

Addiction Medicine Annual Review of the Literature

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Disclosures

- ◆ Joshua D Lee MD MSc
 - ◆ In kind study drug donation: Alkermes, Indivior
 - ◆ Science Advisor: OarHealth.com

- ◆ Talia Rosen
 - ◆ None

- ◆ Sarah E. Wakeman, MD, FASAM
 - ◆ UpToDate author; Springer textbook editor

Learning Objectives

At the conclusion of this session, participants will be able to have:

- Increased awareness of recent key studies in the field of addiction medicine
- Increased working knowledge of key findings from recent cutting edge or important research in addiction medicine
- Discuss the clinical utility and methods for applying the knowledge and findings from key research articles in addiction medicine

2023-2024...The years that were

Fully post-COVID and back to normal?

"New" drugs, not good drugs: Xylazine and Nitazenes

Overdoses: Worsening fentanyl and stimulant driven overdose crisis in US; Worsening racial and ethnic disparities in overdose deaths

Opioid and Related Policies:

Elimination of the X waiver

Oregon drug decriminalization

SCS/Overdose Prevention Centers

Telehealth flexibilities extended

OTP rule evolutions: 'liberating methadone'

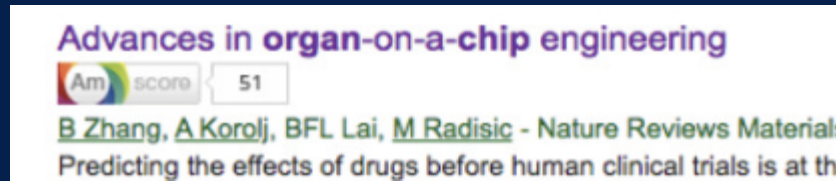
Housing and homelessness



Methods: Literature scan and article selection

1. Lit Scan of all of PubMed for 2023:

- **Search terms:** 'addiction', 'substance use disorders', 'addiction treatment', nicotine, opioid, fentanyl, harm reduction...**35** different key words which map to **MESH terms**
- Publication Dates: **1/1/2023 - 12/31/2023**
- **Ranked by Altmetric score** (media and social media posts):
 - Altmetric for Pubmed Chrome browser extension



2. Journal Index search (redundant with Step 1):

- **Highest impact general medical or psychiatry journals:** NEJM, The Lancet, JAMA, AJP, JAMA Internal Medicine, JAMA Psychiatry, JAMA Network Open, Annals Internal Medicine
- **Addiction Specialty Journals:** Addiction, Am Jo Addiction, Jo Addiction Med, JSAT, Drug Alcohol Dependence, Substance Use & Addiction, Alcohol Clin Express
- **Ranked by Altmetric Score**

4. Newsletter scans: BU's Alcohol, Other Drugs, and Health; ASAM Weekly

5. Final Selection: **Altmetric score ranking plus our editorial perspective and opinions**

Literature Scan: Results

- All of Pubmed Year for '2023': 4,096 articles
- Abstracts reviewed: 178
- Altmetric score range if score >0: 4 - 2502
- Mean score if score >0: 335
- Top 10 + 15 others = today's slides: 25 papers
- Literature Scan Results on Google/Drive:
<https://docs.google.com/spreadsheets/d/16xalgOrxIHrBewwWvcAFb2dFqFG0HkJ1/edit?usp=sharing&oid=105957773192103431397&rtpof=true&sd=true>
- This presentation:
<https://docs.google.com/presentation/d/10cckSetbeQRHpR5giph2Iek85N2wGB2D/edit?usp=sharing&oid=105957773192103431397&rtpof=true&sd=true>

Top 10 Addiction Medicine Papers - 2023

Title	1st Author	Journal	Altmetric Score
#1 Association Between Daily Alcohol Intake and Risk of All-Cause Mortality: A Systematic Review and Meta-analyses	Zhao J	<i>JAMA Net Open</i>	2648
#2 Illicitly Manufactured Fentanyl-Involved Overdose Deaths with Detected Xylazine - United States, January 2019-June 2022	Karissa	<i>MMWR</i>	2615
#3 Evaluating the impact of alcohol minimum unit pricing on deaths and hospitalisations in Scotland: a controlled interrupted time series study	Wyper GMA	<i>Lancet</i>	2340
#4 One-Year Association of Drug Possession Law Change With Fatal Drug Overdose in Oregon and Washington	Joshi	<i>JAMA Psych</i>	1861
#5 Pharmacological and electronic cigarette interventions for smoking cessation in adults: component network meta-analyses	Lindson N	<i>Cochrane Database Syst Rev</i>	1846

Top 10 Addiction Medicine Papers - 2023

#6 Cannabis Use Disorder and Subsequent Risk of Psychotic and Nonpsychotic Unipolar Depression and Bipolar Disorder	Jefsen	<i>JAMA Psych</i>	1493
#7 Spatiotemporal Analysis Exploring the Effect of Law Enforcement Drug Market Disruptions on Overdose, Indianapolis, Indiana, 2020–2021	Ray	<i>AJPH</i>	1459
#8 Treatments Used Among Adolescent Residential Addiction Treatment Facilities in the US, 2022	King	<i>JAMA</i>	1402
#9 Population-Level Health Effects of Involuntary Displacement of People Experiencing Unsheltered Homelessness Who Inject Drugs in US Cities	Barocas	<i>JAMA</i>	1366
#10 Alcohol Intake and Blood Pressure Levels: A Dose-Response Meta-Analysis of Nonexperimental Cohort Studies	Di Federico	<i>HTN</i>	1353

2023 top addiction medicine paper!




University of Victoria | Canadian Institute for Substance Use Research

IAS | Institute of Alcohol Studies

#1. Association Between Daily Alcohol Intake and Risk of All-Cause Mortality: A Systematic Review and Meta-analyses

Dr. Adam Sherk



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Zhao J, et. al.; JAMA Network Open



Dr. Jinhui Zhao



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Moderate drinking does not impact mortality (no J-curve)

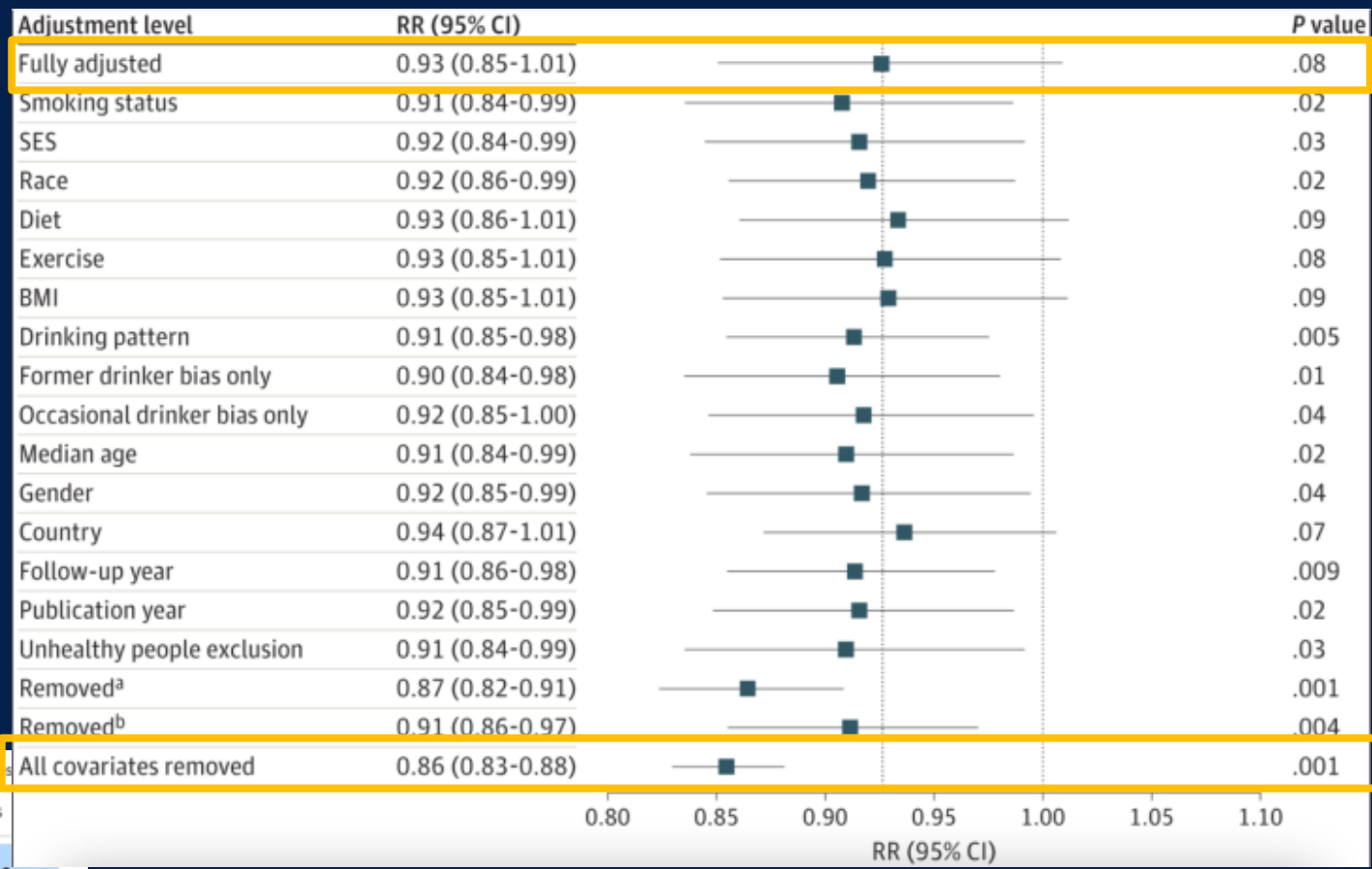
#1. Association Between Daily Alcohol Intake and Risk of All-Cause Mortality: A Systematic Review and Meta-analyses. Zhao, JAMA Net Open, 2023

Data Design: systematic search of PubMed and Web of Science was performed to identify studies published between January 1980 and July 2021, then mixed linear regression models

Conclusions and Relevance

- daily low or moderate alcohol intake was not significantly associated with all-cause mortality risk
- increased risk was evident at higher consumption levels & at lower levels for women

Figure. Relative Risk (RR) of All-Cause Mortality Due to Low-Volume Alcohol Consumption (1.3-24.0 g Ethanol per Day) With and Without Adjustment for Potential Confounding by Each Covariate or Set of Covariates



THE WALL STREET JOURNAL.

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A Little Alcohol Won't Kill You or Make You Stronger

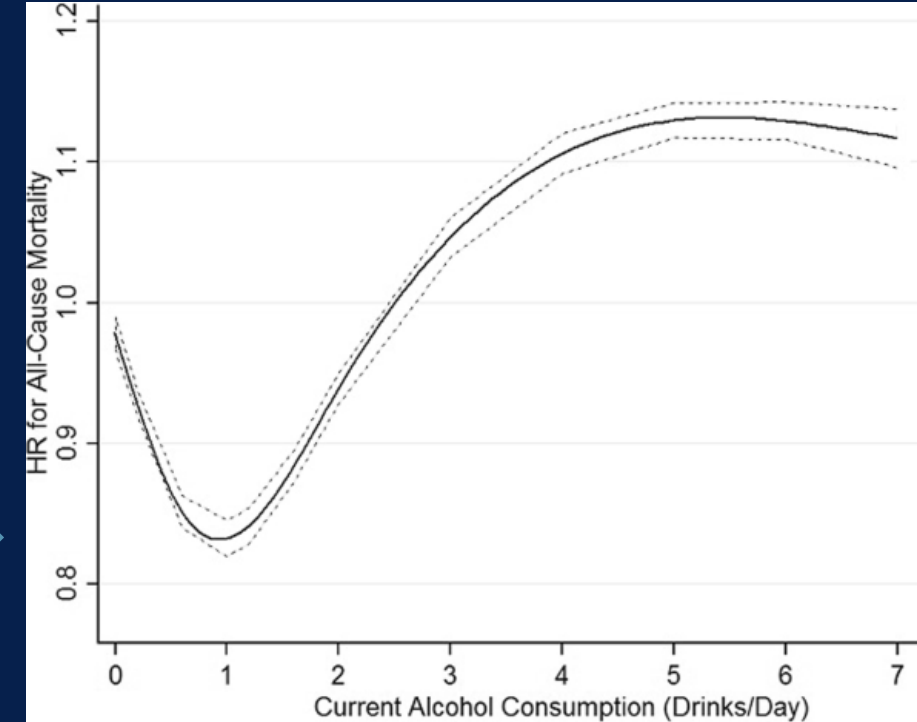
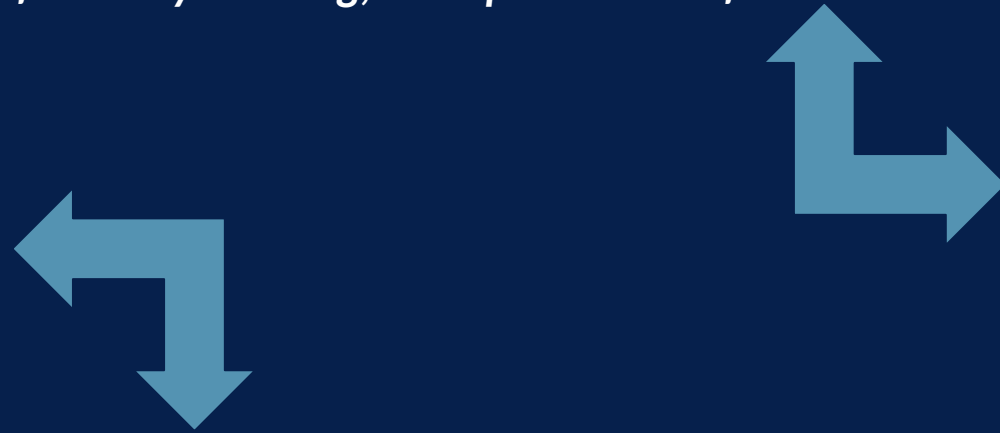
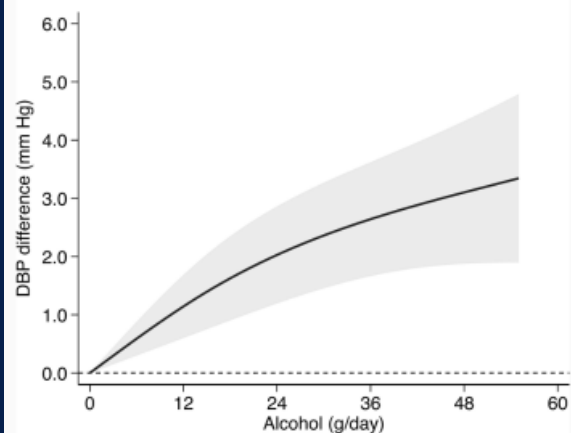
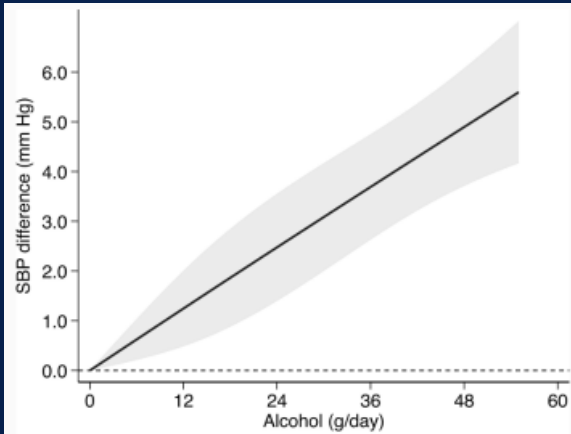
People who drink a little don't die sooner than people who never drank, study shows



