

Drug Overdose Crisis in America

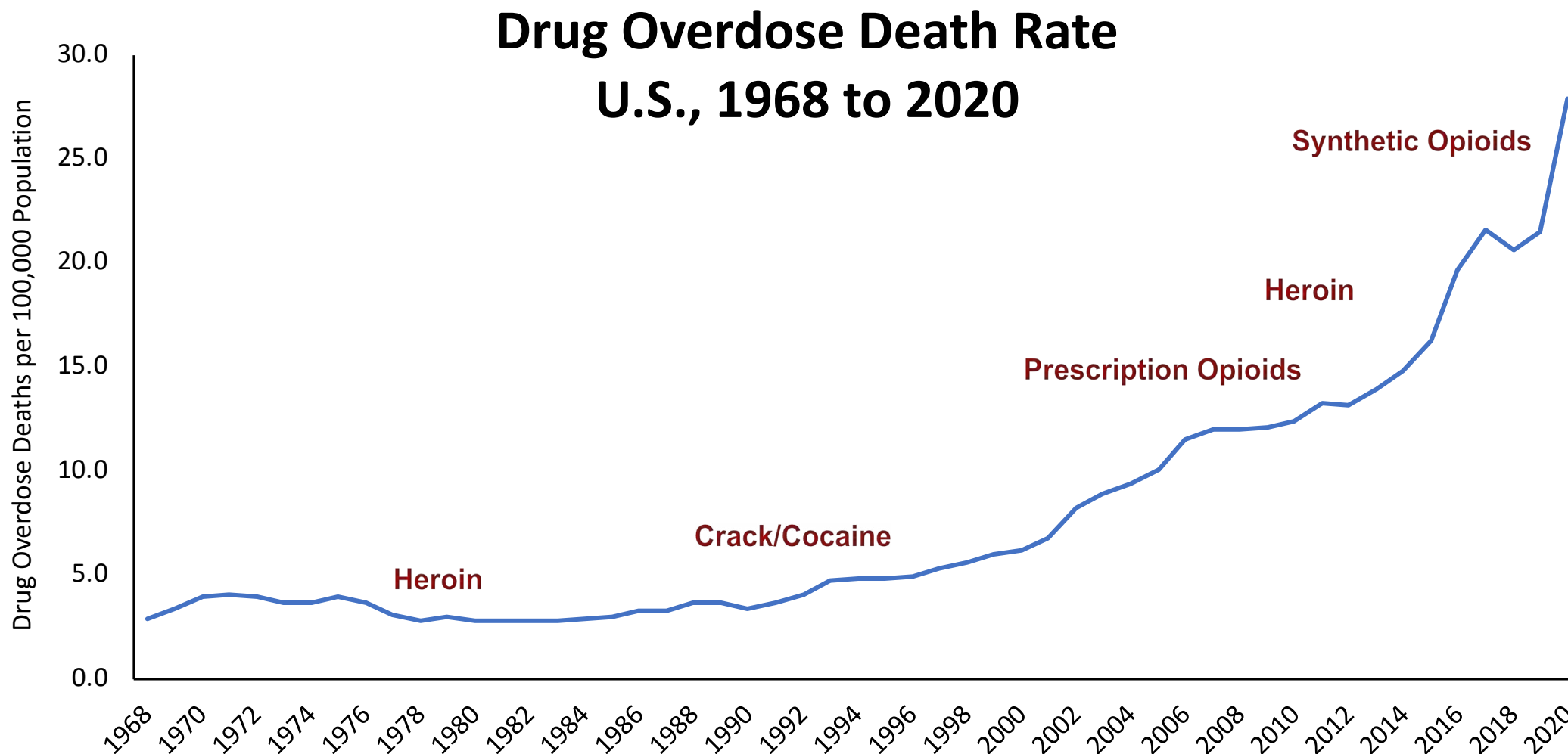
Wilson M. Compton, M.D., M.P.E.

Deputy Director

National Institute on Drug Abuse



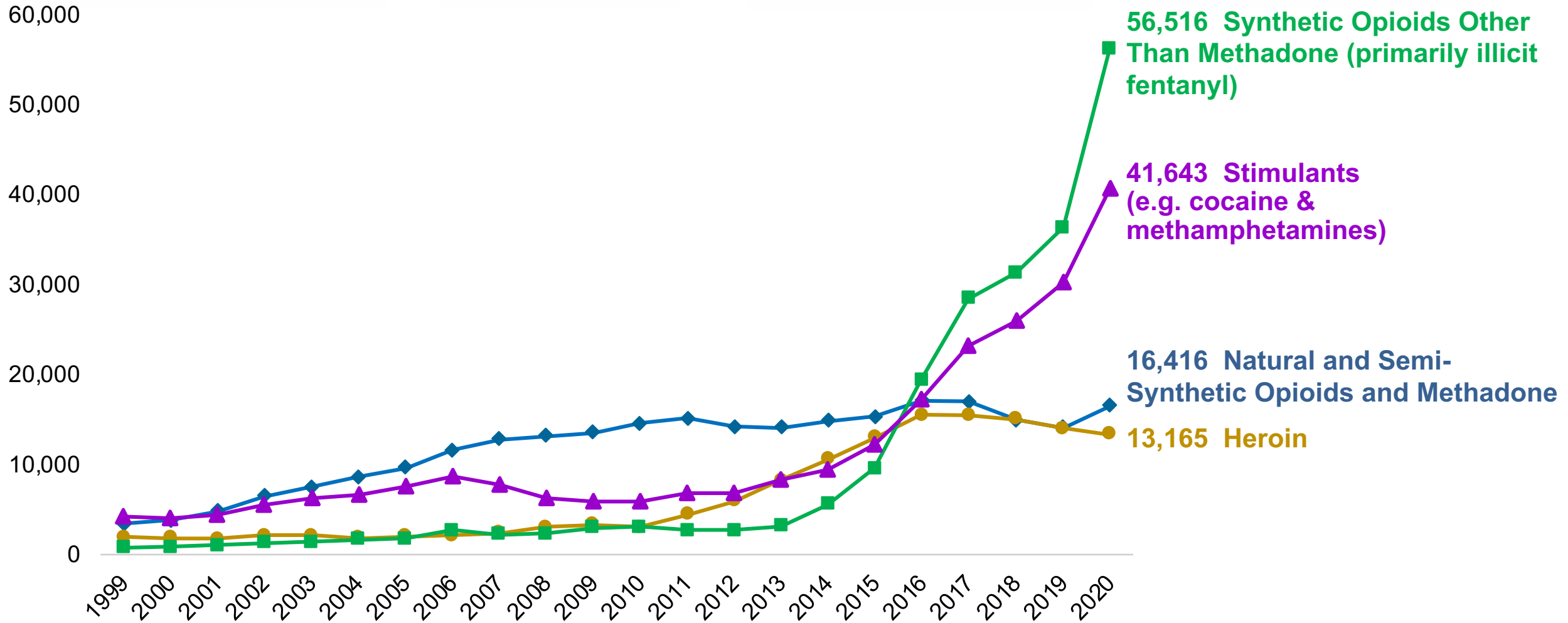
40 Year Exponential Increases in U.S. Overdose Deaths



