Effectiveness of Syringe Services Programs

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to conduct timely, rigorous, and independent systematic reviews to support VA clinicians, program leadership, and policymakers improve the health of Veterans. ESP reviews have been used to develop evidence-informed clinical policies, practice guidelines, and performance measures; to guide implementation of programs and services that improve Veterans' health and wellbeing; and to set the direction of research to close important evidence gaps. Four ESP Centers are located across the US. Centers are led by recognized experts in evidence synthesis, often with roles as practicing VA clinicians. The Coordinating Center, located in Portland, Oregon, manages program operations, ensures methodological consistency and quality of products, engages with stakeholders, and addresses urgent evidence synthesis needs.

Nominations of review topics are solicited several times each year and submitted via the ESP website. Topics are selected based on the availability of relevant evidence and the likelihood that a review on the topic would be feasible and have broad utility across the VA system. If selected, topics are refined with input from Operational Partners (below), ESP staff, and additional subject matter experts. Draft ESP reviews undergo external peer review to ensure they are methodologically sound, unbiased, and include all important evidence on the topic. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. In seeking broad expertise and perspectives during review development, conflicting viewpoints are common and often result in productive scientific discourse that improves the relevance and rigor of the review. The ESP works to balance divergent views and to manage or mitigate potential conflicts of interest.

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Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

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Disclosures

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The findings and conclusions in this document are those of the author(s) who are responsible for its contents and do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. The final research questions, methodology, and/or conclusions may not necessarily represent the views of contributing operational and content experts. No investigators have affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

Main Report

Evidence Synthesis Program

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ABBREVIATIONS TABLE

AHRQ	Agency for Healthcare Research and Quality
AIDS	Acquired immunodeficiency syndrome
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
IDU	Injection drug use
IRB	Injection risk behavior
KQ	Key question
OAT	Opioid agonist therapy
OR	Odds ratio
OUD	Opioid use disorder
PWID	People who inject drugs
RCT	Randomized controlled trial
RoR	Review of reviews
RR	Risk ratio
SSP	Syringe services program
SR	Systematic review
SUD	Substance use disorder
US	United States
VA	Department of Veterans Affairs
VHA	Veterans Health Administration
WHO	World Health Organization

BACKGROUND

The US Centers for Disease Control and Prevention (CDC) predicts that the total number of drug overdose deaths in the 12-month period that ended in February 2023 will be nearly 110,000.[50,51] While the increase in drug-related overdose deaths in the early 2000s was first attributed to prescription opioids and later to heroin use, the current trend of drug-related deaths is attributed to use of illicit synthetic opioids (*eg*, fentanyl and fentanyl analogs) as well as stimulants (*eg*, methamphetamine and cocaine) and exposure to these drugs in combination.[52] From 2013 to 2019, the synthetic opioid-involved death rate increased by 1,040% and the stimulant-involved death rate increased by 317%.[53]

The extent to which US Veterans use substances with high risk of overdose has not been well studied,[54] but deaths related to opioids have mirrored the rise seen in the general population.[55] Other substance use-related harms, such as the transmission of bloodborne pathogens via nonsterile syringes or other drug injection supplies, have also been increasing alongside drug overdose deaths. In 2014, rates of HIV infection in the US began to increase among persons who inject drugs for the first time in 2 decades.[56] Between 2013 and 2020, the incidence of acute hepatitis C (HCV) infection doubled.[57] In response to these trends, VHA has implemented several initiatives to reduce substance use-related harms, including expanding access to medications to treat opioid use disorder (OUD), providing naloxone rescue kits to Veterans at risk of overdose, and developing guidance for VHA health care facilities to develop syringe services programs (SSPs) to provide sterile syringes and other supplies.[58,59]

SSPs, which have also been referred to as needle exchanges, were first implemented in European countries and Australia in the 1980s as community-based efforts to distribute sterile syringes and provide safe injection information to people who inject drugs (PWID) in response to rising HIV infection rates.[60] These programs are guided by the principles of *harm reduction*, which has been defined as "a set of practical strategies and ideas aimed at reducing negative consequences associated with drug use."[61,62] The term *SSP* broadly refers to the provision of sterile syringes and other supplies and is inclusive of any setting that provides these supplies for the intended injection of drugs (including fixed locations, mobile units, and pharmacies).[62]

SSPs can vary widely in terms of their delivery models as well as the types and extent of additional health care services they provide.[63] SSPs with comprehensive services may offer naloxone and overdose education, fentanyl test strips, testing for infectious disease, vaccinations, linkages to addiction treatment, and (less commonly) medications for OUD.[63,64] These services are sometimes referred to collectively as *wraparound services* to emphasize that they are in addition to the core service of providing sterile syringes and supplies. In some cases, SSPs exclusively offering injection supplies may distribute these supplies by mail-order or through pharmacies.

In the US, public support for SSPs has varied regionally and over time. A variety of concerns about SSPs have emerged over the past several decades, including that SSPs promote or facilitate drug use, increase the frequency of injection drug use, attract PWID to communities where SSPs are located, risk public health due to unsafe syringe disposal, increase neighborhood crime, and divert funding away from addiction treatment.[62,65] Starting in the 1980s, many states prohibited SSPs or passed laws criminalizing the possession and distribution of syringes for purposes of illicit drug use, and the federal government previously implemented a near-total ban on the use of federal funds to support SSPs.[65] Whether SSPs are allowed to provide PWID with syringes based on need, rather than via 1-for-1 exchange, has also been a source of controversy with rules varying by state.[66]

While many restrictions were gradually rescinded starting in 2015 in response to increasing HIV and HCV infections in rural areas, an inconsistent legal framework and relative lack of public funding has limited the spread of SSPs in the US.[67,68] According to the North American Syringe Exchange Network (NASEN) directory of SSPs[69] (which relies on voluntary information sharing and is not a comprehensive list), the US currently has approximately 500 SSPs unevenly distributed across the country. For example, California has 58 SSPs and Kentucky has 45 listed on the NASEN website, while Kansas, Mississippi, Nebraska, South Dakota, and Wyoming have none.

VA currently offers SSPs in several locations including Danville, IL, Orlando, FL, and San Francisco, CA.[70] The number of programs is expected to increase in response to recommendations from VHA leadership that medical centers develop SSPs or otherwise ensure Veterans enrolled in VHA care have access to SSPs where not prohibited by state, county, or local law. Through VHA initiatives including the Pain Management, Opioid Safety and Prescription Drug Monitoring Program (PMOP),[58] VA facilitates have received funding and other supports to develop local SSPs.

Important changes in substance use trends, approaches to substance use prevention and treatment, public awareness of substance use harms, and legal and regulatory environments have occurred over the past 4 decades. Moreover, epidemiological features of HIV and HCV infection, approaches to prevention, and options for treatment of these diseases have evolved over time. A result of these changes and developments is a large and complex evidence base on SSPs. The present report is an attempt to provide an overall picture of what is known about the benefits and potential harms of SSPs. This report was requested by the VA Offices of Mental Health and Suicide Prevention, Research and Development, and Specialty Care Services to inform VA efforts to meet the goals of the Office of National Drug Control Policy[71] and to implement best practices for harm reduction in VHA settings.

METHODS

REGISTRATION AND REVIEW

A preregistered protocol for this review can be found on the PROSPERO international prospective register of systematic reviews (CRD42023438525).

KEY QUESTIONS AND ELIGIBILITY CRITERIA

The following key questions were the focus of this review:

Key Question 1	What are the benefits and harms of syringe services programs?
Key Question 1a	Do benefits and harms of syringe services programs vary by exchange model (needs-based vs 1-for-1) or presence/absence of program components?

Study eligibility criteria are shown in the table below. Systematic reviews were required to meet predefined methodological criteria established by the AHRQ Evidence-based Practice Program[72] to merit inclusion: 1) have an explicit and adequate search, 2) apply predefined eligibility criteria to select studies, 3) conduct risk of bias assessment for included studies, and 4) present a synthesis of results.

