Principles of Addiction Medicine: High Impact Research from 2022 (+ early 2023)

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Live Session: Sat April 15, 2023

National Harbor, MD

Disclosure Information

- Sarah Wakeman @DrSarahWakeman
  - Author: UpToDate
  - Textbook royalties: Springer

- Joshua D Lee @DrJoshuaDLee
  - Current In-kind study drug : Indivior, Alkermes
  - Recent ISS Research Funding : Indivior
  - Science Advisor to OarHealth

Methods: literature scan and article selection

1. Highest impact general medical or psychiatry journals:
- NEJM, The Lancet, JAMA, JAMA Internal Medicine, JAMA Psychiatry, JAMA Network Open, Annals Internal Medicine, Amer Jo Psychiatry

2. Addiction Medicine Specialty Journals:
- Addiction, Jo Addiction Medicine, JSAT, Drug Alc Dependence, Am Jo Addictions, Substance Abuse, Alcohol Clin Express

3. Newsletters: BU's Alcohol, Other Drugs, and Health; ASAM Weekly

4. Altmetric Scores, our own edits and opinions:
- Altmetric.com compiles an 'attention score' based on media, tweets, citations

2022…the year that was

Late COVID-19…Omicron…Ukraine…Inflation

Worsening fentanyl and stimulant driven overdose crisis in US

Worsening racial and ethnic disparities in overdose deaths

Ongoing contamination of the drug supply (xylazine etc.)

Policy changes including X the X waiver, SCS/OPCs in NYC, RI

More drinking, smoking, overdoses as COVID Era endured into 2022

Results: # Reviewed and Chapters

Papers ranked: ~50

Altmetric mean score: 560

Final presentation:
24 articles and web-based publications

Scan results and slides:
ASAM Conference App
Google/drive:
https://drive.google.com/drive/folders/18aeUEAXc4AkKSZ4e8xcSgwUZuICoEhJy?usp=sharing

Theme#1: Psychedelic Therapies : biggest AM paper 2022

Bogenschutz, JAMA Psych, 2022

Percentage of Heavy Drinking Days Following Psilocybin-Assisted Psychotherapy vs Placebo in the Treatment of Adult Patients With Alcohol Use Disorder: A Randomized Clinical Trial

New Online | Views 90,566 | Citations 3 | Altmetric 3630 | Comments 1

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Original Investigation | ONLINE FIRST

August 24, 2022

Percentage of Heavy Drinking Days Following Psilocybin-Assisted Psychotherapy vs Placebo in the Treatment of Adult Patients With Alcohol Use Disorder

A Randomized Clinical Trial

Michael P. Bogenschutz, MD[1]; Stephen Ross, MD[1]; Snehal Bhatt, MD[2]; et al

Author Affiliations | Article Information

JAMA Psychiatry. Published online August 24, 2022. doi:10.1001/jamapsychiatry.2022.2096

Why psilocybin for AUD?

- **Neuro rationale: serotonin 2A receptor agonism**
  - downstream effects on neurotransmission, intracellular signaling, epigenetics, and gene expression
  - **enhanced plasticity** at multiple levels, including neuronal structure, neural networks
  - improved cognition, affect, and behavior
  - Plus: we don't really know but these drugs seem to work
- **Prelim studies:**
  - 6 randomized clinical trials published between 1966 and 1971 w LSD
  - 2015 open-label study: moderately high doses of psilocybin (21 to 28 mg/70 kg) were well tolerated by participants with alcohol dependence, w large reductions in drinking over 32-weeks

Psilocybin for AUD: Methods

- 95 AUD participants, recruited from NYU and UNM through advertisements in local media:
  - mean age 45.78, mean gender 44.2% female, 78.9% Non-Hispanic White)
- Randomization: weight-based psilocybin vs diphenhydramine at weeks 4 & 8
- 12 psychotherapy sessions from 2 therapists
  - 4x before 1st dosing session, 4x between, 4x after 2nd dosing
- Dosing Day: stay in room with therapist for 8 hours
  - BP and HR checked every hour or more in first 6 hours.
  - Participant must stay, cannot leave

Figure 2. Effects of Treatment on Continuous Drinking Outcomes

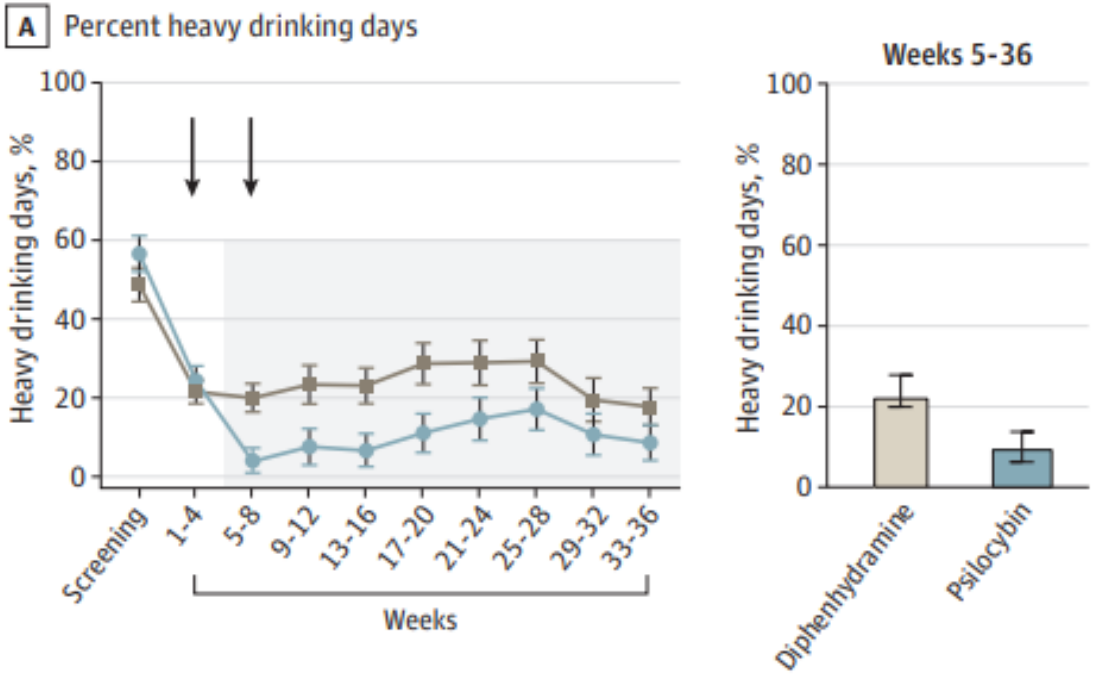


Table 3. Treatment Effects on Dichotomous Drinking Outcomes

	Follow-up period	No. (%)[a] Diphenhydramine (n = 45)	Psilocybin (n = 48)	NNT	OR (95% CI)[b]	*P* value[b,c]
Abstinence	Weeks 5-36	4 (8.9)	11 (22.9)	7.1	3.05 (0.89-10.40)	.06
	Weeks 33-36	11 (24.4)	23 (47.9)	4.3	2.84 (1.17-6.89)	.02
No heavy drinking	Weeks 5-36	5 (11.1)	16 (33.3)	4.5	4 (1.32-12.10)	.01
	Weeks 33-36	18 (40.0)	30 (62.5)	4.4	2.5 (1.08-5.76)	.03
WHO risk level[d]						

Psilocybin for AUD: Discussion

Psilocybin together with psychotherapy was efficacious for AUD

Strengths:

- novel protocol, exciting results for psilocybin
- high retention rate over 32-weeks (not typical of AUD treatment)
- psychotherapy ala addiction treatment programs (MI, CBT)

Limitations:

- blinding compromised
- mostly white participants w moderate AUD
- small proof-of-concept trial; *Funding : Heffter Institute, Donors*

