



Center on
Rural Addiction
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Rural Addiction**
UNIVERSITY OF VERMONT

Community Rounds Workshop Series

Illicit Drug Supply 2023: Fentanyl and Xylazine

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Disclosures

There is nothing to disclose for this UVM CORA Community Rounds session.

Potential Conflict of Interest:

All potential conflicts of Interest have been resolved prior to the start of this program.

All recommendations involving clinical medicine made during this talk were based on evidence that is accepted within the profession of medicine as adequate justification for their indications and contraindications in the care of patients.

This activity is free from any commercial support.



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INTERPROFESSIONAL CONTINUING EDUCATION

Objectives

- Describe the current status of adulterants fentanyl and xylazine in the drug supply
- Discuss specific effects of these agents
- Outline interventions such as harm reduction and drug checking
- Discuss how adulterants affect members of rural populations

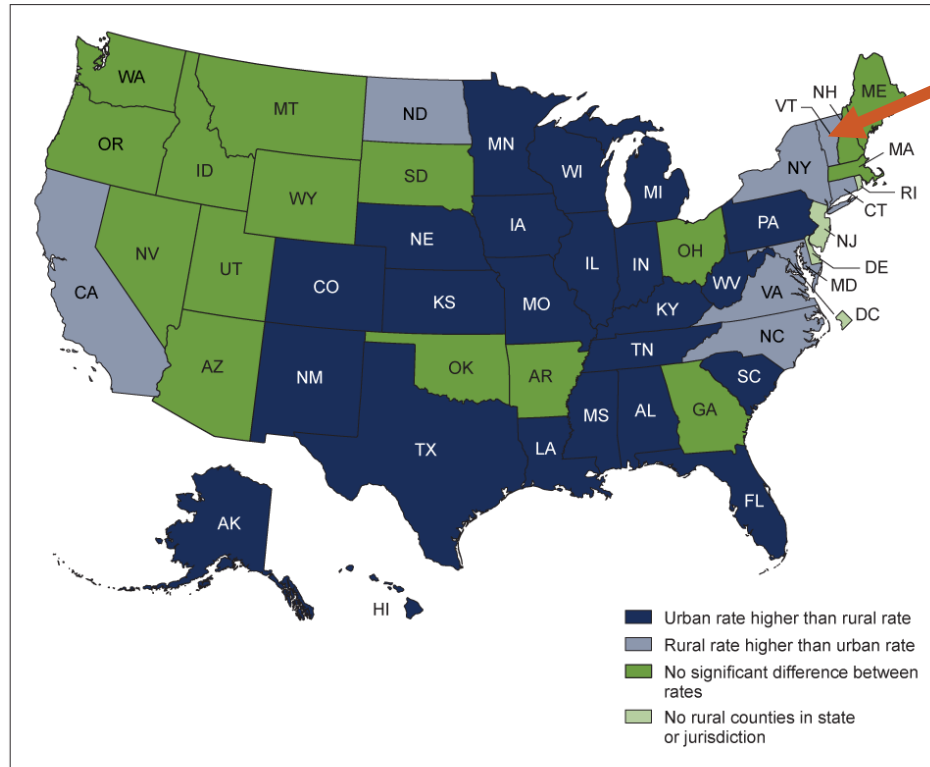


Drug Overdose Deaths* Continue to Increase in 2021

	ALL DRUGS	HEROIN	NAT & SEMI SYNTHETIC	METHADONE	SYNTHETIC OPIOIDS (mainly illicit fentanyl)	COCAINE	OTHER PSYCHO-STIMULANTS (mainly meth)
11/2020*	92,366	13,698	13,667	3,593	56,595	19,953	23,894
5/2021	101,075	11,633	13,909	3,802	64,871	21,235	28,890
11/2021*	106,854	9,504	13,643	3,619	70,420	23,908	32,476
Percent Change 11/20-11/21	15.7%	-30.6%	-0.2%	0.7%	24.4%	19.8%	36.0%

*NCHS Provisional drug-involved overdose death counts are PREDICTED VALUES, 12 months ending in select months.

Figure 4. Urban–rural differences in age-adjusted rates of drug overdose deaths, by jurisdiction of residence: United States, 2020



NOTES: Drug overdose deaths were identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Age-adjusted death rates were calculated using the direct method and the 2000 U.S. standard population. Decedent's county of residence was classified as urban or rural based on the 2013 NCHS Urban–Rural Classification Scheme for Counties. Access data table for Figure 4 at: <https://www.cdc.gov/nchs/data/databriefs/db440-tables.pdf#4>.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality.

