

A Look at Hepatitis C, Drug Use Trends, and Implications

Where Do We Go From Here?

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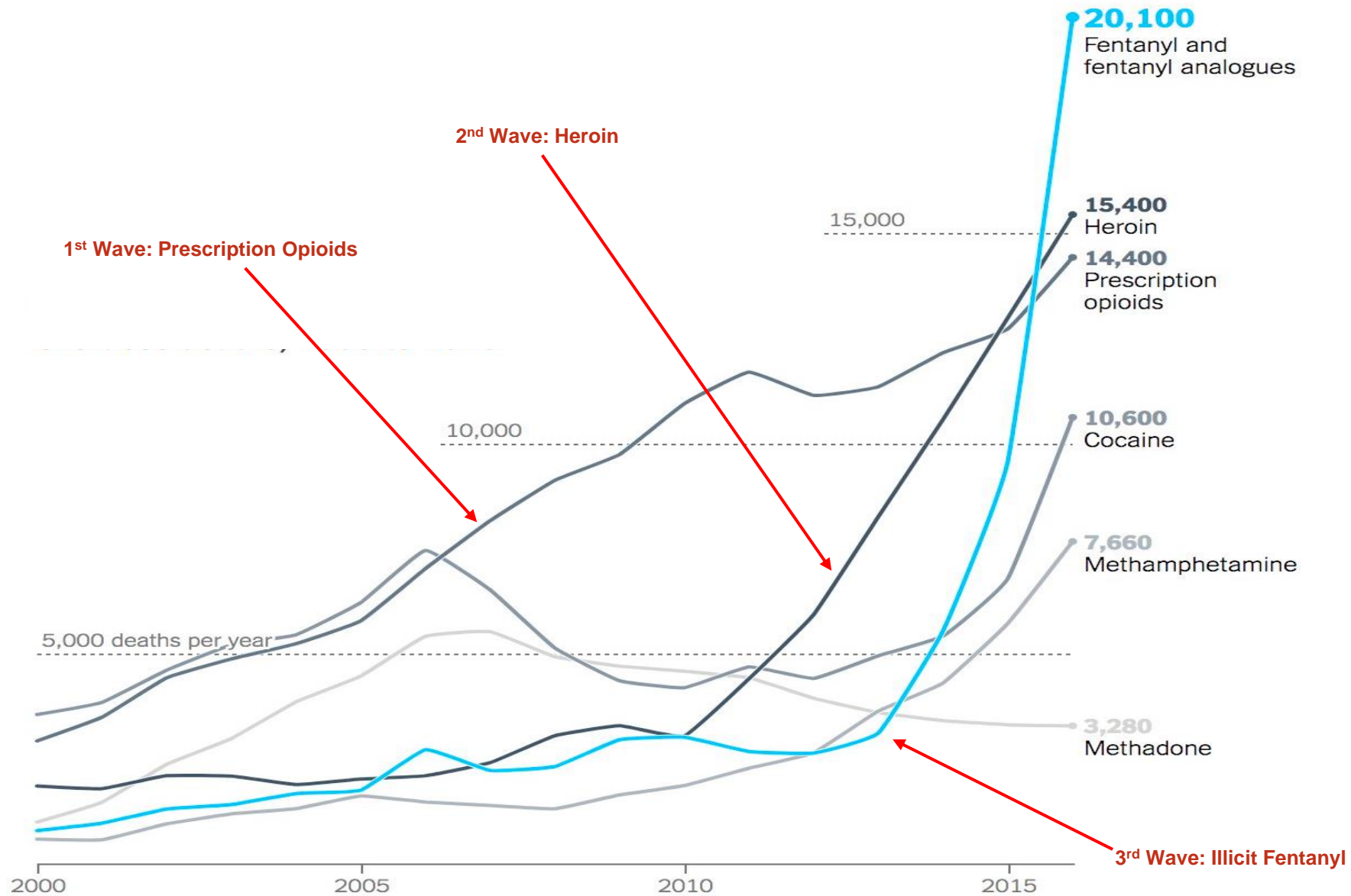
RTI International

Atlanta, GA

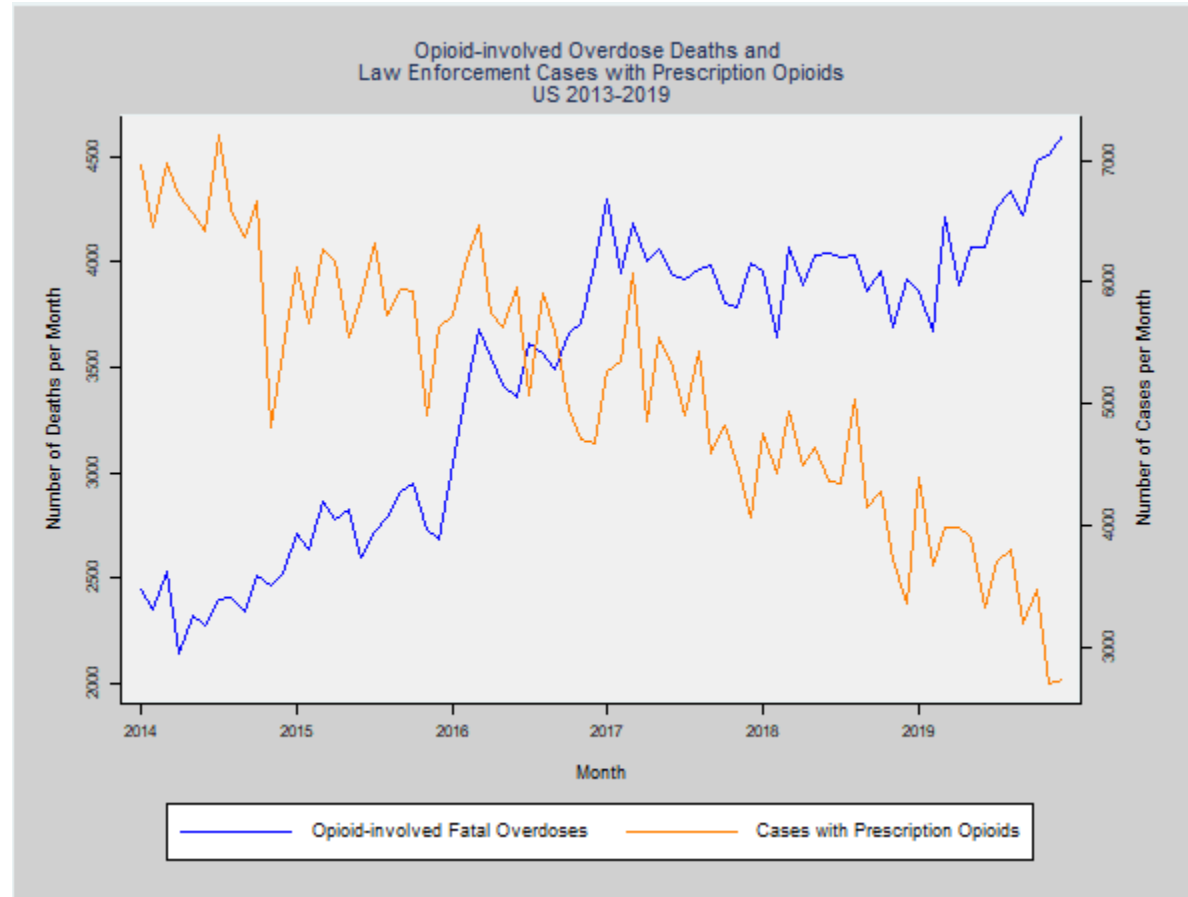
Investigating the Behavioral & Health Impacts of the Illicit Drug Supply

Illicit drug market → drug use behavior → health outcomes

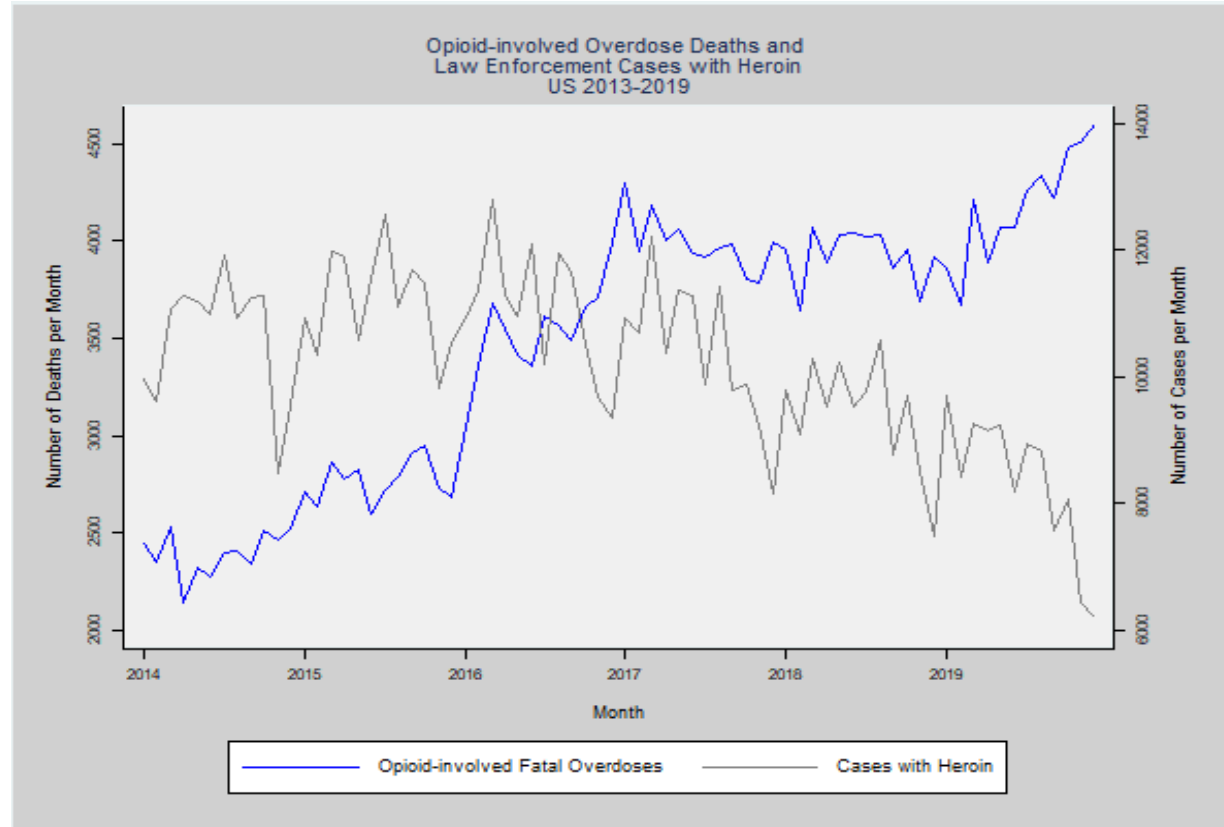
Drugs Involved in OD Deaths, U.S., 2000-2016*