Also: Ketamine for AUD

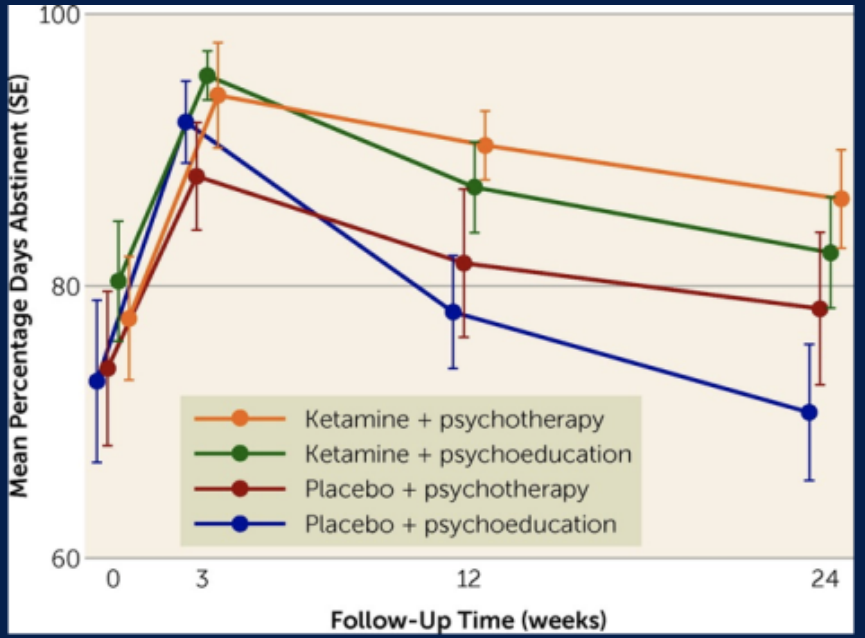
Grabsky, Am J Psychiatry, 2022

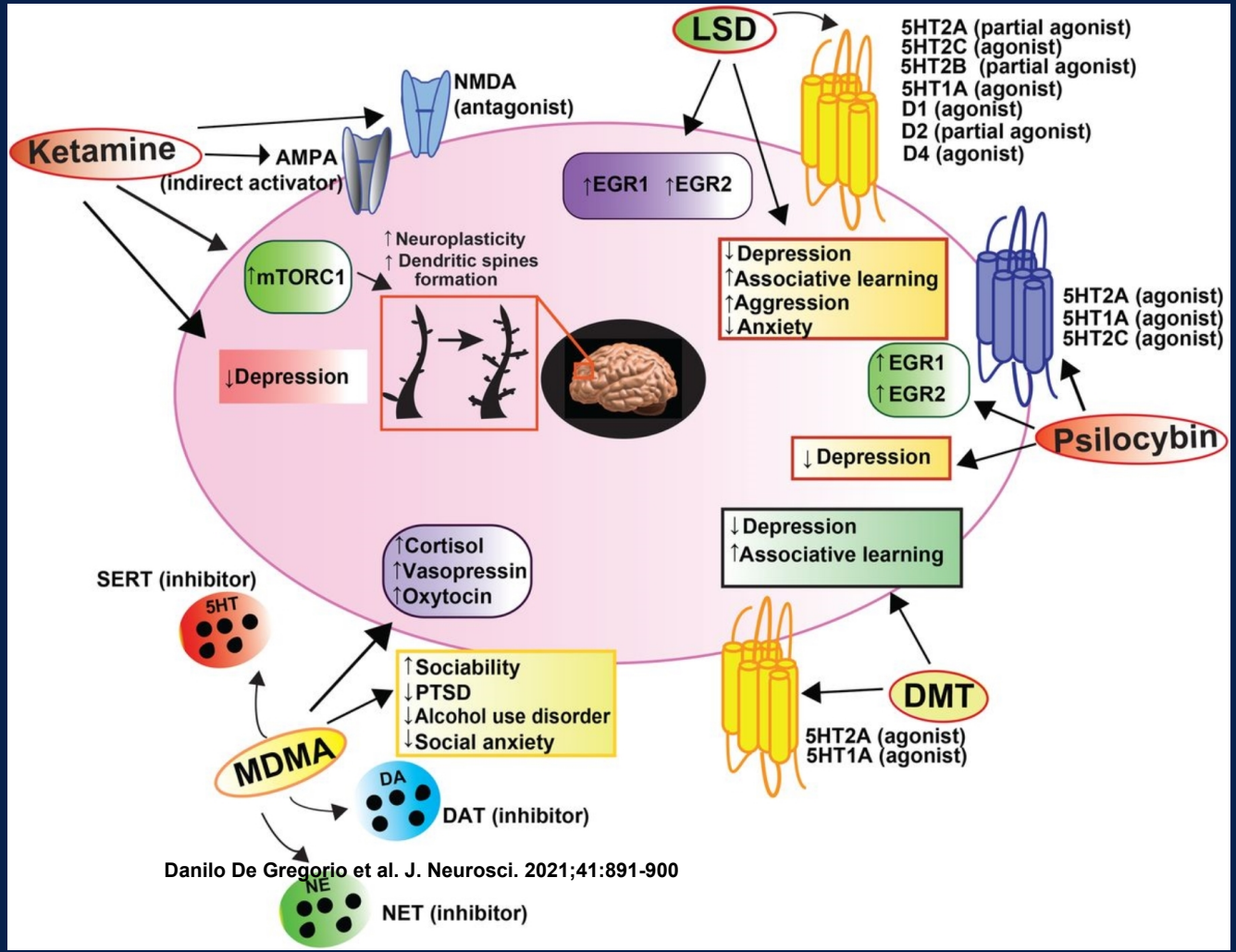
Adjunctive Ketamine With Relapse Prevention-Based Psychological Therapy in the Treatment of Alcohol Use Disorder,

double-blind placebo-controlled phase 2 clinical trial, 96 patients with severe alcohol use disorder

1) three weekly ketamine infusions (0.8 mg/kg i.v. over 40 minutes) plus psychological therapy, 2) three saline infusions plus psychological therapy, 3) three ketamine infusions plus alcohol education, or 4) three saline infusions plus alcohol education.

three infusions of ketamine was well tolerated in patients with alcohol use disorder and was associated with more days of abstinence from alcohol at 6-month follow-up



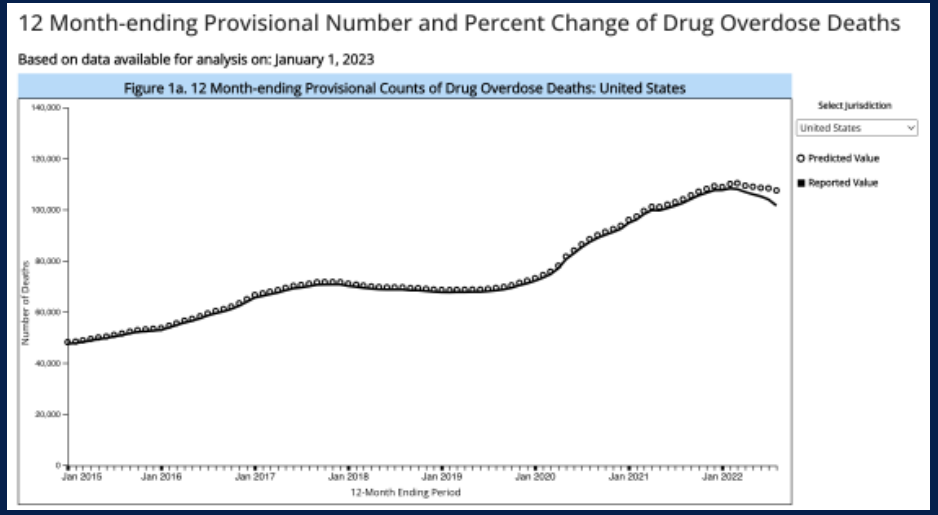


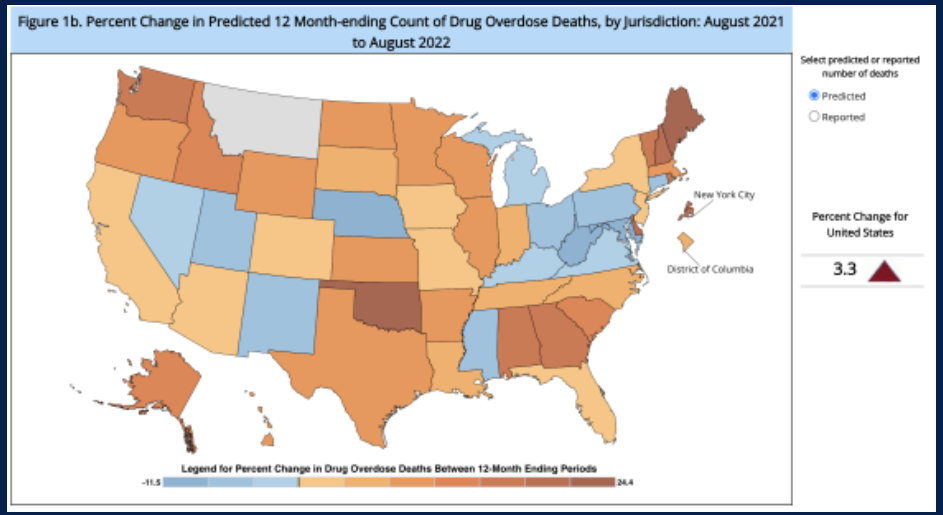
Danilo De Gregorio et al. J. Neurosci. 2021;41:891-900

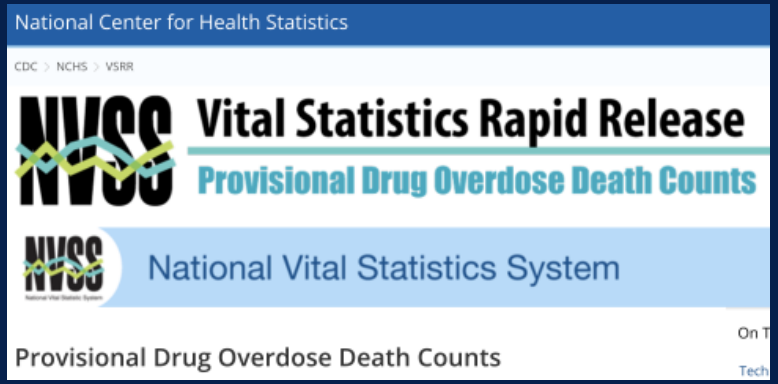
Theme#2: COVID Era saw worsening deaths related to addiction

- New data in 2022: US OD rates through Aug-2022, alcohol related deaths, cigarette consumption, overall worsening US mortality curves
- US Opioid and other drug-related ODs at all-time highs
- Worsening racial and ethnic disparities, rising deaths among youth
- Alcohol-related: also got worse
- On the other hand: MOUD Telehealth seems to have worked well and promising policy changes

2022 US OD Rates: cdc.gov







Have we peaked? OD deaths otherwise continue to set all time highs each year

3.3% increase from 2021

<u>101,000 deaths</u> related to ‘drug poisonings’ annually in Aug-2022, down from 108,000 in Feb-2022

CDC Overdose Death Data: Worsening trends, fentanyl dominant, increasing stimulant

Figure 1. National Drug-Involved Overdose Deaths*, Number Among All Ages, by Gender, 1999-2021

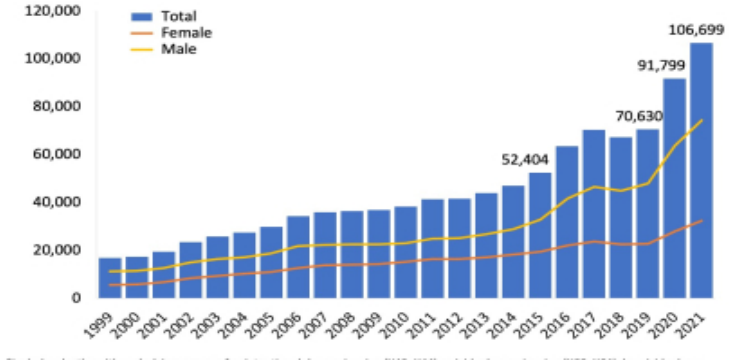


Figure 3. National Overdose Deaths Involving Any Opioid*, Number Among All Ages, by Gender, 1999-2021

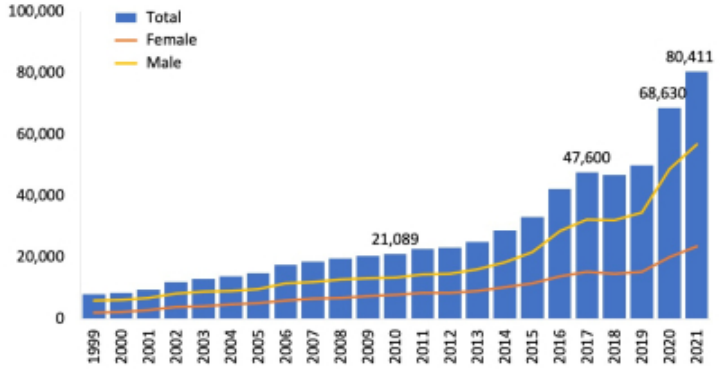


Figure 2. National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2020

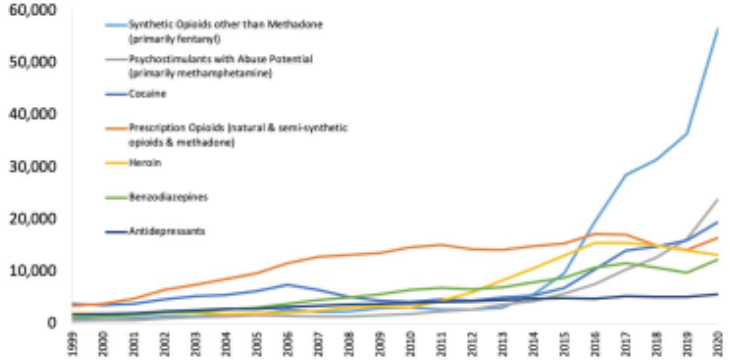
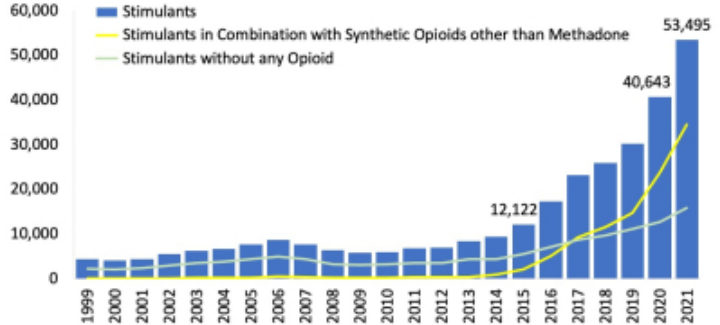


