Getting Specific
New tools for understanding overdose and the drug supply

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University of North Carolina

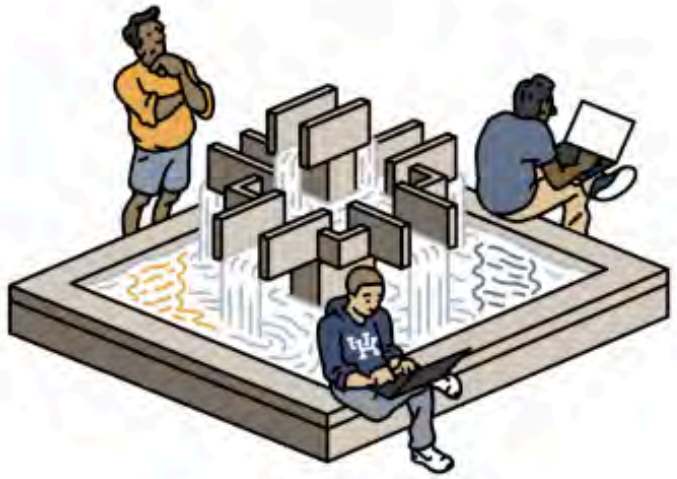
August 28, 2024 • RMPDS Annual Meeting

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
- Vital statistics
- Harm reduction

Lived Experience

Science in Service

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

Part 1

More Specific Overdose Data

This research was funded by the US Food and Drug Administration via UNC to UKY (BAA #167, Contract 75F40122C00193)

The views presented do not necessarily reflect the views of the Funder, and should not be construed as Guidance or policy.

PDMP dispensing linked to OD mortality data

We observe 2 points in time:
Prescription dispensed → overdose death

Limitations

- Limited by what is assayed and noted on death records
- Causal emphasis can vary examiner
- Little/none mental and social antecedents
- Cannot distinguish intentional vs. accidental polysubstance use
- Dispensing records do not capture street drug exposure
- Can't tell if people left or died of other causes

Still, I feel these data can be insightful.

Large collaboration led by Univ. of Kentucky

Key Personnel

- Svetla Slavova, PhD
- Trish Freeman, RPh, PhD
- Doug Oyler, PharmD
- Krassimir Slavov, MS
- Peter Akpunonu, MD
- Sarah Hargrove, MS
- Amber Kizewski, MA

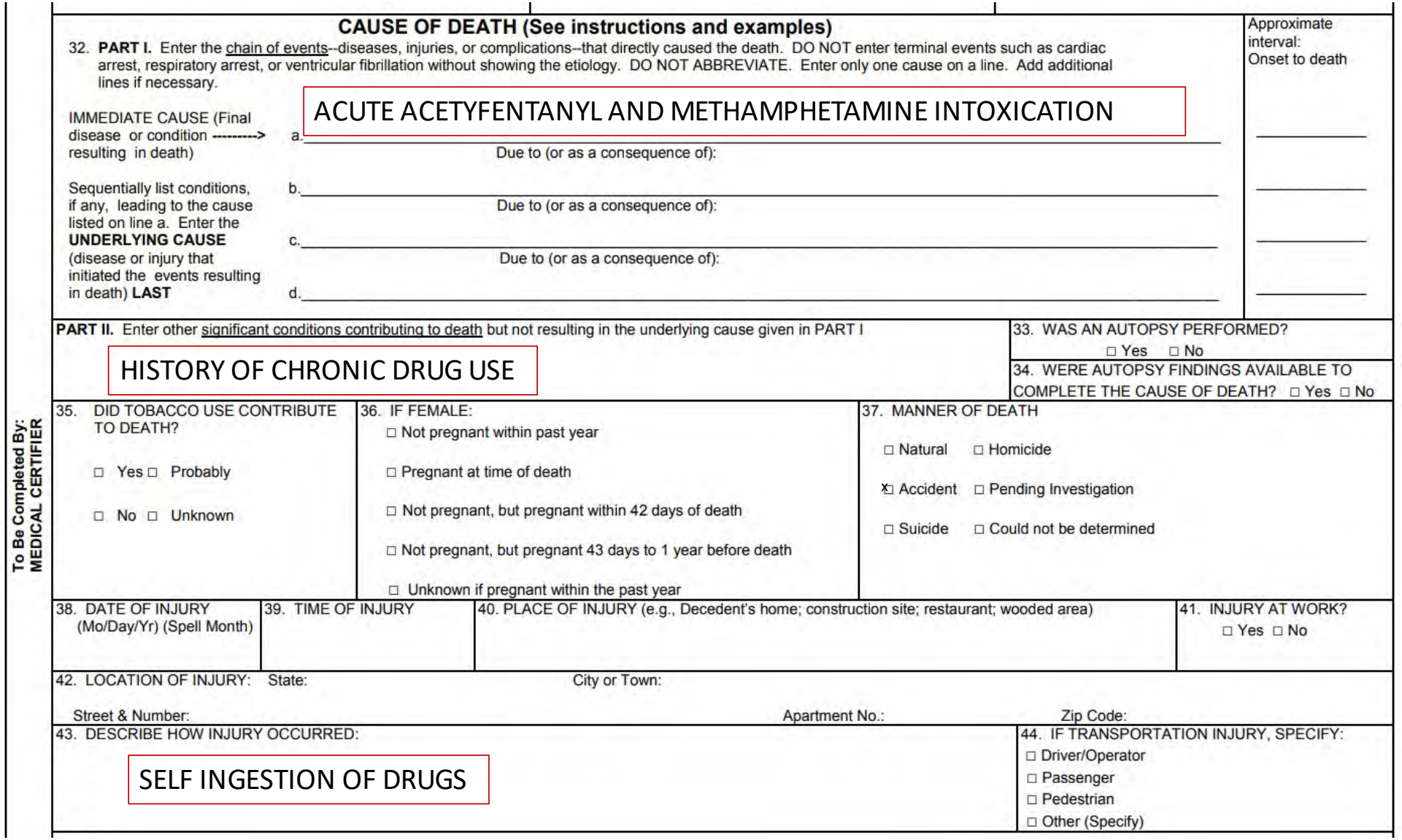
Collaborators

- Jana McAninch, MD, MPH
- Matthew Daubresse, PhD
- Nabarun Dasgupta, PhD, MPH
- Saranrat Conrad, PhD
- Margaret Warner, PhD
- Farida Ahmad, MPH

Consultants

- Holly Hedegaard, MD
- Bruce Goldberger, PhD

Literal Text Analysis of Drug Overdose Death Certificates



To Be Completed By: MEDICAL CERTIFIER

CAUSE OF DEATH (See instructions and examples)

32. **PART I.** Enter the chain of events--diseases, injuries, or complications--that directly caused the death. DO NOT enter terminal events such as cardiac arrest, respiratory arrest, or ventricular fibrillation without showing the etiology. DO NOT ABBREVIATE. Enter only one cause on a line. Add additional lines if necessary.

Approximate interval: Onset to death

IMMEDIATE CAUSE (Final disease or condition ---------> resulting in death)

a. ACUTE ACETYFENTANYL AND METHAMPHETAMINE INTOXICATION

Due to (or as a consequence of):

Sequentially list conditions, if any, leading to the cause listed on line a. Enter the **UNDERLYING CAUSE** (disease or injury that initiated the events resulting in death) **LAST**

b.

Due to (or as a consequence of):

c.

Due to (or as a consequence of):

d.

PART II. Enter other significant conditions contributing to death but not resulting in the underlying cause given in PART I

HISTORY OF CHRONIC DRUG USE

33. WAS AN AUTOPSY PERFORMED? ☐ Yes ☐ No

34. WERE AUTOPSY FINDINGS AVAILABLE TO COMPLETE THE CAUSE OF DEATH? ☐ Yes ☐ No

35. DID TOBACCO USE CONTRIBUTE TO DEATH?

☐ Yes ☐ Probably

☐ No ☐ Unknown

36. IF FEMALE:

☐ Not pregnant within past year

☐ Pregnant at time of death

☐ Not pregnant, but pregnant within 42 days of death

☐ Not pregnant, but pregnant 43 days to 1 year before death

☐ Unknown if pregnant within the past year

37. MANNER OF DEATH

☐ Natural ☐ Homicide

☒ Accident ☐ Pending Investigation

☐ Suicide ☐ Could not be determined

38. DATE OF INJURY (Mo/Day/Yr) (Spell Month)

39. TIME OF INJURY

40. PLACE OF INJURY (e.g., Decedent's home; construction site; restaurant; wooded area)

41. INJURY AT WORK? ☐ Yes ☐ No

42. LOCATION OF INJURY: State: City or Town:

Street & Number: Apartment No.: Zip Code:

43. DESCRIBE HOW INJURY OCCURRED:

SELF INGESTION OF DRUGS

44. IF TRANSPORTATION INJURY, SPECIFY:

☐ Driver/Operator

☐ Passenger

☐ Pedestrian

☐ Other (Specify)

CSTE Epi Tool to Analyze Overdose Death Data

CSTE

Council of State and Territorial Epidemiologists

Leaders in Applied Public Health Epidemiology

National Headquarters
2872 Woodcock Boulevard | Suite 250
Atlanta, Georgia 30341
770.458.3811 | fax 770.458.8516

www.cste.org

CSTE is an organization that supports epidemiologists practicing at the state, territorial, tribal, and local levels.

