What's in our Illicit Drug Supply Across the County and Maine

Nabarun Dasgupta, MPH, PhD
University of North Carolina
Chapel Hill, NC, USA
@nabarund

March 15, 2024 • Maine SUD Learning Community Conference

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.

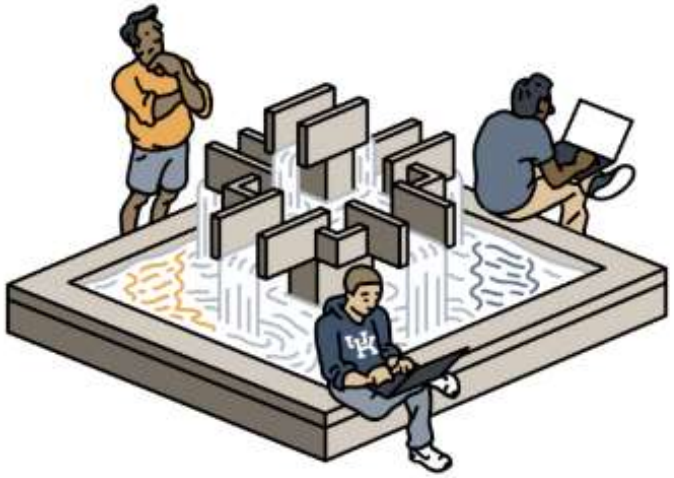
PICK UP
HERE
That first
sip feeling.

University of Kentucky UF FLORIDA UNC

Home Studies Code + Data Team News Contact

Opioid Data Lab

Theory



Foundational Studies

- Biostatistics
- Epidemiology methods
- Psychology of communication
- Pharmacology

Practice

Applied Research

- Pharmacy
- Medicine
- Public health surveillance
- Forensic toxicology

Lived Experience

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
- Dimtheylsulfone
- 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

“What Fresh Hell Is This?”

Understanding the illicit drug supply for better health

Quote from the International Network of Health and Hepatitis in Substance Users conference, October 2022, describing the ever-changing drug supply.

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 model[2] 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

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 report[9] 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

HUFFPOST Log In Join HuffPost

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.

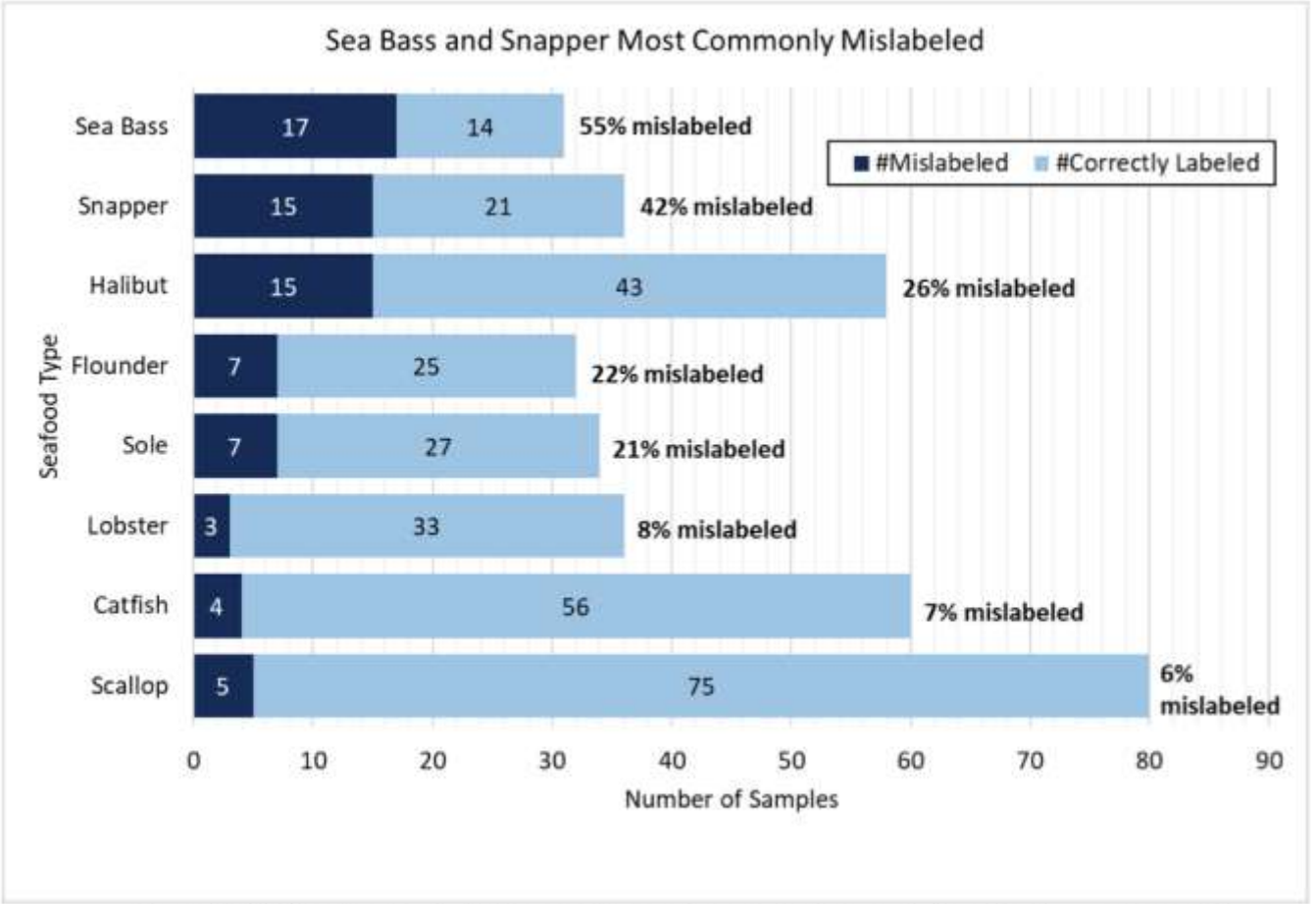


Figure 2. Mislabeling levels (%) among the most commonly sampled seafood types in our study.

https://usa.oceana.org/wp-content/uploads/sites/4/march_2019_oceana_seafood_fraud_report_final.pdf

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?
S 90 3
Alprazolam
mprint: S 90 3
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

Consumer Reports

Sign In

Find the Best....

BECOME A MEMBER | DONATE

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
Vol. 191, No. 2
https://doi.org/10.1093/aje/kwab129
Advance Access publication:
May 11, 2021
© The Author(s) 2021. Published by Oxford University Press on behalf of the Johns Hopkins Bloomberg School of Public Health. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

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-lt@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.

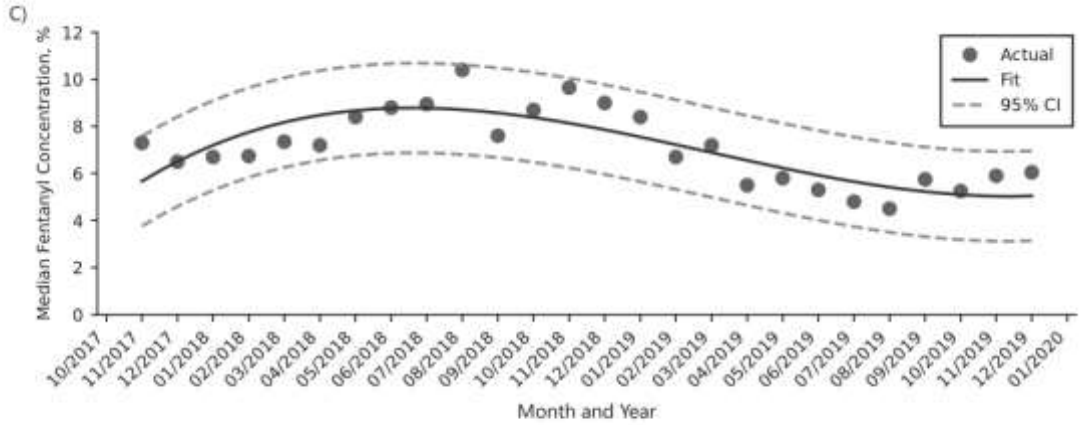


Figure 1. Monthly median fentanyl concentration of expected opioid samples brought to a drug-checking service in Vancouver, British Columbia. First- (A), second- (B), and third-degree (C) polynomial models are indicated by the solid lines and 95% confidence intervals (CIs) by the dotted lines.

S. H. James,[1] B.S., Bruce Calendrillo,[1] B.S., and S. H. Schnoll,[2] M.D.

Medical and Toxicological Aspects of the Watkins Glen Rock Concert

Journal of Forensic Science **1975**

The outdoor rock concert has been well established as an important feature in the life of young people both in this country and abroad. The frequent use of psychoactive chemicals at these large gatherings is to be anticipated, as shown by evaluations of such events in the past [*1-3*]. This phenomenon is concurrent with prevailing permissive attitudes of youth toward drug usage in our society. The evolution of the use of psychoactive drugs, especially the psychedelics, has been associated with the popularity of rock music.

The misrepresentations and adulterations of street drugs and their variable dosage levels have been well documented, reaching proportions as high as 70% of samples analyzed from anonymous sources [*4-6*]. The problems of treating acute drug overdosage are compounded for the physician by this street deception, especially when adequate information from toxicology laboratories is absent or not easily available. This is apparent at large outdoor rock concerts, many of which are held in rural, isolated areas of the country. The physicians in the vicinity who may be asked to staff the medical facility at such events may not be familiar with urban patterns of drug consumption practiced by the majority of rock concert participants. This lack of knowledge may be coupled with a general disinterest in drug-taking youth.

Over the weekend of 26-29 July 1973, the Summer Jam Rock Festival was held in Watkins Glen, N.Y. A CBS news report at 7:55 p.m. on 28 July 1973 made the historic announcement: "The Watkins Glen Music Festival has surpassed Woodstock, which until today was the granddaddy of the music festivals. An estimated 600,000 people have jammed into Watkins Glen, New York, for Summer Jam. The crowd in general is well behaved, orderly and enjoying the music. . . ."

A medical facility was established to care for the people attending the concert. As part of this facility, a toxicology laboratory was established on the site to analyze drug samples and biological fluids for overdosed patients. To our knowledge, this was the first time a toxicology laboratory had been included as part of the medical facility at a rock festival.

Preparation, Materials, and Methods

The basic plan taken for providing toxicological analysis to the medical facility was twofold. The first objective was to survey the solid dose forms of drugs circulating at the

Presented as "Emergency Toxicology in the Field" at the 26th Annual Meeting of the American Academy of Forensic Sciences, Dallas, Texas, 14 Feb. 1974. Received for publication 7 March 1974; revised manuscript received 28 June 1974; accepted for publication 29 June 1974.

[1]Toxicology Department, Wilson Memorial Hospital, Johnson City, N.Y. 13790.
[2]Assistant professor of psychiatry, University of Pennsylvania Medical School, Philadelphia, Pa. 19104.

