

Silent Intruder: Xylazine's impact on Public Health

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Conflicts of Interests

NOTHING TO DISCLOSE



"Pero la droga aquíes muy diferente a la de Puerto Rico...[but the drugs here are very different from what they're using in Puerto Rico] over there they're lacin' it with that stuff...horse tranquilizer, what they call anestesia de caballo...for like 8 years now...and they inject it, and you see them fast asleep on the street corner. And also, they say that when they shoot up and skin it, you know your skin gets, like, kind of f**ked up and you get these big craters. And those craters over there, I mean, they're not like the ones that the dopefiends from here got."

-Isabel, 40, Puerto Rican Resident of Philadelphia, interviewed in



Xylazine (zie-luh-zeen)

Bayer 1470, Abandoned Human Antihypertensive

Side Effects; sedation, hypotension, bradycardia

Currently FDA approved as a common veterinary tranquilizer

NON-opioid sedative with analgesic and muscle relaxant properties

Not federally recognized controlled substance

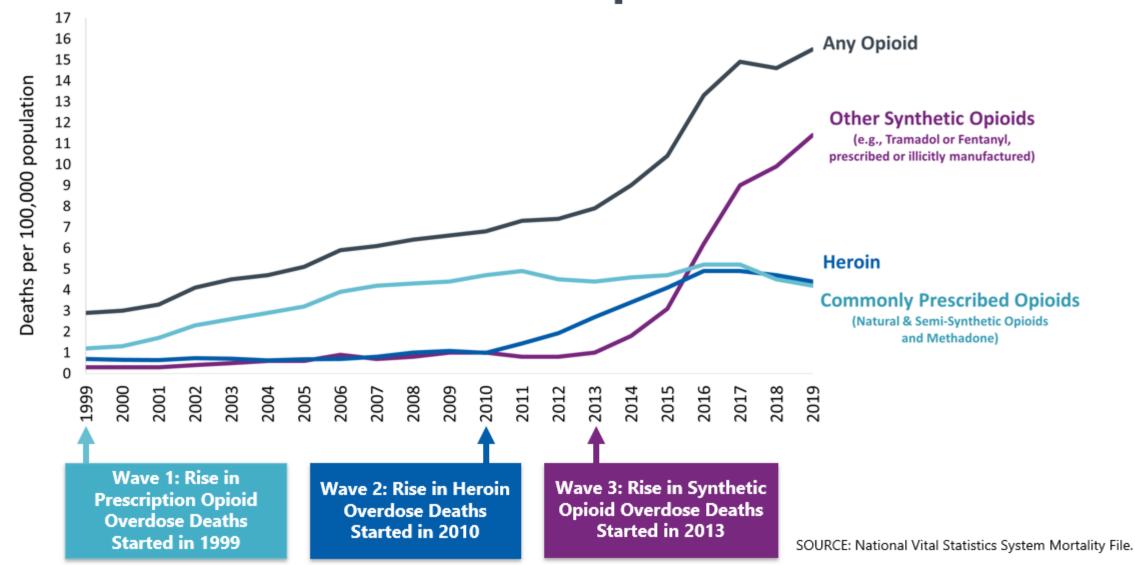
Names: Rompun®, Anased®, XylaMed® Sedazine™, Chanazin®



"Anestesia de caballo"

- Street names include "tranq" or "tranq dope" "sleep cut" "zombie"
- Recreationally used to extend euphoric effects of shorter-acting fentanyl
- Huge problem in Puerto Rico for 20+ years,
 - -->East Coast, Chicago, and Texas (2000s)
 - Post mortem toxicology testing, Drug Seizures by US Drug Enforcement Agency
 - Xylazine cases are frequently undercounted because it is <u>not a universally</u> <u>controlled substance</u> and is inconsistently reported in crime lab data
- Adulterant versus primary agent

Three Waves of the Rise in Opioid Overdose Deaths





Yeah I like a good tranq-fent bag. Some people don't like it, but plenty of people do. It's sought after. Certain stamps [brands printed on drug bags] that are known for tranq have better business, you know what I mean? I like it cuz, fentanyl is such a short-lived high... It's a good high, but it's so short that the nod is over real quick and you get sicker faster. 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. But then other times, they straight put bags out there that are just all tranq. You shoot it, you feel no rush, and you're just out, you're asleep for at least 40 min. You're sitting there one second talking, and then you're waking up 2–3 h later in a weird position."

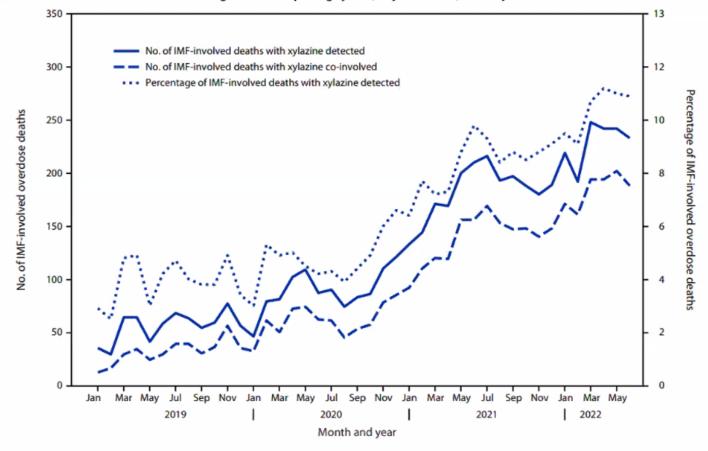
-Henry, White 30, Injects Opioids, Xylazine, Methamphetamine, Cocaine



Illicitly Manufactured Fentanyl–Involved Overdose Deaths with Detected Xylazine — United States, January 2019–June 2022

