



# Zeroing in on Xylazine

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www.mass.gov/dph/bsas





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- Participants who complete and return the evaluation and stay for entire session will be awarded 1.0 contact hours
- None of the planners or speakers have a financial relationships to disclose with ineligible companies





# Conflicts of Interest & Support

## Conflicts of Interest

• Jawa: None

 Murray: consulting for the Federal government, MA Department of Public Health, and several municipal governments around the country

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 Jawa: NIDA K12DA050607-03 University of Pittsburgh Collaboration in Addiction Training Scholars (PittCATS) Program





# Objectives

Describe the trends of xylazine in U.S. illicit drug supply

 Recognize physiologic effects and manifestations of intoxication in persons using xylazine

 Review risks of xylazine on severe sedation, overdose and skin wounds and appropriate harm reduction response







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## Xylazine



Xylazine, a non-opioid veterinary tranquilizer not approved for human use, has been linked to an increasing number of overdose deaths nationwide in the evolving drug addiction and overdose crisis. Studies show people exposed to xylazine often knowingly or unknowingly used it in combination with other drugs, particularly illicit fentanyl. 1-4



# FDA alerts health care professionals of risks to patients exposed to xylazine in illicit drugs

# Xylazine (zie-luh-zeen)

Discovered 1962 as an antihypertensive agent

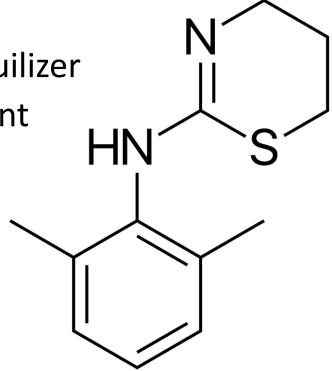
 Noted to have hazardous side effects of sedation, hypotension and bradycardia

Currently FDA approved as a common veterinary tranquilizer

NON-OPIOID sedative with analgesic and muscle relaxant properties

NOT a controlled substance

- Names:
  - AnaSed, Rompun, XylaMed, Sedazine, and Chanazine
  - TRANQ, sleep-cut, Anastesia de caballo [horse tranquilizer]







## Where did it come from?

Torruella Substance Abuse Treatment, Prevention, and Policy 2011, 6:7 http://www.substanceabusepolicy.com/content/6/1/7



- In 2000s was described as an additive in the unregulated drug supply of Puerto Rico
- Usually found in conjunction with opioids
- Early 2010: Increasing knowledge PWUD in especially Puerto Rican community of Philadelphia

### SHORT REPORT

Open Access

## Xylazine (veterinary sedative) use in Puerto Rico

Rafael A Torruella

#### Abstract

Human xylazine use in Puerto Rico merits particular attention for its unprecedented scale and depth. Although Puerto Rican injecting drug users (IDUs) have reported using this drug since the early 2000s, little is being done in the research and service delivery sectors as it is claimed that xylazine severely impacts the health of its users. This report provides information on xylazine use and its associated harms. Data from one semi-structured interview collected in New York City (2007-2008) as part of a larger research study with migrant Puerto Rican drug users is presented as a case study. Xylazine, a veterinary sedative, is an adulterant and complement to other drugs and its chronic use is reported to be associated with physical deterioration. Because human xylazine use has been reported in other locations outside of Puerto Rico, this substance could also emerge as an adulterant in other markets to the levels currently experienced in Puerto Rico. Research and interventions are needed to provide adequate services on the island, better understand how the use of xylazine affects its users, and to reduce the possibility of increased xylazine use on the state-side.

