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Evidence of the Impact of Harm Minimization Programs

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Abstract

People who use drugs (PWUD) account for around 275 million worldwide, with a prevalence of those who inject drugs (PWID) ranging from 0.18–0.30%. Drug injecting behaviors are often associated with harmful forms of use, leading users to higher risk of infectious diseases, overdose, and death caused, among others, by unsafe practices such as shared needles and syringes. Additional burden from drug use includes costs related to crime combating, social consequences of drug behavior, and lost productivity. From a public health perspective, harm minimization measures – defined as a range of interventions aiming at addressing the negative effects of drug use on both individuals and society – can be implemented for those who are unable or unwilling to stop using drugs. The most common interventions to minimize drug-related harm include access to naloxone, opioid substitution therapy, supply reduction interventions for opioids, integration of testing and treatment of blood-borne diseases, nonprescription sales or provision of sterile syringes, and supervised drug consumption facilities. In this chapter, we provided a brief overview of drug use disorders and synthetized the evidence around the impact of the available interventions to reduce the harm associated, especially, with injectable drug use. Moreover, the contribution of pharmacists to harm minimization interventions was also revised and discussed in the context of pharmacy practice.

Keywords

Harm minimization · People who inject drugs · Needle and syringe exchange program

Introduction

Around 83 million people or 30% of adults (aged 15–64) in the European Union are estimated to have used illicit drugs (i.e., abuse substances prohibited under international drug control treaties including opioids, cocaine, amphetamines, and

Z.-U.-D. Babar (ed.), *Encyclopedia of Evidence in Pharmaceutical Public Health and Health Services Research in Pharmacy*, https://doi.org/10.1007/978-3-030-50247-8_18-1

cannabis) at least once in their lifetime, with patterns of drug use ranging from occasional and recreational to dependence (European Monitoring Centre for Drugs and Drug Addiction 2021). Globally, in 2019, it was estimated that around 275 million people use drugs – PWUD (Elflein 2021). These figures may be underestimated given, among others, the disproportionate impact of the global COVID-19 pandemic in consumption patterns. While the consumption of certain illicit substances, such as cocaine and heroin, decreased in the initial months of the pandemic – probably given declines in social gatherings and disruptions in supply, consumption of other substances such as prescription medications increased (European Monitoring Centre for Drugs and Drug Addiction – EMCDDA 2020; Ali et al. 2021).

This chapter focuses on drug use disorders that may arise from the consumption of drugs (either licit or illicit). The term "drug" can also be considered a synonymous to "medicine," however, in the context of this chapter, that is only the case when referring to opiates. We intentionally omit the term "illicit" because drug policy varies widely across the world.

Cannabis (marijuana) is still the most used drug worldwide (i.e., consumed up to five times more frequently than any other drug) followed by opioids and opiates. Yet, polydrug consumption (i.e., drugs combined) is also very common (European Monitoring Centre for Drugs and Drug Addiction 2021; Mental Health Services Administration – SAMHSA 2019). The continual introduction in the market of novel addictive substances alongside with this polydrug consumption significantly increases the related health risks (e.g., side effects, intoxication and, co-occurring chronic conditions, including mental health disorders) and the need to adapt preventive and treatment measures. Globally, drug use is responsible for over 750,000 deaths every year, resulting from premature death caused by injury (including suicide and overdose) or diseases related to drug dependency (including liver disease, hepatitis, cancer, and human immunodeficiency virus – HIV). Because the profile of PWUD dying in the USA is of a younger age, the impact of these behaviors on years lost is worrisome (European Monitoring Centre for Drugs and Drug Addiction 2021; Mental Health Services Administration – SAMHSA 2019).

Although drug injecting behaviors have been declining in several regions, including in Europe, for the past decade, they are often associated with harmful forms of use, leading people who inject drugs (PWID) to have higher risk of acquiring blood-borne infectious diseases (e.g., HIV; hepatitis B and C virus – HBV and HCV) from unsafe practices, including shared drug use material. The global prevalence of PWID was estimated between 0.18% (low-risk use) to 0.30% (high-risk use) in 2017 (United Nations Office on Drugs and Crime (UNODC) 2017). Among injecting drugs, heroin (31% are used through this route) and methamphetamines (29%) appear on top; yet, other illicit drugs may also be injected (e.g., 3% of amphetamine users and 2% of cocaine users) (European Monitoring Center for Drugs and Drug Addiction 2021). It is estimated that 0.73–1.55% of the global population (aged 15–64) have used opioids in the past year, while approximately 0.46% have used amphetamines (Elflein 2021). In Europe, the prevalence of high-risk opioid use among adults is estimated at 0.35%, equivalent to 1 million high-risk opioid users in 2019 (European Monitoring Centre for Drugs and Drug Addiction 2021). These figures are important as opioids are responsible for the largest number of drug overdoses, associated with 76% of fatal cases reported in the European Union in 2019. In this same year, opioid users accounted for 26% of drug treatment requests (European Monitoring Center for Drugs and Drug Addiction 2021). In the USA, overdoses were the leading cause of death in adults under 50 years in 2017 (Elflein 2021). An increase of around 90%, compared to the previous year, in suspected illicit drug toxicity deaths was reported in Canada shortly after the pandemic started (British Columbia Coroners Service 2020; The Ontario Drug Policy Research Network – ODPRN 2020).

Globally, it is estimated that 17.9% of PWID engaged in receptive needle/syringe sharing at last injection, 23.9% in the previous month, and 32.8% in the previous 6–12 months (Tran et al.

2020). These unsafe injection practices among PWID led to rising rates of viral, severe bacterial, and fungal infections. In 2019, 5.5% of the new HIV diagnoses were attributed to unsafe drug use in Europe. In 2018 in the USA, this same rate was of 9%. The incidence of HCV transmission is also high among PWID; between 2018 and 2019, a HCV antibody prevalence varying from 15–86% was reported across 15 European countries. Even though the lowest, the prevalence of active HBV infection was of 4% between 2018 and 2019 in Europe (ranging from 0.4% in Latvia to 8% in Spain) (European Monitoring Center for Drugs and Drug Addiction 2021; Centers for Disease Control and Prevention – CDC 2019, 2020).

Drug use also carries additional burdens, namely costs associated with combating crime, health care needed, social consequences of drug behavior, and lost productivity. Therefore, from a public health perspective, there are two possible approaches to manage PWID: rehabilitation, where drug use is abandoned and people may then find and establish a productive life, or harm minimization measures for those who are not ready to quit (e.g., unable or unwilling to stop), aiming at reducing the chances of contracting and transmitting infection diseases by injecting drugs in an unsafe manner (Sawangjit et al. 2017). In many countries policy initiatives have been developed to reduce drug use–related harm, including outreach programs, rehabilitation clinics, and replacement therapies, and supply of sterile needles (Des Jarlais et al. 2013; Kaplan et al. 1994; van Ameijden et al. 1995; Lennings 2000). As of 2020, over 90 countries had one or more programs using a harm reduction approach to drug use (Harm Reduction International – HRI 2020).

