

# Introduction to Xylazine

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*UPMC Addiction Medicine Lecture Day*

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I have no financial relationships to disclose with ineligible companies

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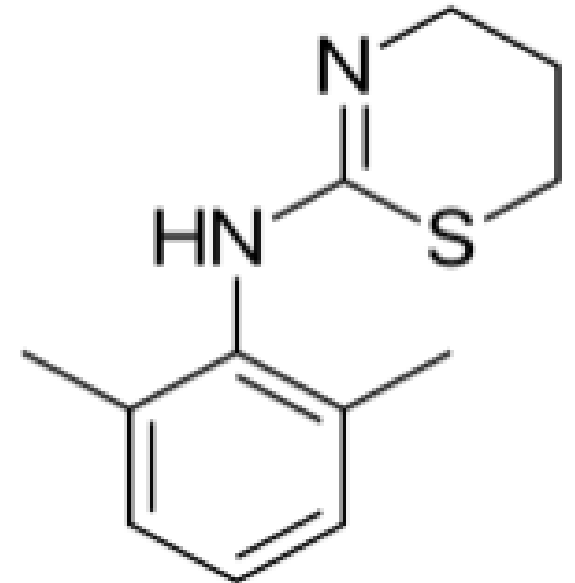


# Learning Objectives

- Describe the trends of xylazine in U.S. illicit drug supply
- Recognize physiologic effects and clinical risks in persons using xylazine and appropriate harm reduction response
- Review clinical strategies for implementation for xylazine-harms

# Xylazine (zie-luh-zeen)

- Central  $\alpha_2$  adrenergic receptor agonist that causes central nervous system depression
- Has sedative, analgesic and muscle relaxant properties
- Names:
  - AnaSed, Rompun, XylaMed, Sedazine, Chanazine
  - **Tranq**, sleep-cut, *Anastesia de caballo*



Greene S et al. J Vet. pharm and therapeutics 1988

# Rising national prevalence of xylazine

DEA Forensic Laboratory Identifications of Xylazine in exhibits by region

Region	2020	2021	% Increase
Northeast	346	556	61%
South	198	580	193%
Midwest	110	118	7%
West	77	163	112%

"Xylazine is making the deadliest drug threat our country has every 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."

## The Biden-Harris Administration's Actions to Address the Dangers of Fentanyl Mixed with Xylazine

- ✓ **Designated** Fentanyl Mixed with Xylazine as an Emerging Threat
- ✓ **Launched** First-of-Its-Kind National Response Plan for this Emerging Threat
- ✓ **Restricted** Unlawful Entry of Xylazine-Active Ingredients and Products Into the Country
- ✓ **Issued** Public Safety Alert on the Sharp Increase in Xylazine-Laced Fentanyl Trafficking
- ✓ **Convened** Leaders on Best-practices for Xylazine Testing, Wound Care, and Drug Treatment

WHITEHOUSE.GOV



DEA. Joint intelligence Report October 2022

# Xylazine + opioid are common BUT the concentrations of each vary

Date	Suspected	Drugs Identified
9/13/2022	Dope	Fentanyl (18.4%), Xylazine (26.9%), 4-ANPP (10.6%) [OPI=1.84]
9/21/2022	Dope	Fentanyl (6.6%), Xylazine (40.5%), 4-ANPP (1.0%), Procaine, Caffeine [OPI=0.69]
9/21/2022	Dope	Fentanyl (7.7%), Xylazine (32.4%), para-Fluorofentanyl (0.3%), 4-ANPP (0.7%) [OPI=0.78]
9/21/2022	Dope	Fentanyl (7.8%), Xylazine (26.6%), 4-ANPP (1.5%) [OPI=0.78]
9/21/2022	Dope	Fentanyl (8.2%), Xylazine (58.4%), 4-ANPP (0.6%) [OPI=0.82]
9/21/2022	Dope	Fentanyl (8.3%), Xylazine (26.3%), 4-ANPP (1.6%) [OPI=0.83] ①
9/21/2022	Dope	Fentanyl (8.8%), Xylazine (30.1%), 4-ANPP (1.7%) [OPI=0.88]
9/21/2022	Dope	Fentanyl (10.0%), Xylazine (36.8%), 4-ANPP (1.7%) [OPI=1.00] ②
9/21/2022	Dope	Fentanyl (11.2%), Xylazine (43.7%), 4-ANPP (1.7%) [OPI=1.12]
9/21/2022	Dope	Fentanyl (11.9%), Xylazine (38.0%), 4-ANPP (3.0%) [OPI=1.19]
9/21/2022	Dope	Fentanyl (13.2%), Xylazine (64.8%), 4-ANPP (2.0%) [OPI=1.32] ③

