



2013

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### Recommended Citation

Shoptaw, S. (2013) "HIV prevention for people who use substances: Evidence-based strategies," *Journal of Food and Drug Analysis*: Vol. 21 : Iss. 4 , Article 33.  
Available at: <https://doi.org/10.1016/j.jfda.2013.09.042>

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# HIV prevention for people who use substances: Evidence-based strategies

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## ABSTRACT

### Keywords:

Combination therapy  
Drug therapy  
Human immunodeficiency virus prevention  
Substance users

Evidence-based strategies to guide human immunodeficiency virus (HIV) prevention for people who use substances can be grouped into approaches that lower infectiousness among substance users living with HIV and those that prevent HIV acquisition among those who are uninfected. Dramatic successes in HIV prevention involving access to antiretroviral therapy, opioid substitution therapies, and needle and syringe exchange programs have reduced both prevalence and incidence in the United States for people who use injection drugs, and modeling studies suggest that scale-up of these approaches will have a parallel impact worldwide. Medical HIV-prevention strategies that reduce infectiousness (“treatment as prevention” or early antiretroviral therapy initiation) and that block HIV acquisition (pre-exposure prophylaxis and post-exposure prophylaxis) can constitute key elements of novel combination HIV-prevention approaches to the goals of reducing infectiousness and reducing acquisition of HIV among people who use substances. For individuals who use substances but do not inject, drug dependence treatments as HIV prevention have a meager evidence base, with most consistent findings being reduction of sexual transmission behaviors that correspond with reductions in substance use, although not with prevention of HIV transmission. This approach may have value, however, when working with groups of substance users who face high rates of HIV prevalence and incidence. Some evidence exists to support HIV prevention interventions that target reduction of sexual risk behaviors in the setting of active stimulant use.

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## 1. Introduction

People who use substances can face multiple transmission risks for human immunodeficiency virus (HIV) when the substances are used in the context of HIV prevalence. These include behaviors related to injection drug use (e.g., needle sharing or reusing needles) and to unprotected sexual

behaviors engaged in while under the influence of substances. Remarkable successes in HIV prevention among people who use injection drugs are evident where there is simultaneous access to antiretroviral therapy (ART), opioid substitution therapy, and needle and syringe exchange programs, including impressive reductions in both incidence and prevalence of HIV [1]. By contrast, incidence continues to rise for men who have

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<http://dx.doi.org/10.1016/j.jfda.2013.09.042>

sex with men (MSM) [2], with data showing that substance use can facilitate sexual transmission risks, especially among MSM who incorporate stimulants [3] and alcohol [4] with their sexual behaviors. Among non-substance using MSM, biomedical HIV prevention strategies reduce HIV transmission when implemented with consistent condom use [5], although no data are available to suggest whether this protective benefit can be extended toward MSM who integrate substance use with their sexual behaviors. This paper outlines evidence-based strategies that can be used to guide a rational strategy for HIV prevention among substance users; particularly for those who engage in substance-related risks in the setting of high HIV prevalence, and points toward future research and clinical efforts.

HIV prevention can be grouped into two approaches [6]: strategies that prevent transmissions by reducing infectiousness in those living with HIV; and strategies that increase protection against acquisition of HIV infection among those who are at high risk (Table 1) [5,7–14].

## 2. Lowering infectiousness in substance users living with HIV

Suppressing viremia using ART in people living with HIV increases the health of HIV-infected individuals and reduces odds for transmission [15]. In a landmark trial, findings showed that compared to standard ART, those randomized to receive comprehensive ART early in HIV infection had less HIV-related morbidity. Moreover, the likelihood for HIV transmission to the uninfected partner from the partner receiving early ART was reduced by 96% [7]. The provision of ART early in HIV infection, which protects against HIV transmission in stable serodiscordant partners, has been named “treatment as prevention” (TasP).

No one knows whether TasP confers parallel health and prevention benefits for substance users living with HIV and who are in serodiscordant partnerships. Studies now are being planned to test whether implementing ART early in HIV infection in the context of opioid substitution therapy, consistent condom use, and access to needle and syringe exchange will enhance health for people who use injection drugs and prevent transmission to serodiscordant partners. Although there are no data to address whether TasP will work in the setting of active injection drug use, it is known that ART taken consistently produces viral suppression in a parallel

fashion for people living with HIV who inject drugs and those who do not use drugs [16]. Among HIV-positive MSM, the immune-enhancing effects of adherence to ART are significantly greater than the modest cumulative negative effects on immune function due to reported use of either cocaine or methamphetamine [17]. Despite this, people who use drugs face consistent barriers to acquiring access to ART. Findings from a Canadian cohort show that people who use drugs (both injection and non-injection) have between a 53% and 38% lower likelihood (respectively) of ever having access to ART compared to people living with HIV who do not use drugs [18].