TLDR/ More alcohol = more blood pressure, BUT, single drinking cohort studies still show J-shaped curve

#101. Alcohol consumption and all cause and cause specific mortality among US adults: prospective cohort study, Tian, BMC Med 2023

- National household survey study 1997-2014 linked to NDI
- *Lower mortality w/ infrequent, light, moderate drinking*
- *Higher all cause mortality for heavy drinking, most pronounced for cancer*



#10. Alcohol Intake and Blood Pressure Levels: A Dose-Response Meta-Analysis of Nonexperimental Cohort Studies; Di Federico, Hypertension, 2023

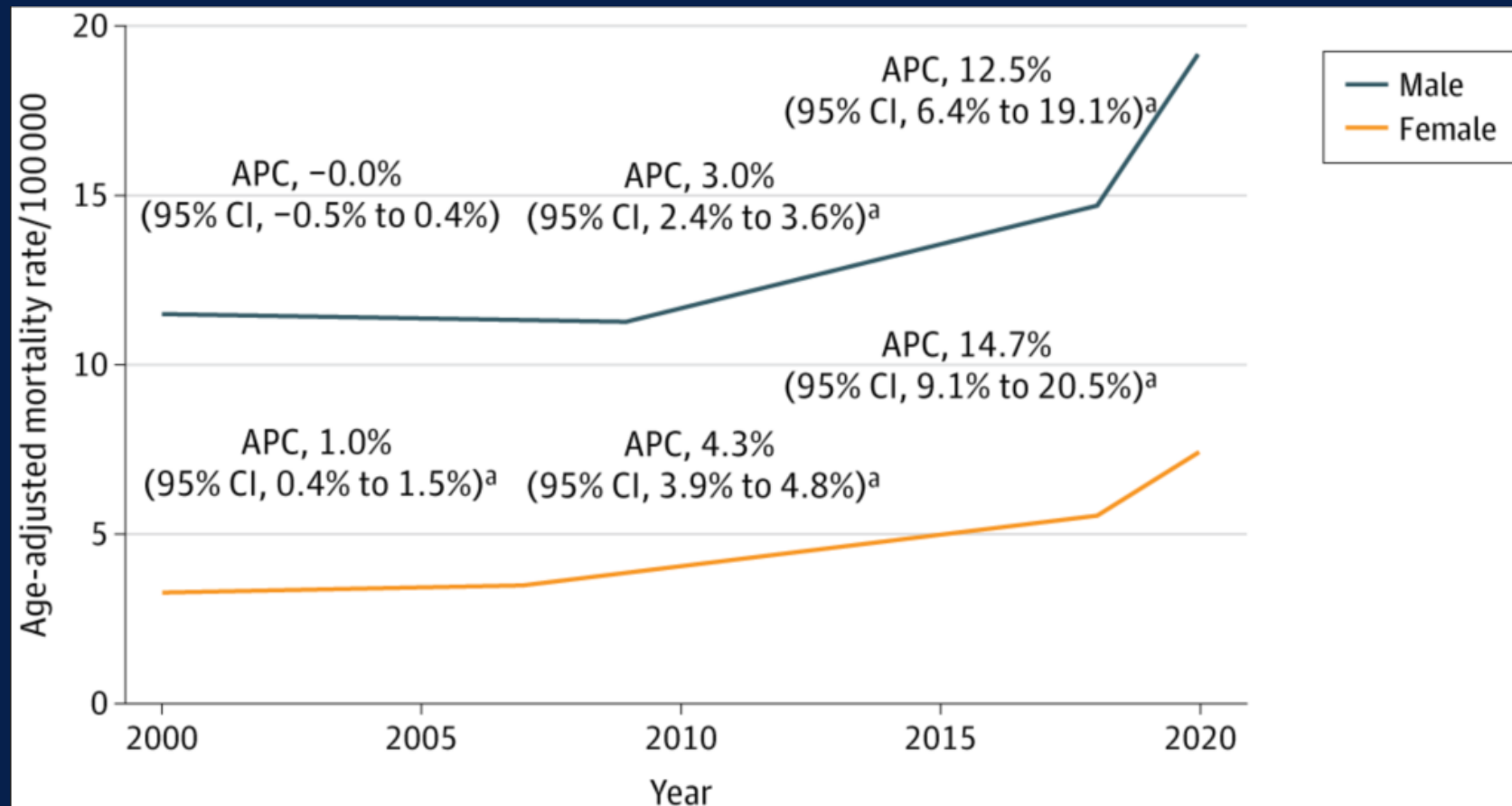
- *Linear increase in SBP with increasing alcohol intake*
- *We used to think BP possibly lower w moderate alcohol intake*

Women catching up to men w alcohol-related mortality: #13 Trends in Alcohol-Related Deaths by Sex US, 1999-2020

Karaye, JAMA Net Open, 2023



- Cross-sectional study of 605 948 alcohol-attributed deaths:
- Males had a significantly higher burden of alcohol-involved mortality than did female
- Temporal trends revealed a significantly higher rate of increase observed for female

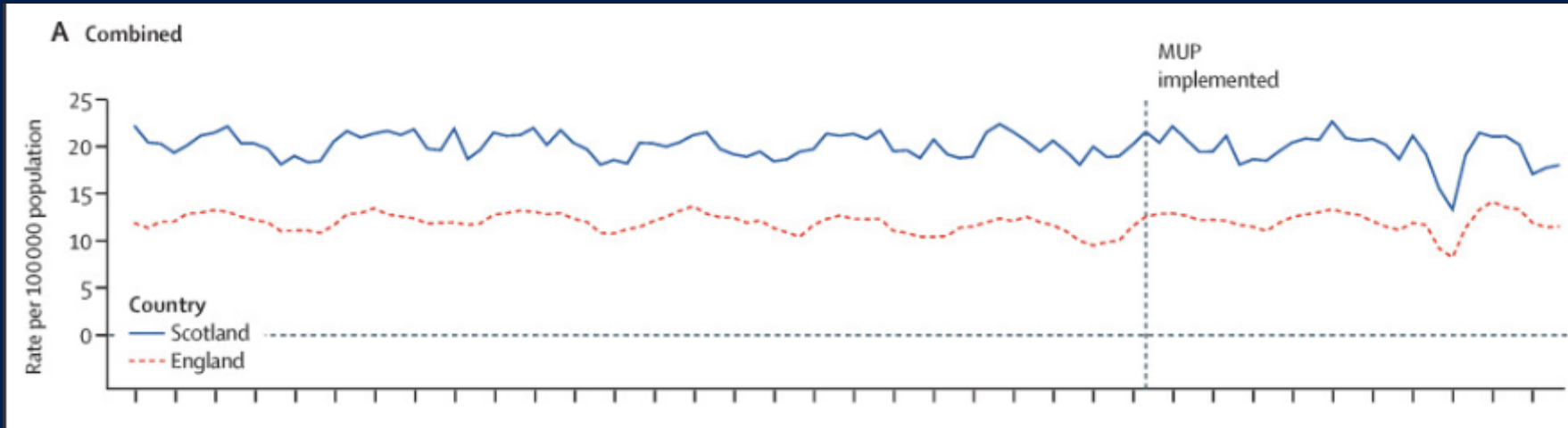


How to drink less? : make alcohol more expensive

#2. Evaluating the impact of alcohol minimum unit pricing on deaths and hospitalisations in Scotland: a controlled interrupted time series study; **Wyper, Lancet, 2023**



Raising prices per unit alcohol in Scotland lowered death and hospitalization rates compared to England



#14. Impact on alcohol selection and online purchasing of changing the proportion of available non-alcoholic versus alcoholic drinks: A randomised controlled trial. **Clarke, PLOsMed, 2023**.



People bought substantially less alcohol if presented with more non-alcohol beverage choices in both a simulation trial and then in real life



More from 2023; Major Themes:

Alcohol Updates

Two big papers: cannabis-mood DOs and Cochrane Review of Smoking Cessation

Opioid and stimulant overdose trends

Racial Inequities, Social Determinants, SUD

Telehealth, m-health and Novel Approaches to MOUD

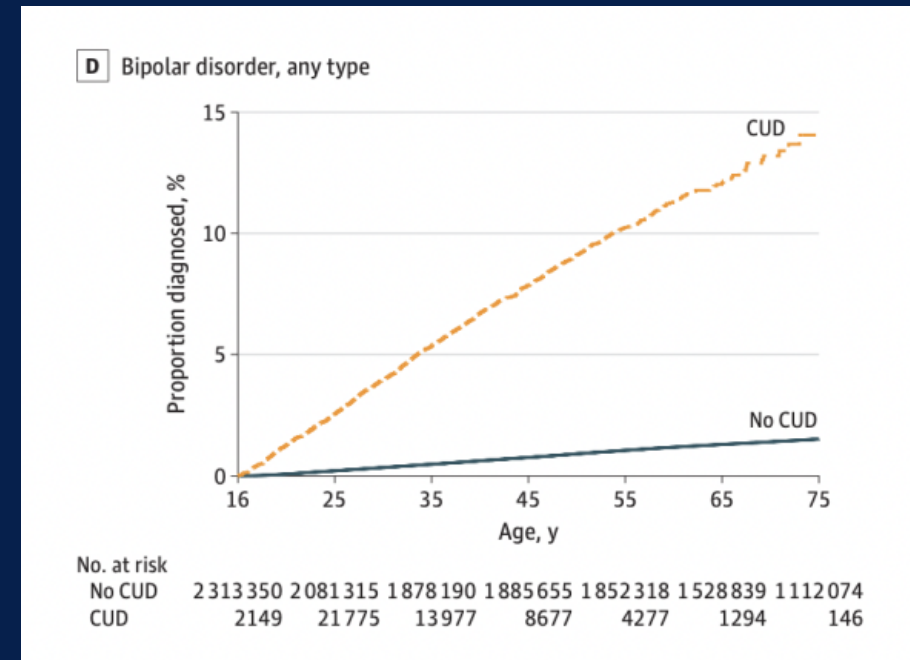
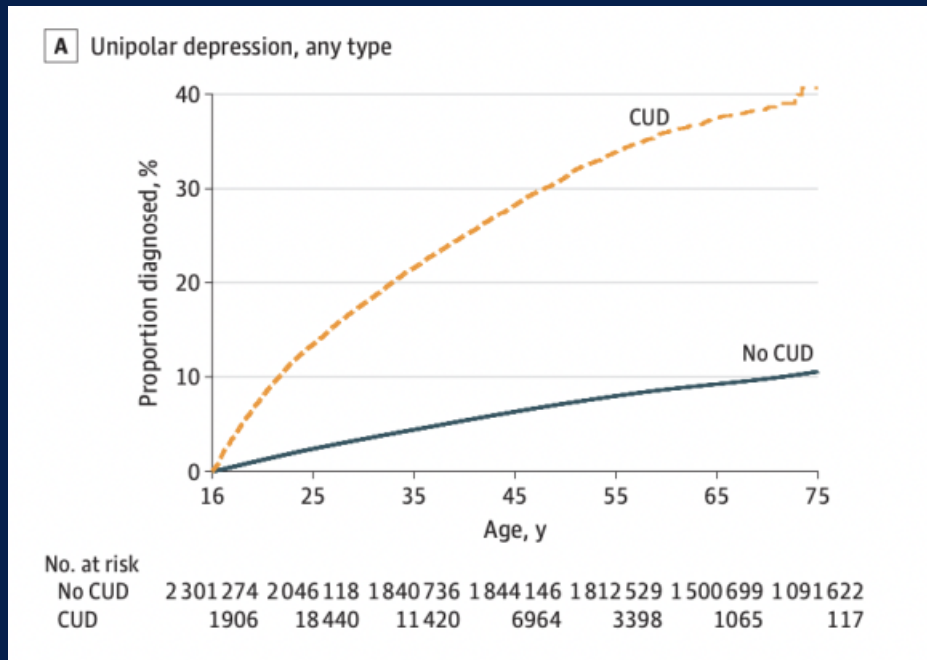


#6 Cannabis Use Disorder (CUD) and Subsequent Risk of Psychotic and Nonpsychotic Unipolar Depression and Bipolar Disorder



Jefson et al. JAMA Psychiatry, 2023

- Prospective, population-based cohort study; Danish registry:
 - ~6.6 million individuals, 16+ yo, 1995-2021
- *Do people with Cannabis Use DO have increased Unipolar Depression (Psychotic and Nonpsychotic) and Bipolar Disorder (Psychotic and Nonpsychotic)?*
- among n=56k with CUD treatment episode(s) : increased risk of both depression and bipolar disorders



#5 Pharmacological and electronic cigarette interventions for smoking cessation in adults: component network meta-analyses