ALLEGED CONTENT \ TRUE CONTENT	Amphetamine	LSD	MDA	Mescaline	Methaqualone	PCP	Psilocybin	Secobarbital	THC	Marijuana	Antihistamine	Ephedrine	DMA	Negative	Total Samples
Amphetamine	2										1	1			4
LSD		10										1			11
MDA			2			1									3
Mescaline		12	1			1							9		23
Methaqualone					4										4
PCP						1									1
Psilocybin		2													2
Secobarbital								1							1
THC						14									14
Marijuana										1					1
Unknown		5			2	4								1	12
Totals	2	29	3		6	21		1		1	1	2	9	1	76

FIG. 1—*Survey of drugs circulating at Watkins Glen rock concert (alleged versus true content).*

Festival Drug Checking

Drug Checking Tech

Test strips

anywhere

Reagents

table top

FTIR

program sites

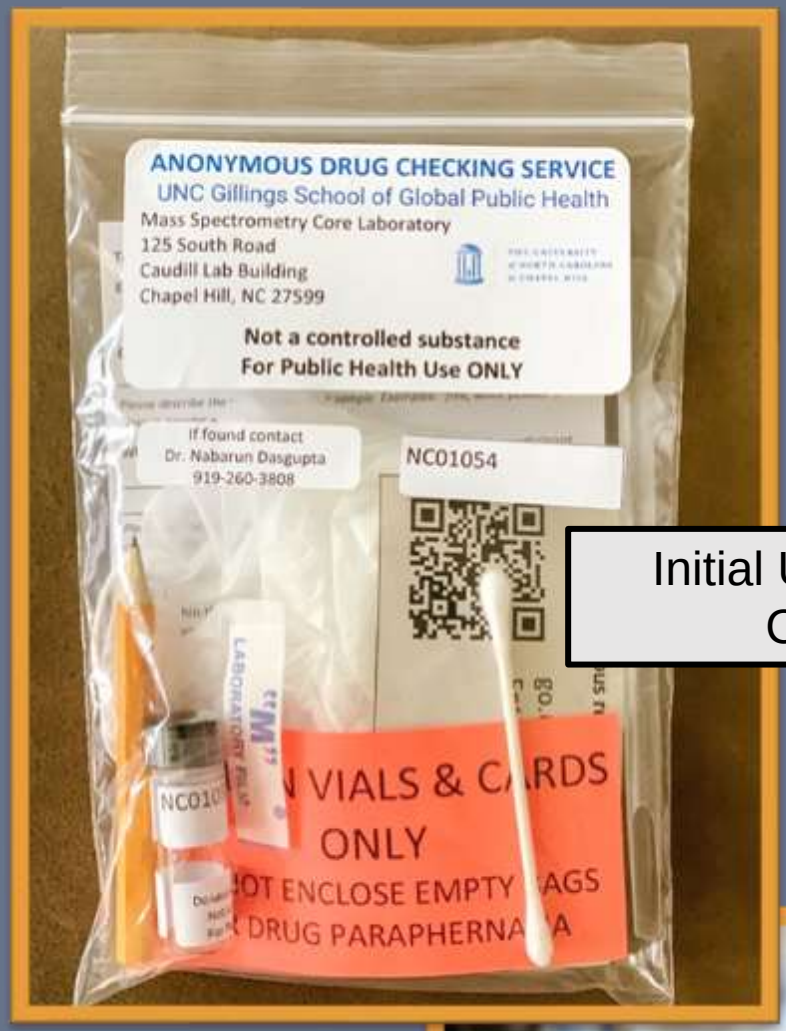
LC/GCMS, QTOF

lab

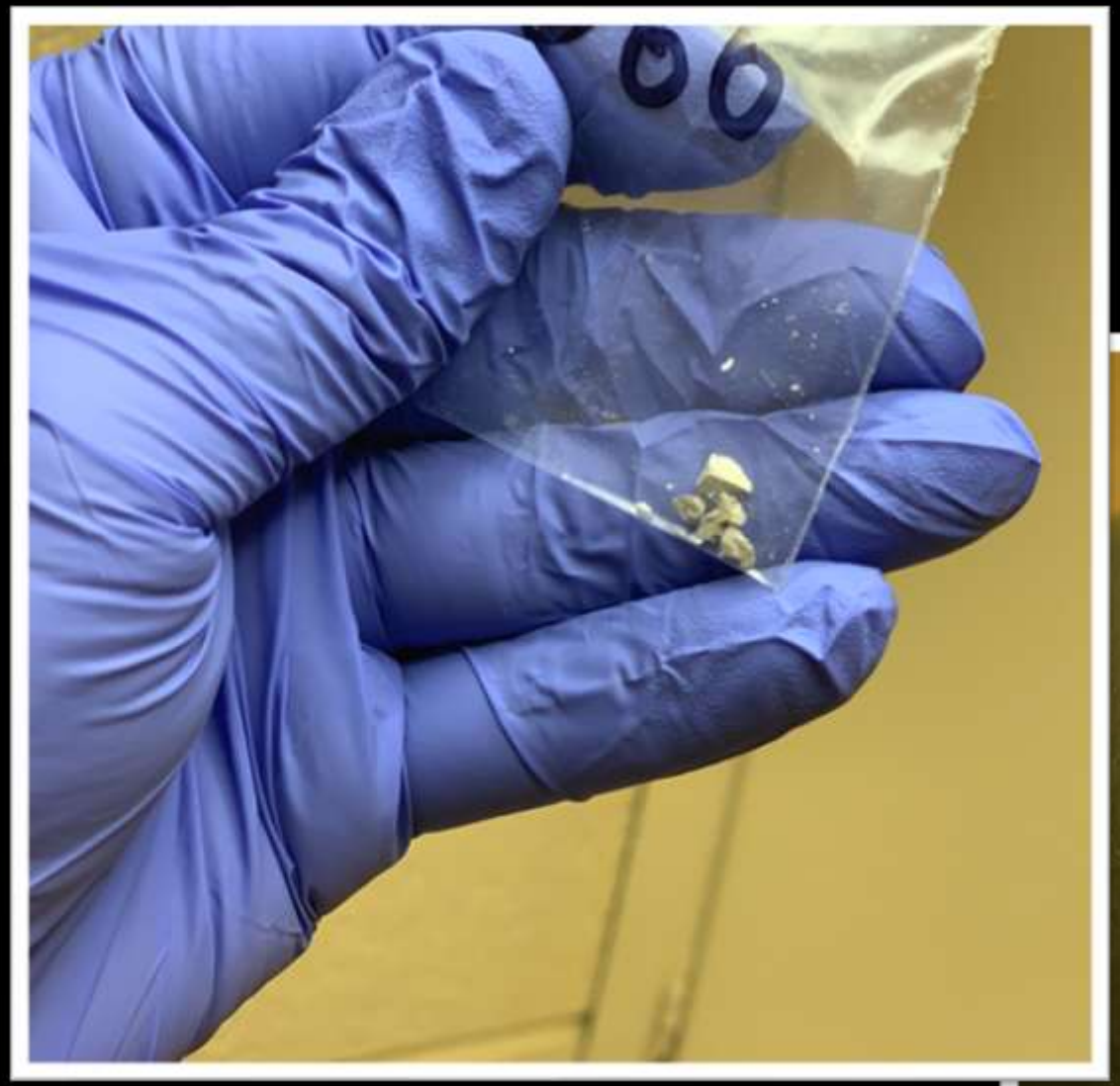
cost, time, complexity

COVID-19 PCR kits

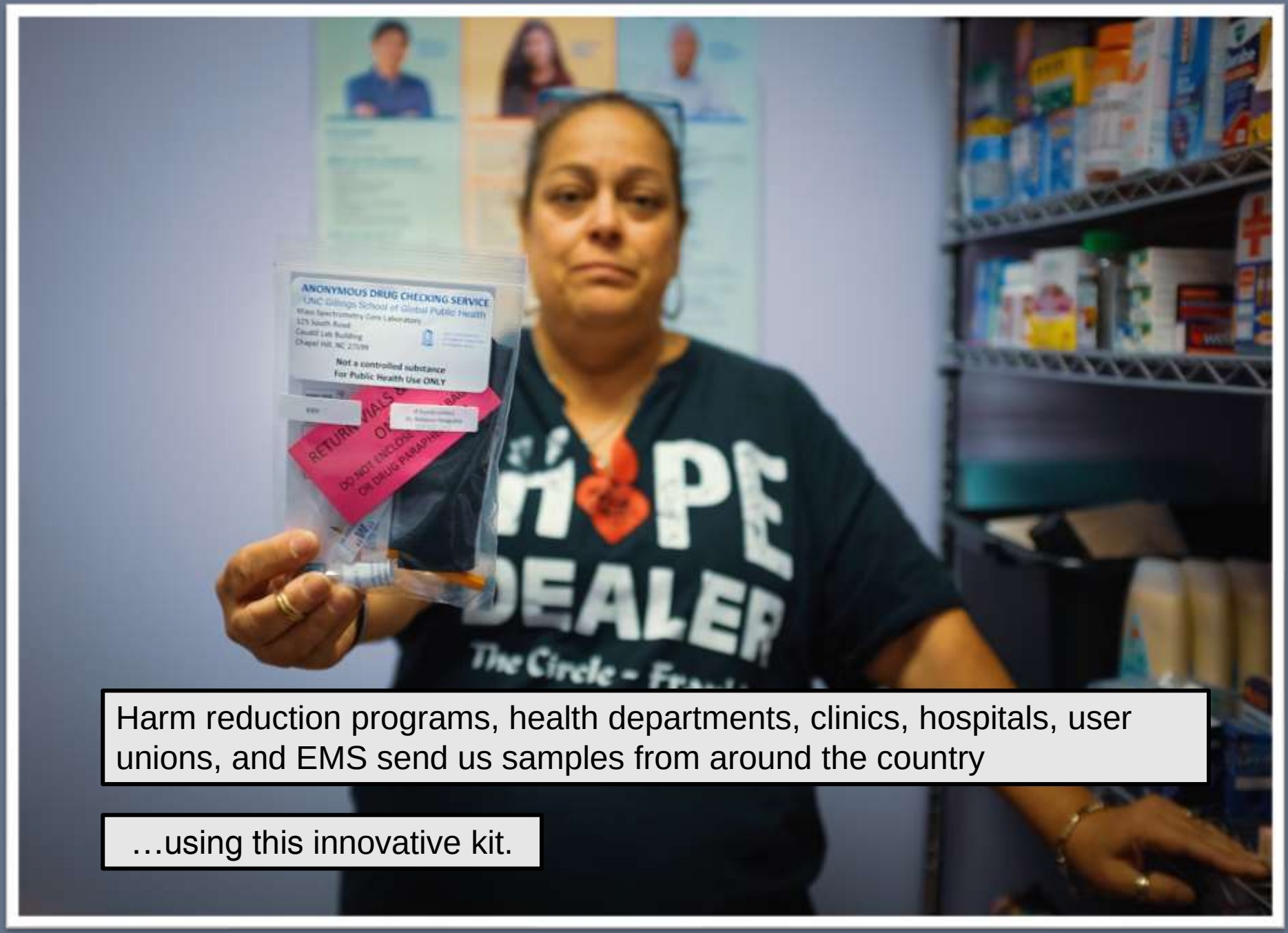
Initial UNC Street Drug Checking kit



Street drugs change constantly.



