GREATER SOUTHERN CALIFORNIA NODE - **FALL DIGEST**

GSCN Quarterly Digest

NOV 2023

Lillian Gelberg, MD, MSPH
Professor, Department of Family Medicine & Health Policy and Management, UCLA

GSCN UPDATES

Congratulations to Dr. Gelberg for receiving the 2023 Maurice Wood Award for Lifetime Contribution to Primary Care Research. The Wood Award is given annually to honor a researcher who has made outstanding contributions to primary care research.

IN THIS ISSUE

Greater Southern California Node (GSCN) of the Clinical Trials Network (CTN) Updates

Introduction to Xylazine

Xylazine-related Resources

Ask an Expert: Joseph Friedman, PhD, MPH

Webinars & Trainings

NEW CTN STUDIES INVOLVING THE GSCN

- **CTN-0139** Collaborative Care for Polysubstance use in Primary Care Settings ("Co-Care")
  - Lead Investigators: Jennifer McNeely, MD, MS (New York Node) and Jane Liebschutz, MD, MPH, FACP (Appalachian Node)
    - Co-Investigator: Lillian Gelberg, MD, MSPH (GSCN)
- **CTN-0143** Social Determinants of Health (SDOH); Needs and Consequences Associated with Substance Use Disorder
  - Lead Investigator: Yih-Ing Hser, PhD (GSCN)

Looking forward to highlighting these exciting new projects in our Winter Digest. Stay tuned!

PUBLICATIONS

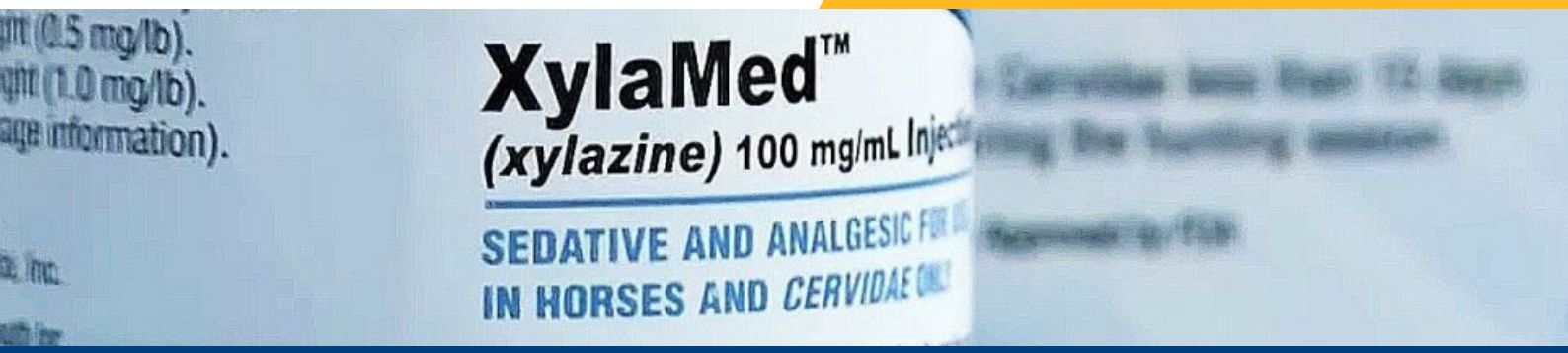
The CTN-0102-Feasibility Study Team, including CTN Node collaborators and clinic personnel, published a paper in *The Journal of Rural Health* titled "Care coordination between rural primary care and telemedicine to expand medication treatment for opioid use disorder: Results from a single-arm, multisite feasibility study," *accessible here*.

GSCN researchers, in collaboration with the Pacific Northwest Node (PNWN), recently published a paper in *The Journal of Rural Health* titled "Medication treatment for opioid use disorder among rural primary care patients," *accessible here*.

The PNWN, GSCN, and collaborating research sites recently published a paper in *Addiction* titled "Identifying patients with opioid use disorder using International Classification of Diseases (ICD) codes: challenges and opportunities," *accessible here*.

WE WANT YOUR FEEDBACK

If you have clinical questions, feedback, or want to share ideas for research collaboration, please complete ***this survey***.



