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REVIEW ARTICLE (INVITED)

Opportunities to Offer Harm Reduction to People who Inject Drugs During Infectious Disease Encounters: Narrative Review

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Increased rates of overdose (OD) and blood-borne infections have been associated with injection drug use (IDU). This increasing overlap between IDU-related infectious diseases (ID) is a byproduct of the opioid OD crisis, especially with the transition to synthetic opioids with faster onset and shorter duration leading to potentially more frequent injections. ID specialists are uniquely positioned to positively impact the opioid OD crisis by capitalizing on opportunistic moments of engagement during clinical encounters with people who inject drugs (PWID). Harm reduction services should therefore be expanded and offered to PWID in ID settings to reduce rates of OD, infection, and hospitalization. Major target areas include (1) teaching and distribution of materials related to safer injection practice such as sterile injection supplies, fentanyl test strips, and naloxone; (2) increased screening and access to pre-exposure prophylaxis and postexposure prophylaxis; and (3) initiation of medications for opioid use disorder. Incorporating these strategies in various treatment settings can expand treatment access, improve patient outcomes, and reduce stigma associated with IDU.

Keywords.: harm reduction; infectious disease; opioid use disorder; people who inject drugs; substance use disorders.

Harm reduction refers to a spectrum of strategies that mitigate the medical consequences and social stigmas perpetuated by injection drug use (IDU) [1]. This approach aims not only to improve the health and safety of people who inject drugs (PWID), but also to protect their families and communities [1]. Its methods are personalized to the individual (or community), regardless of their interest in treatment, and focus on diminishing the harmful effects of IDU rather than achieving abstinence or ignoring harms altogether [1]. Some harm reduction strategies include, but are not limited to, supply of sterile injection materials ("safe injection kits"), syringe exchange/services programs (SSPs), supervised consumption sites (SCS), overdose (OD) and infection prevention, and naloxone provision [2, 3]. SSPs are community-based prevention programs that provide sterile injection equipment, safe disposal of used syringes, testing and in some cases vaccinations, low-barrier access to medication, therapy, counseling, groups, and other services [4]. SCS are services comprising trained staff that can teach safer injection techniques, monitor IDU, test substances for the presence of fentanyl, fentanyl analogues, or other contaminants, and administer naloxone in the event of OD to decrease fatal ODs [5]. These types of programs may serve as a bridge to substance use disorders (SUD) clinics, testing sites for sexually transmitted infections, HIV, and hepatitis C virus (HCV), vaccinations, case management, housing assistance, and more [6, 7].

The opioid crisis has resulted in alarming repercussions in our communities. In the setting of infectious diseases (ID), one particular byproduct of IDU is the increased incidence of ID complications [8]. The surge in microbial infections relating to IDU is particularly worrisome given that the illicit manufacturing of fentanyl and other synthetic analogues not only dominate the opioid OD crisis, but also, the synthetic analogues now produced are typically more potent and provide faster onset, and shorter duration of action than that of fentanyl, which leads to increased risk of OD and potentially more frequent IDU, respectively [9, 10]. IDU-related infections include, but are not limited to, infective endocarditis (IE), osteomyelitis, skin and soft tissue infections (SSTIs), hepatitis B virus (HBV), HCV, and HIV [11]. The practice of sharing syringes is one of the primary risk factors that precipitate HIV and other transmittable diseases, yet an alarming 40% of PWID share injection supplies [12].

The World Health Organization estimates that >13 million people engage in IDU worldwide, and 1.7 million of these individuals have HIV [13]. According to the Centers for Disease Control and Prevention (CDC), 9% of almost 40 000 diagnoses

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of HIV in the United States in 2016 were due to IDU [14]. The ongoing opioid crisis is also associated with increased rates of community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) [15, 16]. PWID have an estimated 16.3 times higher likelihood to develop MRSA than people who do not engage in IDU [15]. From 2011 to 2016, the rate of MRSA infections among PWID more than doubled, with the most frequent infection type associated with nonsterile IDU [16]. As the opioid crisis continues to evolve, nonsterile IDU will continue to fuel a surge in ID complications. However, this public health crisis is not irreparable—clinicians across all specialty settings can take measures to better mitigate this converging epidemic by incorporating harm reduction strategies, and ID specialists are uniquely positioned to promote these measures [17].