Population	Adults at risk for substance use-related harms.
Intervention	Syringe services programs. The primary intervention should be dispensing of sterile syringes, but programs may also include other components such as naloxone distribution, infectious disease testing, education on overdose prevention, safer injection practices, and/or infectious disease prevention, and/or referral to treatment and/or prevention services. The efficacy of these components as standalone interventions will not be evaluated.
Comparator	Any comparator or no comparator (*ie*, pre-post studies).
Outcomes	HIV/HCV prevalence or incidence, injection risk behaviors (sharing, borrowing, lending, reuse, or unsafe disposal of syringes); amount, speed, or frequency of injection drug use; naloxone distribution/use, knowledge of overdose risk; linkage to treatment for substance use disorder(s), HIV/HCV, HIV pre-exposure prophylaxis, or other medical needs; utilization of referred services; neighborhood crime rates or property values.
Study Design	Any, but we may prioritize studies using a best-evidence approach. Existing systematic reviews may be included to address some outcomes.

We did not examine primary studies for a given outcome when we identified a recent, rigorously conducted systematic review that included that outcome. This was the case for the outcomes of HIV/HCV prevalence and incidence and injection risk behaviors, which were covered in a recent review of reviews.[1] Similarly, we identified a 2010 systematic review[2] comparing SSP models and therefore restricted inclusion of primary studies relevant to Key Question 1a to more recent studies not included in that review.

SEARCHING AND SCREENING

To identify articles relevant to the key questions, a research librarian searched Ovid MEDLINE, CINAHL, PsycINFO, and the Cochrane Database of Systematic Reviews through March 2023 using terms for *syringe services programs* (see Appendix for complete search strategies). Additional

citations were identified from grey literature searches and hand-searching reference lists of included studies. The Cochrane Central Register of Controlled Trials was searched for underway studies. English-language titles, abstracts, and full-text articles were independently reviewed by 2 investigators, and disagreements were resolved by consensus.

DATA ABSTRACTION AND RISK OF BIAS ASSESSMENT

Effect information and population, intervention, and comparator characteristics were abstracted from all included studies. The internal validity (risk of bias) of each study was rated using the Cochrane risk of bias tools for systematic reviews,[73] randomized controlled trials,[74] and nonrandomized comparison studies.[75] We did not assess risk of bias of cross-sectional studies individually. All data abstraction and internal validity ratings were first completed by 1 investigator and then checked by another; disagreements were resolved by consensus or discussion with a third investigator (see Appendix for risk of bias ratings).

SYNTHESIS

We synthesized studies narratively using a "best evidence" approach, meaning that we focused on the studies most germane to our Key Questions and of the highest methodological quality.[76] We organized findings by outcome. Because we identified a recent, rigorously conducted review of reviews[1] on HIV/HCV prevalence and incidence and injection risk behaviors, we relied on syntheses from this review for these outcomes. For included primary studies, we prioritized evidence from longitudinal studies when available.

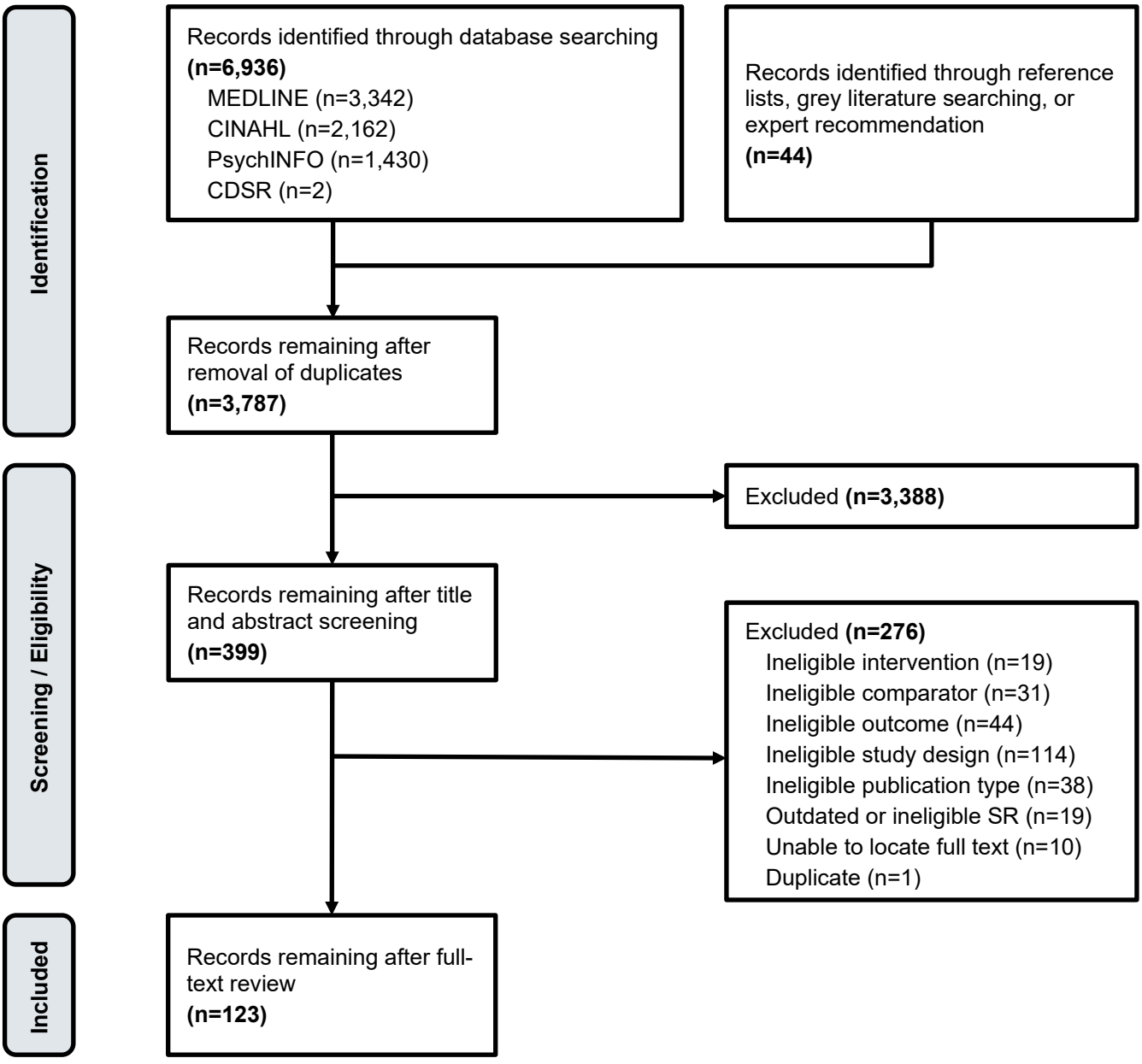
Strength of Evidence

After synthesizing available evidence, we rated the strength of evidence for each Key Question 1 outcome based on the methodology and risks of bias of available studies, the consistency and certainty of findings, and the directness of outcomes (whether reported outcomes are relevant to patients and providers).[77] For the outcomes of HIV/HCV prevalence and incidence and injection risk behaviors, we report the strength of evidence conclusions from the review of reviews described above.[1] For other outcomes, we applied the following general algorithm: *high strength* evidence consisted of multiple, large studies with low risk of bias, consistent and precise findings, and clinically relevant outcomes; *moderate strength* evidence consisted of multiple studies with low to unclear risk of bias, consistent and precise findings, and clinically relevant outcomes; *low strength* evidence consisted of multiple small or moderate-size studies, with unclear to high risk of bias, and inconsistent or imprecise findings; and *insufficient* evidence consisted of a single study or several small studies with an unclear or high risk of bias or no available studies.

RESULTS

LITERATURE FLOW DIAGRAM

The literature flow diagram summarizes the results of the study selection process. A full list of excluded studies is provided in the Appendix.



Notes. 17 SRs in 18 records; 100 primary studies in 105 records.

Abbreviations. CDSR=Cochrane Database of Systematic Reviews; CINAHL=Cumulative Index of Nursing and Allied Health.

