

ECHO IDAHO

**Opioids, Pain and
Substance Use Disorders**

Xylazine

April 24, 2025

Cathy Oliphant, PharmD

Professor, Idaho State University

None of the planners or presenters for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



University of Idaho
School of Health and Medical
Professions



Learning Objectives

- Identify what xylazine is
- List the adverse effects of xylazine use
- Describe potential withdrawal treatment strategies
- Explain harm reduction strategies related to xylazine use

What is Xylazine?

- Non-opioid veterinary tranquilizer
 - Used for sedation, pain relief and muscle relaxation
 - Developed by the Bayer Corporation in 1962
- Not approved for use in humans
 - Misuse was initially detected in the early 2000s in Puerto Rico
- FDA approved for animal use only
- Not a controlled substance
- Available as:
 - Liquid solutions at 20, 100, and 300 mg/mL



Xylazine: Street Names

- Tranq
- Tranq dope
- Philly dope
- Sleep cut
- Zombie drug
- Anesthesia de caballo
- Rompun
- AnaSed

How does Xylazine Work?

- Alpha-2 adrenergic receptor agonist
 - Centrally:
 - Inhibit release of epinephrine and norepinephrine
 - This leads to hypotension, bradycardia, sedation, analgesia and muscle relaxation
 - Peripheral:
 - Vasoconstriction
- Same drug class as clonidine, lofexidine, and dexmedetomidine

Xylazine - Pharmacokinetics

** Lack of pharmacokinetic data in humans **

- Quickly absorbed
 - Effects are rapid (within minutes) and last for ≥ 8 hours
 - The 'high' can last up to 6 hours
- Large volume of distribution
- Rapidly metabolized by P450 enzymes
- Half-life = 23-50 minutes
- Excreted via kidney
- Doses that cause toxicity/death in humans range from 40 – 2400 mg

Xylazine Effects

- Profound sedation/loss of consciousness
- CNS depression
- Respiratory depression
- Hypotension
- Bradycardia
- Disorientation
- Hyperglycemia
- Hypothermia
- Skin wounds/necrosis
- Constricted ('pinpoint') pupils
- Dry mouth
- Amnesia

How is it Used?

- Almost always used in combination with other substances
 - Enhances and prolongs the effects of other agents
- Routes of administration
 - **Route of administration based on substance it is mixed with
 - Injection
 - Subcutaneous (SQ), intramuscular (IM) or intravenous (IV)
 - Insufflation (snorting)
 - Ingestion (swallowing)
 - Inhalation

Why is Xylazine so Dangerous?

- Xylazine is used to cut illegal drugs – fentanyl, heroin, benzodiazepines, cocaine, methamphetamine
- Extends the duration of co-substance(s) effect
- Often unknown agent in illicit substances
- No reversal agent
- Potent side effects
- Significant withdrawal

