WELCOME TO
AK LIVER DISEASE ECHO

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

NPAIHB
Indian Leadership for Indian Health

This project is supported by a grant from the Northwest Portland Area Indian Health Board and funding is provided from the HHS Secretary's Minority HIV/AIDS Fund.

PLEASE PUT IN THE CHAT BOX:

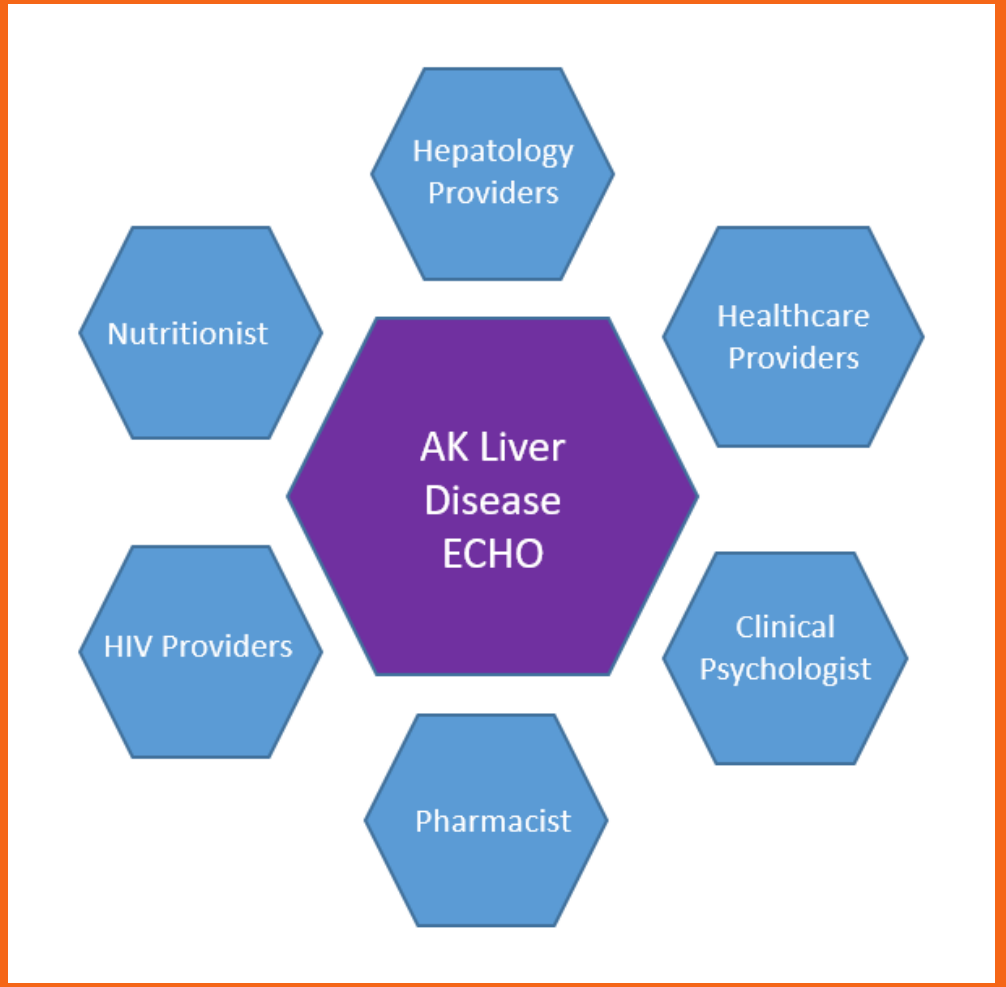
Your name
Where you are located
What brings you to the LD ECHO today

WHAT WE DO

- Didactic Presentations pertaining to ECHO topics
- We're accepting **case presentations and questions pertaining to:**
  - Elevated Liver Function Tests
  - Cirrhosis
  - Managing Complications of Decompensated Cirrhosis – Ascites, encephalopathy, esophageal varices
  - Alcohol-related liver disease, including Alcohol Hepatitis
  - Autoimmune liver disease – Autoimmune Hepatitis, Primary Biliary Cholangitis, Overlap
  - Nonalcoholic fatty liver disease/Nonalcoholic steatohepatitis
  - Hepatocellular carcinoma
- Provide Expert Panelists

CONSULTANT TEAM

- Brian McMahon, MD Hepatologist
- Youssef Barbour, MD Hepatologist
- Lisa Townshend, ANP Hepatology Provider
- Annette Hewitt, ANP Hepatology Provider
- Leah Besh, PA-C HIV/Hepatology Provider
- Anne Fleetwood, MS, RDN, NDN
- Brittany Keener, PharmD, MPH, BCPS
- Kena Desai, MD, Internal Medicine Specialist



Welcome to Alaska Liver Disease ECHO

Approved Provider Statements:

JOINTLY ACCREDITED PROVIDER™
INTERPROFESSIONAL CONTINUING EDUCATION

In support of improving patient care, Alaska Native Medical Center (ANMC) is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Contact Hours:

ANMC designates this activity for a maximum of 12 contact hours, including 3 total pharmacotherapeutics contact hours, commensurate with participation.

Financial Disclosures:

Youssef Barbour, MD & Lisa Townshend-Bulson, APRN / faculty for this educational event, are primary investigators in an ANTHC sponsored hepatitis C study funded in part by Gilead Sciences. All of the relevant financial relationships listed have been mitigated.

Requirements for Successful Completion:

To receive CE credit please make sure you have actively engaged in the entire activity, your attendance is recorded by the facilitator, and complete the course evaluation form found here: https://forms.gle/R8vibUZgMbRcoScw9.

For more information contact
jlfielder@anthc.org or (907) 729-1387

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

LIVER DISEASE ECHO SCHEDULE AT A GLANCE

- December 15 - HCC Surveillance – Are We Doing Enough?
- Survey to help plan 2023 sessions

ANTHC Liver Connect Nov 2022

Update on Medications for Addiction Treatment

Objectives

- Discuss new recommendations and common misconceptions around the treatment of opioid and alcohol use disorders
- Review efficacy of MAT for reducing mortality and expected course of disease including relapse and length of treatment needed
- Explore the regulations related to prescribing buprenorphine
- Explore novel dosing and formulations of buprernophine
- MAT for stimulant use

Financial Disclosures

- I have no financial conflicts of interest to disclose

- I am currently employed by the Ninilchik Traditional Council

- I work as a treatment consultant for the Opioid Response Network in Alaska, ANTHC, as well as for other non-profit agencies.