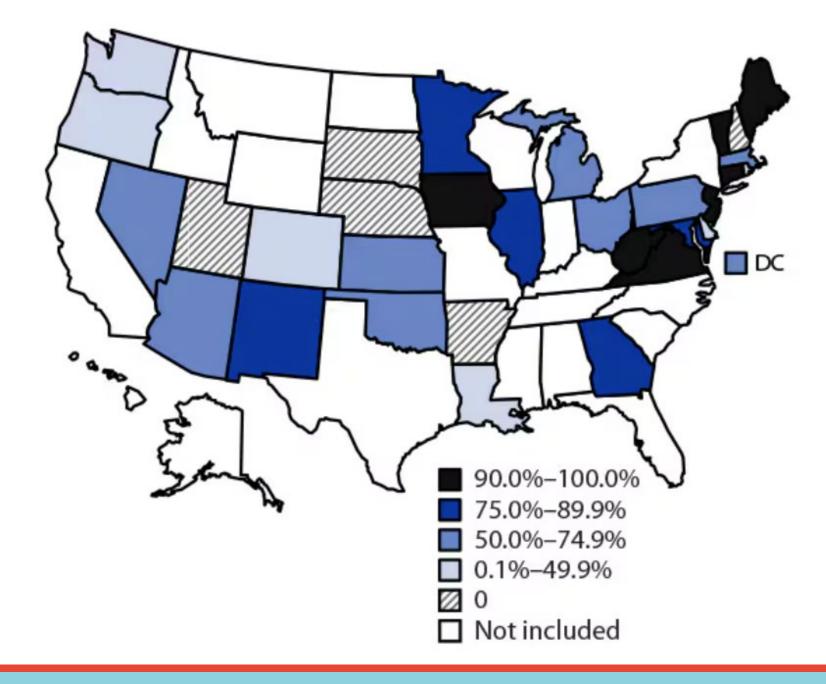
Weekly / June 30, 2023 / 72(26);721-727

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



Kariisa M, O'Donnell J, Kumar S, Mattson CL, Goldberger BA. Illicitly Manufactured Fentanyl-Involved Overdose Deaths with Detected Xylazine - United States, January 2019-June 2022. MMWR Morb Mortal Wkly Rep. 2023 Jun 30;72(26):721-727.

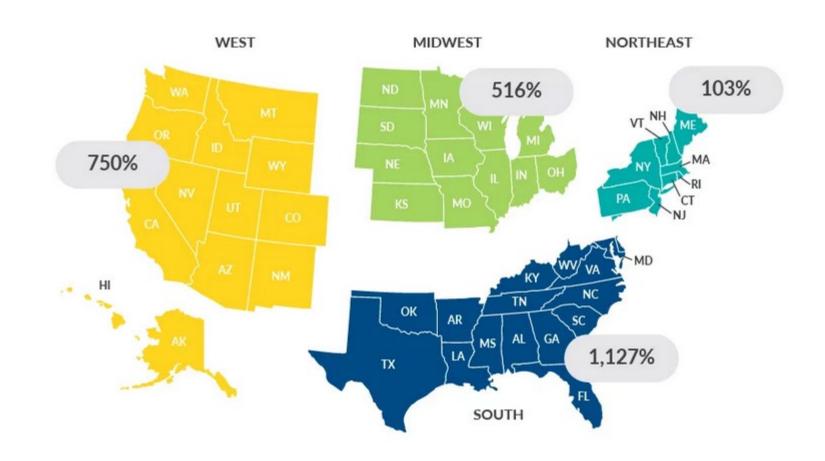




2019-2022



Xylazine Positive Deaths from 2020-2021





(U) Figure 2. Number of Xylazine-Positive Overdose – Deaths by Region

| Region | 2020 | 2021 | Percent Increase |
|-----------|------|-------|---------------------|
| Northeast | 631 | 1,281 | 103% |
| South | 116 | 1,423 | 1,127% |
| Midwest | 57 | 351 | 516% |
| West | 4 | 34 | 750% |

Source: DEA



TABLE. Characteristics of drug overdose decedents with xylazine detected on postmortem toxicology (xylazine-positive) or listed as a cause of death (xylazine-involved) — State Unintentional Drug Overdose Reporting System, 38 states and the District of Columbia,* 2019

| | Classification of deaths, no. (%) | | | | |
|-------------------------------------|---|---|--|--|--|
| Characteristic | Xylazine-positive [†] (n = 826) | Xylazine-involved [§] (n = 531) | | | |
| Sex | | | | | |
| Male | 602 (72.9) | 388 (73.1) | | | |
| Female | 224 (27.1) | 143 (26.9) | | | |
| Race [¶] | | | | | |
| White, non-Hispanic | 604 (74.8) | 396 (75.4) | | | |
| Black, non-Hispanic | 106 (13.1) | 68 (13.0) | | | |
| Hispanic | 90 (11.1) | ** | | | |
| Other | 11 (1.4) | ** | | | |
| Age group, yrs | | | | | |
| 15-24 | 60 (7.3) | 41 (7.7) | | | |
| 25-34 | 265 (32.1) | 181 (34.1) | | | |
| 35-44 | 227 (27.5) | 138 (26.1) | | | |
| 45-54 | 147 (17.8) | 91 (17.1) | | | |
| 55-64 | 109 (13.2) | ** | | | |
| ≥65 | 18 (2.2) | ** | | | |
| U.S. Census region ^{††} | | | | | |
| Northeast | 568 (68.8) | 356 (67.0) | | | |
| Midwest | 144 (17.4) | 91 (17.1) | | | |
| South | 104 (12.6) | ** | | | |
| West | 10 (1.2) | _** | | | |
| Co-occurring drugs listed | as a cause of death ^{§§,¶¶} | | | | |
| Any fentanyl (including analogs) | 815 (98.7) | 526 (99.1) | | | |
| Heroin*** | 215 (26.0) | 151 (28.4) | | | |
| Benzodiazepines | 141 (17.1) | 105 (19.8) | | | |
| Prescription opioids ^{†††} | 94 (11.4) | 71 (13.4) | | | |
| Cocaine | 265 (32.1) | 157 (29.6) | | | |
| Alcohol | 98 (11.9) | 67 (12.6) | | | |
| Methamphetamine | 102 (12.4) | 62 (11.7) | | | |



Classification of deaths, no. (%)

| Xylazine-positive [†] | Xylazine-involved§ | | |
|--------------------------------|--------------------|--|--|
| (n = 826) | (n = 531) | | |

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Pharmacology

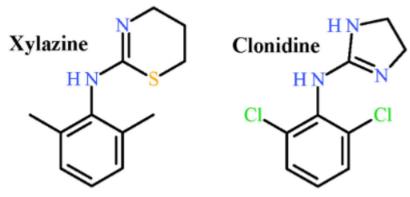


Figure 1. Chemical structures of xylazine and clonidine.

Non-opioid veterinary sedative and muscle relaxant Lipophilic, Rapid uptake into Central Nervous system Structurally similar to clonidine (an antihypertensive agent) Alpha 2 agonist

Xylazine decreases neurotransmitter presynaptic release → decreasing an adrenergic physiologic response (sedation) Implications:

- 1. Limited imidazoline receptor activity: limited bradycardia and hypotension
- 2. Sedation, but limited respiratory depression when by itself, may see synergistic features with other CNS depressants



Pharmacokinetics

Time to Onset: ~1-2 minutes

Peak effects: 30 minutes

Duration of effect: up to **4 hours***however, human case reports duration up to 72 hours*

Human Toxicity dose: 40 – 2,400 mg. Fatal Serum concentrations of xylazine from trace to 16 mg/L.