Our search identified 399 potentially relevant articles after deduplication and title and abstract screening. Of these, 100 primary studies (in 105 publications) met eligibility criteria. We included 17 relevant SRs (in 18 publications; see Appendix for full list) and prioritized 2 that we determined were the most recent and comprehensive, a review of reviews[1] of HIV/HCV transmission and injection risk behaviors and a systematic review[2] comparing different approaches to the organization and delivery of SSPs. Both reviews were assessed as low risk of bias overall. The primary methodological limitation of the review of reviews[1] of HIV/HCV transmission and injection risk behaviors was that risk of bias of included primary studies was not assessed using an established assessment tool. Instead, the authors relied on study design as a proxy for risk of bias. However, risk of bias of included systematic reviews was assessed using a formal assessment tool. The primary methodological limitation of the review of SSP approaches[2] was that methodological quality was not addressed within the narrative synthesis. However, assessment of study quality was conducted and addressed in the discussion.

Review of Reviews on HIV/HCV Transmission and Injection Risk Behaviors

A 2022 review of reviews[1] on HIV/HCV transmission and injection risk behaviors was an update of a 2010 review of reviews[78] on the same topic. These reviews were broad in scope and included several other harm reduction interventions in addition to SSPs (*eg*, opioid agonist therapy). For the 2022 update, the authors used a stepwise approach to search the literature for new evidence. Specifically, they conducted an initial search for systematic reviews on a given intervention and outcome before proceeding to searches of the primary literature, and only searched the primary literature when evidence identified in systematic reviews was considered insufficient. The authors evaluated the quality of systematic reviews using the AMSTAR-2[79] tool and used a pragmatic approach to critical appraisal of primary studies by using study design as a surrogate for quality. Statements regarding the effectiveness of SSPs on preventing HIV/HCV transmission and mitigating injection risk behaviors were categorized as "sufficient," "tentative," or "insufficient" based on the available evidence.

HIV AND HCV TRANSMISSION

The 2022 review of reviews[1] described above found sufficient evidence that SSPs prevent HIV transmission among PWID (Table 1). This conclusion was based on findings from a 2014 systematic review and meta-analysis[80] of 12 primary studies (10 cohorts, 1 case-control, 1 cross-sectional). A meta-analysis of the 6 higher-quality studies indicated that SSPs are associated with significantly lower risk of HIV transmission (pooled risk ratio [RR] = 0.42, 95% CI [0.22, 0.81]). When the 6 low-quality studies were included, the risk reduction was somewhat smaller and bordered on significance (pooled RR = 0.66, 95% CI [0.43, 1.01]).

The same 2022 review of reviews[1] found tentative evidence that SSPs prevent HCV transmission among PWID. This conclusion was primarily informed by a Cochrane systematic review and meta-analysis[81] of primary studies comparing HCV transmission among individuals with high SSP coverage, defined as regular SSP attendance or at least 100% syringe coverage (having at least the supply needed to use a new needle and syringe for every injection), and those with low or no SSP coverage. Pooling adjusted estimates from 5 studies indicated a small and nonsignificant impact of SSP coverage on HCV transmission risk (pooled RR = 0.79, 95% CI [0.39, 1.61]). In contrast, when the analysis was limited to 2 studies that used syringe coverage as the measure of sterile syringe use (rather than SSP attendance), high SSP coverage was associated with a 76% reduction in HCV transmission risk (pooled RR = 0.24, 95% CI [0.09, 0.62]). Findings from additional primary studies were mixed and did not inform the authors' overall evidence statement.

INJECTION RISK BEHAVIORS

The same 2022 review of reviews[1] found sufficient evidence that SSPs reduce injection risk behaviors. This conclusion was informed by the authors' earlier 2010 review of reviews[78] in which evidence from 3 reviews[82–84] of 43 primary studies supported the effectiveness of SSPs in reducing injection risk behaviors. No further literature searching was conducted in 2022 given the already-sufficient level of evidence.

Table 1. Evidence Statements from 2022 Review of Reviews[1] on the Effect of SSP Utilization[a] on HIV/HCV Transmission and Injection Risk Behaviors

Outcome	Evidence[b]	Synthesis	Evidence Statement
HIV transmission	1 review[80] with a meta-analysis of 12 studies	Pooled effect size was equivocal when all studies were included; meta-analysis only including 6 higher quality studies found a 58% reduction in risk of HIV associated with use of SSP (RR = 0.42, 95% CI [0.22, 0.81]).	There is **sufficient** evidence that SSP use is effective in the prevention of HIV transmission among PWID.
HCV transmission	1 review[81] of 15 studies; 5 primary studies	A meta-analysis of 5 studies found an equivocal pooled effect (RR = 0.79, 95% CI [0.39, 1.61]); when meta-analysis was limited to 2 studies that used syringe coverage as the measure of sterile syringe use (rather than SSP attendance), the effect size was consistent with a 76% reduction in HCV incidence (RR = 0.24, 95% CI [0.09, 0.62]). Findings from additional primary studies were mixed.	There is **tentative** evidence to support the effectiveness of SSPs in the prevention of HCV transmission among PWID.
Injection risk behaviors[c]	3 reviews[82–84] of 43 primary studies (21 cohort studies, 21 cross-sectional studies, 1 ecological study)	Clear statement of evidence in support of SSPs from 2 SRs and consistent evidence from primary studies (39 positive studies, 1 negative, 1 no association).	There is **sufficient** review-level evidence to support the effectiveness of SSPs in reducing self-reported injection risk behaviors among PWID.

Notes. [a] SSP utilization compared with non-attendance or low SSP utilization; [b] Evidence from 2022 review of reviews update covering 2011-2020; [c] Level of evidence was sufficient in 2010 review of reviews and no update was undertaken.

Abbreviations. CI=confidence interval; HIV=human immunodeficiency virus; OR=odds ratio; PWID=people who inject drugs; SSP=syringe services program; RR=risk ratio.

Overview of Included Primary Studies

We identified 100 primary studies addressing the remaining outcomes of interest. While 69 studies evaluated injection frequency, we prioritized 16 studies with longitudinal data. Similarly, we identified 16 studies evaluating linkages to treatment and utilization of referred treatment services but prioritized synthesis of 9 studies with longitudinal data. All of these studies evaluated linkage to drug treatment or drug detoxification. We did not identify any studies evaluating whether SSP use is associated with referral to other forms of treatment, such as treatment for HIV or HCV. Of the remaining outcomes, 21 studies (1 RCT, 2 pre-post, 11 cross-sectional, and 7 ecological studies with outcomes that were assessed at a population level) reported on unsafe disposal of syringes, 5 cross-sectional studies reported on naloxone distribution or use, 2 cross-sectional studies reported on knowledge of overdose risk, 2 ecological studies reported on neighborhood crime rates, and 2 RCTs compared SSPs with different exchange models or program components. Exposures and outcomes were defined differently across studies. Most studies relied on participant self-report of SSP use or attendance, injection risk behaviors, and injection frequency. In total, we prioritized synthesis of 48 primary studies (see Appendix). We identified 2 underway studies (see Appendix).

Most studies were conducted in large US cities, and more studies were conducted in Baltimore, MD than in any other city. Eight were conducted outside the US (2 in Canada,[15,39] 3 in the UK,[11,12,23] 1 in Australia,[13] 1 in the Netherlands,[5] and 1 in Sweden[85]). Four studies[14,19,20,34] were conducted within a rural setting (West Virginia, Indiana, or Ohio), and 5 studies[12,13,18,23,31] were conducted within both urban and rural settings. The median sample size across studies was 431 (range: 54 – 6,321). All studies that reported gender were comprised of predominately male participants, except for a single study[28] with an equal number of men and women. Of the studies that reported the racial or ethnic makeup of their sample, 9 studies[7,16,17,21,25–27,32,33] were comprised predominately of Black participants, 5[8,29,30,36,41] were comprised predominately of Hispanic or Latino participants, and 14 studies[3,4,6,10,14,15,20,22,24,31,34,35,37,38] were comprised predominately of White participants. Most studies were conducted prior to the current era of increased illicit synthetic opioids and psychostimulants. Study participants mostly used IV heroin, often in combination with cocaine.