http://dhss.alaska.gov/dbh/Pages/Initiatives/EvidenceBasedPractices/MAT.aspx

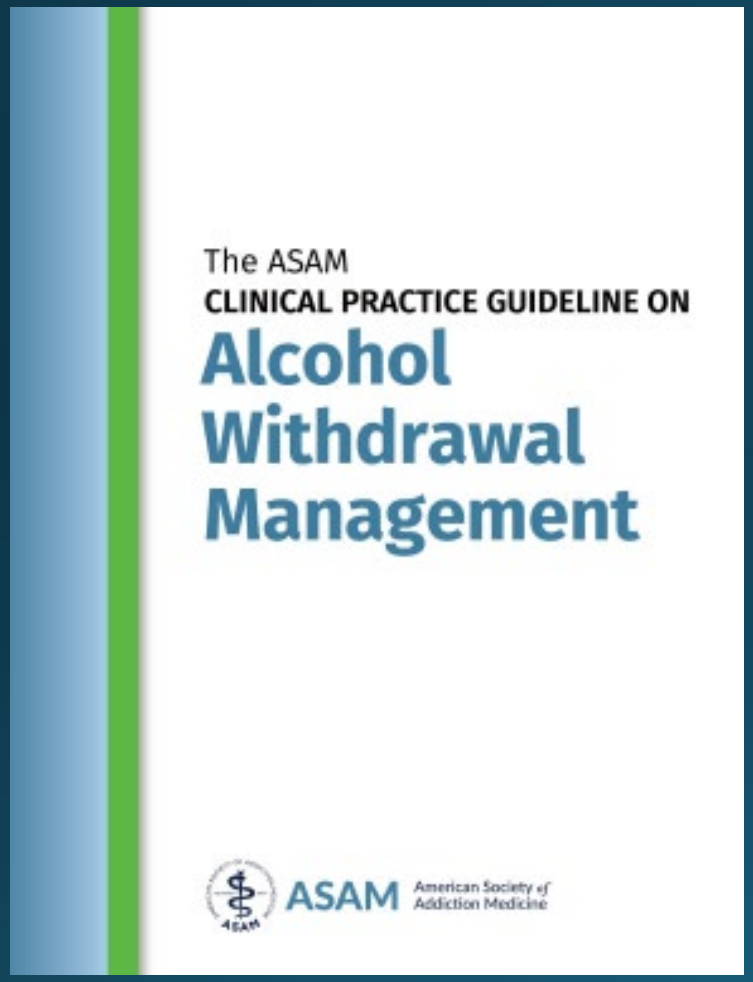
The ASAM

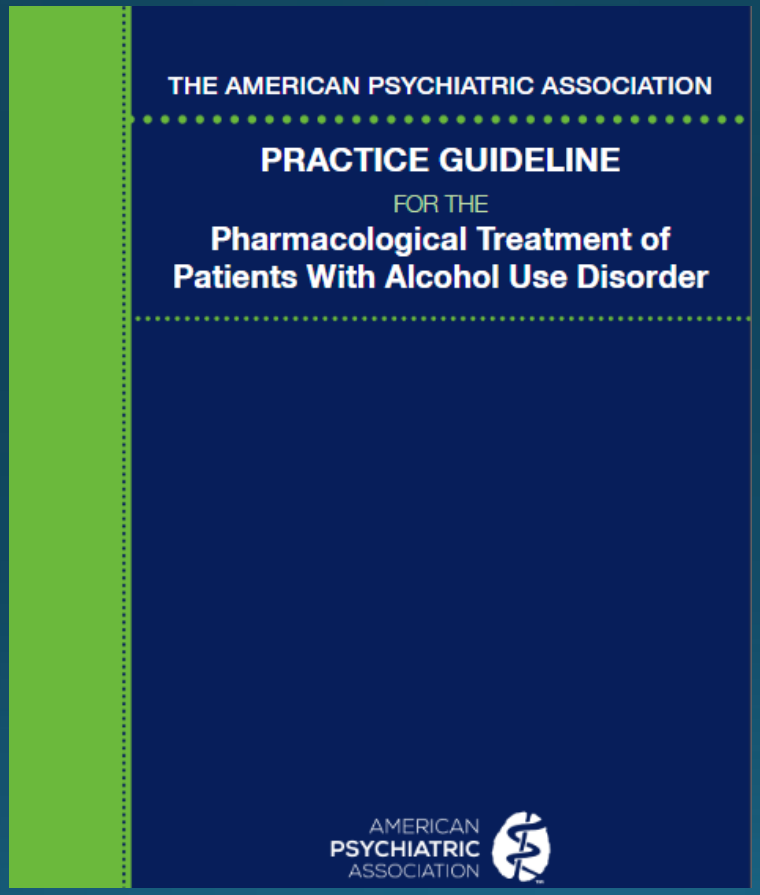
NATIONAL PRACTICE GUIDELINE

For the Treatment of Opioid Use Disorder

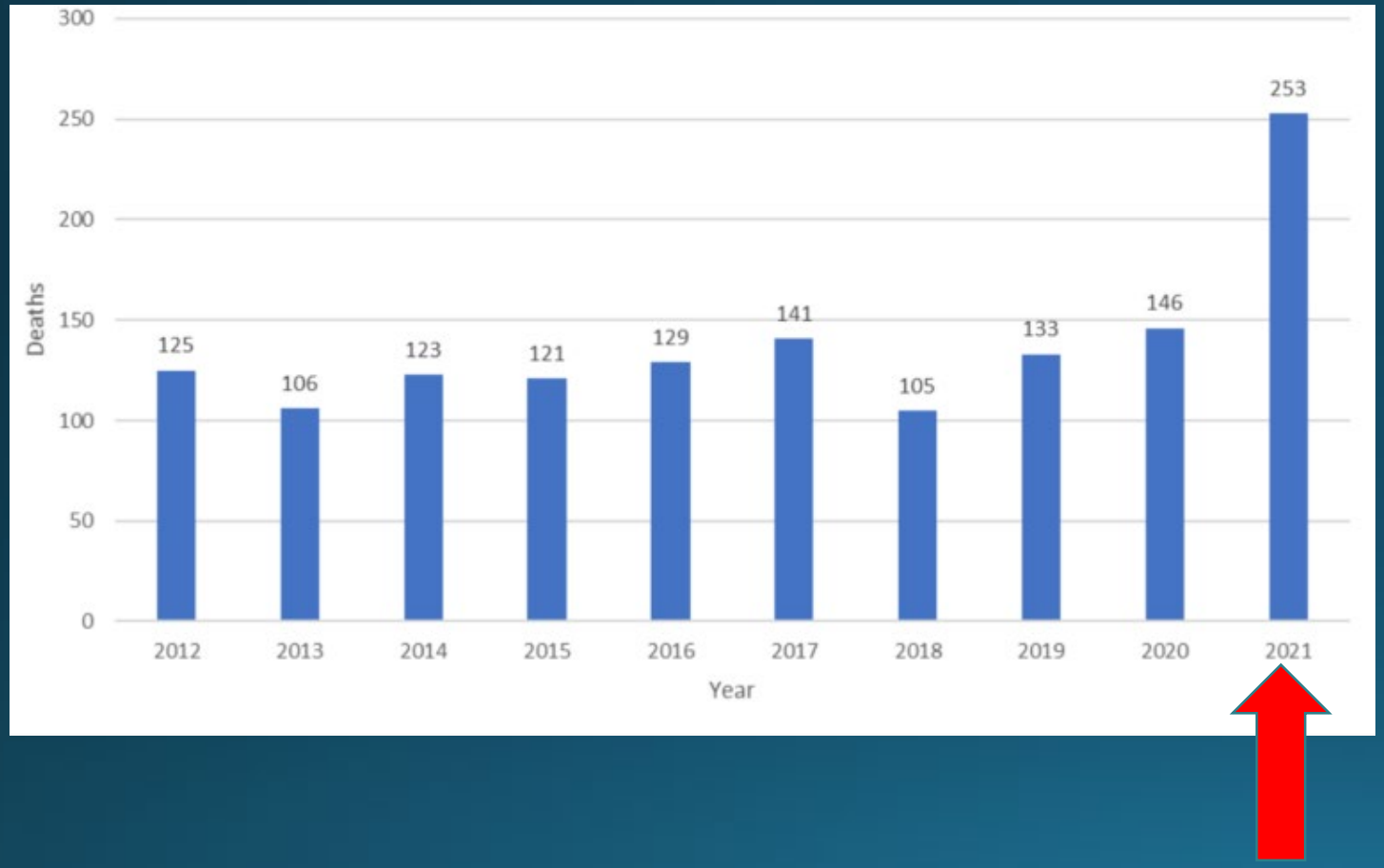
2020 Focused Update

NATIONAL PRACTICE GUIDELINES





Overdose deaths in Alaska rose by 75% in 2021, highest increase nationwide



- Alaskan Natives
OD rate 77/110K

- White
OD rate 28/100K

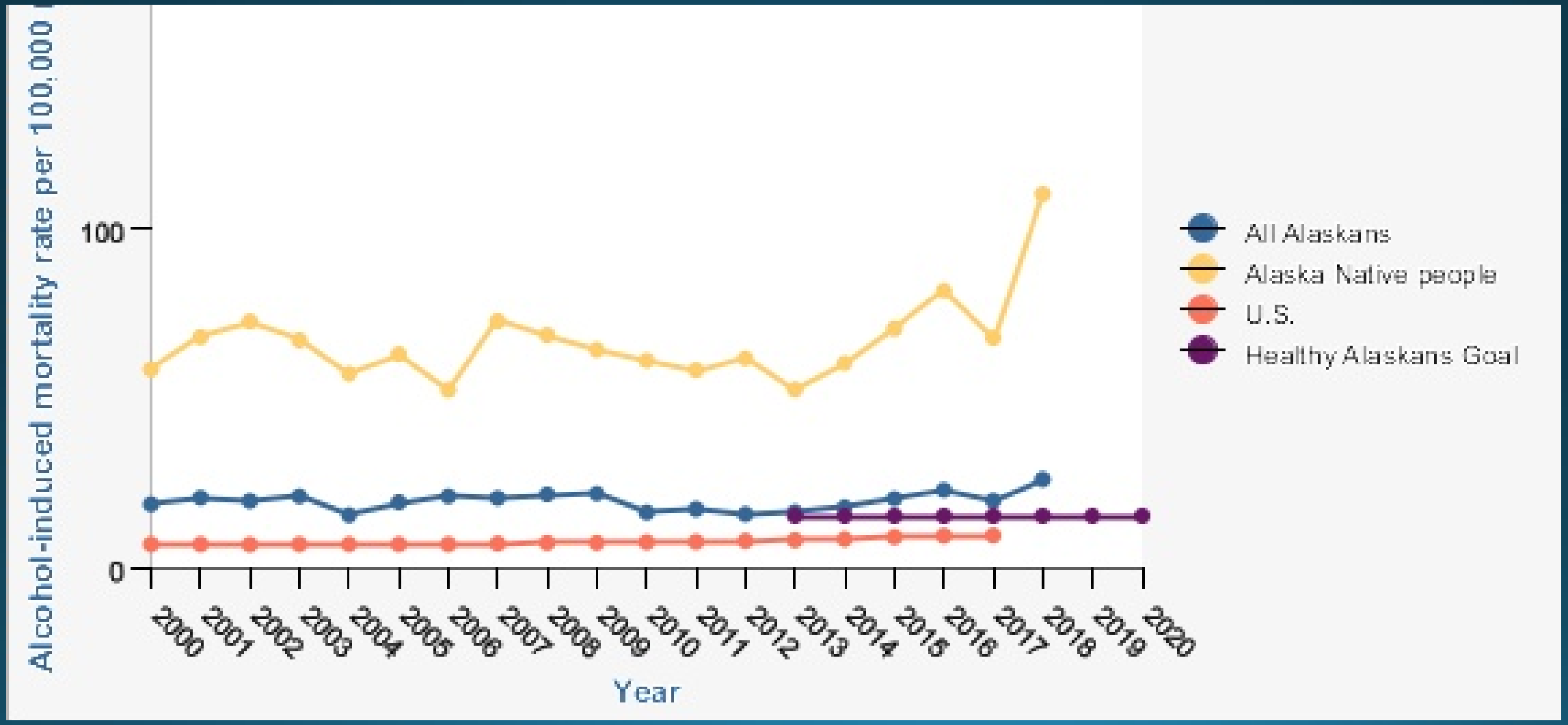
- Meth OD up 150%

- Fentanyl OD up 150%

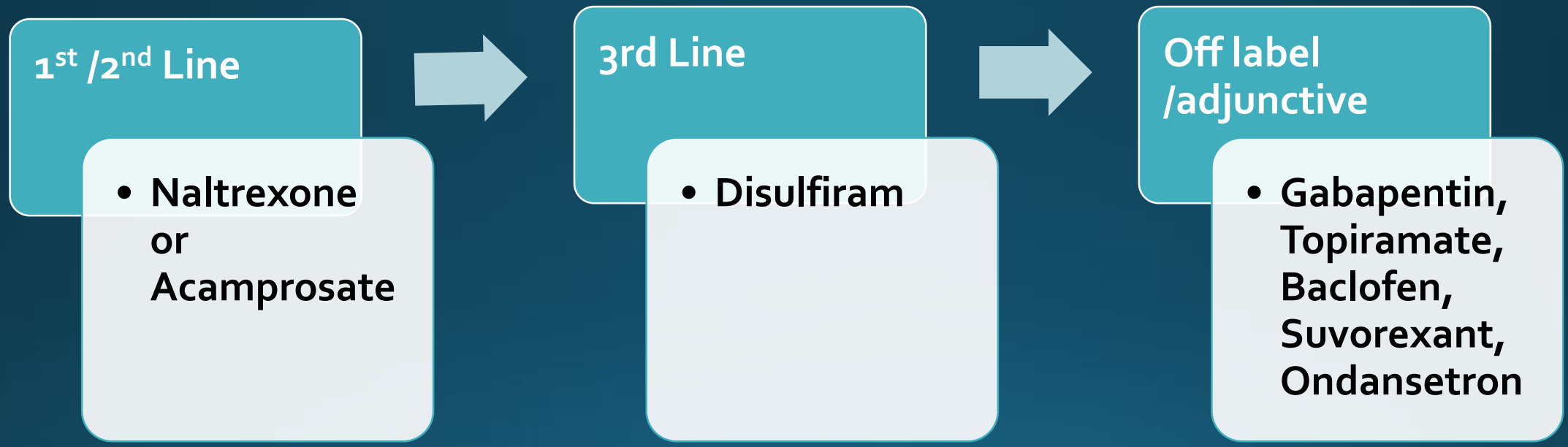
https://health.alaska.gov/dph/VitalStats/Documents/PDFs/DrugOverdoseMortalityUpdate_2021.pdf

cdc.gov/alcohol

Alaska Native people at 110.3 per 100,000 had rates of alcohol-induced mortality that were 8 times higher than those experienced by non-Hispanic whites at 13.0 per 100,000 in 2018



Medications for Alcohol Use Disorder (AUD) treatment



Naltrexone

