



## Xylazine awareness, desire, use and exposure: Preliminary findings from the Rhode Island community-based drug checking cohort study

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### HIGHLIGHTS

- Xylazine was an unexpected and unwanted substance in Rhode Island.
- However, xylazine was frequently detected in the fentanyl supply using drug checking.
- Drug checking services could improve awareness of xylazine's presence in illicit fentanyl supplies.

### ARTICLE INFO

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### ABSTRACT

**Background:** Xylazine is an  $\alpha 2$  adrenergic receptor agonist and a veterinary sedative that can cause severe health complications yet interventions to detect and treat human exposure remain underdeveloped. Community-based drug checking services (DCS) involve the testing of small amounts of drugs to increase community knowledge of unregulated supplies and decrease harms. This study characterized xylazine awareness, desire, use and exposure among people who use drugs (PWUD) in Rhode Island, US.

**Methods:** We analyzed data from an ongoing PWUD cohort study. In 2023, 125 PWUD were enrolled and surveyed. Using point-of-care Fourier Transform infrared spectroscopy (FTIR-S), we tested a drug sample from each participant onsite and confirmed the results offsite at a laboratory. Results were conveyed in real-time, along with harm reduction education, referrals to resources and care.

**Results:** Virtually all participants (99.2 %) wanted to avoid xylazine exposure. Half (51.2 %) knew what xylazine was, and a quarter (26.1 %) suspected previous exposure. Xylazine exposure was primarily surmised through sedating (45.2 %) and ulcerative (29.0 %) effects. Only 8.8 % of participants submitted a sample that they expected to contain xylazine. Xylazine was detected in 14.5 % of samples using FTIR-S and in 21.4 % of samples using a dual laboratory approach of gas chromatography mass spectrometry (GC-MS) and liquid chromatography quadrupole-time-of-flight mass spectrometry (LC-QTOF-MS). Participants thought that these xylazine-positive samples were fentanyl (78.3 %), heroin (13.0 %), or Percocet® (8.7 %).

**Conclusion:** Implementing point-of-care DCS at harm reduction organizations could be useful in rapidly increasing xylazine awareness and engaging at-risk individuals in prevention, harm reduction, treatment, and rapid care for xylazine-related wounds.

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## 1. Introduction

The opioid epidemic costs the US economy over one trillion dollars annually (Joint Economic Committee, 2022). Opioids, including illicit fentanyl, heroin, and counterfeit opioid pills, accounted for three in four US overdose deaths in 2022 (Spencer et al., 2024). Xylazine is a veterinary sedative and an  $\alpha$ 2 adrenergic receptor agonist (Gupta et al., 2023; Kariisa et al., 2021, 2023). Xylazine can cause severe clinical effects including central nervous system depression (i.e., ranging from long periods of sedation to unconsciousness) and necrotizing skin/soft tissue infections (Ruiz-Colón et al., 2014; Alexander et al., 2022). Xylazine-associated overdoses may require more extensive medical care than other overdoses (Zagorski et al., 2023). Additionally, xylazine-induced skin lesions occur both at injection and peripheral sites, and appear even if the drug is smoked or snorted. These wounds can take several weeks to heal and lead to amputations (Bishnoi et al., 2023). Between 2018 and 2021, xylazine involvement in unintentional overdoses increased by 1238 % (Gupta et al., 2023). Though data are limited, case reports and data are emerging on xylazine-associated morbidity and mortality (Kariisa et al., 2021, 2023; Johnson et al., 2021).

Fentanyl test strip (FTS) programs allow people to test their drugs for the presence of fentanyl however there is a need to develop similar tools for xylazine detection. Comprehensive drug checking services (DCS) involve the consensual collection and testing of small amounts of drugs including xylazine using sophisticated instruments such as spectroscopy or spectrometry (Maghsoudi et al., 2022; Palamar et al., 2020; Harper et al., 2017). Additionally, DCS can promote harm reduction behaviors and linkages to care among people who use drugs (PWUD), including fentanyl and stimulants, and help drug surveillance efforts (Park et al., 2021; Peiper et al., 2019; Bailey et al., 2023; Collins et al., 2023; Russell, 2023). There are more than 16 DCS in North America that have tested 49,786 samples (Park et al., 2023). However, unlike fentanyl, the study of xylazine detection, prevention, and treatment is relatively new. Accordingly, we sought to understand xylazine awareness, use, and exposure among a preliminary cohort of PWUD from RI.

