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## Associations Between Methamphetamine Use and Lack of Viral Suppression among a Cohort of HIV Positive Persons who Inject Drugs in Hai Phong Vietnam

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### Abstract

**Objective:** We assessed the association between methamphetamine use and lack of viral suppression among a cohort of HIV seropositive persons who inject drugs (PWID) in Hai Phong, Vietnam.

**Design:** Cohort study with random effects logit modeling and mediation analysis for ART adherence.

**Methods:** PWID were recruited from October 2016–October 2017; HIV seropositive PWID were enrolled in a cohort to assess HIV viral loads, changes in drug use, risk behaviors, and ART adherence during 24-month follow-up. Methamphetamine use in last 30 days was divided into three categories: 0 days (no use), 1–19 days (intermediate), and 20 or more days (heavy). Bivariate and a multivariable random effects logit models were used to assess the relationship between methamphetamine use and not being virally suppressed. We also assessed self-reported ART adherence as a mediating factor.

**Results:** A total of 645 HIV seropositive PWID were included at baseline; 95% male, average age 40 (SD=6.4). At baseline, methamphetamine use in last 30 days was 64% no use, 32% intermediate use, 4% heavy use. Approximately 74% of PWID reported high/complete adherence;

76% were at viral suppression. In random effects analysis, recent methamphetamine use was associated with not being virally suppressed during follow-up (AOR: 1.84, 95% CI: 1.06, 3.17); the effect was not explained by a mediating effect of self-reported adherence to ART.

**Conclusions:** Recent methamphetamine use is associated with not being virally suppressed among PWID. The results of this study indicate the need for targeted interventions for methamphetamine use with special focus on those with HIV infection.

### Keywords

Methamphetamine; Persons who inject drugs; Viral suppression; Antiretroviral therapy; Hai Phong Vietnam

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### Introduction

The HIV epidemic in Hai Phong Vietnam has disproportionately affected persons who inject drugs (PWID). In 2005, HIV prevalence among PWID had reached 66% [1], decreasing to 48% in 2009 [2] and further decreasing to 25% in 2014, with HIV incidence among new injectors approximately 1/100 person years at risk. Several notable interventions have been implemented to address the increased prevalence of HIV among PWID [3], including needle/syringe provision, opiate substitution treatment (OST), and antiretroviral therapy (ART) for HIV seropositive PWID which is provided free of cost to all HIV seropositive persons through over 300 public health clinics throughout Vietnam [4].

Methamphetamine use is associated with higher HIV viral loads [5], ART failure [6] and greater CD4+ and CD8+ T-cell spontaneous proliferation, activation, and exhaustion [7]. HIV seropositive persons using methamphetamine are more likely to exhibit different neurological complications compared to non-users [8], including deficits in working memory, learning, recall, and motor skills [9], which can interfere with adherence to ART [10, 11].

Methamphetamine use in Hai Phong Vietnam has increased significantly in recent years, from 30% among PWID in a respondent driven sampling (RDS) study conducted in 2014 to over 50% among PWID recruited in a RDS study conducted in 2016 [12]. Similar increases have been seen in other locations in Asia, including Bangkok [13]. In Hai Phong, the primary method of using methamphetamine is through smoking; in our initial sample of participants recruited in 2016, the prevalence of smoking methamphetamine was greater than 99% [14]. Due to the elevated levels of methamphetamine use among PWID, there is concern that increased use may directly impact the success of ART and lead to reduced viral suppression, resulting in poor health outcomes among HIV seropositive persons and to increased HIV transmission to HIV negative persons.

There is a lack of evidence at the population level with respect to methamphetamine use, ART adherence, and HIV viral loads, especially among PWID with dual methamphetamine/heroin use disorders and in low- and middle-income countries such as Vietnam. The ongoing spread of methamphetamine in Hai Phong and elsewhere in southeast Asia [15] raises the

question of how methamphetamine use may affect the success of ART treatment and adherence among HIV positive PWID over time.

In this study, we use random effects modeling to assess the association between recent methamphetamine use, and HIV viral load among a cohort of PWID followed for 24 months in Hai Phong Vietnam who reported recent ART use. To account for ART adherence, we consider self-reported ART adherence as a possible mediator in the association between methamphetamine use and HIV viral load.

## Methods

### Participants:

Study participants were recruited in Hai Phong, Vietnam from in September 2016 and again in October 2017 using RDS [16]. Participants were eligible for the study if they were currently injecting drugs, 18 years of age, and capable of giving informed consent. Current injecting drug use was verified through examination of injection marks and urinalysis (participants had to be positive for an injectable drug--heroin and/or methamphetamine; it should be noted that while nearly the entire sample was injecting heroin, less than 1% reported injection of methamphetamine; the primary mode of methamphetamine use in Hai Phong is through smoking).

