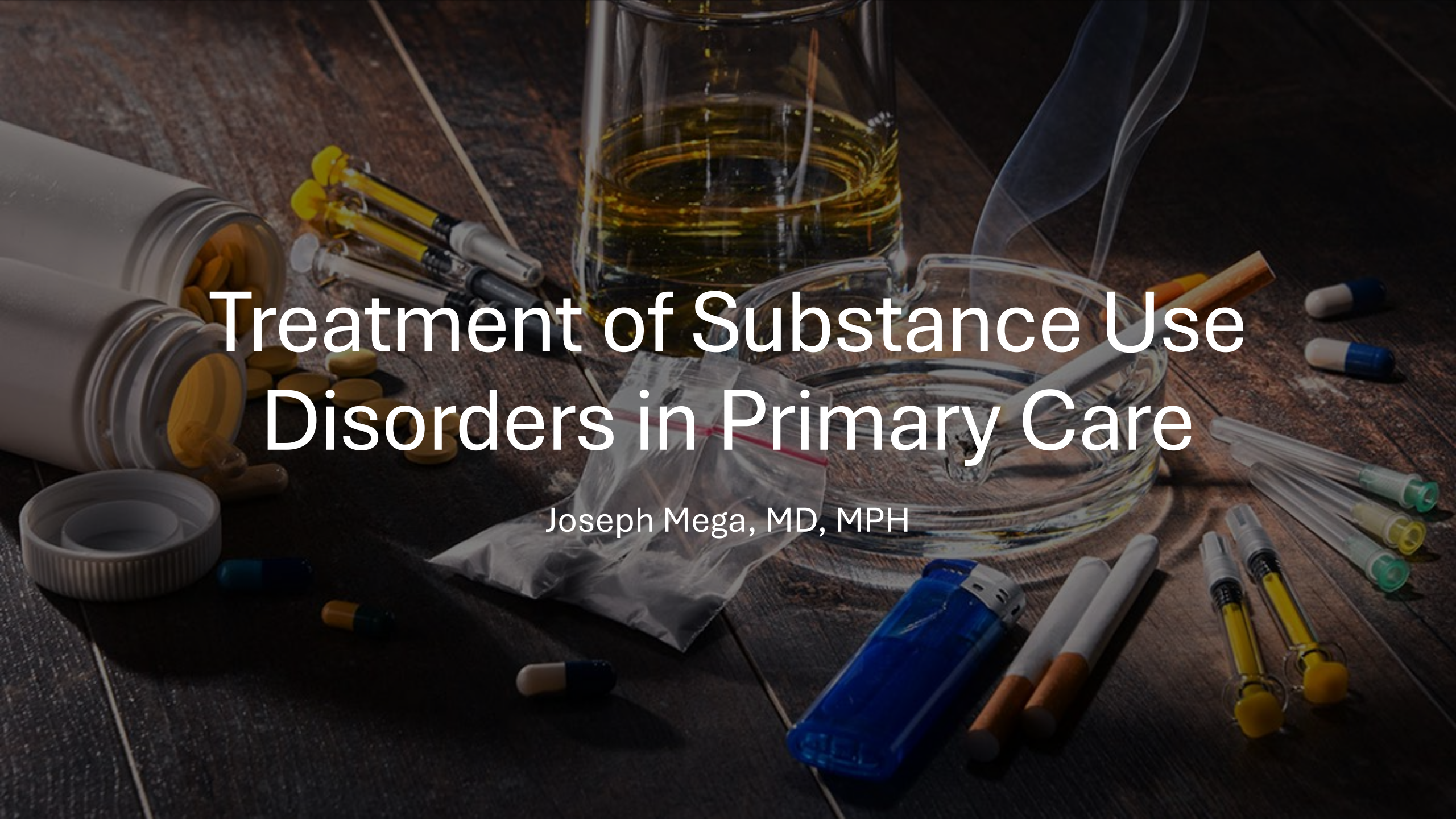


Treatment of Substance Use Disorders in Primary Care

Joseph Mega, MD, MPH

Disclosures & Disclaimers

- No financial conflicts of interest
- I will be discussing the off-label use of multiple medications in this talk

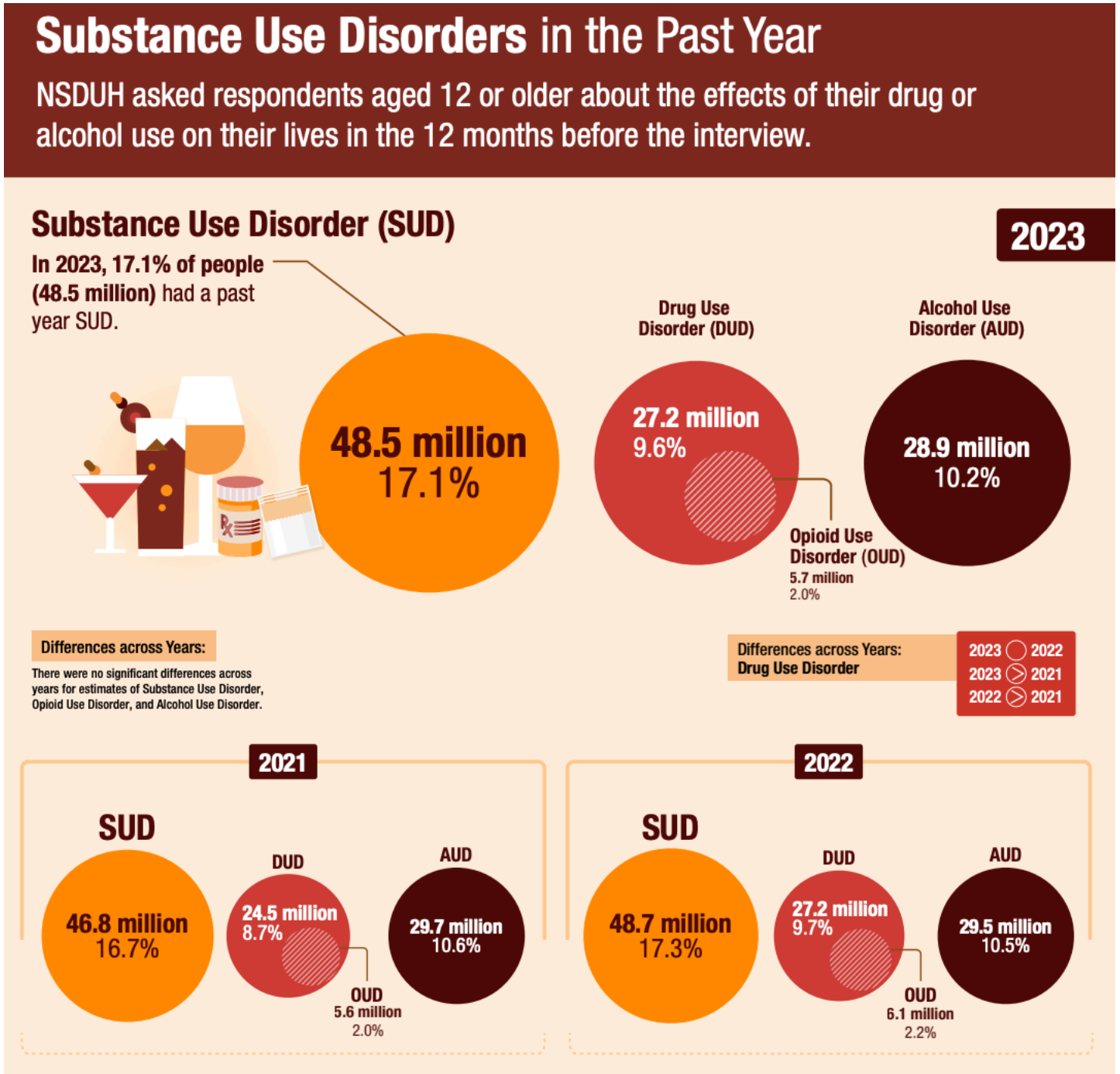
Educational Objectives

- Understand the prevalence of Substance Use Disorders (SUDs) in the US and the disparities in AI/NA populations
- Review tools for screening for SUDs in primary care
- List ways to expand options for treating SUDs in primary care
- Review practical office-based medication assisted treatment (MAT) options for several SUDs

Brief Bio

- Family Medicine Residency – Contra Costa California
- Emergency Room Physician Contra Costa
- Medical Director Health Care for the Homeless, CC
- Contra Costa County Jail Physician
- Prison Re-Entry Program
- Addiction Medicine Board Certification
- Whiteriver Indian Health Service Emergency Room/Bridge Clinic since Feb 2021

Epidemiology of SUD in US



Impact of Alcohol and Opioids
in the United States

Alcohol

Past-Year Use
% of population
177,278,000
62.5%

Alcohol Use Disorder (AUD)
% of population
28,859,000
10.2%

Emergency Department Visits
4,126,082
All alcohol-related

Deaths*
178,307
Annual deaths

61,063	117,245
Acute (e.g., injury)	Chronic (e.g., liver disease)

