

Resilience in the Face of Unrelenting Increases in Overdose

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University of North Carolina

Chapel Hill, NC, USA

@nabarund

March 6, 2024 • TTI Vanguard – Carolina Inn

Funders

Views in this presentation do not necessarily represent the views of funders or partners.

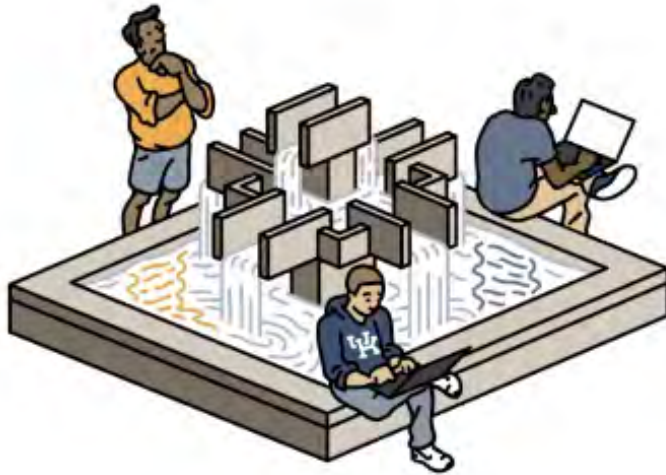
- North Carolina General Assembly via the [NC Collaboratory](#), using Opioid Settlement Funds (2023-25, operations & equipment)
- [US Food and Drug Administration](#) (2023-2025), single study on overdose and naloxone utilization.
- [Vital Strategies](#), operations and outreach (2023-25)
- [Injury and Violence Prevention Branch](#) of the NC Department of Health and Human Services, via funding from the Centers for Disease Control and Prevention (2023, data visualizations)
- [Foundation for Opioid Response Efforts](#) (2022-24, startup)
- The GCMS instrument was funded through a NIH grant to the Department of Chemistry.



Opioid Data Lab



Theory



Practice



Lived Experience



Foundational Studies

Biostatistics
Epidemiology methods
Psychology of communication
Pharmacology

Applied Research

Pharmacy
Medicine
Public health surveillance
Forensic toxicology

Science in Service

Drug checking
Sociology (qualitative)
Evidence-making interventions
History of asylums

Our Approach is Different

Science

in

Service

42%

Adults who have personally known
someone who died of a drug overdose

Athey A. American Journal of Public Health. 2024 Mar;114(3):276-9.

What is “heroin” anymore?

Sold as: Heroin
Raleigh, NC

October 11, 2021

- Xylazine
- Heroin
- Fentanyl
- Caffeine
- 4-ANPP
- Lidocaine
- Quinine
- Flurofentanyl
- 6-MAM
- Acetaminophen

Sold as: Heroin
High Point, NC

September 11, 2021

- Heroin
- 6-MAM
- Fentanyl
- ANPP
- Dimethylsulfone
- Tramadol
- Cocaine

Sold as: Heroin
High Point, NC

September 17, 2021

- Fentanyl
- ANPP

Sold as: Fake blue M30
Myrtle Beach, SC

September 8, 2021

- Fentanyl
- 4-ANPP

Opioid Crisis: No Easy Fix to Its Social and Economic Determinants

The accepted wisdom about the US overdose crisis singles out prescribing as the causative vector. Although drug supply is a key factor, we posit that the crisis is fundamentally fueled by economic and social upheaval, its etiology closely linked to the role of opioids as a refuge from physical and psychological trauma, concentrated disadvantage, isolation, and hopelessness.

Overreliance on opioid medications is emblematic of a health care system that incentivizes quick, simplistic answers to complex physical and mental health

Nabarun Dasgupta, PhD, MPH, Leo Beletsky, JD, MPH, and Daniel Ciccarone, MD, MPH

The accepted wisdom about the US opioid crisis singles out opioid analgesics as causative agents of harm, with physicians as unwitting conduits and pharmaceutical companies as selfish promoters.¹ Although invaluable for infection control, this vector model² of drug-related harm ignores root causes. Eroding economic opportunity, evolving approaches to pain treatment,^{1,3} and limited drug treatment have fueled spikes in problematic substance use, of which opioid overdose is the most visible manifestation. By ignoring the

death.”^{7(p301)} A decade later, US medicine was shaken by revelations of undertreated chronic pain, motivating normative practice and policy shifts.⁸ Previously, chronic pain was managed largely with cognitive behavioral therapy, even hypnosis.

An Institute of Medicine report⁹ attributed the rise in chronic pain prevalence during the 1990s to the following:

1. greater patient expectations for pain relief,

chronic pain was big business. Withdrawals from the market of popular nonopioid analgesics because of cardiovascular risk and acetaminophen toxicity raised concerns about nonopioid alternatives.¹⁰ Short lived but indelible, some pharmaceutical marketing improperly minimized addiction potential (OxyContin)¹¹ and promoted off-label use (Actiq),¹² later giving rise to physician kickback schemes (Subsys),¹³ lucrative speaking fees,¹⁴ and lobbying.¹⁵ In addition, a small proportion of

// 1 //

Counterfeits

Fake pills containing unregulated drugs

POLITICS

The Fish On Your Plate May Not Be What You Ordered

A new investigation finds that one-fifth of U.S. seafood tested is mislabeled.

By Chris D'Angelo

Mar. 7, 2019, 05:52 AM EST



Seafood on display at a fish market in New York City. TUPUNGATO VIA GETTY IMAGES

If you eat [seafood](#), even occasionally, there's a good chance you've been served a fish species you didn't order.

A new monthslong investigation by ocean advocacy group [Oceana](#) finds widespread and persistent [fraud in the U.S. seafood industry](#). The organization tested 449 fish from more than 250 restaurants, seafood markets and grocery stores across the country and found that 21 percent of samples were mislabeled.

Sea Bass and Snapper Most Commonly Mislabeled

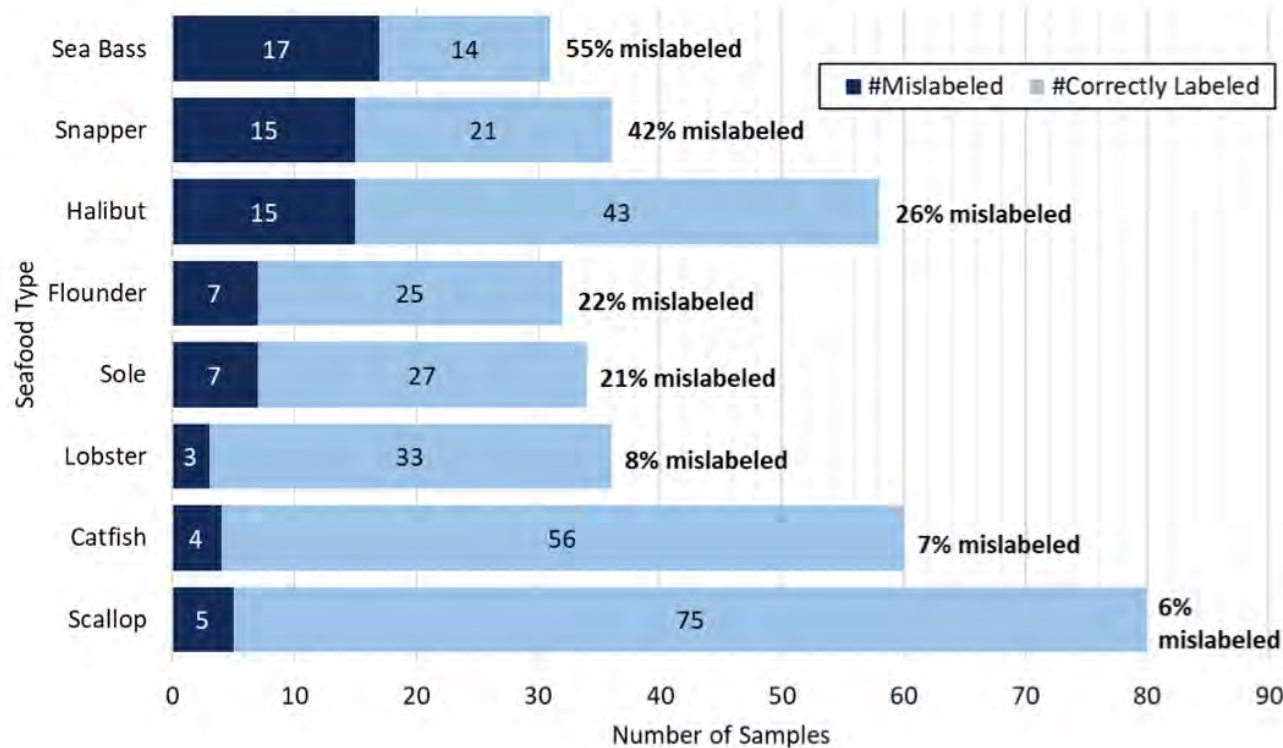


Figure 2. Mislabeling levels (%) among the most commonly sampled seafood types in our study.