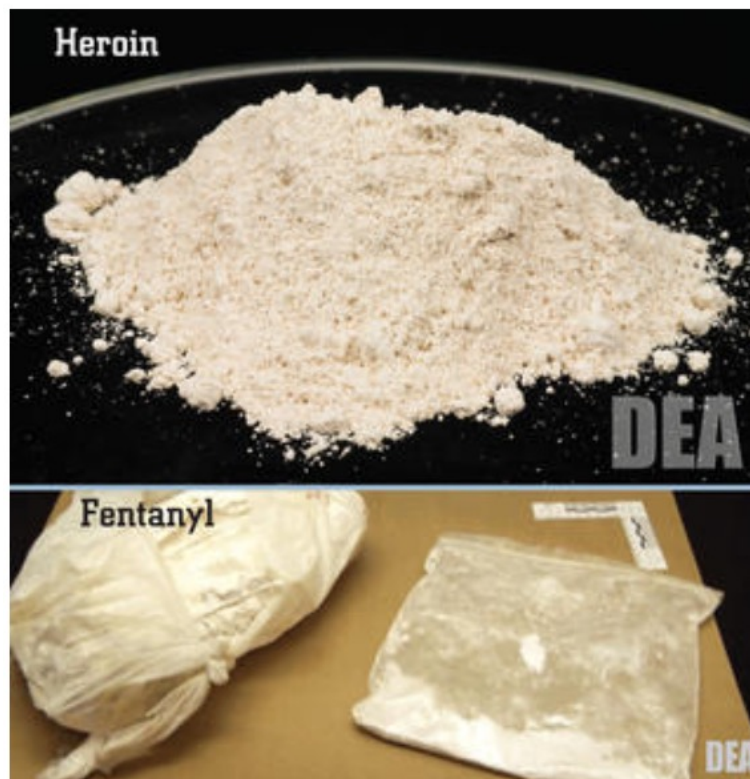


2022 Opioid-Related Vermont Overdose Fatalities - by Month & Substances

Month	Rx Opioids	Heroin	Fentanyl	Total
January	9	0	19	23
February	2	1	13	14
March	1	1	11	12
April	3	4	19	20
May	1	4	14	15
June	3	1	16	16
July	3	2	28	29
August	8	4	22	23
September	3	2	15	16
October				
November				
December				
Total	33	19	157	168

Fentanyl

Fentanyl and heroin



A lethal dose





Overdose and Origins

- From May 2020 to April 2021 more than 100,000 Americans died for a drug overdose.
- 64% of these deaths were due to synthetic opioids like fentanyl.
- Fentanyl is synthesized in China, Mexico and, India and exported to The U.S. as a powder or pressed in pills.
- Fentanyl can be purchased on the dark web and delivered through traditional delivery services including the U.S Postal Service.





The images of legitimate and fake pills are examples and do not represent the many variations of fake pills. Never trust your own eyes to determine if a pill is legitimate. The only safe medications are ones prescribed by a trusted medical professional and dispensed by a licensed pharmacist.



Fake “Oxys” M30s



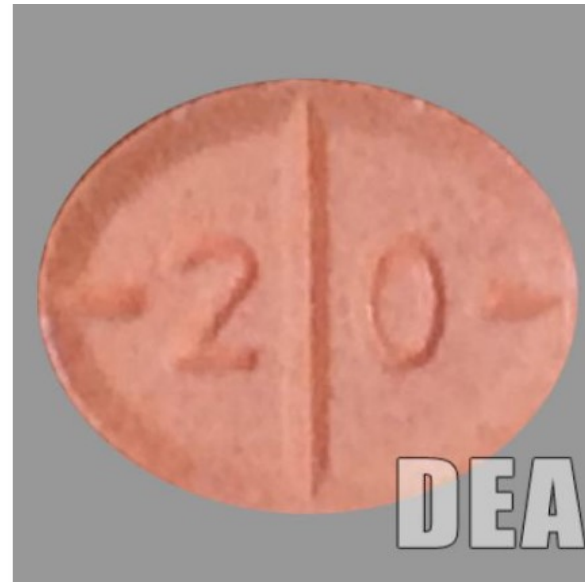
Rainbow fentanyl

Rainbow Fentanyl: A Dangerous Trend

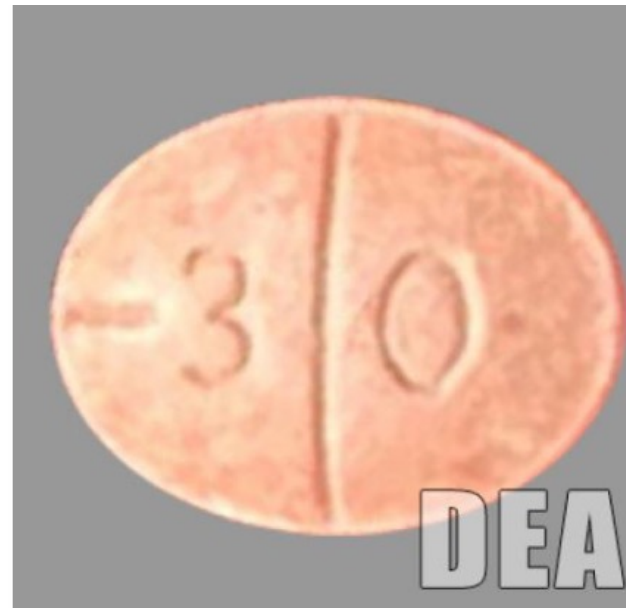
Sep 27, 2022



Authentic Adderall



Fake Adderall





Overdose Risk and Prevention

- Fentanyl is sold both alone and as an adulterant to allow trafficking of smaller quantities but with no reduction in drug effect.
- Small quantities of fentanyl can be deadly and especially if the user is not aware of the presence of fentanyl.
- Preventing overdose can be helped by distributing naloxone, increasing availability effective treatment such as methadone and buprenorphine, lowering barriers to treatment, and providing fentanyl test strips.





