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A systematic review to study the global patterns and policies of HIV harm reduction programs and their impact among people who inject drugs

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Abstract:

Aim: This study aims to provide an updated estimate of HIV prevalence among people who inject drugs (PWID) globally, as well as investigate different policies and methods for applying harm reduction. This article focuses on the two major and the most frequently used harm reduction techniques, Syringe-Service Programs (SSPs) and Opioid Agonist Therapy (OAT). **Methods:** A comprehensive systematic review was undertaken across multiple international databases during the period of (August-December 2021). For studies conducted before 2005, we used data from a previous published systematic review. Thirty-six studies were included, including studies that had performed HIV testing and had a confirmed diagnosis of HIV through repeating the enzyme-linked immunosorbent assay (ELISA) or Western immunoblot assay (WB) and Polymerase Chain Reaction (PCR). **Results:** Both methods similarly achieve a significant decline in the incidence of new HIV cases among PWID. In fact, 22 out of 36 studies show a reduction in HIV incidence as a result of harm reduction programs implementation, where the highest reduction is noticed in the already high incidence countries and the lowest impact lies inside the low incidence countries.
Keywords: HIV, PWID, Harm reduction, SSP, OAT

Introduction

HIV (*human immunodeficiency virus*) is a member of the retrovirus family in the genus of Lentiviruses, and attacks the immune system making the human body vulnerable to various infections and diseases (1). If left untreated, HIV can lead to AIDS (*Acquired Immunodeficiency Syndrome*) which is a chronic life-threatening that suppresses the human immune system and impairs the body's vital functions (2), HIV is usually incurable, it lasts for a lifetime once the virus enters the human body (3) .The high incidence of HIV/AIDS is still the underlying cause of many devastating health conditions and subsequently high rate of global mortalities worldwide (4) **.**

Since the outbreak of the pandemic, there are more than 30 million aids related deaths and 37.6 million people living with HIV (as of 2020) (4) (5)

There are different routes for HIV transmission as unprotected sex, blood transfusion, sharing contaminated needles and mother to child transmission (during pregnancy, childbirth and breastfeeding) (5) (6)**.** Moreover, recent studies showed that the rate of HIV transmission through sexual behavior continues to fall off and injection-induced transmission is currently becoming the predominant route in new cases (7) (8)· This is mainly attributed to the ability of HIV to survive in a previously used needle for up to 42 days, which explains the high rate of infection among PWID(9) (10). In other words, equipment sharing among PWID accounts for approximately one in every ten new HIV infections globally (11) . Accordingly, there was a clear recognition that (PWID) were an important demographic for HIV control in the general population in many countries (12) (13). This has led to declaration of harm reduction techniques among PWID as key to preventing the spread of HIV by the World Health Organization (14) (15)

Harm reduction is a concept that has been widely used in the public health sector for a long time (16). It includes Syringe-Service Programs (SSPs), a public health initiative to decrease blood-borne diseases, such as HIV and HCV among PWID by distributing sterile syringes, and Opioid Agonist Therapy (OAT), an approach involving use of an agonist (a substance having a sub-optimal effect on opioid receptors) (17) to lessen cravings for opioids and reduce consumption of Syringes (18) . Even though scientific debate about harm reduction is now over, harm reduction has been shown convincingly to be effective in reducing HIV, as well as safe and cost-effective (19) (20). It essentially means that reducing the adverse consequences associated with drug comes prior to eliminating drug consumption (21) . However, various stigmas still threaten the success of harm reduction campaigns, such as the debate on whether harm reduction can encourage injections among drug users (22). Also, drug users are often considered criminals (23) which acts as a barrier to their access to HIV protection programs (24)Those people face several violations in their search for harm reduction programs in the form of harassment, beating, and denial of basic services (13) (25) (26)While harm reduction is still opposed in many countries including the majority of the Middle East countries (14) (25), it is currently accepted and applied in more than 60 countries in Asia, Europe, and Canada (14) Moreover, harm reduction is admitted by most of the UN essential agencies including WHO, UNICAF, and UNAIDS, and supported by many

international federations and committees such as the Red Cross (25)(27). Methadone maintenance treatment and needle syringes programs are the leading programs among all the reduction programs. Both of them are applied in the 25 countries of the EU. (27) (28)