## 2. Methods

### 2.1. Setting

The Community Use and Testing Study (CUTS) is an 18-month prospective cohort study of 600 Rhode Island (RI) participants that combines point-of-care DCS with biannual surveys. Enrollment of the first 125 participants occurred through community outreach and word-of-mouth between February and August 2023; recruitment locations included harm reduction organizations, housing services, and public spaces where overdoses occur. Eligible participants underwent informed consent. The interviewer-administered baseline survey (Qualtrics, Provo, UT) took 45–60 minutes. Participants were compensated \$40. The study was approved by the Lifespan Institutional Review Board and developed in consultation with the COBRE on Opioid and Overdose Community Advisory Board (Green et al., 2021a).

### 2.2. Participants

Eligible participants were  $\geq 18$  years; spoke and understood English; used an illicit drug in the past 30 days; RI residents; and provided  $\geq 1$  eligible sample for testing. Eligible samples included drug packaging (i.e., baggie, wax fold) containing remnant drug in powder or pill form; or a once-used cooker, cotton, or straw, and excluded storage containers, syringes, pipes, and used crack stems due to potential signal interference (e.g., contamination from reuse).

### 2.3. Survey measures

The survey contained previously-developed measures (Hughto et al., 2023; Green et al., 2021b; Carroll et al., 2020) and included: (1) socio-demographics (e.g., age, sex, gender identity, race/ethnicity, primary language, education, employment, housing); (2) medical co-morbidities; (3) overdose; (4) drug treatment; (5) FTS use; (6) drug use and social network characteristics; and (7) xylazine awareness, concerns, and expectations, among other measures.

### 2.4. Drug checking

At least one remnant drug sample was collected from each participant and tested by trained staff in community spaces using Fourier Transform infrared spectroscopy (FTIR-S) and FTS, then sent for laboratory-based confirmatory testing. At the time of enrollment, FTS were available through local service organizations but xylazine test strips/kits were not being distributed in RI.

Our DCS protocols were based on two North American DCS (McCrae et al., 2022; MADDs, 2022). The entire process took 15–20 minutes. First, samples were scraped onto a sterilized scanning plate and scanned via the FTIR-S. Staff cleaned the FTIR-S between each tested sample using isopropyl alcohol. Next, they transferred the sample into a disposable 1 oz cup, and diluted as described below for testing with FTS. The remaining sample in its original packaging was secured in a mylar envelope and transferred to a laboratory. Any untested samples and packaging were discarded using a drug-neutralizing disposal bag.

### 2.5. Immunoassay-based fentanyl test strips (FTS)

Staff dissolved each sample with 5 mL of sterile water. For samples suspected to be methamphetamine (crystal or powder) or Adderall, the solution was further diluted to 30 mL of water due to concerns of false positives, and testing was repeated. The Rapid Response FTS (BTNX, Pickering, Ontario) was placed into the solution for ten seconds and read after 5 minutes.

### 2.6. Fourier-transform infrared spectroscopy (FTIR-S)

FTIR-S (Bruker Alpha Inc., Billerica, Massachusetts) was previously validated for use (Ti et al., 2020; Green et al., 2020). FTIR-S can rapidly determine multiple active and inactive components and their relative proportion to one another. We adapted the testing protocol outlined in a program in British Columbia and the technician accessed trainings and technical support from the MADDs team (McCrae and Stunden, 2022; MADDs 2024).

Trained technicians examined generated spectra and compared data to known spectra in library databases (e.g., Bruker pharmaceutical libraries, the Science Working Group for the Analysis of Seized Drugs library, the British Columbia Centre on Substance Use library, and the TICTAC library). A spectrum for xylazine is contained in the latter three libraries.

Staff explained limitations of FTIR-S and FTS before conveying results to the participant. These limitations included: 1) drug checking does not provide a guarantee of safety; 2) drug checking does not provide evidence of purity or dose; 3) people respond differently to drugs and drug checking does not provide personalized information about how you or anyone else will respond; 4) the information you receive is not an endorsement of a drug or of how a drug is used and is provided for the purpose of reducing harm; and 5) the FTIR-S and FTS may occasionally miss fentanyl, fentanyl analogues, or other dangerous substances such as xylazine. Participants also received the limitations of the results and disclaimers in writing during the informed consent process.