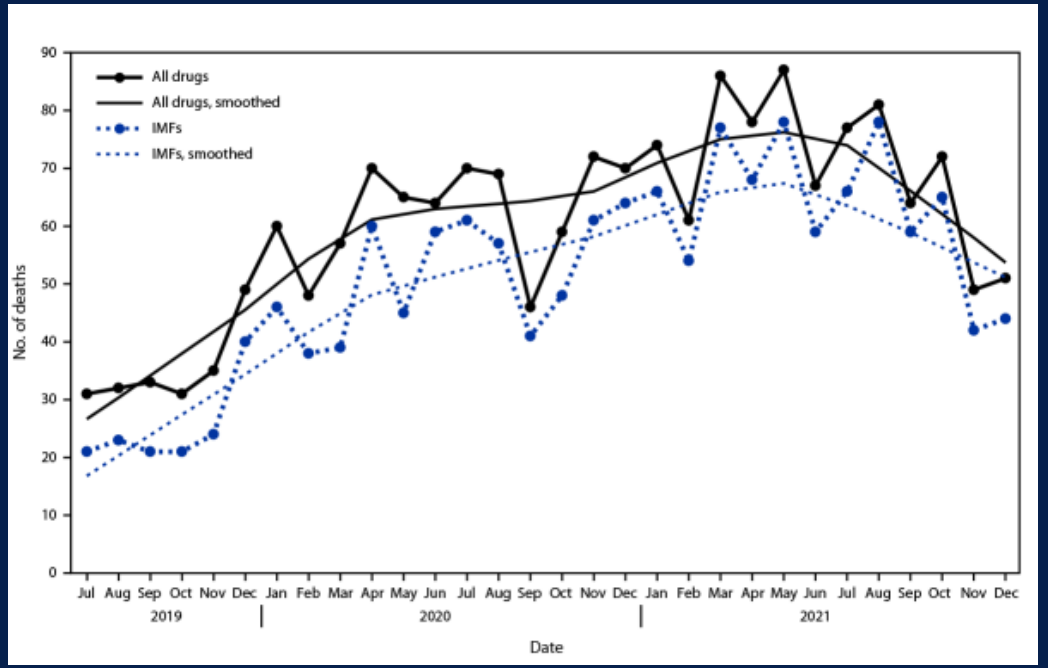
Figure 6. National Overdose Deaths Involving Stimulants (Cocaine and Psychostimulants*), by Opioid Involvement, Number Among All Ages, 1999-2021



Overdose Among Adolescents

Tanz et al. MMWR 2022

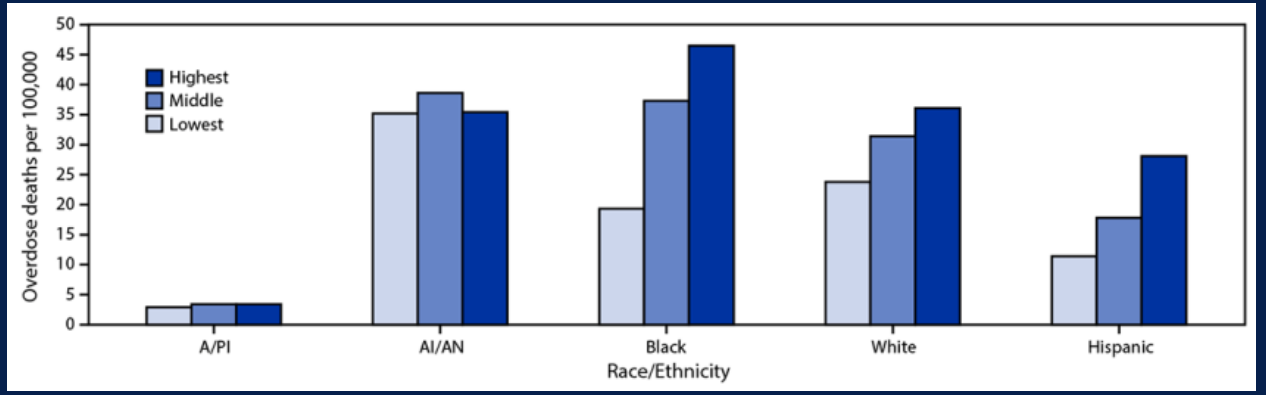
- Median monthly OD deaths among 10-19 yo increased 109% between same 3-month period in 2019 vs 2021
- IMF related deaths up 182%
- Counterfeit pills present 25%
- Majority of deaths had bystander present but most provided no OD response



Worsening Racial and Ethnic Disparities in Overdose

Kariisa et al. MMWR 2022

- Overdose death rates increase was greatest among Black (44%) and AI/AN (39%) individuals

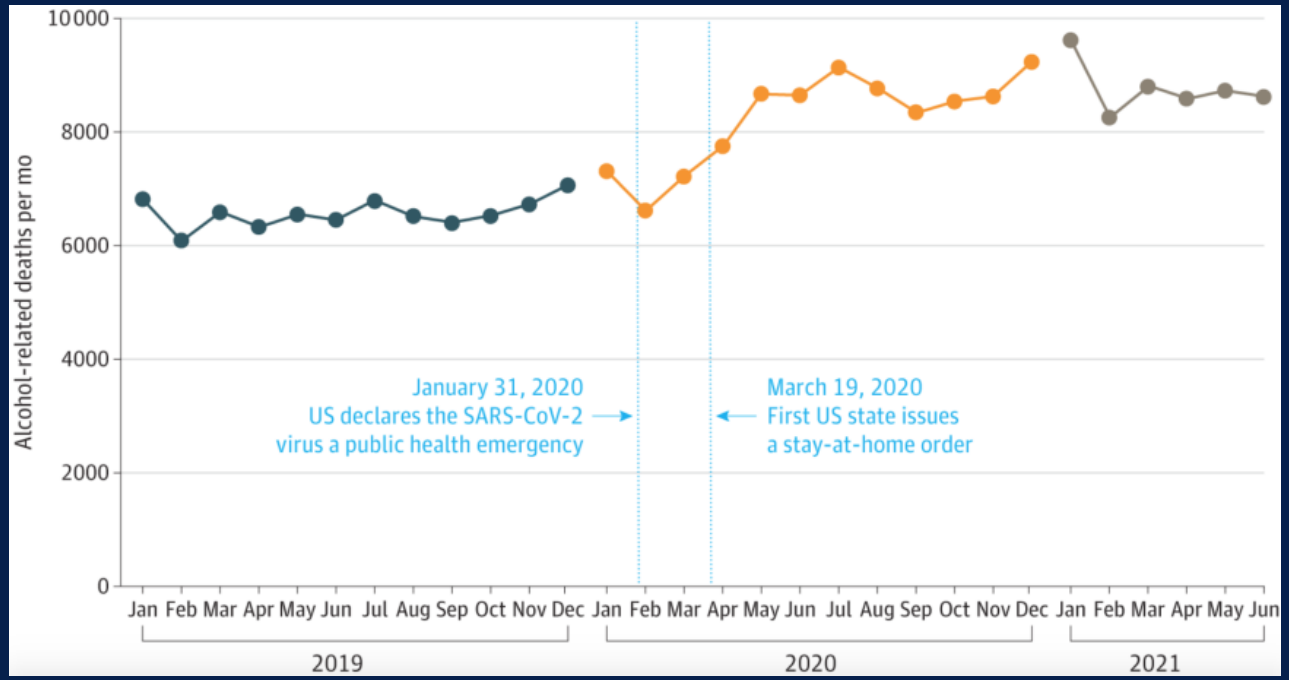


- Rates highest among older Black men and in areas w/ greatest income inequality

- Past treatment rates highest among white (16.4%) and lowest among Black decedents (8%)

White, KoobG (NIAAA), JAMA, 2022

Alcohol-Related Deaths During the COVID-19 Pandemic



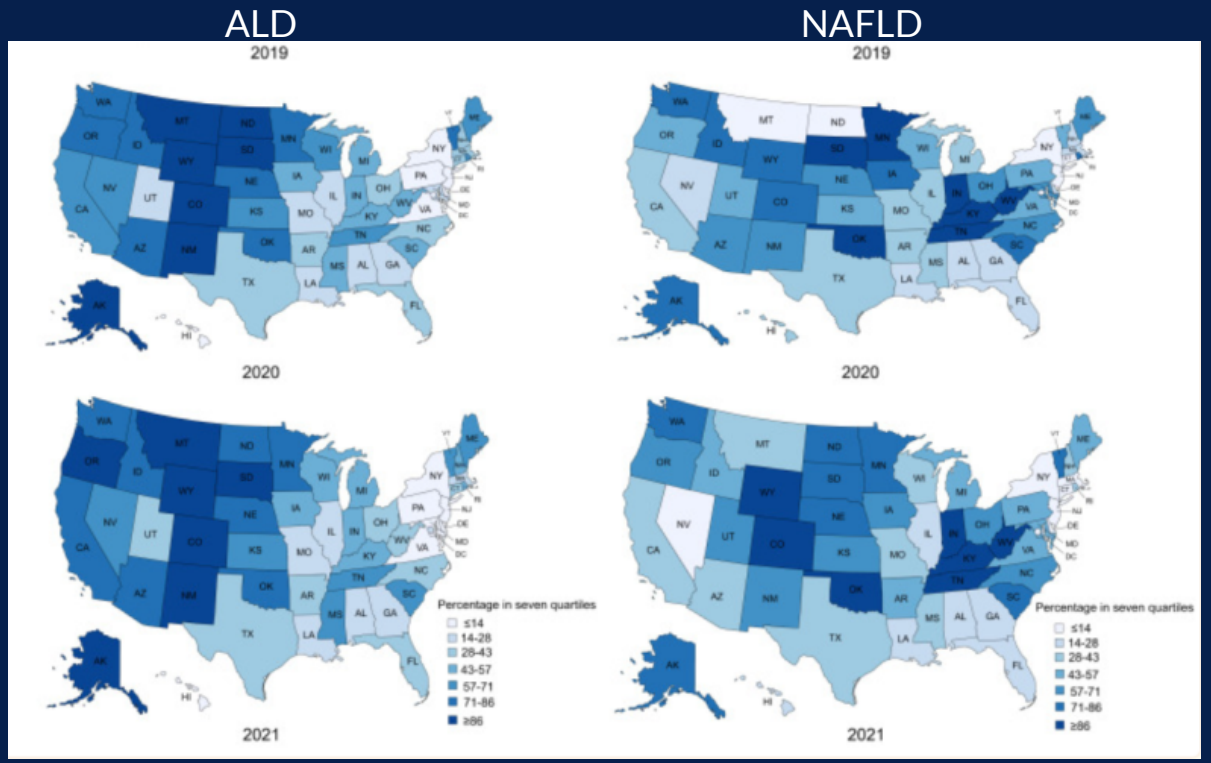
- All deaths involving alcohol increased between 2019 and 2020 (from 78 927 to 99 017 [relative change, 25.5%])
- Alcohol-related deaths accounted for 2.8% of all deaths in 2019 and 3.0% in 2020.
- Largest 35-44 yo [39.7%] and 25-34 yo [37.0%]

