Towards combination HIV prevention for injection drug users: addressing addictophobia, apathy and inattention

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Purpose of review
Recent breakthroughs in HIV-prevention science led us to evaluate the current state of combination HIV prevention for injection drug users (IDUs). We review the recent literature focusing on possible reasons why coverage of prevention interventions for HIV, hepatitis C virus (HCV) and tuberculosis among IDUs remains dismal. We make recommendations for future HIV research and policy.

Recent findings
IDUs disproportionately under-utilize voluntary HIV counseling and testing (VCT), primary care and antiretroviral therapy (ART), especially in countries that have the largest burden of HIV among IDUs. IDUs present later in the course of HIV infection and experience greater morbidity and mortality. Why are IDUs under-represented in HIV-prevention research, access to treatment for both HIV and addiction, and access to HIV combination prevention? Possible explanations include addictophobia, apathy, and inattention, which we describe in the context of recent literature and events.

Summary
This commentary discusses the current state of HIV-prevention interventions for IDUs including VCT, needle and syringe program (NSP), opioid substitution therapy (OST), ART and pre-exposure chemoprophylaxis (PrEP), and discusses ways to work towards true combination HIV prevention for IDU populations. Communities need to overcome tacit assumptions that IDUs can navigate through systems that are maintained as separate silos, and begin to take a rights-based approach to HIV prevention to ensure that IDUs have equitable access to life-saving prevention and treatments.

Keywords
drug abuse treatment, HIV, injection drug use, needle and syringe exchange programs, pre-exposure prophylaxis

INTRODUCTION

These are heady times for HIV prevention. *Science* named the findings from the HIV Prevention Trials Network (HPTN) 052 as the 'scientific breakthrough' for 2011 [1▪▪]. HPTN 052 showed that early initiation of antiretroviral therapy (ART) for HIV-positive partners in HIV-serodiscordant couples dramatically reduced transmission to the HIV-negative partner (96%) and significantly reduced health problems (41%) in the HIV-positive partner. Moreover, combination approaches that integrate ART with behavioral interventions demonstrated significant and relevant reductions in acquiring HIV [2]. For the first time, there exists a variety of efficacious tools for HIV prevention – both medical and behavioral – that can be used in combination to optimally address the specific prevention needs of distinct communities.

Yet not all communities have equal access to HIV prevention and care, especially to interventions that involve medications and an infrastructure

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KEY POINTS

- Addictophobia, apathy and inattention can contribute to under-utilization of combination HIV-prevention approaches that integrate anti-HIV medications, even though IDUs represent a subgroup that may experience differential benefits to these interventions.
- Inclusion of IDUs in clinical trials of combination HIV prevention is rare, even though doing so would yield data to describe whether or not anticipated problems (e.g. attrition, medication nonadherence) would in any way limit use of these new prevention approaches in IDUs.
- Especially in resource-limited settings, some of the most cost-effective approaches to reduce HIV infections and deaths may be existing, proven tools such as needle and syringe programs (NSP), opioid substitution therapy (OST), voluntary HIV counseling and testing (VCT) and interventions promoting linkage to care.
- Providing access to combination prevention outside contexts in which treatment and prevention services are provided to IDUs (e.g. NSP, OST, VCT) will limit uptake, ensuring combination prevention is under-utilized and may contribute to morbidity and mortality – even when we have the best of intentions.

needed to deliver them. A historical case in point is the development and implementation of guidelines for postexposure prophylaxis (PEP). Initial efforts [3] that guided use of anti-HIV drugs as PEP were published in 1990 and updated [4] in the form of guidelines through 2005. Early recommendations for PEP were constrained to healthcare workers who experienced HIV exposures in the workplace and were based on data from primate studies, studies of peri-natal prophylaxis and one case-control study of healthcare workers [5]. For individuals potentially exposed to HIV in settings other than work, a consensus statement cited an overall lack of evidence to support initiating PEP and instead noted '. . .medical treatment after sexual, injection drug use or other nonoccupational HIV exposure is less effective than preventing HIV infection by avoiding exposure' [6]. Not until 15 years after recommendations for initiating PEP for occupational exposures was the guideline broadened to include individuals who experienced nonoccupational exposures – largely without the controlled data that had previously been a major reason for excluding them. Still, citing concerns over ethics, morals and economics, PEP was considered efficacious but expensive [7], and policy makers responded by offering recommendations that reflected a hierarchy: healthcare workers who experienced occupational exposures obtained access first. Later and less consistently, victims of rape received access. Much later and far less consistently today, individuals who experience sexual or injection-related potential exposures are recommended for PEP.

