Utilizing Low-threshold XR Buprenorphine to Address Stimulant-Fentanyl Overdose Risk in Rural Alaska

Sarah Spencer DO, FASAM
Ninilchik Traditional Council Community Clinic
Ninilchik, Alaska

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CHERP

Opioid Response Network

Disclosure Information

Sarah Spencer DO, FASAM

I have no financial conflicts of interest to disclose

I am currently employed by the Ninilchik Traditional Council

I work as an addiction treatment consultant for non-profit agencies including the Opioid Response Network and the Alaska Native Tribal Health Consortium

I am the volunteer medical director of Alaska's first rural syringe access program in Homer

Land Acknowledgment

I live and work on the ancestral lands of the Ninilchik tribe on the rural southern Kenai Peninsula. While stigma has prevented other tribes and clinics from offering MOUD to their patients, the Ninilchik traditional council has been instrumental in expanding access to addiction care and harm reduction services to all the tribes on the Kenai peninsula and to the general community.

Chin'an gheli (Thank You) to the Ninilchik Tribal Council.

https://www.ninilchiktribe-nsn.gov/about-the-tribe/#history

Learning Objectives

1.Examine the epidemiology of comorbid stimulant and opioid use disorders and related overdose risk, especially in NA/AI populations, and explore barriers patients with severe SUDs face in accessing MOUD and harm reduction services in rural areas

2. Summarize the pharmacology of XRBUP and its utility in increasing access to care and reducing risk of fentanyl induced respiratory depression and explore strategies to offer off-label, harm-reduction based approaches to utilizing XRBUP

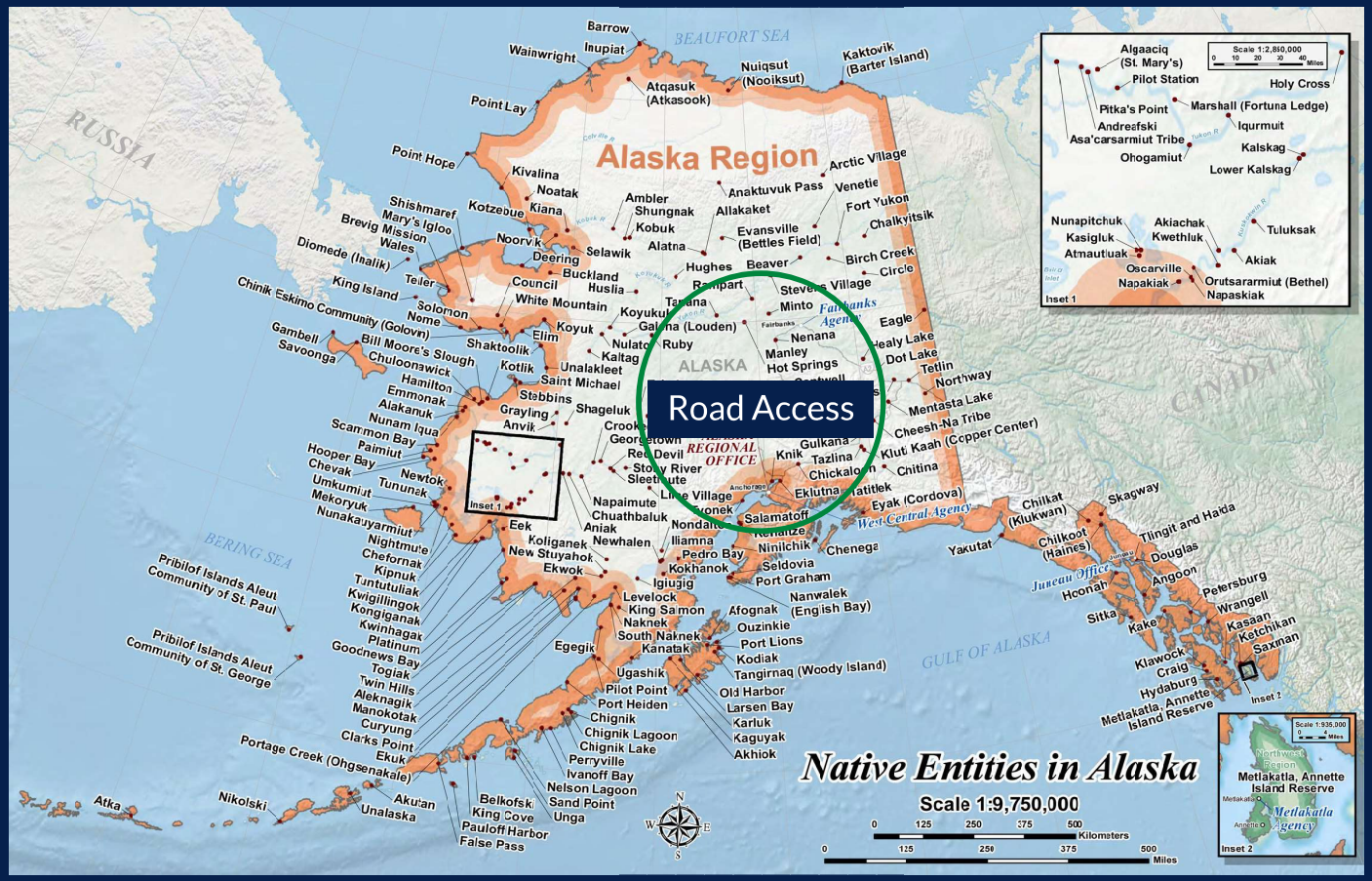
3. Understand the components of low-threshold care and how it can reduce barriers to access and increase treatment retention for patients with co-morbid stimulant and opioid use disorders

4. Review evidence-based treatment of stimulant use disorders

5. Review case presentations to improve clinical skills in triaging and problem-solving complex patient presentations when treating co-morbid stimulant and opioid use disorders

Abbreviations

- OTP: Opioid Treatment Program (methadone clinic)
- MOUD: medication for opioid use disorder (not MAT)
- SLBUP: sublingual buprenorphine
- XRBUP: monthly injectable extended-release buprenorphine
- CHAP: Community Health Aide Practitioner
- ANTHC: Alaska Native Tribal Health Consorsium
- ANMC: Alaska Native Medical Center



