5/2020.
169. Banta-Green C, Newman A, Kingston S. Washington State Syringe Exchange Health Survey: 2017 Results. 2020; https://adai.uw.edu/pubs/pdf/2017syringeexchangehealthsurvey.pdf.

170. The Centre for Global Public Health University of Manitoba. Estimation of Key Population Size of People who Use Injection Drugs (PWID), Men who Have Sex with Men (MSM) and Sex Workers (SW) who are At Risk of Acquiring HIV and Hepatitis C in the Five Health Regions of the Province of British Columbia. 2016; http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/STI/PSE%20Project%20Final%20Report.pdf.
171. Chen YH, McFarland W, Raymond HF. Estimated Number of People Who Inject Drugs in San Francisco, 2005, 2009, and 2012. *AIDS Behav.* 2016;20(12):2914-2921.
172. Jacka B, Larney S, Degenhardt L, et al. Prevalence of Injecting Drug Use and Coverage of Interventions to Prevent HIV and Hepatitis C Virus Infection Among People Who Inject Drugs in Canada. *Am J Public Health.* 2020;110(1):45-50.
173. Massachusetts Department of Public Health. Number of Opioid-Related Overdose Deaths, All Intents by City/Town 2015-2019. https://www.mass.gov/doc/opioid-related-overdose-deaths-by-citytown-june-2020/download. Accessed 9/1/2020.
174. DEA Seattle Field Division. Opioid Overdose Deaths Remain High in Seattle and King County. https://www.dea.gov/sites/default/files/2018-07/BUL-153-17%20Opiate%20Overdose%20Deaths%20Remain%20High%20%281%29.pdf. Accessed 9/1/2020.
175. Philadelphia Department of Public H. Opioid Overdoses. https://hip.phila.gov/EmergentHealthTopics/Opioids. Accessed 9/1/2020.
176. Sabatini J. Drug overdose deaths surpass 300 in San Francisco - The San Francisco Examiner. https://www.sfexaminer.com/news/in-san-francisco-drug-overdose-deaths-surpass-300/. Accessed 9/1/2020.
177. Fulton County GA. Interactive Charts of Opioid Overdose Deaths in Atlanta Metro Region (33N). 2020; https://gisdata.fultoncountyga.gov/datasets/af31fc5890124e6c84395eaf783b6bf6. Accessed 9/1/2020.
178. Baltimore City Health Department. Baltimore City's Response to the Opioid Epidemic. 2015; https://health.baltimorecity.gov/opioid-overdose/baltimore-city-overdose-prevention-and-response-information. Accessed 9/1/2020.
179. Jones CM, Logan, J., Gladden, M., Bohm, M. K. . Vital Signs: Demographic and Substance Use Trends Among Heroin Users — United States, 2002–2013. *Morbidity and Mortality Weekly Report (MMWR).* 2015;64(26):719-725.
180. McNeil R, Small W. 'Safer environment interventions': a qualitative synthesis of the experiences and perceptions of people who inject drugs. (1873-5347 (Electronic)).
181. Kennedy M, Kerr T. Overdose Prevention in the United States: A Call for Supervised Injection Sites. *American Journal of Public Health.* 2017;107(1):42-43.
182. Lange BCL, Bach-Mortensen AM. A systematic review of stakeholder perceptions of supervised injection facilities. *Drug and Alcohol Dependence.* 2019;197:299-314.
183. Pardo B, Caulkins JP, Kilmer B. Assessing The Evidence on Supversied Drug Consumption Sites. *RAND Corportation.* 2018.
184. Milloy M-JS KT, Mathias R, Zhang R, Montaner JS, Tyndall M, et al. Non-fatal overdose among a cohort of active injection drug users recruited from a supervised injection facility. *The American Journal of Drug and Alcohol Abuse.* 2008;34(4):499–509.

Appendix A. Search Strategic Results

Table A1. PRISMA 2009 Checklist

		Checklist Items
TITLE		
Title	1	Identify the report as a systematic review, meta-analysis, or both.
ABSTRACT		
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.
INTRODUCTION		
Rationale	3	Describe the rationale for the review in the context of what is already known.
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).
METHODS		
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.

		Checklist Items
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.
RESULTS		
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).
DISCUSSION		
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.
FUNDING		
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data), role of funders for the systematic review.

From: Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Table A2. Search Strategies for Supervised Injection Facilities: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other NonIndexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE and Versions(R) 1946 to Present + PsycInfo

#	Search Term
1	((Supervised or safe* or drug) adj2 (inject* or shooting or consumption or smok* or inhal*) adj3 (facilit* or room* or galler* or cent* or site* or service*)).ti,ab.
2	(overdose adj3 prevention adj3 (site* or service*)).ti,ab
3	1 or 2
4	(addresses OR autobiography OR bibliography OR biography OR clinical trial, phase I OR comment OR congresses OR consensus development conference OR dictionary OR directory OR duplicate publication OR editorial OR encyclopedia OR guideline OR interactive tutorial OR newspaper OR commentaries).pt
5	3 not 4
6	(animals not (humans and animals)).sh.
7	5 not 6
8	limit 7 to English language
9	remove duplicates from 8

Table A3. Search Strategies for Supervised Injection Facilities: EMBASE

#	Search Term
1	((supervised OR safe* OR drug) NEAR/3 (inject* OR shooting OR consumption OR smok* OR inhal*) NEAR/3 (facilit* OR room* OR galler* OR cent* OR site* OR service*)):ti,ab
2	(overdose NEAR/3 prevention NEAR/3 (site* OR service*)):ti,ab
3	#1 OR #2
4	#3 NOT (('animal'/exp OR 'nonhuman'/exp OR 'animal experiment'/exp) NOT 'human'/exp)
5	#4 NOT [medline]/lim
6	#5 AND [english]/lim

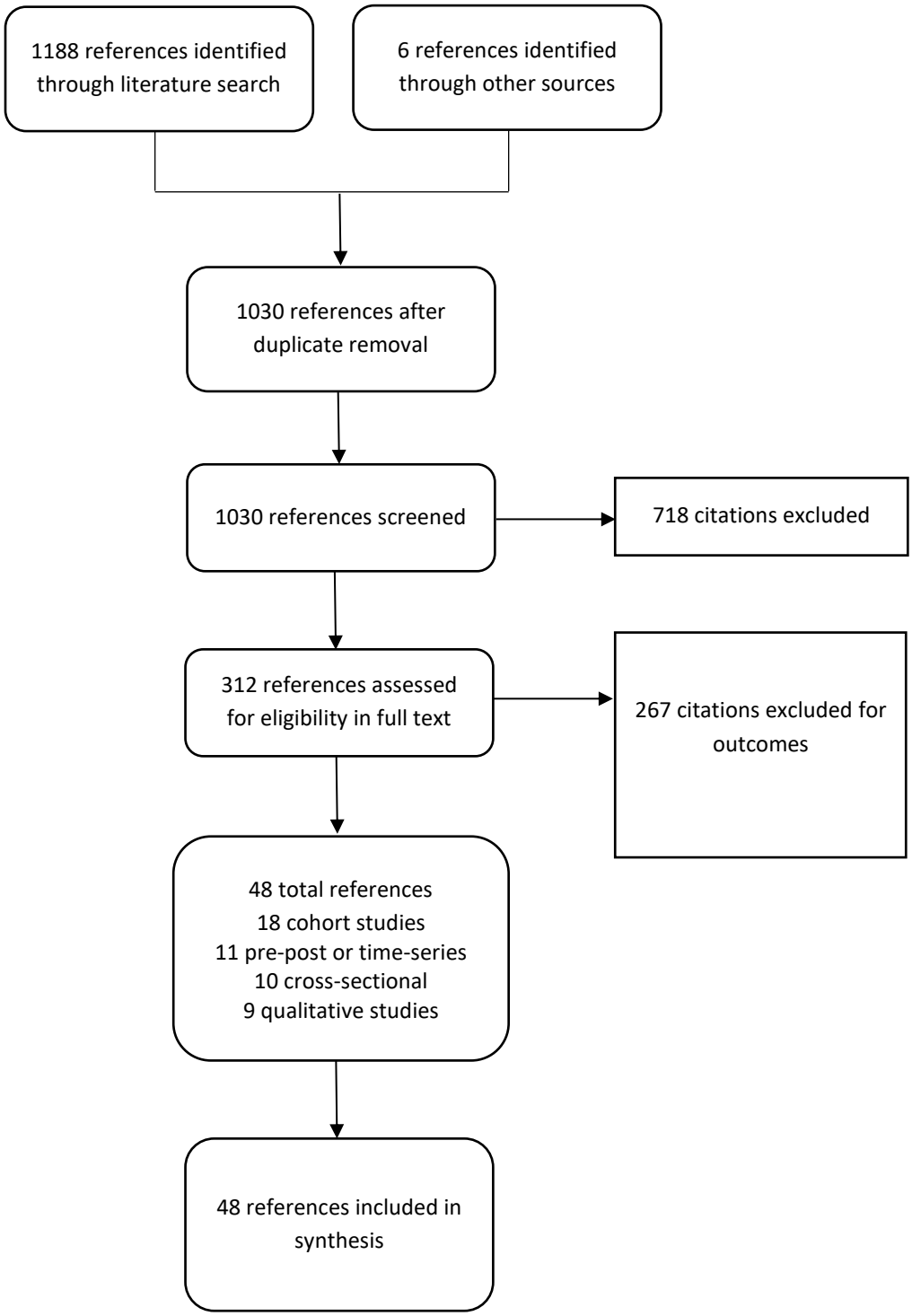
Table A4. Search Strategy for Supervised Injection Facilities: Web of Science (Limited to English language; Year: 1900-2020); Database: Excluding Medline and refined by WOS

#	Search Term
1	TS= ((“SUPERVISED” OR “SAFE*” OR “DRUG”) NEAR/2 (“SMOK*” OR “INHAL*” OR “INJECT*” OR “CONSUMPTION” OR “SHOOT*”) NEAR/2 (“FACILIT*” OR “SERVICE*” OR “ROOM*” OR “GALLER*” OR “CENT*” OR “SITE*”))
2	TS= “OVERDOSE PREVENTION SITES” OR TS=“OVERDOSE PREVENTION SERVICE*”
3	#1 OR #2
4	#3 Refined by: [excluding] Databases: (MEDLINE) AND Databases: (WOS)

Table A5. Search Strategy for Syringe Service Programs: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other NonIndexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE and Versions(R) 1946 to Present + PsycInfo

#	Search Term
1	Needle-Exchange Programs/
2	((needle* or syringe* or inject*) adj3 (program* or service* or exchange* or distribut* or dispens*)).ti,ab.
3	1 or 2
4	(systematic review or meta-analysis).pt.
5	((systematic* adj2 review*) or meta-analys* or ((evidence or quantitative) adj2 synthes*)).ti,ab.
6	4 or 5
7	3 and 6
8	(animals not (humans and animals)).sh.
9	7 not 8
10	limit 9 to english language
11	remove duplicates from 10

Figure A1. PRISMA flow Chart Showing Results of Literature Search for Supervised Injection Facilities



Appendix B. Previous Systematic Reviews and Technology Assessments

Potier, C., Laprévote, V. et al. (2014) "Supervised Injection Services: What Has Been Demonstrated? A Systematic Literature Review".[30]

A systematic review was identified on the data available on supervised injection services (SISs) to determine whether they have achieved their desired objectives. The review included 75 articles in the final analysis including descriptive, cross-sectional, and analytical assessments. Of these, 68% (n= 51) were related to a SIS in Vancouver, 17% (n= 13) from Sydney, and 3% (N=2) from Europe.