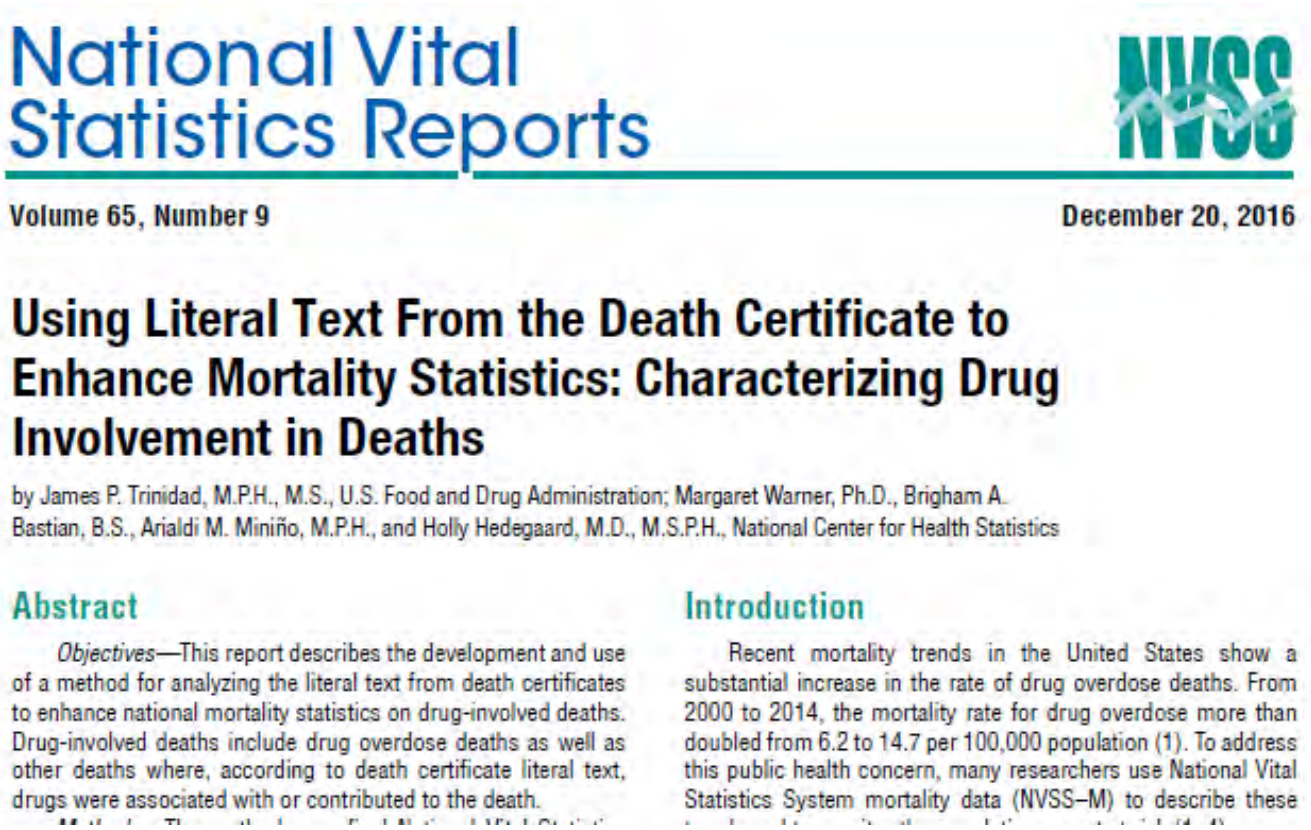
Search tool to identify specific drugs and other terms associated with drug overdose deaths from the death certificate literal text

Prepared by the CSTE Overdose Subcommittee on literal text analysis including Jennifer Sabel, Jim Davis, Dagan Wright, and Svetla Slavova from CSTE; Margaret Warner, Ari Minino, Lily Chen from NCHS; and Len Paulozzi, and Rose Rudd from NCIPC.

Why create a search tool for the literal text?

Drug overdose deaths are currently the leading cause of injury death in the US. The current version of the International Statistical Classification of Diseases coding system is limited in its ability to identify the specific drugs involved in drug overdose deaths

Literal Text Analysis of Drug Overdose Death Certificates



National Vital Statistics Reports

NVSS

Volume 65, Number 9 December 20, 2016

Using Literal Text From the Death Certificate to Enhance Mortality Statistics: Characterizing Drug Involvement in Deaths

by James P. Trinidad, M.P.H., M.S., U.S. Food and Drug Administration; Margaret Warner, Ph.D., Brigham A. Bastian, B.S., Arialdi M. Miniño, M.P.H., and Holly Hedegaard, M.D., M.S.P.H., National Center for Health Statistics

Abstract

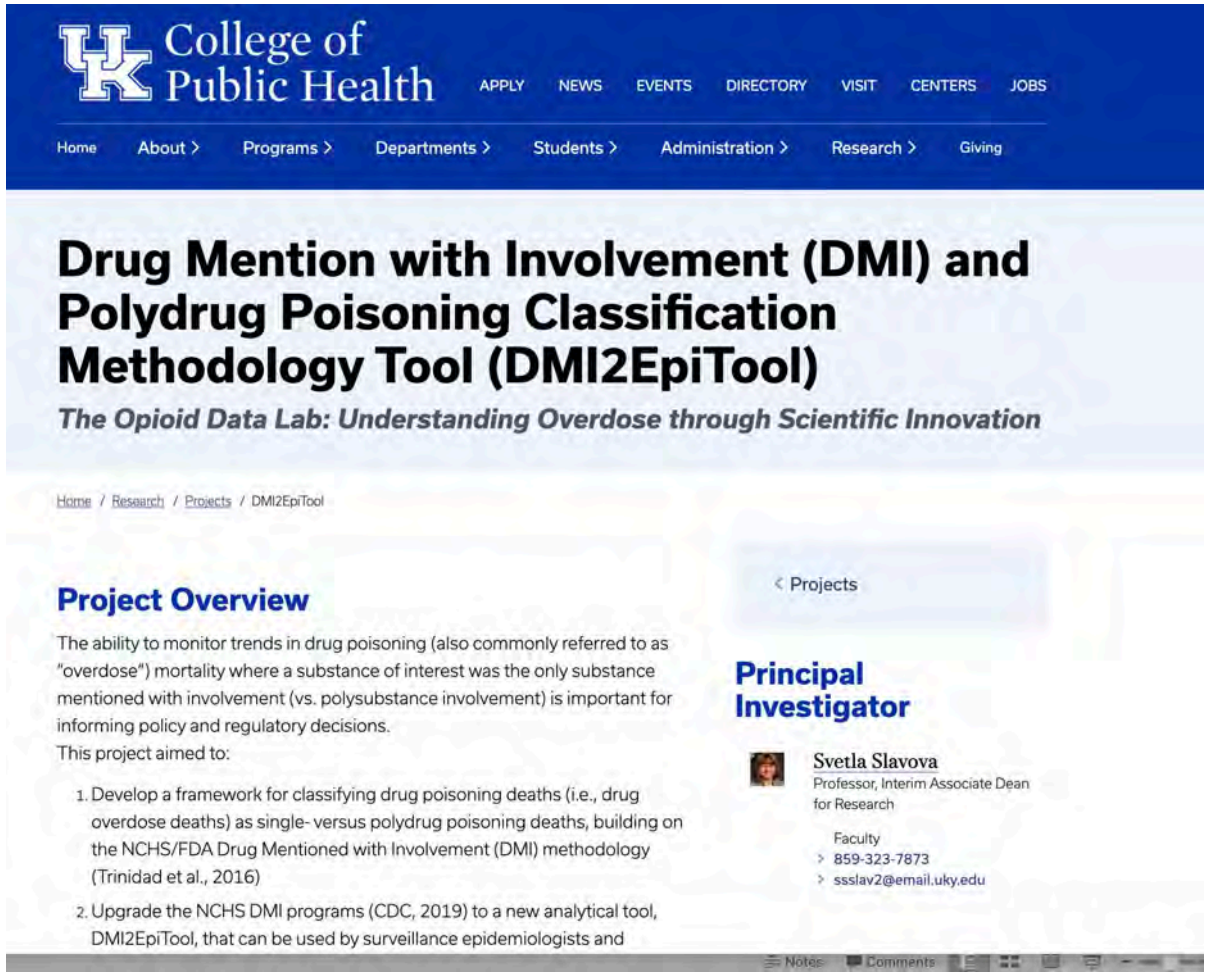
Objectives—This report describes the development and use of a method for analyzing the literal text from death certificates to enhance national mortality statistics on drug-involved deaths. Drug-involved deaths include drug overdose deaths as well as other deaths where, according to death certificate literal text, drugs were associated with or contributed to the death.