Introduction to Xylazine

BY LAYLA TONDRAVI
STAFF RESEARCH ASSOCIATE

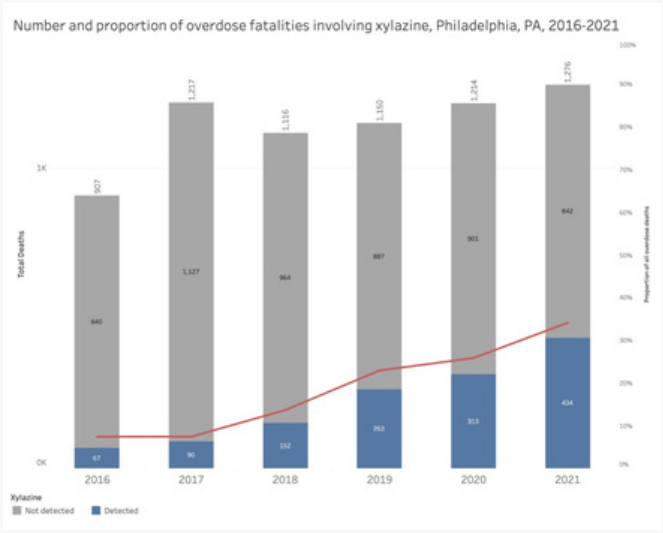
Xylazine is a non-opioid veterinary tranquilizer that is not approved for human use by the Food and Drug Administration (FDA) as it depresses the central nervous system, leading to drowsiness, amnesia, slowed breathing and heart rate, and dangerously low blood pressure (NIH, 2023). Colloquially referred to as "tranq," "tranq dope," or "sleep cut," xylazine is becoming increasingly prevalent in the illicit drug supply in the United States (Pennsylvania DOH, 2023). It has been linked to an increasing number of overdose deaths nationwide as people exposed to xylazine often knowingly or unknowingly use it in combination with other drugs, particularly illicit fentanyl (NIH, 2023).

In areas with a high prevalence of the use of xylazine mixed with fentanyl or heroin, abscesses and painful skin ulcers are often reported (Malayala et al., 2023). Prolonged use can lead to decreased perfusion and impaired wound healing, leading to higher chances of infection of these ulcers (Malayala et al., 2023). Continued use can even cause necrosis (the rotting of human tissue), which can lead to amputation (Malayala et al., 2023). In addition to the topical effect of vasoconstriction, xylazine also leads to hypotension, bradycardia, and respiratory depression (NIH, 2023).

Xylazine poses a serious threat to communities as, in addition to its harmful short term and long-term effects, routine toxicology screens do not detect it and no medication approved for human use is useful in reversing xylazine's effects on respiration and sedation (FDA, 2022).

Although xylazine-adulterated opioids are an emerging threat in the United States, its presence in the illicit drug supply is not new; in the early 2000s, xylazine gained prevalence as an adulterant in Puerto Rico (Pennsylvania DOH, 2023). Shortly after, xylazine entered the United States, and it has had the largest impact in Northeastern states (e.g., Pennsylvania, Vermont) (Pennsylvania DOH, 2023).

Xylazine first showed up in Philadelphia's toxicology reports in 2006 and was found in over 90% of drug samples tested in the city in 2021 (Substance Use Philly, 2021). Preliminary overdose data for 2022 indicate that xylazine contributed to 644 deaths across 38 counties in Pennsylvania, an increase of more than 1,000% since 2018 (Pennsylvania DOH, 2023).



Introduction to Xylazine (*cont.*)

This steep increase in overdose deaths led to the White House officially designating fentanyl adulterated or associated with xylazine as an emerging threat to the U.S. in April of this year (The White House, 2023). With this declaration, the Office of National Drug Control Policy was tasked with creating a response plan, which was posted in July (The White House, 2023). Since then, the FDA responded with certain measures to limit xylazine manufacturing (FDA, 2023).

The treatment landscape is undergoing a transformation in response to the emergence of xylazine, presenting specific challenges in overdose management. While Narcan® (i.e., naloxone) has proven effective in preventing overdose fatalities related to fentanyl, it is unable to counteract the effects of xylazine due to its action on distinct receptors (Washington Post, 2023). Regrettably, there is currently no established method for reversing the effects of xylazine. Exposure to both xylazine and opioids can result in a decline in heart rate and a potentially lethal slowing of breathing (Washington Post, 2023). Moreover, xylazine complicates the process of aiding individuals seeking treatment for opioid use disorder, prolonging the already intricate withdrawal from fentanyl. Despite its short duration of action, fentanyl may persist in the bodies of long-term users, due to its ability to accumulate in fat cells. Consequently, individuals must await the clearance of fentanyl from their system before initiating treatment with buprenorphine, which is designed to alleviate withdrawal symptoms and curb opioid cravings. The presence of xylazine further extends this waiting period, intensifying the challenges of treatment and raising the likelihood of a patient discontinuing care under a healthcare provider (Washington Post, 2023).