Fourteen studies described the characteristics of the most frequent SIS users. Most SIS users were described as male, aged 30-35 years, experiencing housing and employment insecurity and with a previous history of incarceration. The most frequently used drugs were heroin, cocaine, opiates, and amphetamines. Seven studies concluded that no death by overdose had been reported at a SIS; in Vancouver, the SIS led to a 35% decrease in fatal overdoses. In Vancouver and Sydney, regular SIS use was associated with reduced syringe sharing (aOR = 0.30, 95%CI = [0.11–0.82]), syringe reuse (aOR = 2.04, 95%CI = [1.38–3.01]), and public-space injection (aOR = 2.79, 95%CI = [1.93–3.87]); a meta-analysis determined that the SIS was associated with a 69% reduction in syringe sharing. According to six studies, SIS users received care for injection-related problems and five studies reported that SIS use resulted in an increase referral to addiction treatment (OR= 1.32, 95%CI = [1.11-1.58]: P=0.002). Seven surveys evaluated perceptions of local residents, police, and professionals. In Sydney, 70% of residents and 58% of business owners favored the SIS and saw a decrease in drug use and syringe waste. However, most business owners and residents still related SIS use to a negative image of the district and the "honey-pot" effect.

McNeil, R., Small, W. (2014) "Safer Environment Interventions: A Qualitative Synthesis of the Experiences and Perceptions of People Who inject Drugs".[180]

McNeil and Small conducted a systematic review to evaluate the influence of social, structural, and environmental factors on access and engagement with Safe Environment Interventions (SEIs) among people who inject drugs (PWID). The review included 29 references referring to 21 studies in the final evaluation. The included articles were published in Canada (n=16), the USA (n=6), Russia (n=4), and other settings (n=4). The four themes described in the analysis were- SEIs as a refuge, increased use of social services, SEIs impact on survival, and the social-structural impact on the SEIs.

Multiple studies emphasized on the importance of the SEIs as a refuge from violence on the streets. SEIs promoted safer injecting by redefining the social and environmental contexts of injection drug use. In addition to being a refuge from violence, SEIs also enabled safer drug use practices by

enabling harm reduction. The use of these facilities allowed clients to access safer injection equipment which in turn allowed them to practice safer habits and access to a safer space to contributing to reductions in risky injection behavior. Rushed injections and syringe sharing was reduced and enabled more autonomy for the clients. These facilities mediated access to social and healthcare services. Trust was identified as a critical component; trust between clients and staff was associated with increased acceptance of drug treatment referrals and other services.

Kennedy, M C., Karamouzian, M., Kerr, Thomas. (2017) "Public Health and Public Order Outcomes Associated with Supervised Drug Consumption Facilities: A Systematic Literature Review"[181]

Kennedy et al, conducted a systematic review to assess health and community outcomes related to use of supervised drug consumption facility (SCF) use. A total of 47 studies were included in the final analysis including cohort, pre-post, cross-sectional, or time-series analyses. 28 studies were conducted in Vancouver, Canada, 10 in Sydney and the remaining in Europe (n=9).

Overall, the review found that the use of SCFs was associated with a decrease in overdose deaths, an increase in PWID receiving addiction and medical treatment, and a decrease in substance use in public. Eight studies examined overdose-related outcomes, of which six studies found an association between the establishment of a SIF and reduction in overdose-related deaths. For example, the establishment of Insite, Vancouver was correlated with a 35% decline in overdose related deaths near the vicinity of the SIF, compared to a 9% decline outside of this vicinity. In Sydney, Australia opening of SIF was associated with a reduction in ambulance calls as well as opioid related poisoning presentations near the SIF. Four studies reported that frequent SIF use was associated with a decrease in injection risk behaviors including syringe sharing. A cross-sectional study based in Vancouver reported that SIF users are 70% less likely to borrow or lend a used syringe and two additional studies from Denmark and Vancouver found an association between SIF use and a reduction in other unsafe injection behaviors including injecting outdoors, rushed injections, and reusing syringes. SIF use was also reported to be positively associated with an increase in safer injection practices. Further, four studies reported that frequent SIF use was associated with an increased likelihood of entry into and uptake of addiction treatment. At Insite, Vancouver, use of detox services increased by more than 30% in the year after the SIF was opened, compared to the year before; rapid entry into detox services was also associated with contact with an addiction counselor at a SIF. Three other studies report similar data. Five studies reported that implementation a SIF in Vancouver and Sydney was associated with a reduction in the number of people injecting publicly, publicly discarded syringes, and injection-related litter. Besides, four studies conducted in Sydney found no changes in drug-related crime, and similar results were reported in two studies from Vancouver.

Lange, B. Bach-Mortensen, A M. (2019) "A Systematic Review of Stakeholder Perceptions of Supervised Injection Facilities".[182]

Stakeholder perceptions of supervised injection facilities (SIFs) were evaluated in this systematic review. Of the 47 included articles, the majority were conducted in Canada (n=26) and Australia (n= 8). The mean sample size of the included studies was 55.8 (SD: 64). Patients who use drugs (PWUD), including women, reported that the largest benefit to SIFs (sanctioned or unsanctioned) was their ability to provide a safe space from violence, theft, and police harassment. The increased safety of PWUD at a SIF was attributed to several factors such as education on drug use, a hygienic environment, availability of necessary supplies, and supervision especially in the case of an overdose. Business sector, community workers, and health professionals also reported a reduction in publicly discarded syringes. On the other hand, the most highlighted concerns with sanctioned SIFs were associated with current restrictions, age, and pregnancy. Across four studies, PWUD expressed concerns that SIFs did not allow assisted injections, whereas staff described disruptive client behavior and personnel safety as their main concern. For sanctioned SIFs, stakeholders suggested revising restrictions and regulations, to allow drug sharing and injecting drugs other than heroin. These stakeholders also suggested to increase the operating hours of a SIF.

Rand Report. (2018) "Assessing the Evidence on Supervised Drug Consumption Sites". [183]

Researchers conducted a systematic review to assess the existing evidence on supervised consumption sites (SCSs) using PubMed, Embase, Scopus, Web of Science, and WorldCat. Seventeen reviews were identified as quasi-experiments and simulation studies, while five systematic reviews were identified, and one piece of grey literature.

Overall, the authors concluded that the scientific evidence on the effectiveness of SCSs is limited. The authors note that not many scientific studies exist and of those that do, they were limited to only a few locations such as Vancouver and Sydney; in addition, there are no randomized controlled trials (RCTs) evaluating individual or population-level outcomes. According to the research evaluated, clients who attend an SCS and overdose in the presence of staff are much more likely to live thanks to the staff being equipped with naloxone. According to a study conducted in Vancouver, there is a significant reduction in fatal drug overdoses in the area surrounding the SCS compared to outside of the area, and studies conducted in Vancouver and Sydney identified a significant decrease in opioid-related emergency service calls. Several cross-sectional studies concluded that frequent SCS uses adopt better safer injection practices than those who use the SCS less frequently.

Appendix C. Ongoing Studies

Table C1. On-going Studies for Supervised Injection Facilities

Title/Trial Sponsor	Study Design	Comparators	Patient Population	Primary Outcomes	Estimated Completion Date
The Vancouver Injection Drug Users Study (VIDUS) **Canadian Institutes of Health Research (CIHR)**	Prospective cohort N= 2,700 PWID	n/a	People who inject drugs	Impact of prescription opioid misuse, risk behaviors for HIV, non-fatal and fatal overdose	Unclear
The AIDS Care Cohort to Evaluate Exposure to Survival Services (ACCESS) **National Institute on Drug Abuse (NIDA)**	Survey/ Questionnaire	n/a	Individuals living with HIV who use illicit drugs	Estimate the effects of social, policy, physical and economic aspects of the HIV risk environments on the individual and community	Unclear
At-Risk Youth Study (ARYS) **Canadian Institutes of Health Research (CIHR)** **National Institute on Drug Abuse (NIDA)** **SickKids Foundation**	Multi-year study, survey N= 900	n/a	Street-involved youth	Demographic data as well as information about drug use patterns, HIV and sexually transmitted infection (STI), risk behavior including sexual practices and risks related to drug use, access to health and social services, and engagement in the criminal justice system	Unclear
SuperMIX: The Melbourne Injecting Drug User Cohort Study **Burnet Institute**	Multi-year cohort study	n/a	People who inject drugs in Melbourne, Australia	Information on how injecting drug use evolves, focused on periods during which cohort members cease injecting drug use and if they subsequently relapse and the drivers of this cessation and relapse.	2021

Source: bccsu.ca, Burnet Institute

Appendix D. Comparative Clinical Effectiveness Supplemental Information

We performed screening at both the abstract and full-text level. Four investigators screened all abstracts identified through electronic searches according to the inclusion and exclusion criteria described earlier. We did not exclude any study at abstract-level screening due to insufficient information. For example, an abstract that did not report an outcome of interest would be accepted for further review in full text. We retrieved the citations that were accepted during abstract-level screening for full text appraisal. One investigator reviewed full papers and provided justification for exclusion of each excluded study.

Further, we will use 12-item National Heart Lung and Blood Institute (NHLBI) Quality Assessment Tool to assess the quality of the pre-post studies with no control group and 14- item NHBLI Quality Assessment Tool for observational cohort and cross-sectional studies, using the categories as "good," "fair," or "poor" quality. [116]

Good: *A study has the least risk of bias, and results are valid*.

Fair: *A study susceptible to some bias deemed not sufficient to invalidate its results. The fair-quality category is likely to be broad, so studies with this rating will vary in their strengths and weaknesses*.