During 2010 and 2011, findings from key modeling scenarios demonstrated the importance of combination HIV-prevention interventions for IDUs at the population level. Using modeling, Degenhardt *et al.* [8▪▪] showed that when simultaneous scale-up of needle and syringe programs (NSPs), voluntary counseling and testing (VCT), opioid substitution treatment (OST) and ART were implemented when CD4 cell counts drop below 350 cells/mm^3, HIV incidence could be reduced by up to 63%. Similarly, Strathdee *et al.* [9▪▪] showed that in countries where HIV epidemics among IDUs are established or emerging, the benefits of these combinations of interventions were amplified by structural interventions that optimized either access or efficacy of these intervention components. Furthermore, in settings in which the force of infection is high (as is the case in an HIV outbreak), interventions that have an impact on syringe sharing (e.g. NSP, OST) need to operate at very high levels of efficacy to have an impact on syringe sharing [9▪▪]. This situation underscores assertion by Kurth *et al.* [10▪▪] that combination HIV prevention should address both infectiousness and susceptibility.

Research is still needed to identify the most effective combination of interventions for IDUs and other key populations and settings [11▪], without assuming that 'one-size-fits all' [10▪▪]. There is also a need to 'unpack' combinations of interventions to determine which components generate the greatest preventive fraction, and whether some components act synergistically or compete. Yet, in contrast to ripples of excitement in peer-reviewed literature over combination HIV-prevention approaches, including antiretroviral pre-exposure chemoprophylaxis (PrEP) [12,13], empirical data on PrEP and other combination-prevention strategies among IDU populations are virtually absent – and thus cannot inform the discourse on the value of PrEP in IDUs.

Impressive research also emerged with respect to treatment for hepatitis C virus (HCV) and tuberculosis (TB), which are the most common co-infections among HIV-positive IDUs and those at risk, especially in lower and middle-income countries. Sherman *et al.* [14▪] found that a 24-week course of response-guided telaprevir combination HCV treatment was as effective as the standard 48-week course. The recent trend towards oral combinations of antiviral drugs for treatment of HCV

infection without interferon should lead to ART-like interventions for HCV-infected IDUs. Also in 2011, the US Centers for Disease Prevention and Control published guidelines for a shortened course of treatment for latent TB infection [15]. Taken together, IDUs should soon be able to access more manageable treatment regimens for treating HCV and TB; 'combination prevention' should be extended to interventions for important comorbid conditions affecting IDU populations.

Yet the international literature is rife with continued reports that IDUs are disproportionately under-utilizing VCT, primary care and ART, especially in countries that have the largest burden of HIV among IDUs [16▪▪,17]. Consequently, IDUs often present later in the course of HIV infection and experience greater morbidity and mortality than other risk populations [18], even in countries like Brazil, which has a relatively high coverage of ART among IDUs [19]. Why are IDU populations underrepresented in terms of HIV-prevention research, access to treatment for both HIV and drug addiction, and access to HIV combination prevention interventions? Possible explanations include addictophobia, apathy, and inattention.

ADDICTOPHOBIA

Addictophobia is a term that appeared in the literature in 1991, which was described as the exaggerated fear, aversion and/or discrimination against drug users [20]. Since the beginning of the HIV epidemic, IDUs have been vilified, stigmatized, marginalized and blamed for their HIV infection. A 2011 report by Harm Reduction International [21▪] identifies at least 12 places with legislation allowing judicial corporal punishment for drug and alcohol offences, which is a violation of international human rights law [i.e. Singapore, Malaysia, Iran, Yemen, Saudi Arabia, Qatar, United Arab Emirates, Libya, Brunei, Darussalam, Maldives, Indonesia (Aceh) and Nigeria (northern states)]. In several countries, including China, Cambodia, Laos, and Vietnam, drug users are subject to incarceration in compulsory drug centers where forced labor, inadequate medical care, and abuses have been reported [22]. In Thailand, a 'war on drug users' has been underway in response to methamphetamine epidemics [23]. Ongoing prosecution, including the death penalty, are reportedly driving the tendency for IDUs to transition towards more harmful polydrug injection [24]. Methamphetamine injection is also increasing [25].

