

### **FACTS ABOUT XYLAZINE**

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**JUNE 07, 2024** 

### WE NEED A HEALTH APPROACH TO XYLAZINE.

Due to drug prohibition, xylazine is increasingly part of our drug supply. Learn more about how drug decriminalization and investing in health, overdose prevention centers, and safer supply can keep people safer.

# 1. WHAT IS XYLAZINE AND WHAT ARE THE EFFECTS OF XYLAZINE ON THE BODY?

We need a health approach to xylazine.

The general public knows very little about xylazine, and so much of the information on xylazine promotes fear and criminalization instead of helping people. To address our collective safety and well-being—and save lives—information on xylazine must be factual so people can make safer choices. Our responses to people who use drugs must be rooted in health. Here is what you need to know:

## XYLAZINE IS A SEDATIVE INCREASINGLY DETECTED IN THE ILLICIT DRUG SUPPLY.

Xylazine, also known as tranq, sleep cut, or anestetico de caballo, is a sedative drug that has been increasingly detected in fatal overdoses in some parts of the U.S. In these regions, it is being mixed into underground opioid and fentanyl supplies. Xylazine is not approved for medical use in humans. It is only FDA-approved for veterinary use with large mammals as a sedative and pain reliever.

It is appearing in the drug supply more now because it is relatively inexpensive and easy for distributors to procure. Xylazine typically is sourced from online suppliers in the underground market. Xylazine was first detected as an adulterant in underground heroin supplies in Puerto Rico¹ over 20 years ago. However, it has spread and become more common stateside in recent years. It emerged in Philadelphia, PA, over three years ago. By 202I, xylazine was detected in 90% of street opioid samples² in Philadelphia. It has been increasingly detected³ in overdose deaths and drug seizures in the northeast, including in New York City⁴, Maryland⁵ and Connecticut⁶.

## XYLAZINE IS TYPICALLY ADDED TO OPIOIDS TO PROLONG THEIR EFFECTS.

Research suggests7 that xylazine is synergistic with opioids, prolonging the duration and effect of drugs such as fentanyl and heroin. Because opioids have a short half-life, the effect wears off quickly. This is particularly true for people who use opioids often. This means they must seek out the drug frequently to manage opioid cravings and withdrawal symptoms. Xylazine mimics the drowsy feeling of an opioid high and extends the sensation of euphoria. Because of this, xylazine is typically added to opioids and not consumed in isolation.

# DRUG PROHIBITION LEADS TO NEW DRUGS LIKE XYLAZINE ENTERING THE ILLICIT DRUG SUPPLY.

It is also likely that xylazine is being added to the fentanyl supply due to increased penalties and crackdowns on fentanyl and fentanyl analogues. When an underground supply chain is disrupted due to drug seizures, manufacturers and distributors often add various adulterants to their drugs to stretch their supplies farther. It is likely that xylazine is added to fentanyl to extend the effects

of a much smaller quantity and purity of fentanyl in our drug supply.8

## XYLAZINE CAN CAUSE HARMFUL SIDE EFFECTS.

Xylazine is an adulterant. That means people are often not aware of its presence or the amount of it in their drug supply. This lack of control over polysubstance (using more than one drug) exposure can cause harmful side effects. This is because people are unable to prevent accidental exposure.

When taken in large doses or with opioid drugs, xylazine can lead to drowsiness, heavy sedation, and loss of consciousness.

The acute effects of xylazine include9:

- profound sedation,
- blurred vision,
- dry mouth,
- low blood pressure,
- low heart rate,
- weak reflexes,
- respiratory depression,
- disorientation,
- drowsiness,
- slurred speech,
- and risk of overdose.

Chronic effects can include:

- incontinence,
- high or low blood sugar,
- anemia,
- and in some cases, severe skin wounds.

Xylazine withdrawal presents its own challenges since tranquilizer withdrawal is associated with anxiety and mood disturbances, and there are currently no approved medications for xylazine treatment or withdrawal management.