Preliminary results included the chemical components detected, including active and inactive cuts. When these results were verbally communicated to participants at the time of testing, the team also

provided harm reduction education and information on the services available, including referrals to local medical and harm reduction organizations (e.g., wound care guidance and kits), further information from regional DCS (e.g., StreetCheck bulletins), and reinforcement on the use of extant harm reduction tools (e.g., how to use FTS).

### 2.7. Laboratory testing

The first sample collected per participant was transported to the Center for Forensic Science Research and Education (CFSRE, Horsham, PA) for confirmatory testing. Testing was conducted using combined qualitative and quantitative methods (when mass was sufficient). The laboratory used an Agilent Technologies (Santa Clara, CA) gas chromatograph mass spectrometer (GC-MS) for qualitative and quantitative analysis, and a SCIEX (Framingham, MA) liquid chromatograph quadrupole time-of-flight mass spectrometer (LC-QTOF-MS) for qualitative analysis. Samples were aliquoted, weighed (quantitative only), and prepared by a basic liquid-liquid extraction for GC-MS analysis, and subsequent mobile phase dilution for LC-QTOF-MS analysis. Datafiles were acquired in a non-targeted fashion to detect the presence of all relevant components with processing against an extensive in-house library database containing more than 1200 targets. Only results confirmable through verification concurrent with standard reference materials were reported.

Qualitative results were reported in parts (e.g., fentanyl 1p, xylazine 5p, 4-ANPP 0.1p), where the primary drug was set to 1p and all other components were determined based on peak area ratio to the primary drug. Quantitative results were reported in percent composition (e.g., fentanyl 10 %, xylazine 50 %, 4-ANPP 1 %) compared to the total mass taken for analysis (e.g., fentanyl 10 % = 0.3 mg fentanyl of 3 mg total weight). Quantitation was performed via an external calibration model with internal standard comparing instrument response of the samples to known responses generated by analysis of standard reference materials at increasing increments. Both assays were validated prior to use and quality controlled within batch.

### 2.8. Sample-based questions and communication of confirmatory results

StreetCheck is an open-source platform designed to standardize and support the expansion of DCS created by MADDs in collaboration with community partners (Green et al., 2022). It is an efficient, secure, and flexible environment for collecting and managing DCS data. The platform allows for follow-up questions and relies upon anonymous numeric and QR sample codes for tracking sample entry, analysis, and reporting. StreetCheck also contains detailed and standardized pharmacological and medical information on detected chemicals that is relayed back to participants.

Staff entered the following data into StreetCheck: date of collection, a photo of the substance, suspected substance(s), whether it was consumed and, if so, any reactions. They also conversed with each participant to obtain valuable information about their experience with the drug. This information was crucial to provide context to the sample analysis and offered more personalized and in-depth messaging when communicating the results. The public-facing website (streetcheck.org) organized sample-level data by sample ID and locality, and provided aggregate trends. Each participant received a unique anonymous weblink for each sample. Participants could also request their results from staff during visits.

### 2.9. Data analysis

Analysis was accomplished by merging the baseline survey and DCS data using a common sample ID. Using Stata/MP Version 16 (StataCorp, TX), descriptive characteristics were calculated. Cohen's Kappa coefficient was used to measure the pairwise concordance between various detection methods (expected vs. FTIR vs. laboratory). The Kappa

coefficient ranges from  $-1$  to  $+1$  and a score of  $0.4$ – $0.59$  indicates weak agreement,  $0.6$ – $0.79$  indicates moderate positive agreement, and  $>0.8$  indicates strong agreement between the variables (McHugh, 2012).

## 3. Results

Of the preliminary cohort ( $N=125$ ),  $55.2\%$  were male, and median age was 40 years. The cohort was racially and ethnically diverse (Table 1). Most completed high school ( $64.0\%$ ). Only  $22.4\%$  had stable housing. Most reported using cocaine ( $92.0\%$ ), fentanyl ( $67.2\%$ ), heroin ( $65.6\%$ ), and/or methamphetamine ( $46.4\%$ ) in the past 6 months. Half ( $53.9\%$ ) had a history of overdose and survived a median of 4 overdoses. Most participants carried naloxone ( $81.2\%$ ); some reported current receipt of methadone ( $28.8\%$ ) or buprenorphine ( $9.6\%$ ) treatment.