= NO SAFE BLOOD CONCENTRATION



Routes

Swallowed

Inhaled (smoked)

Snorted

Injected (Intramuscular or Intravenous)



XYLAZINE IMPACTS

Clinical Effects

CNS Effects

- Analgesia
- Sedation
- Amnesia
- Coma



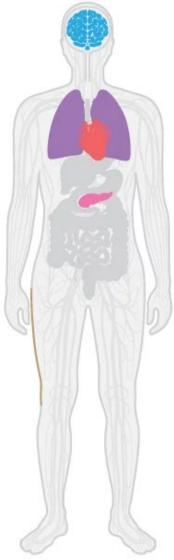
Respiratory System

· Respiratory depression



Skin Disorders

- Ulcers
- · Tissue necrosis





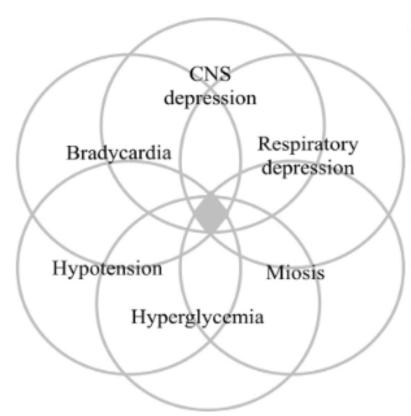
Cardiovascular

- Hypotension
- Bradycardia
- Tachycardia
- Vasoconstriction



Metabolic/Endocrine

Hyperglycemia





"I got some friends out here that got really torn up by it, you know they got holes in them, abscesses, basically it's like the body is rotting. People here are losing limbs like with gangrene. Whatever they're doing with the tranq....everybody is getting these scabby sores all over their bodies... and many of them don't shoot meth. So it's from the dope. You know what I mean, you had the dope, then the fentanyl, now it's the "tranq-fent," the rhinoceros tranquilizer, the horse tranquilizer, you know? Cooked up and it's broken down and it's added to the dope and we seek that out, you know what I mean? Our habits are fentanyl and tranquilizer."

-Annie, White 25, Injects Opioids, Xylazine, Methamphetamine



| CURRENT LIVING ARRANGEMENT | + Xylazine | - Xylazine | |
|-------------------------------|-------------------|-------------------|--------|
| 0. On street | 25 (64.1%) | 27 (37.0%) | 0.009 |
| 1. In a shelter | 0 | 1 (1.4%) | ns |
| 2. With unrelated person(s) | 0 (0%) | 5 (6.9%) | ns |
| 3. In a rented room/apartment | 1 (2.6%) | 0 (0%) | ns |
| 4. With relative(s) | 5 (12.8%) | 9 (12.3%) | ns |
| 5. With parent(s) | 7 (17.9%) | 19 (26.0%) | ns |
| 6. In own house | 1 (2.6%) | 12 (16.4%) | 0.029 |
| PREVALENCE OF SKIN ULCERS | 15 (38.5%) | 5 (6.8%) | <0.001 |

People using xylazine reported poorer health more frequently than those who did not (29/39 vs. 39/73; p = 0.04)



*** WARNING: GRAPHIC PICTURES ON NEXT SLIDE ***

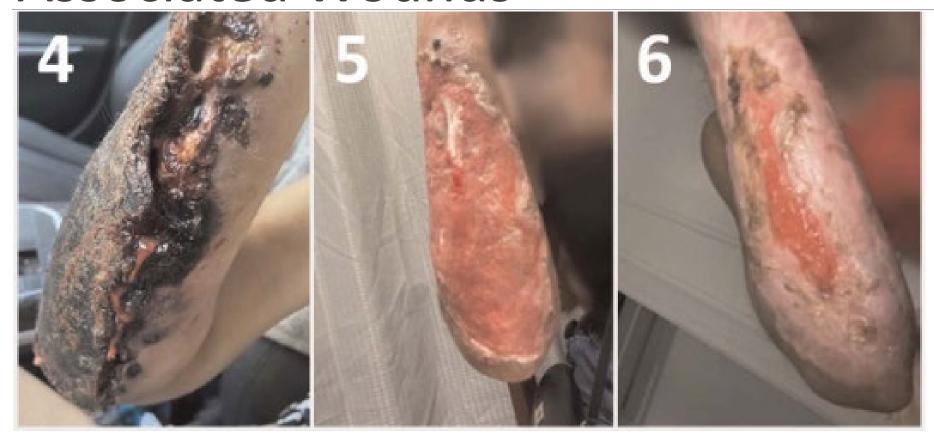
Progression and Healing of Xylazine Associated Wounds

WASHINGTON





Progression and Healing of Xylazine **Associated Wounds**









Cause of Skin Wounds?

Possible causes of xylazine-associated wounds include:

- Cytotoxic effects of xylazine and/or contaminants in the drug supply
- •Infectious
- Peripheral vasoconstriction caused by the drug
- •Increased frequency of injections
- Compression from prolonged sedation
- Vasculitis
- Skin Picking Behaviors

None of these theories completely explain the clinical observations

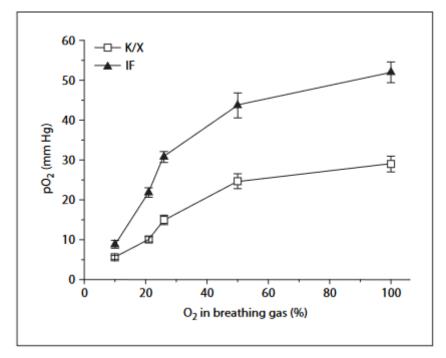
Influence of different anesthetics on skin oxygenation studied by electron paramagnetic resonance in vivo

Z Abramovic ¹, M Sentjurc, J Kristl, N Khan, H Hou, H M Swartz

Affiliations + expand

PMID: 17143012 DOI: 10.1159/000097654

Mice skin oxygenation evaluated by electron paramagnetic resonance oximetry following anesthetized with ketamine/xylazine or isoflurane





Stigma Limitations in Access

- Patients may avoid hospital care due to fear of stigmatization, unmanaged pain and withdrawal, and previous traumatic healthcare experiences
- Patients are often labeled as "junkies" or "drug-seeking"
- Hospital staff often search and confiscate personal belongings, cutting off social support through visitation restrictions
- Disposition limitations with dual diagnosis
- Specialty clinics may be inaccessible due to rigid schedules and sobriety requirements
- Shelter is crucial for wound healing, but housing-first options are scarce



adapted from Prevention Point Philadelphia Wound Care Clinic Approach to Xylazine Associated Wounds