After the discovery of AIDS in 1981, harm reduction became important not only for managing SUD, but also for reducing transmission of blood-borne infection [18]. Since its introduction, harm reduction programs have gradually developed a persuasive body of literature to bolster its positive impact on IDU outcomes. A common misconception about harm reduction is that its interventions are dichotomous to abstinence-oriented strategies. This belief stems from many sources, including 2 landmark prospective cohort studies in the 1990s that found an association between SSP and higher risk of HIV seroconversion [19, 20]. However, critics have pointed out that there are a number of selection biases that could account for these findings, such as the inclusion of people engaging in cocaine injection (who typically inject more often than those using heroin), the limited number of syringes that PWID could have access to in early SSP, and the ready availability of sterile injection equipment through pharmacies (which could have attracted marginalized, higher-risk individuals). Follow-up studies in the same settings, conducted after addressing the aforementioned concerns, found no such increase in risk or decrease in HIV prevalence [21].

It has been estimated that eliminating nonsterile injection techniques can prevent 43% of incident HCV infections between 2018 and 2030 [22]. There is also substantial evidence that these programs are cost-effective and often cost-saving by preventing and reducing risks associated with IDU [23]. In an economic evaluation of SSPs in preventing HIV transmission among PWID, a single SSP in a city with a population of 450 000 was estimated to prevent 24 new HIV infections over 5 years, providing a cost savings of $1.3 million [24]. While policies and attitudes in the United States have advanced substantially in recent years, they still lag behind more advanced jurisdictions in Europe and elsewhere; for example, SSPs are legal in only 38 states, while SCS are currently not sanctioned in the United States [25].

Harm reduction serves as an important vehicle to mobilize response to not only the opioid crisis, but also the other aforementioned epidemics, such as HIV/AIDs, viral hepatitis, and various infections. The clinical overlap between SUD and ID suggests that integration of harm reduction strategies within ID would improve health outcomes. A recent article proposed a subspecialty within ID to address ID-related complications from SUDs [26]. Additionally, there have been many recent publications that highlight the importance of harm reduction to reduce new infections among PWID [27], the unmet need to integrate OUD and ID prevention and treatment [28], and specific strategies for ID clinicians to optimize OUD care during and after hospitalization [29].

Opening conversations with PWID about IDU faces its own set of challenges, as stigma often instills feelings of shame and embarrassment for the patient. It is therefore important to approach patients with empathy and utilize person-first language ("person who uses or injects drugs" vs "drug user," or worse, "addict" and "junkie") to facilitate a comfortable environment, which can open conversation about IDU and harm reduction strategies [30]. Many of the harm reduction services provided by SSPs and SCS can be incorporated into an ID setting to leverage the role of ID specialists to positively impact the opioid crisis.

Herein, we discuss harm reduction strategies that could be incorporated into ID settings aimed at preventing infections, minimizing ID-related complications, and preventing OD.

INFECTION PREVENTION

A study completed in 2016 assessed the contextual and health care environment factors that associate with a patient's ability to achieve viral suppression at an HIV clinic in patients who engage in IDU [31]. Among the patients at the conclusion of the study, 74% met standards for retention in care, 95% were prescribed antiretroviral therapy, and 87% were virally suppressed [31]. In the interviews conducted with both providers, the study found that harm reduction (example provided: SSP) served as a key providing factor in these positive outcomes [31]. A separate study conducted in 2017 found that the success behind this particular facility's harm reduction strategies lay with their humanistic approach to PWID [32].