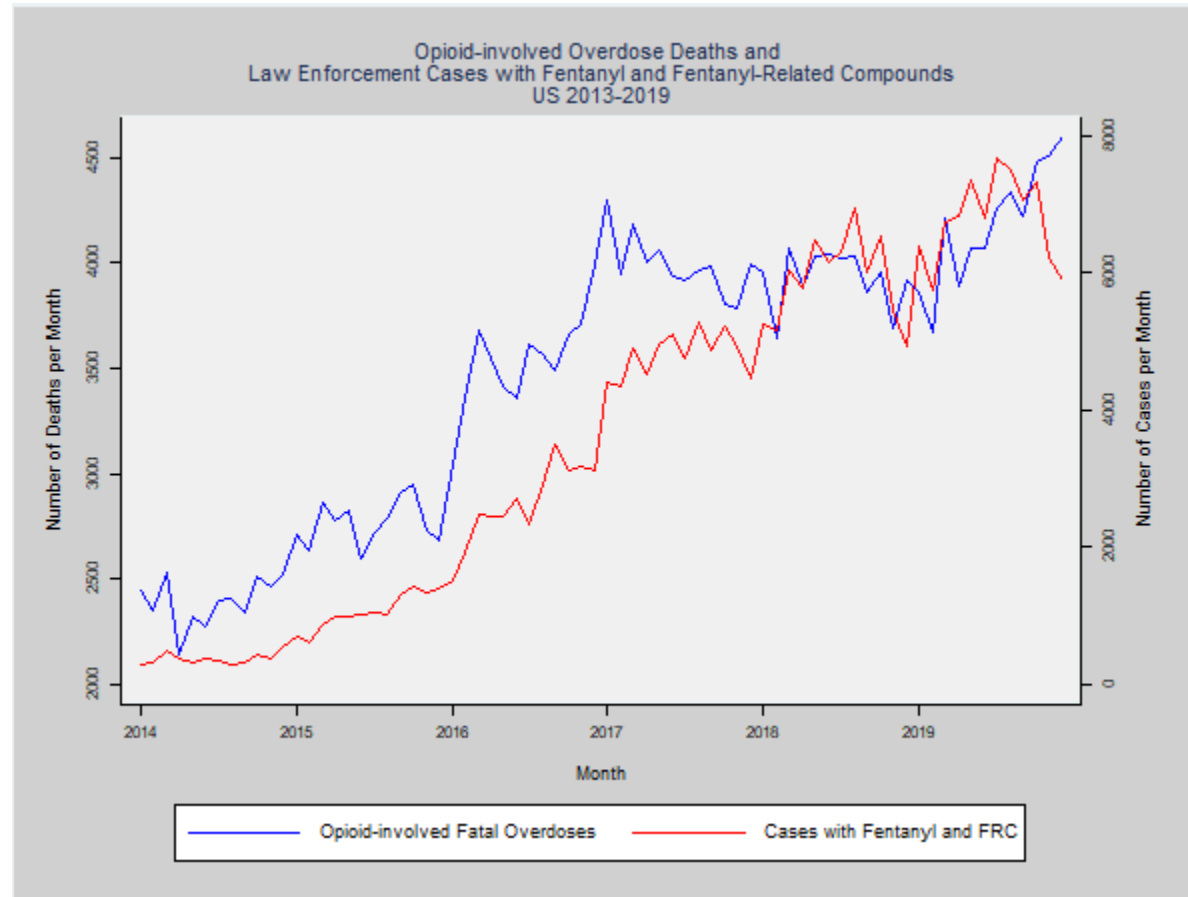
Opioid-Involved OD Deaths & Law Enforcement Cases with Prescription Opioids, United States, 2014-2019



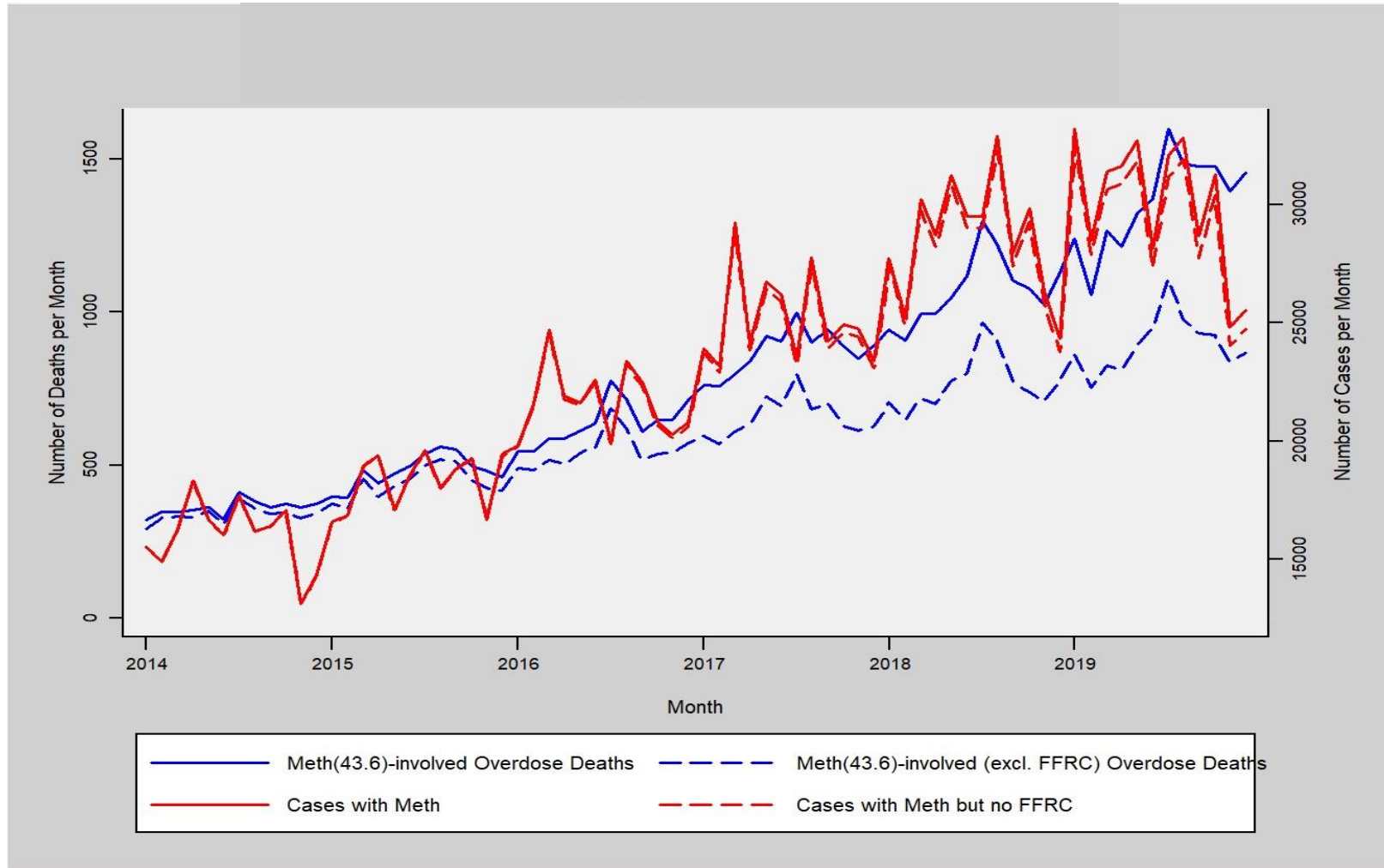
Opioid-Involved OD Deaths & Law Enforcement Cases with Heroin, United States, 2014-2019



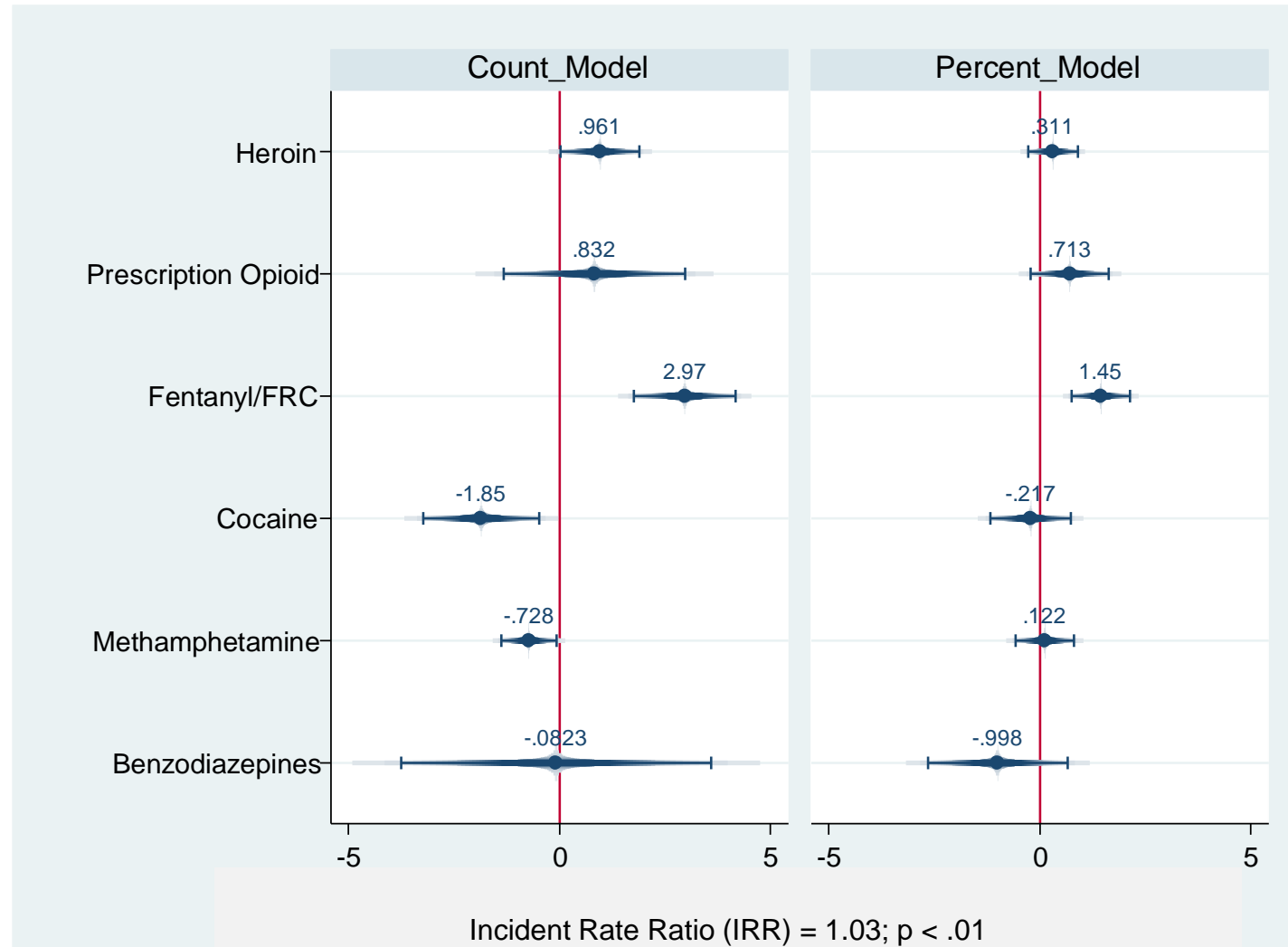
Opioid-Involved OD Deaths & Law Enforcement Cases w/ Fentanyl & Fentanyl Related Compounds, US, 2014-2019