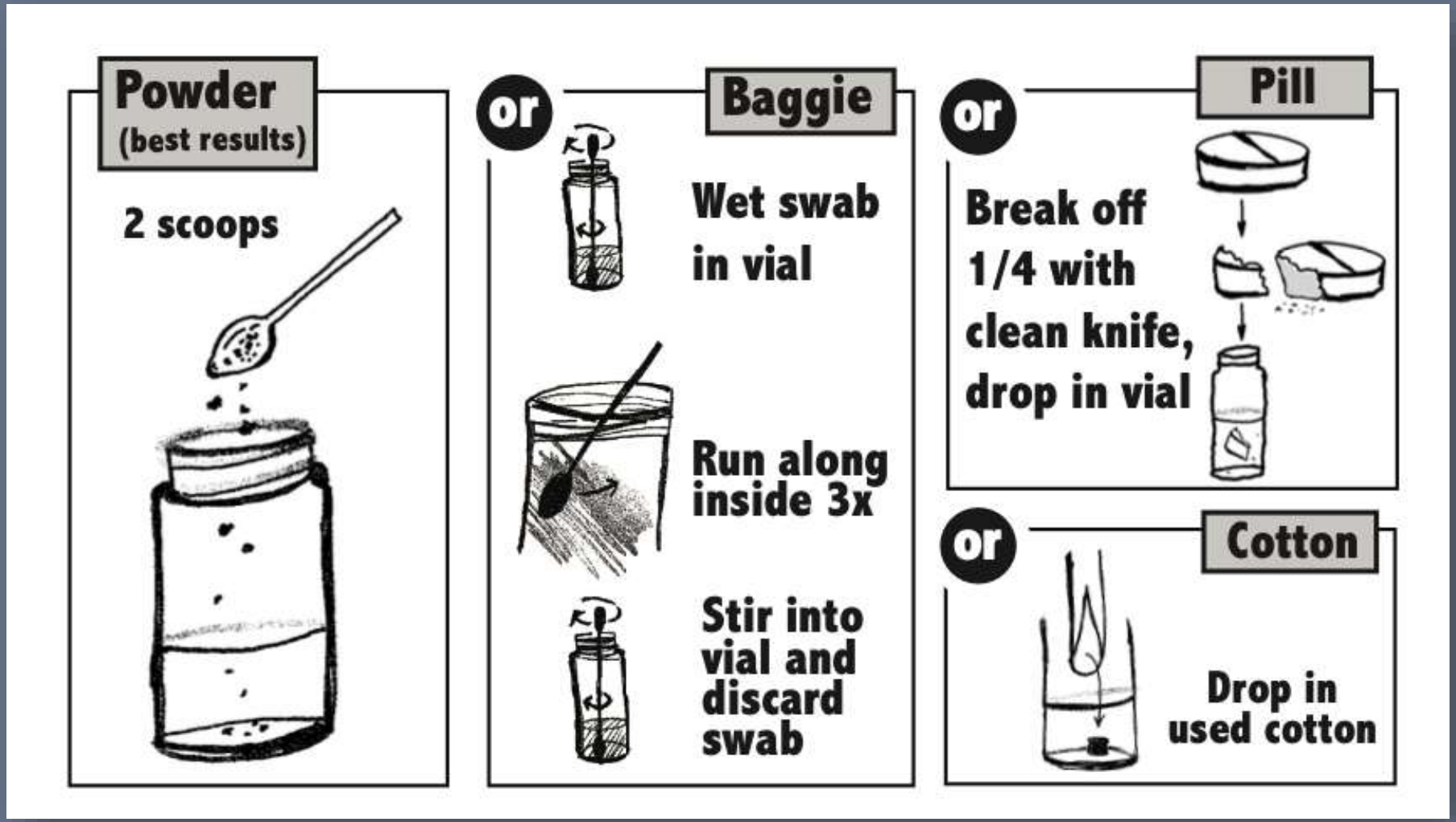
we monitor street drugs



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

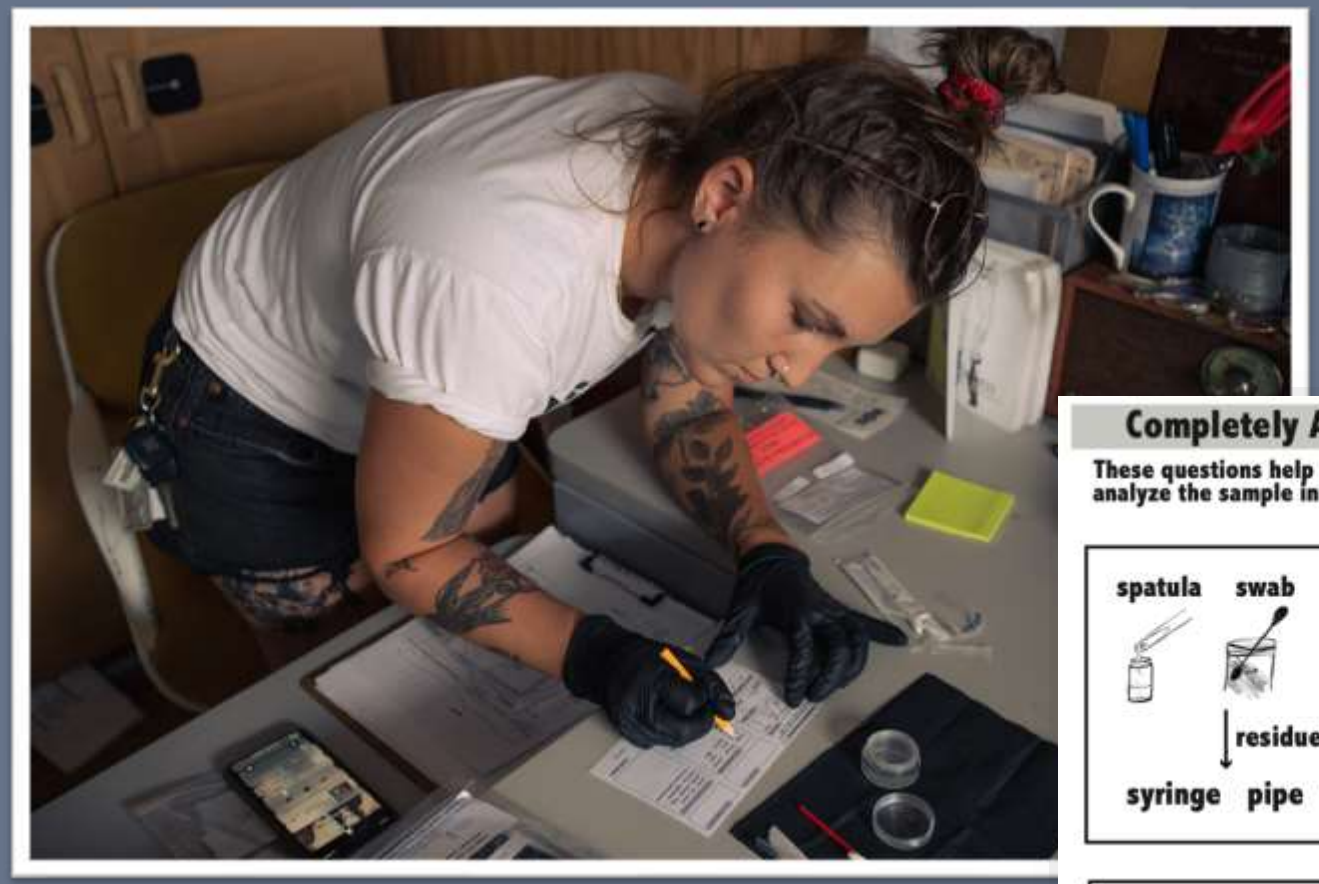
…using this innovative kit.

Samples can be collected via scoop, reside swab, pill fragment, or used cotton.



Samples are given voluntarily.

The tests are anonymous.



Programs share health information with us

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

today's date

month date

circle if involved in overdose

yes no don't know

describe the overdose to warn others:

overdose

describe color and markings

city or neighborhood

circle expected drugs

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

circle & describe sensations

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

describe:

sensations

circle textures

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

sample number

v7

to give human context beyond molecules.

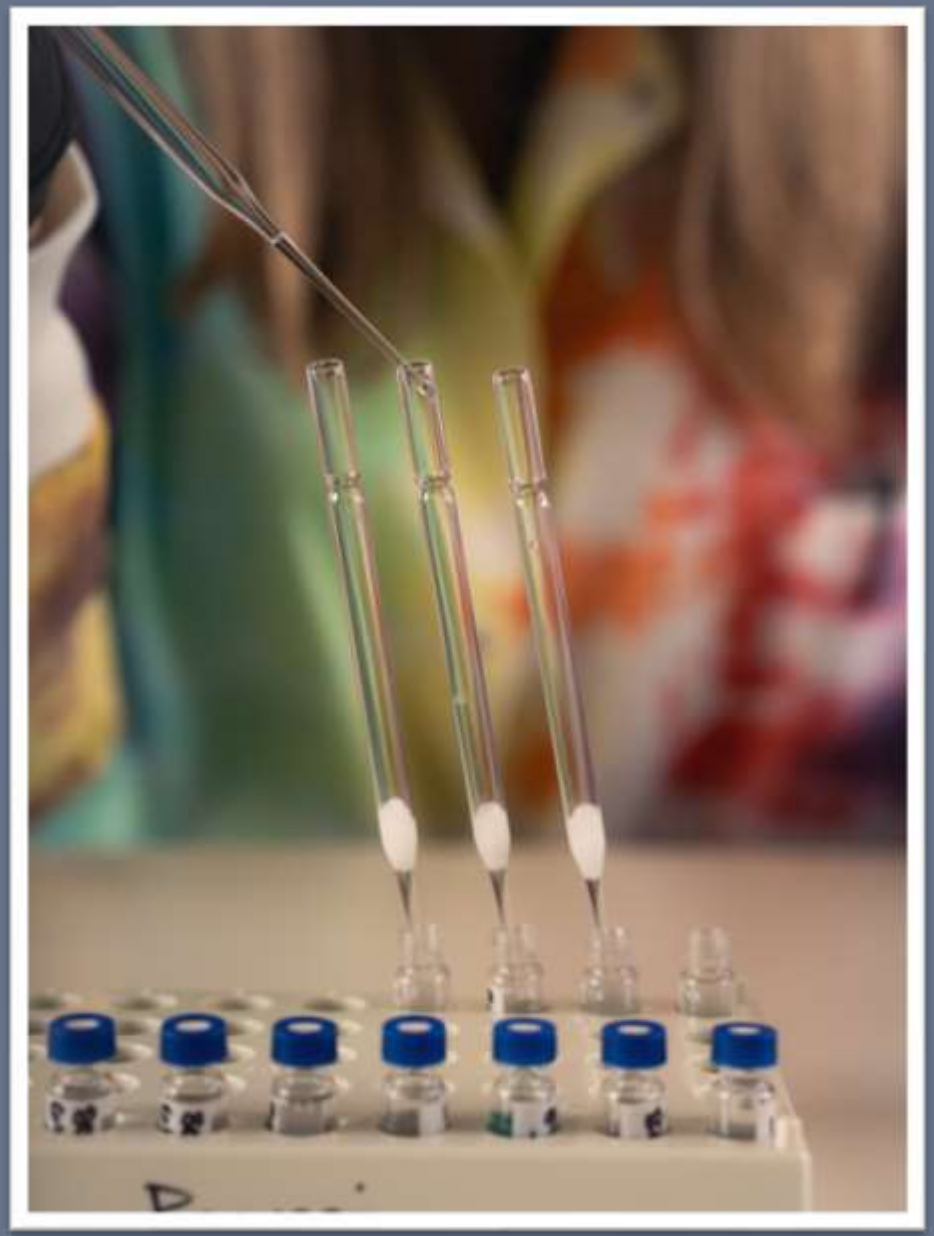
Packages arrive on campus

in compliance with drug and postal laws.

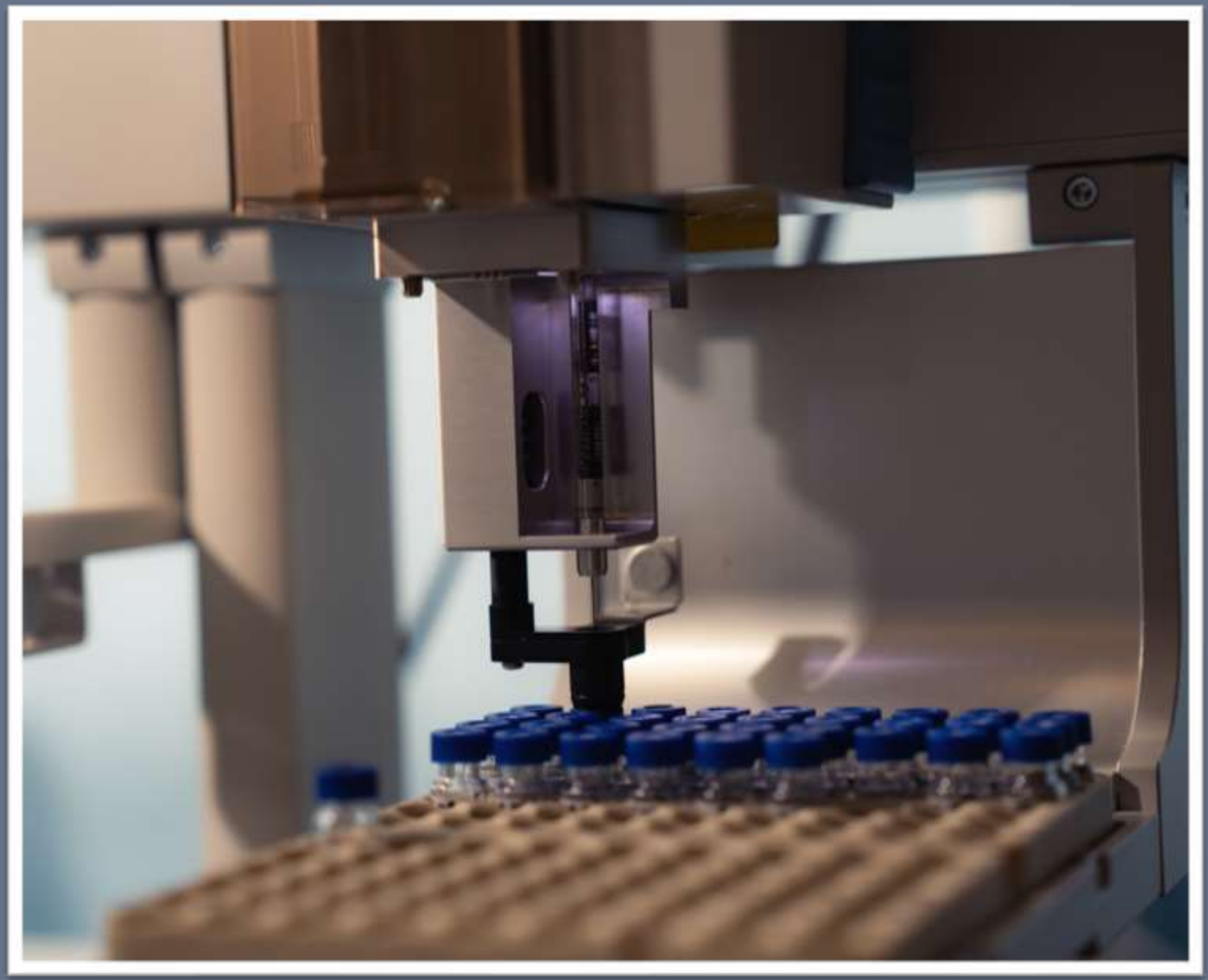
We record the information

and catalog the samples.