Poor: *A study that has a significant risk of bias. Studies rated poor are excluded from the body of evidence.*

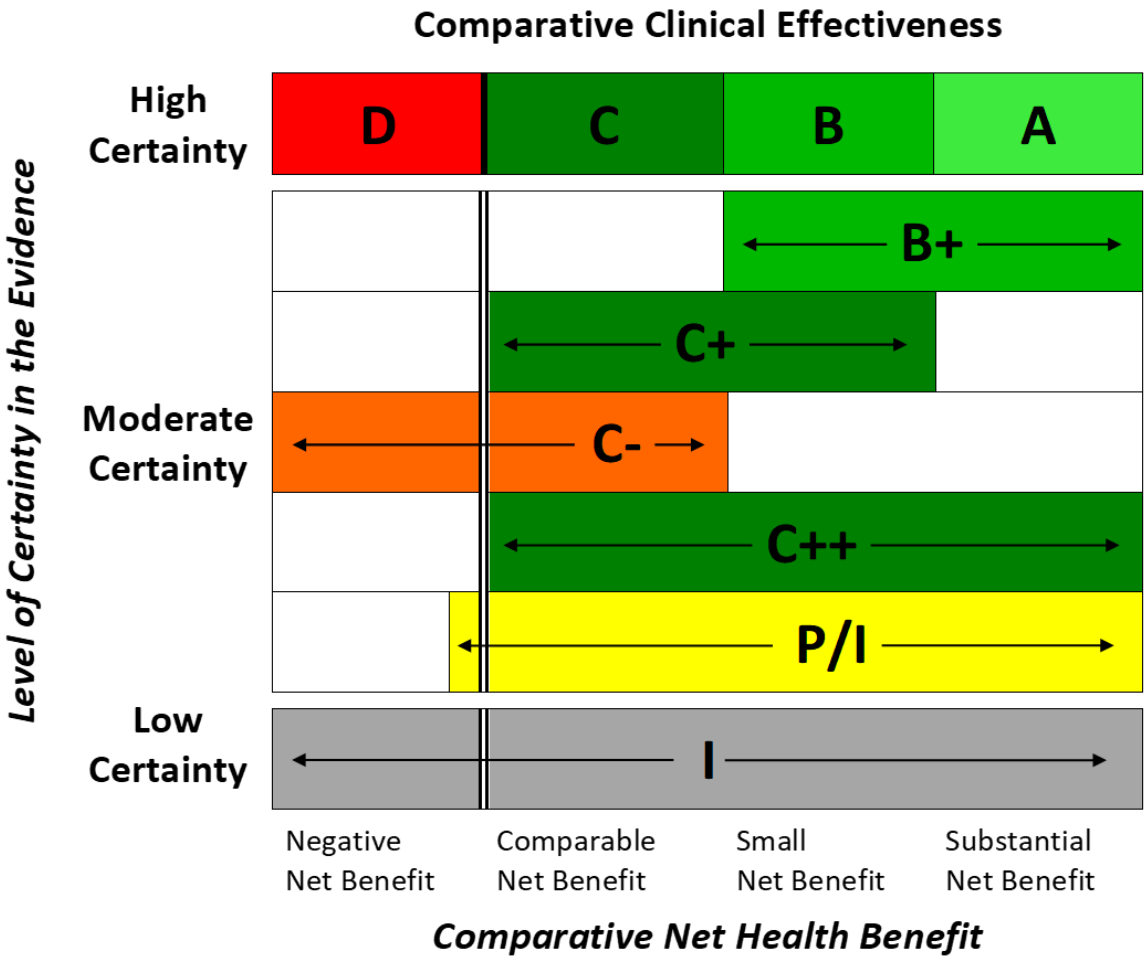
ICER Evidence Rating

We used the ICER Evidence Rating Matrix (see Figure D1) to evaluate the evidence for a variety of outcomes. The evidence rating reflects a joint judgment of two critical components:

1. The magnitude of the difference between a therapeutic agent and its comparator in "net health benefit" – the balance between clinical benefits and risks and/or adverse effects; and

2. The level of certainty in the best point estimate of net health benefit.[117,118]

Figure D1. ICER Evidence Rating Matrix



A = "Superior" *- High certainty of a substantial (moderate-large) net health benefit*
B = "Incremental" *- High certainty of a small net health benefit*
C = "Comparable"- *High certainty of a comparable net health benefit*
D= "Negative"- *High certainty of an inferior net health benefit*
B+= "Incremental or Better" – *Moderate certainty of a small or substantial net health benefit, with high certainty of at least a small net health benefit*
C+ = "Comparable or Incremental" - *Moderate certainty of a comparable or small net health benefit, with high certainty of at least a comparable net health benefit*
C- = "Comparable or Inferior" *– Moderate certainty that the net health benefit is either comparable or inferior with high certainty of at best a comparable net health benefit*
C++ = "Comparable or Better" - *Moderate certainty of a comparable, small, or substantial net health benefit, with high certainty of at least a comparable net health benefit*
P/I = "Promising but Inconclusive" *- Moderate certainty of a small or substantial net health benefit, small (but nonzero) likelihood of a negative net health benefit*
I = "Insufficient" – *Any situation in which the level of certainty in the evidence is low*

Table D2. Evidence Tables

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
Canada					
Wood et al 2004† [53] **Study quality: Good**	Pre-post study	6 weeks pre-SIF opening to 12 weeks post SIF opening (Sept 22, 2003)	Mean number of visits in first week of SIF opening= 184; after 2 months of SIF opening, visits= 504	Public Injecting, Publicly discarded syringes, Injection related litter	SIF opening was associated with reductions in number of people injecting in public (daily mean: 2.4, 95% CI: 1.9 – 3.0) after vs. 4.3, 95% CI: 3.5 – 5.4) before SIF opening, publicly discarded syringes (daily mean: 5.4, 95% CI: 4.7 – 6.3) after vs. (11.5, 95% CI: 10.0 – 13.2) before SIF opening, and injection-related litter (daily mean: 310, 95% CI: 305 – 317) after vs. (601, 95% CI: 590 – 613) before SIF opening.
Wood et al 2005_a† [132] **Study quality: Fair**	Cross-sectional	March 2004 to October 2004	582 PWID from the SEOSI cohort HIV-positive: 17.3%	Syringe sharing	Exclusive SIF use (i.e., use of SIF for 100% of injections) compared to some SIF use was associated with reductions in syringe sharing among HIV-negative individuals (OR: 0.14; 95% CI 0.00 to 0.78) but was not associated with reductions in syringe lending among HIV-positive individuals (OR: 0.94; 95% CI 0.00 to 7.90).
Wood et al 2005_b† [136] **Study quality: Fair**	Cross-sectional	May 2003 to October 2004	874 PWID from the SEOSI cohort; 293 (33.5%) received safer injecting education	Safer injecting education	Daily SIF use was marginally associated with reporting safer injecting education (p=0.085) in univariate analyses.
Kerr 2005† [36] **Study quality: Fair**	Cross-sectional	December 2003 to June 2004	431 active PWIDs from the VIDUS cohort SIF use (most, all, or some of the injections): 20.9% Syringe sharing: 11.4%	Syringe sharing	Use of SIF was associated with reduced syringe sharing (aOR: 0.30, 95% CI: 0.11-0.82, p=0.02). Between SIF users versus non-users, the rates of syringe sharing were similar prior to the SIF opening (X^2= 0.46, p = 0.50), suggesting that the observed reduction was not due to the SIF

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
					selecting PWIDs at inherently lower risk of syringe sharing.
Kerr and Stoltz 2006† [52] **Study quality: Good**	Pre-post study	March 2002 to March 2003	Pre-SIF IDUs: 674 Post-SIF IDUs: 700 Use injected drug pre-SIF: 17% Use injected drug post-SIF: 15%	Injection behaviors	No substantial differences in the relapse rate in the community (17% vs. 20%), stopping injections (17% vs. 15%), introduction and discontinuation of methadone (11% vs. 7% and 13 vs. 11%, respectively). The only difference that exceeded 5% cut-off was increase in number who started smoking crack cocaine (21% v 29%).
Kerr and Tyndall 2006 [32] **Study quality: Not assessed**	Descriptive study	March 2004 to August 2005	285 unique participants from the SEOSI cohort accounted for overdoses	Non-fatal overdose	There were 336 overdose events at the SIF corresponding to a rate of 1.33 (95% CI: 0.0-3.6) overdoses per 1000 injections. Of these events, 28% required transport to the hospital and 27% resulted in the administration of naloxone.
Wood et al 2006† [46] **Study quality: Good**	Prospective cohort	December 2003 to March 2005	1031 PWID who used the SIF Males: 71% Regular SIF use: 58%	Attendance at SIF, Use of services	At least weekly SIF use (aHR = 1.72; 95% CI: 1.25 – 2.38, p=0.001) and contact with a SIF addictions counsellor (aHR = 1.98; 95% CI: 1.26 – 3.10, p=0.003) were associated with more rapid time to entry into a detoxification program.
Wood et al 2006 [60] **Study quality: Good**	Time series	Oct 2003-Sept 2004 (pre-SIF) to Oct 2004-Sept 2005 (post-SIF)	NA- Crime Statistics	Drug trafficking, Assaults and Robbery, Vehicle theft	Post SIF opening, no significant increase was observed in drug trafficking: (124 vs 116, MD=7.9, p=0.803), assaults/robbery: (174 vs 180, MD=-6.2, p=0.565). Significant declines were observed in vehicle break-ins/theft: (302 vs 227, MD=75.7, p=0.001), post SIF opening.

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
Kerr and Small 2007† [124] **Study quality: Not assessed**	Qualitative	November 2005 – February 2006	50 PWID from the SEOSI cohort Age, Range: 25-60 years Males: 56%	Overdose mortality, SIF Use, Overdose requiring hospitalization	Ability to rapidly respond to an overdose and ability to provide naloxone, made the SIF stand out compared to other settings where it takes longer for people to respond or they receive no care at all. Reduced risk when injecting at INSITE versus alone or in an alley and an increased sense of security
Stoltz et al 2007† [131] **Study quality: Fair**	Cross-sectional	July 2004 to June 2005	760 PWID from the SEOSI cohort Age, median: 39.3 years Male: 70%	Consistent vs inconsistent SIF use stratified by characteristics + changes in injection practices associated w/ consistent SIF use	Consistent SIF use (≥25% of injections) was positively associated with decreased public injections (aOR = 2.70, 95%CI: 1.98-3.87, p<0.001); safer syringe or paraphernalia disposal (aOR = 2.13, 95%CI: 1.47-3.09, p<0.001); decreased reuse of syringes less often (aOR: 2.04, 95% CI: 1.38-3.01, p<0.001); less rushed injection (aOR: 2.79 95% CI: 2.03-3.85, p<0.001); using clean water for injecting (aOR = 2.99; 95% CI: 2.13 – 4.18, p<0.001); cooking or filtering drugs prior to injecting (aOR = 2.76; 95% CI: 1.84 – 4.15, p<0.001); tie off prior to injection (aOR = 2.63; 95% CI: 1.58 – 4.37, p<0.001) and it promoted injecting in a clean location (aOR = 2.85, 95%CI: 2.09-3.89, p<0.001).
Wood et al 2007†[48] **Study quality: Good**	Prospective cohort	December 2003- March 1, 2005 (pre-SIF and post-SIF)	1031 PWID from the SEOSI cohort Age, median (IQR): 39(33-46) years Male: 71%	Uptake of detoxification service Injection cessation	There was a significant increase in uptake of detoxification services post-SIF opening, compared to pre-SIF opening (aOR: 1.32, 95% CI: 1.11-1.57, p=0.002). Use of detoxification service was positively associated with a more rapid entry into the