Guidance on Handling the Increasing Prevalence of Drugs
Adulterated or Laced with Fentanyl
2021, National Council for Mental Wellbeing





The Fentanyl Problem

- Fentanyl and its analogs are the primary drivers of death in the opioid overdose crisis.
- Fentanyl can be used knowingly or unknowingly.
- It has been pressed into counterfeit pills mimicking prescription medicines.
- It is 50 times stronger than heroin.
- Unintended use, particularly by people with no or low opioid tolerance, has resulted in a spike in drug overdose deaths.



The Fentanyl Problem

- Overdose can occur by ingestion, injection, or inhalation.
- Overdose by fentanyl can not occur by exposure through skin.
- Reversal of fentanyl overdose may require repeated doses of naloxone.
- This paper offers recommendations for remediating the impact of fentanyl.





Four Principles to Address the Fentanyl Crisis

1. Pursue an incremental approach to behavior change (that is, harm reduction).
 - Goal is reducing risk vs abstinence.
 - Only 20%-30% are in the active stage of change.
2. Emphasize engagement.
 - Programs should offer whatever information or services the potential patient is open to receiving.
 - Encourage return for a follow-up visit.





Four Principles to Address the Fentanyl Crisis

3. Use integrated care to initiate engagement and treatment.
 - Medical settings and primary care are where initial screening and intervention may occur.
4. Be vigilant for fentanyl as the rule rather than the exception.
 - Clinical staff should assume the street drugs are contaminated with fentanyl and every overdose involves fentanyl.



Fentanyl in Rural Areas

There is less opportunity to use methadone as an alternative to buprenorphine, which can be challenging

Addressing Fentanyl in Rural Areas

- Prescribers need extra support and training (such as ECHO sessions)
- Develop options for mobile methadone

CORA Resource – Research Spotlight


Increased Fatal Overdoses Involving Stimulants and Fentanyl

uvmcora.org
Research Spotlight

The Problem: Overdoses Involving Both Stimulants and Fentanyl Are Rising

Over the past decade, drug overdose deaths involving psycho-stimulants have dramatically increased in rural U.S. counties¹ and opioids are involved in a growing proportion of stimulant (e.g., cocaine and methamphetamine) overdoses². Although the increase in overdoses involving both opioids and stimulants may be attributed to opioids adulterated with stimulants, as well as intentional stimulant use among people who use opioids, recent reports suggest that fentanyl is increasingly present as a contaminant in illicit stimulants.^{2,3}

A 2022 examination of National Poison Control data found a 374% increase in the proportion of fentanyl poisoning reports involving cocaine (1.5% in 2015; 7.3% in 2021), as well as a 669% increase in the proportion of fentanyl poisonings involving methamphetamine (1.1% in 2015; 8.7% in 2021).⁴ These are consistent with a 2020 examination of national overdose rates, which showed significant recent increases in stimulant overdose deaths involving synthetic opioids (e.g., fentanyl) in non-metropolitan areas.⁵ Vermont has seen a dramatic increase in the number of deaths involving both cocaine and fentanyl (Figure 1), with 46% of all fatal opioid-related overdoses involving this combination in 2021.⁶ These data suggest that the contamination of illicit stimulants with fentanyl may be becoming more common and highlights the importance of harm reduction, especially in rural communities with limited emergency care access.

Interventions: Harm Reduction and Education

Fentanyl Test Strips. Traditionally promoted among people who use opioids, fentanyl test strips can detect the presence of fentanyl and many fentanyl analogs in a range of substances, including cocaine and methamphetamine, and are essential tools for reducing the risk of overdose. Knowing whether fentanyl is present allows people who use drugs to make informed choices about their use. Providing broad access to fentanyl test strips and promoting their correct and consistent use among people who use stimulants is increasingly important as contamination of illicit stimulants with fentanyl and associated overdoses increase.

Naloxone. Also traditionally promoted among people who use opioids, naloxone (intranasal or injectable) can be administered to reverse an opioid overdose and is an essential tool for people who use illicit stimulants as well as their friends and family members because of the risk of fentanyl-adulterated stimulants. Access to naloxone is critical in rural areas where distance, transportation, and other barriers might delay or limit access to medical care following an overdose.

Education is needed to ensure that people who use stimulants, first responders, and the larger community are aware of the risk of fentanyl-adulterated stimulants and the importance of harm reduction resources for overdose prevention and response.

For more information or to access these and other resources, please contact cora@uvm.edu.