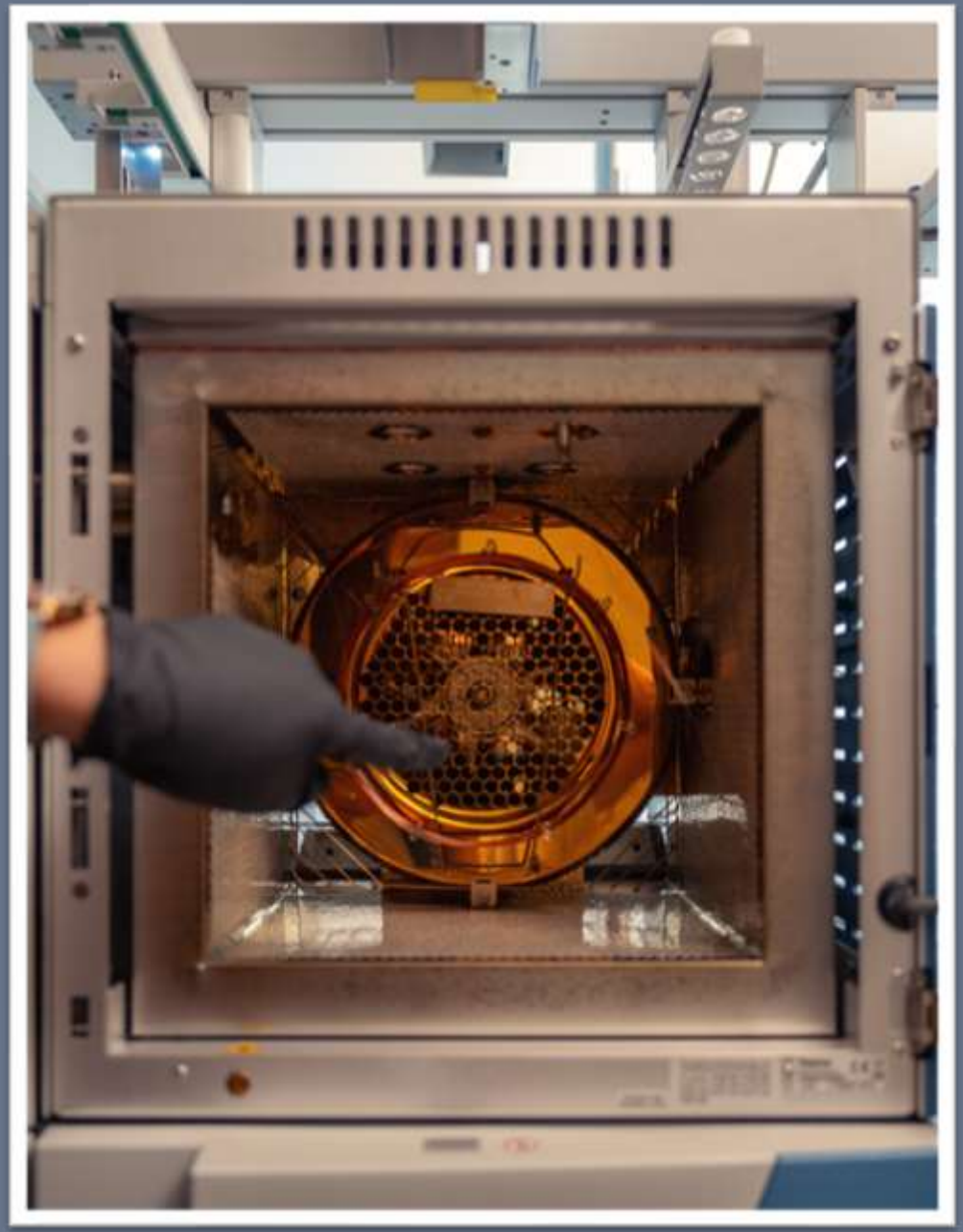
We prep the samples



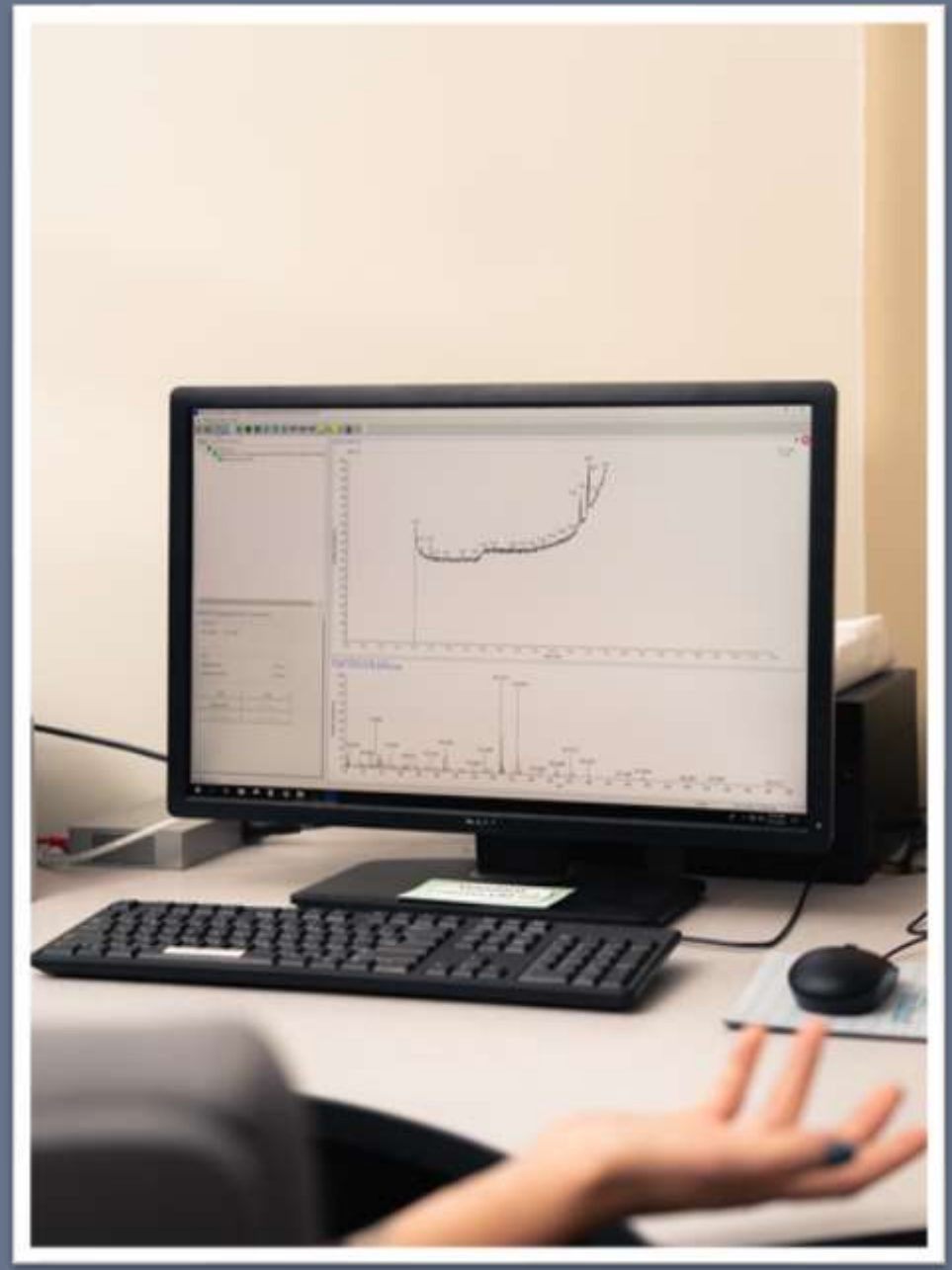
and load them on a GCMS (mass spec).



We interpret the high resolution results,



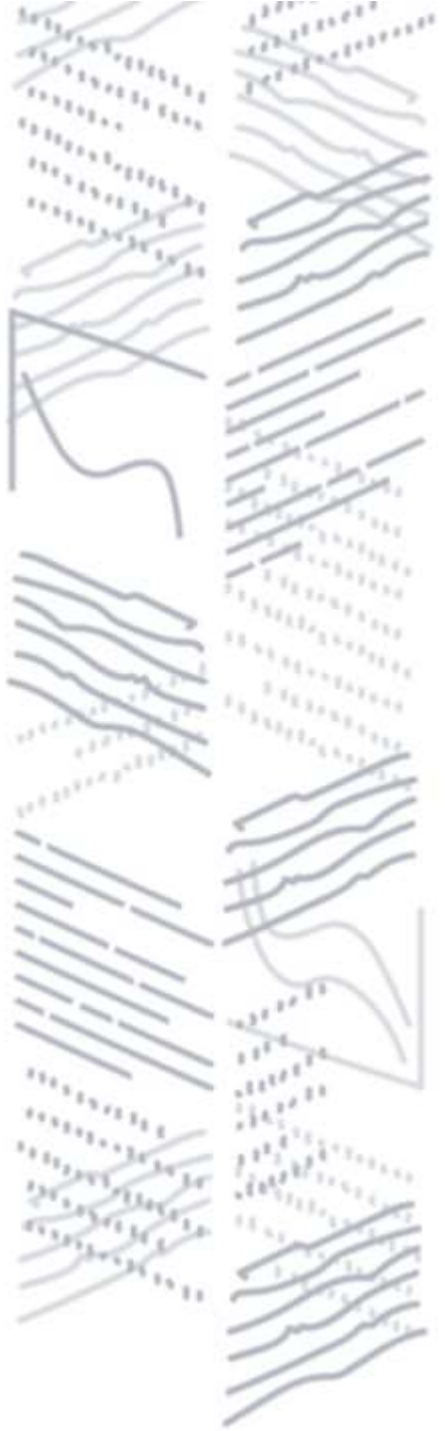
to determine exactly what's in the sample.

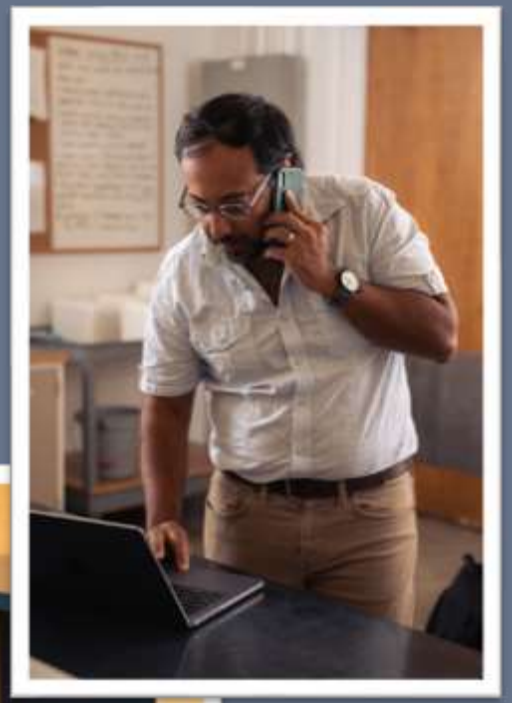


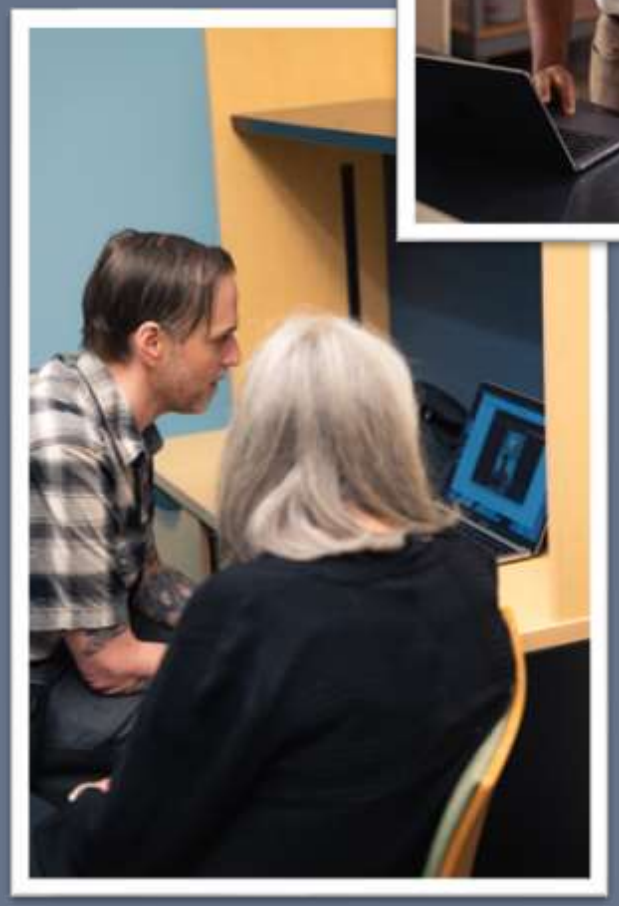
We’ve detected a multitude of substances in drug supply.