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
			Regular SIF use (weekly): 58%		MMT (aHR: 3.73, 95% CI: 2.57-5.39). Of those enrolled in the detoxification program, a significant decline in monthly SIF use was observed after discharge from detoxification, compared to 1-month period before enrollment (19 vs 24 visits, p=0.002)
McKnight et al 2007†[54] **Study quality: Fair**	Retrospective cohort	June 6, 2004 – July 31, 2005	714 PWID from the SEOSI Age, median (range): 39 (33-45) years Male: 71% History of incarceration: 30% Unstable housing or homelessness: 7% HIV seropositive: 21% Public injection use: 30%	Community and environmental outcomes	Waiting time at SIF affected SIF use that was associated with increased likelihood of public injecting (aOR: 3.26, 95% CI: 2.11-5.6, p<0.001) Homelessness also increased the likelihood of injecting in public (ORa: 3.10, 95% CI: 1.46-6.58, p<0.001)
Petrar 2007†[13] **Study quality: Fair**	Cross-sectional	December 1, 2003, and September 30, 2005	1082 PWID from the SEOSI cohort Age, median (IQR): 38.4 (32.7–44.3) years Female: 28% HIV positive: 16.5% Daily heroin use: 50.5%	Injection behaviors	Of the 1,082 PWID who utilized Insite that were surveyed, 74.8% (n=809) reported changing their injection behaviors since using a SIF. Among these clients who changed their injection behaviors, 71% indicated that utilizing the SIF has led to less outdoor injections, and 56% reported less unsafe syringe disposal.
Milloy et al 2008† [184] **Study quality: Good**	Prospective cohort	December 1, 2003 to December 31, 2005	1090 PWIDs from SEOSI cohort Age, median (IQR): 38.42 (32.7-44.3) years Female: 29% History of non-fatal overdose: 58.53%	Non-fatal overdose	Frequent SIF use (≥75% of injections) was not associated with recent non-fatal overdose (aOR: 1.01, 95% CI: 0.77-1.32, p=0.96)

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
Fast et al 2008[137] **Study quality: not assessed**	Qualitative	November 2005 to February 2006	50 PWID from the SEOSI cohort Age, median (range): 38 (25-60) years Male: 56%	Community and environmental outcomes	Participants indicated that there have been substantial gaps in knowledge about safer injecting practices among local PWIDs. These gaps lead to unsafe injecting behaviors and negative health outcomes. Based on users' perspectives, the SCS was found to help clients identify and address these gaps in knowledge through a range of mechanisms that are unique to this facility (e.g., targeted educational messaging).
Small et al 2008† [144] **Study quality: Not assessed**	Qualitative	NR	50 PWID from the SEOSI cohort Age, range: 25-60 years Males: 56%	Barriers to care, Access to care Referrals	SIF facilitated access to on-site nursing attention and care for injection-related infection and facilitated uptake of health services. SIFs have potential to overcome many of the social and structural barriers to care.
Wood et al 2008† [135] **Study quality: Good**	Prospective cohort	March 2004 to March 2005	1,087 PWID from the SEOSI cohort Age, median (IQR): 38.5 (32.8-44.4) years Males: 71%	Patients receiving SIE (safe injection education) stratified by different characteristics	Frequent use of SIF (≥75% of injections) was associated with an increased likelihood of receiving safer injection education (aOR: 1.47, 95% CI: 1.22-1.77, p<0.001).
Lloyd-Smith et al 2008† [42] **Study quality: Good**	Prospective cohort	January 2004 to December 2005	1,065 PWID from the SEOSI cohort Age, median (IQR) of those with CIRI at BL: 36 (31-43) years; those without CIRI at BL: 39 (33-45) years	Cutaneous injection-related infections (CIRI)	SIF use was not significantly associated with development of a CIRI (aOR = 0.58; 95% CI: 0.29-1.19).
Lloyd-Smith 2009† [155] **Study quality: Good**	Prospective cohort	December 2003 to January 2008	1083 PWIDs from SEOSI cohort	Provision of care at the SIF (CIRI)	About 27% received care, 65% of whom attended the SIF for this purpose. Among SIF clients, factors associated with receiving care

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
					included, unstable housing (aHR = 1.39, 95%CI = 1.02–1.88), and daily heroin injection (aHR = 1.52, 95%CI = 1.13–2.4).
Milloy et al 2009† [61] **Study quality: Good**	Prospective cohort	July 2004 to November 2005	902 PWID from the SEOSI cohort Age, median (IQR): 40.9 (35.6-47.3) years Male: 72%	Incarceration/crime	Frequent SIF use (all/most injections vs few/some/none) was not associated with recent incarceration (aOR = 0.99; 95% CI: 0.79 – 1.23, p=0.92).
Small et al 2009† [143] **Study quality: Not assessed**	Qualitative	November 2005 – February 2006	50 PWID from SEOSI cohort Age, range: 25-60 years Males: 56%	Stigma, Integrated care, Access to social services	SIF provided assessment and care for injection-related infections, as well as enhanced access to off-site medical services. Presence of professional nursing staff aided clients to overcome certain social and structural barriers to care.
Krusi 2009†[138] **Study quality: not assessed**	Qualitative	May 2007 to June 2007	22 PWID attending a harm reduction room in Vancouver Age, mean (range): 43.8 (28-54) years Male: 68% HIV Seropositive: 100%	Use of treatment and recovery support services, Injection behaviors, Receipt of services, Skin and soft tissue infection, HIV, Hepatitis C	The Harm Reduction Room (HRR) influenced access to care by building trusting relationships and encouraging use of other services, such as SEI and care for infections. The most common reasons for using the HRR were hygiene, overdose risk, and physical safety especially among female participants. Participants and staff noted that reduction in infections could be due to SEI and having a safer place to inject.
Milloy et al 2010† [154] **Study quality: Good**	Prospective cohort	July 2004 to June 2006	889 PWID from the SEOSI cohort Age, median: 39 years Male: 70%	Access addiction treatment	20% of SIF users were unable to access any type of drug or alcohol treatment in the previous 6 months. Frequent use of SIF (≥75% of injections) was not associated with trying but being unable to access addiction treatment (aOR = 1.08; 95% CI: 0.84 – 1.40, p=0.54).

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
Lloyd-Smith et al 2010† [139] **Study quality: Good**	Prospective cohort	January 2004 to January 2008	1083 PWID from the SEOSI cohort Age, median (IQR): 38.4 (32.7-44.3) years Male: 71%;	Hospitalization for cutaneous injection-related infections (CIRI)	Referral to the hospital by a SIF nurse was associated with an increased likelihood of hospitalization for CIRI in multivariate analyses (aHR: 5.38; 95% CI: 3.39, 8.55). Referral by SIF nurse was associated with shorter hospital stays (4 days [IQR: 2-7] vs 12 days [IQR: 5-33], p=0.001 after adjustment
Marshall 2011 [12] **Study quality: Good**	Analytical Study (Pre-post ecological)	Pre-SIF (Jan 2001 to Sep 2003) Post-SIF (Sep 2003 to Dec 2005)	Pre-SIF (<500 m) = 56 Post SIF (<500 m) = 33 Pre-SIF (>500 m) =113 Post-SIF (>500 m) =88	Overdose mortality	In two years, post-SIF opening, fatal overdose decreased by 35% within 500m from SIF (253.8 to 165.1 deaths per 100,000 PYs, p=0.048), compared to two-years pre-SIF opening. During the same period, fatal overdose decreased by 9.3% in the rest of the city (7.6 to 6.9 deaths per 100,000 PYs, p=0.49). The rate difference between these two periods was significant (1·6–175·8 per 100 000 PYs, p=0·048).
DeBeck et al 2011†[47] **Study quality: Good**	Prospective cohort	December 2003 to June 2006	1090 PWID from SEOSI cohort Age, median (IQR): 39 (33-35) years Female: 29% Homelessness: 19% Regular SIF use (in past 6-months): 37% Current MMT: 23%	Drug use; Use of services	Regular use of SIF use at baseline (aHR = 1.33, 95% CI:1.04–1.72) and having contact with the addiction counselor in the SIF (aHR = 1.54, 95% CI: 1.13–2.08) were independently and positively associated with initiation of addiction treatment. Enrolment in MMT (aHR: 1.57, 95% CI: 1.02-2.40) and other addiction treatment program (aHR: 1.85, 95% CI: 1.06-3.24) were positively associated with injection drug use cessation.
Lloyd-Smith et al 2012† [140] **Study quality: Good**	Prospective cohort	January 2004 to January 2008	1,083 PWID from the SEOSI cohort Age, median (IQR): 39.7 (33.7-45.3) years	Infections	During the study period, 289 (27%) participants used the ED for a CIRI. Referral to hospital by SIF nurses was independently and positively

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
			Male: 70%		associated with ED use for CIRI among (aOR= 4.69, 95% CI: 2.76 – 7.97).
McNeil et al 2014 [44] **Study quality: Not assessed**	Qualitative	November 2010 to August 2011	13 Dr. Peter Center residents (DPC) Age, mean (range): 48 (36-62) years	Drug use healthcare interactions Healthcare access HRQoL	Participants highlighted that DPC aided in providing better access to healthcare services. It provided clients with a comfortable space to have discussions about their drug use and decreased stigmatization. Environmental support by facility decreased drug-related risks and improved health outcomes, including HAART adherence and survival.
Gaddis et al 2017† [45] **Study quality: Fair**	Prospective cohort	November 2010 to December 2012	1316 PWIDs from VIDUS & ACCESS cohort Age, median (IQR): 46.2 (40.2 - 52.1) years Males: 67% Unstable housing: 80% Frequent use of SIF: 60.8%	Factors associated with on-site detoxification services	11.2% of clients reported enrolling in detoxification services co-located with the SIF at least once during the study period. Frequent use of SIF was associated with enrollment into the detoxification program (aOR: 8.15, 95% CI: 5.38-12.34, p<0.001)
Myer and Belisle 2018† [62] **Study quality: Fair**	Time series	January 2002 to December 2004	N/A – Crime statistics	Community and environmental outcomes	Compared to the 89 weeks pre-Insite, Vancouver, the police district that contains Insite observed a significant (per-week) reduction with 6.0 less violent crimes, 34.5 fewer property crimes, and 42.3 less all crimes post-Insite opening; three other police districts observed no significant changes in crime post-Insite opening.
Kinshella et al 2018† [126]	Descriptive study	October 2016 to April 2017	1581 overdose events 497 atypical overdose presentations	Non-fatal overdoses (atypical presentations)	Of 1581 overdose events at Insite, Vancouver, 31.4% were atypical overdose presentations (dyskinesia, confusion, and muscle rigidity). Of 497 atypical overdose presentations, 84.5% were treated with oxygen, 69% with naloxone,

