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# Withdrawal Signs and Symptoms Among Patients Positive for Fentanyl With and Without Xylazine

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**Background:** Xylazine is not approved for human use, yet it has emerged as a common adulterant of illicit fentanyl. It is currently unclear whether there is a withdrawal syndrome associated with xylazine and the potential impact of fentanyl coexposure.

**Methods:** A retrospective cohort study of patients with opioid use disorder admitted to an inpatient medically monitored withdrawal facility was performed. Patients positive for fentanyl were compared to patients copositive for fentanyl and xylazine. Outcomes were self-directed discharge and completion of treatment. Independent variables included Clinical Opioid Withdrawal Scale (COWS) scores, heart rate, and blood pressure. Associations between individuals with or without xylazine were measured.

**Results:** Among 71 patients admitted for opioid withdrawal management positive for fentanyl, 51.4% were copositive with xylazine. There was no difference detected in average COWS scores ($P = 0.12$–$0.78$) or average heart rate ($P = 0.33$–$0.80$) between groups. Xylazine copositive patients had higher average systolic blood pressure on days 1 (129.0 vs 123.0, $P = 0.01$) and 2 (127.9 vs 116.3, $P = 0.04$) although unclear if clinically meaningful. Individuals copositive for xylazine were less likely to complete treatment (43.2% vs 55.9%, $P = 0.23$) and more likely to have self-directed discharge (67.6% vs 44.1%; OR, 2.64; 95% CI, 1.0–6.9) although not statistically significant.

**Conclusions:** Among 71 patients admitted for medically monitored withdrawal, individuals who were copositive for xylazine at the time of admission had higher average blood pressure and were more likely to have a self-directed discharge. Additional research is needed to determine the impact of xylazine on withdrawal.

**Key Words:** opioid use disorder, medically monitored withdrawal, detox, xylazine, fentanyl

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Opioid use disorder (OUD) continues to be a major public health concern in the United States. Of the 106,699 overdose deaths reported by the Centers for Disease Control and Prevention (CDC) in 2021, 80,411 involved an opioid.[1] Provisional data for 2022 from the CDC show that 68% of the 107,081 overdose deaths involve synthetic opioids other than methadone.[2] One factor fueling the rise in overdoses is a diversification of opioids available in the illicit drug supply, from predominantly heroin to predominantly illicitly manufactured fentanyl, with other novel psychoactive substances introduced regularly, including xylazine.[3]

Assessment of withdrawal may be complicated by the presence of substances other than opioids. The recent, widespread incorporation of xylazine into the illicit drug supply has introduced a new, nonopioid cause of central nervous system depression. Xylazine is a central α-2 adrenergic agonist, which causes sedation, respiratory depression, bradycardia, hypotension, and, potentially, cardiac arrest.[4,5] The presence of substances in other drug classes (nonopioids) in the illicit opioid drug supply may result in a secondary withdrawal syndrome when exposed repeatedly. Therefore, providers may benefit from knowing what substances are present in the local illicit drug supply and local toxicology findings from biological specimens.

In this study, we investigate whether the presence of xylazine in the fentanyl drug supply impacts the clinical withdrawal syndrome. The purpose of this study is to investigate whether there is a "xylazine withdrawal syndrome" that should be assessed for and potentially treated separately when managing patients with fentanyl use and suspected or confirmed xylazine exposure. To that aim, clinical measures were compared between individuals presenting for inpatient withdrawal management who positive for fentanyl (control group) compared to those copositive for fentanyl and xylazine (cases). We hypothesized that objective measures of Clinical Opiate Withdrawal Scale (COWS), heart rate, blood pressure, and/or rates of self-directed discharge (SDD) and treatment completion will be different between cases and controls.

