Updates in Addiction Medicine: Emerging Substances & Novel Treatments

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June 6, 2026

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Disclosures

I have no relevant financial relationships that create a conflict of interest related to the content of this presentation.

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STOP THE STIGMA

Learning Objectives

1) Describe the changing epidemiology of the overdose crisis & novel interventions to combat its "fourth wave"
2) Explore current gaps in alcohol use disorder treatment and existing but underutilized as well as new & innovative pharmacotherapy for closing them
3) Identify risks of unregulated, commercially available products containing opioid-like compounds
4) Recognize emerging psychoactive substances adulterating the illicit drug market and their associated medical complications

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We'll tackle these objectives through…

- 4 cases
- Some inpatient, some outpatient
- Internal medicine physicians at the heart of their care
- Internal medicine physicians best positioned to change their trajectories

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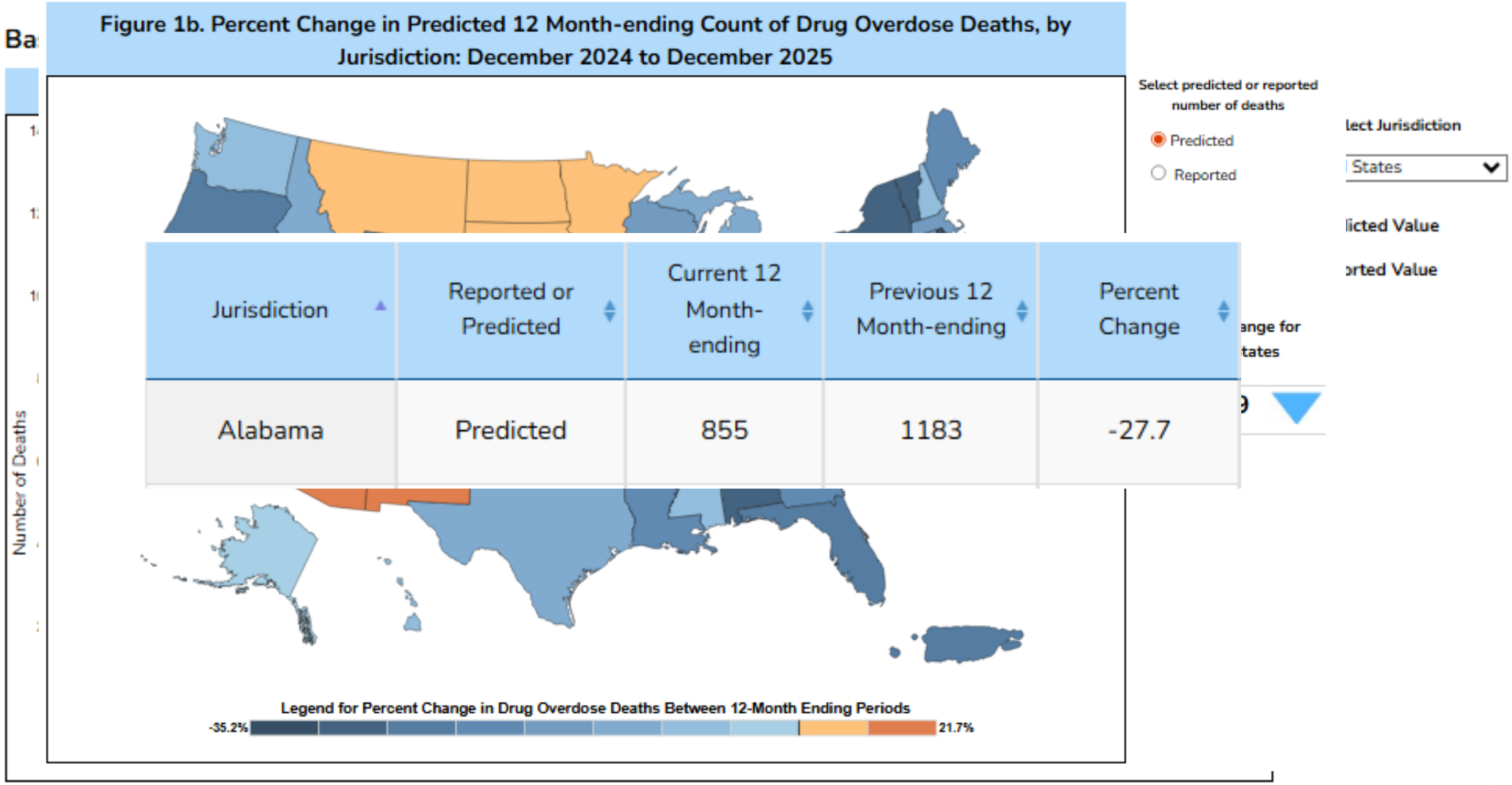
First, how have we been doing in addressing the overdose crisis?

Let’s start with the good news…

Overdose deaths have begun to decline (but still remain higher than 10 years ago).



Jurisdiction	Reported or Predicted	Current 12 Month-ending	Previous 12 Month-ending	Percent Change
Alabama	Predicted	855	1183	-27.7

Ahmad FB, et al. *National Center for Health Statistics*. 2026.

Case 1

29-year-old woman with depression, tobacco use disorder, and intermittent methamphetamine use presents to Gardendale ED after being found down by boyfriend.

- Substance history: 1 ppd, no alcohol, smokes methamphetamine once weekly
  - No past or current opioid use
  - Started methamphetamine over last year
- Current medications: OTC O-pill
- Social History: Lives alone in Gardendale, no children, works as store manager

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Case 1

29-year-old woman with depression, tobacco use disorder, and intermittent methamphetamine use presents to Gardendale ED after being found down by family member.

- Vital Signs: T 98.5°F | HR 102 | BP 107/69 | RR 6 – 8 | SpO2 91%
- Physical exam & ED course:
  - Initially somnolent, unable to fully arouse, pupils symmetric and reactive (neither dilated nor constricted), no crackles or wheezing
  - Administered naloxone 1 mg IV
  - Becomes alert with RR 12 – 14 & SpO2 98 – 100%
- UDS:
  - Positive for amphetamine only
  - Negative for buprenorphine, opiates, oxycodone, & methadone

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What happened?

This is not a diagnostic dilemma…
She undoubtedly experienced an opioid overdose.

How do we explain the lack of opioids on test drug screen?

29-year-old wor r, and
intermittent me ale ED after
being found do

- Vital Signs: T 98.5
- Physical exam & E
  - Initially somno ve (neither dilated nor constricted), nc
  - Administered n
  - Becomes alert
- UDS:
  - **Positive for am**
  - **Negative for bu**

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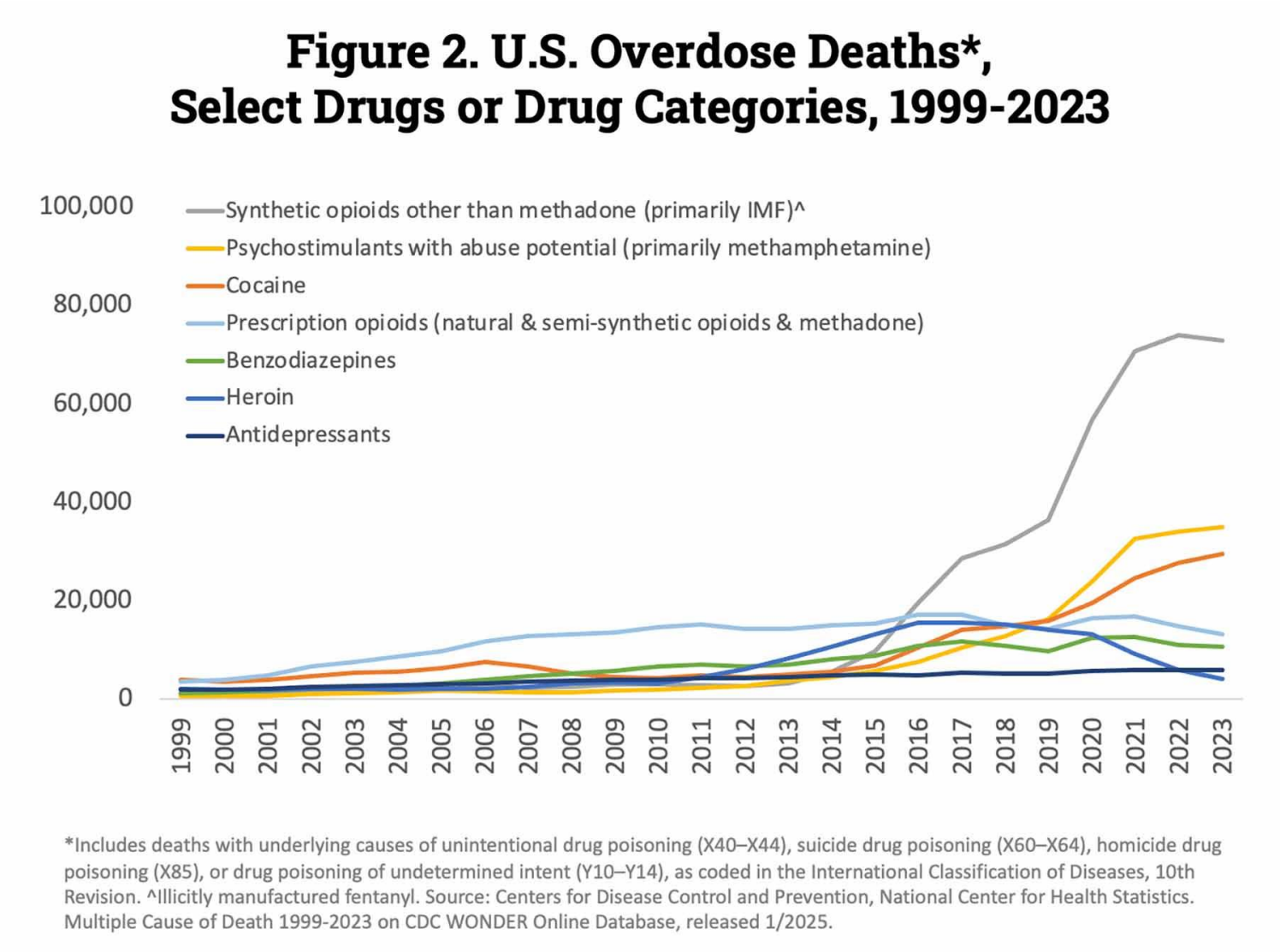
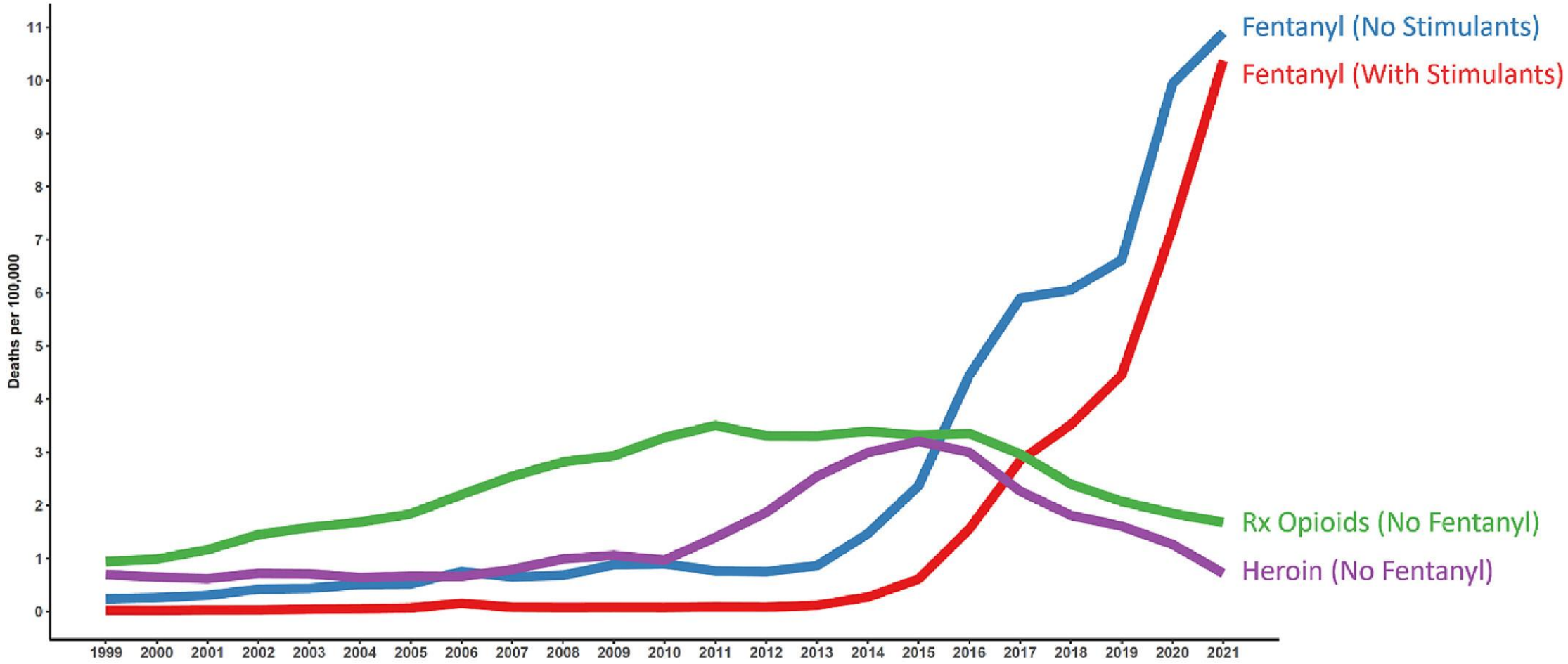
Over the last several years, our efforts have focused on fentanyl.