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
Study quality: Not assessed					and 15.1% were transferred to hospital by ambulance.
Notta et al 2019† [33] **Study quality: Good**	Time series	January 2010 to June 2017	N/R	Overdose	Overdose rate per 100 visits increased from 2010-2017 (1.5 vs 9.5, p<0.001) with an increase in overdose events requiring naloxone administration (48.4% to 57.1%, p<0.001). No overdose deaths reported within the facility. In the recent period clients were more likely to experience an overdose events as compared to baseline if they consumed cocaine (RR: 10.4, 95% CI: 6.7-16.1, p<0.001) or heroin (RR: 4.8, 95% CI: 4.3-5.3, p<0.001)
Kennedy et al 2019† [31] **Study quality: Good**	Retrospective cohort	December 2006 to June 2017	811 PWIDs Age, median (IQR): 39(33-46) years Males: 65.7% Unstable housing: 81.9% HIV seropositive: 30.3% Hep C: 85.3%	All-cause mortality	13.8% participants died during the study period with a CRM of 22.7 per 1000-PY (95% CI: 18.7-27.4). Frequent use of SIF was inversely associated with a risk of all-cause mortality (aHR: 0.46; 95% CI: 0.26-0.80, p=0.006).
Sydney, Australia					
Freeman et al 2005† [57] **Study quality: Good**	Time series	January 1999 to September 2002	N/A- Crime statistics	Police recorded incidents of robbery, Drug-related loitering or dealing	Theft, robbery, or drug-related loitering in front of SIF was not associated with the opening of SIF (p>0.05). Increase in drug-related loitering at the back of the SIF were reported post-SIF opening (p<0.05)
Salmon et al 2007† [55] **Study quality: Good**	Time series	2000, 2002 and 2005	Year 2000: Residents (n=515), Business owners (n=209)	Witness public injections, publicly discarded syringes,	From 2000 to 2005, a significant decline in witnessing public injecting drug use was reported by both, residents (33%, 28%, and 19%, p<0.001) and business owners (38%, 32%,

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
			Year 2002: Residents (n=540), Business owners (n=207) Year 2005: Residents (n=316), Business owners (n=210)	drugs offered for purchase in the last month	and 28%, p=0.03). Business owners located beyond 500m of SIF were less likely to see this change (p<0.001) Similarly, a significant decline in witnessing publicly discarded syringes was reported by both, residents (67%, 58%, and 40%, p<0.001) and business owners (72%, 64%, and 57%, p=0.01). Business owners located beyond 500m of SIF were less likely to see this change (p<0.001) Variable change was observed in drugs been offered for purchase was reported by both, residents (28%, 29%, and 26%, p=0.80) and business owners (33%, 34%, and 28%, p=0.26) over time.
Kimber, Mattick et al 2008† [49] **Study quality: Good**	Prospective cohort	May 2001 to Oct 2002	3715 PWIDs who used MSIC 1385 referrals to 577 clients Overall referral uptake: 35%	Number of referrals drug characteristics	16% SIF clients with drug treatment referrals had confirmed drug treatment uptake. Frequent SIF use was associated with receiving written referral to drug treatment (aHR: 1.6, 95% CI: 1.2-2.2, p<0.01)
Salmon et al 2010†[34] **Study quality: Good**	Ecological Pre-post	May 1998 to April 2006	N/A – Ambulance calls	Non-fatal overdose, Health system utilization	Significant decrease in average monthly ambulance attendances in MSIC vicinity, compared to rest of the city (61% vs 68%, p=0.002) Significant decline in average monthly ambulance attendances was observed during SIF operating hours, compared to rest of the city (80% vs 60%, p<0.001)

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
Fitzgerald et al 2010 [58] **Study quality: Good**	Time series	May 2001 to March 2010	N/A – Crime statistics	Police recorded incidents related to robbery, property, illicit drug offenses	Incidence of robbery and property related crimes declined in both the vicinity of SIF (MSIC) and the rest of Sydney between 1999 and 2010 Illicit drug related offense incidents declined vicinity of SIF (MSIC) between 1999 and 2003 and then remained stable until 2009 A similar trend was reported in the rest of Sydney. Illicit drug related arrests declined from 1999 to 2003, with a slightly upward trend from 2003 to 2010
Donnelly 2013† [59] **Study quality: Fair**	Pre-Post study	May 2001 through December 2012	N/A – Crime statistics	Community and environmental outcomes	In 2002, a significant decline in robbery rates was reported near Kings Cross (281 to 112 incidents). Between 2002-2012, a decline in robbery rates per 100,000-persons was reported (1,646 to 563). Significant reduction was reported in thefts in Kings Cross (36,174 to 16,724 incidents per 100,000-persons) and rest of NSW (6,399 vs 3,359 incidents per 100,000 persons). Total illicit drug offences increased in both the Kings Cross LAC and the rest of Sydney. ($p < 0.001$ for all comparisons)
Latimer 2016† [127] **Study quality: Fair**	Retrospective clinical audit	September 2016 to August 2015	189,203 injections undertaken by 4,177 unique individuals Current drug use: Heroin (25%), Other opioids (58%), Crystal meth (13%), Cocaine (4%)	Fentanyl overdose	Overdose events were highest among users of fentanyl (4.4%) with a significantly higher overdose risk (crude RR: 2.21, 95% CI: 1.8-2.6), $p<0.0001$), as compared to heroin users

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
Roxburgh et al 2017 [128] **Study quality: Good**	Prospective cohort	Jan 2007 to April 2014	909 PWIDs who used the SIF experiencing 2860 overdose Heroin overdose: 62% Oxycodone: 30% Fentanyl: 0.73%	Heroin and oxycodone overdose	During the period 2007–2014, there were 12.7 heroin overdoses per 1000 injections compared to 4.1 oxycodone overdoses per 1000 injections. Heroin overdoses appeared to be more severe than oxycodone overdoses and risk of experiencing overdose with heroin was significantly higher than with oxycodone (OR: 3.1, 95% CI: 3.0-3.2).
Denmark					
Van der Poel et al 2003# [142] **Study quality: Not assessed**	Exploratory	2000	67 PWUD	Use of services	Average SIF visits for four facilities (prior to the interview) was six days (median: 7 days) and two-times (median: 2.5) in last 24hrs. DCR use led to 30% reporting more attention to hygiene, while 59% reported seeing no effect of visiting a DCR on their drug use.
Kinnard 2014# [56] **Study quality: Poor**	Cross-sectional	February 2013 to August 2013	41 PWIDs who use the DCR Age, median (IQR): 37 (30-43) years Males: 90.2% Unstable housing: 26.8% Daily DCR use: 29.3%	Disposal of syringes Behavior change Injection frequency	After SIF opening, 59% reported safer disposal of syringes; 76% reduction in injection risk behaviors [including decline in rushed injection (63%), public injecting (56%) and ceasing syringe sharing (54%)]; p<0.001).
Toth et al 2016# [51] **Study quality: Poor**	Cross-sectional	January 2015 to February 2015	154 PWID who use at least one of 5 SCFs	Injection behaviors, Use of treatment and recovery support services	SIF users receiving SEI were more likely to have access to sterile equipment (68.8% vs 25.9%, p=0.02). SIF users who were advised to seek medical help were more likely to receive treatment for disease, compared to those who

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
					were not advised to seek medical help (51.3% vs 25.7%, p<0.05).
Spain					
Bravo 2009[# 133] **Study quality: Fair**	Cross-sectional	2002 to 2005	249 PWID Age ≤25 years: 37.3% Males: 44.3% SIF users: 39% Unstable housing: 48.5% NEP use: 96%	Injection practices	Among 249 PWID in two cities with SIFs, clients had significantly higher likelihood of not borrowing used syringes (aOR: 3.30, 95% CI: 1.4-7.7), compared to non-SIF clients. Obtaining sterile syringes for free at the NEP was associated with not borrowing (aOR: 2.6, 95% CI: 1.0-6.8) and not sharing injection equipment (aOR: 3.2, 95% CI: 1.4-7.3), compared to not accessing NEP.
Folch 2018[#38] **Study quality: Fair**	Cross-sectional	2014 to 2015	520 PWID who used a DCR Age, mean (SD): 37(8.1) years Male: 81.8% Homelessness: 26.9% Regular SIF use (frequent): 21.2% In prison (ever): 73.1%	Injection behaviors, Use of treatment support services	SIF use in Catalonia, Spain was associated with significantly lower odds of public injection (aOR: 0.27, 95% CI: 0.12-0.62), and sharing syringes (aOR: 0.39, 95% CI: 0.20-0.78) and significantly higher odds of safe disposal of syringes (aOR: 5.77, 95% CI: 3.41-9.77) and accessing drug dependence services (aOR: 2.12, 95% CI: 1.18-3.81).
Germany					

Study / First Author and Year	Study design	Study period (month and year)	Population characteristics	Outcomes reported	Findings
Zurhold et al 2003[#50] Germany **Study quality: Poor**	Cross-sectional	2000	616 PWID using consumption rooms in Germany Age, mean: 32.6 years Male: 80% Years of drug use, mean: 11 Regular SIF use: 33% Heroin use at baseline: 84%	Use of treatment and recovery support services, Receipt of services	Frequent use of SCS was significantly associated with use of syringe exchange services (59% vs 54% and 44%, p<0.05); counselling services (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), compared to occasional or rare visitors
Scherbaum 2010[43] **Study quality: Good**	Prospective cohort	November 2002 to December 2003	129 PWID using DCFs in Germany Age, mean: 31 years Male: 75% History of incarceration: 37% Length of attendance (median): 5 weeks Years of drug use, mean (SD): 11 (6) years	Injection behaviors, Use of treatment support services	Regular and consistent DCF attendance [n (%)]: 9 (7%) of clients. SIF attendance for >3 months: 29 (22%); Left DCR by week 4: 26 (20%); attended the facility for less than a week: 29 (22%). 3months prior to DCF: 83% of clients were in contact at least once with low-threshold ancillary services (e.g., emergency shelter, canteen/cafeteria facility located within the DCF building, and mobile medical unit. After attending DCF: 46% Clients reported regular use of available services and facilities (46%); did not use any service (40%). Reasons for stopping DCF use included transfer to health insurance treatment system facilities (37%), enrollment in methadone maintenance, and imprisonment (17%). Clients stopped attending without providing a reason (21%) and two clients died (one from suicide, one from unknown reasons).