Each participant received counseling and testing for HIV. HIV antibody testing was conducted using Bioline HIV1/2 3.0 rapid test (Standard Diagnostics Inc., Gyeonggi-do, Republic of Korea) plus the VIKIA® HIV1/2 (Marcy l'Étoile, Lyon, France). Confirmation testing was conducted using Determine™ HIV-1/2 (Alere™, Waltham, MA, USA). HIV viral load was measured on banked blood samples at the national reference laboratory (NIHE, Hanoi) using the COBAS Taqman HIV-1 test v2.0 (Roche diagnostics, Hanoi, Vietnam). HCV serology relied on a rapid test SD BIOLINE HCV (SD standard Diagnostic Inc., South Korea). We restricted our analysis to PWID who were HIV seropositive, reported receiving ART and had self-report ART adherence scores and laboratory viral load measurements.

### Interview and Follow-up:

After eligibility was confirmed, informed consent was obtained, and a structured questionnaire was administered by a trained interviewer. The questionnaire examined demographic factors in addition to drug and alcohol use, sexual and injection risk behaviors, mental health (including nervousness and anxiety) and participation in harm-reduction and treatment programs (all questions reported on the last six months of behavior). Each participant that was HIV seropositive was also asked about utilization of ART; if they responded that they were currently on ART, they were asked to use a visual analog scale for their level of adherence to ART in the last six months, from a score of 1 (lowest level of adherence) to 10 (highest level of adherence/complete adherence).

Viral suppression was defined as viral load of less than 1000 copies/ml (the WHO definition of viral suppression used by the NIHE laboratory).

Participants who were HIV seropositive were invited to enroll in the cohort after the first RDS visit in the fall of 2016 (cohort entry 1), and again at the second RDS visit in fall 2017 (cohort entry 2), for two waves of cohort entry from the RDS samples. We collected data on PWID who entered the cohort at baseline (during the RDS visit) and every six months after enrollment (information collected every six months included self-report receiving ART, self-report ART adherence, viral load, and self-reported methamphetamine use). A participant was considered loss to follow-up if they were not present at the 24-month cohort visit.

### **Substance use and adherence scoring:**

Drug and alcohol use were assessed based on self-report of use in the previous six months or the last thirty days for recent use. We divided the number of days using methamphetamine in the last 30 days into three different categories; no use, intermediate use (defined as using 1–19 days), and heavy use (defined as 20 or more days); these categories were chosen based on the distribution of our data along with review of previous studies examining frequency of methamphetamine use [17]. We also divided adherence scores into two categories; low-moderate adherence (defined as scores 1–8) and high/complete adherence (defined as scores 9–10).

### **Statistical Analysis:**

Descriptive statistics for the two cohort entry samples that entered into the cohort in 2016 and 2017 were tabulated along with ART adherence scores and viral suppression, stratified by days of methamphetamine use in the last 30 days (0, 1–19 days, and 20+ days).

We used random effects logit models to assess the association between methamphetamine use and HIV viral load and other important demographic and drug use factors which could impact viral suppression, including heroin and methadone use [18]. The association of each potential predictor or important factor with viral load was first tested in univariate logistic models. All variables that were at least moderately associated with positive viral load in univariate models (i.e.,  $p < 0.15$ ) were then entered into the multivariable model and tested using backward elimination, following Agresti's approach [19], until we arrived at the final models.

We assessed self-report ART adherence as a possible mediator of the association between methamphetamine use and viral suppression, using vanderWeele's approach [20] and the "paramed" package in Stata [21]. Stata software version 15 was used for statistical analyses [22].

The study was approved by the Hai Phong Medical University and Pharmacy and New York University Institutional Review Boards.

## **Results**

### **Demographics, Risk Behaviors, and methamphetamine use:**

A total of 412 PWID were included in the baseline sample from cohort entry 1, and 233 were included in the follow-up sample for cohort entry 2. At baseline, methamphetamine use in the last 30 days was as follows: 322 reported no use (64%), 164 reported intermediate use

(4%) (defined as 1–19 days in the last 30 days), and 21 reported heavy use (defined as 20+ days in the last 30 days).

The two cohorts were relatively similar with respect to baseline demographics including age (39.9 in cohort entry 1 vs 40.7 in cohort entry 2) and gender (93.9% male and 5.6% female in in cohort entry 1 vs 96.1% male and 3.9% female in in cohort entry 2). There were, however, noticeable differences in other variables at baseline including depression (33.3% in cohort entry 1 vs 23.6% in cohort entry 2,  $p=0.01$ ), street methadone use (39.3% in cohort entry 1 vs 29.2% in cohort entry 2,  $p=0.01$ ) and HCV prevalence (91.5% in cohort entry 1 vs 80.3% in cohort entry 2,  $p=0.001$ ). There were also significant differences in methamphetamine use by cohort entry; cohort entry 1 reported 61% no methamphetamine use, 33.8% intermediate use, and 5.1% heavy use compared to cohort entry 2, which reported 52% no methamphetamine use, 27.3% intermediate use, and 2.3% heavy use ( $p=0.042$ ).