Torruella, R. Substance Abuse Treatment, Prevention, Policy, 2011

Rodriguez et. al. Drug and Alcohol Dependence, 2008

Wong et al., Journal of Forensic Science, 2008

Friedman et al. PLOS ONE, 2019





# States/Jurisdictions reporting xylazine



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

Xylazine is detected in 91% of fentanyl/heroin samples in Philadelphia

DEA. Joint intelligence Report October 2022 Adapted from D'Orazio. Toxicity of Xylazine. COBRE on Opioids and Overdose. 2022 Friedman et al. Drug and Alcohol Dependence 2022





# Where is xylazine sourced?



Examples of xylazine samples collected by MADDS







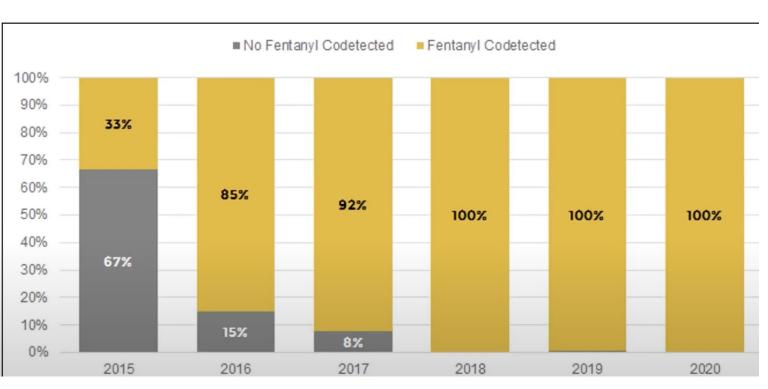
Source: Drug Enforcement Administration Philadelphia Division



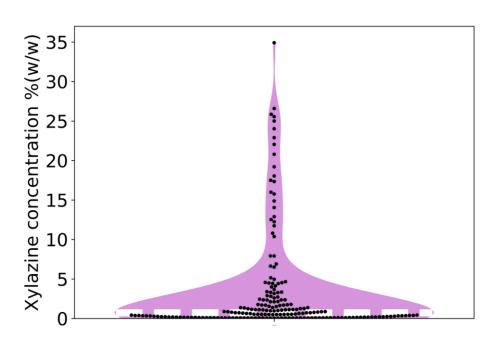


AnaSed®

# Xylazine has varying concentration and is often present with opioids



Philadelphia Medical Examiner's Office



Hutchinson, A. Kielty C. Vancouver Island Drug Checking Project. Sep 2022.





# Xylazine diagnostic testing challenges

- Xylazine can be detected in serum and urine, can be part of a send out test to specialty lab (turn around time ~1 week)
  - Thin layer chromatography (TLC)
  - Gas chromatography mass spectrometry (GC-MS)
  - Liquid chromatography mass spectrometry (LC-MS)
- Point-of-care urine immunoassay not available at this time
- Xylazine test strips may be in the works





Reed M. K. et al. DAD 2022 Christopher Moraff. Twitter 11/2022





# Pharmacology

- Non-opioid sedative, pain-reliever, and muscle relaxant
- Agonist at central alpha-2 adrenergic receptor
  - Sedation
  - May blunt the response to hypoxia
- Anticholinergic effects
- Similar effects to clonidine



## Pharmacokinetics

- Time to effect 1-2 minutes
- Time to drug effect peaks 30 minutes
- Duration of effect up to 4 hours
- Seems to be synergistic with opioids (from veterinary data):
   can improve euphoria and prolong the duration of fentanyl

"See, the tranq like extends the high, it gives the dope more of a heroin effect, it's a good rush with the heroin-like effect"

"Tranq seems to give fentanyl legs"

