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Association between methamphetamine use and retention among patients with opioid use disorders treated with buprenorphine

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ABSTRACT

Background: Methamphetamine use is increasing in parts of the U.S., yet its impact on treatment for opioid use disorder is relatively unknown.

Methods: The study utilized data on adult patients receiving buprenorphine from Washington State Medication Assisted Treatment-Prescription Drug and Opioid Addiction program clinics between November 1, 2015 and April 31, 2018. Past 30-day substance use data were collected at baseline and 6-months, as well as date of program discharge. Cox proportional hazards regression was used to estimate the relative hazards for treatment discharge comparing methamphetamine users at baseline with non-users, adjusting for site, time period, age, gender, race, ethnicity, and education. For a subset of patients with data, we describe the proportion of individuals reporting methamphetamine use at baseline versus 6-months.

Results: The sample included 799 patients, of which 237 (30%) reported using methamphetamine in the past 30 days; of those, 156 (66%) reported 1–10 days of use, 46 (19%) reported 11–20 days of use, and 35 (15%) reported 21–30 days of use. Baseline methamphetamine use was associated with more than twice the relative hazards for discharge in adjusted models (aHR = 2.39; 95% CI: 1.94–2.93). In the sub-sample with data (n = 516), there was an absolute reduction of 15% in methamphetamine use: 135 (26%) reported use at baseline versus 57 (11%) at follow-up.

Conclusions: In summary, this study found that patients who concurrently used methamphetamine were less likely to be retained in buprenorphine treatment compared to non-users. For persons who were retained, however, methamphetamine use decreased over time.

1. Introduction

The United States is currently in the midst of an opioid crisis; recently, methamphetamine use has also emerged as an additional major public health threat. In 2017 an estimated 2.1 million Americans had an opioid use disorder (OUD), and 964,000 had a methamphetamine use disorder (Substance Abuse and Mental Health Services Administration, 2018a). Medications for opioid use disorders, such as buprenorphine and methadone, are effective in reducing illicit opiate use (Fullerton et al., 2014; Mattick, Breen, Kimber, & Davoli, 2014; Saxon, Hser, Woody, & Ling, 2013) and reducing downstream social and health consequences such as incarceration and spread of HIV, hepatitis C, and overdose (Dolan et al., 2005; Gowing, Farrell, Bornemann, Sullivan, & Ali, 2008; Larochelle et al., 2018; MacArthur et al., 2012; Nolan et al., 2014; Oliver et al., 2010; Schwartz et al., 2013; Tsui, Evans, Lum, Hahn, & Page, 2014; Werb et al., 2008; White, Dore, Lloyd, Rawlinson, & Maher, 2014). In response to the opioid crisis there has been a national effort to expand treatment for opioid use disorder with buprenorphine, which can be prescribed by waivered providers (physicians, nurse practitioners, and medical assistants) in office-based settings.

Although methamphetamine use is less prevalent than opioid use, it appears to be on the rise nationally (Substance Abuse and Mental Health Services Administration, 2018a). Methamphetamine use also varies considerably by region of the country and therefore the national estimates can mask these differences. Data from sentinel sites suggest increasing public health burden (i.e. treatment admissions, overdose

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and law enforcement interventions) due to methamphetamine use in states west of the Mississippi (Artigiani, Hsu, McCandlish, & Wish, 2018). Concurrent use of heroin and methamphetamine appears to be increasing on the West coast (Al-Tayyib, Koester, Langegger, & Raville, 2017; Glick et al., 2018). Among persons who inject drugs, the practice of mixing heroin and methamphetamines has been associated with overdose risk (Al-Tayyib et al., 2017). It is unclear how methamphetamine use impacts treatment outcomes among persons who are treated with medications for opioid use disorders. Some studies have demonstrated negative impacts of other substance use (e.g., cocaine, methamphetamines, and cannabis) on buprenorphine treatment retention (Bhatraju et al., 2017; Gryczynski et al., 2014; Hser et al., 2014; Weinstein et al., 2017), although not all studies demonstrate worse outcomes (Cunningham et al., 2008; Soeffing, Martin, Fingerhood, Jasinski, & Rastegar, 2009; Stein, Cioe, & Friedmann, 2005). It is also unknown whether patterns of methamphetamine use change over time among persons who are treated for opioid use disorders with buprenorphine. Prior research suggests buprenorphine treatment is associated with reduced methamphetamine craving (Salehi, Emadossadat, Kheirabadi, Maracy, & Sharbafchi, 2015), and cocaine use was shown to decline over time among persons living with HIV who were treated with buprenorphine (Fiellin et al., 2011).