A variety of samples were submitted for testing; most samples were expected to contain crack cocaine ( $52.0\%$ ) or fentanyl ( $32.0\%$ ) with few submitting what they expected to be xylazine ( $8.8\%$ ), heroin ( $7.2\%$ ) and methamphetamine ( $4.8\%$ ). Participants rarely submitted non-medical prescription opioids e.g., Percocet® ( $1.6\%$ ) and powder cocaine ( $1.6\%$ ). Most ( $70.4\%$ ) had used the drug prior to submission.

Xylazine desire, knowledge, and experiences varied substantially (Table 2). Half ( $51.2\%$ ) knew what xylazine was and less than  $1\%$  wanted xylazine. A quarter ( $26.1\%$ ) suspected previous exposure. In contrast,  $52.9\%$  of the sample wanted fentanyl (data not shown). At baseline, xylazine exposure was primarily deduced from use experience (e.g., through its sedating ( $45.2\%$ ) and ulcerative ( $29.0\%$ ) effects) rather than known by individuals prior to its use (e.g., drug testing kits, DCS, urine testing, communications from their supplier).

While only  $8.8\%$  of participants submitted a sample purportedly containing xylazine, it was detected in  $14.5\%$  of samples using FTIR-S and in  $21.4\%$  of samples using laboratory methods (Table 2 and

**Table 1**

Baseline demographic, drug use and service use characteristics of the Community Use and Testing Study (CUTS) Cohort, Rhode Island ( $N=125$ ).

Variable	n	(%)
Gender		
Male	69	55.2
Female	53	42.4
Gender non-conforming or Non-binary	3	2.4
Age		
18–34	26	20.8
35–44	47	37.6
45–54	24	19.2
55–64	16	12.8
65+	12	9.6
Race		
Non-Hispanic White	61	48.8
Non-Hispanic Black	12	9.6
Hispanic or Latino/a	31	24.8
Other race	21	16.8
Completed high school	80	64.0
Stably housed, current	28	22.4
Drugs used in past 6 months (self-report)		
Fentanyl	84	67.2
Heroin	82	65.6
Cocaine	115	92.0
Crack	115	92.0
Methamphetamine	58	46.4
Ecstasy	2	1.6
Overdose		
Ever	62	53.9
Median no. of times (range)	4	(1–51)
Service use		
Naloxone, current	99	81.2
Methadone, current	36	28.8
Buprenorphine, current	12	9.6
FTS, past year (n=125)	85	68.0
Other DCS (n=125)	16	12.8

**Table 2**  
Xylazine desire, knowledge and experiences among the Community Use and Testing Study (CUTS) cohort, Rhode Island (N=125).

Variable	Total		Xylazine detected by laboratory		p
	n/N	column %	No column %	Yes column %	
Aware of xylazine	62/121	51.2	46.6	68.0	0.059
Wanted xylazine	1/121	<1.0	–	–	–
Reported having a xylazine exposure in past 6 months	31/119	26.1	18.6	56.0	<0.001
If yes, detection method (select all that apply)					
Very sedating effects	14/31	45.2	37.5	57.1	0.282
Ulcers	9/31	29.0	–	–	–
Worse drug withdrawal than usual, did not reduce dope withdrawal	4/31	12.9	–	–	–
Other side effects (endocarditis, diarrhea, cramps, irritation)	2/31	6.5	–	–	–
Feel, color, look, taste, smell	4/31	12.9	–	–	–
Told by dealer or friend	3/31	9.7	–	–	–
DCS tested it	3/31	9.7	–	–	–
Drug sample submitted and tested at baseline					
Expected to contain xylazine by submitter (self-report)	11/125	8.8	2.2	36.0	<0.001
Xylazine detected using point-of-care FTIR-S	18/124	14.5	1.1	68.0	<0.001
Xylazine detected using laboratory-based mass spectrometry	25/125	21.4			

FTIR-S = Fourier-Transform Infrared Spectroscopy  
– omitted due to small cell size

Fig. 1). Eight samples were of sufficient size for xylazine quantification and contained 0.4 %-11.8 % xylazine (Table 3). Xylazine was detected among a range of other active substances, at both minor and trace levels. Xylazine was not detected in any samples without the presence of fentanyl. Xylazine-positive samples (n=23) were marketed to participants as fentanyl (78.3 %), heroin (13.0 %), or oxycodone/Percoct® (8.7 %).