Christopher Moraff

@moraffreports

Real Dava Pharma 2mg Alprazolam next to a presser I acquired yesterday. These are pumped out by the hundreds. Could you tell the difference?



3:42 PM · Feb 2, 2022 · Twitter for iPhone

11 Retweets 4 Quote Tweets 30 Likes

// 2 //

Adulterants

Unexpected and harmful additions
in street drugs

Lead and Cadmium Could Be in Your Dark Chocolate

Consumer Reports found dangerous heavy metals in chocolate from Hershey's, Theo, Trader Joe's, and other popular brands. Here are the ones that had the most, and some that are safer.



Photo Illustration: Melissa Paterno Plonchak/Consumer Reports, Getty Images

December 15, 2022

By Kevin Loria

Data visualizations by Andy Bergmann

High in Both Lead & Cadmium



Theo
Organic Pure Dark
70% Cocoa

LEAD
120%
CADMIUM
142%



Trader Joe's
The Dark Chocolate
Lover's Chocolate
85% Cacao

LEAD
127%
CADMIUM
229%



Theo
Organic Extra Dark
Pure Dark
Chocolate
85% Cocoa

LEAD
140%
CADMIUM
189%



Lily's
Extremely Dark
Chocolate
85% Cocoa

LEAD
143%
CADMIUM
101%



Green & Black's
Organic Dark
Chocolate
70% Cacao

LEAD
143%
CADMIUM
181%

// 3 //

Potency

Unexpected fluctuations in potency drive
overdose risk.



NEWS

Mini-bottles of Fireball Cinnamon don't actually contain whisky and it's led to a lawsuit

Surprise! Those mini-bottles of Fireball Cinnamon at gas stations don't actually have any whisky in them.



A mini bottle of Fireball Cinnamon which does not contain any whisky.

TODAY illustration / Fireball



Jan. 24, 2023, 5:58 PM EST

By Joseph Lamour

A class-action lawsuit has been filed in Cook County, Illinois against the makers of Fireball Cinnamon over



Potency Fluctuation



American Journal of Epidemiology
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<https://doi.org/10.1093/aje/kwab123>
Advance Access publication:
May 11, 2021

Original Contribution

Time-Series Analysis of Fentanyl Concentration in the Unregulated Opioid Drug Supply in a Canadian Setting

Samuel Tobias, Cameron J. Grant, Richard Laing, Jaime Arredondo, Mark Lysyshyn, Jane Buxton, Kenneth W. Tupper, Evan Wood, and Lianping Ti*

* Correspondence to: Dr. Lianping Ti, British Columbia Centre on Substance Use, 1045 Howe Street, Suite 400, Vancouver, BC, Canada, V6Z 2A9 (e-mail: bccsu-ti@bccsu.ubc.ca).

Initially submitted December 14, 2020; accepted for publication April 13, 2021.

North America has been contending with an unregulated street drug supply in which opioids are often adulterated with illicitly manufactured fentanyl. The unpredictability of composition may result in an increased risk of overdose due to unexpected elevated concentrations of the high-potency drug. Using data from a community-based drug-checking project, we evaluated trends in fentanyl concentration of illicit opioids in the context of an overdose epidemic. Using a quantification model for fentanyl hydrochloride, historical Fourier-transform infrared spectra from opioid drug-checking samples were analyzed to determine fentanyl concentrations. Median monthly fentanyl concentrations were plotted, and polynomial and autoregressive time-series analyses were performed to examine trends over time. A total of 3,621 fentanyl-positive samples were included in the study, spanning November 2017 to December 2019. Monthly median fentanyl concentrations ranged from 4.5% to 10.4%. Time-series analyses indicated that a third-degree polynomial model fit the data well ($R^2 = 0.639$), suggesting a cyclical pattern in median concentration over time. Notably, absolute variance in fentanyl concentration decreased by an average 0.1% per month ($P < 0.001$). Future research should explore the relationship between fentanyl concentration and overdose to identify potential targeted harm-reduction interventions that can respond to changes in observed fentanyl concentration.

drug checking; fentanyl; harm reduction; time-series modeling

Abbreviations: FTIR, Fourier-transform infrared; PWUD, people who use drugs; qNMR, quantitative nuclear magnetic resonance.

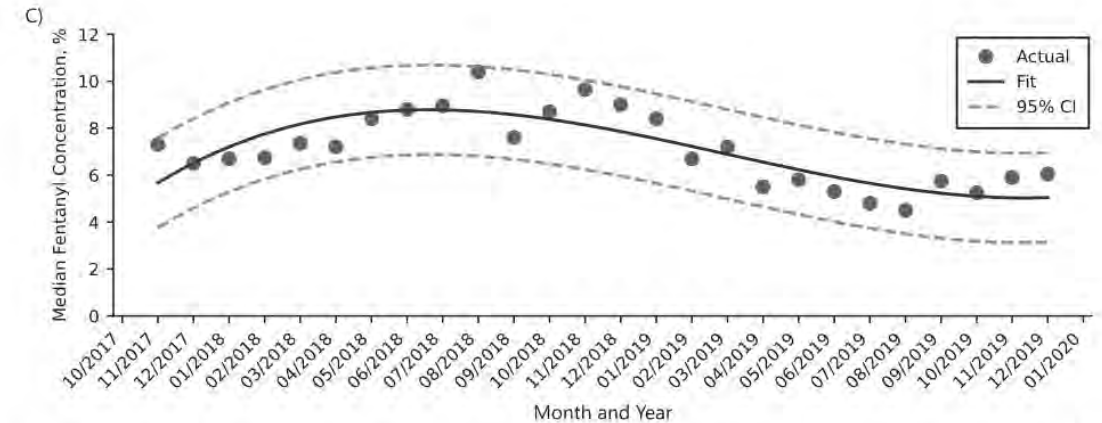
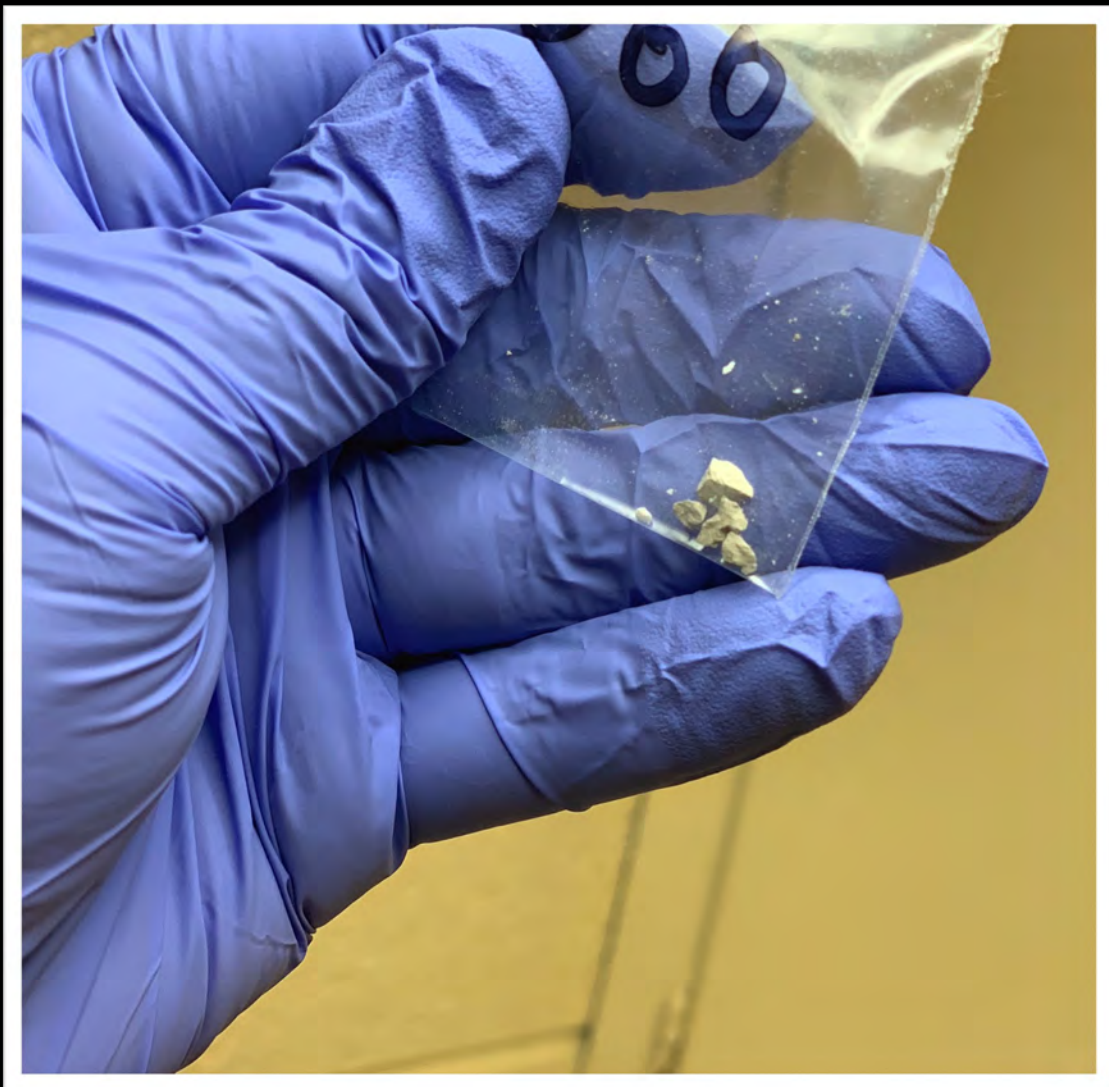


Figure 1. Monthly median fentanyl concentration of expected opioid samples brought to a drug-checking service in Vancouver, British Columbia. First- (A), second- (B), and third-degree (C) polynomial models are indicated by the solid lines and 95% confidence intervals (CIs) by the dotted lines.



