



Overdoses Involving Xylazine Mixed with Fentanyl: Clinical and Public Health Implications

Clinician Outreach and Communication Activity (COCA) Call

Thursday, February 29, 2024

Free Continuing Education

- Free continuing education is offered for this webinar.
- Instructions for how to earn continuing education will be provided at the end of the call.

Continuing Education Disclosure

- In compliance with continuing education requirements, all planners, presenters, and moderators must disclose all financial relationships, in any amount, with ineligible companies over the previous 24 months as well as any use of unlabeled product(s) or products under investigational use.
- CDC, our planners, and presenters/moderators wish to disclose they have no financial relationship(s) with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.
- Content will not include any discussion of the unlabeled use of a product or a product under investigational use.
- CDC did not accept financial or in-kind support from ineligible companies for this continuing education.

Objectives

At the conclusion of today's session, the participant will be able to accomplish the following:

1. Discuss the history and epidemiology of xylazine in the drug supply and among overdoses.
2. Describe the current understanding of adverse health effects from exposure to xylazine mixed with fentanyl and acute overdose treatment strategies.
3. List laboratory testing options and harm reduction activities to minimize disease and death from overdoses involving xylazine mixed with fentanyl.
4. Identify opportunities for public health and clinical partnerships to improve communication, outreach, and outcomes in people exposed to xylazine mixed with fentanyl.

To Ask a Question

- Using the Zoom Webinar System
 - Click on the “Q&A” button
 - Type your question in the “Q&A” box
 - Submit your question
- If you are a patient, please refer your question to your healthcare provider.
- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

Today's Presenters

- **Josh Schier, MD, MPH**
CAPT, U.S. Public Health Service
Senior Medical Officer, Health Systems and Research Branch
Division of Overdose Prevention
National Center for Injury Prevention and Control
Centers for Disease Control and Prevention
- **Lewis Nelson, MD**
Chair, Department of Emergency Medicine
Director, Division of Medical Toxicology and Addiction Medicine
Rutgers New Jersey Medical School
- **Rachel S. Wightman, MD**
Associate Professor Emergency Medicine and Epidemiology
Alpert Medical School of Brown University
Consultant Medical Director, Rhode Island Department of Health

INJURY CENTER

Allison Arwady, MD, MPH

Director

**National Center for Injury Prevention and Control
CDC**



An Introduction to Xylazine and the Epidemiology of Overdoses involving Xylazine mixed with Fentanyl

**CAPT Josh Schier MD MPH USPHS
Commissioned Corps**

**Senior Medical Officer, Division of
Overdose Prevention, CDC (Atlanta, GA)**



Disclaimer

The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Learning Objectives

- To understand
 - What xylazine is and how it entered the illicit drug supply
 - The rationale for this COCA call
 - What is known about the epidemiology of overdoses involving xylazine mixed with fentanyl

Xylazine

What is it?

- Studied for human use in the 1960s
- Pharmaceutical
 - Sedative
 - Analgesic
 - Muscle relaxant properties
- Not FDA approved for human use

D'Orazio J, Nelson L, Perrone J, Wightman R, Haroz R. Xylazine Adulteration of the Heroin-Fentanyl Drug Supply : A Narrative Review. *Ann Intern Med.* 2023 Oct;176(10):1370-1376. doi: 10.7326/M23-2001. Epub 2023 Oct 10. PMID: 37812779.

Robert S. Hoffman (2023) Closing the xylazine knowledge gap, *Clinical Toxicology*, 61:12, 1013-1016, DOI: 10.1080/15563650.2023.2294619

Xylazine

What is it?

- Alpha-2-adrenergic agonist
 - Similar mechanism of action to other drugs such as clonidine and dexmedetomidine
- Street names include:
 - *"Tranq"*
 - *"Anestesia de caballo"* (in Puerto Rico)
 - *"Zombie"*
 - *"Tranq dope"* when combined with opioids such as fentanyl

Xylazine

How did it become a drug overdose issue?

- First identified in Puerto Rico among drug samples around 2001
 - Since 2006
 - Found in post-mortem toxicology tests
 - Drugs seized by the US Drug Enforcement Administration (DEA)
 - Adulterant
 - What is an adulterant?
 - Why are adulterants used?
 - What are historical examples of adulterants?
 - Public health concerns
 - Media interest
- Torruella RA. Xylazine (veterinary sedative) use in Puerto Rico. *Subst Abuse Treat Prev Policy*. 2011;6(1):7. doi: 10.1186/1747-597X-6-7.
- D'Orazio J, Nelson L, Perrone J, Wightman R, Haroz R. Xylazine Adulteration of the Heroin-Fentanyl Drug Supply : A Narrative Review. *Ann Intern Med*. 2023 Oct;176(10):1370-1376. doi: 10.7326/M23-2001. Epub 2023 Oct 10. PMID: 37812779.
- Vagi SJ, Sheikh S, Brackney M, Smolinske S, Warrick B, Reuter N, Schier JG. Passive multistate surveillance for neutropenia after use of cocaine or heroin possibly contaminated with levamisole. *Ann Emerg Med*. 2013 Apr;61(4):468-74. doi: 10.1016/j.annemergmed.2012.10.036. Epub 2013 Jan 29. PMID: 23374417.

Xylazine

Media and News Reports

The New York Times

Tranq Dope: Animal Sedative Mixed With Fentanyl Brings Fresh Horror to U.S. Drug Zones

A veterinary tranquilizer called xylazine is infiltrating street drugs, deepening addiction, baffling law enforcement and causing wounds so severe that some result in amputation.



Xylazine

Are overdoses involving xylazine mixed with fentanyl an emerging public health threat?

FENTANYL ADULTERATED OR ASSOCIATED WITH XYLAZINE RESPONSE PLAN

JULY 2023

THE WHITE HOUSE
EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF NATIONAL DRUG CONTROL POLICY

Xylazine

What factors limit the ability to accurately and completely describe overdoses involving xylazine mixed with fentanyl?

- Biological testing availability (blood, urine, etc.) for non-fatal overdose
- Dedicated surveillance and reporting
- Clinical management and decision-making

SUDORS Dashboard: Fatal Overdose Data | Drug Overdose | CDC Injury Center

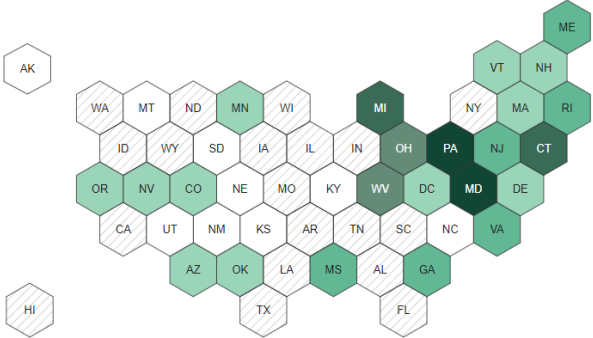
Color Legend

- ≥ 150 deaths
- 100–149 deaths
- 50–99 deaths
- 10–49 deaths
- 1–9 deaths
- 0 deaths
- Data not available