Opioid-Involved Overdose Deaths and NFLIS* Cases with Methamphetamine, U.S., 2014–2019



Count and Percent Change in Opioid Involved Overdose Deaths per 100,000 Persons by Drug Exhibits, U.S., 2014–2019*



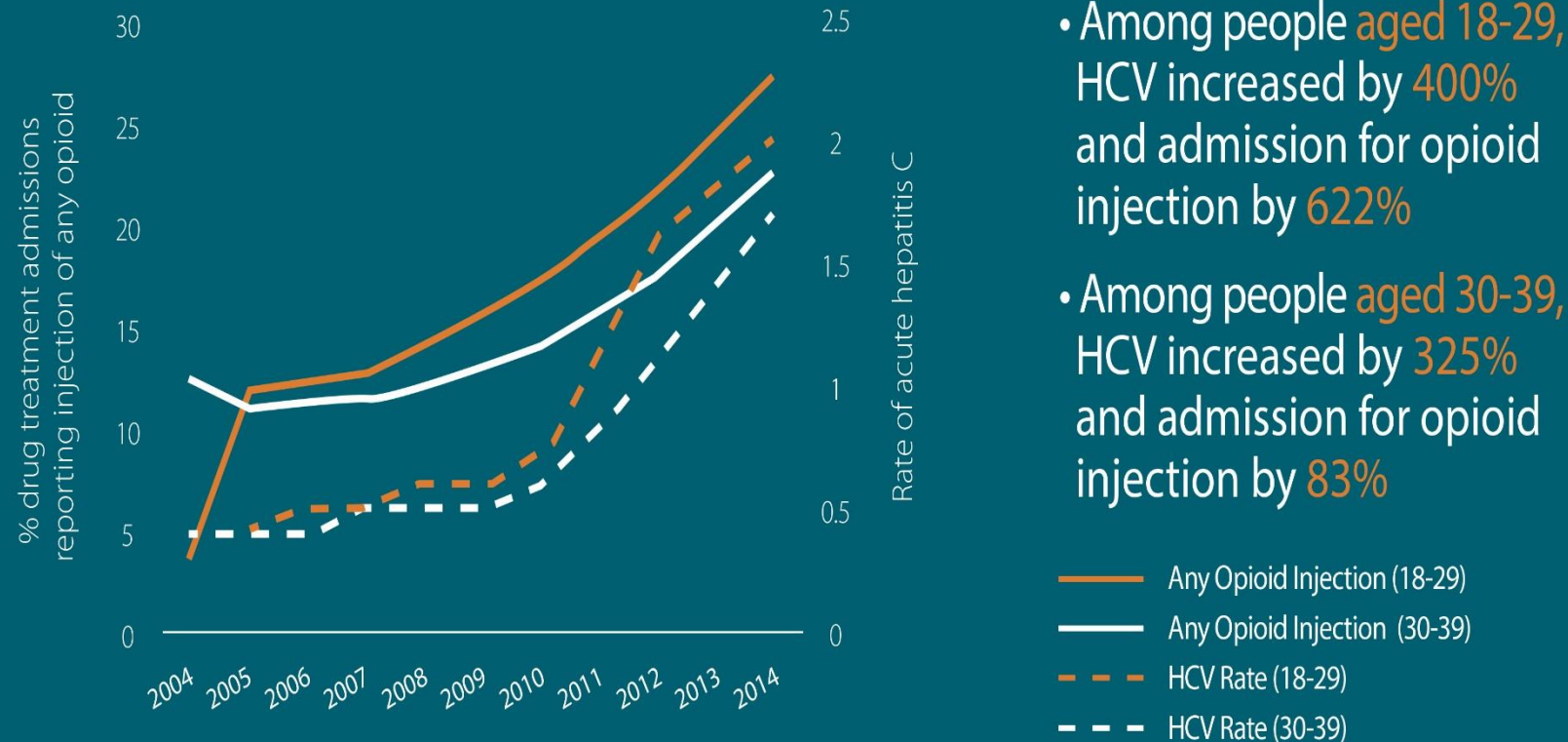
*Results for NFLIS Drug exhibits from state-quarter difference-in-differences models

Estimated number of people who inject drugs in the United States

- ❑ The first update to the number of people who inject drugs in the U.S. in nearly ten years.
- ❑ There were an estimated **3,694,500 PWID in the U.S. in 2018**
 - (95% CI: 1,872,700–7,273,300)
 - 1.46% of the adult population (95% CI: 0.74% – 2.87%)
- ❑ From 1.5 million in 2012 to more than 3.5 million in 2018
- ❑ Findings suggest the population size of PWID has substantially grown in the past decade
- ❑ The estimated prevalence of injection drug use was highest among:
 - male persons (2.1%; 95% CI: 1.1–4.2%)
 - non-Hispanic White persons (1.8%; 95% CI: 0.9–3.6%)
 - adults aged 18–39 years (1.8%; 0.9–3.6%)

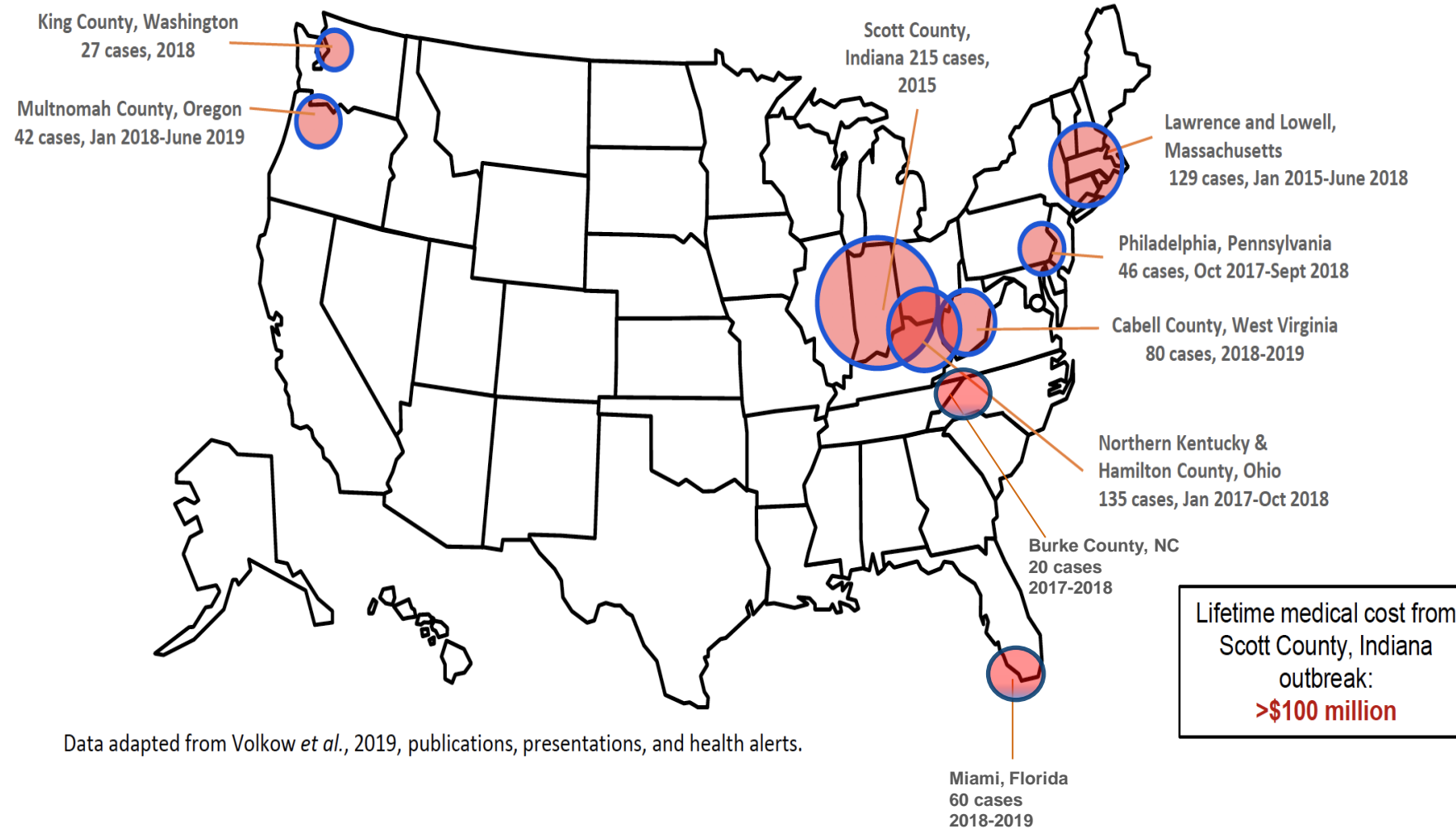
CDC Report on Hepatitis C and Opioid Injecting

HEPATITIS C AND OPIOID INJECTION ROSE DRAMATICALLY IN YOUNGER AMERICANS FROM 2004-2014



Source: Centers for Disease Control and Prevention and Substance Abuse and Mental Health Services Administration

Increasing HIV Cluster Outbreaks among PWID in the U.S.

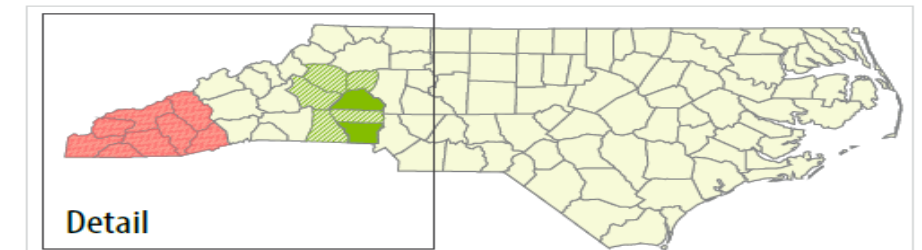
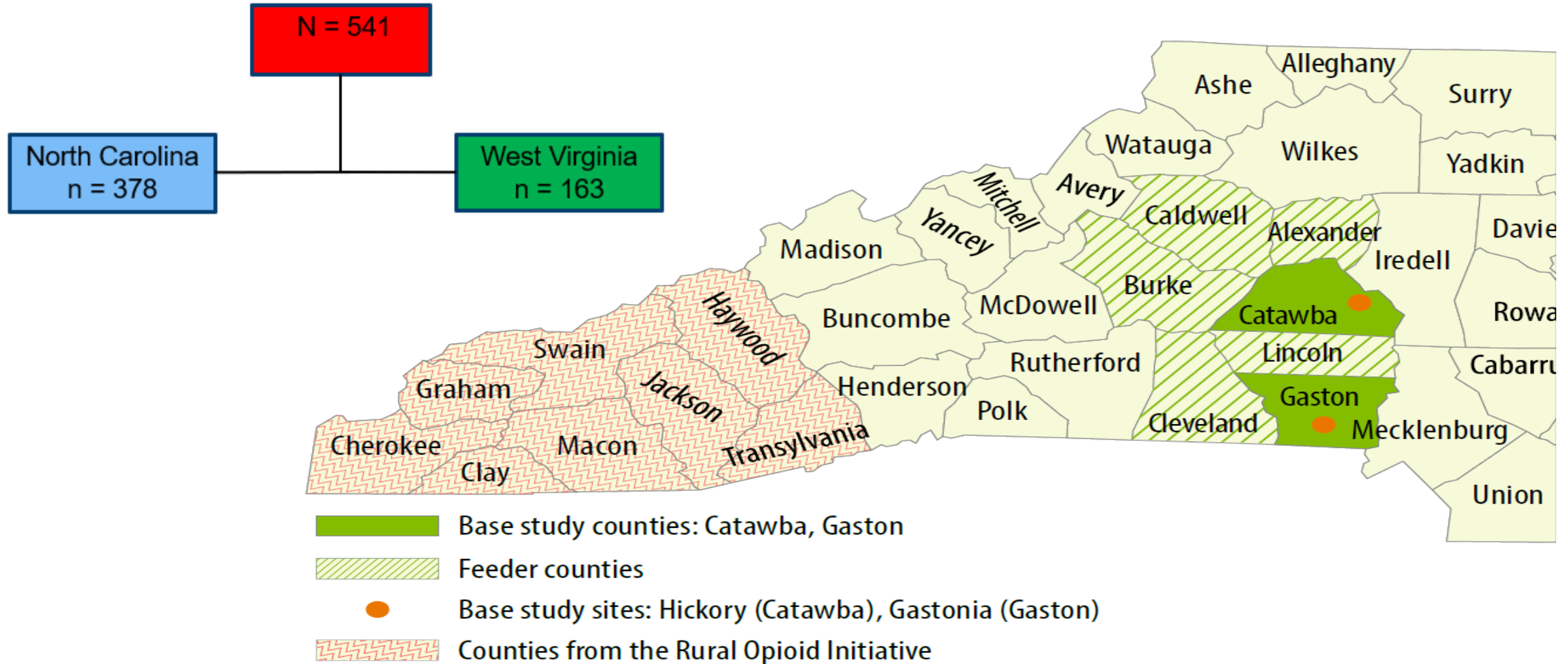


