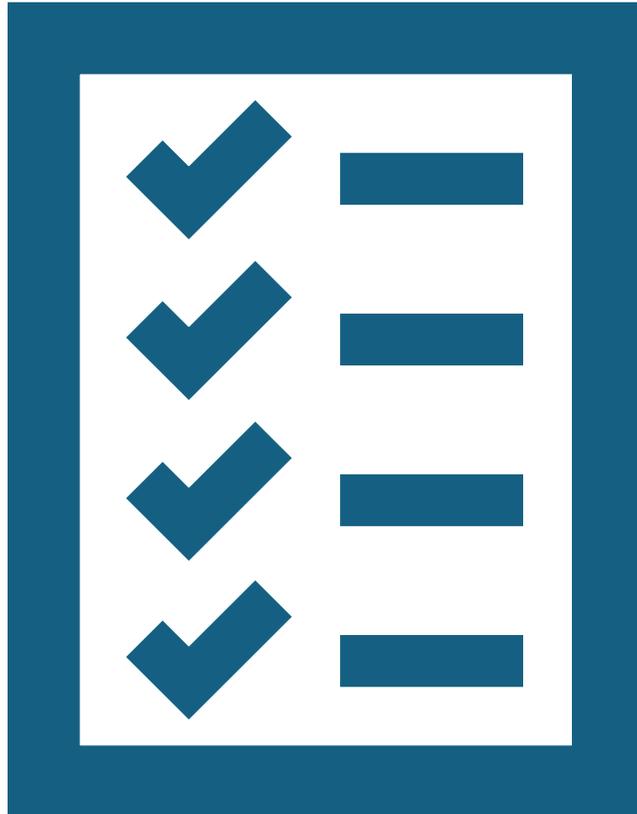




Alcohol and Substance Misuse Workshop



Agenda

- Sneak preview of Alcohol cases
- Alcohol didactics
- Alcohol case discussions
- Sneak preview of Opioid and benzodiazepine abuse cases
- Opioid and benzo didactics
- Opioid and benzo case discussions
- Psychedelic case
- Psychedelic microdosing didactics
- Case discussions

Alcohol case 1: 38 yr old male smoker applying for 1 million whole life

- 38 yo male president of his family business, admits to 1-2 drinks 3 x/week; MVR clear
- 6'5" 249 lbs BP 152/90
- APS review: CPE one year ago. PMH Esophagitis/GERD. Fhx: parents and siblings healthy
Social hx- exercises regularly, wine 2-3 times/week. Owns motorboat use on weekends
APS labs: normal CBC with MCV 90, platelets 188K, normal LFTs, chol 243, HDL 69
Insurance labs: AST 27 (0-41) ALT 35 (0-45), GGT 75 (2-65) , Alb 4.9, HDL 85

Risk assessment based on 1: No CDT

2: CDT **negative**

3: CDT **positive**

Alcohol case 2: 40 yr old male nonsmoker building contractor applying for 1 million whole life

- 6'0" 185 lbs, BP 110/70
- 12/22 PAF hospitalization; F/u visits with brief PAF episodes per patient
- 6 beer daily before PAF onset
- Current etoh reports 3 beers daily,
- Alcohol and substance abuse hx: 15 yrs ago cocaine. Current recreational use MJ legal in state

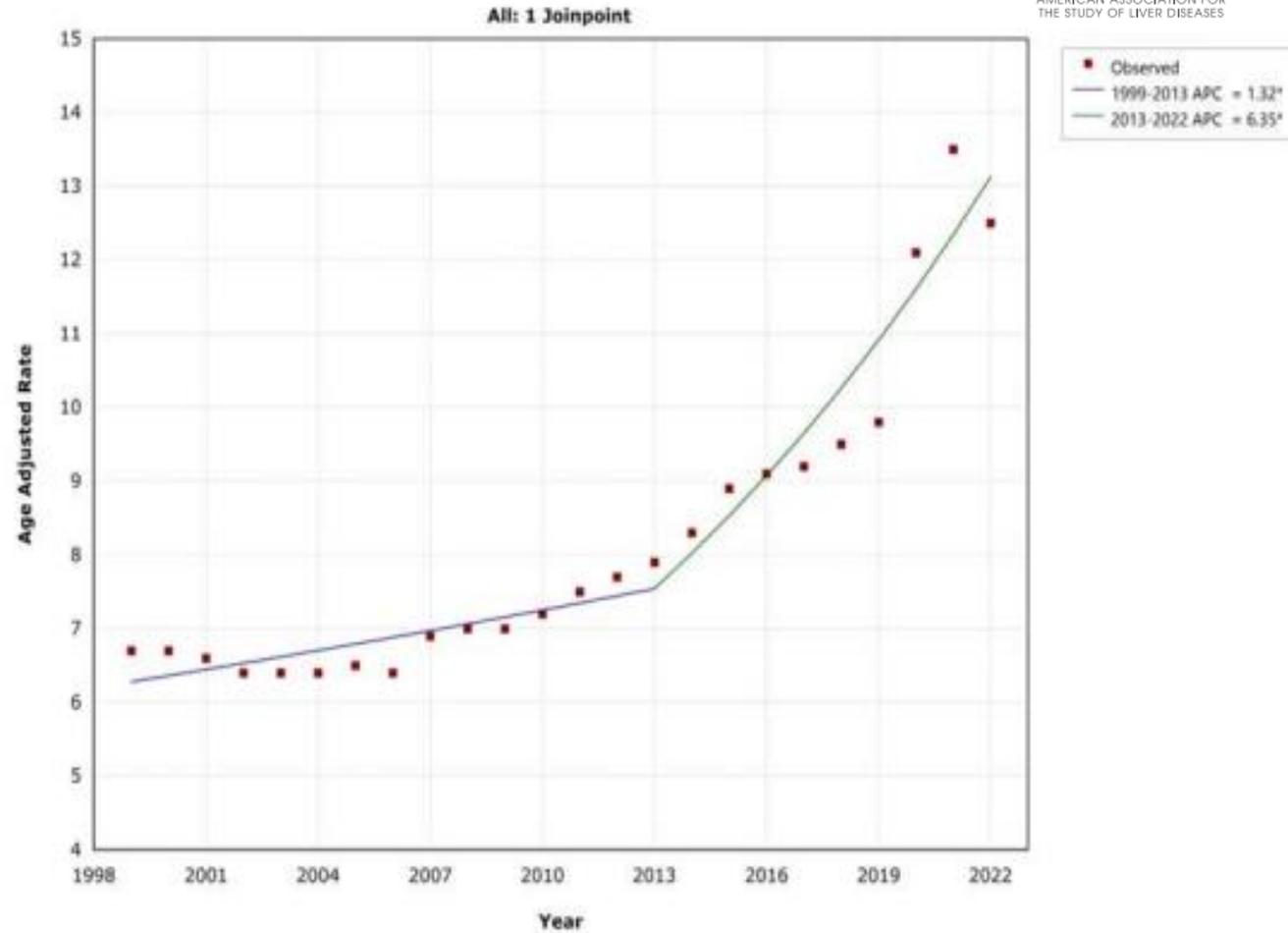
Insurance labs: AST 24, ALT 23, GGT 46, alb 4.4, HDL 35

Alcohol case 3: 42 yr old female businesswoman applying for 5 million whole life

- nonsmoker 5”5” 155 pounds, BP 125/74
 - RX: no meds
 - APS review: CPE last year : physical noted acne rosacea, otherwise normal.
 - Routine labs: CBC with MCV 110, platelets 144,000, Chol 200 HDL 75, trigs 200
 - Social hx: ETOH 1 drink/day occasionally more on business trips and girls' night out
- Family history: Mother and father alive, healthy; sister in good health
- Insurance labs: A1C 5.7, AST 65(1-40), ALT 44 (0-45), GGT 25 (2-65) Albumin 3.7 (3.5-6.0), BUN 18, Cr 1.2
- Urine: no proteinuria, cotinine negative
- Hep BS Ag nonreactive, Hep CAB nonreactive, BAL neg

Alcohol epidemiology: Trends in alcohol associated mortality from 1999 to 2022 in USA

Hepatology Communications.
2023;7:e00180



AAMRs – Age adjusted mortality rates per 100,000 population

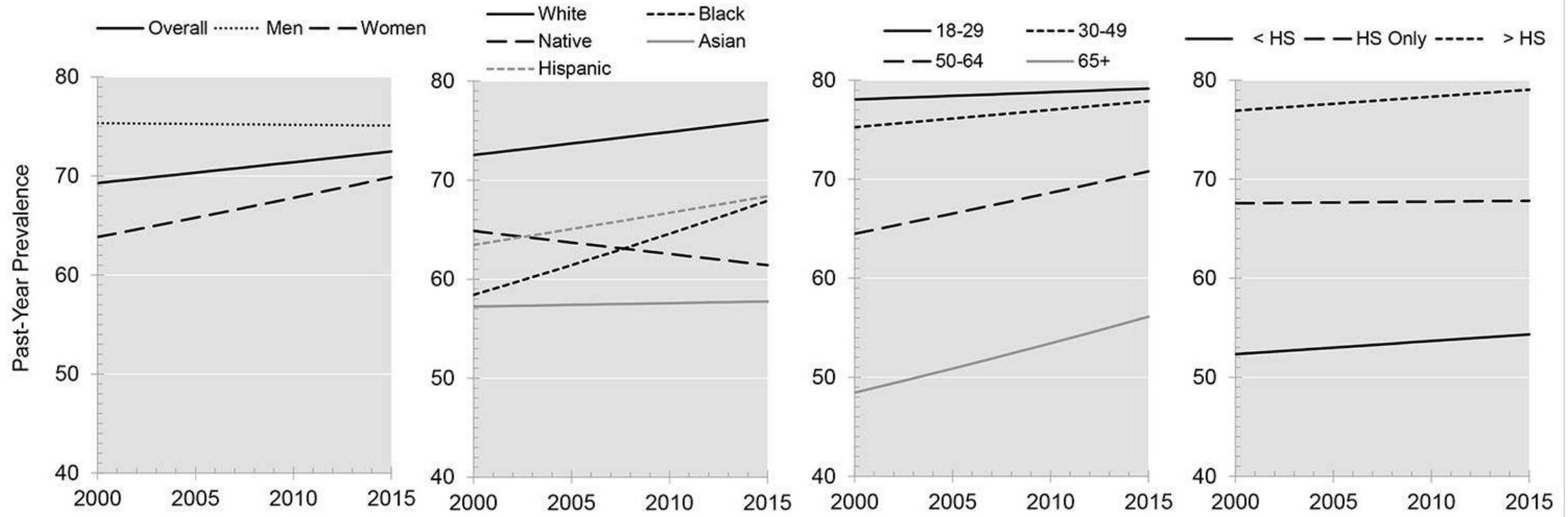
AAPC – average annual percent change

Between 1999 and 2022, 436,651 deaths related to ALD.

AAMR increased from 6.6/100,000 in 1999 to 13.5/100,000 in 2022

Greatest rise was in women

Trends in Adult Alcohol Use and Binge Drinking in the Early 21st Century United States: A Meta-Analysis of Six National Survey Series



Conclusion: Number of women 18 and older who drink each year rose by 0.6% each year as well as number of women who binge drink. Gaps in alcohol related harm between men and women is narrowing – A Cause for **ALARM**

Alcoholism Etiology



The exact cause of alcoholism is unknown.



Alcoholism is a primary, chronic, progressive, and often fatal disease. Life expectancy is shortened.



There is a strong genetic component to alcoholism:

There is a higher concordance of alcohol dependence in monozygotic twins compared to dizygotic twins.

Adopted children with a biologic parent who is alcoholic have a 2-3x increased risk of alcoholism compared to adopted children whose biologic parents are not alcoholic.



Youth who start drinking before age 15 are 6 times more likely to develop alcohol dependence/abuse than those who begin drinking at or after age 21.



Center for Behavioral Health Statistics and Quality. 2015 National Survey on Drug Use and Health: Detailed Tables. Substance Abuse and Mental Health Services Administration, Rockville, MD; 2016.

Alcohol Use Definition Problems

In contrast to
assessing risk for DM
using A1C or CAD
using CTA

- Cannot differentiate per blood test, the drinker at highest risk for alcohol related fatalities
- ETOH: none>occasional ETOH use>occasional ETOH use with light intoxication>binge drinking (episodic >5 drinks to the point of intoxication)>daily drinking>heavy daily drinking>ETOH abuse>alcohol dependence/alcoholism
- Alcohol misuse definition is drinking alcohol in ways that cause harm to oneself or others, or drinking in risky situation
 - Alcohol misuse can manifest as binge drinking and heavy drinking or drinking before driving. This increases risk in developing AUD
- Alcohol use disorder (AUD) is a **medical condition** characterized by inability to control or stop drinking despite negative consequences; it is a more severe chronic form of problematic alcohol use that involves addiction
- DSM-5 changed the definition by dropping the criterion for legal problems and **added the craving criterion**. There are **11** criteria regardless of age.

Two of the following symptoms/behaviors must be present for at least 1 year, and be co-occurring with significant distress or impairment:

1. More alcohol is consumed than intended or is consumed over a longer period of time than intended.
2. Efforts to cut back or control drinking have not succeeded.
3. Excessive time is spent obtaining, using, or recovering from alcohol.
4. Alcohol cravings and urges persist.
5. Use of alcohol has impaired follow-through on education, employment, or home obligations.
6. Interpersonal problems have been caused or intensified by use of alcohol.
7. Alcohol use has led to a reduction in or cessation of recreational, social, and employment activities.
8. Use of alcohol has occurred in situations where it is dangerous.
9. Alcohol use has continued despite knowledge of the problems it is causing.
10. Tolerance to alcohol is evident-ie, drinking the same amount has little effect, or heavier use occurs to maximize alcohol's effects.
11. Withdrawal is evident-ie, physiologic signs (tremors, nausea) occur or closely related drugs (eg, benzodiazepines) are taken to avoid withdrawal.