Seventeen studies provided detail about the syringe dispensation policies of the SSPs evaluated. Some of these studies evaluated multiple SSPs with different dispensation policies or SSPs whose dispensation policies changed over time and are counted more than once. Of these, 11[5,9,10,12,16,17,19,32,39,42,45] reported policies requiring exchange of a used needle for a clean needle (exchange), 7[8,14,18,19,32,34,42] reported distribution of clean syringes without requiring exchange of used needles (distribution), and 2[31,46] reported sale of up to 10 clean syringes. Of the SSPs with exchange policies, 7[5,10,12,16,17,19,45] had strict 1-for-1 exchange policies, and 4[9,32,39,42] allowed for the distribution of a small number of extra syringes (for example, as a starter pack for new SSP clients). Of the SSPs with distribution models, 2[18,32] allowed for distribution of a set number of syringes (*eg*, up to 10 per visit), while 6[8,14,18,19,34,42] distributed clean syringes based on need, without a set limit (needs-based distribution).

Sixteen studies provided information about services offered at the SSP in addition to needle exchange or distribution. Most SSPs ($N = 9$[3,8,10,14–17,20,45]) provided materials related to safer injecting practices, such as sterile injection equipment, bleach, cotton, water, and/or alcohol wipes. Eight studies[5,8,10,14,17,34,45,85] describe provision of education or educational materials on risk reduction and safer injecting practices. Three studies[10,20,34] describe provision of overdose prevention education or resources, with 2[10,34] distributing or administering naloxone. SSPs commonly provided HIV prevention

and education resources ($N = 7$[5,12,15–18,35]), as well as distribution or sale of condoms ($N = 8$[3,5,8,12,15–17,45]), and 6[14,16,17,20,34,85] offered testing for HIV and HCV. Few SSPs provided on-site medical care. One SSP[34] had co-located primary care services, while others offered basic medical care,[35,85] provided referrals for medical treatment,[8,14,16] or distributed wound care kits.[14,34] One SSP[34] had co-located drug treatment services. Eight SSPs[15–18,20,26,35,45] provided referrals to drug treatment, 2 of which[16,17] had a limited number of prepaid spots in methadone maintenance treatment available for SSP clients.

Most studies prioritized for synthesis were retrospective cohorts, pre-post, or cross-sectional. Overall, these studies are less reliable (higher risk of bias) due to selection bias and the potential for uncontrolled confounding (see Appendix for full risk of bias ratings). Other common limitations included high levels of missing data, unclear handling of missing data, and inappropriate exclusion of potential study participants. Cohort studies were also limited by unclear description of classification of the intervention. Absence of information about blinding of study personnel and deviations from the assigned intervention, as well as potential for recall bias, were limitations of included RCTs.

INJECTION FREQUENCY

SSP use does not appear to increase injection frequency among PWID. Most studies found that PWID using SSPs as a source of injection supplies may inject drugs less often over time or the same amount compared to those obtaining injection supplies from other sources (Table 2). A 2003 RCT[3] of 600 PWID in Alaska randomized to SSP access (intervention group) or training on how to purchase injection supplies from pharmacies (comparator group) found that the mean number of past 30-day injections decreased in both groups over time and was not modified by group assignment. This finding was largely supported by results of prospective cohort and pre-post studies, although in general these studies are less reliable due to risk of selection bias and confounding. In 1 pre-post study[14] in which SSP injection frequency seemed to increase over time among SSP users, a discrepancy was noted between data collected on a standard form and information obtained from private interviews, in which almost all participants reported no change in injection frequency per day. In a second study in which the percentage of participants injecting more than 5 times per day seemed to increase over time, authors did not speculate on the reasons for this finding but did note that the cohort participating in longitudinal assessments was a higher-risk group (with more reported high-risk injection behaviors) than the cohort only providing baseline data.[10]

Table 2. Injection Frequency

Study	Study Design	N	Results
Fisher 2003[3]	RCT	600	Randomization to SSP access or training on pharmacy purchase of injection supplies did not significantly modify the association between time under observation and injection.
Hagan 2000[4]	Prospective cohort	1079	Compared former, current, new, and never use of SSP controlling for drug treatment, drug usually injected, and number of injections per month at enrollment. Former exchangers were more likely to report reduced injection frequency of more than 75% compared with never exchangers (aRR = 2.85, 95% CI [1.47, 5.51]). The odds of reduced injection frequency in former exchangers vs never exchangers were greater among individuals injecting daily at enrollment (OR = 3.44, 95% CI [1.46, 8.09]). There was no significant difference between never exchangers and new or current exchangers.
Hartgers 1989[5]	Prospective cohort	54	32% of SSP users said they had injected irregularly (rather than regularly) in the last 6 mos compared with 70% of non-SSP users ($p < 0.05$).
Marmor 2000[6]	Prospective cohort	328	Mean rates of change with time in standardized drug injection rates (negative values represent a decrease in drug injection rate): SSP nonusers: -1.22, 95% CI [-1.46, -0.98]; SSP sporadic users: -0.69, 95% CI [-1.04, -0.35]; SSP consistent users: -0.41, 95% CI [-0.71, -0.10]. Injection frequency decreased in all groups, but the rate of decline was significantly less among consistent SSP users compared to non-users and sporadic users.
Monterroso 2000[7]	Prospective cohort	2306	Reduced injection frequency in participants who ever used an SSP (compared to never used SSP) OR = 0.43, 95% CI [0.31, 0.59].
Schoenbaum 1996[8]	Prospective cohort	329	Among active injectors, SSP users injecting >30 times per month 1989 to 1993: 72.6 to 49.5% ($p < 0.01$); non-exchange users change was 70.9 to 45.2% ($p < 0.001$). 43% of SSP users reduced or stopped injecting compared with 82% of non-SSP users ($p < 0.001$ for both groups).

Study	Study Design	N	Results
Bartholomew 2021[10]	Pre-post	115	Average # of injections per day among PWID who attended an SSP: baseline (n, %): <5 64 (57.7); ≥5 47 (42.3); 1st follow-up: <5 58 (53.2); ≥5 51 (46.8); 2nd follow-up: <5 47 (48.0); ≥5 51 (52.0).
Cox 2000[11]	Pre-post	370	Among PWID who attended an SSP, 70/104 (67%) who reported injecting >4 times per day reduced their injection frequency to <1 time per day ($p < 0.05$).
Donoghoe 1989[12]	Pre-post	142	Mean # of injections in the previous 4 weeks: 53 at first month of attendance vs 45 2-4 months later.
Iversen 2013[13]	Pre-post	724	Daily injection use (N, %) among PWID who attended an SSP across 3 time periods: 1995-1999: 143 (52); 2000-2003: 107 (61); 2004-2010: 110 (50) ($p = .06$).
Huo 2006[9]	Prospective cohort	707	Changes in the injection frequency of SSP users and non-users were not significantly different.
Patel 2018[14]	Pre-post	148	Among PWID who attended an SSP and completed a standardized form reporting injection behaviors, median injection times per day (IQR) first visit: 5 (3–9) compared to most recent visit 9 (5–15); $p < 0.001$. However, in private interviews, almost all participants reported no change in injection frequency per day.
Schechter 1999[15]	Pre-post	694	Among frequent SSP attendees, baseline and first follow-up visits OR injecting ≥4 times per day = 1.28, 95% CI [0.87, 1.87].
Vertefeuille 2000[16]	Pre-post	112	Among HIV-positive PWID enrolled in an SSP, past-2 weeks mean number of injections decreased 82.5 vs 60.2 ($p = .03$) at 6-month follow-up.
Vlahov 1997[17]	Pre-post	335	Mean injections per day decreased from 5.9 to 4.9 (mean change = -1.09, 95% CI [-1.50, -0.68]) at 2-week follow-up. Daily injections decreased from 5.6 to 4.1 from baseline to 6-month follow-up (mean change = -1.50, 95% CI [-2.09, -0.91], $p < .001$).
Vogt 1998[18]	Pre-post	208	Among 208 participants with repeat interviews, 100 (48%) reported a decrease in frequency of injection from the first to the most recent interview, 81 (39%) reported no change in frequency of injection, and 27 (13%) reported increase in frequency of injection.