## COMPLICATIONS OF XYLAZINE CONSUMPTION CAN BE DEBILITATING.

Xylazine causes profound sedation and loss of awareness, leading to blackouts that can last for up to 4 hours. While unconscious, sometimes the person cannot be awakened. If they fall or collapse, they may stay in the same position for hours, cutting blood flow off at limbs and extremities. When sedated on xylazine, one may also be vulnerable to heat or cold exposure if outdoors. There is also the risk of choking or being unable to breathe if airways are blocked off.

It's important that we have a health approach to xylazine that invests in addiction services and social supports. This includes voluntary treatment, housing, employment, harm reduction (including overdose prevention centers), recovery services, and peer support. We also need to start conversations about safer supply so that people know what's in the drugs they are getting.

# 2. ARE THERE ANY MEDICAL USES OF XYLAZINE?

Xylazine is not approved for medical use in humans. And it is not a controlled substance. It is only FDA-approved for veterinary use with large mammals as a sedative and pain reliever.

# 3. HOW LONG DOES XYLAZINE STAY IN THE SYSTEM?

Xylazine effects can be felt for up to 4 hours. Someone who recently used xylazine may test positive on a urine drug test for several days after consuming the drug. However, most standard urine drug screens do not test for xylazine. Xylazine is rapidly eliminated from blood, so there may be a risk of false negatives in blood testing.<sup>10</sup>

# 4. WHAT HAPPENS IF YOU MIX XYLAZINE WITH OTHER DRUGS?

Xylazine is typically added to opioids and not consumed in isolation. Mixing xylazine with other drugs can increase the risk of an overdose, especially if the other drugs are opioids or depressants. Depressant drugs include alcohol, benzodiazepines (like Valium® and Xanax®), sedatives, and tranquilizers. When xylazine is taken with these types of drugs, it can lead to drowsiness, sedation, unconsciousness, overdose, and death.

Naloxone (also called Narcan® and RiVive™) is a drug that works to reverse an opioid overdose, including fentanyl overdose. A new study shows that naloxone can be effective during an overdose of xylazine of an overdose involving an opioid like fentanyl, and xylazine". Overdoses that involve xylazine may need extra medical attention.

# 5. CAN YOU OVERDOSE ON XYLAZINE?

Yes, you can overdose on xylazine.

People often overdose on xylazine when it's combined with fentanyl or other potent opioids or sedatives. Xylazine is a central nervous system depressant that depresses breathing. Those effects combined with an opioid can stop someone's breathing and cause an overdose. Drugs in the underground market are not labeled and tested. This means people may accidentally consume high doses of xylazine without their knowledge, putting them at risk of overdose. The risk of a xylazine overdose is higher if consumed with other opioids or depressant drugs, like fentanyl, alcohol, benzodiazepines, or tranquilizers.

## XYLAZINE OVERDOSES CAN BE REVERSED BY NALOXONE

Since it is not an opioid drug, xylazine does not respond to naloxone. However, it is still important to administer naloxone to anyone who is overdosing because most xylazine is mixed with opioid drugs and the opioids may respond to the naloxone. When responding to a xylazine-involved overdose, administer naloxone, make sure the person is breathing and to place them in the recovery position, so they do not hurt themselves. If the person does not take at least 10 breaths a minute, it is important to call 911 for help and to administer rescue breaths until help arrives.

Read this helpful fact sheet by the National Harm Reduction Coalition for more information.

### 6. CAN YOU BECOME ADDICTED TO XYLAZINE AFTER USING IT FOR THE FIRST TIME?

No, you cannot become addicted to xylazine or any drug after using it only one time.

# PHYSIOLOGICAL DEPENDENCE IS DIFFERENT FROM SUBSTANCE USE DISORDER.

People can develop a physiological dependence upon xylazine if they use it repeatedly for several days or weeks in a row. Physiological dependence means that someone has developed an increased tolerance for a drug. They need to use more to get a desired effect. It also means they may experience physical withdrawal symptoms if they suddenly stop using a drug. Unfortunately, there is no FDA approved treatment for xylazine dependence and there are no established protocols for managing xylazine withdrawal symptoms.

## ADDICTION AND SUBSTANCE USE DISORDER.

A person only meets the criteria for a substance use disorder if they continue to use a drug repeatedly despite experiencing numerous harms and negative consequences.