In a study of risk behavior among 1082 PWID at an SCS, 75% reported positive changes in injection behaviors, such as fewer rushed injections, fewer shared syringes, and a greater likelihood of using sterile supplies as a direct result of the services and counseling provided [33]. In addition, SCS services lead to greater uptake of addiction and other treatment resources, retain people in care, and expand medical services [6, 7]. To expand access to services provided by SSPs and SCS, ID clinicians are uniquely positioned to provide resources and patient education to PWID. Preventative measures, such as supplying sterile equipment, educating on proper injection techniques, and providing postexposure prophylaxis (PEP) or pre-exposure prophylaxis (PrEP) to those who qualify can be taken to attenuate risk of infections. The following is a noncomprehensive list of strategies that ID clinicians could familiarize themselves

Table 1. Ideal and Alternative Supplies to Promote Safer Injection Practices

Equipment	Purpose	Alternative Options (in Descending Order of Sterility)	Avoid
Syringe	Inject drugs into the vein	None	• Reuse and sharing • Sharpening
Cookers	Basin to dissolve or cook drugs for injection Ideally, a cooker with a handle should be used to maintain distance between the fingers and flame	• Spoon • Bottle cap with a makeshift handle (bobby pin, twist ties, paperclips)	• Reuse and sharing
Filters	Remove unwanted particulate matter and utilize every drop of drug solution	• Sterifilt • Cotton balls • Cotton from Q-tips • Filter paper • Tampons	• Reuse and sharing • Cigarette filters as they contain fiberglass particles that may cause a host of complications • "Cotton shots" as fungi and bacteria may gather inside the saved cottons, leading to cotton fever
Sterile saline	Dissolve drug for injection	• Sterile water • 10-minute boiled water • Cold tap water • Bottled water • Toilet water from the tank over the bowl	• Puddle water • Saliva
Ascorbic acid	Acidify drugs that do not easily dissolve in water (eg, crack cocaine)	• Citric acid	• Lemon juice: can transmit bacteria • Vinegar: can irritate veins
Tourniquets	Create easier access and visibility to veins	• Stockings, lubricated condoms, slick neckties • Note: also encourage hydration	• Sharing
Condoms	Prevent transmission of HIV, tourniquet alternative	None	• Condomless sex
Alcohol swab	Sanitize area of injection before injecting	• Chlorhexidine gluconate wipes	• Wiping area of injection after injecting
Dry swab	Allows the blood vessels to heal and platelets to aggregate around the punctured vein	None	• Alcohol swab

with and incorporate into a harm reduction–informed service within their practice.

Sterile Injection Equipment

The practice of sharing syringes is one of the primary risk factors that precipitates blood-transmitted diseases, yet >40% of PWID share injection supplies [12]. Patients should be counseled to use their own injection equipment, as sharing compromises sterility and repeated use may dull the needle point, which can lead to both ID and trauma to the veins and surrounding tissue [34]. Although sharing syringes is of utmost concern, all injection equipment should be unique to the individual and not shared to align with best practices, as HCV may remain infectious at room temperature for up to 6 weeks and potentially transmitted from fomites, such as a cooker [35].

However, the limited availability of sterile syringes and other supplies results in frequent reuse and sharing [34, 36]. To address this unmet need, ID clinicians should consider offering sterile syringes or safe injection kits, prescribing syringes for pickup at a local pharmacy, or assisting PWID in finding the nearest SSP. Measures such as this have resulted in reduced HIV and HCV seroprevalence, parallel to a decline in syringe sharing after changes in syringe access policy [37]. As a last resort, if equipment must be shared, each piece of equipment should be thoroughly cleaned.

To properly clean syringes, first rinse with cold water and then fill completely with undiluted household bleach and shake for 2 minutes [2, 34]. Bleach is a disinfecting agent that, if used according to the recommendations of the CDC, has shown efficacy as an HIV prevention strategy for PWID [36]. The bleach should be discarded, and both the needle and syringe barrel should be flushed with cold water once more [2, 34]. Sharpening syringes should also be discouraged, as this can cause a burr on the needle (causing damage to veins) and weaken the point (which could break off in the vein) [2, 34].