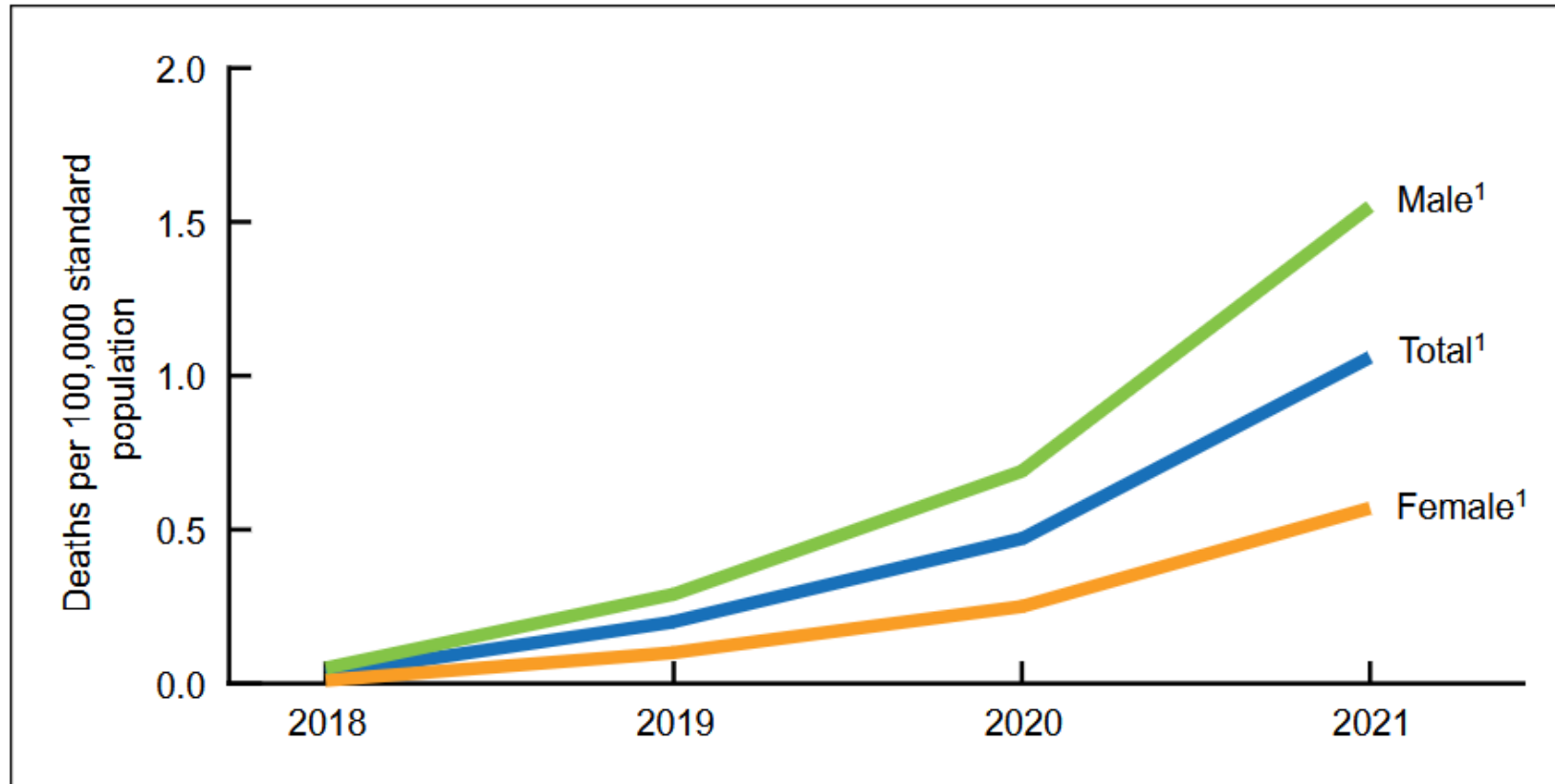


“Xylazine is making the deadliest drug threat our country has ever faced, fentanyl, even deadlier,” said Administrator Milgram. “DEA has seized xylazine and fentanyl mixtures in 48 of 50 States. The DEA Laboratory System is reporting that in 2022 approximately 23% of fentanyl powder and 7% of fentanyl pills seized by the DEA contained xylazine.”

How Common is Xylazine?

- Individuals may not be aware of the presence of xylazine in the substances they are using
- DEA has seized xylazine and fentanyl mixtures in 48 of 50 states
- DEA reported that ~ 23% of fentanyl powder and 7% of fentanyl pills in 2022
- White House declared fentanyl laced with xylazine an ‘emerging threat’ in April of 2023
- CDC reported that the monthly percent of fentanyl related deaths with xylazine increased 276% from Jan 2019 – June 2022

Figure 1. Age-adjusted rate of drug overdose deaths involving xylazine, by sex: United States, 2018–2021



¹Increasing trend from 2018 through 2021 ($p < 0.05$).

NOTES: Drug overdose deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the referent (listed) drug. Age-adjusted death rates were calculated using the direct method and adjusted to the 2000 U.S. standard population. When comparing rates across years, note that trends may be influenced by improvements in drug reporting. The reporting of at least one specific drug or drug class in the literal text, as identified by multiple cause-of-death codes T36–T50.8, improved from 92.0% of drug overdose deaths in 2018 to 95.2% in 2021.