See: Jalal, et al. Science 2016, and Compton, Einstein, Jones. International Journal of Drug Policy. 2022.

Evolution of Drivers of Overdose Deaths:

Analgesics ➔ *Heroin* ➔ *“Fentanyl”* ➔ *Stimulants*



Compton WM & Jones CM, Ann NY (2019) Acad Sci.; Updated for 2020 from WONDER Database

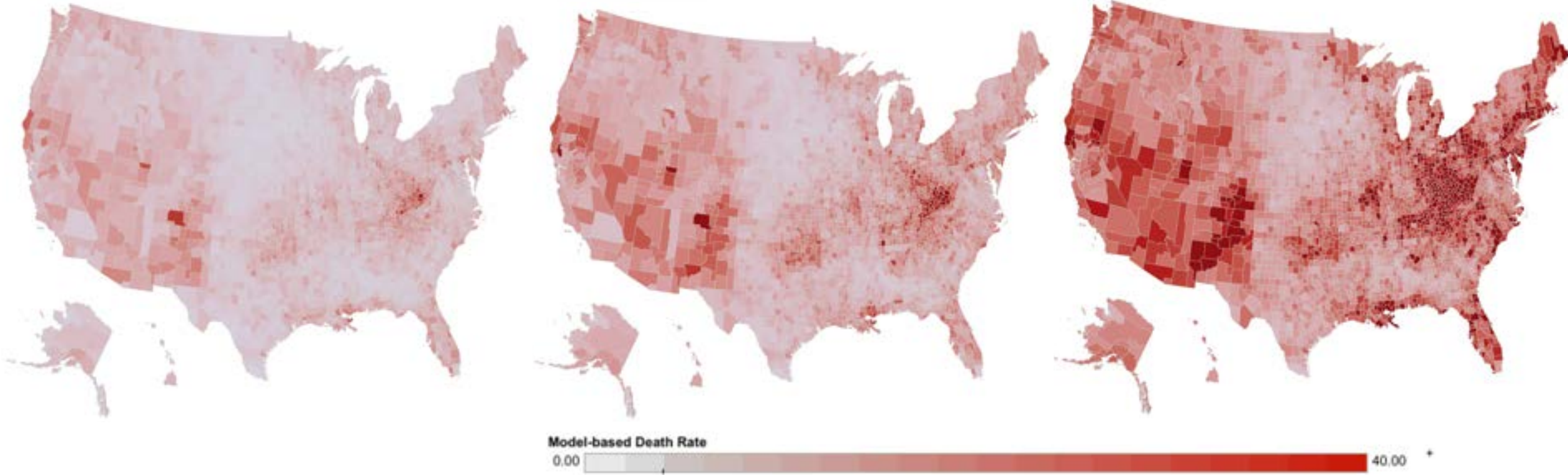
Virtually All U.S. Regions Have Increased Drug Overdoses *But Rates Vary*

Estimated Age-adjusted Death Rates per 100,000 for Drug Poisoning by County

2003

2013

2020



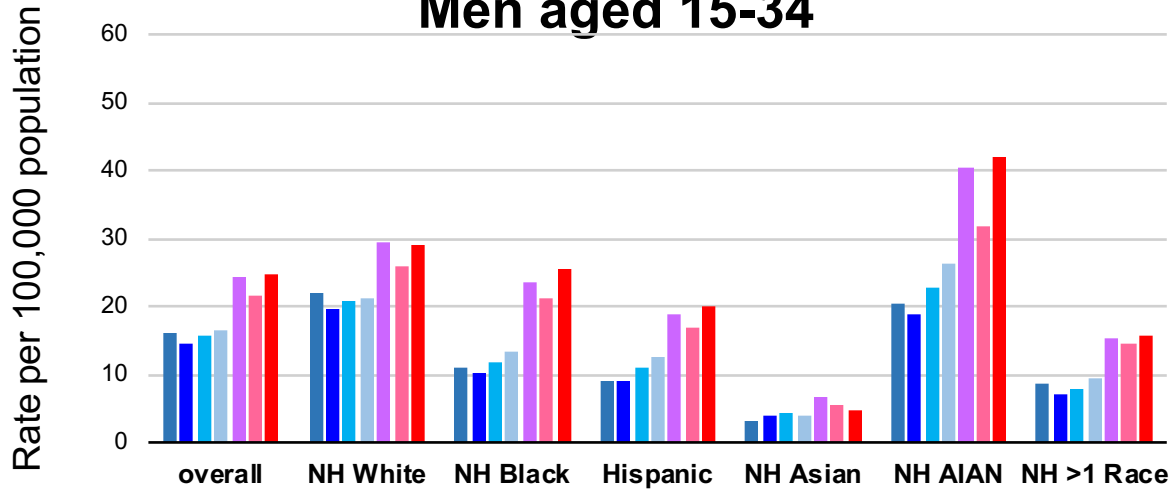
Drug Overdose Deaths* Continue to Increase