The current study was conducted to assess the association between methamphetamine use and treatment retention among patients receiving treatment for opioid use disorders with buprenorphine, and to describe changes in methamphetamine that occurred over time with treatment. We hypothesized that individuals receiving buprenorphine treatment for opioid use disorders who were also users of methamphetamines at baseline would have lower rates of treatment retention compared with non-users of methamphetamines. For the subset of patients who had 6-month follow-up data on substance use, we also describe the change in methamphetamine use compared to baseline.

2. Materials and methods

2.1. Study sample/data source

The sample was comprised of adult patients 18 years of age or older who initiated buprenorphine treatment in a Washington State Medication Assisted Treatment-Prescription Drug and Opioid Addiction (WA-MAT-PDOA) program clinic between November 1, 2015 and April 31, 2018. WA-MAT-PDOA was a 3-year Substance Abuse and Mental Health Services Administration (SAMHSA) funded project intended to expand access to medications for opioid use disorder in Washington State through partnerships with Harborview Medical Center (HMC) and Evergreen Treatment Services (ETS), a federally certified opioid treatment program. The 3 sites were HMC Adult Medicine Clinic (HMC AMC) in Seattle and 2 ETS sites that were located in Hoquiam and Olympia, WA. Hoquiam is a town of approximately 8500 individuals in western WA near the coast, while Olympia, the state capital, lies due south of Seattle at the southern edge of the Puget Sound. The HMC AMC was an office-based program integrated into an urban hospital-based primary care clinic, while the ETS rural-serving sites provided buprenorphine through a telemedicine model. All sites treated adults with heroin and/or prescription opioid use disorders using a collaborative nurse care manager model originally developed in Massachusetts (Alford et al., 2011; LaBelle, Han, Bergeron, & Samet, 2016). Sites used similar approaches to the frequency of monitoring and visits. Analyses were limited to patients' first treatment episode.

2.2. Data collection

Data were collected as part of program activities using the Government Performance and Results Act (GPRA) Client Outcomes Measures survey (SAMHSA, 2017) provided by SAMHSA to track client characteristics and outcomes. The GPRA survey is a structured interview, conducted face-to-face. It was administered to all WA-MAT-PDOA participants by clinic staff during in-person interviews at baseline (i.e., client enrollment in MAT services) and 6 months after enrollment. Participants that had discharged from the program and were unavailable to clinic staff were tracked and interviewed by Washington State program evaluation staff and reimbursed $20 for follow-up surveys. Staff entered completed surveys into the SAMHSA's Performance Accountability and Reporting System (SPARS), and Washington State project evaluation staff downloaded the data from SPARS to create analytic SAS data files necessary for performance monitoring, including this analysis. GPRA data included demographic characteristics, past 30-day substance use, and prior treatment history. Clinic staff provided data on date of discharge from program and reason for discharge. Patients provided verbal consent for GPRA data collection prior to enrollment, and the Washington State Institutional Review Board determined the project to be exempt from IRB oversight as it was considered program evaluation of an evidence-based practice.

2.3. Measures

2.3.1. Main dependent variable/outcome

The primary outcome of interest was time to treatment discharge. Patients were discharged if they had not had an active prescription for buprenorphine and had not had contact with the program for > 30 days. Date of discharge was the day that patients' final buprenorphine prescription was scheduled to end. Patients could leave the program for both voluntary and involuntary reasons. Individuals were considered discharged if they did not return to the clinic and were then considered 'lost to follow-up'; transfer to another addiction treatment program for a higher level of care and death were also considered to be discharges.

2.3.2. Main independent variable/predictor

The main independent variable of interest was self-report of current methamphetamine use at baseline. At intake, patients reported the number of days they had used a given substance in the past 30 days. A dichotomous variable was created for any methamphetamine use based on the patients' endorsement of one or more days of methamphetamine use at intake. Secondary analyses were conducted with methamphetamine use as a categorical variable with the following categories of past 30 day use: none, 1–10 days, 11–20 days, and 21–30 days.

2.3.3. Additional covariates

Other variables for analysis included age, gender, clinic site, period of enrollment in treatment (in 6-month increments to account for changes in clinical policies), race (black, white, Asian, Hawaiian/Pacific Islander, American Indian/Alaskan Native, multi-race, and other), ethnicity (Hispanic/Latino v. non-Hispanic/non-Latino), education level (less than high school, high school, some college, bachelor's degree or higher), transfer from another program already on buprenorphine, and past 30 day use of other non-methamphetamine substances (non-prescribed opioids, cannabis, alcohol, and benzodiazepines).