National Institute of Drug Abuse. August 2024.

However, a "Fourth Wave" in the overdose crisis is emerging.



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Hedegaard H, et al. *NCHS Data Brief*. November 2018. | Friedman J, Shover CL. *Addiction*. December 2023.

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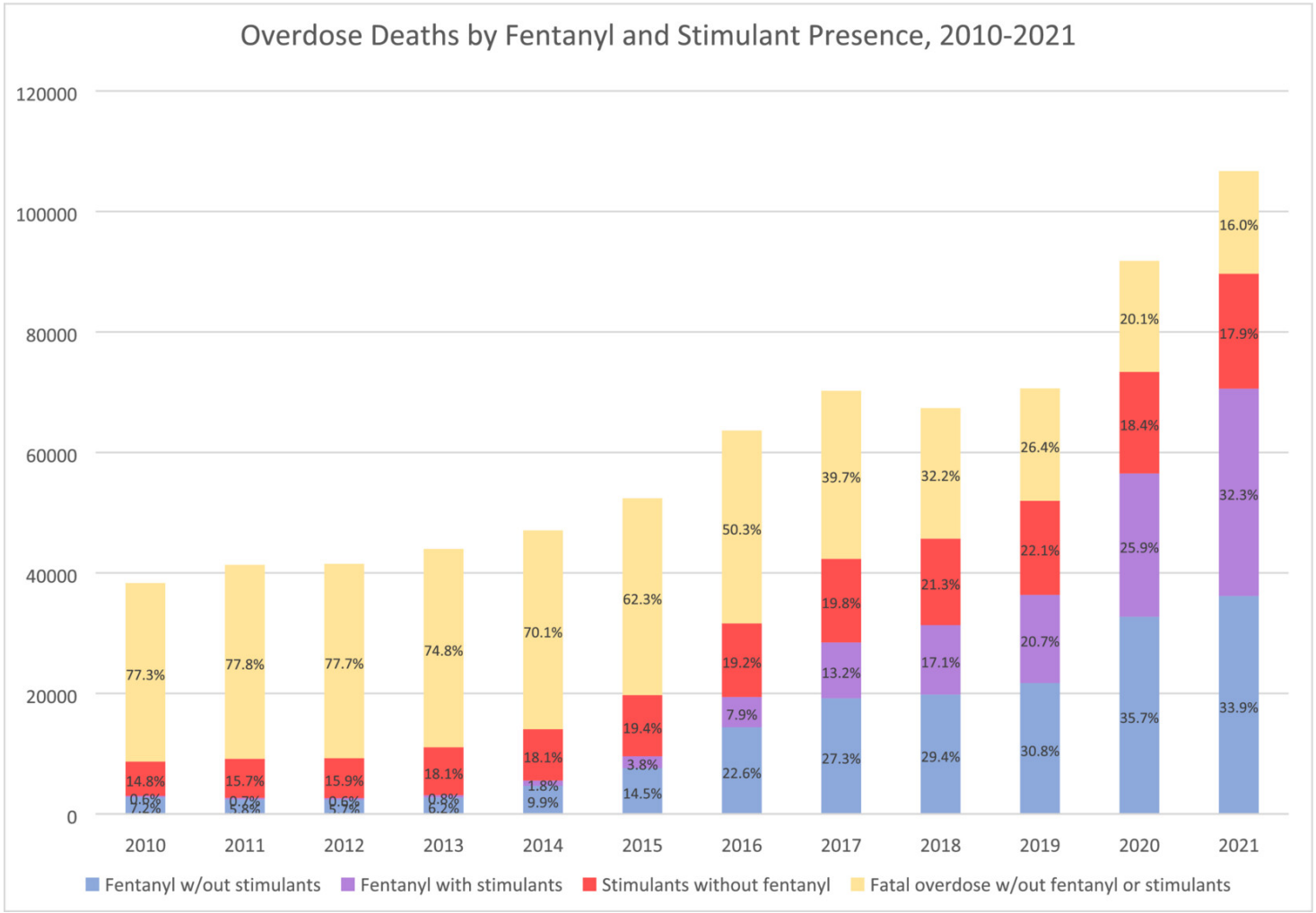
Patients using stimulants without intentional opioid use are being exposed to fentanyl and dying of overdoses.



Fatal overdose w/out fentanyl or stimulants

Stimulants without fentanyl

Fentanyl with stimulants

Fentanyl w/out stimulants

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Friedman J, Shover CL. *Addiction*. December 2023.

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This trend is not a new one in Alabama.

Ranking of Top 10 drugs involved in AL overdose deaths					
Rank	**2013**	**2014**	**2015**	**2016**	**2017**
1	Methadone (39)	Heroin (123)	Heroin (105)	Fentanyl (140)	Fentanyl (161)
2	Heroin (37)	Methadone (42)	Fentanyl (59)	Heroin (126)	Heroin (128)
3	Cocaine (28)	Cocaine (43)	Methadone (41)	Cocaine (81)	Meth (110)
4	Oxycodone (24)	Hydrocodone (34)	Cocaine (39)	Meth (45)	Cocaine (98)
5	Hydrocodone (16)	Fentanyl (32)	Oxycodone (36)	Methadone (34)	Alprazolam (78)
6	Fentanyl (15)	Oxycodone (28)	Meth (28)	Oxycodone (31)	Oxycodone (68(
7	Opiate (15)	Alprazolam (28)	Hydrocodone (25)	Alprazolam (30)	Hydrocodone (54)
8	Morphine (13)	Meth (19)	Morphine (19)	Hydrocodone (30)	Methadone (32)
9	Alprazolam (12)	Opiate (15)	Alprazolam (18)	Morphine (21)	Morphine (24)
10	Meth (13)	Morphine (14)	Opiate (17)	Tramadol (11)	Tramadol (23)

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Overdose Surveillance Summary. *Alabama Department of Public Health*. July 2019.

STOP THE STIGMA

Cocaine has consistently contributed to the larger overdose epidemic

Ranking of Top 10 drugs involved in AL overdose deaths					
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Overdose Surveillance Summary. *Alabama Department of Public Health*. July 2019.

STOP THE STIGMA

while methamphetamine-related overdoses accelerated early.

Ranking of Top 10 drugs involved in AL overdose deaths					
Rank	**2013**	**2014**	**2015**	**2016**	**2017**
1	Methadone (39)	Heroin (123)	Heroin (105)	Fentanyl (140)	Fentanyl (161)
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Overdose Surveillance Summary. *Alabama Department of Public Health*. July 2019.

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Our patient is discharged from the ED.
She establishes a month later with you for primary care.
You gently ask about her ED encounter
and how she's been doing since.

She discloses that she's continued to struggle with methamphetamine.

What could you offer her today for her methamphetamine use disorder?

A. Bupropion

B. Mirtazapine

C. Naltrexone

D. There aren’t any FDA-approved pharmacotherapies

The 2021 ADAPT-2 trial demonstrated the most effective pharmacotherapy combination to date.

Intervention

ER-Naltrexone 380 mg
IM q3weeks

+

Bupropion XL 450 mg
PO daily

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Trivedi MH, et al. *N Engl J Med*. January 2021.

STOP THE STIGMA

However, extended-release naltrexone on a non-FDA approved dosing schedule is unlikely to be affordable for any patient.

With a NNT of 9, this combination is promising.

Study characteristics

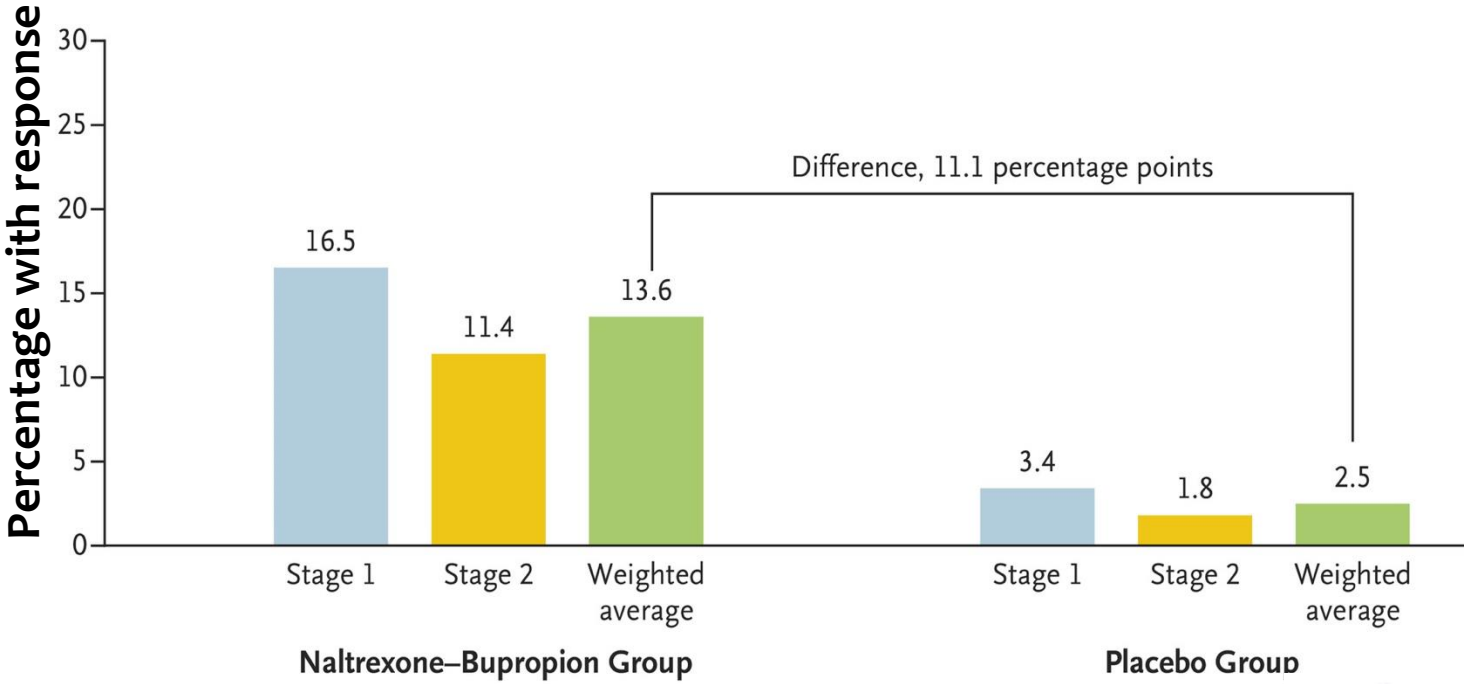
Multisite

Double-blind, placebo-controlled

Two-phase, sequential parallel design

403 participants randomized in Phase I

Outcome



Trivedi MH, et al. *N Engl J Med*. January 2021.

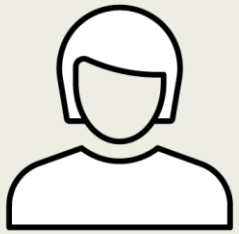
Mirtazapine… a more affordable option?

