**UW PACC**

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

# XYLAZINE


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UW Medicine
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project ECHO

# Speaker disclosures

- ✓ No conflicts

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# Objectives

- Name 2 medical risks of xylazine use.
- Xylazine acts as an agonist at what receptor?
- Name 2 harm reduction tips you can tell patients concerned about xylazine related medical complications.

# What is Xylazine?

- Synthetic alpha 2-adrenergic agonist – synthesized in 1962
- Used as a sedative, anesthetic, muscle relaxant, and analgesic for animals
- Not approved for humans secondary to significant CNS depressant effects

- Found in illicit drug supplies, particularly fentanyl
- Called "tranq" or "tranq dope" when combined with opiates

# What is Xylazine?

- Liquid solution for injection in various strengths 20mg/ml-300mg/ml
- Solution can be dried into powder – typically white or brown and easily mixed into other powders or compressed pills
- Routes of administration
  - IV
  - IM
  - Intranasal
  - Oral
  - No information about inhalation

# Xylazine - Effects

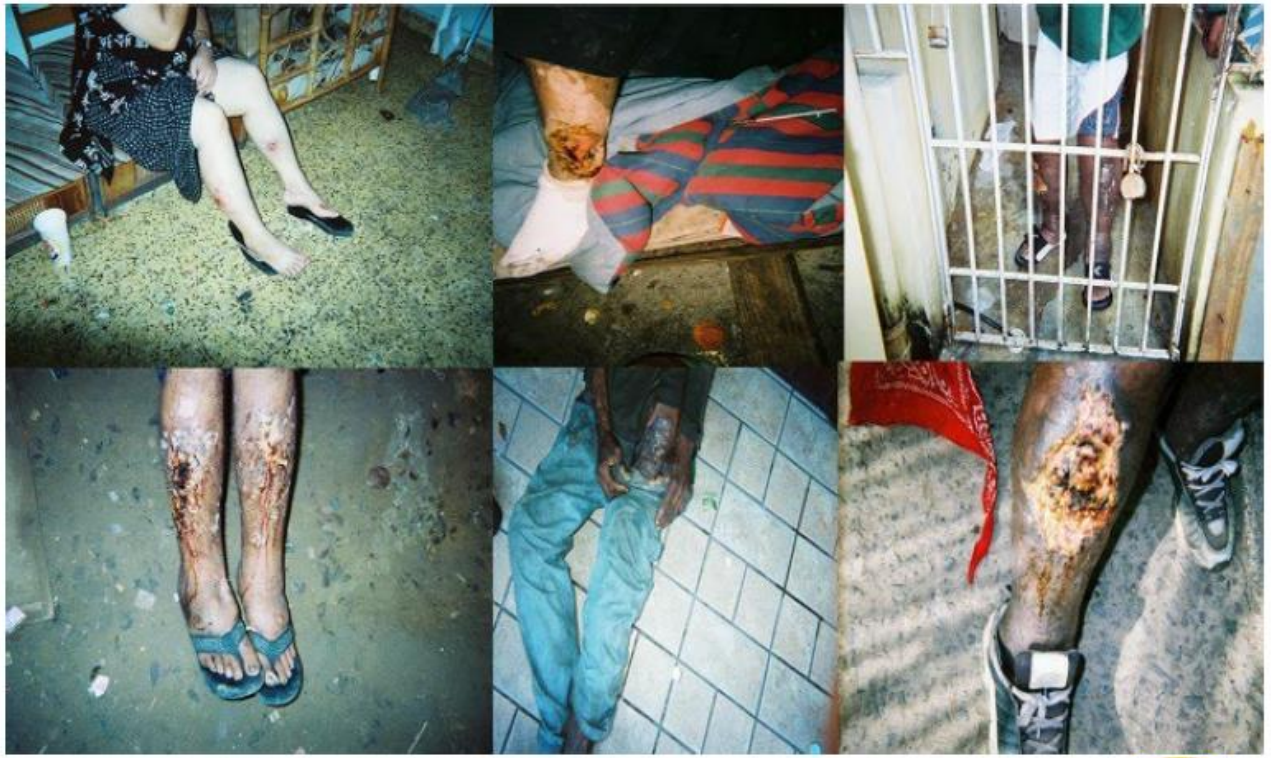
- Rapid onset within minutes
- Can last 8 hours or longer depending upon the dose, route, and whether it was mixed with an opioid or other drug(s)
- CNS depressant
  - Drowsiness
  - Amnesia
  - Slowed breathing and heart rate
  - Significant hypotension
  - Dry mouth
  - Loss of consciousness at higher doses
- When mixed with other substances
  - Complicates withdrawal
  - Intensifies effects, particularly with other CNS depressants

# Why Do People Use?

- Xylazine may extend or potentiate effects of fentanyl
- Unintentional use is common in patients seeking fentanyl or other powder substances