SOURCE: National Center for Health Statistics, death certificate literal text from the National Vital Statistics System as of May 24, 2023.

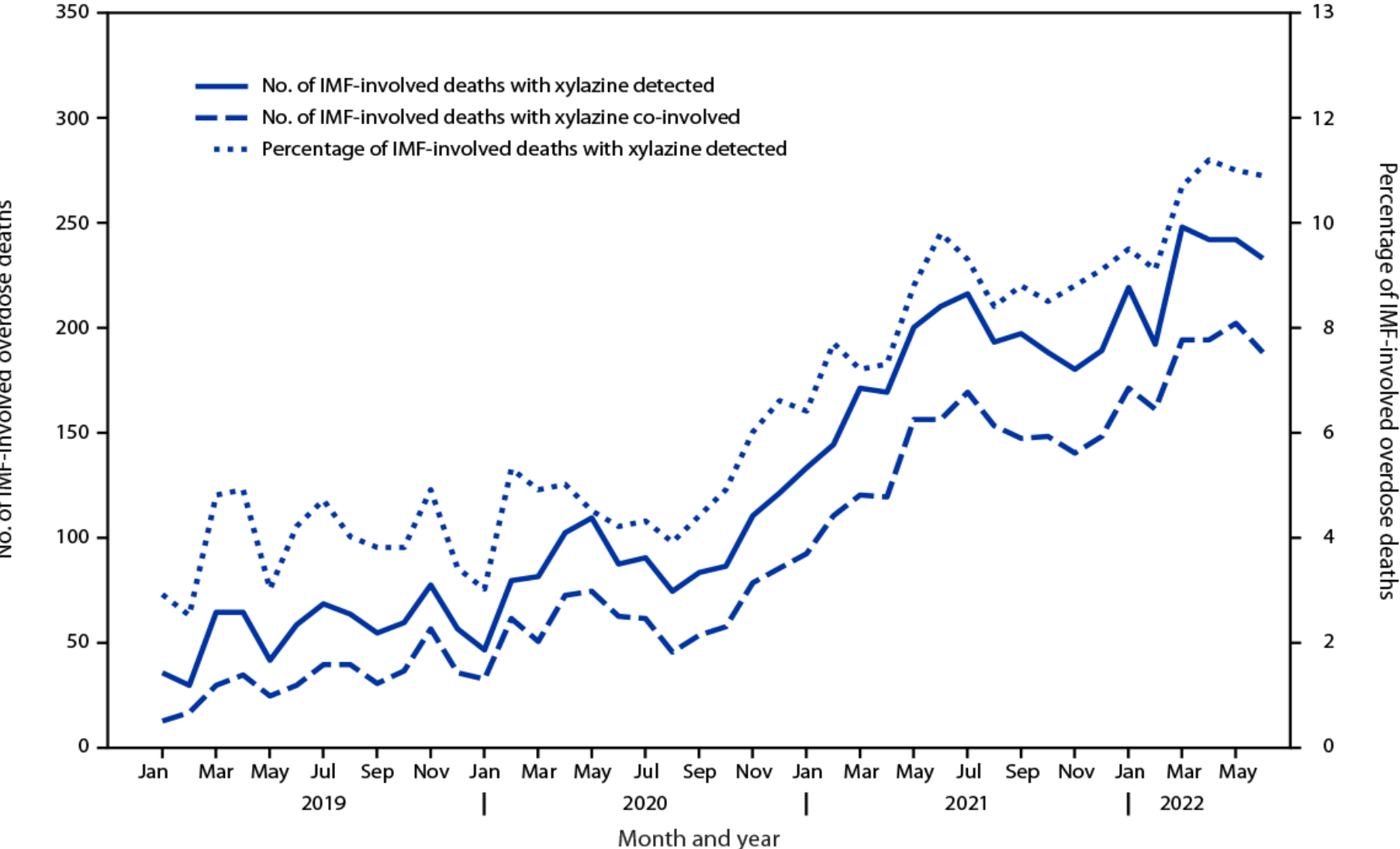
Table. Most frequent concomitant drugs for drug overdose deaths involving xylazine: United States, 2018–2021