Street drugs change constantly.



COVID-19 PCR kits



ANONYMOUS DRUG CHECKING SERVICE

UNC Gillings School of Global Public Health
Mass Spectrometry Core Laboratory
125 South Road
Caudill Lab Building
Chapel Hill, NC 27599



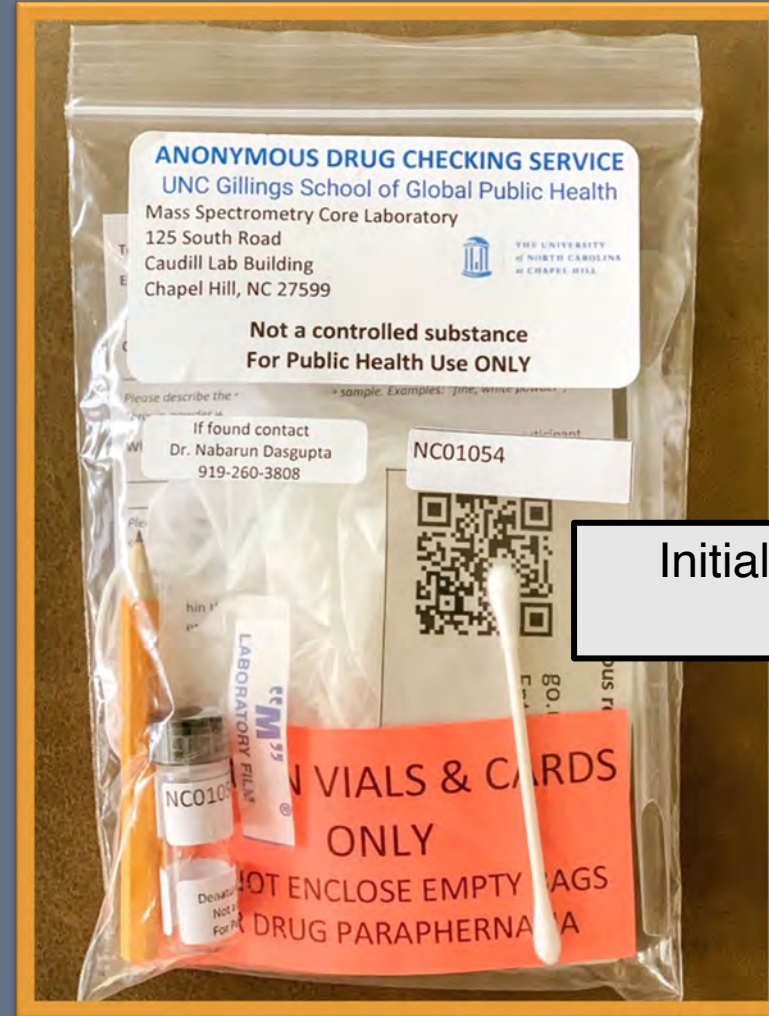
Not a controlled substance
For Public Health Use ONLY

If found contact
Dr. Nabarun Dasgupta
919-260-3808

NC01054



Initial UNC Street Drug Checking kit



In our lab on campus



we monitor street drugs



as a public service.



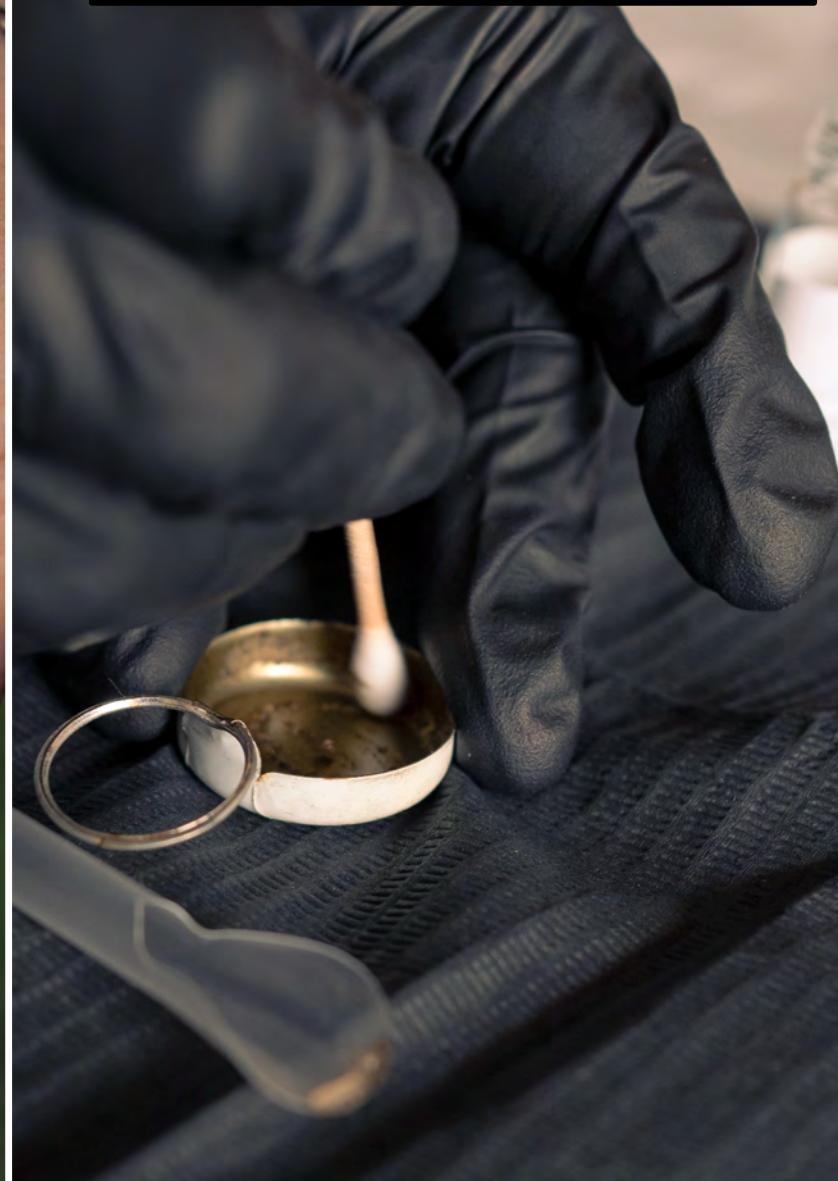
Harm reduction programs, health departments, clinics, hospitals, user unions, and EMS send us samples from around the country

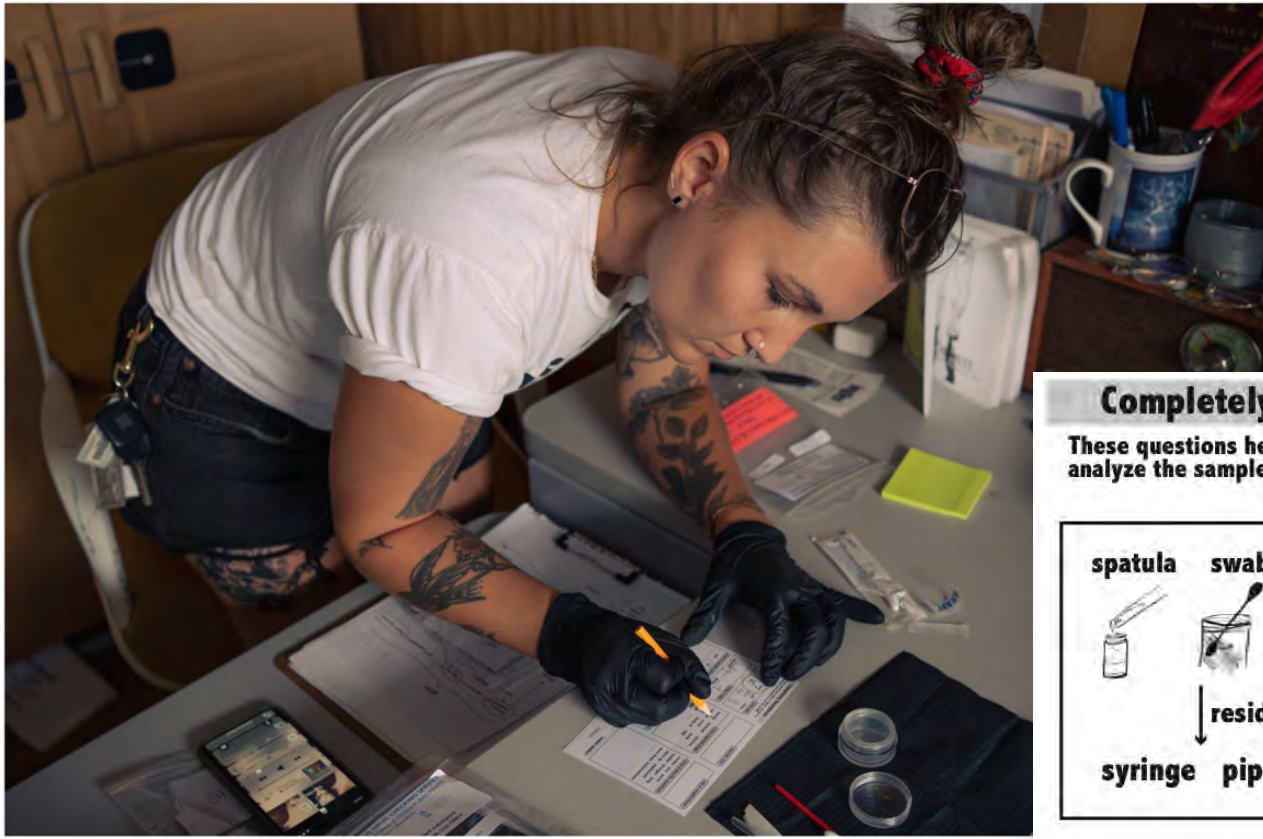
...using this innovative kit.