JAMA Psychiatry

RCT: Mirtazapine for Methamphetamine Use Disorder

POPULATION

213 Male, 126 Female

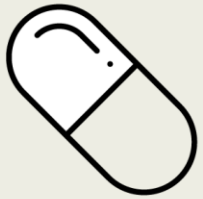


Adults with moderate to severe methamphetamine use disorder

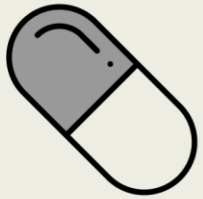
Mean (SD) age, 42.0 (8.6) y

INTERVENTION

344 Participants randomized



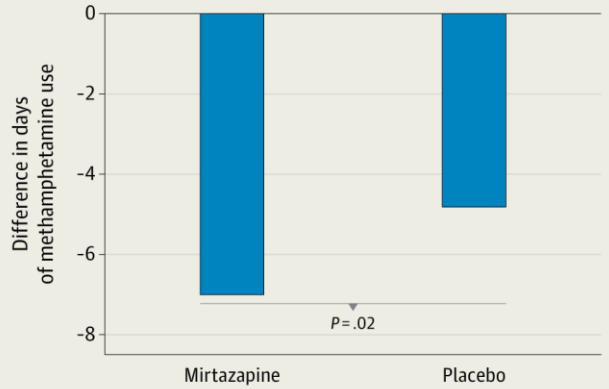
172 Mirtazapine
Mirtazapine, 30 mg/d for 12 wk



172 Placebo
Matched placebo

FINDINGS

The mirtazapine group had a greater reduction in days of methamphetamine use in the past 28 d from baseline to wk 12 than the placebo group



Difference in days of methamphetamine use:
Mirtazapine group: -7.0 d; 95% CI, -8.5 to -5.6
Placebo group: -4.8 d; 95% CI, -6.3 to -3.4
Mean group difference: -2.2 d; 95% CI, -4.2 to -0.2; *P* = .02

SETTINGS / LOCATIONS

6 Outpatient clinics in Australia

PRIMARY OUTCOME

Change in self-reported days of methamphetamine use in the past 28 d from baseline to week 12 (possible range, 0-28 d of the past 28 d). Self-reported days of methamphetamine use was assessed at baseline and wk 4, 8, and 12.

McKretin R, Shoptaw S, Saunders L, et al. Mirtazapine for methamphetamine use disorder: a randomized clinical trial. *JAMA Psychiatry*. Published online April 1, 2026. doi:10.1001/jamapsychiatry.2026.0159

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McKetin R, et al. *JAMA Psychiatry*. April 2026.

Mirtazapine was effective but not with as robust of a response.

Table 2. Primary and Secondary End Points for the Intention-to-Treat Estimand

End point	Placebo (n = 167)	Mirtazapine (n = 172)	Treatment estimand (95% CI)	*P* value
Primary end point				
Mean change in days of methamphetamine use	−4.8	−7.0	−2.2 (−4.2 to −0.2)	.02
Secondary end points				
Methamphetamine-negative oral fluid samples, %	12.0	13.2	1.3 (−4.7 to 7.2)	.68
Mean change in PHQ-9 score	−2.3	−2.5	−0.2 (−1.3 to 1.0)	.77
Mean change in AIS-5 score	−1.2	−1.8	−0.6 (−1.4 to 0.2)	.13
Mean change in HIV risk behavior score	−1.1	−1.4	−0.3 (−1.0 to 0.3)	.32
Mean change in EQ-5D quality of life utility score	1.3	2.2	0.9 (−3.1 to 4.9)	.66

Abbreviations: AIS-5, Athens Insomnia Scale, 5-item version; EQ-5D, EuroQol-5D; PHQ-9, Patient Health Questionnaire-9.

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McKetin R, et al. *JAMA Psychiatry*. April 2026.

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We can use these medications off-label
(not yet FDA-approved)
for select patients…

But we can mitigate the risks
associated with inadvertent fentanyl exposure
for every patient.

EN ESPAÑOL

Naloxone and/or Fentanyl Test Strip Training Registration

Naloxone is available at no cost to individuals, families, and community members across Alabama. A phone number OR email address is required to complete the online naloxone training. If you are unable to provide a phone number or email, please call (205) 933-9110 for assistance.

If you are part of law enforcement, a volunteer fire department, or another first responder organization, please follow the instructions below to request Naloxone through the appropriate channels:

- Law Enforcement & Providers: Contact the Alabama Department of Mental Health at narcanadmh@mh.alabama.gov
- Volunteer Fire Departments in Alabama: Contact Lisa Olson at lrolson1@ua.edu to access Naloxone through Project Freedom.

A ***phone number*** OR ***email address*** is required to complete the online naloxone training. If you are unable to provide a phone number or email, please call (205) 930-1065 for assistance.

Fentanyl Test Strips and Naloxone Kit

NO JUDGEMENT, NO SHAMING, NO PREACHING, JUST LOVE!

(800) 484-3731

If you are going to use by yourself, call us! You will be asked for your first name, location, and the number you are calling from. An operator will stay on the line with you while you use. If you stop responding after using, the operator will notify emergency services of an \"unresponsive person\" at your location.

This American Life

809 | September 8, 2023

The Call

One call to a very unusual hotline and everything that followed.

Learning Objectives

1) Describe the changing epidemiology of the overdose crisis & novel interventions to combat its "fourth wave"
2) **Explore current gaps in alcohol use disorder treatment and existing but underutilized as well as new & innovative pharmacotherapy for closing them**
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Case 2

49-year-old man with obesity, OSA, HTN, and depression presents for primary care visit with concern about his blood pressure and weight.

- HPI: concerned about his blood pressure and sleep
- Current medications: amlodipine, sertraline, OTC ibuprofen PRN
- Social History:
  - Married with 2 kids
  - Electrician
  - No smoking, drinks 4 – 5 beers on weeknights and 2 – 3 6-packs on weekends, no illicits

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STOP THE STIGMA

Case 2

49-year-old man with obesity, OSA, HTN, and depression presents for primary care visit with concern about his blood pressure and weight.

- Vital signs: T 98.2°F | HR 91 | BP 164/91 | BMI 36
- Weight trend: 50-pound gain over last year
- Other details obtained during the visit:
  - Stable mood & wears CPAP nightly
  - Alcohol intake has increased slowly after COVID-19 pandemic
  - No previous withdrawal or known health complications from alcohol
  - Not interest in quitting completely, but open to decreasing though worried may be challenging

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What medication would you consider adding?

A. Acamprosate

B. Disulfiram

C. Oral Naltrexone

D. Extended-release intramuscular Naltrexone

E. Semaglutide

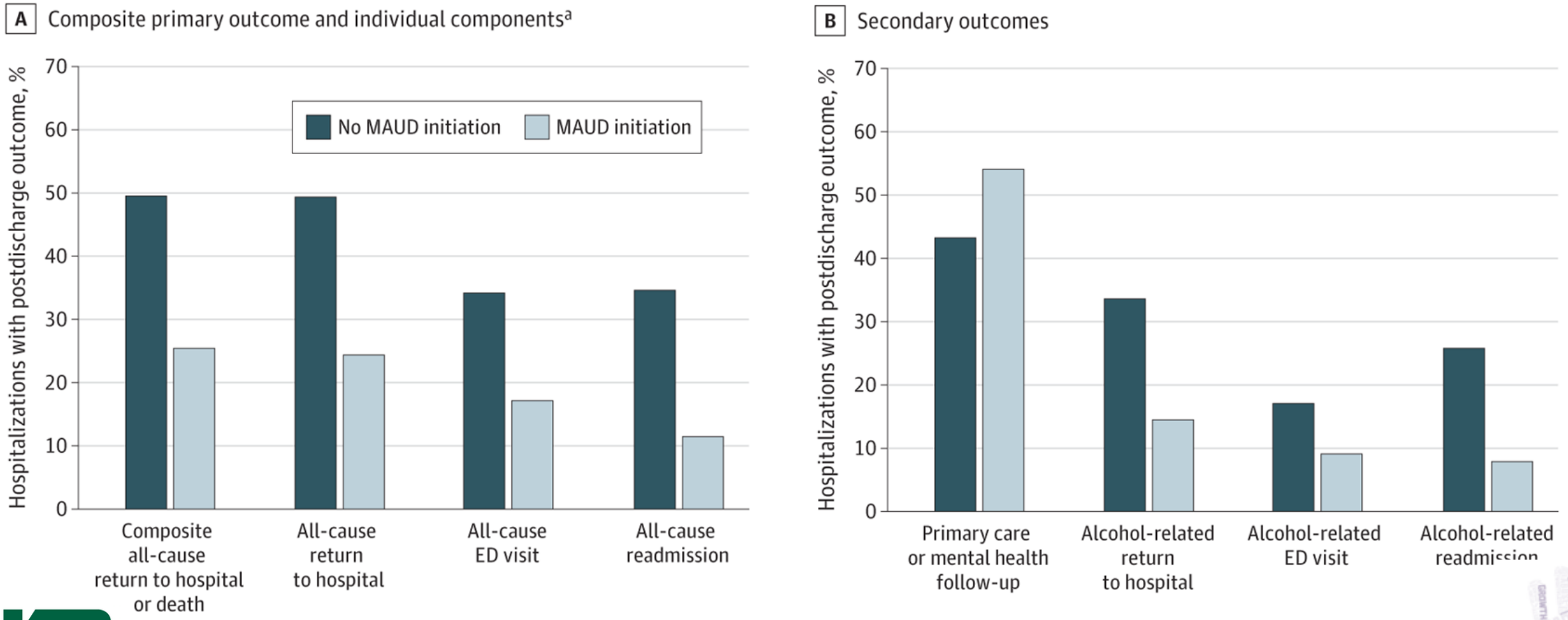
Before we learn about semaglutide's effect on drinking…

How are we doing with utilizing the medications that we already have approved for alcohol use disorder?

Discharge MAUD initiation was associated with an adjusted absolute risk reduction of 18% in the composite outcome*.

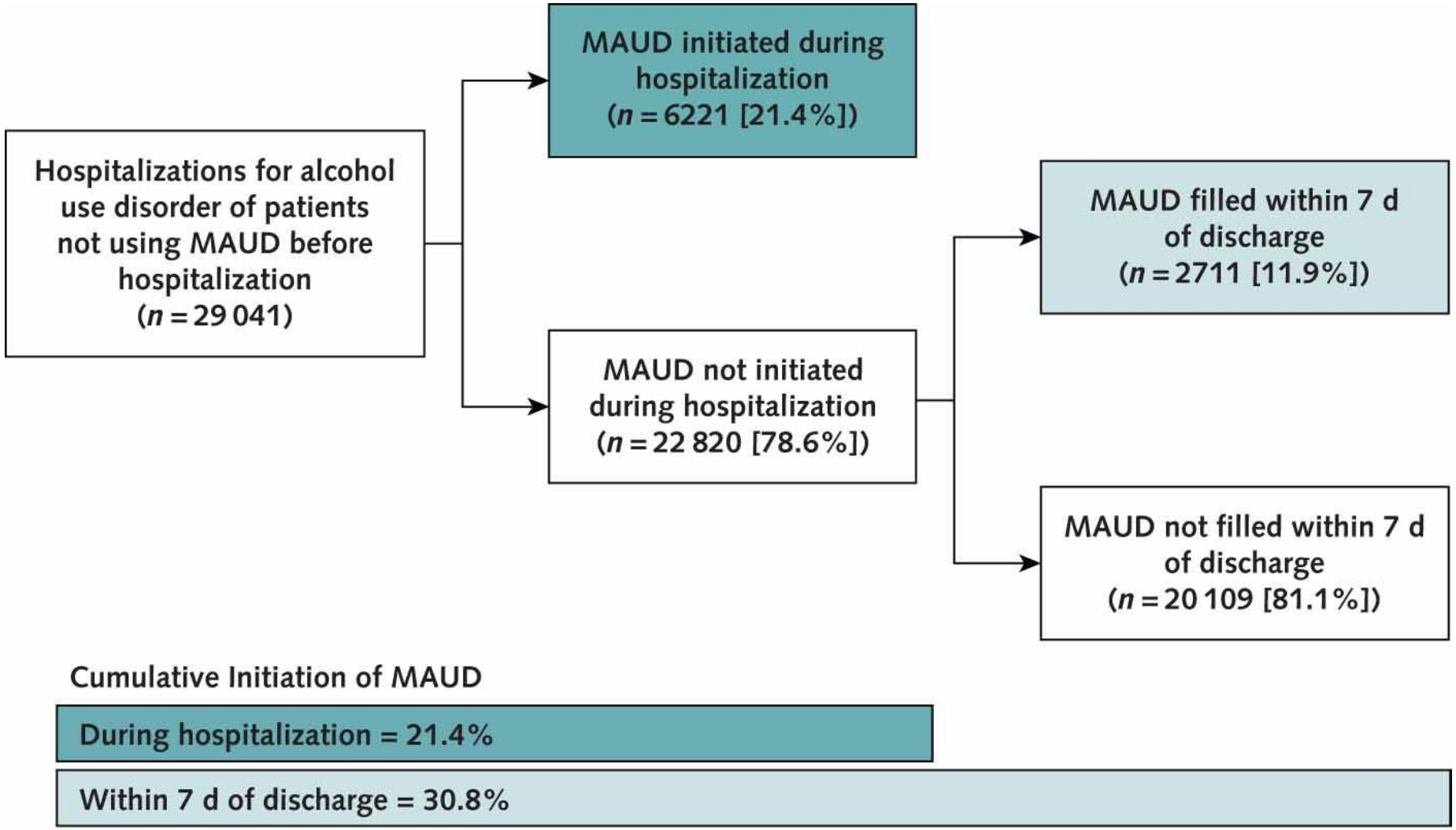
However, only 2% of the 9384 alcohol-related hospitalizations involved discharge initiation of a medication for alcohol use disorder.