2.4. Statistical analysis

Descriptive statistics were used to characterize demographics and baseline patterns of substance use in the sample overall and by program site. The association between baseline methamphetamine use and time to discharge was assessed using Kaplan-Meier survival curves with statistical significance assessed by the log-rank test. Survival time was defined as time from induction or enrollment date to earliest date of discharge or July 2018. Project data collection ended July 2018; therefore retention times were censored after this time. Patients who died or were lost to follow-up were considered "discharged" as per outcome definition. Cox proportional hazards regression was used to estimate the relative hazards for treatment discharge comparing

methamphetamine users with non-users and adjusting for baseline covariates (age, gender, race, ethnicity, education, time period, and clinic site), which were specified "a priori". We chose not to adjust for other substance use, as our primary question of interest was whether the presence of baseline methamphetamine use in a patient initiating treatment with buprenorphine is a marker for future non-retention. We were not seeking to answer the question of whether methamphetamine use was independently associated with retention after excluding effects from other substances. Adjusted hazard ratios (AHR) and 95% confidence intervals (CI) are reported. Sensitivity analyses were conducted using Cox regression models adjusting for site only as well as site plus each covariate (age, gender, race, ethnicity, education, and time period) separately. Subgroup analyses were conducted to assess effect modification (i.e., interaction) for time period, age, gender, race, and ethnicity. Cox models were checked for violation of the proportional hazards assumption by assessing scaled Schoenfeld residuals and log-minus-log survival plots for patterns of non-proportionality.

Exploratory analyses were conducted to describe the proportion of individuals reporting methamphetamine use at baseline compared to the 6-month follow-up GPRA survey. In addition, in a sub-sample of persons who reported methamphetamine use at baseline we describe 1) the frequency of reporting no methamphetamine use at 6-month follow-up and 2) the change in frequency of use of methamphetamines in past 30 days (mean, SD, IQR) at 6 months compared to baseline.

All analyses were performed using SAS statistical software version 9.4. (SAS Institute Inc, 2013)

3. Results

The sample included 799 unique individuals who received treatment with buprenorphine for opioid use disorder at 1 of the 3 sites. Table 1 summarizes baseline demographic factors, buprenorphine treatment status, and substance use for the total sample and by site. Overall, slightly less than half (44%) of the sample were women, the mean age was 38 (± SD12.2), and the majority were white (80%). Most (58%) had a high school education or less. Only a quarter transferred into the program already on a buprenorphine prescription, which typically occurred after inpatient addiction treatment with buprenorphine initiated. Demographic factors were similar among the two ETS sites; compared to the ETS sites, the HMC patients were older and more often male, black, and having a bachelor's degree or higher. Overall among sites, the most common non-opioid substance reported used in the past 30 days at baseline was cannabis (40%) followed by methamphetamines (30%); for the HMC AMC site only alcohol was slightly more common than methamphetamine use (38% v. 31%). Among the 237 participants who reported using methamphetamine in the past 30 days, 156 (66%) reported 1–10 days of use, 46 (19%) reported 11–20 days of use, and 35 (15%) reported 21–30 days of use. The most common route of administration of methamphetamine use was smoking (72.6%), followed by intravenous use (21.1%), oral (3.4%) and intranasal use (2.9%).

Fig. 1 shows the Kaplan-Meier survival curves for time to discharge for methamphetamine users and non-users with 95% confidence bands. Methamphetamine users had significantly shorter treatment duration, being more likely to discharge or drop out early in treatment, i.e. immediately within the first 3 months. The probability of survival (i.e. retention) within the first 90, 180 and 365 days for methamphetamine non-users was 0.80, 0.63 and 0.56, respectively, compared to 0.54, 0.36 and 0.27 among methamphetamine users. The causes for non-retention were: loss to follow-up (65%), transfers to other programs (including for higher level of care) (27%), clinic discharges (4%), known incarceration (2%), death (1%) and other (1%). Table 2 demonstrates results from the Cox proportional hazards models adjusted for site, time period, age, gender, race, ethnicity, and education. These multivariate models were based on the analytic sample of 768 participants with complete data. Baseline reports of any past 30 day use of methamphetamine was associated with a more than two times greater relative hazards for non-retention (HR = 2.39; 95% CI: 1.94–2.93), and a model that used the 4-level covariate for frequency of methamphetamine found that the magnitude of the effect size increased with increased frequency of past 30 day use (Table 2). In models that were adjusted for each individual covariate, the estimates for hazards ratios were similar, ranging from 2.43 to 2.50 (see Supplemental Tables in Appendix). Finally, we conducted analyses to test for effect modification (i.e., interaction) in sub-groups (time period, age, gender, race, and ethnicity). We found no significant interactions at a $p < 0.05$ significance level.