Harm minimization refers to a range of public health interventions aiming at addressing the negative consequences of drug use (from a health, societal, and economic perspectives) on individuals and society. These include a decrease in the need for health care by PWID, a decrease in side effects associated with unsafe consumption patterns, lower risks of overdose, a decrease in mortality rates, an increase in social productivity, and a decrease in criminal activity, to name a few (Lennings 2000; Department of Health – Australian Government 2004). The first harm reduction policy developed emerged in 1985 in response to the outbreak of HIV/AIDS, implemented through the exemption of the criminality associated with the issue of individual rights and sexual behaviors that led to the spread of this disease and placed the responsibility on the rest of society to prevent harm. In time, this same policy was adopted in respect of PWID as it was assumed that injecting drugs was a primary means of transmission of HIV and other infections. Thus, the paradigm of focusing the treatment of drug use disorders by aiming to change addictive behaviors shifted toward harm reduction, through which there was a recognition that by providing PWID with the means to safe practices (e.g., sterile injecting equipment, condoms) their chances of acquiring HIV would significantly reduce (McKeganey 2006; Steenholdt et al. 2015).

Key features and principles that should be considered during harm minimization measures include the following (Steenholdt et al. 2015):

- The primary aim should be reducing harm rather than drug use per se.
- All measures should be grounded on evidence-based analysis (i.e., strategies to demonstrate, on balance of probabilities, a net reduction in harm).
- It is important to accept that drug use is deeply embedded in society and will hardly ever be eliminated.
- Harm minimization should provide a comprehensive public health framework.
- Priority should be placed on immediate and achievable goals.
- Pragmatism and humanistic values should underpin harm minimization strategies.

Today, 35 years after of the introduction of the harm minimization concept, strategies are broadly classified into three: (i) harm reduction – helping to reduce harm arising from drug use for those who continue to use drugs; (ii) supply reduction – reducing and controlling the amount of drug available; and (iii) demand reduction – encouraging

people not to use, to delay use, or to use less of a drug (Department of Health – Australian Government 2004; Zinberg 1984). These strategies should consider the interaction between the individual, the environment, and the drug (according to Zinberg's Interaction Model – Zinberg 1984) and may be delivered in several settings, by varied providers, including, but not restricted to, health care professionals. Most common interventions to harm minimization include:

- Access to naloxone (i.e., naloxone dispensing without an outside prescription such as take-home naloxone programs or THN)
- Opioid substitution therapy – OST (e.g., methadone)
- Supply reduction interventions for opioids (e.g., prescription monitoring programs, tamper-resistant formulations, and prescribing limits)
- Integration of testing and treatment of blood-borne diseases (HIV, HCV, and HBV), by screening and point-of-care testing initiatives, and promoting access to treatment, including PrEP (pre-exposure prophylaxis) and PEP (post-exposure prophylaxis) consultation
- Nonprescription sales or provision of sterile syringes (needle and syringe exchange programs – NSEP or SSP) including in supervised drug consumption facilities or supervised injection facilities (SCF, SIF)

NSEP, one of the most common harm minimization interventions, aimed at effectively counseling PWID about safe injection techniques (e.g., drug preparation and injection equipment), reducing the transmission of infections by decreasing equipment sharing, delivering overdose prevention/education, administering vaccinations, and also facilitating referrals for medication for drug use disorders (Des Jarlais et al. 2013; Thakarar et al. 2021; US Agency for International Development – USAID 2010). Barriers in access to sterile syringes experienced by PWID has been acknowledged in certain areas. Having a sterile syringe available when needed is the basic assumption of any intervention focused on supply of needles, including programs developed to motivate discarding used ones (Meyerson et al. 2019). These services can be provided through pharmacies, primary health clinics, nongovernmental organizations (NGOs) or health workers running vans conveniently located, and vending machines. The first NSEP was introduced in the Netherlands in 1984 by a drug user organization (van Ameijden and Coutinho 1998) and many more countries have followed. In 1993, Portugal created its own NSEP, making it available through NGOs and through community pharmacies, including the distribution of sterile syringes but also material for safe injection (e.g., distilled water and bleach) and safe sex (e.g., condoms). Although many other factors come into play for the changes in the patterns of new HIV or hepatitis infections, it is worth mentioning the notable reduction among PWID from 57.3% in 1998 to 1.8% in 2017 in Portugal (Direção Geral de Saúde 2018). Similarly, NSEP in other countries showed substantial benefit by reducing infections transmission safely, effectively, and cost-effectively (Logez et al. 2005; Heinzerling et al. 2006; Kwon et al. 2019).

Thus, this chapter aims to provide a brief overview of drug use disorders as a reason for concern in public health and to synthetize the evidence around the impact of the available interventions to reduce or minimize the harms associated, especially, with injectable drug use. Moreover, the contribution of pharmacists to harm minimization interventions is also revised and later discussed in the context of pharmacy practice.

Methods for Searching the Literature

A systematic review was conducted on PubMed (https://pubmed.ncbi.nlm.nih.gov/) in August 2021, aiming at identifying studies on the effect of harm minimization or harm reduction interventions targeting injectable drug users. No filters were used for language or period of publication. Limits were only imposed on the type of publication, where only overviews, systematic reviews, or meta-analysis were analyzed (see Complete Search Strategy in Appendix I). After duplicates

removal, recovered studies had their titles screened for the initial selection and a subsequent analysis of their abstract led to the decision to include them in the pooled records. The selection of papers was made by two independent authors and then discussed. Articles' consensus about their relevance to this chapter was established, as well as had their data (e.g., articles' authors and year of publication, description of the intervention, setting, and main outcomes) extracted and qualitatively summarized.

Main Findings and Discussions

Overall Evidence of the Effect of Harm Minimization Interventions

The review initially identified 61 records after duplicates removal, of which 25 were considered relevant to be briefly addressed in this chapter (see Table 1 for studies' overall information). These studies were published between 2000 and 2021, being mostly designed as qualitative systematic literature reviews ($n = 14$; 56%), including different primary studies (ranging from randomized controlled trials, observational studies to clinical audits). Nine systematic reviews additionally performed statistical analyses (i.e., meta-analysis or meta-synthesis). The most evaluated intervention was NSEP in PWID ($n = 8$; 33%). Combined or mixed interventions including behavioral and engagement interventions accounted for another eight systematic reviews. Naloxone access programs (i.e., THN), HIV/HCV testing and treatment interventions, and supervised facilities (SCF or SIF) were evaluated in two studies each. Only two articles (8.0%) published by Fernandes et al. (2017) and Sawangjit et al. (2017) specifically synthetized evidence on the impact of pharmacist-led harm minimization interventions (see section "Evidence of Impact of Pharmacist-Led Harm Minimization Interventions" of this chapter).