	ALL DRUGS	HEROIN	NAT & SEMI SYNTHETIC	METHADONE	SYNTHETIC OPIOIDS (mainly illicit fentanyl)	COCAINE	OTHER PSYCHO-STIMULANTS (mainly meth)
3/2021*	99,567	12,733	14,061	3,893	63,389	20,780	27,435
9/2021	105,654	10,227	14,023	3,733	68,880	23,127	31,647
3/2022*	109,247	8,328	13,376	3,527	73,473	25,959	33,994
Percent Change 3/21-3/22	9.7%	-34.6%	-4.9%	-9.4%	15.9%	24.9%	23.9%

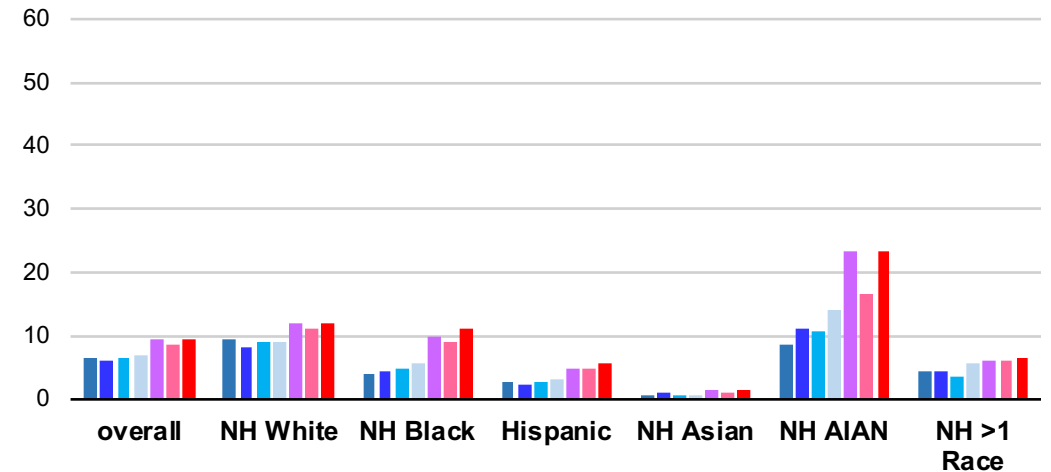
*NCHS Provisional drug-involved overdose death counts are PREDICTED VALUES, 12 months ending in select months.
<https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>