Of the 799 participants included in the study sample, 517 participants completed a 6-month follow-up survey, of which one person was missing baseline data on methamphetamine use. In this sub-sample with baseline and follow-up survey data on methamphetamine use ($n = 516$), there was an absolute reduction of 15% in

Table 1
Baseline demographic characteristic and history of prior treatment overall and by site ($n = 799$).

Characteristic	HMC[a] ($n = 282$)	ETS site A[b] ($n = 260$)	ETS site B[c] ($n = 257$)	Total ($n = 799$)
Time period, n (%)				
11/1/15–4/30/16	45 (16%)	29 (11%)	34 (13%)	108 (14%)
5/1/16–10/31/16	61 (22%)	63 (24%)	67 (26%)	191 (24%)
11/1/16–4/30/17	52 (18%)	47 (18%)	44 (17%)	143 (18%)
5/1/17–10/31/17	71 (25%)	72 (28%)	66 (26%)	209 (26%)
11/1/17–4/30/18	53 (19%)	49 (19%)	46 (18%)	148 (19%)
Age (yrs), mean (SD)	41.3 (13.0)	36.6 (12.1)	35.7 (10.7)	38.0 (12.2)
Male gender, n (%)	183 (65%)	129 (50%)	133 (52%)	445 (56%)
Missing	0 (0%)	1 (0%)	0 (0%)	1 (0%)
Race, n (%)				
Black	35 (12%)	[d]	[d]	48 (6%)
Asian	[d]	[d]	[d]	13 (2%)
Native Hawaiian/ Pacific Islander	[d]	[d]	[d]	12 (2%)
White	200 (71%)	218 (84%)	220 (86%)	638 (80%)
American Indian	[d]	25(10%)	[d]	46 (6%)
More than one race	20 (7%)	[d]	[d]	27 (3%)
Other	[d]	[d]	[d]	12 (2%)
Missing	2 (1%)	1 (0%)	0 (0%)	3 (0%)
Hispanic ethnicity, n (%)	24 (9%)	16 (6%)	19 (7%)	59 (7%)
Missing	0 (0%)	1 (0%)	0 (0%)	1 (0%)
Education, n (%)				
Less than high school	45 (16%)	54 (21%)	40 (16%)	139 (17%)
High school	78 (28%)	112 (43%)	135 (53%)	325 (41%)
Some college	24 (9%)	[d]	[d]	40 (5%)
Bachelor's degree or higher	119 (42%)	81 (31%)	65 (25%)	265 (33%)
Missing	16 (6%)	4 (2%)	10 (4%)	30 (4%)
Buprenorphine transfer, n (%)	42 (15%)	65 (25%)	91 (35%)	198 (25%)
Past 30 day methamphetamine use	87 (31%)	89 (34%)	61 (24%)	237 (30%)
Missing	15 (5%)	4 (2%)	10 (4%)	29 (4%)
Past 30 day cannabis use	132 (47%)	109 (42%)	82 (32%)	323 (40%)
Missing	15 (5%)	4 (2%)	10 (4%)	29 (4%)
Past 30 day alcohol use	106 (38%)	48 (18%)	56 (22%)	210 (26%)
Missing	16 (6%)	4 (2%)	10 (4%)	30 (4%)
Past 30 day benzodiazepine use	36 (13%)	13 (5%)	15 (6%)	64 (8%)
Missing	15 (5%)	4 (2%)	10 (4%)	29 (4%)
Past 30 day cocaine use	43 (15%)	[d]	[d]	52 (7%)
Missing	15 (5%)	3 (1%)	9 (4%)	27 (3%)

[a] HMC = Harborview Medical Center, Seattle, WA.
[b] ETS site A = Evergreen Treatment Services South Sound Clinic, Olympia, WA.
[c] ETS Site B = Evergreen Treatment Services Hoquiam Clinic, Hoquiam, WA.
[d] Due to privacy concerns, cell values are suppressed when there are 11 or fewer observations or if a combination of cell values can be used to calculate the number of observations in a suppressed cell.