Mu receptor antagonist, interrupts the reward pathways in the brain

Dosing 50-100 mg po daily, or 380 mg IM monthly

Hold for LFT >5 times normal, OK in cirrhosis as long as compensated and no acute failure

Nausea is most common side effect (also watch for depression)

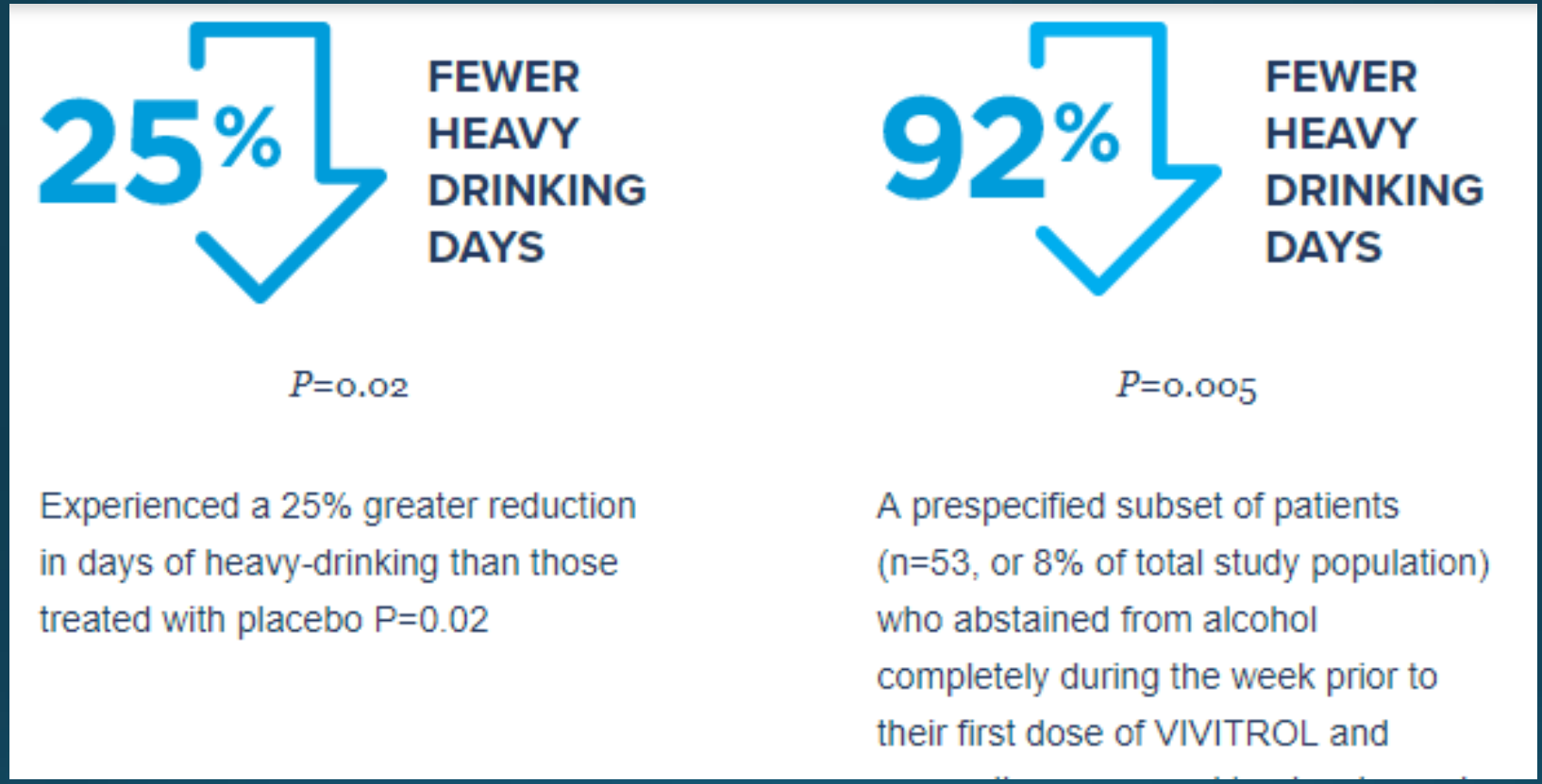
Off Label use: dosed prn prior to anticipated drinking episode

The utility of naltrexone is the ability of the drug to reduce cravings for alcohol and to result in a reduction in the amount of alcohol consumed per sitting.

Using naltrexone alone does not generally result in abstinence from alcohol

Naltrexone does not block the intoxicating effects of alcohol or cause unpleasant side effects when patients drink

XR Naltrexone (Vivitrol)



0.2 heavy-drinking days on Naltrexone vs 2.5 heavy-drinking days on placebo

The same results were not seen in the subset of patients (n=571, or 92% of the total study population) who were actively drinking at the time of starting treatment.