# 7. WHAT ARE TREATMENT OPTIONS FOR PEOPLE WHO USE XYLAZINE?

There are no approved medications for xylazine treatment. But most people are exposed to xylazine because they are using opioid drugs.

People with opioid use disorder and those who use fentanyl have several treatment options<sup>12</sup> if they want help. Substance use disorder treatment involves professionally delivered psychosocial treatment and/or medications to reduce problematic drug use and improve health and quality of life. These services are provided in a variety of settings. This includes specialized treatment facilities like outpatient, inpatient, or

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residential centers. It can also include medical settings, such as hospitals and clinics. We at DPA believe that people should be able to choose the options that work best for them.

Of these treatments, medication assisted therapies have proven to be the most effective forms of treatment for opioid use disorder. There are 3 medications approved by the Food and Drug Administration (FDA) to treat opioid use disorder. These are methadone, buprenorphine (e.g., Suboxone), and naltrexone (e.g., Vivitrol).

Methadone is seen as the "gold standard" treatment for opioid use disorder. Research has shown for decades that it helps people to cut down on street opioids. It also helps patients to gain stability in their lives so they can reach their goals. To obtain methadone in the U.S., patients must visit special clinics. Due to strict regulations, most patients are required to be observed while taking their doses there, on a daily or near-daily basis.

**Buprenorphine** is a medication with similar benefits to methadone. Patients do not need to visit specially regulated clinics to obtain buprenorphine. However, until the recent passage of the MAT Act in Congress, medical professionals had to undergo additional training and get a special DEA waiver, commonly called the X-waiver, in order to prescribe buprenorphine.

Research shows that patients who take methadone or buprenorphine are less likely to experience cravings and withdrawal<sup>14</sup> and are less likely to overdose<sup>15</sup> than people who do not take these medications for their opioid use disorder.

The research on **naltrexone** is more mixed<sup>16</sup>, but it can be helpful for some people who voluntarily choose this option.

# 8. WHAT ARE HARM REDUCTION STRATEGIES FOR PEOPLE WHO USE XYLAZINE?

There are several important harm reduction strategies<sup>17</sup> for people who use xylazine.

#### **USE STERILE AND NEW EQUIPMENT.**

Xylazine can be swallowed, injected, smoked, or snorted. When possible, people who use xylazine should use sterile and new equipment every time. Supplies may include syringes, cookers, pipes, and straws. People should also avoid sharing equipment with others. Reusing or sharing equipment can place users at risk of skin and soft tissue infections, and spread diseases like HIV and hepatitis C. In some cases, xylazine can cause severe skin wounds. It's important to practice good vein hygiene and seek medical care for wounds before they progress to necrosis.

#### **NEVER USE ALONE.**

People should avoid using xylazine alone. Although it is not an opioid, new research shows that xylazine responds to the opioid overdose reversal medication, naloxone<sup>18</sup>. Therefore, it is still important to have naloxone available and to give it to anyone who is overdosing.

#### **MONITOR BREATHING.**

When responding to a xylazine-involved overdose, make sure the person is breathing. And place them in the recovery position so they do not hurt themselves.

#### IF THE PERSON DOES NOT TAKE AT LEAST

10 BREATHS A MINUTE,

IT IS IMPORTANT TO CALL 911 FOR HELP AND TO ADMINISTER RESCUE BREATHS UNTIL HELP ARRIVES.

#### **CHECK DRUGS IF POSSIBLE.**

People should use xylazine test strips or other available drug checking technologies to test their drugs for other adulterants. Xylazine test strips are sometimes available at harm reduction programs. They can tell someone if xylazine is present. But they cannot tell someone how much xylazine is present.

#### **GO SLOW.**

People should "go slow," dilute their drugs, or take a little bit at a time to reduce the risk of an overdose by accidentally taking too much. It is also advised that people do not take xylazine in combination with other opioids or depressant drugs, including alcohol. This can increase the risk of an overdose.

# 9. WHY DO WE NEED A HEALTH APPROACH, NOT MORE CRIMINALIZATION FOR XYLAZINE?

Xylazine is not a controlled substance. Oriminalizing xylazine, including scheduling it on the federal Controlled Substances Act (CSA), will likely result in an even more unknown and potentially dangerous drug supply.