Abbreviations. CI=confidence interval; mos=months; IQR=interquartile range; OR=odds ratio; PWID=people who inject drugs; SSP=syringe services program.

NALOXONE DISTRIBUTION AND OVERDOSE EDUCATION

PWID who have used an SSP are more likely to have received naloxone or say that they are carrying naloxone compared to those who have not used an SSP based on consistent, statistically significant results from 4 cross-sectional studies,[20–23] (Table 3). Receiving overdose education was less frequently studied, but also appears to be positively associated with SSP use based on results from 2 cross-sectional studies.[21,24] A small cross-sectional study[21] of 263 PWID in Philadelphia examined naloxone possession and receipt of overdose education according to SSP use and race and found that Black and White SSP clients were both more likely than Black non-SSP clients to possess naloxone and receive overdose training.

Table 3. Naloxone Distribution and Overdose Education

Study	Study Design	N	Results
Naloxone Distribution			
Allen 2021[20]	Cross-sectional	420	Having accessed sterile syringes at an SSP: aPR[a] received naloxone in the past 6 mos = 1.36; 95% CI [1.18, 1.57].
Jones 2021[21]	Cross-sectional	263	Black SSP clients (aOR[b] = 4.21, 95% CI [2.0, 8.87]), White SSP clients (aOR[b] = 3.54, 95% CI [1.56, 8.04]), and White non-SSP clients (aOR[b] = 4.49, 95% CI [1.5, 13.37]) were more likely to possess naloxone compared to Black non-SSP clients.
Reed 2019[22]	Cross-sectional	571	SSP as primary source for syringes in the past 12 mos compared to a pharmacy or secondary source (friend, relative, sex partner, dealer, shooting gallery, or off the streets): aOR[c] carrying naloxone = 2.92, 95% CI [1.68, 5.09].
Spring 2022[23]	Cross-sectional	2,139	Past-year contact with SSP: aOR[d] carrying naloxone = 1.74, 95% CI [1.39, 2.18].
Turner-Bicknell 2020[19]	Serial cross-sectional	NR	Naloxone distribution increased from 29 kits prior to SSP implementation (July 2017) to 88 kits in September 2017 (post-implementation) but decreased to 69 in December 2017).
Overdose Education			
Jones 2021[21]	Cross-sectional	263	Black SSP clients (aOR[b] = 3.85, 95% CI [1.88, 7.92]) and White SSP clients (aOR[b] = 2.73 95% CI [1.29, 5.75]) (but not White non-SSP clients aOR[b] = 0.54 [0.19, 1.55]) were more likely to have received overdose training compared to Black non-SSP clients.
Kim 2021[24]	Cross-sectional	458	Accessed an SSP: aOR[e] received overdose training = 3.51, 95% CI [1.41, 8.79].

Notes. [a] Adjusted for age, single status, food insecurity, injection drug use past 6 mos, prescription opioid pain relievers, heroin, fentanyl, receptive syringe sharing past 6 months. [b] Adjusted for sociodemographic and drug use variables. [c] Adjusted for homeless status and law enforcement interactions. [d] Adjusted for region of recruitment, gender, born in UK, injecting duration, ever engaged in transactional sex, currently homeless, been in prison in the past year, prescribed treatment for drug use, heroin use and use of other central nervous system depressants in the past month, overdosed in the past year. [e] Adjusted for demographic factors, homeless in the last 12 months, experience of overdose, witnessed overdose in last 12 months, currently own naloxone, drug most frequently injected, and frequency of injection.

Abbreviations. aOR=adjusted odds ratio; aPR=adjusted prevalence ratio; mos=months; NR=not reported; SSP=syringe services program.

LINKAGE TO SUD TREATMENT AND UTILIZATION OF TREATMENT SERVICES

SSP use may be associated with increased treatment linkage and/or use of treatment services among PWID compared to no SSP use (or less use) (Table 4). The most recent and direct evidence is from a 2006 retrospective cohort study[25] of 440 PWID in Baltimore which found that after adjusting for gender, employment status, type and method of drugs used, and HIV status, individuals who used an SSP in the past 6 months were more likely than those who did not to enter drug treatment, which was broadly defined to include drug detoxification, residential treatment, methadone maintenance, and outpatient drug-free treatment (aOR = 1.71, 95% CI [1.12, 2.62]). Similarly, an earlier cohort study[86] also conducted in Baltimore found that HIV-negative PWID who used an SSP were more likely to enter methadone treatment in the subsequent 6 months than those who had not used an SSP, particularly early in the study period when the SSP was able to offer dedicated treatment slots for its

clients (OR 1994-1995 = 1.9, 95% CI [1.34, 2.62]; OR for the study period = 1.48, 95% CI [1.13, 1.75]). In this cohort, SSP attendance was also associated with entry into a medically supervised withdrawal facility for both HIV-positive (aOR = 3.2, 95% CI [1.38, 7.53]) and HIV-negative individuals (aOR = 1.38, 95% CI [1.02, 1.87]).[27]

Two cohorts evaluated treatment retention among those referred to treatment from an SSP compared to another source. In a cohort study[28,87] of 325 PWID in Baltimore, 6- and 12-month treatment retention was no different for those referred by the SSP compared to those referred by other means (self-referral, family referral, other healthcare provider referral, *etc*) after adjusting for demographic variables, employment status, and days of heroin, cocaine, and IDU in the month prior (6 months aHR = 1.39, 95% CI [0.61, 2.04]; 12 months aHR = 1.23 95% CI [0.78, 1.94]). In another cohort study[4] conducted in Seattle, those who stopped attending the SSP during the 12-month study period were more likely to continue methadone treatment compared to those who never used the SSP (aRR = 1.55, 95% CI [0.90, 2.68]), although this finding was not statistically significant. Retention in methadone treatment was similar for current SSP users or those who started using the SSP during the study period compared to those who never used the SSP.

Table 4. Linkage to SUD Treatment and Utilization of Treatment Services

Study	Study Design	N	Results
Initiated Treatment			
Hagan 2000[4]	Cohort	Variable	Participants who started attending the SSP during the 12-month study period (new SSP users) were more likely to enter a methadone program (aRR = 5.05, 95% CI [1.44, 17.7])[a] compared with those who formerly, currently, or never used the SSP.
Hartgers 1989[5]	Cohort	145	At baseline, individuals using an SSP > 90% of the time in the last 6 mos had been in contact with methadone programs more often in the last 5 years than less frequent or non-SSP users (76% vs 48%, $p < 0.01$).
Latkin 2006[25]	Cohort	440	Individuals who utilized an SSP in the past 6 mos were more likely to have entered drug treatment than individuals without past 6-mos SSP use (aOR = 1.71, 95% CI [1.12, 2.62]).[b]
Kuo 2003[26]	Cohort	163	70% of SSP users referred for drug treatment using LAAM (an opioid agonist no longer on the US market) enrolled in the program (114 vs 41). Treatment entry did not differ according to the number of SSP visits prior to accepting the referral.
Strathdee 1999;[27]Shah 2000[86]	Cohort	1,483	HIV-negative participants who attended the SSP were more likely to enroll in methadone maintenance in the subsequent 6 mos compared to those who did not attend the SSP (aOR = 1.48, 95% CI [1.13, 1.75]).[c] SSP attendance was associated with entry into a medically supervised withdrawal facility for both HIV-positive (aOR = 3.2, 95% CI [1.38, 7.53])[d] and HIV-negative individuals (aOR = 1.38, 95% CI [1.02, 1.87]).[b]
Cox 2000[11]	Pre-post	370	There was a nonsignificant increase in the percentage of participants attending other drug treatment services at 3-month follow-up (26% at follow-up vs 20% at baseline, $p < 0.075$).
Vertefeuille 2000[16]	Pre-post	112	Participation in SUD treatment increased between baseline and 6-month follow up in HIV-seropositive SSP participants (8% vs 18.8%, $p = 0.01$).