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## METHODS

### Setting and Study Design

This retrospective cohort study evaluated clinical specimens obtained from April through June 2023 among patients admitted for medically monitored withdrawal (MMW) (ASAM level, 3.7) at a single inpatient treatment facility in an urban area of East Tennessee. Study site (McNabb Center) IRB approval was obtained prior to commencing the study. The inclusion criterion for the study was a fentanyl-positive urine drug screen (UDS) (Fig. 1). Chart review was conducted to collect clinical measures that would help determine differences in withdrawal severity between the two groups by comparing COWS scores, vital signs, and rates of SDD and treatment completion. Sample size was determined based on a sample size calculation to be able to detect a difference in COWS of 5 points between cases and controls. STROBE guidelines were used for reporting.[6]

### Cases and Controls

Two groups were evaluated: (1) individuals with LC-MS/MS urine drug testing results positive for fentanyl (controls) and (2) individuals with LC-MS/MS urine drug testing results copositive for fentanyl and xylazine (cases).

### LC-MS/MS Testing

All urine drug screens positive for fentanyl were sent to Aegis Sciences Corporation in Nashville, TN, and underwent testing using liquid chromatography–tandem mass spectrometry (LC-MS/MS) to confirm the presence of fentanyl and to test for xylazine and other novel psychoactive substances. Testing included fentanyl, designer opioids (including fentanyl analogs and nitazene analogs), opiates, heroin, methadone, buprenorphine, benzodiazepines, designer benzodiazepines, synthetic cannabinoids, hallucinogens, synthetic stimulants, barbiturates, amphetamines (including methamphetamine), gabapentin, alcohol, nicotine, antipsychotics, and sedative hypnotics (see Supplementary Table 1, http://links.lww.com/JAM/A581) for all compounds tested). The level of detection for xylazine using this assay was 2 ng/mL.

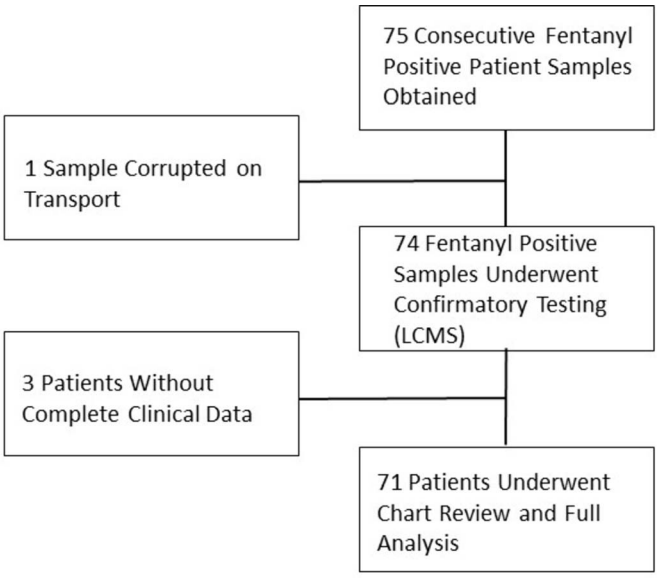


**FIGURE 1.** Sample inclusion flow chart.

### COWS Scoring and Vital Signs

The Clinical Opiate Withdrawal Scale was first published in 2003 by Wesson and Ling.[7] It is a clinician-administered instrument that includes 11 items designed to assess a patient's degree of withdrawal: resting heart rate, sweating, restlessness, pupil size, bone or joint aches, runny nose or tearing, gastrointestinal upset, tremor, yawning, anxiety or irritability, and gooseflesh skin.[7] It was later validated against the Clinical Institute Narcotic Assessment scale in 2009.[8]

COWS scoring and vital sign measurement were performed as a part of routine medical care. Nurses conducting COWS scoring were blinded to LC-MS/MS urine drug test results, including the presence or absence of xylazine, but were privy to the screening results done at the time of admission which included fentanyl. COWS scoring was performed by one of four nurses. COWS scoring was done at least once per day but up to three times per day for the first 3 days. The maximum COWS score for each day was abstracted to indicate maximal withdrawal symptoms each day.