Step 1: Premedicate if possible

Step 2: Remove soiled dressing

- Soak with water/saline to decrease pain with dressing removal
- Offer patient the option to remove own dressing

Step 3: Cleanse

- Normal saline, generic wound washes, soap/water, chlorhexidine
- Test cleaners on small amount of wound to assess tolerance
- Heavy burden of nonviable tissue? Vashe, Dakin's Solution 0.125%



adapted from Prevention Point Philadelphia Wound Care Clinic Approach to Xylazine Associated Wounds

Step 4: Debridement

- Enzymatic versus Autolytic
 - Enzymatic debridement:
 - Santyl: Requires prescription; costly, can be painful
 - Autolytic:
 - Medihoney
 - Hydrogel silver
 - Silver gel/Silver sulfadiazine
- Topicals debridement agents may be applied to primary dressing to avoid directly touching sensitive wounds



adapted from Prevention Point Philadelphia Wound Care Clinic Approach to Xylazine Associated Wounds

Step 5: Apply other topicals

- Skin protectant to peri-wound tissue
 - Example: A&D ointment, no sting skin prep, Coloplast Triad
 - Topical antibiotic if indicated (and compatible)

Step 6: Primary Dressing

Cut to shape of wound to avoid periwound breakdown

Step 7: Apply secondary Dressing

 Super Absorbent Dressing, Layers of woven gauze, abdominal pads or nonstick gauze



adapted from Prevention Point Philadelphia Wound Care Clinic Approach to Xylazine Associated Wounds

Step 8: secure

- Apply self-adherent or ACE bandages snugly enough to keep the underlying dressings in place, but not for compression.
- Warning: Self-adherent dressings should be changed daily to prevent skin breakdown.



Patient monitoring Instructions

- Don't inject near the wound.
- Don't pick at your skin; keep the wound covered
- Watch for serious signs:
 - Signs of being very sick
 - Painful bump that feels squishy
 - Fast changes in wound color
 - Extreme pain, new numbness, or spotted skin around the wound
 - Visible bones or tendons
 - Chunks of tissue falling out
 - If the wound is near a joint, watch for joint pain, swelling, redness, or trouble moving joint



Harm Reduction/ Trauma induced care

- Assess the patient's wound care history
- Offer the patient the option to remove the dressing themselves for engagement, autonomy, and pain minimization
- Address distress and stigma related to wound odor with air fresheners, aromatherapy, and frequent trash changes
- Provide oral antibiotics/medications in a lanyard-attached container to prevent theft or loss (for unhoused individuals)
- •Set a feasible wound dressing change schedule and supply enough materials for multiple changes
- If injecting, encourage safe use (needle exchange, clean needles, alcohol wipes)
- Collaboration



TABLE 2. Survey Results: Demographics, Patterns of Drug Use, and Experiences with Xylazine

| Demographics | | | | | | | |
|--|------|---|------|--|------------|--|-----|
| Age Range (n = 51) | | Gender $(n = 51)$ | | Race $(n = 50)$ | | Geography $(n = 50)$ | |
| <20 y | 8% | Male | 67% | White, non-Hispanic | 79% | Northeast* | 50% |
| 20–29 y | 33% | Female | 29% | White, Hispanic | 4% | Southeast | 14% |
| 30–39 y | 47% | Nonbinary/other | 4% | African American | 4% | Midwest | 14% |
| 40-49 y | 12% | | | Asian | 5% | Southwest | 0% |
| ≥50 y | 0% | | | American Indian | 4% | West | 10% |
| | | | | Native Hawaiian/Pacific Islander | 4% | Other country† | 12% |
| Patterns of Drug Use | | | | | | | |
| Intentionally Seek Out to Buy Drugs That Contain Xylazine (n = 61) | | Drug Use on a Typical Day (n = 60) | | Method of Xylazine Exposure (n = 61) | | Frequency of Xylazine Use (n = 61) | |
| Yes | 26% | Any opioids | 93% | Inhalational (smoking) | 20% | Daily | 39% |
| No | 74% | Fentanyl | 80% | Intranasal (snorting) | 57% | 1–6 times per week | 19% |
| | 7470 | Cannabis | 45% | Injection | 43% | 1–4 times per month | 15% |
| | | Stimulants | 41% | Oral | 3% | A few times per year/rarely | 27% |
| | | Benzodiazepines | 21% | Olai | 570 | 71 few times per year/tatery | 2// |
| | | Hallucinogens | 10% | | | | |
| Experiences With Xylazine | | Tiditucinogens | 1070 | | | | |
| Adverse Effects From Xylazine Use (n = 48) | | Have You Experienced Withdrawal From Xylazine? (n = 59) | | What Xylazine Withdrawal Symptoms Have You Experienced? (n = 35) | | How Has Withdrawing From Other Drugs Changed Since You Started Using Xylazine? (n = 51) | |
| Increased overdoses/passing out | 81% | Yes | 53% | Body aches | 63% | Worse | 57% |
| Skin wounds or infections | 43% | No | 47% | Cravings | 49% | The same | 39% |
| Increased emergency room visits | 17% | | | Anxiety Depressed Mood | 91% 74% | Better | 4% |







Overdose Features?



Unresponsive, extreme drowsiness



Pinpoint pupils



Blue/gray lips, skin or nails



Slow or weak pulse



Slow, shallow or absent Breathing



Intoxication versus Overdose

Intoxication

Overdose

Normal skin tone Pale, clammy skin, cyanosis

Normal breathing Slowed/infrequent breathing, RR <8-10bpm

Deep snoring, gurgling or choking sounds

Normal HR Slowed/irregular HR

Looks sleepy Unconscious, unable to wake up

Speech slurred or slow

Responsive to stimuli

Not responsive to stimuli

Pinpoint pupils* Pinpoint pupils



What to do if Someone is Not Breathing





Side Effects of Naloxone



Side Effects of Naloxone

....Breathing



What is Naloxone? (brand name Narcan)

- Naloxone is a life-saving medication that reverses an opioid overdose
- Naloxone works by blocking the opioid receptor sites (opioid antagonist), thereby reversing the toxic effects of the overdose
- Works in minutes
- Safe even for accidental exposure, pregnancy, children, etc.