Lindson, Cochrane Database Syst Rev, 2023

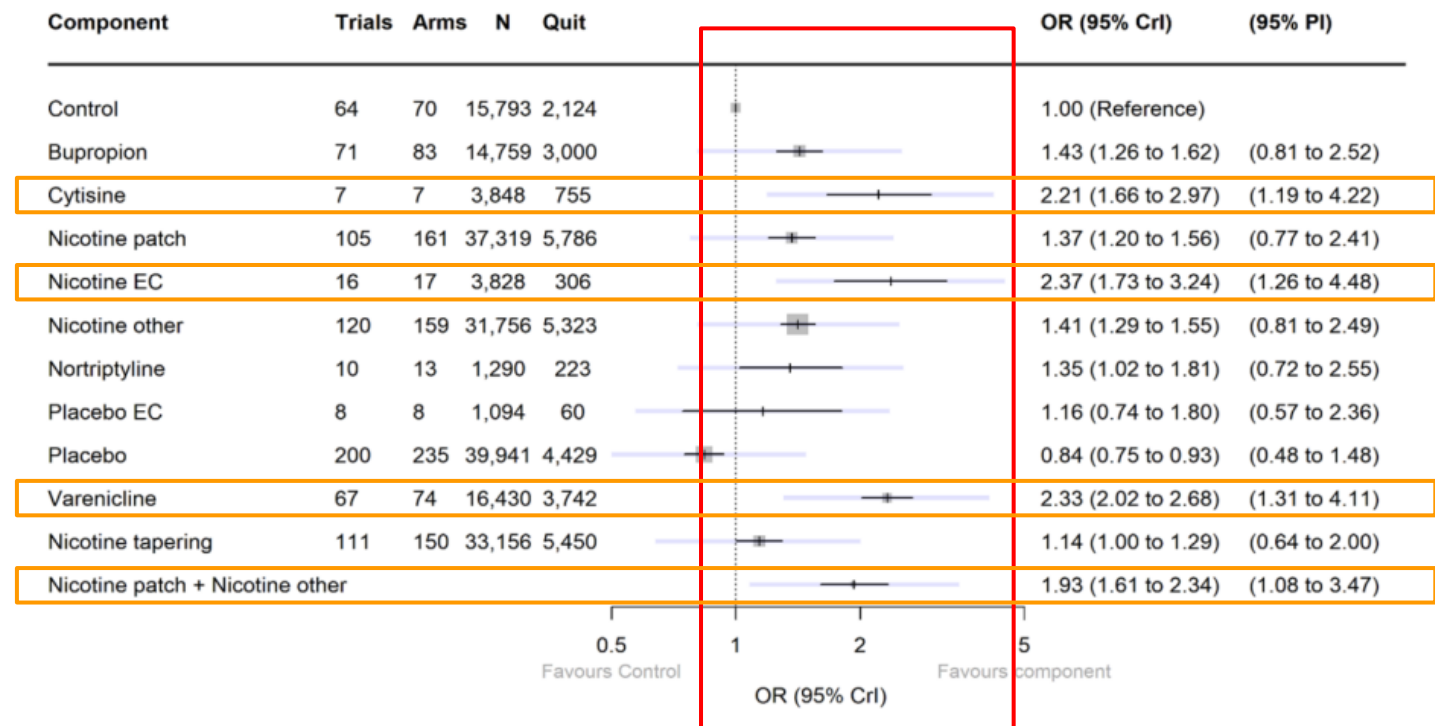
- See also: 2024 Cochrane Review of E-Cigs
- Bayesian component network meta-analyses (*cNMA*) to examine intervention type, delivery mode, dose, duration, timing in relation to quit day and tapering of nicotine dose
- **Nicotine e-cigarettes** (OR 2.37), **varenicline** (OR 2.33) and **cytisine** (OR 2.21) were associated with higher quit rates than control
- Also : **NRT patch + gum/lozenge** also effective but estimate less certain
- **Cytisine** is not labeled for SC in US; available as a supplement



Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

Figure 3. Forest plot illustrating final model for abstinence (efficacy) outcome. Note, darker intervals represent CrI and lighter intervals represent PI. Control: no pharmacological or EC intervention. Abbreviations
CrI: credibility interval; EC: e-cigarette; N: number of participants; OR: odds ratio; PI: prediction interval



Alcohol Updates

Cannabis-Mood DO and Cochrane Review of Smoking Cessation

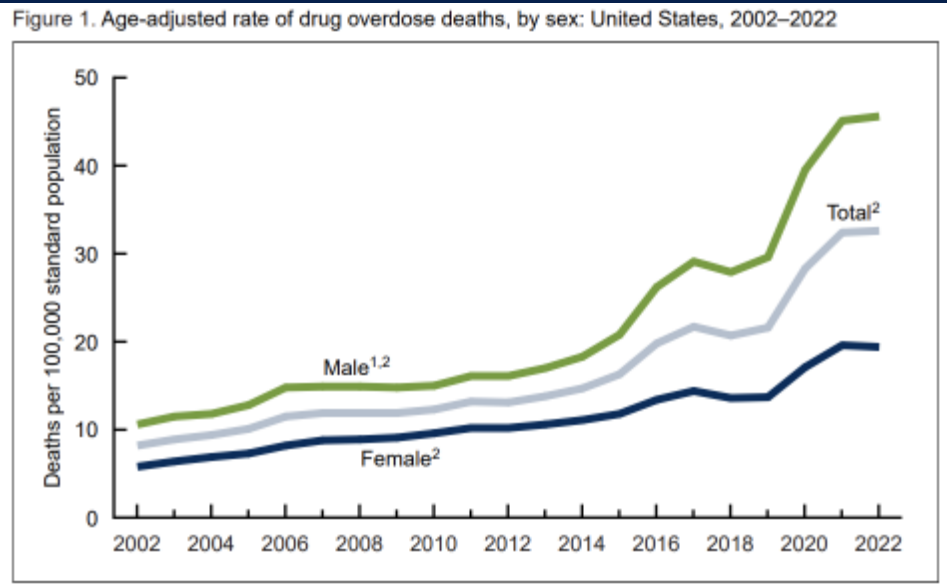
Opioid and stimulant overdose trends

Racial Inequities, Social Determinants, SUD

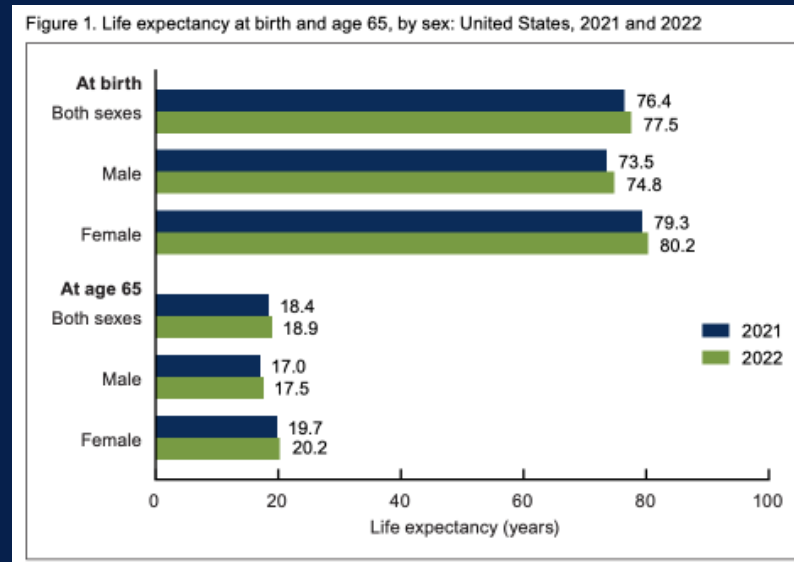
Telehealth, m-health and Novel Approaches to MOUD



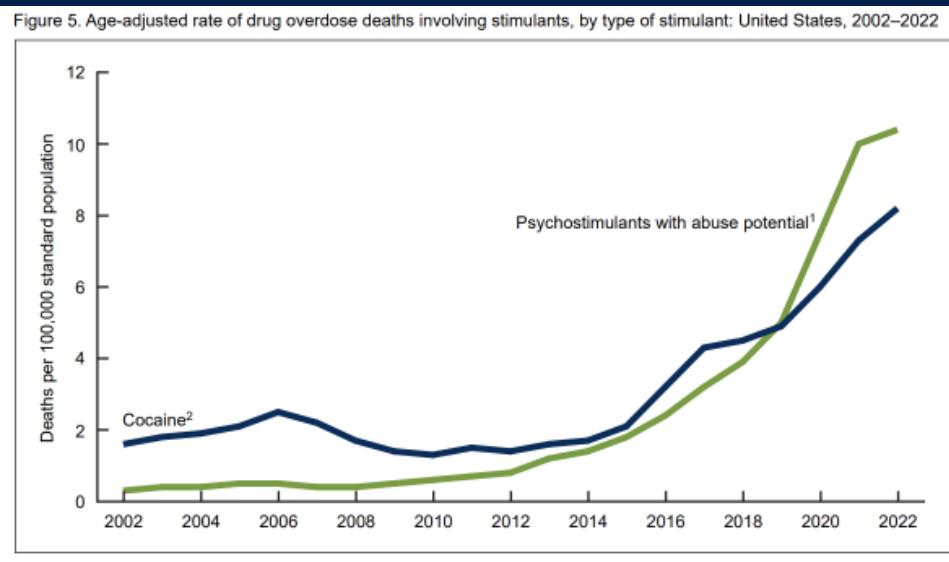
CDC Breaking News 3/20/2024: OD rates high but steady in 2022; life expectancy increased



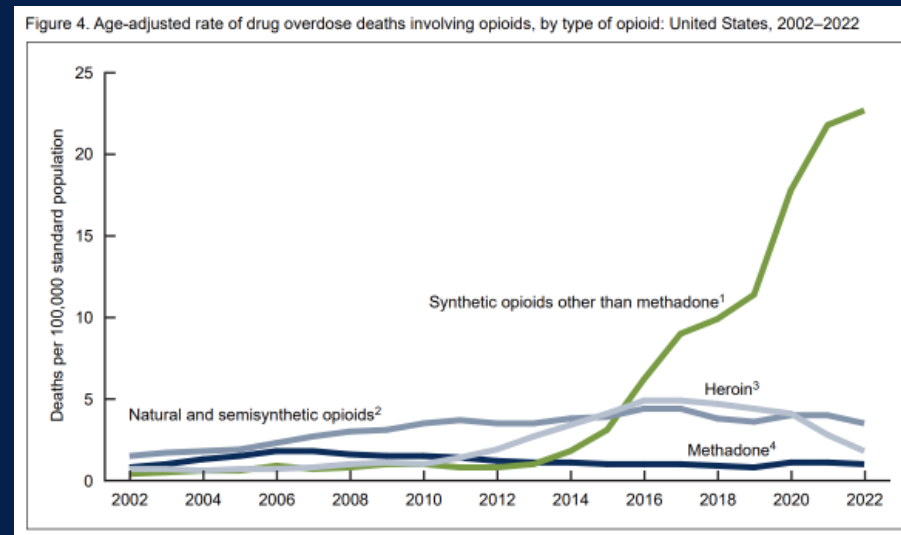
Age-adjusted rate of drug overdose deaths was 32.6 in 2022; no significantly change 2021 to 2022.



2022: US life expectancy at birth was 77.5 years; increase of 1.1 years from 2021