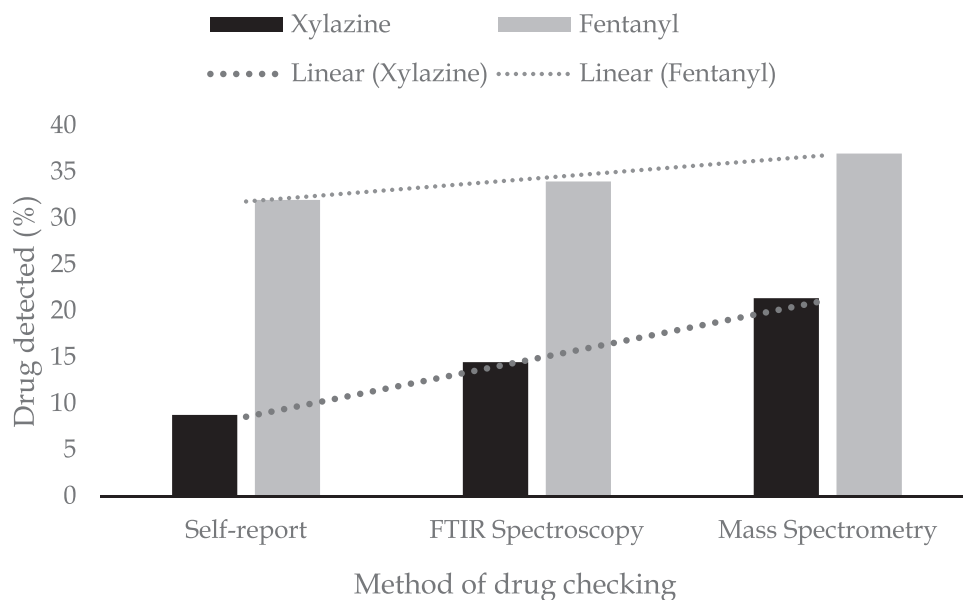
Fentanyl detection was more consistent across the three methods (Fig. 1). Whereas 32.0 % expected that their sample contained fentanyl, 33.9 % and 36.8 % of samples tested positive for fentanyl using FTIR-S and laboratory testing, respectively.

Measure of concordance between expected (i.e., self-reported) and laboratory-confirmed xylazine using Kappa statistic was 0.42 (Z=5.14; p < 0.001). For fentanyl, it rose to 0.85 (Z=9.24, p < 0.001). The concordance between expected and FTIR-detected xylazine was 0.57 (Z=6.64, p < 0.001) and for fentanyl it rose to 0.78 (Z=8.71, p < 0.001); the concordance between FTIR-S and laboratory-confirmed xylazine was 0.74 (Z=8.18, p < 0.001) and for fentanyl it rose to 0.96 (Z=10.38, p < 0.001). However, in comparing the full range of other active drugs detected by the FTIR-S and laboratory to the submitter’s expectations of the sample’s contents (Table 3), there was substantial variability and clear gaps in knowledge.

**4. Discussion**

This study implemented and analyzed preliminary findings on xylazine awareness, desire, intentional use, and exposure from a prospective community-based drug checking cohort study. We found xylazine presence to be largely unexpected, exclusively in samples expected to be fentanyl, and most likely detected through laboratory testing. Our findings extend previous literature that has detected xylazine in drug supplies and documented its clinical effects (Kariisa et al., 2021, 2023; Ruiz-Colón et al., 2014; Alexander et al., 2022; Bishnoi et al., 2023; Johnson et al., 2021; Zagorski et al., 2023).

The prevalence of xylazine varies across geographies. A DCS in Philadelphia employing the same laboratory to generate confirmatory results recently detected xylazine in over 90 % of fentanyl/heroin samples with concentrations ranging from 5 % to 70 % (CFSRE, 2022). In Rhode Island, data suggest that xylazine has entered but not inundated the opioid supply (Collins et al., 2023). Xylazine awareness was



**Fig. 1.** Xylazine and fentanyl detection using multiple methods among the first 125 Community Use and Testing Study (CUTS) cohort drug samples, Rhode Island. Note: The slope of the linear trend visually represents the differences between self-reported and laboratory-confirmed xylazine detection (black line) and fentanyl detection (grey line). Statistical agreement between self-reported and actual xylazine detection was weak (kappa<0.6). In contrast, the agreement observed between self-reported and actual fentanyl detection was strong (kappa >0.8).