Introduction

Recent mortality trends in the United States show a substantial increase in the rate of drug overdose deaths. From 2000 to 2014, the mortality rate for drug overdose more than doubled from 6.2 to 14.7 per 100,000 population (1). To address this public health concern, many researchers use National Vital Statistics System mortality data (NVSS–M) to describe these

Available from: https://www.cste.org/blogpost/1084057/211072/Epi-Tool-to-Analyze-Overdose-Death-Data

New Tool, available now! DMI2EpiTool



https://cph.uky.edu/research/projects/DMI2EpiTool

College of Public Health

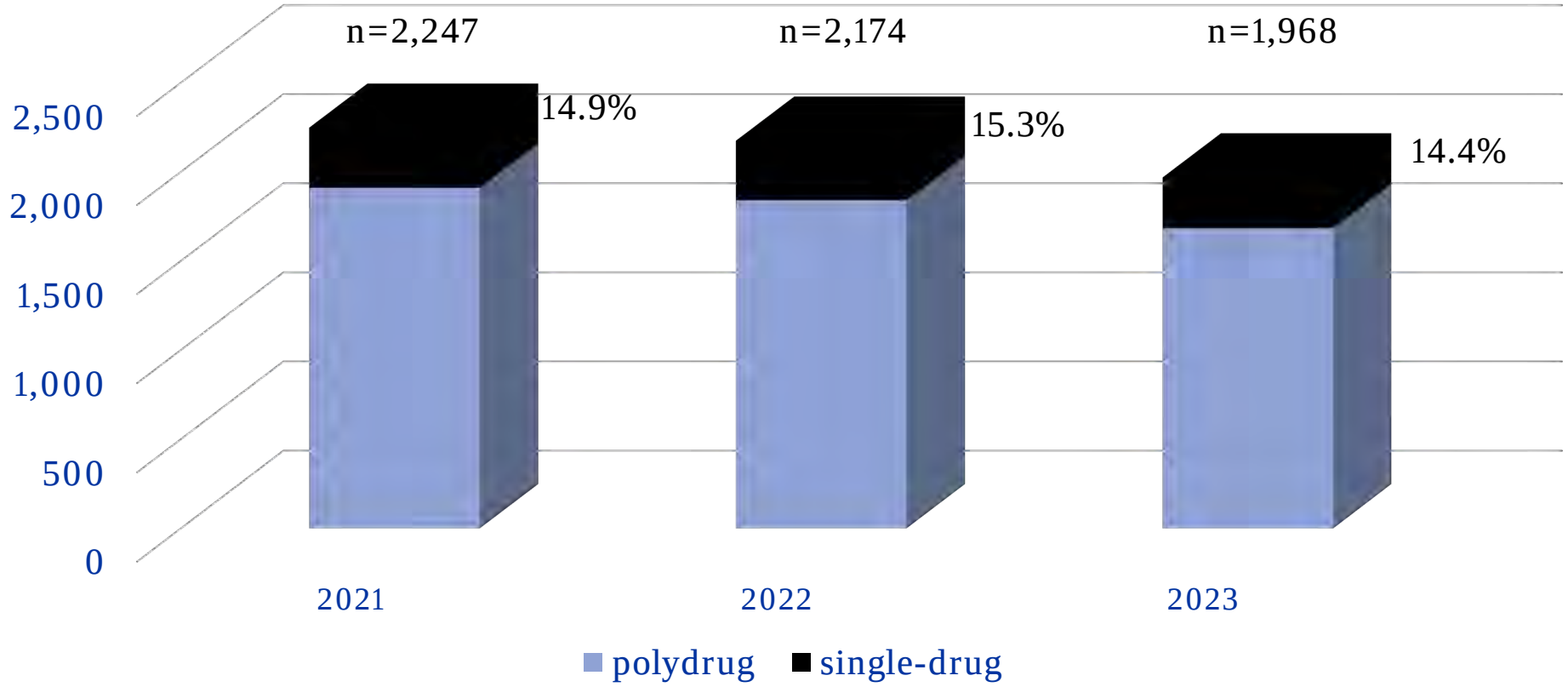
College of Pharmacy

What % of OD deaths are single substance?

Kentucky 2021-2023

10% · 15% · 20% · 25%

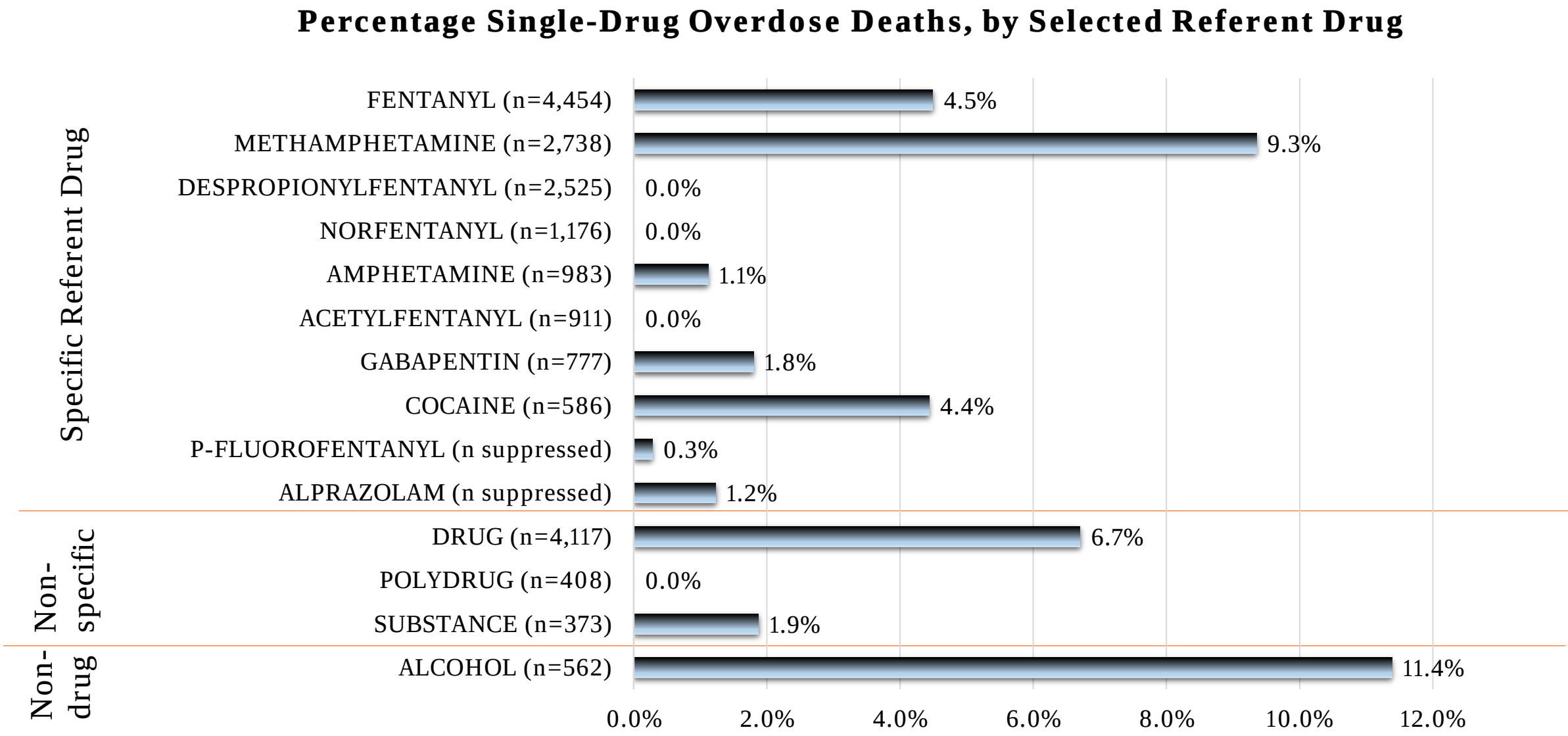
Kentucky Drug Overdose Deaths, 2021-2023



- 12% decline in drug overdose deaths from 2021 (n=2,247) to 2023 (n=1,968)
- About 15% of the drug overdose deaths each year are single-drug overdose deaths

Note: 2023 data are provisional and subject to change

KY Single Drug Overdose Deaths, 2021-2023



Note: 2023 data are provisional and subject to change

Part 2
Applying Tools for New Insights

This research was funded by the US Food and Drug Administration via UNC to UKY (BAA #167, Contract 75F40122C00193)

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What's Not Obvious

Most studies on Rx → OD do not match the prescribed substance with the fatal drug.

Freeman *et al. Substance Abuse Treatment, Prevention, and Policy* (2023) 18:53
https://doi.org/10.1186/s13011-023-00561-y

Substance Abuse Treatment, Prevention, and Policy

RESEARCH Open Access

Drugs involved in Kentucky drug poisoning deaths and relation with antecedent controlled substance prescription dispensing

Patricia R. Freeman[1*], Jana McAninch[2], Nabarun Dasgupta[3], Douglas R. Oyler[1], Krassimir Slavov[4], Candice Collins[2], Sarah Hargrove[5], Edward Freeman[6], Dustin Miracle[1] and Svetla Slavova[4,5]

Abstract

Background The shift from prescription to illicit drugs involved in drug poisoning deaths raises questions about the current utility of prescription drug monitoring program (PDMP) data to inform drug poisoning (overdose) prevention efforts. In this study, we describe relations between specific drugs involved in Kentucky drug poisoning deaths and antecedent controlled substance (CS) dispensing.