# Xylazine and tissue injury

- Xylazine use is associated with severe tissue injury
  - Injury can be at sites remote from injection site
  - Underlying cause is likely multi-factorial
    - Direct vasoconstriction and local tissue damage
    - Ischemic injury due to profound analgesic effect of drug (pressure sore and/or ischemic limb injury





Cureus 14(8) 2022 e28160

# Xylazine: What Clinicians Need to Know (New York State Department of Health)

- Toxicology:
  - Xylazine is **not included in routine immunoassay toxicology screens – requires GC or MS send out**
  - Even with appropriate testing, **xylazine may not be detected due to xylazine's rapid elimination from the body**, with a half-life of 23-50 minutes

- **Overdose Management:**
  - Naloxone should be administered for respiratory depression because xylazine and fentanyl are typically found together
  - Patient may breathe normally after receiving naloxone, but still be sedated from the xylazine.
  - Xylazine can potentiate the effects of other depressants, such as fentanyl and heroin.
  - No reversal agent
    - Supportive care
    - Rescue breathing
    - Blood pressure monitoring/management

# Withdrawal Management

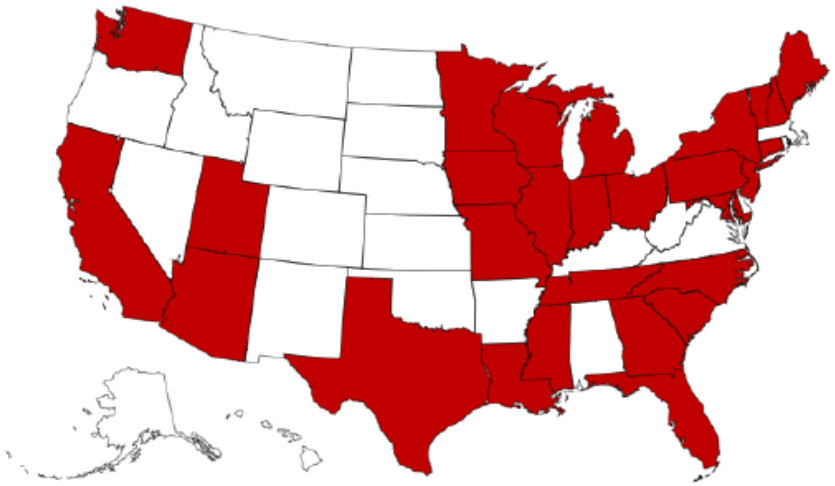
- Managing Withdrawal:
  - Benzodiazepines and/or alpha-2 adrenergic agonists, clonidine, dexmedetomidine, tizanidine, guanfacine
  - Xylazine withdrawal is not a well-defined syndrome.
    - Anxiety, irritability, and restlessness.
    - Severe hypertension is also possible.
  - Concurrent management of opioid withdrawal often required.
    - Liberal use of medications for opioid withdrawal: no clear preferred agent
    - Mitigate symptoms that could further exacerbate the manifestations of xylazine withdrawal or lead to discharges against medical advice.