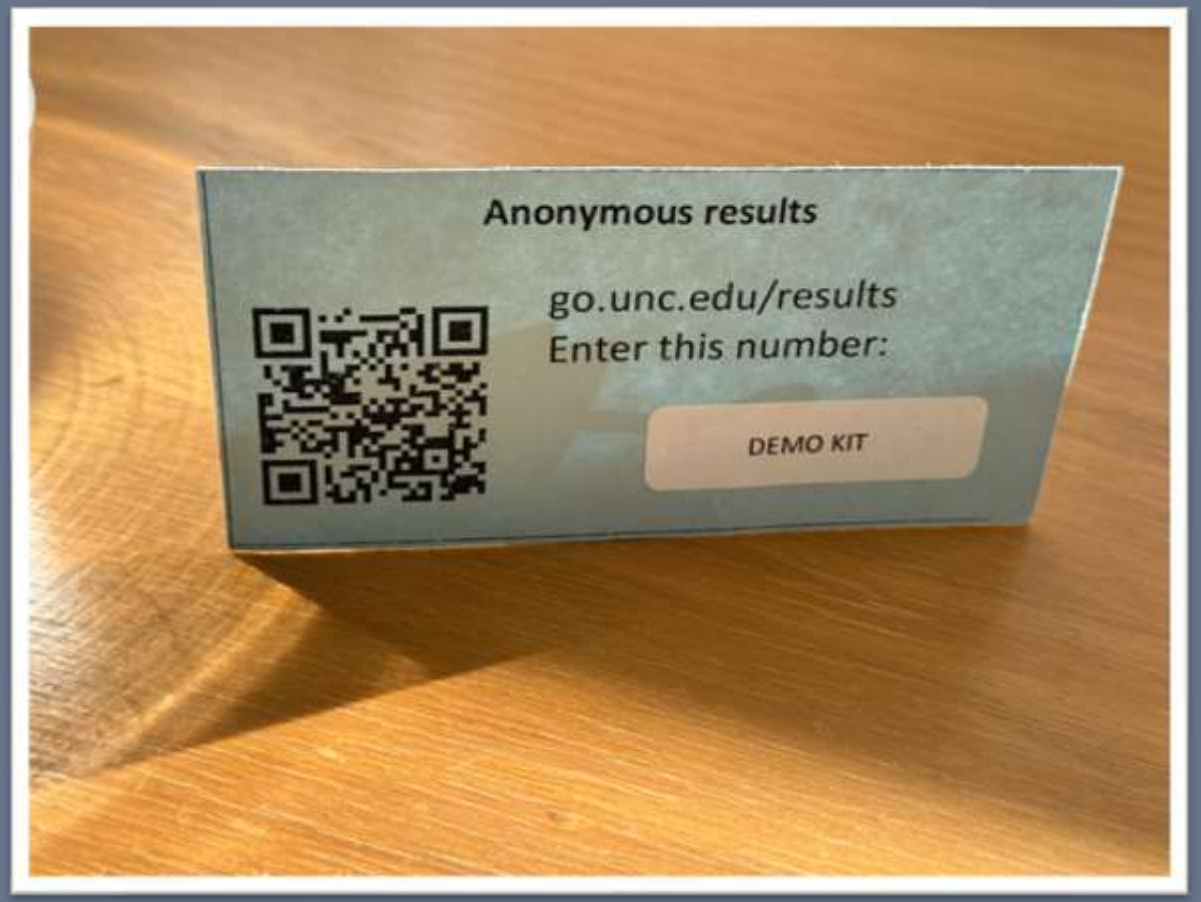
Advanced statistics help detect hidden patterns.

We make our data public daily.









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

https://www.streetsafe.supply

Location, date
Sold as
Physical description

Primary substances detected

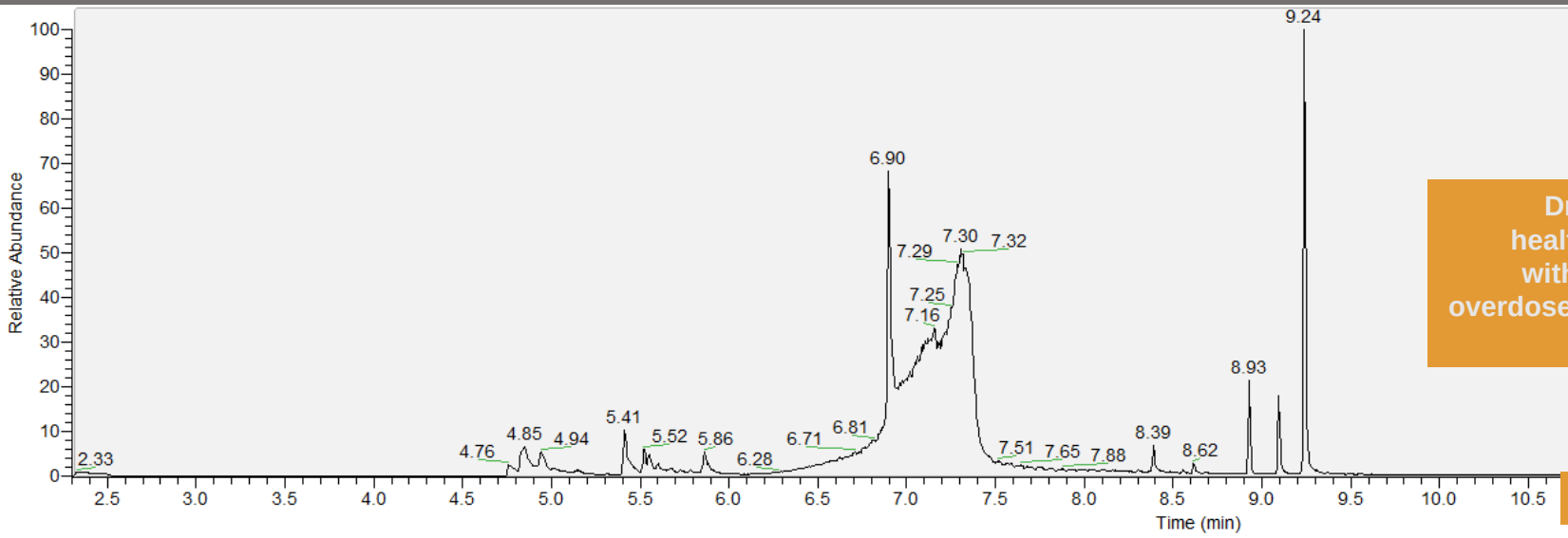
Traces

Drug-specific health warnings with actionable overdose prevention advice

New drugs

Getting help locally

Scientific accountability



NL:
2.53E9
TIC MS
300298-a

300298

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

This is a messy brew of 7 major substances:

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

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

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.

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

National

High-Tech Strategy to Prevent Overdoses Tests Drugs, Not Users

Solving medical mysteries

Psychiatrist.com

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

Answering community questions

Synthesizing complex information

Drug and Alcohol Dependence 252 (2023) 110985

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

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

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 [d,e], Nabarun Dasgupta [d,*]

[a] Department of Health Behavior, Policy, and Administration Sciences, School of Public Health, University of Nevada, Reno, NV 89557, USA
[b] The Mountain Center, Española, NM 87606, USA
[c] Department of Internal Medicine, University of New Mexico Health Sciences Center, Albuquerque, NM 87131, USA
[d] Injury Prevention Research Center, University of North Carolina, CB 7505, 725 Martin Luther King Jr. Blvd, Chapel Hill, NC 27599, USA
[e] Department of Pharmacy, University of Washington, Seattle, WA 98195, USA

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. Hosey[2], Christopher Moraff[3], Aaron Ferguson[4], Mary Figgatt[5], Shoshana Aronowitz[6], Natalie E. Stahl[7], Lucas G. Hill[1], Zoe McElligott[8] and Nabarun Dasgupta[9]

Abstract

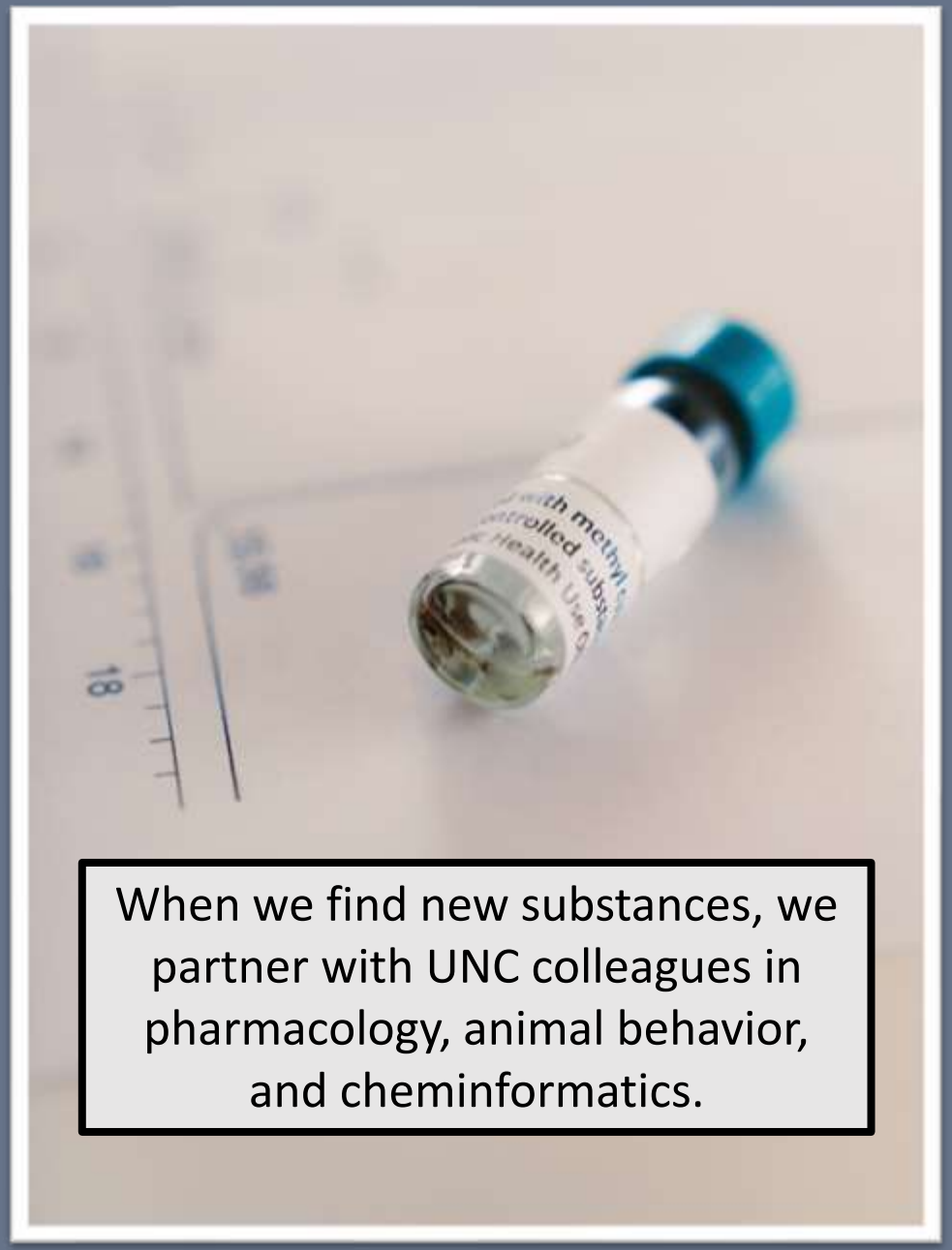
Objectives Xylazine has emerged as a consistent part of the unregulated drug supply in recent months. We discuss major domains of xylazine's harm, current knowledge deficits, clinical and harm reduction strategies for minimizing harm, and xylazine's public health and policy context. As an interdisciplinary 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.