2020

Xylazine Metric: Count Percent

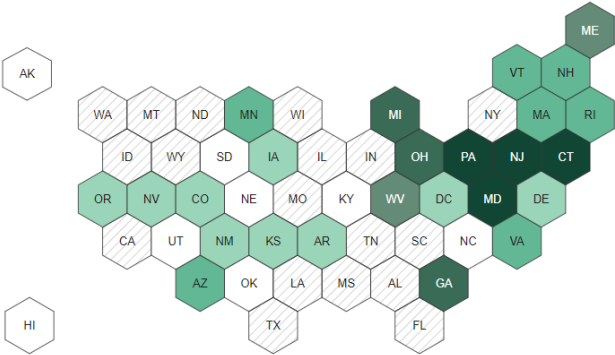
Overall (32 jurisdictions): 1,572 deaths



2021

Xylazine Metric: Count Percent

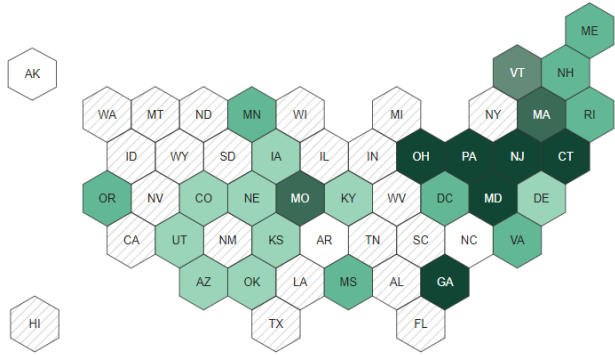
Overall (33 jurisdictions): 2,838 deaths



2022

Xylazine Metric: Count Percent

Overall (29 jurisdictions): 2,950 deaths



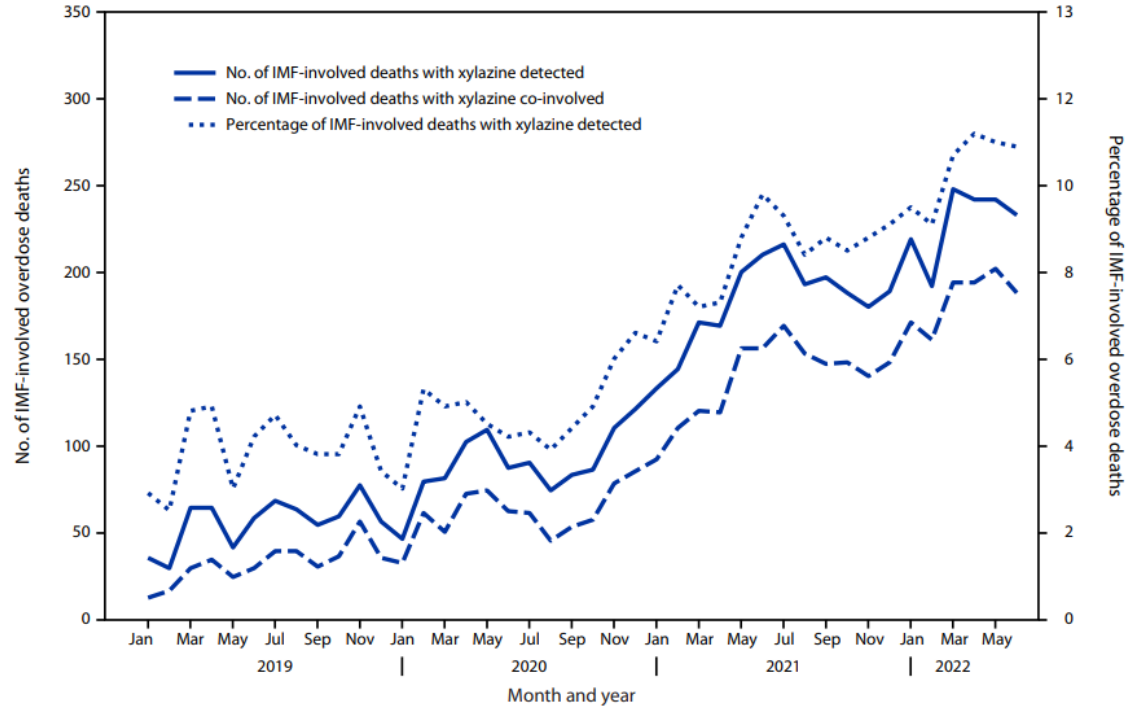
Xylazine

Epidemiology

Illicitly Manufactured Fentanyl-Involvement Overdose Deaths with Detected Xylazine — United States, January 2019–June 2022

Weekly / June 30, 2023 / 72(26);721–727

FIGURE 1. Number and percentage of drug overdose deaths involving* illicitly manufactured fentanyls,† by month and xylazine detection or co-involvement — State Unintentional Drug Overdose Reporting System, 21 jurisdictions,‡ January 2019–June 2022



Kariisa M, O'Donnell J, Kumar S, Mattson CL, Goldberger BA. Illicitly Manufactured Fentanyl-Involvement Overdose Deaths with Detected Xylazine - United States, January 2019-June 2022. MMWR Morb Mortal Wkly Rep. 2023 Jun 30;72(26):721-727.

Xylazine

Epidemiology

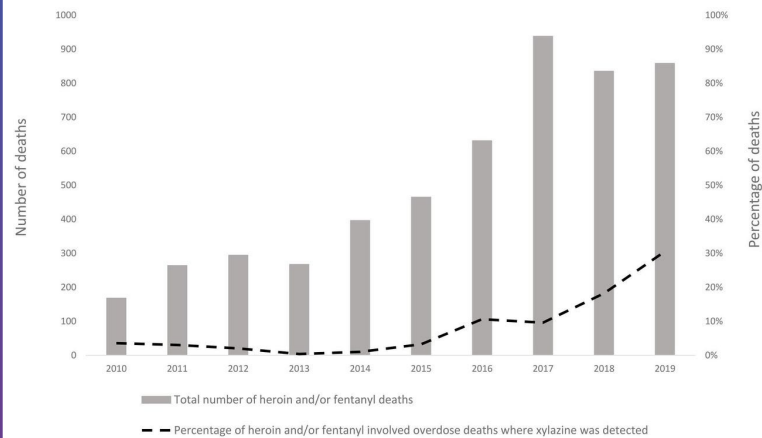


Figure 1 Number and percentage of heroin and/or fentanyl unintentional overdose deaths involving xylazine, Philadelphia, Pennsylvania, 2010–2019.

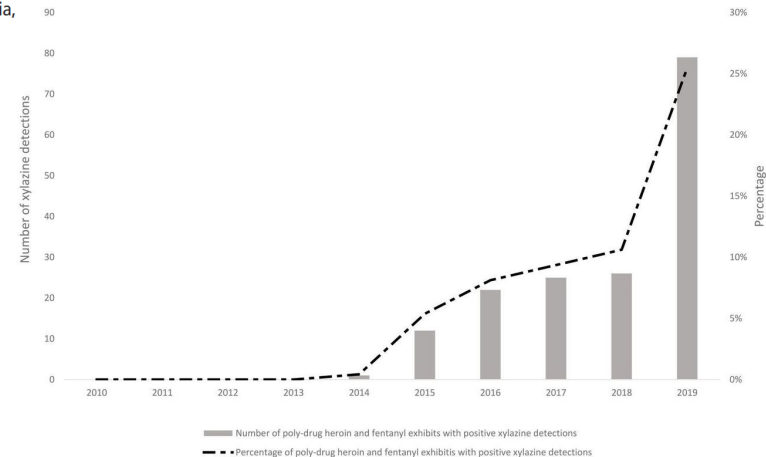


Figure 2 Number and percentage of xylazine detections in polydrug exhibits seized where the primary drug detected was fentanyl or heroin, Pennsylvania, 2010–2019.