Samples are given voluntarily.



The tests are anonymous.





Programs share health information with us

to give human context beyond molecules.

Completely Anonymous
 These questions help us figure out how to analyze the sample in our lab at UNC.

circle

spatula 	swab 	pill 	cotton
residue?			
syringe	pipe	foil	

describe color and markings

circle expected drugs

heroin	fentanyl	xylozine
cocaine	crack	meth
ketamine	weed	M30
benzo	other:	
MDMA		
unknown		

circle textures

crystals	pill	fake pill
powder	edibles	oil/wax
chunky	plant/leaf	tar
shiny	other:	
flaky		
dull		

circle if involved in overdose

yes no don't know

describe the overdose to ward others:

overdose

city or neighborhood

circle & describe sensations

normal nice weird
 weaker stronger long
 more up unpleasant
 more down hallucinations
 sedating unusual taste

describe:

sensations

sample number

Packages arrive on campus



in compliance with drug and postal laws.



We record the information



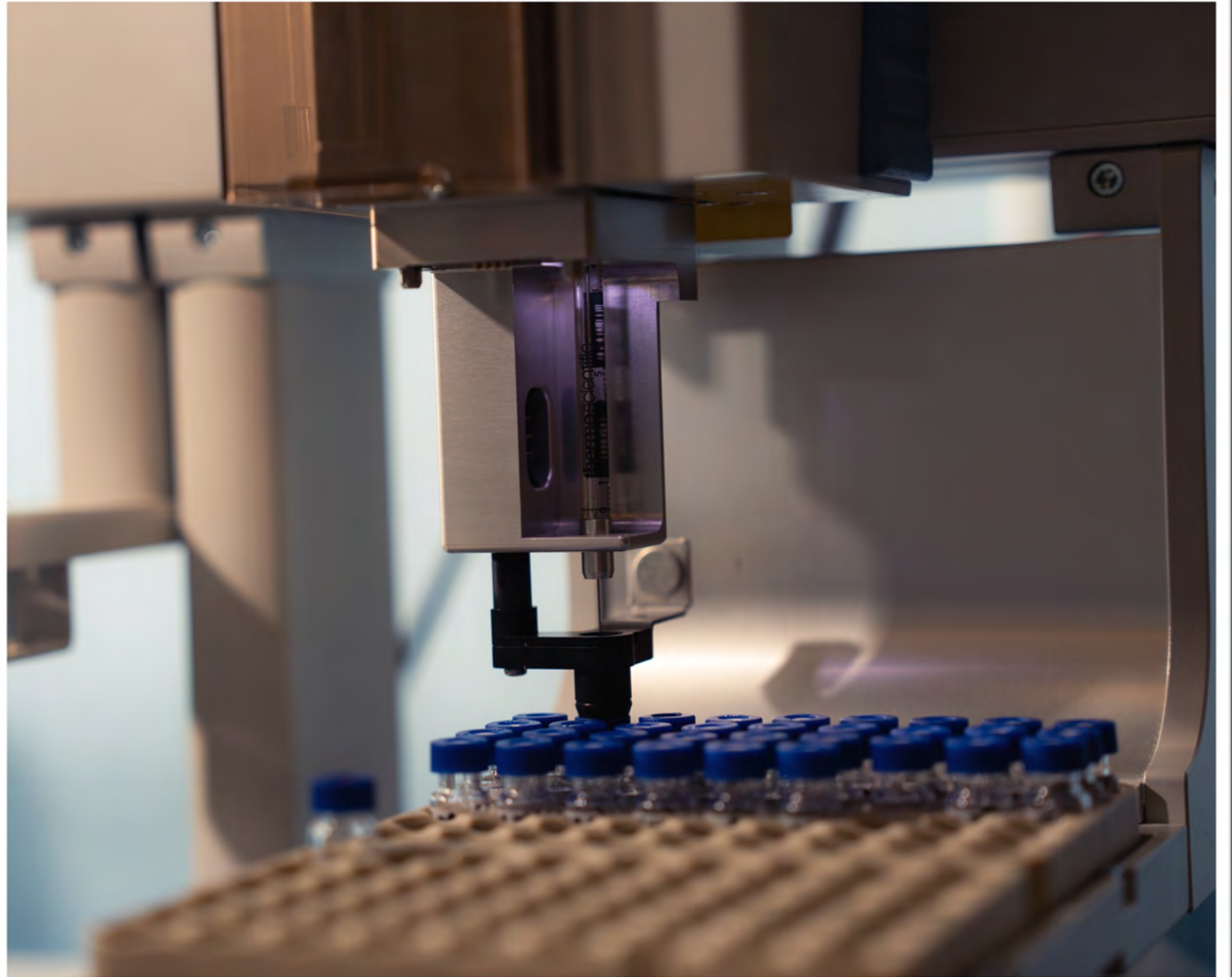
and catalog the samples.



We prep the samples



and load them on a GCMS (mass spec).



We interpret the high resolution results,



to determine exactly what's in the sample.



We've detected a multitude of substances in drug supply.



Advanced statistics help detect hidden patterns.



We make our data public daily.





Most importantly, we provide timely results back to the individual.

Location, date Sold as Physical description

From Winston-Salem, North Carolina on 5/18/2022 Assumed to be fentanyl

Primary substances detected

This is a messy brew of 7 major substances:

- xylazine
- mannitol
- 4-ANPP
- p-fluorofentanyl
- non-specific sugars
- fentanyl
- heroin

Traces

And we also found traces of dimethyl sulfone (methylsulfonylmethane MSM) + acetylcodeine + 6-monoacetylmorphine (6-MAM). Trace substances in small quantities can sometimes be harmless, but other times can cause health problems. If you have unexpected sensations, it may be due to these.

Fentanyl is potent and the amount changes by batch. If you weren't expecting it, consider getting test strips online or from a harm reduction program. Carry naloxone (Narcan) to reverse overdoses. Don't use alone so someone can help if you go out.

Xylazine causes serious skin problems. These can happen anywhere on the body and don't heal quickly. And, xylazine can come on stronger than traditional dope and knock you out, so be mindful of your surroundings. It's best to avoid dope with xylazine. You might need medical attention to prevent long-term damage.

There are a lot of different substances in this sample. We don't know the harms that some of these can cause. Be careful and be prepared for unexpected reactions.

Fluorofentanyl is showing up recently. It's the result of different raw materials being used to make fentanyl. We don't know yet if it causes any specific problems.