Methods The study used linked death certificates and PDMP data for 2,248 Kentucky resident drug poisoning deaths in 2021. Death certificate literal text analysis identified drugs mentioned with involvement (DMI) in drug poisoning deaths. We characterized the concordance between each DMI and the CS dispensing history for this drug at varying timepoints since 2008.

Results Overall, 25.5% of all decedents had dispensed CS in the month before fatal drug poisoning. Over 80% of decedents were dispensed opioid(s) since 2008; the percentage was similar regardless of opioid involvement in the poisoning death. One-third of decedents had dispensed buprenorphine for treatment of opioid use disorder since 2008, but only 6.1% had dispensed buprenorphine in the month preceding death. Fentanyl/fentanyl analogs were DMI in 1,568 (69.8%) deaths, yet only 3% had received a fentanyl prescription since 2008. The highest concordance in the month preceding death was observed for clonazepam (43.6%).

Conclusion Overall, concordance between CS dispensing history and the drugs involved in poisoning deaths was low, suggesting a need to reevaluate the complex relationships between prescription medication exposure and overdose death and to expand harm reduction interventions both within and outside the healthcare system to reduce drug poisoning mortality.

Keywords Drug poisoning, Overdose death, Opioid, Prescription monitoring program, Stimulant

What is the average length of time between last opioid Rx and overdose death?

For hydrocodone & oxycodone, in KY, 2008-2021

<90 days · 8 mon · 1.5 yr · 3.5 yr

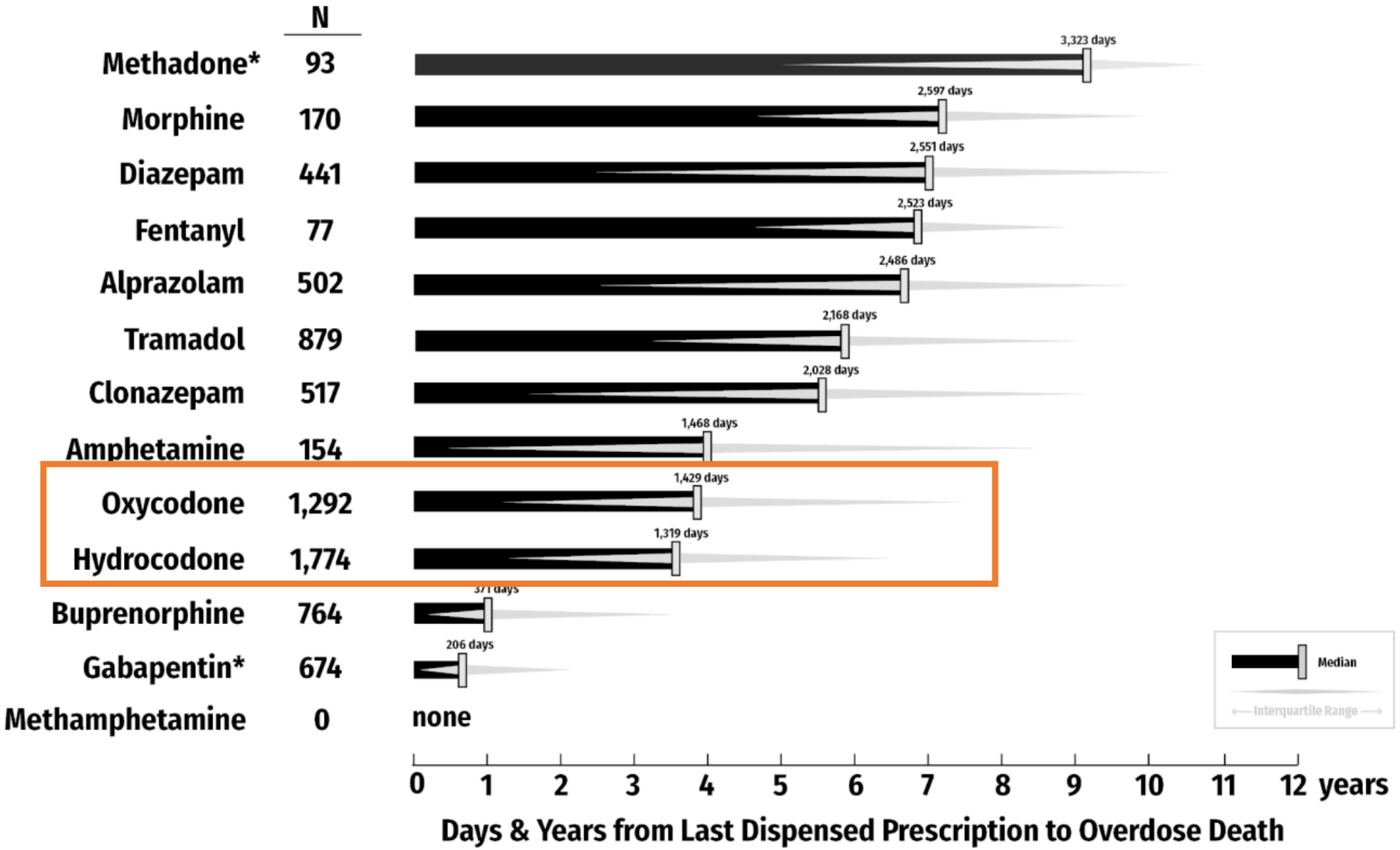


Fig. 1 Median time (years/days from the last dispensed prescription for specific medications to drug poisoning deaths, Kentucky drug poisoning decedents, 2021

* Methadone for treatment of opioid use disorder is not reported to the Kentucky All Schedule Prescription Electronic Reporting (KASPER) system. Gabapentin became a Schedule V controlled substance in Kentucky, reportable to KASPER on July 1, 2017

Note: The reported number of decedents with history of specific dispensed controlled substance includes everyone with such history, regardless of the involvement of the substance in the drug poisoning death

1,400 days to intervene

The Rx → OD relationship is not based just on toxicity.

What happens between the last prescription and overdose?

What should we be doing in that time to prevent these deaths?

Causal Pathways: Rx → Overdose

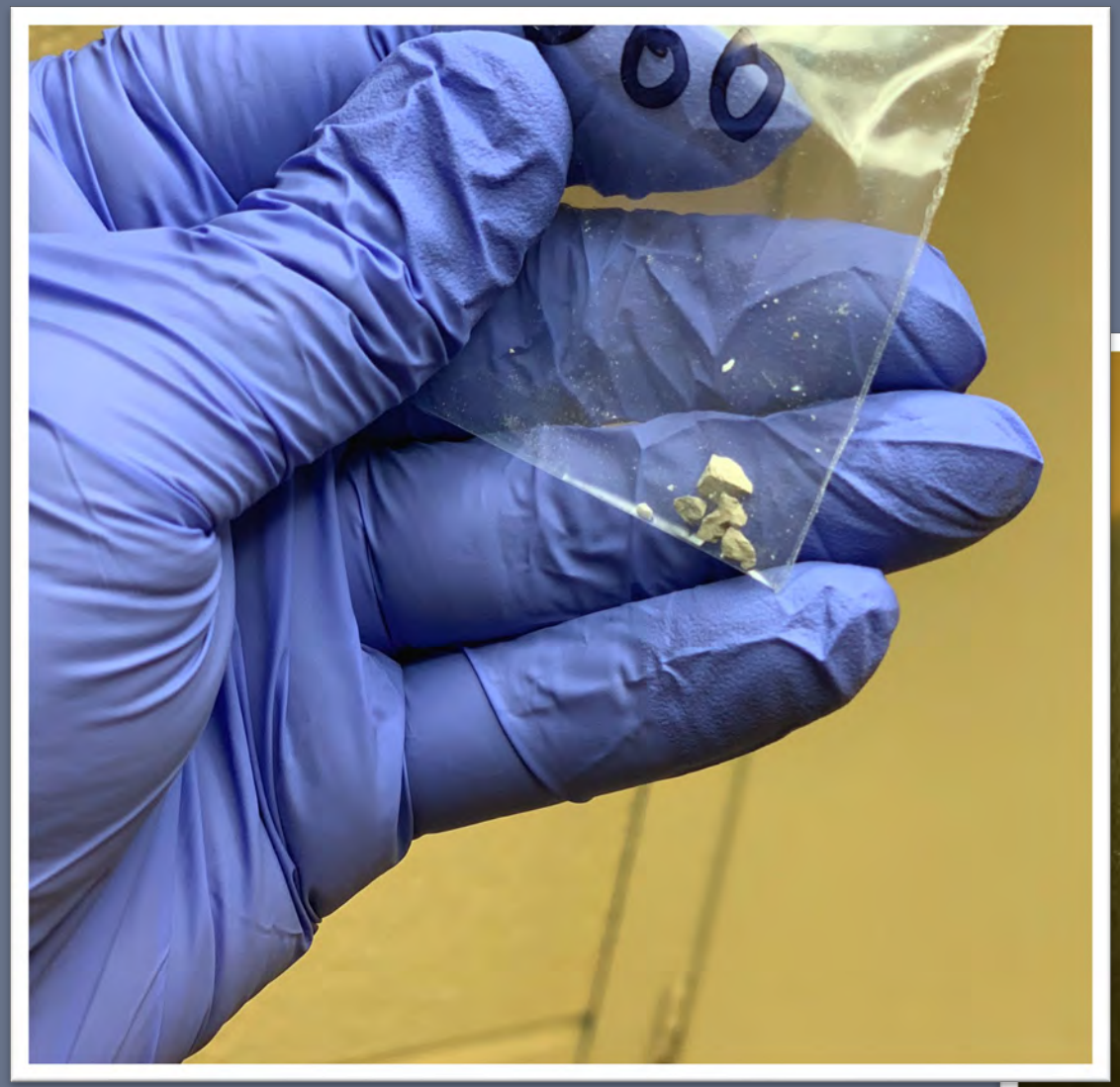
What is it about Rx opioid exposure that leads to overdose?