ACAMPROSATE

Modulates overactive GABA activity that occurs with alcohol cessation (more effective if patient has stopped drinking)

May be particularly helpful in patients whose cravings are triggered by anxiety symptoms, can help with insomnia

Dose 333 mg 2 pills TID → compliance difficulties

Renal dosing: for CrCl 30-50 cut reduce dose by half
avoid in CrCl <30
Most common side effect is diarrhea (in early treatment)

No significant drug-drug interactions

Acamprosate was shown only to support abstinence; it did not influence alcohol consumption after the first drink. When the efficacy profiles of the two drugs were compared, acamprosate was found to be more effective in preventing a lapse, whereas naltrexone was better in preventing a lapse from becoming a relapse. (Rosner 2018)

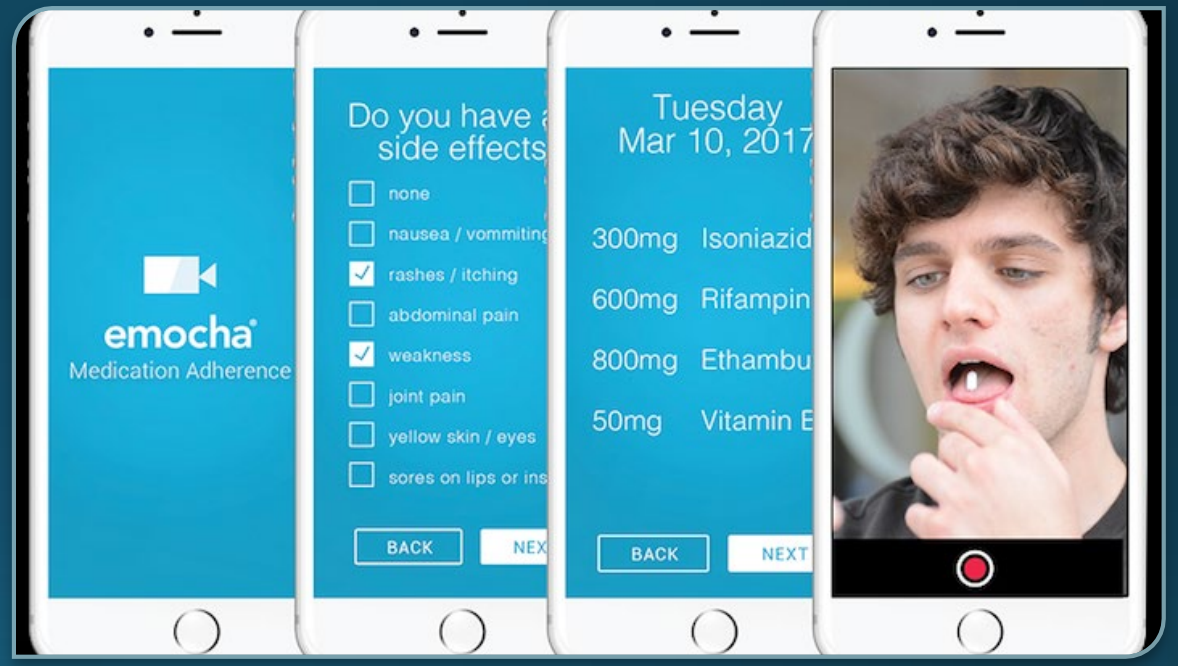
Acamprosate had a significantly larger effect size than naltrexone on the maintenance of abstinence, and naltrexone had a larger effect size than acamprosate on the reduction of heavy drinking and craving. For naltrexone, requiring abstinence before the trial was associated with larger effect sizes for abstinence maintenance and reduced heavy drinking compared with placebo. For acamprosate, detoxification before medication administration was associated with better abstinence outcomes compared with placebo. (Maisel 2013)

DISULFIRAM

- Enforces abstinence through accumulation in acetaldehyde inducing unpleasant side effects if alcohol is consumed (nausea, vomiting, flushing, tachycardia, hypertension)
- Dose 250-500 mg po qd
- Many drug-drug interactions (benzos, warfarin, metronidazole, rifampin)
- Consider avoiding in patients with severe CAD/autonomic dysfunction
- Monitor for worsening neuropathy and liver dysfunction (rare)

DISULFIRAM

- Limited evidence for efficacy (poor compliance)
- Establish plan for directly observed therapy (family member or App)
- Monitor for signs of return to use



Off-Label MAT for AUD

Topiramate: GABA mediated neuronal inhibition, start at 25 mg/d, increase by 25-50 mg weekly to 300 mg/d,

Gabapentin: balances GABA/glutamate dysregulation, 600 mg tid,

Ondansetron: serotonin receptor type 3 antagonist, 0.2 mg bid

Baclofen: GABA receptor antagonist, 5mg tid, titrate to 20 mg tid, preferred in cirrhosis

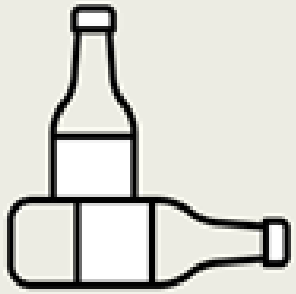
Suvorexant: dual orexin receptor antagonist, for co-morbid AUD and insomnia

JAMA Psychiatry

RCT: Psilocybin-Assisted Treatment of Alcohol Use Disorder

POPULATION

53 Men, 42 Women



Adults with alcohol dependence

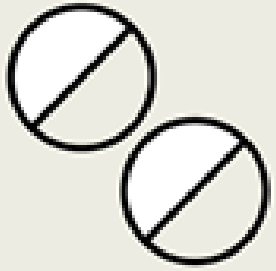
Mean age, 45.8 y

SETTINGS / LOCATIONS

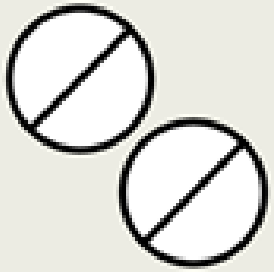
2 Academic centers in New York and New Mexico

INTERVENTION

95 Individuals randomized



49 Psilocybin
Administered orally in 2 all-day sessions (dose range, 25-40 mg/70 kg)



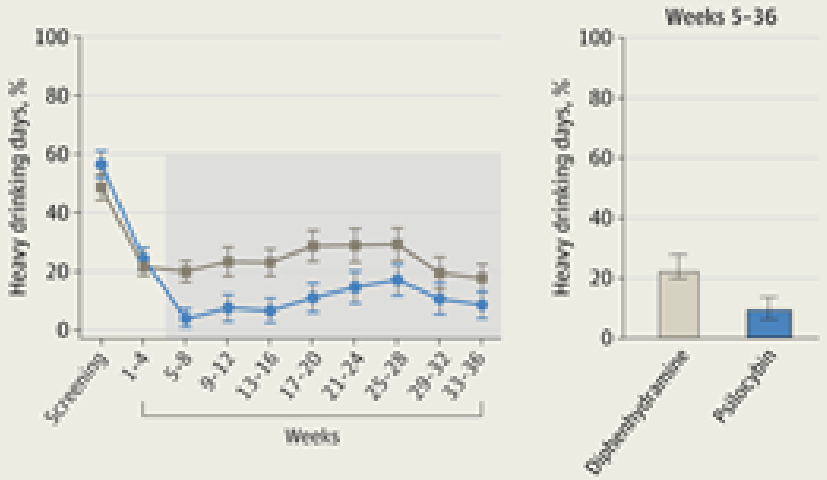
46 Diphenhydramine control
Administered orally in 2 all-day sessions (dose range, 50-100 mg)

PRIMARY OUTCOME

Percent heavy drinking days (scale, 0-100), assessed using the timeline followback interview, contrasted between groups over the 32-wk period following the first administration of study medication.

FINDINGS

Percent heavy drinking days during the 32-wk double-blind period was lower in the psilocybin group compared with the diphenhydramine group



Percent heavy drinking days
Psilocybin=9.7%
Diphenhyramine=23.6%

Mean difference, 13.9 (95% CI, 3.0-24.7; *P* = .01)

Bogenschutz MP, Ross S, Bhatt S, et al. 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. *JAMA Psychiatry*. Published online August 24, 2022. doi:10.1001/jamapsychiatry.2022.2096

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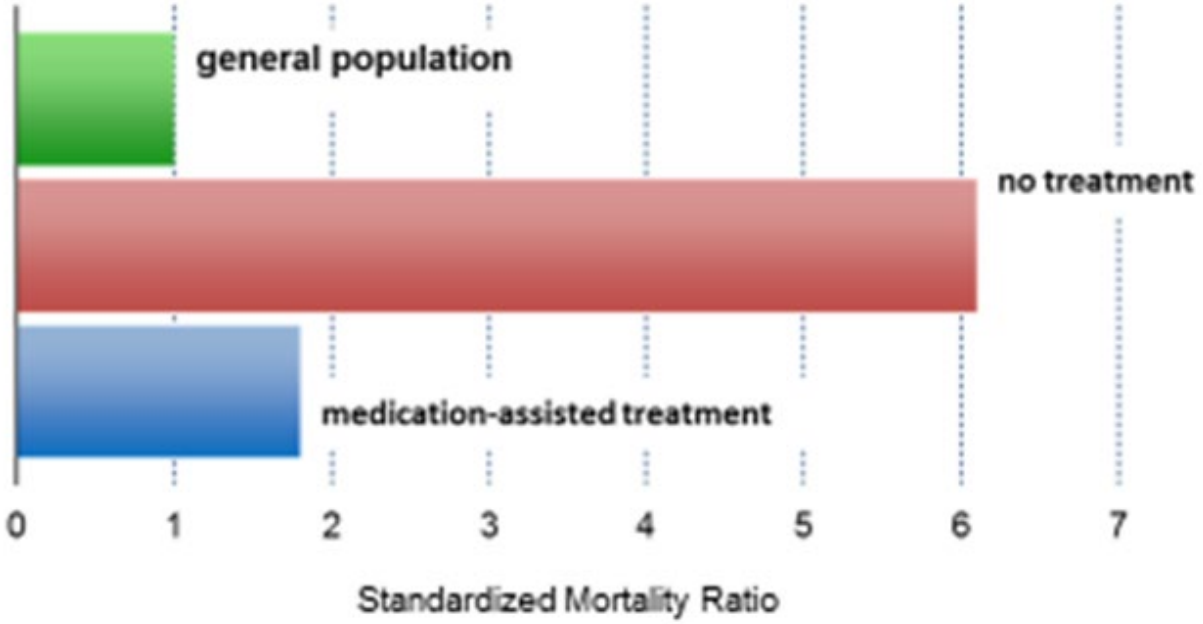
Medication for Opioid Use Disorder (MOUD)