Looks = white powder, chunky

Need free supplies and advice to keep you safe? Find your nearest harm reduction program at harmreduction.org

Major substances in graph:

- Peak 6.9 = xylazine
- Peak 7.3 = mannitol
- Peak 8.39 = 4-ANPP
- Peak 8.93 = heroin
- Peak 9.1 = p-fluorofentanyl
- Peak 9.24 = fentanyl

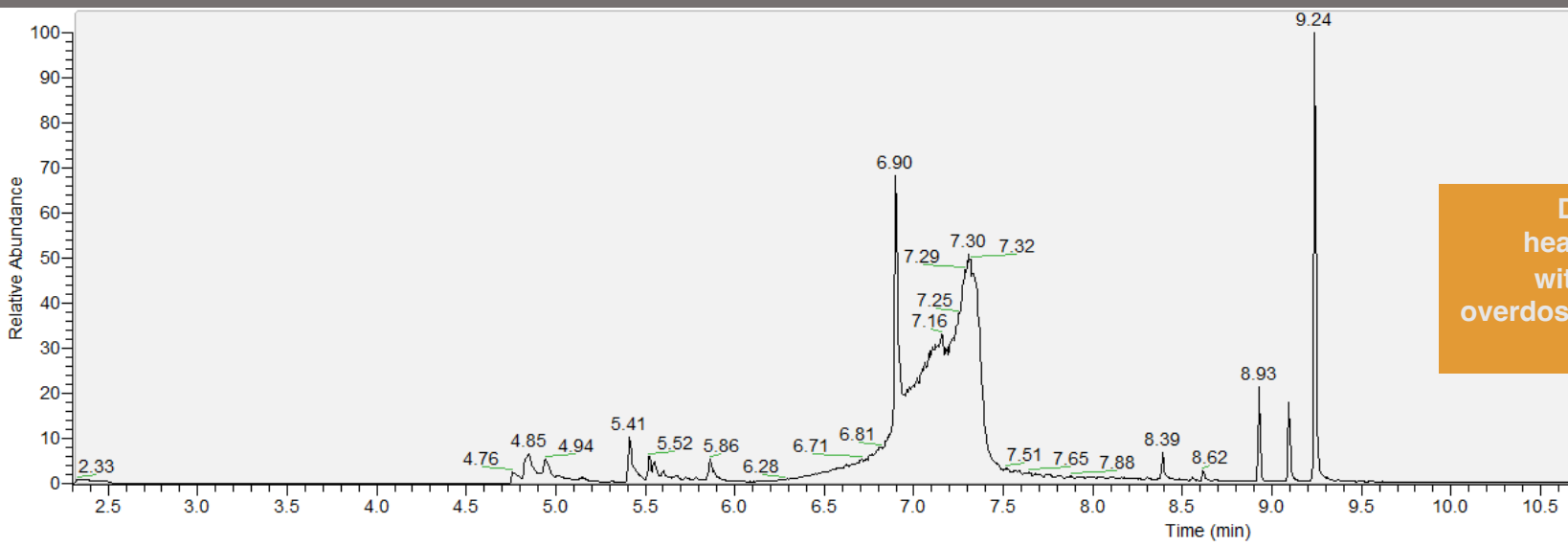
Drug-specific health warnings with actionable overdose prevention advice

New drugs

Getting help locally

Scientific accountability

Method(s): GCMS + Derivatized GCMS Peaks that don't appear on the graph were detected using other advanced methods. If a peak appears on the graph but isn't listed above, then we reviewed it and determined it's unimportant. Contact us if you want details.



NL: 2.53E9 TIC MS 300298-a

Our information empowers people to answer questions of local relevance.



Questions we have helped answer

Is there fentanyl in black tar heroin?

Are nitazenes causing these overdoses?

What is causing a patient's atypical withdrawal?

Can xylazine explain these skin wounds?

How accurate are these test strips?

Can black lights identify xylazine and fentanyl?

Preventing amputations



Solving medical mysteries







CASE REPORT

Xylazine Masking Benzodiazepine Withdrawal

Gregg Robbins-Welty, MD, MS, HEC-C; Jakayla Hart, MD; Nicole Dussault, MD; and Noel Ivey, MD, FACP

Published: February 8, 2024

Xylazine, or “tranq,” is a veterinary anesthetic recognized as a highly potent and potentially lethal adulterant in community supplies of opioids, benzodiazepines, and cocaine.¹ Here, we report a case that suggests a xylazine-induced masking of benzodiazepine withdrawal, which resulted in a withdrawal seizure in our patient. The importance of vigilant monitoring for withdrawal symptoms in patients using multiple substances and the value of drug testing for impurities and additives in the community drug supply are highlighted.

CASE REPORT

A 35-year-old man with a history of polysubstance use disorder (opioids, cocaine, benzodiazepines, THC, methamphetamine, and tobacco), including a recent hospitalization for opioid overdose, presented to the emergency department after being found cyanotic at home. He was successfully

Drug and Alcohol Dependence 252 (2023) 110985

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugaldep

Prevalence of fentanyl in methamphetamine and cocaine samples collected by community-based drug checking services

Karla D. Wagner^a, Phillip Fiuty^b, Kimberly Page^c, Erin C. Tracy^d, Maryalice Nocera^d, Colin W. Miller^d, Lina J. Tarhuni^{e,g}, Nabarun Dasgupta^{d,*}

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ARTICLE INFO

Keywords:
 Drug checking
 Fentanyl
 Methamphetamine
 Cocaine
 Epidemiology
 Harm reduction

ABSTRACT

Background: Overdose deaths involving stimulants and opioids simultaneously have raised the specter of widespread contamination of the stimulant supply with fentanyl.

Methods: We quantified prevalence of fentanyl in street methamphetamine and cocaine, stratified by crystalline texture, analyzing samples sent voluntarily to a public mail-in drug checking service (May 2021–June 2023). Samples from 77 harm reduction programs and clinics originated in 25 US states. Sample donors reported expected drug and physical descriptions. Substances were identified by gas chromatography-mass spectrometry. Negative binomial models were used to calculate fentanyl prevalence, adjusting for potential confounders related to sample selection. We also examined if xylazine changed donors' accuracy of detecting fentanyl.

Results: We analyzed 718 lab-confirmed samples of methamphetamine (64%) and cocaine (36%). The adjusted prevalence of fentanyl was 12.5% (95% CI: 2.2%, 22.9%) in powder methamphetamine and 14.8% (2.3%, 27.2%) in powder cocaine, with notable geographic variation. Crystalline forms of both methamphetamine (Chisq=57, p<0.001) and cocaine (Chisq=18, p<0.001) were less likely to contain fentanyl: less than 1% of crystal methamphetamine (2/276) and no crack cocaine (0/53). Heroin was present in 6.6% of powder cocaine samples. Xylazine reduced donors' ability to detect fentanyl, with correct classification dropping from 92% to 42%.

Conclusions: Fentanyl was detected primarily in powder forms of methamphetamine and cocaine. Recommended interventions include expanding community-based drug checking, naloxone and fentanyl test strip distribution for people who use stimulants, and supervised drug consumption sites. New strategies to dampen variability in street drug composition are needed to reduce inadvertent fentanyl exposure.

Zagorski et al. *Harm Reduction Journal* (2023) 20:141
<https://doi.org/10.1186/s12954-023-00879-7>

Harm Reduction Journal

PERSPECTIVE **Open Access**

Reducing the harms of xylazine: clinical approaches, research deficits, and public health context

Claire M. Zagorski^{1*}, Rebecca A. Hosey², Christopher Moraff³, Aaron Ferguson⁴, Mary Figgatt⁵, Shoshana Aronowitz⁶, Natalie E. Stahl⁷, Lucas G. Hill¹, Zoe McElligott⁸ and Nabarun Dasgupta⁹

Abstract

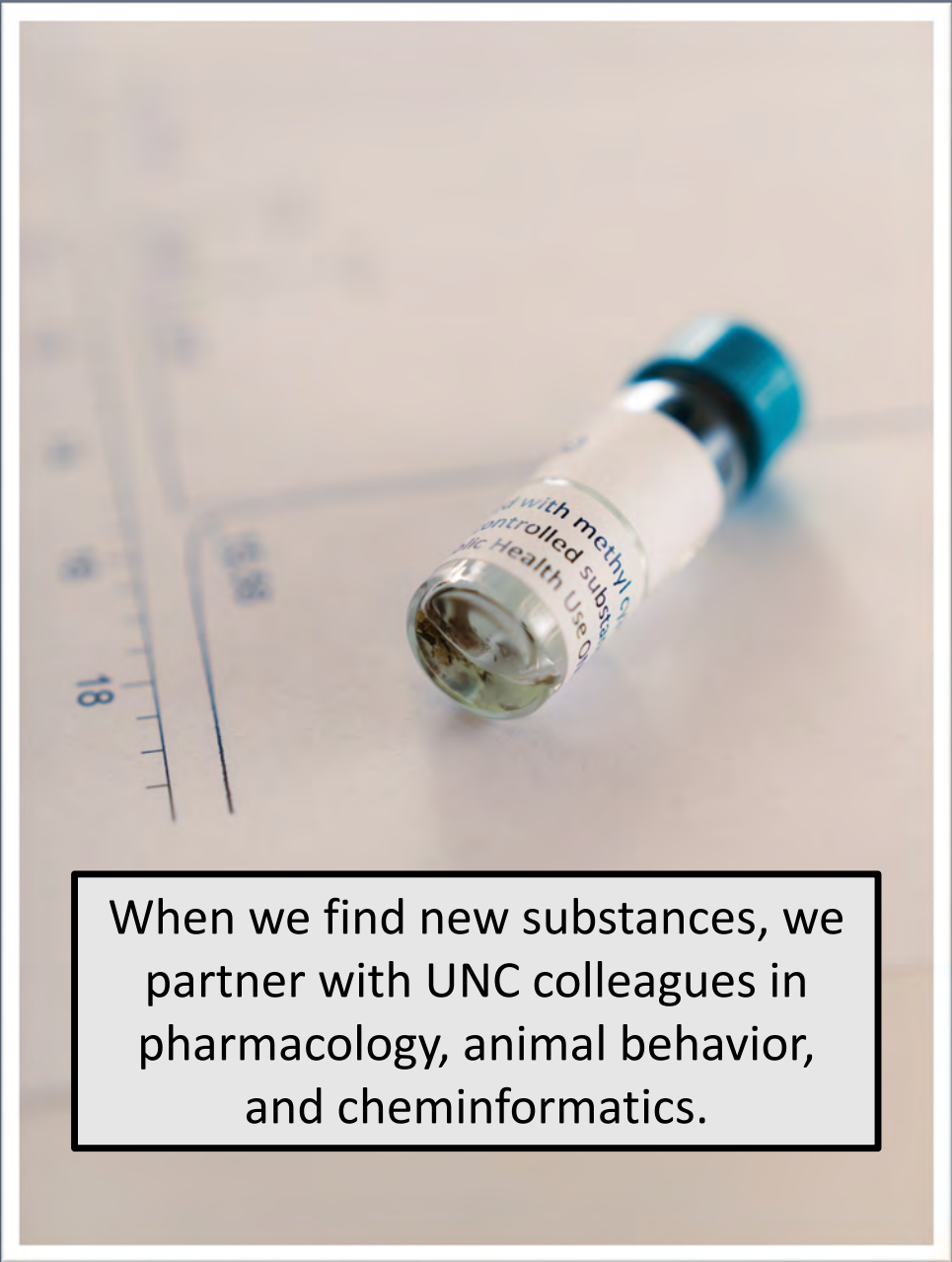
Objectives Xylazine has emerged as a consistent part of the unregulated drug supply in recent months. We discuss major domains of xylazine's harm, current knowledge deficits, clinical and harm reduction strategies for minimizing harm, and xylazine's public health and policy context. As an interdisciplinary team from across the USA, we have pooled our knowledge to provide an overview of xylazine's current and emerging contexts.