Overdoses Before and During the COVID-19 Pandemic

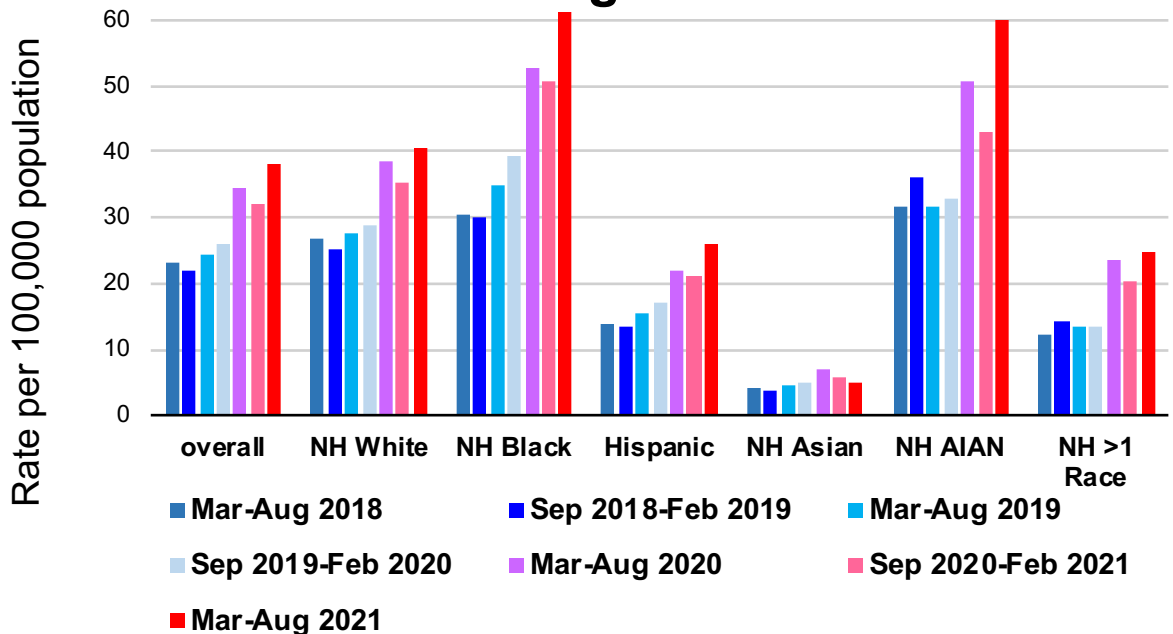
Men aged 15-34



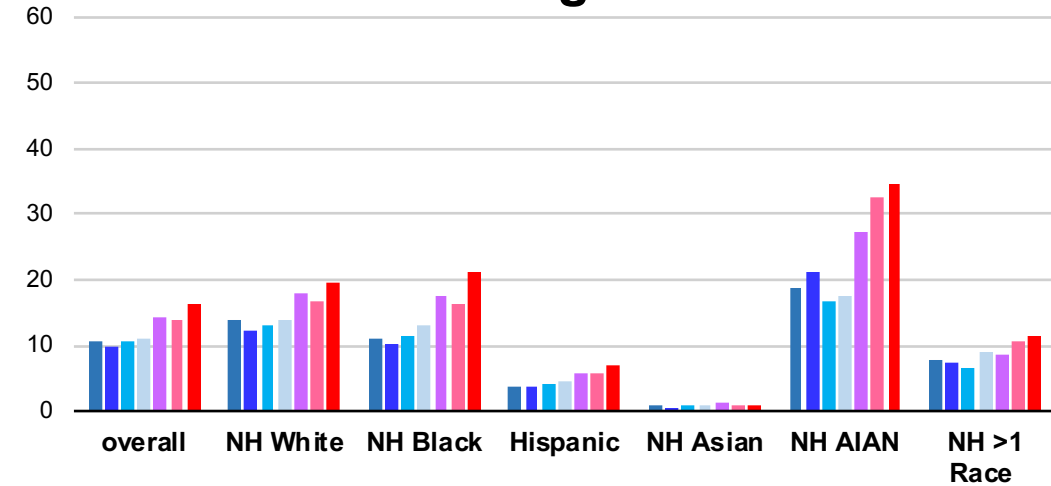
Women aged 15-34



Men aged 35-64

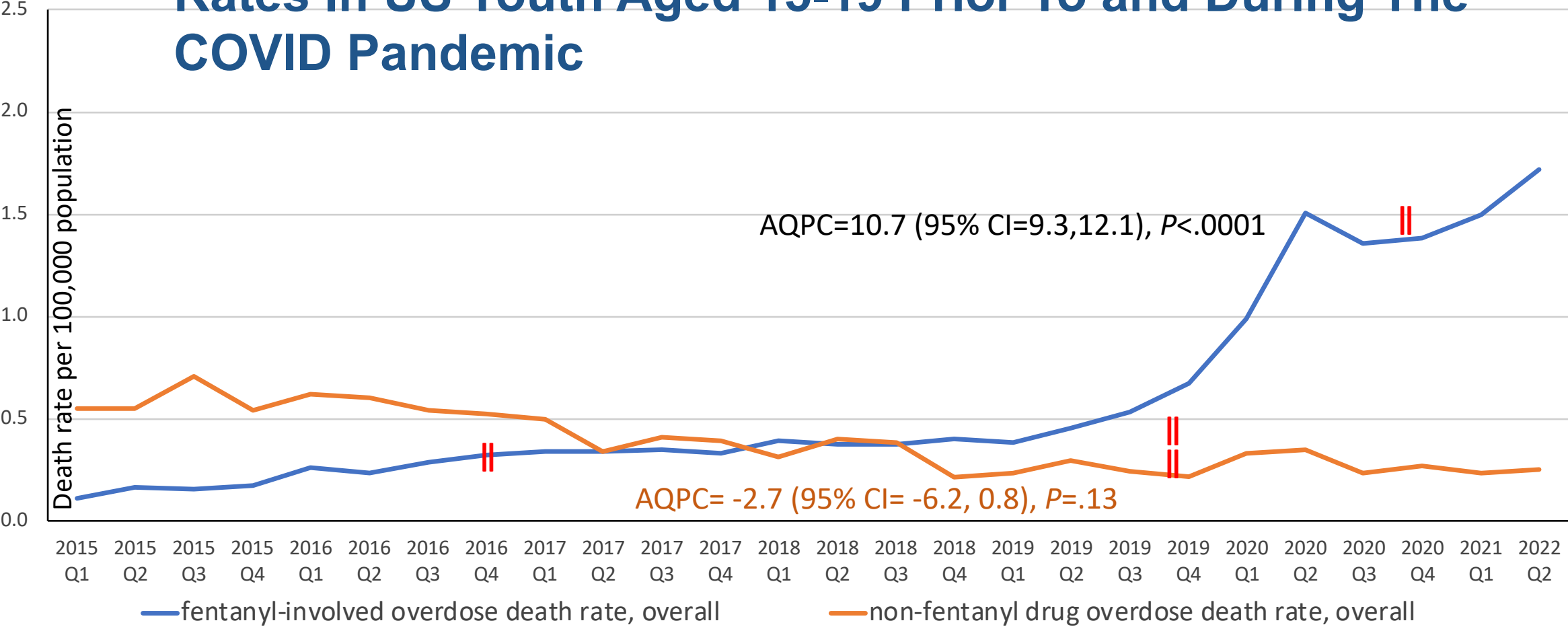


Women aged 35-64



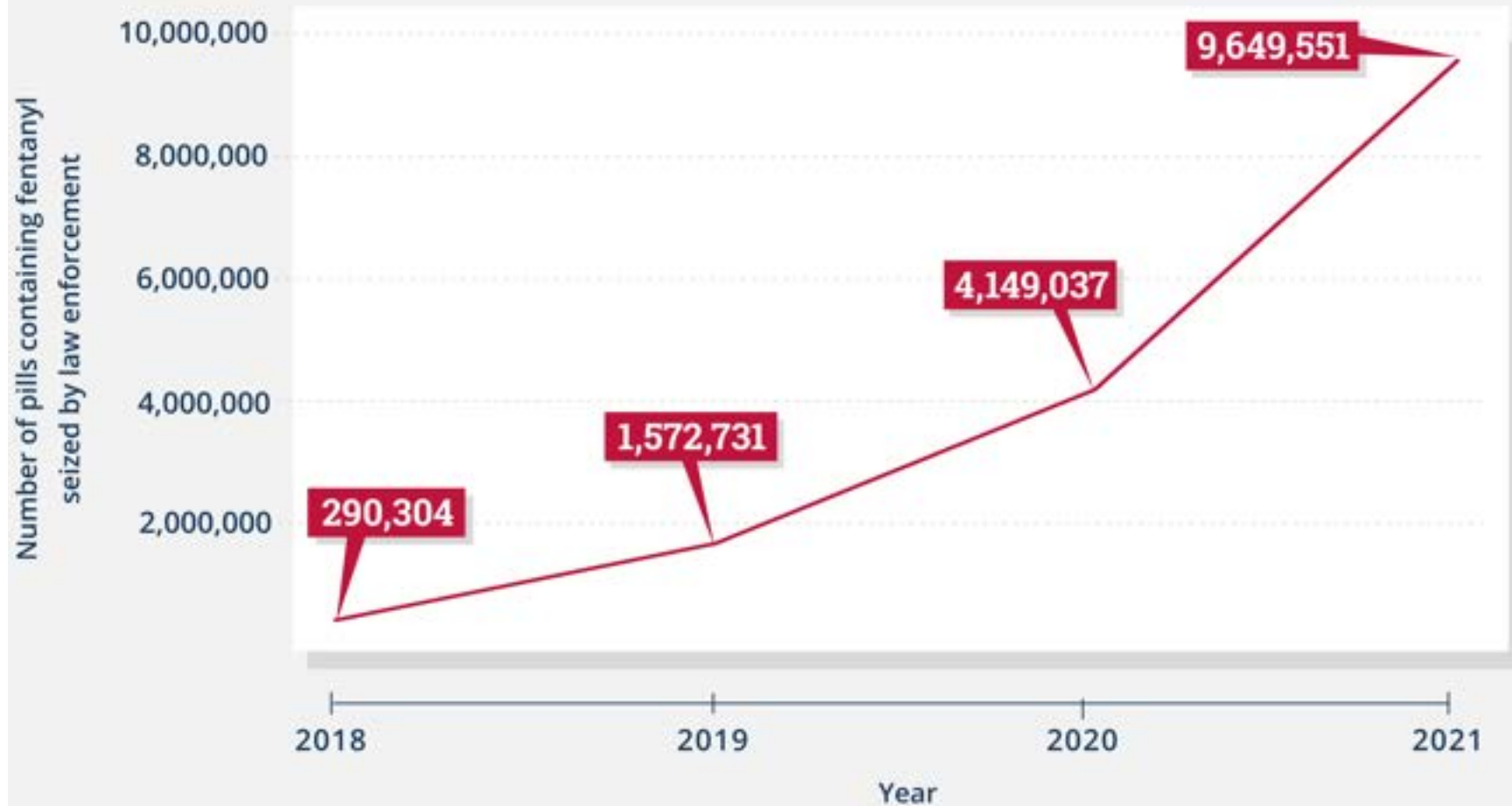
NH: non-Hispanic. AIAN: American Indian/Alaska Native. March-August 2020: COVID-19 pandemic.