Study	Study Design	N	Results
Vlahov 1997[17]	Pre-post	335	Self-reported engagement in treatment increased from 6.3% at baseline to 9.0% at 2-week follow-up (p = .117).
Retained in Treatment			
Brooner 1998;[28]Neufeld 2008[87]	Cohort	325	6- and 12-month treatment retention was no different for those referred by the SSP compared to those referred by other means (self-referral, family referral, other health care provider referral, *etc*) after adjusting for baseline variables (6 mos Ahr = 1.39, 95% CI [0.61, 2.04]; 12 mos aHR = 1.23, 95% CI [0.78, 1.94]).[e]
Hagan 2000[4]	Cohort	Variable	Former SSP users who stopped attending the SSP during the 12-month study period were more likely to remain in methadone treatment at 12-month follow up compared to those who never used the SSP (aRR 1.55, 95% CI [0.90, 2.68]).[f] Retention in methadone treatment was similar for current SSP users or those who started using the SSP during the study period compared to those who never used the SSP.

Notes. [a] Adjusted for gender; [b] Variables controlled for in adjusted analysis not reported; [c] Adjusted for gender, employment status, sniff/snort cocaine, sniff/snort heroin, history of mental illness, HIV positive status; [d] Adjusted for interaction between lagged SSP attendance and calendar year; [e] Adjusted for demographic variables, employment status, and days of heroin, cocaine, and IDU in the prior month; [f] Adjusted for frequency of injection at study enrollment.

Abbreviations. AE=adverse events; aOR=adjusted odds ratio; aPR=adjusted prevalence ratio; aRR=adjusted risk ratio; HIV=human immunodeficiency virus; HR=hazard ratio; IVDU=intravenous drug use; LAAM=levomethadyl acetate hydrochloride; mos=months; NR=not reported; PWID=people who inject drugs; RCT=randomized controlled trial; SSP=syringe services program; SUD=substance use disorder.

SYRINGE DISPOSAL

SSP use and/or presence of an SSP does not appear to increase unsafe syringe disposal practices based on 1 RCT, 2 pre-post studies, 11 cross-sectional studies, and 7 ecological studies (3 of which also included cross-sectional data) evaluating whether SSP use or presence of an SSP within a community was associated with safe (*eg*, return to SSP) or unsafe (*eg*, dispose in trash or leave on street) methods of syringe disposal (Table 5). Three cross-sectional studies[33,38,39] with a combined sample of more than 1,500 participants in large cities (Baltimore, New York City, San Francisco, and Vancouver, BC) found that safe syringe disposal was 2.28 to 5.79 times more likely among those who used an SSP compared to those who did not.

Table 5. Syringe Disposal

Study	Study Design	N	Results
Lewis 2015[29]	Cluster RCT	482	Safe syringe disposal (N, %) among PWID receiving supplies at control group pharmacies: 96 (39.5) at baseline and 91 (46.4) at 3 mos, p = .1263; Safe syringe disposal (N, %) among PWID receiving supplies at intervention group pharmacies: 74 (33.5) at baseline and 72 (42.1) at 3 mos, p = .040; between-group differences non-significant.
Vertefeuille 2000[16]	Pre-post	112	Baseline and 6 mos proportion of participants discarding of syringes in the garbage (48.6% vs 37.8%, p = .13) and in the street (7.5% vs 2.5%, p = .32).

Study	Study Design	N	Results
Vlahov 1997[17]	Pre-post	335	Proportion of participants who discarded needles in a street, alley, sewer, or gutter (28.2% vs 15.6%; $p < .001$) and in the garbage or a dumpster (42.4% vs 29.1%; $p < .001$) before and after enrolling in SSP.
Cleland 2007[30]	Serial cross-sectional	1030	Syringes obtained from an SSP were more likely to be disposed of safely than syringes from other sources: SSP syringe source vs other aOR safe vs unsafe disposal = 22.39, 95% CI [12.93, 38.78]; SSP syringe source vs other aOR safe vs possibly safe disposal = 20.98, 95% CI [12.95, 33.99].[a]
Cotten-Oldenburg 2001[31]	Serial cross-sectional	566	Pre/post legislation allowing for voluntary pharmacy sales of syringes/needles without a prescription for an accompanying drug; safe syringe disposal aOR = 1.32,[b] 95% CI [0.84, 2.06].
Bluthenthal 2004[32]	Cross-sectional	584	PWID received syringes from SSP within 30 days ($N = 155$)[c]: return to SSP: 85.2%; trash: 20.6%; leave at place of injection: 2.6%; flush down toilet: 1.9%; PWID with no direct receipt of syringes from SSP within 30 days ($N = 412$)[c]: return to SSP: 6.1%; trash: 70.6%; leave at place of injection: 7.3%; flush down toilet: 4.4%.
Coffin 2007[33]	Cross-sectional	680	Ever been to SSP compared to never used SSP: aOR safe syringe disposal = 5.79, 95% CI [3.13, 10.69].
Dasgupta 2019[34]	Cross-sectional	200	Among those injecting drugs before and after the public health response[d] ($N = 124$), disposal of used syringes in a designated medical waste container increased from 17% to 82%.
Khoshnood 2000[35]	Cross-sectional	373	Compared to pharmacy as the usual source of syringes, SSP source: OR threw away syringe "sometimes to always" = 0.03, 95% CI [0.006, 0.15]; both SSP and pharmacy source: OR threw away syringe "sometimes to always" = 0.11, 95% CI [0.02, 0.51]; source other than SSP or pharmacy: OR threw away syringe "sometimes to always" = 0.29, 95% CI [0.02, 3.5].
Quinn 2014[36]	Cross-sectional	412	SSP main syringe source aOR[e] improper disposal last 30 days = 0.44, 95% CI [0.26, 0.75]; aOR[f] improperly disposed of >50% total syringes disposed last 30 days = 0.19, 95% CI [0.10, 0.36].
Riley 2010[37]	Cross-sectional	105	Obtaining syringes from an SSP aOR[g] unsafe disposal = 0.17, 95% CI [0.05, 0.95].
Sherman 2004[38]	Cross-sectional	294	Safe syringe acquisition (SSP or pharmacy) aOR[h] safely disposing syringes = 2.28, 95% CI [1.20, 4.37].
Wood 2003[39]	Cross-sectional	587	Use of an all-night SSP compared to other sources (including fixed SSP) aOR[i] safer syringe disposal = 2.69; 95% CI [1.38, 5.21].
Zlotorzynska 2018[40]	Cross-sectional	6321	Obtaining syringes primarily from pharmacies vs SSPs: aOR[j] any unsafe syringe disposal = 1.47, 95% CI [1.38, 1.56].
Levine 2019[41]	Ecological and serial cross-sectional	930, 775 census blocks	Total 371 syringes/1,000 blocks found pre-SSP implementation compared to 191 syringes/1,000 blocks found post-SSP implementation (49% decrease); improper syringe disposal post-SSP implementation compared to pre-implementation aRR = 0.61,[k] 95% CI [0.55, 0.69].
Tookes 2012[42]	Ecological and serial cross-sectional	1050	Miami (city without SSP) syringe density = 371/1000 census blocks and syringe prevalence = 4.9/1000 people; San Francisco (city with SSP) syringe density = 44/1000 census blocks and syringe prevalence = 0.3/1000 people; Miami compared to San

Study	Study Design	N	Results
			Francisco: aOR[l] public syringe disposal = 34.2, 95% CI [21.9, 53.5].
Wenger 2011[m43]	Ecological and cross-sectional	602	Obtained syringes from SSP compared to other source: aOR[g] improper syringe disposal = 0.20; 95% CI [0.10, 0.40].
Broadhead 1999[44]	Ecological	1 town	From fall 1996 to fall 1997 (following SSP closure), the rate of discarded syringes increased from 26.1 per month 39.8 per month (53% increase).
Doherty 1997[45] Doherty 2000[88]	Ecological	32 city blocks	Block mean of number of needles per 100 trash items was 2.42 pre-SSP and 1.30 2 years post-SSP (mean within-block change = −0.028, $p < .05$).
Fuller 2002[46]	Ecological	27 blocks	Decrease in block mean ratios of syringe to background trash pre-SSP (1.17 and 1.03) compared with post-SSP (0.81, 0.53, 0.73).[n]
Oliver 1992[47]	Ecological	1 neighbor-hood	5.14 syringes found per month pre-SSP implementation compared with 1.9 post-SSP implementation, $p < .05$.