- Alcohol-associated liver diseases up to 29,504 (+22.4%)
- Alcohol-related mental and behavioral disorders to 15,211 (+35.1%)
- Opioid overdose deaths involving alcohol 11,969 (+40.8%)
- Fentanyl + alcohol 10,032 (+59.2%)

COVID Impact on ALD Mortality

Gao, J Hepatol. 2023

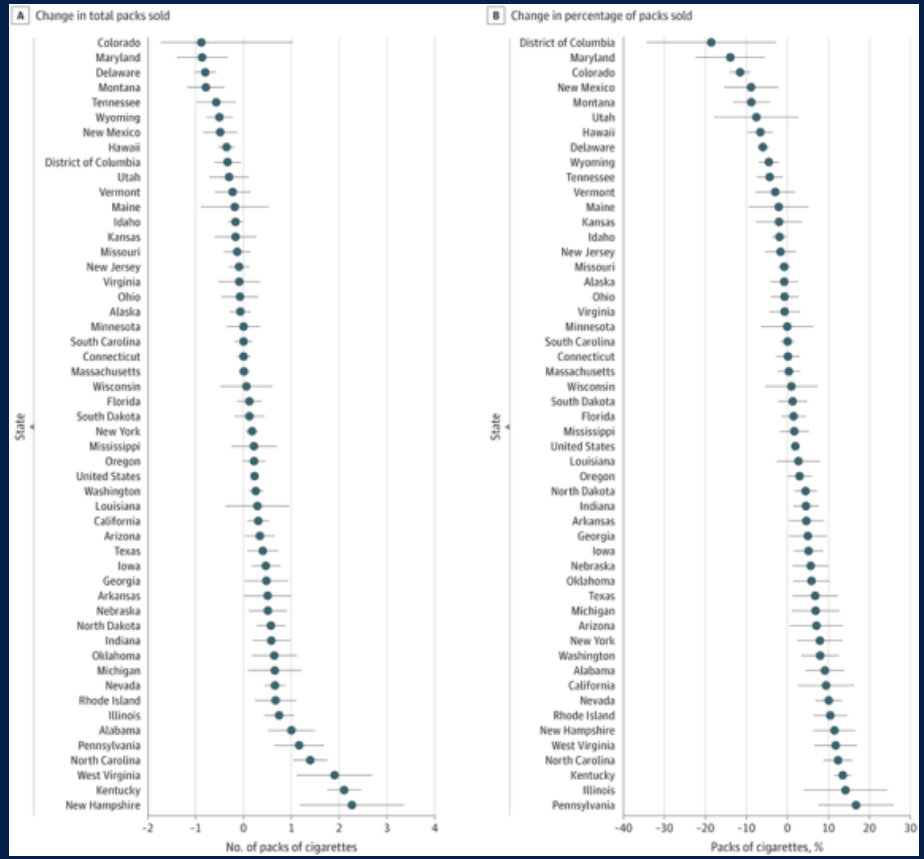
- Age-standardized mortality ratios for chronic liver disease 2010-2021
- 620K CLD related deaths, ALD top cause (55%)
- Accelerated increase in ALD related deaths 2019-2021 compared
- ASMR increased dramatically for ALD
- Annual % change highest for AI/AN individuals (18%)



Cigarette sales tick up during COVID

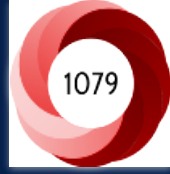
Asere, JAMA Netw Open. 2022

- Interrupted time series analysis of 2008-2020 vs 2020-2021
- Overall there was a 0.23 pack increase per capita Changes in cigarette sales after the onset of the COVID-19 pandemic when calculated as the mean difference between observed and expected quarterly cigarette sales
- Cigarette sales per capita increased in 22 states, unchanged in 20, decreased in 8 post-pandemic
- Colorado had biggest decrease
- New Hampshire had biggest increase (2.3 packs)



But…Telehealth for MOUD During COVID helped

Receipt of Telehealth Services, Receipt and Retention of Medications for Opioid Use Disorder, and Medically Treated Overdose Among Medicare Beneficiaries Before and During the COVID-19 Pandemic



Jones et al. JAMA Psychiatry. 2022 & 2023

- Two cohort study of Medicare beneficiaries looking at telemed-MOUD
- First study found receipt of OUD-related telehealth services was associated with increased odds of MOUD retention (aOR1.27) and lower odds of medically treated overdose (aOR, 0.67)
- Second study limited to those newly initiating OUD treatment during the pandemic
- Those who received OUD-related telehealth services had 33% lower adjusted odds of fatal drug overdose, even after accounting for OUD and non-OUD care engagement and MOUD

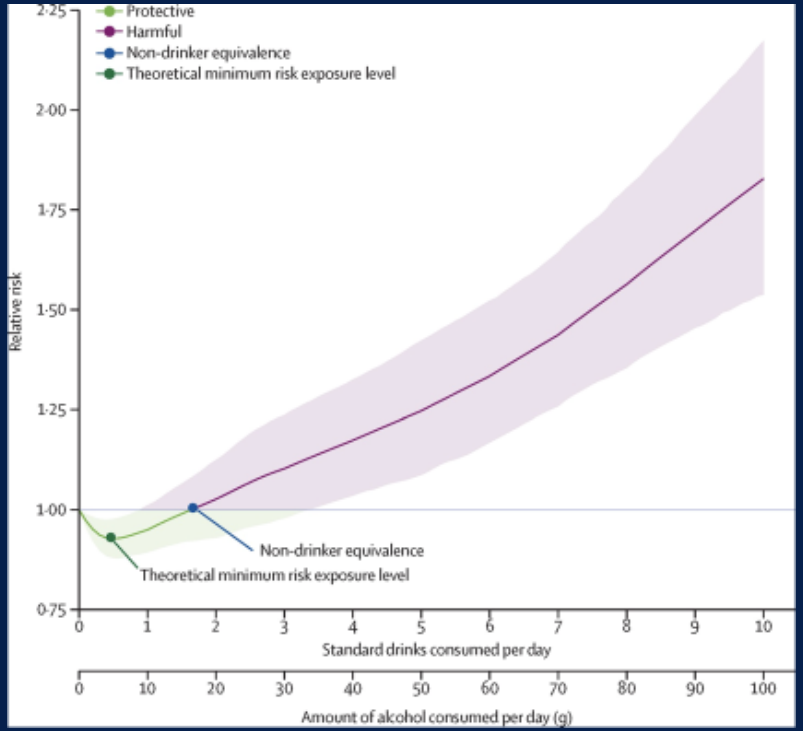
Table 3. Characteristics Associated With Fatal Drug Overdose During Study Period Among Beneficiaries With Opioid Use Disorder in the Pandemic Cohort[a]

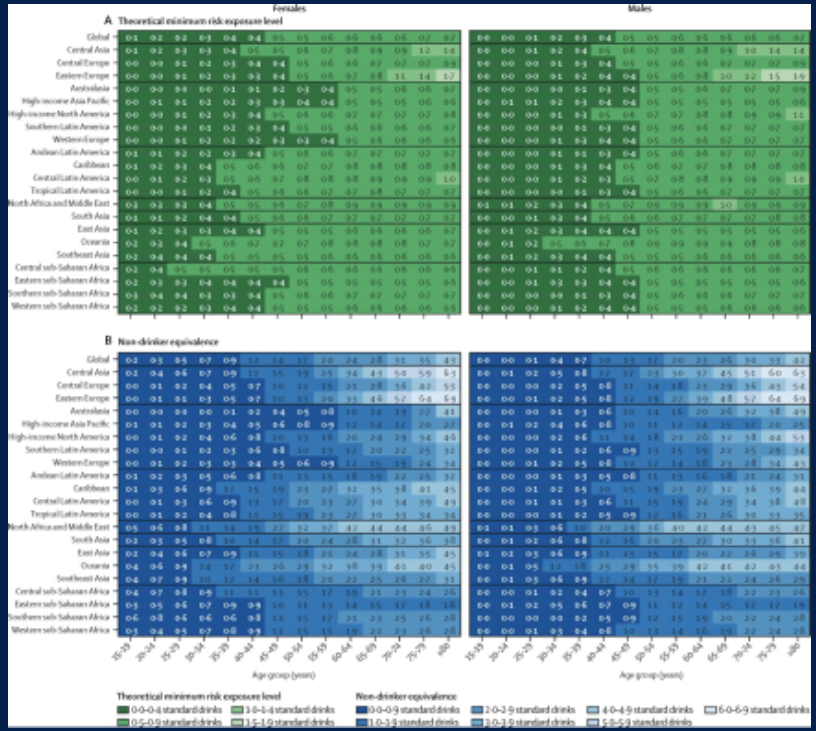
Characteristic	Beneficiaries, No. (%)	aOR (95% CI)[b]
Receipt of OUD-related telehealth service	13 809 (19.6)	0.67 (0.48-0.92)[c]
Receipt of MOUD during study period		
No MOUD	61 626 (87.5)	1 [Reference]
MOUD from OTPs	2774 (3.9)	0.41 (0.25-0.68)[c]
ER naltrexone in office-based settings	170 (0.2)	1.16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

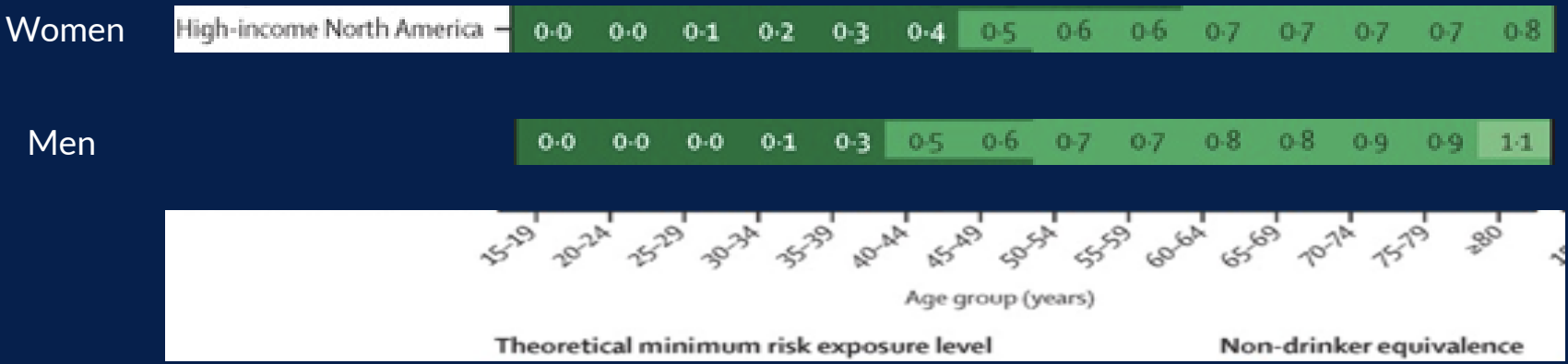
Theme #3: What about 'Alcohol=0'?