A recent example of addictophobia is the return of the United States' Congressional ban on use of federal funds to support NSPs both domestically and internationally that was approved by both houses of Congress at the end of 2011. The use of US federal funds for NSPs was enacted in 1988, but had been repealed in 2009, after eight US government commissioned reports and a plethora of international research consistently showed that NSPs can reduce syringe sharing, HIV prevalence and incidence and are cost-effective. In response to this political about-face, Laura Thomas of the San Francisco Drug Policy Alliance stated, 'Reinstating the ban is murderous. It's saying that people who use drugs should contract fatal and expensive diseases and die. . ..this is a truly shameful moment, when we go backward instead of forward, and let a politics of ignorance, of stigma, of hate, win out over compassion, science and a desire for a healthy community' [26]. Furthermore, in at least 36 US states, legislation has been introduced requiring applicants to public assistance programs (e.g. food stamps, unemployment benefits and heating subsidies). Around the world, policies that address addiction and the health of addicts are steeped in attributions of self-blame, moral failure and psychopathy. This contrasts with over 30 years of scientific findings that have articulated the medical basis of opiate addiction, opiate-seeking behavior, and effectiveness of OST. With rare exception, decisions about providing access for IDUs to health protecting interventions continue to be driven by morality rather than empirical data.

Another example is the general lack of inclusion of IDUs in controlled trials of combination prevention interventions. Whereas few protocols expressly exclude IDUs, all contain a provision allowing an investigator to exclude any individual whose behavior would interfere with safe, consistent participation, such as active injection drug use. Concerns are frequently articulated about drug toxicities from interactions between ART and illicit drugs, about drug users' inability to adhere to treatment, and about concomitant risks for development of drug resistance [2]. As a result, trials often include former, but not active IDUs. IDUs are not only under-represented in trials, they are under-represented among those receiving ART in many countries, both rich and poor. There are exceptions, such as Vancouver, Canada, where additional outreach efforts are employed to engage IDUs [27▪] but even so, Vancouver researchers report subgroups of IDUs that have sub-optimal highly active antiretroviral therapy (HAART) access, such as sex workers and the homeless [28].

APATHY

Apathy – or indifference to the suffering of drug users and their right to access HIV prevention and

treatment – may be a consequence of addictophobia, a lack of political will, or the extreme marginalization that often prevents drug users from having a place at the bargaining table to advocate for services. How do we advocate for HIV treatment as a prevention strategy, when HIV treatment is not even being delivered to IDUs for its primary purpose (i.e. reducing morbidity and mortality)? Before we can justify incorporating PrEP into combination prevention interventions for IDUs, we need to do a better job of ensuring that the components that have already been shown to be effective are brought to scale. Indeed, the United Nations Office on AIDS articulated nine HIV interventions as essential to prevent HIV among IDUs, including sterile syringe access through NSPs, OST (methadone and buprenorphine), HIV counseling and testing, ART, prevention and treatment of sexually transmitted infections (STIs), condom distribution programs, information and education campaigns, vaccination and treatment of viral hepatitis, and prevention and treatment of tuberculosis [29]. It is time to challenge the policies of countries and agencies unwilling to support harm minimization as an excuse to reallocate prevention resources towards unproven interventions at the expense of proven, cost-effective interventions. Moreover, efforts to divert prevention resources that would otherwise be used for IDUs to more socially acceptable populations (e.g. mothers and children) should be challenged.