Opioids

Past-Year Misuse
% of population
8,902,000
3.1%

Opioid Use Disorder (OUD)
% of population
5,679,000
2.0%

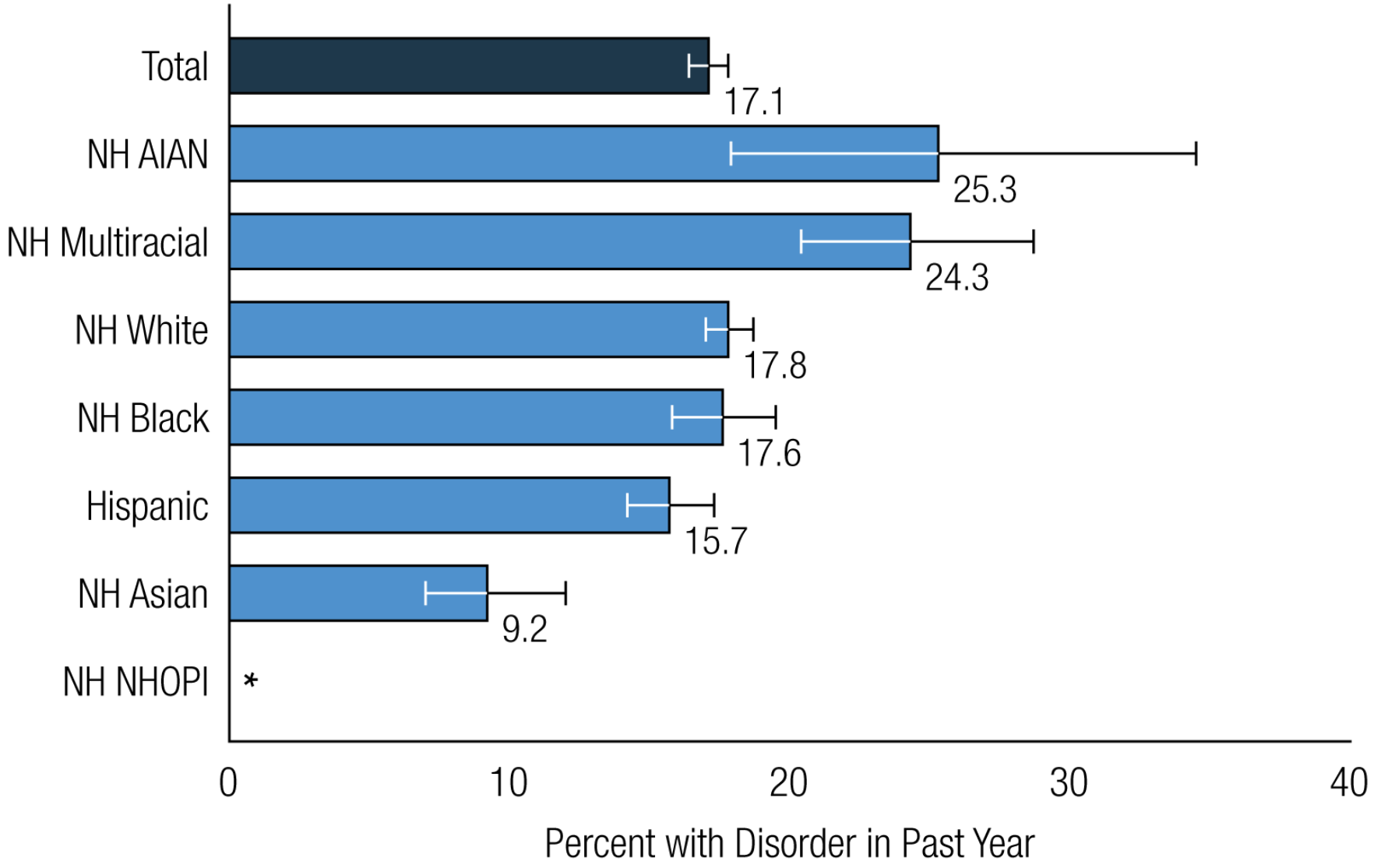
Emergency Department Visits
2,151,264
All opioid-related

Deaths*
81,806
2022 overdose deaths

73,838	5,871	14,716
Synthetic Opioids	Heroin	RX Opioids

Sources: 2023 NSDUH Tables 2.1A&B, 1.1A&B, 5.1A&B; 2021 HCUP-NEDS; 2020–2021 CDC ARDI; 2022 NIDA Drug Overdose Death Rates.
* Acute and chronic alcohol-related deaths do not add to the total due to rounding. The number of deaths from various opioids sum to greater than the total because more than one drug can be involved in a single death.

SUD by Race (≥12 years old)



Alcohol-Related Deaths are much higher in AI/AN populations

Race	Death Rate per 100,000 People
American Indian/ Alaskan Native	50.5
White	11.1
Hispanic or Latino	10.6
Black or African American	7.5
Asian or Pacific Islander	2.4

Synthetic Opioid Deaths are Rising, especially in the West

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

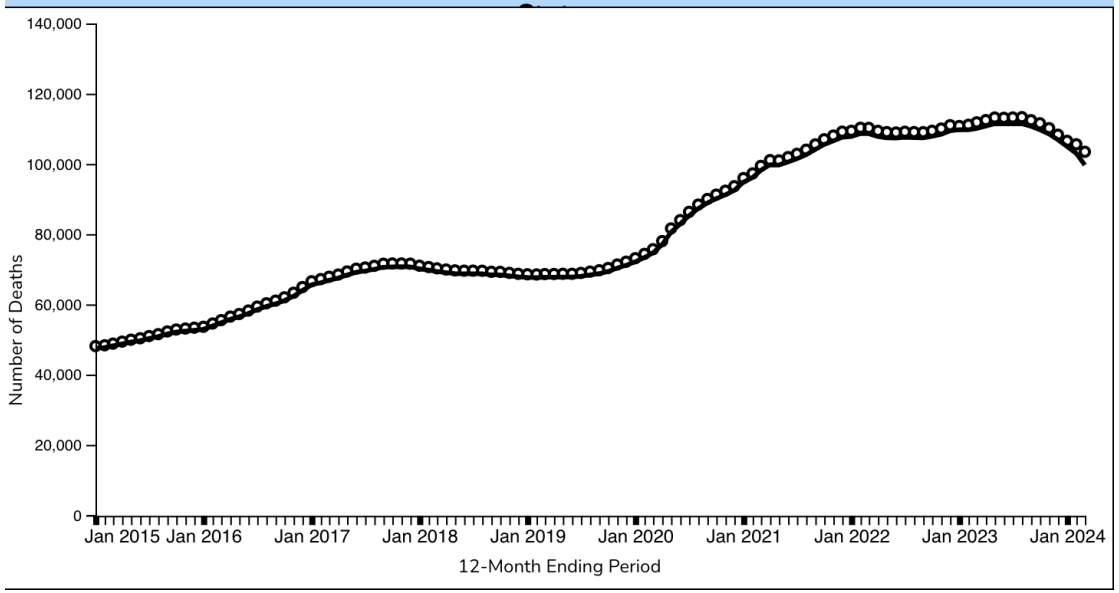
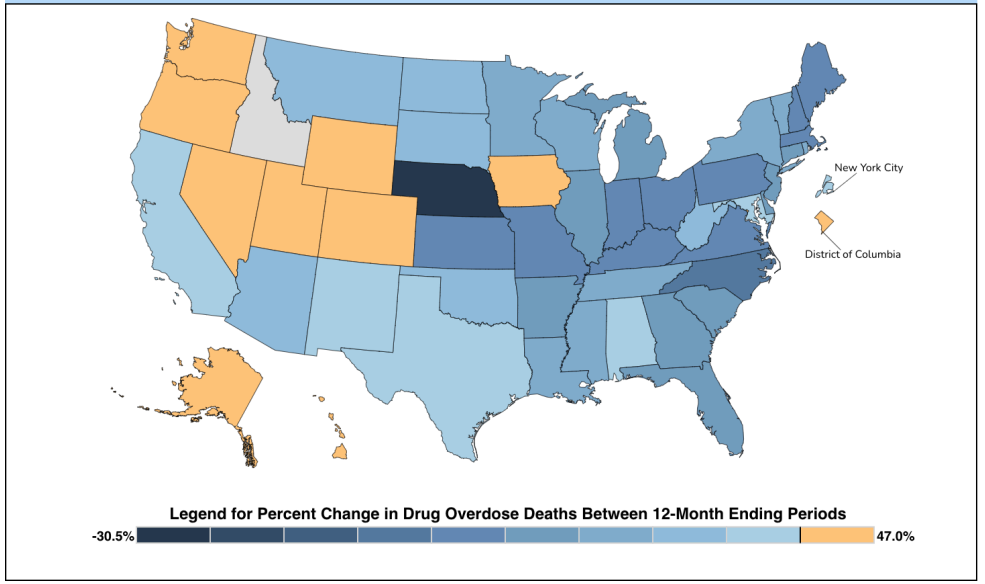
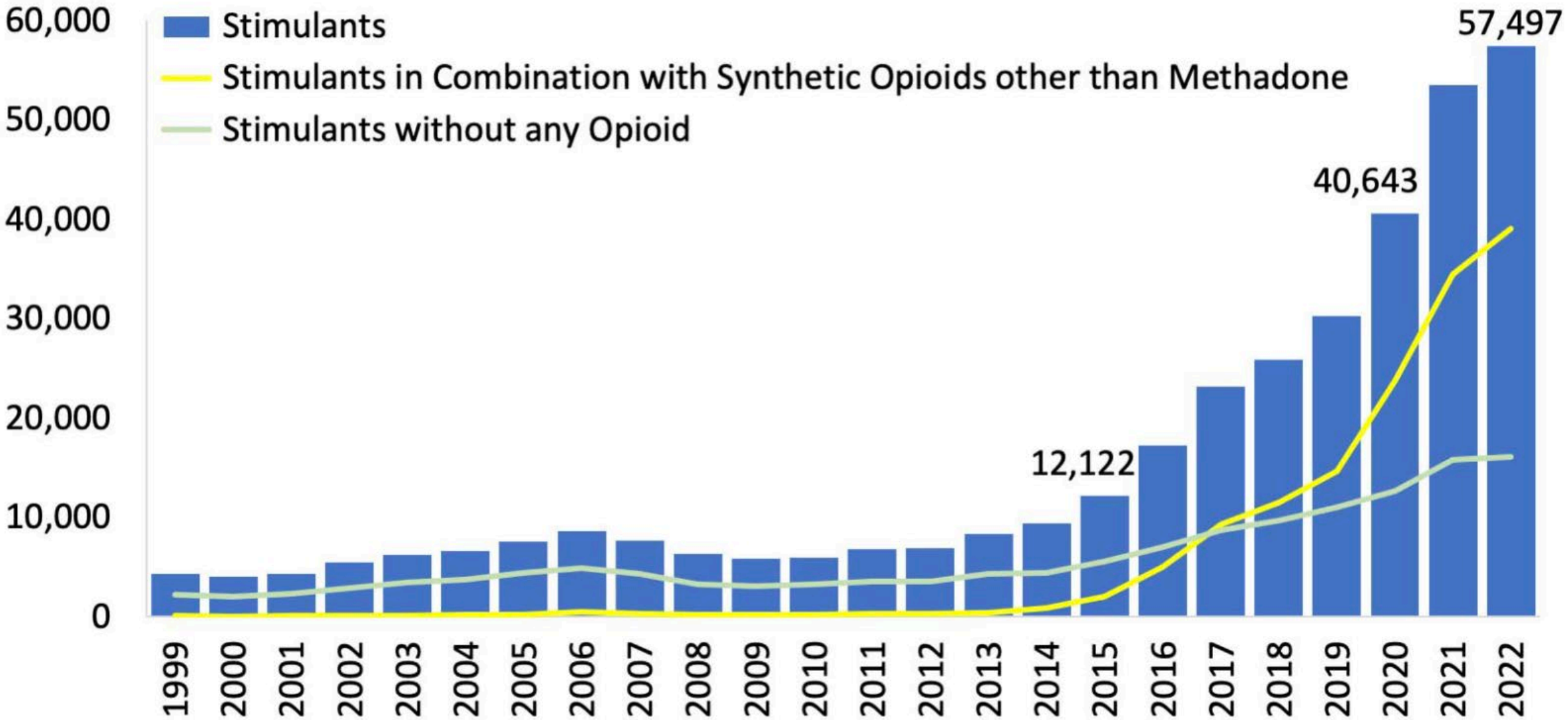