Year	Referent drug	Number of drug overdose deaths involving referent drug	Most frequent concomitant drug		Second most frequent concomitant drug		Third most frequent concomitant drug	
			Concomitant drug	Number and percent of deaths involving both drugs	Concomitant drug	Number and percent of deaths involving both drugs	Concomitant drug	Number and percent of deaths involving both drugs
2021.	Xylazine	3,468	Fentanyl	3,437 (99.1)	Cocaine	1,216 (35.1)	Methamphetamine	652 (18.8)
2020.	Xylazine	1,499	Fentanyl	1,490 (99.4)	Cocaine	489 (32.6)	Methamphetamine	232 (15.5)
2019.	Xylazine	627	Fentanyl	621 (99.0)	Cocaine	194 (30.9)	Heroin	151 (24.1)
2018.	Xylazine	102	Fentanyl	99 (97.1)	Cocaine	41 (40.2)	Heroin	30 (29.4)

NOTES: Drug overdose deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to xylazine. Age-adjusted death rates were calculated using the direct method and adjusted to the 2000 U.S. standard population. When comparing rates across years, note that trends may be influenced by improvements in drug reporting. The reporting of at least one specific drug or drug class in the literal text, as identified by multiple cause-of-death codes T36–T50.8, improved from 92.0% of drug overdose deaths in 2018 to 95.2% in 2021.

SOURCE: National Center for Health Statistics, death certificate literal text from the National Vital Statistics System as of May 24, 2023.

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



https://www.cdc.gov/mmwr/volumes/72/wr/mm7226a4.htm#F1_down

Xylazine – Drug Screens

- Not included in routine screens or toxicology screens
- Short half-life of 20-50 minutes makes it difficult to detect due
- Urine drug testing is available from reference labs

Symptoms – Acute Toxicity

- Unresponsiveness/decreased consciousness
 - Falls
 - Hypothermia/Over-heated
 - Damage to muscles/nerves/organs due to restricted blood flow
- Hypotension
- Bradycardia
- CNS depression
- Respiratory depression
- Hyperglycemia

Management of an Overdose

- Give naloxone
 - Xylazine is often mixed with opioids
- Administer rescue breaths
 - Xylazine causes breathing to slow
- Call 911

** Consider xylazine in drug overdoses when the individual does not respond to naloxone

** No xylazine reversal agent

- Supportive care
- Airway management
- Supplemental oxygen
- Treat hypotension

Xylazine Withdrawal

- Potential for physiological dependence and withdrawal symptoms
- Withdrawal symptoms
 - Anxiety
 - Irritability, agitation, restlessness
 - Dysphoria
 - Hypertension, tachycardia
- Lack of standard treatment for xylazine withdrawal
 - Traditional MOUD are not effective for xylazine withdrawal symptoms
- The severity of symptoms may result in continued use

Personal Experiences With Xylazine and Behavior Change: A Qualitative Content Analysis of Reddit Posts

Negative personal experiences

“Better quit. I quit cold turkey 11 days ago from tranq dope, and I feel fantastic. Its not worth it. You will ruin yourself if you continue. There is no possible way to be functional on tranq. You will pass out constantly, you will be sore from bending over so far. It will hinder you from doing any normal activities with the ones you love. Say goodbye to a normal job, because you won't be able to stay awake long enough to work. Bite the bullet, deal with the withdrawals and never look back.”

“It's effects are so bad ...you pass out after a few minutes. Well, passing out or pouring sweat. People just don't understand how bad it is. It's terrible on the body, leading to faster rates of infections, heart, and kidney issues. It's similar to blood pressure meds. It's like Clonidine but 100× worse. Heavy, uncomfortable sedation, trouble breathing, nausea, dry mouth like sandpaper, uncomfortable physically at high doses like you've got weights on your bones and joints, it's like the worst, dirtiest, most dangerous high ever.”