Syringes with smaller needle gauges will result in smaller puncture wounds and therefore decrease the likelihood for infection to occur [2, 34]. Syringes for intravenous (IV) injections typically should not exceed 25G [2, 34]. When the needle is too short, it may miss the vein, and if it is too long, it may go through the vein. The ideal lengths are one-half inch for insulin needles and five-eighths inch for tuberculin needles [2, 34].

In the absence of safe injection kits or sterile equipment access, patients should be counseled on proper and alternative equipment (Table 1).

Injection Technique

Education on proper equipment and cleaning should include counseling on proper injection technique. The Harm Reduction Coalition provides a manual guiding these practices [34], though

a few key points have been extracted and included below. PWID should be advised to rotate sites, even if it is uncomfortable initially [2, 34]. Injecting into the same locations repeatedly can interfere with circulation and cause phlebitis, and veins can collapse or become leaky if they are not given adequate time to heal [2, 34]. Additionally, loss of peripheral vein function or venous sclerosis may occur, which increases the risk of other serious complications, noted below, due to use of alternative, potentially dangerous central injection sites [2, 34, 38]. Crushed pills should be avoided for injection if possible, as they can be difficult to dissolve, which increases the risk of thrombus formation after IV injection, or abscesses if injected subcutaneously [2, 34].

To encourage rotation of injection sites, it is best to align with the patient to identify their preferred sites and maintain a log (written or mental) of when sites were last used. It is important to identify safer sites versus dangerous sites that should not be utilized. For IV injection, preferred sites include the forearms, followed by the backs of the hands [2, 34]. Dangerous sites that should not be utilized due to high risk for complications or potentially fatal outcomes include the neck, groin, tops of the feet, ankles, ventral wrists, and palms [2, 34]. A review of these dangers and complications can be found elsewhere [34], and expert guidance is recommended to maximize safety and monitoring if patients wish to inject in these higher-risk areas. To help patients find vein access in preferred, safer sites, one can encourage hydration or use of a tourniquet or assist with other strategies that encourage blood flow/enlargement of veins such as applying a heat pack for a few minutes, utilizing gravity by dangling the arm for a few minutes, or completing a few push-ups.

In line with evidence-based best practices for sterile injection technique, hands should be washed before injecting. The injection can then be prepared utilizing a sterile cooker, sterile saline, and a sterile filter or other alternatives (Table 1). The injection site should then be cleaned using an alcohol pad/swab or chlorhexidine gluconate wipes to reduce risk of skin microbes entering the bloodstream when the needle pierces the skin [2, 34]. A tourniquet should be used to tie off above the injection site utilizing a slip knot to ensure easy removal [2, 34]. The needle should be inserted at a 15°–35° angle with the bevel facing up to reduce trauma to the tissue and veins, and the injection should always be in the direction of the heart [2, 34]. After inserting the needle, the plunger should be pulled back to ensure that dark red, slow-moving blood comes up, which means a vein has been successfully punctured and injection may proceed [2, 34]. If an artery is accessed, identifiable by bright red blood return that is forced or "pulsing," immediate action is necessary including untying the tourniquet, removing the needle, applying pressure to the injection site, and raising the injection site above the heart to slow the bleeding [34]. If the bleeding has not stopped in 10 minutes, medical attention is required [34]. Additionally, if the vein is missed, the injection will likely be painful and could lead to the formation of abscesses [34].

After the vein has been accessed and injection has occurred, the needle should be removed at the same angle it was inserted [2, 34]. A dry swab can be used to apply to the injection site, which allows for the blood vessels to heal and platelets to aggregate around the punctured vein [2, 34]. Do not use alcohol swabs to clean the wound afterwards, as this may prevent the wound from healing/clotting [34]. Lastly, individuals may be open to other routes of administration that carry less risk of ID complications and OD such as oral, intranasal, and smoking [34]. Therefore, it is important to discuss these alternative routes with individuals wishing to minimize risks associated with IDU.