Fentanyl-involved and Non-fentanyl Overdose Death Rates In US Youth Aged 15-19 Prior To and During The COVID Pandemic



National Vital Statistics System multiple-cause-of-death 2015-2020 final and 2021 provisional data U.S. census monthly data. ||: Joinpoints indicate significant changes in nonlinear trends using Bayesian Information Criterion. AQPC=average quarter percentage change during 2015 Q1-2022 Q2. ICD-10 cause of death code: synthetic opioids other than methadone (T40.4, primarily fentanyl and analogs).

Number of Pills Containing Fentanyl Seized by Law Enforcement in the United States, 2018 – 2021



Estimates based on data reported by the Office of National Drug Control Policy's High Intensity Drug Trafficking Areas program

Reference: JJ Palamar, et al. *Drug and Alcohol Dependence*. DOI: 10.1016/j.drugalcdep.2022.109398 (2022)

Current State of the Overdose Crisis

- Overdose crisis continues to be dominated by illicit synthetic opioids such as illicitly made fentanyl (IMF) and fentanyl analogs, but most overdose deaths also involve other drugs
- Patterns of substances used and how they are being used is changing, with rising stimulant use and co-use of opioids and stimulants, especially injection use
- Substance use and overdose patterns are tied to changes in supply:
 - Westward expansion of IMF and analogs
 - Eastward expansion of methamphetamine
 - Counterfeit pills containing IMF and analogs
- Proliferation of highly potent synthetic opioids into an unpredictable illicit drug supply increases overdose risk, especially among those using multiple substances and those unknowingly exposed
- Many missed opportunities for intervention and response