Access to Naloxone: Take-Home Programs (THN)

In the past years, THN programs became an integral overdose prevention strategy aiming at reducing the number of overdose deaths related to the growing epidemic of opioid use being implemented in Australia, Europe, and the USA. In these programs, participants are trained to recognize and respond to an opioid overdose and provide them with a packaged kit that includes naloxone, an opioid antagonist that temporarily reverses opioid toxicity. Previous studies showed an important association between THN programs and overdose survival, with successful overdose reversals rates (Bird et al. 2016; McDonald and Strang 2016; Chronister et al. 2018). Among the included studies in this chapter, Ansari et al. (2020) and McAuley et al. (2015) systematically reviewed the literature on the effect of naloxone programs as opioid policy interventions (Ansari et al. 2020; McAuley et al. 2015).

The recent review published by Ansari et al. (2020) focused on six studies performed in the USA and Canada on the distribution of naloxone kits as part of a harm minimization strategy for PWUD. Other policies broadly discussed by the authors included prescription drug monitoring programs, pain clinic regulations, and clinical guideline changes. The evidence on the impact of THN was mixed; while some studies showed a decrease in overdose deaths after a police naloxone training and distribution of the kits in some states of the USA ($p = 0.03$), others demonstrated no changes on opioid-related overdose. No benefits were observed in studies examining combined overdose education and naloxone distribution. No studies assessed the impact of harm minimization interventions on transmitted infections. Authors concluded that naloxone distribution programs are still understudied and that this inconclusive evidence is a consequence, among others, of the scarcity of well-designed and conducted studies in this field and lack of standardized outcome measures (Ansari et al. 2020).

On the other hand, McAuley et al. (2015) determined the effect size for THN program as a primary response to PWUD by means of a descriptive meta-analysis. Overall, six studies were included, resulting in a 9.2 (ranging from 5.2–13.1) rate of naloxone uses every 3 months for every 100 PWUD trained. This means that around 9% of naloxone kits distributed are likely to be used for peer administration within the first

Evidence of the Impact of Harm Minimization Programs, Table 1 Summary of studies on the impact of harm minimization interventions

Author, year	Study design	Main goal	Included studies[a]	Intervention delivered[a]	Setting	Population included	Outcomes reported	Main findings
Ansari et al. (2020)	SLR	To assess the effect of policies and interventions on opioid use, overdose, and deaths	Six comparative studies (RCT, cross-sectional, pre-pros design)	Naloxone distribution programs	Any health facility in the USA or Canada	PWUD	Opioid use Opioid-related overdose Opioid-related death	Mixed and inconclusive evidence on the effect of naloxone distribution programs given the scarcity of well-performed studies
Aspinall et al. (2014)	SLRMA	To assess between NSEP and HIV transmission	12 observational studies (cohort, cross-sectional, case-control)	NSEP	Fixed sites, pharmacies, outreach services	PWID	HIV incidence	NSP is effective in reducing the transmission of HIV among PWID, although other harm reduction interventions can contribute to these findings. Most studies had moderate-high quality
Awungafac et al. (2017)	SLR	To evaluate the effectiveness of SW interventions in sub-Saharan Africa	Two studies (RCT, cross-sectional)	Combined interventions to reduce harm	Adapted health services	SW PWUD or alcohol users	HIV incidence Frequency of violence Engagement in SW Number sex partners Frequency of drinking Condom use STI incidence	Evidence on harm minimization combined interventions in this setting is extremely poor; initial data show a slightly decrease of violence and sex partners; increase of condom use and reduction of drinking. No impact on HIV were found.
Caven et al. (2019)	SLR	To evaluate the effect of HCV treatment on substance use behavior in PWID	Five quantitative or mixed-method studies	Hepatitis C diagnosis and treatment (combined intervention)	Hospitals, GP/primary care, community clinics, provision services	PWID	Injecting behavior Sharing needle/syringe Sharing equipment	Evidence was inconclusive due the high heterogeneity among studies; treatment engagement may have a positive impact in PWID equipment sharing behavior

Coats and Dillon (2015)	SLR	To evaluate the impact of novel testing methods in the number of HCV diagnosis in PWID	Six studies (RCT, cohort, ecological clinical audit)	DBS or PoC testing	Clinics, prisons, provision services, and health boards	PWID	Test uptake New HCV diagnosis	No studies with PoC were found. Five of the six studies provided moderate-high methodological quality evidence that DBS testing increased the number of tests and new diagnoses
Copenhaver et al. (2006)	SLRMA	To evaluate behavioral HIV risk reduction interventions in PWID	37 RCT	Group or individual behavioral HIV prevention intervention	Any health setting	PWID	Injection frequency Entry drug treatment Sharing needle/ syringe Sharing equipment Condom use Trading sex for drugs Unprotected sex	Behavioral interventions reduced injection ($p < 0.001$) and noninjection drug-use ($p = 0.028$), trading sex for drugs ($p = 0.052$), increased condom use ($p = 0.017$) and drug treatment entry ($p = 0.013$). No effects on needle/syringe borrowing were observed
Davis et al. (2017)	SLRMA	To assess the association between NSEP and HCV prevention	Six observational studies (cohort, case-control)	NSEP	Any health setting	PWID	Association between HCV seroconversion and participation in NSEP	Evidence is mixed and inconclusive; no consistent association on NSEP and reduction of HCV was found. Studies have substantial heterogeneity and large inconsistency
Fernandes et al. (2017)	Overview	To assess the effect of community-based NSEP on HIV, HCV, HBV, and bacteremia or sepsis	13 systematic reviews	Pharmacy-based NSEP	Any health facility excluding prisons and consumption rooms	PWID	HIV transmission HCV transmission HVB transmission Injecting behavior	NSEP was effective in reducing HIV transmission and injecting risk behaviors among PWID Data on HCV was mixed and inconclusive The heterogeneity and the overall low quality of evidence highlights the

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Evidence of the Impact of Harm Minimization Programs, Table 1 (continued)

Author, year	Study design	Main goal	Included studies[a]	Intervention delivered[a]	Setting	Population included	Outcomes reported	Main findings
								need for future community-level studies of adequate design
Gillies et al. (2010)	SLR	To determine whether NSEP reduces injecting risk behaviors or HCV transmission	13 observational studies (cohort, cross-sectional)	NSEP	Provision services, safer injection facilities	PWID	HCV incidence HCV prevalence Injecting behavior	Eight studies presented adjusted odds ratios, ranging from 0.3 to 0.9, suggesting a reduced likelihood of sharing of equipments However, estimates are uncertain given the low quality of studies and volume of evidence
Islam et al. (2012)	SLR	To assess data on strategies to enhance the access of PWID-target primary care interventions	35 documents (primary studies, reports)	Primary care interventions (e.g., NSEP, OST)	Any clinical facility such as outreach or drop-in	PWID	Access to the intervention Acceptability of the intervention Operational challenges	Different interventions and models proven accessible and acceptable such as NSEP, OST, HCV/HIV treatment, social and welfare services, being provided by medical, nursing, counseling staff. However, the heterogeneity among studies hampers further systematic evaluations
Jones et al. (2010)	SLR	To assess the effectiveness of NSEP	16 studies (RCT, cohort, cross-sectional, pre-post design)	NSEP	Any health setting	PWID	Injecting behavior Incidence of BBV Prevalence of BBV Entry drug treatment	Most studies ($n = 11$) showed no evidence of an impact of different NSEP on drug injecting behaviors Given the reduced quality of studies, it is difficult to draw further conclusions