Figure 1b. Percent Change in Predicted 12 Month-ending Count of Drug Overdose Deaths, by Jurisdiction: March 2023 to March 2024

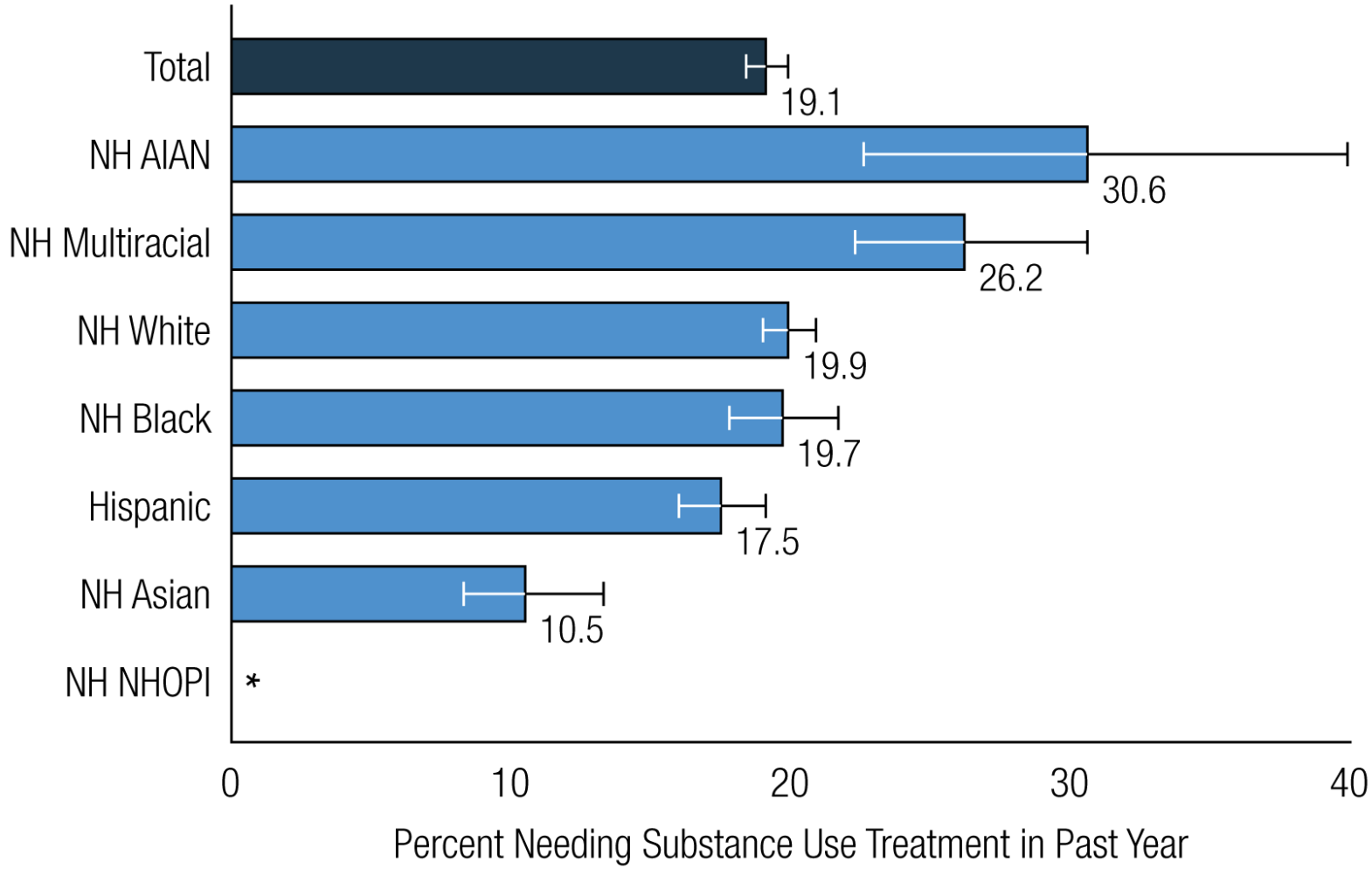


DRUG TYPE*	(ESTIMATED DEATHS 2023)	(ESTIMATED DEATHS 2022)
Synthetic Opioids (fentanyl)	74,702	76,226
Psychostimulants (including methamphetamine)	36,251	35,550
Cocaine	29,918	28,441
Natural/semi-synthetic	10,171	12,135

