

Xylazine and Fentanyl: A Deadly Duo

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Presenter information

- Work with northeastern Minnesota Tribal Nations and rural community partners on community engagement to address substance use:
 - Community forums
 - Focus groups
 - Harm reduction trainings
 - Funding: HRSA, SAMHSA, USDA for prevention, treatment, recovery, and harm reduction

Objectives

- Review the history of fentanyl and xylazine in the current United States Drug supply
- Compare the pharmacology of fentanyl and xylazine
- Describe how fentanyl and xylazine can cause toxicity and overdose, separately and together
- Review the pharmacology of naloxone and its utility in reversing opioid overdose
- Describe harm reduction strategies to reduce overdose and other harm resulting from fentanyl and xylazine use

Foundation of Person-Centered Practice

- Self-Awareness/Biases/Personal Beliefs
- Most people want and value: a family, a home, control over one's life, social acceptance, positive self-image, sense of acceptance, sense of accomplishment, friends
- Appreciate their life before the need for intervention

*Carl Rogers – Person Centered Therapy & Beth Mount – Person Centered Practice

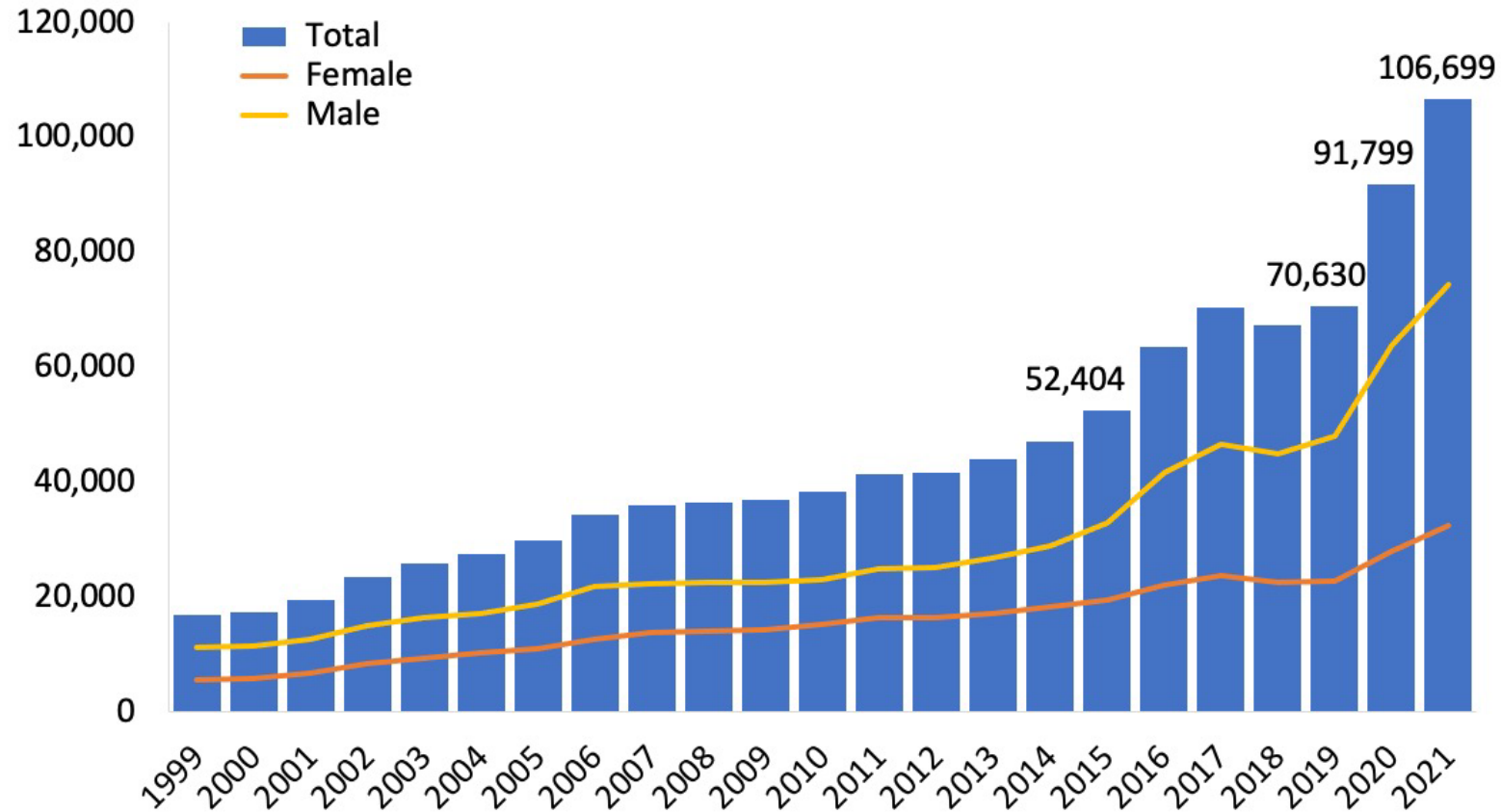
The importance of language

- Person with an opioid use disorder or person who uses drugs
- Neonatal Abstinence Syndrome/Neonatal Opioid Withdrawal Syndrome
- Medications for addiction treatment, medications for opioid use disorder
- Positive/negative, expected/unexpected urine drug test findings
- Sterile/Used syringes
- Breathing emergency

Trends in US overdose deaths

- 2000-2006: Cocaine
- 2007-2013: Prescription opioids
- 2013-2014: Heroin
- 2016-present: Illicitly manufactured fentanyl
- 2018-present: Xylazine implicated in a growing number of overdose deaths

Figure 1. National Drug-Involved Overdose Deaths*, Number Among All Ages, by Gender, 1999-2021



*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999–2021 on CDC WONDER Online Database, released 1/2023.

Setting the stage: fentanyl vs. xylazine

Similarities:

- Both are adulterants in the US drug supply
- Both cause deadly respiratory depression
- We have harm reduction tools (testing strips) to test for both

Differences:

- Fentanyl is a *mu* opioid receptor agonist, xylazine is an *alpha-2* receptor agonist
- The effects of fentanyl can be reversed with naloxone (*mu* opioid antagonist) if it is given early enough, there is no similar drug for xylazine reversal

What is xylazine?

- Non-opioid agent approved in 1972 by FDA as a sedative and analgesic for veterinary medicine
 - NOT approved for use in humans
- Structurally, xylazine “looks” like clonidine and tizanidine and may share some clinical effects
- *Alpha-2 receptor agonist* in brainstem
 - Causes a rapid decrease in the release of norepinephrine and dopamine in CNS

How are individuals exposed to xylazine?

- People who use street/illicit drugs may not know that they are getting xylazine