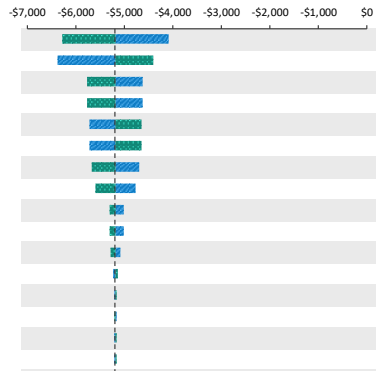
Insite, Vancouver and MSIC, Australia - fixed stand-alone or specialized model (†)
Dr. Peter Centre, Vancouver – Integrated model (‡)

Paris, East Side Frankfurt, and Luxembourg – Embedded model (§)
Some centers in Spain, Germany, and Denmark - Mobile model (#)

Appendix E. Comparative Value Supplemental Information

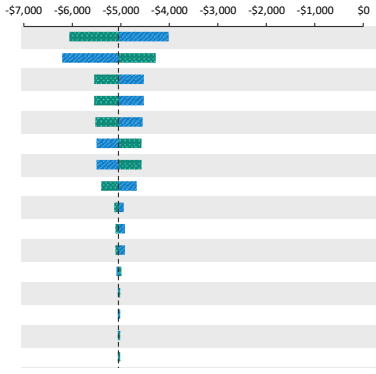
Figure E1a-f. Tornado Diagrams: Cost per Ambulance Ride Avoided, SIF+SSP vs. SSP-Only

a. Boston



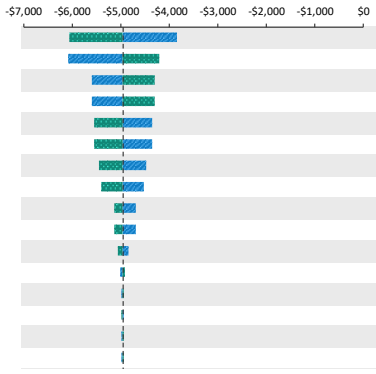
Parameter	Low Value	High Value	Low Result	High Result	Spread
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$4,095	-$6,277	$2,182
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$6,377	-$4,397	$1,980
Hospitalization Cost: Boston	$6,704	$10,055	-$4,613	-$5,759	$1,146
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$4,613	-$5,759	$1,146
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$5,727	-$4,645	$1,083
Cost of Living Ratio vs. Vancouver: Boston	0.99	1.49	-$5,727	-$4,645	$1,083
Cost of ED VIsit: Boston	$2,761	$4,141	-$4,694	-$5,678	$983
First Year SSP Cost	$1,226,623	$1,839,934	-$4,761	-$5,610	$849
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$5,021	-$5,296	$276
Total annual injections in the SIF	144,000	216,000	-$5,021	-$5,296	$276
Cost of Ambulance Ride: Boston	$418	$628	-$5,081	-$5,290	$209
Number of Unique SIF Clients/Month	1,680	2,520	-$5,236	-$5,136	$99
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$5,212	-$5,160	$52
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$5,170	-$5,202	$33
Cost/sqft Commercial Property: Boston	$440	$660	-$5,201	-$5,170	$31
Commercial Mortgage Loan Interest: Boston	5%	9%	-$5,195	-$5,176	$20

b. Philadelphia



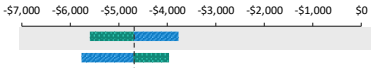
Parameter	Low Value	High Value	Low Result	High Result	Spread
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$4,015	-$6,073	$2,059
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$6,208	-$4,274	$1,935
Hospitalization Cost: Philadelphia	$6,001	$9,002	-$4,531	-$5,557	$1,026
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$4,531	-$5,557	$1,026
Cost of ED VIsit: Philadelphia	$2,761	$4,141	-$4,552	-$5,536	$983
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$5,502	-$4,586	$917
Cost of Living Ratio vs. Vancouver: Philadelphia	0.84	1.26	-$5,502	-$4,586	$917
First Year SSP Cost	$1,226,623	$1,839,934	-$4,673	-$5,415	$741
Cost of Ambulance Ride: Philadelphia	$390	$585	-$4,947	-$5,141	$195
Total annual injections in the SIF	144,000	216,000	-$4,927	-$5,122	$195
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$4,927	-$5,122	$195
Number of Unique SIF Clients/Month	1,680	2,520	-$5,087	-$5,001	$87
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$5,069	-$5,019	$49
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$5,028	-$5,060	$32
Cost/sqft Commercial Property: Philadelphia	$166	$248	-$5,050	-$5,038	$12
Commercial Mortgage Loan Interest: Philadelphia	5%	9%	-$5,048	-$5,040	$7

c. San Francisco



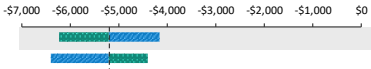
Parameter	Low Value	High Value	Low Result	High Result	Spread
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$3,846	-$6,071	$2,224
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$6,080	-$4,216	$1,865
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$5,600	-$4,317	$1,283
Cost of Living Ratio vs. Vancouver: San Francisco	1.18	1.76	-$5,600	-$4,317	$1,283
Hospitalization Cost: San Francisco	$6,946	$10,419	-$4,365	-$5,552	$1,188
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$4,365	-$5,552	$1,188
Cost of ED VIsit: San Francisco	$2,761	$4,141	-$4,467	-$5,450	$983
First Year SSP Cost	$1,226,623	$1,839,934	-$4,515	-$5,401	$886
Total annual injections in the SIF	144,000	216,000	-$4,699	-$5,131	$432
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$4,699	-$5,131	$432
Cost of Ambulance Ride: San Francisco	$453	$680	-$4,845	-$5,072	$227
Number of Unique SIF Clients/Month	1,680	2,520	-$5,010	-$4,907	$104
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$4,985	-$4,932	$53
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$4,943	-$4,974	$31
Cost/sqft Commercial Property: San Francisco	$240	$360	-$4,967	-$4,950	$17
Commercial Mortgage Loan Interest: San Francisco	5%	9%	-$4,964	-$4,953	$11

d. Atlanta



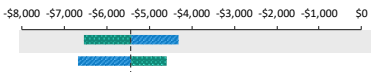
Parameter	Low Value	High Value	Low Result	High Result	Spread
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$3,770	-$5,603	$1,833
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$5,766	-$3,972	$1,794
Cost of ED VIsit: Atlanta	$2,761	$4,141	-$4,195	-$5,179	$983
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$5,093	-$4,281	$812
Cost of Living Ratio vs. Vancouver: Atlanta	0.74	1.12	-$5,093	-$4,281	$812
Hospitalization Cost: Atlanta	$4,712	$7,068	-$4,284	-$5,090	$806
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$4,284	-$5,090	$806
First Year SSP Cost	$1,226,623	$1,839,934	-$4,324	-$5,050	$727
Cost of Ambulance Ride: Atlanta	$369	$554	-$4,595	-$4,779	$185
Total annual injections in the SIF	144,000	216,000	-$4,625	-$4,728	$103
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$4,625	-$4,728	$103
Number of Unique SIF Clients/Month	1,680	2,520	-$4,729	-$4,644	$85
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$4,709	-$4,665	$44
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$4,672	-$4,702	$30
Cost/sqft Commercial Property: Atlanta	$195	$293	-$4,694	-$4,680	$14
Commercial Mortgage Loan Interest: Atlanta	5%	9%	-$4,691	-$4,682	$9

e. Baltimore



Parameter	Low Value	High Value	Low Result	High Result	Spread
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$4,174	-$6,233	$2,059
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$6,407	-$4,407	$2,000
Hospitalization Cost: Baltimore	$6,001	$9,002	-$4,691	-$5,717	$1,026
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$4,691	-$5,717	$1,026
Cost of ED VIsit: Baltimore	$2,761	$4,141	-$4,712	-$5,695	$983
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$5,618	-$4,789	$829
Cost of Living Ratio vs. Vancouver: Baltimore	0.76	1.14	-$5,618	-$4,789	$829
First Year SSP Cost	$1,226,623	$1,839,934	-$4,846	-$5,562	$716
Cost of Ambulance Ride: Baltimore	$394	$591	-$5,105	-$5,302	$197
Total annual injections in the SIF	144,000	216,000	-$5,125	-$5,256	$130
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$5,125	-$5,256	$130
Number of Unique SIF Clients/Month	1,680	2,520	-$5,246	-$5,162	$84
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$5,228	-$5,179	$49
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$5,187	-$5,220	$33
Cost/sqft Commercial Property: Baltimore	$162	$242	-$5,209	-$5,198	$11
Commercial Mortgage Loan Interest: Baltimore	5%	9%	-$5,207	-$5,200	$7

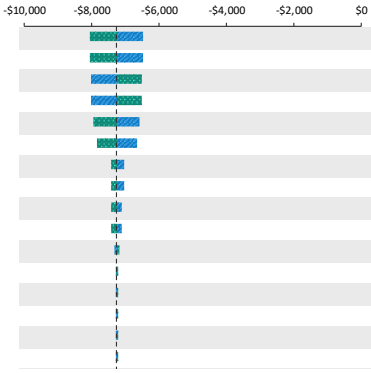
f. Seattle



Parameter	Low Value	High Value	Low Result	High Result	Spread
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$4,320	-$6,544	$2,224
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$6,688	-$4,601	$2,087
Hospitalization Cost: Seattle	$6,946	$10,419	-$4,838	-$6,026	$1,188
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$4,838	-$6,026	$1,188
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$5,947	-$4,917	$1,030
Cost of Living Ratio vs. Vancouver: Seattle	0.94	1.42	-$5,947	-$4,917	$1,030
Cost of ED VIsit: Seattle	$2,761	$4,141	-$4,940	-$5,924	$983
First Year SSP Cost	$1,226,623	$1,839,934	-$5,008	-$5,856	$849
Total annual injections in the SIF	144,000	216,000	-$5,304	-$5,517	$213
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$5,304	-$5,517	$213
Cost of Ambulance Ride: Seattle	$413	$620	-$5,329	-$5,535	$207
Number of Unique SIF Clients/Month	1,680	2,520	-$5,482	-$5,382	$99
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$5,459	-$5,405	$53
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$5,415	-$5,449	$34
Cost/sqft Commercial Property: Seattle	$331	$497	-$5,444	-$5,420	$24
Commercial Mortgage Loan Interest: Seattle	5%	9%	-$5,439	-$5,424	$15