DrugsData.org  
Drug Checking Quarterly Report (Q3 2022): Philadelphia, PA

# Patient's experience using xylazine-opioids vary

**Many are UNAWARE that it is contaminating their drugs!**

1. Extends the duration of sedation
2. May delay withdrawal
3. May assist in regulating sleep
4. Affordability

1. Dislike the sedating sensation
2. Worry it can cause:
  - An unintentional dependence
  - Risk for assault or injury when sedated
  - Negative clinical side effects

Reed, MR et al. DAD 2022

Jawa et al. Pending publication

# UNC Street Drug Analysis Lab

# 500951

From Pittsburgh, Pennsylvania on 5/23/2023  
Assumed to be xylazine, fentanyl

### 3 major substances detected:

- xylazine
- 4-ANPP
- fentanyl

# 500589

From Pittsburgh, Pennsylvania on 6/6/2023  
Assumed to be fentanyl

### 2 major substances detected:

- xylazine
- fentanyl

# Pittsburgh: xylazine + opioids

Bags to watch for:

<u>Date</u>	<u>Name</u>	<u>Location</u>	<u>info</u>
7/23/23	Hennesy	Northside	very strong
7/23/23	Guerrilla Glue (Purple Stamp)	Penn Hills, Homewood	very strong, Purple dope
7/23/23	1017 Records	East Pgh	+ for fent + xylazine
7/23/23	Black Jack	Penn Hills	+ for xylazine
7/27/23	Show Time (Blue Bag)	South Hills	very strong
8/1/23	Crack Cocaine	Northside	+ for fent, Ammonia
8/1/23	Balloons (dope)	Hill District	very strong, ODs
8/2/23	Easy Pass (Double Seal Blue Bag)	West Side	+ for xylazine
8/2/23	Ferrari (double seal)	?	+ for xylazine
8/3/23	Crash (Black stamp)	Swissvale	+ for fent + xylazine, ODs
8/6/23	Call of Duty (Blue stamp)	Homewood	for xylazine
8/6/23	Hot Pussy (Pink Stamp)	?	for xylazine
8/6/23	Venom	?	for xylazine
8/8/23	Northface (Green stamp)	Northside	very strong
8/10/23	Dray Sprite (Red stamp)	Carroll	+ for xylazine
8/16/23	Mike (Black stamp)	Hill District	for xylazine





# Xylazine diagnostic testing

- Xylazine **can be detected** in blood and urine tests, BUT it is not routinely included in toxicology screens at UPMC
- Send out tests to specialty labs, BUT they take several days, have variable availability, and are less helpful to patients
- Need more research as unclear clinical utility and caution with interpretation, but may be helpful for surveillance



# Xylazine test strips (XTS)

- Are a rapid visual immunoassay for qualitative presumptive detection of xylazine
- A **low-cost, high-impact** harm-reduction strategy and patients are interested in testing their drugs prior to use
- Compatible with most injectable, powder, or pill drugs
- Multiple commercially available AND range in cost and dilution ratios



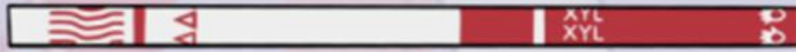
**Magee Cares Award: Drs Hull, Jawa, Shang**

Peiper NC, et al . IJDP. 2019

Reed M. K. et al. DAD 2022

Shuda S, Lam H.Y. CFSRE. October 2022

## Xylazine Test strip



Sterile water (5mL)



Cooker



*Images Courtesy of M. Shang 2023*

Don't interpret before 5 min or after 10 min. **ONE** red line is **POSITIVE**. **TWO** red lines is **NEGATIVE**.



