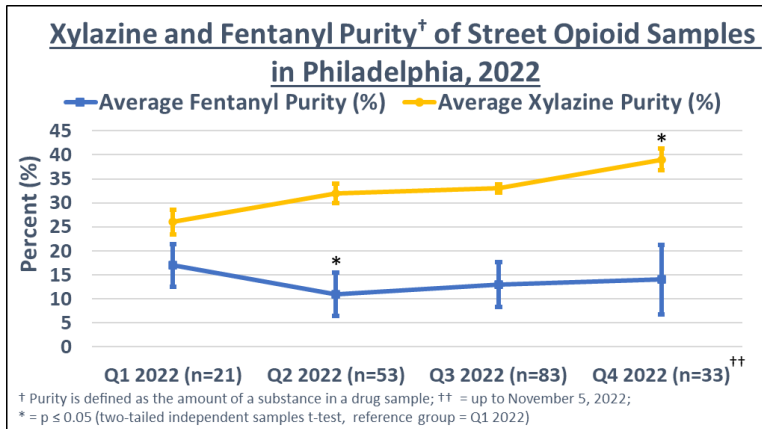


Health Update

Xylazine (tranq) exposure among people who use substances in Philadelphia December 8th, 2022



On November 8th, 2022, the U.S. Food and Drug Administration issued an [alert](#), warning health professionals about the presence of xylazine in the illicit drug supply. Xylazine is a non-opioid veterinary tranquilizer not approved for human use that is often added to street fentanyl to prolong its effects. First detected in Philadelphia in 2006, xylazine has been associated with increasing fatal overdoses and chronic wounds.¹ From 2015 to 2021, the number of fatal overdoses involving xylazine per year increased from 15 to 434.² Point of care testing for xylazine is not yet available, so people who use substances may not be aware that they have been exposed to xylazine.

Xylazine is an unscheduled drug and easily accessed. In 2021, 90% of street opioid samples contained xylazine. As fentanyl has overtaken heroin in Philadelphia, fentanyl is no longer considered an adulterant but is a primary composite, meaning that drugs sold as street opioids or “dope” are accepted to be fentanyl. Xylazine is now the most common adulterant in the drug supply. Drug checking of street opioids in 2022 revealed increasing xylazine, suggesting that xylazine is becoming more well established in the local illicit drug supply. (See graph) Thus, people who use illicit opioids in Philadelphia are almost certainly being exposed to xylazine. In March, 2022, the Philadelphia Department of Public Health released a [Health Alert](#) on the risks of xylazine use. Below is an update to guide xylazine-related clinical management.

Xylazine Withdrawal Management

When xylazine is abruptly stopped, severe withdrawal symptoms may develop that clinicians need to diagnose and manage. Opioid withdrawal symptoms not responsive to medications for opioid use disorder with associated hypertension, tachycardia, and/or anxiety should increase suspicion of co-occurring xylazine withdrawal. Laboratory testing is becoming available, but xylazine has a short half-life of 23-50 minutes and may not be present in urine samples even among routine users. Xylazine withdrawal can look like clonidine or dexmedetomidine “rebound”, characterized by sympathetic overactivity such as hypertension, anxiety, and jitteriness, and should be actively managed with high clinical suspicion even when laboratory tests are negative. Long-term symptoms may include insomnia, anxiety, and dysphoria. Treatment of xylazine withdrawal may require inpatient monitoring for vital sign instability.

SUMMARY POINTS

- People who use illicit opioids in Philadelphia are almost certainly being exposed to xylazine.
- Co-occurring xylazine and opioid withdrawal can be managed with alpha-2-adrenergic agonists and management of pain, insomnia, and anxiety.
- Xylazine increases risk of fatality associated with opioid overdoses and is not responsive to naloxone.
- Individuals who use xylazine may develop necrotic wounds that typically require debridement and may require medical management.
- Referrals to emergency departments and inpatient care for wound care should be accompanied with a plan to manage xylazine and opioid withdrawal.
- Harm reduction approaches can improve the health and well-being of people who use substances.

and benzodiazepine tapers. While no medication is FDA approved for xylazine withdrawal, the following approaches are being used:

Replacement therapy with alpha-2-adrenergic agonists:

- Clonidine
- Dexmedetomidine
- Tizanidine
- Guanfacine

Symptom management:

- Pain: short acting opioids, Ketamine, Gabapentin, Ketorolac, Acetaminophen, NSAIDs
- Insomnia: Trazadone, Quetiapine, Mirtazapine
- Anxiety: Hydroxyzine, Benzodiazepines (judiciously)

Treat opioid use disorder and opioid withdrawal:

- If a patient is on opioid agonist therapy, then split dosing can increase analgesic effect and improve pain control.
- If a patient is undergoing induction, then microdosing buprenorphine allows for concurrent use of short acting opioids that can improve pain control.