**Table 3**

Unique samples submitted by Community Use and Testing Study (CUTS) participants that tested positive for xylazine in laboratory testing (N=25).

Sample sold as...	Sample expected to contain...	Psychoactive drugs detected using point-of-care FTIR	Psychoactive drugs detected using Laboratory-based mass spectrometry*	Percentage of Xylazine detected <sup>^</sup>
Fentanyl	Fentanyl, Methamphetamine	Fentanyl	Acetylfentanyl, Fentanyl, 4-ANPP, <b>Xylazine</b>	-
Heroin	Heroin, Fentanyl, <b>Xylazine</b>	Fentanyl, Caffeine, <b>Xylazine</b>	Fentanyl, Caffeine, 4-ANPP, Phenethyl-4-ANPP, <b>Xylazine</b>	-
M30 Pill (Percocet, Perc30)	Fentanyl	Sertraline	Sertraline, Fentanyl, <b>Xylazine</b>	0.4 %
M30 Pill (Percocet, Perc30)	Fentanyl	Sertraline	Sertraline, Fentanyl, <b>Xylazine</b>	-
Unknown	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b>	Acetylfentanyl, Fentanyl, 4-ANPP, <b>Xylazine</b> , Ethyl-4-ANPP, Phenethyl-4-ANPP	-
Fentanyl	Fentanyl	Fentanyl, <b>Xylazine</b>	<b>Xylazine</b> , Fentanyl, Phenethyl-4-ANPP, Acetylfentanyl, 4-ANPP, Ethyl-4-ANPP	11.8 %
Fentanyl	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b>	<b>Xylazine</b> , Fentanyl, Cocaine, Phenethyl-4-ANPP, 4-ANPP, Ethyl-4-ANPP	4.3 %
Fentanyl	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b> , 4-ANPP, Phenethyl-4-ANPP	5.6 %
Fentanyl	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b> , 4-ANPP, Phenethyl-4-ANPP	-
Fentanyl	Fentanyl	Fentanyl, <b>Xylazine</b>	<b>Xylazine</b> , Fentanyl, 4-ANPP	-
Fentanyl	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b>	<b>Xylazine</b> , Fentanyl, Cocaine, 4-ANPP, Phenethyl-4-ANPP	-
Fentanyl	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b>	<b>Xylazine</b> , Fentanyl, 4-ANPP	-
Fentanyl	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b>	<b>Xylazine</b> , Fentanyl, 4-ANPP	6.8 %
Fentanyl	Fentanyl	Fentanyl, <b>Xylazine</b>	<b>Xylazine</b> , Fentanyl, 4-ANPP, Phenethyl-4-ANPP	6.5 %
Unknown	Heroin	Fentanyl	Fentanyl, 4-ANPP, Acetylfentanyl, para-Fluorofentanyl, Heroin, Caffeine, Phenethyl-4-ANPP, Ethyl-4-ANPP, <b>Xylazine</b> , Lidocaine	-
Heroin	Heroin	Fentanyl, Lidocaine	Fentanyl, 4-ANPP, para-Fluorofentanyl, Lidocaine, Caffeine, <b>Xylazine</b>	-
Heroin	Heroin	Fentanyl, Lidocaine	Fentanyl, 4-ANPP, para-Fluorofentanyl, Caffeine, <b>Xylazine</b> , Lidocaine	-
Fentanyl	Fentanyl	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b> , 4-ANPP, Caffeine	-
Fentanyl	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b> , 4-ANPP, Cocaine, para-Fluorofentanyl, Acetylfentanyl, Phenethyl-4-ANPP, Caffeine, Ethyl-4-ANPP	5.7 %
Unknown	Fentanyl	Acetaminophen, Caffeine, Fentanyl, Lidocaine	Fentanyl, Acetylfentanyl, Caffeine, 4-ANPP, <b>Xylazine</b> , Acetaminophen, Cocaine, Phenethyl-4-ANPP, Ethyl-4-ANPP, Lidocaine	3.8 %
Fentanyl	Fentanyl	Fentanyl, Lactose	Fentanyl, <b>Xylazine</b> , 4-ANPP, Cocaine, Phenethyl-4-ANPP, Caffeine	-
Fentanyl	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b>	Fentanyl, <b>Xylazine</b> , 4-ANPP	-
Fentanyl	Fentanyl	Fentanyl	Fentanyl, 4-ANPP, Diphenhydramine, Cocaine, <b>Xylazine</b> , Phenethyl-4-ANPP	-
Fentanyl	Fentanyl	Fentanyl, <b>Xylazine</b> , Caffeine	Fentanyl, 4-ANPP, para-Fluorofentanyl, Cocaine, <b>Xylazine</b> , Caffeine, Phenethyl-4-ANPP, para-Fluoro-Phenethyl-4-ANPP, Diphenhydramine, Ethyl-4-ANPP	-
Fentanyl	Fentanyl	Fentanyl	Fentanyl, 4-ANPP, Cocaine Diphenhydramine, Phenethyl-4-ANPP, <b>Xylazine</b>	-
Fentanyl	Fentanyl	Fentanyl	Fentanyl, <b>Xylazine</b> , 4-ANPP, Phenethyl-4-ANPP	-