¹Hedegaard H, Sporenc MR. Urban-rural differences in drug overdose death rates, 1999-2019. NCHS Data Brief, no 403. Hyattsville, MD: National Center for Health Statistics; 2021. DOI: <https://www.ncbi.nlm.nih.gov/doi/10.1562/0161-0289>

²Hoets et al. (2020). The rise in non-fatal and fatal overdoses involving stimulants with and without opioids in the United States. *Addiction*. 115(5): 946-958.

³Farrs et al. (2020). Fentanyl and fentanyl analogs in the illicit stimulant supply: Results from U.S. drug seizure data, 2011-2016. *Drug and Alcohol Dependence*. 218(3): 108416.

⁴Palamar et al. (2022). Trends in characteristics of fentanyl related poisonings in the United States. *American Journal of Drug Alcohol Abuse*. 15: 1-10.

⁵Vermont Department of Health (2022). Opioid-Related Fatal Overdoses Among Vermonters. Retrieved from: <https://www.healthvermont.gov/alcohol-drugs/reports/data-and-reports>.

This publication is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling \$17,032,587 with zero percentage financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, HRSA, HHS or the U.S. Government.



Figure 1. Number and percent of Vermont fatal overdoses involving the combination of cocaine and fentanyl, 2010-2021.⁶

Year	# of Overdoses (Left Axis)	% of Overdoses (Right Axis)
2010	1	0%
2011	0	0%
2012	0	0%
2013	3	0%
2014	4	0%
2015	3	0%
2016	6	0%
2017	24	0%
2018	42	0%
2019	44	0%
2020	50	0%
2021	93	46%

Find *Increased Fatal Overdoses Involving Stimulants and Fentanyl* at:

uvmcora.org/resources




Testing for Fentanyl

- Fentanyl test strips (FTS) can detect the presence of fentanyl in drug samples.
- FTS cost is \$1.00 per strip.
- Testing is 96% accurate and can detect at least 10 fentanyl analogs.
- The legality of FTS varies from state to state (some states view FTS as illegal drug paraphernalia).



Testing for Fentanyl

- One study of FTS found 85% of people using illicit drugs wanted to know about the presence of fentanyl.
 - Positive changes as a result of tests included:
 - Using a smaller dose.
 - Snorting instead of injecting.
 - Pushing the syringe plunger more slowly to gradually assess drug effect.
 - Having naloxone nearby.
 - Not using the drug.
 - Not using alone.
 - There is no evidence that use of FTS has a permissive effect on promoting drug use.
- 

CORA Supplies

To request fentanyl test strips and fentanyl test strip guides, email the Best Practices Core at:

cora.bp@uvm.edu



The University of Vermont Center on Rural Addiction Fentanyl Test Strips User Guide

Methamphetamine or MDMA

For Step 1 If testing MDMA or methamphetamine:

Put small amount of residue in about half a cup of water. **Sample MUST be heavily diluted for most accurate results!** Then follow Steps 2-5

Heroin or injectable substances

For Step 1 If testing heroin or anything you inject:

Prepare shot as normal in UNUSED cooker, draw up into your syringe, and then add ¼ inch of clean water to the residue in the cooker. Then follow Steps 2-5

Pills or substance to be snorted

For Step 1 If testing pills or anything you snort:

Put a small chip of the pill or a very small pinch of powder into an UNUSED cooker and add ¼ inch of clean water. Then follow Steps 2-5

Tips for safer use

- Don't mix substances
- Try a small test amount first
- Don't use alone
- Know the signs of an overdose and carry naloxone

Use sterile supplies, to find a SSP near you go to www.nasen.org

Tips for safer use

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All drug use carries inherent risks. Call 911 if you suspect an overdose.

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1 Add sterile rinse water to cooker or empty baggie

2 Dip test strip in water, don't go past first line and hold in water for 10-15 sec

3 Place on sterile surface or across top of cooker

4 Wait for results for 1 min

5 Interpret the results

POSITIVE: one line
product contains fentanyl

NEGATIVE: two lines
MAY contain a fentanyl analogue or no fentanyl

POSITIVE: one line
product contains fentanyl

NEGATIVE: two lines
MAY contain a fentanyl analogue or no fentanyl

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POSITIVE: one line
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Fentanyl Test Strip Guide – wallet sized



Duhart Clarke SE, Kral AH, Zibbell JE. Consuming illicit opioids during a drug overdose epidemic: Illicit fentanyls, drug discernment, and the radical transformation of the illicit opioid market. *Int J Drug Policy*. 2022 Jan;99:103467. doi: 10.1016/j.drugpo.2021.103467. Epub 2021 Oct 15. PMID: 34662847; PMCID: PMC8755588.




Introduction

- Uncertainty of the presence of fentanyl in opioids has led to some safer practices among people who inject drugs (PWID).
 - Tester shots
 - Micro-dosing
 - Staggering injections with peers
 - Fentanyl test strips
- This qualitative study was to better understand how PWID came to recognize fentanyl by sight, taste, and subjective drug effects in order to prevent overdose.