WHEN IN DOUBT, GIVE IT





| | XYLAZINE-RELATED | | | | ALL SUSPECTED HEROIN | | |
|----------------|------------------|--------|---------------|-----|----------------------|---------------|--|
| YEAR | SUBMI | SSIONS | GLASSINE BAGS | | SUBMISSIONS | GLASSINE BAGS | |
| 2019 | 368 | 3% | 9,038 | 1% | 13,010 | 680,807 | |
| 2020 | 855 | 11% | 30,236 | 6% | 7,814 | 500,715 | |
| 2021 | 3,052 | 30% | 239,998 | 29% | 10,341 | 821,171 | |
| 2022 | 2,614 | 35% | 138,818 | 29% | 7,374 | 475,826 | |
| 2023 (TO 9/30) | 2,529 | 50% | 144,637 | 47% | 5,039 | 310,665 | |

| ANALYZED 1/1/2015 - 12/31/2022 | | | | | |
|--|-----------|------|--|--|--|
| FENTANYL/4-ANPP/XYLAZINE | 82,612 | 19% | | | |
| HEROIN/FENTANYL/4-ANPP/XYLAZINE | 42,408 | 10% | | | |
| FENTANYL/XYLAZINE | 28,826 | 7% | | | |
| HEROIN/FENTANYL/XYLAZINE | 19,871 | 5% | | | |
| HEROIN/FENTANYL/FLUOROFENTANYL/ | 15,256 4% | | | | |
| TRAMADOL/XYLAZINE | 15,256 | 470 | | | |
| XYLAZINE ONLY (MONO DRUG) | 724 | 0.2% | | | |
| OTHER FENTANYL & XYLAZINE | 220 101 | 54% | | | |
| COMBINATIONS | 228,101 | 54% | | | |
| OTHER DRUGS OR COMBINATIONS | 7,664 | 2% | | | |
| TOTAL 425,462 | | | | | |
| Content is listed in the order of amounts found in the sample. | | | | | |

Xylazine positive

Data from New Jersey State Police



Naloxone Take Home

- •Overdose management should focus on clinical findings, ventilation, and oxygenation. Use naloxone per standard guidelines.
- •Xylazine, not reversed by naloxone, is often combined with opioids, making naloxone effective for ventilatory effort
- •"Naloxone-resistant overdose" often involves polysubstance use (e.g., benzodiazepines, xylazine) or metabolic issues (hypoxia, hypercarbia)= NEED MEDICAL ATTENTION
- •Aim for improved ventilation, not awakening, to avoid multiple naloxone doses and risk of opioid withdrawal.
- •Treat opioid-xylazine overdose with supportive care and naloxone as needed.

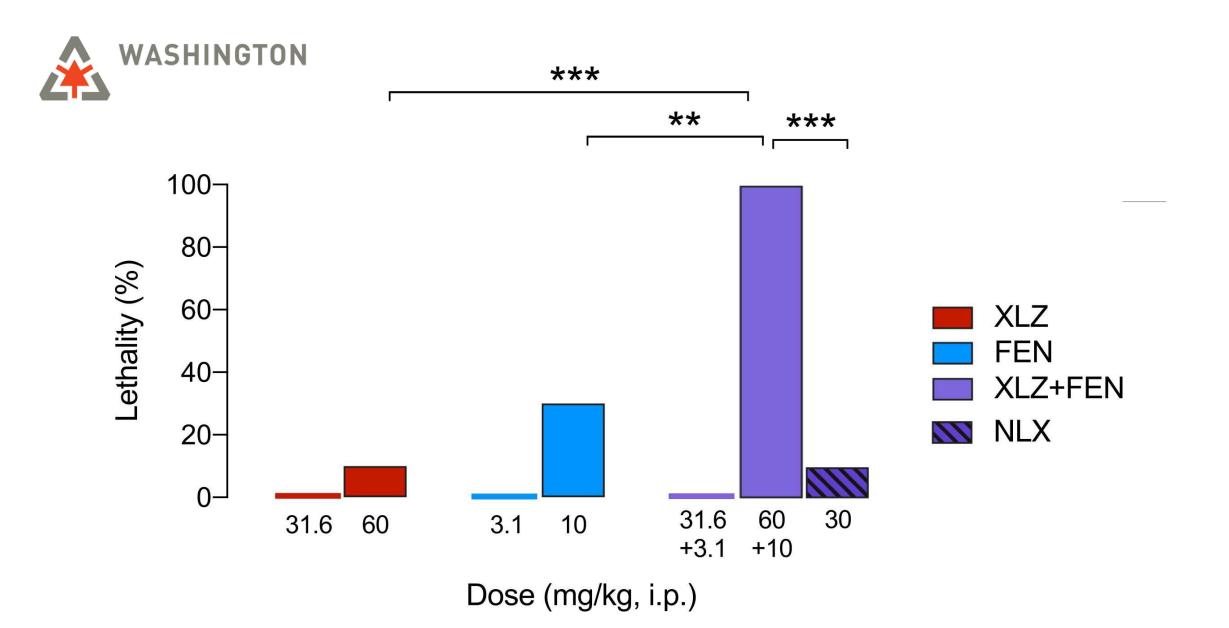




Table 2. Clinical outcomes in xylazine vs. control patients.

| Clinical outcome variables | Xylazine (<i>n</i> = 90) | Xylazine absent ($n = 231$) | P-Value |
|---|---------------------------|-------------------------------|---------|
| Cardiovascular outcomes | | | |
| Received CPR | 4 (4.4%) | 33 (14.3%) | 0.013 |
| Bradycardia | 2 (2.2%) | 4 (1.7%) | 0.77 |
| Pulmonary outcomes | | | |
| Intubated within 4h | 2 (2.2%) | 13 (5.6%) | 0.193 |
| Non-invasive positive pressure within 4 h | 1 (1.1%) | 4 (1.7%) | 0.689 |
| Any ventilatory support within 4 h | 3 (3.3%) | 17 (7.4%) | 0.182 |
| Intubated after 4 h | 2 (2.2%) | 11 (4.8%) | 0.298 |
| Non-invasive positive pressure after 4 h | 2 (2.2%) | 2 (0.9%) | 0.327 |
| Any ventilatory support after 4 h | 4 (4.4%) | 13 (5.6%) | 0.67 |
| Central nervous system outcomes | | | |
| Coma within 4 h | 24 (26.7%) | 87 (37.7%) | 0.063 |
| Coma after 4 h | 12 (13.3%) | 35 (15.2%) | 0.682 |
| Overall outcomes | | | |
| Death | 1 (1.1%) | 5 (2.16%) | 0.528 |
| Discharged from the ED | 59 (65.6%) | 147 (63.6%) | 0.528 |
| ICU Admissions | 11 (12.2%) | 39 (16.9%) | 0.30 |
| Miscellaneous | | | |
| Length of hospitalization (h); median (IQR) | 10 (5–28) | 9 (5–36) | 0.806 |
| Total naloxone dose (mg) | 3.68 (1.3-4.05) | 2.8 (2-4.1) | 0.448 |

Abbreviations: IQR, interquartile range; CPR, cardiopulmonary resuscitation; ED, emergency department; ICU, intensive care unit. The bold values indicate variables that are statistically significant (P < 0.05).