Adapted from the DSM-5; American Psychiatric Association (2013).

Severity of Alcohol Misuse:

- Mild: 2-3 symptoms
- Moderate: 4-5 symptoms
- Severe: 6 or more symptoms

Alcohol Mortality Concerns

Motor vehicle accidents, accidents-falls, hypertension, cardiomyopathy, arrhythmias, GI bleeding, liver disease, cancer, suicide-not a complete list

95% of all suicides have a mental disorder: 80% with depression, 10% with schizophrenia, 5% with dementia. 75% of suicide victims have comorbidity. **At least 25% also have alcohol abuse.**

With alcoholism, recent life disruption, loss of a close relationship, MDD (75%), health problems (50%), unemployment (50%), and living alone (33%) were factors at the time of suicide.

Carbohydrate Deficient Transferrin (CDT)

Chronic heavy alcohol consumption reduces the number of carbohydrate moieties attached to transferrin, leading to increased CDT levels. An average daily consumption of **more than 60 grams** of alcohol (~4 drinks) during the previous 2 weeks increases the percentage of transferrin that has a deficient carbohydrate content.

- **CDT** is thus used as a biomarker to detect heavy daily alcohol consumption.
- **CDT** typically normalizes within several weeks of abstinence of alcohol use.
- **CDT** is currently the only FDA-approved test for the detection of heavy alcohol use.
- **PEth** indicates alcohol consumed in last 2-4 weeks. And cut offs can provide a clue as to how much. A CDT can be negative with the PEth result suggesting heavy drinking
- Different laboratories and commercial kits report wide ranges in CDT sensitivities and specificities. Sensitivity of CDT remains a controversial issue.

PEth (phosphatidylethanol)

Carbohydrate Deficient Transferrin (CDT)

- According to the Mayo clinic, specimen stability for CDT measurement is 7 days at room temp and 28 days, if refrigerated.
- Congenital disorders of glycosylation (CDGs), hereditary fructose intolerance, galactosemia, and liver disease may result in increased levels of CDT.
- In addition, pre-analytic variables such as bacterial contamination may cause falsely elevated CDT values.
- Several factors may cause variability in CDT analysis, including: pregnancy, body mass index, drug interactions, chronic medical illness.

Carbohydrate Deficient Transferrin (CDT)

CDT AND SERUM ALCOHOL: WHAT IS THE RISK? VF Dolan, Stouts and Fulks : ON THE RISK vol.27 n.1 (2011)

- Accepting a real-world **specificity of 98.5% (true negatives)** (published values of 98-100%), **sensitivity of 75% (true positives)**, and a heavy alcohol use prevalence in applicants of 7.5%, the positive predictive value (PPV) is only 0.3. The low PPV argues against using CDT as a general population screening test.
- Based on CRL research, GGT elevation triple the pre-test likelihood of heavy alcohol use, HDL >50 doubles it, and positive tobacco may cause a 4-fold increase.
- If any two of these conditions are present and CDT is positive, we estimate the pre-test likelihood increases sufficiently so that the final PPV is 0.7 or better.

Sensitivity and Specificity of Alcohol Biomarkers

<u>Biomarker</u>	<u>Sensitivity (%)</u>	<u>Specificity (%)</u>
AST	15-69	47-68
ALT	18-58	50-57
GGT	34-85	11-95
MCV	34-89	26-95
CDT	39-94	82-100
CDT + GGT	90 †	98
Alcohol	0-100	0-100

*Values vary considerably according to gender, age, drinking pattern, prevalence of alcohol abuse/dependence, and prevalence of comorbidity, among other factors

Keep in mind, any and all combination of abnormalities of the above tests can occur with alcohol misuse and all tests can also be normal.

Dr. Bob Stout's research article from OTR on positive BAL and CDT

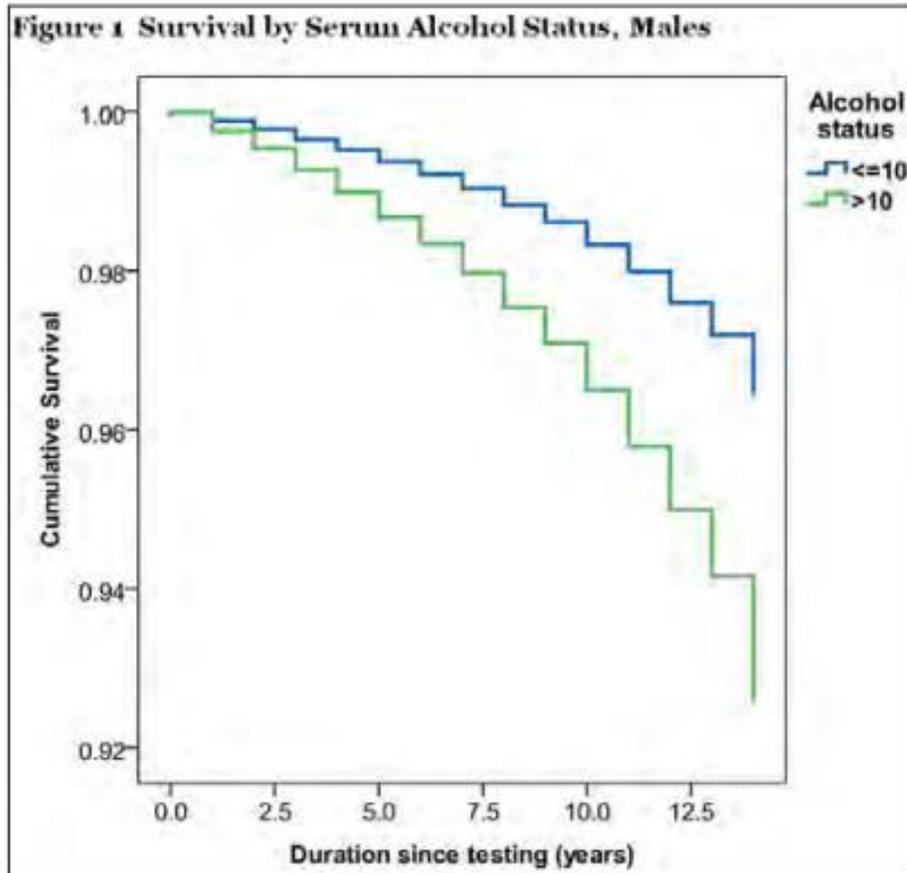
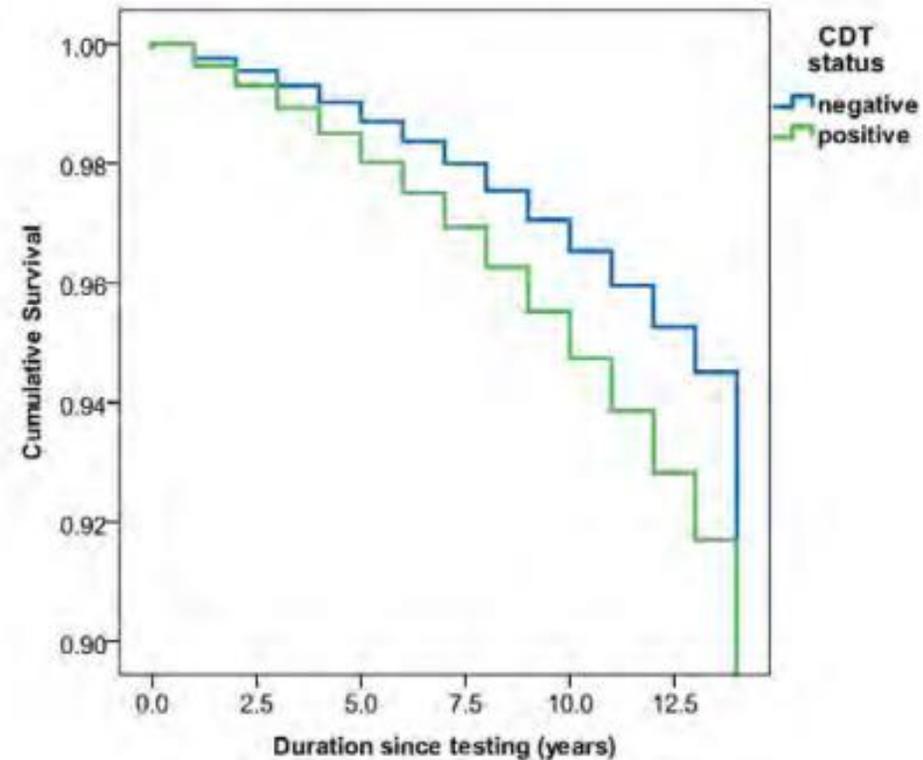


Figure 2 Survival by CDT Status, Males



What Do the Study Results Contribute to Risk Assessment? Both positive CDT and serum alcohol have a similar impact on relative mortality below age 60, although the impact of CDT, while still increased, is reduced at older ages. This may be due partly to the favorable impact of alcohol on HDL and cardiovascular risk, and possibly due to less excess alcohol-related harm among older individuals. The degree of mortality found for CDT positivity is consistent with that noted for heavy regular alcohol use by others.¹⁻⁷ The elevated risk appears to be sustained over the long term, and can be quantified using simple mortality ratios that we found to not vary dramatically by sex or tobacco status.

Dr. Steven Rigatti on Bad Habits and Pandemic

- Comparison of positive BAL prior to pandemic revealed an increase from Jan 2019 to March 2020 from 4.2 per thousand to 4.7 per thousand. Highest seen in lower face amounts (<100k) however more sharply increased in highest face amounts (2.5 mil)
- Also found uptick among smokers, noting 5 times the comparable rates in nonsmokers

Key takeaway: rates of BAL up especially among smokers and those applying for larger life insurance, even though tobacco usage rates across board are down.

Alcohol case 1: 38 yr old male smoker applying for 1 million whole life

- 38 yo male president of his family business, admits to 1-2 drinks 3 x/week; MVR clear
- 6'5" 249 lbs BP 152/90
- APS review: CPE one year ago. PMH Esophagitis/GERD. Fhx: parents and siblings healthy
Social hx- exercises regularly, wine 2-3 times/week. Owns motorboat, uses on weekends
APS labs: normal CBC with MCV 90, platelets 188K, normal LFTs, chol 243, HDL 69
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Risk assessment based on 1: No CDT

2: CDT **negative**

3: CDT **positive**



how would you
assess risk for
these choices?

Alcohol case 2: 40 yr old male NS building contractor applying for 1 million whole life

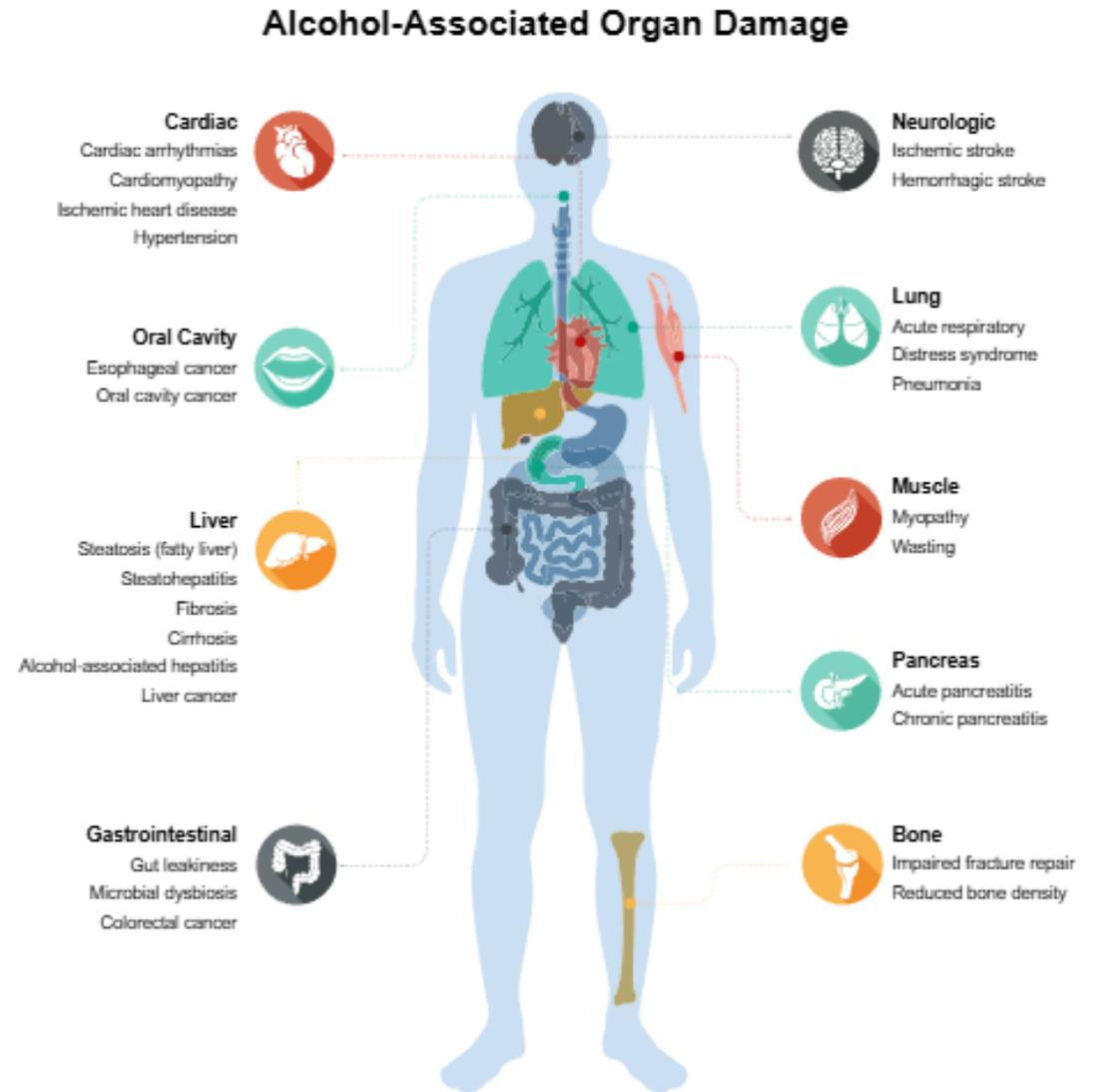
- 6'0" 185 lbs, BP 110/70
- 12/22 PAF hospitalization; F/u visits with brief PAF episodes per patient
- 6 beer daily before PAF onset
- Current etoh reports 3 beers daily,
- Alcohol and substance abuse hx: 15 yrs ago cocaine. Current recreational use MJ legal in state

Insurance labs: AST 24, ALT 23, GGT 46, alb 4.4, HDL 35

Before commenting, let me provide some more didactics.