Data adapted from Volkow *et al.*, 2019, publications, presentations, and health alerts.

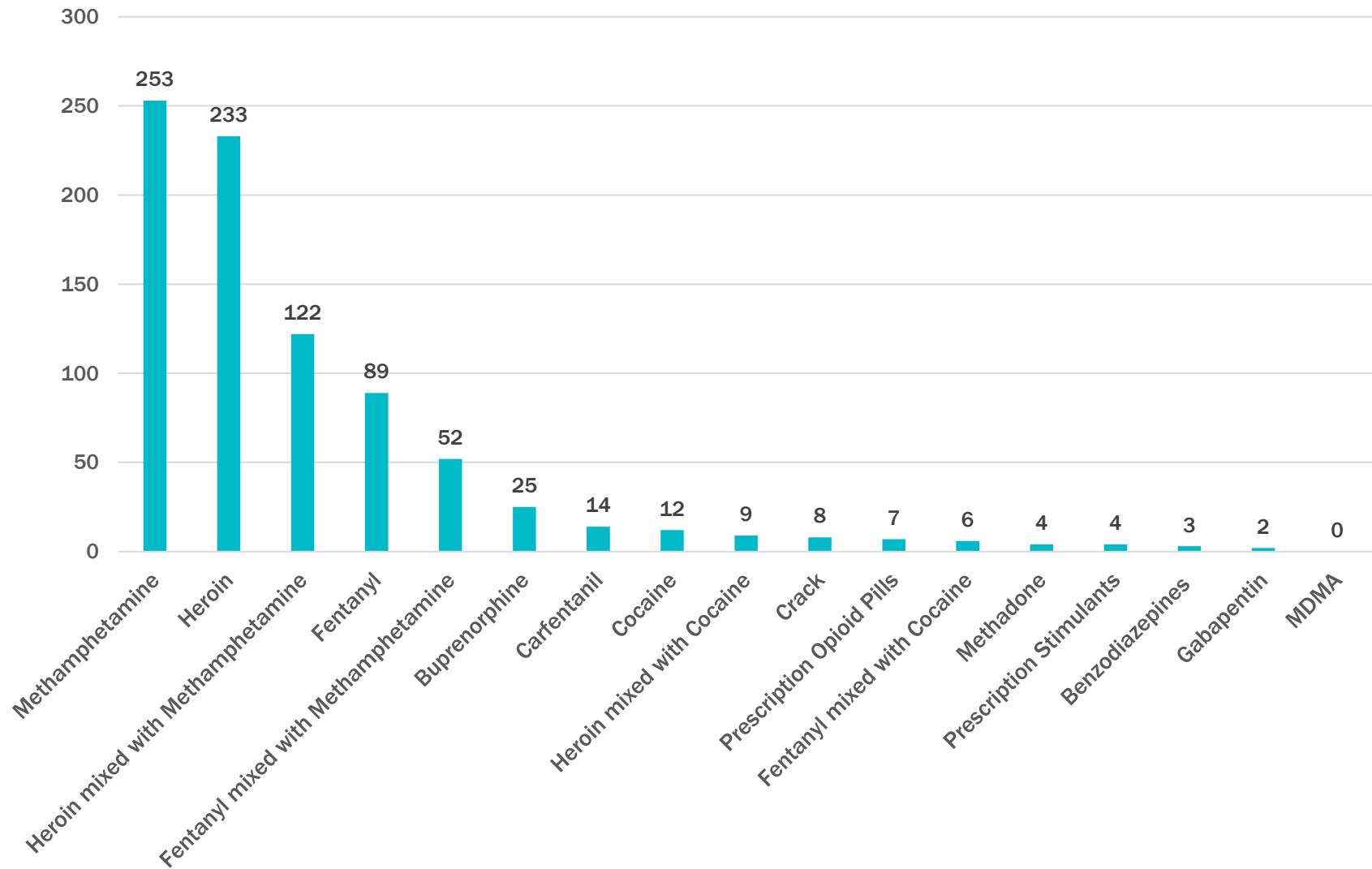
Evolving Drug Landscape Associated with HCV Epidemic & HIV Cluster Outbreaks

- **[2012] MMWR** identified increasing HCV infections among young (<30 yrs.) persons who inject drugs in KY, WV, VA, TN
 - Cases associated with injection of prescription opioids
 - Urban and Rural Increases
- **[2016] CDC Report** linked HCV epidemic to the Growing Opioid Epidemic
 - Cases associated with the injection of prescription opioids and heroin
- **[2016] HIV Outbreak** in Scott County, Indiana
 - HIV infections linked to the injection of oxymorphone (*MIPIE* behavior)
 - 98.5% of newly HIV infected persons were co-infected with HCV
- **[2015-2019] HIV Cluster Outbreaks** in Eastern Regions of US
 - Linked to fentanyl and illicit stimulants
- **[2019-2020] Acute HCV Outbreak**, Upstate NY.
 - Cases linked to the injection of methamphetamine
 - Injection of methamphetamine is a developing constant in HCV/HIV outbreaks post-2018

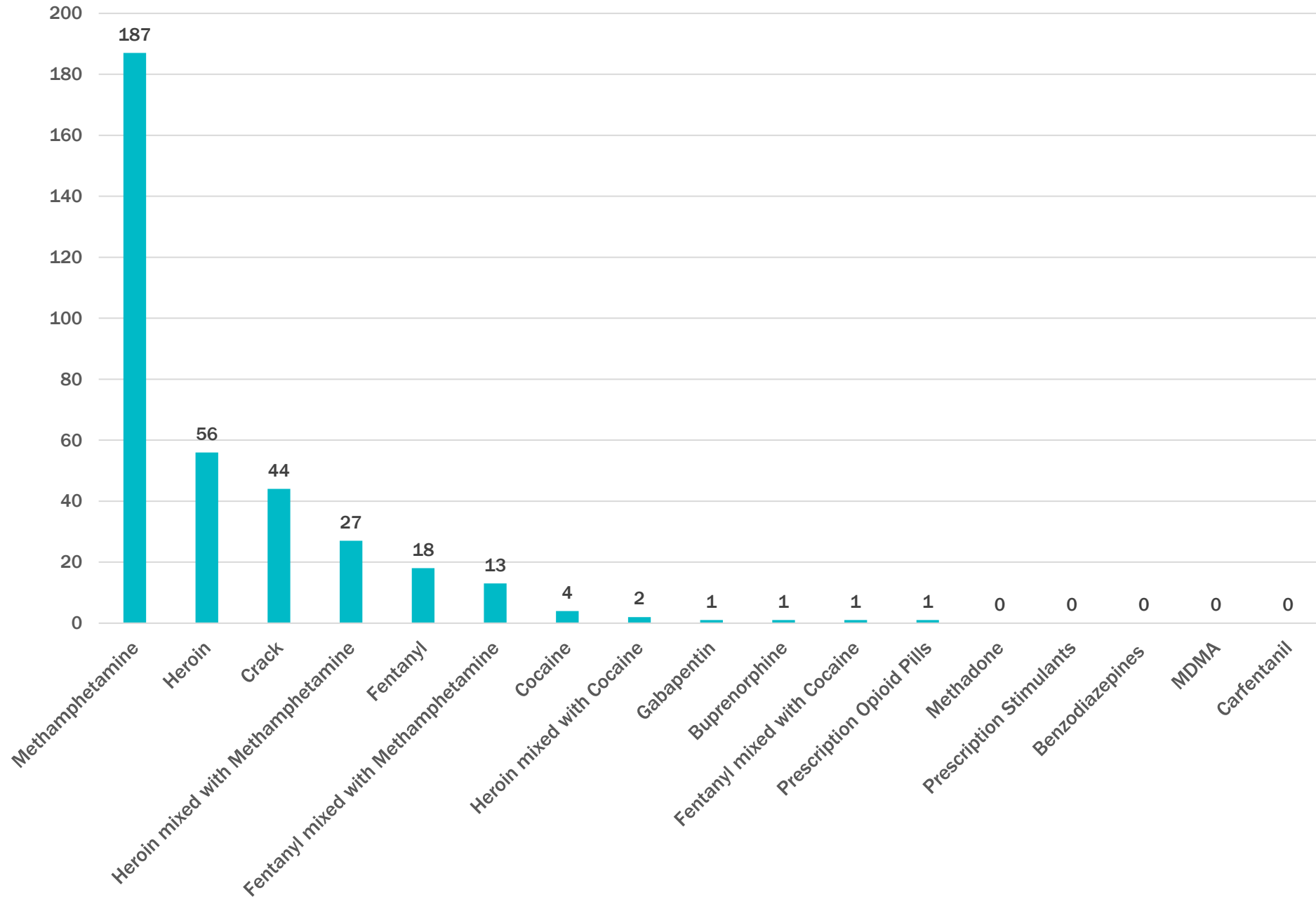
Fentanyl Test Strip Study in NC and WV



FTS Study, Past 30-Day Injection by Drug, NC, 2022, @Baseline (N=378)



FTS Study, Drugs Smoked Past 30 Days, NC, 2022, @Baseline (N=372)



Past 30-Day Use of Heroin, Fentanyl, and Meth (N=541), Baseline Findings, FTS Study, NC & WV, 2022

	All (N=541)	
	Freq (%)/ Mean(SD)	
Used Fentanyl but no Heroin in past 30 days	33	(6.1)
Used Heroin but no Fentanyl in past 30 days	170	(31.4)
Used Both Fentanyl and Heroin in past 30 days	214	(39.6)
Used Fentanyl but no Methamphetamine in past 30 days	18	(3.3)
Used Methamphetamine but no Fentanyl in past 30 days	237	(43.8)
Used Both Fentanyl and Methamphetamine in past 30 days	229	(42.3)
Prefer Fentanyl over Heroin	39	(7.2)
Prefer Heroin over Fentanyl	298	(55.1)
Prefer Both Fentanyl and Heroin in Combination	72	(13.3)

A New Fentanyl Risk Environment:

Highlights from Interviews with People who Inject Drugs (PWID) in NC

Respondents detected rapid changes to the illicit opioid market using physical and physiological indicators.