Xylazine

Epidemiology

FIGURE 3 Trend of xylazine growth from 2015 to 2022 at the MDME.

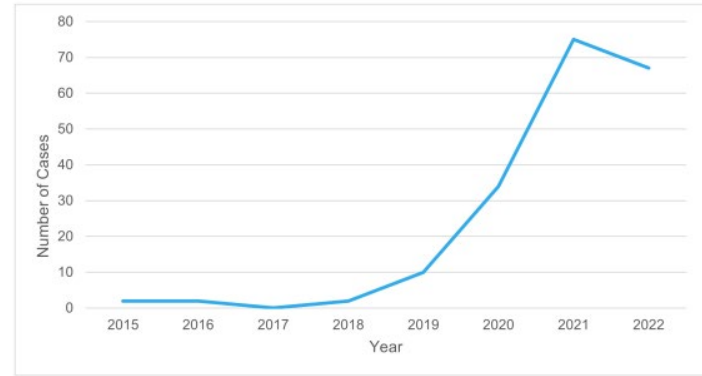
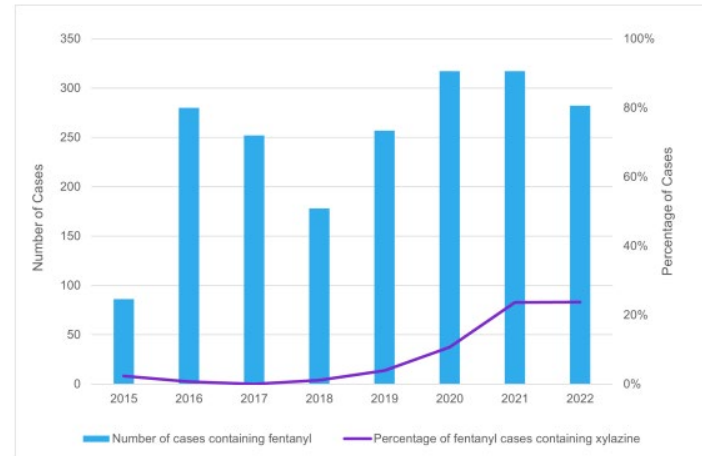


FIGURE 4 Relationship between fentanyl-positive cases and xylazine-positive cases.



Potoukian RB, Gonyea J, Shoff EN, Hime GW, Moore DM. Prevalence of xylazine in overdose cases: An analysis of Miami-Dade County medical examiner case data. *J Forensic Sci.* 2023 Nov;68(6):2205-2210. doi: 10.1111/1556-4029.15375. Epub 2023 Sep 1. PMID: 37658657.

Xylazine

Epidemiology

NFLIS
NATIONAL FORENSIC LABORATORY INFORMATION SYSTEM

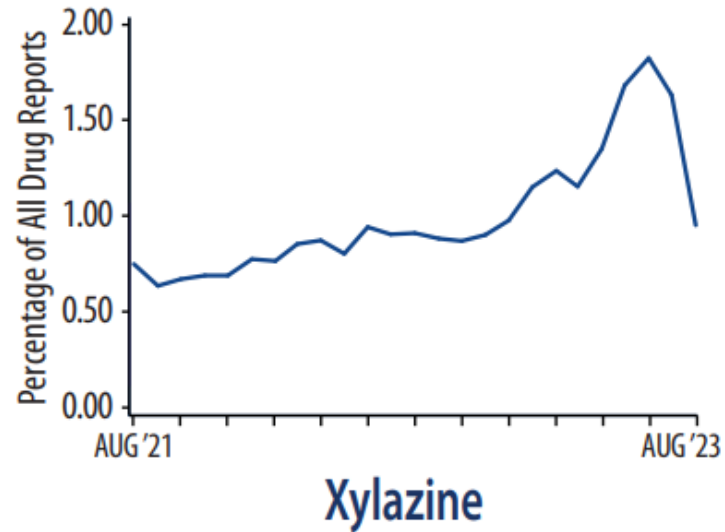


DRUG

snapshot



September 2023

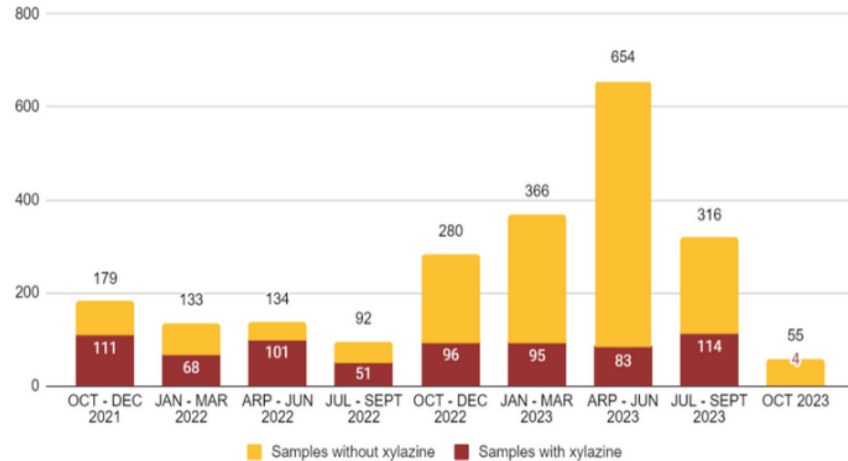


Xylazine

Epidemiology

RAD: Rapid Analysis of Drugs (program that tests drugs samples in MD)

Figure 5: Xylazine in RAD Samples, October 2021 - October 2023



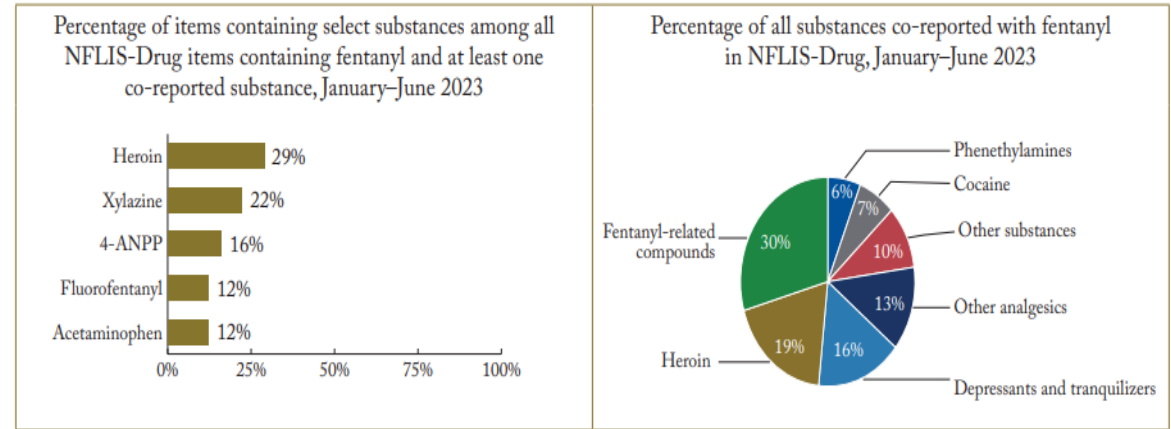
In the past year, xylazine has decreased in prevalence throughout RAD results (Figure 5). This trend has been seen in Maryland law enforcement seizure data. However, RAD continues to see Xylazine in greater than 20% of samples on average, and shows great variation by jurisdiction (with some consistently over 75%-80% prevalence. An increase in wounds in people who use drugs is also linked to xylazine's presence in the drug supply.