*Ehrman-Dupre et al. – Journal of Addiction Medicine 2022*

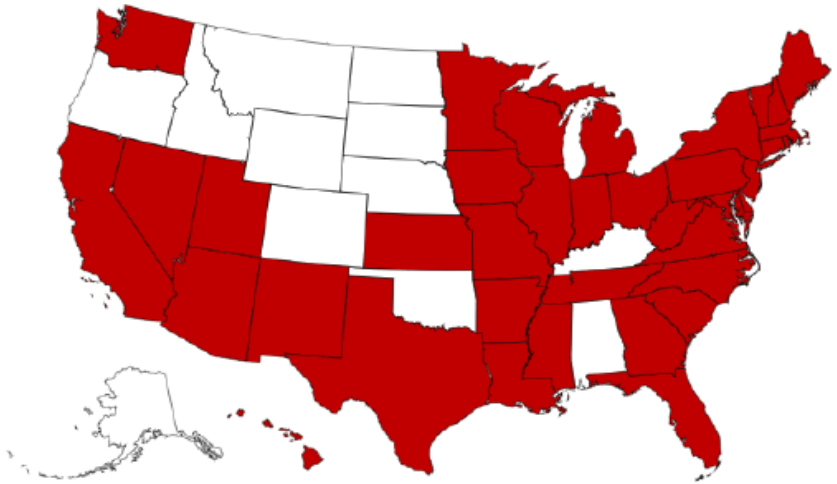
# Expansion of xylazine-involved deaths

Jan 2019

Jan 2020



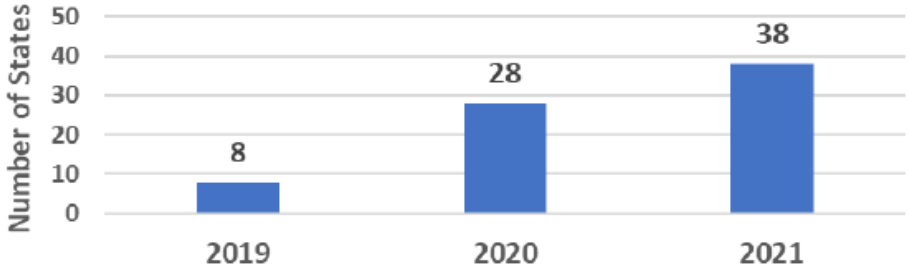
Jun 2021



Office of National Drug Control Policy

Kacinko, S. L., Mohr, A. L., Logan, B. K., & Barbieri, E. J. (2022). Xylazine: Pharmacology Review and Prevalence and Drug Combinations in Forensic Toxicology Casework. *Journal of Analytical Toxicology*, *46*(8), 911-917.

States with Xylazine-Involved Overdose Deaths, 2019-2021



# Local Trends – Washington State

- Xylazine has been identified in less than 1% of fentanyl-involved overdose deaths in 2021 and 2022.
- Xylazine is seen in much less than 1% of police evidence that has also tested positive for fentanyl in 2021 and 2022.
- These proportions are generally much lower than seen in recent years in the Eastern United States.

UW – ADAI Risks of the Unregulated Drug Market/Xylazine | Stopoverdose.org

# ToxIC Fentalog Study Group — Quarterly NPS Report

**CLINICAL** | **Q2 2023**

**PURPOSE:** This report provides new information regarding comprehensive drug testing of clinical toxicology specimens collected after suspected opioid overdoses in cities across the United States (U.S.).

**OVERVIEW:** Drug use can lead to adverse events and overdose scenarios where individuals present to emergency departments (EDs) for clinical evaluation and/or treatment. The culprit can be traditional drugs (e.g., heroin, fentanyl, cocaine, methamphetamine) or novel psychoactive substances (NPS); however, proper drug testing methodologies must be used for accurate identification and characterization. Street-level drug preparations can contain undeclared or unwanted substances (e.g., toxic adulterants or NPS) which can potentiate effects or lead to adverse reactions. Understanding emerging drug trends and drug testing results can help direct new or revised approaches to clinical treatment and harm reduction.

**OBJECTIVE:** A partnership between the American College of Medical Toxicology (ACMT) and the Center for Forensic Science Research and Education (CFSRE) was established to comprehensively assess the role and prevalence of synthetic opioids and other drugs among suspected overdose events in the U.S.

**SAMPLE SOURCE:** Patients presented to EDs within ACMT's Toxicology Investigators Consortium (ToxIC) experiencing a suspected opioid overdose. Residual, discarded biological samples were obtained for testing against an expansive library of drugs and other substances. Our findings provide a near real-time assessment of the drug market and allude to resulting implications on clinical institutions.

**TOXICOLOGY TESTING:** Analysis was performed via liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS). The scope of testing targeted more than 1,000 drugs, including a vast majority of NPS and metabolites. Drug classes included opioids, benzodiazepines, cannabinoids, stimulants, and hallucinogens, among other drugs.

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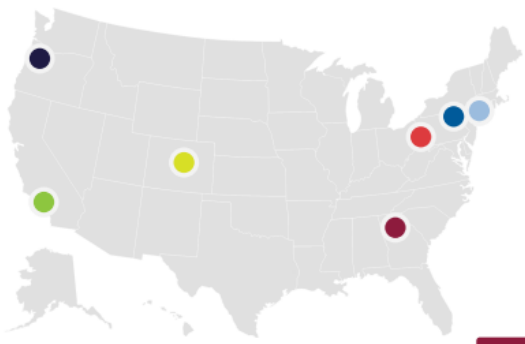
**SUGGESTED CITATION:** Manini et al. (2023) ToxIC *Fentalog Study Group — Quarterly NPS Report Q2 2023* Center for Forensic Science Research and Education, United States.



**NEW CLINICAL SITES!**

Atlanta, GA & Denver, CO

## PORTLAND, OR

- 100% positive for at least one opioid
- Fentanyl (56%) commonly detected, followed by heroin (22%)
- Opioid and stimulant use commonly detected (67%); opioid and benzodiazepine use also common (44%)
- *Note: Xylazine and Fluorofentanyl not detected*
- **NPS: Clonazolam (11%)**

## BETHLEHEM, PA

- 75% positive for at least one opioid
- Fentanyl (63%) only traditional opioid
- Opioid and stimulant (25%) and opioid and benzodiazepine (25%) use observed
- Xylazine found alongside fentanyl (25%)
- **NPS: Bromazolam (25%), *N*-Cyclohexyl Butylone (25%), *p*-Fluorofentanyl (13%), Flubromazepam (13%)**