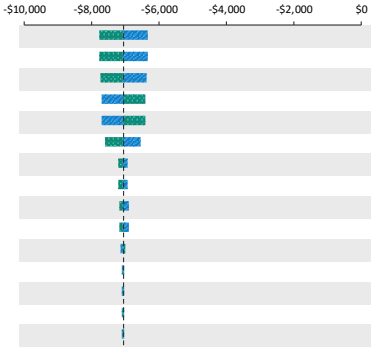
Figure E2a-f. Tornado Diagrams: Cost per Emergency Department Visit Avoided, SIF+SSP vs. SSP-Only

a. Boston



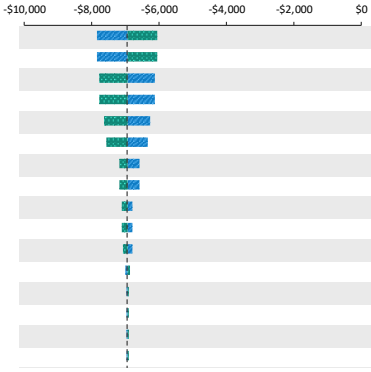
Parameter	Low Value	High Value	Low Result	High Result	Spread
Hospitalization Cost: Boston	$6,704	$10,055	-$6,474	-$8,083	$1,609
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$6,474	-$8,083	$1,609
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$8,039	-$6,519	$1,519
Cost of Living Ratio vs. Vancouver: Boston	0.99	1.49	-$8,039	-$6,519	$1,519
Cost of ED VIsit: Boston	$2,761	$4,141	-$6,589	-$7,969	$1,380
First Year SSP Cost	$1,226,623	$1,839,934	-$6,683	-$7,875	$1,192
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$7,047	-$7,434	$387
Total annual injections in the SIF	144,000	216,000	-$7,047	-$7,434	$387
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$7,129	-$7,428	$299
Cost of Ambulance Ride: Boston	$418	$628	-$7,132	-$7,426	$294
Number of Unique SIF Clients/Month	1,680	2,520	-$7,349	-$7,209	$139
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$7,229	-$7,312	$83
Cost/sqft Commercial Property: Boston	$440	$660	-$7,301	-$7,257	$44
Commercial Mortgage Loan Interest: Boston	5%	9%	-$7,292	-$7,265	$28
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$7,281	-$7,276	$5
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$7,280	-$7,278	$2

b. Philadelphia



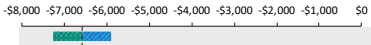
Parameter	Low Value	High Value	Low Result	High Result	Spread
Hospitalization Cost: Philadelphia	$6,001	$9,002	-$6,360	-$7,800	$1,440
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$6,360	-$7,800	$1,440
Cost of ED VIsit: Philadelphia	$2,761	$4,141	-$6,390	-$7,770	$1,380
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$7,723	-$6,436	$1,287
Cost of Living Ratio vs. Vancouver: Philadelphia	0.84	1.26	-$7,723	-$6,436	$1,287
First Year SSP Cost	$1,226,623	$1,839,934	-$6,559	-$7,600	$1,041
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$6,941	-$7,219	$278
Cost of Ambulance Ride: Philadelphia	$390	$585	-$6,943	-$7,217	$274
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$6,916	-$7,189	$273
Total annual injections in the SIF	144,000	216,000	-$6,916	-$7,189	$273
Number of Unique SIF Clients/Month	1,680	2,520	-$7,141	-$7,019	$122
Cost/sqft Commercial Property: Philadelphia	$166	$248	-$7,088	-$7,072	$17
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$7,087	-$7,075	$12
Commercial Mortgage Loan Interest: Philadelphia	5%	9%	-$7,085	-$7,074	$10
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$7,082	-$7,077	$5

c. San Francisco



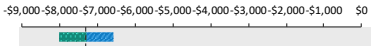
Parameter	Low Value	High Value	Low Result	High Result	Spread
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$7,860	-$6,059	$1,801
Cost of Living Ratio vs. Vancouver: San Francisco	1.18	1.76	-$7,860	-$6,059	$1,801
Hospitalization Cost: San Francisco	$6,946	$10,419	-$6,126	-$7,793	$1,667
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$6,126	-$7,793	$1,667
Cost of ED VIsit: San Francisco	$2,761	$4,141	-$6,269	-$7,650	$1,380
First Year SSP Cost	$1,226,623	$1,839,934	-$6,338	-$7,581	$1,244
Total annual injections in the SIF	144,000	216,000	-$6,596	-$7,202	$606
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$6,596	-$7,202	$606
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$6,798	-$7,121	$324
Cost of Ambulance Ride: San Francisco	$453	$680	-$6,801	-$7,119	$318
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$6,790	-$7,072	$282
Number of Unique SIF Clients/Month	1,680	2,520	-$7,032	-$6,887	$145
Cost/sqft Commercial Property: San Francisco	$240	$360	-$6,972	-$6,948	$24
Commercial Mortgage Loan Interest: San Francisco	5%	9%	-$6,967	-$6,952	$15
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$6,963	-$6,956	$6
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$6,962	-$6,957	$6

d. Atlanta



Parameter	Low Value	High Value	Low Result	High Result	Spread
Cost of ED VIsit: Atlanta	$2,761	$4,141	-$5,888	-$7,269	$1,380
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$7,148	-$6,009	$1,140
Cost of Living Ratio vs. Vancouver: Atlanta	0.74	1.12	-$7,148	-$6,009	$1,140
Hospitalization Cost: Atlanta	$4,712	$7,068	-$6,013	-$7,144	$1,131
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$6,013	-$7,144	$1,131
First Year SSP Cost	$1,226,623	$1,839,934	-$6,068	-$7,088	$1,020
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$6,447	-$6,710	$264
Cost of Ambulance Ride: Atlanta	$369	$554	-$6,449	-$6,708	$259
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$6,492	-$6,636	$145
Total annual injections in the SIF	144,000	216,000	-$6,492	-$6,636	$145
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$6,656	-$6,527	$128
Number of Unique SIF Clients/Month	1,680	2,520	-$6,638	-$6,519	$119
Cost/sqft Commercial Property: Atlanta	$195	$293	-$6,588	-$6,569	$19
Commercial Mortgage Loan Interest: Atlanta	5%	9%	-$6,584	-$6,572	$12
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$6,581	-$6,576	$5
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$6,577	-$6,580	$3

e. Baltimore



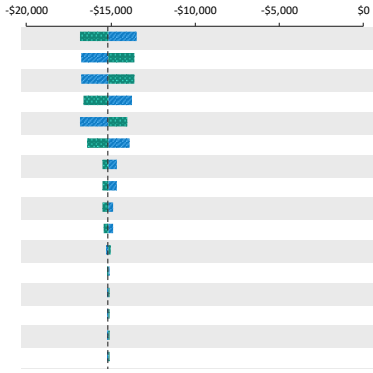
Parameter	Low Value	High Value	Low Result	High Result	Spread
Hospitalization Cost: Baltimore	$6,001	$9,002	-$6,584	-$8,024	$1,440
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$6,584	-$8,024	$1,440
Cost of ED VIsit: Baltimore	$2,761	$4,141	-$6,614	-$7,994	$1,380
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$7,886	-$6,722	$1,164
Cost of Living Ratio vs. Vancouver: Baltimore	0.76	1.14	-$7,886	-$6,722	$1,164
First Year SSP Cost	$1,226,623	$1,839,934	-$6,802	-$7,806	$1,004
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$7,163	-$7,445	$281
Cost of Ambulance Ride: Baltimore	$394	$591	-$7,166	-$7,442	$277
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$7,194	-$7,377	$183
Total annual injections in the SIF	144,000	216,000	-$7,194	-$7,377	$183
Number of Unique SIF Clients/Month	1,680	2,520	-$7,363	-$7,245	$118
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$7,369	-$7,261	$108
Cost/sqft Commercial Property: Baltimore	$162	$242	-$7,312	-$7,296	$16
Commercial Mortgage Loan Interest: Baltimore	5%	9%	-$7,309	-$7,299	$10
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$7,306	-$7,301	$5
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$7,303	-$7,305	$2

f. Seattle

Parameter	Low Value	High Value	Low Result	High Result	Spread
Hospitalization Cost: Seattle	$6,946	$10,419	-$6,791	-$8,458	$1,667
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$6,791	-$8,458	$1,667
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$8,347	-$6,901	$1,446
Cost of Living Ratio vs. Vancouver: Seattle	0.94	1.42	-$8,347	-$6,901	$1,446
Cost of ED VIsit: Seattle	$2,761	$4,141	-$6,934	-$8,315	$1,380
First Year SSP Cost	$1,226,623	$1,839,934	-$7,029	-$8,220	$1,191
Total annual injections in the SIF	144,000	216,000	-$7,445	-$7,744	$300
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$7,445	-$7,744	$300
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$7,477	-$7,772	$295
Cost of Ambulance Ride: Seattle	$413	$620	-$7,479	-$7,769	$290
Number of Unique SIF Clients/Month	1,680	2,520	-$7,694	-$7,555	$139
Cost/sqft Commercial Property: Seattle	$331	$497	-$7,641	-$7,608	$33
Commercial Mortgage Loan Interest: Seattle	5%	9%	-$7,634	-$7,614	$21
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$7,627	-$7,622	$5
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$7,626	-$7,623	$2

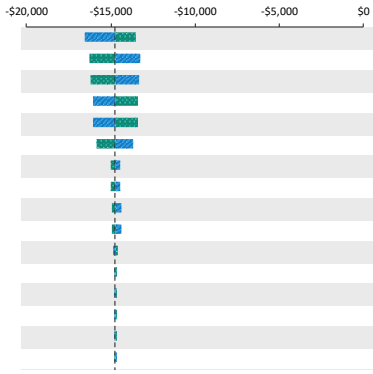
Figure E3a-f. Tornado Diagrams: Cost per Hospitalization Avoided, SIF+SSP vs. SSP-Only

a. Boston



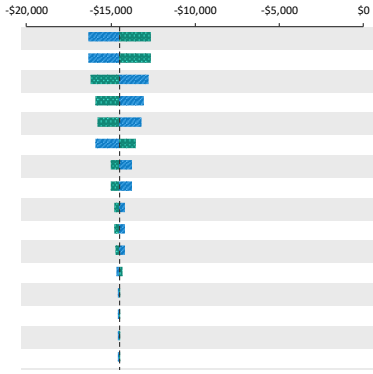
Parameter	Low Value	High Value	Low Result	High Result	Spread
Hospitalization Cost: Boston	$6,704	$10,055	-$13,488	-$16,840	$3,352
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$16,747	-$13,582	$3,165
Cost of Living Ratio vs. Vancouver: Boston	0.99	1.49	-$16,747	-$13,582	$3,165
Cost of ED VIsit: Boston	$2,761	$4,141	-$13,726	-$16,602	$2,876
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$16,861	-$14,034	$2,827
First Year SSP Cost	$1,226,623	$1,839,934	-$13,923	-$16,406	$2,483
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$14,681	-$15,487	$806
Total annual injections in the SIF	144,000	216,000	-$14,681	-$15,487	$806
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$14,853	-$15,476	$622
Cost of Ambulance Ride: Boston	$418	$628	-$14,858	-$15,470	$612
Number of Unique SIF Clients/Month	1,680	2,520	-$15,310	-$15,019	$290
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$15,060	-$15,233	$173
Cost/sqft Commercial Property: Boston	$440	$660	-$15,210	-$15,119	$91
Commercial Mortgage Loan Interest: Boston	5%	9%	-$15,192	-$15,135	$58
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$15,170	-$15,159	$11
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$15,166	-$15,162	$4