Approximately 16% of PWID were loss to follow-up in the study (defined as missing two or more follow-up visits); there were several notable differences among those lost to follow-up vs those included in the follow-up analysis; those loss to follow-up were more likely to be report greater numbers of days injecting heroin (in last 30 days), number of days smoking methamphetamine (in last 30 days), and not being virally suppressed. Additionally, those loss to follow-up were less likely to have positive urine toxicology for methadone.

#### **ART Adherence and Viral Suppression:**

The percentage of high/complete self-reported adherence scores at baseline were similar among the two cohorts: 79.8% for cohort entry 1 and 76.8% for cohort entry 2. Viral suppression at baseline was also similar: 74.5% for cohort entry 1 and 76.8% in cohort entry 2.

Adherence scores by self-report of methamphetamine use is presented in table 2a and viral suppression by self-report methamphetamine use is presented in table 2b. There are important differences in the adherence scores when examining different levels of self-reported methamphetamine use. For example, among cohort entry 1 PWID, those with high/complete adherence among those with no methamphetamine use increased modestly from 65.9% at baseline to 72.8% at 24-month follow-up, compared to a modest decrease in self-reported high/complete adherence among those with heavy methamphetamine use, from 4.7% to 2.8% over the same time period. For cohort entry 2, those with high/complete self-reported adherence among those with no methamphetamine use increased modestly from 71.9% at baseline to 73.9% at 24-month follow-up, compared to a modest decrease in self-reported high/complete adherence among those with heavy methamphetamine use, from 3.2% to 2.1% over the same time period.

Similar trends were noted for viral suppression. Among cohort entry 1 PWID, viral suppression among those with no methamphetamine use increased from 62.1% at baseline to 74.7% at 24-month follow-up. There was a modest decrease in viral suppression among heavy methamphetamine users, from 4.6% to 1.3% over the same period. Among cohort entry 2 PWID, viral suppression among those with no methamphetamine use increased from

69.4% at baseline to 72.8% at 24-month follow-up. There was no change in viral suppression among heavy methamphetamine users, which remained stable at approximately 2%.

### **Modeling methamphetamine use and viral suppression:**

In order to assess the relationship between methamphetamine use and HIV viral load, we used random effects logit modeling (with the three levels of methamphetamine use as an ordered exposure with no methamphetamine use set to the referent group), controlling for demographic factors, heroin injection and positive methadone in urine. Table 3 presents the results of the multivariable analysis. Self-reported methamphetamine was associated with not being virally suppressed during follow-up (AOR 1.83, 95% CI: 1.06, 3.17); additionally, age (AOR 0.92, 95% CI: 0.86, 0.98) and methadone use (AOR 0.29, 95% CI: 0.16, 0.53) were negatively associated with viral suppression. Mediation analysis showed that direct effect of methamphetamine use remained significant (OR (direct effect (DE)) = 1.59; 95% CI 1.07 – 2.36) and accounted for the greatest proportion of the total effect.

### **Discussion**

Among HIV positive PWID, we observed a statistically significant association between methamphetamine use and not being virally suppressed, after controlling for important demographic factors and substance use; the association remained significant after including self-report ART adherence scores as a possible mediating factor. This is one of the first studies to document this association among a sample of PWID with dual heroin/methamphetamine use in southeast Asia, and our results are consistent with and support results of other studies showing similar associations between methamphetamine use and not being virally suppressed [23].

Although there is no direct biological in vivo evidence linking methamphetamine to altered ART drug metabolism, and the effect in humans on HIV viral replication is still not completely understood, there are mechanisms that have been proposed that support the role of methamphetamine in interacting with and affecting ART effectiveness. Methamphetamine causes increased HIV replication in dendritic cells, monocyte derived macrophages [24], and monocyte activation [25]. As a result it may directly interact with ART, leading to lower effectiveness of ART medication [26]. Methamphetamine intoxication is associated with several negative outcomes, including failure to adhere to medication regimens, including ART [15].

Methamphetamine use, particularly among PWID, has recently increased in Vietnam, as drug use has traditionally been dominated by heroin [27]. Due to the low cost and increased production of methamphetamine in southeast Asia, the use of methamphetamine has increased significantly in the last 5–10 years, and among the PWID included in our study, nearly 50% had reported recent methamphetamine use, and over 70% had reported lifetime use of the drug.

Stimulant use presents unique challenges in that there is not a comparable treatment such as methadone for heroin dependence, and many users of methamphetamine suffer from mental



health issues including depression and psychosis [28] and may also suffer from antisocial behavior [29], factors that are all associated with non-adherence to ART [30].

Hai Phong has good coverage for methadone treatment for heroin users in the city; these programs could potentially offer harm reduction services for those with not only heroin addiction but those with methamphetamine use disorder as well (who may or may not be daily attendees of the methadone program). It should be noted, however, that there may be under-reporting of participation in methadone programs by PWID, and this introduces unique challenges in linking PWID to harm reduction and care if they do not want to be associated with methadone programs.