Xylazine

Epidemiology

NFLIS-Drug Brief: Substances Co-Reported with Fentanyl in NFLIS-Drug and DEA-Tox, January 2013–June 2023

Figure 13. Submission date: January–June 2023 ($n = 10,730$ items containing fentanyl and at least one co-reported substance)



Self Knowledge Check

Commonly reported effects of xylazine include which of the following?

- a. Sedation
- b. Hypertension
- c. Seizures
- d. Ulcers

Self Knowledge Check

Answer

Commonly reported effects of xylazine include which of the following?

- a. Sedation
- b. Hypertension
- c. Seizures
- d. Ulcers

Rationale: Xylazine is a drug that depresses the central nervous system, so options b and c are incorrect. Ulcers are not a commonly reported effect of xylazine.

LEWIS S. NELSON, MD, MBA

Professor and Chair,
Department of Emergency Medicine
Chief, Division of Medical Toxicology
and Addiction Medicine
Rutgers New Jersey Medical School

“CURRENT UNDERSTANDING OF THE
HEALTH RISKS AND OVERDOSE
TREATMENT STRATEGIES ASSOCIATED
WITH EXPOSURE TO XYLAZINE MIXED
WITH FENTANYL”

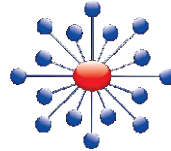
LEARNING OBJECTIVES

- Discuss the pharmacology of xylazine and how it impacts the risks of opioid use
- Describe the adverse consequences associated with exposure to xylazine mixed with fentanyl.
 - Overdose and death
 - Withdrawal
 - Wounds
- Explain how patients exposed to xylazine mixed with fentanyl overdose are best managed
- Describe approaches to address the adverse consequences of xylazine mixed with fentanyl

ARTICLES ABOUT XYLAZINE-ADULTERATED OPIOIDS IN THE UNITED STATES DRUG SUPPLY



National Drug Abuse Treatment Clinical Trials Network
**Managing Patients Taking Xylazine-Adulterated Opioids
in Emergency, Hospital, & Addiction Care Settings**



June 14, 2023
9:00 a.m. – 12:30 p.m.

<https://nida.nih.gov/news-events/meetings-events/2023/06/managing-patients-taking-xylazine-adulterated-opioids-emergency-hospital-addiction-care-settings>

REVIEW

Annals of Internal Medicine

Xylazine Adulteration of the Heroin-Fentanyl Drug Supply

A Narrative Review

Joseph D'Orazio, MD; Lewis Nelson, MD, MBA; Jeanmarie Perrone, MD; Rachel Wightman, MD; and Rachel Haroz, MD

Xylazine is an animal sedative, approved by the U.S. Food and Drug Administration, that is commonly used in veterinary medicine and is not approved for human use. Since 2016, xylazine has consistently appeared in the illicitly manufactured fentanyl supply and has significantly increased in prevalence, likely due to its low cost, easy availability, and presumed synergistic psychoactive effect. Clinical experience along with the available pertinent research were used to review xylazine adulteration of the drug supply and provide

guidance on the care of patients exposed to xylazine. This review discusses xylazine pharmacology, animal and human clinical effects, and what is known to date about care of patients experiencing acute overdose, xylazine-fentanyl withdrawal, and xylazine-associated wounds.

Ann Intern Med. 2023;176:1370-1376. doi:10.7326/M23-2001 **Annals.org**
For author, article, and disclosure information, see end of text.
This article was published at Annals.org on 10 October 2023.

<https://www.acpjournals.org/doi/10.7326/M23-2001>

XYLAZINE – PHARMACOLOGY/TOXICOLOGY

Alpha-2a adrenergic agonist (xylazine)

- Decreases sympathetic outflow via locus coeruleus
- Sedation

Imidazoline-1 agonist (clonidine)

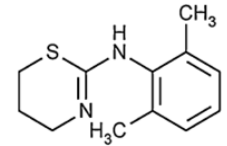
- Decreases sympathetic outflow via rostral ventrolateral medulla
- Bradycardia and hypotension

Implications

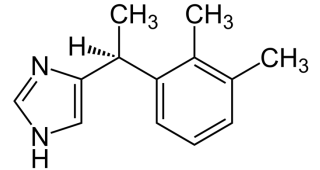
- Xylazine lacks significant imidazoline receptor activity → limited bradycardia and hypotension
- No significant respiratory depression → limited mortality expected

Pharmacokinetics

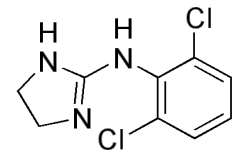
- Time to effect is 1-2 minutes with IV administration
 - Can be given IM, SC, PO, IN
- Duration of effect up to 4 hours (in animals)



Xylazine (α₂)



Dexmedetomidine
(α₂)



Clonidine (I₁)

Lowry JA, Brown JT. Clin Toxicol (Phila). 2014 Jun;52(5):454-69

Bosquet P. Pharmacol Rev 2020, 72 (1) 50-79;

https://www.deadiversion.usdoj.gov/drug_chem_info/Xylazine.pdf Nov 2022

OVERDOSE HUMAN SELF HARM ATTEMPTS WITH XYLAZINE

Human Overdose with the Veterinary Tranquilizer Xylazine

DAVID G. SPOERKE, MS, RPh,* ALAN H. HALL, MD,*
MICHAEL J. GRIMES, MD,†
BERTRAND N. HONEA, III, MD,‡ BARRY H. RUMACK, MD*

Three patients self-injected the veterinary tranquilizing agent xylazine (Rompun®). The first patient developed mild bradycardia and hypotension, miosis, and a feeling of disorientation. The other two patients became apneic and required intubation and mechanical ventilation. Initial mild hypertension followed by mild hypotension and a mildly elevated blood glucose was seen in the second patient, whereas both the second and third patients developed mild bradycardia. Xylazine has structural similarity to the phenothiazines and pharmacological activity similar to clonidine. With increasing veterinary use, the availability and potential for human exposures may also increase. (*Am J Emerg Med* 1986;4:222-224)

- Intentional self-injection of xylazine
 - Patient 1: mild bradycardia, hypotension, miosis, disorientation
 - Patient 2: initial hypertension, then hypotension, elevated glucose, apnea requiring intubation
 - Patient 3: mild bradycardia, apnea requiring intubation

Opioid overdoses involving xylazine in emergency department patients: a multicenter study

Table 2. Clinical outcomes in xylazine vs. control patients.