Over 200 Alaska Native tribes/villages

Spread over 660,000 mi^2

Most off the road system

550 Community Health Aides/Practitioners (CHAPs) in 170 tribal clinics

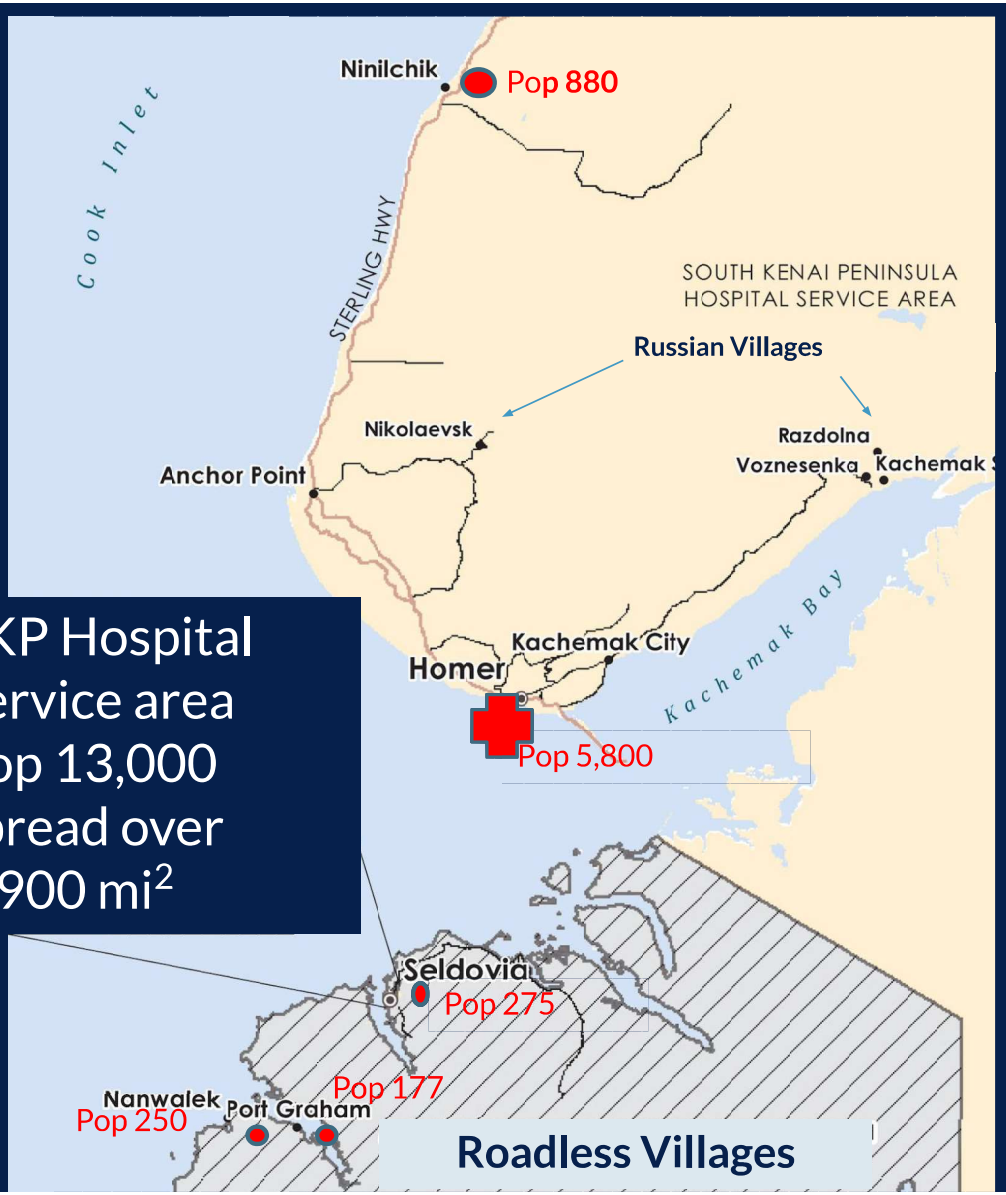
- Currently MOUD offered by 2/3 of the regional healthcare hubs

Kenai Peninsula of Alaska

Tribal Entities

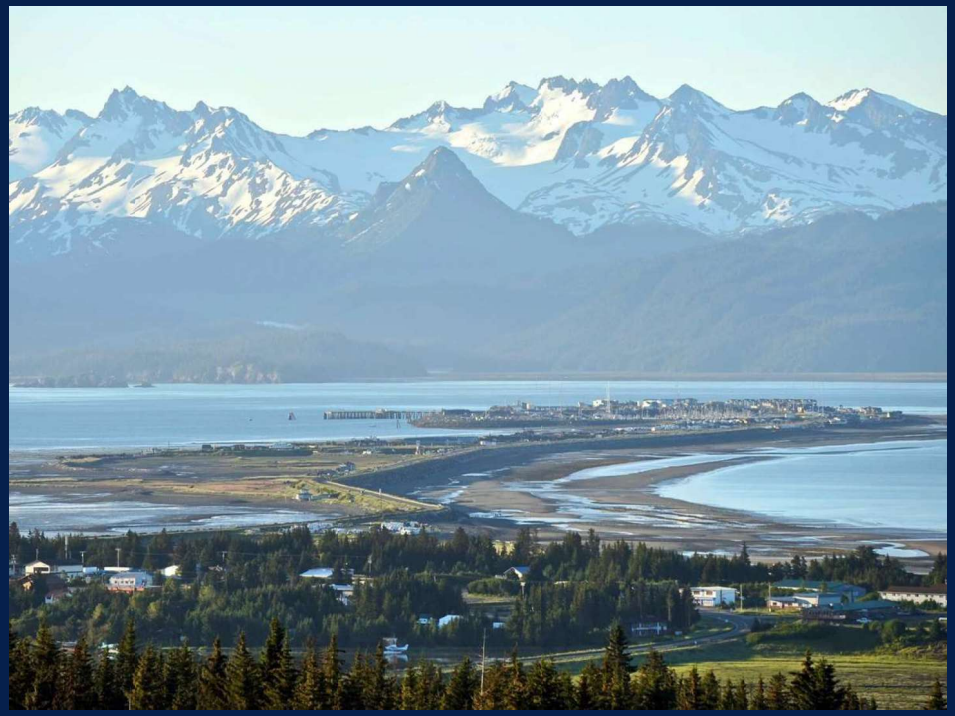
- Ninilchik Traditional Council
- Seldovia Village Tribe
- Chugachmiut
- Kenaitze Indian Tribe

- About 20% AK Native
- 200 miles from nearest OTP
- 1 addiction med specialist



What barriers do NA/IA patients face when accessing MOUD, especially in rural areas?

Barriers to MOUD Access in Rural AK



- Travel/Transportation/Gas
- Weather Holds/ Rx delayed in the Mail
- No local licensed medical providers (only CHAPS)
- No local pharmacies
- **STIGMA**

Words Matter:
How Language Choice Can Reduce Stigma

> *"Protest any labels that turn people into things. Words are important. If you want to care for something, you call it a 'flower;' if you want to kill something, you call it a 'weed.'"* [i]

The Real Stigma of Substance Use Disorders

In a study by the Recovery Research Institute, participants were asked how they felt about two people *"actively using drugs and alcohol."*

One person was referred to as a "substance abuser"

The other person as "having a substance use disorder"

No further information was given about these hypothetical individuals.

THE STUDY DISCOVERED THAT PARTICIPANTS FELT THE "SUBSTANCE ABUSER" WAS:

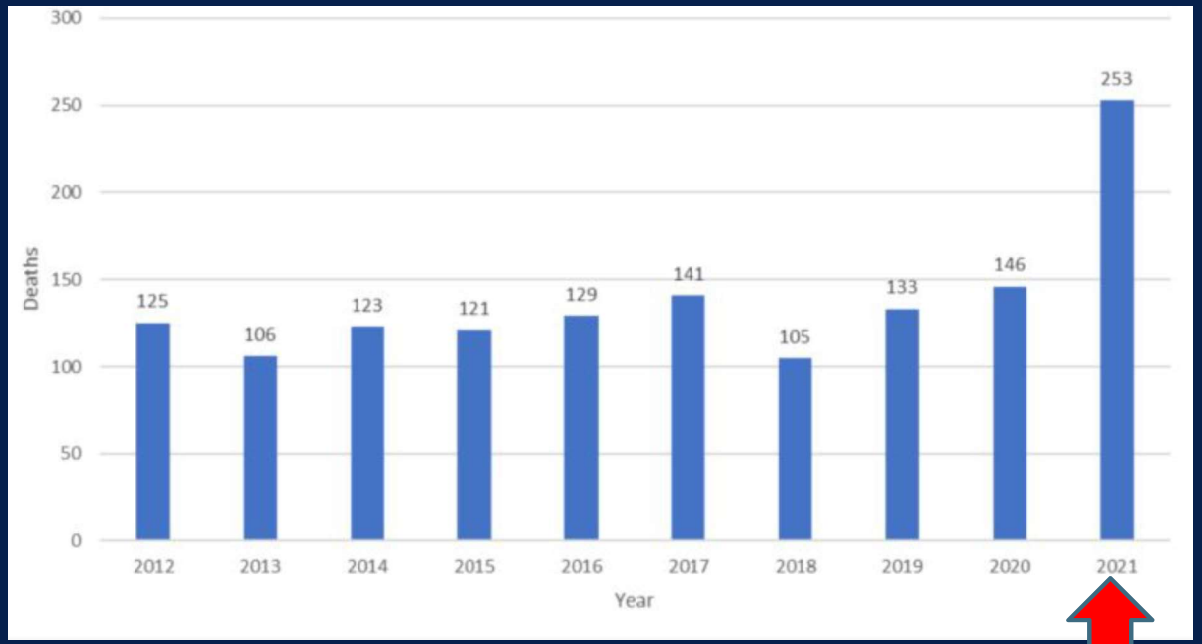
- less likely to benefit from treatment
- more likely to benefit from punishment
- more likely to be socially threatening
- more likely to be blamed for their substance related difficulties and less likely that their problem was the result of an innate dysfunction over which they had no control
- they were more able to control their substance use without help