Vital signs were measured during each COWS scoring. Maximum and average systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) for each day were calculated. All clinical data were abstracted from the patient's chart and linked with a unique identifier to the LC-MS/MS xylazine test results.

### Routine Clinical Care

Routine withdrawal management included a medical intake with measurement of vital signs and initial COWS scoring as well as obtaining an initial presumptive UDS followed by the appropriately timed initiation of buprenorphine for withdrawal management. Drug screening was performed using iScreen 14 panel drug screen cups.[9] All urine samples were obtained as a part routine clinical care during admission to an inpatient MMW setting. Urine samples are collected at the time of presentation for treatment (typically within the first 30 minutes of presenting). Patients admitted for opioid withdrawal management are started on a routine opioid withdrawal protocol that starts with COWS scoring and then follows one of two induction pathways: pathway 1: patients who present in moderate to severe withdrawal — when patients present with a COWS ≥18 without fentanyl use in the prior 24 hours, we initiate a rapid low-dose buprenorphine induction on the day of admission; day 1: 2 mg of buprenorphine SL every hour for 3 hours for a total dose of 6 mg buprenorphine; day 2: start maintenance, 16 mg daily; and pathway 2: alternatively, for patients who present for treatment and report recent opioid use with little or no current withdrawal symptoms — they undergo serial COWS scoring performed until clinically apparent opioid withdrawal or COWS ≥12 and then start a protocolized low-dose induction consisting of the following: day 1, 1 mg three times daily; day 2, 2 mg three times daily; and day 3, 4 mg twice daily and then either remain on buprenorphine

 

maintenance treatment (typically 16 mg daily) or taper off for induction onto opioid antagonist maintenance treatment.

## Outcome Measures

Primary and secondary outcome measures were selected to capture any differences in withdrawal trajectory between cases and controls: primary outcomes were COWS scores throughout treatment and vital sign measures (HR and BP). These were selected as primary outcomes because they were part of the routine medical care and documentation and were objective measures. COWS scores and HR/BP were compared to determine if the objective measures differed in the setting of xylazine (due to xylazine's known α adrenergic agonism). Rates of SDD or not completing MMW treatment was included as a secondary outcome to determine if the presence of xylazine on admission would reduce rates of treatment completion.

## Statistical Analysis

Descriptive statistics were used to summarize characteristics of study participants comparing cases and controls. To identify predictors of outcome variables, the analysis was restricted, to patients who had full information available in their clinical chart with no imputation conducted. *t* Tests, Wilcoxon-Mann-Whitney tests, $\chi^2$ tests, and Fisher's exact tests (where applicable) were used to assess the associations between patient groups with or without the presence of xylazine. Data were assessed to be normally distributed unless otherwise indicated. Two multivariable logistic regression models were developed, one with SDD as the outcome (SDD model) and the other with treatment completion as the outcome (completion model). The outcome measure for the completion model is not completing treatment for reading consistency with the SDD model. The following candidate variables were determined a priori to be potentially associated with remaining in treatment and were entered into the initial multivariable logistic regression models: COWS on admission, insurance, home, employment status, protocol utilized, and selected illicit substance presence based on LC-MS/MS testing. Candidate variables with a *P* value of <0.1 in the initial models were included in the final models as well as xylazine presence. Adjusted odds ratios and 95% confidence intervals (CIs) were calculated for the models. A 2-tailed *P* value <0.05 was considered statistically significant. SAS statistical software version 9.4 (SAS Institute Inc, Cary, NC) was used for all analyses.