Notes. [a] Safe methods of disposal included clinic, doctor, hospital, SSP, pharmacy, disposal mailbox, and sharps box. Unsafe methods of disposal included bushes, toilet, sewer, stranger, ground, owner, and left. Possibly safe methods of disposal included garbage at home and garbage elsewhere; [b] Adjusted for speedball injection and prison history; [c] ESP calculated; [d] The public health response included establishment of the state's first legal SSP (other components of the public health response were not described);[e] Controlled for recruitment site; [f] Controlled for income; [g] Variables controlled for in adjusted analysis not reported; [h] Controlling for ethnicity, gender, education level, and age; [i] Adjusted for age, HIV positivity, unstable housing, residence in the HIV epicentre, involvement in the sex trade, frequency of heroin use, reuse of syringes, and injecting alone; [j] Adjusted for age, race/ethnicity, gender, education, current homelessness, self-reported HIV status and injection frequency; [k] Adjusting for gender, age, race/ethnicity, homelessness, and HIV-positive status; [l] Adjusting for age, gender, homelessness, and self-reported HIV seropositivity; [m] Sample includes San Francisco participants from Tookes 2012 study; [n] Counts were made at 2 time points prior to SSP (October 25, 2000 and January 30, 2001) and 3 time points following SSP (April 25, 2001, June 27, 2001, and December 5, 2001).

Abbreviations. AOR=adjusted odds ratio; ARR=adjusted risk ratio; CI=confidence interval; mos=months; OR=odds ratio; PWID=people who inject drugs; SSP=syringe services program.

NEIGHBORHOOD CRIME RATES

Presence of an SSP may not be associated with any change in neighborhood crime rates. We identified 2 ecological studies[48,49] measuring community crime rates based on proximity to an SSP or pharmacy selling syringes (Table 6). While a study in New York City found that SSP access was associated with increased arrests, a study in Baltimore evaluating the same outcome found no difference in arrest trends. Neither study controlled for other variables that could account for local arrest trends, but the study conducted in Baltimore likely provides more reliable information because it more directly measured arrest trends relative to the start of an SSP.

Table 6. Neighborhood Crime Rates

Study	Study Design	N	Results
Cooper 2012[48]	Ecological	42 health districts in New York City	On average a 1-unit increase in logged SSP access over time was associated with an increase of 11.18 arrests/1000 residents ($p < 0.0001$).
Marx 2000[49]	Ecological	Baltimore areas within 0.5-mile radius of an SSP site	No significant differences in arrest trends by category after SSP introduction relative to before SSP introduction in program vs non-program areas ($p > .05$)

Abbreviations. SSP=syringe services program.

SSP DISTRIBUTION MODELS

Use of SSPs that offer more syringes per visit or supply syringes based on need (regardless of how many used syringes are returned) may be associated with less syringe re-use compared to use of SSPs with more restrictive syringe distribution policies, such as caps on the number of syringes that may be supplied per visit or requirements for 1-for-1 syringe exchange (*ie*, 1 sterile syringe is supplied for every used syringe that is returned) (Table 7). A 2010 systematic review[2] of SSP effectiveness included 3 cross-sectional studies[32,89,90] evaluating SSPs according to syringe distribution policies. Two of these cross-sectional studies[32,89] compared injection risk behaviors among PWID using SSPs or pharmacies with variable syringe dispensation policies and/or limits on the number of syringes that could be supplied. A third cross-sectional study[90] compared injection risk behaviors among PWID in Hartford, CT when the number of syringes permitted to be dispensed by SSPs increased from 5 to 10. Results were consistent across studies showing that use of SSPs with more permissive syringe distribution practices (*eg*, needs-based) was associated with less reported syringe re-use. No differences were found for reports of syringe sharing in 2 studies.

Table 7. SSP Exchange Models

Syringe Policy	Evidence	Findings
Needs based or >1 for 1 exchange vs 1-for-1 exchange	1 SR[2] (2 cross-sectional studies[32,89])	Syringe re-use: Less syringe re-use with needs-based or >1 for 1 syringe access compared to 1-for-1 or limited syringe exchange[32,89] Syringe sharing: No difference in receptive syringe sharing according to SSP syringe exchange policies[32,89]
Increase in the number of syringes dispensed from 5 to 10	1 SR[2] (1 cross-sectional study[90])	Mean percent of injections using a pre-used syringe decreased from 14% to 11% when syringe distribution cap increased from 5 to 10

Abbreviations. SR=systematic review; SSP=syringe services program.

SSP PROGRAM COMPONENTS

Combined SSP and OUD Treatment Programs

The 2022 review of reviews[1] on HIV/HCV transmission and injection risk behaviors evaluated evidence on combined SSPs and OUD treatment programs, finding that while evidence was insufficient for the outcome of HIV transmission (no studies were identified), sufficient evidence existed regarding a benefit of combined programs on reducing HCV transmission. This conclusion was

largely based on a systematic review and meta-analysis, Platt et al,[81] of 3 types of studies, which found that use of an SSP combined with opioid agonist therapy resulted in a significantly lower risk of HCV transmission (RR = 0.26, 95% [CI 0.07, 0.89], with a larger effect size than was seen for SSP use or opioid agonist therapy alone. This finding was consistent with another meta-analysis[91] of 2 cohorts and 4 cross-sectional studies included in the original 2010 review of reviews.[78] That meta-analysis also reported that combined SSP and opioid agonist therapy was associated with 48% reduction in odds of self-reported needle sharing (aOR = 0.52, 95% CI [0.32, 0.83]).

Additional Harm Reduction and Referral Services

Whether motivational interviewing or strengths-based case management improves treatment enrollment among PWID using an SSP is unclear (Table 8). A trial[92] of a motivational interviewing intervention among PWID accessing a SSP in Baltimore found no difference in treatment entry. Findings were mixed with regard to strengths-based case management, with 1 trial[93] conducted among PWID using an SSP in Baltimore finding that case management after treatment referral resulted in greater treatment entry (OR = 1.84, 95% CI [1.07, 3.16]), and another trial of a similar case management intervention among PWID in Sweden with high enrollment rates overall finding no effect.[85] In the Baltimore trial, intention-to-treat analysis controlling for distance to travel, access to care, and clustering by SSP site did not show a difference in treatment enrollment between intervention and control groups, leading authors to conclude that benefits of case management could be attributed to the provision of transportation.

Whether harm reduction education and referral to services offered by staff at a pharmacy-based SSP improves injection risk behaviors, safe syringe disposal, or treatment uptake is also unclear (Table 8). In a trial[29] conducted in New York City in which pharmacies were randomized to offer harm reduction services or usual care, no benefit was seen among PWID using intervention group pharmacies in regard to injection frequency, syringe sharing, safe syringe disposal, or receipt of detoxification or drug treatment.

Table 8. Additional Harm Reduction Services[a]

SSP Approaches	Evidence	Findings
Motivational interviewing	1 SR[2] (1 RCT[92])	Treatment enrollment: No difference in treatment entry with a motivational interviewing intervention
Strength-based case management services	1 SR[2] (1 RCT[93]), 1 RCT[85]	Treatment enrollment: A strength-based case management intervention delivered after treatment referral resulted in greater treatment entry,[93] while a similar intervention delivered prior to treatment referral did not result in greater treatment enrollment among a population with high enrollment rates overall (95% in the intervention group and 94% in the control group)[85]
Harm reduction education and referral to services	1 RCT[29]	No difference in injection frequency, syringe sharing, safe syringe disposal, or receipt of detoxification or drug treatment between pharmacy-based SSPs randomized to offer harm reduction services[b] compared to usual care

Notes. [a] Two RCTs were included in the Jones 2010 SR and 2 were published after this review and were included as primary studies in our review; [b] HIV prevention/medical/social service referrals, syringe disposal containers, and harm reduction print materials.