Overdose experience

“I survived unintentional ODs. From a combination of Fentanyl, Heroin and Xylazine. It felt as if I went to sleep and just total darkness. No memory of anything. Each time I felt no pain, I had no knowledge of what was happening, it was just total darkness.”

“My area is heavy with Xylazine... Those bags are so toxic... Over 14 yrs on dope with no overdoses or infections and the last few years, I ODD more times than I can count, and almost lost my arm and my leg on separate occasions. It's literally like an anesthetic, the combo knocks out so hard that you can instantly collapse while walking and slam your head... You're not getting up until it wears off.”

Withdrawal experiences

“...every time I go into withdrawal...my heart is in excruciating electrical type pain like I'm minutes away from a seizure or something. haven't gone longer than 20mins into those feelings without dosing because of how scary they are... I can't get that long now [12 hours] with these tranq withdrawals starting in a matter of 3 hours or LESS, tremoring so bad I can't stand up & my heart pounding out my chest until I'm seeing stars & almost passing out when I try to stand and my whole heart shooting electrical pain. I truly feel for the first time in my life, like I AM going to die this way”

“...It got so bad for me I had withdrawals within 3 hours. I couldn't sleep longer than 3 hours and I'd wake up SHAKING from how cold I was, my heart in electrical shocks, my hands locking up, my vision blacking out, soooo much pressure in my head and chest, crazy pains in my back and sides...”

Xylazine Withdrawal Management: Alpha-2 Agonists

- When an individual stops using xylazine, there is a rebound in norepinephrine (similar to opioid withdrawal)
- Alpha-2 agonists reduce norepinephrine release
- Mimics some of the effects of xylazine (due to having the same mechanism of action as xylazine)

Xylazine Withdrawal Management

- Limited data to support the use of other alpha-2 agonists for the management of xylazine withdrawal symptoms
- Treat concurrent opioid withdrawal
- Treatment with limited data
 - *Dexmedetomidine – ICU
 - *Clonidine
 - *Tizanidine
 - *Benzodiazepines
 - Guanfacine
 - Lofexidine

Xylazine Withdrawal Protocol - Example

- Prophylaxis and treatment of xylazine withdrawal (initial management):
- First-line, for use in all patients unless contraindicated
 - Clonidine: alpha2-adrenergic agonist; antihypertensive; efficacy in opioid withdrawal attributed to binding to central alpha-2 adrenergic receptor that shares potassium channels with opioids and blunts symptoms of withdrawal
 - 0.1mg PO q6-8h scheduled (not PRN) and titrated to effect, up to a
 - maximum dose of 0.3 mg PO Q8h
- Monitor for signs of hypotension and oversedation especially in patients with ESRD, advanced age or compromised renal function.

Symptoms - Chronic

- Skin ulcers
 - Severe, necrotic skin ulcers/abscesses
 - Independent of the route of xylazine administration
- Dependence
- Withdrawal

Skin Ulcers

- Chronic use associated with severe, necrotic skin ulcers
- Should have a suspicion for xylazine use in individuals who inject drugs and have non-healing, necrotic ulcers
- Distinctly different from other skin and soft tissue infections associated with injection drug use
- May or may not be associated with an injection site
 - Develop irrespective of IV injection site
 - Occur remotely from the injection site
- Thought to be secondary to direct vasoconstrictive effect and further precipitated by hypotension leading to reduced tissue oxygenation/perfusion
 - Impaired wound healing
 - Risk of secondary infection

Xylazine wounds

Beginning xylazine wounds showing as bruises and discoloration.



<https://www.masslive.com/galleries/4VB6RA5CWBAE3HGQ7LRKYETQHQ/>

+ - One Day

+ - Five Days



Courtesy of PAARI

Xylazine wounds

A progression of xylazine wounds over five days.

<https://www.masslive.com/galleries/4VB6RA5CWBAE3HGQ7LRKYETQHQ/>



Courtesy of PAARI

Xylazine wound

Infected xylazine sores.