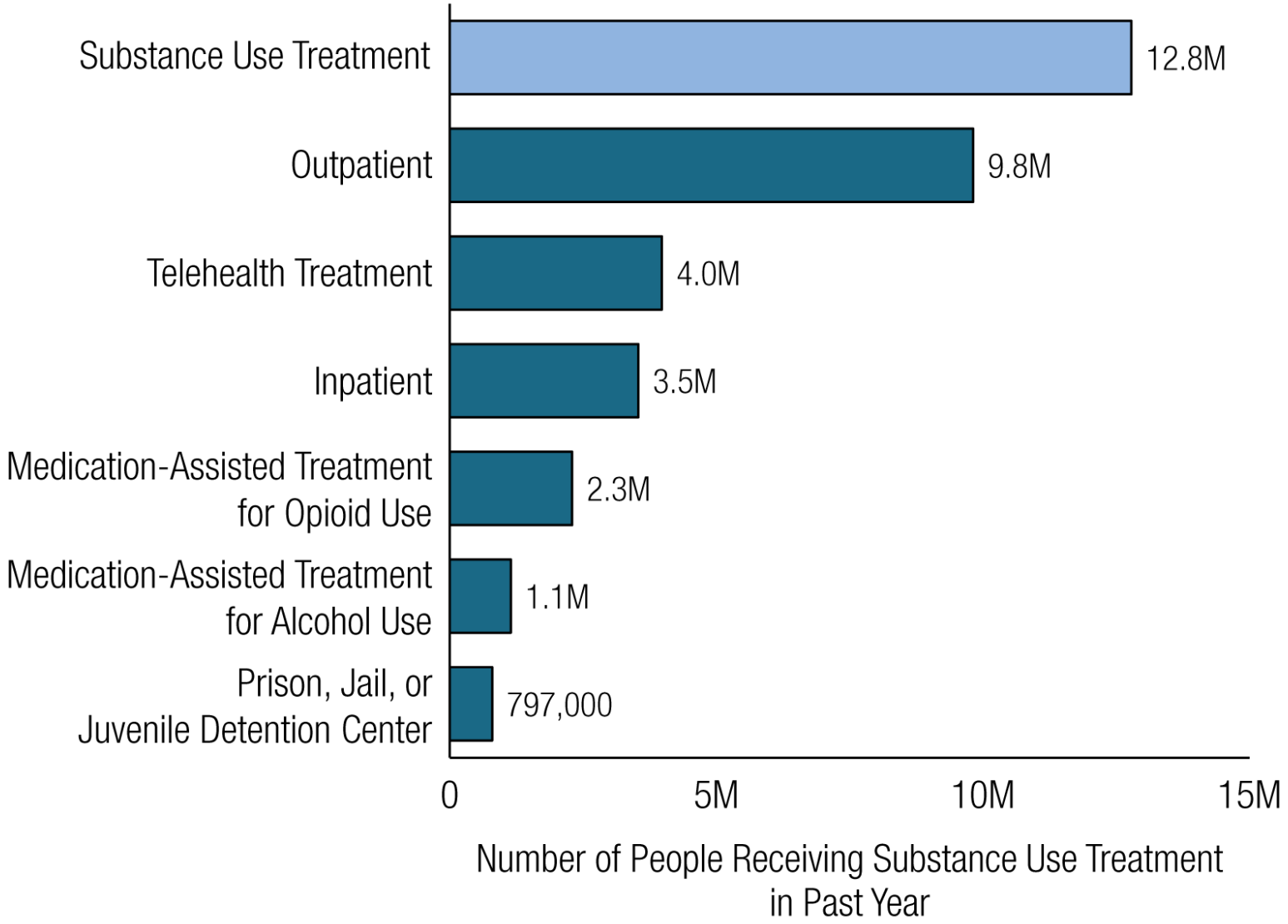
Stimulant Deaths are also on the Rise

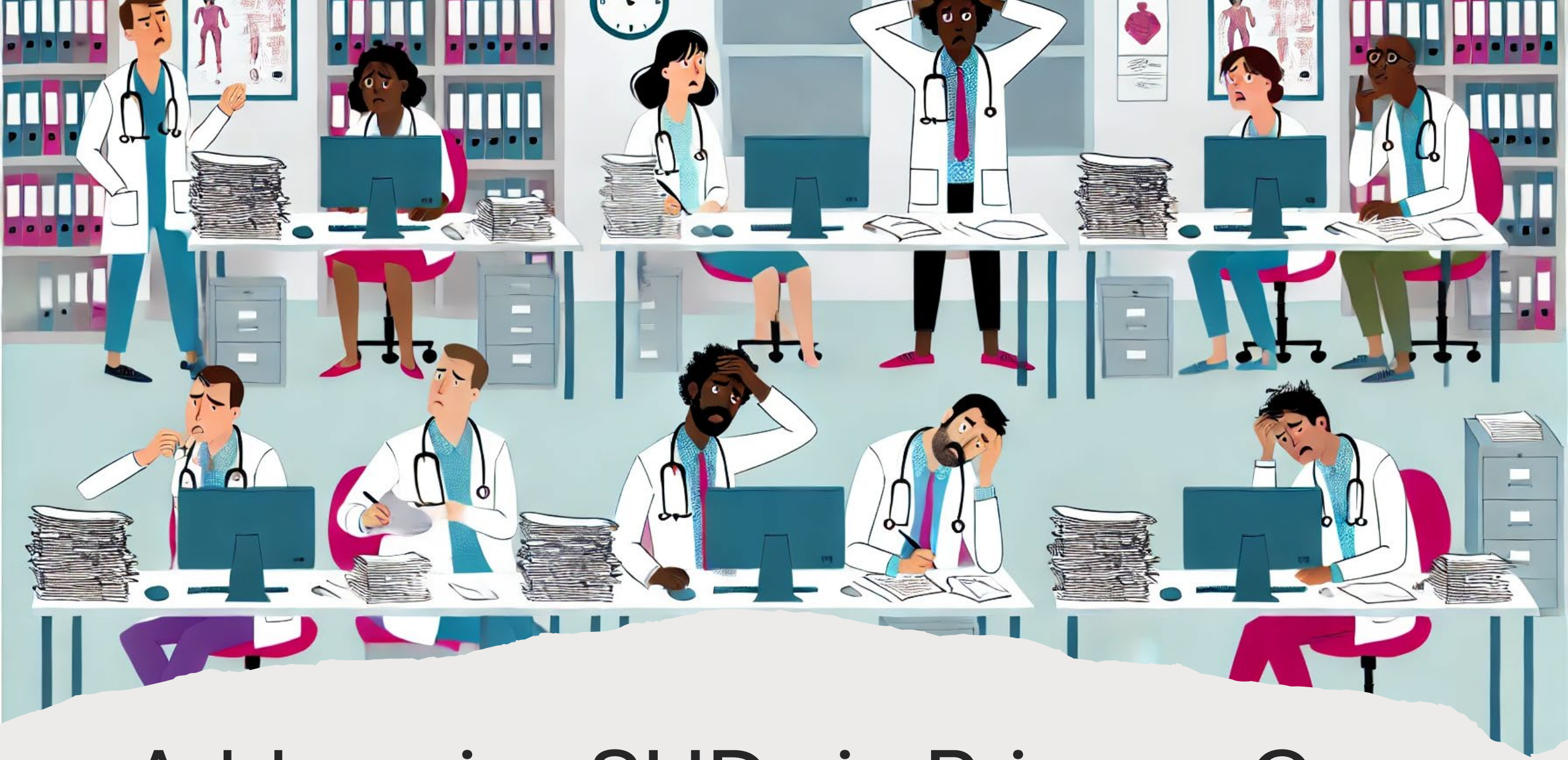


Self-Reported Need for SUD Treatment (≥12 yo)



Types/Locations of SUD Treatment (≥12 yo)





Addressing SUDs in Primary Care

Harm Reduction is not a Fringe Idea

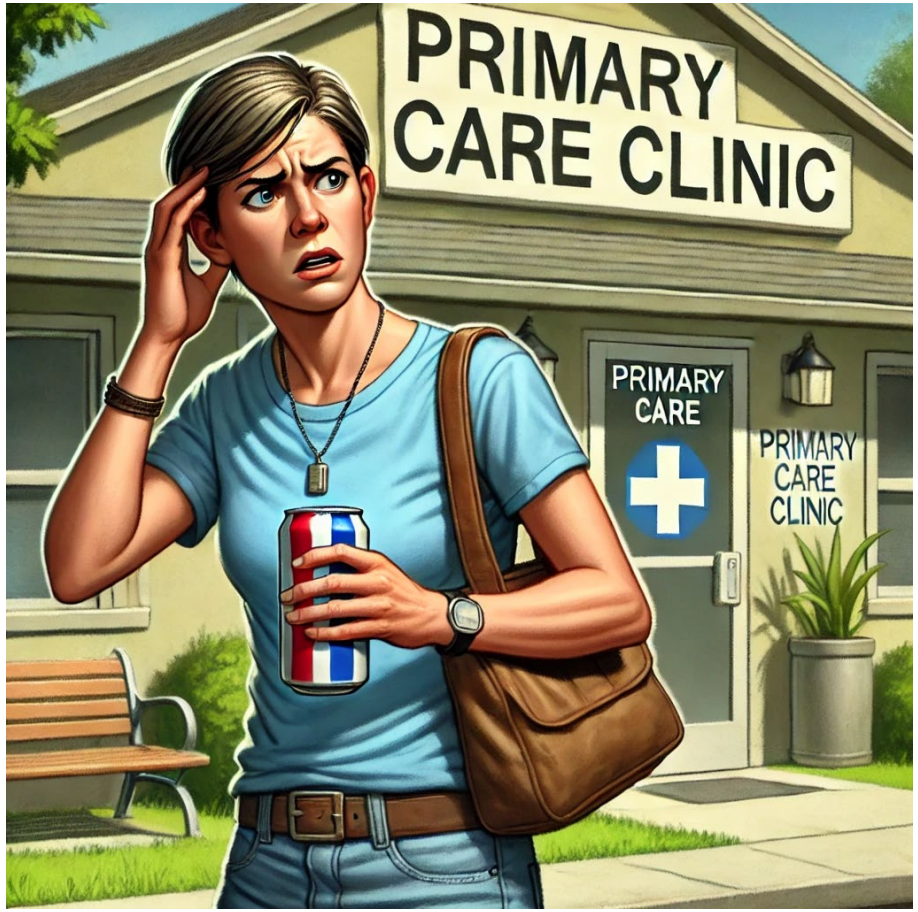
“We cannot treat dead people”

- White House Drug Czar

Dr Rahul Gupta

Traditional Teaching is SBIRT (Screening, Brief Intervention, Referral for Treatment)

In a perfect world



Reality

Cut out the Middle Man!
Screen & Treat in Clinic Today

Options for Screening for SUD

Grade B screening recommendation by USPSTF for adults

- SISQ
- TAPS 2-4 min
- AUDIT (10 items)
- AUDIT-C (first 3 of AUDIT)
- DAST

https://nida.nih.gov/nidamed-medical-health-professionals/screening-tools-resources/chart-screening-tools

Opioid Use Disorder (OUD)

DSM-5 Criteria for OUD:

1. Unable to fulfill role obligations
2. Social or interpersonal problems due to use
3. Hazardous use
4. Tolerance *
5. Withdrawal/physical dependence *
6. Taken in larger amounts of over longer period
7. Unsuccessful efforts to cut down or control
8. Great deal of time spent to obtain substance
9. Important activities given up or reduced
10. Continues use despite harm
11. Craving

Severity: Mild 2-3 symptoms, Moderate 4-5 Symptoms, Severe >6 symptoms

*If opioids are prescribed, this criterion does not apply.

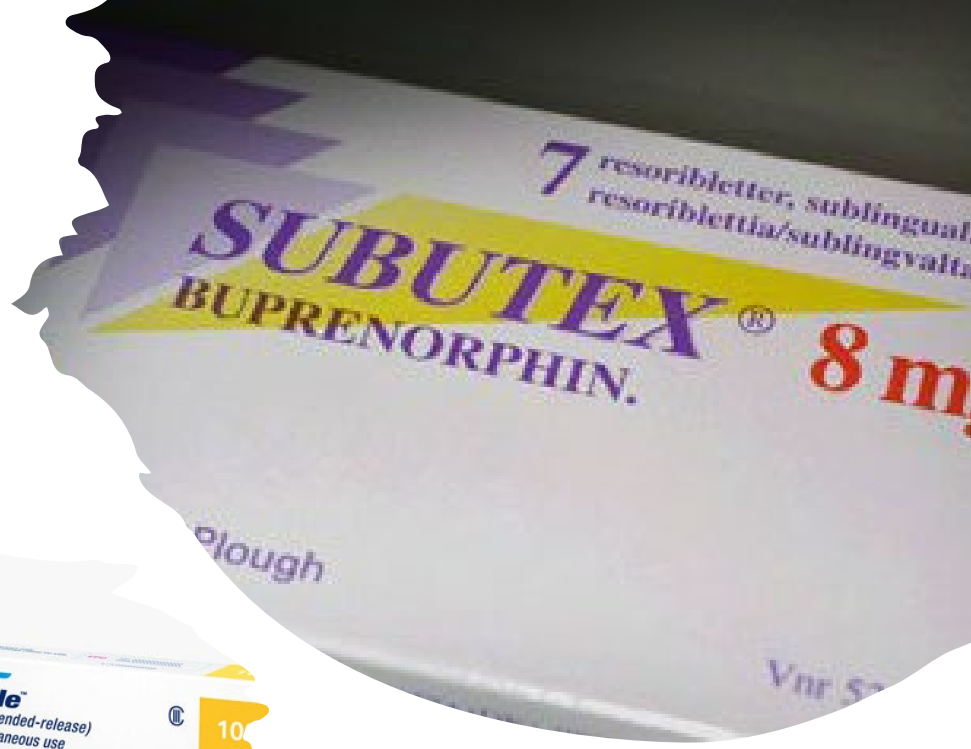
Medication Assisted Treatment (MAT) for OUD

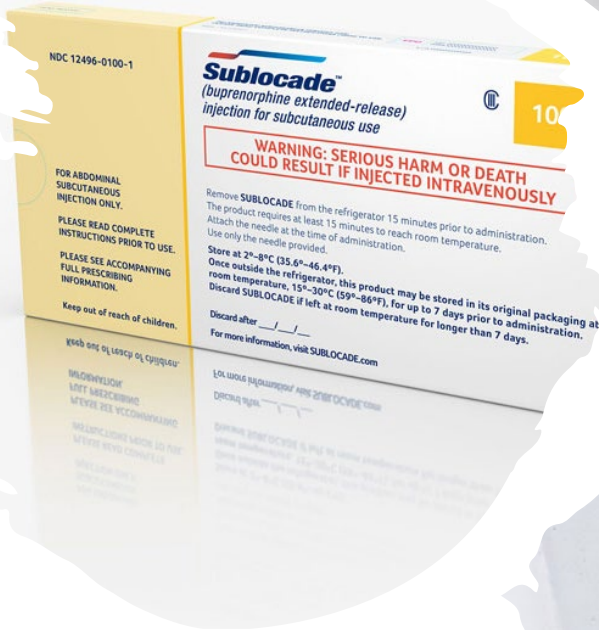
1. Methadone – full agonist therapy
   - Effective in certain patients, not patient centered, limited availability
2. Naltrexone – Antagonist therapy, generally long-acting IM
   - Effective but high barrier to initiate
   - Less realistic in the fentanyl era
3. Buprenorphine – partial agonist therapy
   - Lowest barrier to start
   - One of the most effective interventions for any disease
   - NNT for buprenorphine maintenance v placebo: **2**
     - 39 for Statins to prevent MI in those with known CVD
     - 50 for ASA for secondary prevention post-MI
     - 100 for anti-hypertensives to prevent MI