2022, Stimulant-related deaths increased



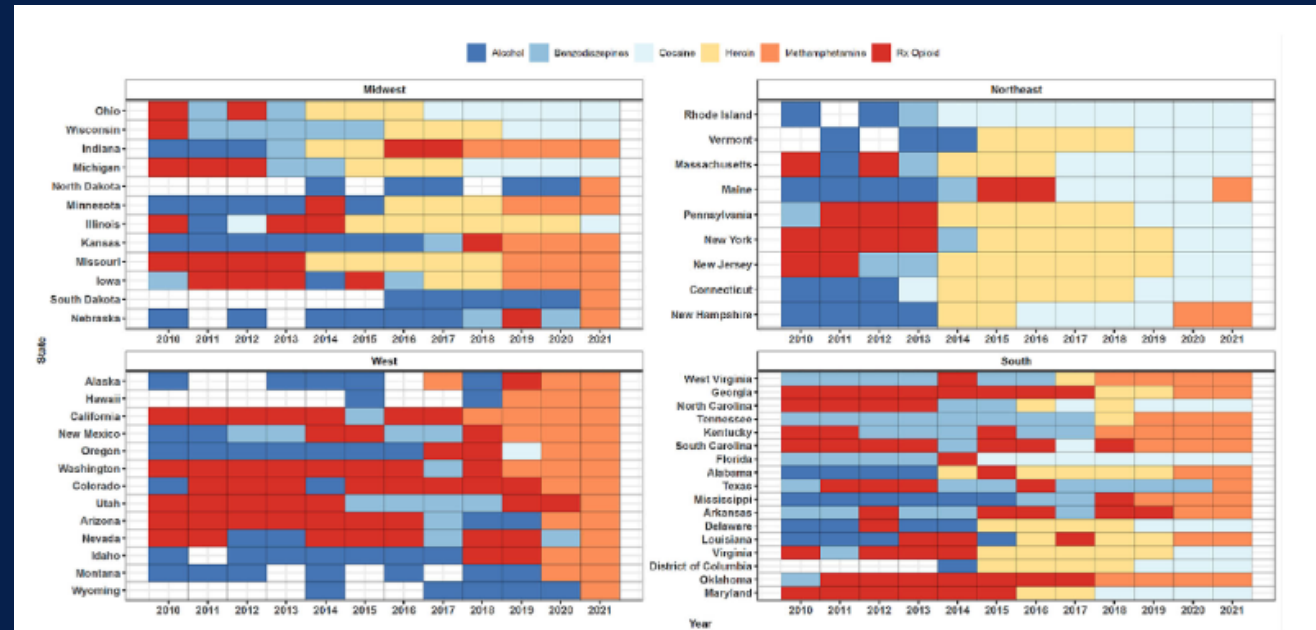
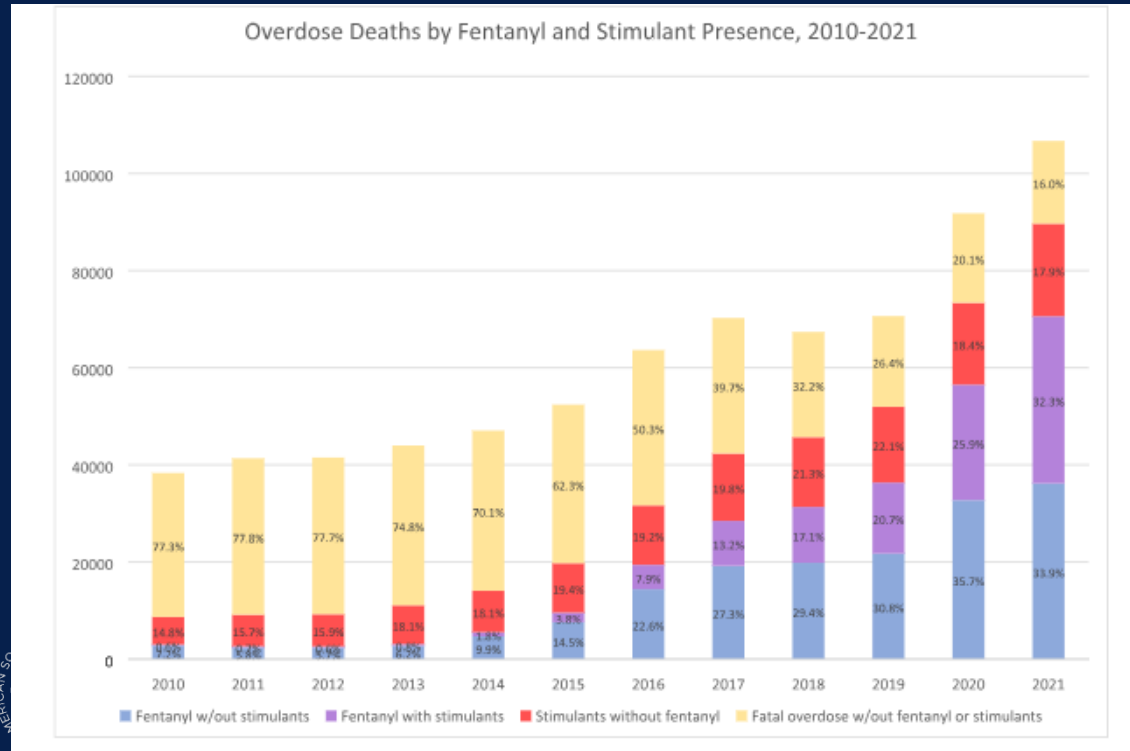
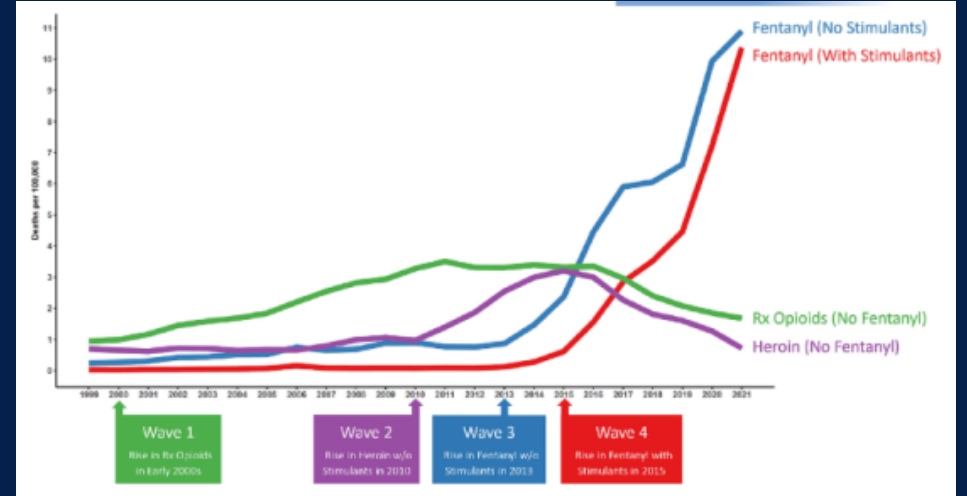
Fentanyl-related deaths increased; heroin and other opioid deaths decreased

(#11) Charting the fourth wave: Geographic, temporal, race/ethnicity and demographic trends in polysubstance fentanyl overdose deaths in the United States, 2010-2021.

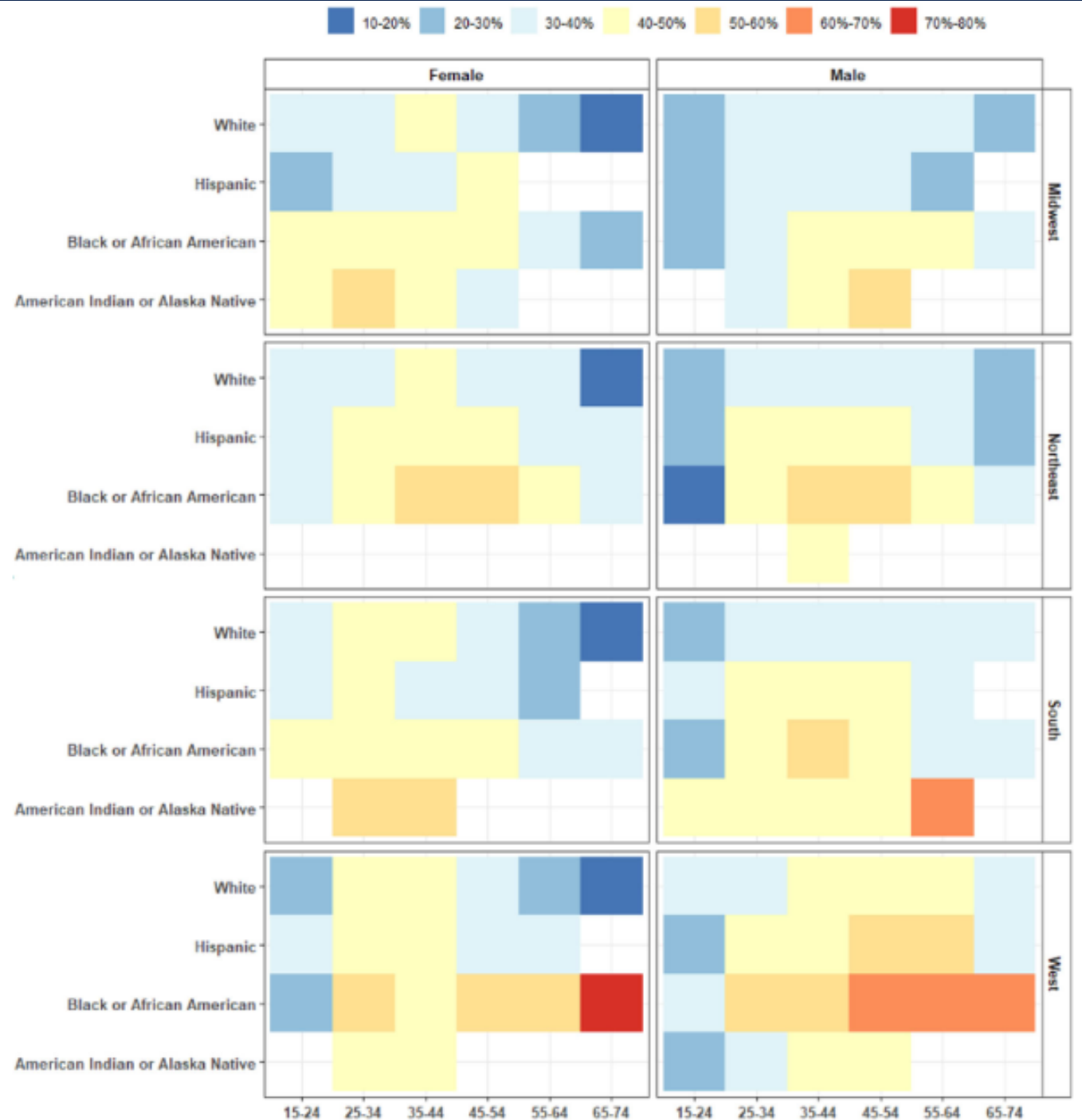


Friedman, Addiction 2023

- Population-based study of national death records
- Polysubstance characteristics of fentanyl-involved overdose mortality shifted from 2010 to 2021 period. Percent involving both fentanyl and stimulants rose from 0.6% to 32.3%



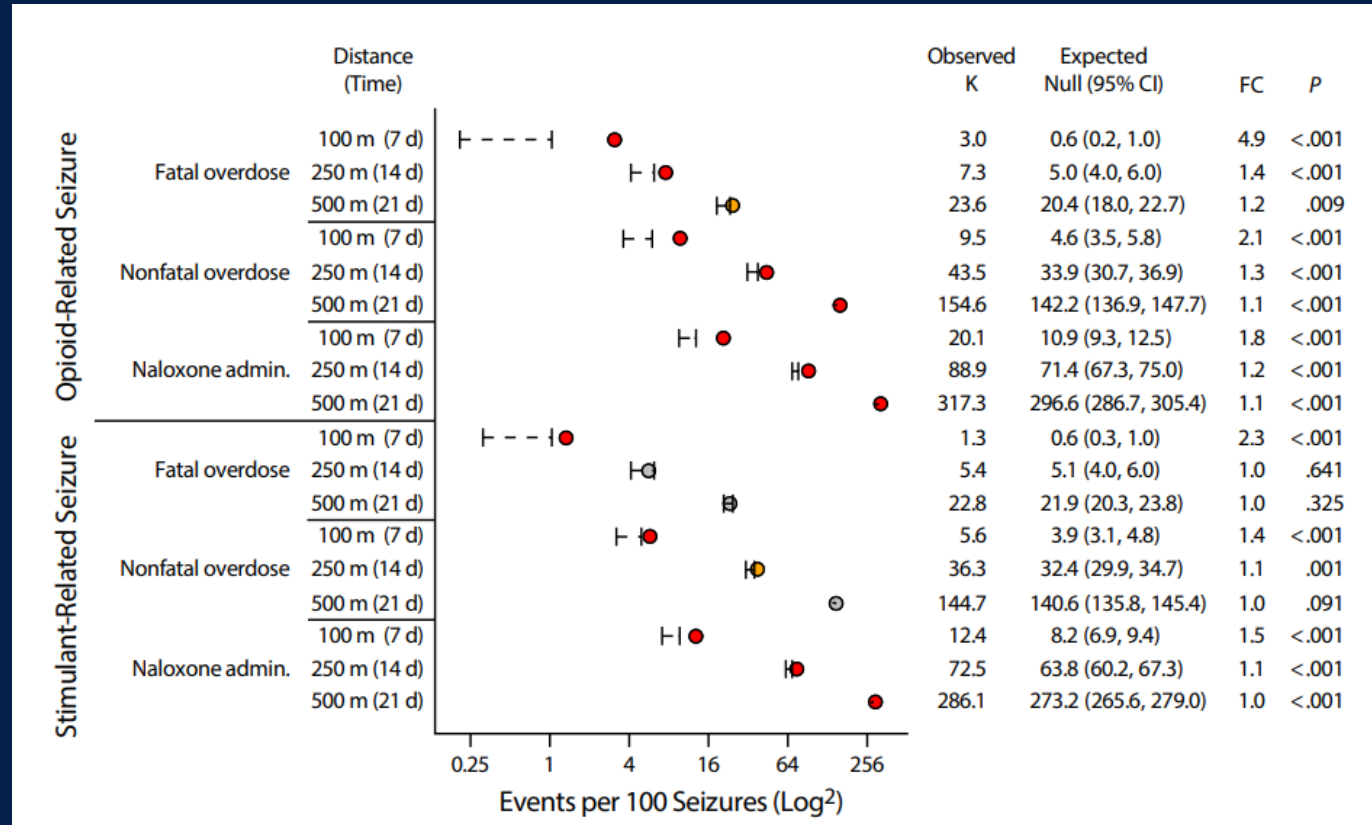
- the highest prevalence of stimulant involvement in fentanyl overdose deaths was observed in individuals ages 25 through 54 through 54
- The intersectional groups with the highest proportions included Black women age 65-74 and Black men 55-65 living in the West



#7 Changes in Overdose after Drug Seizure Ray, AJPH



- Retrospective population-based cohort study in Marion County, Indiana comparing opioid & stimulant seizures with changes in fatal overdose, emergency medical services nonfatal overdose calls for service, and naloxone administration in the geographic area and time following the seizures.
- Looked at pre-post differences 7, 14, 21 days after seizure
- Police opioid seizures were significantly associated with spatiotemporal clustering of fatal overdoses, nonfatal overdoses, and naloxone administrations at all time and distance parameters used in the analysis (100 m at 7 days, 250 m at 14 days, 500 m at 21 days)