Abbreviations. HIV=human immunodeficiency virus; RCT=randomized controlled trial; SR=systematic review; SSP=syringe services program.

DISCUSSION

This review aimed to integrate a large and complex evidence base on the effectiveness and potential harms of SSPs to inform VHA policies and program development. Reducing harms due to substance use is a goal of the Office of National Drug Control Policy,[71] as well as VA Offices of Mental Health and Suicide Prevention, Research and Development, and Specialty Care Services.

Findings of this review are based on more than 4 decades of research on SSPs. Despite broad changes in drug use patterns and shifts in policies related to how SSPs are permitted to operate, findings regarding the effectiveness of SSPs have been largely consistent over time. A 2022 review of reviews[1] found sufficient evidence that SSPs prevent HIV transmission among PWID and tentative evidence that SSPs prevent HCV transmission. Studies of HCV prevention had less consistent results compared to studies of HIV prevention, but it is unknown whether the weaker benefit in terms of HCV prevention is primarily due to study factors (such as the ways SSP use was defined and measured in studies evaluating HCV transmission) or differences in HIV and HCV transmissibility. Additionally, the relatively recent availability of curative therapy options for HCV is likely altering the epidemiology of HCV in ways that have not yet been reflected in available evidence. Combined SSP and opioid agonist treatment may improve HCV prevention to a greater degree than either intervention alone.

The same 2022 review of reviews[1] found sufficient evidence that SSP use reduced injection risk behaviors, an important intermediate outcome when considering that a primary aim of SSPs is to prevent infectious disease transmission. SSP use may also be associated with increased treatment linkage and/or use of treatment services among PWID compared to no SSP use (or less use).

SSP use does not appear to increase injection frequency among PWID, result in an increase in unsafe syringe disposal practices, or directly increase neighborhood crime rates. Authors of a 2012 ecological study[48] of arrest trends in proximity to SSP locations in New York City noted "the spatial overlap of these two features of the risk and protective environment likely reflects their shared target population and target behaviors." This framing underscores the point noted by several study authors that SSPs serve a segment of the PWID population with a higher baseline risk for drug-related harms, including legal system involvement. Despite this higher baseline risk, we found no evidence that SSP use further heightens risk to PWID or communities.

Studies of public health interventions in real-world settings often must rely on observational research methods that are intrinsically less rigorous than study designs available in clinical contexts. These methodological limitations lower the strength of available evidence for individual SSP outcomes (see Appendix). However, when looking across outcomes, the preponderance of evidence demonstrating the potential benefits of SSPs and relative lack of harms is more than sufficient to support SSP implementation when possible. This overall conclusion is consistent with recommendations from several public health organizations and professional societies regarding the role of SSPs in harm reduction, including statements from the CDC describing SSPs as "safe, effective, and cost-saving" (see Table 9).

Table 9. Public Health Organization and Professional Society Statements Regarding SSPs

American Academy of Addiction Psychiatry[94]	Supports the funding and development of programs that assist people, who are injecting drug users, to have increased access to clean needles and syringes to help them eliminate all reusing and sharing of needle syringes.
American Bar Association[95]	Expressed support in 2011 for continuation of federal funding for syringe exchange programs, which the association maintains are an effective public strategy for reducing the transmission of HIV/AIDS in the United States.
American Medical Association[96]	The AMA strongly supports needle and syringe exchange programs as part of a wider harm reduction approach to treating substance abuse and addiction.
American Public Health Association[97]	State and local health departments, tribal leaders and/or councils, and community agencies should implement comprehensive SSPs for people who inject drugs to mitigate the risk of blood-borne infections (HIV and HCV) at the community level.
Centers for Disease Control and Prevention[98,99]	Nearly 30 years of research shows 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.
European Centre for Disease Prevention and Control and European Monitoring Centre for Drugs and Drug Addiction[100]	2011 guidance states that provision of, and legal access to, clean drug injection equipment, including sufficient supply of sterile needles and syringes, free of charge, as part of a combined multi-component approach implemented through harm-reduction, counseling, and treatment programs, is a key intervention component for prevention of infections among PWID.
Joint United Nations Progamme on HIV/AIDS (UNAIDS)[101]	Given the prominence of unsafe injecting drug use due to the limited availability of needle and syringe programs in the HIV epidemics in many countries, comprehensive harm reduction services are vitally important, including in prisons and other closed settings. The services therefore should include needle and syringe programs, opioid substitution therapy and naloxone, and should address the specific needs of women who use drugs.
World Health Organization[102]	Evidence from 20 years of research shows that needle and syringe programs prevent, control, and ultimately reduce prevalence of HIV and other blood-borne infections among injecting drug users.

Abbreviations. AMA=American Medical Association; HCV=hepatitis C virus; HIV=human immunodeficiency virus; PWID=people who inject drugs; SSP=syringe services program.

Limitations

The existing evidence base has several limitations. First, studies used different measures for SSP exposure (*eg*, number of visits, percent of syringe coverage, *etc*) and outcomes, limiting our ability to compare results across studies in some cases. Second, many studies relied on participant self-report for both SSP use and outcomes of interest. In general, participant self-report has potential for recall bias and social desirability bias. Third, observational studies have potential bias due to uncontrolled confounding. While several studies used adjusted analyses to minimize the effect of confounding variables, effect estimates could still be skewed by unmeasured confounders. Finally, even though study periods span 4 decades, most studies were conducted in urban populations and prior to the current era of substance use in which illicit fentanyl and methamphetamine use is more common.

Although most findings discussed in this review are broadly applicable to a range of populations and settings, whether specific benefits of SSPs apply to all segments of PWID is unclear.

FUTURE RESEARCH

Despite some evidence gaps, additional research on existing SSP models may not be of practical value to health care policymakers given that available evidence is sufficient to support SSP implementation when possible. However, given that drug use patterns are constantly evolving and often regionally specific, future research on strategies to improve the responsiveness of SSPs to shifts in drug use patterns would be informative. For example, studies included in this review were largely conducted prior to the emergence of xylazine as a more common component of the illicit drug supply.[103] Future research could examine best practices to provide PWID with tools and information needed to reduce harms associated with xylazine exposure.

We note that studying SSPs presents several methodological challenges. One challenge is how to compare findings across SSPs, which may have inconsistent approaches to defining and measuring outcomes.[104] Another challenge is integrating data sources to derive valid and meaningful conclusions. A recent study using administrative data to evaluate links between SSPs openings and drug-related health outcomes illustrates this point.[105] In this study, the author concluded that SSPs increase rates of opioid-related mortality based on an analysis of county-level data on SSP openings and overdose fatalities. However, this analysis has been criticized for assuming that because an association exists between an exposure and an outcome at the population level, it exists at the individual level (a concept known as ecological fallacy).[106] Future researchers have the benefit of learning from decades of research on SSPs and should take care to avoid known causes of data misinterpretation.

CONCLUSIONS

SSP utilization likely results in lower HIV transmission and reduced injection risk behaviors, and may result in lower HCV transmission, promote carrying naloxone, increase exposure to overdose education, and facilitate referral to and enrollment in treatment services. SSP use and presence in communities does not appear to increase injection frequency, unsafe syringe disposal practices, or neighborhood crime rates. Combined SSP and opioid agonist treatment may improve HCV prevention to a greater degree than either intervention alone. The effectiveness of other SSP program components or practices has been less frequently studied and evidence is insufficient to draw conclusions regarding best practices. Overall, when viewed as a harm reduction intervention, SSPs appear to offer a range of potential benefits without evidence suggesting that SSPs introduce harms or other unintended consequences.

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