PWID reported that, compared to heroin, fentanyl causes a stronger rush, a shorter high, and heavier sedation

"Fentanyl makes you nod out real bad. Regular heroin does that too, but the fentanyl is a lot stronger"

"Fentanyl hits you right away, but it doesn't last . . . If you got something that lasts for more than 10 minutes, you found some really amazing shit"

Fentanyl saturation of the illicit opioid market directly contributed to changes in drug use behavior

Because of fentanyl's shorter high, PWID are injecting more frequently to maintain the opioid effects

Many respondents reported modifying their method of consumption from injecting to smoking or snorting

"The fact that I have to inject more is tearing my veins up. It's harder to find places to shoot and I'm losing sensation in my fingers; my legs now swell because I'm using the veins in my legs"

PWID reported increasingly using illicit stimulants to combat the unwanted heavy sedation of fentanyl

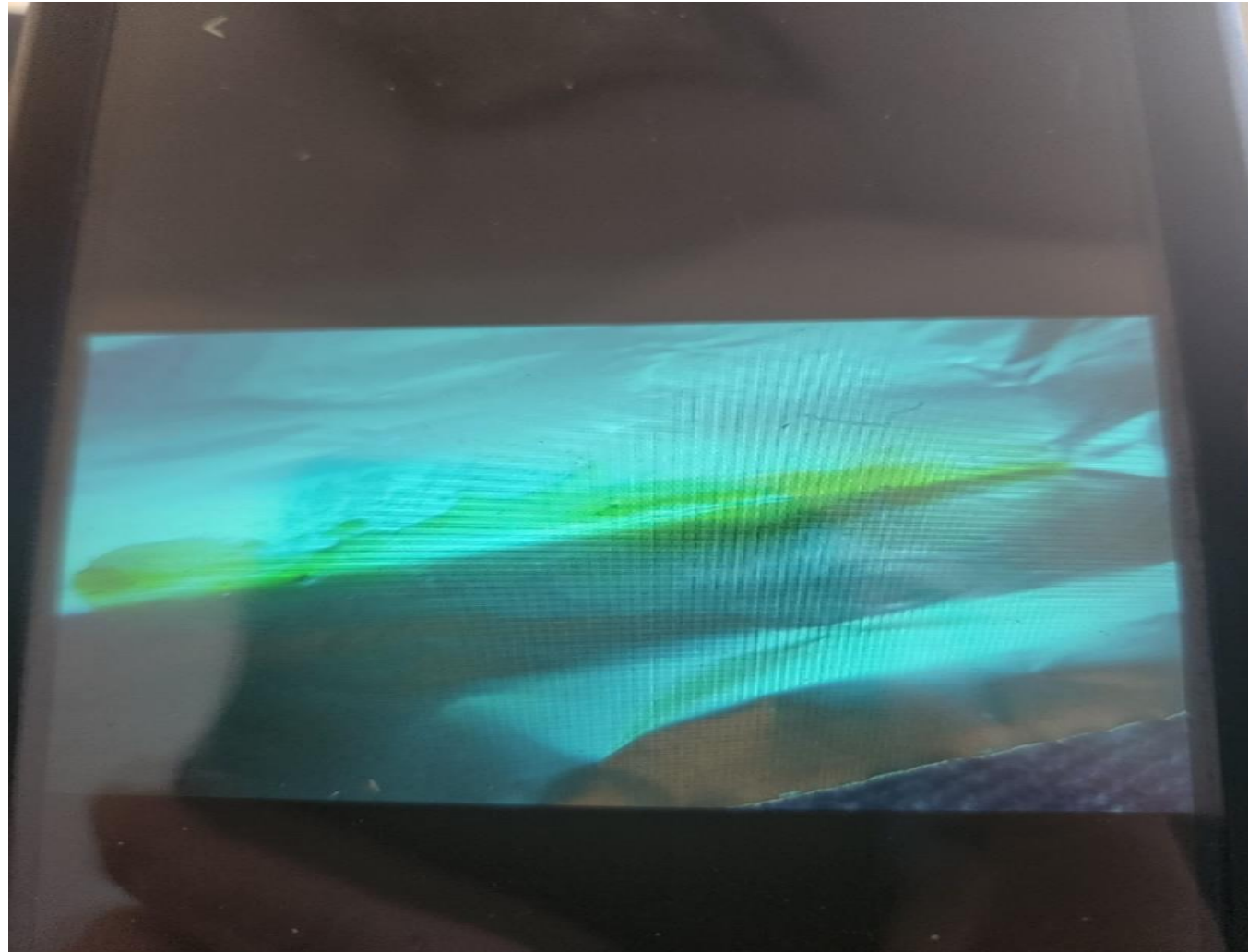
"These days the meth I do to counteract the sedation of fentanyl"

72%
of respondents reported co-using crack/cocaine with opioids

44%
reported co-using methamphetamine and opioids

PWID reported increasingly using gabapentin, primarily to ease opioid withdrawal symptoms but also to potentiate the opioid high

Fentanyl under black light on foil after heat has been applied and the oil has run



Changing Supply of Methamphetamine in NC, 2022

"I only use meth these days. The fatty doesn't even get me high—just makes me sleep."
So what's the fuckin' point, right? (Female, 36)

I still inject meth but it's not the same as it was back in the day. It makes me sleepy. We call it 'sleepy meth' around here. (Male, 44)

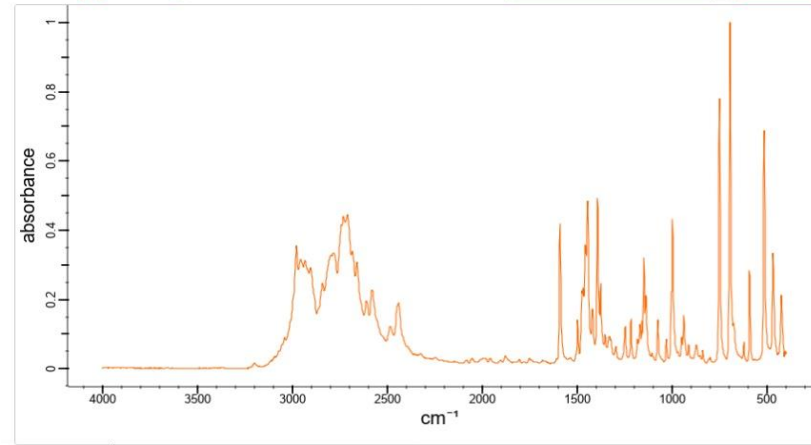
The meth has changed around here, man, over the last bunch of years. It used to be fire; \$20 would keep you up for days. Now I can do a \$20 shot and fall asleep. It's fucked up. Feels like fentanyl or some other 'down' is in it. (Male, 52)

People are making meth out of ant and roach spray. They're called 'waspsers.' They take a screen and spray the bug spray on it and then electrocute it with battery cables. Makes it turn to crystals and it looks just like ice. The shit is fucking people up, too. I have seen people have mental breaks after slammin' and never come back from it. (Female, 32)

Different Forms of 'Methamphetamine' in the Illicit Drug Supply

Attenuated Total Reflectance Infrared (ATR-IR) Spectrum

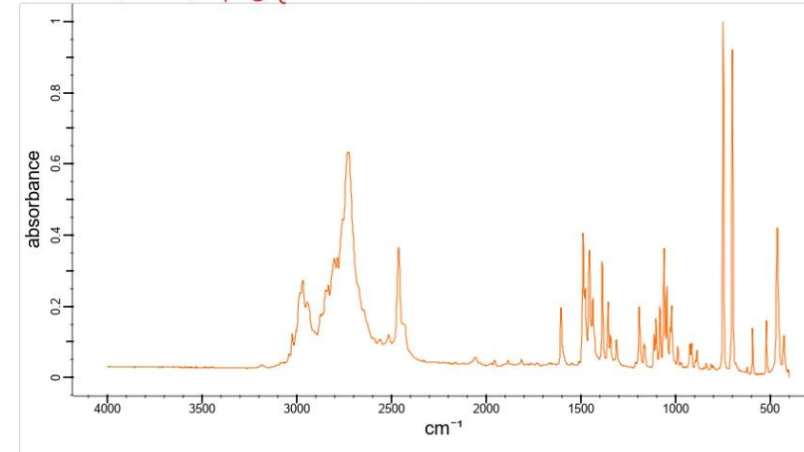
N-iso HCl



N-isopropylbenzylamine HCL

Attenuated Total Reflectance Infrared (ATR-IR) Spectrum

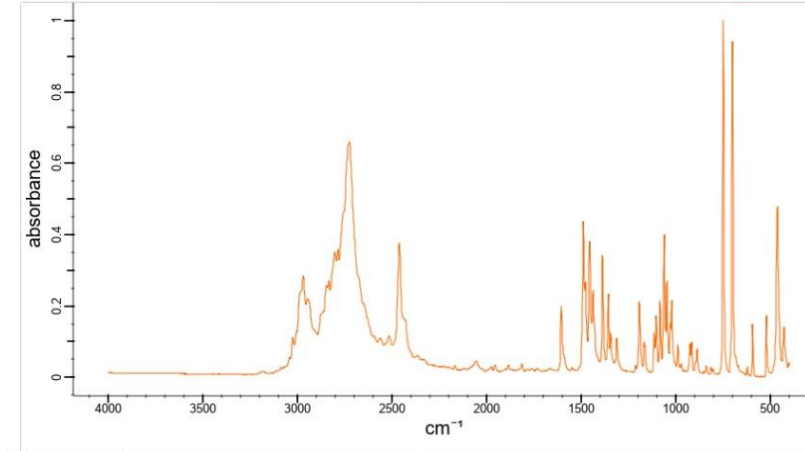
D-Meth HCl



Dextromethamphetamine HCL

Attenuated Total Reflectance Infrared (ATR-IR) Spectrum

DL-Meth HCl



Levomethamphetamine HCL

Methamphetamine and Sex

With some of the girls I hang with it's understood that we fuck right after getting high. The meth makes them instantly wet. I mean you can see it through their pants right after [they inject]. I'm not fucking with you, man. I've seen it. (Male, 47)

Folks are having a lot more sex these days because of the meth. Guys are even having sex with other guys who never showed signs of wanting men before. The meth is turning them feminine; I swear. They are tricking other men and some women are even pimping them out. There is no question in my mind that it's the meth. It is removing all inhibitions (Female, 39)

When I do meth, I hate to say it, but I just wanna fuck. It hits me real hard, and I get horny as fuck. I will invite girls over to get high and we both know what we are going to do after [using]. We both want it but I always seem to want it more. (Male, 48)