If no lines or only this line  appears, test is invalid. Lines can be faint so look with a bright light.

## How to use XTS

- Dissolve a tiny amount of product in water, dip the strip in the solution, wait a few minutes for the test result
- We recommend to **only test for opioids**
- No validation studies in non-opioids

# Xylazine toxidrome and effects

## ACUTE EFFECTS:

- **Prolonged sedation**
- Blurred vision
- Dry mouth
- Low blood pressure
- Bradycardia
- Weak reflexes
- Disorientation
- Drowsiness
- Slurred speech
- **Risk of overdose**

## CHRONIC EFFECTS

- **Skin wounds**
- Abnormal blood glucose
- Anemia

Kacinko SK et al. Journal of Analytical Toxicology 2022  
Xiao, YF et al. BMC Anesthesiology 2013  
Pending publication. Courtesy of N. Dasgupta 2023

# Xylazine withdrawal

- Not well-defined syndrome, can present with hypertension, anxiety, irritability, restlessness
- \*\*Consider if protracted withdrawal symptoms despite on appropriate MOUD or adjunctive medications\*\*
- **Prophylaxis and treatment of xylazine withdrawal**
  - Clonidine: 0.1mg PO q6-8h scheduled and titrated to effect, up to a max dose 0.3 mg PO Q8h
- **Pain and opioid withdrawal management**
  - **Initiate on medications for opioid use disorder**
  - Gabapentin 300-600 mg PO q8h + 300mg QHS or Pregabalin 50-100mg PO TID
  - Ketamine
  - Adjuncts: olanzapine, hydroxyzine, GABA agonists, dexmedetomidine

Penn CAMP. Best Practices for Management of Xylazine Withdrawal and Xylazine-related Overdose. 2023  
Bettigole, et al, "Xylazine (Tranq) Exposure Among People Who Use Substances in Philadelphia."  
Ehrman-Dupre, R. et al. Journal Addiction Medicine 2022.

# Prolonged sedation and loss of awareness

*"I'm having more problems with the tranq than I am with the fentanyl down here. I have basically blackouts from the tranq. I lose days at a time. Like I'll lose four, five, six hours, and then when I come out of the blackout..."*