Effects of Alcohol on the Body

- Neurologic: Wernickes, ataxia, memory, PNS (peripheral nervous system from folate and B12 deficiency) myopathy, psychiatric comorbidities
- Gastrointestinal: esophagus, stomach, pancreas, liver
- Cardiac: atrial fib, dilated cardiomyopathy, HTN
- Hematologic: macrocytic anemia, sideroblastic anemia, thrombocytopenia, neutropenia
- Endocrine: lipids, uric acid
- Cancer: oropharynx (worsened with smoking), esophagus, pancreas, liver, colon, breast, cervix, prostate
- Fetal Alcohol Syndrome: ~31 to ~99 per 1000 children



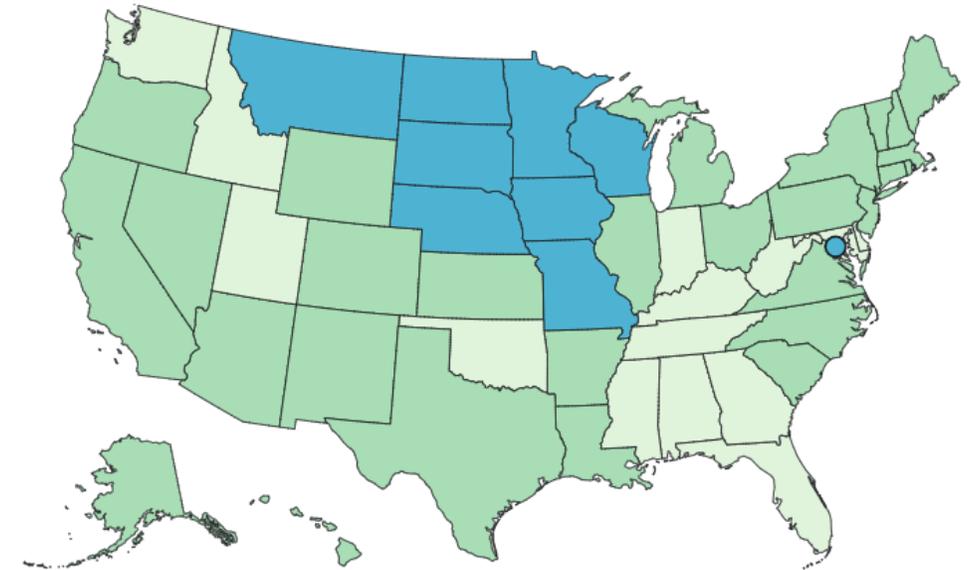
<https://www.niaaa.nih.gov/alcohols-effects-health/alcohols-effects-body>

CDC Binge Drinking Facts

- Binge drinking is the most common, costly, and deadly pattern of excessive alcohol use in the US.
- National Institute on Alcohol Abuse and Alcoholism binge drinking definition: drinking that results in blood alcohol concentration >0.08 grams percent. It occurs when **men consume ≥ 5 drinks or women consume ≥ 4 drinks in 2 hrs.**
- 1 in 6 US adults binge drink ~4 times a month, consuming ~8 drinks per binge. Most binge drinkers are not alcohol dependent.
- Binge drinking is most common among younger adults aged 18–34 years, but is reported across the lifespan.
- The prevalence of binge drinking among men is twice the prevalence among women.

Kanny D, Liu Y, Brewer RD, Lu H. Binge drinking — United States, 2011. MMWR Suppl. 2013;62(suppl 3):77–8

Percentage[†] of adults who binge drink* by state, 2022



Prevalence (percentage of adults who binge drink), during the past 30 days

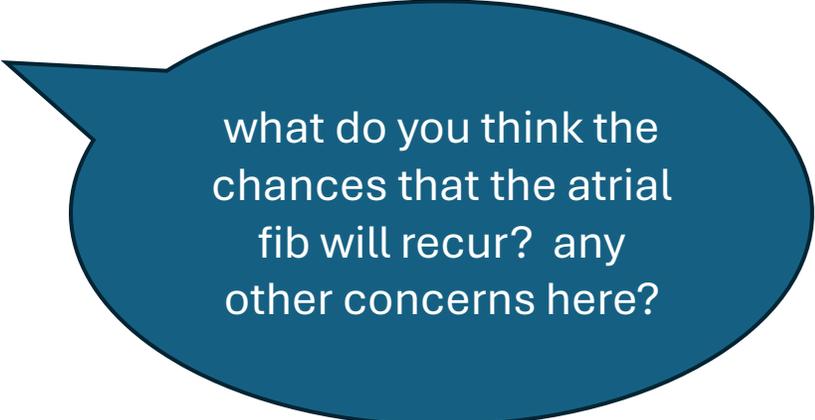


Source: Prevalence of binge drinking among U.S. adults 18 and older, by state — Behavioral Risk Factor Surveillance System, 2022

Alcohol case 2: 40 yr old male NS building contractor applying for 1 million whole life

- 6'0" 185 lbs, BP 110/70
- 12/22 PAF hospitalization; F/u visits with brief PAF episodes per patient
- 6 beer daily before PAF onset
- Current etoh reports 3 beers daily,
- Alcohol and substance abuse hx: 15 yrs ago cocaine. Current recreational use MJ legal in state

Insurance labs: AST 24, ALT 23, GGT 46, alb 4.4, HDL 35



what do you think the chances that the atrial fib will recur? any other concerns here?

Alcohol case 3: 42 yr old female businesswoman applying for 5 million whole life

- nonsmoker 5”5” 155 pounds, BP 125/74
 - RX: no meds
 - APS review: CPE last year : physical noted acne rosacea, otherwise normal.
 - Routine labs: CBC with MCV 110, platelets 144,000, Chol 200 HDL 75, trigs 200
 - Social hx: ETOH 1 drink/day occasionally more on business trips and girls' night out
- Family history: Mother and father alive, healthy; sister in good health
- Insurance labs: A1C 5.7, AST 65(1-40), ALT 44 (0-45), GGT 25 (2-65) Albumin 3.7 (3.5-6.0), BUN 18, Cr 1.2
- Urine: no proteinuria, cotinine negative
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Alcohol case 3: 42 yr old female businesswoman applying for 5 million whole life

nonsmoker 5'5" 155 pounds, BP 125/74

- APS review: CPE last year : physical noted **acne rosacea**, otherwise normal.
- Routine labs: CBC with MCV 110, **platelets 144,000**, Chol 200 **HDL 75**
- Social hx: ETOH 1 drink/day occasionally **more on business** trips and **girls' night out**

Insurance labs: A1C 5.7, **AST 65**(1-40), **ALT 44** (0-45), GGT 25 (2-65) **Albumin 3.7** (3.5-6.0), BUN 18, Cr 1.2

Urine: **no proteinuria**, cotinine negative

Hep BS Ag nonreactive, Hep CAB nonreactive, BAL neg

Fib-4 Calculator

Age

Use with caution in patients <35 or >65 years old, as the score has been shown to be less reliable in these patients

42

years

AST

Aspartate aminotransferase

65

U/L

ALT

Alanine aminotransferase

44

U/L

Platelet count

144

$\times 10^3/\mu\text{L}$ ↵

2.86 points

Advanced fibrosis (METAVIR stage F3-F4) likely (McPherson 2017)

Approximate fibrosis stage: Ishak 2-3 (Sterling et al 2006)

Underwriting Considerations for Alcohol Use

Volume

Frequency including binging

Problems

- health: Physical, psychological comorbidities – depression
- Social/relationships
- occupation/hobbies/sports
- legal
- Financial

Gender

Age

Underwriting Considerations for Alcohol

Lower risk

Moderate volume

Chronic drinking

Older age

No health complications

No psyche comorbidities

Non-treatment center

Higher risk

Heavy volume

Binge drinking

Younger age

Major, chronic or recurrent health complications

Psyche co-morbidities

Treatment center

Opioids and Benzos Oh MY!!

Opioid/Benzo Case 1: 52 yr old male contractor applying for 3 million whole life

Hx of lumbar fusion surgery 2008; ESI 2010-11; Treated at Pain Clinic currently

PMH: Depression, Anxiety, OSA on Cpap

SHx: Quit smoking 2011; Hobby Skis on weekends from Dec – March; ETOH 2-3 drinks/day;

MVR: DUI 2011

RX inquiry: Hydrocodone/Acetaminophen 10/325 mg #120 tablets, Soma (Carisoprodol) 350 mg #90, Alprazolam 1mg #60, Viagra, Flonase, OTC Allegra

Paramed: 5'10" 205 lbs BP 145/90

Insurance Labs: normal however AST 50 ALT 20, HDL 82

Opioid Case 2: 55 yo F applying for 2 million whole life

- Medical Hx: migraine headaches, Fibromyalgia and GAD.
- Surgical Hx: Breast implants, maxillofacial cosmetic surgery
- Social Hx: Divorced, 2 yrs ago moved from LA to CT, works as office manager for her brother's internal medicine practice in CT. Smoker ½ ppd x 20 yrs and quit 2016. ETOH 3 glasses wine per week
- Family Hx: unremarkable other than father died age 62 of lung cancer
- RX inquiry: 7/25: Relpax 40 mg, HCTZ 25 mg, Amitiza (Lubiprostone), Darvocet
- APS: 1/25 Office note: Reported increased migraines unrelieved with Relpax. Also was sick when on vacation in Florida over Xmas with flu and still with cough, requesting Tussionex as it was effective in past. Prescribed Tussionex elixir 4 oz and given #12 Percocet 5/325. Referred to neurology.
- 2/25 Office note: Cannot get into neuro for another 2 months. Requesting more Percocet and when refused, asked for Fioricet. Given #20 Fioricet and with recommendation to start Amitriptyline 10 mg at bedtime and a week later to titrate up to 2 tablets until she sees neurologist.
- 4/25 Urgent Care visit: URI symptoms. Cough, no fever. RX: Augmentin, Tussionex elixir 4 oz and Ultracet #30.
- 6/25 Establishing with New PCP with chief complaint of headache and constipation. Wearing dark glasses in exam room complaining of photophobia and nausea. She described daily headaches of mild severity but once a week would get a severe HA often requiring Percocet 10/325. She was also to fly in 2 weeks to LA, requesting Xanax. And lastly, requested RX for constipation as no relief with OTC laxatives.
- When agent asked for Neurology APS, there were none.
- Paramed: BP 145/88, 5'4", 135 lbs
- HOS: + Cotinine, otherwise neg
- Labs: ALT 95, AST 75, T. Bili 1.9, GGT 75, BUN 28, Creatinine 1.5
- Chol 205, HDL 35, CDT Negative, Hep B S Ag nonreactive
- Hep C AB nonreactive