Benefits of MAT: Decreased Mortality

Overdose risk the first 2 weeks after leaving treatment is 10-30 times higher

Death rates:



MOUD can reduce death rates by 80%

Dupouy et al., 2017
Evans et al., 2015
Sordo et al., 2017

PCSS Providers Clinical Support System

Features of Methadone

- Full opioid agonist
- Stimulates opioid receptors to reduce cravings and illicit opioid use
- Provides some opioid blockade at higher doses
- Available only at an opioid treatment program (Methadone clinic), daily observed dosing (ANC, Mat-Su, Fairbanks)
- Long acting, once daily dosing
- OTP provides counseling and social support services with methadone
- Many drug-drug interaction and QT prolongation
- Also treats chronic pain
- Best retention in treatment of all forms of MAT

Features of Naltrexone

- Opioid Antagonist
- Binds strongly to opioid receptors and blocks opioids from binding
- Monthly injection (Do not use oral naltrexone for OUD)
- Not a controlled substance, no physical dependence
- Requires 1-2 weeks of opioid abstinence before 1st injection
- Inpatient withdrawal management can increase success with initiation
  - Still 30% failure to initiate medication
  - Once patient successfully inducted, abstinence rates may be similar to OAT in selected patients

The least commonly used medication to treat OUD so there is less evidence for effectiveness/retention

Naltrexone does not provide any agonist effect so it cannot cause intoxication or euphoria or be abused, and there is no physical dependence on the medication, so it can be discontinued without withdrawal syndrome.

Thus, Naltrexone does not provide any positive or negative reinforcing effects.

Patients do not feel any better when they take the medication.

Patients do not feel any worse if they skip their medication.

<u>This can result in poor retention in treatment</u>

especially in patients with severe OUD

Rewards for medication compliance (contingency management), can increase retention in treatment in high-risk groups.

Not as effective to reduce overdose risk

Pharmacology of Buprenorphine

Buprenorphine is a partial opioid agonist/antagonist

Treats withdrawal symptoms and minimizing cravings = positive reinforcement

- The agonist effects of buprenorphine reach a **plateau** and no longer continue to increase with further increases in dose—the "ceiling effect."
  - **lower risk of abuse, addiction, and side effects** compared to full opioid agonists.
  - Maximal effects are less than those of full agonists like heroin and methadone, **Hard to get "high" off it**
- Buprenorphine binds very tightly to the opioid receptor and **blocks other full agonists from binding** and can precipitate withdrawal symptoms if administered to an opioid-dependent individual while a high dose of full agonist is in the bloodstream.
- **Kappa antagonist: Antidepressant effect**

RECOVERY RESEARCH INSTITUTE

MGH 1811

Even 3 years into treatment, patients that stay on their medication have 2/3 less relapse
5 years in have ½ the relapse rate

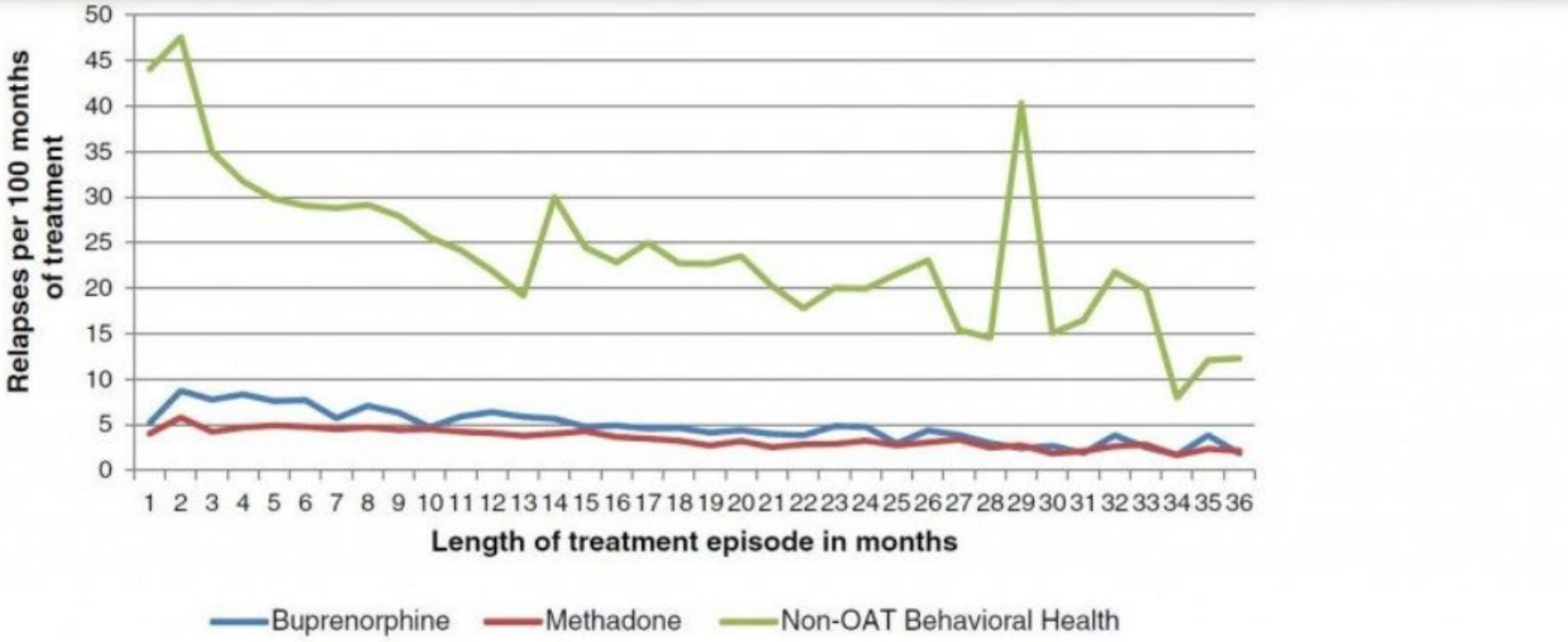


Fig. 1. Relapses during treatment among MassHealth members who received treatment for opioid addiction between 2003 and 2010[1]. [1] N = 18,866 episodes of buprenorphine treatment, 24,309 episodes of methadone treatment and 31,220 episodes of non-OAT behavioral health treatment in month 1. 33% of buprenorphine episodes, 52% of methadone episodes, and 12% of non-OAT treatment episodes lasted 12 months or more. 13% of buprenorphine treatment episodes, 27% of methadone episodes, and 1% of non-OAT treatment episodes lasted 24 months or longer.

Buprenorphine Prescribing Regulations

New Practice Guidelines Allow Expanded Access to Treatment for Patients with Opioid Use Disorder

On April 27, 2021, the US Department of Health and Human Services (HHS) announced *Practice Guidelines for the Administration of Buprenorphine for Treating Opioid Use Disorder* to expand patient access to buprenorphine (Buprenex®, Suboxone®, Subutex®) for the treatment of opioid use disorder. Buprenorphine treatment for opioid use disorder reduces overdose and overdose deaths, and significantly increases positive outcomes for people with opioid use disorder.[1]

HHS's updated practice guidelines were made effective April 28, 2021. Key highlights include:

Eligible Healthcare Providers:

- Practitioners who are eligible to prescribe buprenorphine under this revised guideline include physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, and certified nurse midwives who are licensed under State law and possess a Drug Enforcement Administration (DEA) registration to prescribe controlled substances.

Exemption from Mandatory Training:

- Exempts the training requirements for eligible practitioners to treat up to 30 patients at any one time.

Exemption from Mandatory Training:

- Exempts the training requirements for eligible practitioners to treat up to 30 patients at any one time.

Exemption from Referral to Counseling and Ancillary Services:

- Eliminates the counseling and ancillary services referral requirement for practitioners who treat up to 30 patients.

Continued Registration with the Substance Abuse and Mental Health Services Administration (SAMHSA) and the DEA:

- Under this exemption, providers are still required to submit a Notice of Intent to obtain an "X-waiver" to prescribe buprenorphine for the treatment of opioid use disorder. *Please note: It will require 45 days for SAMHSA to process these notifications.*
- Buprenorphine prescriptions will still need to have an x-number listed on them.

For additional details, please reference SAMHSA's *FAQs About the New Buprenorphine Practice Guidelines* and the full announcement here.