# RESULTS

## Overall

Seventy-five consecutive presumptive fentanyl-positive urine samples were collected during routine clinical care over the course of 3 months at a single facility representing 68 unique individuals (7 patients had a repeat admission). One urine sample was compromised during transport to the testing laboratory, did not undergo LC-MS/MS testing, and was removed from analysis (chart 1). Of the 74 presumptive fentanyl-positive samples that

**TABLE 1.** Demographics

| | Overall | Xylazine Positive | Xylazine Negative | |
|---|---|---|---|---|
| **Variable** | **N = 71** | **n = 37** | **n = 34** | ***P*** |
| Demographics | | | | |
| Sex, male | 40 (56.3%) | 19 (51.3%) | 20 (58.8%) | 0.53 |
| Age (mean), y | 37.28 | 37.24 | 37.44 | 0.92 |
| Race | | | | 0.28 |
| White | 65 (91.5%) | 36 (97.3%) | 29 (85.3%) | |
| Black | 2 (2.8%) | | 2 (5.9%) | |
| Unknown | 4 (5.6%) | 1 (2.7%) | 3 (8.8%) | |
| Withdrawal protocol | | | | 0.43 |
| Opioid Withdrawal Protocol | 58 (81.6%) | 30 (81.1%) | 28 (82.3%) | |
| Combined Opioid and Benzodiazepine/Alcohol Protocol | 9 (12.7%) | 6 (16.2%) | 3 (8.8%) | |
| Other | 4 (5.6%) | 1 (2.7%) | 3 (8.8%) | |
| Induction pathway | | | | 0.08 |
| One | 10 (14.1%) | 2 (5.4%) | 8 (23.5%) | |
| Two | 44 (62.0%) | 26 (70.3%) | 18 (53.0%) | |
| N/A | 17 (24.0%) | 9 (24.3%) | 8 (23.5%) | |
| Insurance | | | | 0.59 |
| Uninsured | 47 (66.2%) | 23 (62.2%) | 24 (70.6%) | |
| Medicare and/or Medicaid | 22 (30.9%) | 12 (32.4%) | 10 (29.4%) | |
| Other | 2 (2.8%) | 2 (5.4%) | 0 (0%) | |
| Employment status | | | | 0.9 |
| Unemployed | 56 (78.9%) | 30 (81.1%) | 26 (76.5%) | |
| Employed | 12 (16.9%) | 6 (16.2%) | 6 (17.6%) | |
| Other | 3 (4.2%) | 1 (2.7%) | 2 (5.9%) | |
| Housing status | | | | 0.96 |
| Unhoused | 25 (35.2%) | 14 (37.84%) | 11 (32.3%) | |
| Recovery housing | 4 (5.6%) | 2 (5.4%) | 2 (5.9%) | |
| Stable | 39 (54.9%) | 20 (54.1%) | 19 (55.9%) | |
| Unknown | 3 (4.2) | 1 (2.7%) | 2 (5.9%) | |

Comparison of demographic data between fentanyl positive patients with (n = 37) and without (n = 34) xylazine. The two groups were similar with no statistically significant differences in race, withdrawal protocol, insurance status, employment status, or housing status.

underwent LC-MS/MS testing, all were positive for fentanyl, and 51.4% were copositive for xylazine. Only 6.8% samples were positive for fentanyl without any other substances. The majority (66.2%) of samples were positive for fentanyl and methamphetamine. In addition, 44.6% were positive for fentanyl with "designer opioids," which include nitazene analogs and fentanyl analogs.

Of the 74 patient samples that underwent LC-MS/MS testing, clinical data were able to be abstracted from the charts of 71 (95.9%). Of the 3 charts that were excluded, one patient did not require MMW based on the remote time of their last use of fentanyl and two patients self-discharged prior to completing the admission process. Of the 71 samples that underwent chart review, 34 were fentanyl positive (controls), and 37 were fentanyl and xylazine copositive (cases). Demographic characteristics between the cases and controls were similar (Table 1). Overall, the sample was majority male (56.3%), White (92.9%), uninsured (67.6%), and unemployed (78.9%). In addition, 36.6% of the sample were unhoused.