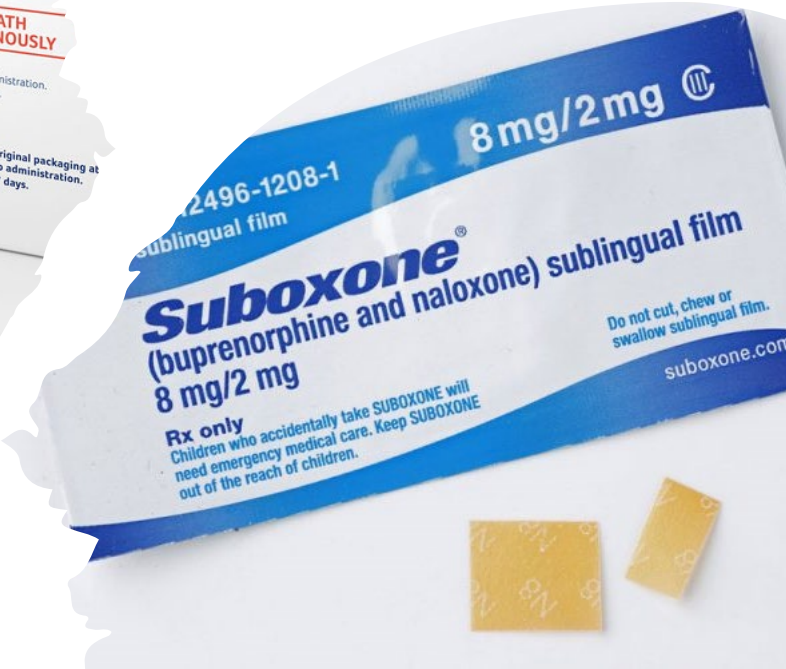
Buprenorphine

“effective…doesn’t just mean preventing death, which, on its own is pretty awesome. Suboxone erases need. It allows patients to swap the destructive cycle of addiction with the super-boring cycles of routine living. It doesn’t just prevent death; it fosters life”

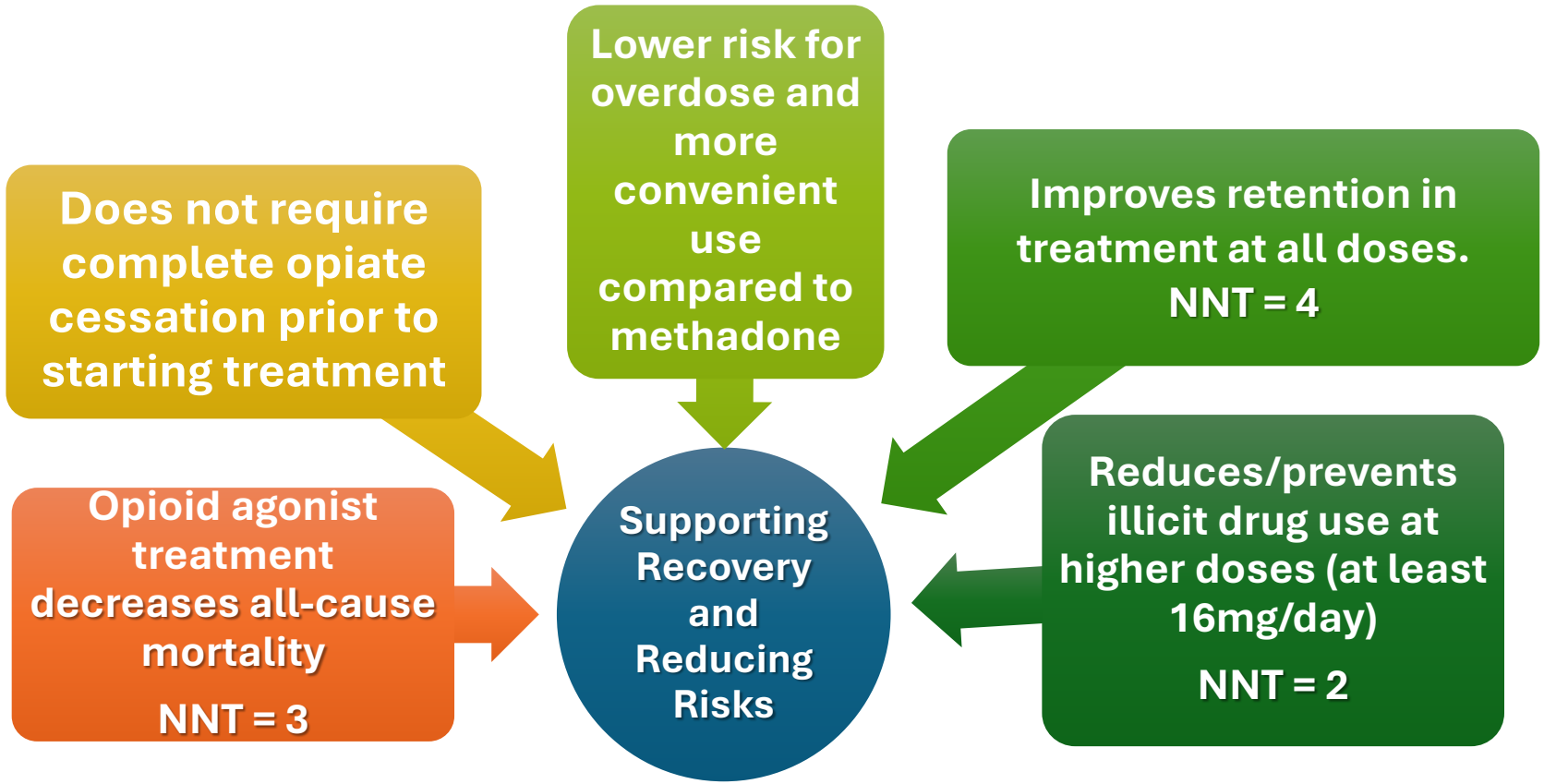
Ethan Brooks, *The Atlantic Aug 2024*



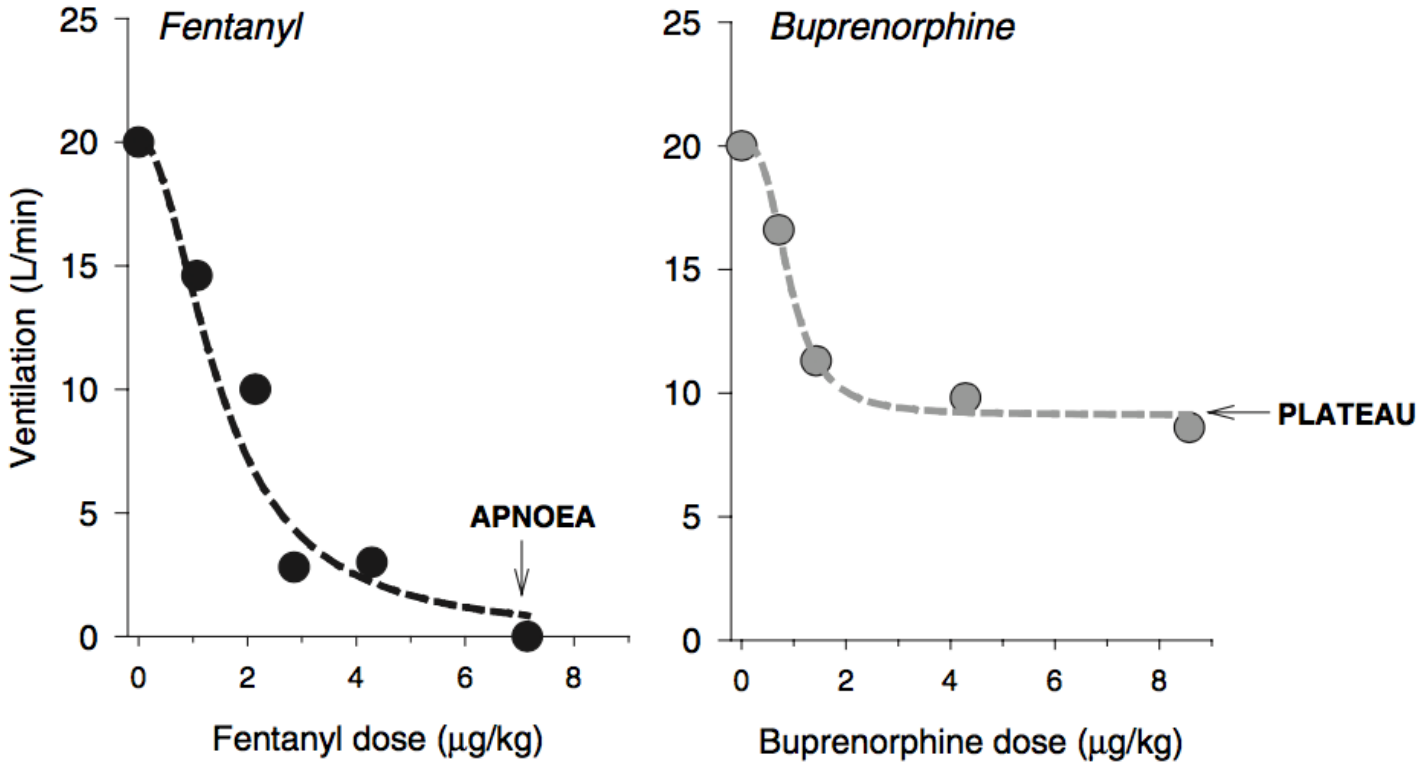




Buprenorphine



Buprenorphine is SAFE



Suboxone = Buprenorphine/Naloxone

- Combo formulation developed in attempt to decrease abuse
- Practically no difference between suboxone and buprenorphine only