Among people who inject drugs, opioid substitution therapy is an efficacious HIV-prevention strategy. Compared to people not in opioid substitution therapy, people who inject drugs and who are in opioid substitution therapy are more likely to initiate ART and, once started, are more likely to adhere to ART [19,20]. Even among homeless individuals, methadone maintenance doubles the odds for viral suppression compared to those not on methadone [21]. Opioid substitution therapies (methadone and buprenorphine) act to prevent HIV transmission along multiple mechanisms, including reduction of illicit opioid use (and number of injections), sharing of injection equipment (and potential transmission events), and multiple sex partners and exchanges of sex for drugs or money (and number of drug-associated sexual transmission episodes) [8].

Whether or not people who inject drugs are engaged in opioid substitution therapy, needle and syringe exchange programs provide protection against HIV transmission by facilitating access to sterile injection equipment, to supplies that promote health and prevent disease, and to linkages to primary and HIV medical care [10]. Indeed, simultaneous scale-up of access to ART, opioid substitution therapy, and needle and syringe exchange programs is estimated to reduce HIV incidence among people who inject drugs by >60% [22,23]. Additional HIV-prevention approaches are recommended for people who inject drugs by the World Health Organization, UNAIDS, and the United Nations Office on Drugs and Crime, and include HIV counseling and testing, prevention and treatment of sexually transmitted infections, condom programs for people who use substances and their sexual partners, targeted information, education and communication programs, prevention vaccination and treatment for viral hepatitis, and voluntary medical male circumcision [24]. Interestingly, one randomized controlled trial showed efficacy for sustained reduction of HIV sexual transmission behaviors among non-treatment-seeking stimulant users [13].

**Table 1 – Evidence-based HIV-prevention strategies for people who use substances.**

Substance users living with HIV	Substance users uninfected with HIV
Antiretroviral therapy as HIV prevention [7]	Pre-exposure prophylaxis [5]
Opioid substitution therapy [8]	Post-exposure prophylaxis [9]
Needle and syringe exchange programs [10]	Drug dependence treatments [11,12]
Behavioral prevention programs [13]	Behavioral prevention programs [14]

HIV = human immunodeficiency virus.

## 3. Preventing acquisition of HIV for substance users

Acquisition of HIV can be prevented using pre-exposure prophylaxis (PrEP), which entails providing ART prophylactically to HIV-negative individuals who experience regular exposures to HIV. Evidence for the approach is a randomized placebo controlled trial involving 2499 MSM or transgender women who were assigned to receive a daily combination tablet of tenofovir and emtricitabine or placebo. Those assigned to active medication showed 43% reduction in HIV infection

(incidence) compared to placebo, with 73% reduction among participants in the active condition who were highly adherent to their medication [5]. Initial evidence suggests that people who inject drugs may experience protection using PrEP, with one placebo-controlled randomized trial of daily oral tenofovir in the context of methadone maintenance and needle and syringe exchange programs showing efficacy over placebo in preventing HIV acquisition, particularly at long-term follow-up evaluations [25]. Although preliminary, this evidence suggests a PrEP strategy is appropriate for high-risk substance users, although the specifics defining the sample of substance users (injection, non-injecting, MSM, heterosexual, opioids, stimulants) and the contextual components in which the prophylactic medication is delivered (addiction treatment, harm reduction, sexually transmitted infection clinics) have yet to be articulated.

Although no randomized clinical trials of HIV medication or behavioral prevention interventions have demonstrated significant reductions in HIV incidence among HIV-negative individuals (independent of substance use), post-exposure prophylaxis (PEP; starting ART among HIV-negative individuals within 72 hours after potential exposure to HIV) is recommended in occupational and nonoccupational contexts [26]. PEP strategies have been evaluated favorably when used among MSM [9]. When PEP is integrated with contingency management among MSM who have methamphetamine dependence and engage in concomitant high-risk sexual behaviors, positive response to contingency management increased completion rates for the PEP regimen [14]. Showing a preliminary signal for stimulant-drug-dependence treatment as HIV prevention, one randomized controlled trial showed that methamphetamine-dependent MSM assigned to receive mirtazapine (30 mg/day) significantly reduced methamphetamine use and high-risk sexual behaviors [11]. More careful evaluations are needed to determine whether drug-dependence treatments can function in part or in whole as HIV-prevention strategies in groups of substance users at high risk for HIV acquisition due to drug-related sexual transmission behaviors.

#### 4. Summary and conclusions

Taken together, a database exists that can guide composition of novel combination HIV-prevention approaches for people who use drugs and encounter HIV transmission risks. Strong evidence suggests that people who use substances can benefit from TasP; weaker evidence indicates PrEP may provide prophylaxis against HIV transmission when delivered in specific contexts for people who inject drugs. Strong signals demonstrate that opioid substitution therapy enhances immune functioning among people who use drugs receiving ART and is efficacious on its own as an HIV-prevention strategy among HIV-negative people who inject drugs. Future directions in research will articulate ways in which ART and efficacious medications for substance dependence can constitute novel combination HIV-prevention strategies that will ultimately reduce infectiousness among HIV-positive substance users and prevent HIV acquisition among those who are HIV negative.

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