A Rapidly Changing Risk Environment

- **Surging rates of illicit stimulant use** are occurring across the US
 - ❑ 4th wave of opioid epidemic
 - ❑ Linked to combatting fentanyl's heavy sedation
- **Methamphetamine is contributing to increases in both injection-related risk and sexual activity among PWID.**
 - ❑ Increased risk of sex-related infections (e.g., syphilis, HIV infection)
 - ❑ Increases in transactional sex
 - ❑ Sex-acquired HIV infections may facilitate virus entry into social networks of PWID wherein injection drug use serves to facilitate rapid community spread
- **Injections of fentanyl and illicit stimulants** are contributing to higher injection frequency
 - ❑ Increased risk for infectious disease (bacterial and viral)
 - ❑ Increase in skin and soft tissue infections
- **Shifting HCV risk** may be proxy for increasing injection-related HIV risk
 - ❑ Recent reports show a shift from prescription opioids and heroin associated with HCV infection to methamphetamine and fentanyl
 - ❑ Numerous HIV outbreak investigations report methamphetamine as the main drug injected by newly-infected persons

Distinguishing HCV Epidemic as a Health Crisis from a Public Health Epidemic

- ❖ **The largest population burden for chronic HCV infection** are among persons born between 1945 and 1965 commonly known as the *Birth Cohort*. This population needs to be treated to reduce HCV-related morbidity and mortality
- ❖ Yet, **most of this population *does not* currently inject drugs**. The Birth Cohort is not the source of new infections and not an active component of the current public health crisis
- ❖ People who actively inject drugs present **the largest population of acute and recent infections**. This population needs to be treated if we are to stop incident infections and achieve *HCV elimination*
- ❖ We therefore **need a plan to reach and treat the population of PWID** for HCV infection, but we also need to retain them into care to monitor and treat other drug-related health outcomes

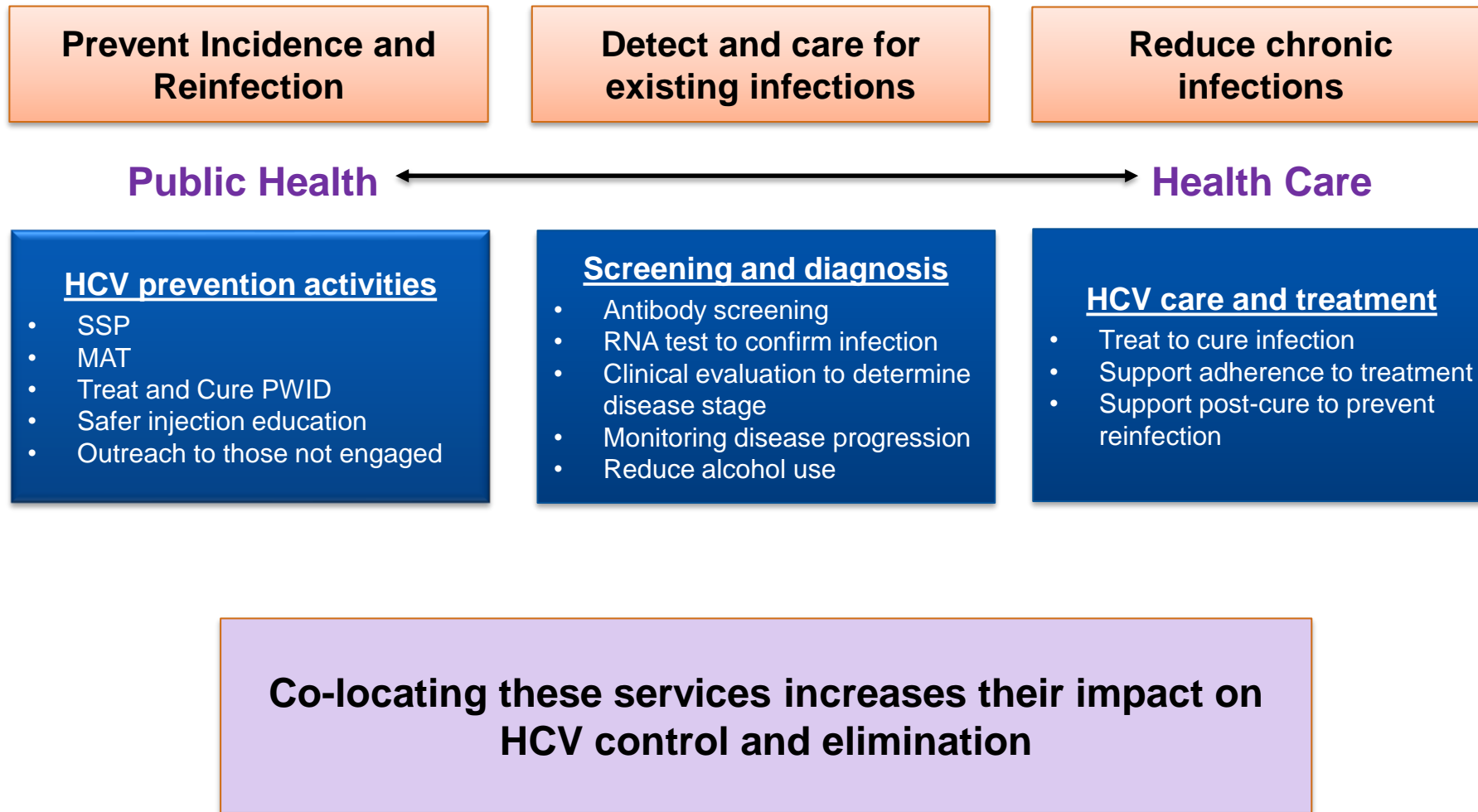


SUPPLEMENT ARTICLE

Recommendations for the Management of Hepatitis C Virus Infection Among People Who Inject Drugs

Geert Robaeys,^{1,2,3,a} Jason Grebely,^{4,a} Stefan Mauss,⁵ Philip Bruggmann,⁶ Joseph Moussalli,^{7,8} Andrea De Gottardi,⁹ Tracy Swan,¹⁰ Amber Arain,^{1,3} Achim Kautz,¹¹ Heino Stöver,¹² Heiner Wedemeyer,¹³ Martin Schaefer,^{14,15} Lynn Taylor,¹⁶ Markus Backmund,^{17,18} Olav Dalgard,¹⁹ Maria Prins,^{20,21} and Gregory J. Dore;^{4,22} on behalf of the International Network on Hepatitis in Substance Users

Strategic Model of HCV Prevention and Control for PWID



Multi-Component Interventions (MCI)

- An approach to risk reduction where programs are combined as “packages” and offered concurrently in the form of a “one-stop shop.”
 - ❖ Syringe service program with HCV/HIV testing; linkage to health care; naloxone, safer injection education; Fentanyl Test strips, hepatitis A/B vaccines; PReP, etc.
- Rather than providing one service at a time, MCI incorporates myriad services simultaneously, increasing the likelihood that PWID will traverse health services based on the status of their drug use—not by disease risk or disease status.
- MCI shown to reduce:
 - Injecting Risk
 - New HIV and HCV infections
 - HCV Re-infection

Syringe Services Programs: Vital Part of Efforts to Combat Opioid, HIV, and Hepatitis Epidemics

What is an SSP? A community-based program that provides key pathway to services to prevent drug use, HIV, and viral hepatitis



Free sterile needles and syringes



Safe disposal of needles and syringes



Referral to mental health services



Referral to substance use disorder treatment, including medication-assisted treatment



HIV and hepatitis testing and linkage to treatment



Overdose treatment and education



Hepatitis A and B vaccination



Other tools to prevent HIV and hepatitis, including counseling, condoms, and PrEP (a medicine to prevent HIV)



SSPs DON'T increase illegal drug use or crime but DO reduce HIV hepatitis risk.

Syringe services programs: <http://bit.ly/2dhkAsq>

Find an SSP: <http://bit.ly/2dhktgB>

**HIV diagnoses are down among PWID.
More access to SSPs could help reduce HIV and hepatitis further.**

PWID - People who inject drugs

SOURCE: Vital Signs, December 2016

Integrating SSPs with Low Threshold Medical Services

- National support for SSPs at all-time high due to the current opioid epidemic and its democratizing of drug-related harm
- Syringe service programs provide direct health services to PWID without requiring abstinence as a precondition to receive services
- SSPs are now located in states hardest hit by the opioid epidemic
- SSPs reduce stigma. They have gained trust with PWID and staff can transfer this “street cred” to medical professionals when forming partnerships
- SSPs are the only programs with deep reach into networks of persons who actively inject drugs community, relationships that are required if we are to effectively test, treat, and cure enough PWID to achieve the goal of HCV elimination in the U.S. by 2030
- Harm reduction providers are forming partnerships with NPs and PAs to coordinate co-localization of treatment services and improve access to comprehensive health care for people who use drugs

Growing incidence of novel and severe wounds among PWID is an **emerging** public health crisis

- Lost among skyrocketing OD deaths is an alarming burden of IWSSTIs and invasive bacterial infections among PWID
- Abscesses and bacterial infections have been a concern for PWID for decades but factors driving recent increases in prevalence and change in characteristics are poorly understood
- The *Evolving and Emerging Drug Threats* Committee of the Office of National Drug Control Policy recently listed xylazine as an emerging threat based on the criterion “novel clinical illness [*read*: chronic wounds] by suspected exposure to a drug.”
- In this era of increasing contamination of the illicit drug supply with novel and synthetic drugs, a new public health crisis is emerging.

Emerging Synthetic Drug Crisis Involving Sharp Increases in Novel Psychoactive Substances in the Illicit Opioid Market

[Politics](#)[World](#)[Culture](#)[Events](#)[Shop](#)[Current Issue](#)

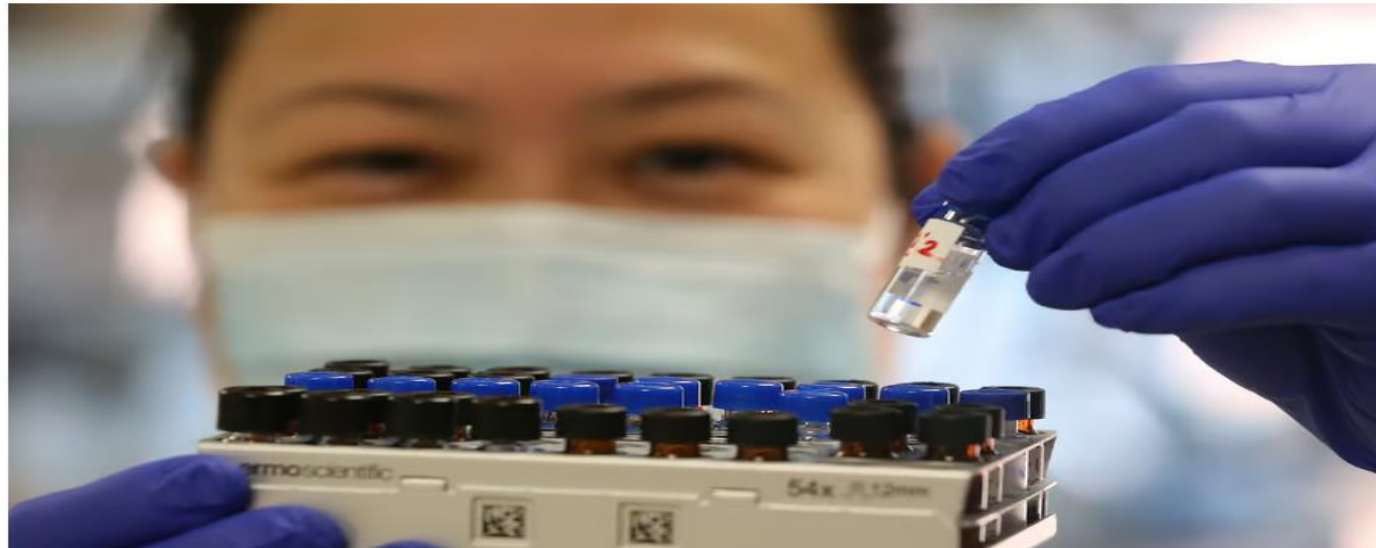
DRUG WAR AND DRUG POLICY DRUG TESTING ILLICIT DRUGS

Synthetic Drugs Are Sending the Overdose Crisis Into Overdrive

US policy is keeping public health officials, scientists, and emergency-room doctors in the dark about a growing manufactured plague.