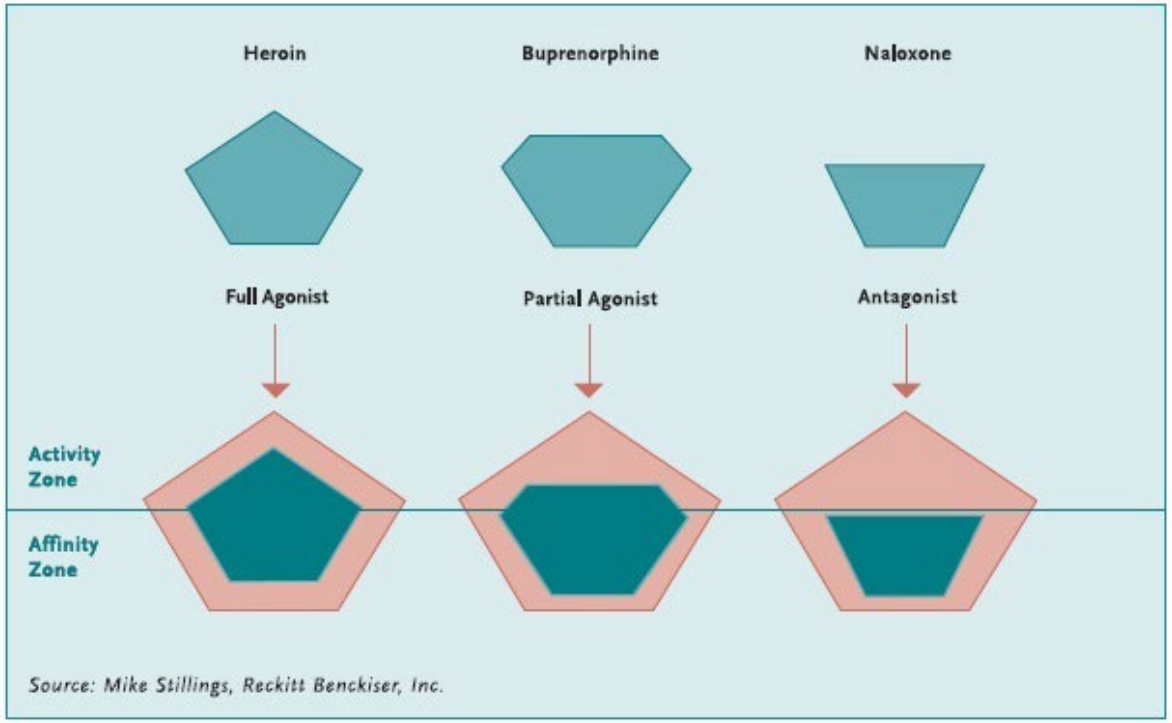
Buprenorphine

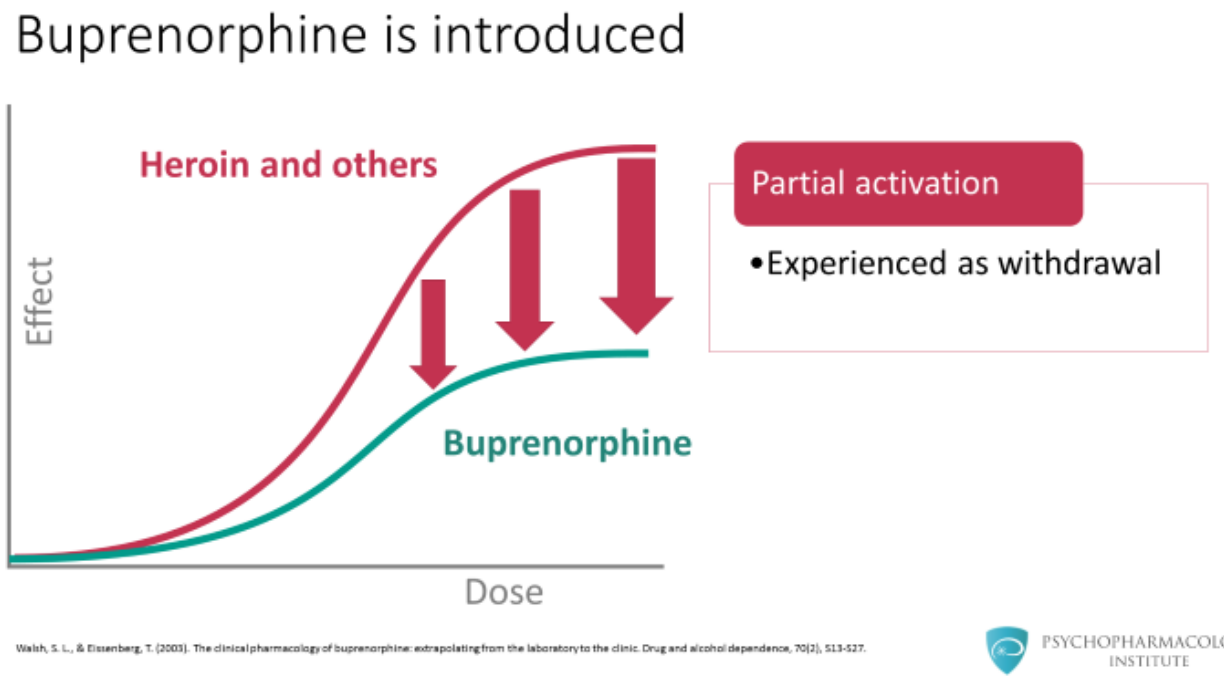
- Active ingredient when taken sublingually provides partial agonist effect
- Blocks use of other opioids
- Higher affinity for mu receptors
- May cause precipitated withdrawal in presence of other opioids

Naloxone

- Low sublingual bioavailability
- No clinical effects when taken sublingually
- If injected may precipitate withdrawal
- Not the cause of precipitated withdrawal when taken sublingually

“Precipitated Withdrawal”

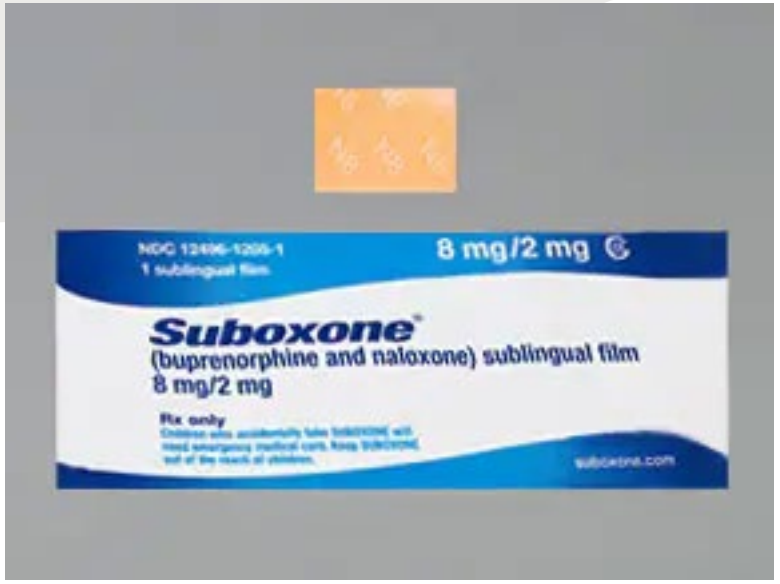




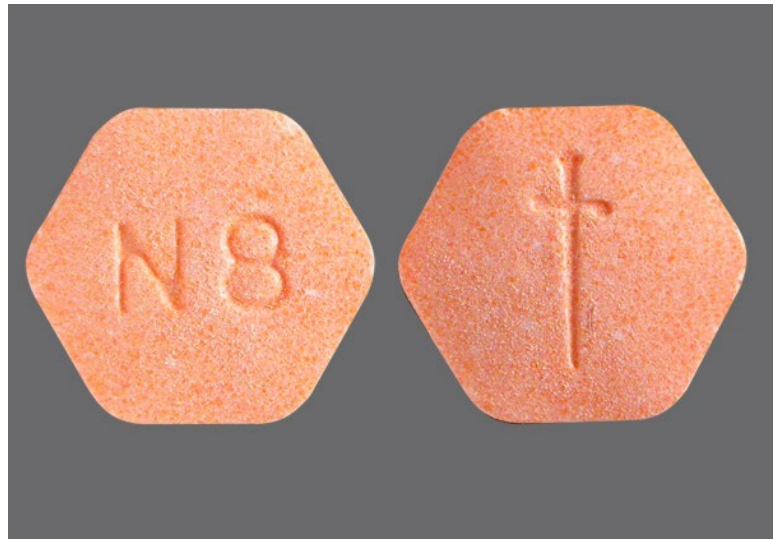
Walsh, S. L., & Eissenberg, T. (2003). The clinical pharmacology of buprenorphine: extrapolating from the laboratory to the clinic. Drug and alcohol dependence, 70(2), 513-527.

PSYCHOPHARMACOLOGY INSTITUTE

Dose Ranges



- Tabs and films come in 2,4, or 8mg formulations
- 8-16mg average dose range
- Doses are patient dependent
- Doses of 8-16mg effective in treatment retention
- >16mg doses more effective in reducing illicit drug use



- Recent data suggesting some patients need 24-32mg and this is helpful in retention

Initiating Buprenorphine

1. Diagnose OUD
2. Any other substances used? *Alcohol/benzos are NOT a reason to withhold buprenorphine*
3. Upreg on first visit +/- Utox
4. Review treatment history, experience with MAT in past
5. Review Prescription Monitoring Program
6. Review past medical/psych history
7. Offer screening for communicable diseases (HIV, RPR, Chronic Hep panel, GC/CT; PrEP?)
8. Review current opioid use and make clear to patient honesty is important to the success of treatment

“Induction”

CHECK COWS

- If >12 patient can start NOW
- If not in withdrawal, home “induction” is safe and indicated. No need to check COWS

Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-

COWS Clinical Opiate Withdrawal Scale

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 Pulse rate 80 or below 1 Pulse rate 81-100 2 Pulse rate 101-120 4 Pulse rate greater than 120	GI Upset: *over last 1/2 hour* 0 No GI symptoms 1 Stomach cramps 2 Nausea or loose stool 3 Vomiting or diarrhea 5 Multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 No report of chills or flushing 1 Subjective report of chills or flushing 2 Flushed or observable moistness on face 3 Beads of sweat *on* brow or face 4 Sweat streaming off face	Tremor *observation of outstretched hands* 0 No tremor 1 Tremor can be felt, but not observed 2 Slight tremor observable 4 Gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 Able to sit still 1 Reports difficulty sifting still, but is able to do so 3 Frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds	Yawning *Observation during assessment* 0 No yawning 1 Yawning once or twice during assessment 2 Yawning three or more times during assessment 4 Yawning several times/minute
Pupil size 0 Pupils pinned or normal size for room light 1 Pupils possibly larger than normal for room light 2 Pupils moderately dilated 5 Pupils so dilated that only the rim of the iris is visible	Anxiety or irritability 0 None 1 Patient reports increasing irritability or anxiousness 2 Patient obviously irritable anxious 4 Patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 Not present 1 Mild diffuse discomfort 2 Patient reports severe diffuse aching of joints/ muscles 4 Patient is rubbing joints or muscles and is unable to sit still because of discomfort	Gooseflesh skin 0 Skin is smooth 3 Piloerrection of skin can be felt or hairs standing up on arms 5 Prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 Not present 1 Nasal stuffiness or unusually moist eyes 2 Nose running or tearing 4 Nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing Assessment:_____

Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal

Home induction is normal

Scenario one:

Patient presents to clinic with COWS >12 (i.e. in active withdrawal)

- OR -

COWS <12 no self-reported opioid use in past 3 days (i.e. already detoxed)

- Patient can take 4-8mg once picked up from pharmacy
- Take initial dose per above, take 4mg as needed q4-6 hours day one up to max 16mg
- Day 2 patient takes single dose of 8mg in morning, repeat 4-8mg if needed in pm
- Day 3 take full day 2 dose in am

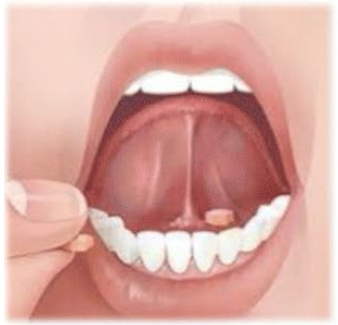
Home induction

Scenario two (most likely):
Patient presents to clinic with recent opioid use, NOT in withdrawal

- Educate on precipitated withdrawal. “when you start feeling sick, wait another 1-2 hours”
- Average time until withdrawal:
    - *Heroin or short acting pills* (oxycodone, hydrocodone): wait AT LEAST 12 hours
    - *Long acting pills* (morphine SR, oxyCONtin): wait at least 24 hours
    - *Fentanyl*…sort of depends
- Recommend consultation/referral for current methadone use

Once in withdrawal:
- 4mg buprenorphine, wait 1-2 hours, if feeling BETTER take another 4m
- 4mg every 4-6 hours as needed up to max 16 mg on day 1
- Day 2 patient takes single dose of 8mg in morning, repeat 4-8mg if needed in pm
- Day 3 take full day 2 dose in am

Buprenorphine in the Era of Synthetic Opioids



Day	Total dose
1	0.25 mg
2	0.5 mg
3	1 mg
4	2 mg
5	4 mg
6	8 mg
7	12 mg

Rozylo et al 2020

Urine Drug Screens

- Establish early NOT punitive
- Opportunity to explore use of other substances and referrals
- Unlike with narcotic chronic pain management **opioids and other substances in urine are NOT an indication to stop treatment**
- Bup screens early on and randomly if necessary

- Treatment of OUD should be like any chronic disease management. Remember, Harm Reduction!
  - Do you stop Lasix in patients eating salty food?
  - Do you stop Insulin in diabetics who continue to eat carbs?

Follow up

- Weekly to bi-weekly visits for first 1-2 months – can be phone check ins
- Patients should be seen at minimum monthly for first 3 – 6 mos
- YOU can provide office-based MI as counseling, data shows bup is effective without adjunctive counseling
- Consider NA, outpatient programs for additional support
- Clinic nurses or other staff to check in/answer questions outside of visits

MAT for Alcohol Use Disorder (AUD)

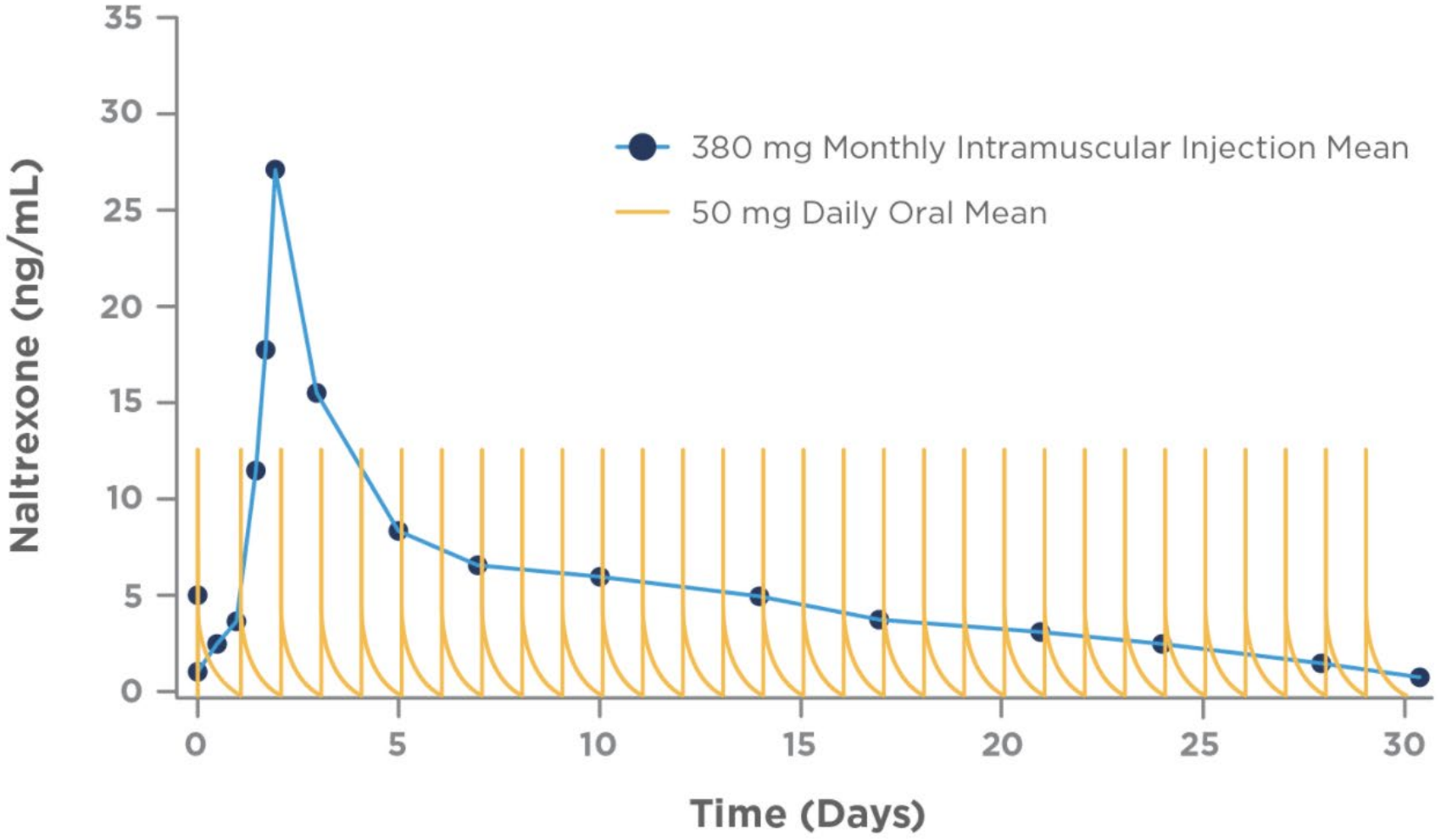
Naltrexone

- Daily pill or monthly shot (vivitrol)
- Reduces cravings for alcohol
- Reduces total drinking days, median drinks per day and number of heavy drinking days (NNT 12)
- Increases abstinence rates, percentage of days abstinent, length of continuous abstinence, time to first drink and time to first heavy drinking day (NNT 20)
- Recent meta-analysis of studies assessing effectiveness of IM naltrexone compared to oral naltrexone shows:
  - Reduction in heavy drinking days, longer refill persistence and longer medication persistence with XR-NTX

Side Effects/Contraindications for Naltrexone

- Side effects may include injection site pain for IM, nausea and headaches (5-10%) and flu-like syndrome in small number of patients and these symptoms self-resolve
- Ensure no co-occurring OUD
- Possibility of increase in LFTs (only 2% in largest studies)
- Not recommended if AST/ALT > 5X upper limit of normal
- LiverTox database assigned drug grade E, which is the lowest likelihood score for DILI; a score that reflects suspected, unproven correlation.
- I give it regardless of LFTs/cirrhosis, unless there is severe acute hepatitis
- Not recommended in pregnancy, though weigh risk/benefit

▶ MEAN NALTREXONE CONCENTRATION[1-3]