## DRUG PROHIBITION LEADS TO STRONGER, MORE POTENT ILLICIT DRUGS.

Restricting prescription opioids did not end demand for opioids. Instead, it just sent people to the underground heroin supply. Crackdowns on heroin led suppliers to produce cheaper, potent and easily smuggled fentanyl. Harsh fentanyl penalties incentivized fentanyl analogues to flood our markets. And now, history is once again repeating itself. The classwide scheduling of fentanyl-related substances—which criminalizes all fentanyl-related substances more harshly, regardless of whether they are harmful or not—and the criminalization of fentanyl analogues more generally is leading to new and even more unknown drugs, like xylazine. We are increasingly seeing xylazine<sup>19</sup>, etizolam, benzodiazepines,20 and nitazenes overtaking some markets as a result of harsh crackdowns on

fentanyl analogues.

# SIMPLY PUT: CRACKDOWNS PUT US IN A GAME OF

### WHACK-A-MOLE.

When we try to eradicate one drug, a new one comes up. Often, it is a drug that consumers are not prepared for or has unpredictable effects. As a result, it creates more harms, because people who use drugs are not aware of what they are using or how strong it is.

# CRIMINALIZING XYLAZINE WILL DETER PEOPLE FROM SEEKING LIFESAVING SUPPORT.

Harsher penalties and criminalization can even prevent people from calling for help when someone is experiencing an overdose. This is because they are afraid of being prosecuted or facing other kinds of repercussions. This can include loss of employment, housing, or custody of their children.

## WE NEED A HEALTH APPROACH TO XYLAZINE.

Our elected officials need to invest in a health approach that invests in addiction services and social supports. This includes voluntary treatment, housing, employment, harm reduction (including overdose prevention centers), recovery services, and peer support. We also need to start conversations on safer supply so that people know what's in the drugs they are getting.

# 10. WHAT ARE DRUG POLICIES TO HELP PEOPLE WHO USE XYLAZINE TO BE SAFER?

There are many ways we can help people who use xylazine to be safer. This includes public education and policies we can pass at the local, state, and federal level.

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- Expand access to lifesaving overdose prevention services.
  - This includes the overdose reversal drug naloxone, drug checking tools like xylazine and fentanyl test strips, and syringe service programs.
  - Authorize overdose prevention centers (OPC) on the state and local level.
- Expand and protect 9II Good Samaritan laws.
- Expand methadone and buprenorphine access to treat opioid use disorder since most people exposed to xylazine are using opioid drugs.
- Expand addiction services and social supports, including evidence-based treatment and recovery services.
- Provide fact-based public education about xylazine for people who may be accidentally exposed to xylazine-adulterated drugs.
- Oppose attempts to schedule xylazine as a controlled substance and oppose calls for criminal penalties for xylazine use, possession, and distribution. Scheduling drugs can make it more difficult for researchers to study these drugs and develop effective treatments for the people who use them. Criminalization discourages individuals from seeking health services.

- Fund more research to better understand xylazine's effects on the human body and how to prevent and manage xylazine-related wounds.
   We also need more research on how to manage xylazine intoxication, how to reverse its effects, and how to provide treatment to people who may be experiencing xylazine withdrawal.
- Provide training for medical and emergency staff on how to appropriately treat xylazine-related wounds and how to care for patients who may be experiencing xylazine withdrawal.

Drug Policy Alliance (DPA) recommends a comprehensive, health-based response to the overdose crisis to keep people safe and healthy.

#### THERE IS GROWING PUBLIC ACCEPTANCE OF THE FACT THAT DRUG USE IS A HEALTH ISSUE, NOT A CRIMINAL ONE.

Unfortunately, some elected officials and members of law enforcement continue to call for draconian criminal policies to drive up support for policies that hurt people instead of helping them.

When it comes to xylazine and other substances emerging in the illicit drug supply, we must ensure that any new laws take a health approach. This includes decriminalizing drugs, safer supply, and overdose prevention centers.