<sup>^</sup> If missing, mass was insufficient for quantification or quantification was unavailable at the time of sample processing

\* laboratory results are reported in decreasing detection levels of active drug components.

moderate in our baseline cohort, a vulnerable population comprised of mostly unstably housed and polysubstance-using RI residents at risk of overdose. We found that in the absence of DCS, PWUD in RI relied on subjective health effects to decipher xylazine exposure as related to experiences of sedation and ulcerative wound appearance. Notably, the statistical agreement between what was expected by PWUD and detected through laboratory testing was weak ( $\kappa < 0.6$ ). In contrast, the agreement observed between expected and actual fentanyl exposure was strong ( $\kappa > 0.8$ ).

Point-of-care DCS could rapidly fill knowledge gaps when newer drugs enter the illicit market by directly affirming and expanding the public’s awareness of local drug supplies. Unlike traditional drug surveillance programs, point-of-care models provide a rich opportunity for learning from PWUD about their experiences with the drug sample, communicating results and providing access to harm reduction supplies.

In the absence of a regulatory framework for DCS, validation studies for xylazine tests will need to be conducted for rapid point-of-care testing tools. DCS models that include laboratory-based confirmation testing are advantageous over single-drug rapid tests as the former is more comprehensive and can be rapidly expanded to include novel psychoactive drugs as the drug supply evolves.

**4.1. Limitations**

To our knowledge, this is one of few prospective studies in the US that have integrated DCS into research. However, we caution that the experiences in RI may not be generalizable outside of the state. The clinical and public health significance of trace amounts of xylazine detected in submitted samples remains unknown and will require further evaluation. The percentages of xylazine detected in this study cannot be interpreted as population-level prevalence estimates as non-random sampling was used to collect samples and because samples were non-standardized. Lastly, given that no DCS is 100 % accurate, we conveyed to participants the uncertainty in the point-of-care results. In the context of the overdose crisis, our study shows that DCS is acceptable to some PWUD in Rhode Island. The current scenario that harm reduction organizations face is similar to take-home COVID test kits that were approved for use that vary greatly in their accuracy. Our hope is that drug checking instruments only become more accurate and affordable.

**5. Conclusions**

In this DCS study, we detected substantial knowledge gaps regarding the composition of the local drug supply. Implementing DCS at harm reduction organizations could rapidly increase community awareness of



xylazine and other contaminants and engage PWUD into prevention and other critical supports such as wound care. Substantial federal and state investments for DCS development, implementation and research (Cepeda et al., 2023; Park et al., 2023), as well as policy supports (e.g., drug paraphernalia law reform) (LAPPA, 2023) will be required to scale up DCS across the country.

### CRedit authorship contribution statement

**Elyse R. Grossman:** Writing – review & editing, Investigation. **Traci C. Green:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Alex J. Krotulski:** Writing – review & editing, Writing – original draft, Validation, Supervision, Investigation, Data curation. **Adina Badea:** Writing – review & editing, Supervision, Formal analysis, Data curation. **Michelle McKenzie:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation. **Jessica Tardif:** Writing – review & editing, Data curation. **Rachel Serafini:** Writing – review & editing, Writing – original draft, Validation, Project administration, Methodology, Formal analysis, Data curation. **Merci Ujeneza:** Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation. **Ju Nyeong Park:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

### Declaration of Competing Interest

None.

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### Disclosures

None to declare.

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