By Joseph Friedman and Eric Reinhart

AUGUST 9, 2022

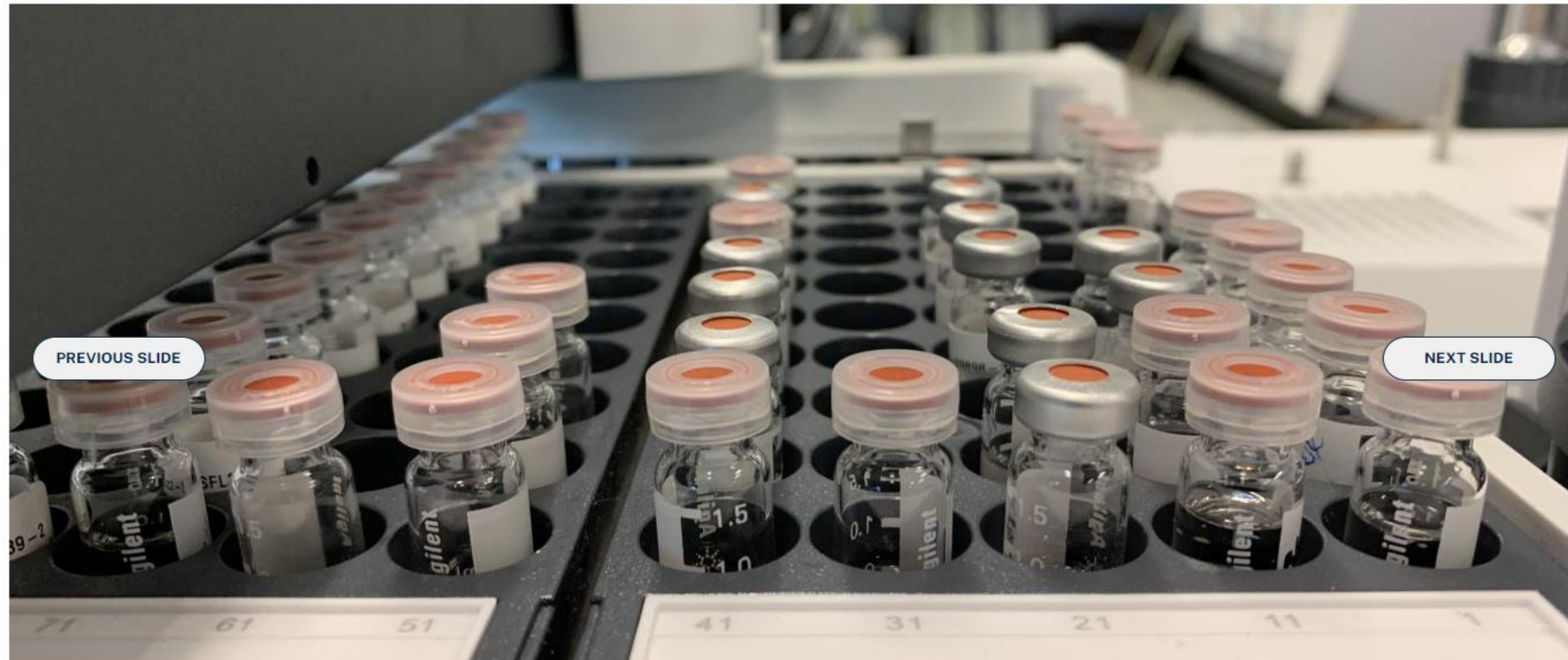


Sharp Increases in Novel Illicitly Manufactured Fentanyls, 2015-2017

- **2015: 524** Fentanyl Law Enforcement Exhibits
 - 524 fentanyl
 - 160 fentanyl analogs (**4 distinct analogs**)
 - 8 exhibits of 4-ANPP (fentanyl precursor chemical)
- **2016: 877** Fentanyl Law Enforcement Exhibits
 - 877 fentanyl
 - 409 fentanyl analogs (**15 distinct analogs**)
 - ~60% of substance were seized and reported for the first time
- **2017: 1873** Fentanyl Law Enforcement Exhibits
 - 1873 fentanyl
 - 952 fentanyl analogs* (**17 distinct analogs**)
 - ~117% increase in identification from 2016-2017
 - 7 substance seized and identified for the first time
 - 81 exhibits of 4-ANPP (fentanyl precursor chemical)

New, Dangerous Synthetic Opioid in D.C., Emerging in Tri-State Area

DEA Washington, DC Division - Public Information Office



The DEA Washington Division is warning area residents of a new drug, emerging in the D.C. metropolitan area that is as dangerous and deadly as fentanyl.

This week, the DEA Washington Division brought local news outlets into their regional laboratory to see and discuss a dangerous class of drugs they are seeing emerge in the region--nitazenes. A drug that was never approved for medical use, nitazenes are being sourced from China and being mixed into other drugs.

[Isotonitazene \(aka nitazene or "ISO"\)](#) is a particular synthetic opioid the DEA is seeing move into the area.





Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™



Morbidity and Mortality Weekly Report (*MMWR*)

Notes from the Field: Illicit Benzodiazepines Detected in Patients Evaluated in Emergency Departments for Suspected Opioid Overdose — Four States, October 6, 2020–March 9, 2021

Weekly / August 27, 2021 / 70(34);1177–1179

Kim Aldy, DO^{1,2}; Desiree Mustaquim, PhD³; Sharan Campleman, PhD¹; Alison Meyn, MPH¹; Stephanie Abston¹; Alex Krotulski, PhD⁴; Barry Logan, PhD^{4,5}; Matthew R. Gladden, PhD³; Adrienne Hughes, MD⁶; Alexandra Amaducci, DO⁷; Joshua Shulman, MD⁸; Evan Schwarz, MD⁹; Paul Wax, MD^{1,2}; Jeffrey Brent, MD, PhD¹⁰; Alex Manini, MD¹¹; the Toxicology Investigators Consortium Fentalog Study Group ([VIEW AUTHOR AFFILIATIONS](#))

FDA alerts health care professionals of risks to patients exposed to xylazine in illicit drugs

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[11-8-2022] Health care professionals should be cautious of possible xylazine inclusion in fentanyl, heroin, and other illicit drug overdoses, as naloxone may not be able to reverse its effects. FDA is aware of increasing reports of serious side effects from individuals exposed to fentanyl, heroin, and other illicit drugs contaminated with xylazine.

Xylazine is FDA-approved for use in animals as a sedative and pain reliever. Xylazine is not safe for use in humans and may result in serious and life-threatening side effects that appear to be similar to those commonly associated with opioid use, making it difficult to distinguish opioid overdoses from xylazine exposure. However, we do not know if side effects from xylazine exposure can be reversed by naloxone. Since we do not know if reversal agents regularly used in veterinary medicine (e.g., yohimbine hydrochloride, tolazoline hydrochloride) are safe or effective in humans, they should not be used.

Routine toxicology screens do not detect xylazine, and additional analytical techniques are required to detect xylazine when it might be involved in illicit drug overdoses, particularly when there are other signs or symptoms of xylazine exposure.

Health care professionals should continue to administer naloxone for opioid overdoses and consider xylazine exposure if patients are not responding to naloxone or when there are signs or symptoms of xylazine exposure (e.g., severe, necrotic skin ulcerations). Health care professionals should provide appropriate supportive measures to patients who do not respond to naloxone.

FDA issued a letter to stakeholders providing clinical information about the risks of

CDC: Xylazine Detection & Involvement in OD Deaths, US, 2019

Morbidity and Mortality Weekly Report

Notes from the Field

Xylazine Detection and Involvement in Drug Overdose Deaths — United States, 2019

Mbabazi Kariisa, PhD¹; Priyam Patel, MSPH^{1,2};
Herschel Smith, MPH^{1,2}; Jessica Bitting, MS^{1,3}

Xylazine is a drug used in veterinary medicine as an animal sedative with muscle relaxant and analgesic properties (1). It is not approved by the Food and Drug Administration for use in humans, in whom it acts as a central nervous system depressant and can cause respiratory depression, slowed heart rate, and hypotension (2). When used as a toxic adulterant in illicitly produced opioids such as fentanyl or heroin (3), xylazine might potentiate sedation and respiratory depression, increasing the risk for fatal overdose. In addition, because xylazine is not an opioid, it does not respond to opioid reversal agents such as naloxone; therefore, if illicit opioid products containing xylazine are used, naloxone might be less effective in fully reversing an overdose. Several states have reported increases in xylazine-involved overdose deaths; however, the prevalence of xylazine involvement in drug overdose deaths (overdose deaths) has not been extensively studied, particularly in the United States (4). To better understand the impact of xylazine adulteration on the evolving drug overdose epidemic in the United States, CDC analyzed unintentional and undetermined intent overdose death data from the State Unintentional Drug Overdose Reporting System (SUDORS) in 38 states and the District of Columbia (DC).^{*,†}

A SUDORS case was defined as xylazine-positive if xylazine was detected on postmortem toxicology or if xylazine was listed on the death certificate as a contributing cause of death