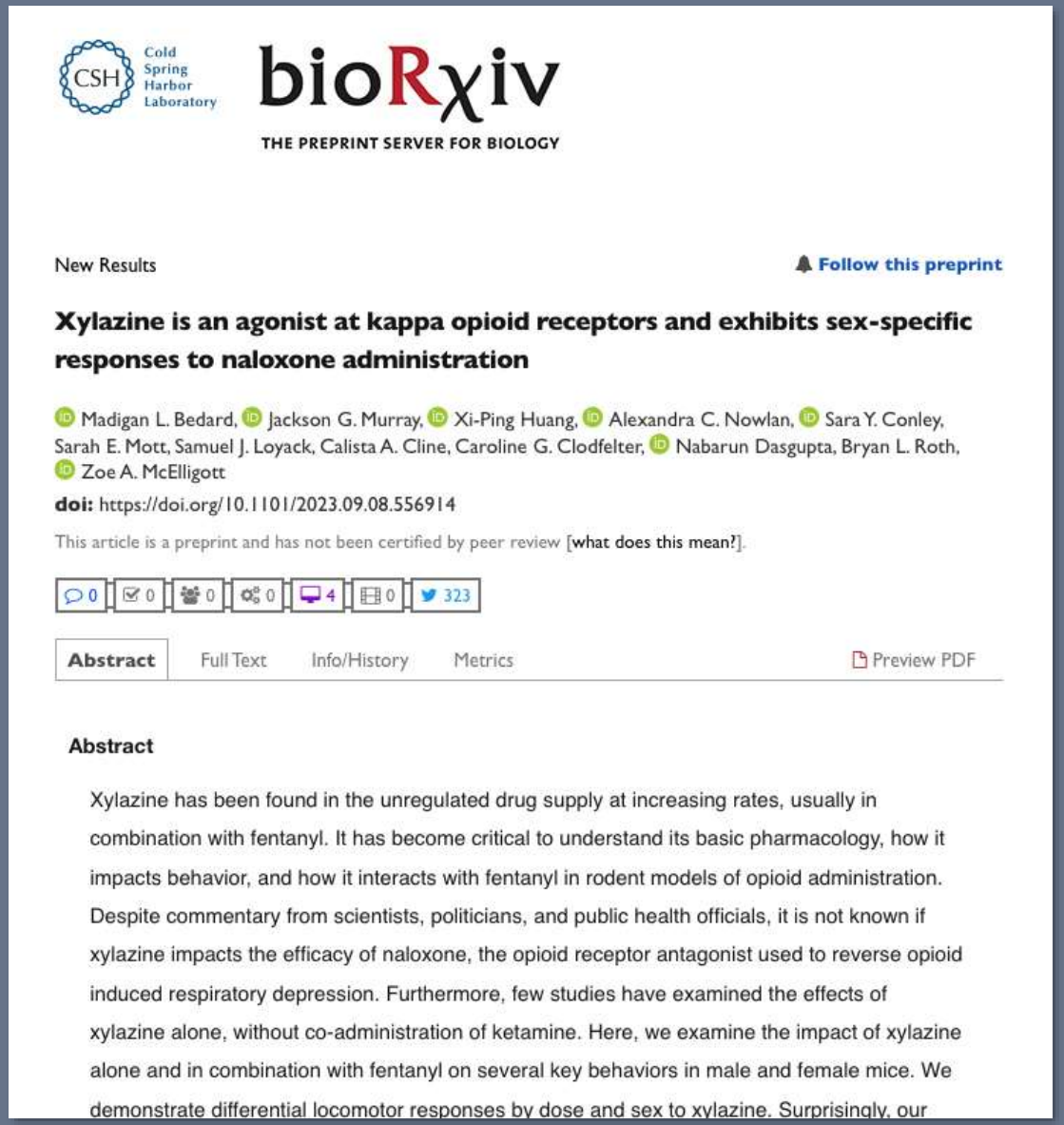
Conclusions Addressing the harms of xylazine requires interdisciplinary participation, investment in community-based harm reduction strategies, and improved drug supply surveillance. The relatively unique context of xylazine demands buy-in from public health professionals, harm reduction professionals,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



Cold Spring Harbor Laboratory

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?].

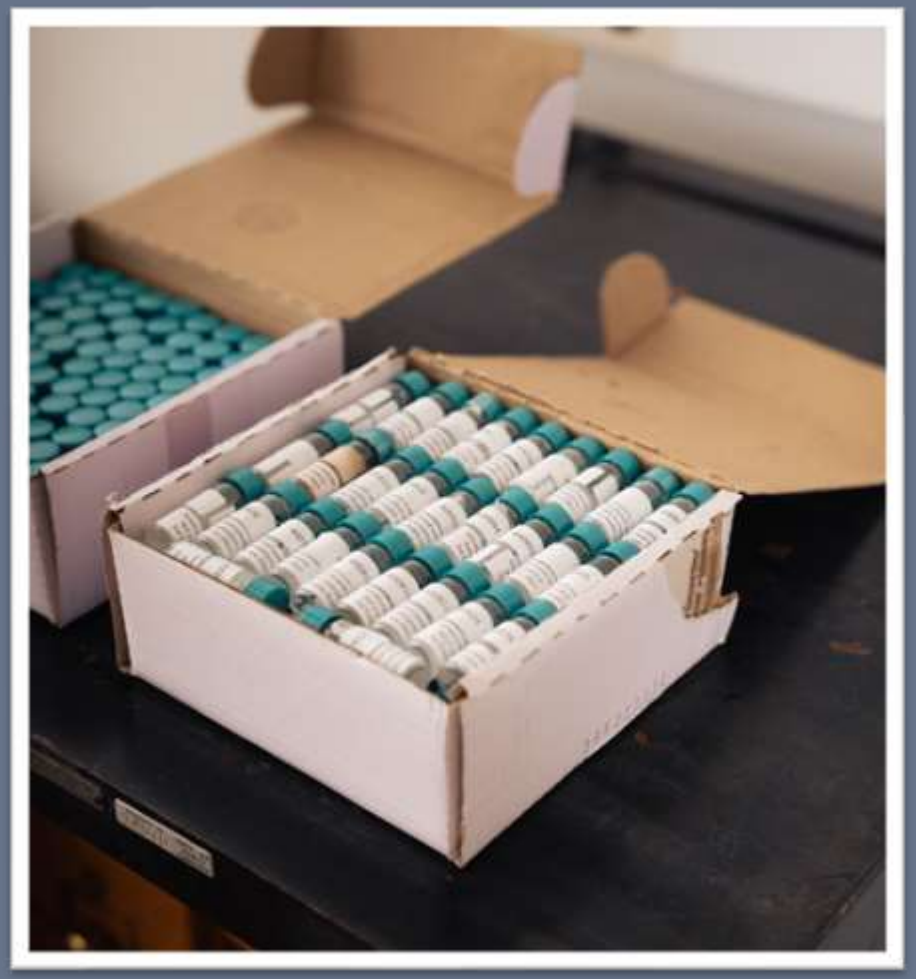
0 0 0 0 4 0 323

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

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



March 2022 to March 5, 2024

N = 4,748 samples analyzed
160+ programs
35+ US states

300731

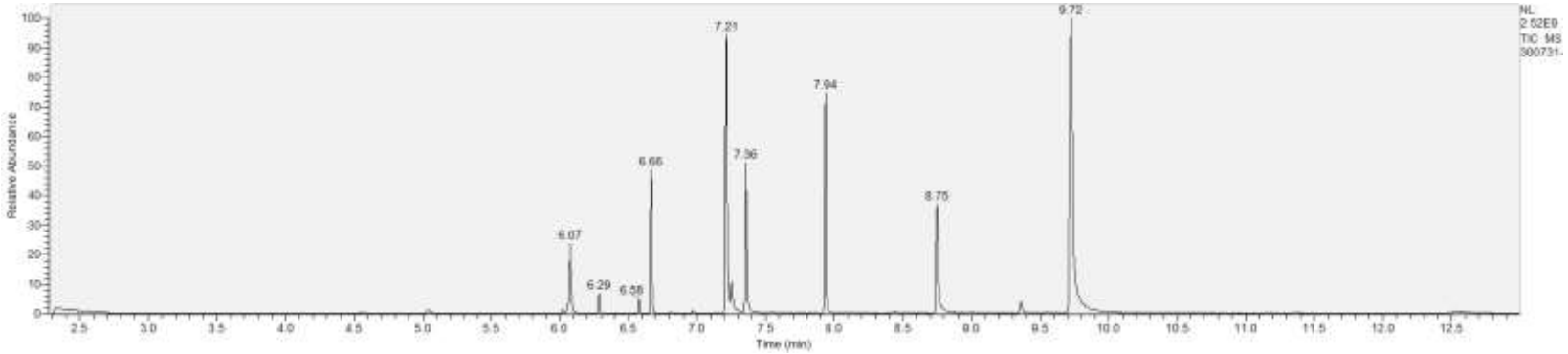
From Asheboro, North Carolina on II/2/2022
Assumed to be heroin

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 sustancías



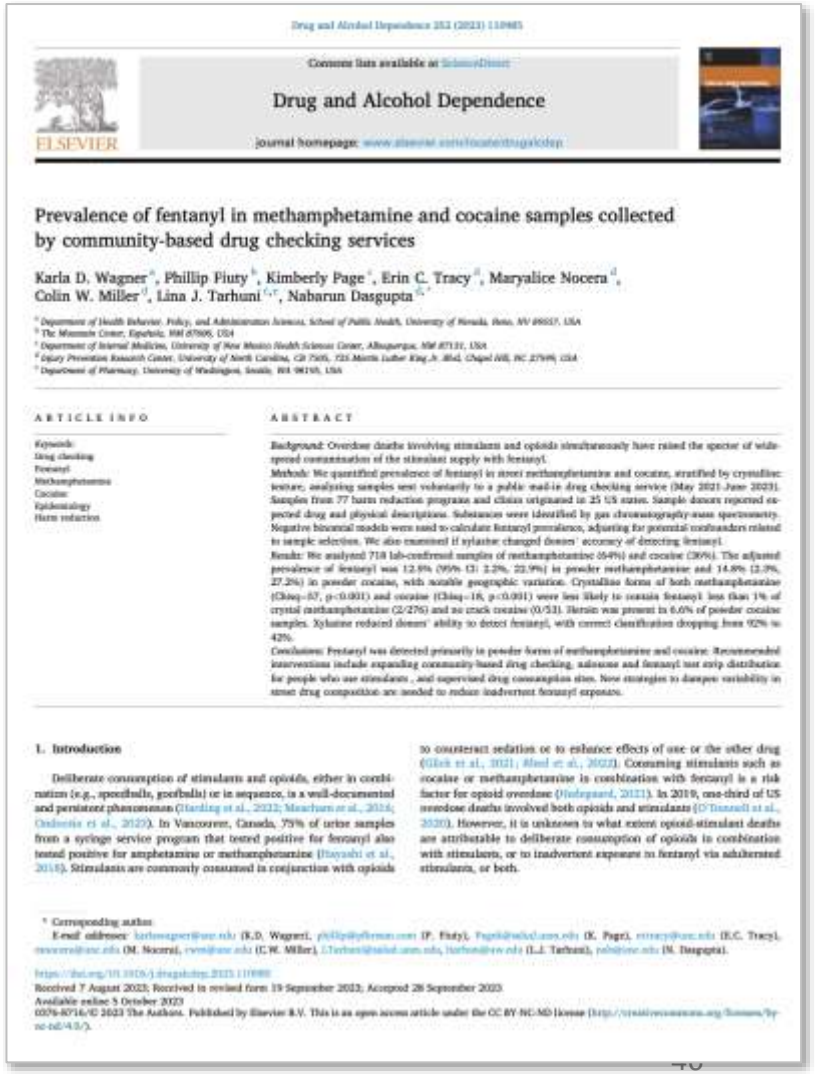
Medicina: phenacetin, paracetamol, melatonin
Medicina veterinaria: levamisole, xylazine
Entumecedor: procaine
Estimulantes: cafeína, cocaína
Origen vegetal: noscapine, meconin, hydrocotarnine, heroin
Opioides sintéticos: fentanyl
Subproducto: 4-ANPP, N-phenylpropanamide, MSM

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?

What is the prevalence of fentanyl in street stimulants?

- N=718 samples
  methamphetamine 64%, cocaine 36%
- May 5, 2021 to June 15, 2023
- 25 states, 96 counites
- GCMS, untargeted search
- Modeling: negative binomial, GEE
- Bias correction
  “weird” samples, FTIR programs, swabs, consumed before testing, and xylazine; time & location



Drug and Alcohol Dependence

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

Karla D. Wagner, Phillip Fiuty, Kimberly Page, Erin C. Tracy, Maryalice Nocera, Colin W. Miller, Lina J. Tarhuni, Nabarun Dasgupta

ARTICLE INFO

ABSTRACT

1. Introduction

Powder forms of street stimulants have twice as many substances as crystalline forms.

Table 1. Adulterant substances detected in methamphetamine and cocaine, by stimulant type.