PrEP and PEP

While there are limited data regarding PrEP among PWID, evidence suggests that PrEP has been associated with a 49% reduction in HIV acquisition compared with placebo during a follow-up of 4.6 years (n = 2413) [39]. According to the CDC, PrEP should be initiated in individuals at high risk of HIV infection, which includes PWID, with the highest risk associated with sharing syringes or having an HIV-positive partner who injects drugs [40]. The current standard recommended regimen is tenofovir disoproxil fumarate with emtricitabine, which is available as a combination formula and can be taken once daily [40]. The CDC notes that for PWID, PrEP is likely a better treatment option to prevent HIV; however, PEP should be offered to those not receiving PrEP who are HIV-negative and have experienced a single high-risk exposure event within the past 72 hours [40].

Infection prevention measures among PWID are essential to maximize the health of the individual and the public. Without these, there can be clusters of outbreaks, as seen with HCV and HIV recently in many areas around the world, particularly within the United States in Scott County, Indiana, from 2015 to 2016 and in 2 cities in Massachusetts from 2015 to 2018 [41, 42]. In these areas, HIV outbreaks among PWID were identified with high rates of HCV co-infection which, in just a few years, blossomed to a few hundred cases in total. The risk of IDU-related outbreaks can be significantly reduced with sterile injection equipment, safer injection technique, PrEP, PEP, and OUD treatment. As such, these resources should be readily accessible.

IDENTIFYING TECHNIQUES TO REDUCE ID COMPLICATIONS

The primary etiology of infections from IDU derives from the endothelial damage caused by the injection of particulate matter, followed by a proliferation of high bacterial loads associated with relative immune suppression [43]. Two concerns arise from this practice—the injection technique and the type of bacteria injected. Therefore, in the setting of ID, particular attention should be paid to not only incorporate harm reduction strategies to target injection technique as discussed above,

but also to understand the underlying cause behind the infection. While there are a variety of infectious complications that may occur due to IDU, the diseases discussed in the following portion of this section are of particular interest, as not only can specific preventative measures be taken to attenuate the risk of these infections, but treatment modalities may also be adjusted based on the underlying cause of an infection that has already taken place.

HIV

According to the CDC's 2018 HIV Surveillance Supplemental Report, IDU or men who have sex with men (MSM) and inject drugs (men who endorse both) account for 1 in 10 new HIV diagnoses, yet males with HIV infection attributed to IDU were least likely to receive medical care after diagnosis, with only 51% reported to have received continuity of care [44]. As of 2015, only 52% of PWID with HIV were virally suppressed, meaning the remainder of this population (48%) could transmit the infection to others [44]. Particular preventative strategies to reduce risk of HIV transmission include incorporation of condoms in safe injection kits, PrEP, and PEP [44, 45].

Hepatitis C Virus

IDU is a primary risk factor for HCV, the most common chronic blood-borne infection in the United States, with IDU reported in >60% of cases each year HCV is assessed [46]. HCV is often overlooked as the disease has fostered a false sense of security due to its high cure rates [46]. However, a study found that the number of HCV-related deaths increased by an annual percentage of 6.2% from 2003 to 2013, while in contrast, the number of deaths from 60 other nationally notifiable infectious diseases—including HIV, *Staphylococcus aureus*, and pneumococcal infections—decreased by an annual percentage of 3.4% [47]. The increasing mortality rate despite highly effective treatments is attributed to potential ineligibility due to co-infection with HIV, incomplete treatment, and economic burden, all of which are already particularly concerning in the context of IDU [47]. High prevalence of HCV among PWID has also been associated with prolonged virus survival in contaminated syringes [48] and other possible equipment [35], which, in the setting of ID, further bolsters the need for patient counseling on safe injection techniques.

Additionally, it is important to offer HCV treatment as usual, even if IDU is ongoing, as lack of treatment will not break the cycle of HCV transmission and will decrease the likelihood of global eradication of HCV. Treating HCV amid ongoing IDU can still lead to successful eradication of virus [49], has been associated with low rates of reinfection [50], and is dually beneficial for improving OUD-related outcomes such as the 79% uptake of newly starting buprenorphine in this study, with fewer subsequent opioid-positive urine drug screens and a lower rate of opioid OD [51].