Apply for your waiver at: https://buprenorphine.samhsa.gov/forms/select-practitioner-type.php

ASAM 2020 OUD Treatment Guideline Summary of Changes

- Counseling should not be required to obtain MOUD
- Do not withhold MOUD due to polysubstance use (including ETHO/Benzos)
- MOUD should be started in the ED/Hospital before discharge whenever possible
- Doses of =/>16 mg/day buprenorphine work better
- MOUD should be continued for at least 2-3 years minimum with no time limit on therapy
- Pregnant women with OUD should be maintained on Bup or Methadone, Bup has less severe NAS (unrelated to dose), combo product considered OK now
- Buprenorphine should not be held pre-operatively or post-operatively

ADA protections for patients with OUD

- Treatment facilities (residential SUD, skilled nursing) cannot deny admission to patients who are taking MOUD
- Jails/prisons must allow patients taking MOUD to continue their prescribed medication
- Hospitals/clinics cannot deny/refuse to care for patients because they have OUD or are taking MOUD

https://www.ada.gov/opioid_guidance.pdf, 2022

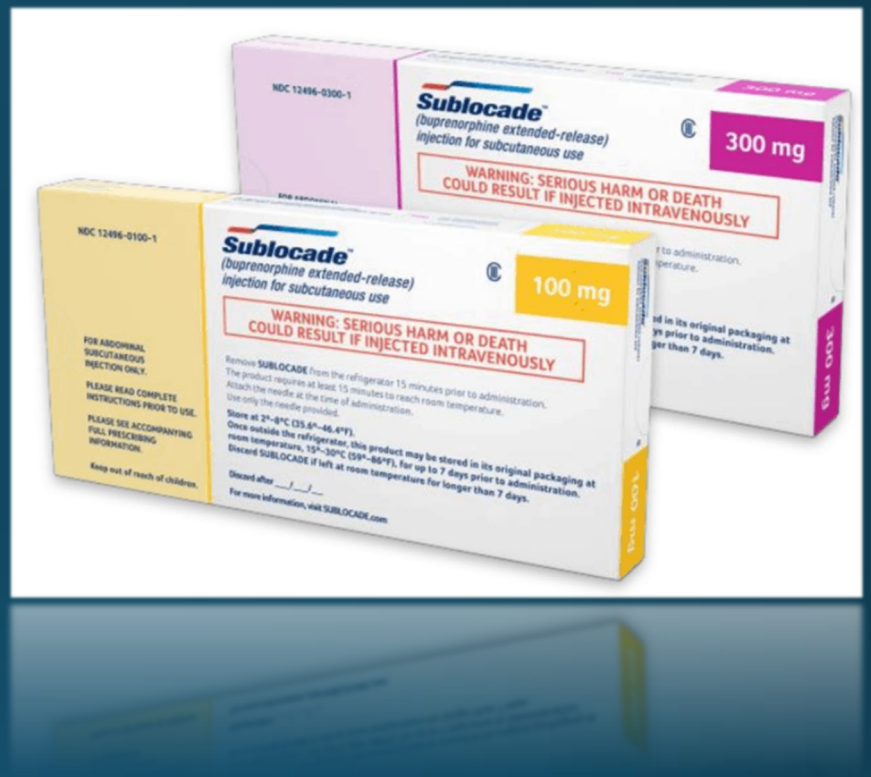
Buprenorphine low-dose and high-dose starts (Micro/macro-dosing)

Low-dose start (microdose)

- Continue full agonist during the induction period
- No need to be in withdrawal before starting Bup
- Good for patients on Methadone, hospitalized acute/chronic pain, heavy fentanyl use, h/o PW
- Start 0.5 mg on day 1, double dose daily and continue full opioid of choice until 16 mg of bup

High-dose start (macrodose)

- Good in ED, risk of loss to f/u, post OD, heavy use, severe WD/PW
- First dose typically 16 mg, up to 32 mg of Bup taken on day 1
- Safe in ED studies



Monthly Injectable Buprenorphine (Sublocade)

Advantages of Monthly Injectable Buprenorphine In Remote Native Alaskan Villages

No concern for diversion

Diversion concerns and stigma around sublingual buprenorphine can be a huge barrier to patient access as providers/clinic administrators are hesitant to offer this treatment

Monitoring medication compliance can be very difficult in remote locations

Not easy to access facilities for random medication counts and urinalysis

Reduces risk of withdrawal and relapse related to Rx interruption

Mail delivery in the bush can be frequently interrupted due to weather holds and other logistical concerns (reduced flights during COVID) that can result in Rx refills not arriving on time, leading to acute withdrawal which can trigger relapse and overdose

Flexible dosing q4-6 weeks, slow reduction in levels reduces withdrawal sxs

Excellent and long-lasting opioid blockade

Provides protection from overdose, even for patients with extended lack of clinic access such as those in fishing industry or who may become incarcerated, reducing risk of overdose in this remote population

Monthly XR Buprenorphine

Who would benefit?

Patients who would benefit from buprenorphine but have difficulty taking daily medications

Patients with high risk of overdose

Patients at risk for med interruption (incarceration/fishing)

Patients with limited transportation or who cannot reliably attend appointments

Patients with a high diversion risk

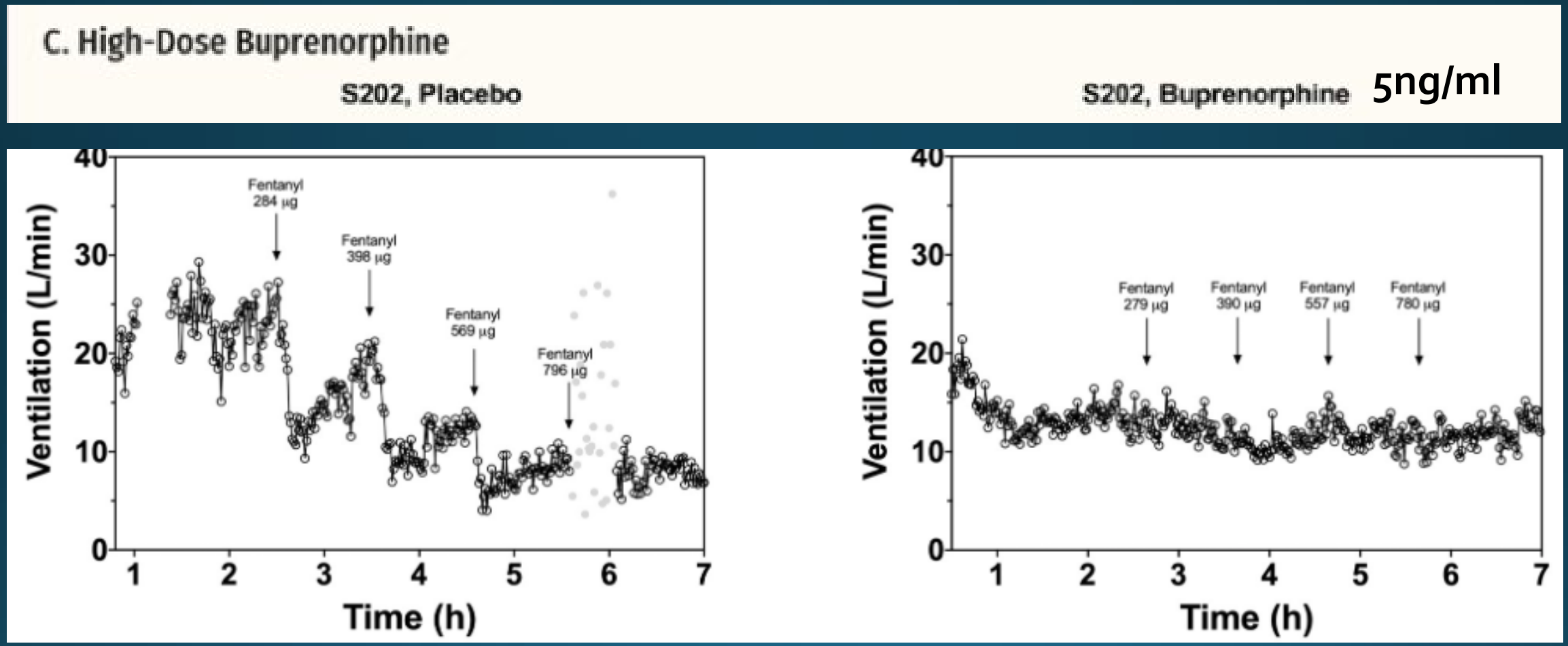
Patients who like flexible dosing (Once every 4-6 weeks)