^{*}Percentage of entire cohort.



Future Treatment Agents?

Yohimbine- α2 adrenergic antagonist

Atipamezole- α 2-antagonist that is used as a reversal agent for α 2-agonist toxicity in animals

Tolazoline- mixed central and peripheral α_2 -antagonist

?Given the limited contribution of xylazine to overdose mortality, the pursuit of xylazine specific reversal agents is not clearly necessary

For the time being treatment should be focused on the opioid component of the overdose

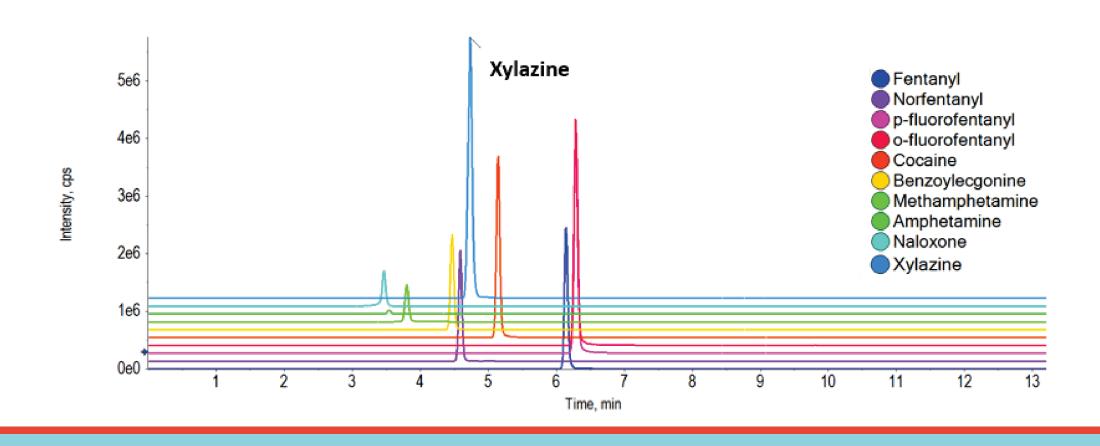


Testing limit

Animal models and human data suggest xylazine has a short detection window in biological matrices, with urine having a longer detection window than blood

- A cohort of 128 opioid use disorder patients (March 2022 February 2023) had urine samples tested for xylazine using GC/MS
- No xylazine was detected in any tests performed after 43 hours from the last reported use
- Two out of three tests were positive after 30 hours, but these involved inhospital substance use
- The likely detection duration for xylazine in urine is less than 30 hours

Extracted ion chromatograms standard for Target Drugs including xylazine, NPS Discovery

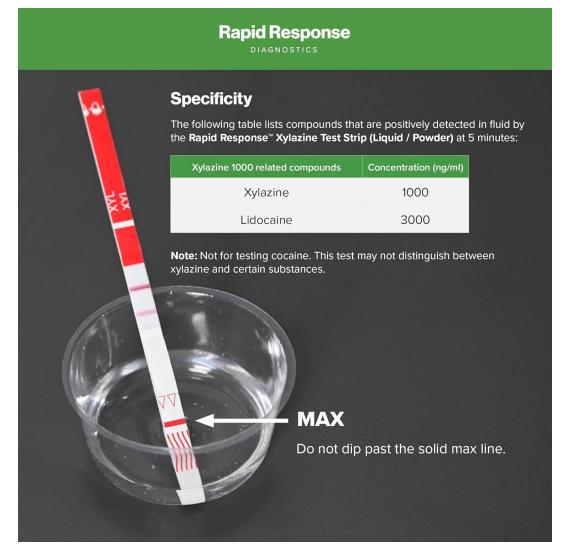




Laboratory and Testing

- Point of Care Immunoassay not currently available
- Most hospital laboratories are unable to run analysis for Xylazine, need TLC or GCMS evaluation
- NMS, ARUP, Mayo, Others
- Turn around time-week(s) may not be clinically useful
- Often costly, hundreds to thousands of \$\$\$, who pays?
- Send off labs offers testing for clients such as reference labs, hospital laboratories, medical personnel, medical examiners/coroners, jails, and the







Test Strips:

~\$100-200 per box of 100

Rapid visual Qualitative immunoassay

While test strips are decriminalized under existing paraphernalia and testing laws in at least 23 states, some states maintain drug paraphernalia laws that may inhibit or criminalize to possession of test strips*

Potential false positives: lidocaine, diphenhydramine, levamisole



Withdrawal Presentation

XYLAZINE WITHDRAWAL SYMPTOMS

- Anxiety
- Dysphoria
- Restlessness
- •+/- Hypertension

OPIOID WITHDRAWAL SYMPTOMS

- Anxiety
- Dysphoria
- Restlessness
- •GI Distress (Nausea, Vomiting, Diarrhea)
- Muscle Soreness
- Runny Nose
- Tremors
- Yawning
- Goosebumps



Withdrawal Management

Not well defined syndrome

The widespread co-exposure to opioids and increasing fentanyl dependence make xylazine dependence and its withdrawal syndrome unclear

Anxiety, irritability, restlessness, dysphoria, severe hypertension

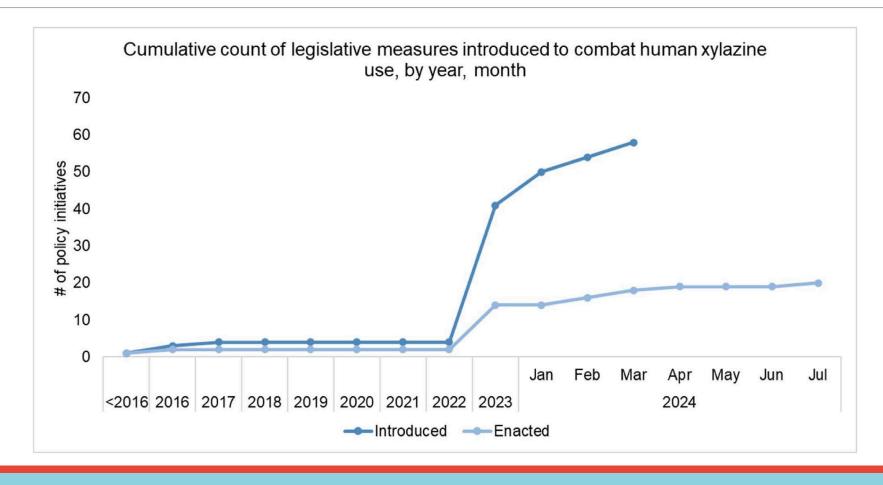
- If patients are admitted inpatient be prepared to treat xylazine withdrawal symptoms simultaneously with opioid withdrawal
- Consideration of benzodiazepines and/or alpha-2 adrenergic agonists, clonidine, dexmedetomidine, tizanidine, guanfacine