Hepatitis B Virus

The 2 most commonly reported sources of HBV infection are IDU and having multiple sex partners [52]. HBV is largely preventable through vaccinations [52]. In an ID setting, clinicians can recommend prevaccination serologic testing in high-risk individuals including persons with HIV, MSM, and past or current IDU, per CDC recommendations [52]. Although HBV vaccination at birth is preferred to confer long-term protection against HBV, there are data that suggest that the vaccination's efficacy may wane over time [53]. Vaccination is indicated in PWID who test negative for antibodies to core (HBcAb), antibodies to surface antigens (HBsAb), and surface antigen (HBsAg) [54]. The caveat with HBV vaccination is the extended follow-up necessary for completion of the vaccination schedule (0, 1, and 6 months), which can be a barrier to care in this population [54]. However, 1 study found that an accelerated vaccination schedule (0, 1, and 2 months) offered through SSPs, with the initial vaccination dose given at screening, could improve completion rates [54].

Infective Endocarditis

Almost 30% of hospitalizations for IE are related to IDU [55–57]. While IE typically presents as left-sided, a majority of IE associated with IDU is right-sided [55–57]. PWID with HIV also have a compounded risk for developing IE, with right-sided involvement being more likely [57]. Furthermore, the type of bacteria varies based on its underlying cause [57]. While IE primarily involves *Staphylococcus aureus* and *Streptococcal species*, IE among PWID has been associated with gram-negative organisms, fungi, and diphtheroids [57]. Additionally, the practice of licking needles has been associated with oral anaerobes, such as *Actinomycosis odontolyticus*, *Veillonella* species, *Prevotella melaninogenica*, and *Eikenella* [58]. It is therefore pertinent to assess the potential underlying cause of the infection, as treatment modalities may be completely altered.

Skin and Soft Tissue Infections

SSTIs are the most common ID-related reason for hospital admission among PWID [59]. Among all community-acquired SSTIs, 17% are attributed to IDU [60]. Heroin and heroin-cocaine combination injections are independent risk factors for SSTIs, with methamphetamine injection having lower rates [61]. A cross-sectional study compared those using black tar heroin with those using powder heroin and found that those using black tar heroin were more likely to have vein occlusion and abscess formation [62]. Secondary to loss of vein access, PWID reported purposeful soft tissue injection (as opposed to "missed hits," which is when one misses a vein during injection), which can independently contribute to abscess formation [62]. Similar to IE, treatment modalities for SSTIs may be adjusted based on the underlying cause of the infection. An observational study examined the risk factors among PWID in

San Francisco associated with SSTIs from 2011 to 2014 [63]. The injection practices that were associated with SSTIs were injection of nonpowder drugs, needle licking before injection, injecting with another user's pre-used equipment, receiving the injection from another person, and frequent injections [63]. Syringe sharing remained statistically significant after multivariate analysis (adjusted odds ratio, 6.38). These data propose that both injection practice and type of drug administered IV can carry their own independent risk of infection and must be examined alongside safe injection practices, which, altogether, can reduce the level of SSTIs among PWID [64].

OVERDOSE PREVENTION

According to the CDC, overdose rates have increased roughly 5-fold since 1990 [65], in line with the increasing potency of opioids, as the crisis is dominated by illicitly manufactured fentanyl and fentanyl analogues [9, 10]. PWID should be made aware of OD prevention strategies such as the use of fentanyl test strips and proper administration of naloxone.

Naloxone

Naloxone is a rapid-acting opioid antagonist that can reverse an opioid OD. The importance of the availability of naloxone and how to use it are central to the concept of harm reduction because it is one of the most direct ways to prevent fatal OD [66]. Implementing naloxone counseling interventions has been shown to not only successfully reverse ODs, but also engage patients in opioid use discussions and improve provider–patient relationships [67]. A study completed in 2013 evaluated the impact of OD education and naloxone distribution programs on rates of opioid-related OD in Massachusetts and found a reduced number of unintentional ODs at a rate ratio of 0.82 from 2002 to 2013 [68]. However, naloxone prescribing should extend beyond just those who use nonprescribed opioids, as co-prescribing to individuals receiving chronic prescription opioid therapy is associated with substantial reduction in emergency department visits and hospitalizations as well [69]. Additionally, those who have been offered naloxone reported that this was acceptable and beneficial and that they would not have had access otherwise [70]. Therefore, offering naloxone to all should be standard of care.