Since harm-reduction approaches recently gained popularity worldwide and became globally accepted, the international HIV/AIDS community urged countries to take steps to prevent HIV transmission among injecting drug users in 2010(29). Accordingly, six countries of the highest burden countries, accounting for half of the global population of PWID were reviewed for progress in policy adjustments (29) (30). Several countries subsequently changed their policies including China, Malaysia, Vietnam, and Ukraine to improve coverage of important PWID interventions. Promising improvements include an increase in PWID obtaining OAT in both Vietnam and China, as well as a move in Malaysia from a punitive law enforcement strategy to evidence-based treatment (16) (31)

On the other hand, there have been no advancements in PWID to SSPs and OAT in the United States and Russia. Instead, there have been several policy setbacks in these countries(32), with Russia expressing its opposition to OST and blocking access to methadone information, and the United States reinstituting its congressional restriction on federal funding for NSPs (30) (31). In fact, harm reduction is of extreme importance in the so-called ‘closed settings’ such as jails and prisons. Once behind bars, HIV infection risk is multiplied many times, reasons behind that include for example, the large number of injecting equipment sharing partners, the severely degraded condition of needles and syringes and the mixing of diverse demographic and geographical groups in prison (33) (34). Despite the evidence for harm reduction and widespread endorsement by international public health and drug policy bodies, provision remains extremely limited in prison settings globally (34)(35). Several obstacles are responsible for this crisis, as the lack of political leadership and a major shortage of funding (36) (37). It is impossible to solve the HIV epidemic without the participation of injecting drug users, who are the market for harm reduction strategies. To put this collaboration in motion, it is necessary to "turn a blind eye" to illegal activity and allocate a percentage of public funding to what many call promoting drug use. Advocates of zero tolerance view all illicit drug use as inherently evil, while harm reduction professionals focus on preventing harm. With this rather pragmatic approach, some continued use of psychotropic drugs seems inevitable (16)(38).

In this paper we will be reviewing the different patterns and policies of HIV harm reduction interventions including service syringe program (SSP) and opioid agonist therapy (OAT) in several countries and their role in HIV prevention globally.

Methodology:

A comprehensive search of all literature of relevance to harm reduction in relation to HIV prevalence was conducted , and more than 53 references were obtained. We then reviewed these references to eliminate those that did not cover injecting drug use, or illicit drug use (such as studies on changing sexual risk behavior in non-drug users); and the prevalence of HIV in relation to sexual transmission. The following resources were accessed: SAGE, PubMed and AUC library, Cochrane library. Hence, an already existing framework was used to aid in the identification of harm reduction in controlling HIV among people who inject drug (PWID), that included search strategy in all the mentioned used articles through screening of the titles by the whole team, followed by screening the whole full texts also by the whole team of reviewers that went in depth of the details. Original studies with a variety of designs including cross-sectional, cohorts, case–control studies, and qualitative studies were considered for inclusion. The following inclusion and exclusion criteria was agreed on by the authors.

Inclusion and Exclusion Criteria

Included studies involved (a) studies reporting the prevalence of HIV in PWID (b) studies where HIV testing was performed and a diagnosis of HIV confirmed through ELISA, WB and PCR, and (c) studies where HIV prevalence has been reported in a sample size of at least 30 PWID. Exclusion studies included (a)

(1)case reports and case–series;