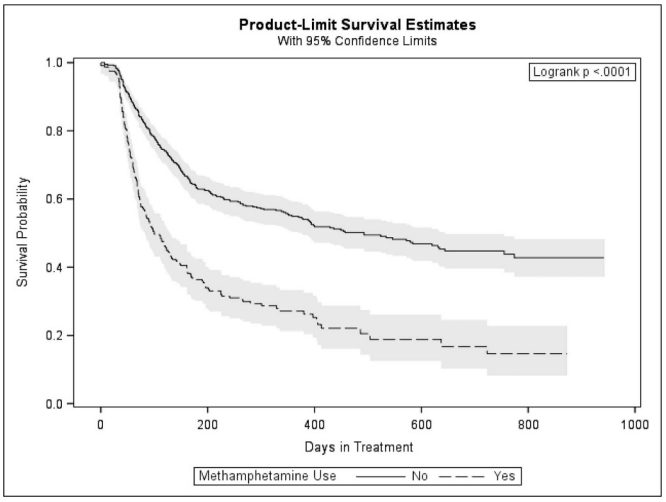

Fig. 1. Kaplan-Meier survival curves for methamphetamine users and non-users with 95% confidence bands (n = 770).

Table 2
Estimates of hazard ratios for non-retention associated with past 30 day methamphetamine use at baseline: results from Cox proportional hazards regression analysis (n = 768).[a]

Model	Hazard Ratio (95% CI)
Any methamphetamine use	2.39 (1.94–2.93)
Days used methamphetamine	
None	Reference
1–10	2.05 (1.63–2.57)
11–20	3.04 (2.12–4.23)
21–30	3.61 (2.40–5.23)

[a] Adjusted for site, time period, age, gender, race, ethnicity, and education; sample includes 768 with complete data.

methamphetamine use reported: 57 (11%) reported using methamphetamines at follow-up, compared to 135 (26%) at baseline. Among those participants who used methamphetamines at baseline (n = 135), 98 (73%) reported no longer using at the 6-month follow-up survey. Of those 367 participants who did not use methamphetamines at baseline, 19 (5%) had initiated methamphetamine use at the 6-month survey. Overall, methamphetamine use decreased on average by 6.10 days (± SD 9.11) among baseline users.

4. Discussion

This study evaluated the effect of methamphetamine use on treatment retention among patients receiving buprenorphine for opioid use disorders at three SAMHSA-funded programs in Washington State. Results demonstrated that methamphetamine use was relatively common among these patients engaging in treatment for opioid use disorders: at baseline, slightly less than one-third (30%) reported that they were also current users of methamphetamines. Methamphetamine use was significantly associated with lower retention in buprenorphine treatment. Patients who reported baseline use of methamphetamine had a > 2-fold relative hazard for not being retained in treatment, with most treatment discharges occurring within the first 6–8 months of treatment and primarily due to loss to follow-up. On a positive note, over time there appeared to be reductions in methamphetamine use among these patients who received buprenorphine for OUD.

The results of this study add to the existing reports of adverse health consequences of concurrent methamphetamine and opioid use. Methamphetamine use has been demonstrated to be associated with increased risk for overdose among persons who inject drugs (PWID) (Al-Tayyib et al., 2017) and with sexual risk taking and HIV among men who have sex with men (MSM) (Nerlander et al., 2018). A study of PWID in the Seattle metropolitan area demonstrated that methamphetamine use has been steadily increasing among non-MSM between 2009 and 2017, with 53% of PWID reporting simultaneous injection of heroin and methamphetamine use (i.e., “goofballs”) in the most recent year (Glick et al., 2018). Our study provides additional evidence of the growing burden of methamphetamine use among persons seeking treatment for opioid use disorders in Washington State. Our results can also be contrasted with studies of samples of patients receiving office-based treatment for buprenorphine on the East Coast where cocaine rather than methamphetamine appears to be the most common stimulant used (Bhatraju et al., 2017; Cunningham et al., 2013; Weinstein et al., 2017).