### **END NOTES**

- Torruella, Rafael A. 2011. "Xylazine (veterinary sedative) use in Puerto Rico." Substance Abuse Treatment, Prevention, and Policy 67. https://substanceabusepolicy.biomedcentral.com/ articles/I0.II86/I747-597X-6-7
- Bettigole, Cheryl, Andrew Best, and Daniel Teixeira da Silva. 2022.
   "Xylazine (tranq) exposure among people who use substances in Philadelphia." <a href="https://hip.phila.gov/document/3154/PDPH-HAN\_Update\_13\_Xylazine\_12082022.pdf/">https://hip.phila.gov/document/3154/PDPH-HAN\_Update\_13\_Xylazine\_12082022.pdf/</a>
- Friedman, Joseph, Fernando Montero, Phillippe Bourgois, Rafik Wahbi, Daniel Dye, David Goodman-Meza, and Chelsea Shover. 2022. "Xylazine spreads across the US: A growing component of the increasingly synthetic and polysubstance overdose crisis." Drug and Alcohol Dependence, Volume 233. https://www. sciencedirect.com/science/article/abs/pii/S037687I62200II7X
- 4. Giftos, Jonathan and Alex Harocopos. 2022. "Advisory #33: Xylazine and Fentanyl in the New York City (NYC) Drug Supply." New York City Department of Health and Mental Hygiene. https://www.nyc.gov/assets/doh/downloads/pdf/han/advisory/2022/xylazine-and-fentanyl.pdf
- Friedman, Joseph, Fernando Montero, Phillippe Bourgois, Rafik Wahbi, Daniel Dye, David Goodman-Meza, and Chelsea Shover. 2022. "Xylazine spreads across the US: A growing component of the increasingly synthetic and polysubstance overdose crisis." Drug and Alcohol Dependence, Volume 233. https://www. sciencedirect.com/science/article/abs/pii/S037687I62200II7X
- 6 Connecticut Department of Public Health Drug Overdose Monthly Report. April 2023. <a href="https://portal.ct.gov/-/media/DPH/">https://portal.ct.gov/-/media/DPH/</a> Injury-and-Violence-Prevention/Opioid-Overdose-Data/Monthly-Death-Reports/2019-March-2023. <a href="https://doi.org/10.1007/JPH.2015">Drug-Overdose-Data/Monthly-Reports/2019-March-2023</a>. <a href="https://doi.org/10.1007/JPH.2015">Drug-Overdose-Data/Monthly-Reports/2019-March-2015</a>. <a href="https://doi.org/10.1007/JPH.2015">Drug-Overdose-Data/Monthly-Reports/2019</a>. <a href="https://doi.org/10.1007/JPH.2015">Drug-Overdose-Data/Monthly-Data/JPH.2015</a>. <a href="https://doi.org/10.1007/JPH.2015">Drug-Overdose-Data/JPH.2015</a>. <a href="https://doi.org
- Gupta, Rahul, David R. Holtgrave, and Michael A. Ashburn. 2023.
   "Xylazine Medical and Public Health Imperatives." The New England Journal of Medicine. <a href="https://doi.org/10.1056/NEJMp2303120">https://doi.org/10.1056/NEJMp2303120</a>
- Montero, Fernando, Philippe Bourgois, and Joseph Friedman. 2022. "Potency-Enhancing Synthetics in the Drug Overdose Epidemic: Xylazine ("Tranq"), Fentanyl, Methamphetamine, and the Displacement of Heroin in Philadelphia and Tijuana." Journal of Illicit Economies and Development. <a href="https://jied.lse.ac.uk/articles/I0.3I389/jied.l22">https://jied.lse.ac.uk/articles/I0.3I389/jied.l22</a>
- Grayken Center for Addiction Training & Technical Assistance, Boston Medical Center. 2022. "Zeroing in on Xylazine" Training. <a href="https://addictiontraining.org/training/register/event/?category=99&start=82&id=II86&pkIDed=I236">https://addictiontraining.org/training/register/event/?category=99&start=82&id=II86&pkIDed=I236</a>
- D'Orazio, Joseph. 2022. "Toxicity of Xylazine and How it Impacts People Who Use Drugs." COBRE on Opioids and Overdose Lecture Series. <a href="https://www.youtube.com/watch?v=Rqpf0]luyCo">https://www.youtube.com/watch?v=Rqpf0]luyCo</a>
- II. Bedard, Madigan L, Xi-Ping Huang, Jackson G. Murray, Alexandra C. Nowlan, Sara Y. Conley, Sarah E. Mott, Samuel J. Loyack, Calista A. Cline, Caroline G. Clodfelter, Nabarun Dasgupta, Brian Krumm, Bryan L. Roth, and Zoe A. McElligott. "Xylazine is an agonist at kappa opioid receptors and exhibits sex-specific responses to opioid antagonism." Addiction Neuroscience II (2024): 100155. https://doi.org/10.1016/j.addicn.2024.100155.