GBD Authors, Lancet, 2022

Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020







Age 15–39 years: TMREL = 0 - 0·603
NDE = 0·002 - 1·75

Age 40 +years: + J-shaped curve for all regions:
TMREL 0·114 - 1·87
NDE 0·193 - 6·94 drinks/day

Among individuals consuming harmful amounts of alcohol in 2020, 59·1% (54·3–65·4) were aged 15–39 years and 76·9% (73·0–81·3) were male.

Remember this?: #1 Addiction Paper, 2018 (San Diego!)

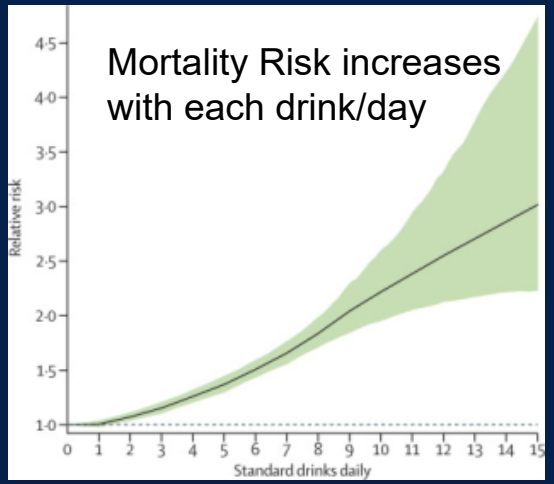
Global Burden of Disease 2016 Alcohol Collaborators, The Lancet, 2018 (Top 100 of 2018: #3):

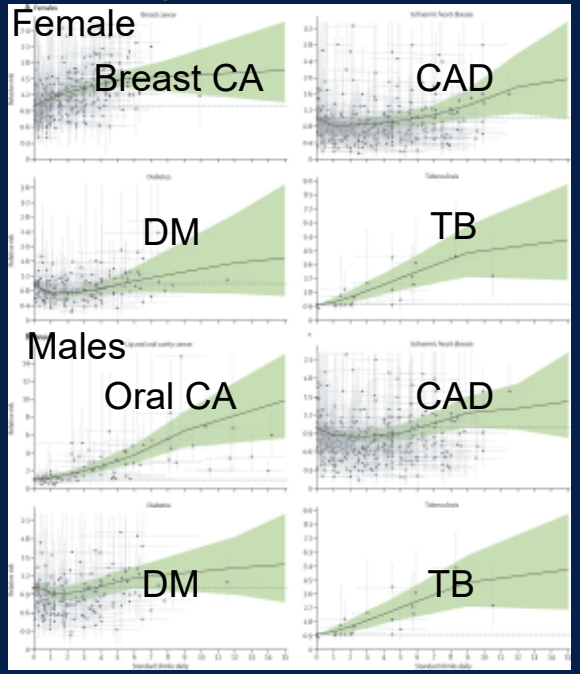
Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016

- 694 data sources of individual and population-level alcohol consumption, along with 592 prospective and retrospective studies on the risk of alcohol use
- Added sales and national prevalence and consumption data (new approach) to self-report data (old approach)

- The level of alcohol consumption that minimised harm across health outcomes was zero (95% UI 0·0–0·8) standard drinks per week

- Among the population aged 15–49 years, alcohol use was the leading risk factor globally in 2016, with 3·8% (95% UI 3·2–4·3) of female deaths and 12·2% (10·8–13·6) of male deaths attributable to alcohol use.





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Related, 2022: Health Canada says Alcohol=0

Canada's New Guidelines for Alcohol Say 'No Amount' Is Healthy

The guidance builds on growing evidence, after decades of sometimes conflicting research, that even small amounts of alcohol can have serious health consequences.

Canadian health officials have overhauled their guidelines for alcohol consumption, warning that no amount is healthy and recommending that people reduce drinking as much as possible.

The new guidelines, issued Tuesday, represent a major shift from the previous ones introduced in 2011, which recommended that women consume no more than 10 drinks per week and that men limit themselves to 15.

Canadian Centre on Substance Use and Addiction

- There is a continuum of risk associated with weekly alcohol use where the risk of harm is:
  - **0 drinks per week** — Not drinking has benefits, such as better health, and better sleep.
  - **2 standard drinks or less per week —** You are likely to avoid alcohol-related consequences for yourself or others at this level.
  - **3–6 standard drinks per week —** Your risk of developing several types of cancer, including breast and colon cancer, increases at this level.
  - **7 standard drinks or more per week** — Your risk of heart disease or stroke increases significantly at this level.
  - **Each additional standard drink** radically increases the risk of alcohol-related consequences.
- Consuming more than 2 standard drinks per occasion is associated with an increased risk of harms to self and others, including injuries and violence.

Just last week: Meta-A showing no J-shaped curve

Zhao, JAMA Net Open, 2023

Association Between Daily Alcohol Intake and Risk of All-Cause Mortality

A Systematic Review and Meta-analyses

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

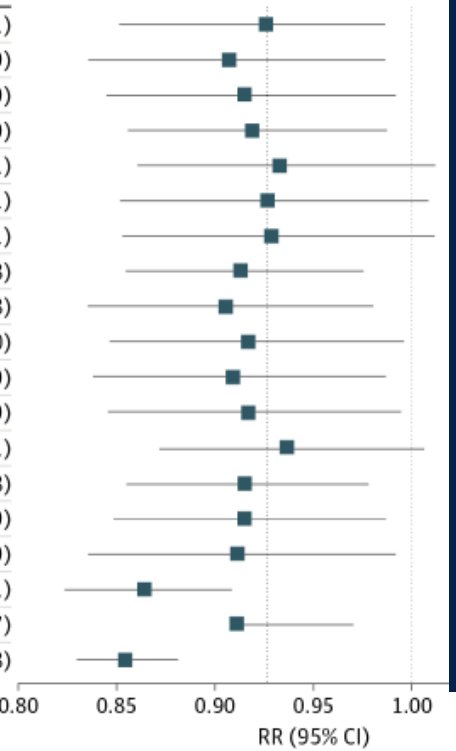

THE WALL STREET JOURNAL

Home World U.S. Politics Economy Business Tech Markets Opinion Book

A Little Alcohol Won't Kill You

People who drink a little don't die sooner than people who

Adjustment level	RR (95% CI)
Fully adjusted	0.93 (0.85-1.01)
Smoking status	0.91 (0.84-0.99)
SES	0.92 (0.84-0.99)
Race	0.92 (0.86-0.99)
Diet	0.93 (0.86-1.01)
Exercise	0.93 (0.85-1.01)
BMI	0.93 (0.85-1.01)
Drinking pattern	0.91 (0.85-0.98)
Former drinker bias only	0.90 (0.84-0.98)
Occasional drinker bias only	0.92 (0.85-1.00)
Median age	0.91 (0.84-0.99)
Gender	0.92 (0.85-0.99)
Country	0.94 (0.87-1.01)
Follow-up year	0.91 (0.86-0.98)
Publication year	0.92 (0.85-0.99)
Unhealthy people exclusion	0.91 (0.84-0.99)
Removed[a]	0.87 (0.82-0.91)
Removed[b]	0.91 (0.86-0.97)
All covariates removed	0.86 (0.83-0.88)



Theme#4: Cannabis-Pain-OUD

JAMA: Cannabis for Pain and Placebo Response

Annals of Internal Medicine: Cannabis and CBD for Chronic Pain

NEJM: THC and MVAs in Canada

JAMA: Opioid Prescriptions after Fatal OD Notifications to Providers

Annals of Internal Medicine: VA/DOD Chronic Pain Guidelines 2022

NEJM: CDC Chronic Pain Guidelines 2022

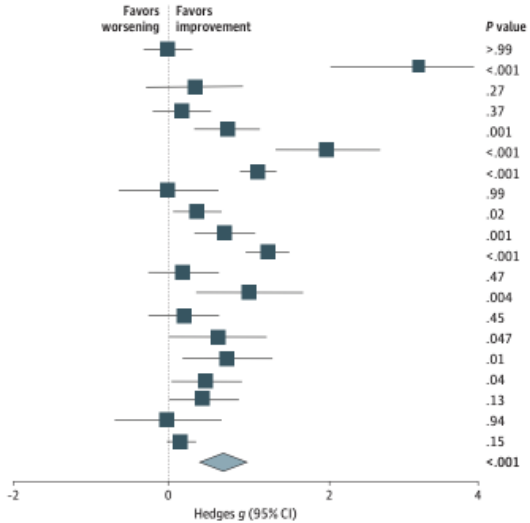
Gedin, JAMA, 2022

Placebo Response and Media Attention in Randomized Clinical Trials Assessing Cannabis-Based Therapies for Pain: A Systematic Review and Meta-analysis

- Systematic review and meta-analysis
- To determine size and magnitude in placebo response in cannabinoid trials for clinical pain and if magnitude is associated with media attention on the trials
- Meta analysis of 20 studies of 1459 individuals found significant pain reduction in response to placebo
- The amount of media attention and dissemination linked to each trial was proportionally high, with a strong positive bias, but was not associated with the clinical outcomes