							Use of health services	
Kennedy et al. (2017)	SLR	To evaluate health and community impacts of SCFs	47 quantitative studies (cohort, cross-sectional, ecological)	SCF	SCF in any country/region	PWID	Individual- or population-level health or social outcomes	Overall evidence demonstrates that SCFs mitigate overdose-related harms and unsafe drug use behaviors Yet, no meta-analyses were performed; outcomes are not standardly reported
Ksobiech (2006)	SLRMA	To evaluate the societal impact of NSEP in controlling the spread of HIV/AIDS	31 observational studies	NSEP	Any health setting	PWID	Risky context Injection frequency Sharing needle/ syringe Syringe use	NSEP attendance was inversely related to decline of most outcomes; however, given the high heterogeneity among studies, data should be carefully interpreted
Levengood et al. (2021)	SLR	To assess the effectiveness of SCF/SIF	22 comparative studies	SCF/SIF	SCF/SIF in any country/ region	PWID	Overdose-induced mortality Overdose-induced morbidity Injecting behavior Access to treatment Crime, public nuisance	In some studies, SIF were associated with reductions in overdose morbidity/ mortality ($n = 5$), improvements in injection behaviors ($n = 7$), access to addiction treatment ($n = 7$), but heterogeneity in outcomes' measures hampers further conclusion
Marshall et al. (2015)	SLR	To evaluate the role of PWID in harm reduction initiatives, programs, and policies	164 documents (primary studies, reports)	Education Support Counseling Direct harm reduction Policy creation	Any health setting	PWID	Approaches to interventions delivery Obstacles, facilitators for interventions implementation	Current evidence provides good descriptive content, but the field lacks agreed-upon approaches to documenting the ways PWID contribute to harm reduction initiatives

(continued)

Evidence of the Impact of Harm Minimization Programs, Table 1 (continued)

Author, year	Study design	Main goal	Included studies[a]	Intervention delivered[a]	Setting	Population included	Outcomes reported	Main findings
McAuley et al. (2015)	SLRMA	To assess the impact of THN programs	9 observational studies (cohort, cross-sectional)	THN	SCF/SIF, drug treatment centers, prisons	PWUD	Number of peer naloxone administration Opioid-related overdose	The meta-analysis showed a range of 5.2–13.1 (point estimate 9.2) naloxone uses every three months for every 100 PWUD trained in THN Evidence shows successful reversals and the lack of reported adverse events
McNeil and Small (2014)	SLR	To evaluate PWID's experience with tree safer environment interventions	22 qualitative studies	NSEP SCF/SIF Peer-based harm reduction interventions	Urban or semiurban settings	PWID	Individual, collective experiences with interventions	Safer environment interventions may mitigate drug-related harms by providing refuge from street-based drug scenes, safer injecting, and mediated access to resources/health services Qualitative synthesis in this field is needed
Merson et al. (2000)	SLR	To review the effectiveness of programs to reduce sexual transmission of HIV	34 documents (primary studies, reports)	Behavior change Education, counseling Harm reduction interventions	Any health setting	PWID	Transmission of HIV	HIV prevention interventions can be effective in changing risk behaviors and preventing transmission in low- and middle-income countries. Few studies have evaluated harm reduction interventions in PWID; evidence is scarce
Platt et al. (2017) and Platt et al. (2018)	SLRMA	To assess the effect of interventions (NSEP, OST) for preventing HCV in PWID	28 observational studies (cohort)	NSEP OST	Any health setting	PWID	HCV incidence HCV acquisition risk	HCV incidence ranged from 0.09–42 cases per 100 person-years. OST reduced the risk of HCV (RR 0.50 [95% CI

								0.40–0.63]); NSEP did not change this outcome (RR 0.79 [95% CI 0.39–1.61]). Most studies had serious/critical risk of bias (low quality)
Sawangjit et al. (2017)	SLRMA	To evaluate the effectiveness of pharmacy-based NSEPs on risk behaviors, HIV/HCV prevalence and economic outcomes	14 comparative studies (cohort, cross-sectional, pre-post design)	Pharmacy-based NSEP	Pharmacies	PWID	Risk behaviors (RBs) HIV prevalence HCV prevalence Economic outcomes	Pharmacy-based NSEP programs appear to be effective for reducing risk behaviors among PWID (OR 0.50 [95% CI 0.34–0.73], I2 = 59.6%), but their effect on HIV/HCV prevalence and economic outcomes are still unclear
Singh et al. (2014)	SLR	To evaluate the effectiveness in response to HIV in Pakistan	97 documents (primary studies, reports)	Harm reduction interventions	Any health setting	HIV patients	Risk analysis of HIV burden Discuss implemented interventions	Injecting drug users accounted for 36.4% of HIV cases Implemented harm minimization measures included: NSEP, OST, condoms, STI, prevention education through outreach, and peer and social support
Stockings et al. (2016)	SLR	To assess the effectiveness of prevention, early intervention, harm reduction, and treatment of problem	15 documents (primary studies) focusing on illicit drug use	Brief interventions (reduce drug use) Roadside drug testing Harm reduction interventions (injection related)	College-based Primary care General settings	Young users of tobacco, alcohol, or illicit drugs	Drugs used Problematic use Injury or harm	Mixed findings and insufficient evidence were reported regarding BI and harm reduction interventions in PWUD. Scarce availability of research with young people indicates the need to test further interventions

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Evidence of the Impact of Harm Minimization Programs, Table 1 (continued)

Author, year	Study design	Main goal	Included studies[a]	Intervention delivered[a]	Setting	Population included	Outcomes reported	Main findings
Suthar et al. (2013)	SLRMA	To review the evidence on community-based testing and counseling facilities	19 studies (RCT, observational studies)	HIV mobile testing and counseling for PWID	Facility based for testing and counseling	People at risk or with HIV	Uptake Proportion receiving first HIV test CD4 value at diagnosis Linkage to care HIV incidence Facility coverage	Uptake among PWID ranged to 14–94% with heterogeneity related to how testing was offered. No differences between community versus facility-based approach were found
Turner et al. (2011)	SLRMA	To evaluate the effect of NSEP and OST in HCV transmission in PMID	Six individual-level data studies	NSEP OST	Any health setting	PWID	HCV incidence Injecting behavior Number of injections	Using individual-patient data, OST and NSEP led to a reduction in new HCV infection (AOR 0.41 [95% CI 0.21-0.82] and 0.48 [95% CI 0.25–0.93], respectively) OST + NSEP (full harm reduction) decreased needle sharing by 48% and mean injecting frequency by 20 injections/month. Data heterogeneity was moderate

[a]Data related only to harm minimization or harm reduction interventions

AOR adjusted odds ratio, *BBV* blood-borne viral infections, *CI* confidence interval, *DBS* dried blood spots testing, *NSEP* needle and syringe exchange program, *PoC* point-of-care testing, *PWID* people who inject drugs, *PWUS* people who use drugs, *RR* risk ratio *OST* opioid substitution therapy, *RCT* randomized controlled trial, *SCF* supervised drug consumption facilities, *SIF* supervised injection facility, *SLR* systematic literature review, *SLRMA* systematic literature review and meta-analysis *STI* sexually transmitted infections, *SW* sex workers, *US* USA, *THN* take-home naloxone program

trimester of supply for this population. Further studies should assess the effectiveness of these THN programs and differences among training structures as this may affect the rate of naloxone use (McAuley et al. 2015).