Friedman et al. Drug and Alcohol Dependence 2022

Adapted from D'Orazio: Toxicity of Xylazine. COBRE on Opioids and Overdose. 2022

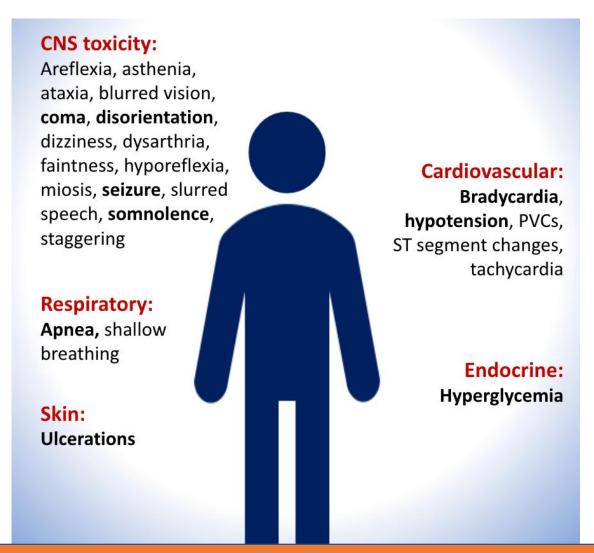




# Xylazine toxidrome and effects

## **ACUTE EFFECTS:**

- Profound sedation
- Blurred vision
- Super dry mouth
- Low blood pressure
- Bradycardia
- Weak reflexes
- Disorientation
- Drowsiness
- Slurred speech
- Risk of Overdose



## **CHRONIC EFFECTS**

- Severe skin wounds
- Dysglycemia
- Anemia

CriticalCareNow.com 2022.





# Xylazine withdrawal

• Not well-defined syndrome, can overlap with opioid withdrawal syndrome

Can present with hypertension, anxiety, irritability, restlessness

May require inpatient monitoring for vital sign instability

 Emerging literature on treatment protocols, but likely can treated similar with sedative hypnotic withdrawal syndromes

> Bettigole, et al, "Xylazine (Tranq) Exposure Among People Who Use Substances in Philadelphia." Ehrman-Dupre, R. et al. Journal Addiction Medicine 2022.





# Xylazine pros & cons

- Opioid-xylazine extends duration of intoxication and delays withdrawal
- May help patients regulate sleep
- Affordability

- No control over xylazine and other adulterants
- Exposure to poly-substances
- Disliking sensation of mixture of substances
- Worry of tranquillizer dependence
- Higher risk of assault or injury when sedated

Reed, M.R. et al. DAD 2022.





## 1. Profound sedation and loss of awareness

"I'm having more problems with the tranq then 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..."

M.K. Reed, N.S. Imperato, J.M. Bowles et al. DAD 2022





# Profound Sedation: Complications

- Extended immobility increases the risk for:
  - Blood clots and soft tissue breakdown (decubitus ulcers)
  - Imped blood flow (if in hyper-flexed or unusual positions)
  - Muscle and nerve damage
  - Rhabdomyolysis (muscle breakdown → kidney damage)
- If combined with other sedating drugs, ↑ central nervous system depression, and ↑ risk of overdose



Adapted from Claire Zagorski, MSc, LP- Be Well Texas ECHO 2022





# Profound Sedation: Harm reduction strategies for patients

- Be aware of the presence of xylazine
- Sit or lay down in a safe place after using
- Never use alone

- Watch for patients who are sedated or unconscious longer than usual
- Make sure to check that breathing and heart rate are adequate
- Put people in recovery position, avoid atypical positions
- Roll from one side to another every 1-2 hours
- Place padding under boney areas (heels, hip, shoulder ankles, etc.)





## 2. Risk of overdose

• Xylazine may be synergistic with opioid agonists and 个个 overdose risk

 Naloxone may not fully reverse overdose symptoms from opioid-xylazine formulation

 Individuals may continue to have period of profound sedation after naloxone is administered

**Xylazine and naloxone:** Xylazine can contribute to oversedation alongside opioids. **Naloxone WILL NOT** reverse the effects of xylazine, but ALWAYS administer naloxone in a suspected overdose. Naloxone will reverse the effects of any opioids present. The person may remain unresponsive if xylazine is present. Give rescue breaths to support their breathing.

Johnson et al. BMJ Injury Prevention 2021 Nunez et al., Am. J. Forensic Med. Pathol. 2021





# 个个 Number of Xylazine-positive overdose deaths

- Overdose deaths with xylazine present have increased 20-fold from 2015-2020
- Account for ~1.8% of overdose deaths (in 2020)

Region	2020	2021	% Increase
Northeast	631	1281	103%
South	116	1423	1,127%
Midwest	57	351	516%
West	4	34	750%

Johnson, J et al. BMJ Injury Prevention 2019 DEA. Joint intelligence Report October 2022