Figure 3. Association Between Placebo and Change in Pain Intensity Ratings

Study, year	Hedges g	SE (95% CI)	z Value
Berman et al,[13] 2004	0.00	0.16 (-0.31 to 0.31)	0.00
Buggy et al,[14] 2003	3.32	0.62 (2.11 to 4.54)	5.35
Chaves et al,[15] 2020	0.38	0.34 (-0.29 to 1.06)	1.11
Corey-Bloom et al,[16] 2012	0.18	0.20 (-0.21 to 0.56)	0.89
de Vries et al,[17] 2017	0.77	0.23 (0.33 to 1.22)	3.40
Issa et al,[18] 2014	2.06	0.36 (1.36 to 2.76)	5.78
Langford et al,[24] 2013	1.16	0.11 (0.93 to 1.38)	10.23
Malik et al,[25] 2017	0.00	0.34 (-0.68 to 0.67)	0.00
Nurmikko et al,[26] 2007	0.36	0.15 (0.06 to 0.66)	2.36
Rog et al,[23] 2005	0.73	0.21 (0.31 to 1.52)	3.42
Schimrigk et al,[19] 2017	1.30	0.14 (1.03 to 1.57)	9.43
Skrabek et al,[20] 2008	0.18	0.25 (-0.31 to 0.67)	0.73
Toth et al,[21] 2012	1.05	0.36 (0.34 to 1.77)	2.90
Turcott et al,[22] 2018	0.18	0.24 (-0.29 to 0.66)	0.76
Wade et al,[28] 2003	0.65	0.33 (0.01 to 1.29)	1.98
Wallace et al,[27] 2015	0.77	0.30 (0.18 to 1.36)	2.57
Ware et al,[29] 2010	0.51	0.25 (0.23 to 0.99)	2.07
Weizman et al,[30] 2018	0.43	0.28 (-0.12 to 0.98)	1.53
Zadikoff et al,[31] 2011	-0.03	0.36 (-0.74 to 0.68)	-0.08
Zajicek et al,[32] 2012	0.14	0.10 (-0.05 to 0.32)	1.44
Combined	**0.64**	**0.13 (0.38 to 0.89)**	**4.82**

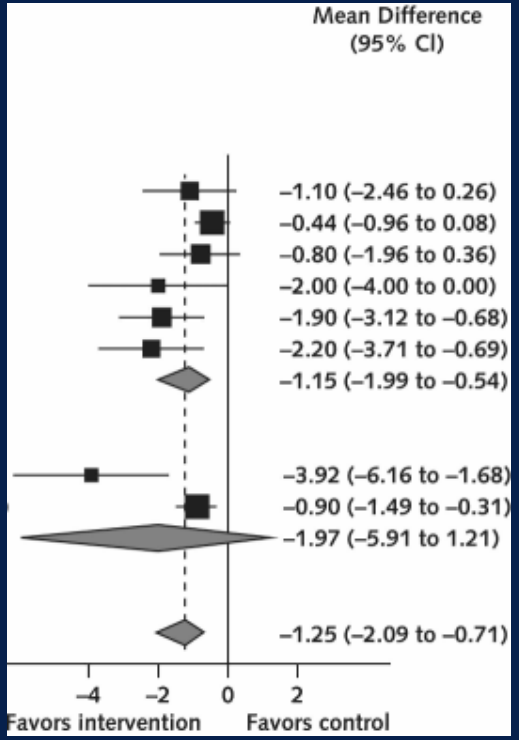


The overall treatment response to placebo was statistically significant. The blue squares to the right of the midline represent improvements in pain intensity after treatment, squares on the midline represent no change, and squares to the left of the midline represent worsening of pain intensity after treatment.

McDonagh, Annals IM, 2022

Cannabis-Based Products for Chronic Pain : A Systematic Review

- Systematic review evaluating the benefits and harms of cannabinoids in chronic pain
- 18 randomized placebo-controlled trials (n=1740) and 7 cohort studies (n=13,095)
- 56% enrolled patients with neuropathic pain
- Synthetic products with >98% THC may be associated with moderate improvement in pain severity and response (>30% improvement)
- Increased risk of sedation and dizziness
- Oral synthetic cannabis products with high THC-CBD ratios and comparable extracted cannabis products may be associated with short-term chronic pain improvement and increased risk of dizziness and sedation



Brubacher, NEJM, 2022

Cannabis Legalization and Detection of Tetrahydrocannabinol in Injured Drivers

- Study of drivers THC levels treated after collisions in 4 British Columbia trauma centers from 2013 to 2020
- Before legalization, a THC level >0 was detected in 9.2% of drivers, a THC level of at least 2 ng per ml in 3.8%, and a THC level of at least 5 ng per ml in 1.1%.
- After legalization, the values were 17.9%, 8.6%, and 3.5%, respectively.
- Increase in THC levels more prevalent in older, male drivers

Table 2. Substance Levels in Moderately Injured Drivers before and after Cannabis Legalization.*

Substance	Entire Study Period: Jan. 2013–Mar. 2020 (N=4409)	Before Legalization: Jan. 2013–Sept. 2018 (N=3550)	After Legalization: Nov. 2018–Mar. 2020 (N=789)	Prevalence Ratio: After vs. Before Legalization (95% CI)†	
				Crude‡	Adjusted§
	number (percent)				
Cannabis					
THC level = 0 ng/ml	3923 (89.0)	3225 (90.8)	648 (82.1)	—	—
THC level >0 ng/ml	486 (11.0)	325 (9.2)	141 (17.9)	1.95 (1.63–2.34)	1.33 (1.05–1.68)
THC level ≥2 ng/ml	209 (4.7)	136 (3.8)	68 (8.6)	2.25 (1.70–2.98)	2.29 (1.52–3.45)
THC level ≥5 ng/ml	69 (1.6)	38 (1.1)	28 (3.5)	3.32 (2.05–5.37)	2.05 (1.00–4.18)
Alcohol					
Blood alcohol level = 0%	3912 (88.7)	3141 (88.5)	712 (90.2)	—	—
Blood alcohol level >0%	497 (11.3)	409 (11.5)	77 (9.8)	0.85 (0.67–1.07)	0.90 (0.71–1.14)
Blood alcohol level ≥0.08%	399 (9.0)	331 (9.3)	64 (8.1)	0.87 (0.67–1.12)	0.98 (0.74–1.30)
Cannabis and alcohol					
THC level >0 ng/ml and blood alcohol level >0%	103 (2.3)	75 (2.1)	24 (3.0)	1.44 (0.92–2.27)	0.84 (0.49–1.45)
THC level ≥2.5 ng/ml and blood alcohol level ≥0.05%	24 (0.5)	17 (0.5)	7 (0.9)	1.85 (0.77–4.45)	2.88 (0.76–10.9)

* Date on prevalence during the month of legalization (October 2018) are provided in Table S2 in the Supplementary Appendix. THC denotes tetrahydrocannabinol.
† Confidence intervals (CIs) have not been adjusted for multiplicity; no statistical inferences may be drawn.
‡ Shown are Wald confidence intervals (excluding the month of legalization).
§ Adjusted prevalence ratios were obtained from a log-binomial regression model that was adjusted for annual trend (year), season (winter, spring, summer, or fall), sex (male or female), age group (<30, 30 to 49, or ≥50 years), health authority (Vancouver Coastal Health, Fraser Health Authority, Vancouver Island Health Authority, or Interior Health Authority), injury severity (admission to hospital or discharge from emergency department), time of collision (daytime or nighttime), and type of collision (single-vehicle or multivehicle).

Doctor, JAMA, 2022

Effect of Prescriber Notifications of Patient's Fatal Overdose on Opioid Prescribing at 4 to 12 Months: A Randomized Clinical Trial

- Randomized clinical trial
- Whether clinicians notified of patient's overdose from schedule II or IV drug were more likely than clinicians not notified to reduce opioid prescribing
- 167 patients who received prescriptions from 826 clinicians from 2015-2016
- 9.7% decrease in prescriptions filled for MMEs up to 3 months after letter receipt and a decrease in new patients taking high dose opioids in panels of clinicians who received the letter

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)

Sandbrink, Annals IM, 2022

The Use of Opioids in the Management of Chronic Pain: Synopsis of the 2022 Updated U.S. Department of Veterans Affairs and U.S. Department of Defense Clinical Practice Guideline

- Updated guideline for clinicians prescribing opioids for chronic pain
- Reviews recommendations for initiation and continuation of opioid therapy; dose, duration, tapering, screening, assessment, and risk mitigation
- New additions since 2017:
  - recommendations about use of buprenorphine over full agonist opioids
  - assessing for behavioral health conditions + other risk factors
  - use of pain and opioid education to reduce the risk of prolonged use