Results: Physical Sensations

- The fentanyl high was described as much briefer (sometimes just minutes) compared to heroin (4 to 8 hours).
 - Many described fentanyl as “having no legs.”
 - “If you got something that lasts for more than 10 minutes (after the initial rush) you found some really amazing shit.”
 - “It wears off faster than heroin...so people use a lot more--every fucking 30 minutes to an hour.”
 - Fentanyl effects were described as being more like a sedative with tranquilizing effects and periods of unconsciousness.
- 



Results: Modifying Drug Preferences

- The prevalence of fentanyl has had the effect of altering drug consumption patterns and preferences particularly the increased use of stimulants.
- 72% reported smoking or injecting cocaine or crack.
- 44% reported using methamphetamine.
- Two approaches to stimulant use were reported:
 - Concurrent use in a single injection (speedball or goofball).
 - Sequential use in separate injections.





Results: Modifying Drug Preferences

- Participants reported the use of stimulants was related to the extreme sedative effect of fentanyl requiring a counteracting drug.
- “Yeah, as methamphetamine goes now, everybody calls it ice and it’s definitely out there. I would say 8 of 10 people that inject heroin love to do ice because it’s a speedball...Me personally, I like to rush off one and then I wait a while and I like the rush of the other.”
- “...the meth is going to keep you awake, which is important when using fentanyl, since what overdoses you is that you fall asleep and then you stop breathing...”





Results: Changing Patterns of Drug Consumption

- All reported using opioids more frequently because of fentanyl's short high.
- The higher number of daily injections resulted in physical harm.
 - “The fact I have to inject more is tearing my veins up. I'm losing sensation in fingers; my legs swell now because I'm using the veins in my legs.”
- Some who used opioids and stimulant reported smoking the stimulant to save their veins for injecting opioids.
- Some switched from injecting to smoking or sniffing opioids also.



Discussion

- The strong rush and short high reported is consistent with fentanyl's pharmacologic profile as a synthetic opioid with high lipophilicity resulting in a rapid onset of action and short duration of effect.
- The higher frequency of injection increases the number of times per day people are exposed to blood-borne pathogens (e.g., HIV/HCV).
- Mounting evidence that stimulants are used to manage fentanyl-induced sedation suggests that overdose deaths involving fentanyl and stimulants are largely due to intentional mixing rather than an adulterated supply.



Trecki J, Gerona RR, Ellison R, Thomas C, Mileusnic-Polchan D. *Notes from the Field: Increased Incidence of Fentanyl-Related Deaths Involving Para-fluorofentanyl or Metonitazene — Knox County, Tennessee, November 2020–August 2021*. MMWR Morb Mortal Wkly Rep 2022;71:153–155.

DOI: <http://dx.doi.org/10.15585/mmwr.mm7104a3>





New Fentanyl Compounds

- Other fentanyl compounds are appearing in heroin, counterfeit pills and in autopsy findings.
- Para-fluorofentanyl was developed through research efforts in the 1960's and classified as a schedule I substance.
- Para-fluorofentanyl is showing up now in seized heroin, counterfeit pills, and autopsy findings.
- Carfentanil (100 times more potent than fentanyl) has been reported in a very few cases in the Midwest.



New Opioid Class

- Benzimidazole was developed in the 1950's as a new opioid analgesic and is now showing up as a heroin adulterant.
- Metonitazene, an opioid in the benzimidazole class, is also showing up more frequently.



Xylazine



Use of Xylazine in veterinary medicine

Xylazine and its antidote Tolazoline is an essential tool universally used by veterinarians who work on livestock. Many surgical procedures would not be possible or would be inhumane without such a short-term sedative/analgesic. It is extremely effective for bovine, sheep and goats. Administered intravenously or intramuscularly by a veterinarian Xylazine is a systemic anesthetic lasting about an hour. The reversing drug Tolazoline is used to reverse xylazine effects.





Xylazine – Pharmacology/Clinical Effects

Alpha-2 adrenergic agonist that stimulates central alpha-2 receptors

- Sedation
- CNS DEPRESSION - No effect on respiratory rate, blunted response to airway occlusion similar to other sedatives, synergistic effect with opioids
- Similar effects to imidazoline compounds such as clonidine, dexmedetomidine, oxymetazoline, tetrahydrozoline, tizanidine, and lofexidine

Clinical Effects

- Major clinical effect is profound sedation
- Imidazoline receptor activity → hypotension/bradycardia
- Pharmacokinetics • Typical anesthesia dose ranges (0.2-1 mg/kg IM or IV)
- Time to effect is a 1-2 minutes
- Duration of drug effect up to 4 hours



Xylazine has been studied in humans for its potential use as an analgesic, hypnotic, and anesthetic, but these clinical trials were terminated due to **its severe hypotension and central nervous system depressant effects.**



Xylazine information from NIDA

- Also known as “tranq,”⁵ xylazine is a central nervous system depressant that can cause drowsiness and amnesia and slow breathing, heart rate, and blood pressure to dangerously low levels.^{6,7} Taking opioids in combination with xylazine and other central nervous system depressants—like alcohol or benzodiazepines increases the risk of life-threatening overdose.