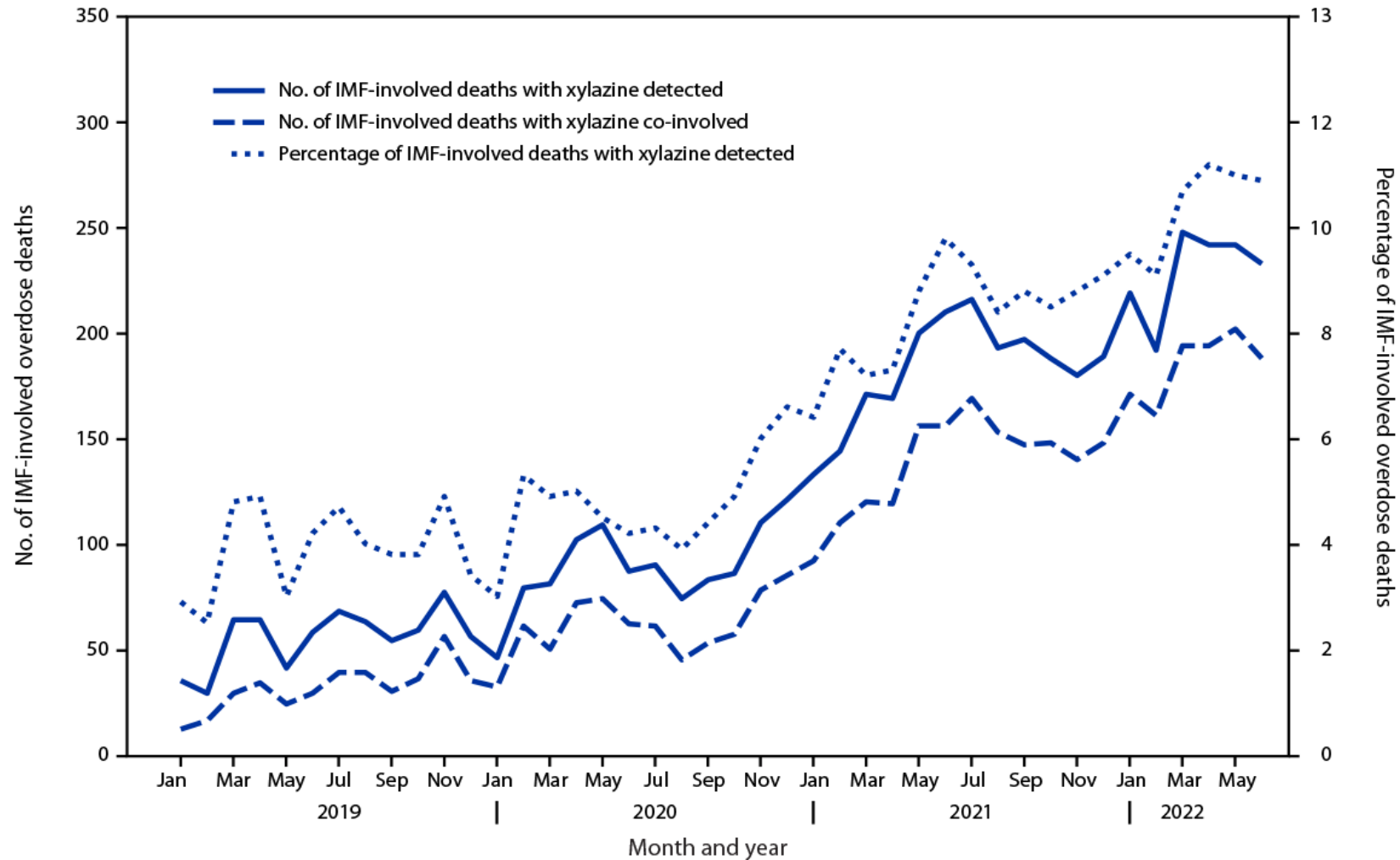
by the medical examiner or coroner based on postmortem toxicology detection, evidence of drug use at the scene, or witness reports of drug use. SUDORS cases in which xylazine is listed on the death certificate as a contributing cause of death by the medical examiner or coroner were defined as xylazine-involved. Thus, a xylazine-involved case would also be considered to be xylazine-positive by definition; however, a xylazine-positive case would not always mean that xylazine contributed to the death (i.e., xylazine-involved). Using data from 38 states and DC, CDC examined xylazine-positive and xylazine-involved overdose deaths that occurred during 2019. In addition, detailed narrative text for each case was reviewed for information about xylazine use or presence among drug products or paraphernalia found at the scene.

Among 45,676 overdose deaths reported to SUDORS during January–December 2019, xylazine-positive (826; 1.8%), and xylazine-involved (531; 1.2%) deaths were identified in 25 and 23 states, respectively. Xylazine was listed as a cause of death in 64.3% of deaths in which it was detected. The majority of xylazine-involved deaths were among males (73.1%), non-Hispanic White persons (75.4%), and from states in the Northeast Census region (67.0%).[§] Among all xylazine-involved deaths, one or more other drugs, particularly illicit drugs, were also listed as a cause of death, and 98.7% of xylazine-positive deaths and 99.1% of xylazine-involved deaths had fentanyl (including analogs) listed as a cause of death. Cocaine and heroin were listed as a cause of death in 32.1% and 26.0% of xylazine-positive deaths respectively and in 29.6% and 28.4% of xylazine-involved deaths respectively (Table).

The findings in this report are subject to at least one limitation. Estimates of xylazine detection in overdose deaths might be underestimated. Data reviews revealed instances where

^{*}SUDORS captures data on fatal unintentional and undetermined intent

Recent CDC Report on Xylazine Involvement in Drug OD Deaths

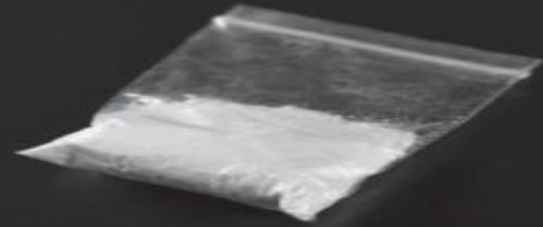


Surging Prevalence of Xylazine in Illicit Opioid Markets and Opioid OD Deaths

DEA NFLIS-Drug Identifications of Xylazine by Region			
Region	2020	2021	% Increase
Northeast	346	556	61%
South	198	580	193%
Midwest	110	118	7%
West	77	163	112%

Number of Xylazine-Positive OD Deaths by Region			
Region	2020	2021	% Increase
Northeast	631	1281	103%
South	116	1423	1,127%
Midwest	57	351	516%
West	4	34	750%

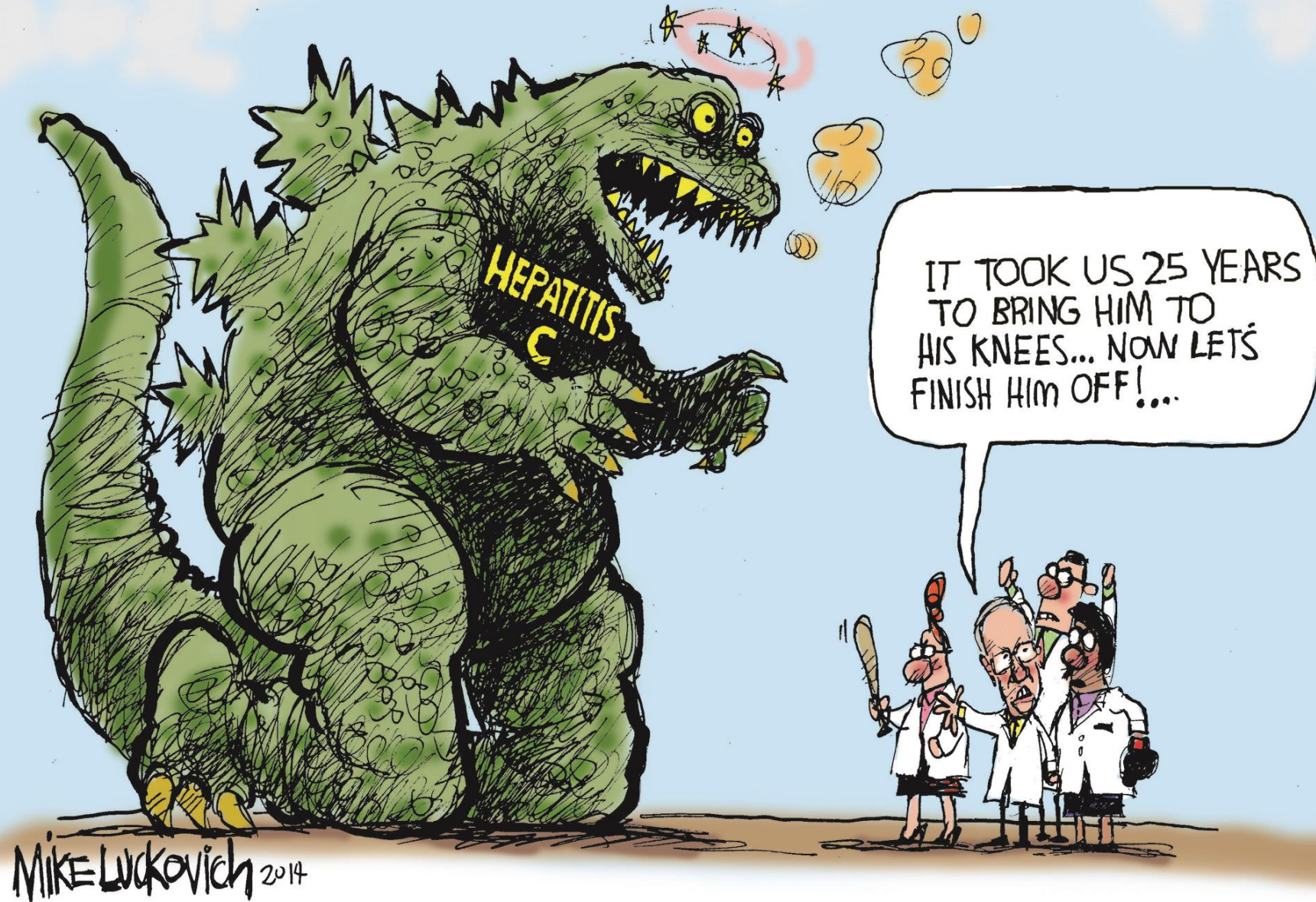
WHAT'S THE DEAL WITH XYLAZINE (‘TRANQ’)?



- A very strong sedative; not an opioid
- Potent Alpha 2 Adrenergic Receptor agonist; analog of clonidine
- Not approved for humans
- Discovered as an antihypertensive agent in 1962 by Bayer in Germany
- Used as a veterinary anesthetic and the recommended dose varies between species
- Due to hazardous side effects, including hypotension and bradycardia, it was not approved by the FDA for human use.
- Xylazine's mechanism of action in humans remains unknown, particularly

Injection-Related Wounds and Skin and Soft Tissue Infections (IWSSTIs) among PWID

	Etiological Factors	Characteristics
Novel Injection-Related Wounds (IW)	Impaired healing capacity	Often non-infectious
	Venous insufficiency; venous pooling	Distal to injection site
	Illicit opioid adulterants (e.g., xylazine)	
Skin & Soft Tissue Infections (SSTIs)	High injection frequency	Proximate to injection site
	Subcutaneous injections from "missed shots"	Cutaneous Nodules
	Non-sterile injecting equipment	
	Unhygienic injection environments	



Special Thanks To:

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- ❖ **Sarah Duhart Clarke** (RTI International)
- ❖ **Dr. Judith Feinberg** (West Virginia University)
- ❖ **Megan Grabenauer** (RTI International)
- ❖ **Bernadine Kwan** (West Virginia University)
- ❖ **Bobby Lane** (West Virginia University)
- ❖ **Michelle Mathis** (Olive Branch Ministry]
- ❖ **DeMia Pressley** (Drug Enforcement Administration)
- ❖ **Bradley Ray** (RTI International)
- ❖ **Hope Smiley McDonald** (RTI International)
- ❖ **Lynn Wenger** (RTI International)
- ❖ **Laura Jones** (Milan Puskar Health Right, West Virginia)