According to Mueller et al. (2015), THN studies usually focus on overall program evaluation, experiences, and attitudes of program participants; willingness of medical providers to prescribe naloxone; and comparison of different routes of naloxone administration. The literature on the long-term effectiveness and cost-effectiveness of these programs, especially in community-based settings, is heterogenous and somewhat inconclusive, which may be a barrier for the implementation of the programs and the enrollment of participants (Ansari et al. 2020; Mueller et al. 2015).

NSEP and OST Approaches

As previously mentioned, the implementation of NSEP and similar programs has been associated with benefits (e.g., reduction in new HIV and hepatitis infections) according to some reports in different countries (Direção Geral de Saúde 2018; Logez et al. 2005; Heinzerling et al. 2006; Kwon et al. 2019). However, given the complexity of these interventions, implementation, and performance (e.g., accounting for several components), as well as the differences across settings (e.g., type of facility/delivery, as well as participants characteristics) and geographical regions, results are usually heterogenous and the true effect of these programs in real-world settings may be over or underestimated. We found eight different systematic reviews assessing the effects of NSEP or OST interventions in different scenarios.

Aspinall et al. (2014) synthetized the evidence on the association between NSEP and HIV (n = 12 studies) and found a potential reduction in the transmission of this disease among PWID beneficiaries of this program (odds ratio – OR of 0.66 [95% confidence interval – 95% CI 0.43–1.01]) for all studies. By restricting the analysis to studies considered of high quality (n = 6 trials), a significant result favoring the intervention was obtained: OR 0.42 [95% CI 0.22–0.81]. Yet, authors believe that it is likely that other harm reduction interventions have contributed to the observed reduction in HIV risk, which should be further investigated (Aspinall et al. 2014).

Davis et al. (2017) focused on the association between NSEP and HCV prevention in PWID (n = 6 studies) and found mixed results indicating no consistent effects of this intervention (OR 0.51 [95% CI 0.05–5.15]), probably given the substantial heterogeneity ($p \leq 0.10$) and moderate to large inconsistency ($I^2 \geq 66\%$) among studies included. Concerns over participant representativeness, unclear adjustments for confounders, and bias from participant nonresponse and losses to follow-up were noted (Davis et al. 2017). Similarly, Gillies et al. (2010) assessed the effects of NSEP on the reduction of injecting risk behaviors and HCV transmission among PWID (n = 13 studies) and concluded that the evidence is currently limited by an insufficient volume and quality of studies (Gillies et al. 2010).

Platt et al. published two articles (Platt et al. 2017, 2018) addressing the effects of both NSEP and OST programs (alone or in combination) for preventing the acquisition of HCV in PWID (n = 28 studies). The overall incidence of HCV ranged from 0.09 cases to 42 cases per 100 person-years across studies. Most studies (>85%) were classified as with serious or critical risk of bias, meaning the quality of evidence was overall low and should be considered when interpreting the findings. Meta-analyses show that OST reduces the risk of HCV by 50% (risk ratio – RR of 0.50 [95% CI 0.40–0.63], I^2 = 0%, n = 12 studies). No similar evidence was shown for NSEP (RR 0.79 [95% CI 0.39–1.61, I2 = 77%, n = 5 studies). Combined NSEP and OST (n = 3 studies) resulted in a 74% reduction of the risk of HCV acquisition (RR 0.26 [95% CI 0.07–0.89]), probably attributable to the OST component (Platt et al. 2017, 2018). A similar meta-analysis previously performed by Turner et al. (2011) also demonstrated a potential association of OST and NSEP coverage with a reduction in new HCV infections (adjusted OR 0.41 [95% 0.21–0.82] and 0.48 [95% CI 0.25–0.93], respectively, with I2 = 50%). The combination of interventions as a full harm reduction strategy (OST plus high NSEP) may reduce the odds of new HCV

infection by nearly 80% (adjusted OR 0.21 [95% CI 0.08–0.52]) of self-reported needle sharing by 48% (adjusted OR 0.52 [95% CI 0.32–0.83]) and of mean injecting frequency by 20.8 injections per month (95% CI -27.3 to -14.4) (Turner et al. 2011).

The systematic review published by Jones et al. (2010) sought to determine which approaches and delivery of NSEP are effective ($n = 16$ included studies). Based on 11 studies, there was no evidence of an impact of different NSEP settings or syringe dispensation policies on drug injecting behaviors. Only one study reported data on the combination of methadone treatment and full participation in NSEP and found a potential association with a lower incidence of HIV and HCV. Thus, it is difficult to draw conclusions on the effect of these interventions considering the range of harm reduction services available and their differences (Jones et al. 2010). Similarly, Ksobiech (2006), by evaluating data on NSEP (n = 31 studies with 86 different reported outcomes) concluded that although attendance to this service may lead to a decline in most unsafe practices (e.g., injection frequency and sharing equipments), results should be cautiously interpreted as the between-studies heterogeneity was extremely high (especially due the lack of standard outcome measures) (Ksobiech 2006).

Access to primary health care interventions including NSEP or OST as well as their impact on health outcomes, cost implications, and logistic challenges were revised by Islam et al. (2012). Authors reported that different interventions and models (provided by medical, nursing, and counseling staff) are accepted by PWID; however, the lack of rigorous and systematic evaluations of their effect hamper further conclusions (Islam et al. 2012).

Supervised Drug Consumption Facilities (SCF) or Supervised Injection Facilities (SIF)

SIF, broadly known as SCF, have increasingly been implemented in response to public health and public order concerns associated with drug use. They are usually located in areas where there is an open drug scene and injecting is common in public places. Typically, SCF provide drug users with sterile injecting equipment; counseling services before, during, and after drug consumption; emergency care in the event of overdose; and primary medical care and referral to appropriate social health care and addiction treatment services (Kennedy et al. 2017; Levengood et al. 2021). We found two systematic reviews on this topic:

Kennedy et al. (2017) reviewed the literature on the health and community impacts of SCF and highlighted that this approach can mitigate overdose-related harms and unsafe drug use behaviors, as well as facilitate uptake of addiction treatment and other health services among PWUD. The recent systematic review of Levengood et al. (2021) on the effectiveness of SIF for harm reduction and community outcomes ($n = 22$ studies) also demonstrated an association of this strategy with reductions in opioid overdose morbidity and mortality, improvements in injection behaviors and harm reduction, improvements in access to addiction treatment programs, and no increase or reductions in crime and public nuisance for PWID. However, in both reviews, quantitative synthesis was not possible given the inconsistent outcome measures across studies, which highlights the need for further well-performed trials on this field to better understand the potential long-term health impacts of SCFs and how innovations in SCF programming may help to optimize the effectiveness of this intervention (Kennedy et al. 2017; Levengood et al. 2021).