## At Risk for:

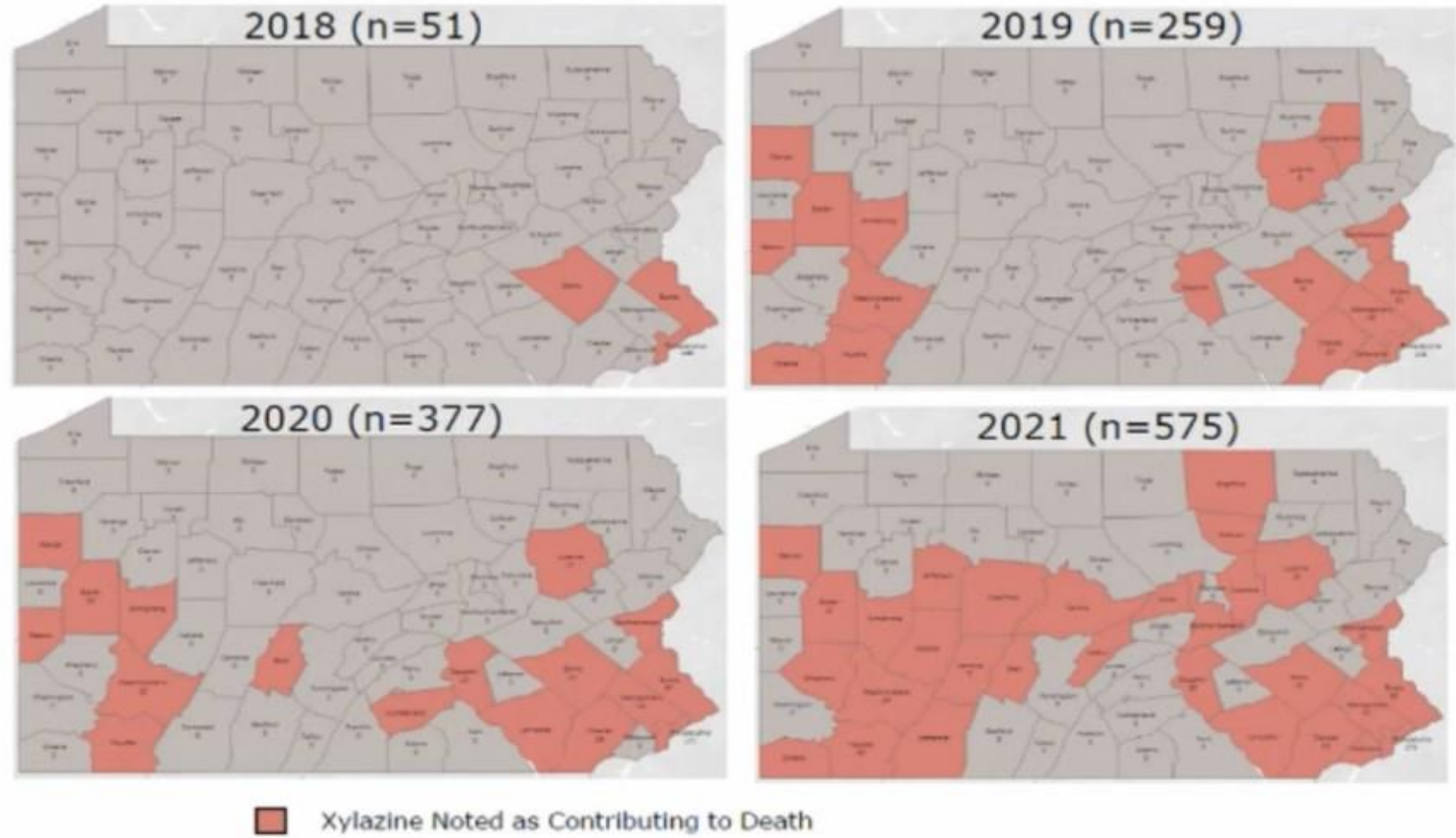
- Environmental Injury
- Extended immobility increases the risk for blood clots, soft tissue breakdown, muscle and nerve damage

## Harm Reduction strategies:

- Never use alone, safer consumption sites
- Rest in a safe place after using
- Place in recovery position, avoid atypical positions

M.K. Reed, N.S. Imperato, J.M. Bowles et al. DAD 2022  
Dasgupta N et al. Pending publication 2023.

# Emerging Overdose Trends - Xylazine



# Harm reduction strategies: xylazine- associated overdoses

- **Dispel the myth of “naloxone resistant overdose”!**
- People may not wake up for several hours after naloxone administration and this is not an indication to give more or higher doses of naloxone
- In an overdose

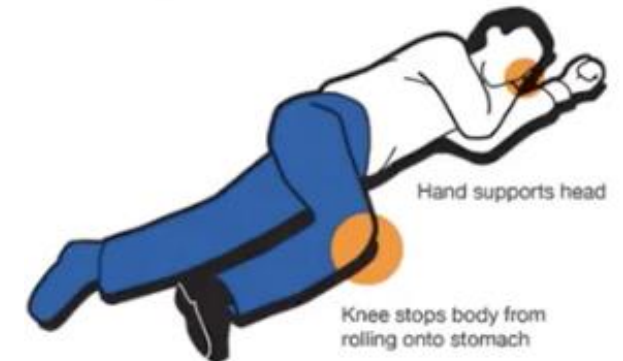
- 1. Administer naloxone!!**

2. Place in recovery position

3. Wait 2-3 minutes before administering another dose if needed

4. Supportive field management until drug wears off and sedation resolves:

- **Rescue breathing, airway maneuvers, continuous pulse oximetry, supplemental O2**
- Rotating positions and massaging limbs



Bettigole, et al, “Xylazine (Tranq) Exposure Among People Who Use Substances in Philadelphia.”