Methods To inform this essay, the pertinent literature was reviewed, clinical knowledge and protocols were shared by multiple clinicians with direct expertise, and policy and public health context were added by expert authors.

Results We describe xylazine's major harm domains—acute poisoning, extended sedation, and wounds, along with anemia and hyperglycemia, which have been reported anecdotally but lack as clear of a connection to xylazine. Current successful practices for xylazine wound care are detailed. Understanding xylazine's epidemiology will also require greater investment in drug checking and surveillance. Finally, approaches to community-based wound care are discussed, along with an orientation to the larger policy and public health context.

Conclusions Addressing the harms of xylazine requires interdisciplinary participation, investment in community-based harm reduction strategies, and improved drug supply surveillance. The relatively unique context of xylazine demands buy-in from public health professionals, harm reduction professionals, clinicians, basic science researchers, policymakers and more.

Keywords Xylazine, Harm reduction, Wounds, Drug injection



When we find new substances, we partner with UNC colleagues in pharmacology, animal behavior, and cheminformatics.

New scientific breakthroughs



bioRxiv
THE PREPRINT SERVER FOR BIOLOGY

New Results

[Follow this preprint](#)

Xylazine is an agonist at kappa opioid receptors and exhibits sex-specific responses to naloxone administration

Madigan L. Bedard, Jackson G. Murray, Xi-Ping Huang, Alexandra C. Nowlan, Sara Y. Conley, Sarah E. Mott, Samuel J. Loyack, Calista A. Cline, Caroline G. Clodfelter, Nabarun Dasgupta, Bryan L. Roth, Zoe A. McElligott

doi: <https://doi.org/10.1101/2023.09.08.556914>

This article is a preprint and has not been certified by peer review [what does this mean?].



Abstract

Full Text

Info/History

Metrics

[Preview PDF](#)

Abstract

Xylazine has been found in the unregulated drug supply at increasing rates, usually in combination with fentanyl. It has become critical to understand its basic pharmacology, how it impacts behavior, and how it interacts with fentanyl in rodent models of opioid administration. Despite commentary from scientists, politicians, and public health officials, it is not known if xylazine impacts the efficacy of naloxone, the opioid receptor antagonist used to reverse opioid induced respiratory depression. Furthermore, few studies have examined the effects of xylazine alone, without co-administration of ketamine. Here, we examine the impact of xylazine alone and in combination with fentanyl on several key behaviors in male and female mice. We demonstrate differential locomotor responses by dose and sex to xylazine. Surprisingly, our



March 2022 to March 5, 2024

N = 4,748 samples analyzed

160+ programs

35+ US states

300731

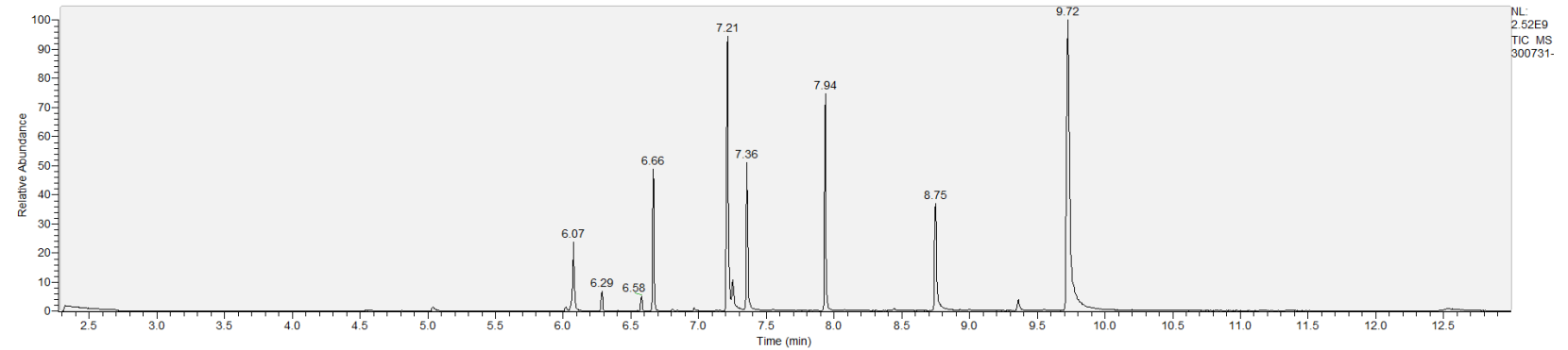
From Asheboro, North Carolina on
11/2/2022
Assumed to be heroin

This is a messy brew of 10 major substances:

- **phenacetin**
- **caffeine**
- **procaine**
- **meconin**
- **hydrocotarnine**
- **fentanyl**
- **levamisole**
- **4-ANPP**
- **xylazine**
- **cocaine**

But we found lots of contaminants too, with traces of acetaminophen + N-phenylpropanamide + melatonin + noscapine + heroin + dimethyl sulfone (methylsulfonylmethane MSM). Trace substances in small quantities can sometimes be harmless, but other times can cause health problems. If you have unexpected sensations, it may be due to these.

Mezcla de 16 sustancias



Medicina: phenacetin, paracetamol, melatonin

Medicina veterinaria: levamisole, xylazine

Entumecedor: procaine

Estimulantes: cafeína, cocaína

Origen vegetal: noscapine, meconin, hydrocotarnine, heroin

Opioides sintéticos: fentanyl

Subproducto: 4-ANPP, N-phenylpropanamide, MSM

Current watch list

1. Nitazenes – Novel opioids of varying potency
2. Potent benzodiazepines – Here to stay in fake pills?
3. Colored drugs – Hype versus reality
4. Fentanyl in stimulants – More in powder forms
5. (dex)medetomidine – Xylazine replacement
6. Tianeptine – Odd withdrawal syndromes
7. Fentanyl analogues – Predictably diversifying
8. Ketamine mixtures – Unexpected combos with stimulants
9. K2/Spice contaminants – Could opioids appear?
10. Substituted cathinones – Will they diversify?

We help people
make better
decisions about
what to put in their
bodies.



Thanks from and to our team!



Tory



Illyana



Allison



Don



Louise

Shelby
Bridgette
Shay
Tushar
William



Drew



Brandie



Maryalice



LaMonda

Rachel Clark @ DanceSafe



Hand drawn by

**BRITAIN
PECK**



Zoë



Nabarun



Colin



Erin

Photos by
Pearson Ridley



erythritol, stevia leaf

sucrose

dextrose, maltodextrin, aspartame, acesulfame potassium, phenylalanine

dextrose, maltodextrin, sucralose

dextrose, sucralose

sucrose

dextrose, maltodextrin, sucralose

sucrose

dextrose, saccharin, cream of tartar, calcium silicate

sucrose



Communication & Drug Checking

Googling chemical names will give you wrong information.

→ **Provide simple summaries (<5 words) to retain attention**

Metonitazene: “Rare but potent opioid”

Inability to pronounce chemical names disconnects people.