Patients who cannot tolerate SL bup/nlx due to nausea/taste

Patients who's cravings are uncontrolled on 24 mg/day

Patients continuing to use drugs- fentanyl exposure risk

High Dose XR Buprenorphine blocks fentanyl induced respiratory depression

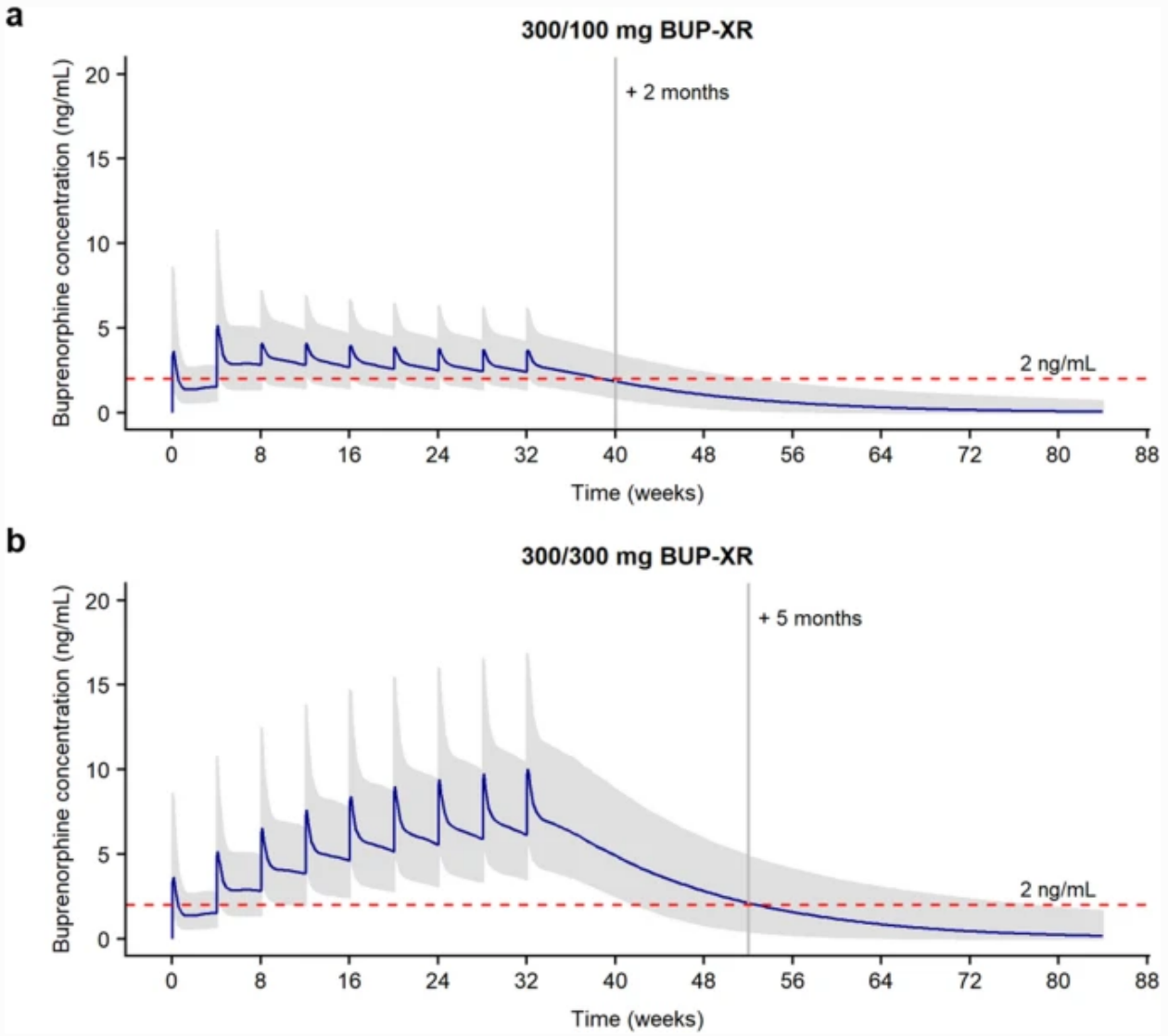


Blockade was lost under 2 ng/ml

https://journals.plos.org/plosone/article/figure?id=10.1371/journal.pone.0256752.g004

Extended opioid blockade after medication cessation

Fig. 6

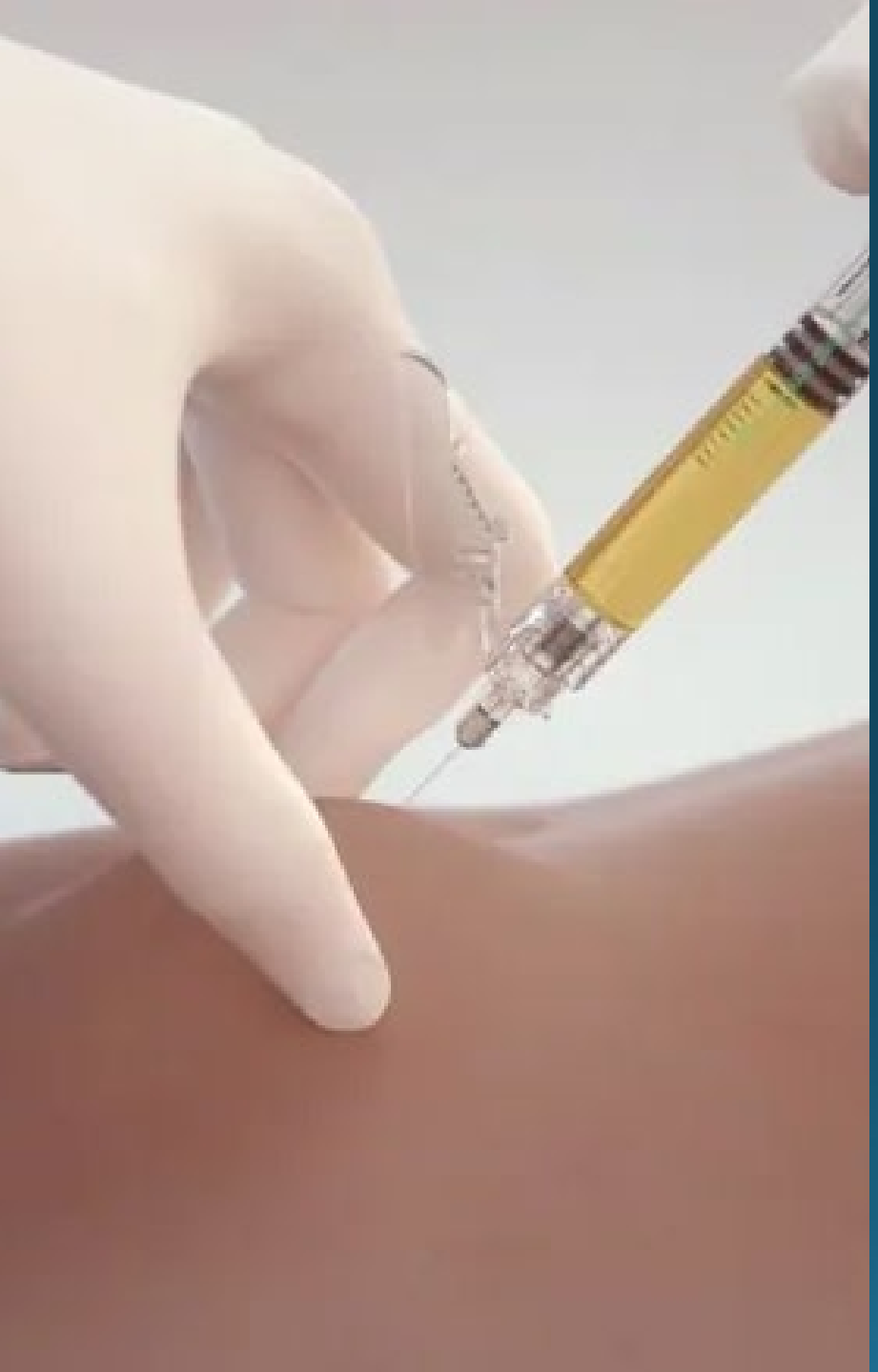


Predicted decrease in buprenorphine plasma concentrations for BUP-XR dosing regimens following treatment interruption. **a** 300/100-mg dosing regimen 2; **b** 300/300-mg dosing regimen. Blue solid lines: median of the simulated data; gray shaded areas: 90% prediction intervals of simulated data. A total of nine subcutaneous injections were simulated in 5000 subjects. The horizontal red dashed line indicates the 2-ng/mL minimum concentration required for opioid blockade, as established from

Patients stable on 100 mg will have blockade for 2 months (1 missed shot)

Patients stable on 300 mg will have blockade for 5 months (4 missed shots)

