

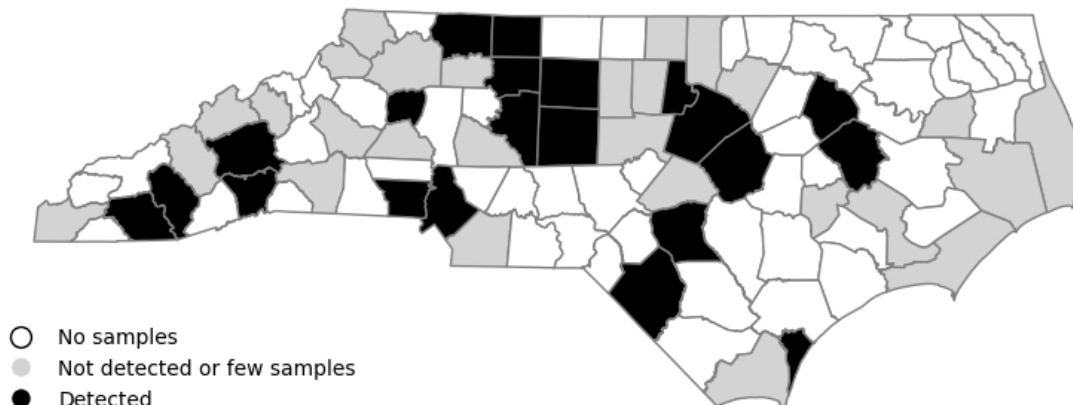
UNC Street Drug Analysis Lab

Xylazine is Different

The Street Drug Analysis Lab is a public service of UNC. Our lab performs chemical composition analysis on drug samples voluntarily sent to us by 32 NC programs: EMS, hospitals, clinics, harm reduction programs, and health departments. GCMS “mass spec” results are updated daily, freely and publicly. We have analyzed 954 samples as of March 12, 2024.

Xylazine was first detected and linked to skin wounds by Don Jackson at the NC Survivors Union in Greensboro in January 2021. Since then, **we have confirmed the presence of xylazine in 21 out of 48 counties** (July 2021 to March 2024). Currently, we see xylazine nearly always with illicitly manufactured fentanyl. Xylazine is toxic, causes heavy sedation, and is not being sought out for psychotropic effects. **Of 516 fentanyl samples, 41% contained xylazine.**¹

Distribution of Xylazine in North Carolina



Source: UNC Street Drug Analysis Lab
January 2022-March 2024
N=230 xylazine samples

Recent Discovery

We discovered that xylazine is both an alpha-2 adrenergic agonist and active at the **kappa opioid receptor**. Kappa is responsible for withdrawal & dysphoria. No activity at mu opioid receptor. **No other drug is known to work like this.**

¹ Programs may have preferentially sent us samples that they suspected had xylazine. Xylazine is surely present in other counties, but we have not received enough samples to confirm it.

Health Harms of Xylazine

<p>Wounds Prevents people from entering treatment, even when mostly healed.</p> <p>Can be treated like chemical burns if detected early. But little emphasis on early intervention.</p> <p>Wound healing takes months, requires regular dressing changes. Medical system not equipped for long-term at-home wound care.</p> <p>Amputations, some unnecessary.</p>	<p>Withdrawal Unique xylazine withdrawal syndrome with severe agitation and anxiety. Lasts longer than opioid withdrawal.</p> <p>Buprenorphine inductions becoming less successful in presence of xylazine. Need to modify medication protocols to address xylazine withdrawal.</p> <p>Can mask withdrawal from benzodiazepines.</p>
<p>Overdose Response Naloxone acts on xylazine alone, and reverses fentanyl overdose. While breathing may normalize, patients may not be reanimated, leading to excessive naloxone administration.</p> <p>Xylazine + fentanyl ODs may be less severe.</p> <p>Xylazine not causally linked to most OD deaths.</p>	<p>Other Harms Hypothesis: severe anemia Hypothesis: hyperglycemia</p>

Current Needs

Wound Care: Emphasis on early intervention and treatment of early wounds. Wound care kits for harm reduction programs to alleviate medical costs.

OD Management: 81% of harm reduction programs having to ration naloxone because of cost and supply. Overdose response trainings need to re-emphasize rescue breathing and supportive oxygen.

Detection: Expand xylazine test strips and community-based drug checking.

Clinical Practice: Provider awareness of how to handle wounds. New treatment protocols for addiction treatment. Substance use treatment facilities without medical staff may be ill-equipped to deal with wounds and overlapping fentanyl + xylazine withdrawal.

Research: Best practices for wound care. Research on sex differences. Trials for treatment of xylazine withdrawal with existing medications, including kappa agonists and methadone. Severe anemia and hyperglycemia hypothesis need to be tested. What's next (dexmedetomidine)? Impact of scheduling on veterinary and medical practice. Accuracy of different manufacturers xylazine test strips.

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<https://www.fda.gov/science-research/advancing-regulatory-science/characterization-impact-xylazine-and-dexmedetomidine-pharmacological-profile-addictive-behaviors-and>

Characterization of the impact of xylazine and dexmedetomidine: pharmacological profile, addictive behaviors, and physiological effects, including wound development

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Project Start Date: September 8, 2023

Regulatory Science Challenge

The unregulated drug supply is an ever-changing chemical landscape with novel additives that are often unknown to both the end users, as well as clinicians and public health officials. One such compound, xylazine, is now detected in the unregulated drug supply at alarming levels. In addition, there remain concerns that xylazine in combination with fentanyl leads to increased drowsiness, increased respiratory distress, and the development of difficult to treat wounds. Researchers and medical professionals currently do not know how xylazine contributes to addictive behaviors and other physiological problems; thus, the principle aim of this research ultimately will determine how xylazine influences fentanyl-related behaviors and physiology. Dexmedetomidine, a closely related FDA approved drug (in medical settings), which is emerging as another adulterant to fentanyl, will also be investigated for its effects compared to xylazine.

Project Description and Goals

This project uses pharmacological approaches including cellular assays and rodent models to examine how xylazine and dexmedetomidine impact physiological functions. This multifaceted study will examine how these drugs interact with receptors in the body, how they affect brain function, and how they influence fentanyl's effects. The effects of xylazine on the physical dependence and withdrawal syndrome associated with fentanyl are currently unknown. Data will be collected from cellular assays, behavioral tests in rats and mice, analysis of respiration, and analysis of skin wound development (thought to be associated with the combined use of fentanyl and xylazine in humans) and healing of skin tissue. Investigators plan to present data from this project at scientific conferences and publish findings in peer-reviewed journals.