Methadone and buprenorphine DO NOT substitute one addiction for another

Addiction is defined by the American Society of Addiction Medicine as compulsive drug use despite harmful consequences. Taking a daily prescribed medication that improves functioning, health, and quality of life, while reducing other drug use and death, does not meet this definition.

People taking opioid agonist therapy depend on a daily medication to keep their disease in remission, the same way that people with diabetes, hypertension, hyperlipidemia, hypothyroidism, and nearly every chronic medical condition do

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



- Alaskan Natives
OD rate 77/110K

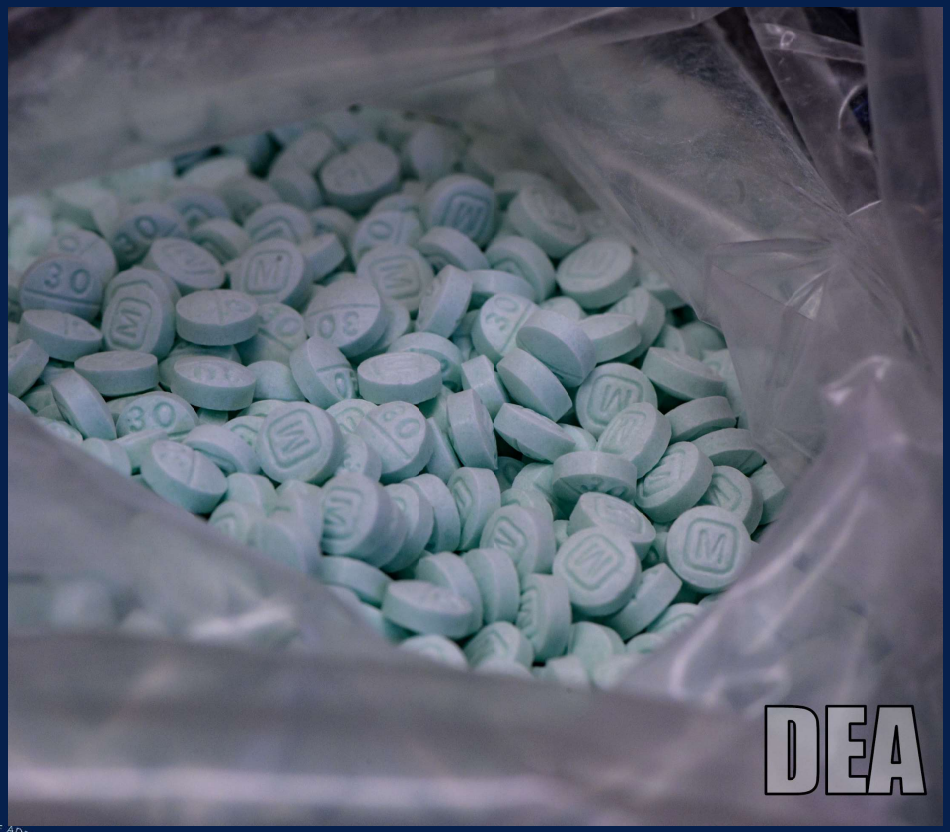
- White
OD rate 28/100K

- Meth OD up 150%

- Fentanyl OD up 150%

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

DEA Laboratory Testing Reveals that 6 out of 10 Fentanyl-Laced Fake Prescription Pills Now Contain a Potentially Lethal Dose of Fentanyl



DEA illustration of 2 mg of fentanyl, a potentially lethal dose

https://www.dea.gov/alert/dea-laboratory-testing-reveals-6-out-10-fentanyl-laced-fake-prescription-pills-now-contain

Use of stimulants with opioids has been increasing nationwide

Past month
methamphetamine use by
people who use heroin

9.0% to 44.0%

from 2015-2019

Strickland et al, The continued rise of methamphetamine use among people who use heroin in the United States. Drug Alcohol Depend. 2021