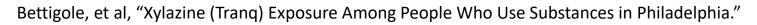




# Risk of overdose: Harm reduction strategies for patients

- Place in recovery position
- Administer naloxone!!
- Keep checking pulse and breathing
- Supportive management until drug wears off and sedation resolves
  - Keep people's airways open (jaw thrust)
  - Provide rescue breathing

- Continuous pulse oximetry, supplemental oxygen if hypoxia Reposition every 2 hours, roll to opposite side, gently massage

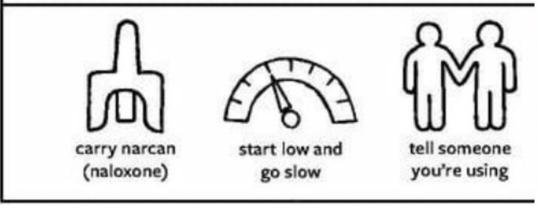






Knee stops body from rolling onto stomach

# Universal overdose prevention

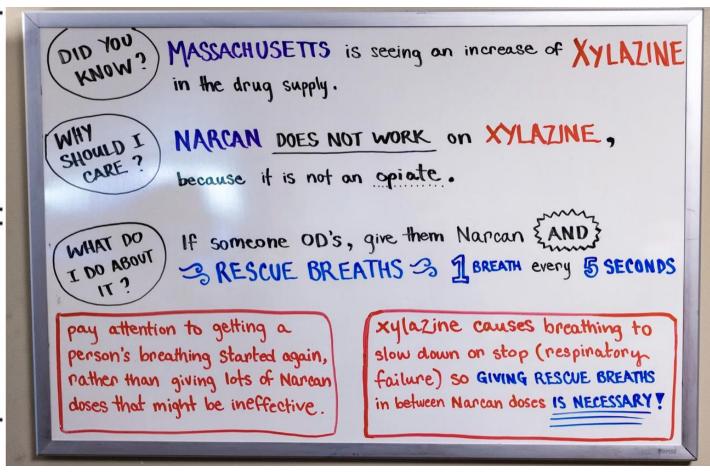


## **Never Use Alone**

English hotline: 800-484-3731 Spanish hotline: 800-928-5330

## The Brave App

download in the app store



Costa, J WBUR 2022





# 3. Xylazine Skin wounds

- Skin wounds reported in PR 2012
- Early data of xylazine + heroin users >
  higher risk injection behaviors
- Severe, difficult to treat
- Can involve loss of fingers/toes
- Risk of secondary bacterial infection



Reyes J. et al. Journal of Urban Health. 2012 Lopez et al. Addiction science and Clinical Practice 2015





## WARNING

The multiple slides contains graphic content about injection drug use related wounds that might disturb some of you.





# Xylazine skin wounds



- Can start as purple/red blisters → may progress to areas of necrosis with thick eschar
- May be at a missed injection (and non-injection sites) and prior areas with scratches
- Risk seems to be irrespective of route of administration
- Can appear as local vasculitis and range from small open sores to large ulcers, chronic osteomyelitis, gangrene
   resulting in limb loss

  Ehrman-Dupre, R. et al. JAM. 2021





# Pathophysiology of xylazine wounds is unknown

- † tissue death and poor wound healing from local tissue hypoxemia
- Inhibits endothelial cell proliferation
- ↓ sensitivity to skin injury
- 个 skin picking
- Injecting at wound site to alleviate the pain
- Tissue compression from extended periods of immobility
- Local effect from drug extravasation or peripheral vasoconstriction
- Obliterative vasculitis from ↑ injections ("shooter's patch")

Silva-Torres, L. A. et al. Tox in Vitro. 2014





# Xylazine skin wounds prevention: Harm reduction strategies for patients

- EDUCATE patients about xylazine in illicit drug supply and ASK about atypical wounds!
- Advise to seek alternate batch, if possible
- Consider other route of use (we aren't sure about this one!)
- Good vein hygiene, rotating injection sites, sterile supplies, skin cleaning, vein finders
- Wipe metal needle on an alcohol pad after you pull up solution and before injecting

\*\*Reports of patients being declined admission to some treatment facilities if wounds present \*\*

Jason Bienert. Experiences with Xylazine-related problems. Wound care nurse, Voices of Hope



# TRANQ IN THE SUPPLY

by Rebecca Hosey MPH RN

### What's goin' on?

Xylazine or Tranq is a potent drug additive that has been seen all over the East Coast. While you may not be able to check your supply for it on the go, you can take some steps to reduce harm.