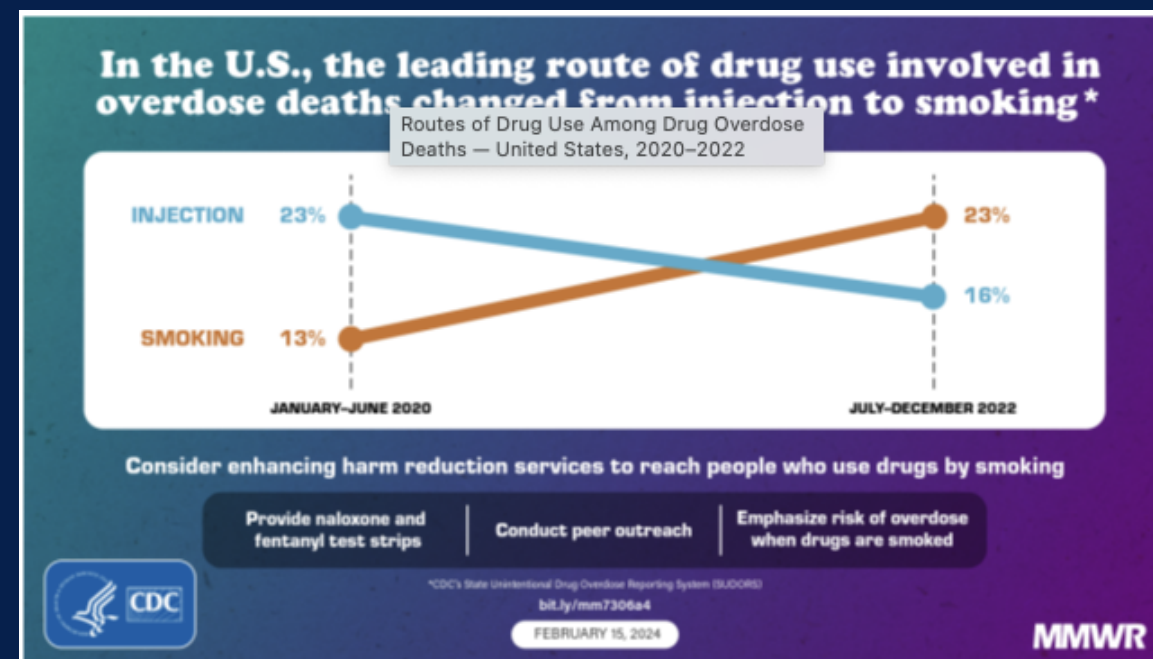
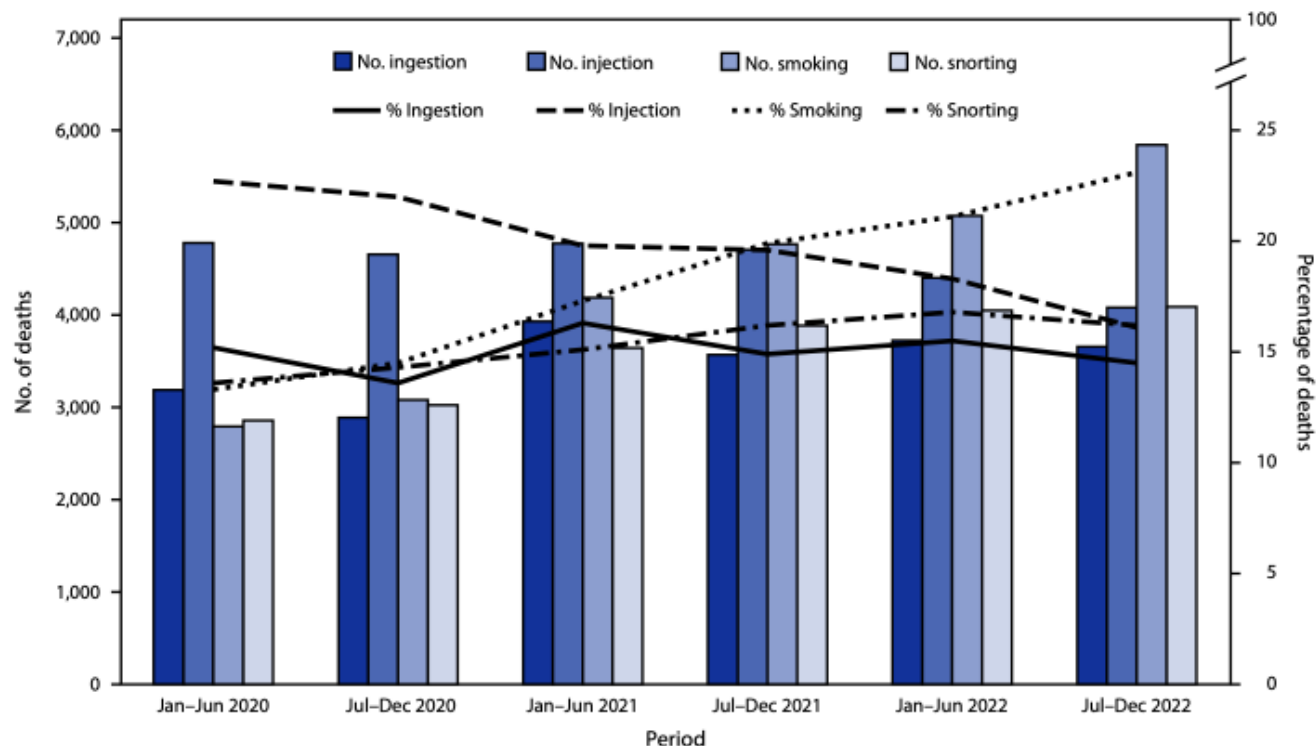
CDC Breaking News 2/15/2024: Smoking fentanyl now a leading route to OD



Routes of Drug Use Among Drug Overdose Deaths — United States, 2020–2022

Tanz, MMWR, 2024

FIGURE 1. Number and percentage of drug overdose deaths with evidence of selected routes of drug use,^{*,†} by 6-month period of death (N = 139,740) — State Unintentional Drug Overdose Reporting System, 28 jurisdictions,^{§,¶} January 2020–December 2022



2022 vs. 2020: smoking vs. IV now leading known route of administration in fatal overdoses

Most OD deaths (60,000+): unknown route of administration



#2 Illicitly Manufactured Fentanyl-Involved Overdose Deaths with Detected Xylazine – United States, January 2019–June 2022



Kariisa, MMWR Morb Wkly Rpt, 2023

- Using data from CDC’s State Unintentional Drug Overdose Reporting System during Jan 2019-Jan 2022
- Among 21 jurisdictions, the monthly percentage of IMF-involved deaths with xylazine detected increased 276% from January 2019 (2.9%) to June 2022 (10.9%).
- During January 2021–June 2022 in 32 jurisdictions, xylazine was detected in a higher percentage of IMF-involved deaths in the Northeast U.S. Census Bureau region
 - Xylazine detected in <12% of IMF-involved deaths overall, varying by jurisdiction from none to 27.7%

FIGURE 1. Number and percentage of drug overdose deaths involving* illicitly manufactured fentanyls,† by month and xylazine detection or co-involvement — State Unintentional Drug Overdose Reporting System, 21 jurisdictions,‡ January 2019–June 2022

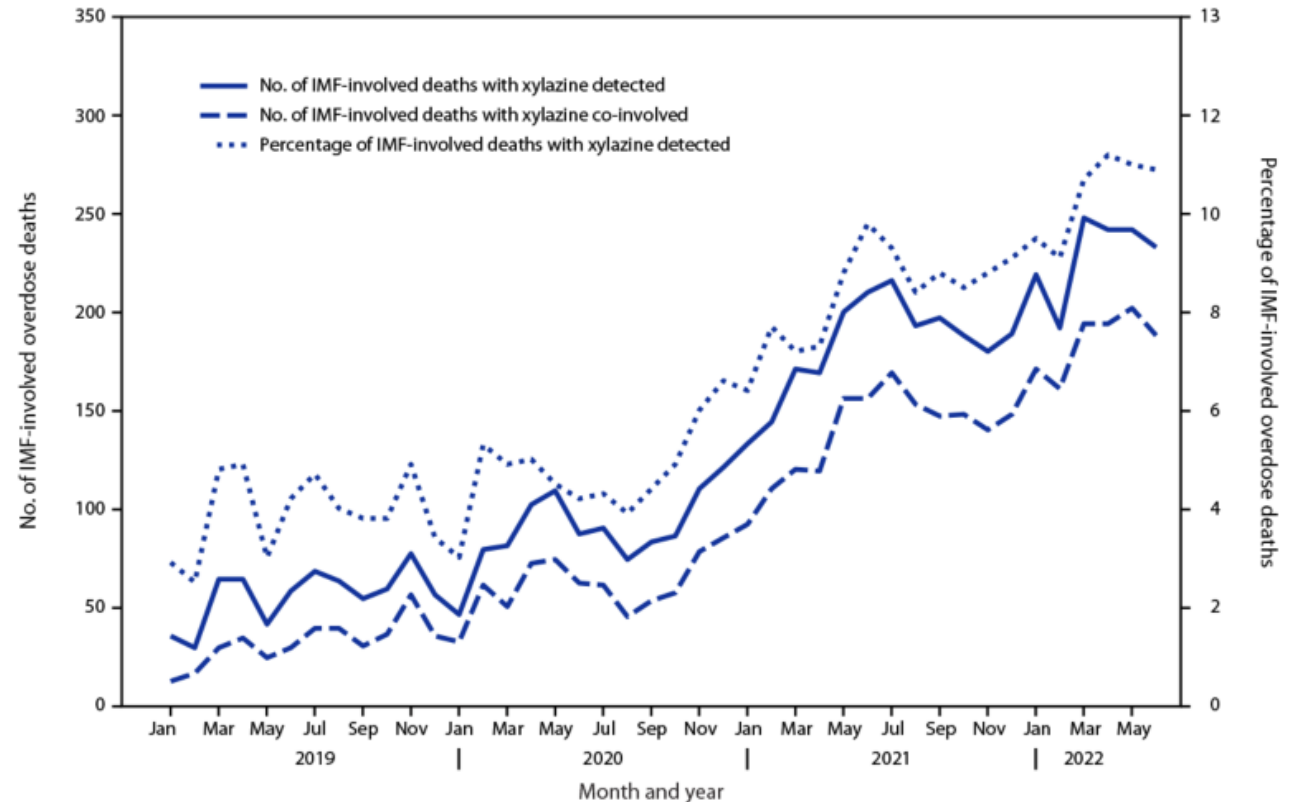
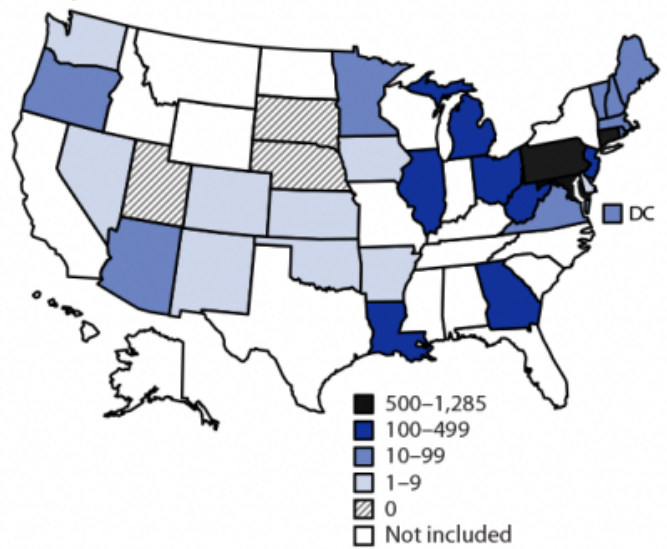
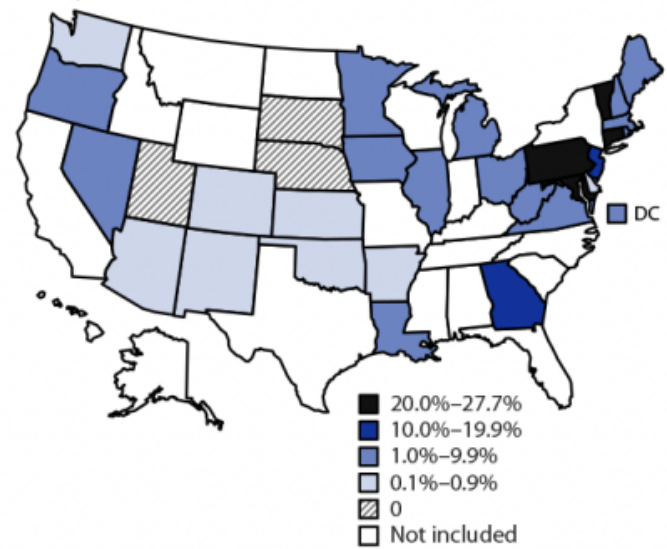


FIGURE 2. Number and percentage of drug overdose deaths involving* illicitly manufactured fentanyl,† by xylazine detection or co-involvement
 — State Unintentional Drug Overdose Reporting System, 31 states and District of Columbia,‡ January 2021–June 2022

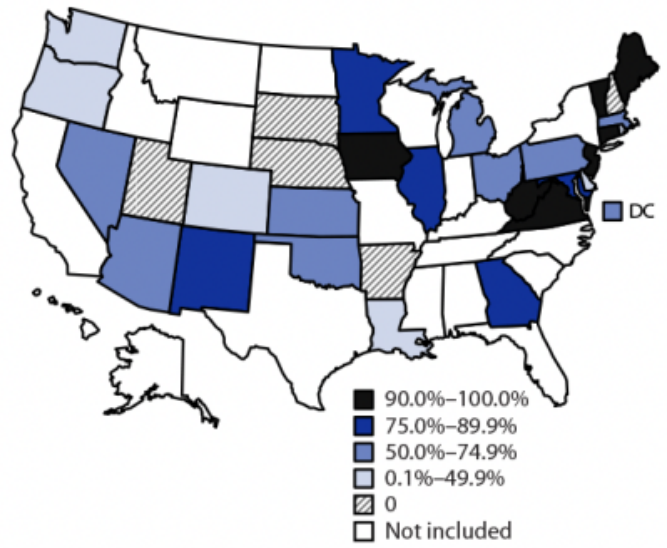
A. No. of IMF-involved overdose deaths with xylazine detected