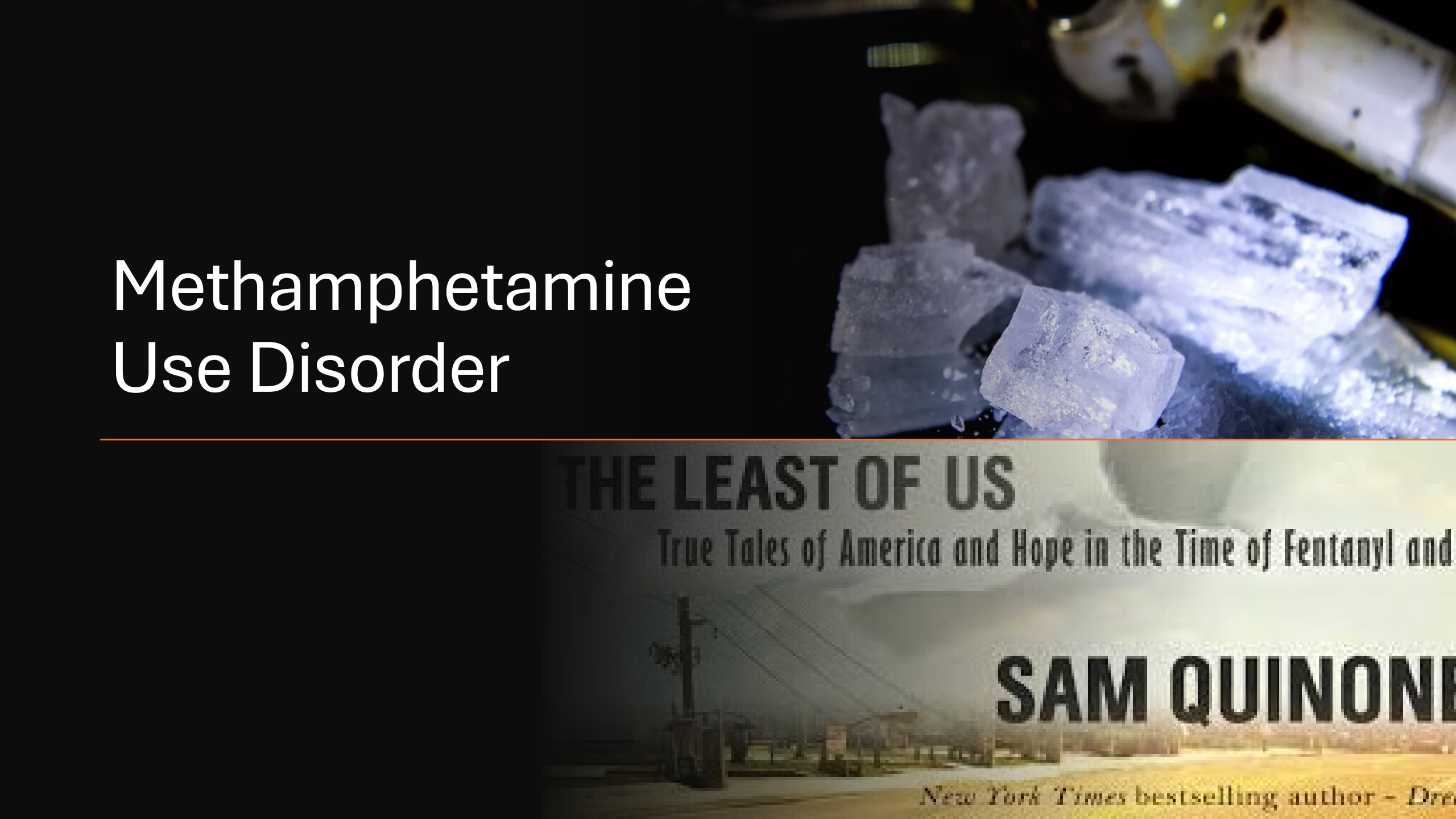
Acamprosate

- Glutamate modulator that depresses NMDA receptor activation
- Most effective in patients in a period of abstinence
- NNT 12 to prevent return to heavy drinking
- Two pills three times daily, difficult dosing for compliance
- Excellent SE profile
- Contraindicated in severe renal dysfunction

Other Treatment Options

- Gabapentin
- Disulfiram
- Topiramate
- Alcoholics Anonymous
- Other 12-step programs
- Counseling
- Intensive outpatient program
- Residential treatment/Detox

Methamphetamine Use Disorder



There are no FDA approved treatments for amphetamine-type substance use disorder

MAT for Methamphetamine Use

- Unlike with opioids and alcohol, fewer medications with benefit
- Bupropion/IM Naltrexone combo
  - Most effective MAT to date
  - Reduces cravings and meth use
  - NNT to reduce use is 9
- Mirtazapine, methylphenidate
- Behavioral interventions are the mainstay of treatment
- Many patients require treatment with antipsychotics for poor sleep, paranoia and disorganized thoughts

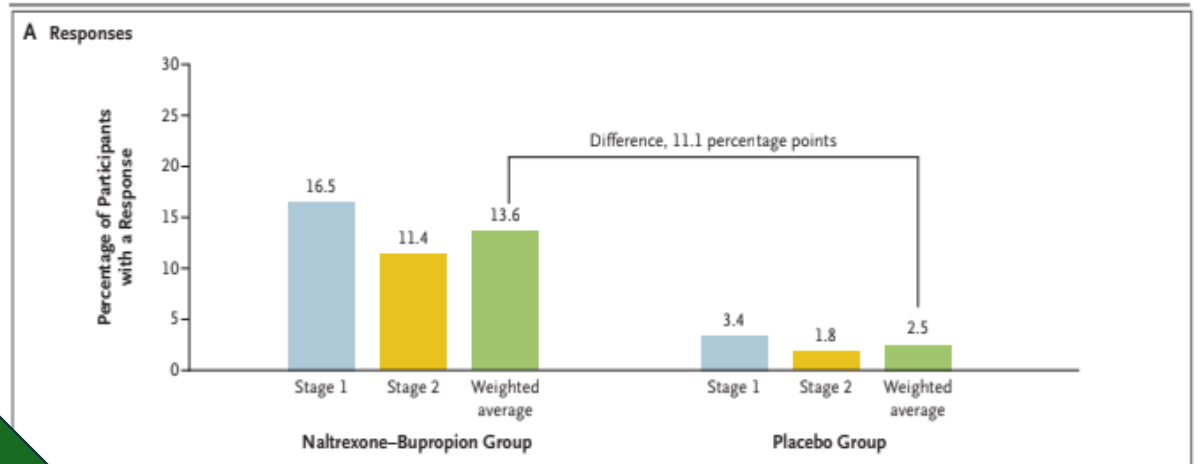
The NEW ENGLAND JOURNAL of MEDICINE

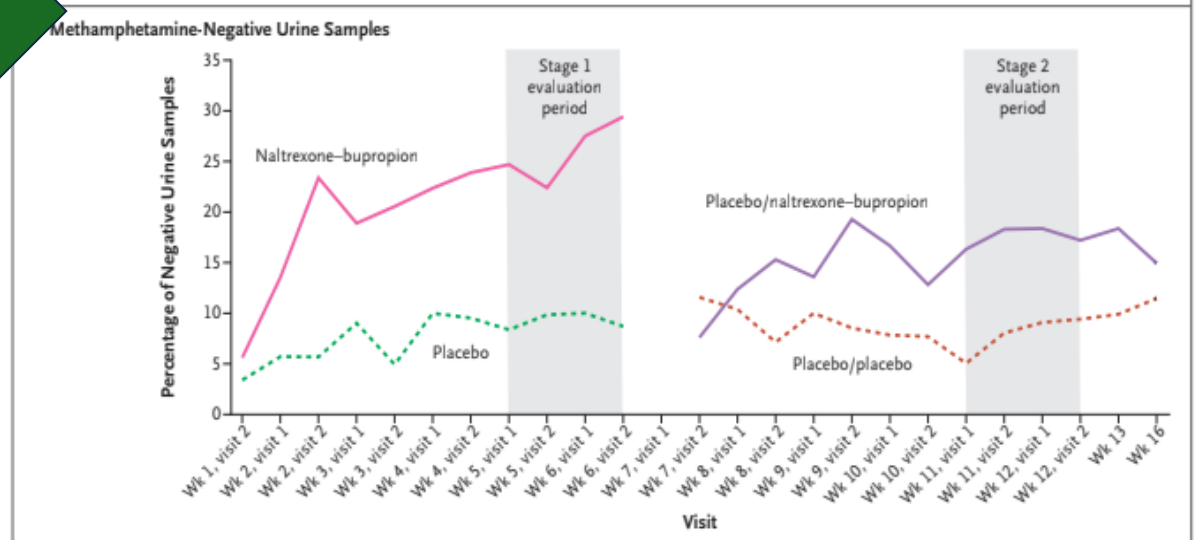
ORIGINAL ARTICLE

Bupropion and Naltrexone in Methamphetamine Use Disorder

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

NNT is 9!!





No. of Urine Samples Obtained at Each Visit	Stage 1											Stage 2											
Naltrexone–bupropion	89	96	77	90	73	85	67	81	67	80	68												
Placebo	265	280	229	266	223	260	210	239	203	240	207												
Placebo/naltrexone–bupropion												92	97	85	103	83	96	78	98	82	98	93	98	87
Placebo/placebo												95	106	84	100	82	102	91	99	87	99	85	101	96

Statistically significant response to treatment but still overall low percentage with response (13.6%) and 11% difference in percentage points

MAT for Tobacco Use

- Varenicline (Chantix)
  - Most effective treatment
  - Decreases desire to smoke
  - Best when combined with NRT
  - Prior FDA concerns of psychiatric side effects have been refuted
- Bupropion
  - Modestly effective
  - Best when combined with Varenicline
  - Limited by SE profile
- Nicotine Replacement Therapy
  - Nicotine patches, gum, lozenges
  - Slowly lower dose and taper off
  - Less effective for long term cessation when used alone

DATION FOR MEDICAL EDUCATION AND RESEARCH. ALL RIGHTS RESERVED.

Cannabis Use Disorder

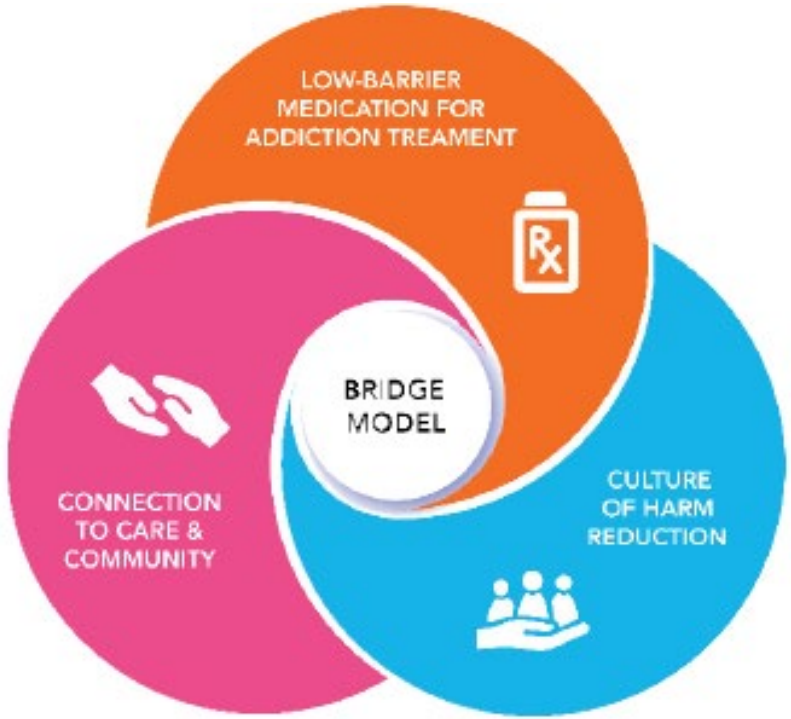
- Average THC levels in cannabis flowers 5-6x higher in past 25 years
- Concentrated products may be as much as 18x higher
- Higher THC levels related to multiple health issues
    - Hyperemesis
    - Psychological disorders

Cannabis Use Disorder

- Psychosocial interventions cornerstone if treatment
- Counseling by PCP shown benefit for adolescents
- CBT/MI
- MAT limited
- Reduced cravings and withdrawal with gabapentin in adults
- N-acetylcysteine in adolescents
- Dronabinol may be helpful to manage withdrawal
- Quetiapine for withdrawal symptoms

What we are doing at Whiteriver IHS

- Bridge Clinic
- IM Naltrexone in the ER and inpatient unit
- ER buprenorphine
- Substance Use Navigators



https://bridgetotreatment.org/

Questions?

joseph.mega@ihs.gov

Citations

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