“For veterinary use only”



“For horses and cervidae”



Widespread Distribution of Xylazine Detected Throughout the United States in Healthcare Patient Samples.

- Holt, Andrew C. PharmD; Schwoppe, David M. PhD; Le, Kathy PharmD; Schrecker, Joshua P. PharmD; Heltsley, Rebecca PhD. *Journal of Addiction Medicine* ():10.1097, January 6, 2023.

Xylazine-related deaths are being increasingly identified in rural states.

- Sibbesen J, Abate MA, Dai Z, Smith GS, Lundstrom E, Kraner JC, Mock AR. Characteristics of xylazine-related deaths in West Virginia—Xylazine-related deaths. *The American Journal on Addictions*. Doi: 10.1111/ajad.13365, December 12, 2022.
- Vermont Department of Health. Xylazine involvement in fatal opioid overdoses among Vermont residents (2021). Available at:<https://www.healthvermont.gov/sites/default/files/documents/pdf/ADAP-XylazineBrief.pdf>. Accessed July 8, 2022.

Conclusions


- Xylazine is geographically spread throughout the United States, indicative of a wide incorporation into the illicit drug supply. These samples originated from healthcare providers in routine care settings, where other reports typically involve overdose deaths.
- Routine testing for xylazine in outpatient settings can afford providers the opportunity to educate individuals and adjust harm reduction measures to potentially mitigate overdose risk.



Alexander RS, Canver BR, Sue KL, Morford KL. Xylazine and Overdoses: Trends, Concerns, and Recommendations. Am J Public Health. 2022 Aug;112(8):1212-1216. doi: 10.2105/AJPH.2022.306881. PMID: 35830662; PMCID: PMC9342814.



CORA Resource – Research Spotlight


Research Spotlight

uvmcora.org

Increasing Prevalence of Xylazine in Fatal Opioid Overdoses

The Problem: *A Growing Number of Overdoses Involve Xylazine and Require Emergency Medical Care*

The drug supply in the United States is increasingly adulterated with synthetic opioids (e.g., fentanyl) and other toxic substances that can increase the risk of fatal overdose. One such substance is xylazine, a veterinary tranquilizer that can cause skin ulcers and abscesses as well as more serious symptoms like respiratory depression, slowed heart rate, and hypotension in humans.¹ Xylazine is often found in combination with fentanyl.² In fact, fentanyl is involved in nearly all fatal overdoses where xylazine is present.³ Xylazine was first identified as a drug supply adulterant in Puerto Rico and is now widespread across the United States.² The presence of xylazine in fatal overdoses increased from <1% in 2015 to 7% in 2020 across 10 regions, with rates in some areas >25%.¹ In Vermont, the presence of xylazine in overdoses has increased dramatically since 2020, with xylazine present in 30% of fatal opioid overdoses in the first quarter of 2022 (Figure 1).⁴ Xylazine is a risk for people who use opioids as it is not detected by fentanyl test strips and, because xylazine is not an opioid, naloxone may not be as effective in reversing an overdose when xylazine is present. However, naloxone should still be administered to reverse the effects of fentanyl, which is likely to be the primary cause of overdose. Emergency medical care, including respiratory and cardiovascular support, is also critical when xylazine is involved or suspected in an overdose.²

The Implications: *Education is Needed to Ensure that People Receive Necessary Medical Care*

In response to the increasing prevalence of xylazine, educational efforts are needed to ensure that people who use drugs and those who respond to overdoses are aware of its risks, the potential limitations of naloxone's efficacy reversing overdoses, and the importance of emergency medical care in the case of overdose when xylazine is involved or suspected. These efforts are particularly important in rural communities where people may have less regular interaction with health care providers and be less likely to seek medical care following an overdose due to transportation barriers, stigma, and other factors. Drug checking services, which are not currently widely available in the United States, are a potential future intervention that could provide people who use drugs and their communities with valuable information about the drug supply. In other countries, these services have been shown to influence the intentions and behavior of people who use drugs, allowing them to make informed choices and potentially reducing harm.⁵

For more information, please contact cora@uvm.edu.

¹ National Institute on Drug Abuse. Research Topics: Xylazine. Available at: <https://nida.nih.gov/research-topics/xylazine>. Accessed July 8, 2022.
² Karissa M et al. Notes from the field: Xylazine detection and involvement in drug overdose deaths United States (2019). MMWR Morbidity and Mortality Weekly Report. 70:3300-3302.
³ Friedman J et al. Xylazine spreads across the US: A growing component of the increasingly synthetic and polysubstance overdose crisis (2022). Drug and Alcohol Dependence. 233:109380.
⁴ Vermont Department of Health. Xylazine involvement in fatal opioid overdoses among Vermont residents (2021). Available at: <https://www.healthvermont.gov/sites/default/files/documents/pdf/ADAP-XylazineBrief.pdf>. Accessed July 8, 2022. 2022 data were obtained via personal communication with the Vermont Department of Health.
⁵ Maghsoudi N et al. Drug checking services for people who use drugs: A systematic review (2022). Addiction. 117(3): 532-544.