B. Percentage of IMF-involved overdose deaths with xylazine detected



C. Percentage of IMF-involved overdose deaths with xylazine detected for which xylazine was co-involved



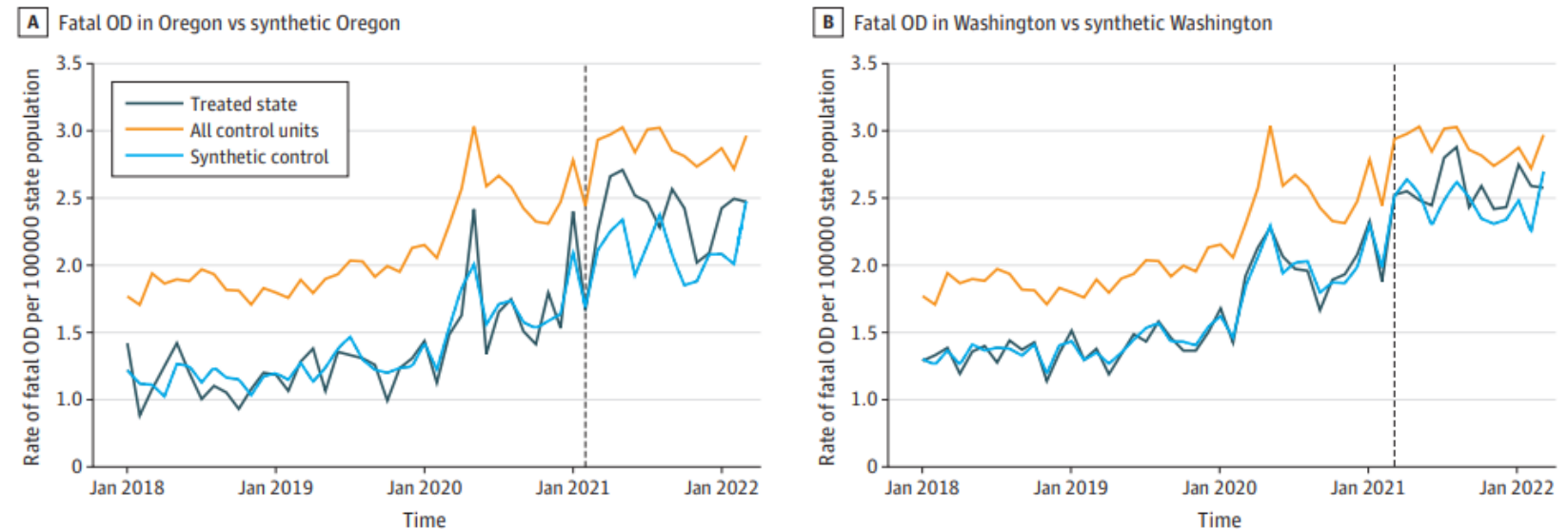
(#4) One-Year Association of Drug Possession Law Change With Fatal Drug Overdose in Oregon and Washington



Joshi, JAMA Psych 2023

- Were changes in drug possession laws and fatal drug overdose rates in Oregon and Washington in the postpolicy period?
- Cohort study using a **synthetic control method** approach: a counterfactual comparison group (synthetic controls) was created for Oregon and Washington, using 48 states and the District of Columbia, that did not implement similar policies during the study period
- **No evidence of an association between legal changes and fatal drug overdose rates.**

Figure 2. Monthly Fatal Drug Overdose (OD) Rates per 100 000 State Population



Oregon vs synthetic Oregon (A) and Washington vs synthetic Washington (B), January 2018-March 2022. The vertical line represents the implementation of Measure 110 and the *Blake* decision. All control units reflect an unweighted

average rate of fatal drug overdose over the study period, inclusive of all 49 control units. The vertical line indicates the implementation of the drug policy change.

What actually happened in OR and WA?

Washington State, 2021-2023:

- 2021: **Washington Supreme Court** struck down the state law making drug possession a felony as unconstitutional (no requirement prosecutors prove someone knowingly had drugs)
- 2023: Legislature w a **compromise drug possession bill** during a special session: penalty for possession of CS now a gross misdemeanor.

Oregon, 2020-2024 and **Measure 110**:

- 2020: “Oregon voters passed the most liberal drug law in the country in November 2020, decriminalizing possession for small amounts of **heroin, cocaine, and methamphetamines**. Measure 110...instead of arresting drug users, police gave them a citation and point them towards treatment.”
 - *This never included **fentanyl** or fentanyl-like opioids*
- 2020-2023: increase in public drug use and overdose deaths
- **2024: New bill just passed re-criminalizing ‘hard drug’ possession**

Small amounts of drugs : probation or up to 180 days in jail
Support and \$\$ for diversion and treatment left intact



The screenshot displays four news articles from different sources, each with a small thumbnail image on the right side. The articles are as follows:

- The Hill:** "Oregon governor signs law recriminalizing drug possession". The thumbnail shows Oregon Governor Tina Kotek.
- BBC:** "Oregon recriminalises drug possession after overdoses rocket". The thumbnail shows a person in a dark jacket, possibly a police officer or someone in custody.
- Forbes:** "Here's Why Oregon Is Walking Back Its Drug Decriminalization Law". The thumbnail shows a person's hands holding a small object, possibly a drug package.
- NBC News:** "Oregon re-criminalizes small amounts of hard drugs after 2020 voter initiative is overturned". The thumbnail shows two people in dark clothing, one appearing to be in custody.

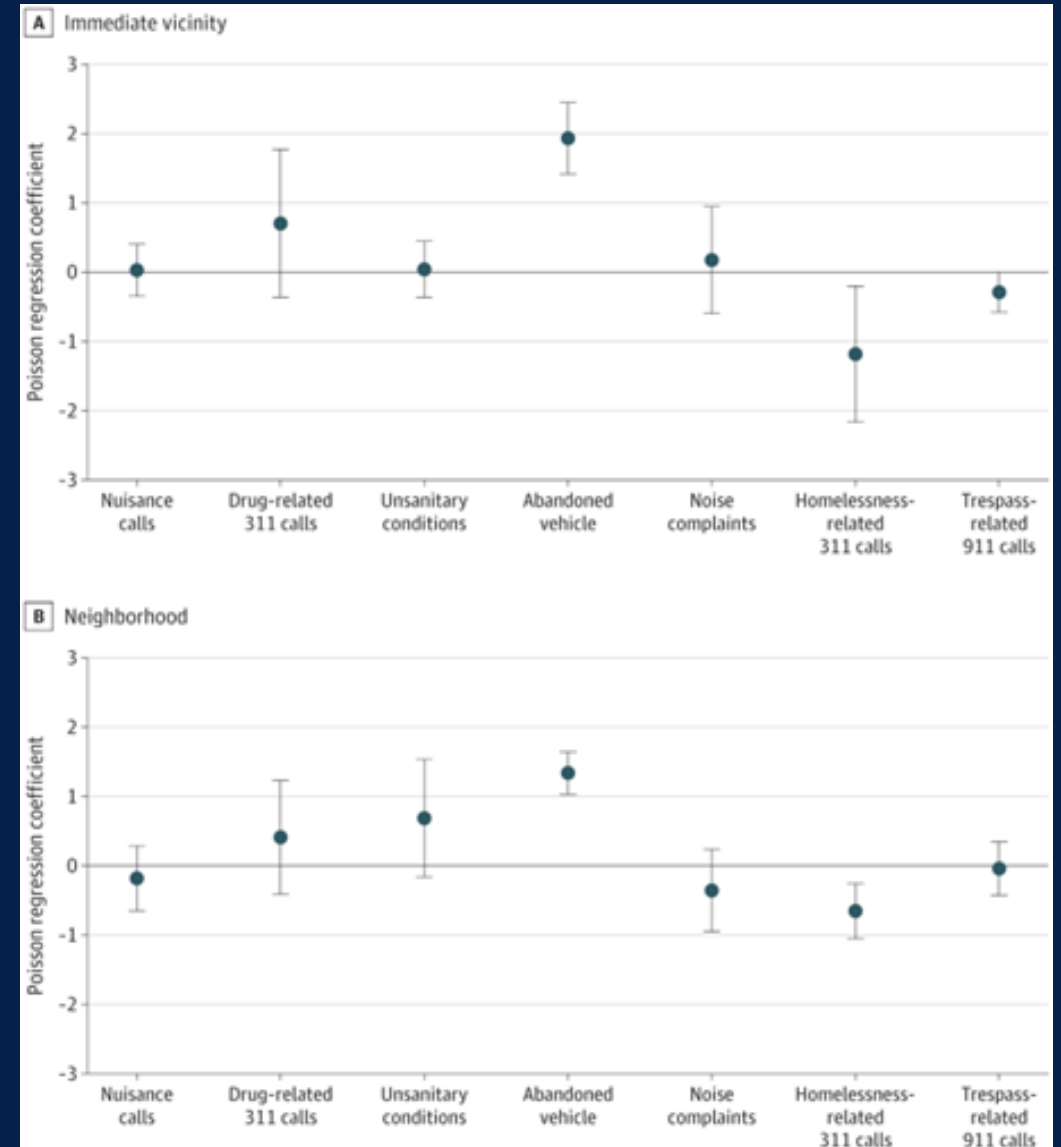
#28 Overdose Prevention Centers, Crime, and Disorder in NYC

Chalfin, JAMA Netw Open 2023



- Cohort study, difference-in-differences between 2 OPCs vs. 17 other syringe service programs
- Compared crimes, 311 calls, and police enforcement
- **No significant changes** in:
 - violent crimes
 - property crimes
 - 911 calls for crime or medical incidents
 - 311 calls regarding drug use or unsanitary conditions
- **Significant decline** in low-level drug enforcement:
 - reduction in arrests for drug possession near the OPCs) of -82.7%
 - reduction in their broader neighborhoods of -74.5%

OPCs in NYC remain open, active, and are constantly navigating complicated local and federal politics



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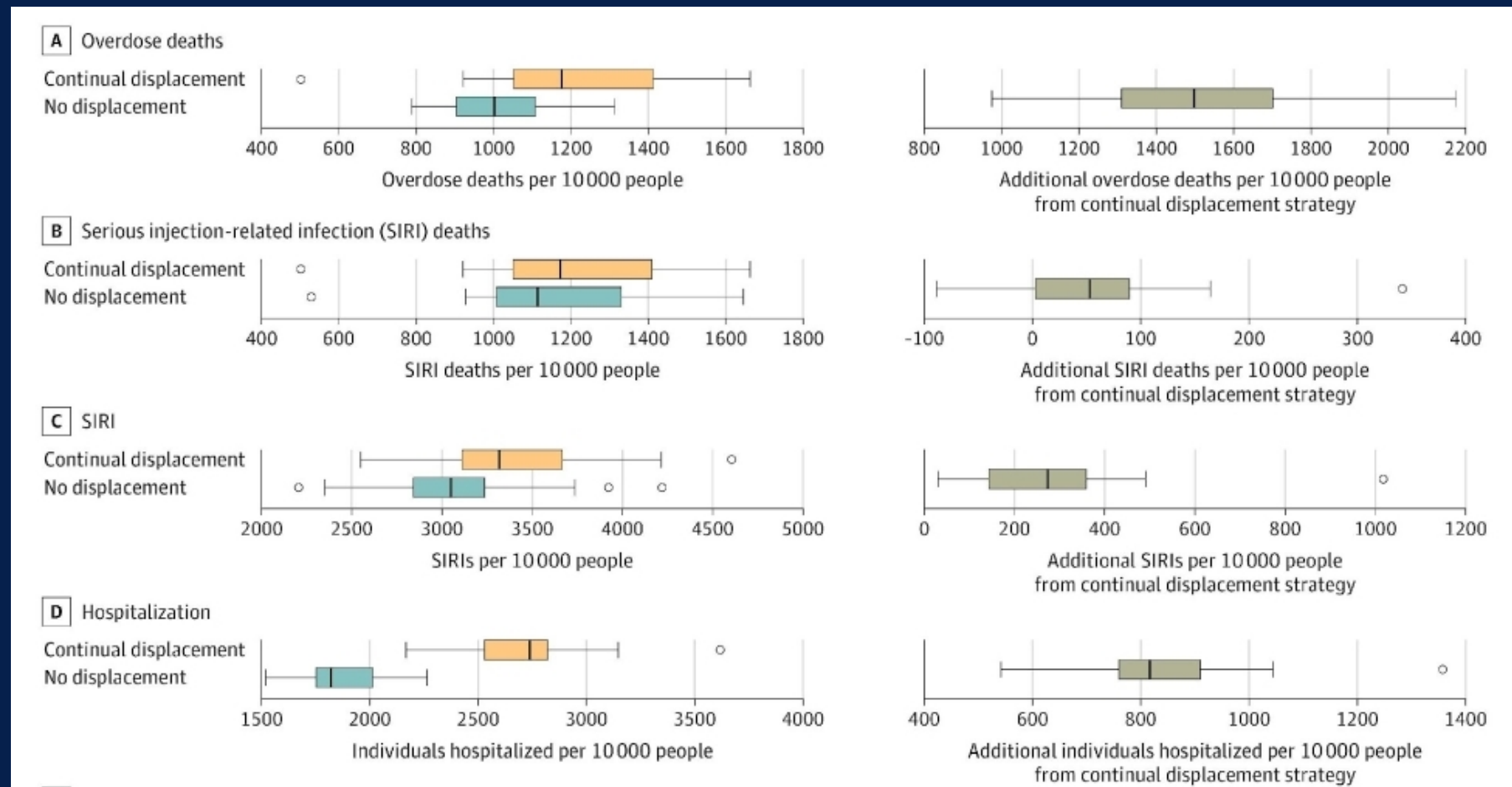


#8 Displacement of PEH Who Inject Drugs



Barocas et al, JAMA 2023

- Closed cohort microsimulation model
- Estimate long-term health effects of involuntary displacement on people experiencing homelessness who inject drugs in 23 US cities
- Involuntary displacement of PEH substantially increases drug-related morbidity and mortality.



#16 Racial Inequality in Receipt of Medications for Opioid Use Disorder



Barnett ML, N Engl J Med, 2023

- Since 2010, Black persons in US had a greater increase in opioid overdose-related mortality
- Medicare claims data 2016–2019; Index event related to OUD; outcomes in 180 days after; ~23K people
- In the 180 days after the index event, patients received buprenorphine after
 - 12.7% of events among Black patients
 - 18.7% of those among Hispanic patients
 - 23.3% of those among White patients
- Patients received naloxone after 14.4%, 20.7%, and 22.9%, respectively
- Black and Hispanic people with opioid use disorder are less likely to receive medications for opioid use disorder than White people.