1. Patient behavior: taking more than prescribed
2. Short-term toxicity: too high starting dose; drug combos
3. Long-term iatrogenic exposure → OUD → illicit/diverted
4. Abrupt tapering of long-term opioid patients
5. Pre-existing mental health → iatrogenic → OUD →OD

Part 3

What's actually in street drugs?

Funding: FORE, Vital Strategies, NC General Assembly via NC Collaboratory

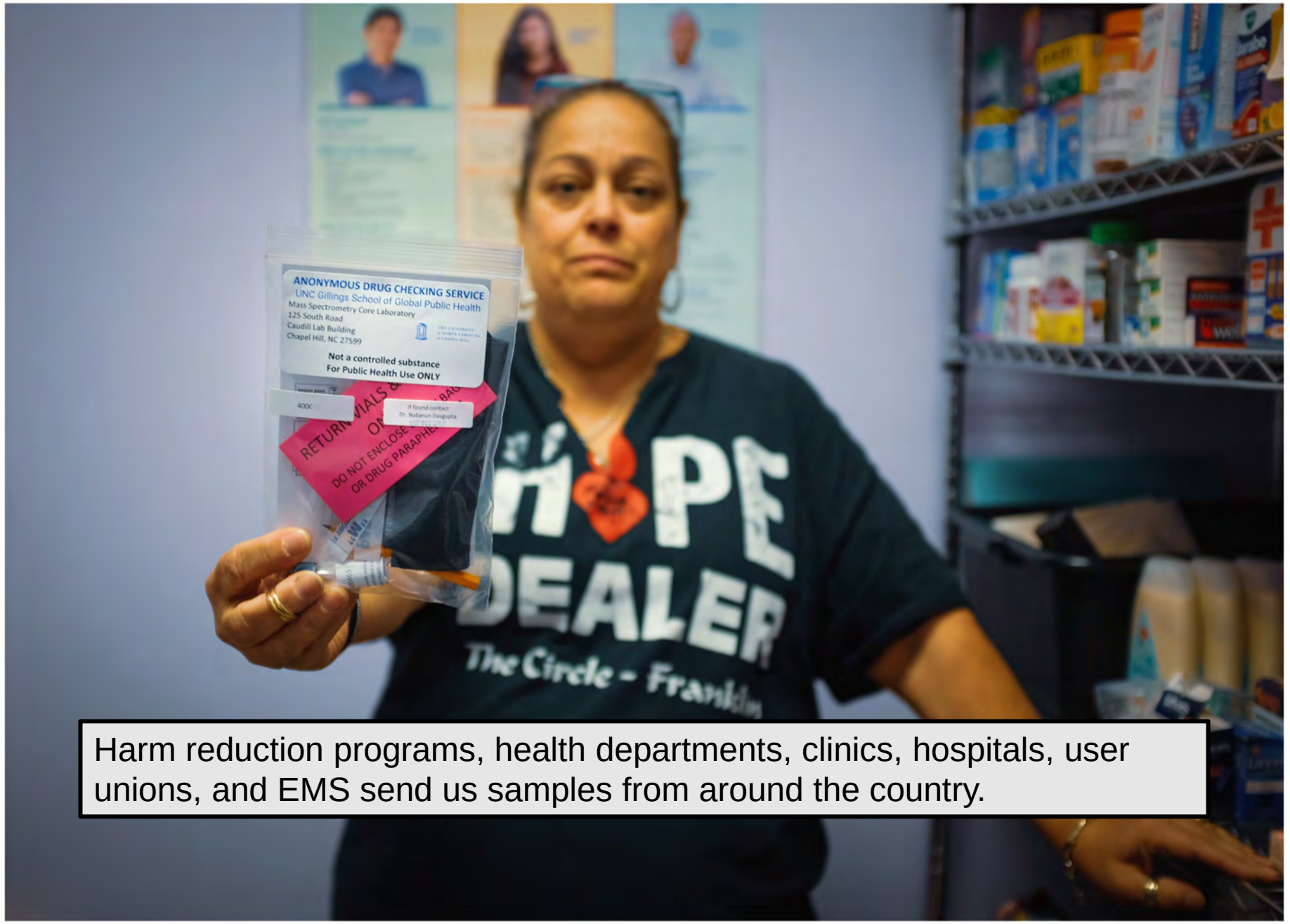


Street drugs change constantly.

In our lab on campus

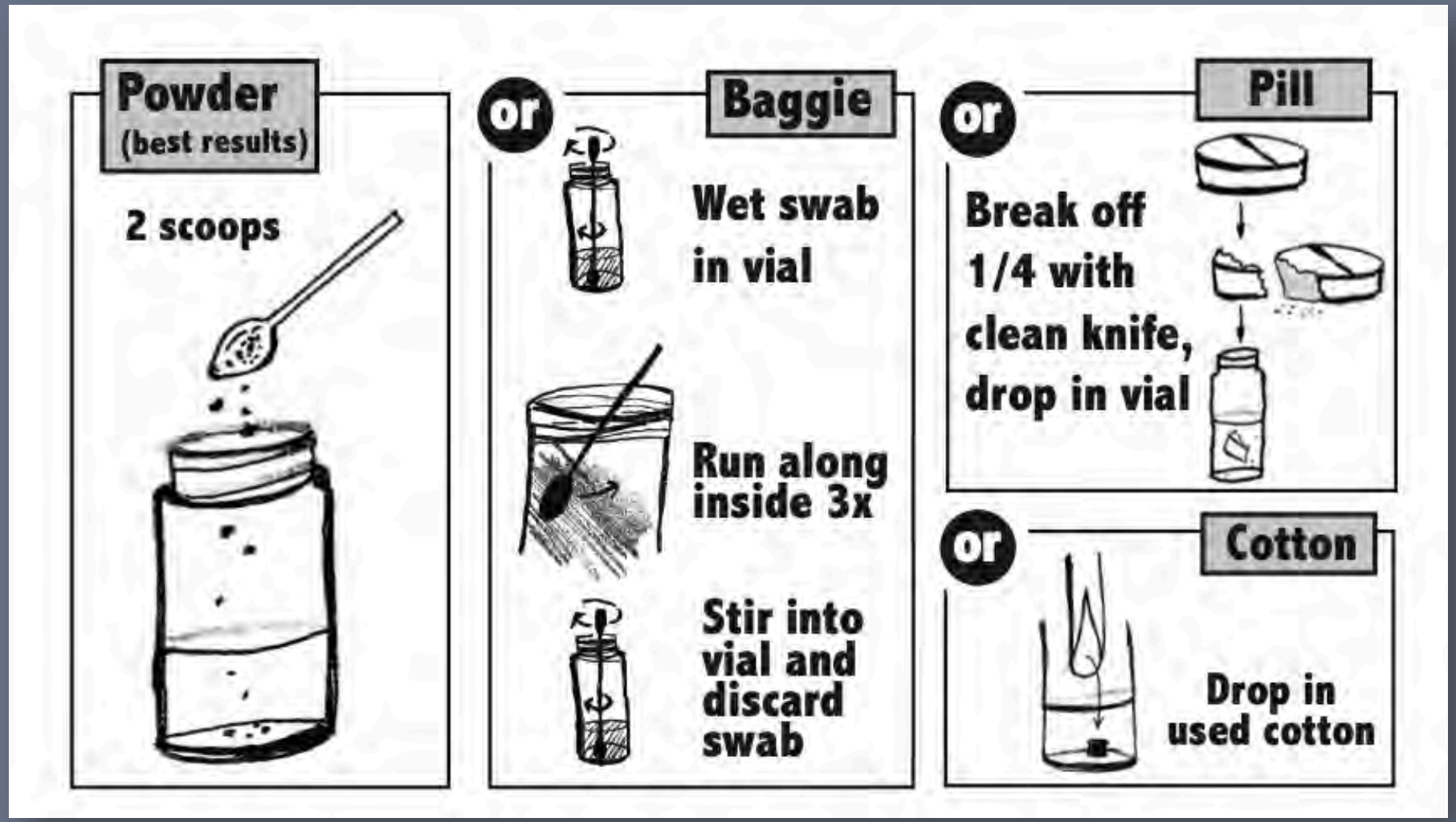
we monitor street drugs

as a public service.