Unfortunately, there is no sign that the low global coverage of HIV prevention interventions and ART among IDUs will improve anytime soon. The recent announcement of the cancellation of the next round of the Global Fund competition and the President's Emergency Plan for AIDS Relief (PEPFAR)'s reduced funding commitment will disproportionately affect the delivery of HIV prevention and care services for IDUs in countries where HIV infections among IDUs continues to surge (e.g. China, Russia, Ukraine, Vietnam) [18]. Legislation that prevents PEPFAR funds from being used to provide syringes in any international setting undermines the successes that this program has achieved with other populations, and is an act we condemn. Rollbacks of Ryan White funding mean that there will be longer delays for HIV care among the poor, who are disproportionately IDUs and under-represented minorities.

INATTENTION

Some subgroups of IDUs remain especially vulnerable. One is adolescent IDUs, many of whom are street youth. In a 2011 study of street youth in Ukraine, Hillis *et al.* [30▪] found that being both orphaned and homeless had additive effects on both injection drug use initiation and HIV risks. In an accompanying editorial, Mastro *et al.* [31] call for structural interventions for this doubly marginalized group, which should include social welfare systems, child protection and support services for victims of violence and abuse. These recommendations underscore the notion that combination HIV prevention should not focus solely on the individual, but on structural factors, systems and processes that are the underlying drivers of individual-level risk behaviors [9▪▪].

As international literature generally indicates that the median age of first injection is about 19 years [32], we need to recognize that almost half of IDUs begin injecting before age 18 and this subgroup is often hidden, and less likely to attend NSP or OST programs. They also are likely to be minors not living with family, which heightens ethical concerns that complicate their inclusion in research. Because of their youth and extreme vulnerability to HIV, we need concerted efforts to overcome these hurdles.

Women who inject drugs are also disproportionately impacted by the epidemic, yet remain understudied. Recent research suggests that female IDUs frequently experience violence from intimate partners, police and sex trade clients [33▪], homelessness [34] and psychiatric comorbidities [35], which may act synergistically, increasing their risk for HIV infection. Yet, many of the women falling into these risk groups are excluded from intervention studies [36].

HIV-prevention research tends to focus on IDUs while overlooking other subgroups of substance users who may not inject, such as stimulant users, and heavy and episodic drinkers. In Thailand, alcohol consumption among IDUs increased rapidly in recent years, and excessive alcohol consumption among IDUs was associated with increased mortality [37]. We echo the call for renewed efforts to extend combination HIV prevention to noninjection drug users [38▪].

CONCLUSION

In 2009, a group of representatives from agencies that guide international public health policies deliberated and recommended that once proof of concept for PrEP is established, its roll-out should be preceded by a delivery and implementation framework that demonstrates its feasibility in different cultural, ethical, legal and political environments [39▪]. In considering IDUs in this context, communities will need to overcome their tacit assumptions

that IDUs can navigate through systems that are maintained as separate silos (e.g. NSP, clinics providing VCT and OST and specialty clinics treating TB, STIs and HCV, reproductive health and mental health services). Providing combination HIV prevention to IDUs under one umbrella, in a point-of-care, one-stop venue that addresses their myriad needs may seem like a Holy Grail, but it is ultimately what substance users need and is likely to be cost-effective. For decades, Amsterdam has offered integrated OST, HIV and primary care services for substance users [40]. In the USA, some early steps have been made to promote a multicity infrastructure that integrates HIV primary care and substance abuse treatment [41].

Research is also needed to develop optimal combination prevention packages which are cost-effective. Even with new advancements in HIV-prevention research, we should keep in mind that to maximize the impact of intervention packages, particularly in resource-limited settings, some of the most cost-effective preventions to reduce HIV infections and deaths may be existing, proven tools such as access to NSP, OST, VCT and linkage to care. We need to avoid over-investment in individually focused interventions that include so many sessions that they are impractical or cost prohibitive. Yet, some IDUs, especially women, need safe spaces to access to deal with trauma, violence and stigma that interfere with health. Most of all, we need to overcome addictophobia, which manifests as the desire to refer drug users somewhere else, anywhere else, or to deny them access to life-saving interventions 'for their own good'. People who use drugs, both by injection or other routes, can be difficult to manage. But if we do not integrate services and make combination prevention interventions truly accessible, effective interventions will remain under-utilized and morbidity and mortality will increase, even when we have the best of intentions.

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Conflicts of interest

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REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 379).

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