There is evidence that methadone interacts and directly affects ART [31]; while we do not have systematic data on methadone treatment among the PWID in our study, future studies should examine the interactions that exist among triply exposed participants (methadone, methamphetamine, and ART) and how these interactions may affect the overall effectiveness of ART. We did note a negative association between methadone use and viral suppression in our model, which is consistent with other studies finding similar protective effects of methadone on viral suppression among drug users and PWID in particular [32].

There are several public health implications for the results of this study. Due to the increased prevalence of methamphetamine use among PWID in Hai Phong and southeast Asia [15], tailored harm reduction programs are needed to address methamphetamine use and associated co-morbidities, with specific emphasis on careful management of HIV positive drug users with methamphetamine use disorders. It is important to continue to monitor HIV viral loads among those who continue to use drugs, particularly methamphetamine and other stimulants such as cocaine (which has also been associated with lack of viral suppression exclusive of ART adherence) [33], and monitor ART regimens accordingly. Education for drug users should focus on the implications of methamphetamine use with respect to HIV transmission and acquisition, particularly among high risk individuals (PWID and those with a history of risky sexual behavior).

Contingency management (CM) programs for methamphetamine users have been proposed as a way to manage and treat methamphetamine addiction, showing that those in CM programs were more likely to achieve methamphetamine abstinence compared to those not exposed to CM [34]. Several procedures have been adopted for use with methamphetamine use disorders including the Matrix model [35] and the 12-step facilitation group model [36]. Integration of CM programs with psychiatric treatment (given the high level of psychological comorbidity among methamphetamine users) could possibly allow for a more holistic treatment strategy, and likely lead to more long lasting positive results in abstinence.

A recent pilot program aimed at reducing methamphetamine use was implemented in methadone clinics in Hanoi, and found reduced methamphetamine and opiate use during follow-up. Among high risk methamphetamine users, there was a reduction in positive methamphetamine urine tests, from 86.9% to 10.5%; there was also a reduction in positive urine tests for illicit opiates, from 43.5% to 10.5%. While the results of this study are promising, they were limited to an eight-week time period; currently there are little to no



ongoing drug treatment programs in Vietnam that are directly aimed at reducing methamphetamine use [37]. Another option is to include methamphetamine users within a broader intervention framework including systems navigation and psychosocial counseling, as was done among a cohort of PWID Vietnam [38].

This study has limitations that should be noted. This analysis was restricted to approximately 645 HIV positive PWID, and although we utilized RDS to recruit a representative population of PWID in the city of Hai Phong for enrollment into the cohort, the sample recruited for our study may not be generalizable to all HIV positive PWID in Hai Phong. The data collected on ART adherence and methamphetamine use is based on self-report; as there may be stigma related to reporting low ART adherence or high levels of methamphetamine use, there may be under-reporting of these behaviors. However, we would note that the increase in perfect ART adherence scores among those with no methamphetamine use, and decreases in perfect adherence among those with heavy methamphetamine use are consistent with other literature assessing methamphetamine use and ART adherence [39]. Finally, we did note that approximately 16% of the PWID were loss to follow-up in the cohort; the differences among those included vs. those loss to follow-up suggest that the observed results of our analyses for the association between methamphetamine and HIV viral load would have been even stronger (greater ORs) had we continued to obtain follow-up data from those who were lost to follow-up.

## Conclusions

We observed that HIV positive PWID on ART with recent methamphetamine use are less likely to be virally suppressed compared to PWID on ART not using methamphetamine after controlling for self-reported ART adherence and important demographic and substance use factors. The results of this study indicate that broader approaches are needed to address the increased use of methamphetamine in Hai Phong and other locations among PWID, with special focus on HIV positive PWID not at viral suppression. Harm reduction programs that can address the dual methamphetamine/heroin epidemic are essential to reducing HIV transmission related harms. Integration with methadone treatment programs is one possible way to begin offering services in conjunction with existing treatment programs already in place, but challenges remain for those HIV seropositive PWID with dual heroin/methamphetamine use disorders and with limited or no interaction with harm reduction services.