# Xylazine OD patient handouts

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## HOW TO STAY SAFER


As xylazine can cause unconsciousness for several hours:


- Keep money and personal items in a safe place
- Pad boney parts of your body
- Sit or lay down after use
- Avoid being alone. Alternate using with trusted friends
- Use in places with stable temperatures


## ADDITIONAL RESOURCES

 **Massachusetts Overdose Prevention Hotline**  
1-800-972-0590

**StreetCheck**  
Free drug checking services to see what's in your supply. Find a location nearest you  
[tinyurl.com/5955crj5](https://tinyurl.com/5955crj5)



Learn more about xylazine 



## XYLAZINE



// zai · luh · zeen //

AKA "Tranq" or "Tranq Dope"


A veterinary sedative making its way into the drug supply. Xylazine increases the risk of sedation, overdose, and wounds that are hard to heal.

This guide focuses on overdose >>>

Last updated: 04/2023; Design by: Maggie Shang MD.



## DID YOU KNOW?



- Xylazine is a **non-opioid** tranquilizer
- Xylazine can be mixed with opioids like fentanyl, which increases overdose risk

**Always give naloxone if you suspect an overdose!**

## WHAT TO LOOK FOR?


Overdoses involving xylazine make people more sedated/sleepy for a much longer time.

Additional signs include:

- Slow, irregular, or no breathing
- Choking, gurgling, or snoring sounds
- Blue-colored lips or nails
- Slow heart rate
- Tiny pupils if opioids present

## WHAT TO DO?

- 1 Call for nearby help. Check for breathing/pulse. If no pulse, begin CPR/chest compressions.
- 2 If slow or shallow breathing, give naloxone. If breathing is regular, skip to step 4
- 3 Give rescue breaths once every 5 seconds. Use a face shield if available
- 4 Once breathing again, place in recovery position. Place padding under bony areas



- 5 Keep checking breathing and pulse. Call 911 if appropriate
- 6 Roll from side to side every 1-2 hours

## OVERDOSE PREVENTION

- Xylazine might be in your drug supply. Ask others about their experiences
- Some places have xylazine test strips or can test your drugs for you
- Start low and go slow
- Avoid using alone
- Always have naloxone available and visible

## KEY TIPS

People experiencing an overdose involving xylazine may remain unconscious or unarousable **EVEN AFTER** getting naloxone.

Remember that naloxone helps restore breathing! Giving more naloxone than needed can cause severe opioid withdrawal symptoms like vomiting.

# WARNING

The following slides contains graphic images of drug use related wounds.

# Xylazine skin wounds

*“Xylazine wounds are a whole other kind of...just horror...if there’s xylazine in it, and if you miss [the vein], you were risking a really deep and necrotizing wound.”*

- Non-specific ulcer morphology, and is distinct from typical injection site infections
- Risk of wound supra-infection
- Anecdotal risk irrespective of route of administration
- Likely multifactorial mechanism

Reyes J. et al. Journal of Urban Health. 2012  
Lopez et al. Addiction science and Clinical Practice 2015  
Ehrman-Dupre, R. et al. JAM. 2021  
Malayala et al. Cureus. 2022  
Friedman, J et al. DAD 2022



# Xylazine associated wounds can heal over time



Wei JJ, et al. JAAD Case Reports. 2023

Shared with patient permission Healthy Streets Outreach Program

# Harm Reduction Strategies: Screening & Prevention

- ASK patients if they have had any about atypical wounds
- Educate patients on **RED flag symptoms**→
- Consider use of XTS and advise to seek alternate batch


