EDITORIAL COMMENT

Managing amphetamine use is critical to achieving HIV control

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People who inject drugs (PWID) accounted for 12% of the 1.7 million new HIV infections globally in 2018, with the following regional proportions: Eastern Europe and Central Asia, 41%; the Middle East and North Africa, 37%; Asia and the Pacific, 13%; Western and Central Europe and North America, 11%; sub-Saharan Africa, 8%; Latin America, 3%; and the Caribbean, 2% [1]. As for all populations impacted by HIV infection, achieving high levels of HIV diagnosis, initiation, and continuation of antiretroviral therapy (ART), and viral suppression are central to HIV control among PWID [1].

Globally, there is a paucity of data on ART coverage among PWID. Where such data exist, ART coverage tends to be low, for example, 14% in Myanmar, 53% in Vietnam, and 69% in China [1]. Ongoing substance use presents challenges to achieving viral suppression and HIV control among PWID. Issues related to punitive laws, stigma and discrimination, and the common requirement for HIV-positive PWID to abstain from illicit drug use before initiation of ART are some key barriers to accessing ART and sustained adherence [2,3]. Moreover, patterns of substance use are dynamic in various regions of the world, including in parts of Asia where amphetamine use increased over the past 2 decades, sometimes displacing heroin use and often leading to dual use [4,5]. Although opioid substitution therapy, including methadone, is effective for managing opioid use disorder, there are no broadly effective pharmacotherapies for stimulant use, including cocaine and amphetamines [6].

Hai Phong, Vietnam, is a city of two million, where an estimated 5000 PWID have experienced a severe HIV epidemic since the 1990s; HIV prevalence was 66% in 2005 among PWID [4,7]. Although HIV prevalence and incidence have decreased among PWID since then, in 2014, prevalence was still 25% and incidence was one per 100 person-years among new injectors [4]. Heroin has been the primary drug of injection in Vietnam, but methamphetamine use, mostly smoked, has increased over the past decade [4,7]. In this issue of *AIDS*, Feelemyer *et al.* [8] present data from a cohort of HIV-positive PWID on ART in Hai Phong, who primarily injected heroin, indicating that recent methamphetamine use was associated with not achieving viral suppression; methadone use was associated with viral suppression. In their analysis, this methamphetamine association was not fully explained by a mediating effect of self-reported adherence to ART. Understanding this association is critical to devising interventions leading to sustained viral suppression among PWID who use amphetamines.

There are a few possible explanations for why amphetamine use may have been associated with not achieving viral suppression in this cohort of PWID. First, adherence

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to an effective ART regimen is the main determinant of viral suppression and self-reported adherence is an imperfect indicator of true adherence. Although the underlying disease of addiction may influence accuracy of self-reporting, there are other biologic explanations. As discussed by Feelemyer *et al.* [8], methamphetamine causes increased HIV replication in dendritic cells, monocyte-derived macrophages [9], and monocyte activation [10]. The data showing direct effects of methamphetamine use on immune function is independent of HIV serostatus [11,12]. Consistent findings linking methamphetamine use with inadequate viral suppression point to a key role of this drug in HIV transmission [13]. A relevant research question is whether pre-exposure prophylaxis medications will remain effective in preventing HIV infection in the face of recent methamphetamine-induced changes in immune function.

In addition to HIV-related effects, methamphetamine causes negative behavioral, social, and economic consequences while impairing brain function. People with methamphetamine addiction are significantly more likely to make decisions of risk in the settings of recent loss compared with people who do not use methamphetamine [14]. Biases in decision-making and impairments in impulse inhibition can lead to disruptive behaviors by people who use methamphetamine in the treatment system [15]. In Vietnam, people in methadone maintenance therapy (MMT) programs who use methamphetamine are more likely to continue using heroin [16]. As methamphetamine use is illegal, there is a rationale for the most disruptive individuals to be expelled from the MMT clinic, with the possibility of imprisonment or detention in treatment centers.

Addiction is a disease. Continued drug use during drug treatment is not a sign of a bad person but of a failed treatment. Providing more of a treatment that doesn't work is not good medicine. The idea of developing evidence-based treatments, especially the issue of contingency management and in the context of Vietnam is ground-breaking. Local champions of evidence-based treatments are implementing contingency management and cognitive behavioral therapies, which is consistent with calls in international addiction medicine to use data to drive interventions [6].

We also need to consider pharmacotherapies for amphetamine use disorder. There finally is some good news on this front: two trials of the US Food and Drug Administration (FDA) approved antidepressant medication mirtazapine showed efficacy for reducing methamphetamine use among MSM in San Francisco [17,18] and other drug trials are underway. Although mirtazapine is not FDA approved for methamphetamine use disorder, ongoing studies of mirtazapine hope to provide data on its efficacy in broad groups of people who use methamphetamine.

Addressing amphetamine use in a comprehensive behavioral and biological manner for PWID and all populations will be critical to achieving HIV control globally. Noninjection amphetamine use is an important cofactor for HIV acquisition in multiple populations around the world [6]. Amphetamine use has been a longstanding important risk factor for HIV acquisition among MSM and transgender individuals and is currently expanding globally, notably in Asia [6]. Of concern is a pattern known as 'chemsex,' a term used to describe sex under the influence of some psychoactive substances, including amphetamines [19,20]. This phenomenon has been found to be associated with higher HIV risk behavior, such as sex without condoms and sex with multiple partners who are often not aware of their HIV serostatus or treatment status [19,20]. Thus, the need to address amphetamine use is not only necessary for improving the chances of achieving viral suppression among PWID, but an important step for combating the further spread of HIV among all at risk populations who use amphetamines.