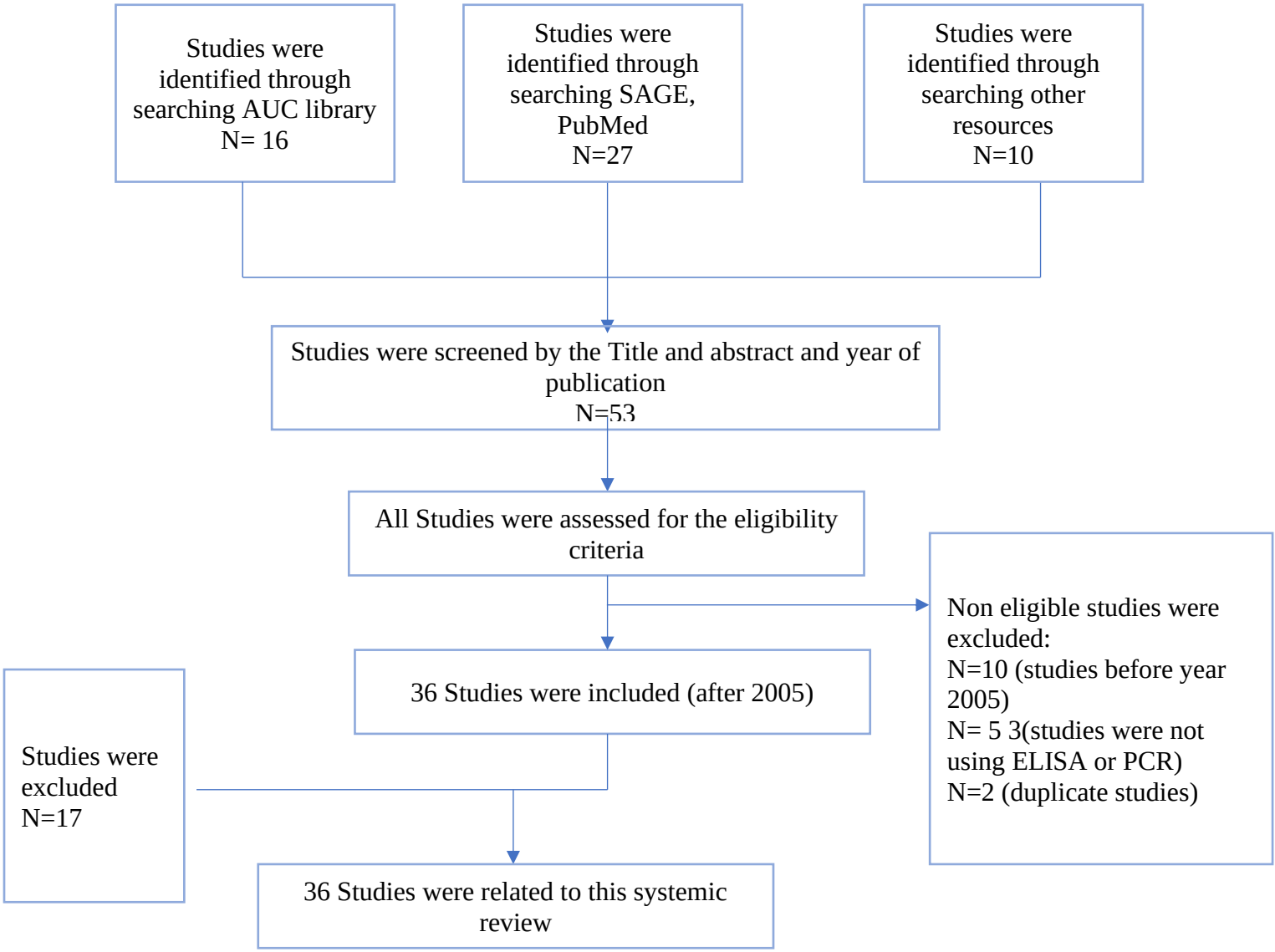
(2) Studies conducted in infectious diseases wards or referral HIV counseling centers;

(3)Studies that suffered discrepancies in their data or their main information, such as sample size.

In addition, we reviewed all studies included in the previous systematic review on HIV prevalence among PWID worldwide conducted since 2010. Studies considered not applicable were double checked to ensure that they won't be included.

When conducting our search and screening we applied a time limitation and excluded studies conducted before 2005.We then further sorted the remaining studies into those reports that covered an intervention, versus those that were epidemiological or descriptive in nature. We retained the epidemiological and descriptive literature to use for background research. Across the all harm reduction intervention studies, that were reviewed; research approaches and methods were greatly different.