Table 2. Receipt of Medications after OUD-Related Event, According to Race and Ethnic Group.*

Variable	Black (N = 3937)	Hispanic (N = 2105)	White (N = 19,862)	Adjusted Difference (95% CI)		
				Black vs. White	Hispanic vs. White	Hispanic vs. Black
Buprenorphine						
Any receipt in 180 days — no. (%)	501 (12.7)	393 (18.7)	4627 (23.3)	-8.7 (-11.3 to -6.0)	-4.2 (-6.7 to -1.8)	4.4 (2.0 to 6.9)
Total days' supply received within 180 days, among recipients	94.1±68.4	111.7±66.9	118.1±66.0	-23.4 (-32.5 to -14.2)	-4.0 (-11.3 to 3.3)	19.4 (8.1 to 30.7)
Treatment retention — no./total no. (%)†	151/501 (30.1)	160/393 (40.7)	2073/4627 (44.8)	-14.0 (-20.3 to -7.8)	-1.9 (-7.3 to 3.6)	12.2 (5.8 to 18.6)
Naloxone						
Any receipt in 180 days — no. (%)	568 (14.4)	435 (20.7)	4546 (22.9)	-6.7 (-9.5 to -3.7)	-2.3 (-5.1 to 0.5)	4.3 (1.5 to 7.1)
Naltrexone						
Any receipt in 180 days — no. (%)	110 (2.8)	70 (3.3)	664 (3.3)	-0.1 (-0.7 to 0.6)	0.1 (-0.9 to 1.1)	0.2 (-0.7 to 1.0)
Total days' supply received within 180 days, among recipients	57.1±49.7	45.9±42.9	55.9±48.3	-1.4 (-18.7 to 15.9)	-7 (-16.7 to 2.7)	-5.6 (-24.7 to 13.6)
Opioid analgesic						
Any receipt in 180 days — no. (%)	921 (23.4)	474 (22.5)	4656 (23.4)	-0.8 (-2.7 to 1.2)	0.1 (-2.1 to 2.3)	0.9 (-1.8 to 3.6)
Benzodiazepine						
Any receipt in 180 days — no. (%)	921 (23.4)	623 (29.6)	7359 (37.1)	-14.1 (-16.7 to -11.6)	-6.7 (-8.4 to -5.1)	7.4 (4.5 to 10.3)



#9 Treatments Used Among Adolescent Residential Addiction Treatment Facilities in the US, 2022: Research Letter



King, JAMA, 2023

- “secret shopper” approach, made cold calls based on SAMSHA treatment locator

“We called as the aunt or uncle of a 16-year-old with a recent nonfatal fentanyl overdose to make calls more plausible if we did not have all requested information about the adolescent.”

- 160 (45.2%) provided residential treatment to patients younger than 18 years:

11% offered buprenorphine maintenance
 54% family therapy
 25% art therapy

Table. Reported Treatment and Supportive Programming Used by Adolescent Residential Addiction Treatment Facilities (N = 160)

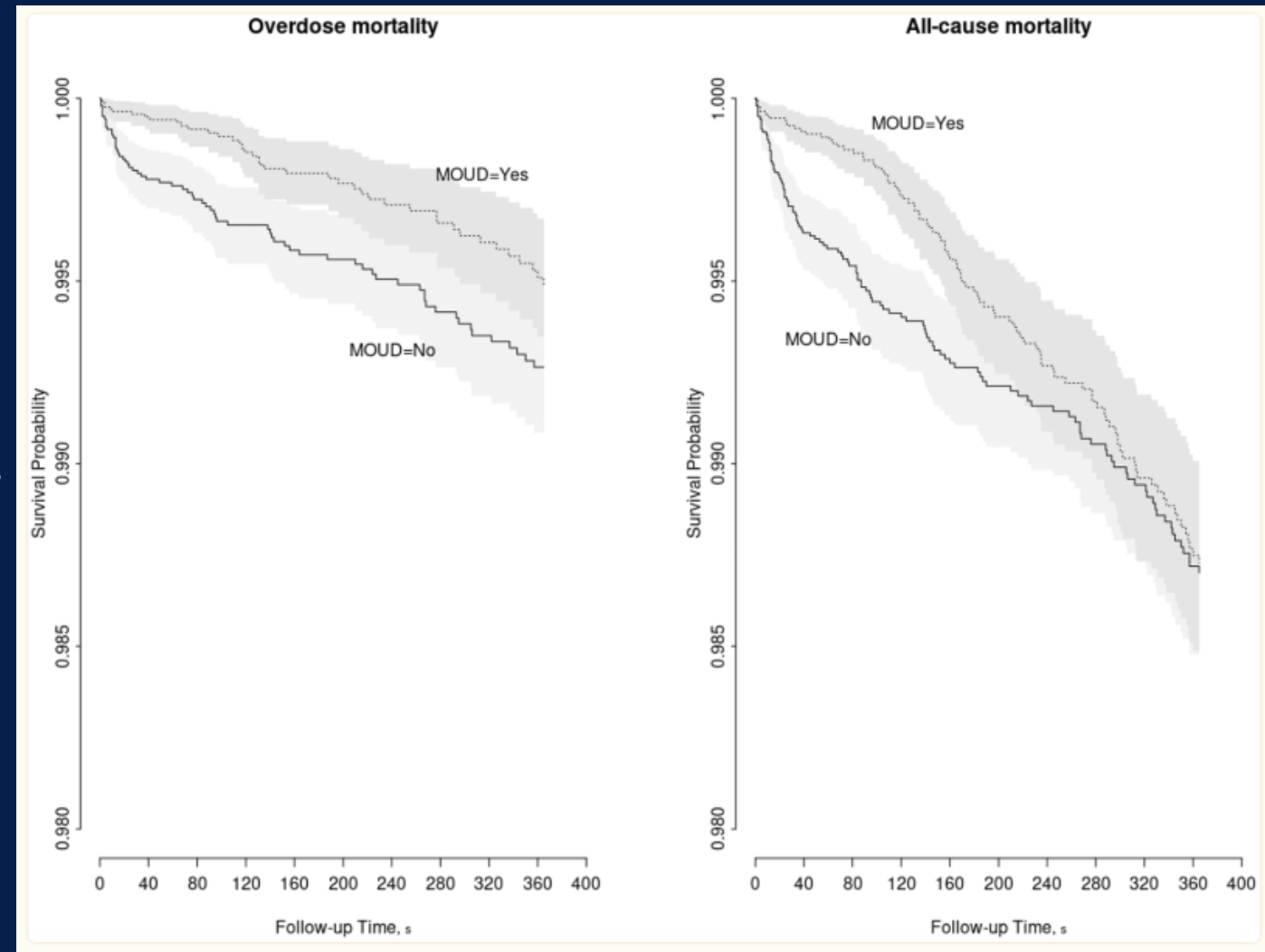
Treatment and support modalities	No. (%) ^a
Pharmacotherapy^b	
Offers any buprenorphine	39 (24.4)
Northeast ^c	6/15 (40.0)
Midwest ^c	11/32 (34.4)
South ^c	11/52 (21.2)
West ^c	11/61 (18.0)
Offers buprenorphine initiation with discontinuation prior to discharge	12 (7.5)
Offers buprenorphine initiation with ongoing treatment	17 (10.6)
Offers buprenorphine for ongoing treatment only	3 (1.9)
Offers buprenorphine to adolescents <16 y	12 (7.5)
Behavior treatment^b	
Family therapy^d	
Cognitive behavior therapy	52 (32.5)
Community reinforcement approach	44 (27.5)
Community reinforcement and family training	26 (16.3)
Dialectical behavior therapy	17 (10.6)
Mutual help	
12-step program or Alcoholics/Narcotics Anonymous	59 (36.9)
Other supportive programming	
Equine therapy	40 (25.0)
Art therapy	40 (25.0)
Music therapy	37 (23.1)
Outdoor adventure	21 (13.1)



#21 Association between jail-based methadone or buprenorphine treatment for opioid use disorder and overdose mortality after release from New York City jails 2011–2017

Lim, *Addiction*, 2023

- NYC jail medical records for methadone and buprenorphine treatment during incarceration
- Matching to NYC vital statistics and cause of death outcomes, 2013-2017
- Majority black (30%) and Hispanic (44%), 18% female incarceration episodes
- **MOUD associated with lower mortality and lower OD deaths rates**
- **Largest US CJS sample of MOUD and mortality to date, N=15 797 adults with n=31 382 incarcerations**



Alcohol Updates

Cannabis-Mood DO and Cochrane Review of Smoking Cessation

Opioid and stimulant overdose trends

Racial Inequities, Social Determinants, SUD

Telehealth, m-health and Novel Approaches to MOUD



#19 Eat, Sleep, Console for NOWS RCT: Eat, Sleep, Console Approach or Usual Care for Neonatal Opioid Withdrawal

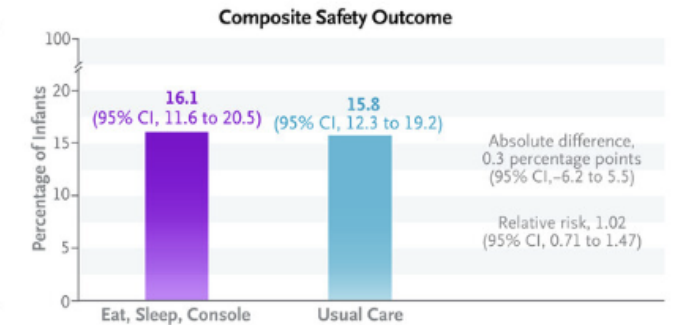
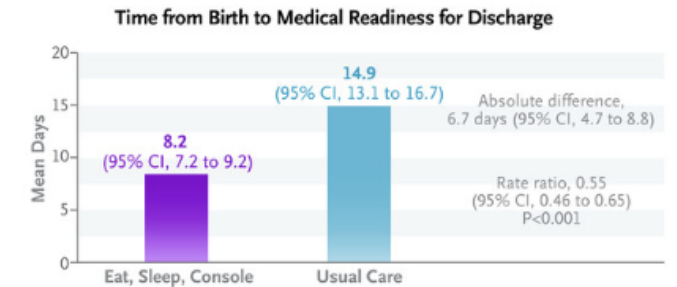
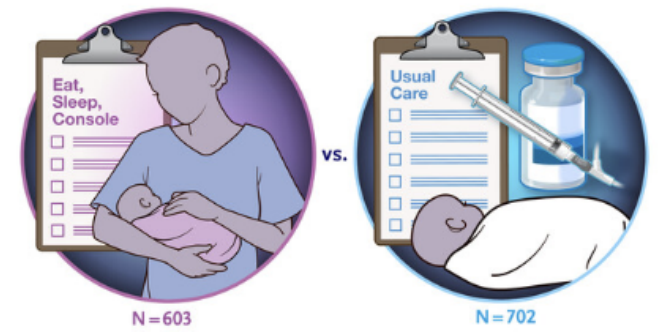
Young, NEJM 2023



- Cluster RCT at 26 hospitals of 1305 infants born at >36 week w/ NOWS. At a randomly assigned time hospitals transitioned to ESC.
- Eat Sleep and Console: bond w baby and don't just dose opioids based on a w/d scale:

“We look at whether the baby is able to eat, sleep and be consoled. If any of these are being impacted by withdrawal, we encourage the mother to try methods like skin-to-skin contact, frequent nursing, and holding her baby in a quiet room with low light”

- ITT results: days to hospital discharge was 8.2 in the ESC group and 14.9 in the usual-care group (adjusted mean difference, 6.7 days; 95% confidence interval [CI], 4.7 to 8.8)



CONCLUSIONS

In infants with neonatal opioid withdrawal syndrome, use of the Eat, Sleep, Console approach significantly reduced the time from birth until medical readiness for discharge, as compared with usual care.

#41 Impact of prescriber notification after overdose on subsequent opioid prescribing: RCT

Doctor, JAMA Netw Open, 2023

- RCT : clinicians who prescribed an opioid within the 12 months before patient’s death
- 2015-2016
- 12 months of data before and after the intervention.
- Mean MMEs and number of new patients prescribed opioids decreased in both groups, with a greater decrease in the intervention group.

Intervention: A courtesy communication informing prescribers of the death of a former patient where prescription drug overdose was the primary cause or contributed to the cause of the death. The letter invited prescribers to review CDC and California state prescribing guidelines.

Table. Adjusted Per-Prescriber Weekly MMEs After Intervention

Parameter	MMEs, mean (95% CI)	
	Letter (n = 385 prescribers)	Control (n = 424 prescribers)
1-3 mo ^a		
Preintervention	328.43 (320.25 to 336.60)	329.14 (321.93 to 336.35)
Postintervention	263.70 (257.17 to 270.24)	288.97 (282.39 to 295.56)
4-12 mo ^b		
Preintervention	328.43 (320.25 to 336.60)	329.14 (321.93 to 336.35)
Postintervention	131.54 (128.29 to 134.79)	141.50 (138.20 to 144.79)

Abbreviation: MME, morphine milligram equivalent.

^a The difference in differences was -24.56 MMEs (95% CI, -34.19 to -14.71 MMEs).

^b The difference in differences was -9.24 MMEs (95% CI, -14.00 to -4.39 MMEs).