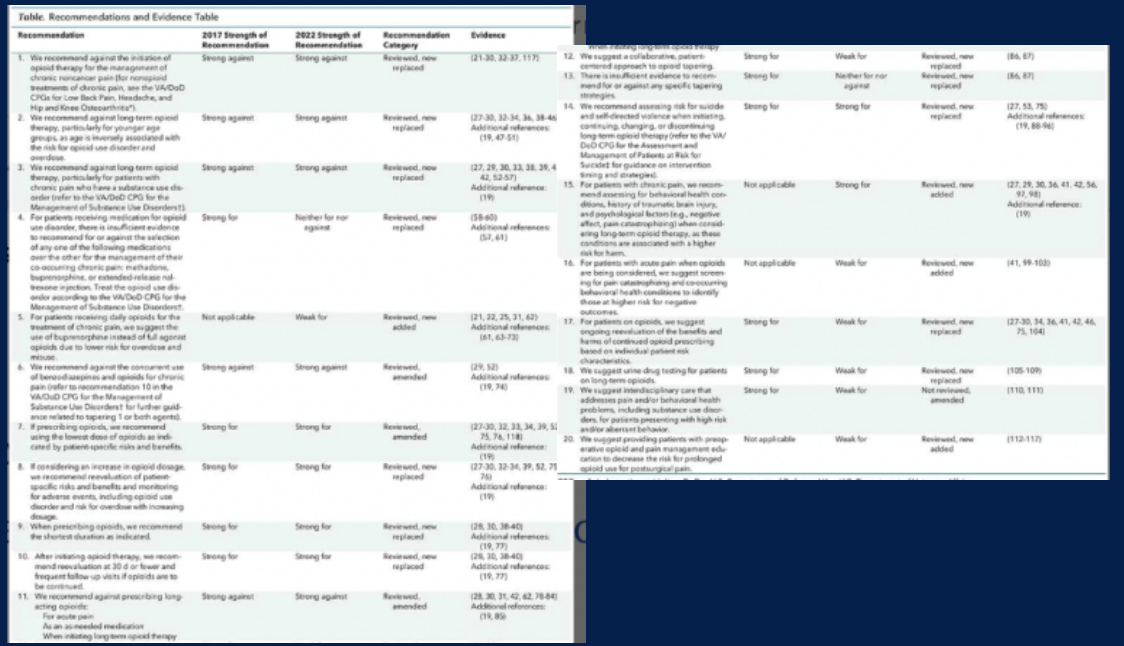


Table. Recommendations and Evidence Table

Recommendation	2017 Strength of Recommendation	2022 Strength of Recommendation	Recommendation Category	Evidence
1. We recommend against the initiation of opioid therapy for the management of chronic noncancer pain (for nonopioid treatments of chronic pain, see the VA/DoD CPGs for Low Back Pain, Headache, and Hip and Knee Osteoarthritis*).	Strong against	Strong against	Reviewed, new replaced	(21-30, 32-37, 117)
2. We recommend against long-term opioid therapy, particularly for younger age groups, as age is inversely associated with the risk for opioid use disorder and overdose.	Strong against	Strong against	Reviewed, new replaced	(27-30, 32-34, 36, 38-46) Additional references: (19, 47-51)
3. We recommend against long-term opioid therapy, particularly for patients with chronic pain who have a substance use disorder (refer to the VA/DoD CPG for the Management of Substance Use Disorders†).	Strong against	Strong against	Reviewed, new replaced	(27, 29, 30, 33, 38, 39, 42, 52-57) Additional reference: (19)
4. For patients receiving medication for opioid use disorder, there is insufficient evidence to recommend for or against the selection of any one of the following medications over the other for the management of their co-occurring chronic pain: methadone, buprenorphine, or extended-release naltrexone injection. Treat the opioid use disorder according to the VA/DoD CPG for the Management of Substance Use Disorders†.	Strong for	Neither for nor against	Reviewed, new replaced	(58-60) Additional references: (57, 61)
5. For patients receiving daily opioids for the treatment of chronic pain, we suggest the use of buprenorphine instead of full agonist opioids due to lower risk for overdose and misuse.	Not applicable	Weak for	Reviewed, new added	(21, 22, 25, 31, 62) Additional references: (61, 63-73)
6. We recommend against the concurrent use of benzodiazepines and opioids for chronic pain (refer to recommendation 10 in the VA/DoD CPG for the Management of Substance Use Disorders† for further guidance related to tapering 1 or both agents).	Strong against	Strong against	Reviewed, amended	(29, 52) Additional references: (19, 74)
7. If prescribing opioids, we recommend using the lowest dose of opioids as indicated by patient-specific risks and benefits.	Strong for	Strong for	Reviewed, amended	(27-30, 32, 33, 34, 39, 5[illegible] 75, 76, 118) Additional reference: (19)
8. If considering an increase in opioid dosage, we recommend reevaluation of patient-specific risks and benefits and monitoring for adverse events, including opioid use disorder and risk for overdose with increasing dosage.	Strong for	Strong for	Reviewed, new replaced	(27-30, 32-34, 39, 52, 75 76) Additional reference: (19)
9. When prescribing opioids, we recommend the shortest duration as indicated.	Strong for	Strong for	Reviewed, new replaced	(28, 30, 38-40) Additional references: (19, 77)
10. After initiating opioid therapy, we recommend reevaluation at 30 d or fewer and frequent follow-up visits if opioids are to be continued.	Strong for	Strong for	Reviewed, new replaced	(28, 30, 38-40) Additional references: (19, 77)
11. We recommend against prescribing long-acting opioids: For acute pain As an as-needed medication When initiating long-term opioid therapy	Strong against	Strong against	Reviewed, amended	(28, 30, 31, 42, 62, 78-84) Additional references: (19, 85)
12. We suggest a collaborative, patient-centered approach to opioid tapering.	Strong for	Weak for	Reviewed, new replaced	(86, 87)
13. There is insufficient evidence to recommend for or against any specific tapering strategies.	Strong for	Neither for nor against	Reviewed, new replaced	(86, 87)
14. We recommend assessing risk for suicide and self-directed violence when initiating, continuing, changing, or discontinuing long-term opioid therapy (refer to the VA/DoD CPG for the Assessment and Management of Patients at Risk for Suicide‡ for guidance on intervention timing and strategies).	Strong for	Strong for	Reviewed, new replaced	(27, 53, 75) Additional references: (19, 88-96)
15. For patients with chronic pain, we recommend assessing for behavioral health conditions, history of traumatic brain injury, and psychological factors (e.g., negative affect, pain catastrophizing) when considering long-term opioid therapy, as these conditions are associated with a higher risk for harm.	Not applicable	Strong for	Reviewed, new added	(27, 29, 30, 36, 41, 42, 56, 97, 98) Additional reference: (19)
16. For patients with acute pain when opioids are being considered, we suggest screening for pain catastrophizing and co-occurring behavioral health conditions to identify those at higher risk for negative outcomes.	Not applicable	Weak for	Reviewed, new added	(41, 99-103)
17. For patients on opioids, we suggest ongoing reevaluation of the benefits and harms of continued opioid prescribing based on individual patient risk characteristics.	Strong for	Weak for	Reviewed, new replaced	(27-30, 34, 36, 41, 42, 46, 75, 104)
18. We suggest urine drug testing for patients on long-term opioids.	Strong for	Weak for	Reviewed, new replaced	(105-109)
19. We suggest interdisciplinary care that addresses pain and/or behavioral health problems, including substance use disorders, for patients presenting with high risk and/or aberrant behavior.	Strong for	Weak for	Not reviewed, amended	(110, 111)
20. We suggest providing patients with preoperative opioid and pain management education to decrease the risk for prolonged opioid use for postsurgical pain.	Not applicable	Weak for	Reviewed, new added	(112-117)

Dowell, NEJM, 2022

Prescribing Opioids for Pain – The New CDC Clinical Practice Guideline

- Updated CDC guideline
- Aim is to promote equitable access to effective, informed, individualized, and safe pain management that improves patients' function and quality of life, while clarifying and reducing the risks associated with opioid use

Recommendations:

- Maximize nonopioid therapies
- Before starting discuss risk/benefit, identify functional goals, plan for discontinuation if risk>benefit
- Check PDMP
- Start low, with IR, not LA/ER
- *"Avoid increasing above levels likely to yield diminishing returns in benefits relative to risks"*
- If benefit>risk, continue opioids. If risks>benefits, work with patient to gradually lower dose.
- Do not abruptly taper unless there is a life-threatening issue
- For acute pain, only prescribe amount needed
- re-evaluate risk/benefit 1-4 weeks after starting
- Re-evaluate periodically, offer naloxone
- Consider benefits/risks of toxicology testing
- Use caution with opioid +benzo rx
- Offer/arrange tx with MOUD if OUD identified

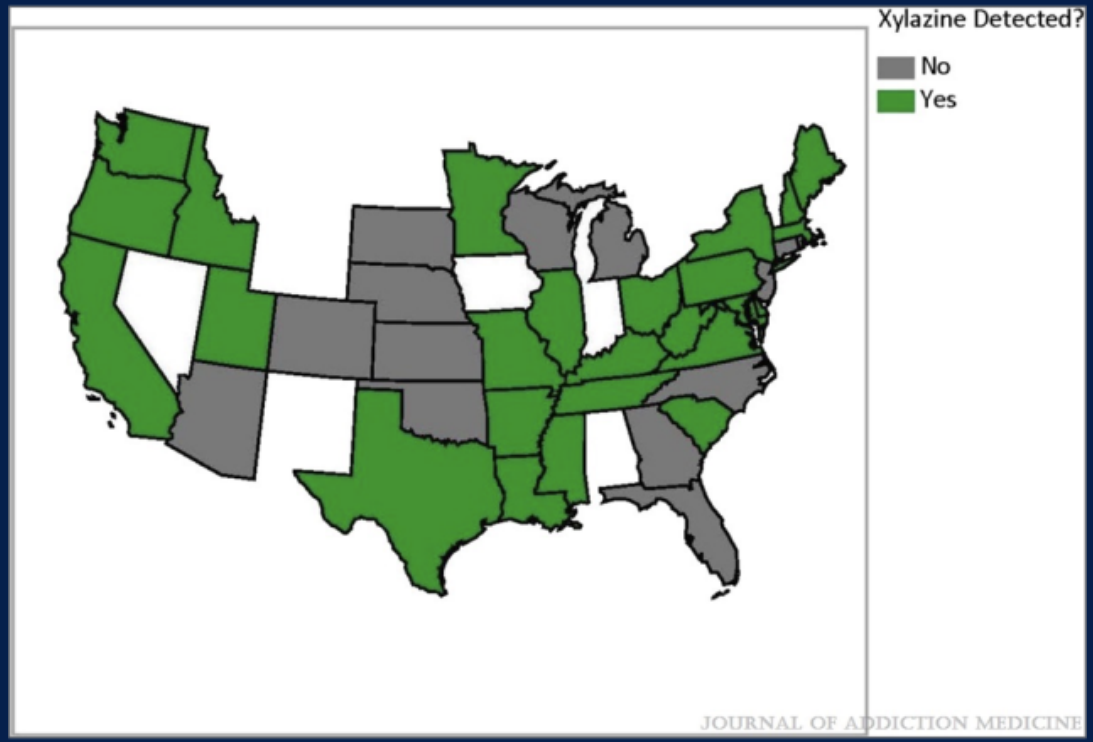
In Closing: 2022-3 Specialty Addiction Journal Highlights

- Journal of Addiction Medicine (2023)
  - Xylazine found nation-wide
- Addiction
  - E-cigs vs. NRT as harm reduction
- Addiction
  - Drug checking: systematic reiew
- JSAT
  - Housing supports for mothers
- Drug and Alcohol Dependence
  - MOUD after rehab
- SAJ
  - alcohol home delivery during COVID-19

Holt, Journal of Addiction Medicine, 2023

Widespread Distribution of Xylazine Detected Throughout the United States in Healthcare Patient Samples

- Samples for which providers ordered testing for xylazine, April 2021 - March 2022
  - liquid chromatography–tandem mass spectrometry.
  - Retrospective analysis of xylazine-positive samples collected from
- Xylazine was identified in 413 of 59,498 samples from adults aged 20–73 years and originated from 25 of the 39 states where xylazine testing was ordered.



Smith, Addiction 2022

E-cigarettes versus nicotine replacement treatment as harm reduction interventions for smokers who find quitting difficult: randomized controlled trial

- Randomized controlled trial of EC (n=68) versus NRT (n=67) with 6 month follow-up
- 135 smokers unable to stop smoking with conventional treatments received either NRT of their choice or EC starter pack
- Smoking reduction or cessation in 26.5% in EC arm and 6.0% in NRT arm
- Sustained abstinence after 6 months 19.1% in EC arm and 3.0% in NRT arm
- EC more effective than NRT

Table 2 Smoking reduction of at least 50% and smoking cessation in the two study arms

	EC arm (n = 68) *n (%)*	*NRT arm (n = 67)* *n (%)*	*RR (95% CI)*	*P-value*
CO-validated reduction in smoking				
At 4 weeks, CO-validated	29 (42.7)	16 (23.9)	1.8 (1.1–3.0)	P = 0.03
At 6 months, CO-validated	18 (26.5)	4 (6.0)	4.4 (1.6–12.4)	P = 0.005
Self-reported[a] reduction in smoking				
At 4 weeks, self-reported	48 (70.6)	35 (52.2)	1.4 (1.0–1.8)	P = 0.03
At 6 months, self-reported	45 (66.2)	25 (37.3)	1.8 (1.3–2.5)	P = 0.002
CO-validated smoking cessation				
At 4 weeks, CO-validated	20 (29.4)	10 (14.9)	2.0 (1.0–3.9)	P = 0.05
At 6 months, CO-validated	13 (19.1)	2 (3.0)	6.4 (1.5–27.3)	P = 0.01
Self-reported[a] smoking cessation				
At 4 weeks, self-reported	32 (47.1)	19 (28.4)	1.7 (1.1–2.6)	P = 0.03
At 6 months, self-reported	20 (29.4)	6 (9.0)	3.3 (1.4–7.7)	P = 0.01

A sensitivity analysis was conducted adjusting for previous use of EC at baseline. This did not change the results. [a]Self-reported groups include all participants reporting the given outcome, whether validated or not. EC = electronic cigarette; NRT = nicotine replacement therapy; RR = relative rate; CI = confidence interval; CO = carbon monoxide.