- Xylazine is usually injected, but can be swallowed or sniffed
- The DEA has seized xylazine and fentanyl mixtures in 48 of 50 states
 - DEA laboratory system reported that approximately 23% of fentanyl powder and 7% of fentanyl pills seized by the DEA in 2022 contained xylazine
 - Xylazine can be purchased on the internet (shipped from international sources)
- Street drugs such as cocaine, heroin, and fentanyl can be mixed with xylazine:
 - to enhance drug effects or
 - increase street value by increasing their weight

<https://www.cdc.gov/drugoverdose/deaths/other-drugs/xylazine/faq.html#:~:text=References-,What%20is%20xylazine%3F,approved%20for%20use%20in%20people.>

What is xylazine?

- Names: Tranq, AnaSed, Rompun, Horse tranquilizer
- Reports from the street (National Harm Reduction Coalition):
 - “It’s found in powder heroin/fentanyl mostly, and sometimes cocaine and methamphetamine”
 - “It’s a deep sedative”
 - “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”

Signs of Xylazine toxicity

- Signs and symptoms of acute xylazine toxicity include:
 - Central Nervous System (CNS) and respiratory depression
 - Hypotension (low blood pressure)
 - Bradycardia (low heart rate)
 - Hypothermia (low body temperature)
 - High blood glucose

Some of these signs look similar to opioid (fentanyl) overdose, so it can be difficult to distinguish

Xylazine-related necrotic skin ulcerations

- Repeated exposure to xylazine by injection is known to cause necrotic skin ulcerations
- Distinctly different from other soft tissue infections (such as cellulitis) often associated with injection drug use
- They may develop in areas of the body away from the injection site
- Thought to be due to its direct vasoconstricting effect on local blood vessels and resultant decrease in skin perfusion and wound healing

Xylazine-related hyperglycemia

- Xylazine-induced reduction of skin sensitivity to insulin leads to acute hyperglycemia in diabetic and normoglycemic monkeys (Xiao et al) and cattle (Hsu et al)
 - Proposed to be due to stimulation of alpha-2 adrenoreceptors and increase in stress hormones
- Result: glucose levels go up in normoglycemic and diabetic monkeys
 - Occurred 10 minutes after administration
 - Peak 35 minutes after administration

Harm reductionist advice to users of xylazine

- It is best to avoid dope with xylazine in it if you can
- 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
- 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
- Get your drugs tested at a harm reduction program

Summary of important information about xylazine

- Xylazine overdose is not reversed by naloxone
- Xylazine is not detected by routine toxicology screens (consider it an adulterant)
- Repeated exposure to xylazine may cause severe, necrotic skin ulcerations
- Individuals with repeated exposure to xylazine may become dependent and experience severe withdrawal symptoms

What is fentanyl?