#12 Association of Receipt of Opioid Use Disorder-Related Telehealth Services and Medications for Opioid Use Disorder With Fatal Drug Overdoses Among Medicare Beneficiaries Before and During the COVID-19 Pandemic

JonesC, JAMA Psychiatry, 2023

- Expanded telehealth for opioid use disorder (OUD) during COVID-19
- Pandemic cohort (70K) vs. pre-P (100k)
- Higher all-cause mortality: 99.9 vs. 76.8 per 1000
- Higher overdose rates: 5.1 vs. 3.7 per 1000
- **Associated with a significantly lower aORs for fatal drug overdose:**
 - Receipt of OUD-related telehealth
 - Receipt of MOUD from opioid treatment programs
 - Receipt of buprenorphine in office-based settings

Table 3. Characteristics Associated With Fatal Drug Overdose During Study Period Among Beneficiaries With Opioid Use Disorder in the Pandemic Cohort^a

Characteristic	Beneficiaries, No. (%)	aOR (95% CI) ^b
Receipt of OUD-related telehealth service	13 809 (19.6)	0.67 (0.48-0.92) ^c
Receipt of MOUD during study period		
No MOUD	61 626 (87.5)	1 [Reference]
MOUD from OTPs	2774 (3.9)	0.41 (0.25-0.68) ^c
ER naltrexone in office-based settings	170 (0.2)	1.16 (0.41-3.26)
Buprenorphine in office-based settings	5882 (8.4)	0.62 (0.43-0.91) ^c

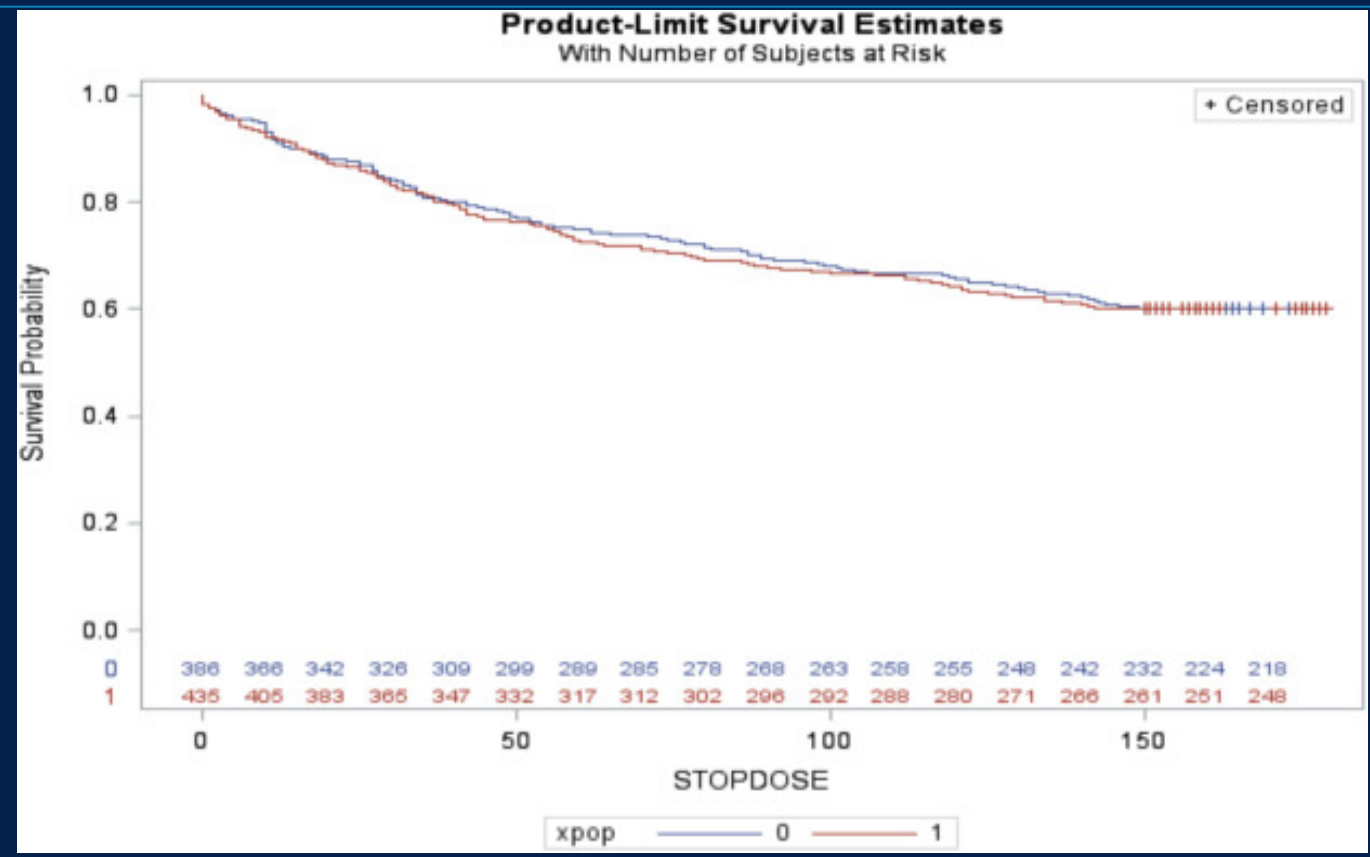


Retention and critical outcomes among new methadone maintenance patients following extended take-home reforms: a retrospective observational cohort study



Williams, Lancet Regional Health, 2023

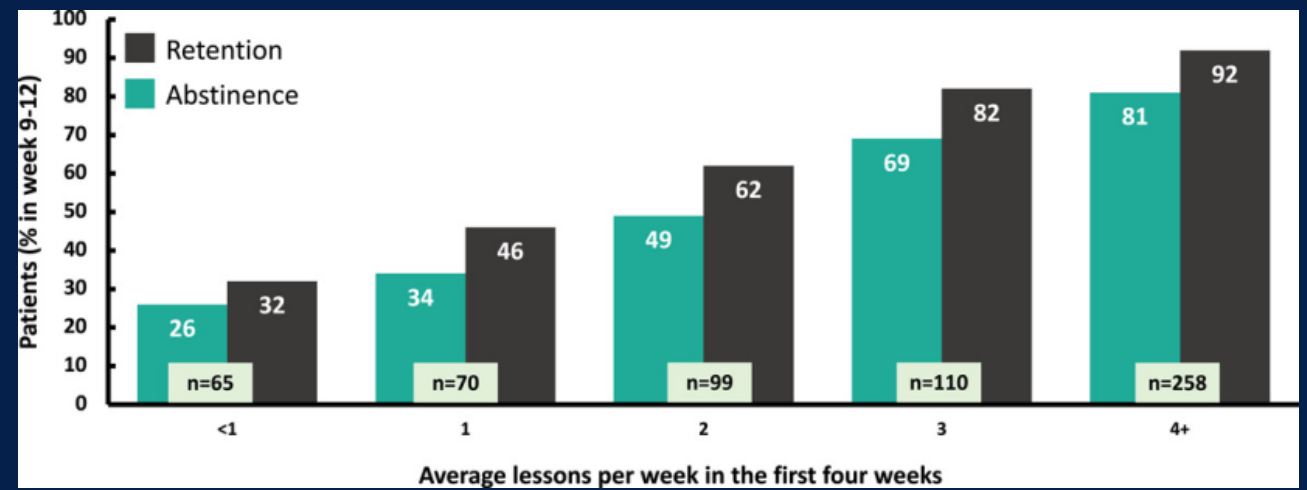
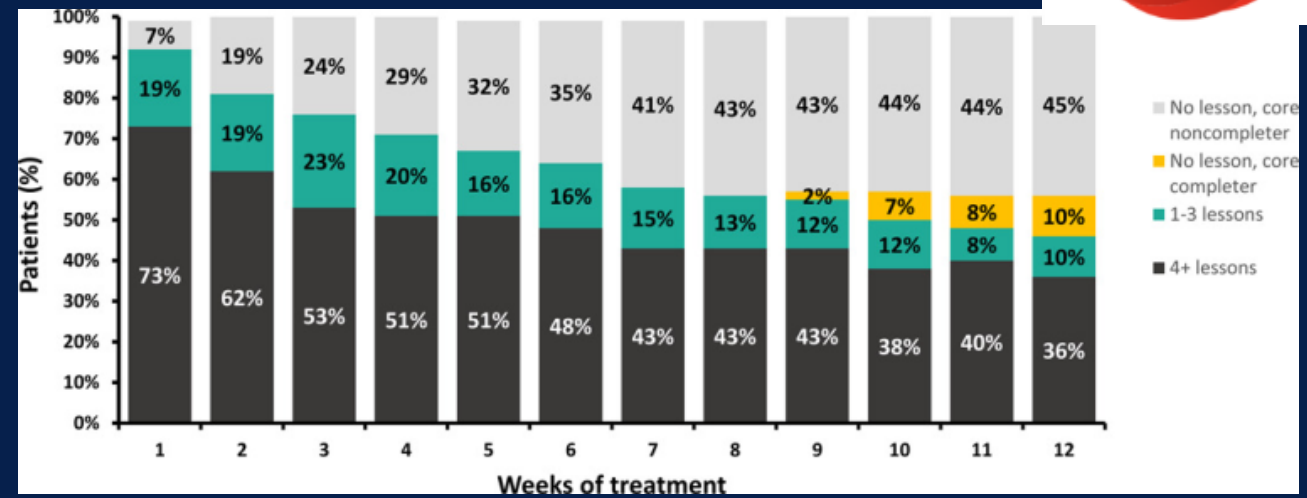
- NIDA CTN retrospective observational cohort study across 9 OTPs
- Newly enrolled patients between 2020 (post-COVID, reform period) v. 2019 (pre-COVID, control period), N=821
- more stimulant use disorder post-COVID (25.7% vs 32.9%, $p = 0.02$)
- Retention was non-inferior (60.0% vs 60.1%) as were hazards of adverse events
- opioid use higher post-COVID (64.8% vs 51.1%, $p < 0.001$)



#104 Evaluation of real-world outcomes associated with use of a prescription digital therapeutic to treat substance use disorders Xiong, A



- Observational evaluation of 602 patients from 28 states who filled an initial prescription for reSET (PEAR) Jan-2019 to Mar-2021
- Substances used by patients were: alcohol (46.7%), opioids (17.9%), stimulants not including cocaine (13.3%), cannabis (7.8%), cocaine (6.5%), and other/unknown (7.8%).
- 55% of patients were still actively using the digital therapeutic at Week 12
- Median total number of therapy lessons completed during 12 weeks was 33 (interquartile range: 13–39) out of 61
- Combining self-report and UDS data, abstinence in Weeks 9–12 was 62% using the “missing data positive” analysis (N = 602)
- 40.9% of patients had an overall abstinence rate $\geq 80\%$ across the duration of the prescription when missing weeks were assumed to be positive.



2023 : PEAR Therapeutics declares bankruptcy
 2023: reSET assets acquired by PursueCare

#49 Enhancing Patient Choice: Using Self-administered Intranasal Naloxone for Novel Rapid Buprenorphine Initiation



Randall, J Addict Med, 2023

- Case report
- The increasing use of illicitly manufactured fentanyl has made initiating BUP-NX more likely to precipitate withdrawal...an experience that deters treatment and causes return to use
- Case: Patient who was able to transition to a therapeutic dose of BUP-NX less than 3 hours after his last fentanyl...by choosing to self-administer intranasal naloxone!
- After the naloxone, the transition took 31 minutes- included 14 minutes of expected moderately severe withdrawal
- Patient remains in care with BUP-NX

CASE REPORT

OPEN

Enhancing Patient Choice: Using Self-administered Intranasal Naloxone for Novel Rapid Buprenorphine Initiation

Adam Randall, DNP, FNP-C, Ilana Hull, MD, MSc, and Stephen A. Martin, MD, EdM, FASAM, FAAFP

Buprenorphine-naloxone (BUP-NX) is a lifesaving treatment for opioid use disorder. The increasing use of illicitly manufactured fentanyl, however, has made initiating BUP-NX more likely to precipitate withdrawal—an experience that deters treatment and causes return to use. If BUP-NX cannot be successfully started, it cannot work. We describe the case of a patient who was able to transition to a therapeutic dose of BUP-NX less than 3 hours after his last illicitly manufactured fentanyl use by choosing to self-administer intranasal naloxone. After the naloxone, the transition took 31 minutes, including 14 minutes of expected moderately severe withdrawal. He remains in care with BUP-NX and would recommend this transition approach to others.

Key Words: opioid use disorder, buprenorphine, retention in care, telehealth, transition to buprenorphine

(J Addict Med 2023;17: 237–240)

fentanyl use—likely because of fentanyl's lipophilicity, which leads to a large volume of distribution and slow dissipation when used chronically.¹ Patients have significant concerns about the severity of withdrawal needed to start buprenorphine as well as the risk of precipitated withdrawal; the possibility of a negative experience understandably fosters hesitance to begin treatment.^{4–6}

Newer methods for BUP-NX initiation have been reported—generally categorized as very low- (or “microdosing”), low-, standard-, and high-dose (or “macrodose”) protocols—each with potential benefits and risks (Table 1).²⁰ Less common methods use transmucosal, buccal sublingual, and intravenous buprenorphine formulations not readily available for this outpatient purpose.⁷ Additional effective, expedited approaches would empower patients, providing more choices regarding when and how quickly they can fully transition to lifesaving treatment.

We present a novel approach for rapid outpatient BUP-NX initiation where a patient chose self-administration of intranasal naloxone to induce withdrawal, followed shortly by 24–6 mg BUP-NX. The patient provided written informed consent for publication, including review of the article.

BACKGROUND

More than 100,000 overdose deaths were reported in 2021, largely driven by illicitly manufactured fentanyl (IMF).¹ Buprenorphine-naloxone (BUP-NX) is a first-line treatment for opioid use disorder (OUD) and, like methadone, reduces morbidity and mortality while increasing retention in care.² Unfortunately, initiating BUP-NX has become more complicated as IMF has largely replaced heroin in the US drug supply.

CASE REPORT

A 33-year-old man with 2 years of daily fentanyl use presented to our telehealth addiction medicine program. His daily use averaged 2, ranging up to 20, pressed fentanyl tablets, which

TABLE 1. Methods for Transitioning From Full Agonists to Buprenorphine Using Readily Available Outpatient Formulations*

Method [†]	Time After Last Use of Full Agonist Until the Initiation Phase [‡] Can Begin	Duration of Initiation Phase	Withdrawal Severity [§] Recommended at Start of Initiation Phase	Medication Taken During Initiation Phase	Expected Change in Withdrawal Symptoms during Initiation Phase	Continued Full Agonist Use During Transition period [†]	Duration of Complete Transition Period
Very low dose ⁷	None	Days to weeks	None	BUP-NX [†] , initial dose <1 mg	N/A	Yes	Days to weeks
Low dose and standard dose ^{2,8}	1–2 d	Days	Moderately severe	BUP-NX, initial dose 1–4 mg	Improve	Patient dependent	Days
High-Dose ^{9b}	12 h	~2–3 h	COWS ≥8	BUP-NX, initial dose >8 mg	Improve	No	~15 h
Case study “Quick Start”	None	29 min	None	Intranasal naloxone, followed by 24 mg BUP-NX	Increased severity withdrawal (COWS 28) for short duration, then improve	No	<1 h

TABLE 2. Chronology of Transition From Fentanyl to Buprenorphine-naloxone

Event	Time Elapsed, min	Time Between Events, min	COWS*
Last use of fentanyl	120 min prior		0
Premedication with clonidine 0.2 mg and gabapentin 600 mg	0	120	0
4 mg (1 spray) intranasal naloxone	36	36	NS†
GI upset (“stomach not feeling right”)	38	2	NS
COWS measured	42	4	9
Vomiting (2 episodes of vomitus, 3 episodes of dry heaving)	45	3	NS
24/6 mg sublingual buprenorphine-naloxone at once	50	5	28
Buprenorphine-naloxone fully dissolved.	60	10	NS
Subjective withdrawal symptoms 0–10; he states that he is at a 4. Feeling tired.			
Discontinued visit to sleep	65	5	NS

*Clinical Opioid Withdrawal Scale (COWS), excluding heart rate.

†COWS not scored.

Thank You, Beyonce!



Discuss!



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