Figure 1 Flow-chart of the search and selection process



Results:

Table 1 Most Recent HIV Harm Reduction Trends and Policies

Study Number	Study (first First Author & Year of Publication	Sc Scope	Harm Reduction Program Implemented		Most Recent Trends and Trends and Policies
			SSP*	OAT*	
1	***Louisa Degenhard et al. 2013***	What has been **achieved in the HIV Harm reduction interventions** in **the six highest HIV burden countries** (27)	✓	✓	Policies are altered to increase harm reduction coverage among PWID in **China, Malaysia, Vietnam and Ukraine** with the **most significant changes** in **Ukraine** and **Vietnam**, witnessing around **1.5% increase** in PWID accessing **NSP*** and almost **7 times increase** in the number of **OAT*** clients respectively over the last decades. In contrast, there were **no further advances** on access of OAT and NSPs in both **Russia** and the **USA**. **Russia** and the **USA harm reduction promoting policies** experienced major **setbacks** over the last few years, the Russian government prolonged its stand against OAT and the USA relaunched its Congressional ban on Federal funding for NSPs.
2	**Katherine La Monaca *et al.* 2019**	Studying **Harm Reduction trends** in **Eastern Europe** and **Central Asia in 2016**(39)	✓	✓	--The **highest** percentages of ***OAT**** coverage among **EECA***countries is in **Lithuania** and **Georgia**, with around **34%** and **22%** respectively, whereas the lowest percentages are in **Azerbaijan** and **Kazakhstan** with **0.5%** OAT coverage. In **Russia, and Uzbekistan** OAT are not available at all.

					As for ***SSP*, Tajikistan** and **Estonia** are the leading countries, with **345** and **230** needles distributed per PWID respectively, whereas **Azerbaijan** and **Russia** witness minor **SSP** with only 34 and 2 needles distributed per PWID respectively.
3	**Gen Sander 2019**	The **availability** and **accessibility** of **Harm Reduction programs** in **prisons** (40)	✓	✓	**NSPs** are very limited in prisons globally, such programs are being implemented in more than **one** prison in only **10** countries, whereas NSPs are available in **86** countries worldwide outside of prisons, which represents **less than 1%** of prisons globally. The availability of **OAT** in prisons is **more common** than **NSPs.** Recently, a type of OAT is offered in no less than **one** prison in **54** countries, which accounts for almost a **4% increase** since **2014** Prisoners still encounter many **challenges** obstacles in **accessing** OATs where it is provided though.

Table 2: Impact of HIV Harm Reduction

Study number	Study (first First Author & Year of Publication	Sco Scope	Harm Reduction Program Implemented		Impact
			SSP*	OAT*	
1	***Javier Cepeda 2020***	Effect **of a 60% increased SSP* coverage** is measured **in 3 different HIV incidence settings** between **2020** and **2030**(21)	✓	✓	--In **high incidence** settings **(Bangkok-like): 65% decrease** -In **middle incidence** settings (**Montrea**l-**like**):**63% decrease** -In **low incidence** settings **(St. Petersburg-like): 22% decrease**
2	***Khalid Tinasti 2016***	A **comparison** of **HIV prevalence** between **countries** that have **effective harm reduction policies** and **countries** where **people don't have access to harm reduction programs**(41)	✓		In **Switzerland**, massive **implementation of SSPs** among PWIDs **lead** to a significant **decline** in HIV infections **over 12 years** to **reach 5 %** in **2009**, whereas in **high drug injection burden countries** including **Russia, China, and the United States**, no harm **reduction services are introduced**, HIV **prevalence rates** are, respectively **37%, 12%, and 16%.**
3	***Ehsan Jozaghi, 2020***	The **role** of **OAT** in **Prisons**(18)		✓	**OAT result** in a **major decline** of **post-release death rates associated with drug-overdose**. Contemporary **findings though show** that **people** tend to **shift** from **prescription opioid misuse** to **street-based forms** (e.g., heroin and fentanyl derivatives) this makes the **government's regulations** on opioid use **a key factor** to guarantee **that alternative harm-reduction programs are effective**
4	***Andrea J. Low 2016***	A recent **meta-analysis** conducted **in North America, Europe and Asia**, to study the **effect** of **OST using methadone maintenance** on the **prevalence of HIV among PWID**(42)		✓	**OST** using methadone maintenance treatment leads to a **54% increase in the odds of** being on Antiretroviral Therapy