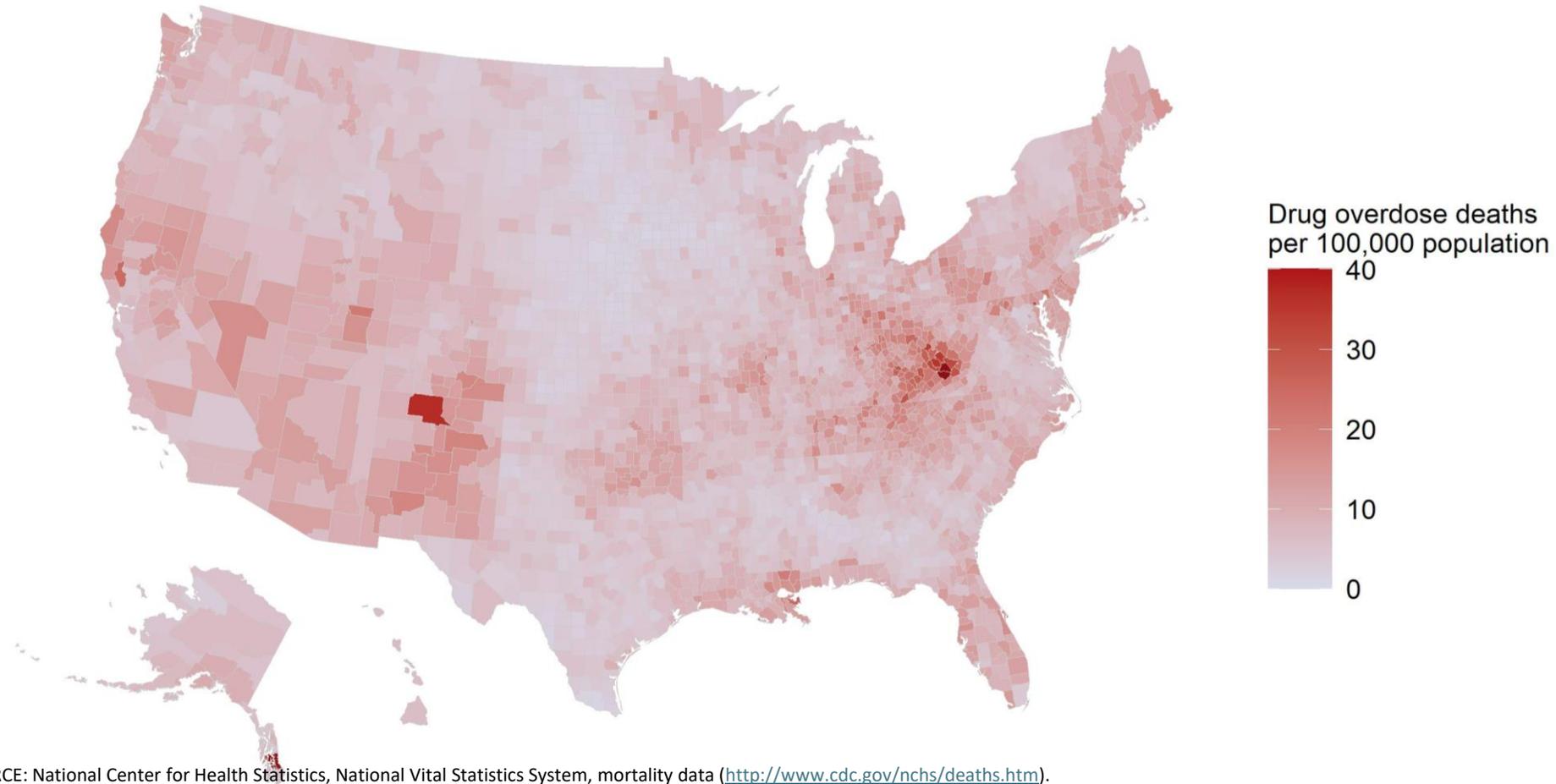


Opioid Crisis is Born: USA



Re

Drug Overdose Mortality USA: 2003

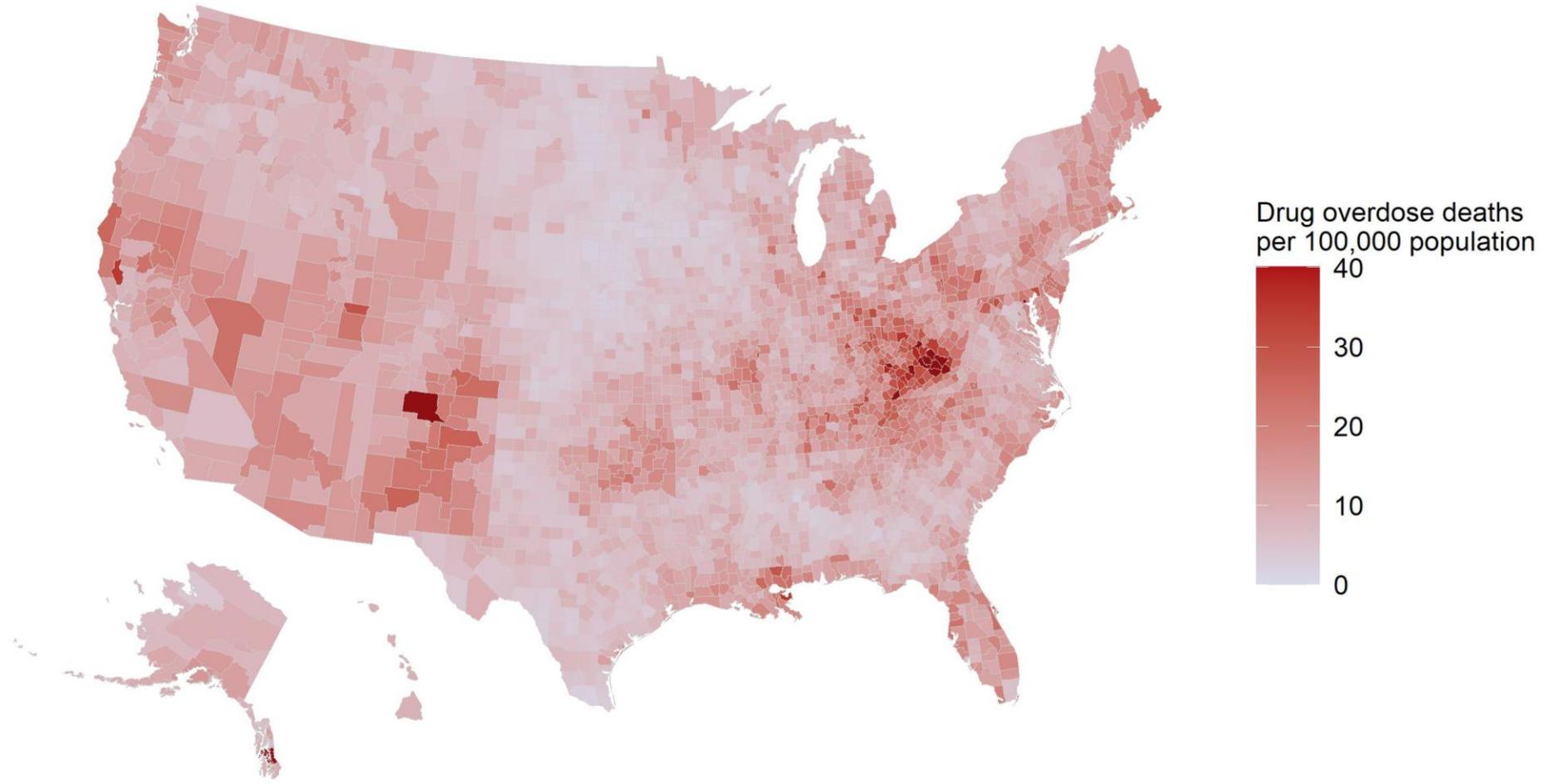


SOURCE: National Center for Health Statistics, National Vital Statistics System, mortality data (<http://www.cdc.gov/nchs/deaths.htm>).

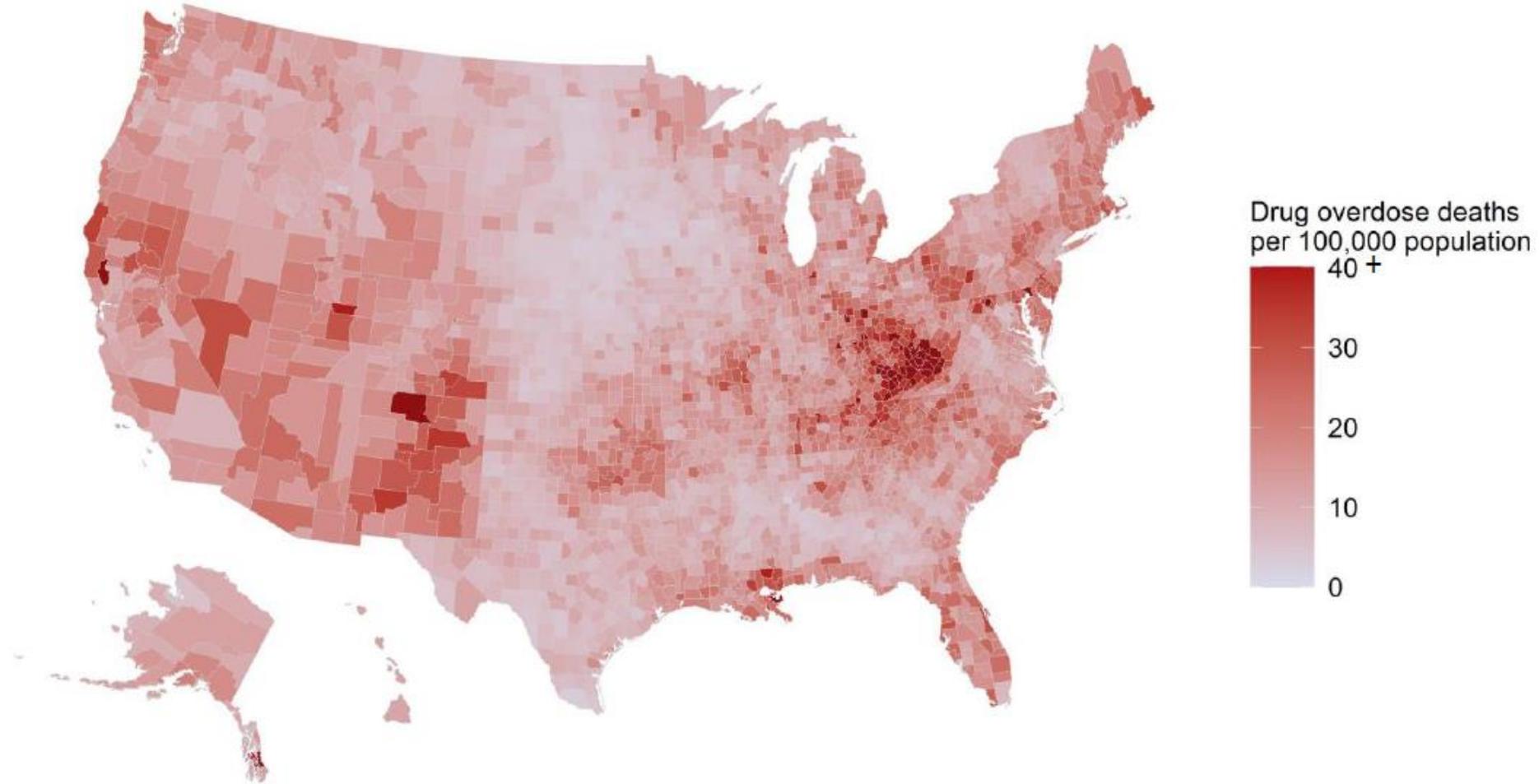
SUGGESTED CITATION: Rossen LM, Bastian B, Warner M, Khan D, Chong Y. Drug overdose mortality: United States, 2003–2021. National Center for Health Statistics. 2022.

(Available from: <https://www.cdc.gov/nchs/data-visualization/drug-poisoning-mortality/>).