In navigating the complexities posed by xylazine in opioid use disorder treatment, implementing effective strategies is crucial. Successful approaches encompass precise timing and vigilant monitoring of withdrawal, implementation of adjunct therapies for symptom management, and meticulous wound care. For a more comprehensive understanding of best practices related to xylazine, please refer to *this document*.

Although xylazine has been detected in California, it does not appear to be widespread. However, given the unpredictable nature of the drug supply, experts are concerned that xylazine may eventually penetrate the California drug supply in greater quantities or higher concentrations and may contribute to overdose and severe skin wounds (CDPH, 2023).

Healthcare providers should maintain a level of suspicion of xylazine exposure when: naloxone appears to be ineffective in reversing a suspected drug overdose; individuals present with concomitant hypotension and bradycardia or cardiac conduction disturbances in the setting of drug use; or necrotic skin ulcerations are present in a person with substance use disorder, especially opioid use disorder (CDPH, 2023). Management is mainly supportive care related to bradycardia, hypotension, respiratory depression, and wound care as needed.

Harm reduction approaches emphasize the importance of real-time information about xylazine in local supplies to best support health-care providers when treating patients. Testing illicit drugs for contamination, both locally and nationally, will be key in healthcare systems' responses to this adulteration of xylazine in the illicit drug market.

XYLAZINE-RELATED RESOURCES

XYLAZINE FACTSHEETS:

- Xylazine information
- Xylazine LA County
- Xylazine CA Department of Public Health
- Xylazine infographic

PROVIDER 'QUICK TIPS' ON XYLAZINE:

- Xylazine Best Practices
- Xylazine and Wound Care for Healthcare Providers
- Xylazine Withdrawal Management

XYLAZINE TESTING:

- Xylazine test strips (XTS) have recently been developed and are available through BTNX
- Residents of LA County can bring their drugs to be tested for free as part of a pilot program being run through UCLA. For more information, contact Chelsea L. Shover, PhD via email at clshover@mednet.ucla.edu.

WOUND CARE:

- Xylazine Wound care handout

HARM REDUCTION:

- Xylazine, Health Risks and Harm Reduction Strategies

ASK AN EXPERT: JOSEPH FRIEDMAN, PHD, MPH

Dr. Friedman, PhD, MPH, is an ethnographer and data scientist who researches addiction and health inequalities at the Center for Social Medicine and Humanities at UCLA's David Geffen School of Medicine. For more information on our expert, including a list of his academic publications, *click here.*

Providers are starting to hear about xylazine, but many are unfamiliar with it. What is it and what are the consequences of prolonged use? Should providers be concerned?

Xylazine is a sedative that has been used for many years as an animal tranquilizer, but it is increasingly used as a synthetic cutting agent for opioids like fentanyl. There is still much that we don't know about xylazine, but there is great concern that exposure to the drug increases the risks of skin infections, overdose not fully responsive to naloxone, and other harm stemming from over-sedation, such as increasing vulnerability to violence, theft, and sexual assault.

Providers who work with patients that use illicit drugs should be aware that xylazine may be arriving to their area, and acutely increasing health risks for their patients.

Any emerging practices for treating people taking xylazine-adulterated opioids? How do we intervene?

Many people who use drugs are unaware that they are consuming xylazine and/or unaware of the risks it may pose to their health. Providing accurate, compassionate, non-stigmatizing education about the ways that the local drug supply is shifting can empower patients to make safer choices. Drug checking technologies, such as point-of-use strips to detect xylazine, can be provided to patients to help them recognize when it may be present in the drugs they are consuming. Helping patients switch onto safer options, such as buprenorphine or methadone, can be transformative, and providing information about the rapidly evolving health risks linked to new drugs in the illicit drug supply can be a helpful first step towards making these changes.

How do you expect the treatment landscape will shift in response to xylazine? How might it impact the delivery of care for SUDs?