10 / 11

<https://www.masslive.com/galleries/4VB6RA5CWBAE3HGQ7LRKYETQHQ/>



1a



1b



2a



2b

<https://pmc.ncbi.nlm.nih.gov/articles/PMC10402246/pdf/nihpp-rs3194876v1.pdf>

Treatment of Skin Ulcers

- Routine wound care
 - Wound cleansing
 - Avoid alcohol or hydrogen peroxide
 - Dressing changes
 - Nonadherent dressing
- Evaluate for secondary infection
 - Sepsis
 - Cellulitis
 - Must cover *Staphylococcus aureus* (including MRSA), group A streptococcus
- Severe wounds may require skin graft, limb amputation
- Avoid xylazine use

TABLE 1. The Prevention Point Philadelphia Wound Care Clinic’s Approach to Care for Xylazine-associated Wounds

Stepwise Dressing Change	Dressing Products Used	Notes
Step 1: Premedicate if possible		In settings where available, advocate for adequate pain/withdrawal management before dressing change
Step 2: Remove soiled dressing		Soak soiled dressing with water/saline to decrease pain with removal. Offer patient option to remove their own dressing.
Step 3: Clean	Normal saline, generic wound washes For wounds with heavy burden of nonviable tissue: <ul style="list-style-type: none">• Vashe, Dakins 0.125%	Test cleansers on small area of wound to assess tolerance.
Step 4: Debride	Enzymatic debridement <ul style="list-style-type: none">• Santyl: Requires prescription; costly Autolytic: <ul style="list-style-type: none">• Medihoney: Consider outdoor exposure and potential insect attraction• Hydrogel silver• Silver gel/Silver sulfadiazine• PHMB topical	Topicals may be applied to the primary dressing (step 6) to avoid directly touching sensitive wounds. Alert patient to the likelihood of increased drainage with use of topical debriding agents. Cross-hatching of eschar, if tolerated, promotes deeper penetration of topical debriding agents and may be appropriate in some settings.
Step 5: Apply other topicals	Skin protectant to periwound tissue (eg no-sting skin prep, A&D ointment, Coloplast Triad) Topical antibiotic if indicated and compatible (eg, Mupirocin)	Preservation of intact periwound tissue is priority, especially with necrotic and heavily exudative wounds. Systemic antibiotics do not penetrate above the wound bed, and a topical may be required to reduce the overall bioburden.
Step 6: Apply primary dressing	Based on assessment of wound drainage: <ul style="list-style-type: none">• Wet/normal wound: Oil-emulsion (e.g. Adaptic)• Dry wound: Petroleum-based (e.g. Xeroform)	Cut to shape of wound to avoid coverage of periwound area, which can promote breakdown. Check compatibility of Xeroform and any topicals used.
Step 7: Apply secondary of dressing	Super absorbent dressing, layers of woven gauze, abdominal pads, or nonstick gauze	
Step 8: Secure	Gauze wrap secured with Tubigrip, IV netting, self-adherent wrap, or ACE bandage	Self-adherent or ACE bandages should be applied just tight enough to secure underlying dressings, not for compression. Self-adherent wrap may contribute to skin breakdown if not changed daily.

Harm Reduction



Strategies to Reduce the Risk of an Overdose

- Never use alone
- Carry naloxone
- Rescue breaths
- Know the risks of using illegal drugs
- Seek medical care for skin wounds
- Reduce injection related risks
- Test before using

Key Points

- Xylazine has increasing use
- Enhances opioid effects as well as associated with significant effects of its own
- No reversal agent
- Withdrawal can be severe
- No standard withdrawal treatment

References

- <https://www.samhsa.gov>
- <https://www.cdc.gov/drugoverdose/deaths/other-drugs/xylazine/xylazine-resources.html>
- <https://nida.nih.gov/research-topics/xylazine>
- Papudesi BN, Malayala SV, Regina AC. Xylazine Toxicity. [Updated 2023 Jul 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK594271/>
- <https://www.health.ny.gov/publications/12044.pdf>
- <https://www.dea.gov>
- <https://www.fda.gov>
- Personal Experiences With Xylazine and Behavior Change: A Qualitative Content Analysis of Reddit PostsJ AddictMed 2025;19: 135–142