*(*return to hospital or death within 30 days)*



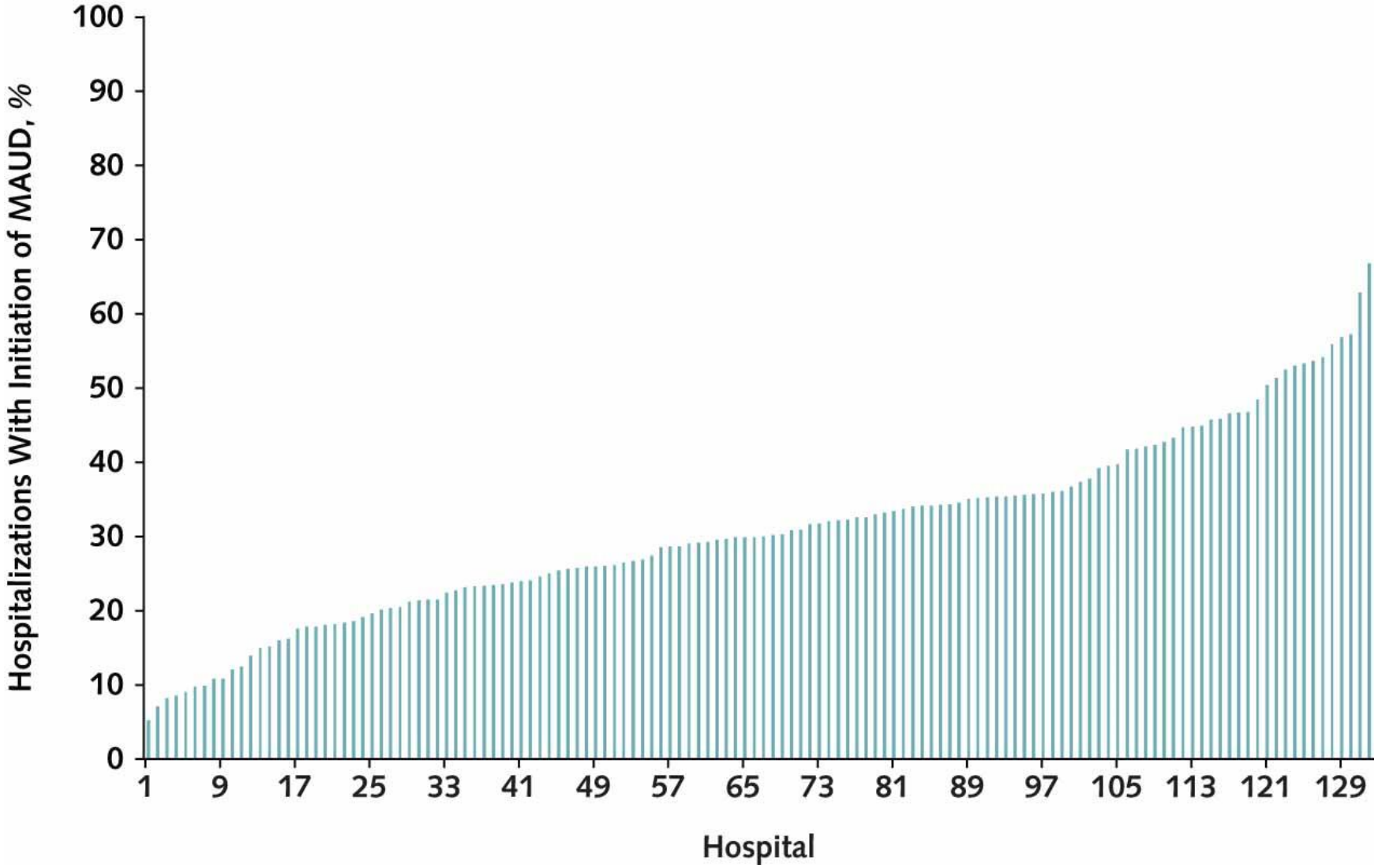
Bernstein EY, et al. *JAMA Netw Open*. March 2024.

MAUD initiation was higher in this VA-based observational study,



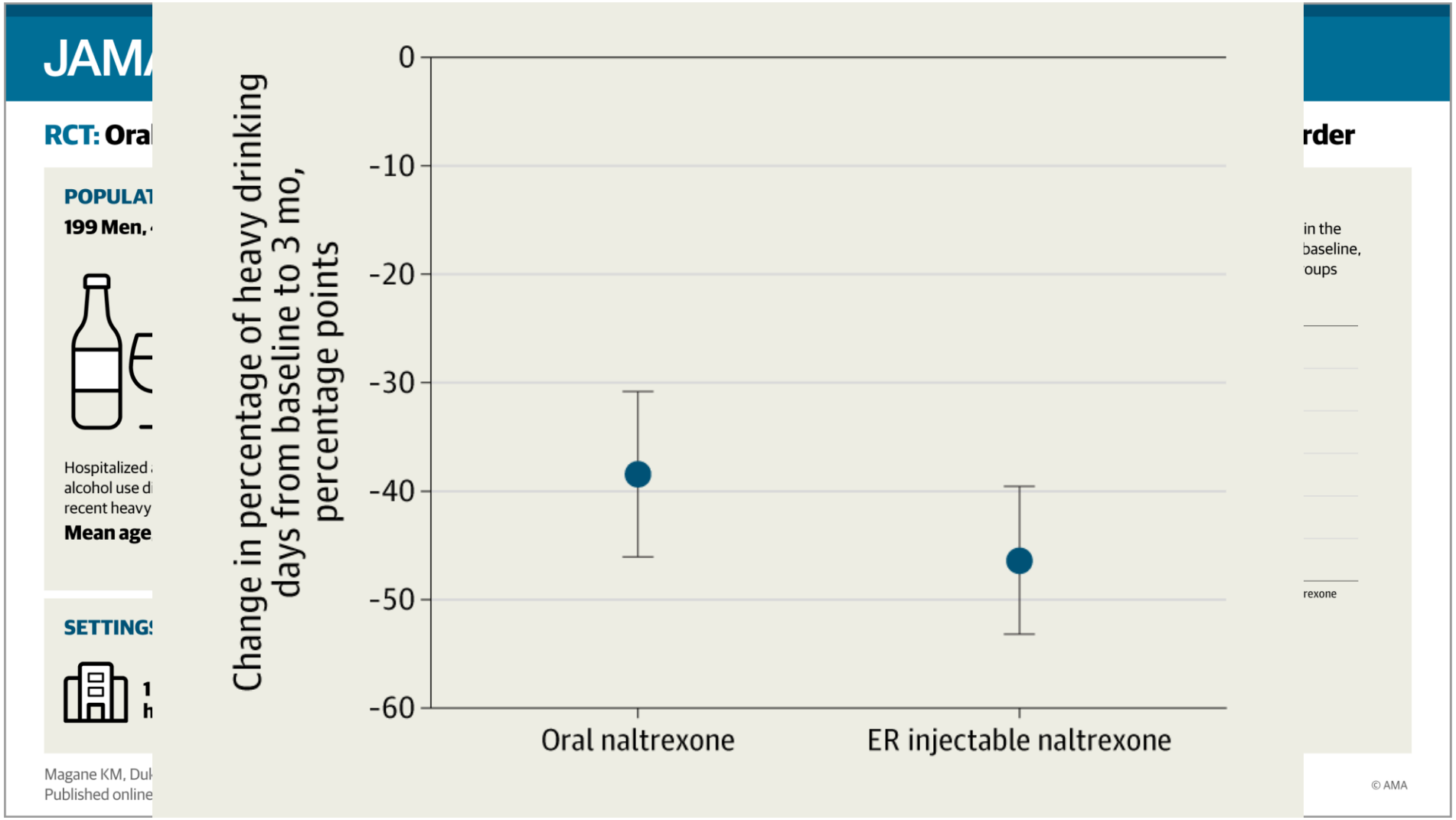
Anderson TS, et al. *Ann Intern Med*. May 2026.

But initiation was also highly variable among hospitals.



Anderson TS, et al. *Ann Intern Med*. May 2026.

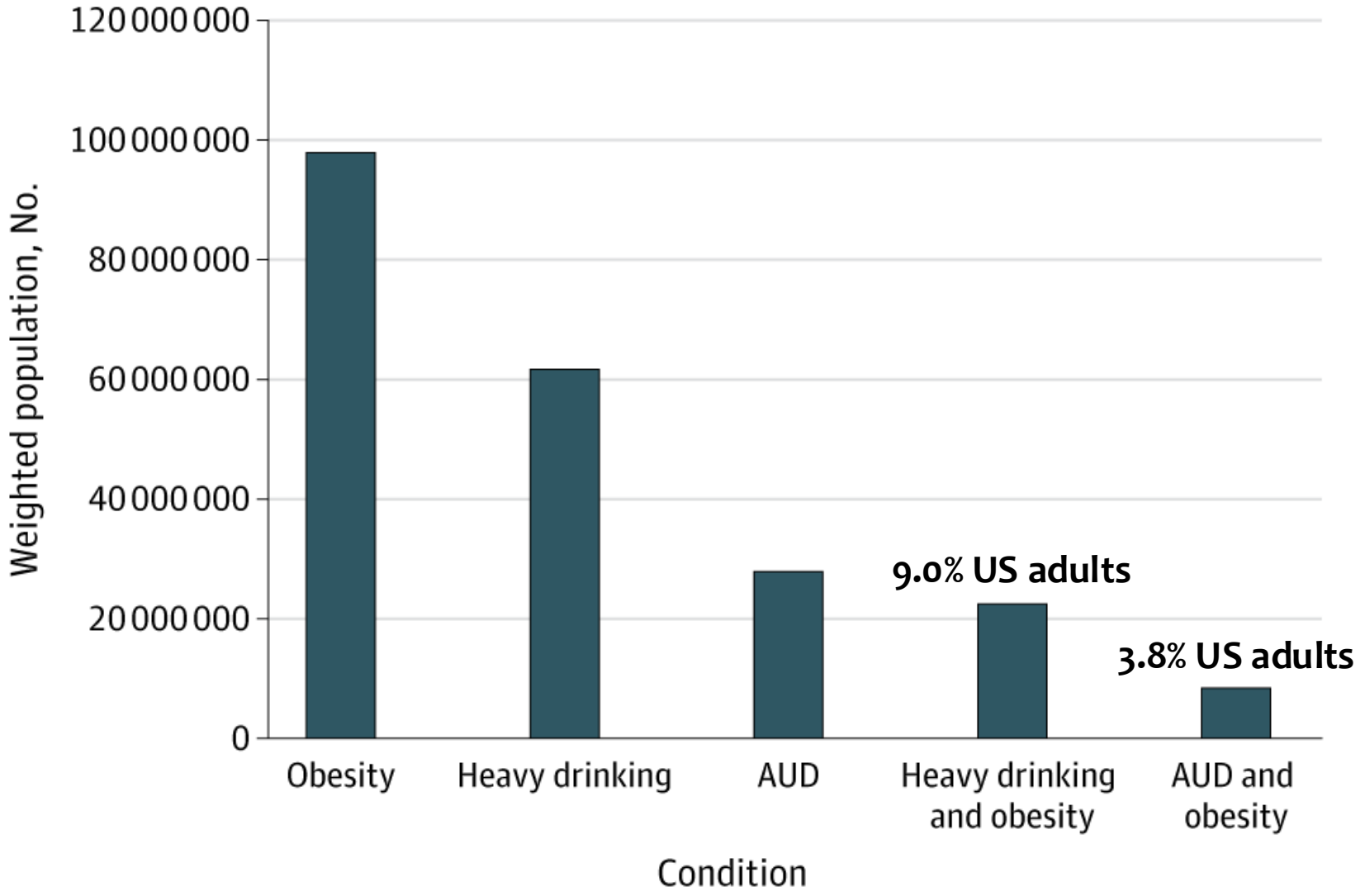
Both naltrexone formulations are similarly effective, so start what makes most sense for your patient!



Magane KM, et al. *JAMA Intern Med*. April 2025.