Increased Overdose Fatality Risk

Xylazine is an alpha-2-adrenergic agonist that acts centrally, producing profound sedation, bradycardia, and decreased perception of painful stimuli. Xylazine has synergistic toxic effects with opioids that increase risk of mental status depression and airway compromise. Naloxone should always be administered when there is suspicion for opioid overdose. Xylazine, however, is not reversed by naloxone, and there are no xylazine reversal agents that are safe for human use. Thus, individuals may remain heavily sedated due to xylazine after reversing respiratory depression due to fentanyl with naloxone. Overdose responders should continue to provide supportive care, such as airway management and supplemental oxygen, to patients with prolonged sedation in the presence of normal respirations.

Wound care

Xylazine use has been associated with necrotic skin wounds that can be progressive and extensive. Xylazine is thought to have partial alpha-1-adrenergic agonist activity that induces peripheral vasoconstriction leading to poor perfusion and necrosis. Wounds can occur at a site of injection as well as other locations, even when xylazine is smoked or snorted, which is not well understood. Wounds are associated with pain, which should be treated using with the multi-model symptom management approach described above. Care for xylazine-associated wounds typically requires debridement, long-term dressings [durable dressings], and an individualized follow-up plan based on access to clean water, housing status, access to medical supplies, comfort accessing healthcare, and comfort with self-care. Individuals may be declined from admission to inpatient behavioral health facilities due to xylazine-associated wounds, including those that are clinically evaluated to be self-manageable. The health department is working to increase the capacity of these settings for wound care.

Not all xylazine wounds require antibiotic treatment. If there is active purulence, surrounding erythema, or edema, antibiotics may be indicated. Antibiotic coverage should include methicillin-resistant *Staphylococcus aureus*, and there should also be a high suspicion for Group A Strep (*Streptococcus pyogenes*). Xylazine-associated wounds may also increase risk of systemic infections, such as bacteremia and endocarditis. Individuals with worsening wounds and/or signs of systemic infection, such as fevers, chills, rigors, nausea, and vomiting, should receive an evaluation for inpatient care. Referrals to emergency departments and inpatient care should be accompanied with a plan to manage xylazine and opioid withdrawal.

Harm Reduction

Individuals who are exposed to xylazine in Philadelphia are likely to be active substance users and providing care to manage complications of xylazine use requires not judging patients for engaging in substance

use. Stigma associated with substance use and shame associated with xylazine-associated wounds can lead to delays in care and worse health outcomes. It should be assumed that anyone injecting street purchased opioids is also using xylazine, however xylazine may also be smoked or snorted. Below are harm reduction approaches to improve the care of patients who use xylazine:

Wound care

- If someone is unable to regularly access hand washing, provide gloves and hand sanitizer for someone who will be caring for their own wounds.
- Provide individuals with the materials they need to take care of their wounds (individual saline, gauze, wraps, ointment).

Safer drug use

- Recommend avoiding injecting into wounds.
- Recommend swabbing skin with alcohol prior to injecting.
- If sniffing/snorting, recommend flushing nasal passages before and after using sterile water or saline.
- Provide sterile syringes using a needs-based model³ to prevent infections related to re-using and sharing.
- Provide patients with naloxone and provide training on how to administer naloxone.
- Provide patients with fentanyl test strips and provide training on how to use and interpret results.
- Recommend patients try not to use alone, and provide resources if that is what they are doing, such as:
 - o Never Use Alone: 800-484-3731 (English) | 800-928-5330 (Spanish)
 - o The Brave App – free to download on app stores

Resources

- [Xylazine web-based training](#) sponsored by the Pennsylvania Department of Drug & Alcohol Program and presented by [Savage Sisters Recovery](#). Instructions to access the training – [link](#).
- Learn how to get and use naloxone – www.phillynaloxone.com
- Get fentanyl test strips – <https://nextdistro.org/philly>
- Learn how to use fentanyl test strips
 - o <https://www.cdc.gov/stopoverdose/fentanyl/fentanyl-test-strips.html>
 - o <https://www.youtube.com/watch?v=GmhE6UOZ9YY>
- Substance Use Disorder Treatment
 - o Behavioral Health Services Initiative (uninsured): 1-215-546-1200
 - o Community Behavioral Health (Medicaid): 1-888-545-2600
 - o Care Connect Warmline: 484-278-1679
 - o National Helpline: 800-662-HELP (4357)

¹ Wong SC, Curtis JA, Wingert WE. Concurrent Detection of Heroin, Fentanyl, and Xylazine in Seven Drug-related Deaths Reported from the Philadelphia Medical Examiner's Office. Journal of forensic sciences. 2008 Mar;53(2):495-8.

² Philadelphia Department of Public Health. Unintentional Drug Overdose Fatalities in Philadelphia, 2021. CHART 2022; 7(3): 1-7

³ Centers for Disease Control and Prevention. Needs-Based Distribution at Syringe Services Program. December 2020.