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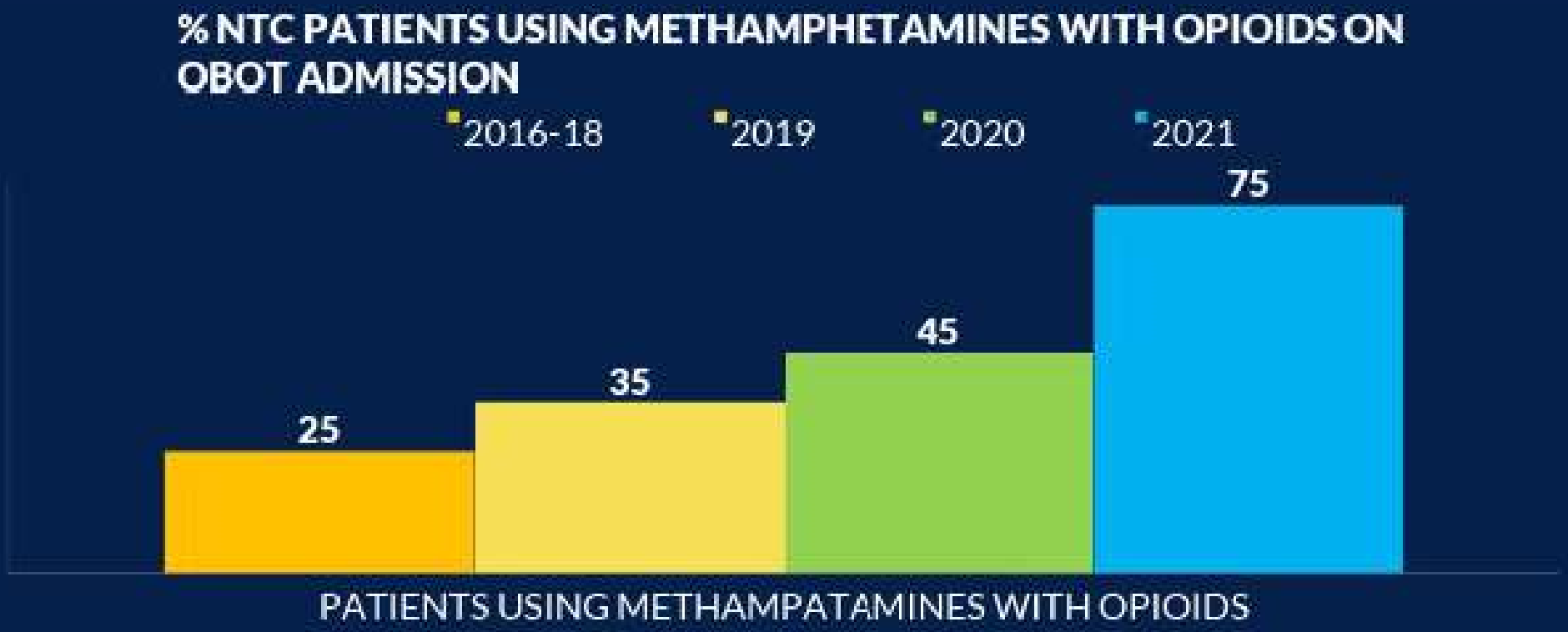
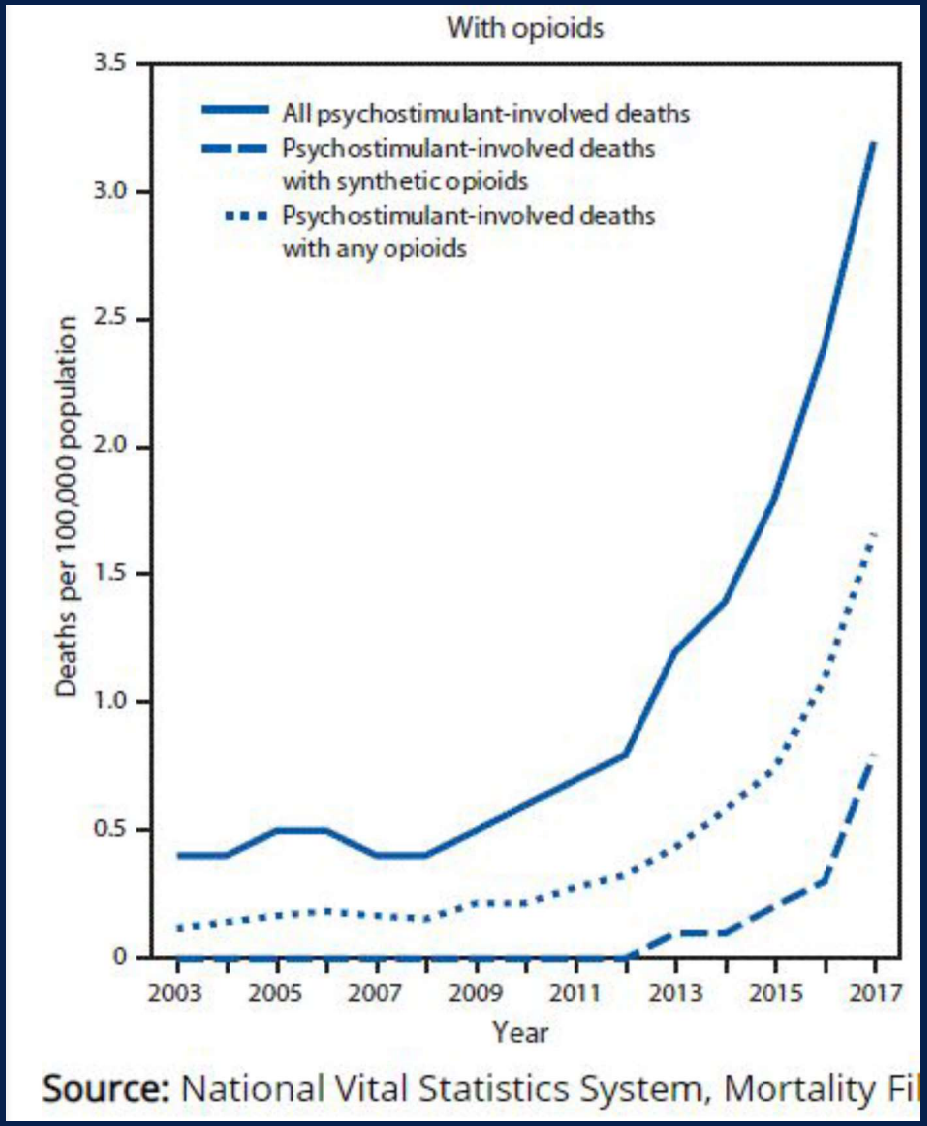


Roughly ½ of methamphetamine overdoses involve fentanyl

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



Why do people use stimulants with opioids?

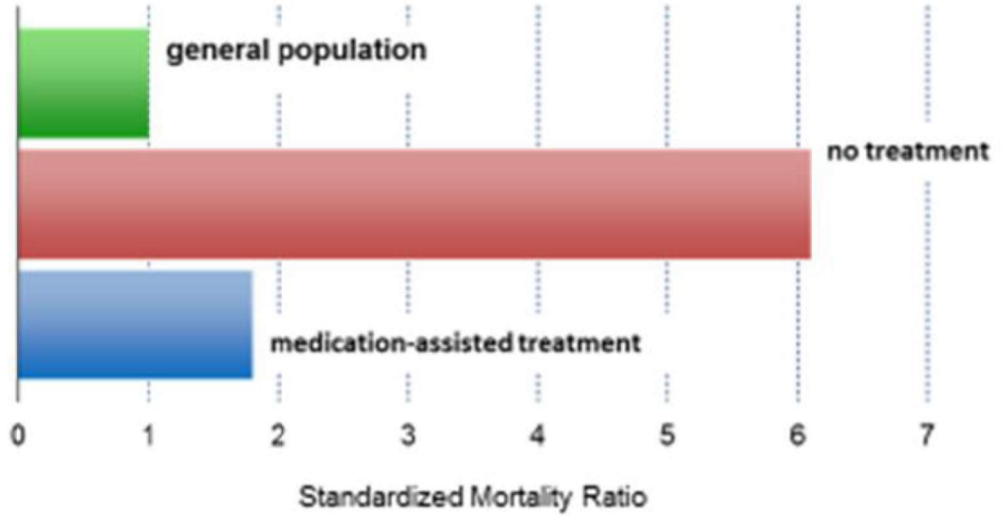
- To prolong the effects of fentanyl
- To counteract the negative effects of opioids (reduce the chance of “nodding out”)
- To foster energy and enhance euphoria

https://www.sciencedirect.com/science/article/abs/pii/S0955395922002079

Benefits of MAT: Decreased Mortality

Overdose risk the first 2 weeks after leaving treatment rises dramatically

Death rates:



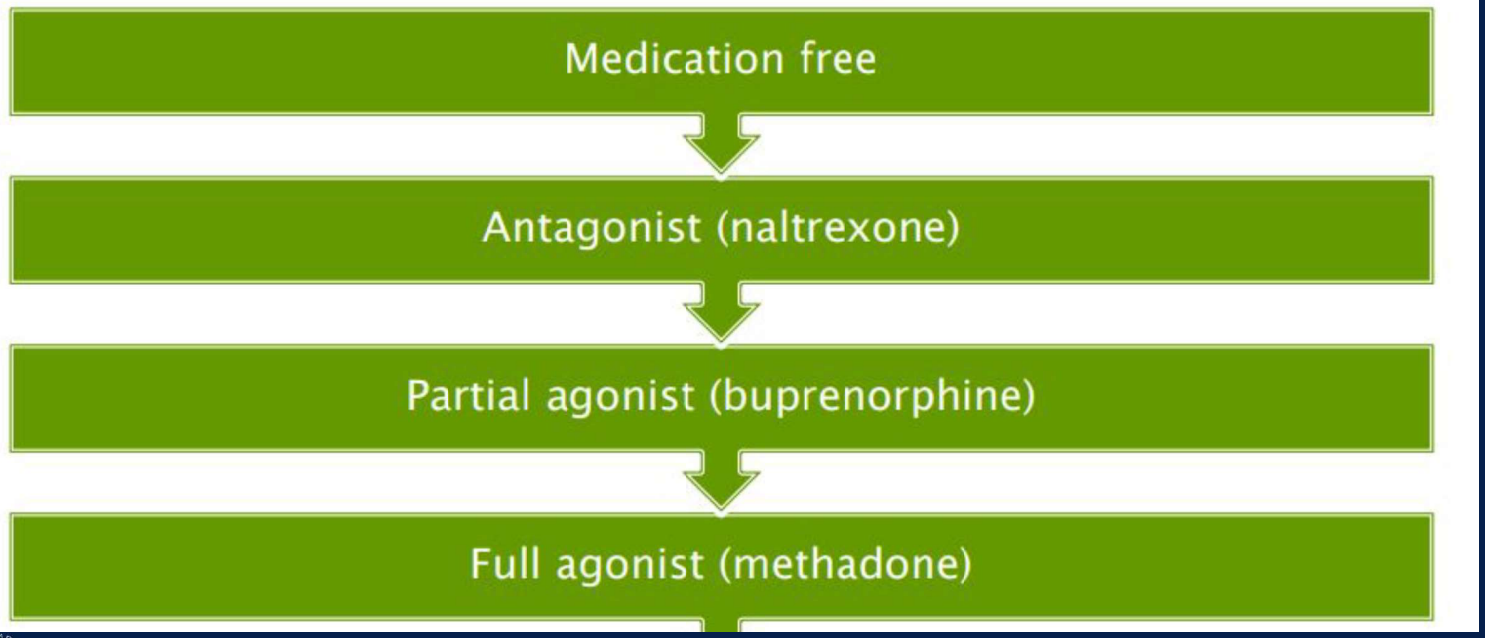
MOUD can reduce death rates by 80%

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

PCSS Providers Clinical Support System

Krawczyk N, Mojtabai R, Stuart EA, et al. Opioid agonist treatment and fatal overdose risk in a state-wide US population receiving opioid use disorder services. Addiction. 2020;115:1683–1694.

Hierarchy of Stigma in OUD Recovery



Least Effective

Most Effective

Waiver Elimination (MAT Act)

Section 1262 of the Consolidated Appropriations Act, 2023 (also known as Omnibus bill), removes the federal requirement for practitioners to submit a Notice of Intent (have a waiver) to prescribe medications, like buprenorphine, for the treatment of opioid use disorder (OUD). With this provision, and effective immediately, SAMHSA will no longer be accepting NOIs (waiver applications).

- No special education required to Rx BUP
- All prescribers authorized to Rx schedule 3 can RX BUP
- No limits on number of patients
- No requirement to track list of patients
- No requirement to refer to counseling
- If you have a waiver, that X-number will be removed from your newly issued DEA card

Retention in MOUD treatment and methamphetamine use

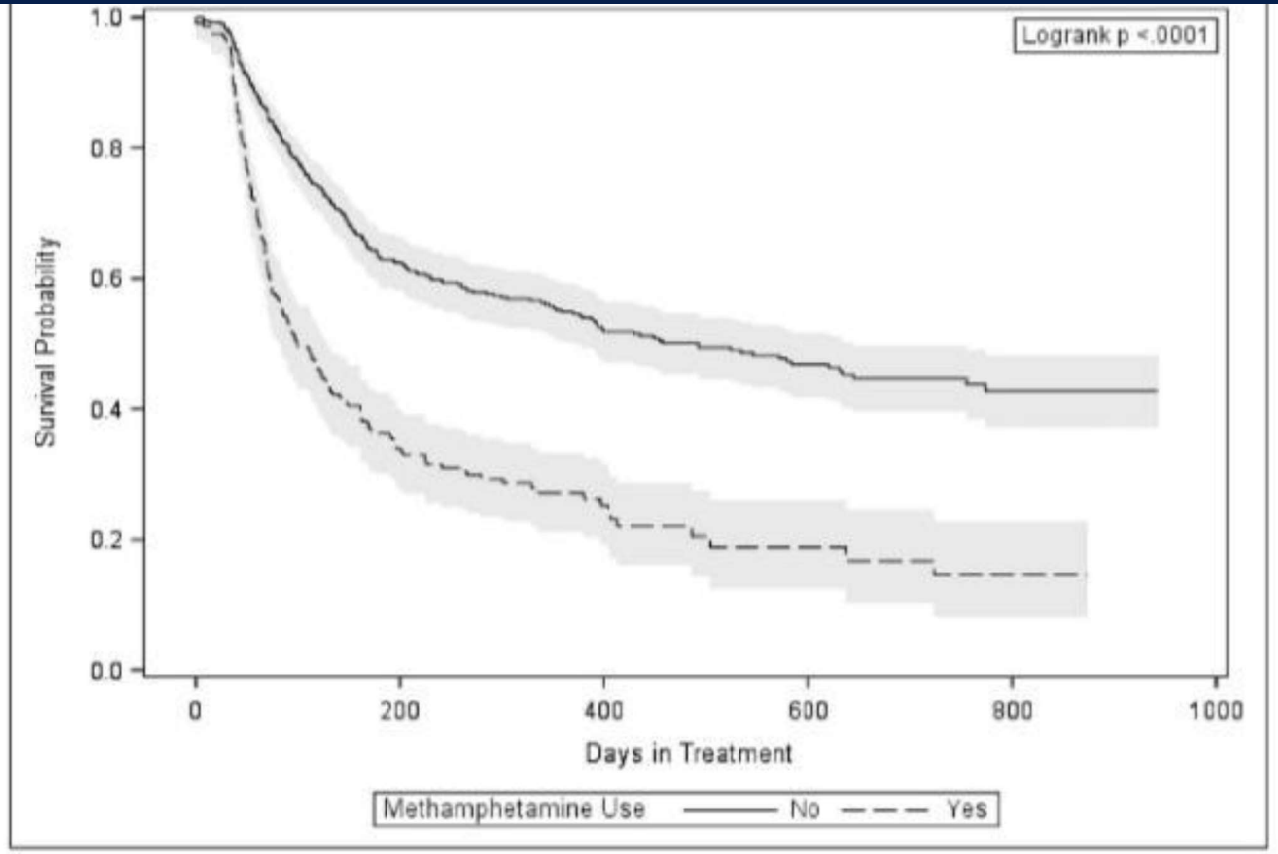


Fig. 1. Kaplan-Meier survival curves for methamphetamine users and non-users with 95% confidence bands (n = 770).

People who use methamphetamine may have poorer retention in MOUD programs

But those who stay in treatment may reduce their use

https://www.journalofsubstanceabusetreatment.com/article/S0740-5472(19)30250-8/fulltext

Why do you think people who use stimulants with opioids have reduced access to and retention in MOUD programs?

Low Threshold Care

A potential strategy to retain people who use stimulants with fentanyl in MOUD treatment

Predictors of engagement and retention in care at a low-threshold substance use disorder bridge clinic https://doi.org/10.1016/j.jsat.2022.108848 , Patient experiences with a transitional, low-threshold clinic for the treatment of substance use disorder: A qualitative study of a bridge clinic https://doi.org/10.1016/j.jsat.2019.09.003

What are the essential components of a low-threshold addiction treatment program?