Clinical outcome variables	Xylazine (n = 90)	Xylazine absent (n = 231)	P-Value
Cardiovascular outcomes			
Received CPR	4 (4.4%)	33 (14.3%)	0.013
Bradycardia	2 (2.2%)	4 (1.7%)	0.77
Pulmonary outcomes			
Intubated within 4 h	2 (2.2%)	13 (5.6%)	0.193
Non-invasive positive pressure within 4 h	1 (1.1%)	4 (1.7%)	0.689
Any ventilatory support within 4 h	3 (3.3%)	17 (7.4%)	0.182
Intubated after 4 h	2 (2.2%)	11 (4.8%)	0.298
Non-invasive positive pressure after 4 h	2 (2.2%)	2 (0.9%)	0.327
Any ventilatory support after 4 h	4 (4.4%)	13 (5.6%)	0.67
Central nervous system outcomes			
Coma within 4 h	24 (26.7%)	87 (37.7%)	0.063
Coma after 4 h	12 (13.3%)	35 (15.2%)	0.682
Overall outcomes			
Death	1 (1.1%)	5 (2.16%)	0.528
Discharged from the ED	59 (65.6%)	147 (63.6%)	0.528
ICU Admissions	11 (12.2%)	39 (16.9%)	0.30
Miscellaneous			
Length of hospitalization (h); median (IQR)	10 (5–28)	9 (5–36)	0.806
Total naloxone dose (mg)	3.68 (1.3–4.05)	2.8 (2–4.1)	0.448

Abbreviations: IQR, interquartile range; CPR, cardiopulmonary resuscitation; ED, emergency department; ICU, intensive care unit. The bold values indicate variables that are statistically significant ($P < 0.05$).

*Percentage of entire cohort.

NALOXONE DOES NOT REVERSE THE EFFECTS OF XYLAZINE, YET IT IS THE DRUG OF CHOICE

YEAR	XYLAZINE-RELATED				ALL SUSPECTED HEROIN	
	SUBMISSIONS		GLASSINE BAGS		SUBMISSIONS	GLASSINE BAGS
2019	368	3%	9,038	1%	13,010	680,807
2020	855	11%	30,236	6%	7,814	500,715
2021	3,052	30%	239,998	29%	10,341	821,171
2022	2,614	35%	138,818	29%	7,374	475,826
2023 (TO 9/30)	2,529	50%	144,637	47%	5,039	310,665

Xylazine positive

SUSPECTED HEROIN GLASSINE BAGS CONTAINING XYLAZINE ANALYZED 1/1/2015 - 12/31/2022		
FENTANYL/4-ANPP/ XYLAZINE	82,612	19%
HEROIN/FENTANYL/4-ANPP/ XYLAZINE	42,408	10%
FENTANYL/ XYLAZINE	28,826	7%
HEROIN/FENTANYL/ XYLAZINE	19,871	5%
HEROIN/FENTANYL/FLUOROFENTANYL/ TRAMADOL/ XYLAZINE	15,256	4%
XYLAZINE ONLY (MONO DRUG)	724	0.2%
OTHER FENTANYL & XYLAZINE COMBINATIONS	228,101	54%
OTHER DRUGS OR COMBINATIONS	7,664	2%
TOTAL	425,462	
Content is listed in the order of amounts found in the sample.		

Data from New Jersey State Police

WHAT IS THE OPTIMAL DOSING STRATEGY FOR NALOXONE?

Remember, we are treating fentanyl not xylazine!

Is there such a thing as “naloxone-resistant” overdose?

Rarely

What is the clinical endpoint for successful reversal?

Breathing

Can “too much” naloxone be administered?

Yes

Is there an alternative agent for xylazine reversal?

Technically, but no.

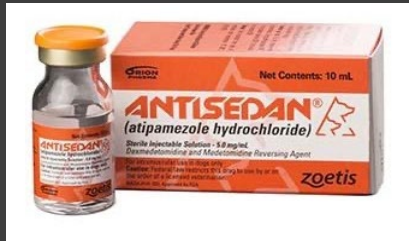
COMPARISON OF ATIPAMEZOLE WITH YOHIMBINE FOR ANTAGONISM OF XYLAZINE

Journal of the American Association for Laboratory Animal Science
Copyright 2017
by the American Association for Laboratory Animal Science

Vol. 56, No. 1
March 2017
Pages 142-147

Comparison of Atipamezole with Yohimbine for Antagonism of Xylazine in Mice Anesthetized with Ketamine and Xylazine

Christopher F Janssen,^{1,2*} Pauline Marella,² M Jerry Wright Jr,² Kara B Krcinovsky,² and Joseph T Newsome^{1,4}



INDICATIONS: ANTISEDAN is indicated for the reversal of the sedative and analgesic effects of DEXDOMITOR (dexmedetomidine hydrochloride), and DOMITOR (medetomidine hydrochloride) in dogs.

It is currently not FDA-approved for human use

<https://www.zoetis.com/products/petcare/antisedan-atipamezole>

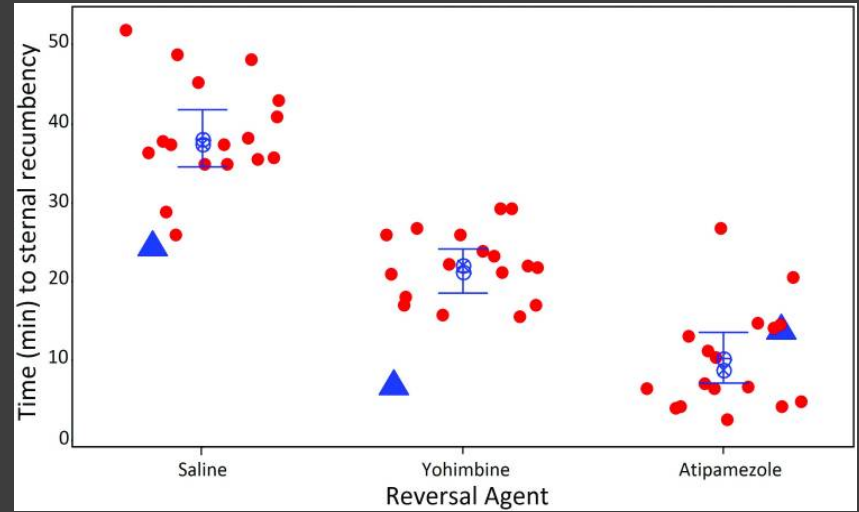


Figure 1. Time to return of the righting reflex in mice anesthetized with $\alpha 2$ agonist xylazine, in combination with ketamine, after intraperitoneal administration of either of the $\alpha 2$ antagonists atipamezole (1 mg/kg IP) and yohimbine (1.5 mg/kg IP) or saline (control). At these dosages, atipamezole (mean \pm 1 SD, 10.3 \pm 6.5 min) resulted in the most rapid recovery of the mice to sternal recumbency, allowing for prompt return of the mice to the home cage after anesthesia, compared with yohimbine (21.3 \pm 5.6 min) and saline (38.2 \pm 7.5 min). The 3 data points designated by triangles indicate a technical error, in which the antagonist was given at 10 min, rather than 15 min, after the anesthetic combination.