- Fentanyl is a prescription drug that is also made and used illegally
 - Introduced as a legal drug in the 1960's
 - Between 2011-2018 synthetic fentanyl analogs created in clandestine labs caused marked increases in death from overdose
- Fentanyl and other opioids sit on the *mu*-opioid receptor when they work in the body (*mu opioid agonist*)
- It is a powerful synthetic opioid that is similar to morphine, but 50-100 times more potent
 - Typically used to treat pain after surgery
 - Sometimes used for chronic pain with patients who are tolerant to other opioids
 - Tolerance is when you need a higher amount or more frequent amount to get the desired effects

What are Opioids?

- Pharmaceutical opioids
 - Opioids/opiates/narcotics/opioid analgesics
 - Prescribed by a provider, dispensed from a pharmacy
 - Include drugs such as morphine, hydrocodone, oxycodone, fentanyl patches
 - Opioids prescribed in veterinary medicine

- *ACMT and AACT Position Statement, J Med Tox, Dec 2017
- Trends and geographic patterns in drug and synthetic opioid OD deaths, MMWR Feb 2021

What are opioids?

- Illegal opioids (some) include
 - Non-pharmaceutical fentanyl*
 - Confirmed in other substances including methamphetamine and cocaine
 - 50-100 x more potent than morphine and 30-50 x more potent than heroin
 - Non-medical, including novel synthetic opioids
 - Fentanyl street names:
 - Apache, China Girl, China Town, Dance Fever, Friend, Goodfellas, Great Bear, He-Man, Jackpot, King Ivory, Murder 8, and Tango & Cash

Signs of opioid use

- Impaired memory and/or attention
- Constricted pupils
- Scratching their skin
- Runny nose
- Nausea
- Sleepiness and nodding off
- Slurred speech
- Stupor
- Slowed breathing

What is an Opioid Overdose?

- Opioid overdose occurs when an opioid(s) alone or mixed with other drugs and/or substances overwhelms the body's ability to handle it.
- Many opioid-related overdoses result from mixing prescription painkillers/heroin with benzodiazepines and/or alcohol/other sedative hypnotics.
- Fentanyl and xylazine are a particularly deadly combination
 - The effects of fentanyl can be reversed if naloxone is given early enough, there is no “antidote” for xylazine

What Leads to Overdose Death?

- Respiratory failure resulting in lack of sufficient oxygen in the blood
- Leads to decreased level of consciousness
- Vital organs like the heart and brain also start to fail
- Can lead to death

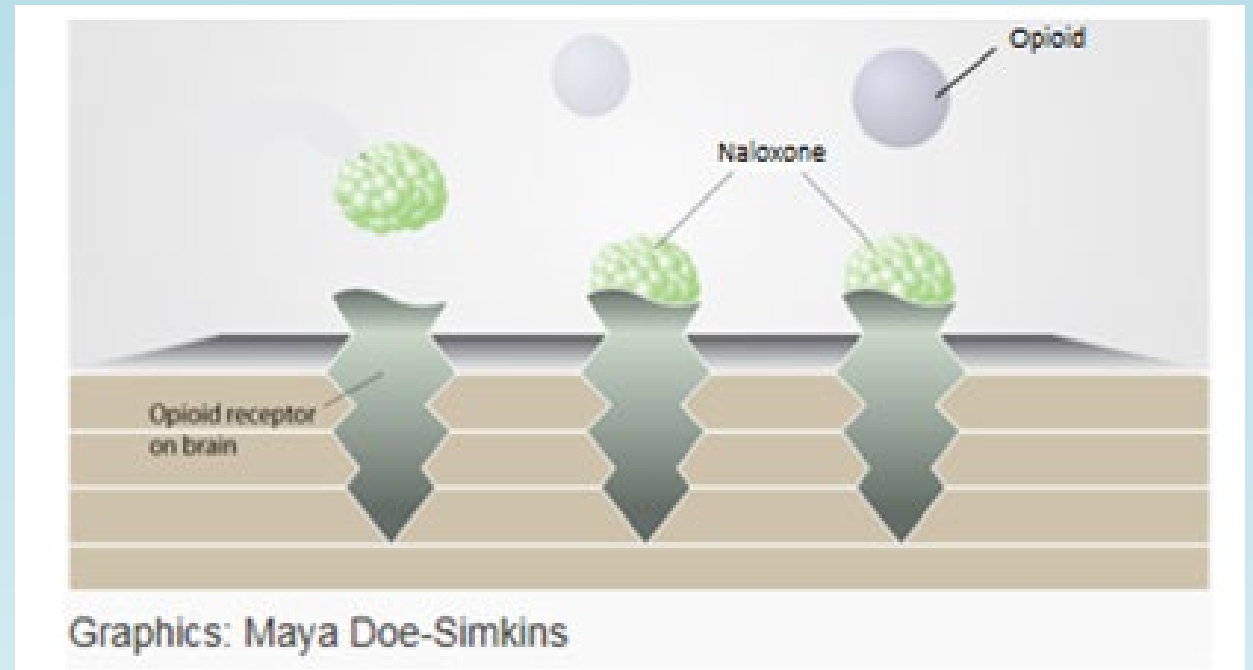
- *Surviving an overdose due to fentanyl or xylazine = BREATHING and OXYGEN*

