

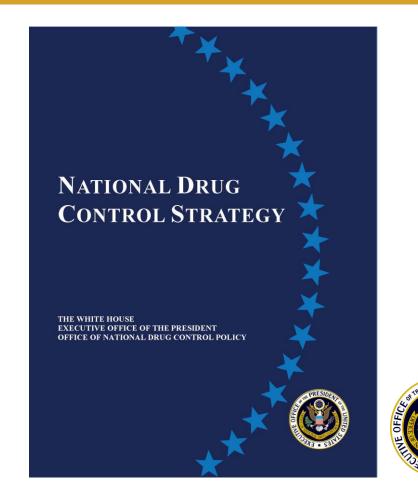
Emerging Threats: Xylazine

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National Drug Control Strategy

- ONDCP coordinates the nation's drug policy, which involves 19 federal agencies with a \$41 billion budget
- First Biden strategy was released April 2022
 - Intended to provide a whole-of-government approach to address addiction and the ongoing overdose epidemic
- Scheduled to be updated 2024



National Drug Control Strategy (2022)

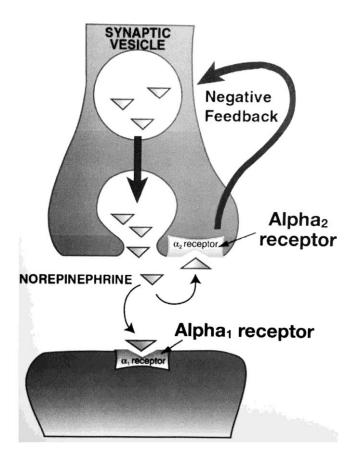
- Addressing untreated addiction for those at-risk of an overdose
- Expand high-impact harm reduction interventions like naloxone
- Ensure those at highest-risk of an overdose can access evidence-based treatment
- Improve data systems and research that guide drug policy development

- Going after drug trafficking and illicit drug profits
- Obstruct and disrupt financial activities of transnational criminal organizations (TCOs) that manufacture illicit drugs and traffic them to the United States
- Reduce the supply of illicit drugs through domestic collaboration of international coordination
- Reduce the supply of illicit drugs smuggled across our borders



Alpha-2 agonist pharmacology

- Centrally acting α -2 agonist
 - Decrease the release of NE and EPI
 - Central effects include sedation, analgesia, euphoria
 - Clonidine partially blocks acute opioid withdrawal symptoms
- Reduced sympathetic outflow from the CNS
 - Decreased peripheral vascular resistance,
 - Decreased heart rate,
 - Decreased BP





Xylazine detection in fentanyl positive specimens (UDS)