XYLAZINE AVAILABLE DATA AND RISK MESSAGING

Bloomberg US Edition

Live Now Markets Economics **Industries** Tech AI Politics Wealth Pursuits Opinion Businessweek Equality Green

Industries
Health

Deaths Linked to Animal-Tranquilizer Use Have Exploded, CDC Data Show



By **Matthew Griffin**
June 30, 2023 at 12:01 AM EDT

Facebook Twitter LinkedIn Email RSS

THE WHITE HOUSE

Administration Briefings The Record Briefing Room Contact

APRIL 30, 2023

Biden-Harris Administration Designates Fentanyl Combined with Xylazine as an Emerging Threat to the United States

ONDCP Briefing Room Press Releases


Xylazine's growing role in overdose deaths nationwide prompts Administration to make this designation for the first time in U.S. history.

ATLANTA, GA – Today, Dr. Rahul Gupta, Director of the White House Office of National Drug Control Policy (ONDCP), has officially designated fentanyl adulterated or associated with xylazine as an emerging threat to the United States. The Bureau of National Drug Control Policy is pleased to announce this designation.

**FENTANYL
ADULTERATED OR
ASSOCIATED WITH
XYLAZINE RESPONSE
PLAN**

JULY 2023

THE WHITE HOUSE
EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF NATIONAL DRUG CONTROL POLICY



Xylazine

U.S. Department of Justice
Drug Enforcement Administration



**The Growing Threat of Xylazine
and its Mixture with Illicit Drugs**
DEA Joint Intelligence Report
DEA-2023-00123
Undiscover

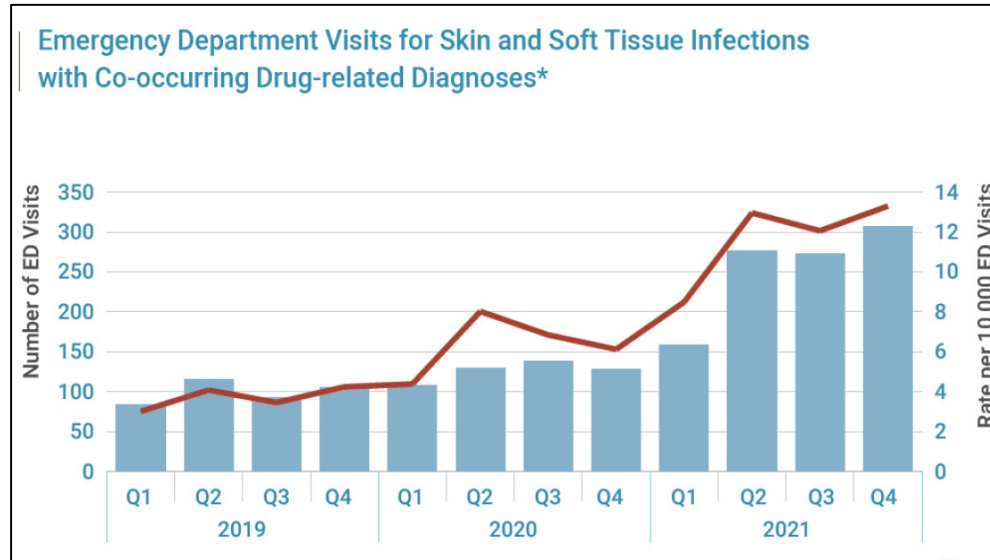


Xylazine	Opioid
<ul style="list-style-type: none">■ Anxiety■ Dysphoria■ Restlessness	<ul style="list-style-type: none">■ Anxiety■ Dysphoria■ Restlessness■ N/V/D■ Myalgia■ Rhinorrhea■ Tremor■ Yawning■ Piloerection

Treatment: As for opioids, including comfort meds

OVERLAPPING “WITHDRAWAL” SYNDROMES

XYLAZINE ASSOCIATED WOUNDS



Data source: Pennsylvania Healthcare Cost Containment Council

XYLAZINE ASSOCIATED WOUND PATHOPHYSIOLOGY

- Longstanding history of skin ulcers with injection drug use
 - Heroin
 - Black tar heroin
 - “Krokodil” (desomorphine)

Potential Causes of Wounds from Injection Drug Use:

- Obliterative vasculitis from repetitive injection (“shooter’s patch”)
- Infectious
- Skin picking causing excoriations and ulcers
- Poor wound healing (various causes)
- Cytotoxic effect of drug (irritant)
- Localized pharmacological effect (hypoxia)
- Compression ulcer

WOUND CARE

Cessation of injection

Clean with soap/water, chlorhexidine, Dakin's Half Strength Solution, or 1% acetic acid

Debridement (enzymatic vs surgical)

Antimicrobial coverage (Silver sulfadiazine cream, bacitracin ointment)

Non-adherent (petroleum gauze or other additive to promote moist wound environment) and absorptive dressing

Biodegradable Temporizing Matrix (BTM), skin grafting, epithelialization/complete closure



FINAL TAKEAWAYS/ SUMMARY

- Xylazine is an alpha-2 agonist found in increasing frequency mixed in heroin/fentanyl especially in the Northeast
- Causes significant sedation, not reversible by naloxone
- Does not appear to directly increase the fatality rate from fentanyl
- Repeated use *may* cause a withdrawal syndrome (unique?) typically described as anxiety and dysphoria
- Repetitive xylazine use is associated with necrotic wound development

SELF KNOWLEDGE CHECK

In the absence of naloxone, after calling 911, what should be done to help a patient with a xylazine/fentanyl overdose?

- a. Inject epinephrine (Epi-pen)
- b. Provide rescue breathing
- c. Stimulate with cold or hot water
- d. Give sublingual buprenorphine

SELF KNOWLEDGE CHECK (CONT.)

In the absence of naloxone, after calling 911, what should be done to help a patient with a xylazine/fentanyl overdose?

- a. Inject epinephrine (Epi-pen)
- b. Provide rescue breathing**
- c. Stimulate with cold or hot water
- d. Give sublingual buprenorphine

Rationale: Because most of the harm from xylazine is due to the fentanyl that is present, death is almost always due to respiratory arrest. Thus, rescue breathing by any means will provide oxygen to help reduce the harms. The other methods are either ineffective, unsafe, or unstudied.

Managing the potential public health threats associated with xylazine mixed with fentanyl in the community

Rachel S. Wightman, MD FACMT

Assistant Professor of Emergency Medicine and Epidemiology

Alpert Medical School of Brown University

Director of Medical Toxicology Education

Consultant Medical Director, Rhode Island Department of Health



BROWN PHYSICIANS, INC.