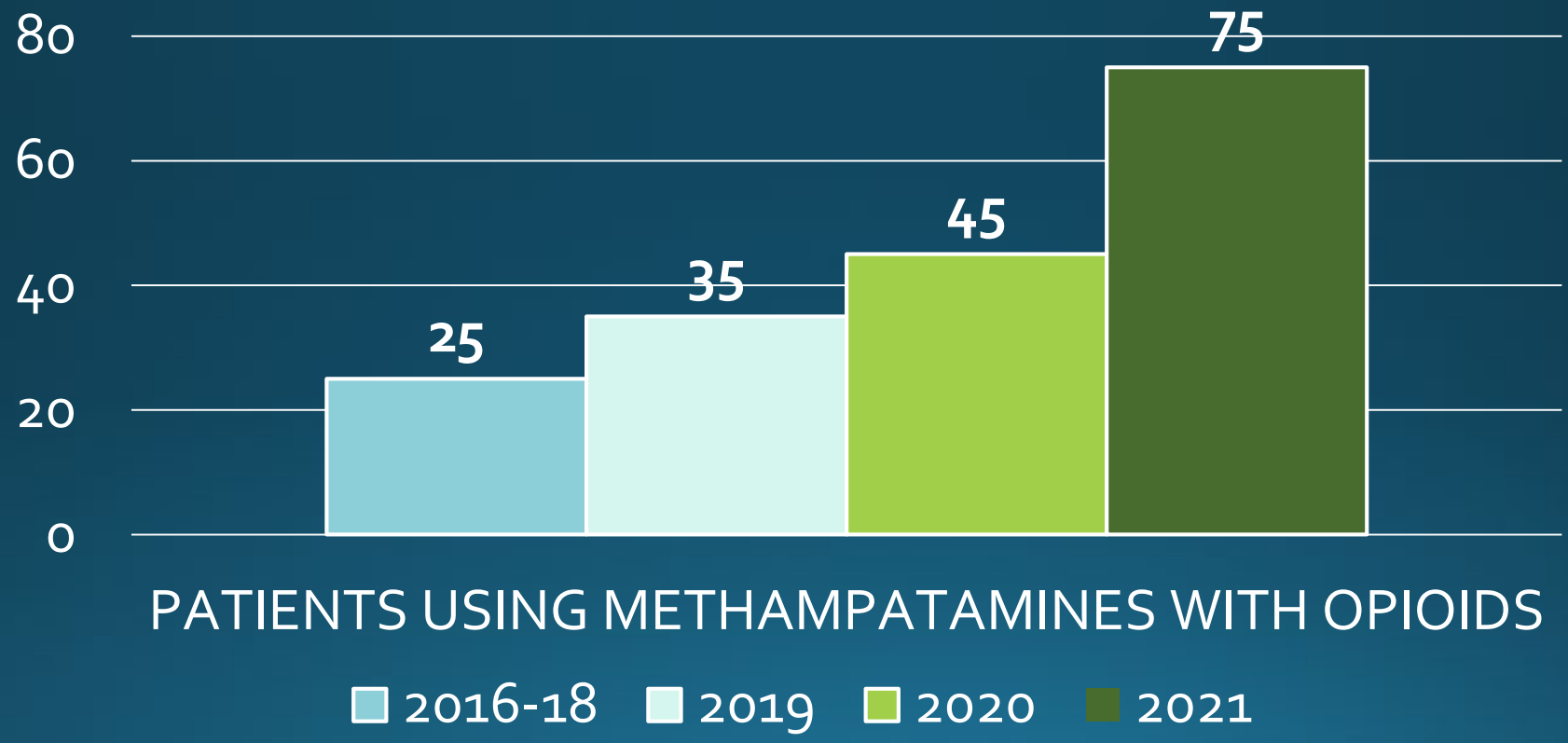
https://link.springer.com/article/10.1007/s40262-020-00957-0



Low Threshold XR-BUP

- Given regardless of active drug/alcohol use
- No required drug testing
- Flexible schedule
- Walk-in appointments for injections
- Single day SL-BUP induction for tolerant patients
- Flexible dose
- SL supplementation available
- Available in pregnancy (2^{nd}/3^{rd} trimester)

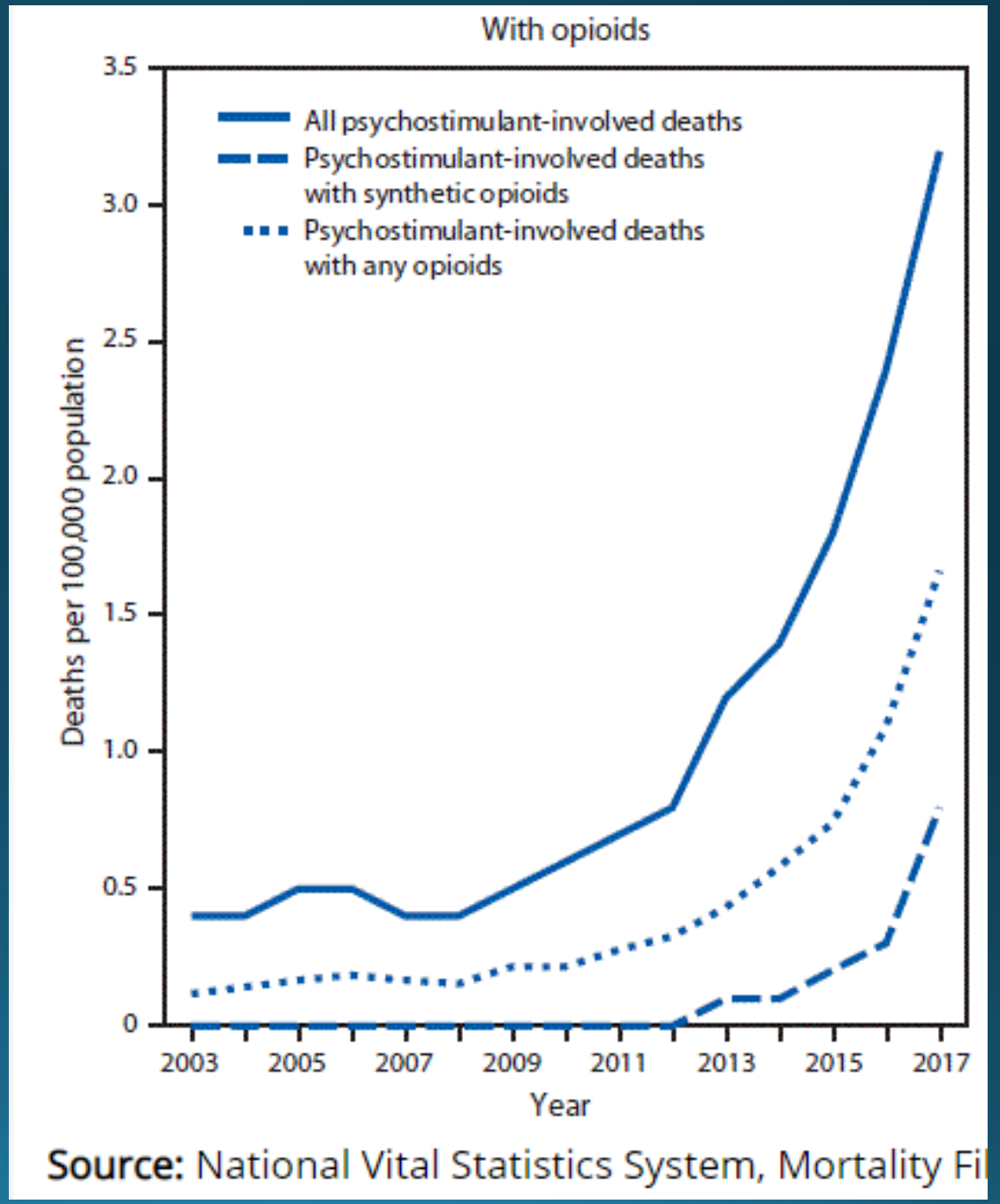
% NTC PATIENTS USING METHAMPHETAMINES WITH OPIOIDS ON OBOT ADMISSION



NTC Community Clinic

Roughly ½ of methamphetamine overdoses involve opioids

Injecting meth with opioids "goof-balling" is 3X more likely to result in overdose than injecting opioids alone



No FDA approved meds to treat stimulant use disorders

Bupropion and Naltrexone in Methamphetamine Use Disorder

January 14, 2021 N Engl J Med 2021; 384:140-153 DOI: 10.1056/NEJMoa2020214

IM Naltrexone 380 mg every 3 weeks, plus bupropion 450 mg/day
Around 10-15% of patient able to show abstinence

Mirtazapine for Methamphetamine dependence in MSM

Colfax 2011

Mirtazapine 30 mg/day reduced UDS+meth by 20%
Even without great medication compliance

ntingency Management is the most effective treatment for stimulant use

Contact FMI

Sarah Spencer DO, FASAM

Ninilchik Community Clinic

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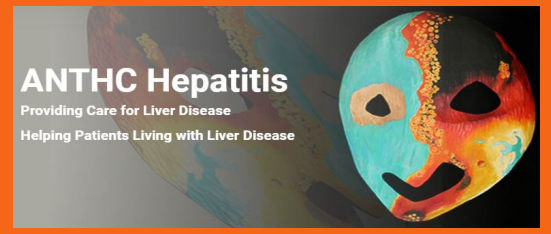
sarahspencerak@gmail.com

ADDITIONAL LEARNING OPPORTUNITIES

- HCV Simplified Treatment Training – Available Online until December 2nd
  https://www.anthc.org/provider-resources/new-provider-webinars/
  - Scroll down to topic titled: **HCV Treatment Training**
- AK ID ECHO: HCV, HIV, PrEP, STIs
  - The 2nd Tuesday of every month from 12:00-1:00PM Alaska Standard Time
    - 1CE/CME offered per session
  - anthc.org/project-echo/hcv-hiv-prep-stis-echo
- LiverConnect Webinar Program
  - Second Tuesday of every month 8:00-9:00AM Alaska Standard Time
    - Full Hour didactic topics on Liver Disease and related topics 1CE/CME offered
  - anthc.org/what-we-do/clinical-and-research-services/hep/liverconnect/



AK LIVER DISEASE ECHO -TEAM CONTACTS

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Thank you

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