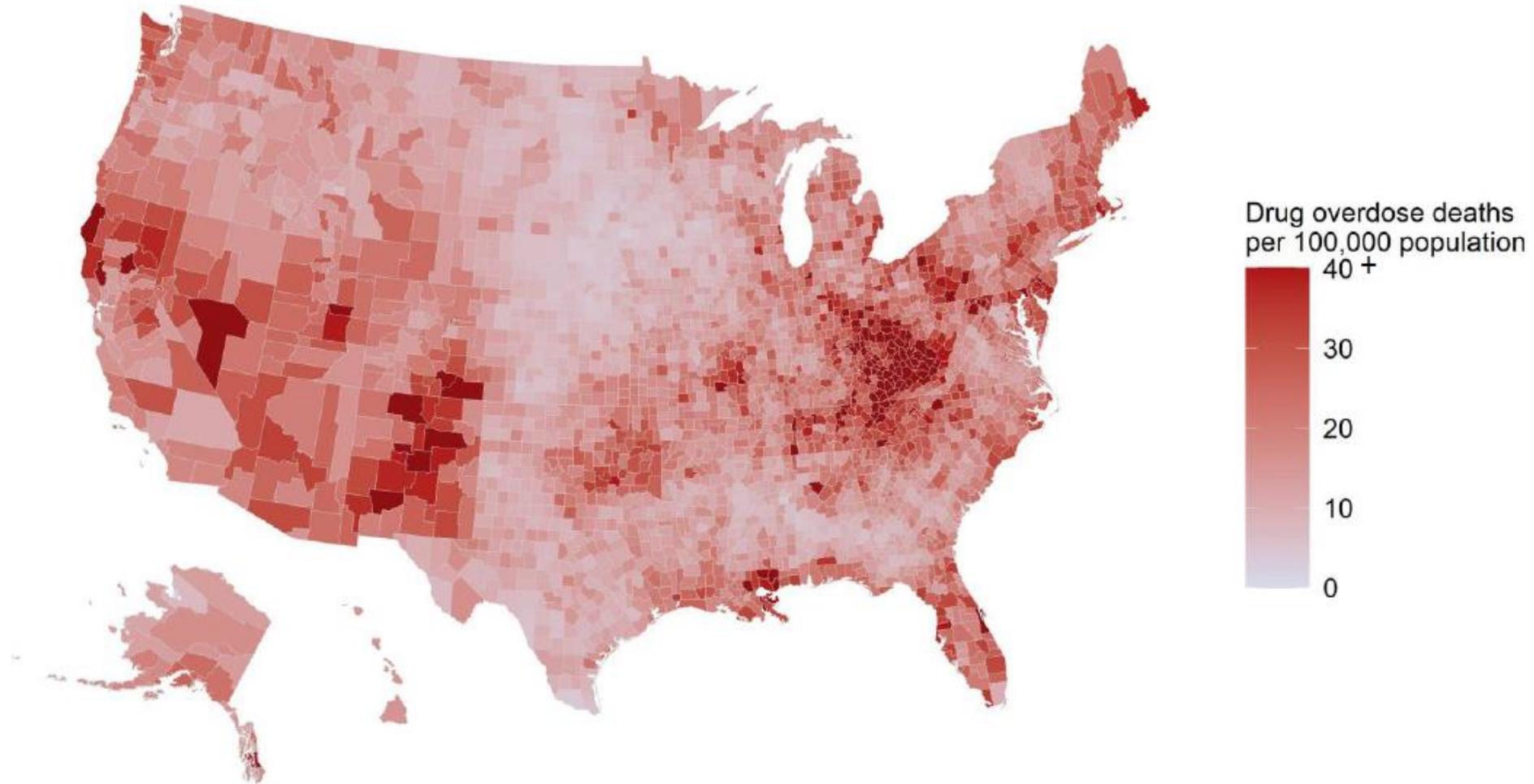
Drug Overdose Mortality USA: 2010



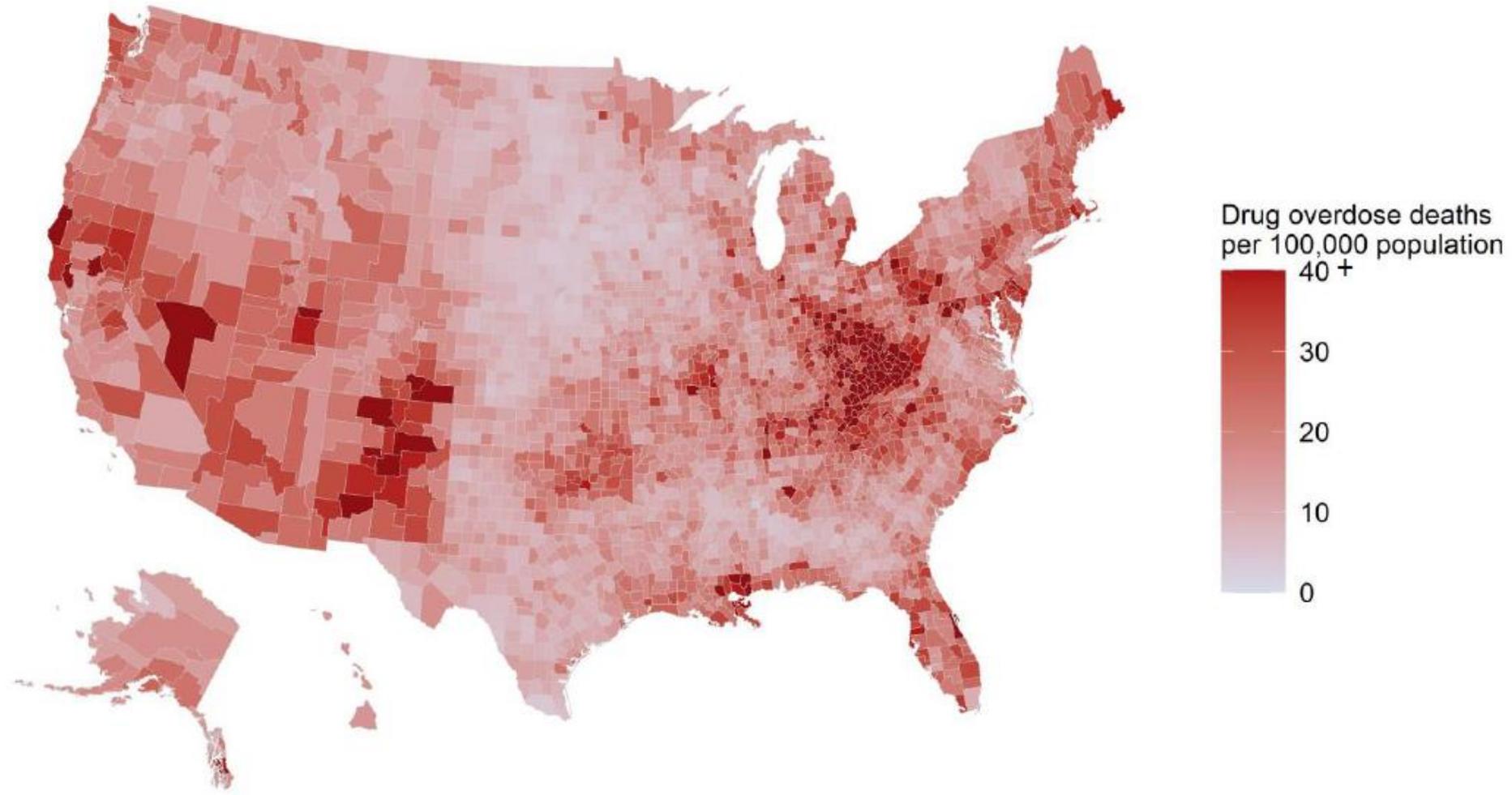
Drug Overdose Mortality USA : 2015



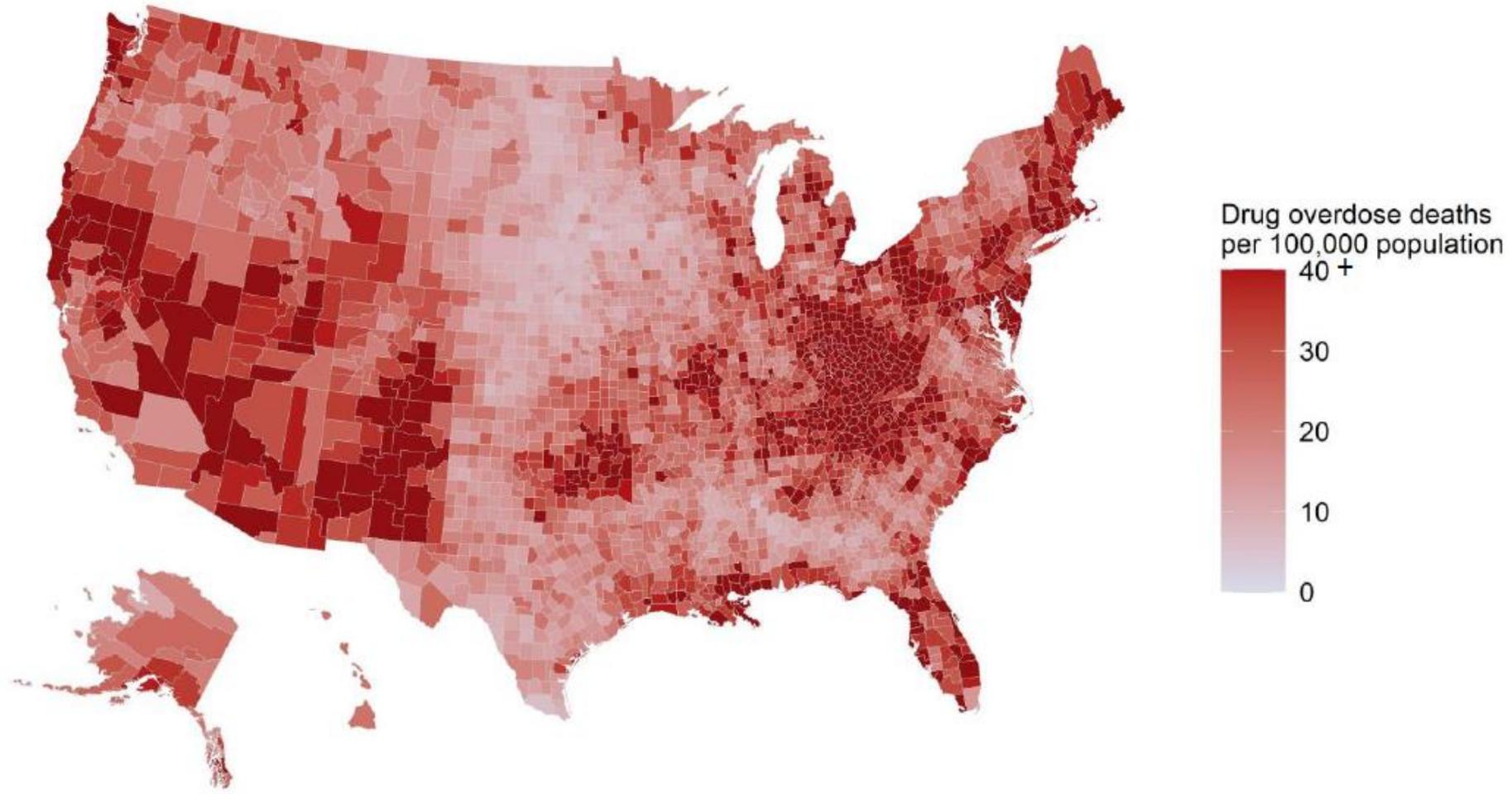
Drug Overdose Mortality USA: 2017



Drug Overdose Mortality USA: 2019



Drug Overdose Mortality USA: 2021



What was responsible for the opioid epidemic at its onset in late 1990s through the height of the Opioid crisis?

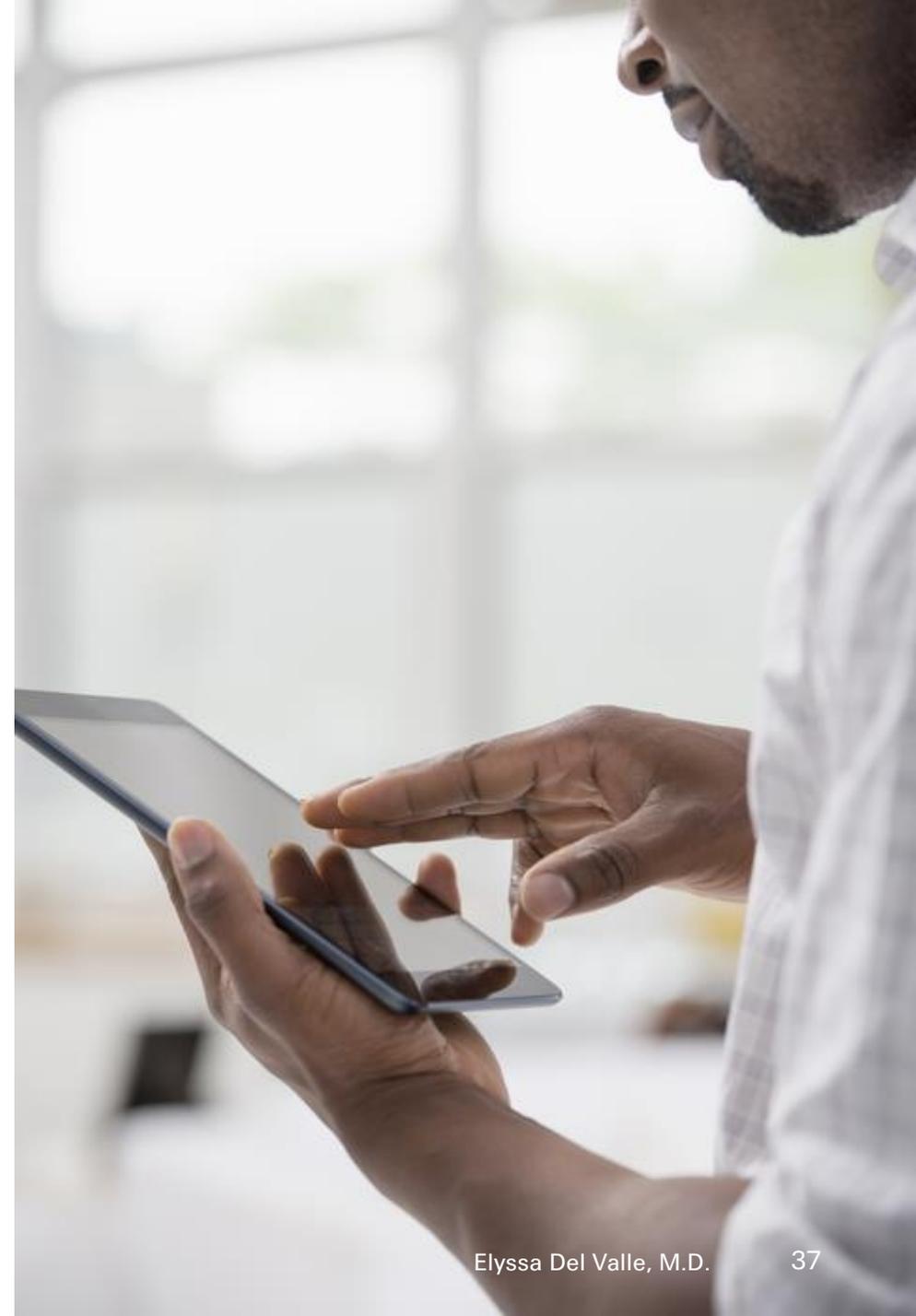
Pre-COVID

An MD's perspective on how opioid crisis came to be

Changes in Prescribing Patterns: Insurgence of Aggressive Pain Management

Editorial in New England Journal of Medicine

- **Previously**, opioids were not indicated in the long-term treatment of chronic pain
- **This philosophy changed drastically** in the late 1990s and into 2000
 - New pain management guidelines from the Joint Commission for the Accreditation of Healthcare Organizations (JCAHO) in 2000
 - In 2001 California mandated all licensed physicians (except radiologists and pathologists) take a full-day course on “pain management”
 - **The self-report of pain was to be treated above any other considerations**
- Patient **satisfaction surveys** and **Internet**
- **Addiction counseling** and **treatment** is time-consuming, poorly reimbursed and **often unavailable**, while **treatment with opiates is profitable** and **pain clinics ubiquitous**