Integration of Testing and Treatment of Blood-Borne Diseases

Effective national and global responses to infections such as HIV and hepatitis require a significant expansion of testing and counseling to improve access to prevention and care and reduce harms (Suthar et al. 2013). According to regional experiences from Georgia – reported to the World Health Organization (WHO), testing simultaneously for several communicable diseases in primary health care settings is feasible and can help to bring down the burden of chronic hepatitis C, HIV, sexually transmitted infections (STI), and tuberculosis in several countries (World Health Organization – WHO 2021). Additionally, as tools to optimize screening and circumvent losses

to follow-up, novel testing methods such as dried blood spots (DBS) and point-of-care (PoC) testing have been developed and may enable easier access to high-risk populations who have less frequent contact with health care professionals. This can contribute to the detection, diagnosis, staging, linkage to care, treatment monitoring, and effectiveness of infection control at the population level (Coats and Dillon 2015). We found two systematic reviews on this topic:

Coats and Dillon (2015) evaluated whether the availability of these novel testing methods increased either uptake or the number of new diagnoses of HCV in PWID. No studies on PoC testing at the time were found; yet $n = 6$ studies on DBS testing (including populations attending substance use clinics, prisons, and NSEP) showed that this intervention may contribute to HCV diagnosis. These findings should be updated considering the high speed of publication on the topic in the past years (Coats and Dillon 2015).

On the other hand, Suthar et al. (2013) systematically reviewed the available evidence on community testing and counseling for HIV (i.e., outside of health facilities) ($n = 117$ records) among PWID, and found that the uptake of mobile interventions was very heterogenous across studies, ranging from 9% to almost 100%, probably related to how testing was offered. Further research is needed to better understand the effects of these strategies and improve the acceptability of community-based testing for key populations (Suthar et al. 2013).

Other Combined Interventions

The eight remaining systematic reviews and meta-analyses reported in this chapter referred to other behavior interventions – mostly combined approaches.

Awungafac et al. (2017) updated the evidence on the effectiveness of sex work (SW) interventions in PWID in sub-Saharan Africa ($n = 25$ studies, but only two referring to harm minimization interventions). Combined interventions to reduce harm included: structural approaches (empower SW), behavioral interventions (reduce susceptibility to HIV), and biochemical interventions (reduce HIV infectiousness/STI burden). Evidence of harm minimization interventions in this setting is extremely poor and heterogeneous; initial data show a decrease of violence, and engagement with SW and sex partners; increase of condom use and reduction of drinking, yet with no persistent findings, were reported in the studies. No impact of these interventions on HIV were found (Awungafac et al. 2017). Merson et al. (2000) and Singh et al. (2014) also reviewed the effect of projects and programs to reduce sexual transmission of HIV or transmission related to injected drug. Although it is possible that behavioral change interventions are effective when targeted at high-risk populations (e.g., female SW), evidence is scarce; few studies on harm reduction interventions in PWID are available in this context (Merson et al. 2000; Singh et al. 2014).

The systematic review of Caven et al. (2019), by assessing the impact of HCV treatment on drug use behavior in PWID ($n = 5$ studies), found no conclusive evidence of changes in frequency of injections and on equipment borrowing/sharing, probably due the high heterogeneity among studies (Caven et al. 2019). Conversely, Copenhaver et al. (2006) reported that behavioral interventions significantly reduced injection ($p < 0.001$) and noninjection drug use ($p = 0.028$) patterns, decreased trading sex-for-drugs rates ($p = 0.052$), and increased condom use ($p = 0.017$) and drug treatment entry ($p = 0.013$) among PWID at HIV risk ($n = 37$ randomized trials; 10,190 participants). Yet, no effects on needle/syringe borrowing were observed. According to authors, behavioral interventions can reduce risk behaviors among PWID, especially when targeting both drug- and sexual-risk behavior, and when they include certain behavioral skills components (Copenhaver et al. 2006).

Stockings et al. (2016) performed an overview (systematic review of reviews) on the effectiveness of prevention, early intervention, harm reduction, and treatment of substance use disorders in young people (including alcohol and illicit drugs [e.g., cannabis, opioids, amphetamines, and cocaine] but also tobacco). Roadside drug testing and interventions to reduce injection-related harms seem to have a moderate-to-large effect,

but mixed findings and insufficient evidence were reported, especially for brief interventions. This scarce availability of literature on interventions for substance use in young people indicates the need to develop and test specific interventions that are effective and accepted by this population (Stockings et al. 2016).

Marshall et al. (2015) focused on the role of PWID in co-creation of harm reduction initiatives, including their involvement in program organization, and studied barriers and facilitators to their engagement ($n = 164$ documents were evaluated). Authors described interventions ranging from education, support, counseling, direct harm reduction, and policy creation and concluded that current evidence, although providing good descriptive content and insights, still lacks agreed-upon approaches to documenting the ways PWID may contribute themselves to harm reduction initiatives (Marshall et al. 2015). McNeil and Small (2014) also evaluated PWID's perspectives and experiences on available interventions (NSEP, SCF, and combined peer-based harm reduction interventions) and suggested safer environment interventions may mitigate drug-related harms by providing refuge from street-based drug scenes, safer injecting, and mediated access to resources/health services. Quantitative syntheses are needed to strengthen these results (McNeil and Small 2014).

Evidence of Impact of Pharmacist-Led Harm Minimization Interventions

Two studies recovered in the search strategy (one overview of systematic reviews and one meta-analysis) focused on the effect of pharmacy-based or pharmacist-led harm minimization interventions. Both of them had a strong focus on NSEP.

Sawangjit et al. (2017), after screening 1568 records, retrieved 14 studies (including a total of 7035 PWID), and concluded that pharmacy-based NSEP were effective in reducing risk behaviors (reported in 13 studies), including sharing syringe behavior and safe syringe disposal. Yet, most studies ($n = 9/14$, 64.3%) were rated as having a serious risk of bias. For sharing-syringe behavior, pharmacy-based NSEP were significantly better than no intervention both in main (OR 0.50 [95% CI 0.34–0.73], I2 = 59.6%) and sensitivity analyses – excluding studies with a serious risk of bias (OR 0.52 [95% CI 0.32–0.84], I2 = 41.4%)). For safe syringe disposal and HIV/HCV prevalence, the evidence was unclear since few studies reported this data. Economic outcomes were only reported in one study, making conclusions not possible (Sawangjit et al. 2017).

The overview by Fernandes et al. (2017) included 13 systematic reviews with 133 relevant unique studies published between 1989 and 2012, among which two reviews were considered to have low risk of bias. The authors reported pharmacy-based NSEP as effective in reducing HIV transmission and injecting risk behaviors among PWID, but found mixed results on the reduction of HCV infection.

Additionally, aiming at providing further evidence on the role and effects of pharmacist-led or pharmacy-based harm minimization interventions on illicit drug use, we gathered some primary studies and references to this chapter, listed in Table 2.