## ATLANTA, GA

- 93% positive for at least one opioid
- Fentanyl (83%) commonly detected, followed by oxycodone (10%) & heroin (7%)
- Opioid and stimulant use common (54%); opioid and benzodiazepine use (27%)
- Xylazine found alongside fentanyl (12%)
- **NPS: Flualprazolam (15%), *p*-Fluorofentanyl (12%), Metonitazene (9.7%), Eutylone (9.7%), Brorphine (7.3%), Bromazolam (4.9%), *N,N*-Dimethylpentylone (2.4%)**

## DENVER, CO

- 90% positive for at least one opioid
- Fentanyl (76%) commonly detected, followed by oxycodone (23%)
- Opioid and stimulant use very commonly observed (76%); followed by opioid and benzodiazepine use (31%)
- *Note: Xylazine not detected*
- **NPS: *N*-Cyclohexyl Butylone (8%), *p*-Fluorofentanyl (6%), Bromazolam (2%)**

## NEW YORK, NY

- 82% positive for at least one opioid
- Fentanyl (73%) most commonly detected, followed by methadone (14%)
- Opioid and stimulant use (37%) and opioid and benzodiazepine (27%) use observed
- Xylazine found alongside fentanyl (26%)
- **NPS: *p*-Fluorofentanyl (8%), Bromazolam (8.2%), Flubromazepam (6.8%), Clonazolam (2.7%), Etizolam (1.4%)**

## LOS ANGELES, CA

- 88% positive for at least one opioid
- Fentanyl (80%) commonly detected
- Opioid and stimulant use commonly observed (70%); while opioid and benzodiazepine use less common (25%)
- *Note: Xylazine not detected*
- **NPS: *p*-Fluorofentanyl (15%), Bromazolam (5%), Flualprazolam (2.5%), Clonazolam (2.5%), *N,N*-Dimethylpentylone (2.5%), Metonitazene (2.5%)**

## PITTSBURGH, PA

- 90% positive for at least one opioid
- Fentanyl (88%) most commonly detected, followed by methadone (13%)
- Opioid and stimulant (33%) and opioid and benzodiazepine (23%) use observed
- Xylazine found alongside fentanyl (45%)
- **NPS: Bromazolam (10%), *p*-Fluorofentanyl (8%), Clonazolam (5%), Etizolam (2.5%), *N*-Desethyl Isotonitazene (2.5%)**

cfsre | NPS DISCOVERY

ACMT American College of Medical Toxicology

ToxIC Toxicology Investigators Consortium

# Xylazine: What Clinicians Need to Know (New York State Department of Health)

- **Harm Reduction Messages**:
  - Educate patients about xylazine in the illicit drug supply and ask about atypical wounds.
  - Providers should be aware of the heightened risk of skin and soft tissue wounds
    - Injection:  use sterile syringes, swab area with alcohol prior to injecting, rotate injection site, and avoid injecting into wounds
    - Try to avoid using alone. If you are using alone, double down on other strategies. Have someone check on you.
    - If you are using in a group, stagger your use so someone is always alert. Carry naloxone and know how to use it. Look out for each other. Call 911, be aware that a xylazine overdose may need more care than naloxone.
    - Go slow. Use less. Sniffing or smoking is probably safer than injecting.
    - Because of the heavy sedation, be aware of your surroundings and your possessions, especially if you're somewhere that's not secure. Be sure the airway is open, as breathing may be blocked in slumped positions.

# Resources


- 2023_Q2_Clinical_ToxIC_Fentalog_Study_Group_Quarterly_NPS_Report.pdf (cfsre.org)

- Xylazine: What Clinicians Need to Know (ny.gov)
- *Friedman, J., Montero, F., Bourgois, P., Wahbi, R., Dye, D., Goodman-Meza, D., & Shover, C. (2022). Xylazine spreads across the US: A growing component of the increasingly synthetic and polysubstance overdose crisis. Drug and alcohol dependence, 233, 109380.*
- *Reyes JC, Negrón JL, Colón HM, et al. The emerging of xylazine as a new drug of abuse and its health consequences among drug users in Puerto Rico. J Urban Health Bull N Y Acad Med. 2012;89(3).*
- *Ehrman-Dupre, R., Kaigh, C., Salzman, M., Haroz, R., Peterson, L. K., & Schmidt, R. (2022). Management of Xylazine Withdrawal in a Hospitalized Patient: A Case Report. Journal of addiction medicine, 16(5), 595–*
- *Kariisa M, Patel P, Smith H, Bitting J. Notes from the Field: Xylazine Detection and Involvement in Drug Overdose Deaths — United States, 2019. MMWR Morb Mortal Wkly Rep 2021; 70:1300–1302.*