Additional Reasons For Insurgence of Aggressive Pain Management



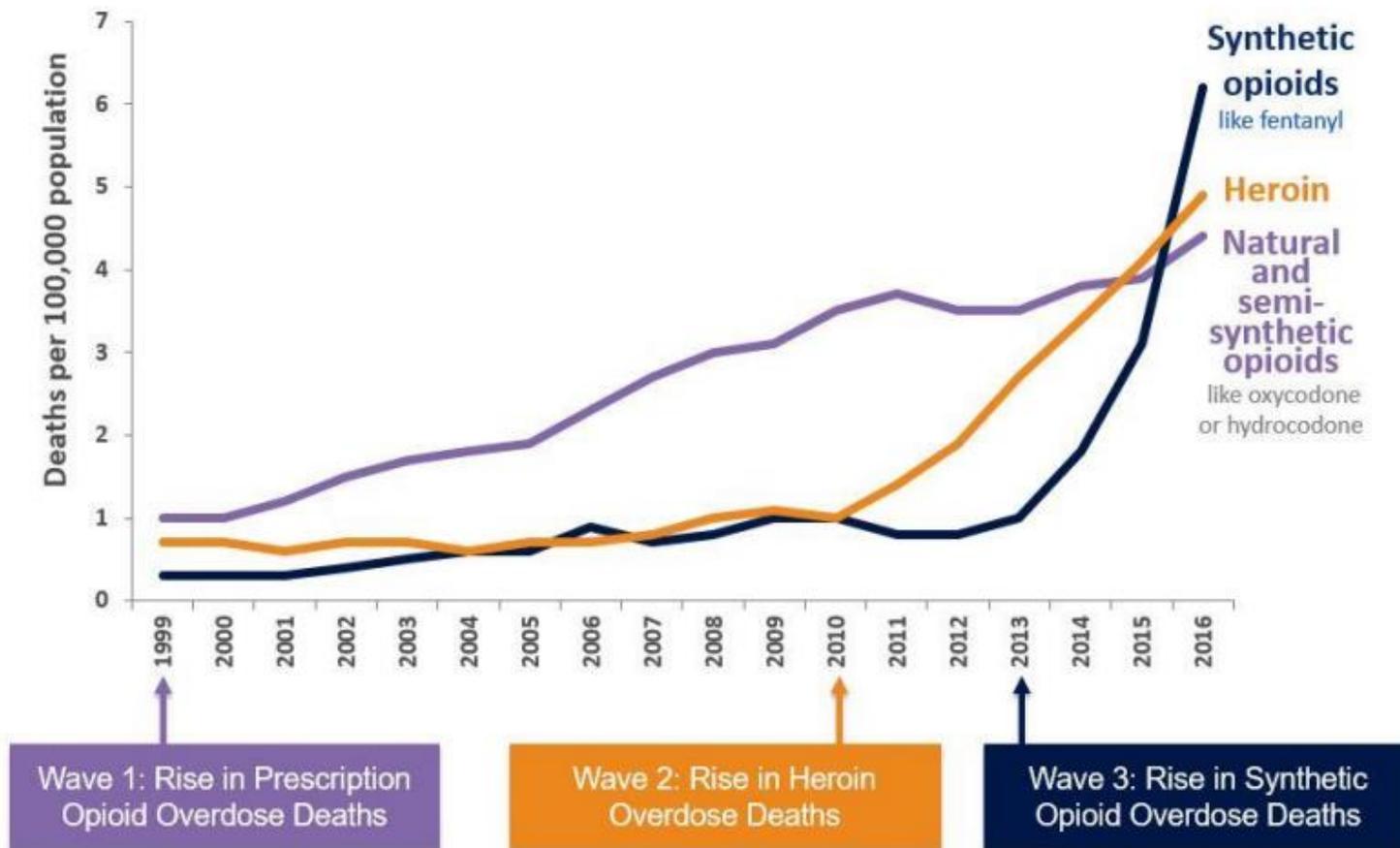
Oxycontin was marketed as a non-addicting opioid pain reliever based on industry-sponsored trials



NSAIDs have been shown to be associated with a higher risk of coronary artery disease, stroke and GI bleeds

Opioids: Overdose Deaths

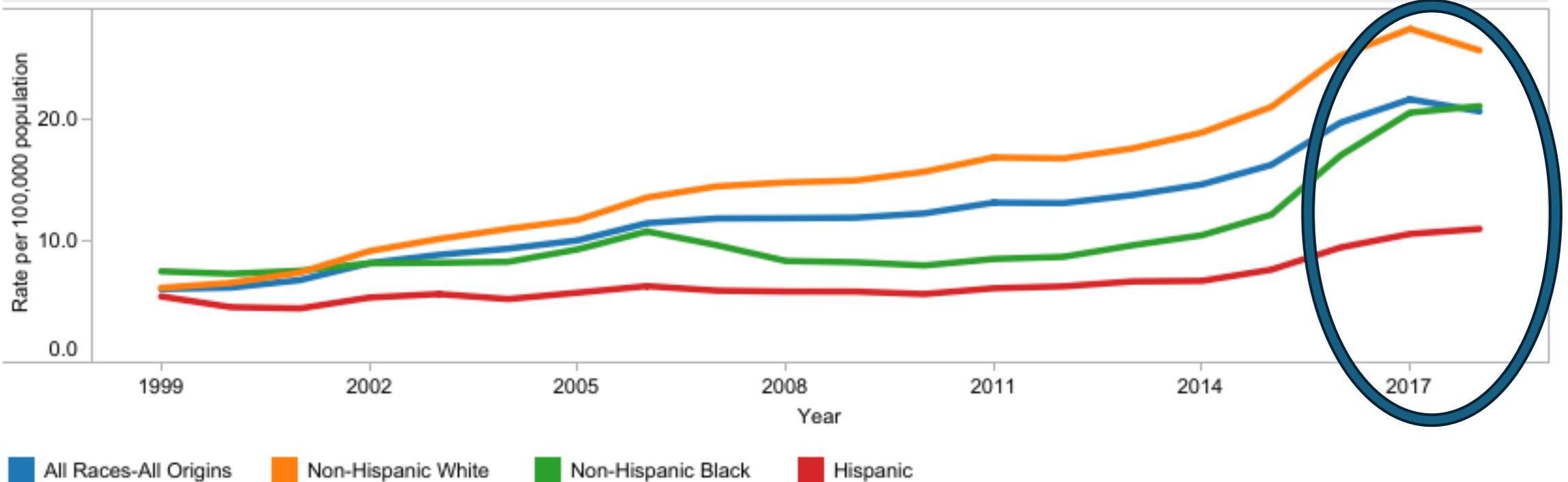
3 Waves of the Rise in Opioid Overdose Deaths



SOURCE: National Vital Statistics System Mortality File.

Opioid crisis was improving prior to Covid

Age-adjusted Death Rate† for Drug Poisoning by Race and Hispanic Origin, All Ages, Both Sexes: United States, 1999–2018

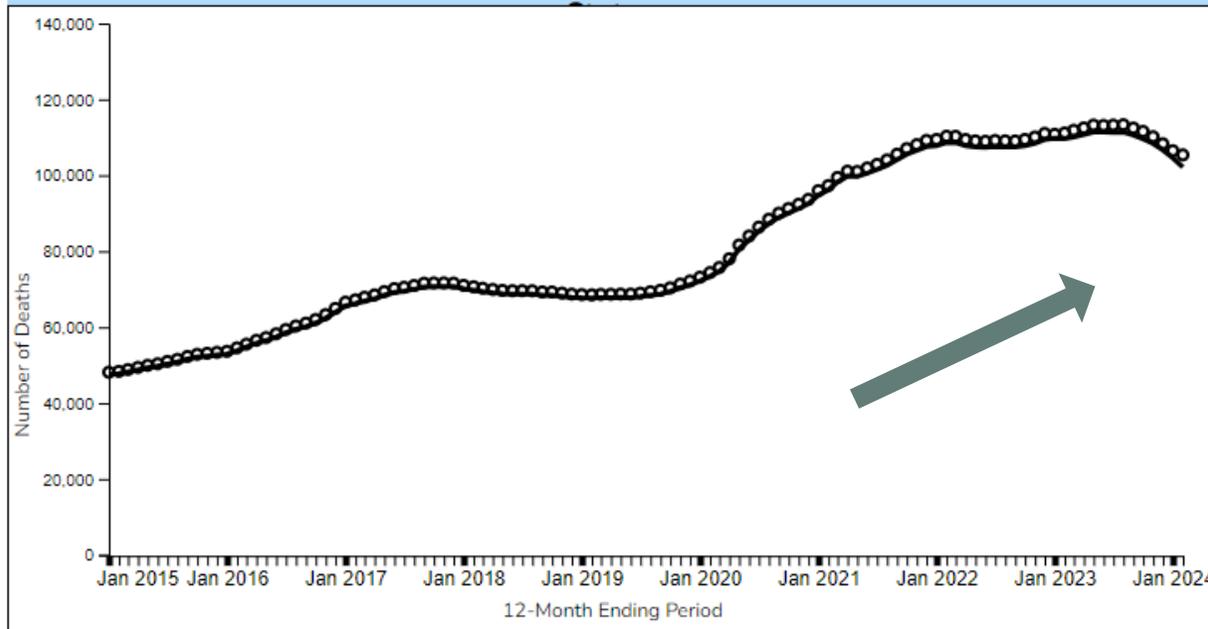


Drug overdose deaths contributing to non-covid increases

Potential peak in drug overdose hopefully passed and decline will continue in many states

Based on data available for analysis on: July 7, 2024

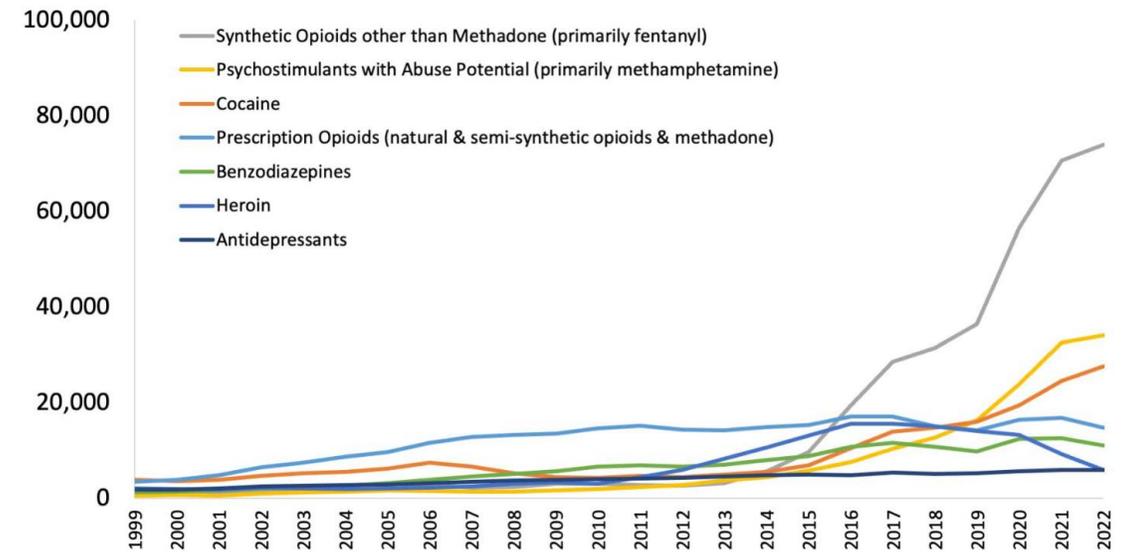
Figure 1a. 12 Month-ending Provisional Counts of Drug Overdose Deaths: United



○ Predicted Value

■ Reported Value

Figure 2. National Drug Overdose Deaths*, Number Among All Ages, 1999-2022



*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999–2022 on CDC WONDER Online Database, released 4/2024.

Per CDC's National Center for Health Statistics

Opioids: Mechanism of action

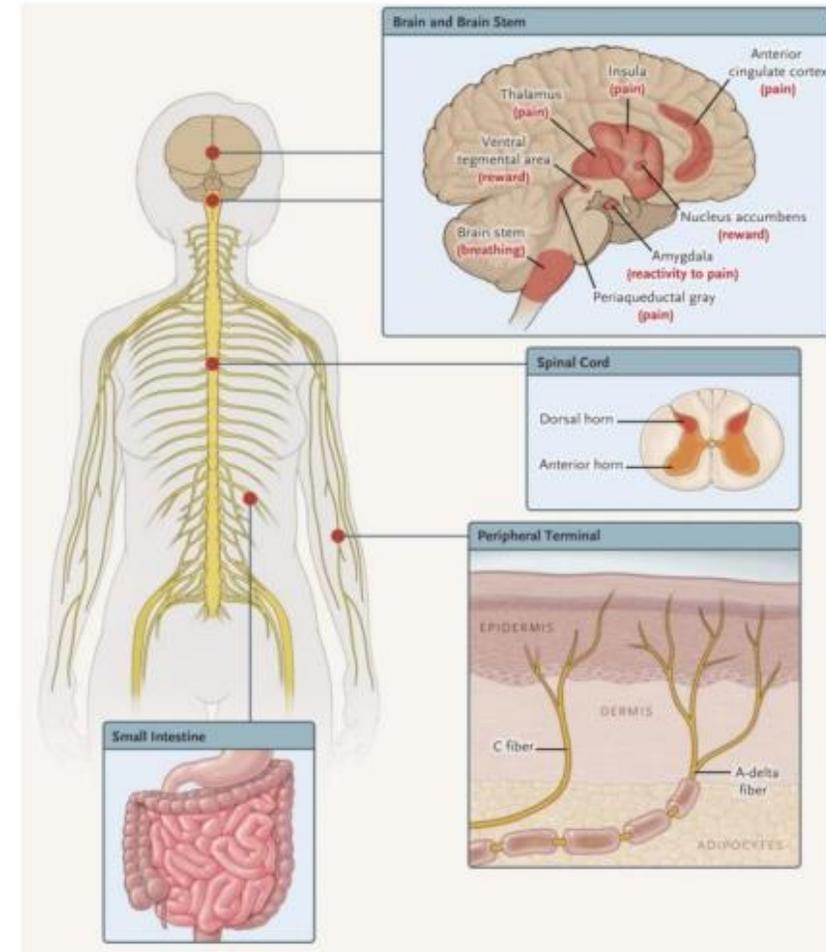
- Opioid receptors — central nervous system (CNS) and peripheral (PNS)

