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# The impact of buprenorphine/naloxone treatment on HIV risk behaviors among HIV-infected, opioid-dependent patients☆

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ABSTRACT

*Background:* Opioid dependence is a major risk factor for HIV infection, however, the impact of buprenorphine/naloxone treatment on HIV risk behaviors among HIV-infected opioid-dependent patients is unknown.
*Methods:* We conducted a longitudinal analysis of 303 HIV-infected opioid-dependent patients initiating buprenorphine/naloxone treatment. Outcomes included self-reported past 90-day needle-sharing and non-condom use. We assessed trends over the 12 months using the Cochran–Armitage trend test. Using generalized estimating equations, after multiple imputation, we determined factors independently associated with needle-sharing and non-condom use, including time-updated variables. We then conducted a mediation analysis to determine whether substance use explained the relationship between time since treatment initiation and needle-sharing.
*Results:* Needle-sharing decreased from baseline to the fourth quarter following initiation of buprenorphine/naloxone (9% vs. 3%, $p < 0.001$), while non-condom use did not (23% vs. 21%, $p = 0.10$). HIV risk behaviors did not vary based on the presence of a detectable HIV-1 RNA viral load. Patients who were homeless and used heroin, cocaine/amphetamines or marijuana were more likely to report needle-sharing. Heroin use fully mediated the relationship between time since treatment initiation and needle-sharing. Women, patients who identified as being gay/lesbian/bisexual, those married or living with a partner and who reported heroin or alcohol use were more likely to report non-condom use. Older patients were less likely to report non-condom use.
*Conclusions:* While buprenorphine/naloxone is associated with decreased needle-sharing among HIV-infected opioid-dependent patients, sexual risk behaviors persist regardless of viral load. Targeted interventions to address HIV risk behaviors among HIV-infected opioid-dependent populations receiving buprenorphine/naloxone are needed.



## 1. Introduction

Opioid dependence continues to fuel HIV transmission, with injection drug use accounting for over 4 million cases of HIV worldwide (Center for Strategic and International Studies (CSIS) Task Force on HIV/AIDS, 2008; Mathers et al., 2008). HIV transmission can occur either through the sharing of drug-injecting equipment or sexual risk behaviors (Des Jarlais et al., 2007; Strathdee and Stockman, 2010). Established interventions for HIV prevention for these populations and their partners include needle and syringe exchange programs; condoms; and expanded combination antiretroviral therapy for HIV-infected individuals (Marshall and Wood, 2010). In addition, there is growing support for the effectiveness of opioid agonist treatment (OAT), including methadone and buprenorphine, at decreasing HIV risk behaviors among uninfected patients (Sullivan et al., 2008; Gowing et al., 2011; MacArthur et al., 2012).

Available in the United States since 2002, buprenorphine is a partial mu-receptor agonist effective at treating opioid dependence (Sullivan and Fiellin, 2008; Mattick et al., 2008) and is included in

☆ More information on the BHIVES Collaborative can be found by accessing the online version of this paper. See Appendix A for more details.

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the World Health Organization's Model List of Essential Medicines (Center for Strategic and Internationa Studies (CSIS) Task Force on HIV/AIDS, 2008). Commonly administered in combination with naloxone, buprenorphine may be prescribed by providers who have obtained a special registration from the Drug Enforcement Agency and have appropriate linkages to clinical services (Sullivan et al., 2008). Recent data demonstrate the impact of integrated buprenorphine/naloxone and HIV treatment on improving HIV and drug treatment outcomes (Altice et al., 2011; Fiellin et al., 2011) and quality of life (Korthuis et al., 2011) for some individuals. Meanwhile, cross-sectional data reveal that ongoing HIV risk behaviors among HIV-infected opioid-dependent patients occur frequently and may be associated with infection with resistant virus (Chaudhry and Botsko, 2011; Tetrault et al., 2013). However, the impact of buprenorphine/naloxone on HIV risk behaviors over time among HIV-infected opioid-dependent patients is unknown.

Therefore, the purpose of the current study was to begin to address this gap, focusing on needle-sharing and non-condom use, over a one year period among HIV-infected opioid-dependent patients initiating buprenorphine/naloxone treatment. Given the increased likelihood of HIV transmission in the setting of a detectable HIV viral load, we also examined whether needle-sharing and non-condom use differed based on the presence of a detectable HIV viral load.

## 2. Methods

### 2.1. Study overview

The Buprenorphine-HIV Evaluation and Support (BHIVES) Project[1] was funded by the HIV/AIDS Bureau of the Health Resources and Services Administration from 2004 to 2009 as a Special Project of National Significance, and the design and patient characteristics are described in detail elsewhere (Chaudhry and Botsko, 2011; Weiss et al., 2011). Through the collaboration of multiple partners, BHIVES led to the creation and evaluation of the integrated provision of buprenorphine and HIV treatment services in 10 HIV primary care settings across the United States. The current analysis relies on data from nine sites as one site was unable to meet the integrated care requirement (Weiss et al., 2011). Among those contributing data to these analyses, six were located in academic medical centers; one in a public hospital; one in a community health center; and one in a community health center located within an academic medical system. Sites developed their own protocols for the delivery of these services, which included integrated HIV and buprenorphine/naloxone treatment, counseling, and linkage to supportive services along with a comparison arm, which varied across sites. This study was approved by the Institutional Review Boards at The New York Academy of Medicine and each of the demonstration sites. Patients were reimbursed for their participation with an in-kind incentive for completing assessments.