5	***David P.Wilson 2015***	**The effect of SSPs** on both **HIV incidence** and the **economic growth** over a **10 years period in Australia** (32)	✓		**SSPs** not only **reduced** HIV incidence by up to **74 percent** in Australia over a ten-years period, but they also saved money, with a **return on investment** of between **$1.3 and $5.5** for every $1 invested.

Discussion: (Noura, Mirna)

This paper updated data on the trends and effects of two major HIV harm reduction interventions (SSP and OAT) among PWID worldwide, which in turn highlighted the absence of harm reduction programs in two of the highest HIV burden countries, namely USA and Russia.

The setbacks observed in harm reduction programs are attributed to significant deficits mandating the cancellation of HIV global funds to the countries that are too wealthy to be financially supported, including Russia and China (43). The Russian NGO's were still entitled to two years grants to proceed with the services that they have already started, however, the cancellation of further funds caused the suspension of many ongoing harm reduction services and the cessation of similar initiatives in the Russian NGO's and HIV harm reduction coalitions (44) The US ban on federal funding for NSP's also crippled the potential SSP's expansion in countries where HIV US funds are essential to support further harm reduction programs, including Ukraine and Vietnam. In fact, this policy shift impedes both, Bush's Emergency Plan for AIDS relief and Obama's administration call for an AIDS free generation (45)and impairs the HIV prevention researchers ability to meet their ethical commitment of providing their trial candidates with a decent level of care(44)

In contrast, there has been some movement by several UN entities towards the declaration of an evidence and rights-based perspective of the rules governing HIV harm prevention among people who inject drugs. For instance, 12 UN agencies (International Labor Organization; Office of the High Commissioner for Human Rights; UN Development Program; UN Educational, Scientific and Cultural Organization; UN Population Fund; UN High Commissioner for Refugees; UN Children's Fund; UN Office on Drugs and Crime; UN Entity for Gender Equality and the Empowerment of Women; World Food Program; World Health Organization; and Joint United

Nations Program on HIV/AIDS) issued a shared statement dictating the closure of mandatory rehabilitation centers and the provision of evidence informed and rights based social and health services among the HIV community (46). The high level, UN-sponsored Commission on HIV and the Law sent a clear message in July 2012 about the HIV prevention needs among PWID and the commitment of nations to provide them, for both legal and human rights purposes (47) (48)

As for the implementation of harm reduction programs in prisons, studies have indicated that harm reduction may be applied safely and successfully in closed settings, with evidence of reduced drug injection, needle and syringe sharing and overdose risk (49). However, harm reduction services and programs were found to be very limited in jails, for instance, only ten nations currently offer NSPs in at least one prison, compared to 86 countries that offer the service outside of prisons and only five of the 19 Middle Eastern and North African countries provide OST services in prisons (50). As a response to the limited availability of harm reduction programs in prisons and their recognized positive impact in such settings, the WHO, UNODC, and UNAIDS, have issued worldwide guidelines on how to implement harm reduction services in jails back in 2013 (51). Then, another global call to make harm reduction interventions more accessible in jails was raised by the outcome of the UN general assembly special session in 2016, urging member states to provide harm reduction measures such as NSP and OAT in jails(40)

Strengths and Limitations

Findings related to the trends of HIV harm reduction interventions were obtained from peer-reviewed data using reliable research engines including PubMed and BioMed Central and from websites demonstrating definitive and global data related to HIV and IDU; websites of national ministries of health, national AIDS committees, UN agencies and relevant NGOs. Websites in languages other than English were also checked to retrieve the non-English documents tackling the research question. Data was then reviewed by a team of researchers to include the most recent information and to take in preference national data over subnational data. The findings were adjusted to be utilized for comparison between countries using common parameters, for instance, if the data were associated with a period of less than or more than a year, a constant rate of access or distribution was estimated, and numbers adjusted for 12 months accordingly. Since the number

of opioid dependent IDUs couldn't be obtained for each country, the percentage of the number of people receiving OAT per 100 IDUs was calculated as well, regardless of the kind of drug injected.