## COWS Scoring, Treatment Induction Pathways, and Vital Signs

On admission, the fentanyl positive controls had a higher COWS than copositive cases (7.0 vs 5.0), although the difference did not achieve statistical significance ($P$ = 0.12). Throughout treatment, COWS scores between the two groups were not statistically different (Table 2). Induction pathway 2 was the most common pathway initiated overall. Pathway 1 (rapid low dose induction) was more common among individuals positive for fentanyl only (23.5% vs 5.4%), although this was not statistically significant. The maximum mean COWS score for each group was lowest on day of admission (day 0) and peaked at day 1 for the control group (8.52) and peaked at day 2 for the xylazine-positive group (8.31). The maximum SBP and DBP were statistically different between groups at points during treatment (Table 2). The maximum SBP was higher in the xylazine-positive group on day 1 (129.0 vs 123.0, $P$ = 0.01) and day 2 (127.9 vs 116.3, $P$ = 0.04). The maximum DBP was higher in the xylazine-positive group on day 1 (86.0 vs 78.0, $P$ = 0.03) and day 2 (86.9 vs 77.8, $P$ = 0.03).

## Completion of Treatment and Self-Directed Discharge

In bivariate group analysis (Table 3), xylazine copositive cases were found to self-discharge at 2.6 times the rate of controls (OR, 2.64; 95% CI, 1.0–6.9), which approached statistical significance ($P$ = 0.05).

In the SDD final multivariable model (Table 4), in which xylazine was included due to clinical interest, presence of buprenorphine (aOR, 3.46; 95% CI, 1.01–13.33) and ethyl glucuronide (EtG) or ethyl sulfate (ES) (aOR, 4.32; 95% CI, 1.04–21.61) on initial urine drug screen were significantly associated with experiencing a SDD. Cocaine (aOR, 0.18; 95% CI, 0.04–0.69) and designer opioids (aOR, 0.21; 95% CI, 0.04–0.85) presence were associated with reduced odds of experiencing a SDD. Other copositive substances were not statistically significant.

In the final multivariable Completion model (Table 4), in which xylazine was included due to clinical interest, presence of ethyl glucuronide (EtG) or ethyl sulfate (ES) (aOR, 5.74; 95% CI, 1.38–32.67) on initial urine drug screen was significantly associated with decreased treatment completion. Cocaine (aOR, 0.27; 95% CI, 0.07–0.86) and heroin (aOR, 0.20; 95% CI, 0.04–1.12) presence were associated with increased likelihood of completing treatment with heroin presence approaching, but not reaching, statistical significance. Other copositive substances were not statistically significant.

## DISCUSSION

This exploratory study aimed to evaluate whether, among patients using fentanyl, the clinical withdrawal syndrome was altered due to the presence of xylazine. Despite anecdotal reports of a xylazine withdrawal syndrome,[10] a clearly defined xylazine withdrawal syndrome has not been described in the literature. To our knowledge, this is the first study comparing withdrawal syndromes between patients positive for fentanyl with and without xylazine. In this small cohort, we found only minimal detectable differences in vital sign measures, which were abstracted to explore if there are signals in a patient's