HHS Overdose Prevention Strategy – Pillars and Cross-Cutting Principles

HHS Overdose Prevention Strategy



Cross-Cutting Principles

Equity

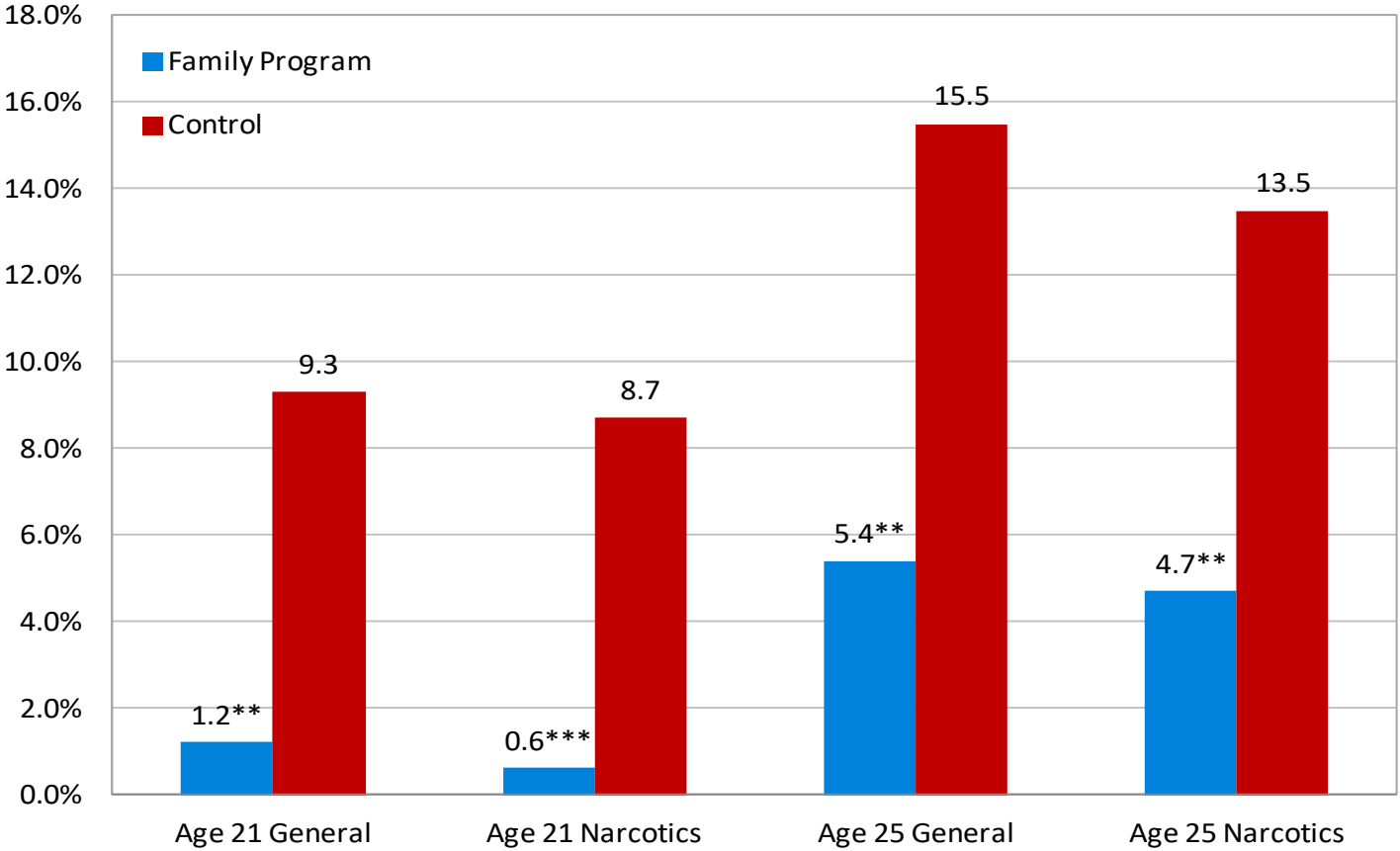
Data & Surveillance

Coordination, Collaboration & Integration

Reducing Stigma

Current strategy broadly focuses on drug overdose and specifically considers increase in methamphetamine harms.

Universal Substance Use Prevention May Reduce Later Misuse of Opioids



Targeting Youth to Prevent Later Substance Use Disorder: An Underutilized Response to the US Opioid Crisis

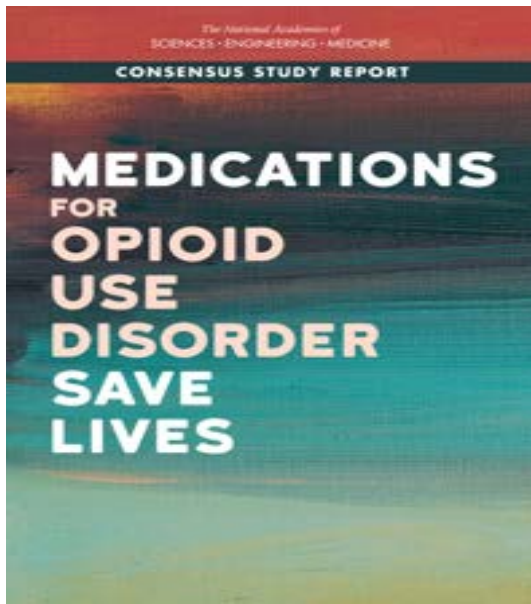
WM Compton, CM Jones, GT Baldwin, et al.
AJPH. 2019;109:2185-S189.

In this study, for 100 young adults in general population starting Rx abuse, only 35 young adults from an intervention community started.

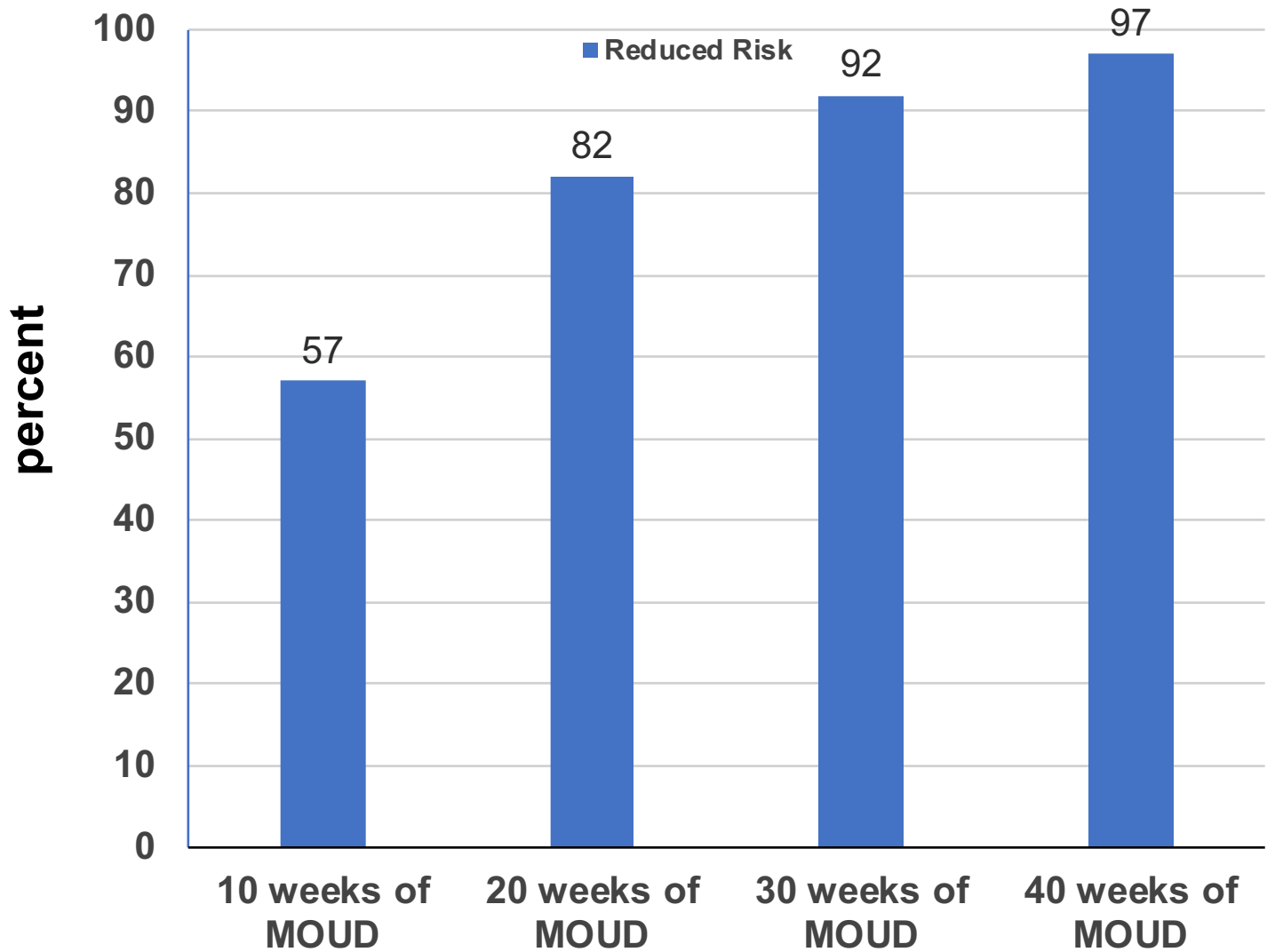
Notes: General=Misuse of opioids or CNS depressants or stimulants. [R Spoth et al. \(2013\) American Journal of Public Health](#)