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## References

1. Hoàng TV. Results from the HIV/STI Integrated Biological and Behavioral Surveillance (IBBS) in Vietnam: 2005–2006. Ministry of Health; 2007.
2. Des Jarlais DC, Thi Huong D, Thi Hai Oanh K, Khue 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.
3. Kurth AE, Celum C, Baeten JM, Vermund SH, Wasserheit JN. Combination HIV prevention: significance, challenges, and opportunities. *Curr HIV/AIDS Rep* 2011; 8(1):62–72. [PubMed: 20941553]
4. FHI360. Characterizing Loss to Follow-up (LTFU) and Mortality Among HIV Infected Patients in Vietnam. UNAIDS; 2015.
5. Jiang J, Wang M, Liang B, Shi Y, Su Q, Chen H, et al. In vivo effects of methamphetamine on HIV-1 replication: A population-based study. *Drug Alcohol Depend* 2016; 159:246–254. [PubMed: 26790825]
6. Kumar S, Rao PS, Earla R, Kumar A. Drug-drug interactions between anti-retroviral therapies and drugs of abuse in HIV systems. *Expert Opin Drug Metab Toxicol* 2015; 11(3):343–355. [PubMed: 25539046]
7. Massanella M, Gianella S, Schrier R, Dan JM, Perez-Santiago J, Oliveira MF, et al. Methamphetamine Use in HIV-infected Individuals Affects T-cell Function and Viral Outcome during Suppressive Antiretroviral Therapy. *Sci Rep* 2015; 5:13179.
8. Skowronska M, McDonald M, Velichkovska M, Leda AR, Park M, Toborek M. Methamphetamine increases HIV infectivity in neural progenitor cells. *J Biol Chem* 2018; 293(1):296–311. [PubMed: 29158267]
9. Rippeth JD, Heaton RK, Carey CL, Marcotte TD, Moore DJ, Gonzalez R, et al. Methamphetamine dependence increases risk of neuropsychological impairment in HIV infected persons. *J Int Neuropsychol Soc* 2004; 10(1):1–14. [PubMed: 14751002]
10. Burton CL, Strauss E, Hultsch DF, Hunter MA. Cognitive functioning and everyday problem solving in older adults. *Clin Neuropsychol* 2006; 20(3):432–452. [PubMed: 16895857]
11. Hinkin CH, Castellon SA, Durvasula RS, Hardy DJ, Lam MN, Mason KI, et al. Medication adherence among HIV+ adults: effects of cognitive dysfunction and regimen complexity. *Neurology* 2002; 59(12):1944–1950. [PubMed: 12499488]
12. Feelemyer J, Duong Thi H, Khue 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(5):382–389. [PubMed: 30183558]
13. 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. *E ClinicalMedicine* 2019; 9:44–51.
14. Michel L, Des Jarlais DC, Thi HD, Hai OKT, Minh KP, Peries M, et al. Intravenous heroin use in Haiphong, Vietnam: Need for comprehensive care including methamphetamine use-related interventions. *Drug Alcohol Depend* 2017; 179:198–204. [PubMed: 28800503]
15. UNODC. Synthetic Drugs in South-East Asia: Trends and Patterns of Amphetamine-type Stimulants and New Psychoactive Substances. In: Global SMART Programme; 2019.
16. Heckathorn DD. Respondent-driven sampling: A new approach to the study of hidden populations. *Soc Problems* 1997; 44(2):174–199.
17. McKetin R, Hickey K, Devlin K, Lawrence K. The risk of psychotic symptoms associated with recreational methamphetamine use. *Drug Alcohol Rev* 2010; 29(4):358–363. [PubMed: 20636650]
18. Westergaard RP, Kirk GD, Richesson DR, Galai N, Mehta SH. Incarceration predicts virologic failure for HIV-infected injection drug users receiving antiretroviral therapy. *Clin Infect Dis* 2011; 53(7):725–731. [PubMed: 21890777]
19. Agresti A *Categorical Data Analysis*. Wiley; 2003.
20. VanderWeele TJ. Mediation Analysis: A Practitioner’s Guide. *Annu Rev Public Health* 2016; 37:17–32. [PubMed: 26653405]