The increasing use of xylazine with fentanyl is complicating the treatment of patients with opioid use disorder, in terms of responding to overdoses, treatment of withdrawal syndromes, and managing associated comorbidities.

Xylazine is likely causing increased rates of overdoses that are not fully responsive to naloxone. In cases of overdose where xylazine is suspected, it's still important to give naloxone as the first step, because we know that xylazine is almost always used together with fentanyl, and almost never by itself. However, for patients who do not become fully responsive after receiving naloxone, additional techniques such as rescue breaths and airway management are needed.

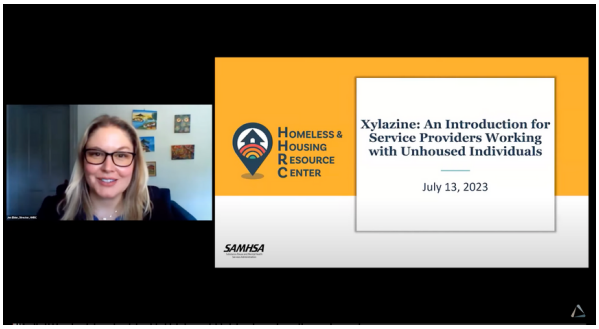
We have established tools to treat withdrawal from opioids, but nothing like that exists for xylazine. Some early research indicates that withdrawing from xylazine and fentanyl is likely more emotionally and physically difficult than withdrawing from opioids alone. Providers can prescribe additional medications to manage withdrawal symptoms, and check in with their patients regularly as they make transitions in the substance use. The management of skin and soft tissue infections stemming from xylazine also requires regular access to low-barrier wound care services.

WEBINARS & TRAININGS

TOXICITY OF XYLAZINE AND HOW IT IMPACTS PEOPLE WHO USE DRUGS

This webinar reviews the human pharmacology of xylazine, a veterinary sedative, differentiates between the findings of xylazine and opioid overdose and demonstrates ability to treat them, and recognizes symptoms of xylazine withdrawal and applies basic treatment concepts.

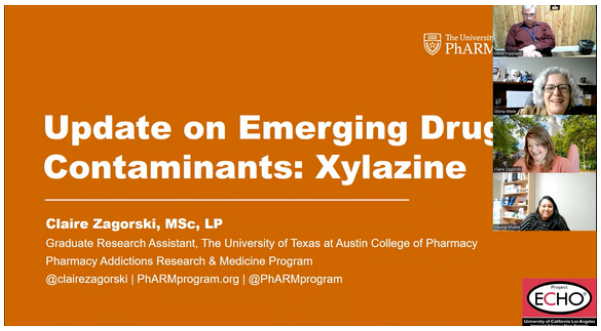
Learn More



XYLAZINE: AN INTRODUCTION FOR SERVICE PROVIDERS WORKING WITH UNHOUSED INDIVIDUALS

In this webinar, panelists will provide a brief overview of Xylazine, a substance newly found in illicit drug supplies, and its impacts on the unsheltered community. Panelists will share their lived expertise with xylazine, its effects, organizational best practices for wound care, overdose response, and harm reduction.

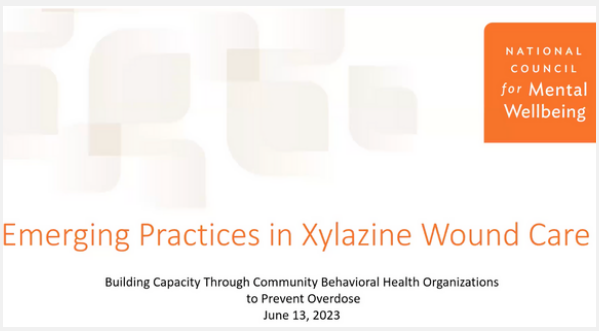
Learn More



UPDATE ON EMERGING DRUG CONTAMINANTS: XYLAZINE

This on-demand course will briefly cover the emerging drug supply contaminant xylazine, what we do and don't know about its effects, major domains of medical harms from xylazine use, and what harm reduction for xylazine looks like today.

Learn More



EMERGING PRACTICES IN XYLAZINE WOUND CARE

This webinar, presented by the National Council for Mental Wellbeing, addresses xylazine wound care, sores, and treatmeant for such afflictions utilizing simple interventions.

Learn More