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Conflicts of interest

There are no conflicts of interest.

References

1. UNAIDS. *UNAIDS data 2019*. Geneva: UNAIDS; 2019.
2. DeBeck K, Cheng T, Montaner JS, Beyrer C, Elliott R, Sherman S, *et al*. **HIV and the criminalisation of drug use among people who inject drugs: a systematic review.** *Lancet HIV* 2017; **4**:e357–e374.
3. Degenhardt L, Peacock A, Colledge S, Leung J, Grebely J, Vickerman P, *et al*. **Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review.** *Lancet Glob Health* 2017; **5**:e1192–e1207.
4. Feelemyer J, Duong Thi H, Khuê Pham M, Hoang Thi G, Thi Tuyet Thanh N, Thi Hai Oanh K, *et al*. **Increased methamphetamine use among persons who inject drugs in Hai Phong, Vietnam, and the association with injection and sexual risk behaviors.** *J Psychoactive Drugs* 2018; **50**:382–389.
5. Martin M, Vanichseni S, Sangkum U, Mock PA, Leethochawalit M, Chiamwongpaet S, *et al*. **HIV incidence and risk behaviours of people who inject drugs in Bangkok, 1995–2012.** *EClinicalMedicine* 2019; **9**:44–51.
6. Farrell M, Martin NK, Stockings E, Borquez A, Cepeda JA, Degenhardt L, *et al*. **Responding to global stimulant use: challenges and opportunities.** *Lancet* 2019; **394**:1652–1667.
7. Des Jarlais DC, Thi Huong D, Thi Hai Oanh K, Khuê Pham M, Thi Giang H, Thi Tuyet Thanh N, *et al*. **Prospects for ending the HIV epidemic among persons who inject drugs in Haiphong, Vietnam.** *Int J Drug Policy* 2016; **32**:50–56.
8. Feelemyer J, Arasteh K, Huong DT, Oanh KTH, Khue PM, Giang HT, *et al*. **Associations between methamphetamine use and lack of viral suppression among a chort of HIV-positive persons who inject drugs in Hai Phong, Vietnam.** *AIDS* 2020; **34**:1875–1882.
9. Liang H, Wang X, Chen H, Song L, Ye L, Wang SH, *et al*. **Methamphetamine enhances HIV infection of macrophages.** *Am J Pathol* 2008; **172**:1617–1624.
10. Carrico AW, Johnson MO, Colfax GN, Moskowitz JT. **Affective correlates of stimulant use and adherence to antiretroviral therapy among HIV-positive methamphetamine users.** *AIDS Behav* 2010; **14**:769–777.

11. Fulcher JA, Hussain SK, Cook R, Li F, Tobin NH, Ragsdale A, *et al*. **Effects of substance use and sex practices on the intestinal microbiome during HIV-1 infection.** *J Infect Dis* 2018; **218**:1560–1570.
12. Fulcher JA, Shoptaw S, Makgoeng SB, Elliott J, Ibarrondo FJ, Ragsdale A, *et al*. **Brief report: recent methamphetamine use is associated with increased rectal mucosal inflammatory cytokines, regardless of HIV-1 serostatus.** *J Acquir Immune Defic Syndr* 2018; **78**:119–123.
13. Ellis RJ, Childers ME, Cherner M, Lazzaretto D, Letendre S, Grant I, HIV Neurobehavioral Research Center Group. **Increased human immunodeficiency virus loads in active methamphetamine users are explained by reduced effectiveness of antiretroviral therapy.** *J Infect Dis* 2003; **188**:1820–1826.
14. Gowin JL, Stewart JL, May AC, Ball TM, Wittmann M, Tapert SF, Paulus MP. **Altered cingulate and insular cortex activation during risk-taking in methamphetamine dependence: losses lose impact.** *Addiction* 2014; **109**:237–247.
15. Tsui JI, Mayfield J, Speaker EC, Yakup S, Ries R, Funai H, *et al*. **Association between methamphetamine use and retention among patients with opioid use disorders treated with buprenorphine.** *J Subst Abuse Treat* 2020; **109**:80–85.
16. Hoang T, Nguyen H, Shiraishi RW, Nguyen M, Bingham T, Nguyen D, *et al*. **Factors associated with concurrent heroin use among patients on methadone maintenance treatment in Vietnam: a 24-month retrospective analysis of a nationally representative sample.** *Int J Drug Policy* 2018; **55**:113–120.
17. Colfax GN, Santos GM, Das M, Santos DM, Matheson T, Gasper J, *et al*. **Mirtazapine to reduce methamphetamine use: a randomized controlled trial.** *Arch Gen Psychiatry* 2011; **68**:1168–1175.
18. Coffin PO, Santos GM, Hern J, Vittinghoff E, Walker JE, Matheson T, *et al*. **Effects of mirtazapine for methamphetamine use disorder among cisgender men and transgender women who have sex with men: a placebo-controlled randomized clinical trial.** *JAMA Psychiatry* 2019; **77**:246–255.
19. Edmundson C, Heinsbroek E, Glass R, Hope V, Mohammed H, White M, Desai M. **Sexualised drug use in the United Kingdom (UK): a review of the literature.** *Int J Drug Policy* 2018; **55**:131–148.
20. Maxwell S, Shahmanesh M, Gafos M. **Chemsex behaviours among men who have sex with men: a systematic review of the literature.** *Int J Drug Policy* 2019; **63**:74–89.