	N	Top other substances detected (n)*	Average Number of Substances Detected by GCMS (95% CI)	Difference (t-test)
Powder methamphetamine	182	• fentanyl (39) • 4-ANPP (33) • heroin (12) • phenethyl 4-ANPP (10) • xylazine (8) • 1,3-Diacetin (7) • dimethyl sulfone** (7) • caffeine (6) • N,N-Dimethylamphetamine (5) • ethyl-4-ANPP (5) • p-fluorofentanyl (5)	2.01 (1.74, 2.28)	t=8.1, df 456, p<0.001
Crystal methamphetamine	276	• dimethyl sulfone (6) • N,N-Dimethylamphetamine (2) • fentanyl (2) • ketamine (2)	1.07 (1.03, 1.11)	
Powder cocaine	207	• fentanyl (56) • 4-ANPP (38) • heroin (22) • xylazine (19) • methyl ecgonidine (15) • caffeine (11) • phenethyl 4-ANPP (10) • 6-monoacetylmorphine (9) • acetylcodeine (8) • lidocaine (8) • phenacetin (8) • levamisole (7) • benzoylecgonine (6) • p-fluorofentanyl (6) • despropionyl p-fluorofentanyl (5)	2.39 (2.08, 2.71)	t=4.1, df 258, p<0.001
Crack cocaine	53	• levamisole (1) • methyl ecgonidine (1) • norcocaine (1) • tropacocaine (1)	1.07 (1.00, 1.23)	

* Top 10 or occurring at least 5 times

** Dimethyl sulfone is also known as methylsulfonylmethane (MSM)

Abbreviations: 1-ANPP= 4-anilino-N-phenethylpiperidine; CI=confidence interval; df=degrees of freedom; GCMS=gas chromatography-mass spectrometry

Powder forms of meth and coke are more likely to have fentanyl than crystalline forms.

Methamphetamine

Overall fentanyl prevalence: 6.2% 95% CI: 1.1%, 11.2%

39/182 powder meth vs. 2/276 crystal meth

Cocaine

Overall fentanyl prevalence: 12.6% 95% CI: 2.4%, 22.8%

3956/207 powder coke vs. 0/53 crack

Detecting Xylazine

Figgatt et al. Harm Reduct J (2021) 18:80
https://doi.org/10.1186/s12954-021-00528-x

Harm Reduction Journal

RESEARCH Open Access

Treatment experiences for skin and soft tissue infections among participants of syringe service programs in North Carolina

Mary C. Figgatt[1,2*], Zach R. Salazar[3], Louise Vincent[3], Diannee Carden-Glenn[4], Kelly Link[5], Lauren Kestner[6], Tyler Yates[7], Asher Schranz[8], Elizabeth Joniak-Grant[1] and Nabarun Dasgupta[2]

Abstract

Introduction: Bacterial and fungal infections, such as skin and soft tissue infections (SSTIs) and infective endocarditis (IE), are increasing among people who use drugs in the United States. Traditional healthcare settings can be inaccessible and unwelcoming to people who use drugs, leading to delays in getting necessary care. The objective of this study was to examine SSTI treatment experiences among people utilizing services from syringe services programs. This study was initiated by people with lived experience of drug use to improve quality of care.

Methods: We conducted a cross-sectional survey among participants of five syringe services programs in North Carolina from July through September 2020. Surveys collected information on each participant's history of SSTIs and IE, drug use and healthcare access characteristics, and SSTI treatment experiences. We examined participant characteristics using counts and percentages. We also examined associations between participant characteristics and SSTI history using binomial linear regression models.

Results: Overall, 46% of participants reported an SSTI in the previous 12 months and 10% reported having IE in the previous 12 months. Those with a doctor they trusted with drug use-related concerns had 27 fewer (95% confidence interval = − 51.8, − 2.1) SSTIs per every 100 participants compared to those without a trusted doctor. Most participants with a SSTI history reported delaying (98%) or not seeking treatment (72%) for their infections. Concerns surrounding judgment or mistreatment by medical staff and self-treating the infection were common reasons for delaying or not seeking care. 13% of participants used antibiotics obtained from sources other than a medical provider to treat their most recent SSTI. Many participants suggested increased access to free antibiotics and on-site clinical care based at syringe service programs to improve treatment for SSTIs.

Conclusions: Many participants had delayed or not received care for SSTIs due to poor healthcare experiences. However, having a trusted doctor was associated with fewer people with SSTIs. Improved access to non-judgmental healthcare for people who use drugs with SSTIs is needed. Expansion of syringe services program-based SSTI prevention and treatment programs is likely a necessary approach to improve outcomes among those with SSTI and IE.

Summer 2020 Something unexpected was happening in the drug supply. We thought it was SSTIs.

January 2021 Don Jackson in Greensboro first identified xylazine using FTIR-based point-of-care drug checking.

Xylazine prevalence varies. East Coast primarily affected.

Samples analyzed
N=3,081

Expected opioids
n=1,570

Xylazine in any amount (including trace)
n=453

Xylazine as **primary** constituent
n=317 (20%)

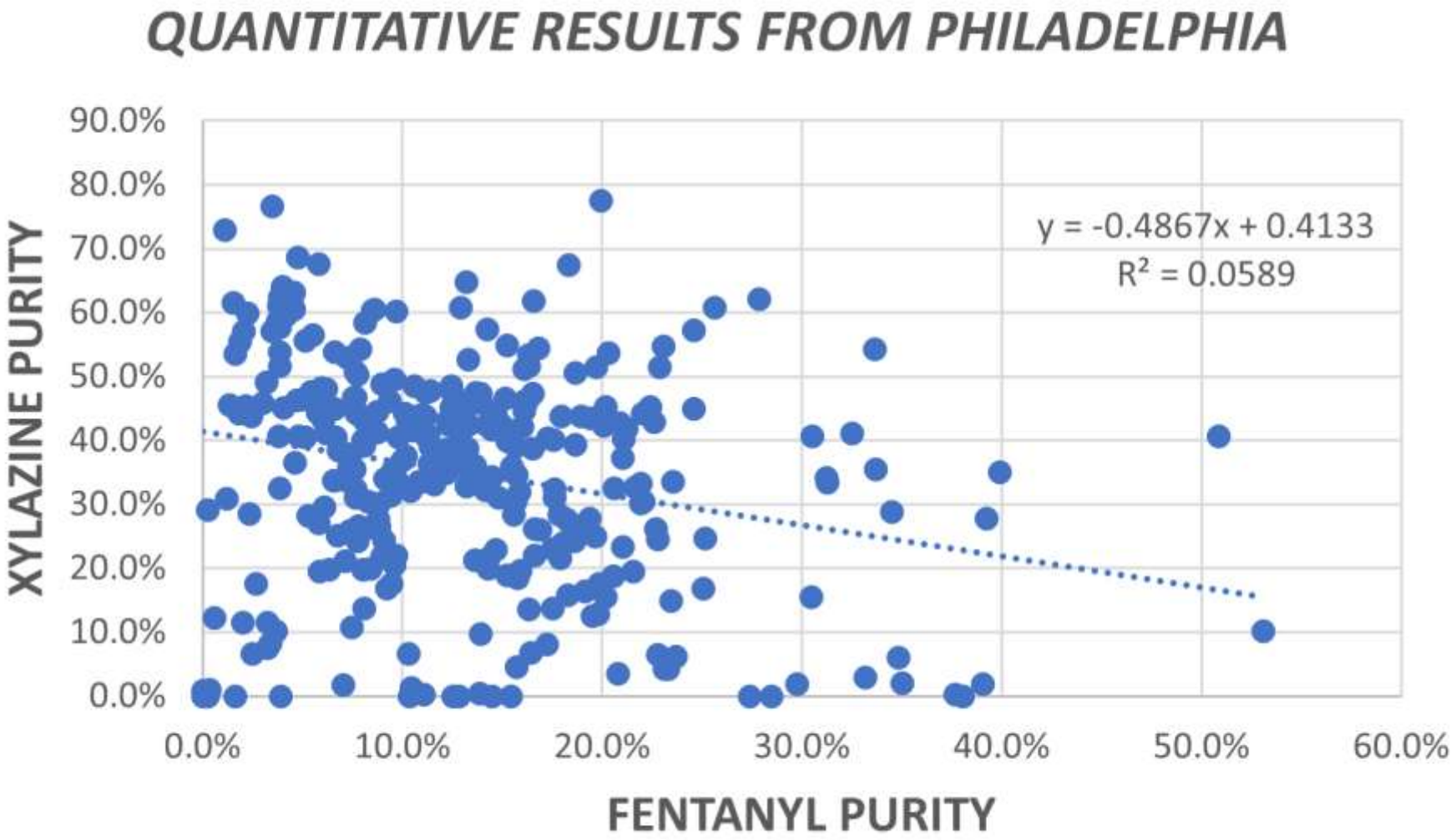
state	xylazine	total	percent
CT	2	2	100
MS	1	1	100
NJ	1	1	100
OR	3	48	6.3
AZ	1	19	5.3
WA	5	256	2
CO	0	6	0
VA	0	5	0
MT	0	1	0
IN	0	2	0
NV	0	3	0
NM	0	18	0
GA	0	3	0
CA	0	37	0

Caveat: Overestimation

People may send us samples because they suspect xylazine.

Data current through Monday October 2, 2023

Xylazine vs. Fentanyl Ratios



Source:
Alex Krotulski
CSFRE
Purity in terms of weight by volume

Xylazine is found mostly alongside fentanyl, but also mixed with other drugs.

	substance	sample
1	xylazine	192
2	fentanyl	187
3	4-ANPP	176
4	phenethyl 4-ANPP	92
5	p-fluorofentanyl	69
6	heroin	53
7	cocaine	51
8	lidocaine	37
9	despropionyl p-fluorofentanyl	36
10	dimethyl sulfone (methylsulfonylmethane MSM)	33
11	ethyl-4-ANPP	33
12	methamphetamine	32
13	N-phenylpropanamide	29
14	1,3-Diacetin	27
15	p-fluoro phenethyl 4-ANPP	25
16	6-monoacetylmorphine (6-MAM)	24
17	caffeine	23
18	acetylcodeine	22
19	tramadol	20
20	acetaminophen	18

How does xylazine get in the drug supply?

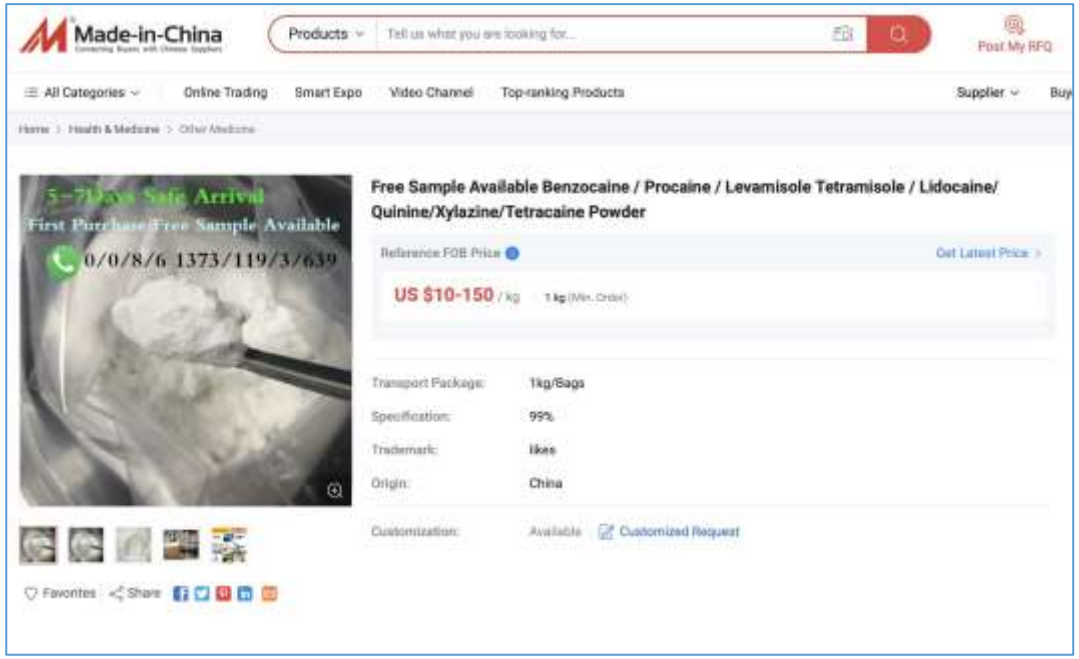
1. Veterinary diversion – rare, niche, cultural, not cost effective

2. Fentanyl-xylazine combo
   No xylazine synthesis impurities!

3. Ridealong cut at end of supply chain

4. Cross-contamination

5. Without fentanyl



Health Harms of Xylazine

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

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. Hosey[2], Christopher Moraff[3], Aaron Ferguson[4], Mary Figgatt[5], Shoshana Aronowitz[6], Natalie E. Stahl[7], Lucas G. Hill[1], Zoe McElligott[8] and Nabarun Dasgupta[9]