This publication is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling \$13,699,254 with zero percentage financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS or the U.S. Government.

Year	Number of Overdoses	Percentage of Total Overdoses
2019	6	5%
2020	9	5%
2021	29	16%
2022 - Q1	18	30%

Find *Increasing Prevalence of Xylazine in Fatal Opioid Overdoses* at:

uvmcora.org/resources



Increasing presence of xylazine in heroin and/or fentanyl deaths, Philadelphia, Pennsylvania, 2010-2019. Inj Prev. (Johnson et al 2021)

- Xylazine is a non-opioid sedative, analgesic, and muscle relaxant used in veterinary medicine and not approved for human use.
- It has been found among people who use drugs in Puerto Rico since the early 2000s and referred to as “anestesia de caballo” (horse anesthetic).
- The Philadelphia Medical Examiner found xylazine in less than 2% of fatal heroin and/or fentanyl overdoses between 2010 and 2015 and an increase to 31% in 2019.

Xylazine in Rural Communities

Due to transportation barriers, stigma and other factors, people may have less regular interaction with health care providers and be less likely to seek medical care following an overdose

Wound Care

- Rural practitioners need training on identification of xylazine wounds and protocols for addressing them

Unfamiliar Characteristics of Overdoses

- Overdoses involving xylazine require breathing support; rural EMTs and first responders need training



Xylazine in Vermont – a Rural State

Xylazine Involvement in Vermont Opioid Overdose Deaths - 2022 (Jan-Sept)

Month	Total Opioid Overdose Deaths	Number of Opioid Overdose Deaths Involving Xylazine	Percent of Opioid Overdose Deaths with Xylazine
January	23	4	17%
February	14	7	50%
March	12	4	33%
April	20	4	20%
May	15	3	20%
June	16	4	25%
July	29	12	41%
August	23	5	23%
September	16	5	31%
Totals	168	48	28.57%



Xylazine in an overdose

In the event of a suspected xylazine overdose, experts recommend **giving the opioid overdose reversal medication naloxone** because xylazine is frequently combined with opioids. However, because xylazine is not an opioid, naloxone does not address the impact of xylazine on breathing.

Assistance with breathing can be useful in assisting with an overdose involving xylazine.



From a Massachusetts clinic

DID YOU KNOW? MASSACHUSETTS is seeing an increase of **XYLAZINE** in the drug supply.

WHY SHOULD I CARE? **NARCAN** DOES NOT WORK on **XYLAZINE**, because it is not an opiate.

WHAT DO I DO ABOUT IT? If someone OD's, give them Narcan **AND** **RESCUE BREATHS** **1 BREATH** every **5 SECONDS**

pay attention to getting a person's breathing started again, rather than giving lots of Narcan doses that might be ineffective.

xylozine causes breathing to slow down or stop (respiratory failure) so **GIVING RESCUE BREATHS** in between Narcan doses **IS NECESSARY!**

Xylazine effects

- In humans xylazine can cause hypotension, central nervous system depression, respiratory depression, and bradycardia.
- It also causes open skin ulcers among injectors who may continually inject affected areas for pain relief.



Treatment of Overdose, Withdrawal, and Wounds
Associated with Xylazine
(From D'Orazio 2022)



Much of the material presented here was adapted from a presentation of Joseph D’Orazio, MD, Department of Emergency Medicine, Director, Division of Medical Toxicology & Addiction Medicine, Lewis Katz School of Medicine.



Management of Xylazine Overdose

- Blunted response to hypoxia due to sedation – airway occlusion is problematic
 - Field management
 - Recovery position, airway maneuvers
 - ED Management
 - Airway monitoring/control, continuous pulse oximetry
- No antidotal therapy available or recommended
 - Yohimbine (alpha-2-antagonist) not recommended
 - Atipamezole not FDA approved drug
 - Naloxone?

The Recovery Position

Keep the Airway Clear



Stay with person. If you must leave them alone at any point, or if they are unconscious, put them in this position to keep airway clear and prevent choking.

Narcan or Narcan't?

- **“Narcan resistant overdose”** - Xylazine is not an opioid, so naloxone will not reverse xylazine
- Xylazine is almost always found in combination with fentanyl
- Naloxone should still be administered whenever an opioid-involved overdose is suspected

Naloxone (Narcan Nasal Spray)

- Indication for use
 - Apnea or cyanosis and decreased mental status in suspected opioid overdose (respiratory rate <8 bpm and PO₂ <92%)
- Bystander naloxone administration saves lives
 - Recovery position, rescue breathing, give second dose after 2-3 minutes if no improvement in breathing
 - Risk of overshoot and precipitating opioid withdrawal in patients with significant opioid dependence



Diagnostic Testing

- Not currently available as POC or urine immunoassay
- The detection of xylazine in (serum and urine):
 - Thin layer chromatography (TLC)
 - Gas chromatography mass spectrometry (GC-MS)
 - Liquid chromatography mass spectrometry (LC-MS)
- Rapidly eliminated from blood
 - 70% excreted in urine as major metabolite 2,6 xylidine