Access to Naloxone

- Naloxone nasal spray was available in 69.5% of community pharmacies across 11 U.S. states from May 2020-April 2021 (n=4,984) ([Hill et al., 2022](#)).
 - In MA, findings suggest increased dispensing of naloxone, in part by naloxone standing orders ([Chatterjee, et al., 2022](#)).
 - Limited availability of naloxone at independent community pharmacies in GA even after the standing order was issued ([Gilbert, et al., 2021](#)).
 - Most pharmacies in TX do not appear to be willing and able to dispense prescribed buprenorphine/naloxone films and naloxone nasal spray to patients with OUD in a timely manner ([Hill, et al., 2021](#)).
- No municipal-level racial/ethnic inequities in naloxone distribution in RI nor MA ([Nolen, et al., 2022](#)), but there are few studies focused on inequity particularly among vulnerable populations (those with physical disabilities or unstable housing) ([Martignetti & Sun, 2022](#)).
- Pharmacists express support of dispensing naloxone in rural and urban pharmacies in NY ([Tofighi, et al., 2021](#)). Still, research findings indicate underutilization of pharmacists with a specific need of programs and training to support their naloxone dispensing.



Reduced Risk Overdose in Pregnant Women Given Medications for OUD



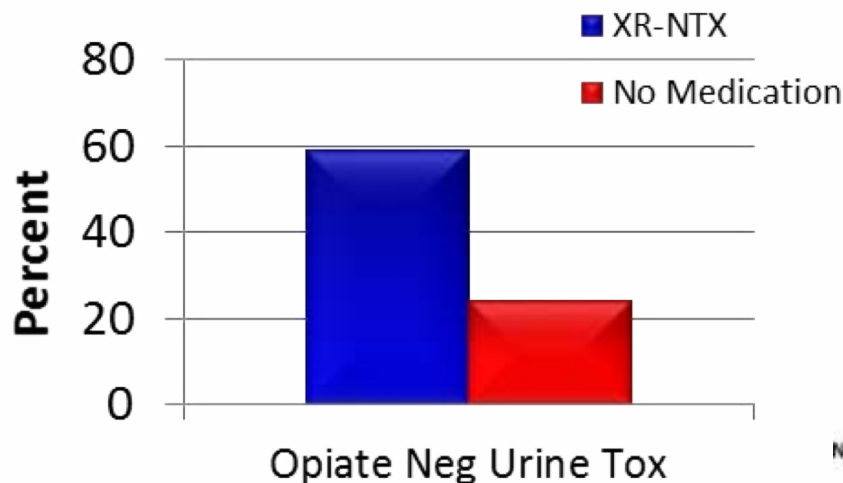
FDA-Approved Medications

<p>Methadone</p>  <p>In use since the 1960s, the slow-acting synthetic opioid agonist effectively treats moderate to severe heroin addiction. It is only available in heavily regulated clinics.</p>	<p>Buprenorphine/Suboxone</p>  <p>Approved in 2002, the long-acting opioid agonist relieves drug cravings with fewer side effects than other opioids and is available by prescription from certain doctors. Suboxone is designed to deter illicit use.</p>
<p>Naltrexone/Vivitrol</p>  <p>Approved in pill form in 1984, it has been available since 2010 as a 30-day time-release injectable medication called Vivitrol. Patients must be completely off all opioids for seven to 10 days. Both block the effect of opioids, do not activate the opioid receptor system, and do not cause physical dependence.</p>	<p>Naloxone</p>  <p>Approved in 1971, the short-acting medication, also known as Narcan and Evzio, reverses opioid overdoses but does not treat opioid addiction.</p>

Science = Solutions: Improving Addiction Treatment

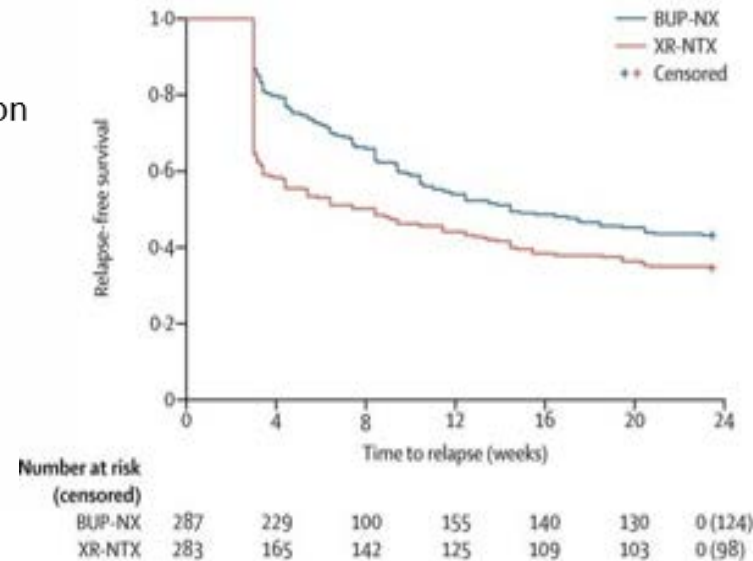
- Initiating buprenorphine treatment in the **emergency department** improves treatment engagement and reduces illicit opioid use
- Extended-release naltrexone initiated in **criminal justice** settings lowers relapse rates and overdoses
- **BUP-Nx** more effective than **XR-Naltrexone** overall but appear equally safe and effective after induction