21. Emsley RLH. PARAMED: Stata module to perform causal mediation analysis using parametric regression models: Statistical Software Components S457581. In. Boston College Department of Economics; 2013.
22. StataCorp. 2017 Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.
23. Shoptaw S, Stall R, Bordon J, Kao U, Cox C, Li X, et al. Cumulative exposure to stimulants and immune function outcomes among HIV-positive and HIV-negative men in the Multicenter AIDS Cohort Study. *Int J STD AIDS* 2012; 23(8):576–580. [PubMed: 22930295]
24. 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(6):1617–1624.
25. Carrico AW, Cherenack EM, Roach ME, Riley ED, Oni O, Dilworth SE, et al. Substance-associated elevations in monocyte activation among methamphetamine users with treated HIV infection. *AIDS* 2018; 32(6):767–771. [PubMed: 29369159]
26. Ellis RJ, Childers ME, Cherner M, Lazzaretto D, Letendre S, Grant I. Increased human immunodeficiency virus loads in active methamphetamine users are explained by reduced effectiveness of antiretroviral therapy. *J Infect Dis* 2003; 188(12):1820–1826. [PubMed: 14673760]
27. UNODC. Synthetic drugs from Asia are fuelling global public health and crime concerns. Hanoi; 2017.
28. Darke S, Kaye S, McKetin R, Dufflou J. Major physical and psychological harms of methamphetamine use. *Drug Alcohol Rev* 2008; 27:253–262. [PubMed: 18368606]
29. Embry D, Hankins M, Biglan A, Boles S. Behavioral and social correlates of methamphetamine use in a population-based sample of early and later adolescents. *Addict Behav* 2009; 34(4):343–351.
30. Villes V, Spire B, Lewden C, Perronne C, Besnier JM, Garre M, et al. The effect of depressive symptoms at ART initiation on HIV clinical progression and mortality: implications in clinical practice. *Antivir Ther* 2007; 12(7):1067–1074. [PubMed: 18018765]
31. Gourevitch MN, Friedland GH. Interactions between methadone and medications used to treat HIV infection: a review. *Mt Sinai J Med* 2000; 67(5–6):429–436. [PubMed: 11064494]
32. Shrestha R, Copenhagen MM. Viral suppression among HIV-infected methadone-maintained patients: The role of ongoing injection drug use and adherence to antiretroviral therapy (ART). *Addict Behav* 2018; 85:88–93.
33. Rasbach DA, Desruisseau AJ, Kipp AM, Stinnette S, Kheshti A, Shepherd BE, et al. Active cocaine use is associated with lack of HIV-1 virologic suppression independent of nonadherence to antiretroviral therapy: use of a rapid screening tool during routine clinic visits. *AIDS Care* 2013; 25(1):109–117. [PubMed: 22670566]
34. Shoptaw S, Huber A, Peck J, Yang X, Liu J, Jeff D, et al. Randomized, placebo-controlled trial of sertraline and contingency management for the treatment of methamphetamine dependence. *Drug Alcohol Depend* 2006; 85(1):12–18. [PubMed: 16621339]
35. Rawson RA, Marinelli-Casey P, Anglin MD, Dickow A, Frazier Y, Gallagher C, et al. A multi-site comparison of psychosocial approaches for the treatment of methamphetamine dependence. *Addiction* 2004; 99(6):708–717. [PubMed: 15139869]
36. Donovan DM, Wells EA. ‘Tweaking 12-Step’: the potential role of 12-Step self-help group involvement in methamphetamine recovery. *Addiction* 2007; 102 Suppl 1:121–129. [PubMed: 17493061]
37. Nguyen HA TT, Nguyen TT, Shoptaw S, Giang LM. Feasibility and Outcomes of Evidence-Based Interventions to Reduce Methamphetamine Use among Patients on MMT in Hanoi, Vietnam. In: CPDD San Antonio TX; 2019.
38. Miller WC, Hoffman IF, Hanscom BS, Ha TV, Dumchev K, Djoerban Z, et al. A scalable, integrated intervention to engage people who inject drugs in HIV care and medication-assisted treatment (HPTN 074): a randomised, controlled phase 3 feasibility and efficacy study. *The Lancet* 2018; 392(10149):747–759.
39. Carrico AW, Johnson MO, Colfax GN, Moskowitz JT. Affective correlates of stimulant use and adherence to anti-retroviral therapy among HIV-positive methamphetamine users. *AIDS Behav* 2010; 14(4):769–777. [PubMed: 19125321]