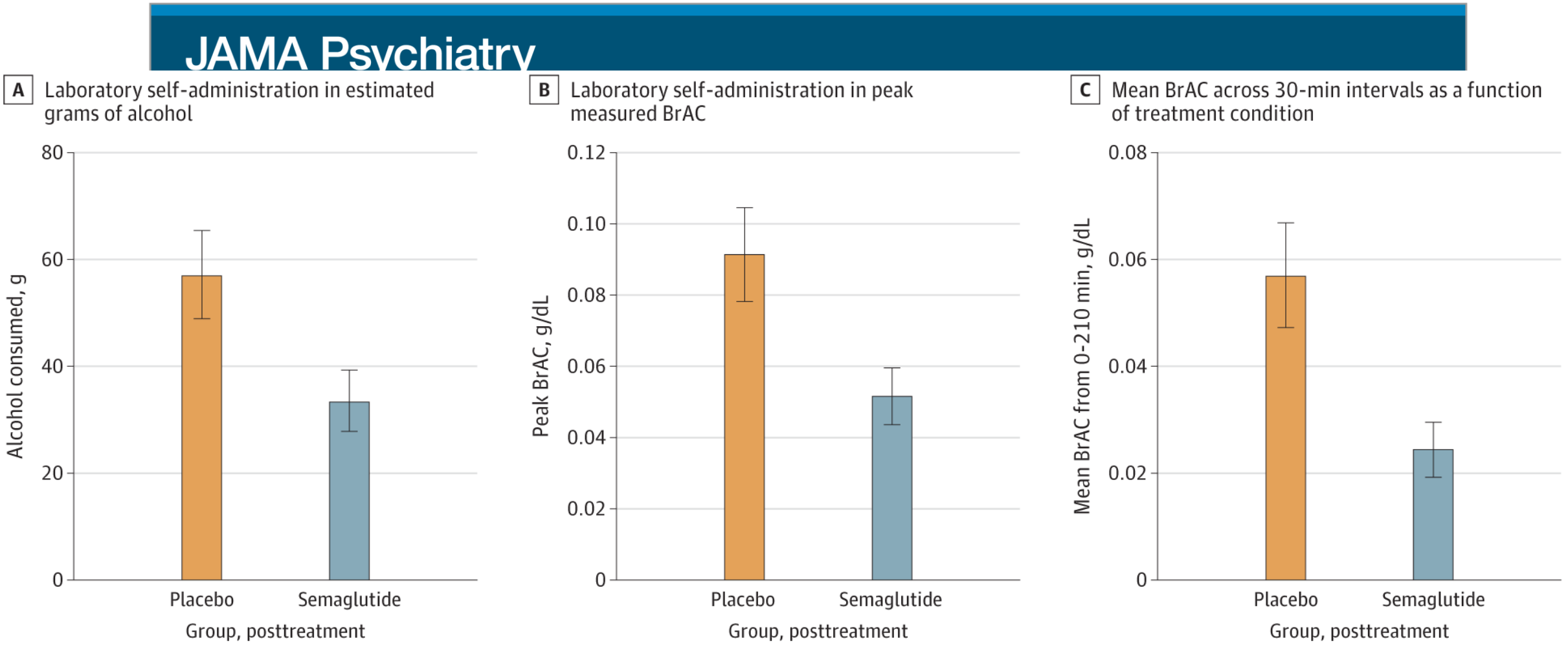
But what about semaglutide?

This patient is not alone.
Nearly 1 in 10 US adults are impacted by obesity and heavy drinking.



Shuey B, et al. *JAMA Intern Med*. April 2026.

Semaglutide showed promise in lab-based alcohol self-administration



Hendershot CS, Bremmer MP, Paladino MB, et al. Once-weekly semaglutide in adults with alcohol use disorder: a randomized clinical trial. *JAMA Psychiatry*.
Published online February 12, 2025. doi:10.1001/jamapsychiatry.2024.4789

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Hendershot CS, et al. *JAMA Psychiatry*. February 2025.

In this recent RCT of patients with comorbid obesity & AUD, semaglutide reduced heavy drinking days.

A B

	Placebo (n=54)	Semaglutide (n=54)	Estimated treatment difference, placebo vs semaglutide (95% CI)	p value
Self-reported drinking and alcohol scales				
Heavy drinking days, percentage points (primary endpoint)*	−26·4 (−34·1 to −18·6)	−41·1 (−48·7 to −33·5)	−13·7 (−22·0 to −5·4)	0·0015
Total alcohol consumption, g/30 days*	−1025·9 (−1260·0 to −791·1)	−1550·2 (−1868·2 to −1232·1)	−467·5 (−739·5 to −195·4)	<0·0009
Days without alcohol consumption, percentage points*	27·6 (19·8–35·5)	38·9 (30·6–47·3)	10·1 (−0·0 to 20·2)	0·051
Change in drinks per drinking day*	−2·1 (−3·1 to −1·1)	−3·5 (−4·5 to −2·6)	−1·5 (−2·6 to −0·5)	0·0051

Table 2: **Change in endpoints from baseline to week 26**

Klausen MK, et al. *Lancet*. May 2026.

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Case 3

43-year-old woman with chronic low back pain and history of opioid use disorder presents with headaches, fatigue, nausea, myalgias, and tremulousness after reducing use of a "natural" mood enhancer purchased at a local gas station.

- Addiction History:
  - Prescribed opioids following back injury at 40
  - Escalated to illicit use of up to 10 tablets of hydrocodone or oxycodone
  - Never insufflated or injected, no heroin or fentanyl use
  - No previous residential treatment or medications for opioid use disorder (MOUD)
  - Last opioid pill use 1.5 years ago → started using gas station product over last 6 months
  - No tobacco, alcohol, benzodiazepines, cannabis, or other illicit substances

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Case 3

43-year-old woman with chronic low back pain and history of opioid use disorder presents with headaches, fatigue, nausea, myalgias, and tremulousness after reducing use of a "natural" mood enhancer purchased at a local gas station.

- Exam:
  - Tachycardic (HR 102), anxious mood, tremor & piloerection present, no mydriasis

- Urine toxicology:
  - Negative for all substances (amphetamine, benzodiazepines, buprenorphine, cocaine, fentanyl, methadone, opiates, oxycodone, and THC)

- Product information: "Better Weather" labeled to contain kava & cat's claw

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BETTER WEATHER
12 PACK
FixElixir
Piper Methysticum & Uncaria Tomentosa Extracts
BETTER WEATHER
FixElixir
BETTER WEATHER
FixElixir
Piper Methysticum & Uncaria Tomentosa Extracts
BETTER WEATHER
12 PACK
FixElixir
Piper Methysticum & Uncaria Tomentosa Extracts
BERRY

What medication would you use to treat her withdrawal?

A. Baclofen

B. Buprenorphine

C. Clonidine

D. Gabapentin

E. Referral to ED for management with benzodiazepines

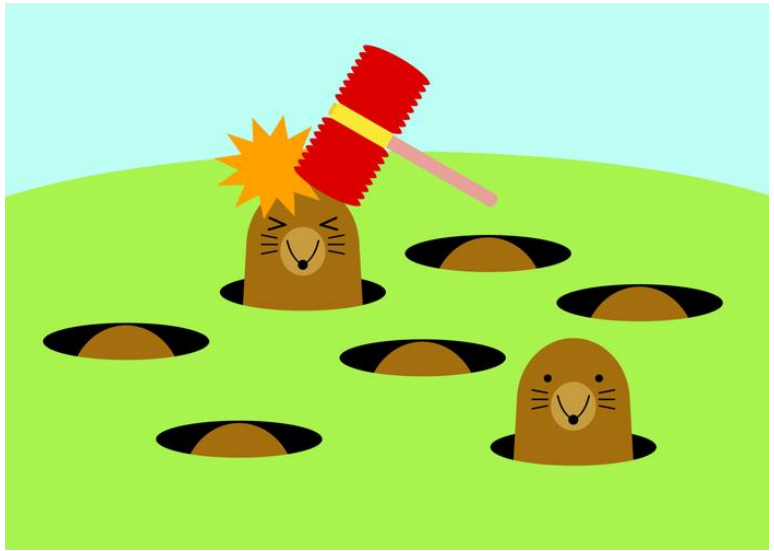
Are we treating withdrawal from
kava (*Piper methysticum*), cat's claw (*Uncaria tomentosa*),
or something else entirely?

In recent testing of these products, we found kratom alkaloids.

Table 1. UPLC-MS/MS Quantitative Analysis of Kava Labeled Products			
Product Name	**Happy Hour Shot 777 Mixed Berry**	**Happy Hour Shot BlueBurstPop**	**Boujee Bliss Strawberry Banana**
Label Claim:	Kavalactone Extract Akuamma Cat's Claw	Kavalactone Extract Akuamma Cat's Claw	Piper methysticum extract Uncaria tomentosa extract
Amount in each Bottle (fl oz):	1.0	1.0	0.5
Total Kratom Alkaloids (µg/Bottle):	263 ± 9.6	258.5 ± 12.0	221.3 ± 4.0
Mitragynine	38.7 ± 1.9	34.3 ± 0.5	38.5 ± 1.1
7-hydroxymitragynine	10.5 ± 0.7	11.5 ± 0.7	3.41 ± 0.0
Mitragynine pseudoindoxyl	207.2 ± 6.9	206.5 ± 10.8	163.4 ± 2.6
Total Kavalactones (mg/Bottle):	167.5 ± 1.2	158.1 ± 0.3	92.8 ± 0.1

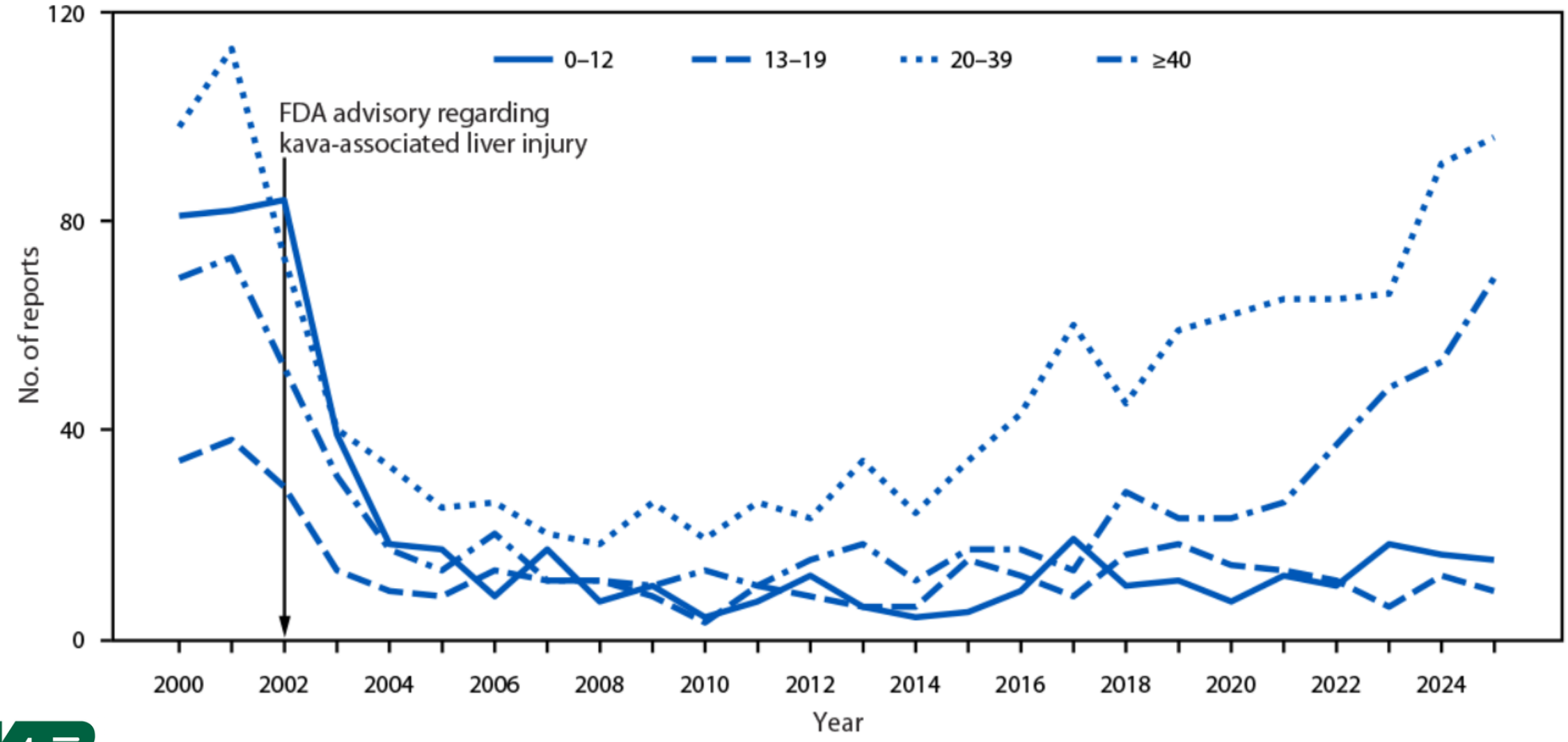
Marshall S, et al. *Clinical Toxicology*. June 2026 (in press).

These “kava” products have turned out to be yet another compound active at the opioid receptor commercially available & unregulated.



NIDA. March 2026.