Table 3 Smoking reduction and cigarette consumption in non-abstainers

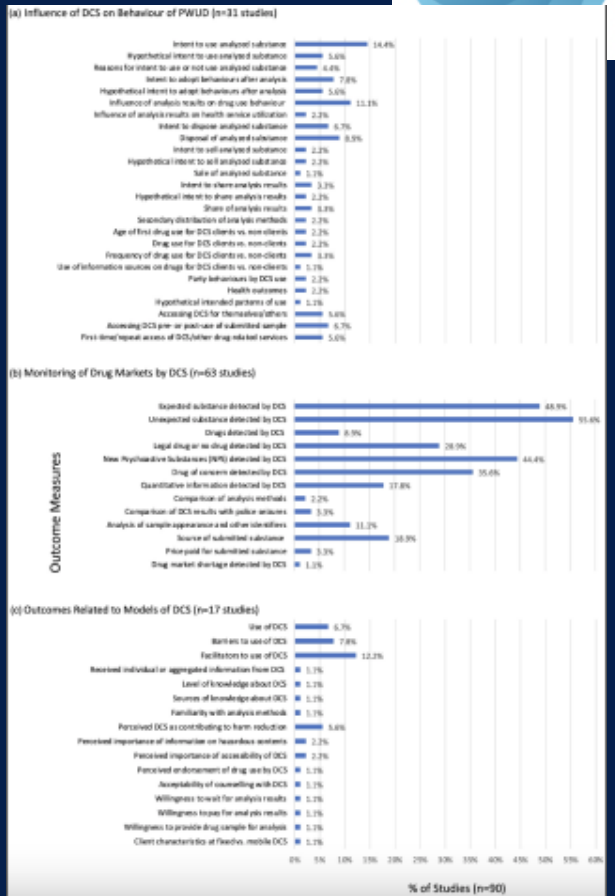
Time-point	*EC arm*	*NRT arm*	*Difference*
Smoking reduction at 6 months[a] (*n*, %)			
Self-reported[c] (*n* = 55 EC, *n* = 65 NRT)	32 (58.2)	22 (33.9)	RR = 1.7 (1.1–2.6) P = 0.009
CO-validated (*n* = 68 EC, *n* = 67 NRT)	5 (9.1)	2 (3.1)	RR = 3.0 (0.6–14.6) P = 0.18
Cigarette consumption[a] (cigarettes per day)			
Baseline, *n* = 68 EC, *n* = 67 NRT, median (IQR)	15 (10–20)	15 (10–20)	Z = −0.2[e], P = 0.83
4 weeks, *n* = 35 EC, *n* = 44 NRT, median (IQR)	2 (0–10)	5.5 (2–15)	Z = −1.7[e], P = 0.08
6 months, *n* = 44 EC, *n* = 41 NRT, median (IQR)	0 (0–10)	7 (0–15)	Z = −2.4[e], P = 0.02
6 months: change from baseline *n* = 44 EC, *n* = 41 NR, mean (SD)	−12.8 (8.9)	−8.1 (8.1)	*t* = −2.5[b], P = 0.01

#ASAMAnnual2023

Maghsoudi, Addiction 2022

Drug checking services for people who use drugs: a systematic review

- Systematic review of 2463 titles and abstracts, 156 full texts, 90 studies
- Sought to synthesize literature on influence of drug checking services on behavior or people who use drugs, monitoring of drug markets by drug checking services, and outcomes related to drug checking services
- DCS appear to influence behaviour of people who use drugs, particularly when results from drug checking services are unexpected or drugs of concern.



Incidence of Precipitated Withdrawal During a Multisite Emergency Department–Initiated Buprenorphine Clinical Trial in the Era of Fentanyl

D'Onofrio et al JAMA Netw Open 2023

- Observational cohort data of individuals across 28 geographically diverse EDs with moderate-severe OUD who had opioid positive, methadone negative urine test, COWS 4+

Table 2. Detailed Data From PW Cases[a]

Enrollment date	Location	Age, decade	Race	Gender	Severity of use, d/wk	Last use, h	Route	Urine drug testing	BUP type	COWS scores, baseline/ peak	Time elapsed, min[b]	Disposition	ED LOS
December 2020	Northeast	50s	Black	Woman	7	16	Injection	Opiates and fentanyl	SL	13/19	20	Discharged	6 h 40 min
January 2021	West	20s	White	Woman	7	8	Smoking	Fentanyl	XR	15/23	25	Discharged	2 h 50 min
February 2021	Northeast	40s	White	Man	7	8	Nasal	Fentanyl	XR	12/20	114	Observation[c]	7 h 50 min
												Discharged	
April 2021	Midwest	60s	Black	Woman	7	24	Nasal	Cocaine, opiates, marijuana, fentanyl	XR	8/16	60	Against medical advice	1 h 41 min
May 2021	Northeast	30s	Multiracial	Man	6	>24	Injection	Cocaine, marijuana, fentanyl	SL	17/23	54	Discharged	7 h 24 min
August 2021	South	30s	Multiracial	Man	6	24	Smoking	Cocaine, fentanyl	SL	13/32	55	Observation[c]	22 h 39 min
												Discharged	
September 2021	Midwest	40s	Black	Man	7	12	Nasal	Cocaine, marijuana, fentanyl	XR	13/20	30	Discharged	8 h 50 min
November 2021	Midwest	20s	American Indian/Alaskan Native	Man	7	16	Smoking	Cocaine, marijuana, fentanyl	SL	10/22	82	Discharged	8 h 43 min
December 2021	South	20s	Black	Man	7	15	Injection	Cocaine, fentanyl	SL	29/>30[d]	116	Observation[c]	20 h 0 min
												Discharged	

Abbreviations: BUP, buprenorphine; COWS, Clinical Opiate Withdrawal Scale; ED, emergency department; LOS, length of stay; PW, precipitated withdrawal; SL, sublingual; XR, extended-release injectable.

[a] Rates of PW by region were as follows: Northeast (10 sites), 3 of 313 participants (0.95%); West (6 sites), 1 of 423 participants (0.24%); Midwest (6 sites), 3 of 207 participants (1.44%); South (6 sites), 2 of 257 participants (0.78%); and total, 9 of 1200 participants (0.76%).

[b] Time elapsed from BUP administration to maximum COWS score.

[c] Patient was placed in ED observation status and then discharged.

[d] COWS score improved to 15 then increased (exact score unobtainable due to patient's condition).

- Randomized to SL or XR bupe, observed for 2 hours
- PW defined as marked escalation in COWS requiring additional buprenorphine or ancillary within 2 hours of buprenorphine administration
- Per initiation protocol COWS of 8+--> buprenorphine 8mg in ED, COWS 4-7→ home induction
- Among 1200 cases, 9 PW (0.76%); 1% among those w/ IMF
- Time since last use ranged 8->24H

Slesnick, JSAT, 2023

Housing and supportive services for substance use and self-efficacy among young mothers experiencing homelessness: A randomized controlled trial

- Randomized controlled trial measuring frequency of drug and alcohol use in homeless mothers with young children
  - 240 women ages 18 to 24 experiencing homelessness with a SUD who also had a biological child under the age of 6 years

Means and standard deviations of substance use and self-efficacy.

	Total sample		Housing + SS		Housing only		SAU	
Variables	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	N	Mean (SD)
Substance use[a]								
Baseline	240	84.78 (24.86)	80	82.61 (27.64)	80	81.73 (25.87)	80	90.00 (19.85)
3-month	224	72.13 (35.67)	77	69.40 (38.03)	77	72.57 (35.48)	70	74.65 (33.41)
6-month	219	68.18 (39.18)	76	61.22 (39.30)	74	75.22 (36.90)	69	68.28 (40.60)
9-month	209	62.94 (41.02)	70	59.31 (42.71)	70	66.27 (39.06)	69	63.22 (41.52)
12-month	218	63.48 (40.87)	73	58.27 (41.67)	73	67.15 (39.05)	72	65.04 (41.89)
Self-efficacy[b]								
Baseline	238	19.92 (3.13)	79	19.63 (3.31)	80	20.29 (2.82)	79	19.82 (3.23)
3-month	219	22.06 (3.18)	75	22.31 (2.77)	75	22.23 (3.23)	69	21.59 (3.53)
6-month	214	22.26 (3.35)	74	22.73 (3.24)	72	22.04 (3.53)	68	21.99 (3.27)
9-month	199	22.51 (3.40)	68	22.68 (3.65)	66	22.56 (3.35)	65	22.28 (3.23)
12-month	206	22.51 (3.41)	69	22.70 (3.70)	68	22.44 (3.28)	69	22.39 (3.29)

[a] Substance use represents percentage of total days of drug use (except for the use of tobacco) in the prior 90 days. The mean scores across five time points represent the average percent days of substance use.
[b] The mean scores across five time points represents the average level of self-efficacy.

- Participants randomly assigned to: housing + support services (n = 80), housing-only (n = 80), or services as usual (SAU) (n = 80)
- All participants showed improvement with more participants showing improvement in housing + support services
- Unexpectedly, more mothers in SAU showed improvement than in housing only

Cole, *Drug and Alcohol Dependence*, 2022

Outpatient follow-up and use of medications for opioid use disorder after residential treatment among Medicaid enrollees in 10 states

- Meta-analysis of medicaid claims, measuring follow-up and use of MOUD after residential treatment
  - 90,639 episodes of residential treatment for OUD for 69,017 enrollees from 2018-2019
- 62.5% didn't receive follow-up after 7 days, 46.9% didn't receive after 30 days
  - 47% of residential treatment episodes for medicaid enrollees are not followed by outpatient visit or MOUD

Grossman, *Substance Abuse*, 2022

Alcohol consumption and alcohol home delivery laws during the COVID-19 pandemic

- Many states responded to COVID-19 by relaxing their alcohol laws, including alcohol delivery
- May 2020, convenience sample of U.S. adults, 21+ of age recruited through social media
    - N=832 completed online survey: 84% were female, 85% were White, and 72% were between the ages of 26 and 49
- 21% of those consuming alcohol had at least some alcohol delivered
- Participants who reported having alcohol delivered :
    - more drinks per month: $\beta = 13.3$ $p < .000$
    - more drinking days: $\beta = 5.0$ $p < .000$
    - 2x binge drinking: $OR = 1.96$ 95% CI [1.3, 3.1]

Final Takeaways/Summary: 2022 Addiction Medicine Literature

- COVID-19 negatively impacted attention and publication metrics for all subjects…while making drug, alcohol, and smoking rates and harms worse
- Psychedelics for alcohol and smoking disorders: watch this space, data is compelling but limited, and lots of practical and regulatory issues
- Treatments for OUD – still effective, but not enough of it, and not for long enough

Thank You!

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