### 2.2. Participants

Participants were identified by providers and through self-referral based on both clinic-based and community-based recruitment efforts. Participants were: 18 years and older; HIV-infected; met Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV; American Psychiatric Association, 2000) criteria for opioid dependence; were initiating buprenorphine/naloxone treatment at baseline; and willing and able to provide written informed consent in English or Spanish. Patients were excluded if they were pregnant; had transaminases five times the normal level or greater; met criteria for benzodiazepine abuse or dependence in the prior six months; met criteria for alcohol dependence; received high doses of methadone; were suicidal or severely psychiatrically impaired; or were inappropriate based on the provider's clinical judgment (Weiss et al., 2011). These criteria were chosen to be consistent with existing guidelines for providers who were new to offering office-based buprenorphine (Center for Substance Abuse Treatment, 2004) and the sites were able to apply the exclusion criteria with some flexibility based on their expertise (Weiss et al., 2011). Our analytic sample was restricted to patients who received at least one dose of buprenorphine/naloxone at study initiation.

[1] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering http://dx.doi.org/10.1016/j.drugalcdep.2014.03.006.

### 2.3. Data sources

Data were collected through interview and medical chart abstraction at baseline and then quarterly for the period of 12 months after buprenorphine/naloxone initiation. Data sources included patient surveys and patients' medical records.

### 2.4. HIV risk behaviors

To determine the impact of buprenorphine/naloxone on HIV risk behaviors, we assessed self-reports of needle-sharing behaviors and non-condom use at each interval. Specifically, patients were asked: *When was the last time you shared needles or works with anyone?*, and among those who reported being sexually active during the past 90 days before the baseline and quarterly follow-up interviews, *When was the last time you had vaginal or anal sex without using a condom?* We categorized the response options accordingly: *within the past 90 days* as recent; *greater than 90 days ago* and *never* as not recent; and *unknown* or *refuse to answer* as missing.

### 2.5. Covariates

Survey data were used to determine demographic information, education, employment, housing status, incarceration history, HIV disease history including likely mode of acquisition, antiretroviral use and adherence. The presence of a detectable viral load was defined as >400 copies/mL (Chaudhry and Botsko, 2011). Substance use behaviors were assessed using the Addiction Severity Index-Lite (ASI-Lite) at baseline (lifetime and past 30 days) and each interval (past 30 days; McLellan et al., 1985). Time-updated variables for employment, housing status, incarceration, antiretroviral use, HIV viral load and substance use were included in the models. Data were abstracted from the medical chart to determine years since HIV diagnosis, CD4 count, HIV-1 RNA viral load, use of antiretroviral therapy, hepatitis B and C serologies, and presence of an AIDS-defining illness. To account for changes over time, time since treatment initiation (quarter) was included as a covariate (SAS Institute Inc., 2009).

### 2.6. Statistical analysis

We performed descriptive statistics to characterize the demographic and clinical characteristics of patients receiving buprenorphine/naloxone at baseline. The proportion of patients with needle-sharing and non-condom use over time was determined and assessed for a trend using the Cochran–Armitage trend test (Cochran, 1954; Armitage, 1955). We assessed bivariate associations between demographic and clinical characteristics and HIV risk behaviors and defined statistical significance based on a threshold of $p < 0.05$. To further identify factors associated with each HIV risk behavior, we constructed multivariate generalized estimating equations (GEE) models to account for within-individual correlation as a result of repeated measures from the same participants over time. Variables included in the multivariate models were those which yielded $p < 0.25$ in bivariate models (Mickey and Greenland, 1989; Demchuk et al., 1999; Bursac et al., 2008) and those thought to be clinically relevant. Potential collinearity was assessed by calculating the correlation between independent variables and covariates, and no pair had a Spearman's correlation >0.40. All analyses were conducted using SAS version 9.3 (Cary, NC). We used multiple imputation with Markov chain Monte Carlo method to handle missing data (Rubin, 1996; McPherson et al., 2013). Twenty imputed datasets were generated using PROC MI and the outcome variables (needle sharing and non-condom use) were dichotomized using adaptive rounding (Bernaards et al., 2007). Results of the GEE analysis on each of the datasets, including 303 participants from five time points (1515 observations each), were combined using PROC MIANALYZE. Given our hypothesis that changes in needle-sharing are due to changes in substance use, we then conducted a mediation analysis to assess whether changes in substance use mediated changes in needle-sharing over time (Baron and Kenny, 1986; Vyavaharkar et al., 2010). To complete this, we assessed whether (1) time since treatment initiation was associated with substance use; (2) time since treatment initiation was associated with needle-sharing; and (3) the relationship between time since treatment initiation and needle-sharing was attenuated after adjusting for substance use.

## 3. Results

### 3.1. Participant characteristics

Three hundred and three participants received at least one dose of buprenorphine/naloxone and were included in the analytic sample (Table 1). Detailed demographic and clinical characteristics have been previously published (Chaudhry and Botsko, 2011). The majority of patients were men, black, heterosexual, single, and had completed at least a high school education. At baseline, 74% were unemployed, 25% were homeless and 13% had been incarcerated in the past 30 days. At treatment entry, patients had