Harm Reduction Based Low Threshold Care
(Our clinic's approach)

- Don't discharge patients for ongoing drug use
- Create patient centered care plans
- Flexible walk-in/same day/tele-med appointments
- Co-located/tele-behavioral health/digital apps
- Motivational interviewing
- Peer support (via text)
- Treatment of co-morbid medical/MH issues
- Contingency Management

Harm Reduction Based Low Threshold Care (continued)

- Assistance with transportation
- Assistance with filling out applications for treatment or social services
- Contraception
- Rapid Hep C/HIV testing
- Hep C treatment/ PREP for active users
- Naloxone kits
- Injection and smoking supplies
- Fentanyl test strips

ANTHC Harm Reduction Training and Supplies

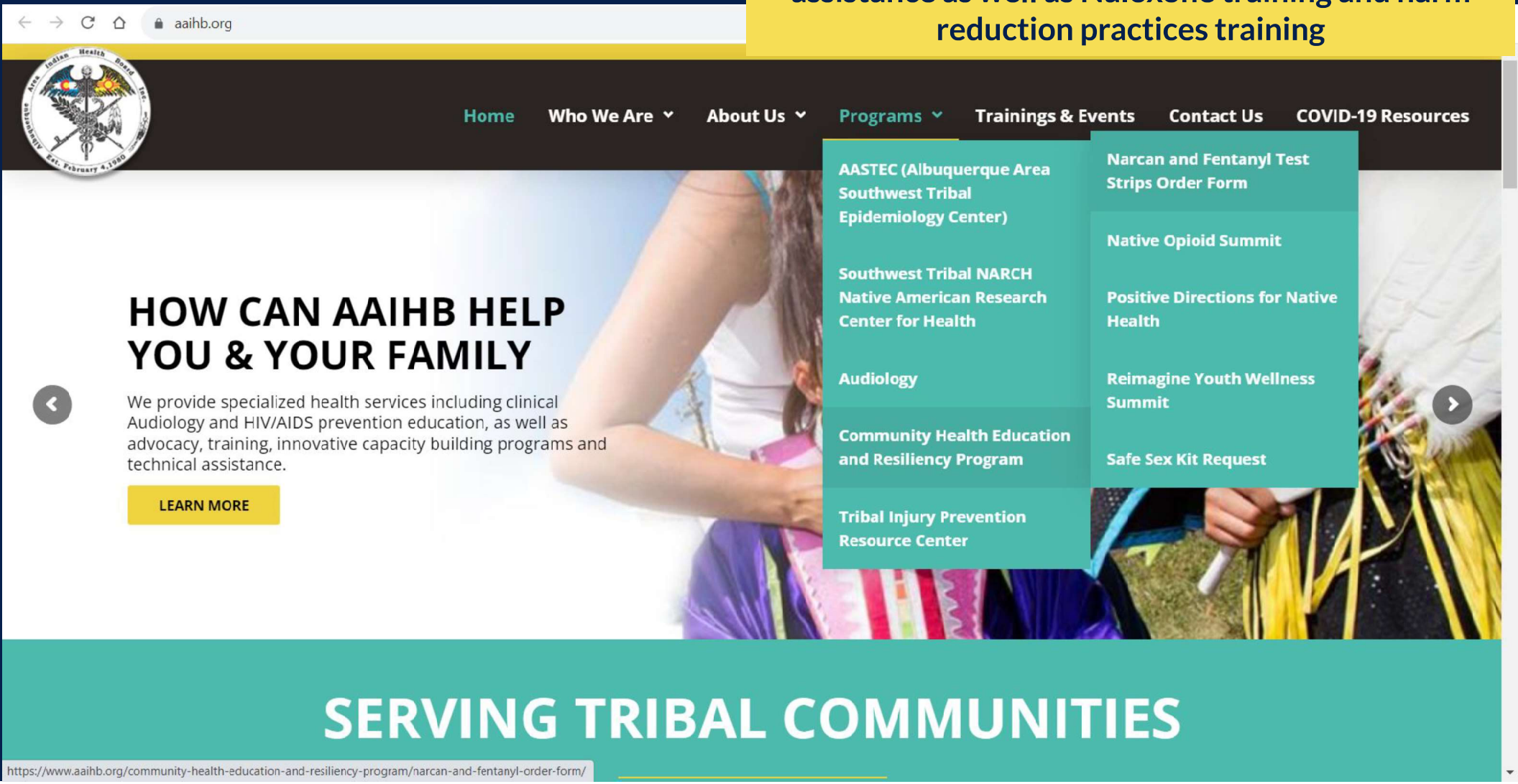
https://www.iknowmine.org/wp-content/uploads/2021/01/ANTHC_Harm-Reduction_Toolkit.pdf

https://www.iknowmine.org/other-cool-stuff/harmreduction

https://www.iknowmine.org/harm-reduction-trainings/

AAIHB Mail order harm reduction supplies

The CHERP team can provide capacity-building assistance as well as Naloxone training and harm reduction practices training



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

Contingency Management is the most effective treatment for

The treatment modality with the most evidence for efficacy for stimulant use disorder is

Contingency Management

What is Contingency Management?

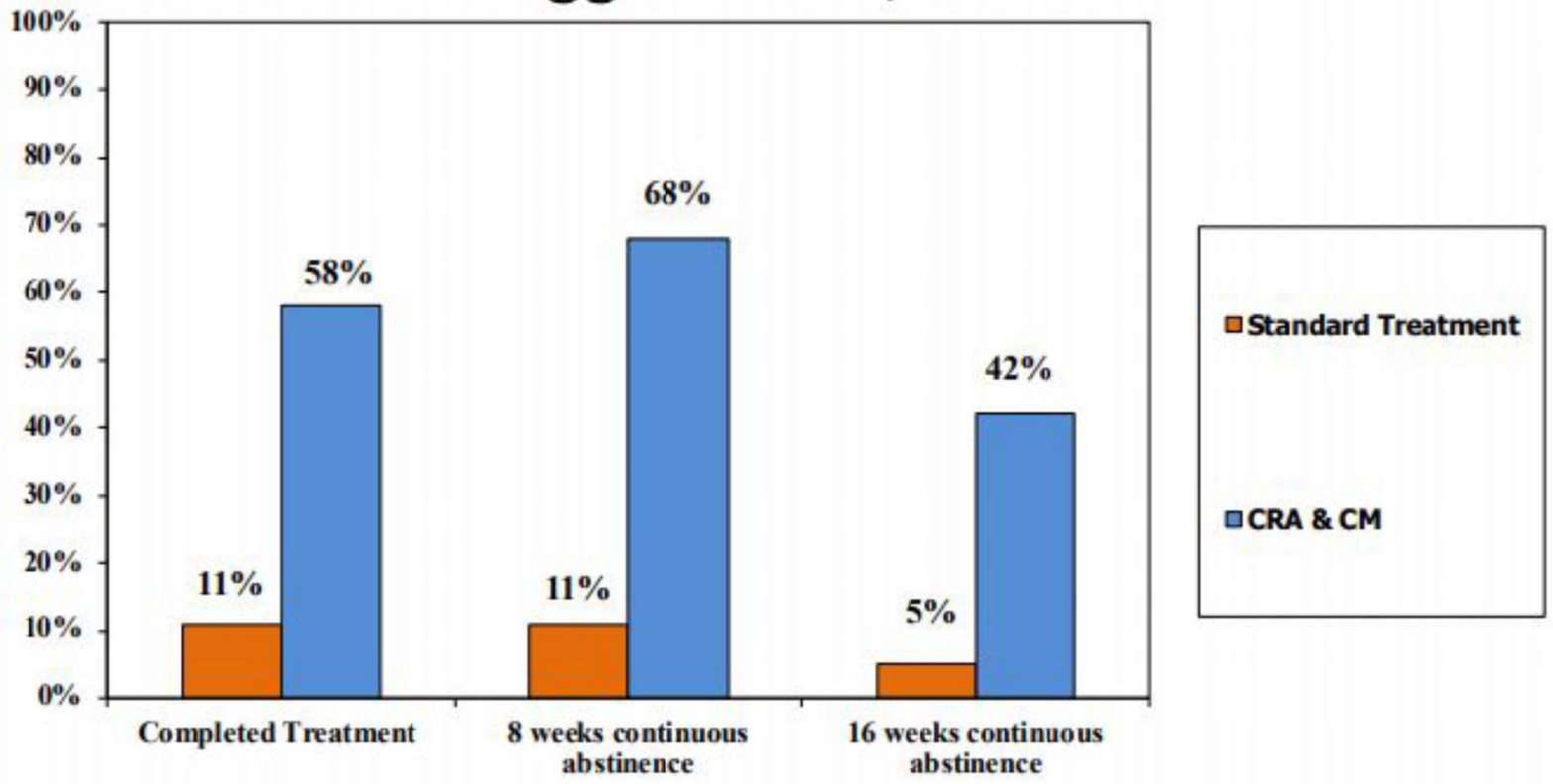
The most effective behavioral health intervention to treat substance use disorders, but also the least utilized.