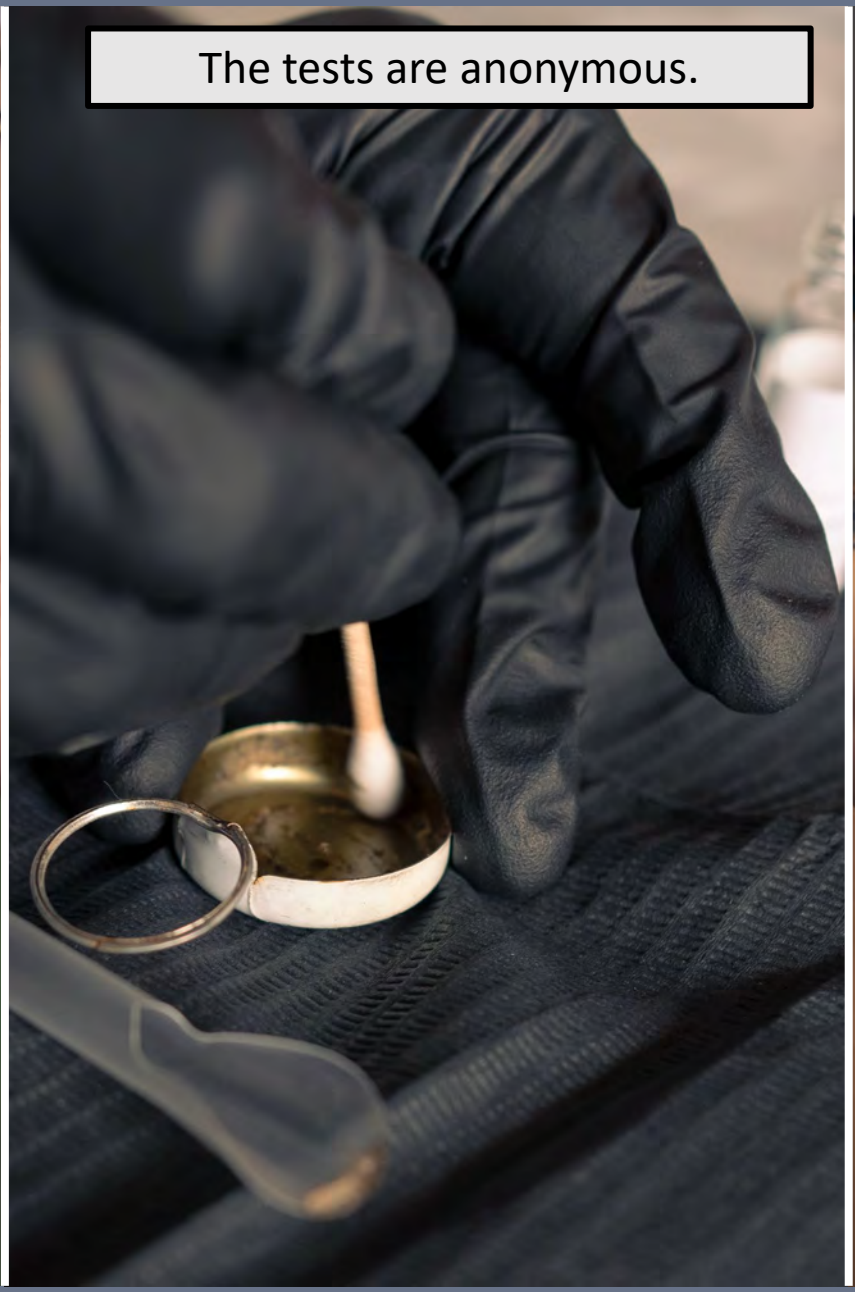


Harm reduction programs, health departments, clinics, hospitals, user unions, and EMS send us samples from around the country.

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




Samples are given voluntarily.


The tests are anonymous.


THIS IS MY
SECOND
RODEO

Programs share health information with us…

…to give human context beyond molecules.

Completely Anonymous

These questions help us analyze samples in the lab. Card info may be public on result website or used for data analysis.

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 overdose to warn others:

overdose

v8

describe color and markings

city or county

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

Packages arrive on campus

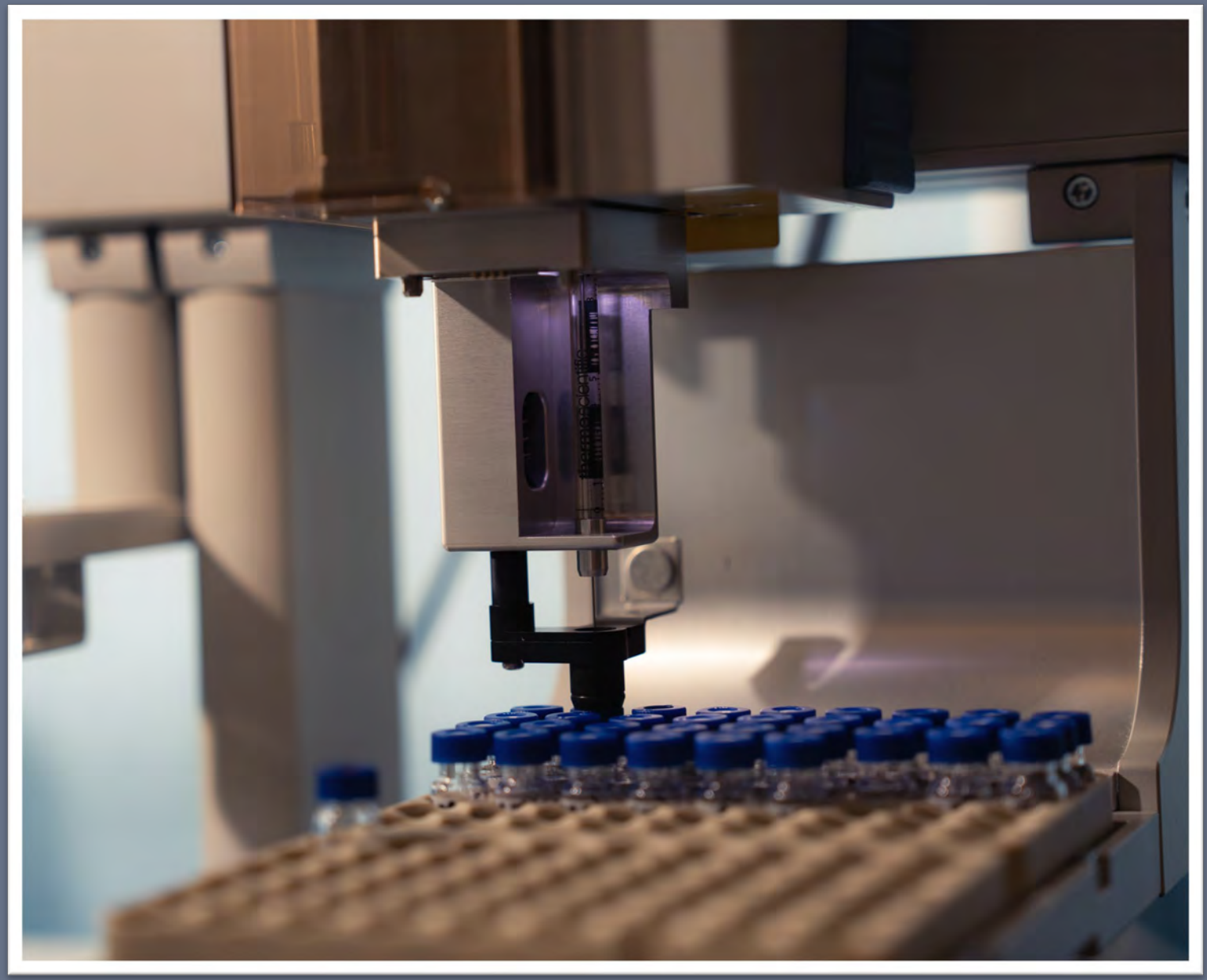
in compliance with drug and postal laws.

We record the information

and catalog the samples.