### **IV** Injecting

- Clean injection site with alcohol pad first, try to avoid injecting in wounds or limbs with wounds
- Remember your tourniquet! and inject towards the heart
- After drawing up into needle, wipe down needle with alcohol pad so tranq is not on the outside of the needle
- Once injected, leave in while counting to 3 to allow for blood flow away from insertion site

Credit: Jessica Blanchard MSN RN

### Tranq may...

- kick in within 30 min. + last for a few days
- cause respiratory depression, but cannot be reversed with naloxone
- initially rapidly increase your heart rate and blood pressure, then decrease both
- may cause small, ulcer type wounds to pop up in unexpected places

### **WOUNDS**

\*Change wraps or bandages
daily if possible\*

Use saline, wound spray, or antibacterial soap and water to clean; Hibiclens is also great!
 Add antibiotic ointment to affected areas but try to avoid putting on intact or healthy skin
 Place non-adherent pad or ointment gauze (yellow or petroleum gauze) over the affected areas, again trying to avoid putting on healthy skin!
 Use ABD pad if it is draining a lot then wrap with gauze roll, Ace wrap or Coflex (brown wrap)

questions? email rhosey@nursing.upenn.edu





# If have a wound, monitor for red flag symptoms

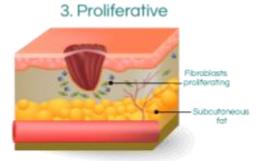
- Don't inject into or near the wound edges
- Avoid skin picking: wear long sleeve shirts, gloves, use A+D ointment on fingertips, put dressings/band-aids over problem areas
- Not all wounds require antibiotic treatment
- Educate and monitor for red flags and early triage!
  - Signs of systemic illness
  - Painful spot with fluctuance  $\rightarrow$  concern for abscess
  - Rapidly progressing change in color
  - Excruciating pain, new numbness, mottled skin, in or around infected area
  - Can see underlying bone/tendons
  - Chunks of tissue falling
  - If close to a joint, ↑ pain, redness, decreased mobility → septic arthritis

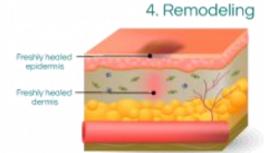




## 4 STAGES OF WOUND HEALING











www.physio-pedia.com





# Suggestions for xylazine wound management

- Avoid alcohol and hydrogen peroxide
- Clean wounds with soap (if available) and bottled/tap water or saline
- Keep skin around wound clean of drainage and moisturized (Vitamin A+D ointment)
- Goal for wound bed ~MOIST (helps dead skin soften/fall on its own) OR debridement

## **Black hardened wounds**

- Chemical debridement: Santyl
- Autolytic debridement: Medihoney
- Mechanical debridement: wet to dry gauze, surgery

## **Open wounds**

- Treat like burns, promote moist wound bed healing
- Can use Medihoney gel and/or Xeroform gauze cut to size
- Calcium alginate cut to size- makes a gel over

Doughty D, Nursing Clinics of North America. 2005





# Dressing 101: xylazine wounds

- Cover the ENTIRE wound
- Ensure the dressing stays in place with adequate tape
- · Can use kerlix/gauze vs non adherent ABD bandages (Pads, diapers) for any wound drainage
- Use wrap on top with Ace bandage or Coban (3M product that is self-adhering)
- Consider fresh socks and gloves, and long sleeve shirts/pants to cover dressings
- Leave bandage on 1-2 days, use saline to wet adherent dressings before removing
- Change bandage if ever soiled or soaked
- Wash wound with warm soapy water and re-bandage as above until wound heals

\*\*It is normal for dead tissue to fall off in the dressing or when washed

as it softens\*\*

Doughty D, Nursing Clinics of North America. 2005





## Thank You!!

Please email us your experience and questions with xylazine so we can have shared learning!