**TABLE 2.** COWS and Vitals

| Observations | Xylazine Positive | Xylazine Negative | *P* |
|---|---|---|---|
| COWS | | | 0.23 |
| Mean admission (n) | 5.0 (n = 34) | 7.0 (n = 27) | 0.12 |
| Mean day 1 maximum (n) | 8.2 (n = 35) | 8.5 (n = 27) | 0.78 |
| Mean day 2 maximum (n) | 8.3 (n = 29) | 6.9 (n = 22) | 0.12 |
| Mean day 3 maximum (n) | 4.5 (n = 15) | 5.4 (n = 8) | 0.45 |
| Vitals | | | |
| Day 1 | | | |
| Systolic Blood Pressure | | | |
| Median, daily max (n) | 129.0 (n = 35) | 123.0 (n = 27) | 0.02 |
| Median, daily average (n) | 122.0 (n = 35) | 113.1 (n = 27) | 0.04 |
| Diastolic BP | | | |
| Median, daily max (n) | 86.0 (n = 35) | 78.0 (n = 27) | 0.03 |
| Mean, daily min (n) | 72.6 (n = 35) | 69.0 (n = 27) | 0.29 |
| Mean, daily average (n) | 79.9 (n = 35) | 74.5 (n = 27) | 0.09 |
| HR | | | |
| Mean, daily max (n) | 89.4 (n = 35) | 84.4 (n = 27) | 0.16 |
| Mean, daily average (n) | 80.7 (n = 35) | 79.1 (n = 27) | 0.60 |
| Day 2 | | | |
| Systolic BP | | | |
| Mean, daily max (n) | 127.9 (n = 29) | 116.3 (n = 23) | 0.04 |
| Mean, daily average (n) | 119.7 (n = 29) | 110.2 (n = 23) | 0.04 |
| Diastolic BP | | | |
| Mean, daily max (n) | 86.9 (n = 29) | 77.8 (n = 23) | 0.03 |
| Median, daily min (n) | 75.0 (n = 29) | 71.0 (n = 23) | 0.15 |
| Median, daily average (n) | 78.0 (n = 29) | 72.0 (n = 23) | 0.06 |
| HR | | | |
| Mean, daily max (n) | 91.6 (n = 29) | 86.3 (n = 23) | 0.19 |
| Mean, daily average (n) | 83.9 (n = 29) | 80.3 (n = 23) | 0.33 |
| Day 3 | | | |
| Systolic BP | | | |
| Mean, daily max (n) | 113.4 (n = 19) | 118.7 (n = 9) | 0.50 |
| Mean, daily average (n) | 111.2 (n = 19) | 111.8 (n = 9) | 0.92 |
| Diastolic BP | | | |
| Mean, daily max (n) | 79.2 (n = 19) | 77.9 (n = 9) | 0.84 |
| Mean, daily min (n) | 75.0 (n = 19) | 60.4 (n = 9) | 0.01 |
| Mean, daily average (n) | 77.0 (n = 19) | 67.9 (n = 9) | 0.10 |
| HR | | | |
| Mean, daily max (n) | 82.6 (n = 19) | 84.0 (n = 9) | 0.78 |
| Mean, daily average (n) | 79.1 (n = 19) | 78.0 (n = 9) | 0.80 |

Comparison of COWS scores and vital signs between fentanyl positive patients with (n = 37) and without (n = 34) xylazine. COWS scores between the two groups were not significantly different on the day of admission or over the subsequent 3 days. The mean systolic BP was significantly higher ($P$ < 0.05) in the xylazine positive group on day 1 and day 2, and the diastolic pressure was significantly higher on days 2 and 3.

**TABLE 3.** Completion of Treatment

| Outcomes | Overall | Xylazine Positive | Xylazine Negative | *P* |
|---|---|---|---|---|
| Completed MMW | | | | 0.23 |
| Yes | 35 (49.3%) | 16 (43.2%) | 19 (55.9%) | |
| No | 36 (50.7%) | 21 (56.8%) | 15 (44.1%) | |
| SDD | | | | 0.05 |
| Yes | 40 (56.3%) | 25 (67.6%) | 15 (44.1%) | |
| No | 31 (43.7%) | 12 (32.4%) | 19 (55.9%) | |

Comparison of treatment completion and SDD rates between fentanyl positive patients with (n = 37) and without (n = 34) xylazine. Xylazine-positive patients were significantly more likely to SDD (OR, 2.64; 95% CI, 1.0–6.9).

CI indicates confidence interval; OR, odds ratio.

clinical presentation that may indicate xylazine presence when laboratory testing is not readily available.

Opioid use is evolving, and in this population studied as well as others,[11] individuals admitted for opioid withdrawal are more likely to be using multiple substances rather than just opioids. In addition, there is a striking prevalence of xylazine, which is not routinely tested for. In this study, xylazine was present in over half (51.4%) of the patients admitted for MMW. The prior year data (2022) from the local (Knox County) medical examiner reported 10% xylazine prevalence in overdose deaths.[12] The current data showing over 50% prevalence in active opioid users in East Tennessee suggest that the prevalence in overdose deaths in this region will also be dramatically higher in the coming year's analysis. This is evidence of the rapid spread of xylazine in the illicit drug supply in Tennessee.