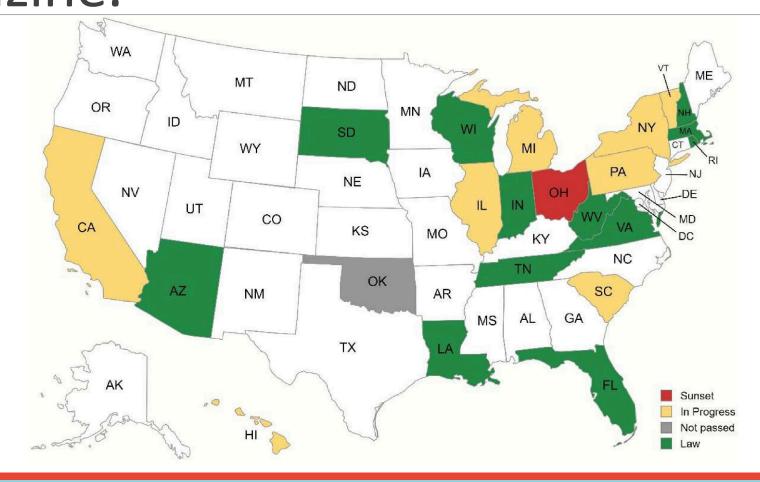
| Drug | Alternatives | Description | |
|-----------------|--------------------------------------|---|--|
| Primary | | | |
| Clonidine | Tizanidine, lofexidine, guanfacine | α -2 Adrenergic agonist; antihypertensive; efficacy in opioid withdrawal attributed to binding to central α -2 adrenergic receptor that shares potassium channels with opioids and blunts symptoms of withdrawal; starting dose 0.1 mg every 8 h recommended as standing dose/prophylaxis if blood pressure can tolerate; caution: sedation, bradycardia, and hypotension | |
| Secondary | | | |
| Olanzapine | Ziprasidone, risperidone, quetiapine | Atypical antipsychotic; 2.5 mg starting dose; 2.5-10 mg daily | |
| Lorazepam | Clonazepam, midazolam, diazepam | GABA agonists; lorazepam 1-2 mg orally/intravenously/intramuscularly; titrate to effect; caution: sedation | |
| Gabapentin | - | Anticonvulsant; reduces transmission of voltage-gated calcium channels reducing excitatory neurotransmitters; best efficacy in neuropathic pain; can optimize sedation effects; 300-600 mg every 8 h and 300 mg once daily at bedtime | |
| Phenobarbital | - | GABA agonist; long-acting barbiturate; 130 mg intravenously; caution: sedation | |
| Dexmedetomidine | - | α -2 agonist; sedation; antihypertensive; use in monitored settings after maxim oral α -2 agonists: dose \geq 0.2-1 mcg/kg/h | |
| Others | | | |
| Ropinirole | - | Non-ergoline dopamine agonist used to treat motor symptoms of Parkinson of as well as to treat restless legs syndrome; it can aid in muscle relaxation, and motor restlessness-myoclonus; starting dose 0.25-0.5 mg every 8 h | |
| Ketamine | - | NMDA receptor antagonist; effective as an opioid-sparing analgesic adjunct; 10 mg postoperatively every 6 h; 0.3 mg/kg intravenously over 15 min; short-acting unless followed by continuous infusion | |
| Pregabalin | - | Anticonvulsant; adjunct treatment for neuropathic pain and anxiety; 100 mg 3 times per day up to 600 mg 3 times per day | |

GABA = γ -aminobutyric acid; NMDA = N-methyl-D-aspartic acid.

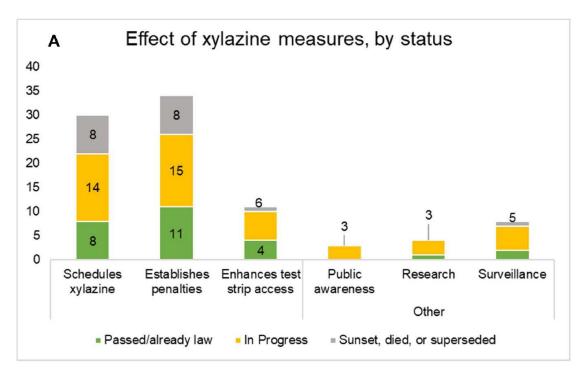
Cumulative count of legislative measures to combat illicit xylazine as of April 16, 2024

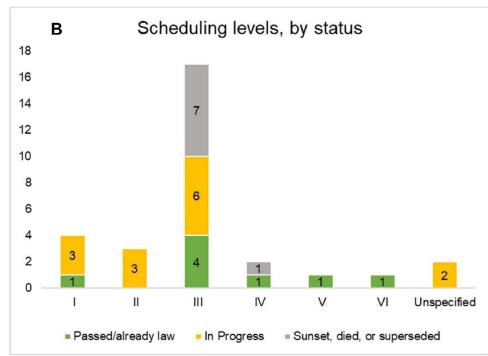


Geographic distribution of proposed legislative initiatives to combat illicit xylazine.