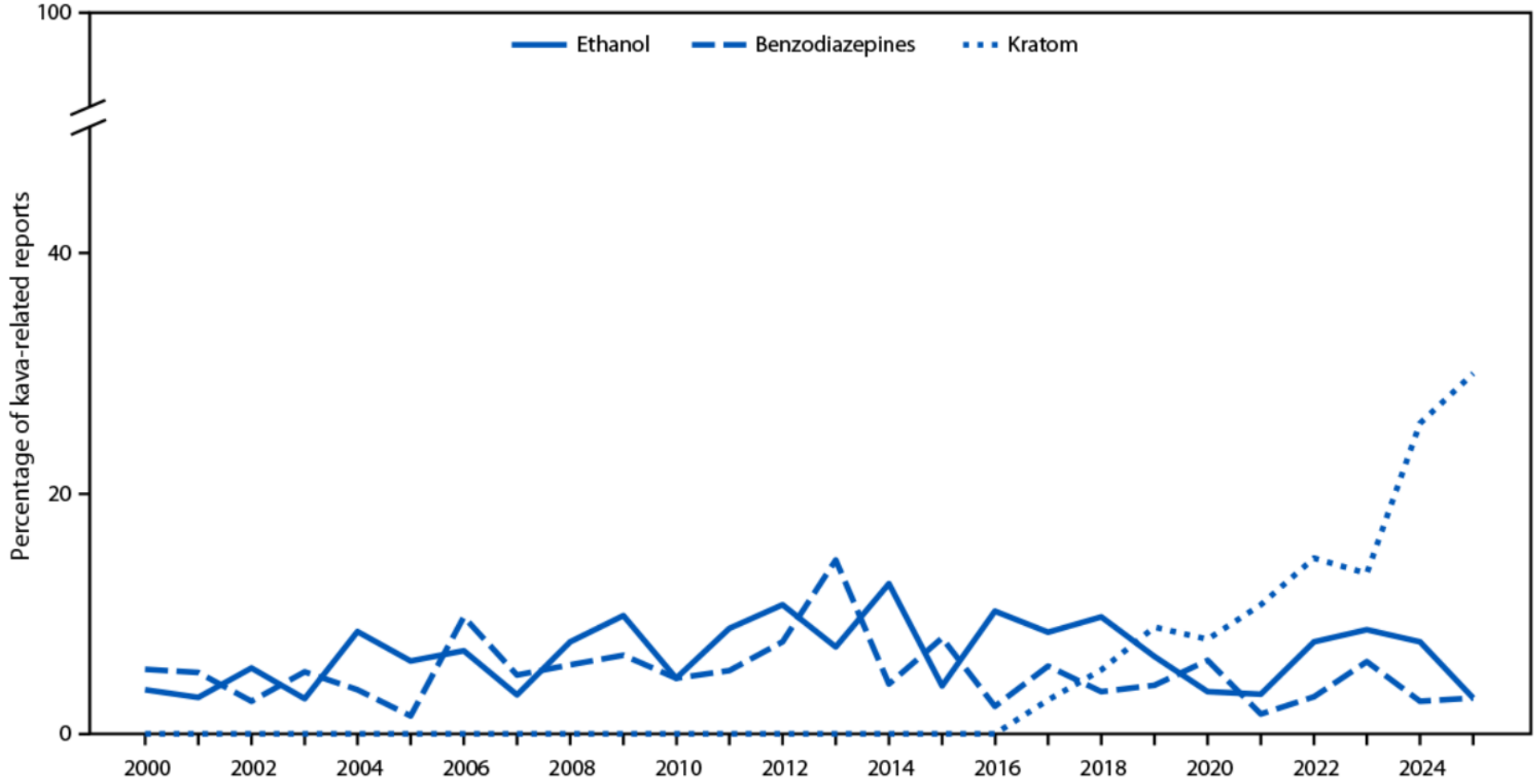
And while kava is not benign…



Tower EB, et al. *MMWR Morb Mortal Wkly Rep*. April 2026.

Insidious marketing has led to an increase in “kratom” use nationally.

FIGURE 3. Percentage of kava-related poison center reports involving ethanol, benzodiazepines, or kratom use — National Poison Data System, United States, 2000–2025



Tower EB, et al. *MMWR Morb Mortal Wkly Rep*. April 2026.

However, these newer products are not simply “kratom.”

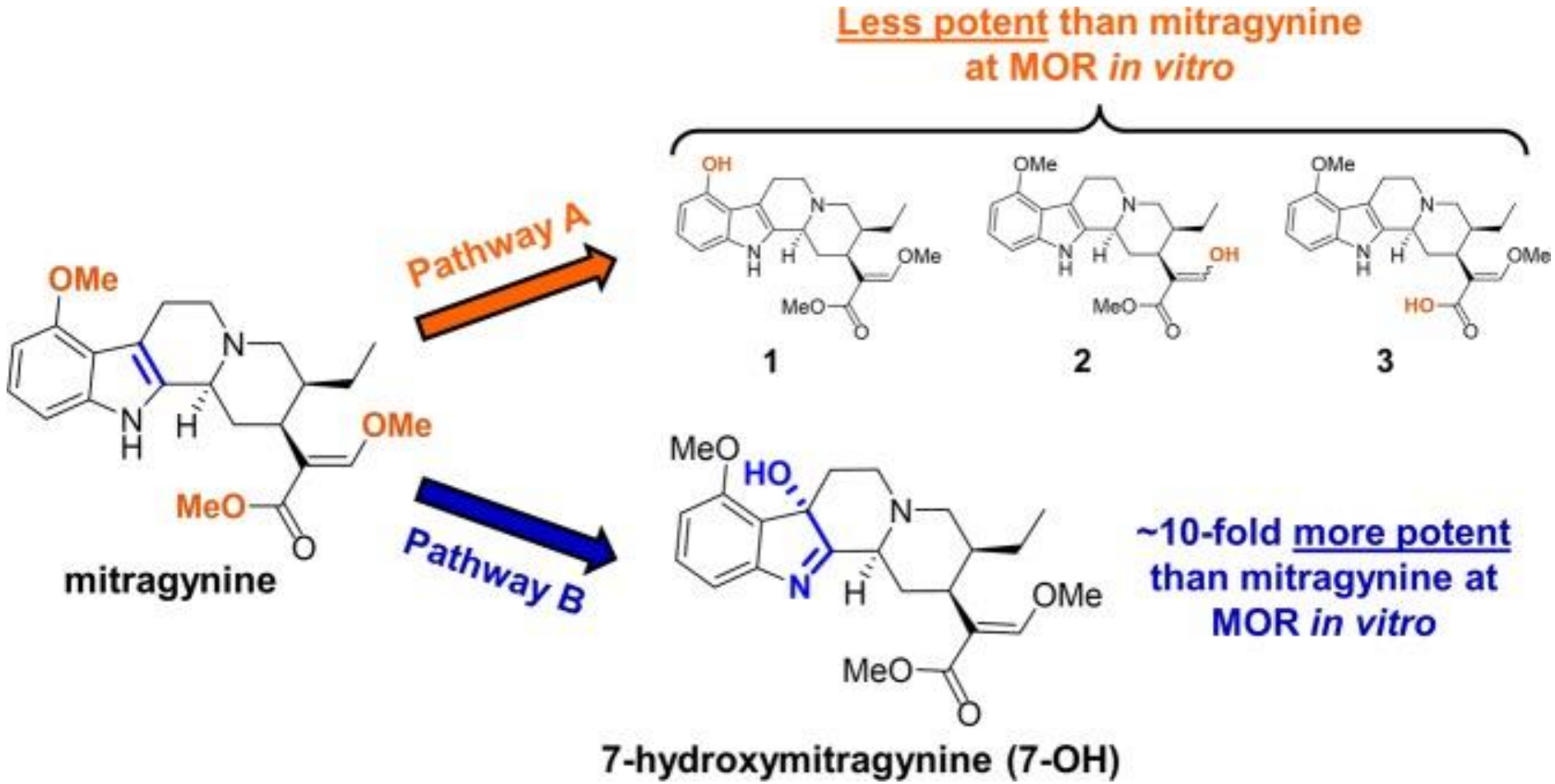
Leaf of kratom tree

Kratom capsules

≠

Drug Enforcement Administration. April 2020.

In its whole plant form, kratom contains mostly mitragynine, which is metabolized primarily to less potent alkaloids.



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Kruegel AC, et al. *ACS Cent Sci*. June 2019.

STOP THE STIGMA

Newer products contain higher amounts of the more potent 7-OH.

Whole Plant Derived Products
1–2% 7-hydroxymitragyine

Leaf of kratom tree

Kratom capsules

≠

Novel Semisynthetic Products
Up to 98% 7-hydroxymitragyine

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Smith KE, et al. *Addiction.* February 2025.

STOP THE STIGMA

So how do we manage her withdrawal?

Given 7-OH's activity at the opioid receptor, buprenorphine has been our most effective treatment.

ORIGINAL RESEARCH

Buprenorphine for the Management of 7-Hydroxymitragynine (7-OH) Use: A Retrospective Case Series

Fenske, Emma DO; Williams, Beth AGNP, MPH, CARN-AP; Hallock-Koppelman, Laurel DNP, FNP-C, APRN, CARN-AP, FAANP; Buchheit, Bradley M. MD, MS

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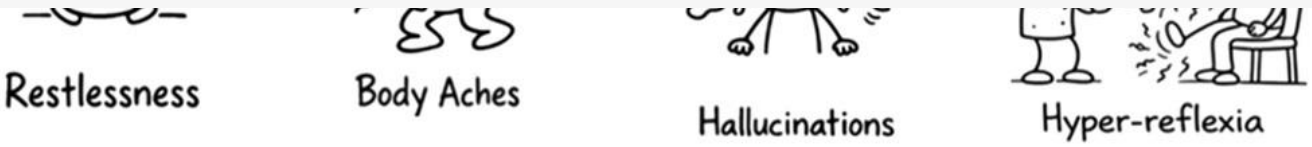
Fenske E, et al. *J Addict Med*. June 2026.

STOP THE STIGMA

Buprenorphine dosing is challenging given lack of labeling, and kava withdrawal contributes to a mixed withdrawal syndrome.

TABLE 2 - Observed Buprenorphine Dosing Patterns Based on Daily 7-OH Use

Estimated Daily 7-OH Use (mg/d)	Estimated Kratom Doses (per Weiss et al),[15] g kratom/d	Rationale	Proposed Buprenorphine Dose Range (mg/d)
<50	<20	Lower physiological tolerance, mild withdrawal risk	2–4
50–150		Moderate dependence, risk of dysphoria/anxiety with cessation	4–8
150–300	>40	Significant opioid-like tolerance and withdrawal	8–16
> 300		High-tolerance pattern similar to high-dose opioid use	12–24+



Fenske E, et al. *J Addict Med*. June 2026. | Kiyokawa M, et al. *J Addict Med*. March 2026.

STOP THE STIGMA

Learning Objectives

1) Describe the changing epidemiology of the overdose crisis & novel interventions to combat its "fourth wave"
2) Explore current gaps in alcohol use disorder treatment and existing but underutilized as well as new & innovative pharmacotherapy for closing them
3) Identify risks of unregulated, commercially available products containing opioid-like compounds
4) **Recognize emerging psychoactive substances adulterating the illicit drug market and their associated medical complications**

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Case 4

36-year-old man with severe opioid (IV fentanyl) use disorder and chronic hepatitis C infection presents after accidental overdose with initial response to intranasal naloxone.

- Arrival to ED & Course:
  - Presenting VS: T 98.6F, HR 66, BP 139/94 , RR 7, 96% RA
  - Experiencing intermittent apneic episodes, so started on naloxone infusion
  - Admitted to MICU due to sluggish to little response after naloxone initiation
  - MICU VS: T 96.9F, HR 53, BP 99/62, RR 8, 97% 2L
- UDS:
  - Positive for cannabis and fentanyl
  - Negative for amphetamines, benzodiazepines, buprenorphine, cocaine, methadone, opiates, and oxycodone

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What are we missing?

An overdose on which of the following substances would not be reversed by naloxone:

A. Nitazenes

B. Medetomidine

C. Xylazine

D. B and C

E. A, B, and C

Cutting agents are inherent to the illicit drug market.