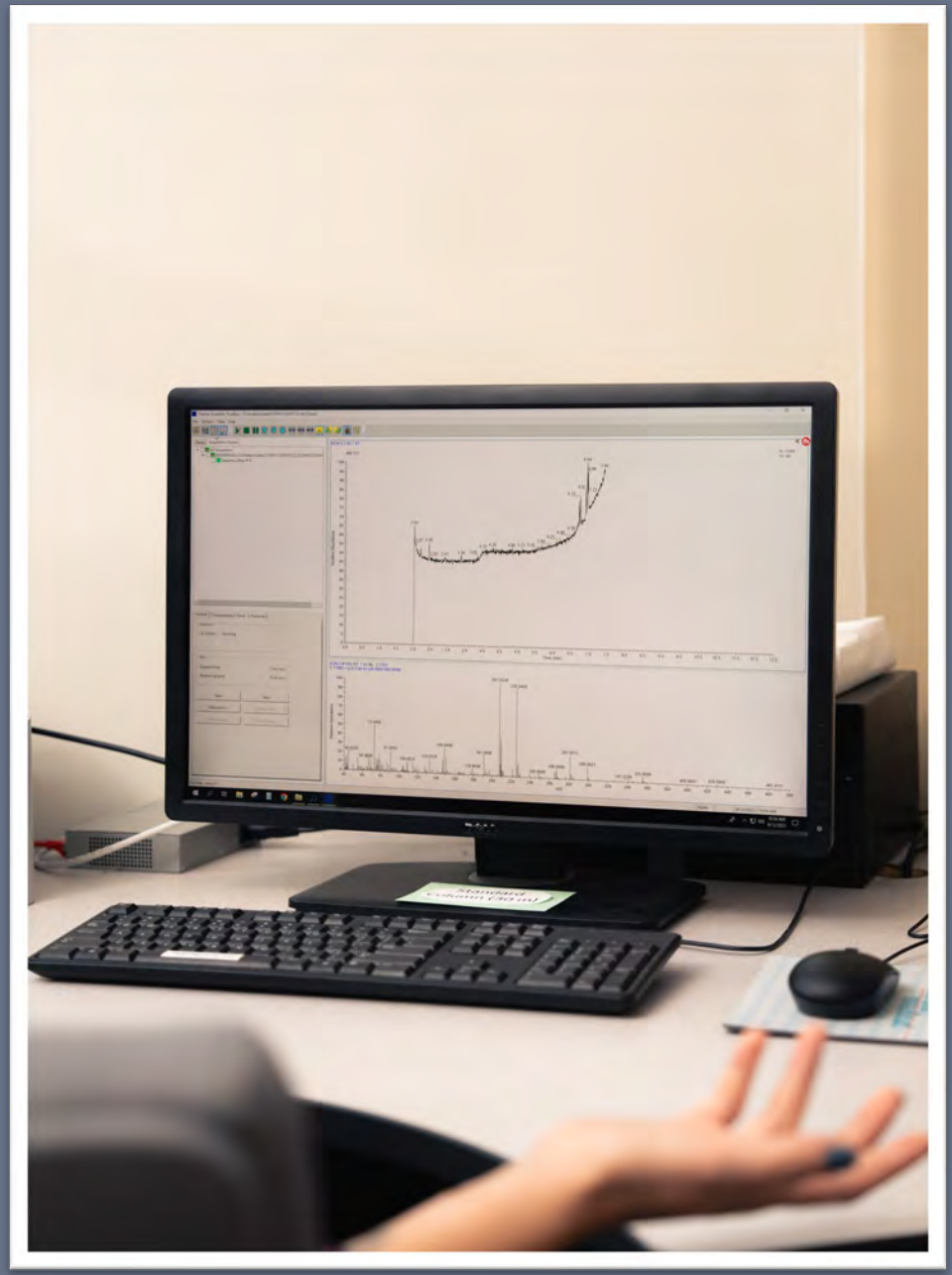
We prep the samples

and load them on a GCMS (mass spec).



We interpret the high resolution results,

to determine exactly what's in the sample.



March 2022 to August 27, 2024

USA

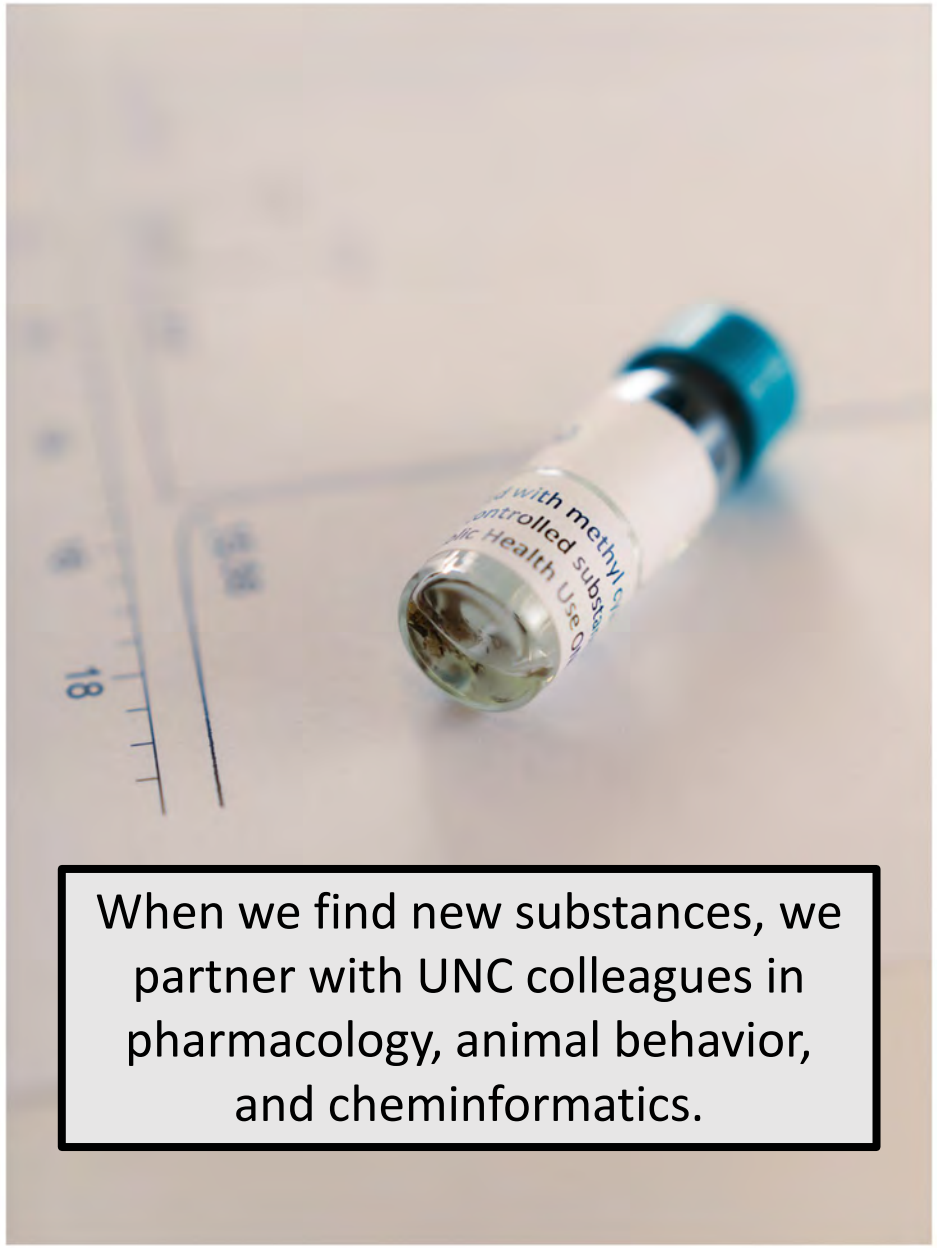
N = 7,243 drug samples

142 programs

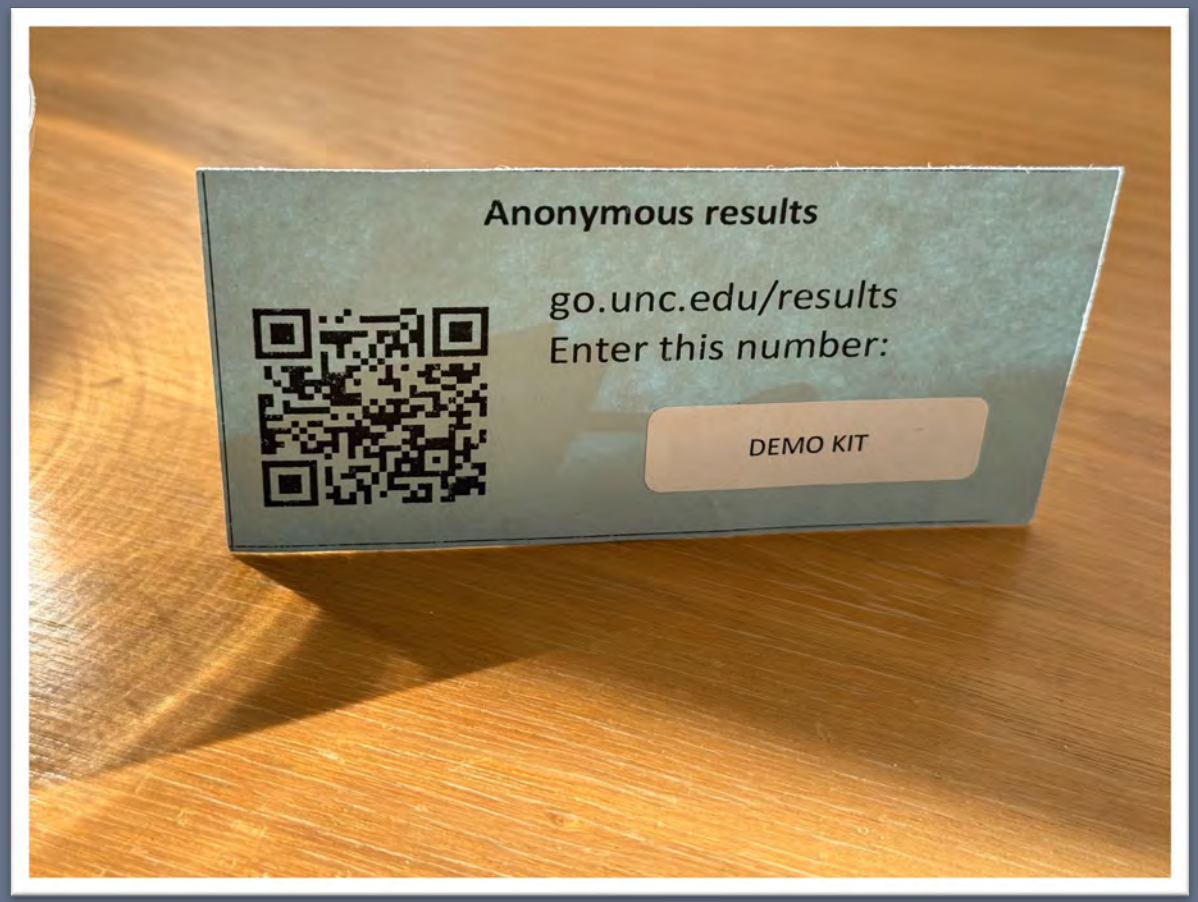
37 US states

212 counties

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



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



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

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 killed my husband?
- Can xylazine explain these skin wounds?
- How accurate are test strips?
- Can black lights identify xylazine and nitazenes?
- Are psychedelic therapy patients obtaining unadulterated MDMA?