**Table 1**

Demographic Characteristics of Sample of DRIVE Cohort PWID

|                                    | Cohort Entry 1 (2016) |              |              |              |              |              | Cohort Entry 2 (2017) |              |              |  |
|------------------------------------|-----------------------|--------------|--------------|--------------|--------------|--------------|-----------------------|--------------|--------------|--|
|                                    | Baseline              | M6*          | M12*         | M18*         | M24*         | Baseline     | Baseline              | M18*         | M24*         |  |
| Total Sample (N)                   | 412<br>N (%)          | 331<br>N (%) | 302<br>N (%) | 274<br>N (%) | 269<br>N (%) | 233<br>N (%) | 233<br>N (%)          | 176<br>N (%) | 169<br>N (%) |  |
| Gender <sup>†</sup>                |                       |              |              |              |              |              |                       |              |              |  |
| Male                               | 387 (94)              |              |              |              |              | 224 (96.1)   |                       |              |              |  |
| Female                             | 23 (6)                |              |              |              |              | 9 (3.9)      |                       |              |              |  |
| Median Age (SD) <sup>†</sup>       | 39.9 (6.29)           |              |              |              |              | 40.7 (6.68)  |                       |              |              |  |
| Depression                         | 137 (33.3)            | 51 (15.4)    | 33 (10.9)    | 26 (9.5)     | 30 (11.2)    | 55 (23.6)    | 15 (8.5)              | 19 (11.2)    |              |  |
| Nervous/Anxiety <sup>†</sup>       | 145 (35.2)            |              |              |              |              | 68 (29.2)    |                       |              |              |  |
| History of Arrest                  |                       | 13 (3.9)     | 21 (7.0)     | 7 (2.6)      | 14 (5.2)     |              | 5 (2.8)               | 12 (7.1)     |              |  |
| Substance Use Characteristics      |                       |              |              |              |              |              |                       |              |              |  |
| Alcohol Use                        | 250 (60.7)            | 194 (59.2)   | 187 (61.9)   | 151 (55.1)   | 138 (51.4)   | 135 (58)     | 104 (59.1)            | 95 (56.2)    |              |  |
| Morphine positive urine toxicology | 410 (99.5)            | 331 (100)    | 186 (61.6)   |              | 163 (60.6)   | 233 (100)    | 176 (100)             | 105 (62.1)   |              |  |
| Street Methadone <sup>†</sup>      | 162 (39.3)            |              |              |              |              | 68 (29.2)    |                       |              |              |  |
| HCV Seropositive                   | 377 (91.5)            | 306 (92.4)   | 279 (92.4)   | 256 (93.4)   | 246 (91.4)   | 187 (80.3)   | 152 (86.4)            | 150 (88.8)   |              |  |
| Methamphetamine Use (days)         |                       |              |              |              |              |              |                       |              |              |  |
| 0                                  | 202 (61)              | 237 (71.6)   | 227 (75.2)   | 211 (77)     | 193 (71.7)   | 120 (52)     | 124 (70.5)            | 119 (70.4)   |              |  |
| 1–19                               | 112 (33.8)            | 79 (23.9)    | 67 (22.2)    | 56 (20.4)    | 68 (25.3)    | 52 (29.5)    | 48 (27.3)             | 46 (27.2)    |              |  |
| 20 <sup>†</sup>                    | 17 (5.1)              | 15 (4.5)     | 8 (2.6)      | 7 (2.6)      | 8 (3)        | 4 (2.3)      | 4 (2.3)               | 4 (2.4)      |              |  |
| ART Adherence Score (0–10)         |                       |              |              |              |              |              |                       |              |              |  |
| 0–8                                | 43 (10.4)             | 53 (17.6)    | 22 (7.9)     | 20 (7.9)     | 13 (5.1)     | 53 (22.7)    | 9 (7.3)               | 5 (4)        |              |  |
| 9–10                               | 170 (41.3)            | 249 (82.4)   | 256 (92.1)   | 233 (92.1)   | 240 (94.9)   | 179 (76.8)   | 114 (92.7)            | 120 (96)     |              |  |
| Viral Suppression                  |                       |              |              |              |              |              |                       |              |              |  |
| Yes                                | 307 (74.5)            | 256 (77.3)   | 255 (84.4)   | 230 (83.9)   | 233 (86.6)   | 179 (76.8)   | 152 (86.4)            | 147 (87)     |              |  |
| No                                 | 99 (24)               | 69 (20.8)    | 47 (15.6)    | 44 (16.1)    | 34 (12.6)    | 53 (22.7)    | 17 (9.7)              | 21 (12.4)    |              |  |

\* M6=month 6 follow-up, M12=month 12 follow-up, M18=month 18 follow-up, & M24=month 24 follow-up

† only collected at baseline visit

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**Table 2a:** Adherence by self-report methamphetamine frequency in last thirty days among DRIVE CohortPWID

|                              | Baseline        |               |  | M6*             |               |  | M12*            |               |  | M18*            |               |  | M24*            |               |  |
|------------------------------|-----------------|---------------|--|-----------------|---------------|--|-----------------|---------------|--|-----------------|---------------|--|-----------------|---------------|--|
|                              | Adherence Score |               |  | Adherence Score |               |  | Adherence Score |               |  | Adherence Score |               |  | Adherence Score |               |  |
|                              | 0-8<br>N (%)    | 9-10<br>N (%) |  | 0-8<br>N (%)    | 9-10<br>N (%) |  | 0-8<br>N (%)    | 9-10<br>N (%) |  | 0-8<br>N (%)    | 9-10<br>N (%) |  | 0-8<br>N (%)    | 9-10<br>N (%) |  |
| <b>Cohort Entry 1 (2016)</b> |                 |               |  |                 |               |  |                 |               |  |                 |               |  |                 |               |  |
| No methamphetamine use       | 17 (39.5)       | 112 (65.9)    |  | 31 (58.5)       | 190 (76.3)    |  | 11 (45.8)       | 208 (78.5)    |  | 12 (57.1)       | 194 (79.2)    |  | 9 (56.3)        | 185 (72.8)    |  |
| Moderate methamphetamine use | 24 (55.8)       | 49 (28.8)     |  | 14 (26.4)       | 54 (21.7)     |  | 13 (54.2)       | 50 (18.9)     |  | 9 (42.9)        | 45 (18.4)     |  | 6 (37.5)        | 62 (24.4)     |  |
| Heavy methamphetamine use    | 2 (4.7)         | 9 (5.3)       |  | 8 (15.1)        | 5 (2)         |  | 0 (0)           | 7 (2.6)       |  | 0 (0)           | 6 (2.5)       |  | 1 (6.3)         | 7 (2.8)       |  |
| <b>Cohort Entry 2 (2017)</b> |                 |               |  |                 |               |  |                 |               |  |                 |               |  |                 |               |  |
| No methamphetamine use       | 18 (58.1)       | 77 (71.9)     |  |                 |               |  |                 |               |  | 10 (66.7)       | 105 (75)      |  | 5 (41.7)        | 105 (73.9)    |  |
| Moderate methamphetamine use | 12 (38.7)       | 28 (26.2)     |  |                 |               |  |                 |               |  | 4 (26.7)        | 34 (24.3)     |  | 7 (58.3)        | 34 (23.9)     |  |
| Heavy methamphetamine use    | 1 (3.2)         | 2 (1.9)       |  |                 |               |  |                 |               |  | 1 (6.7)         | 1 (0.7)       |  | 0 (0)           | 3 (2.1)       |  |