When should naloxone be given?

- **Naloxone should be given in response to any suspected drug overdose to reverse any possible opioid effects!**
- Naloxone will not reverse the effects of xylazine, but because xylazine is often used with opioids like fentanyl, naloxone should still be given.
- It's very important to call 911 for additional medical treatment, especially since the effects of xylazine may continue after naloxone is given.

Naloxone Mechanism

- High affinity *mu* receptor antagonist
 - Displaces opioids to reverse respiratory depression
 - Opioids still circulate in the body
- No dependence or tolerance
- No clinical effects in absence of opioids



Responding to an Overdose

- Identify signs of opioid or xylazine toxicity
- For inadequate breathing such as slow rate, gurgling, or no breathing
 - Attempt to awaken patient
 - **Call 911**
 - **Administer naloxone**
 - Place patient in recovery position on their side
- **All patients need transport to a medical facility**
- Debrief and get support

HOW TO RESPOND TO AN OPIOID OVERDOSE

Signs of an Overdose



Not Responding

Not moving, can't be woken up



Slow or Not Breathing

Not breathing or slower than every 5 seconds



Making Sounds

Snoring, gurgling, or choking sounds



Blue Lips & Nails



Cold or Clammy Skin



Tiny Pupils

Call 9-1-1 right away if you see any of these signs.
When you call 9-1-1 to report an overdose,
you won't be charged with simple drug possession

Fentanyl & Xylazine Test Strips

- Products that are designed for testing drug supply for fentanyl or xylazine
- Inexpensive and sensitive tests
- Cannot detect all fentanyl analogues and can be improperly used, so training is important



Bergh MS, Øiestad ÅML, Baumann MH, Bogen IL. Selectivity and sensitivity of urine fentanyl test strips to detect fentanyl analogues in illicit drugs. *Int J Drug Policy*. 2021 Apr;90:103065.

Krieger MS, Goedel WC, Buxton JA, Lysyshyn M, Bernstein E, Sherman SG, Rich JD, Hadland SE, Green TC, Marshall BDL. Use of rapid fentanyl test strips among young adults who use drugs. *Int J Drug Policy*. 2018 Nov;61:52-58.

Weicker NP, Owczarzak J, Urquhart G, Park JN, Rouhani S, Ling R, Morris M, Sherman SG. Agency in the fentanyl era: Exploring the utility of fentanyl test strips in an opaque drug market. *Int J Drug Policy*. 2020 Oct;84:102900.

Benefits of Test Strips

- More and more of the street drug supply contains fentanyl and xylazine, increasing uncertainty of the contents and potency of many drugs.
- Test strips and proper education can help people who inject drugs to avoid life threatening overdoses.
- Regarding FTS, they are potentially less useful in areas where people believe fentanyl to be in all street drugs.

Bergh MS, Øiestad ÅML, Baumann MH, Bogen IL. Selectivity and sensitivity of urine fentanyl test strips to detect fentanyl analogues in illicit drugs. *Int J Drug Policy*. 2021 Apr;90:103065.

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Research on Xylazine antidotes

- University of Minnesota Medical School Department of Pharmacology
 - Atipamizole – selective alpha 2 antagonist used in animals (but not humans due to side effects)
 - Noradrenaline and atropine – to normalize blood pressure and heart rate
 - Research recommends naloxone due to likelihood of an opioid with xylazine
 - General management supportive of care focusing on ventilation and hemodynamics

Review: fentanyl vs. xylazine

Similarities:

- Both are adulterants in the US drug supply
- Both cause (sometimes deadly) respiratory depression

Differences:

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