Post Prison-Release Outcomes



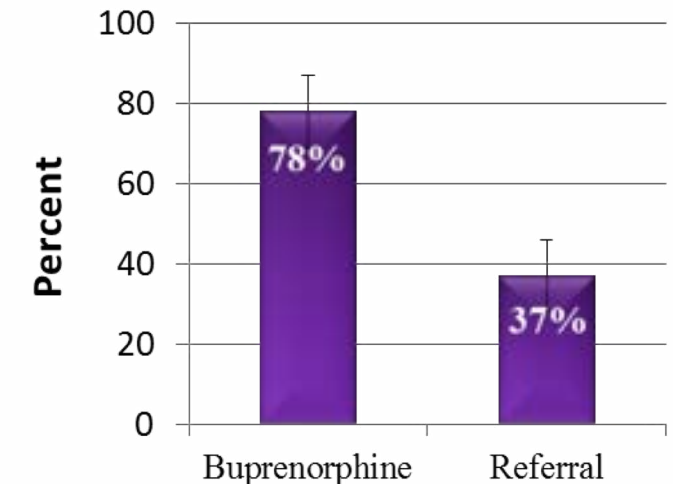
[Lee et al. \(2015\) Addiction](#)
[Lee et al. \(2016\) NEJM](#)

Relapse-free survival



[Lee et al., \(2018\) Lancet](#)

ED-initiated Buprenorphine Increased TX Engagement



D'Onofrio JAMA. 2015.

Treating Stimulant Use Disorder

ADAPT-2 Trial Results Deliver a Breakthrough in Long Search for Methamphetamine Use Disorder Medication

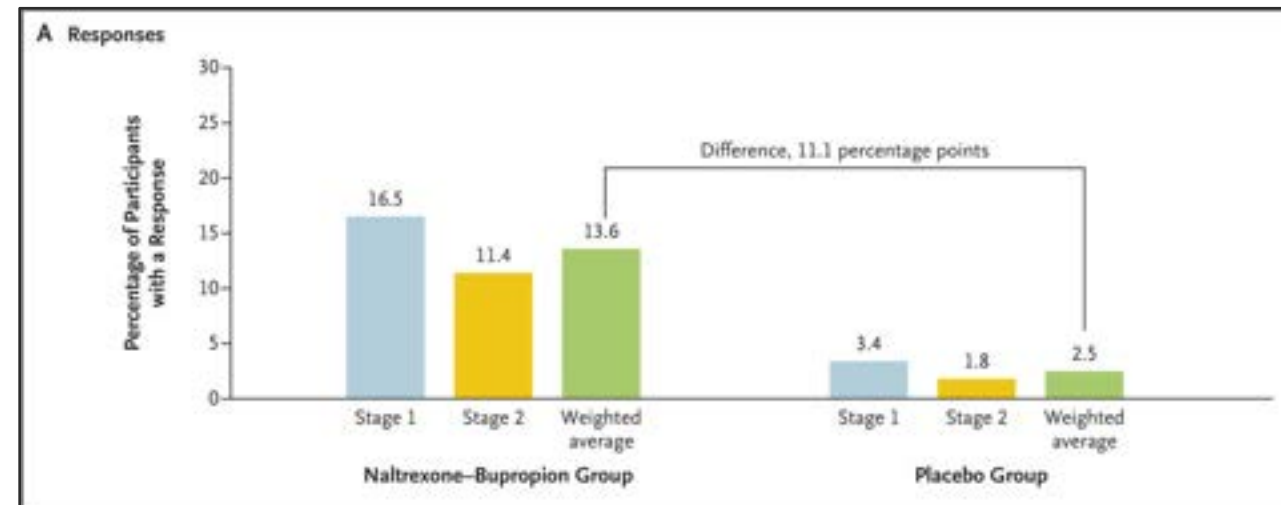
- No FDA approved medications for stimulant use disorder or overdose
- Contingency management is the most effective treatment but is challenging to implement and underutilized
- NIDA prioritizing investment in development of medications to treat stimulant use disorders

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Bupropion and Naltrexone in Methamphetamine Use Disorder

M.H. Trivedi, R. Walker, W. Ling, A. dela Cruz, G. Sharma, T. Carmody, U.E. Ghitza, A. Wahle, M. Kim, K. Shores-Wilson, S. Sparenborg, P. Coffin, J. Schmitz, K. Wiest, G. Bart, S.C. Sonne, S. Wakhlu, A.J. Rush, E.V. Nunes, and S. Shoptaw



Treating Fentanyl OUD and Overdoses

- Limited data on efficacy of medication to treat fentanyl OUD
- Methadone is effective in fentanyl OUD.
 - Methadone protected against death, but relapse rates were high ([Stone, et al., 2018](#), [Stone, et al. 2020](#)).
- Buprenorphine is effective in fentanyl OUD ([Wakeman, et al., 2019](#)).
 - Harder to initiate patients on buprenorphine
- Naltrexone no published data
- Deaths from fentanyl are increasing in spite of naloxone ([Torralva and Janowsky, 2019](#)).
- OD from fentanyl require multiple naloxone doses ([Schumann et al., 2007](#), [Somerville et al., 2017](#))
 - Shorter duration of naloxone (t_{1/2} 1.3–2.4 h) than fentanyl (t_{1/2} 7-8 h)
 - Slower clearance of fentanyl in frequent users
- Chest wall rigidity induced by fentanyl, which might reflect noradrenergic and cholinergic effects.

NIDA Research Pivots to Address Overdose Trends

Treating Overdose, Advancing Research on Fentanyl

- **How do we reverse fentanyl overdose?**
 - Should naloxone doses be higher?
 - Are long-acting formulations of naloxone needed?
 - Are there other medications or medication combinations that would be more effective?
- **What are appropriate detoxification strategies?**
- **How do we treat fentanyl addiction?**
 - In pregnancy and postpartum?
- **How do we treat fentanyl involved neonatal abstinence syndrome?**

Notice of Special Interest (NOSI): Administrative Supplements for research on fentanyl and derivatives

Notice Number:
NOT-DA-21-032

Key Dates

Release Date:	March 25, 2021
First Available Due Date:	April 01, 2021
Expiration Date:	April 01, 2022



Addressing Overdose Deaths in 2022

- Providing effective treatment to pain patients including the appropriate use of opioids when needed is necessary but not sufficient
- Treatment of Opioid Use Disorders is CRUCIAL but not sufficient
- Treatment of Substance Use Disorders in addition to OUD is now necessary to prevent overdose deaths
- Prevention of drug use including illicit prescription drug use is necessary to prevent overdoses