Provides immediate rewards for meeting goals

- Negative UDS
- Coming to appointments
- Getting monthly medication injections
- Attending counseling

Example: Gift cards = $100/month

CRA and Contingency Management: Higgins et al., 1993



CRAFT

I want to help my loved one enter substance abuse treatment

Community Reinforcement Approach and Family Training (CRAFT) is a form of therapy that helps family members improve their personal well-being and learn specific skills to motivate their loved one toward substance abuse treatment. CRAFT is a new therapy being offered in Anchorage at the Aleutian Pribilof Islands Association (APIA) in partnership with ANTHC.

ANTHC Behavioral Health

behavioralhealth@anthc.org

> **More than two thirds of family members who use CRAFT successfully engage their loved one in treatment.**
>
> *— Robert J. Meyers. Ph.D.*
> *From HBO Addiction Series*

Helping Families Help

https://helpingfamilieshelp.com/

What might be some advantages of offering XRBUP to patients in rural areas?

Advantages of XRBUP In Remote Native Alaskan Villages

No concern for diversion

Diversion concerns and stigma around SLBUP can be a barrier. It's difficult to monitor medication compliance in remote locations, and it's difficult to arrange medication counts and drug testing

Reduces risk of withdrawal and relapse related to Rx interruption

Mail delivery in the bush frequently interrupted due to weather holds and logistics (reduced flights during COVID) that can result in delayed Rx refills□ acute withdrawal □ relapse □ overdose

Flexible dosing q4-6 weeks, slow reduction in levels reduces w/d sxs

Excellent and long-lasting opioid blockade

Reduces overdose risk for patients with extended lack of medication access (fishermen, oil field workers, incarcerated)

Which patients can benefit most from XRBUP?

XRBUP Patient Selection

- Useful for patients who have difficulty with medication continuity, who have fallen out of care multiple times
- Patients who cannot reliably attend scheduled appointments or have difficulty filling frequent prescriptions due to transportation (no vehicle or license), location (lives off road system) or employment barriers (slope workers, commercial fishermen) or at risk for med interruption (incarceration, moves, loss of insurance)
- Patients who do better on high dose buprenorphine (still struggle with cravings at 24mg/day)

XRBUP Patient Selection (Continued)

- Patients who don't tolerate SLBUP due to nausea
- Patients who have difficulty securing their medication
- Patients actively using other non-RX substances (stimulants/benzo/ETOH) or otherwise high overdose risk
- Patients who are at high diversion risk, patients who have sold their buprenorphine in the past

Real patient testimonials regarding XR-BUP

"It works great! Anyone that says that it doesn't is full of s#!t!"

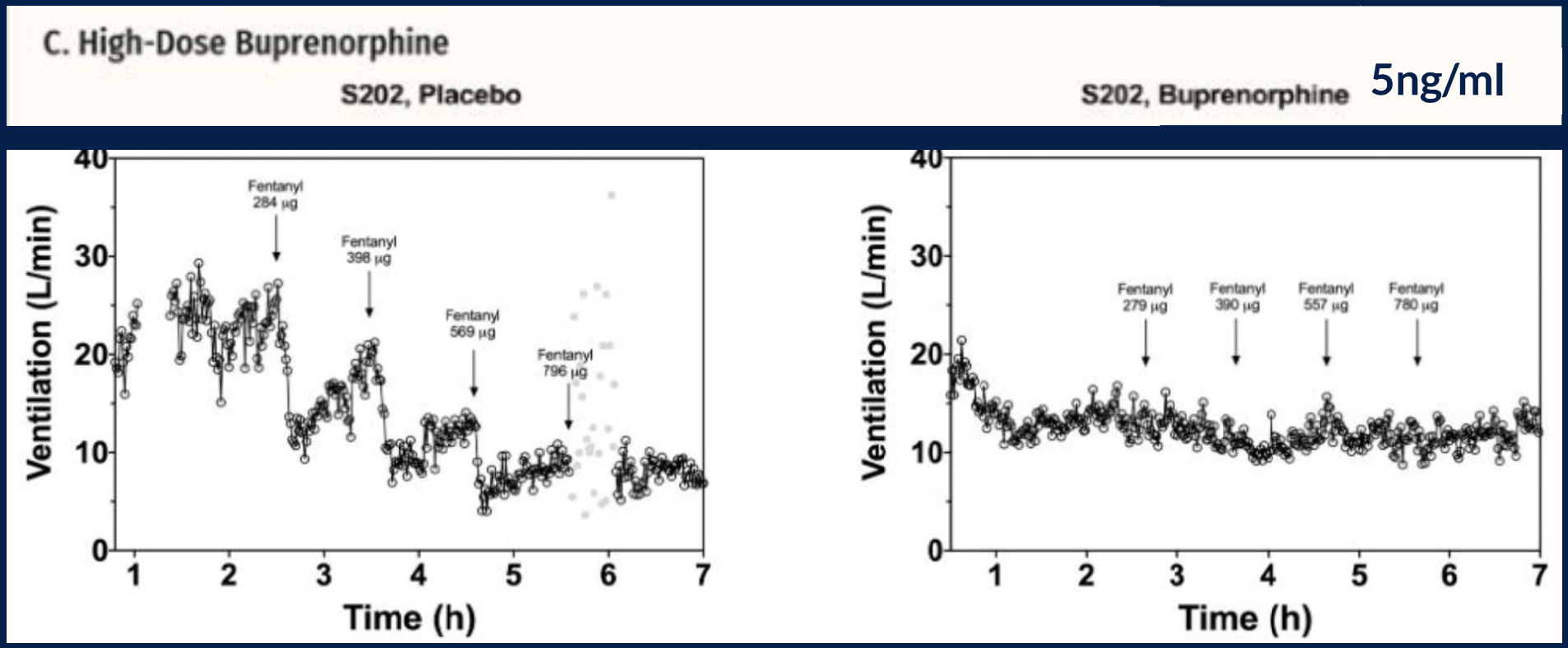
"I love that I just feel normal every day when I wake up."

"I was glad that I didn't feel any withdrawal symptoms when I went to jail."

"I don't even think about heroin anymore."

"I tried using heroin and it was totally blocked."