- Fever or chills
- Skin turns dark or black
- Skin is red, hard, & hot to touch
- Thick, smelly yellow or green drainage
- Severe or worsening pain at wound site
- Pain & decreased ability to move joint
- Pieces of tissue falling off
- Exposed bone or tendon
- New numbness


Images Courtesy of M. Shang 2023




# Framework for wound management

1) Evaluate for infection and need for antibiotics

2) Cleanse  Saline, soap + water, antimicrobial cleanser, dry skin

3) Moisture  Around the wound: Vitamin A+D ointment  
Wound bed: petrolatum

4) Cover/ wrap  1° dressing: bandage OR nonadherent cut to size  
2° dressing: roll gauze loosely


# Examples of wound care kits



Image courtesy of Jen Shinefeld 2023

# Xylazine wound care patient handouts

## WOUND CARE SUPPLIES



### SELF-CARE STEPS

- 1 Clean hands with soap & water or hand sanitizer before touching wounds
- 2 Gently wash wound with soap & water or with saline at least every 2-3 days
- 3 Put ointment on gauze & place on entire wound. Cover with more dry gauze
- 4 Wrap wound with kerlix and secure with medical tape. Make sure wrap is not too tight
- 5 Cover dressing with ACE wrap or coban or with long sleeves/pants if no other option
- 6 Change dressing every 1-3 days. Watch for red flags

## XYLAZINE



// zai · luh · zeen //

### AKA "Tranq" or "Tranq Dope"

A cutting agent making its way into the drug supply. Contamination with xylazine increases risk of sedation, overdose, and wounds that are hard to heal.

**This guide focuses on xylazine wounds >>>**

Last updated: 02/2023; Design by: Maggie Shang MD



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## XYLAZINE WOUNDS

Xylazine wounds can appear anywhere on the body regardless of where you are injecting, particularly in **YELLOW** areas.

Check these areas regularly for any wounds that may develop.

Wounds can occur even if you're just snorting or smoking.



### HELPFUL TIPS

Xylazine wounds can look like a combination of:

- Blisters
- Large ulcers
- Small scabs
- Eschar (dark/black pieces of dead tissue)



- Keep your skin moisturized with A+D ointment
- Avoid using alcohol/hydrogen peroxide on wounds
- Keep wounds covered with a clean bandage
- Wear long sleeves, pants, socks, and gloves to prevent yourself from scratching your skin
- Eat protein & stay hydrated to help with healing
- Avoid injecting into or around your wounds
- Use new supplies every time and avoid sharing
- Not every wound is infected. Avoid taking non-prescribed antibiotics

### RED FLAGS to SEEK MEDICAL CARE

- Fever or chills
- Skin turns dark or black
- Skin is red, hard, & hot to touch
- Thick, smelly yellow or green drainage
- Severe or worsening pain at wound site
- Pain & decreased ability to move joint
- Pieces of tissue falling off
- Exposed bone or tendon
- New numbness



Even though xylazine isn't an opioid, you should still give naloxone in an overdose as opioids are often present.





# What can we do?

## Address Misinformation

- **Xylazine is not naloxone resistant**, it is simply not an opioid.
- Like fentanyl, there is **no known risk** to first responders from xylazine exposure.
- Xylazine does not cause “flesh eating” wounds and the **wounds are not contagious** to first responders.
- Sedation from xylazine will make people who use less able to respond and less able to follow directions.
- **Words Matter!** Xylazine is NOT a “zombie drug”, and further stigmatizes individuals