<u>jawar@upmc.edu</u> Stephen.murray@bmc.org

- University of Pittsburgh Medical Center
- Prevention Point Pittsburgh
- Grayken Center of Addiction
- Responding to Xylazine in the Drug Supply Part 1&2. National Harm Reduction Coalition Office Hours.
   4.8.2022
- 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
- Mary Wheeler, Healthy Streets Outreach Program
- Jason Bienert. Experiences with Xylazine-related problems. From a Wound care nurse, Voices of Hope, Cecil
   & Hartford County, Maryland.







# Grayken Center for Addiction Training & Technical Assistance

## **Boston Medical Center**

addictiontraining.org

Request training and technical assistance: addictiontraining.org/training/request

Questions? Email info@addictiontraining.org



### Massachusetts Drug Supply Data Stream (MADDS)

### Community Drug Supply Bulletin: Two Active Cuts

### **Xylazine in Fentanyl & Heroin**

- Multiple samples sold as fentanyl and heroin have been confirmed to contain the veterinary sedative xylazine in addition to fentanyl, heroin, or tramadol.
- From June 2020 to February 2021, MADDS detected xylazine in 35 samples statewide. Samples contained an increasing ratio of xylazine as an active cut: xylazine increased from a rarely present, low-ratio substance to a high-ratio active drug component for substances sold as dope/heroin/fentanyl.
- Samples containing xylazine included powdered residue in bags and cookers or cottons used for injection.
- Xylazine is a long acting and sedating medication, but it is not an opioid. Most user experiences were not provided ed or were unremarkable. 5 of 35 samples containing xylazine were associated with a fatal or nonfatal overdose that also involved fentanyl.

### **Health Effects**

- Xylazine can cause decreased level of consciousness/ unresponsiveness, low blood pressure, a slow heart rate, and decreased breathing. Because it is often combined with other sedating drugs like opioids, there is an increased risk for overdose or death.
- Narcan has not been documented to reverse xylazine's sedating effects but will stop an opioid overdose if the substance used also contained fentanyl, heroin or another opioid. When responding to a xylazine-involved overdose with Narcan, the person's breathing may return but they may still

  Active cuts are user experience.
- appear sedated. Seek medical assistance if you suspect a xylazine-involved overdose.
- Injecting xylazine may increase risk of skin ulcers.

### Rising Phenacetin in Cocaine

- From June 2020 to February 2021, 29 samples sold as cocaine have been confirmed to contain phenacetin in addition to cocaine statewide.
- Phenacetin is a common active cut for cocaine due to its similar appearance to cocaine. It is also a pain reliever, similar to acetaminophen (Tylenol).
- While not a new additive, phenacetin has become the most prevalent active cut for cocaine in Massachusetts during the pandemic. Phenacetin occurs in a higher ratio to cocaine in these drug samples.
- Samples containing phenacetin were found as powdered residue in bags, rock crystals, and in cookers or cottons used for injection.

### Health Effects

- Phenacetin is a pain medication/fever reducer that was removed from the US and European medications market due to kidney damage and urothelial cancer risk.
   Prolonged use of phenacetin, especially among people with kidney or liver problems, can cause serious organ damage. Ingestion of a high concentration of phenacetin in drug samples may accelerate these health concerns.
- Healthcare providers caring for people who use cocaine should consider increased monitoring of kidney and liver function.

Active cuts are additives that affect the user experience. Inactive cuts are additives that do not affect the user experience.

Active cuts, like xylazine and phenacetin, can have important adverse health effects which is why it is important to learn about additives.

Click for more info and resources or scan:



### How to Identify the Substances

- Both phenacetin and xylazine appear as a white crystalline solid and easily blend into powdered street drugs. They are
  difficult to identify without analytical testing.
- All samples were provided by harm reduction programs or donated by police departments for MADDS testing. If you
  have suspicions about the makeup of a drug, contact MADDS about drug checking.