\* M6=month 6 follow-up, M12=month 12 follow-up, M18=month 18 follow-up, & M24=month 24 follow-up

**Table 2b:** Viral Suppression by self-report methamphetamine frequency in last thirty days among DRIVE Cohort PWID

|                              | Baseline   |           |            | M6*        |           |            | M12*      |            |           | M18*       |           |       | M24*  |         |       |
|------------------------------|------------|-----------|------------|------------|-----------|------------|-----------|------------|-----------|------------|-----------|-------|-------|---------|-------|
|                              | VS#        | Not VS#   | N (%)      | VS#        | Not VS#   | N (%)      | VS#       | Not VS#    | N (%)     | VS#        | Not VS#   | N (%) | VS#   | Not VS# | N (%) |
|                              | N (%)      | N (%)     | N (%)      | N (%)      | N (%)     | N (%)      | N (%)     | N (%)      | N (%)     | N (%)      | N (%)     | N (%) | N (%) | N (%)   | N (%) |
| <b>Cohort Entry 1 (2016)</b> |            |           |            |            |           |            |           |            |           |            |           |       |       |         |       |
| No methamphetamine use       | 162 (62.1) | 39 (59.1) | 191 (74.6) | 191 (74.6) | 42 (60.9) | 196 (76.9) | 31 (66)   | 181 (78.7) | 30 (68.2) | 174 (74.7) | 19 (55.9) |       |       |         |       |
| Moderate methamphetamine use | 87 (33.3)  | 23 (34.8) | 58 (22.7)  | 58 (22.7)  | 20 (29)   | 54 (21.2)  | 13 (27.7) | 45 (19.6)  | 11 (25)   | 56 (24)    | 11 (32.4) |       |       |         |       |
| Heavy methamphetamine use    | 12 (4.6)   | 4 (6.1)   | 7 (2.7)    | 7 (2.7)    | 7 (10.1)  | 5 (2)      | 3 (6.4)   | 4 (1.7)    | 3 (6.8)   | 3 (1.3)    | 4 (11.8)  |       |       |         |       |
| <b>Cohort Entry 2 (2017)</b> |            |           |            |            |           |            |           |            |           |            |           |       |       |         |       |
| No methamphetamine use       | 102 (69.4) | 18 (64.3) |            |            |           |            |           | 109 (74.1) | 14 (50)   | 107 (72.8) | 12 (57.1) |       |       |         |       |
| Moderate methamphetamine use | 42 (28.6)  | 9 (32.1)  |            |            |           |            |           | 35 (23.8)  | 13 (46.4) | 37 (25.2)  | 8 (38.1)  |       |       |         |       |
| Heavy methamphetamine use    | 3 (2)      | 1 (3.6)   |            |            |           |            |           | 3 (2)      | 1 (3.6)   | 3 (2)      | 1 (4.8)   |       |       |         |       |

# VS=virally suppressed

\* M6=month 6 follow-up, M12=month 12 follow-up, M18=month 18 follow-up, & M24=month 24 follow-up



Random Effects Model Table Examining Relationship between Recent Methamphetamine use and not being virally suppressed in DRIVE Cohort

**Table 3:**

|  | <b>OR (95% CI)</b> | <b>AOR (95% CI)</b> |
|--|--------------------|---------------------|
| Age                                    | 0.91 (0.84, 0.98)  | 0.92 (0.01, 0.86)   |
| Heroin Injection                       | 1.01 (0.99, 1.04)  |                     |
| Methamphetamine Use <sup>#</sup>       | 1.99 (1.26, 3.14)  | 1.84 (1.06, 3.12)   |
| Methadone in urine                     | 0.29 (0.16, 0.54)  | 0.29 (0.16, 0.53)   |
| Self-Report ART Adherence <sup>*</sup> | 0.12 (0.05, 0.24)  |                     |

<sup>#</sup> ordered exposure of methamphetamine use in last 30 days (0= no use, 1= 1–19 days use, 2= 20+ days use)

<sup>\*</sup> Adherence score divided into non-perfect adherence (scores 0–8) and perfect adherence (9–10)