This study demonstrates that methamphetamine use is associated with increased risk for non-retention for patients who are treated for opioid use disorders with buprenorphine. We are unaware of other studies that have specifically focused on the effects of methamphetamine use on buprenorphine treatment retention. Prior studies on the impact of cocaine use on retention have shown mixed results (Cunningham et al., 2013; Soeffing et al., 2009; Weinstein et al., 2017). Given that methamphetamine use was not rare in our sample, and it was strongly associated with non-retention, these results underscore the need for additional interventions to be offered early on to improve treatment outcomes in this unique population. As such, buprenorphine treatment programs will need to provide interventions for methamphetamine use as well in the midst of the opioid crisis. Psychosocial treatments such as cognitive behavioral therapy and contingency management have demonstrated efficacy among persons with methamphetamine use disorders in some studies (Rawson et al., 2004; Roll et al., 2006; Roll, Chudzynski, Cameron, Howell, & McPherson, 2013) and therefore could be considered in this population. However, obtaining financial reimbursement for contingency management for substance use treatment remains a challenge (McPherson et al., 2018). There are currently no FDA-approved medications for treatment of methamphetamine use disorder. However, a number of pharmacotherapies have been tested and suggest benefits in some studies, and could be considered (Colfax et al., 2011; Schottenfeld et al., 2018; Elkashef et al., 2012; Jayaram-Lindstrom et al., 2008; Ling et al., 2014). It is worth noting that the majority (66%) of patients in our study with baseline methamphetamine use reported using 1–10 times in the past month and therefore may not have met criteria for having moderate to severe stimulant use disorder that would typically justify such interventions. Twelve-step meeting attendance has been associated with better outcomes for buprenorphine treated patients; however, there was no benefit associated with requiring meeting attendance as a condition of treatment (Monico et al., 2015).

Our results do provide some descriptive evidence that methamphetamine use decreases over time for persons who are treated for OUD with buprenorphine, suggesting benefits of that medication that extend beyond opioids. Another study of persons living with HIV treated with buprenorphine for OUD saw similar declines in cocaine use over time (Fiellin et al., 2011), and a recent study demonstrated decreased craving for methamphetamines with buprenorphine treatment (Salehi et al., 2015). Current guidelines for providing medications for OUD released by SAMHSA do not provide explicit instructions on how to treat patients with co-occurring non-opioid substance use disorders, yet do recommend monitoring for other substances (Substance Abuse and Mental Health Services Administration, 2018b). Our results reinforce the need to provide access to, and maintenance of, buprenorphine treatment for patients who also use methamphetamines, as their polydrug use may decline over time. It may also put into question the need for monitoring for non-opioid/non-buprenorphine substances early in treatment if such information should not prompt action from providers.

This study has a number of limitations. The study sample was comprised of three SAMHSA-funded buprenorphine treatment sites in

Washington State, and therefore, results may not be representative of patients treated in other geographic locations or settings. These data reflect the frequency of methamphetamine use among persons with treated OUD, and therefore should not be construed as representative of the prevalence of methamphetamine use among all patients with OUD. Furthermore, since a small number of participants (15%) were transfers from other buprenorphine programs, methamphetamine use might be under-reported. Our data are observational, and therefore, we cannot assume direct causality in associations. However, our analyses demonstrating a graded "dose response" do provide some suggestion of a causal relationship. Our sample size was fairly robust compared to prior published studies; however, we had limited power for sub-group analyses. Nonetheless, we performed analyses to test for interactions among a limited group of factors and did not detect any substantial interactions. Our data on methamphetamine use over time was restricted to individuals who were not missing 6-month follow-up data (517/799; 65%). Assuming more frequent missing data among methamphetamine users, this would bias our estimates to under-reporting rates of methamphetamine use over time. Our primary outcome of discharge could occur for a variety of reasons, although the most common reason was patient loss to follow-up (65%). Our study does not shed specific information on mechanisms leading to higher likelihood of loss to follow up and discharge among persons who use methamphetamines at baseline. We acknowledge that discharge could be related to a variety of unmeasured factors including those relating to provider judgment and clinic policies. However, we did adjust for site in our models to account for site differences and also adjusted for time period to account for possible changes in clinic policies. We purposefully chose not to adjust for other substance use, as the primary question of interest was whether the presence of baseline methamphetamine use in a patient initiating treatment with buprenorphine is a marker for future non-retention. Further research is needed to confirm our findings and perform additional analyses to understand possible mediators and causal mechanisms.

In summary, this study of persons receiving treatment with buprenorphine for OUD at 3 sites in Washington State found that self-reported use of methamphetamines at baseline was associated with 2-fold greater risk for non-retention in treatment over time. These results underscore the consequences of rising methamphetamine use in parts of the country and how it may impede efforts to engage and retain persons with OUD in buprenorphine treatment. Further research is needed to understand the reasons for non-retention and to develop and test interventions to improve retention among persons with opioid use disorders who use methamphetamines.

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