300731

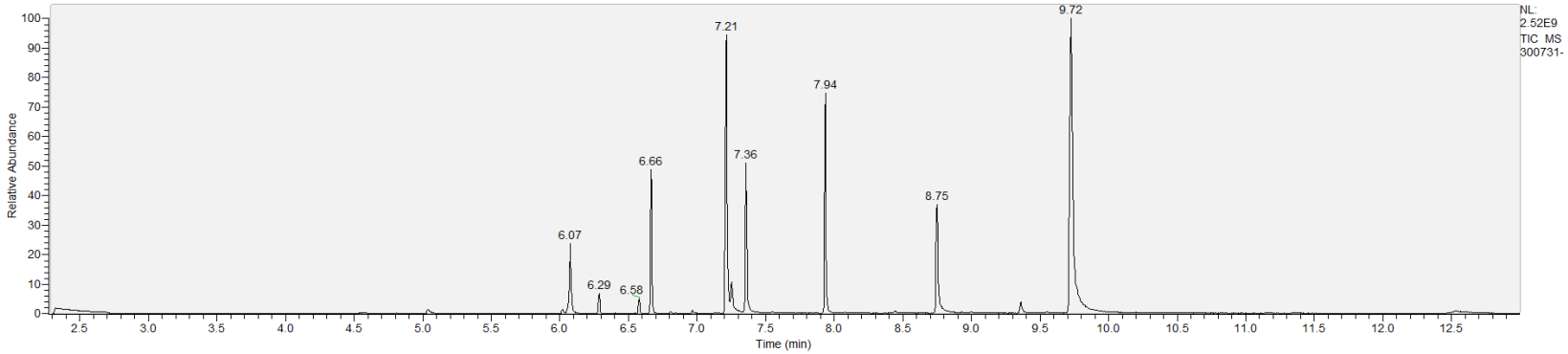
From Asheboro, North Carolina on II/2/2022
Assumed to be heroin

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.

Messy Brew of 16 Substances



Medicine: phenacetin, paracetamol, melatonin
Veterinary medicine: levamisole, xylazine
Numbing agents: procaine
Stimulants: caffeine, cocaine
Organic origin: noscapine, meconin, hydrocotarnine, heroin
Synthetic opioids: fentanyl
Byproducts: 4-ANPP, N-phenylpropanamide
Cuts (bulking agent): MSM

Case Study

2-fluoro-2-oxo-PCE


DRUGS SOLD AS FENTANYL IN GOLDSBORO,
EDGECOMBE CONTAINED 8 DIFFERENT SUBSTANCES
WRAL NEWS
COVERAGE YOU CAN COUNT ON


METHADONE
Pringles
Gatorade
CODE
RED

601834

From Edgecombe, North Carolina on 5/10/2024
Assumed to be fentanyl, xylazine

This is a messy brew of 8 major substances:

- **lidocaine**
- **2-Fluoro-2-oxo PCE**
- **tiletamine**
- **bromazolam**
- **xylazine**
- **fentanyl**
- **procaine**
- **4-ANPP**

804146

From Johnson City, New York on 5/9/2024
Assumed to be heroin

This is a messy brew of 8 major substances:

- **xylazine**
- **erythritol**
- **fentanyl**
- **4-ANPP**
- **2-Fluoro-2-oxo PCE**
- **bromazolam**
- **tiletamine**
- **procaine**

And we also found traces of quinine. Trace substances in small quantities are usually harmless, but can sometimes cause health problems. Unexpected sensations may be due to these.

cahma

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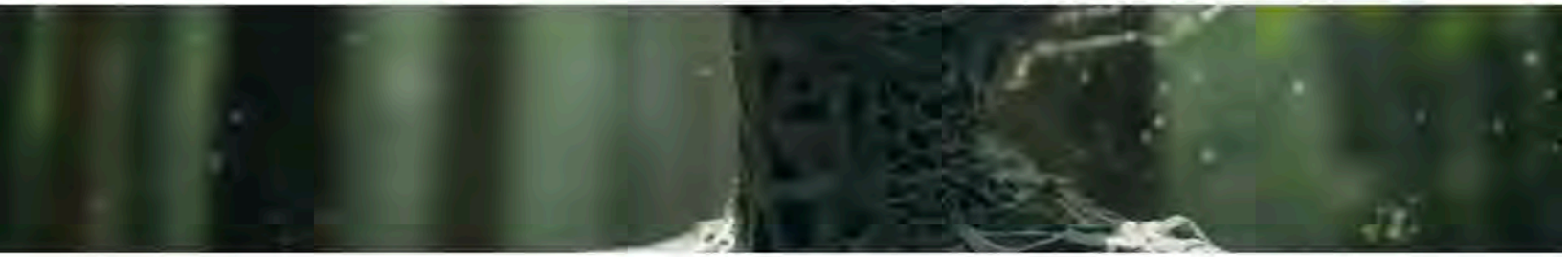
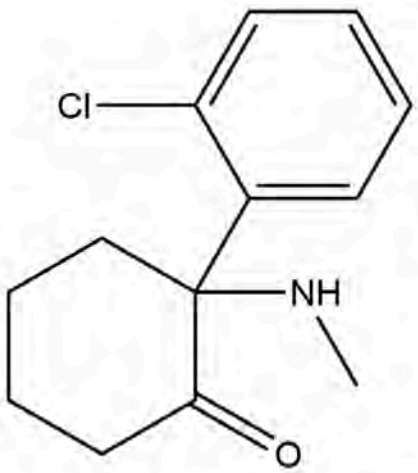


About 2F-NENDCK or "CanKet"

2F-NENDCK (short for 2-**f**luoro-***N***–**e**thyl**n**or**d**es**c**hloro**k**etamine, also known as CanKET, 2'-fluoro-2-oxo-PCE or 2-FXE) is a novel dissociative drug that was initially identified at the CanTEST health and drug checking service as well as a forensic laboratory in China.[1,2] After its identification by researchers at the Australian National University, 2F-NENDCK was initially called 2'-fluoro-2-oxo-PCE after which it became colloquially known as "CanKet" as in "Canberra ketamine".[1] Novel synthetic drugs like 2F-NENDCK are commonly referred to as "designer drugs" or "research chemicals". These drugs often have very little research into their safety and effects on humans, which is indeed the case for 2F-NENDCK.

At CanTEST, 2F-NENDCK has been found numerous times in samples that were expected to be ketamine.[3,4] According to CanTEST's final evaluation, only 57% of the 81 samples expected to be ketamine actually contained ketamine as of April 2023.[5] The remaining 43% of the 81 samples contained other dissociative drugs, including 2F-NENDCK, 2F-DCK, and tiletamine (a veterinary dissociative anaesthetic), as well as other psychoactive and non-psychoactive compounds.[3] According to DrugsData.org, a drug checking service in the US that analyses samples sent by mail, numerous samples sold as ketamine, FXE, 2F, MXE, 2F-DCK, and even heroin, fentanyl and ibogaine, actually contained 2F-NENDCK.[6]

If you suspect your ketamine may be adulterated or contain a different drug entirely, consider taking a



Ketamine

2F-NENDCK

Got a question ? Click here to ask.

Bis (2,2,6,6-tetramethyl-4-piperidyl) sebacate

Dispersions, Resins and Additives, North America

BASF
We create chemistry

TINUVIN® 770 DF

TINUVIN 770 DF is a solid basic hindered amine light stabilizer (HALS) developed for coating, adhesive and sealant applications. It is designed to meet durability requirements of all exterior solvent-based industrial coatings. It protects coatings against surface defects such as gloss reduction, cracking and chalking and it ensures the retention of mechanical properties. It is broadly compatible and can be easily incorporated to achieve long term light stabilization.

Product highlights

Good long term performance

Good thermal stability

Suggested applications:

- Industrial coatings
- Marine

UNC Samples

The live report linked below lists all the samples we have seen containing bis(2,2,6,6-tetramethyl-4-piperidyl) sebacate.

```
Data last updated on Tuesday, August 27, 2024.
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Hosted on Deepnote

```
Unique samples with substance: 122
We detected in 11 states: WI, ME, NC, NY, WA, OR, OH, MI, CA, NM and CO
```

Hosted on Deepnote

Thanks for your attention!

Newsletter, data, more…

Live Data Reports

go.unc.edu/drugsupply