→ **Provide phonetic guides**

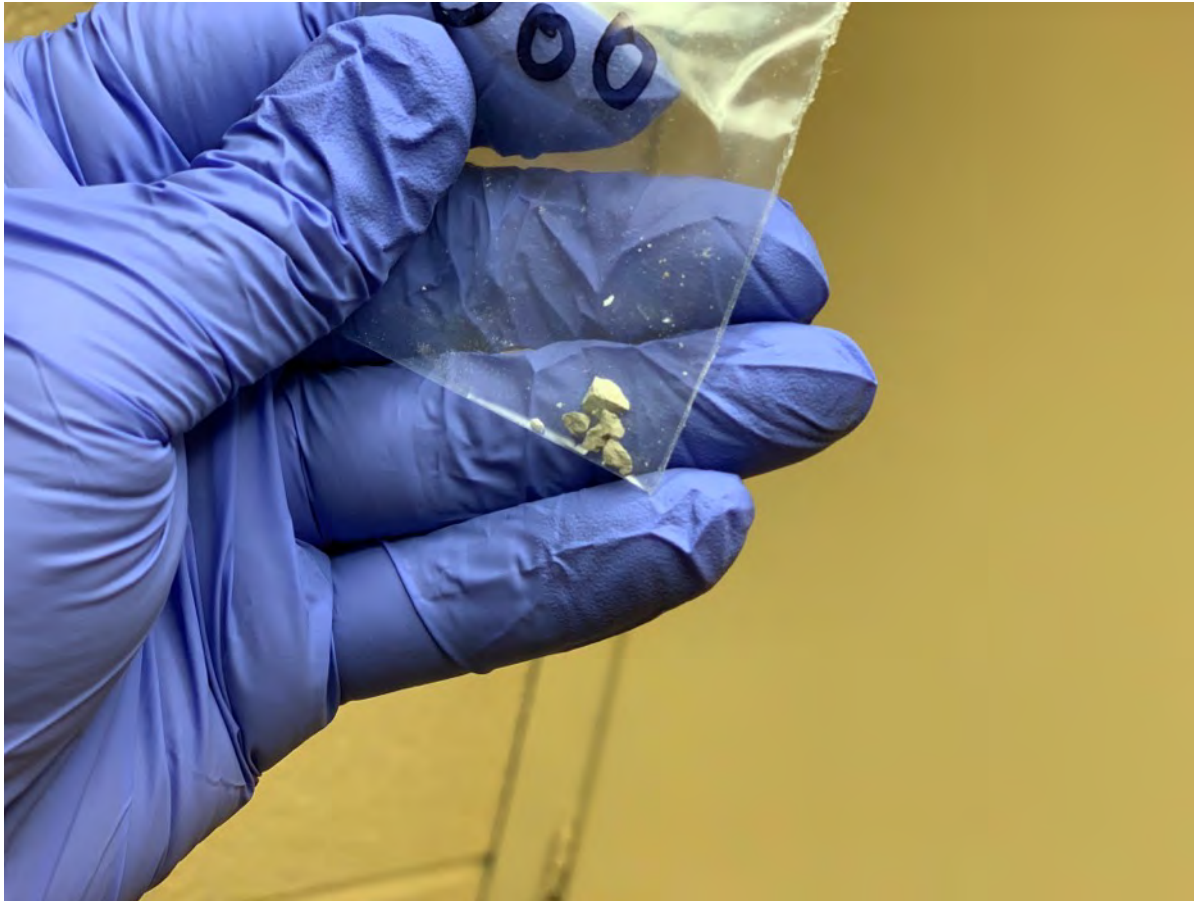
Metonitazene: “met-oh-nit-a-zeen”

People want to know what is “normal.”

→ **Use metrics to benchmark to local supply**

Metonitazene: “Increasing in western NC along TN border.”

Drug alerts are issued every day. But how well do we communicate?



Health departments

Law enforcement

PSA

News media

Schools

Clinics

Harm reduction orgs

Drug checking programs

 Interior Health

⚠️ DRUG ALERT ⚠️

Date Issued: **February 2, 2021**

Community/Region: **Castlegar**

Description of drug: **Light pink powder**

Sold as: **DOWN**

Tested at: **ANKORS with FTIR**

Result: **CONTAINS A HIGH CONCENTRATION OF FENTANYL + BENZODIAZEPINES**

Risk: High risk of OVERDOSE with PROLONGED SEDATION - MAY NOT RESPOND TO NALOXONE – CONTINUE TO GIVE BREATHS AND SEEK MEDICAL ATTENTION.

In effect until: **February 9, 2021**



OVERDOSE SPIKE ALERT

➔ CARRY NALOXONE

➔ DON'T USE ALONE

➔ KNOW YOUR SUPPLY

**AND REMEMBER:
WE ARE HERE FOR YOU.**

Please visit us at 304 Hancock Street for supplies!



Potent synthetic opioids implicated in increase in drug overdoses

Date of issue:	18/08/2021	Reference no:	NatPSA/2021/007/PHE
This alert is for action by: Acute, mental health and community trusts, private and voluntary sector treatment services, ambulance and 999/111 service providers, general practice and community pharmacists.			
This is a safety critical and complex National Patient Safety Alert. Implementation should be co-ordinated by an executive lead (or equivalent role in organisations without executive boards).			

Explanation of identified safety issue:

In the past 10-14 days there have been an unprecedented number of overdoses (with some deaths) in people who use drugs, primarily heroin, in some parts of the country (5 London boroughs, Hampshire, Essex, West Sussex, Dorset, Thames Valley).

Opioid drug deaths are, sadly, not uncommon (averaging 24 a week across England and Wales) but what has been seen in these areas is an unusual increase, with some common patterns and some limited evidence of a common cause.

Testing in two areas (of 3 cases) so far found isotonitazene, a potent synthetic opioid. Isotonitazene has been identified previously in this country but its use has been more common in the USA. It was notified as a subject of concern in Europe in 2019. Its potency and toxicity are uncertain but perhaps similar to, or more than fentanyl, which is about 100x morphine

The adulterated heroin used may be paler in colour than usual and may become darker than usual when dissolved for injection ("cooked up"). However, reports vary considerably

There is good evidence from reports that naloxone, the 'antidote' to opioid overdoses, works in these cases. The treatment required for an overdose that may be related to isotonitazene is the same as for other opioid overdoses, but delivering it rapidly and completely is even more critical, as progression to respiratory arrest, and recurrence of respiratory arrest, are more likely.

Those in contact with heroin users should be alert to the increased possibility of overdose arising from 'heroin' containing synthetic opioids, be able to recognise possible symptoms of overdose and respond appropriately.

There is no evidence for absorption of isotonitazene through the skin but usual precautions, including masks, should be taken when handling unknown substances, especially if they have become airborne.

Actions required

Actions to be completed as soon as possible and no later than 20 August 2021.

- All organisations where staff may encounter people who use drugs should ensure those staff are:**
 - made aware of the risk of severe toxicity resulting from adulteration of heroin with potent synthetic opioids such as isotonitazene
 - made aware of the potency and toxicity of isotonitazene is perhaps similar to, or more than, fentanyl, which is about 100x morphine
 - alert to the symptoms of opioid overdose in known and suspected heroin users
 - communicate these risks to heroin users during any contacts
 - ensure people who use heroin and others who might encounter an opioid overdose have naloxone available ([Widening the availability of naloxone](#))
- All organisations that provide emergency care for opioid overdose should ensure staff are supported to:**
 - treat suspected cases as for any opioid overdose, using naloxone and appropriate supportive care
 - recognise the duration of action of naloxone is shorter than that of many opioids and appropriate monitoring and further doses of naloxone may be required

In the community this could include injectable or intranasal naloxone, administering a single dose and waiting for no response before administering more.

In specialist medical settings only:

 - treatment may involve the intravenous naloxone titration regimen recommended by the National Poisons Information Service (overleaf).
 - intramuscular naloxone can be used as an alternative in the event that IV access is not possible or is delayed.

For further detail, resources and supporting materials see: [Enter specific webpage provided by alert issuer](#)

For any enquiries about this alert contact: NatPSA@phe.gov.uk

1/2

NEW DANGEROUS DRUG ALERT

METONITAZENE/ETONITAZENE, KNOWN COMMONLY AS "ISO", IS A DEADLY DRUG 20 TIMES MORE POTENT THAN FENTANYL.

ISO CAN BE ABSORBED BY THE BODY BY SKIN CONTACT, INGESTION OR INHALATION.

ISO IS NOW TURNING UP IN OVERDOSES AND SUBSTANCE ABUSE CASES.

SIGNS OF AN OVERDOSE:

- BLUE/PURPLE FINGERNAILS
- BLUE/PURPLE LIPS
- DIFFICULTY BREATHING
- UNCONCIOUSNESS
- CLAMMY SKIN
- VOMITING
- PINPOINT PUPILS
- DROWSINESS

ALL OF WHICH CAN OCCUR WITHIN MINUTES OF EXPOSURE.

IF YOU BELIEVE SOMEONE IS OVERDOSING, CALL 911 IMMEDIATELY.



NSW DRUG ALERT

Heroin mixed with Fentanyl

NSW health has released a warning about fentanyl/acetlyfentanyl found in the heroin supply in Sydney (Jan 2021). Fentanyl has been circulating in Sydney & regional NSW since Nov/Dec 2020. It is reported that heroin containing fentanyl/acetlyfentanyl sometimes is purple or turns purple when mixed with water.