#### Harm Reduction and Overdose Prevention

- The drug supply is unpredictable. It is safer to use when other people are present or can check on you frequently.
   People using together should take turns to prevent simultaneous overdose. Administer Narcan and call for help in case of overdose, prolonged sedation, or other adverse reaction. You can get Narcan at <a href="https://harmacies.ncbi.nlm.ncbi
- Use a sterile syringe for every injection to prevent infection.
- Contact a local harm reduction program for help with abscess or wound care, more advice on safer use, and availability of drug checking with MADDS.

MADDS is a state-funded collaboration between Brandeis University researchers, the Massachusetts Department of Public Health, various town police departments and local harm reduction agencies. Contact us at maddsbrandeis@gmail.com

### know what's in your drugs

## TRANQ | XYLAZINE

Xylazine is a veterinary tranquilizer that is cut in dope to give fentanyl longer legs. It's known as "anestesia de caballo" in Puerto Rico and "tranq" in Philly.

#### Trang was found in over

90%

of dope samples tested in Philly in 2021

Dope with tranq was first seen in Puerto Rico. Today, it is being found in more and more places across the US.



When tranq is mixed with another drug (like fentanyl, heroin, or a benzo), the chance of overdose increases. If someone is overdosing administer naloxone like you normally would. If the person starts breathing again but is still sedated, they don't need more naloxone. Put them in rescue position and keep an eye on them.



Tranq has been associated with severe wounds, which spread and worsen very quickly.



These wounds are seen regardless of how people use: smoking, snorting, or injecting. It's very difficult for these wounds to heal on their own so it is important to get medical attention if you have one.

## What can you do if you think there is tranq in your dope?

First, try to ask around and see how the drug is making other people feel before you buy or use it. Since tranq can cause a really heavy nod, try to use somewhere that you will be safe and won't fall and hurt yourself. Finally, if you think there is tranq in your dope let others know--including someone at your local exchange program--so folks know to be careful.



(naloxone)







tell someone

### **Never Use Alone**

English hotline: 800-484-3731 Spanish hotline: 800-928-5330

### **The Brave App**

download in the app store

## XYLAZINE IN THE DRUG SUPPLY

### XYLAZINE (ZIE-LUH-ZEEN)

## NAMES

Tranq AnaSed Rompún Horse tranquilizer Anestesia de caballo

- It's found in powder heroin/fentanyl mostly, and sometimes coke and meth
- It's not an opioid. It's a deep sedative, like clonidine or ketamine.
   It starts quickly and makes you fall out hard for about the first hour if you're not used to it
- Xylazine can give fentanyl legs so you're not sick again in two hours, but can be very dangerous when it shows up in dope unexpectedly
- If you have skin wounds that are not healing, it may be because of xylazine

### THE BAD STUFF

- Xylazine causes really bad skin ulcers when injected, even beyond the site of injection, like anywhere with a bite or cut.

  Missed shots can make skin ulcers worse
- Xylazine may cause a life-threatening drop in your blood's ability to carry oxygen to tissues (low blood iron, but we don't know a lot about this yet)
- Other symptoms may include: High blood sugar; less bladder control; tired all the time; slower reflexes; trouble swallowing; really dry mouth

### HARM REDUCTION TIPS

- · It is best to avoid dope with xylazine in it if you can
- Get your drugs tested at a harm reduction program if you can
- Don't use alone. Because of the heavy sedation, be aware of your surroundings and your possessions, especially if you're somewhere that's not secure

- Some harm reductionists think it may be safer to sniff/smoke/booty-bump dope with xylazine, but we don't know what other harms this can cause
- Try to be in a comfortable seated position, it's important to be in a position that doesn't cut off circulation to arms or legs
- Eat foods high in iron if xylazine is in your drug supply.
   Harm reduction programs can consider testing participants for hemoglobin using handheld devices

### **OVERDOSE**

- If someone is unresponsive, it's very very important to see if they are breathing! If they are taking 10 breaths each
  minute, keep an eye on them for the next hour. You don't need to use naloxone unless their breathing gets slower
- Naloxone doesn't work on xylazine BUT it will help if the opioid/fentanyl is making it hard for them to breathe
- Only if their breathing is slow or shallow, use naloxone the way you normally would (or titrate a lower dose of injectable



National Harm Reduction Coalition, 2022