BROWN
Alpert Medical School

Objectives

- Understand testing options to determine the presence of xylazine in a community
- Identify opportunities for public health, community, and clinician partnerships to improve communication, outreach, and outcomes
- Provide examples of harm reduction initiatives to help minimize morbidity and mortality from xylazine

Xylazine testing overview

- Community drug checking
 - Screening vs. Confirmatory (e.g. MAADS, NYC)
 - Potential legal concerns in many states
- Non-fatal overdose testing
 - Not part of standard testing in health care settings
- Fatal overdose testing
 - Post-mortem testing algorithms vary
 - Delayed reporting
- Drug seizure testing
 - Testing and reporting often delayed
 - Data sharing limited, may lack context

Testing considerations for xylazine

- Rapidly evolving landscape
- Pharmacokinetics in humans
- Clinical Utility
 - point of care (community drug, ED, hospital, office-based testing) vs. surveillance
- Metabolites
- False positives/negatives
- Testing infrastructure which are not siloed and ready to detect and communicate changes
- Interpretation and communication of quantitative testing

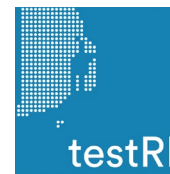
testRI overview



Toxicological and Ethnographic
Drug Surveillance Testing RI

- Two-year community-based research study
(MPIs: Dr. Rachel Wightman and Dr. Alexandra Collins)
- Toxicology testing (n=200 samples) + feedback surveys
- Qualitative interviews with people who use drugs (n=50)
- Rapid dissemination of testing findings across audiences to inform harm reduction efforts
- *Community Advisory Board/Project Partners : People with lived experience, Project Weber Renew, House of Hope, Rhode Island Department of Health, treatment providers*
- Samples are donated: (1) by study participants or (2) anonymously donated
- Collect location and substance the individual reported buying
- Samples include product, equipment (e.g., syringes, choy, cookers, pipes) and refuse (e.g., baggies)
- All samples tested via LC-QTOF-MS at Rhode Island Hospital Laboratory run by Dr. Adina Badea

2022 testing results snapshot

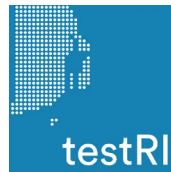


	Used Equipment			Product			Refuse		
	Samples	Xylazine	Fentanyl	Samples	Xylazine	Fentanyl	Samples	Xylazine	Fentanyl
Cocaine powder	1	—	—	4	—	1	2	—	1
Crack cocaine	9	1	3	6	—	1	1	—	1
Methamphetamine	2	—	2	4	2	3	—	—	—
Heroin	—	—	—	1	—	1	—	—	—
Fentanyl / Dope	27	20	27	16	8	16	9	5	9
Percocet	1	1	1	1	1	1	4	4	4
Unknown	8	4	6	—	—	—	—	—	—
MDMA or Ketamine	—	—	—	4	—	—	1	—	—
Xanax or Adderall	—	—	—	2	—	—	—	—	—
Total	48	26	39	38	11	23	17	9	15

Xylazine was present in 63% (33/52) of samples donated as fentanyl and 45% of samples overall

*Xylazine was always detected in the presence of fentanyl

testRI ethnographic snapshot



- Anecdotes of change in drug use experience and observed partner drug use including:
 - New onset incontinence
 - Compression wounds and peripheral nerve injury
 - Deep sedation
- Example quotes from others:
 - *“[It was] no dope. I couldn’t tell you what was in it. [Interviewer: What was the feeling?] Like woozy. Like taking a sleeping pill or something.”*
 - *“Made me feel like, drowsy, like, I was like, sleepwalking, I don’t know. It was weird.”*



Drug Overdose Testing (DOT)

	Xylazine (n)	Fentanyl (n)	Percent fentanyl positive samples with xylazine
76 Urine samples	25 (33%)	67 (88%)	37%
76 Blood samples	11 (14%)	58 (76%)	19%
Both Urine and Blood samples	10 (13%)	58 (76%)	17%
Not Detected	50 (66%)	9 (12%)	

Median time to collection of blood from ED triage time was approximately 4 hours and 50 minutes

Median time to collection of urine from ED triage time was approximately 4 hours and 30 minutes

* Every sample positive for xylazine also tested positive for fentanyl



Xylazine Drug Seizures in RI

- Currently, finding xylazine as a fentanyl adulterant in both powder and counterfeit pill forms
- Xylazine was found in nearly **40% of counterfeit opioid pills tested in 2022**

Xylazine determinations in seized fentanyl incidents in Rhode Island

Q3 21	Q4 21	Q1 22	Q2 22	Q3 22	Q4 22	Q1 23	Q2 23
45%	43%	34%	38%	45%	37%	46%	48%

- *Limitations*

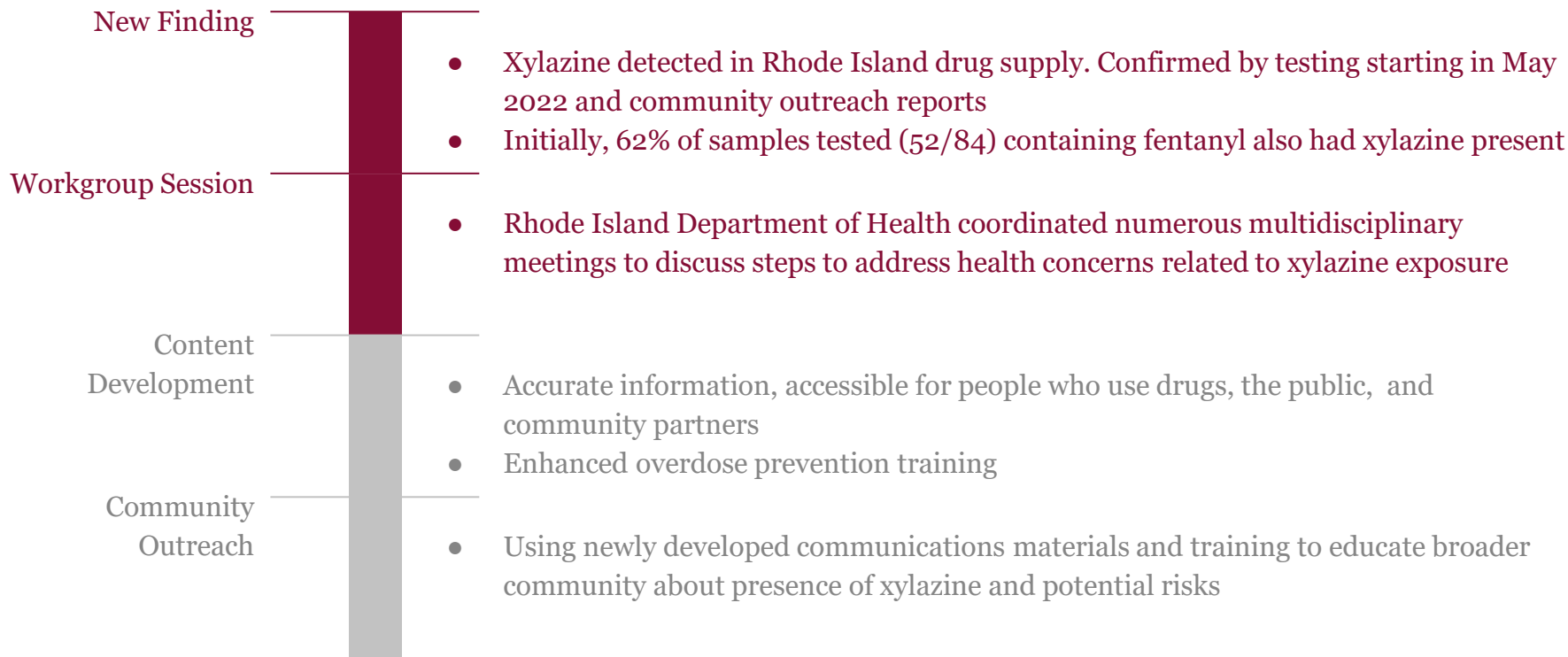
This is only seizure testing data submitted by law enforcement or medical examiner

About 5% of the cases don't have occurrence dates and are not included in this calculation

This does not account for separations of pills, powders, rinse/residue, or if any other drugs were found in the substances

* Data courtesy of the RIDOH Forensic Drug Chemistry Lab

Workflow example



Partner messaging

 **Rhode Island Department of Health** @RIHEALTH · Nov 17, 2022

Check out the latest newsletter from the Governor's #OverdosePrevention and Intervention Task Force. This month's issue includes announcements from @GovDanMcKee, a downloadable resource on #xylazine, upcoming events for #WorldAIDSDay, and more. bit.ly/3AptyiJ



ALT

Four Ways to Stay Safer with Xylazine

Xylazine is a powerful veterinary sedative recently found in the Rhode Island drug supply. Here's how to stay safer:

Use near someone who can check on you

Make sure someone is around to administer naloxone if you overdose.