- National Academies of Sciences, Engineering, and Medicine. 2019. "Medications for Opioid Use Disorder Save Lives." Washington, DC: The National Academies Press. <a href="https://nap.nationalacademies.org/catalog/25310/medications-for-opioid-use-disorder-save-lives">https://nap.nationalacademies.org/catalog/25310/medications-for-opioid-use-disorder-save-lives</a>
- I3. Mattick, Richard P., Courtney Breen, Jo Kimber, and Marina Davoli. 2009. "Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence." Cochrane Database of Systematic Reviews. <a href="https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002209.pub2/full">https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002209.pub2/full</a>
- I4. Thomas, Cindy Parks, Catherine Anne Fullerton, Meelee Kim, Leslie Montejano, D. Russell Lyman, Richard H. Dougherty, Allen S. Daniels, Sushmita Shoma Ghose, and Miriam E. Delphin-Rittmon. 2014. "Medication-Assisted Treatment With Buprenorphine: Assessing the Evidence." Psychiatry Online. https:// ps.psychiatryonline.org/doi/full/IO.II76/appi.ps.201300256
- I5. Larochelle, Marc R., Dana Bernson, Thomas Land, Thomas J. Stopka, Na Wang, Ziming Xuan, Sarah M. Bagley, Jane M. Liebschutz, and Alexander Y. Walley. 2018. "Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality." Annals of Internal Medicine. https://www. acpjournals.org/doi/10.7326/MI7-3107
- 16. Wolfe, Daniela and Roxanne Saucier. 2021. "Biotechnologies and the future of opioid addiction treatments." International Journal of Drug Policy, Volume 88. <a href="https://www.sciencedirectcom/science/article/abs/pii/S0955395920303790?via%3Dihub">https://www.sciencedirectcom/science/article/abs/pii/S0955395920303790?via%3Dihub</a>
- I7. National Harm Reduction Coalition. 2022. "Xylazine in the Drug Supply." <a href="https://harmreduction.org/wp-content/uploads/2022/III/Xylazine-in-the-Drug-Supply-one-pager.pdf">https://harmreduction.org/wp-content/uploads/2022/III/Xylazine-in-the-Drug-Supply-one-pager.pdf</a>
- 18. Bedard, Madigan L, Xi-Ping Huang, Jackson G. Murray, Alexandra C. Nowlan, Sara Y. Conley, Sarah E. Mott, Samuel J. Loyack, Calista A. Cline, Caroline G. Clodfelter, Nabarun Dasgupta, Brian Krumm, Bryan L. Roth, and Zoe A. McElligott. "Xylazine is an agonist at kappa opioid receptors and exhibits sex-specific responses to opioid antagonism." Addiction Neuroscience II (2024): 100155. https://doi.org/10.1016/j.addicn.2024.100155.
- 19. Friedman, Joseph, Fernando Montero, Phillippe Bourgois, Rafik Wahbi, Daniel Dye, David Goodman-Meza, and Chelsea Shover. 2022. "Xylazine spreads across the US: A growing component of the increasingly synthetic and polysubstance overdose crisis." Drug and Alcohol Dependence, Volume 233. https://www.sciencedirect.com/science/article/abs/pii/SO37687I62200IITX
- Bollinger, Katherine, BeLinda Weimer, David Heller, Nichole Bynum, Megan Grabenauer, DeMia Pressley, and Hope Smiley-McDonald.
   2021. "Benzodiazepines reported in NFLIS-Drug, 2015 to 2018."
   Forensic Science International: Synergy Volume 3. <a href="https://www.sciencedirect.com/science/article/pii/S258987IX21000061">https://www.sciencedirect.com/science/article/pii/S258987IX21000061</a>