Table 1 Xylazine harm domains and clinical approaches

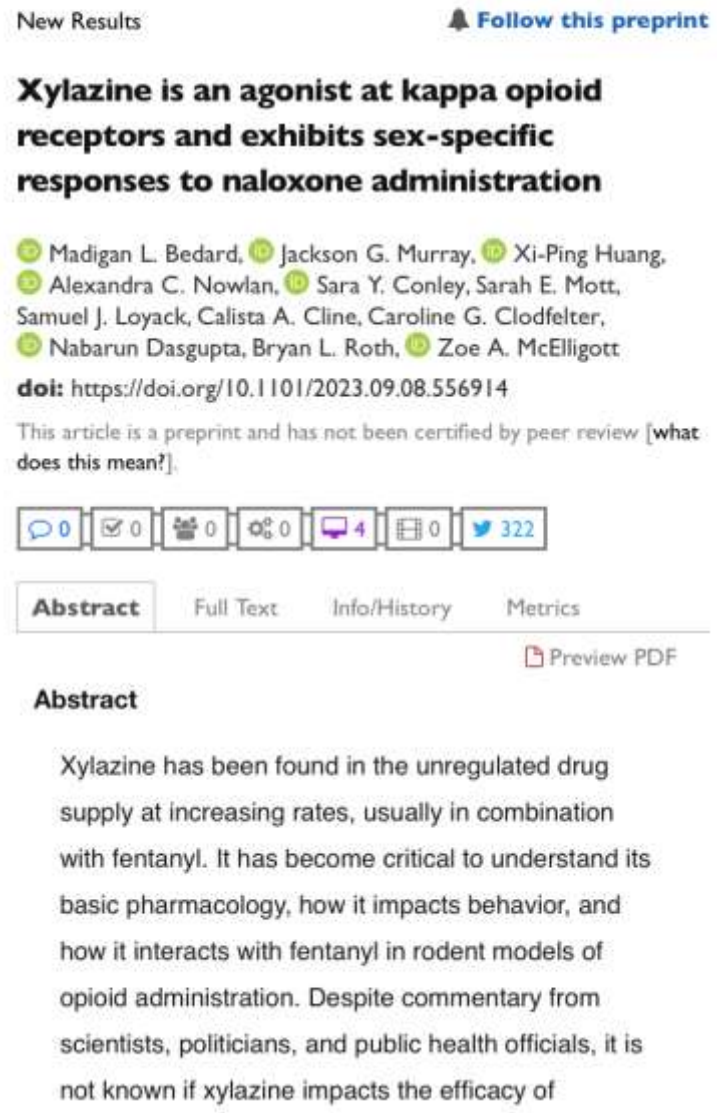
Harm domain	Mechanism	Clinical implications	Harm reduction strategies
Heavy sedation	Alpha-2 receptor agonism	Continued sedation after naloxone administration Pressure ulcers and skin breakdown likely Elevated risk for DVT Elevated risk of compartment syndrome Nerve, muscle, and soft tissue injury Rhabdomyolysis	Encourage using drugs with a friend Roll people nodding onto their side Move people nodding every two hours Pad under bony areas (sacrum, heels, shoulders, etc.) Avoid wrinkled or hard surfaces under nodding person
Skin wounds	Unknown	Bacterial superinfection possible Ensure adequate longitudinal wound care Can cause shame and reduced care-seeking Individuals may be deemed ineligible for in-patient substance use disorder care due to untreated wounds	Coach to avoid injecting into or near wounds Facilitate wound care access Teach individual and friends/family how to care for wounds Provide wound care supplies Teach on signs of worsening condition
Anemia	Unknown; perhaps sympathetic antagonism	Vague symptoms may delay care-seeking Important to rule out dietary or other causes	Coach communities on signs and symptoms; when care-seeking is necessary Encourage and facilitate community support to identify changes in health status in self and others
Dysglycemia	Unknown	Vague symptoms may delay care-seeking Important to rule out other causes of metabolic derangement Potential to worsen skin wound progress	Coach communities on signs and symptoms; when care-seeking is necessary Encourage and facilitate community support to identify changes in health status in self and others

Xylazine is also a kappa opioid.

Xylazine is both an alpha-2 adrenergic agonist and a kappa opioid agonist.

Explains many community observations

1. Naloxone precipitates xylazine withdrawal in mice
2. There are marked sex differences in response to xylazine in mice
3. Wounds bear striking similarity to other kappa opioids, such as pentazocine



Cold Spring Harbor Laboratory

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?**].

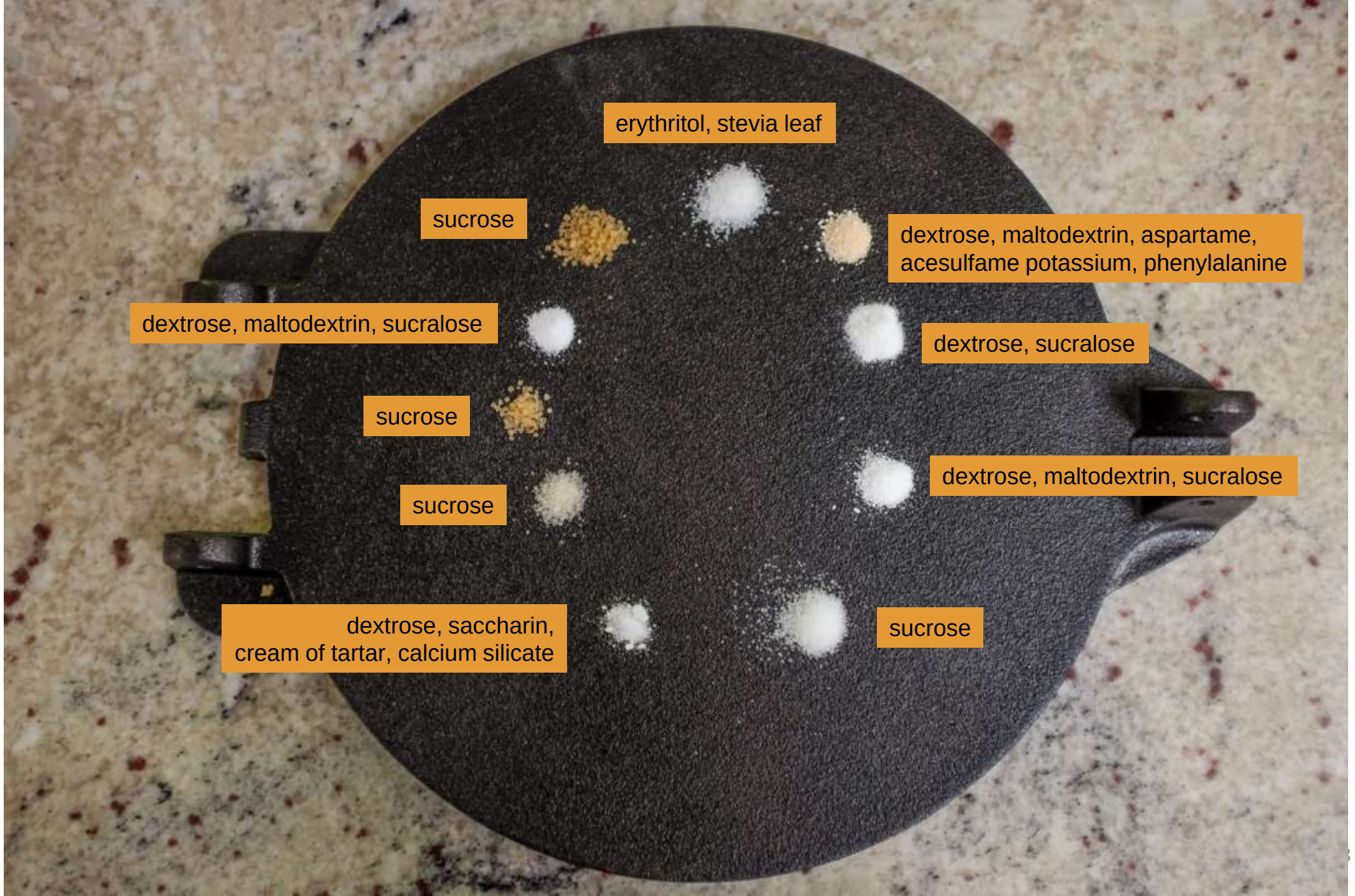
0 0 0 0 4 0 322

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


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

FLORIDA CRYSTALS
Cane Sugar
CAFÉ truvia
STEVIA LEAF
equal original
Granulated Sugar Substitute
Cheney Brothers
ecoStick
Organic Raws
Splenda
ecoStick
Organic Whites
SWEET'N LOW
ZERO CALORIE SWEETENER
Sugar

Communication & Drug Checking

Googling chemical names will give you wrong information.

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

Metonitzene: “Rare but potent opioid”

Inability to pronounce chemical names disconnects people.

→ **Provide phonetic guides**

Metonitzene: “met-oh-nit-a-zeen”

People want to know what is “normal.”

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

Metonitzene: “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

British Columbia

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

Maine

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!

National Patient Safety Alert

Public Health England

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.

1. **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 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)
2. **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

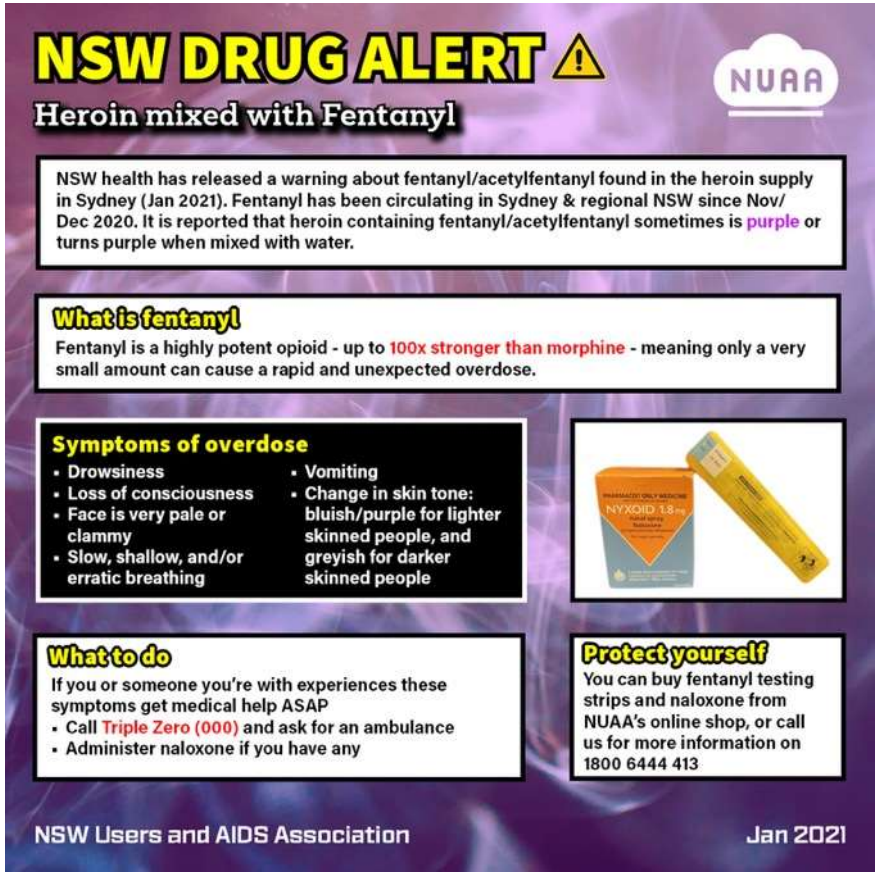
For any enquiries about this alert contact: NatPSA@phe.gov.uk

Failure to take the actions required under this National Patient Safety Alert may lead to CQC taking regulatory action

Florida

Australia

Yemen



https://twitter.com/majedalhoriby/status/1470759434368466946?s=20&t=zH0ASU2zHTh-4Zsj5MIarA

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

Optimized

⚠ 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

- ar
batch, use smaller amounts, and push the syringe plunger slowly if injecting
- Always carry naloxone (Narcan) and know how to use it to reverse an overdose

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

Simple graphics that do not distract

Information Hierarchy

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

All Images Illustrations About Submit

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
Ele

Working at computer
Britain Peck

Water ampoule
Lindsey Morano

Crack Vial
Lindsey Morano

Holding pills
DALL·E

COVID Bus
Britain Peck

Syringe in space
DALL·E

Crack Vials
Lindsey Morano

Gauze
Lindsey Morano

Working on medicine ball
Britain 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!

Thanks from and to our team!

Tory

Illyana

Allison

Don

Louise

Shelby
Bridgette
Shay
Tushar
William

Rachel Clark @ DanceSafe

Drew

Brandie

Maryalice

LaMonda

Hand drawn by BRITTAIN PECK

Zoë

Nabarun

Colin

Erin

Photos by
Pearson Ridley