b. Philadelphia



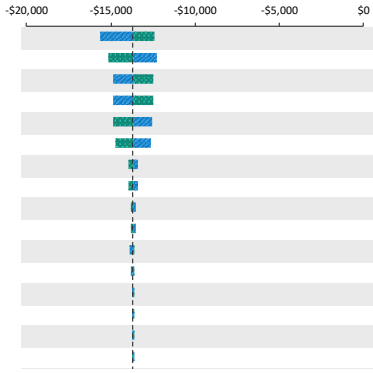
Parameter	Low Value	High Value	Low Result	High Result	Spread
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$16,561	-$13,542	$3,020
Hospitalization Cost: Philadelphia	$6,001	$9,002	-$13,249	-$16,250	$3,001
Cost of ED VIsit: Philadelphia	$2,761	$4,141	-$13,312	-$16,187	$2,876
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$16,090	-$13,409	$2,680
Cost of Living Ratio vs. Vancouver: Philadelphia	0.84	1.26	-$16,090	-$13,409	$2,680
First Year SSP Cost	$1,226,623	$1,839,934	-$13,666	-$15,833	$2,168
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$14,459	-$15,040	$580
Cost of Ambulance Ride: Philadelphia	$390	$585	-$14,464	-$15,035	$570
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$14,408	-$14,977	$570
Total annual injections in the SIF	144,000	216,000	-$14,408	-$14,977	$570
Number of Unique SIF Clients/Month	1,680	2,520	-$14,876	-$14,623	$254
Cost/sqft Commercial Property: Philadelphia	$166	$248	-$14,767	-$14,732	$34
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$14,764	-$14,740	$25
Commercial Mortgage Loan Interest: Philadelphia	5%	9%	-$14,760	-$14,738	$22
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$14,754	-$14,745	$10
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$14,749	-$14,750	$1

c. San Francisco



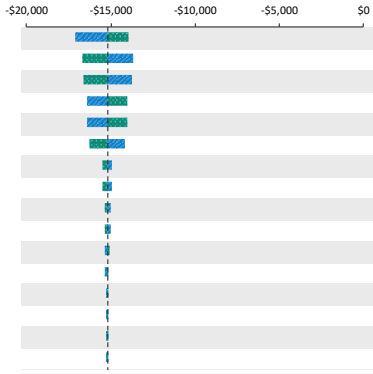
Parameter	Low Value	High Value	Low Result	High Result	Spread
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$16,375	-$12,623	$3,753
Cost of Living Ratio vs. Vancouver: San Francisco	1.18	1.76	-$16,375	-$12,623	$3,753
Hospitalization Cost: San Francisco	$6,946	$10,419	-$12,763	-$16,236	$3,473
Cost of ED VIsit: San Francisco	$2,761	$4,141	-$13,061	-$15,937	$2,876
First Year SSP Cost	$1,226,623	$1,839,934	-$13,204	-$15,795	$2,591
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$15,953	-$13,530	$2,423
Total annual injections in the SIF	144,000	216,000	-$13,742	-$15,004	$1,262
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$13,742	-$15,004	$1,262
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$14,162	-$14,836	$674
Cost of Ambulance Ride: San Francisco	$453	$680	-$14,168	-$14,830	$662
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$14,145	-$14,733	$587
Number of Unique SIF Clients/Month	1,680	2,520	-$14,651	-$14,348	$303
Cost/sqft Commercial Property: San Francisco	$240	$360	-$14,524	-$14,474	$50
Commercial Mortgage Loan Interest: San Francisco	5%	9%	-$14,514	-$14,483	$31
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$14,506	-$14,492	$13
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$14,505	-$14,493	$12

d. Atlanta



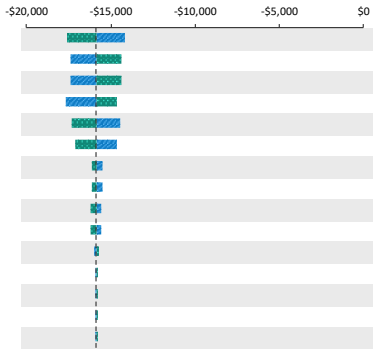
Parameter	Low Value	High Value	Low Result	High Result	Spread
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$15,659	-$12,403	$3,256
Cost of ED VIsit: Atlanta	$2,761	$4,141	-$12,267	-$15,143	$2,876
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$14,892	-$12,518	$2,374
Cost of Living Ratio vs. Vancouver: Atlanta	0.74	1.12	-$14,892	-$12,518	$2,374
Hospitalization Cost: Atlanta	$4,712	$7,068	-$12,527	-$14,883	$2,356
First Year SSP Cost	$1,226,623	$1,839,934	-$12,643	-$14,768	$2,125
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$13,430	-$13,980	$549
Cost of Ambulance Ride: Atlanta	$369	$554	-$13,435	-$13,975	$540
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$13,524	-$13,826	$302
Total annual injections in the SIF	144,000	216,000	-$13,524	-$13,826	$302
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$13,866	-$13,599	$268
Number of Unique SIF Clients/Month	1,680	2,520	-$13,829	-$13,581	$249
Cost/sqft Commercial Property: Atlanta	$195	$293	-$13,725	-$13,685	$41
Commercial Mortgage Loan Interest: Atlanta	5%	9%	-$13,718	-$13,692	$26
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$13,710	-$13,700	$9
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$13,702	-$13,708	$6

e. Baltimore



Parameter	Low Value	High Value	Low Result	High Result	Spread
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$17,145	-$13,931	$3,214
Hospitalization Cost: Baltimore	$6,001	$9,002	-$13,716	-$16,717	$3,001
Cost of ED VIsit: Baltimore	$2,761	$4,141	-$13,779	-$16,654	$2,876
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$16,429	-$14,004	$2,425
Cost of Living Ratio vs. Vancouver: Baltimore	0.76	1.14	-$16,429	-$14,004	$2,425
First Year SSP Cost	$1,226,623	$1,839,934	-$14,170	-$16,263	$2,093
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$14,923	-$15,510	$586
Cost of Ambulance Ride: Baltimore	$394	$591	-$14,928	-$15,505	$576
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$14,988	-$15,369	$381
Total annual injections in the SIF	144,000	216,000	-$14,988	-$15,369	$381
Number of Unique SIF Clients/Month	1,680	2,520	-$15,339	-$15,094	$245
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$15,352	-$15,127	$225
Cost/sqft Commercial Property: Baltimore	$162	$242	-$15,233	-$15,200	$34
Commercial Mortgage Loan Interest: Baltimore	5%	9%	-$15,227	-$15,206	$21
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$15,222	-$15,211	$10
Ppn. of SIF ODs resulting in ED visit	0.0063	0.0095	-$15,214	-$15,219	$5

f. Seattle



Parameter	Low Value	High Value	Low Result	High Result	Spread
Hospitalization Cost: Seattle	$6,946	$10,419	-$14,148	-$17,621	$3,473
Insite Annual Operating Cost	$1,349,829	$2,024,743	-$17,390	-$14,378	$3,012
Cost of Living Ratio vs. Vancouver: Seattle	0.94	1.42	-$17,390	-$14,378	$3,012
Ppn. of ED visits resulting in hospitalization	38.4%	57.6%	-$17,684	-$14,684	$3,001
Cost of ED VIsit: Seattle	$2,761	$4,141	-$14,446	-$17,322	$2,876
First Year SSP Cost	$1,226,623	$1,839,934	-$14,643	-$17,125	$2,482
Total annual injections in the SIF	144,000	216,000	-$15,510	-$16,134	$624
Percent of injections at SIF resulting in OD	0.760%	1.140%	-$15,510	-$16,134	$624
Ppn. of No SIF ODs resulting in ambulance	0.368	0.552	-$15,577	-$16,191	$615
Cost of Ambulance Ride: Seattle	$413	$620	-$15,582	-$16,186	$604
Number of Unique SIF Clients/Month	1,680	2,520	-$16,029	-$15,739	$290
Cost/sqft Commercial Property: Seattle	$331	$497	-$15,919	-$15,850	$69
Commercial Mortgage Loan Interest: Seattle	5%	9%	-$15,905	-$15,862	$43
Ppn. of SIF ODs resulting in ambulance	0.0063	0.0095	-$15,889	-$15,879	$11
Ppn. of No SIF ODs resulting in ED visit	0.264	0.396	-$15,887	-$15,882	$5

Table E1. Scenario Analysis of SIF-Associated Reduction in HIV and HCV Infections

	Boston			Philadelphia			San Francisco		
	SIF+SSP	SSP Only	Difference	SIF+SSP	SSP Only	Difference	SIF+SSP	SSP Only	Difference
HIV Cases	47	49	-2	113	115	-2	56	60	-4
HCV Cases	278	293	-15	668	683	-15	334	357	-23
	Atlanta			Baltimore			Seattle		
	SIF+SSP	SSP Only	Difference	SIF+SSP	SSP Only	Difference	SIF+SSP	SSP Only	Difference
HIV Cases	36	39	-2	27	28	-1	41	43	-2
HCV Cases	215	229	-15	161	167	-6	243	258	-15

Table E2. Two-Way Scenario Analysis of Differential MAT Retention at SIF+SSP vs. SSP-only

Incremental MAT Retention Among SIF+SSP Clients		**Relative Difference in SSP-Only Clients who Access MAT Compared to SIF+SSP**										
		0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%*
MAT Retention for SSP-Only Clients Compared to SIF+SSP	0%	61	61	61	61	61	61	61	61	61	61	61
	10%	61	60	59	59	58	58	57	56	56	55	55
	20%	61	59	58	57	56	55	53	52	51	50	49
	30%	61	59	57	55	53	52	50	48	46	44	42
	40%	61	58	56	53	51	49	46	44	41	39	36
	50%	61	58	55	52	49	46	42	39	36	33	30
	60%	61	57	53	50	46	42	39	35	32	28	24
	70%	61	56	52	48	44	39	35	31	27	22	18
	80%	61	56	51	46	41	36	32	27	22	17	12
	90%	61	55	50	44	39	33	28	22	17	12	6
	100%*	61	55	49	42	36	30	24	18	12	6	0*

*Base case