This evidence confirms that in many countries NSEP has been implemented in community pharmacies and in opioid replacement therapy clinics run and managed by pharmacists, including in Australia Belgium, China, France, Ireland, Kyrgyzstan, the Netherlands, New Zealand, Portugal, Spain, Slovenia, Ukraine, the UK, and the USA (Bonnet 2006; Rudolph et al. 2010; Sendziuk 2007; The Pharmacy Guild of Australia 2010; O'Shea et al. 2009; National Institute for Health and Care Excellence – NICE 2014; Sheridan et al. 2005; Hong and Li 2009). In Scotland, pharmacists have now been involved in the methadone and NSEP for more than 10 years. The implementation of the opiate dependence program surpasses 85%, where most providers have a supplementary contract with the local health board to supervise the consumption of methadone on their premises. Conversely, only a very small proportion of "methadone" pharmacists are involved in the provision of a pharmacy-based needle exchange scheme, even though considered the most cost-effective method of delivering clean injecting

Evidence of the Impact of Harm Minimization Programs, Table 2 Additional studies describing pharmacist-led or pharmacy-based harm minimization interventions

Author, year	Title	Study design/Article type
(Antoniou et al. 2021)	Impact of policy changes on the provision of naloxone by pharmacies in Ontario, Canada: a population-based time series analysis	Population-based time series analysis
(Hill et al. 2019)	Pharmacists are missing an opportunity to save lives and advance the profession by embracing opioid harm reduction	Commentary
(Meyerson et al. 2019)	I could take the judgment if you could just provide the service: nonprescription syringe purchase experience at Arizona pharmacies, 2018	Qualitative interview study
(Meyerson et al. 2020)	Feasibility and acceptability of a proposed pharmacy-based harm reduction intervention to reduce opioid overdose, HIV, and hepatitis C	Exploratory survey study
(Parry et al. 2021)	Pharmacist attitudes and provision of harm reduction services in North Carolina: an exploratory study	Exploratory survey study
(Roberts and Hunter 2004)	A comprehensive system of pharmaceutical care for drug misusers	Review

equipment to injecting drug users (Roberts and Hunter 2004).

In fact, as described by Meyerson et al. (2019, 2020), there are possibly barriers hindering service implementation, namely stigmatization by staff, resulting in frequent refusal of syringe purchase at pharmacies. It is well established that lack of access to sterile syringes reinforces health risk behaviors among PWID, therefore investments must be made in education and training to improve pharmacy practice (Meyerson et al. 2019, 2020).

Pharmacy-based naloxone programs have been described in Canada and in the USA. In Canada, since 2016, the government implemented the Ontario Naloxone Program for Pharmacies, authorizing pharmacists to provide injectable naloxone kits at no charge to residents. The monthly dispensing of these kits over 4 years led to changes in 2018 (adding intranasal naloxone and removing the requirement to present a government health card), which increased pharmacy-based naloxone dispensing uptake, particularly among individuals at high risk of inadvertent opioid overdose (Antoniou et al. 2021). Although provision of nonprescription syringes and naloxone has been reported by a vast majority of US pharmacists, at least occasionally (Parry et al. 2021), lack of readiness among pharmacists to dispense naloxone and little willingness to provide sterile syringes has been described as a barrier to effective service implementation, needing adequate education on opioid harm reduction interventions (Hill et al. 2019).

Meyerson et al. (2020) have used the consolidated framework for implementation research to evaluate a service in the USA combining an intervention for opioid misuse screening, brief intervention, syringe and naloxone dispensing, and referrals provision (PharmNet), suggesting that pharmacy staff perceived this combined service to be beneficial for PWUD and that staff could deliver it when provided with adequate training (Meyerson et al. 2020).

Challenges and Perspectives on Harm Minimization Interventions

Interventions focusing on drug use disorders have always been topics of discussion well beyond the public health arena. The development and implementation of drug policies around the globe are often characterized as a continuous debate between a moral position in which PWUD are portrayed as criminal/deviant versus a public health position where they are seen as individuals that need treatment and care. A balanced approach seems to focus on public safety measures (e.g., reforming criminal justice policies) as well as

using advanced interventions in the prevention and treatment of drug use disorders or in harm minimization (Steenholdt et al. 2015; Davoli et al. 2010).

Over the last 35 years, specific interventions aimed at harm reduction or minimization have changed the way decision-makers and stakeholders respond to drug problems. These interventions aim to identify and support policies and programs that moderate or decrease the deleterious consequences of drug use, both to PWUD and to the society (Lennings 2000; Department of Health – Australian Government 2004). This gives clear primacy to a public health perspective in which the imperative is to minimize immediate harms; questions of long-term abstinence from drug use can be later on decided. So, the current debates on drug policies now focus on the selection of the best harm minimization intervention (or combination of interventions) that fit each scenario (Steenholdt et al. 2015; Davoli et al. 2010). Yet, this is not an easy task and several challenges for the development and implementation of these approaches are common worldwide. In the outer context, low political prioritization, lack of coordination and integration, limited advocacy, and resource limitations for access to these interventions may represent important barriers. Stigma, ethical issues, and patterns of drug consumption may also threaten the implementation, engagement/acceptance, and use of these services in daily practice (Stockings et al. 2016; Irwin and Fry 2007). It is important to consider that the drug market is constantly changing (e.g., introduction of novel drugs) which directly impacts on drug use practices and patterns, meaning that harm minimization strategies and policies should be adapted and innovated accordingly (Greene et al. 2018; Roy et al. 2017). This fit should also consider countries' culture and population characteristics (e.g., sex, age, socioeconomic status, and risk status) (Stockings et al. 2016).

PWID are extremely vulnerable to many infectious diseases given the consequences of substance use on criminalization, stigmatization, and psychological, physical, behavioral, and economic factors. While relationships between drug use and blood-borne and STI are well established, less attention has been paid to other outbreaks, including the COVID-19 pandemic. This disease may increase risks of homelessness, overdoses, and unsafe injecting and sexual practices for PWID, which should be better addressed in future public policies (Vasylyeva et al. 2020).

Most countries' approach to confront drug issues is to develop comprehensive and evidence-based policies. However, the importance given to "evidence" in this perspective can be contrasted with policies that are more ideologically driven. Particularly, when facing an emergency situation, many quick decisions can result in the adoption of policy options that are initially viewed as controversial with no robust evidence-based argument (Steenholdt et al. 2015; Davoli et al. 2010). Another area surely controversial is when public health and safety contrast, in the sense that there might be evidence to support the adoption of harm minimization interventions but in certain contexts, such as places of detention, their adoption implies recognizing drug use occurs inside prison walls. This is one of the reasons why the uptake of such interventions is still limited (Moazen et al. 2020).