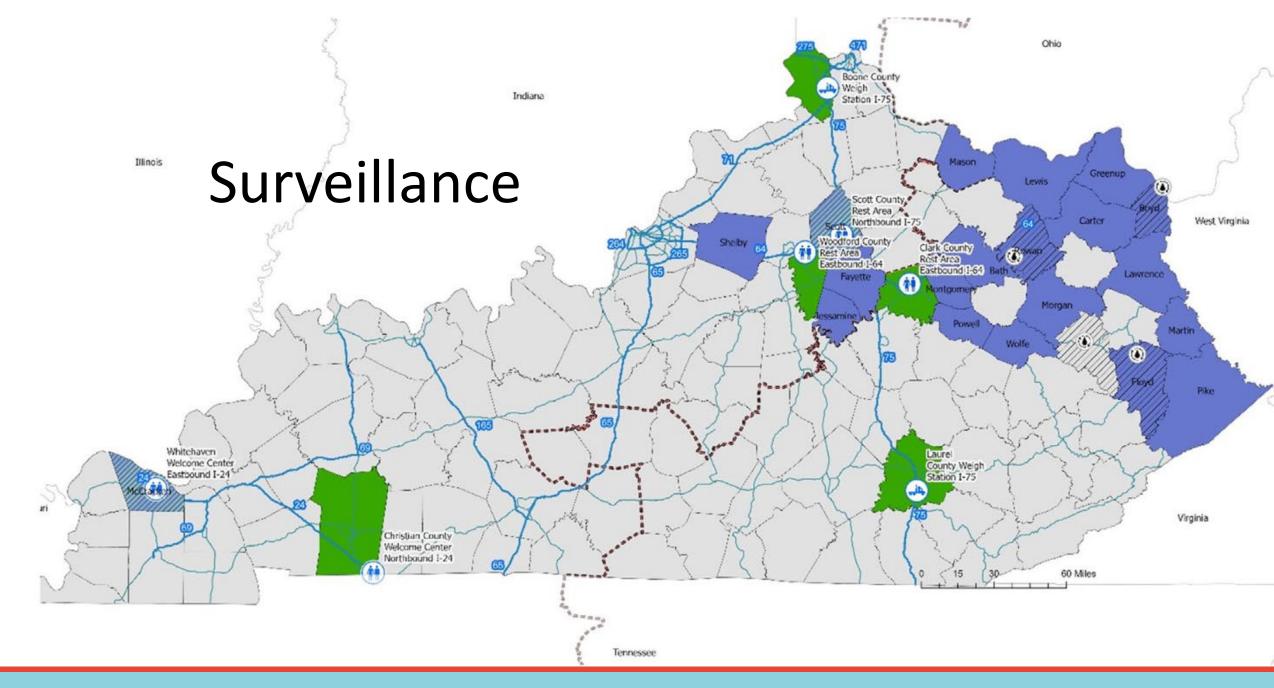


Distribution of proposed legislative initiatives by type, xylazine scheduling levels





Categories are not mutually exclusive. Some policy initiatives had multiple provisions in the same bill (e.g. establish penalties and enhance test strip access)





Public Awareness

Xylazine desire, knowledge and experiences among the Community Use and Testing Study (CUTS) cohort, Rhode Island (N=125).

| Total | | Xylazine detected by laboratory | | | |
|--|------------|---------------------------------|-------------------|--------------------|--------|
| Variable | n/N | column % | No column % | Yes column % | p |
| Aware of xylazine | 62/ 121 | 51.2 | 46.6 | 68.0 | 0.059 |
| Wanted xylazine | 1/ 121 | <1.0 | - | - | - |
| Reported having a xylazine exposure in past 6 months | 31/ 119 | 26.1 | 18.6 | 56.0 | <0.001 |

| Drug sample submitted and | |
|---------------------------|-----|
| tested at baseline | |
| Expected to contain | 11/ |
| xylazine by submitter | 125 |
| (self-report) | |
| Xylazine detected using | 18/ |
| point-of-care FTIR-S | 124 |
| Xylazine detected using | 25/ |
| laboratory-based mass | 125 |
| spectrometry | |

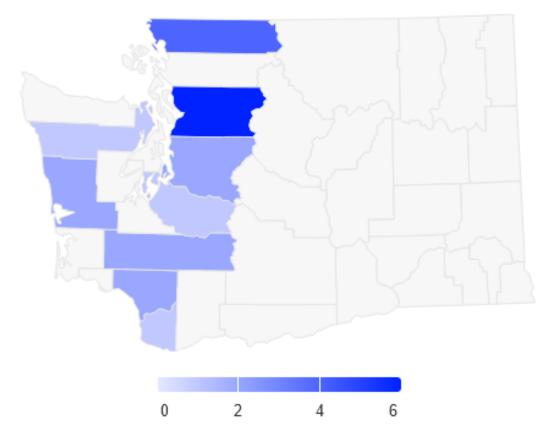


Light at the End of the Tunnel

| DRUG TYPE* | (ESTIMATED DEATHS 2023) | (ESTIMATED DEATHS 2022) |
|--|-------------------------|-------------------------|
| Synthetic Opioids (fentanyl) | 74,702 | 76,226 |
| Psychostimulants (including methamphetamine) | 36,251 | 35,550 |
| Cocaine | 29,918 | 28,441 |
| Natural/semi-synthetic | 10,171 | 12,135 |

^{*}Deaths may involve multiple drugs, while others might not specify any specific drug. As a result, the sum of deaths attributed to specific drugs may not equal the total number of drug overdose deaths.

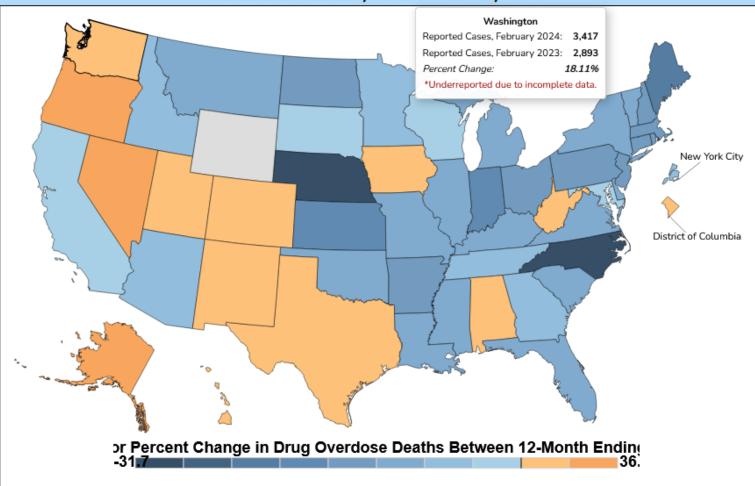
Xylazine cases more than doubling in Q1 2024 versus average quarter in prior 3 years

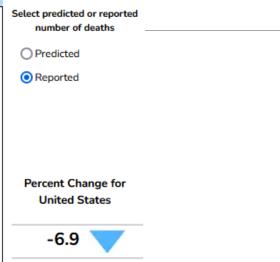


Analysis by UW ADAI. For data sources, see text or adai.uw.edu/WAdata @ USA Census Bureau

iminary data. Data source: Forensic Laboratory Services Bureau, Washington State Patrol

Figure 1b. Percent Change in Reported 12 Month-ending Count of Drug Overdose Deaths, by Jurisdiction: February 2023 to February 2024





"I would say that Xylazine is another trend in concert with K2 [synthetic cannabinoids] in Philly. Part of the reason that people use so much K2 here is because there's this belief that cannabinoids in general increase the half-life of opioids. When the switch to fentanyl happened, drug users were talking about how frustrating it is that fentanyl doesn't have legs. Manufacturers responded by trying to increase the amount of sedation, by adding xylazine. And likewise, people think that K2 can help 'give fentanyl legs' increase the duration of effect]. So xylazine is really part of a larger story of both drug users and dealers adapting to the new world of fentanyl in both safe and unsafe ways."

-Interviewee

Questions?