160,000 tested samples from 73,000 unique patients

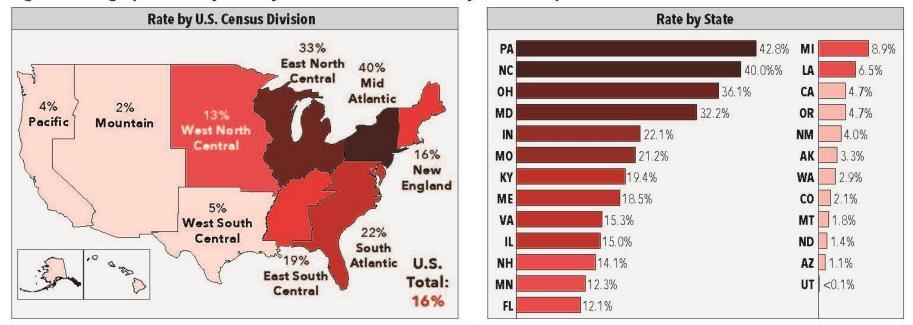


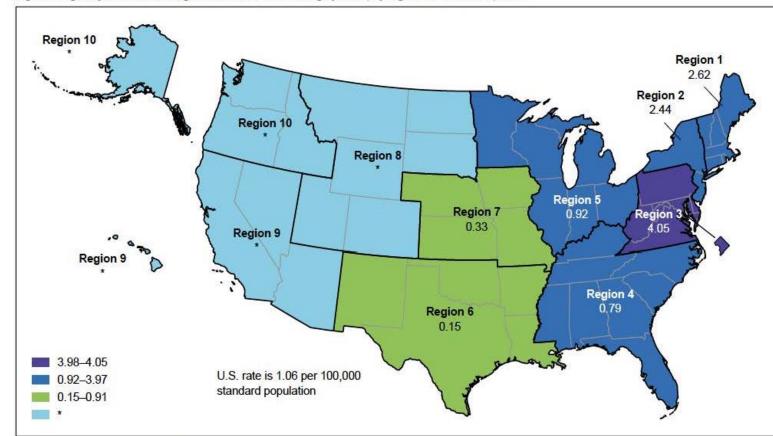
Figure 1. Geographical Analysis of Xylazine Detection in Fentanyl-Positive Specimens

Xylazine urine drug test (UDT) positivity rate in fentanyl-positive specimens by U.S. Census Division (left) and state (right). Logistic generalized estimating equation (GEE) regression models were fit with xylazine detection via LC-MS/MS as the dependent variable. Sex, age (discrete variable), specialty of the referring clinician, payer group and U.S. Census Division (left) or state (right) were treated as model covariates. States listed on the right were restricted to those with 50 or more fentanyl-positive results for accurate xylazine positivity rate estimation. All data were derived from clinician-ordered testing for xylazine on specimens collected between April 12th and July 20th, 2023.



Xylazine-related deaths are spreading across the US

Figure 4. Age-adjusted rate of drug overdose deaths involving xylazine, by region: United States, 2021



CDC Vital Statistics Rapid Release, Report 30, June 2023

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Xylazine, depending on location, is everywhere

- Xylazine was found in over 90% of illicit drug samples tested in Philadelphia in late 2021
 - Limited data on illicit samples tested in NYC
- Xylazine has now been detected in tested seized fentanyl samples in 48 states





Risks associated with xylazine use

Complex overdose treatment

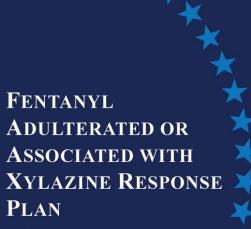
- Naloxone alone will not do the trick
- Severe Withdrawal
 - Not effectively treated with potent opioids
- Xylazine associated tissue injury
 - Requires unique treatment to optimize outcomes
- Increased difficulty with successful addiction treatment
 - Relapse rate very high absent effective treatment of xylazine withdrawal symptoms
 - absent effective treatment of xylazine withdrawal symptoms







- ONDCP Director Rahul Gupta designated fentanyl adulterated or associated with xylazine declared an emerging threat on April 12, 2023
- National Response Plan released July 11, 2023



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- Six pillars of action:
 - Testing
 - Data collection
 - Evidence-based prevention, harm reduction, and treatment
 - Supply reduction
 - Scheduling
 - Research

FENTANYL-ADULTERATED-OR-ASSOCIATED-WITH-XYLAZINE-EMERGING-THREAT-RESPONSE-PLAN-Report-July-2023.pdf



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Improved testing

- Standardizing forensic testing practices
- Develop and implement robust clinical testing
- Develop and implement testing in community settings
 - Focus on ensuring testing gets to those most in need

Expand data collection and reporting

- Improve / modify data collection and reporting to guide policymaking
 - Ensure that detailed data regarding those individuals most impacted by xylazine are well represented



 Support the implementation of evidence-based prevention, harm reduction and treatment

- Identify and disrupt the illicit supply of xylazine
 - Includes exploring rescheduling of xylazine



- Support xylazine-related research
 - Basic science and clinical research
 - Social outcomes related to xylazine use

- Actions are ongoing
 - February 2023: FDA took action to restrict the unlawful entry of xylazine into the US
 - March 2023: DEA issued a public safety alert
 - June 2023: NIDA held a meeting related to care of individuals taking xylazine and issues a NOSI on xylazine-related research
 - CDC has published several manuscripts related to xylazine