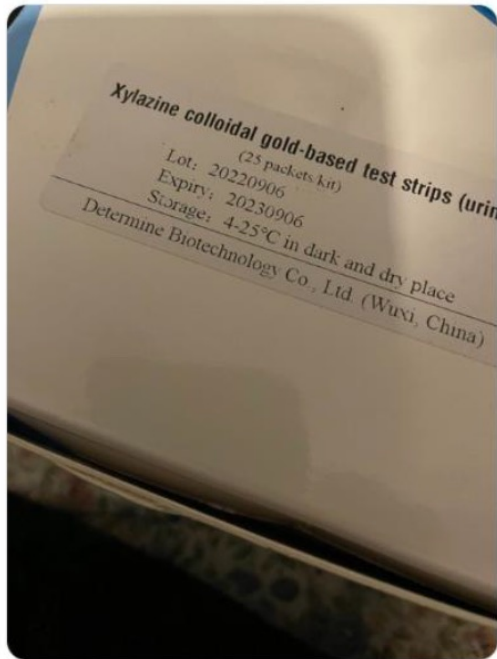
Test Code
4815B/U
Method
LC-MS/MS
Specimen Type
Blood or urine
Turnaround Time
8 days



Test Number	Test Name	Specimen Requirements	Reference Ranges	Stability	Rejection/References	CPT Code
6504	XYLAZINE URINE LCMS	At least 10 ml Urine (plastic urine container)	Cutoff: 5 ng/ml	Room temperature 8 days / Refrigerated 30 days / Frozen 6 months	Leaked in transit, improperly labeled	80375



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BTNX, the Canadian company that popularized fentanyl test strips, releases immunoassay test strip for xylazine



Xylazine Withdrawal

- Not a well-defined syndrome → experiential learning
 - Major symptom is anxiety
 - No severe VS abnormality or associated withdrawal seizures
 - Duration few days to a week
- Some corollary to clonidine and dexmedetomidine withdrawal
 - Hypertension, tachycardia, diaphoresis, anxiety, and agitation
- Overlap with opioid withdrawal syndrome
 - Anxiety, irritability, restlessness

Wesson & Ling, J Psychoactive Drugs, 2003 Apr-Jun;35(2):253-9.

COWS Clinical Opiate Withdrawal Scale

Endings	0 = Not at all 1 = Mild 2 = Moderate 3 = Severe	0 = Not at all 1 = Mild 2 = Moderate 3 = Severe	
1. Nausea	0 = None 1 = Mild 2 = Moderate 3 = Severe	4. Irritability	0 = None 1 = Mild 2 = Moderate 3 = Severe
2. Depressed affect	0 = None 1 = Mild 2 = Moderate 3 = Severe	5. Craving	0 = None 1 = Mild 2 = Moderate 3 = Severe
3. Retention of food	0 = None 1 = Mild 2 = Moderate 3 = Severe	6. Sweating	0 = None 1 = Mild 2 = Moderate 3 = Severe
4. Tremor	0 = None 1 = Mild 2 = Moderate 3 = Severe	7. Headache	0 = None 1 = Mild 2 = Moderate 3 = Severe
5. Anxiousness	0 = None 1 = Mild 2 = Moderate 3 = Severe	8. Total Score	0 = None 1 = Mild 2 = Moderate 3 = Severe

Score: 0-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal

Xylazine Withdrawal Treatment

- No data or evidence-based recommendations available for treatment
- Treat like sedative-hypnotic withdrawal (benzo/alcohol)
- First-line agents:
 - Benzodiazepines, dexmedetomidine, phenobarbital
- Adjunctive
 - Clonidine, tizanidine, lofexidine, gabapentin, antipsychotics
 - Ketamine?





Wounds

- Longstanding history of skin ulcers with injection drug use
Heroin → fentanyl → krokodil → cocaine → methamphetamine → xylazine

Potential Causes of Wounds from Injection Drug Use:

- Obliterative vasculitis from repetitive injection (“shooter’s patch”)
- Skin picking causing excoriations and ulcers
- Poor wound healing (various causes)
- Infectious
- Local effect from caustic agent extravasation (but wounds not always seen at site of injection)
- Compression ulcers
- Drug effect

Wound Treatments

- Cessation of injection
- Clean with soap/water, chlorhexidine, Dakin's Half Strength Solution, or 1% acetic acid
- Debridement (enzymatic → surgical)
- Antimicrobial coverage (Silver sulfadiazine cream, bacitracin ointment)
- Non-adherent and absorptive dressing
- Biodegradable Temporizing Matrix (BTM), skin grafting, epithelialization/complete closure
- Amputation



Infection Prevention Supplies from CORA

- Alcohol wipes
- Bandages
- Benzalkonium antiseptic wipes
- Gauze
- Gauze Roll
- Saline
- Medical tape
- Self-adhesive bandage wrap
- Triple antibiotic ointment



To request, email the Best Practices Core: cora.bp@uvm.edu



Questions?

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