Diluents

- Pharmacologically inactive
- Readily available
- $
- Mimic sight and taste

Adulterants

- Pharmacologically active
- Less available
- $$
- Mimic effects
- Enhance effects
- Ease administration

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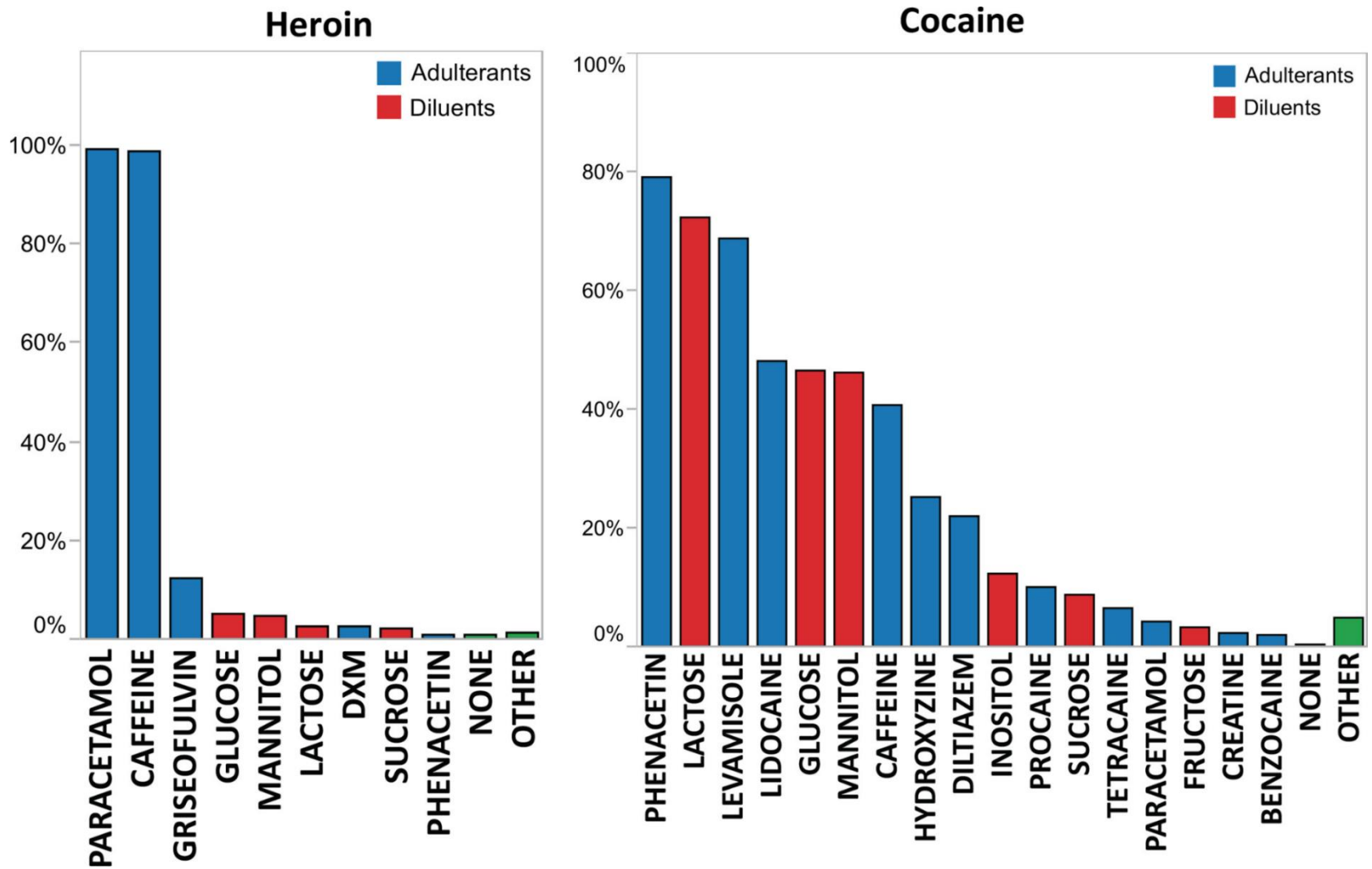
Broséus J, et al. *Forensic Sci Int*. September 2016.

STOP THE STIGMA

Cutting agents are inherent to the illicit drug market.



Broséus J, et al. *Forensic Sci Int*. September 2016.

What more recent adulterant could explain our patient's MICU course?

Case 4

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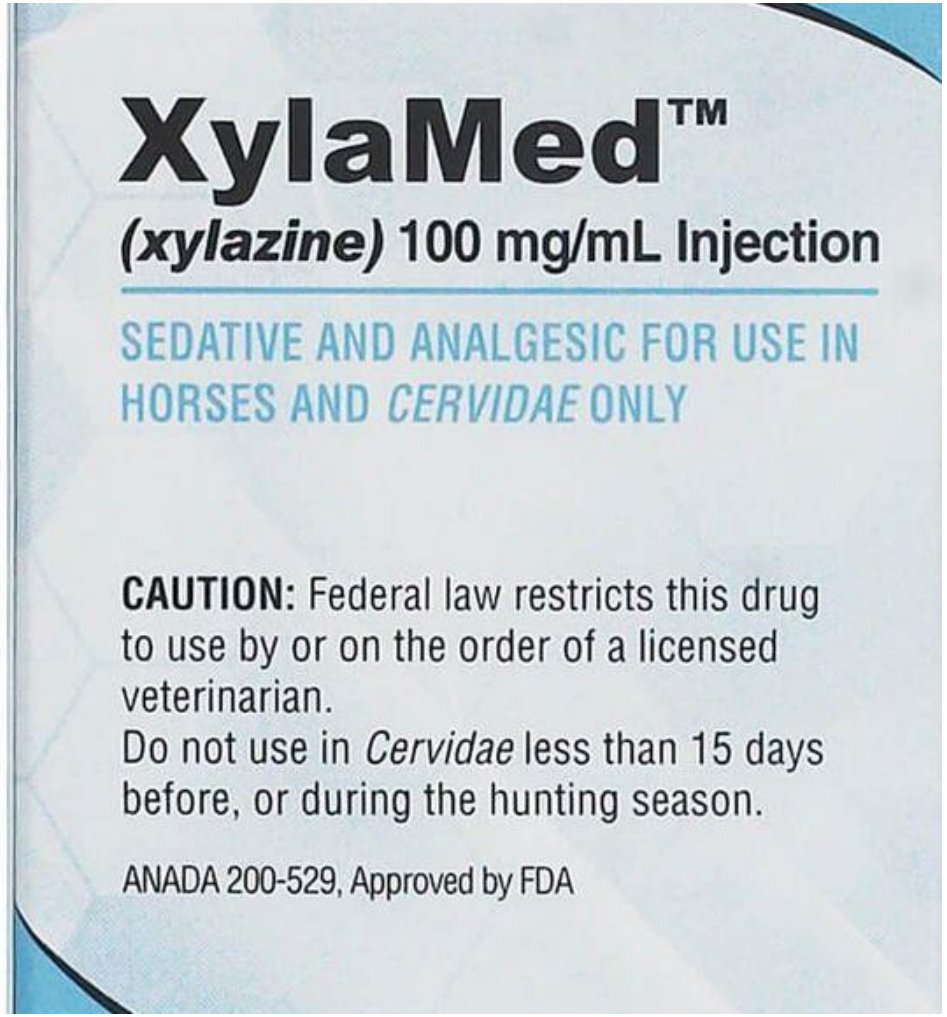
STOP THE STIGMA

Actual horse tranquilizer… xylazine complicates fentanyl overdoses



Xylazine a.k.a. "Tranq"

- Analogue of clonidine
- Bradycardia
- Hypotension
- CNS depression
- Respiratory depression
- Increases OD risk
- Not reversed by naloxone

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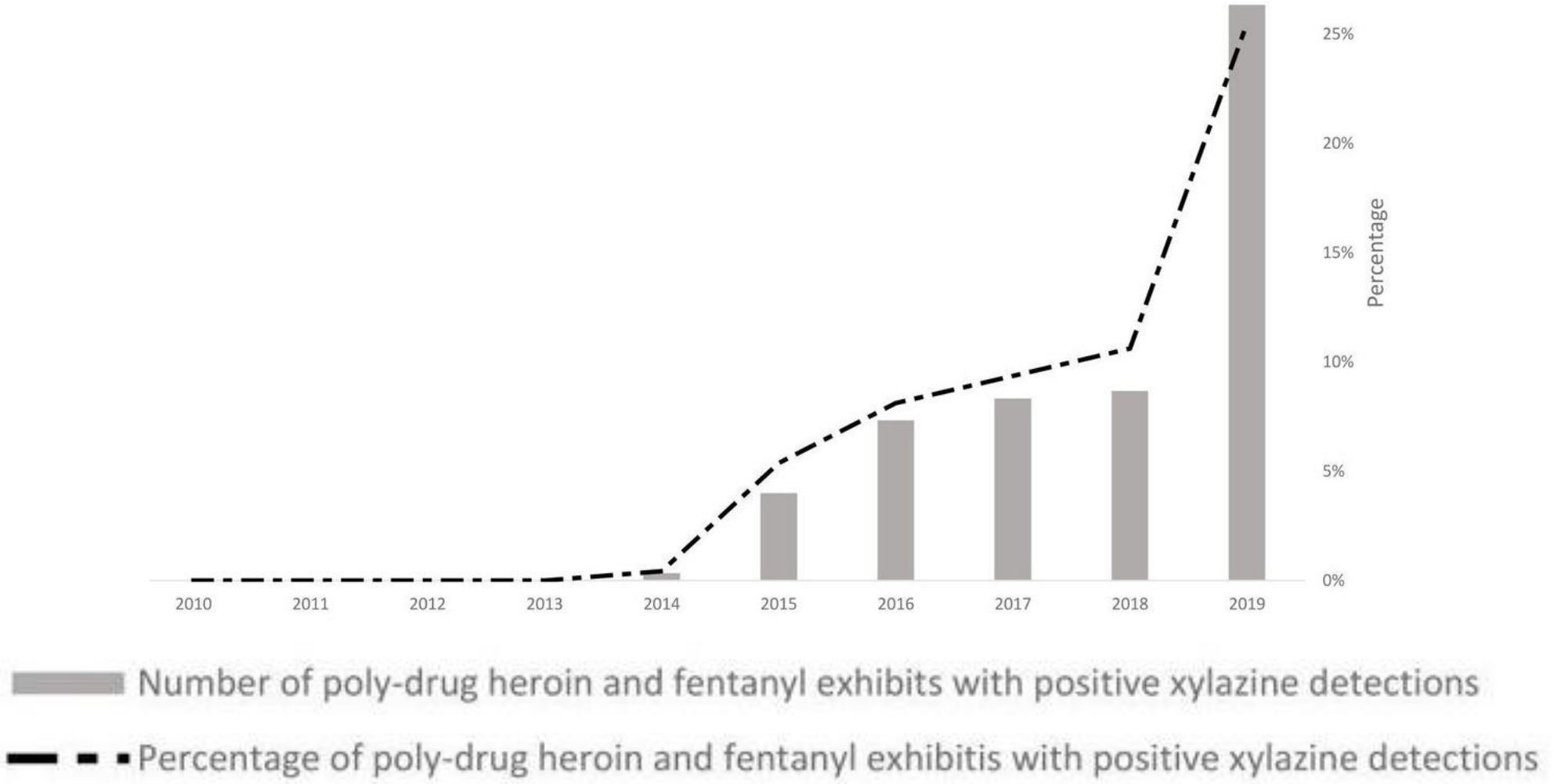
Johnson J, et al. *Inj Prev*. August 2021.

STOP THE STIGMA

Initial reports from Philly detected its emergence over 10 years ago.



Johnson J, et al. *Inj Prev*. August 2021.

Though not always nationally recognized, the South has carried the burden of xylazine-related deaths.