We show that, in addition to skin lesions and severe sedation, compounding the effects of fentanyl's respiratory depression, xylazine exposure may alter opioid withdrawal syndrome, although this was not able to be determined with confidence in this preliminary study. In this single-site study, SDD rates were higher in those copositive with xylazine, but this difference did not achieve statistical significance. These preliminary findings do not clearly show a xylazine withdrawal syndrome and is unable to make any conclusions about ideal clinical management of patients copositive for xylazine. However, these preliminary findings support the need for additional research into this important topic. Larger samples are needed to be able to capture modest differences in vital sign measures and COWS scores, among other measures. Additionally, evaluating COWS subcategory scores rather than the aggregate total score may better identify if any specific withdrawal symptoms differ between groups. Lastly, fentanyl and xylazine quantification at time of admission and a more specific determination of time since last illicit substance use prior to initiation of opioid withdrawal treatment could be helpful in future research.

**TABLE 4.** Multivariate Models

| Patient Characteristics at Time of Study Entry | Adjusted Odds Ratio (95% CI) | *P* |
|---|---|---|
| SDD model | | |
| Xylazine presence | 1.22 (0.32–5.05) | 0.77 |
| Buprenorphine presence | 3.46 (1.01–13.33) | 0.05 |
| EtG or ES presence | 4.32 (1.04–21.61) | 0.05 |
| Cocaine presence | 0.18 (0.04–0.69) | 0.01 |
| Designer opioids presence | 0.21 (0.04–0.85) | 0.03 |
| Completion model | | |
| Xylazine presence | 0.93 (0.32–2.78) | 0.89 |
| EtG or ES presence | 5.74 (1.38–32.67) | 0.02 |
| Cocaine presence | 0.27 (0.07–0.86) | 0.03 |
| Heroin presence | 0.20 (0.02–1.12) | 0.09 |

Multivariate models of treatment completion and SDD rates between fentanyl positive patients with (n = 37) and without (n = 34) xylazine. In the SDD model, buprenorphine and EtG or ES presence increased the odds of self-directed discharge during treatment, whereas cocaine and designer opioids in the admission sample decreased the odds of self-directed discharge. In the completion model, EtG or ES presence increased the odds of unsuccessful treatment, whereas cocaine and heroin increased the odds of completing treatment.

CI indicates confidence interval; EtG, ethyl glucuronide; ES, ethyl sulfate.

## Study Limitations

This was a retrospective cohort study and so only identify correlations. As a convenience sample secondary analysis, this study lacks the power to detect small differences between groups, which may have been clinically significant. All results were reported irrespective of significance. The population reported in this study is disproportionately low socioeconomic status, with many being unhoused and uninsured, which may lead to more severe or untreated disease and therefore limits generalizability. This study was conducted at a single clinical site in a single city with a relatively small sample size, which may also limit generalizability. Also, study authors were not blinded to xylazine positivity when analyzing data.

Furthermore, although testing to identify the presence of xylazine in urine was performed via LC-MS/MS, it is possible that previous use or exposure beyond the period of detection of the validated assay could have occurred. At this time, there is limited information regarding metabolism and elimination of xylazine in humans. Thus, selection of analytical markers to identify the presence of xylazine in biological specimens, as well as determination of an appropriate threshold for testing during method validation, was completed using available information.

# CONCLUSIONS

These exploratory findings suggest that xylazine may be associated with higher SBP during early abstinence; however, the absolute increase in SBP was not clinically significant. Xylazine presence was correlated with increased rates of SDD. It is important for future studies to more rigorously study the effects of xylazine cessation and to better characterize any "xylazine withdrawal syndrome" in order to improve treatment for patients exposed to xylazine.

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