Additionally, it has been suggested that weak evidence pieces (e.g., studies with methodological flaws and high risk of bias, as well as misleading and conflicted reports) can lead to biased recommendations and may distort decision-making in several health areas (Ioannidis 2016; Page et al. 2018; Bonetti et al. 2022) including in drug policy, where evidence base for supporting current approaches is often weak – as demonstrated in this chapter. This scenario reinforces the need of rigorous methodological assessments, transparent reporting (i.e., providing information in an accessible and understandable format), and critical appraisal of the available evidence. Evidence appraisal for an intervention is a complex process requiring methodological rigor, particularly in conducting a comprehensive search of the literature, evaluating quality of primary studies, and summarizing the results. This process aims to systematically assess the value and relevance of scientific research to determine its appropriateness to support decisions (Ioannidis 2016; Page et al. 2018; Bonetti et al. 2022).

To date, the evidence on the impact of naloxone programs in reducing overdose-related outcomes remains insufficient, although studies suggest that further well-designed studies with standardized outcomes are needed to strength these findings. No strong evidence exists to support the concern that these interventions lead to increased harms for PWUD or encourage drug use. On the other hand, evidence is sufficient to support the role of OST in reducing HIV transmission and injecting risk behavior among PWID, while data supporting NSEP in this context is scarcer. Evidence on the effect of other harm minimization interventions or combined measures, as well as in further settings or contexts (e.g., among young people, sex workers, and individuals with or at risk of HCV or HVB) are scarce or led to mixed/controversial findings. The effect of combined strategies is difficult to assess, as one or more components of a program of interventions may reduce harmful outcomes. This includes pharmacy-based or pharmacist-led interventions that are usually grounded on multiple and complex interventions. Yet, studies primarily demonstrated that harm minimization interventions in this setting (especially pharmacy-based NSEP) are effective in reducing the transmission of communicable diseases and risk behaviors among PWID. As such, pharmacists are positioned to play important roles in implementing evidence-based prevention and harm reduction approaches to drug use and related health care outcomes (Agley et al. 2003). The implementation of these programs in pharmacies can additionally contribute to increase access to services and care. However, as the supply of these services is notably lower in rural areas, lower acceptability of such services among rural pharmacists may exist and should be further investigated (Parry et al. 2021). Other barriers for hindering service implementation in pharmacies can include stigmatization and personal belief by staff (e.g., refusal of syringe/needles purchase) and lack of readiness or training among pharmacist to properly deliver the intervention (Meyerson et al. 2019, 2020; Hill et al. 2019).

Finally, in terms of research priorities, further methodologically robust primary studies on the impact of harm reduction interventions (alone or combined with other approaches) on HCV, HVB, and subpopulations (e.g., young adults, sex workers, and prison populations) are needed, as well as studies on standardization of outcome measures related to drug overdose and injecting behavior.

Cross-References

- ▶ Behavioral Medicine/Behavioral Science in Pharmacy
- ▶ Community Health Outreach Services: Focus on Pharmacy-Based Outreach Programs in Low- to Middle-Income Countries
- ▶ Evidence of the Role of Pharmacy-Based Interventions in Sexually Transmitted Infections
- ▶ Pharmacy Practice for Marginalized Communities

Appendix I

Complete Search Strategy (PubMed):

(("drug users"[MeSH Terms] OR ("drug"[All Fields] AND "users"[All Fields]) OR "drug users"[All Fields] OR ("drug users"[MeSH Terms] OR ("drug"[All Fields] AND "users"[All Fields]) OR "drug users"[All Fields] OR ("drug"[All Fields] AND "addicts"[All Fields]) OR "drug addicts"[All Fields]) OR ("inject"[All Fields] OR "injectability"[All Fields] OR "injectant"[All Fields] OR "injectants"[All Fields] OR "injectate"[All Fields] OR "injectates"[All Fields] OR "injected"[All Fields] OR "injectible"[All Fields] OR "injectibles"[All Fields] OR "injecting"[All Fields] OR "injections"[MeSH Terms] OR "injections"[All Fields] OR "injectable"[All Fields] OR "injectables"[All Fields] OR "injection"[All Fields] OR "injects"[All Fields]) OR (("heroin"[MeSH Terms] OR "heroin"[All Fields] OR "diacetylmorphine"[All Fields] OR "diamorphine"[All Fields] OR "heroin s"[All Fields] OR "heroine"[All Fields] OR "heroines"[All Fields]) AND ("user s"[All Fields] OR "users"[All Fields])) OR (("cocaine"[MeSH

Terms] OR "cocaine"[All Fields] OR "cocain"[All Fields]) AND ("user s"[All Fields] OR "users"[All Fields]))) AND (((("harm reduction"[MeSH Terms] OR ("harm"[All Fields] AND "reduction"[All Fields]) OR "harm reduction"[All Fields] OR ("harm"[All Fields] AND "minimization"[All Fields]) OR "harm minimization"[All Fields]) AND ("intervention s"[All Fields] OR "interventions"[All Fields] OR "interventive"[All Fields] OR "methods"[MeSH Terms] OR "methods"[All Fields] OR "intervention"[All Fields] OR "interventional"[All Fields])) OR (("harm reduction"[MeSH Terms] OR ("harm"[All Fields] AND "reduction"[All Fields]) OR "harm reduction"[All Fields]) AND ("intervention s"[All Fields] OR "interventions"[All Fields] OR "interventive"[All Fields] OR "methods"[MeSH Terms] OR "methods"[All Fields] OR "intervention"[All Fields] OR "interventional"[All Fields])) OR (("needle s"[All Fields] OR "needled"[All Fields] OR "needles"[MeSH Terms] OR "needles"[All Fields] OR "needle"[All Fields] OR "needling"[All Fields] OR "needlings"[All Fields]) AND ("exchangable"[All Fields] OR "exchange"[All Fields] OR "exchangeabilities"[All Fields] OR "exchangeability"[All Fields] OR "exchangeable"[All Fields] OR "exchanged"[All Fields] OR "exchanger"[All Fields] OR "exchanger s"[All Fields] OR "exchangers"[All Fields] OR "exchanges"[All Fields] OR "exchanging"[All Fields])) OR (("needle s"[All Fields] OR "needled"[All Fields] OR "needles"[MeSH Terms] OR "needles"[All Fields] OR "needle"[All Fields] OR "needling"[All Fields] OR "needlings"[All Fields]) AND ("syringe s"[All Fields] OR "syringed"[All Fields] OR "syringes"[MeSH Terms] OR "syringes"[All Fields] OR "syringe"[All Fields]) AND ("exchangable"[All Fields] OR "exchange"[All Fields] OR "exchangeabilities"[All Fields] OR "exchangeability"[All Fields] OR "exchangeable"[All Fields] OR "exchanged"[All Fields] OR "exchanger"[All Fields] OR "exchanger s"[All Fields] OR "exchangers"[All Fields] OR "exchanges"[All Fields] OR "exchanging"[All Fields]))) AND ("impact"[All Fields] OR "impactful"[All Fields] OR "impacting"[All Fields] OR "impacts"[All Fields] OR "tooth, impacted"[MeSH Terms] OR ("tooth"[All Fields] AND "impacted"[All Fields]) OR "impacted tooth"[All Fields] OR "impacted"[All Fields] OR ("evidence"[All Fields] OR "evidences"[All Fields] OR "evident"[All Fields] OR "evidently"[All Fields]))) AND (meta-analysis[Filter] OR systematic review[Filter]).

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