Data related to HIV harm reduction programs patterns and effects in prisons was derived from research conducted for Harm Reduction International's *2018; The Global State of Harm Reduction* report. For that report, information was collected using existing sources including reviews and records from several multilateral agencies, non-governmental organizations, researchers opinions and scholarly articles. Regional harm reduction coalitions and HIV harm prevention and reduction advocates provided helped as well in the collection of qualitative data related to the progress and extent of harm reduction programs availability in jails and detention centers on national and international levels.

The information demonstrating the impact of the two harm reduction techniques discussed in this review was also retrieved from studies with reliable statistical analysis. For instance, the meta-analysis used to test the effect of OAT on HIV incidence (table 2, 4th study) has a resulting P value of 0.002, which in turn shows that the reduction of HIV incidence upon the application of OST was not due to chance, the same applies to the data studying the impact of SSP on HIV incidence too. For example, the study used to measure the effect of a 60% increased SSP coverage in 3 different HIV incidence settings (table 2, 1st study) revealed a 95% confidence interval value, which again shows that the decrease in HIV incidence in each of the demonstrated settings that was attributed to the implementation is statistically significant.

Some implicit limitations exist in the proposed findings though. For instance, the main focus of the review was about 2 core evidence-informed implementations (OAT and SSP) to address the complications of HIV among PWID, however, emerging interventions that were also found to be effective such as HIV harm reduction through the implant of sustained release synthetic drugs (52) and interventions that prevent initiation to drug injection (53) were not tackled.

Another limitation to this review is the fact that only quantitative data demonstrating the coverage of HIV harm reduction interventions and their impact were observed, in contrast, the quality of harm reduction programs and any other variables determining their success were ignored. For instance, although the availability of OAT programs in China recently increased, low mean dosages of methadone (an opioid-agonist) and the detention of those who were using illicit

forms of opioids lead to the a high rate of drop out from MMT (Methadone Maintenance Treatment) programs(54). Additionally, any potential further risk among polysubstance-using PWID was neglected, regardless of the fact that HIV prevalence among people who inject primarily stimulants (a broad class of drugs that increase the activity of the central nervous system) (55) was found to be higher than those who use both opioids and stimulants (56)(27)

Conclusion:

The global prevalence of HIV among PWID recently reels in a downward spiral, which can be attributed to the substantial increase in the application of the harm reduction policies since 2010. That followed the United Nations' agencies collaboration in an attempt to urge countries to fairly provide harm reduction techniques for IDUs using OAT and SSPs. Although both OAT and SSPs have had similar results in minimizing the incidence of HIV among IDUs, SSPs is the most widely used, especially in low- and middle-income countries and in high-risk closed settings due to their low cost compared to the extravagant methadone and buprenorphine used as OAT. It is worth mentioning though that OAT holds a distinctive advantage. The Studies reviewed obviously emphasize the psychosocial and social benefits of OAT for individuals and their communities which makes OAT more cost-effective than SSPs despite its high cost. This is why, some countries have developed hybrid programs to get the cumulative advantages of both techniques.

Notably, harm reduction interventions managed to reduce the behavioral risks among injecting drug users significantly in the last few decades, yet, many countries still have constraints on harm reduction implementation policies associated with social stigmas.

Eventually, the proposed systematic review will aide HIV harm reduction advocates who are looking forward to enhance harm reduction promoting policies in high HIV burden countries. That's to say, that the evidence gathered in the review shows the impact of harm reduction policies implementation on the incidence of HIV among PWID and the drawbacks of harm reduction policy setbacks in some places around the world. This will in turn help HIV harm reduction activists worldwide to raise calls to action for HIV harm reduction funding and promotion.

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