- Mu, kappa and delta

- Activation of mu receptors

CNS: analgesia, reward/euphoria, pain-induced emotional responses, respiratory depression

PNS: constipation, cough suppression



Opioids

Tolerance

- Decrease in potency with repeated intake → ongoing longer use typically requiring dose escalation to maintain initial analgesic effect
- Similar tolerance occurs with reward/euphoria effects
- Tolerance to analgesia and reward/euphoria occur quickly vs. tolerance to respiratory depression
- Dose increases to overcome tolerance to analgesia or euphoria markedly increased risk of overdose

Physical dependence

- Withdrawal symptoms if stopped abruptly

Addiction

- Cravings, obsessive thoughts, compulsive use

DSM-V criteria: Opioid Use Disorder (OUD)

DSM-V criteria: Opioid Use Disorder (OUD)

Problematic pattern of use leading to impairment/distress with at least two of the following within 12-month period:

- ✓ Larger amounts or over a longer period of time than intended
- ✓ Persistent desire or unsuccessful effort to cut down or control use
- ✓ A great deal of time spent to obtain, use, or recover from effects
- ✓ Stopped or reduced important activities (social, occupational, recreational) because of use
- ✓ Recurrent use in physically hazardous situations
- ✓ Continued use despite knowledge of having a persistent or recurrent physical or psychological problem
- ✓ Cravings, desire, or urge to use
- ✓ Recurrent use resulting in failure to fulfill major obligations (work, school, home)
- ✓ Continued use despite persistent or recurrent social/interpersonal problems caused by effects of opioids
- ✓ Tolerance*
- ✓ Withdrawal*

* Not considered to be met for those taking opioids solely under appropriate medical supervision

- **Mild: 2-3 symptoms**
- **Moderate: 4-5 symptoms**
- **Severe: 6 or more symptoms**

Risk Factors For Misuse And Overdose

- **Male gender: BUT gap is closing**
- **History of other substance misuse or overdose**
- **Mental health diagnoses (e.g., depression, bipolar, PTSD)**
- **Pulmonary disease or OSA**
- **Family history of alcohol or drug abuse**
- **Prescription opioid misuse highest among ages less than 40 to 45 years old**
- **Prescription opioid overdose highest among ages 25 to 54 years**
- **Recent abstinence**



- **Opioid use risks**
 - Long-term opioid use (>3 months)
 - Higher average daily dose
 - Long-acting formulations (e.g. methadone, transdermal fentanyl)
 - Combination of opioids and benzodiazepines or alcohol
 - Illicit opioids
 - Early refill requests
 - Multiple prescribers

Sources:

Becker, William, et al, *Prescription Drug Misuse: Epidemiology, Prevention, Identification and Management*, UpToDate, July 2018

Gupta, Anita, et al, *Use of Opioids in the Management of Chronic Non-Cancer Pain*, UpToDate, September, 2017

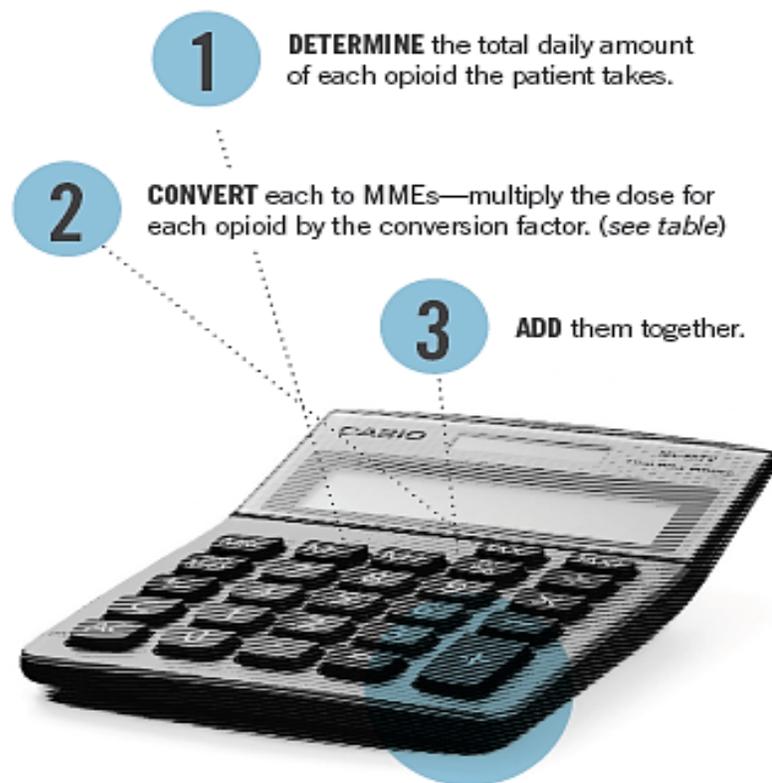
Volkow, ND, *Opioid Abuse in Chronic Pain — Misconceptions and Mitigation Strategies*, New England Journal of Medicine, 2016; 374;13: 1253-1263

Centers for Disease Control and Prevention. Prescription Opioid Overdose Data. Retrieved August 12, 2018. <https://www.cdc.gov/drugoverdose/data/overdose.html>

Underwriting considerations

- Alcohol and drug abuse is an ever-increasing problem encountered by underwriters, with significant mortality implications
- Distinguishing appropriate and inappropriate use is the key to underwriting these individuals
- Recovery is possible, but postpone periods are required before we can reconsider
- New CDC guidelines intended to curtail use and abuse of narcotics
- MME stands for Morphine Milligram Equivalent
- Risk for overdose increases substantially as the MME increases
 - RR of overdose in individuals taking 20 to < 50 MME is between 1.3- 1.9
 - RR of overdose in individuals taking 50 to < 100 MME is between 1.9- 4.6
 - RR of overdose in individuals taking \geq 100 MME is between 2.0 – 8.9

How Should the Total Daily Dose of Opioids be Calculated?



CAUTION:

- Do not use the calculated dose in MMEs to determine dosage for converting one opioid to another—the new opioid should be lower to avoid unintentional overdose caused by incomplete cross-tolerance and individual differences in opioid pharmacokinetics. Consult the medication label.

Calculating morphine milligram equivalents (MME)

OPIOID (doses in mg/day except where noted)	CONVERSION FACTOR
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1-20 mg/day	4
21-40 mg/day	8
41-60 mg/day	10
≥ 61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.

USE EXTRA CAUTION:

- **Methadone:** the conversion factor increases at higher doses
- **Fentanyl:** dosed in mcg/hr instead of mg/day, and absorption is affected by heat and other factors

Opioid/Benzo Case 1: 52 yr old male contractor applying for 3 million whole life

Hx of lumbar fusion surgery 2008; ESI 2010-11; Treated at Pain Clinic currently

PMH: Depression, Anxiety, OSA on Cpap

SHx: Quit smoking 2011; Hobby Skis on weekends from Dec – March; ETOH 2-3 drinks/day;

MVR: DUI 2011

RX inquiry: Hydrocodone/Acetaminophen 10/325 mg #120 tablets, Soma (Carisoprodol) 350 mg #90, Alprazolam 1mg #60, Viagra, Flonase, OTC Allegra

Paramed: 5'10" 205 lbs BP 145/90

Insurance Labs: normal however AST 50 ALT 20, HDL 82

Calculate the MME

Percocet 10/325 gets 120 tablets/month

Drug	HYDROcodone (Vicodin, Norco, Lortab) ▾	
Dosage	10	mg/dose
Doses per day	4	doses/day
Add another drug	<input checked="" type="radio"/> No	<input type="radio"/> Yes

40.0

MME/day

2x higher risk of overdose than <20 MME/day; there is no completely safe opioid dose; use caution when prescribing opioids at any dose and always prescribe the lowest effective dose

Drug(s):
40.0 mg hydrocodone

Copy Results 📄

Next Steps >>>

Any concern with the rest of RX (Alprazolam, Carisoprodol, OTC antihistamines) and his history?

<https://www.mdcalc.com/calc/10170/morphine-milligram-equivalents-mme-calculator>

Opioid Case 2: 55 yo F applying for 2 million whole life

- Medical Hx: migraine headaches, Fibromyalgia and GAD.
- Surgical Hx: Breast implants, maxillofacial cosmetic surgery
- Social Hx: Divorced, 2 yrs ago moved from LA to CT, works as office manager for her brother's internal medicine practice in CT. Smoker ½ ppd x 20 yrs and quit 2016. ETOH 3 glasses wine per week
- Family Hx: unremarkable other than father died age 62 of lung cancer
- RX inquiry: 7/25: Relpax 40 mg, HCTZ 25 mg, Amitiza (Lubiprostone), Darvocet
- APS: 1/25 Office note: Reported increased migraines unrelieved with Relpax. Also was sick when on vacation in Florida over Xmas with flu and still with cough, requesting Tussionex as it was effective in past. Prescribed Tussionex elixir 4 oz and given #12 Percocet 5/325. Referred to neurology.
- 2/25 Office note: Cannot get into neuro for another 2 months. Requesting more Percocet and when refused, asked for Fioricet. Given #20 Fioricet and with recommendation to start Amitriptyline 10 mg at bedtime and a week later to titrate up to 2 tablets until she sees neurologist.
- 4/25 Urgent Care visit: URI symptoms. Cough, no fever. RX: Augmentin, Tussionex elixir 4 oz and Ultracet #30.
- 6/25 Establishing with New PCP with chief complaint of headache and constipation. Wearing dark glasses in exam room complaining of photophobia and nausea. She described daily headaches of mild severity but once a week would get a severe HA often requiring Percocet 10/325. She was also to fly in 2 weeks to LA, requesting Xanax. And lastly, requested RX for constipation as no relief with OTC laxatives.
- When agent asked for Neurology APS, there were none.
- Paramed: BP 145/88, 5'4", 135 lbs
- HOS: + Cotinine, otherwise neg
- Labs: ALT 95, AST 75, T. Bili 1.9, GGT 75, BUN 28, Creatinine 1.5
- Chol 205, HDL 35, CDT Negative, Hep B S Ag nonreactive
- Hep C AB nonreactive

Let's discuss. No MME, but what are the concerns? See abuse? What is most likely cause of abnormal LFTs?

BONUS CASE

60 yr old CEO of major TV network discloses retreat for mental wellness for psilocybin last year. Reports now that he microdoses psilocybin once a quarter for creativity, focus and neuroplasticity.

PMH: No mental condition. No medical conditions. Labs normal. Ekg normal. Seen 6 months ago and had normal screening testing including Cscope and Prostate check. Never smoker. Married with 2 grown children.

MVR clear. RX no medications. never smoker. No hx of recreational drug use. No cannabis
Self prescribes the psilocybin taking 200 mg on Fadiman protocol which is every 3 days for 2 weeks.

Microdose movement

- Institutes such as "microdosing institute"
 - Education, research and community
 - GLOBAL
- Online access to tutorials and "coaching" that helps users in the process of microdosing.
- Research information, protocols, different substances, etc.
- They have a shop where you can access different substances in different parts of the world.
- It goes beyond mental disorders. It refers to **mental health**.

Microdosing Institute is a global education, community, and research platform. We build vital connections in society and bring together ancestral wisdom with modern science to allow for safe, conscious, and effective microdosing with psychedelics.



EDUCATION

Here at Microdosing Institute you'll find everything you need to microdose safely, consciously, and effectively. We provide evidence-based education and guidance in various forms to foster the most transformative microdosing experiences.

[Learn About Microdosing](#)



COMMUNITY

Through our global microdosing community, we aim to provide accessible and honest microdosing education, foster healthy conversations about microdosing and psychedelics, and provide connection and high-quality support for those who need it.

[Join Our Global Community](#)



RESEARCH

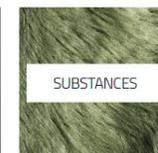
Microdosing research enables us to better understand how, when, and by whom microdosing can be safely and effectively used. Here, we have gathered and summarized most scientific research publications on microdosing and its effects to date.

[Explore Research](#)

Learn How To Microdose

Now, let's get practical.

The practical guide below provides a starting roadmap for your journey. This microdosing guide features detailed, comprehensive information about microdosing substances, protocols, getting started, and optimizing your microdosing experience. Remember, a small dose can lead to big changes – over time and when done with intention.