Have naloxone nearby

Drugs that have xylazine in them very often have fentanyl, too. Make sure you and your friends carry naloxone.



Call 911 first if there is an overdose

911 will instruct you on how to support the person's breathing. If the person is breathing again but still sedated, put them on their side supported by a bent knee. The Good Samaritan Law provides certain legal protection, whether you have drugs on you or not.



Use new supplies and get wounds treated

Xylazine can cause severe wounds that can lead to an infection. Always use new supplies and get care for wounds.



Get FREE safer drug use supplies and other resources:



Project Weber/RENEW
640 Broad Street, Providence, RI 02907
124 Broad Street, Pawtucket, RI 02860
Kennedy Plaza, Providence, RI 02903
Tel: 401-383-4888
Hours: Mon-Wed: Fri, 10 a.m.-4 p.m.
Thurs., 10 a.m.-2:30 p.m.



AIDS Care Ocean State
557 Broad Street, Providence, RI 02907
Tel: 401-781-0665
Hours: Mon-Fri, 8:30 a.m.-4:30 p.m.
Tues. & Thurs. 6 p.m.-8 p.m.



Parent Support Network
535 Centerville Road, Suite 202,
Warwick, RI 02886
Tel: 401-603-6069
Hours: Mon-Fri, 9 a.m.-5 p.m.



Community Care Alliance
245 Main Street, 3rd Floor,
Warwick, RI 02886
Tel: 401-235-6044
Hours: Mon-Fri, 9 a.m. to 4 p.m.

For safer drug use supplies, resources, and more information, visit PreventOverdoseRI.org/xylazine/



PREVENT OVERDOSE RI

Provider dissemination

Audiences Reached

Recipients of provider advisories including:

- Licensed social workers
- Licensed mental health counselors
- Licensed psychologists
- Licensed marriage and family therapists
- Licensed chemical dependency professionals
- Licensed nurses
- Licensed physicians
- Licensed advanced practice providers
- Licensed pharmacists



September 13, 2023

testRI Update: Nitazenes Detected in Local Drug Supply



The Rhode Island Department of Health (RIDOH), in partnership with Brown University School of Public Health and the Alpert Medical School, share these June and July 2023 local drug supply updates from [testRI](#). This study looks at samples of what is in Rhode Island's drug supply and how changes to the supply are impacting people who use drugs.

Toxicological and Epidemiologic
Drug Surveillance Testing RI

Protonitazene, isotonitazene, metonitazene, and etonitazene have been detected in several drug samples tested in Rhode Island over the spring and summer of 2023.

Outreach initiatives

- Continued emphasis of importance of naloxone
 - Xylazine found mainly with fentanyl, naloxone is still of critical importance
- Drug checking including xylazine test strips
 - Utility of test strips in a xylazine saturated market and other limitations
 - Anecdotally have heard preference for single test strip versus combined fentanyl and xylazine strip
 - Potential false positives (e.g., lidocaine)
- Wound care outreach
 - Limited availability, capacity, and accessibility of wound care centers
 - Importance of dedicated professionals and not trainees in the community
 - Wounds cited as barriers to access shelters, residential treatment, etc.

Summary

- Testing and data should not be siloed
- Importance of multidisciplinary teams and community advisory boards not just in outreach, but also decision making
- Approach will be influenced by local factors (e.g., level of xylazine saturation, data sources)
- Continued emphasis of naloxone

Self Knowledge Check

Xylazine test strips can potentially result in false positives.

- a. True
- b. False

Self Knowledge Check (cont.)

Xylazine test strips can potentially result in false positives.

a. True

b. False

Rationale: Xylazine test strips have been shown to have false positives with lidocaine among other substances

Questions?

- Special Thanks
 - Dr. Francesca Beaudoin, Dr. Adina Badea, Dr. Alexandra Collins
 - Rhode Island Department of Health
 - Foundation for Opioid Response Efforts
 - Vartan Gregorian Fox Point Elementary School

To Ask a Question

- Using the Zoom Webinar System
 - Click on the “Q&A” button
 - Type your question in the “Q&A” box
 - Submit your question
- If you are a patient, please refer your question to your healthcare provider.
- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

Joining the Q&A Session

- **Julie O'Donnell, PhD, MPH**

LCDR, US Public Health Service

Team Lead, Overdose Mortality Team

Epidemiology and Surveillance Branch

Division of Overdose Prevention

National Center for Injury Prevention and Control

Centers for Disease Control and Prevention

TRAIN

- **January 1, 2024:** Move from Training and Continuing Education Online (TCEO) to CDC TRAIN (<https://www.train.org/cdctrain>).
- **Existing Activities:** Continue to use TCEO for existing activities that have CE set to expire in 2024, since these courses will not move to CDC TRAIN. You may also use TCEO for existing activities with CE set to expire in 2025, before the courses transition to CDC TRAIN sometime next year. If you begin one of these courses in TCEO, we will let you know when the course will move to CDC TRAIN.
- **Transcripts & Certificates:** You can access and download CE transcripts and certificates in TCEO through the end of 2025.
- Instructions will be available on both platforms and a learner support team will be available to answer questions.

Continuing Education

- All continuing education for COCA Calls is issued online through CDC TRAIN at CDC TRAIN (<https://www.train.org/cdctrain>).
- Those who participate in today's COCA Call and wish to receive continuing education please complete the online evaluation by **April 1, 2024**, with the **course code WC4520R-022924**. The **registration code** is **COCA022924**.
- Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation between **April 2, 2024**, and **April 2, 2026**, and use **course code WD4520-022924**. The **registration code** is **COCA022924**.

Today's COCA Call will be Available to View On-Demand

- **When:** A few hours after the live call ends*
- **What:** Video recording
- **Where:** On the COCA Call webpage
 - https://emergency.cdc.gov/coca/calls/2024/callinfo_022924.asp

**A transcript and closed-captioned video will be available shortly after the original video recording posts at the above link.*

Upcoming COCA Calls & Additional Resources

- Continue to visit <https://emergency.cdc.gov/coca/> to get more details about upcoming COCA Calls.
- Subscribe to receive notifications about upcoming COCA calls and other COCA products and services at emergency.cdc.gov/coca/subscribe.asp.

Thank you for joining us today!



<http://emergency.cdc.gov/coca>

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