# What can we do?

## Educate and Refer

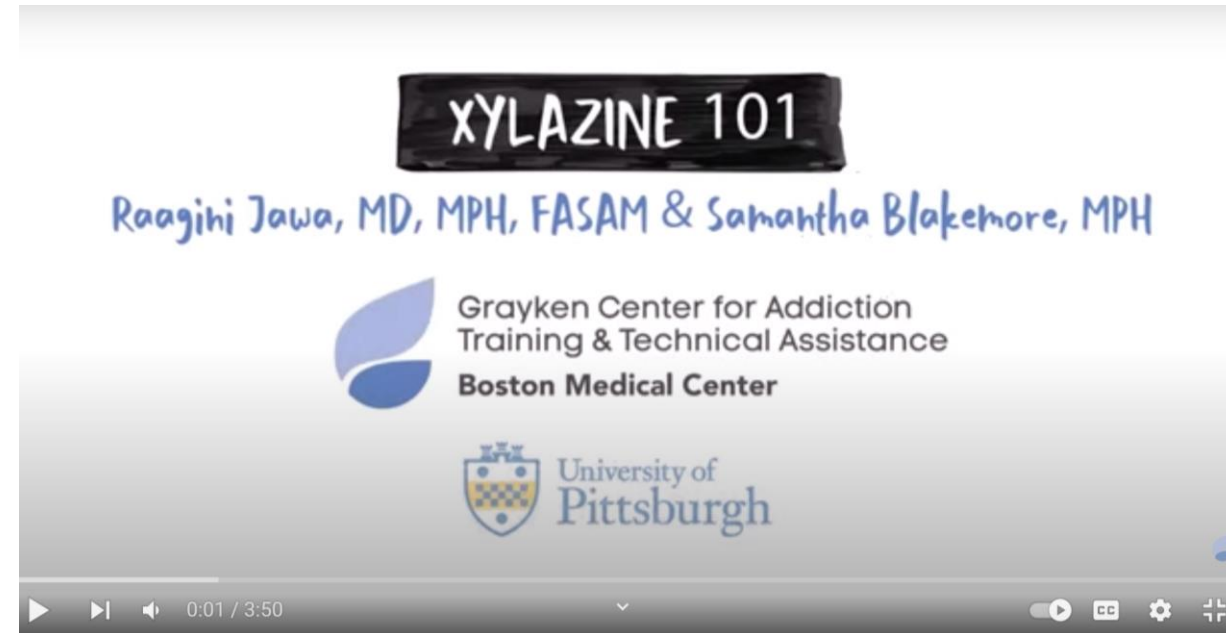


- Upcoming virtual training: 9/13/23 Grayken Center for Addiction TTA: [addictiontraining.org](http://addictiontraining.org)
- Talk to your patients who use drugs about xylazine and screen for xylazine-harms
- Refer patients to get XTS: IM-REP, [Fall 2023 Magee, Latterman, and CPCDS]
- Refer patients for Xylazine Wound Care: UPMC IM-REP Clinic

# What can we do?



- INNOVATE: Develop protocols and to address xylazine-related harms
- ADVOCATE:
  - To local health departments for safe drug supply, offer local drug checking centers, fund xylazine test strips
  - To medical examiners to universally screen for xylazine
- RESEARCH!



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- Sara Wallace-Keeshen, BSN, RN, Rachel McFadden, BSN, RN, CEN, & Rebecca Hosey, MPH, BSN, RN. Basics of Wound Care. Substance Use Response Guidance and Education. 9/2022.
- Claire Zagorski, MSc, LP. What we need to know about Xylazine. Be Well Texas ECHO. 10/6/22
- Dr. Joseph D’Orazio. Toxicity of Xylazine and How it impacts treatment for people who use drugs. COBRE on Opioids and Overdose. 6/16/22
- NASTAD Beyond the Alerts: Practical Guidance for Responding to Xylazine webinar. 2/21/2023
- Dr Ramsey. Learning Thursdays: Xylazine. NYS OASAS. 2/10/2023
- Jason Bienert. Experiences with Xylazine-related problems. From a Wound care nurse, Voices of Hope, Cecil & Hartford County, Maryland.
- Rebecca Hosey. Xylazine effects on wounds: Why and how we care. HRNA AIIRM. 1/10/2023

Please email us your experience and questions with xylazine!

**Email: [rjawa@pitt.edu](mailto:rjawa@pitt.edu)**