The US Food and Drug Administration (FDA) has approved an intranasal naloxone spray and an autoinjector naloxone formulation for community use [71]. The autoinjection device is prefilled and provides verbal instructions to the naloxone user on how to deliver the medication once activated; however, it is not commonly used due to its prohibitive cost [71]. The intranasal formulation is a prepackaged nasal spray that requires no assembly and is sprayed into 1 nostril [71]. To properly administer the intranasal formulation, one should be counseled to peel back the package, hold the device with their thumb on the bottom of the plunger and two fingers on the nozzle, place and hold the tip of the nozzle in either nostril until your fingers touch the bottom of the patient's nose, and then press the plunger firmly to release the dose into the patient's nose [71]. If there is no response within 2–3 minutes, a second dose may be administered [71]. Additionally, a less prevalent option is an intramuscular naloxone formulation that can be administered intramuscularly or adapted for intranasal use by attaching a leur-lock mucosal atomizer device [72].

Fentanyl Test Strips

Fentanyl has been the biggest cause of opioid-related fatal ODs since 2013 [73]. According to the CDC, from 2016 to 2017, the rate of opioid-related fatal ODs increased by 47% [73], and for many, the person was unaware of the presence of fentanyl in the drug supply [74]. The FORECAST study, conducted in 2017, found that the vast majority of people who use drugs would modify their behavior, abstaining from use, slowing down consumption, or using with others who have naloxone, if they were made aware that their drugs contained fentanyl [75, 76]. Testing at the Insite Safe Injection Facility in Vancouver, where drug checking with fentanyl test strips was pioneered, showed that during 1 month in 2016, 79% of all substances tested were positive for fentanyl, whether pills or powder [77]. Other studies examined the behavioral changes among PWID after incorporating fentanyl test strips into their injection practices and found an association between positive change in risk behavior and receiving a confirmatory result on a fentanyl test [78, 79].

Of note, the fentanyl test strips now being used as a harm reduction strategy were originally intended for urinalysis. As such, a special technique is required to enhance usability in this capacity. To properly use fentanyl test strips, the end product to be used should be prepared by the individual and drawn up into the syringe first. Then, 10 drops of water should be added to residual content in the cooker and thoroughly mixed. The test strip can then be dipped in the water up to the first line and held for 15 seconds, and afterwards placed on a sterile surface. One line indicates the presence of fentanyl, whereas 2 lines indicate the absence of fentanyl [34]. Further dilution may be required for certain substances.

Medications for Opioid Use Disorder

Beyond harm reduction is treatment with pharmacotherapy of an underlying SUD if one exists. For MOUD, there are 3 FDA-approved medications including opioid agonist treatment options, methadone, and buprenorphine, in addition to an opioid antagonist treatment option, extended-release naltrexone [80]. Methadone and buprenorphine have been associated with significant reductions in OD and emergency department utilization or hospitalization related to opioids and are considered first-line agents [81–83]. Despite this, methadone and buprenorphine remain underutilized given significant treatment access limitations [80]. Methadone

Table 2. Summary of Harm Reduction Services to Offer in an ID Specialty Practice

Recommendation	Purpose
Offer MOUD to those with OUD	Reduces HCV and HIV risk behaviors and ongoing transmission, improves HIV viral suppression, improves HCV cure and decreases reinfection risk, and reduces OD risk
Implement program for safe injection kit or safer equipment supply access	Avoid use of nonsterile equipment
Incorporate harm reduction–informed services before patient discharge/cessation of outpatient appointment	Educate patients on safe injection techniques and alternative equipment in the absence of preferred equipment or availability of safe injection kit
Screen for risk of HIV and offer PrEP and PEP as appropriate	Reduce HIV transmission rates
Assess underlying cause of IDU-associated infection	Adjust treatment for IDU-associated microbes
Offer and provide naloxone	Reduce OD
Develop relationship with nearest SSP	Connect PWID with readily available access to safer injection equipment