Johns Hopkins Center for Psychedelic & Consciousness Research



2000 – first research since 1970s w/published paper

2006 on positive effects of a single dose of psilocybin, sparking renewal in research on psychedelics

2006- established safety of high dose psilocybin

2008 – Guidelines for Human Psychedelic Research

2011 – Psilocybin increases personality domain of openness

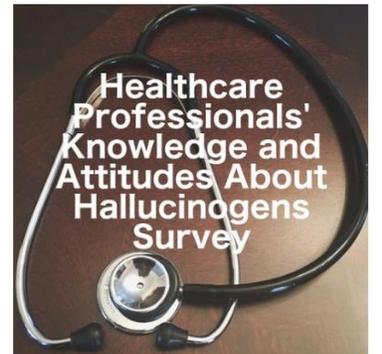
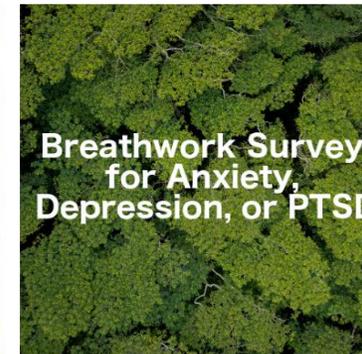
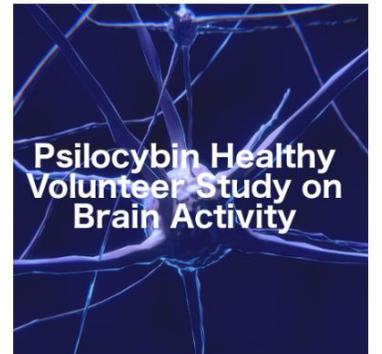
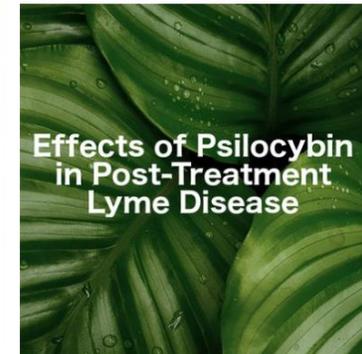
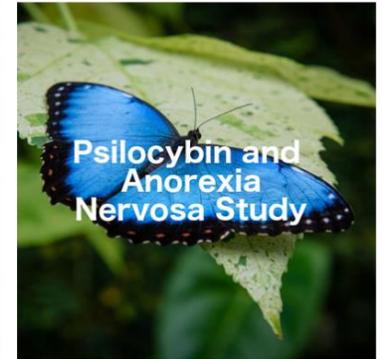
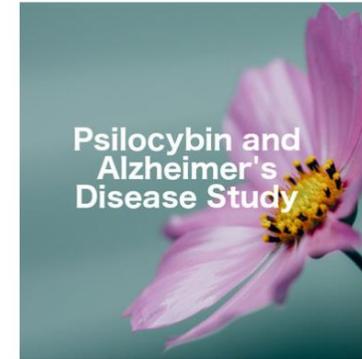
2015 – Research as potential treatment of pain and addiction (opioid, not serotonin 2A receptors)

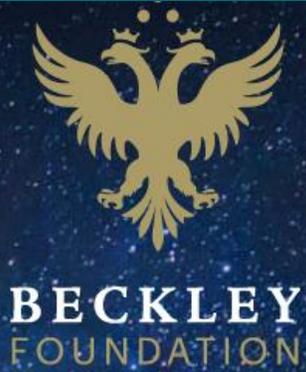
2016 - Palliative Effects of Psilocybin treatment in Cancer Patients

2016 - NIH granted study on effects of psilocybin on brain function

2017 - Pilot study showed 80% of participants were biologically verified as smoke free 6 months after psilocybin treatment compared to 35% with conventional drugs

RESEARCH





Changing Minds, Altering Perceptions

The Beckley Foundation is UK-based non-profit with a long history of pioneering psychedelic research. Founder and Director Amanda Feilding has for the past years been laying the groundwork for an exciting new range of collaborations with leading research institutes around the world, largely focusing on LSD.

Beckley Microdosing Research Program Oxford UK

54

- Specific program focused on micro-dosing (LSD)

🔥 LSD microdosing on mood, cognition & pain relief

🔥 LSD microdosing, brain activity & neuroplasticity

🔥 LSD Microdosing for Alzheimer's Disease

🔥 Microdosing and meditation

🔥 The largest placebo-controlled microdosing study

🔥 Remote microdosing research platform

- McGill University's NEURO



PSYCHEDELICS

Medscape

Research on nearly 7000 individuals who had taken 1 of 27 different psychedelic compounds mapped various experiences to different brain receptors.

Ego dissolution
Associated with 5-HT2A receptor, serotonin receptors (5-HT2C, 5-HT1A, 5-HT2B), adrenergic receptors α -2A and b-2, and the D2 receptor

Sensory perception
Associated with expression of the 5-HT2A receptor in the visual cortex

Transcendence of space, time, and self
Associated with modulation of the salience network by dopamine and opioid receptors

The infographic features three colored callout boxes: an orange box for 'Ego dissolution' with a silhouette of a head containing trees, a grey box for 'Sensory perception' with icons of a nose, ear, eye, and mouth around a brain, and a green box for 'Transcendence of space, time, and self' with a clock icon.

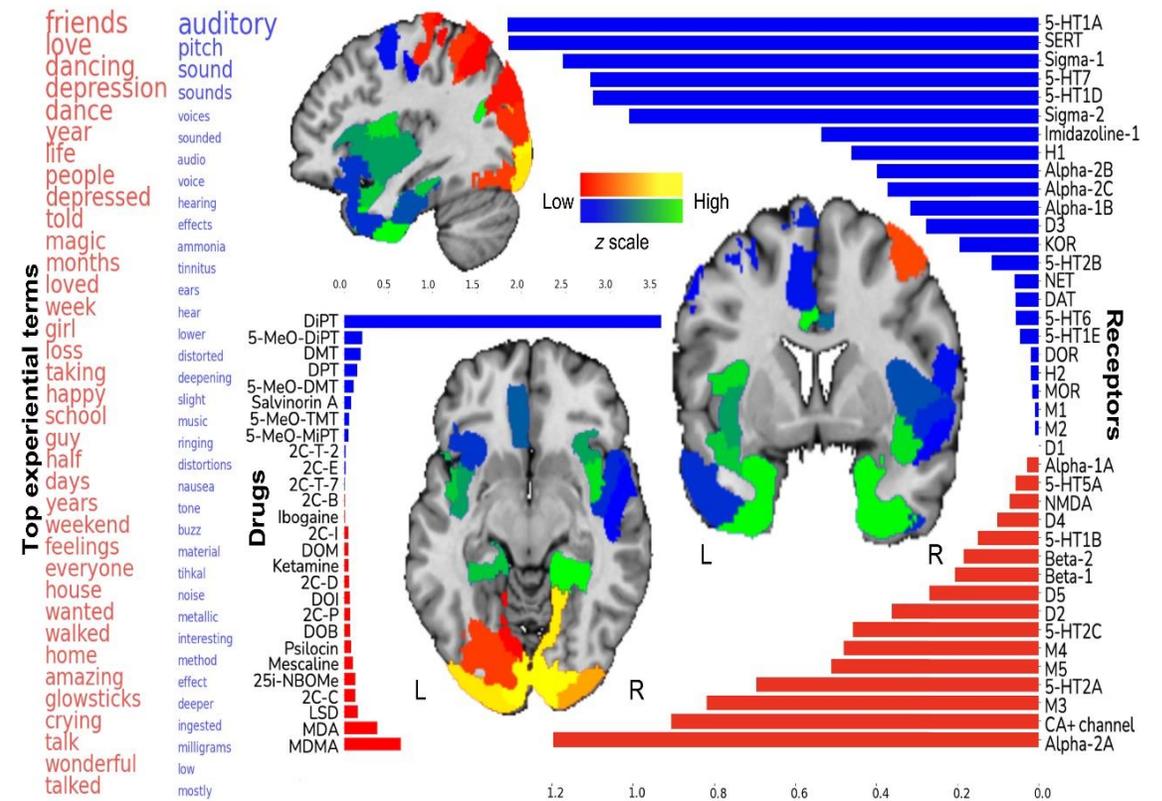
NEURO's research

Trips and neurotransmitters: Discovering principled patterns across 6850 hallucinogenic experiences

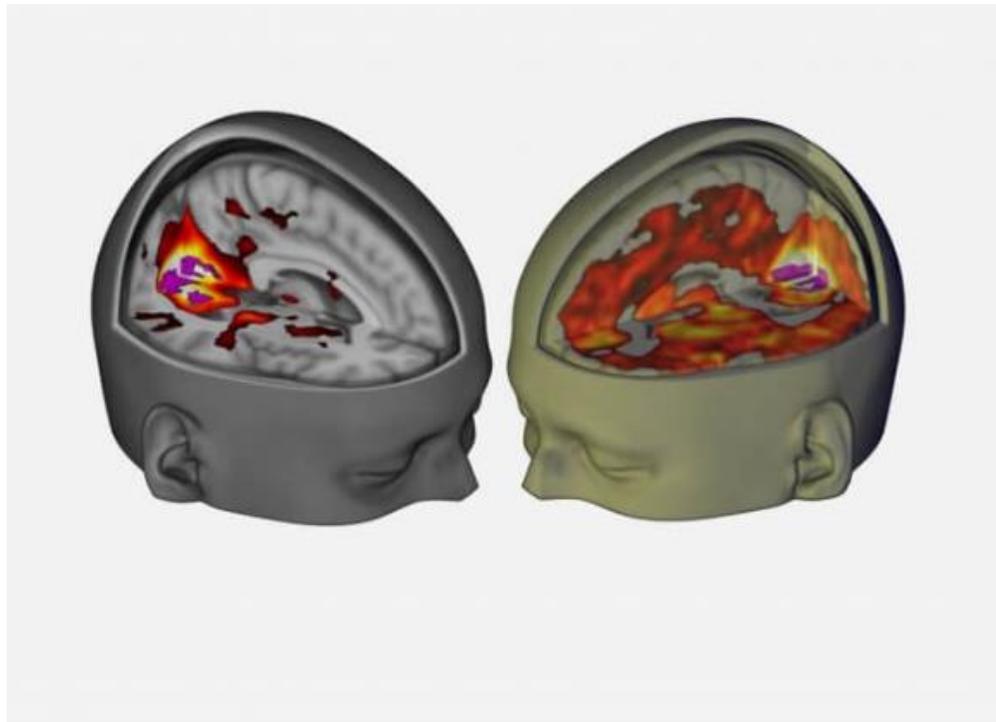
- Published in Science Advances March 2022
- Trips and neurotransmitters: Discovering principled patterns across 6850 hallucinogenic experiences | Science Advances

"Hallucinogenic drugs may very well turn out to be the next big thing to improve clinical care of major mental health conditions," senior author Danilo Bzdok, MD, PhD, associate professor, McGill

University, Montreal, Canada, said in a press release.

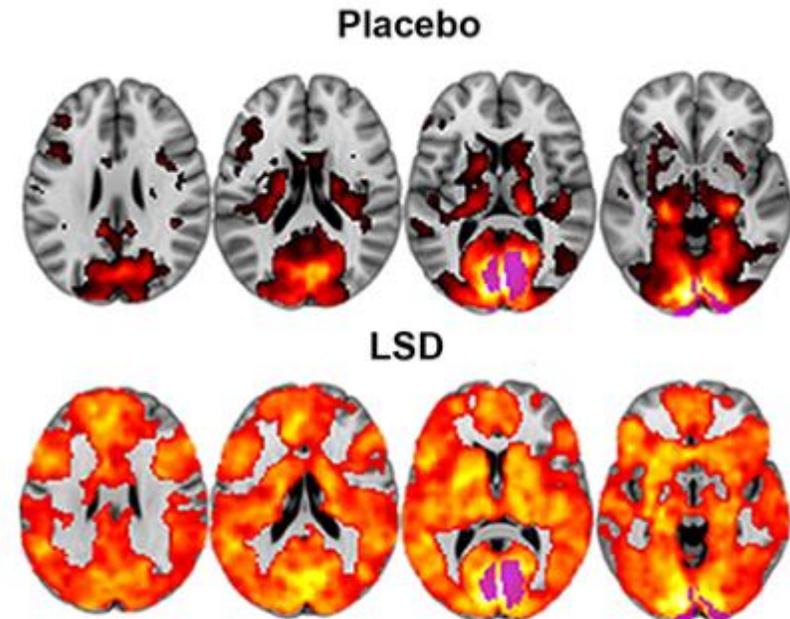


The World's First Images of the Brain on LSD – 2016 via functional MRI brain published in Proceedings of the National Academy of Sciences



Increase in the brain connectivity after LSD (right), compared to placebo (left).

Ego dissociation- DMN disintegrates under LSD, allowing for a magnificent increase in communication between brain networks that are normally highly segregated. This produces a more integrated pattern of connectivity throughout the entire brain, producing more fluid modes of cognition and enriching consciousness



This image shows how, with eyes-closed, much more of the brain contributes to the visual experience under LSD than under placebo. The magnitude of this effect correlated with participants reports of complex, dreamlike visions.

LSD decreases the communications between the brain region of the Default Mode Network – which is like a conductor in orchestra. This DMN controls amount of sensory information and controls and represses consciousness.... that is referred to as the EGO

Micro-dosing Protocols...

- **Stamets's** Protocol --also called the “beginner’s protocol”, and uses “stacking” of Lion’s Mane supplement, psilocybin, and niacin (vitamin B3) on days 1-4 and 8-11 of 14 for 4 weeks, then rest 2 to 4 weeks.
 - Paul Stamets is an American mycologist from Ohio. Advocate of treatment cancer and Alzheimer’s with psilocybin.
 - Also advocates for bioremediation, using living organisms to clean up our environmental contaminants.
- **Fadiman** protocol--microdosing every third day for 4 to 8 weeks, then rest 2 to 4 weeks. Using LSD or psilocybin at dosage of 5-10% of the recreational dose, taken in morning. the 2 days off allows to fully metabolize the substance and avoid potential tolerance or build up.
 - Dr. James Fadiman is an American writer known for research in microdosing psychedelics
 - co founded the Institute of Transpersonal Psychology which later became Sofia University
- **Micro-dosing Institute** Protocol (MDI)—microdosing every second day for 4 to 8 weeks, then rest 2 to 4 weeks.

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MVR clear. RX no medications.

Never smoker, never Cannabis, no hx of recreational drug use.

Self prescribes the psilocybin taking 200 mg on Fadiman protocol which is every 3 days for 2 weeks every 3 months.



how would you assess his
risk?