What is fentanyl
Fentanyl is a highly potent opioid - up to **100x stronger than morphine** - meaning only a very small amount can cause a rapid and unexpected overdose.



Symptoms of overdose

- Drowsiness
- Loss of consciousness
- Face is very pale or clammy
- Slow, shallow, and/or erratic breathing
- Vomiting
- Change in skin tone: bluish/purple for lighter skinned people, and greyish for darker skinned people

What to do
If you or someone you're with experiences these symptoms get medical help ASAP
• Call **Triple Zero (000)** and ask for an ambulance
• Administer naloxone if you have any

Protect yourself
You can buy fentanyl testing strips and naloxone from NAAA's online shop, or call us for more information on 1800 6444 413

NSW Users and AIDS Association Jan 2021

NALOXONE

SAVE ME with Naloxone

- Opioid Reversal Agent
- Invented 1961 & In use 1971
- Non-selective & Competitive opioid receptor antagonist
- Works by reversing the depression of the central nervous system and respiratory system caused by opioids
- Multiple doses required as the action of most opioids are greater
- Naloxone's binding Affinity is highest for the μ -opioid receptor then the δ -opioid receptor, and lowest for the κ -opioid receptor
- It is Synthetic congener of Oxymorphone
- Nasal Spray was approved in 2015
- Naloxone pre-filled syringes, vials, and auto-injector are available

Stimulate Airway
Ventilate Evaluate Muscular In. Evaluate (Next Dose)

Medical Use

Opioid overdose

- Useful in treating both Acute/Chronic opioid overdose and respiratory or mental depression due to opioids
- It is always prescribed when patient is on high dose of opioids
- Initial dose of 0.4mg-2mg administered IV, maximum 10 mg IV

In people with Shock, including Septic, Cardiogenic, Hemorrhagic, or Spinal shock, those who received naloxone had improved blood flow

- Naloxone also used as an antidote in overdose of Clonidine
- Also used to treat Opioid induced severe Pruritus and constipation

Pharmacokinetics & Pharmacodynamics

Routes of Administration : Intranasal, Endotracheal, IV, IM, Intraosseous

- ✓ Bioavailability : 2 % Oral, 50 % Intranasal, 80 % IM, 100 % IV
- ✓ Metabolism : Liver
- ✓ Onset of action: IV-2 m, IM-5 m
- ✓ Elimination half-life : 1-1.5 h
- ✓ Duration of action : 30-60 min
- ✓ Excretion : Urine, bile
- ✓ Storage : At room temperature
- ✓ Molar Mass : 27.380 g·mol⁻¹
- ✓ Formula : C₁₉H₂₁NO₄

Safe in Pregnancy & Lactation


- ✓ Available as a sterile solution for IV, IM and S/C administration in three concentrations: 0.02 mg, 0.4 mg and 1 mg per mL
- ✓ It is repeated at two- to three-minute intervals
- ✓ Dose in children & Neonates is 0.01 mg/kg
- ✓ Careful in giving in Geriatric, Renal and Liver failure patients
- ✓ Maximum dose is 24 mg/24 hrs
- ✓ Always protect from light

Side Effects

- Increased sweating, Nausea, Restlessness, Trembling, Vomiting, Flushing, Headache, Hypotension and Fibrillation
- In rare cases it causes Heart Rhythm Changes, Seizures, and Pulmonary Edema with Cardiac Arrest
- Excessive doses of naloxone in postoperative patients may result in significant reversal of analgesia and may cause agitation
- Shelf life is IV 2 years & Intranasal 1.5 years

Extra Shots

- It is available without prescription in most of the countries
- Naloxone kits are available



Randomized Message Trial

RCT of standard vs. optimized alerts

Adulterant and potency alerts

4 alerts in 10 minutes for \$10 cash incentive

Test saliency based on demographics, drug use, history

N=610

- Sonoran Prevention Works (AZ)
- Maine Access Points (ME)
- Twin Cities Harm Reduction Collective (NC)
- RED Project (MI)
- SANE (CA)
- Connecticut Harm Reduction Alliance (CT)
- Portland People's Outreach Project (OR)

Standard



! DRUG ALERT!!!

High Potency MDMA (Ecstasy)

There have been reports across the state of unusually potent MDMA/Ecstasy pills that have resulted in a number of hospitalizations and one death. The pills are shaped like the "Tesla" logo and have been seen in a variety of colors. A typical MDMA/Ecstasy pill contains 100mg - 150mg of MDMA, whereas these "Tesla" pills have been found to contain three to four times that (300mg-400mg of MDMA).

Follow the tips below to keep you and others safe:

- **Avoid overheating:** MDMA/Ecstasy can cause hyperthermia, or overheating of the body. Be sure to sip water throughout your experience to keep your body hydrated, and take breaks regularly if you are engaging in physical activity such as dancing.
- **Start with a test dose:** Start with 1/4 of a pill and wait at least an hour to assess how you feel. You can always take more, but you can't go back once you've ingested too large of a dose.
- **Do not take other drugs with MDMA/Ecstasy:** alcohol, cocaine, methamphetamine, and other stimulants can contribute to body temperature dysregulation and increase the chances of negative health outcomes.
- **Never use alone:** It's always a good idea to have friends around just in case someone should get overheated or have an adverse reaction.
- **Don't hesitate to get help if you or someone else has an adverse reaction:** call for help as soon as one is feeling unwell or has an adverse reaction.

Optimized



DRUG ALERT!

High Potency "Tesla" MDMA (ECSTASY) found across the state.

 There have been reports of unusually potent **MDMA (ECSTASY)** pills shaped like the Tesla logo that have led to hospitalizations and one death. These have **3X** the typical amount of MDMA.

Avoid OVERHEATING.
Make sure to sip water and **stay hydrated.**

FOLLOW THESE TIPS TO STAY SAFE:

- Start with a test dose
- Avoid using alone so someone can help in an emergency

GET HELP QUICKLY IF SOMEONE HAS AN UNEXPECTED NEGATIVE REACTION

! OVERDOSE ALERT!!!

There have been several overdoses in your county in the last 48 hours, three of which were fatal, linked to purple-colored fentanyl. This potentially fatal type of fentanyl is also known as "purp", "grapes", or "grimace". Knowing the signs and how to respond to an opioid overdose can save lives!



Signs of an Opioid Overdose

- Unresponsive
- Blue or gray lips and finger/toenails
- Slow, shallow, or not breathing
- Vomiting
- Small/"pinpoint" pupils
- Cold, clammy, pale skin
- A gurgling or snoring-like sound of breath (also known as the "death rattle")

If you are using drugs, it is important to utilize the following harm reduction strategies to lower your risk of fatal and non-fatal overdose:

- Never use alone
- If using with someone, use your drugs at different times so that if one of you overdoses the other can respond to the overdose
- Avoid mixing opioids with other drugs, especially benzodiazepines (Xanax, Klonopin, Valium, etc.) and/or alcohol

Simple graphics that do not distract

- Always carry naloxone (Narcan) and know how to use it to reverse an overdose

Information Hierarchy

1. rub your knuckles on the sternum of person you suspect has overdosed. If person is unresponsive, continue to next step.
2. Call 911
3. Administer naloxone and begin rescue breathing
4. If person is still unresponsive after 2-3 minutes, administer another dose of naloxone and continue rescue breathing; repeat until the person's breathing is restored

Formatted for screens and social media

POTENCY ALERT!

Purple Fentanyl linked to multiple overdoses in [Name] County.

Local relevance



There have been several overdoses in [NAME] COUNTY in the last 48 hours, three of which were fatal, linked to **PURPLE FENTANYL**. This potentially fatal fentanyl is called "purp," "grapes," or "grimace."

Time urgency

Carry NALOXONE.

Call to action

Know overdose signs and how to respond **to save lives.**

Motivation



- 🔗 SIGNS OF AN OPIOID OVERDOSE
- 🔗 USING NALOXONE (NARCAN) TO REVERSE AN OPIOID OVERDOSE



More information links

Intervention graphics use the most space

ZeroStigma.Art

It's hard to find imagery that reflects the nuance of drug use and chronic pain. Zero Stigma Art is a library of hand-drawn harm reduction and pain patient illustrations that anyone can use for free.



Surgical Mask
Lindsey Morano



Antibiotic Ointment
Lindsey Morano



Water ampoule
Lindsey Morano



Syringe cap
Lindsey Morano



Game Night
Eje



Working at computer
Brittain Peck



Water ampoule
Lindsey Morano



Crack Vial
Lindsey Morano



Holding pills
DALL·E



COVID Bus
Brittain Peck



Syringe in space
DALL·E



Crack Vials
Lindsey Morano



Gauze
Lindsey Morano



Gauze
Lindsey Morano



Working on medicine ball
Brittain Peck



Benzalkonium Box
Lindsey Morano

The right message, to the right person,
at the right time.

Alerts are short. They are actionable and relevant.

Educational information can be more detailed, but are separate communication tools!