Abbreviations: HCV, hepatitis C virus; ID, infectious diseases; IDU, injection drug use; MOUD, medications for opioid use disorder; OD, overdose; OUD, opioid use disorder; PEP, postexposure prophylaxis; PrEP, pre-exposure prophyalxis; PWID, people who inject drugs; SSP, syringe service program.

access is restricted due to prescribing limitations for OUD outside of a certified opioid treatment program, which preclude low-threshold access from an ID setting. Buprenorphine, on the other hand, can be prescribed and managed in outpatient settings, though obtaining a Drug Addiction Treatment Act (DATA) waiver to prescribe is required first. As such, access is largely restricted by the limited number of clinicians who have obtained the DATA waiver to prescribe buprenorphine [80]. However, access could be readily expanded if ID clinicians obtained the DATA waiver and offered this as a treatment option to PWID alongside harm reduction during ID encounters. Of note, extended-release naltrexone may lead to reduction in opioid craving, use, and OD [83–85]. However, more recent evidence suggests that extended-release naltrexone may be less effective for protection from OD and all-cause mortality when compared with methadone or buprenorphine [81, 82]. Lastly, there is an extensive body of literature associating MOUD with reduced risk of HIV and HCV transmission in addition to improved viral suppression [86–95].

CONCLUSIONS

Nonsterile injection practices among PWID have perpetuated the influx of ID, with certain underlying etiologies associated with specific microbes. Harm reduction can intersect this epidemic by incorporating proper education and providing infection and OD prevention equipment and education in the ID setting. In clinical practice, ID clinicians should familiarize themselves with the aforementioned strategies, incorporate them into a harm-reduction informed service within their practice whenever possible (Table 2), and utilize publicly available harm reduction and SUD treatment resources for additional support and training (Table 3). In the absence of providing safe injection kits, patients should be counseled on safe injection

Table 3. Publicly Available Resources for Harm Reduction and SUD Education, Training, and Support[a]

Content	Resource
DATA waiver training for MD, APRN, PA, and medical students	Providers Clinical Support System • https://pcssnow.org/medications-for-addiction-treatment/ American Society of Addiction Medicine • https://elearning.asam.org/buprenorphine-waiver-course
Find nearby DATA-waivered clinicians and OTPs[b]	Substance Abuse and Mental Health Services Administration • https://www.samhsa.gov/medication-assisted-treatment/find-treatment
Naloxone intranasal device education pamphlet and training video	Narcan • https://www.narcan.com/patients/how-to-use-narcan
Naloxone auto-injector education pamphlet and training video	Evzio • https://evzio.com/
IDU-related harm reduction	National Harm Reduction Coalition • https://harmreduction.org/issues/safer-drug-use/injection-safety-manual/
SSP laws by state[c]	The Policy Surveillance Program • http://lawatlas.org/datasets/syringe-services-programs-laws
Locate nearest SSP[d]	North American Syringe Exchange Network • https://nasen.org/map/

Abbreviations: APRN, advanced practice registered nurse; DATA, Drug Addiction Treatment Act; IDU, injection drug use; MD, medical doctor; OTPs, opioid treatment programs; PA, physician assistant; SUD, substance use disorder; SSP, syringe service program.

[a]This is not a comprehensive list of resources, but rather a starter guide for accessing additional training or support.

[b]Incomplete list as providers must consent to public listing.

[c]Last update: August 1, 2019.

[d]Regularly updated, but last date of update not available.

techniques, proper and alternative equipment, and the location of the nearest SSP and offered PrEP and PEP. Lastly, to further expand treatment access and reduce harm, ID clinicians should offer naloxone and become waivered to initiate buprenorphine for those interested in this treatment pathway.

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