(U) Figure 1. DEA Forensic Laboratory Identifications of Xylazine by Region

Region	2020	2021	Percent Increase
Northeast	346	556	61%
South	198	580	193%
Midwest	110	118	7%
West	77	163	112%

Source: DEA

(U) Figure 2. Number of Xylazine-Positive Overdose Deaths by Region

Region	2020	2021	Percent Increase
Northeast	631	1,281	103%
South	116	1,423	1,127%
Midwest	57	351	516%
West	4	34	750%

Source: DEA

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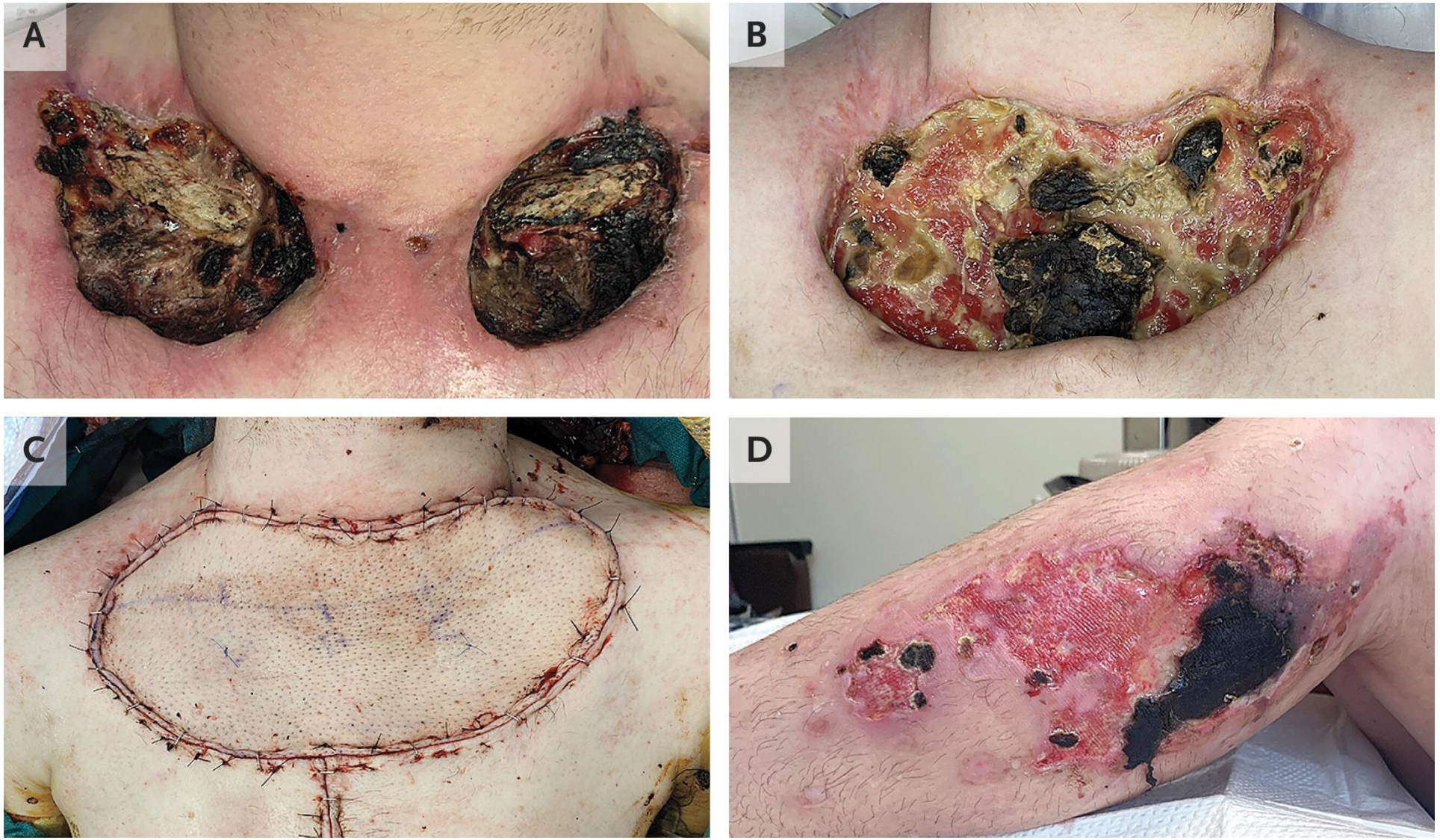
DEA Joint Intelligence Report. *Drug Enforcement Administration*. October 2022.

STOP THE STIGMA

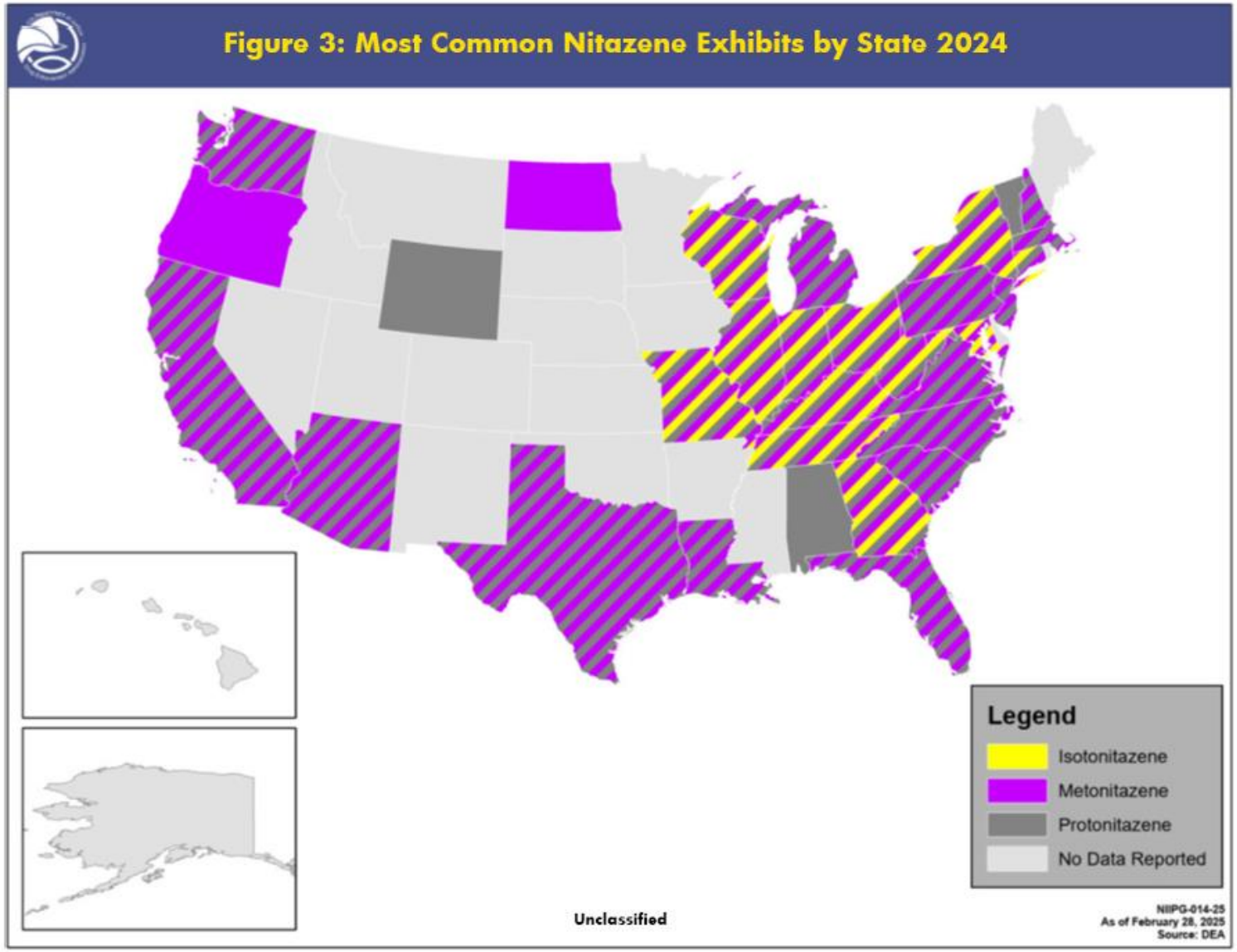
And by now, you have likely seen xylazine-associated skin injuries.



O'Neil J, Kovach S. *N Engl J Med*. June 2023.

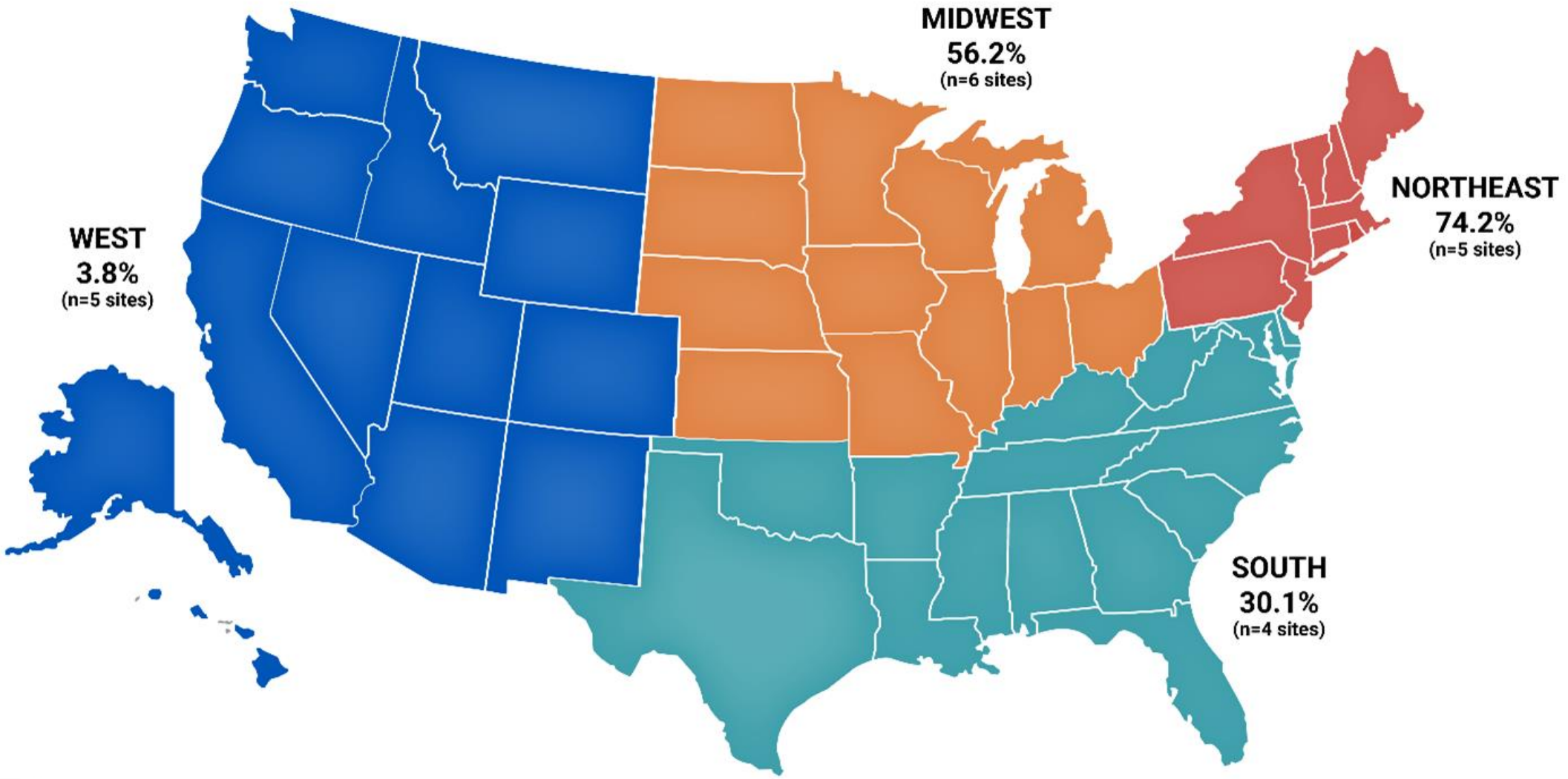
And new threats continue to emerge…

Nitazenes, a diverse group of synthetic opioids, have popped up.



Drug Enforcement Administration. September 2025.

And medetomidine, another alpha-2 agonist, has recently emerged.



Centers for Disease Control & Prevention. April 2026.

And may be eclipsing the prevalence of xylazine.

TABLE 2 - LC-MS/MS Confirmatory Toxicology (System A Only)

Substance Detected (LC-MS/MS)	n (% of tested)
Norfentanyl	43 (100.0)
3-OH-Medetomidine (post-glucuronidase)	43 (100.0)
Xylazine (post-glucuronidase)	29 (67.4)
3-OH-Medetomidine	28 (65.1)
Xylazine	24 (55.8)

London KS, et al. *J Addict Med*. March – April 2026.

An overdose on which of the following substances would not be reversed by naloxone:

A. Nitazenes

B. Medetomidine

C. Xylazine

D. B and C

E. A, B, and C

Takeaways

1) **Remember tools for the Fourth Wave**
   - Bupropion + ER-Naltrexone show the greatest potential for methamphetamine use disorder
   - Mirtazapine may be more cost-effective but with less effect
   - Naloxone, Fentanyl test strips, & Never Use Alone for every patient using stimulants
2) **Treat alcohol use disorder**
   - Naltrexone & Acamprosate are underutilized
   - PO naltrexone & extended-release IM naltrexone are similarly effective
   - Though not yet approved for AUD, semaglutide reduces heavy drinking (maybe even more than naltrexone!)
3) **Suspect 7-OH (semisynthetic kratom) in gas station products**
   - "Kava" products surreptitiously contain mitragynine & 7-oH
   - These extracts contain much higher amounts of 7-OH (more potent) than plant-based products
   - Consider buprenorphine for treating kratom & 7-OH withdrawal and use disorder
4) **Practice vigilance for emerging adulterants in the drug market**
   - Xylazine complicates fentanyl overdoses & may cause necrotic skin lesions
   - Though does not produce skin wounds, medetomidine withdrawal leads to severe sympathetic activation
   - Nitazenes are a diverse group of synthetic opioids – some more potent than fentanyl

As we have looked ahead to emerging threats
but also to hopeful novel treatments,

I'll close with one look back…

JAMA The Journal of the American Medical Association

June 12, 1991

Fentanyl-Laced Heroin

Daniel Fernando, PhD

JAMA. 1991;265(22):2962. doi:10.1001/jama.1991.03460220050029

Fernando D. *JAMA*. June 1991.

Updates in Addiction Medicine: Emerging Substances & Novel Treatments

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