High Dose XRBUP 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

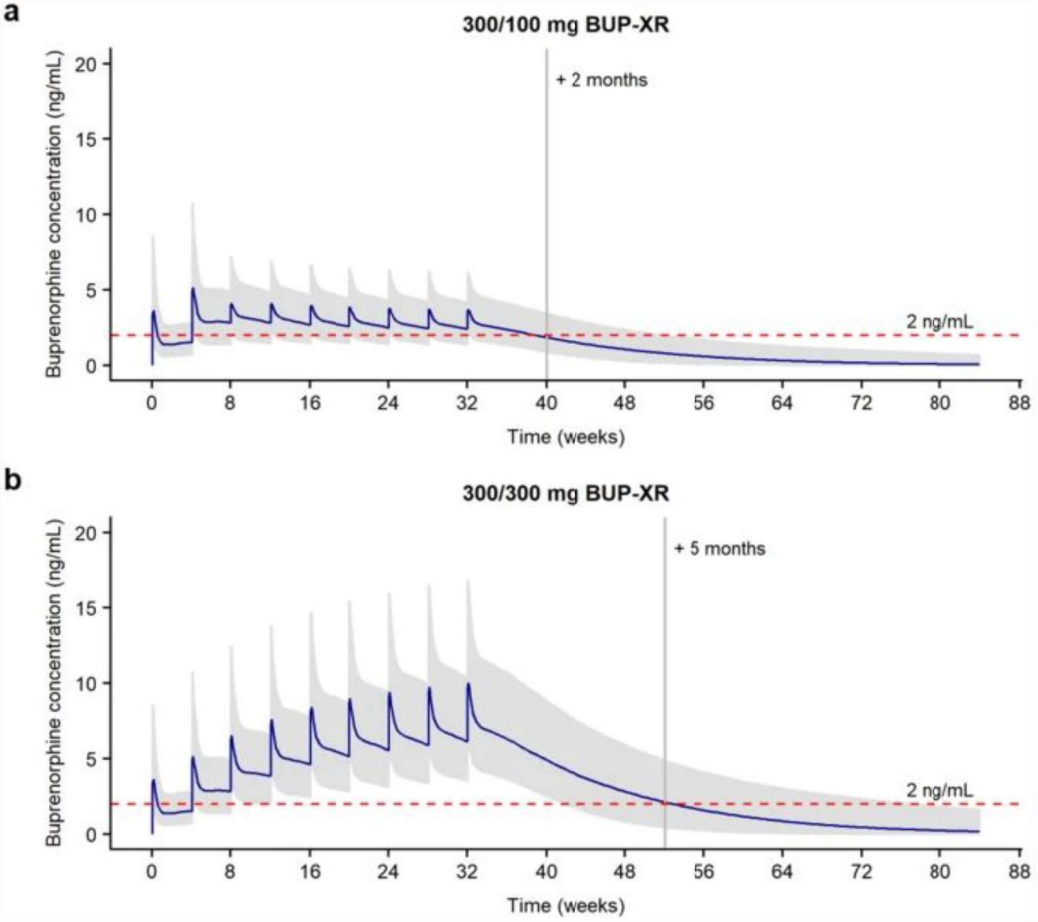
Pharmacokinetic parameters	SUBUTEX daily stabilization		SUBLOCADE		
Mean	12 mg (steady-state)	24 mg (steady-state)	300 mg# (1st injection)	100 mg* (steady-state)	300 mg* (steady-state)
$C_{avg,ss}$ (ng/mL)	1.71	2.91	2.19	3.21	6.54
$C_{max,ss}$ (ng/mL)	5.35	8.27	5.37	4.88	10.12
$C_{min,ss}$ (ng/mL)	0.81	1.54	1.25	2.48	5.01

During the first month of XRBUP, the serum drug levels drop to levels that may not be therapeutic for some patients, thus supplemental SLBUP is indicated in patients who experience craving or withdrawal in early treatment

https://www.sublocade.com/Content/pdf/prescribing-information.pdf

Extended opioid blockade after medication cessation

Fig. 6

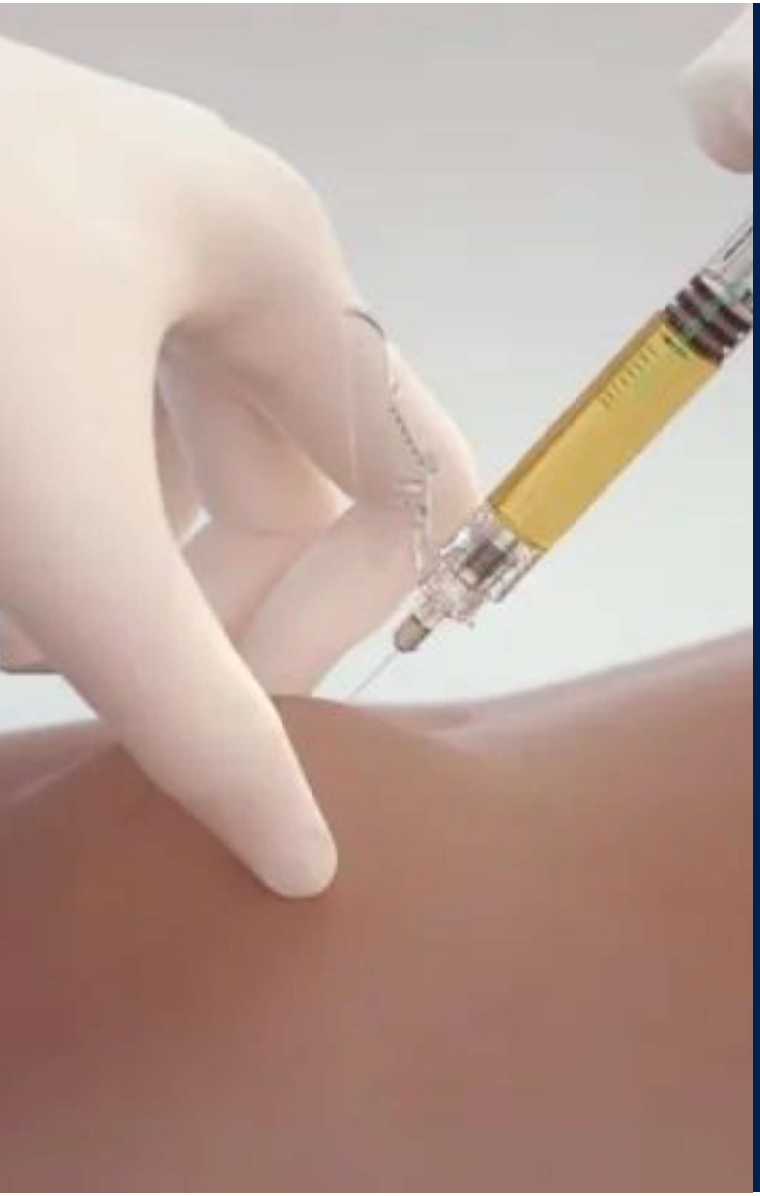


Predicted decrease in buprenorphine plasma concentrations for BUP-XR dosing regimens following treatment interruption. **a** 300/100-mg dosing regimen 2; **b** 300/300-mg dosing regimen. Blue solid lines: median of the simulated data; gray shaded areas: 90% prediction intervals of simulated data. A total 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 may have blockade for 2 months (1 missed shot)

Patients stable on 300 mg may 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 medication start for opioid tolerant patients
- Flexible dose
- SL supplementation available
- Available in pregnancy (2^{nd}/3^{rd} trimester)

Treatment Retention SL vs XR Buprenorphine

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Important considerations for offering low-threshold MOUD

- Basic prescriber education
  - Easy Buprenorphine prescribing for everyone 1 hour webinar
- Basic staff education:
  - Addiction Basics, Stigma and SUD
- Case manager: Can be anyone with interest and passion
- Consider alternative scheduling (block, open access, walk-in, groups)
- Connection to other community resources
  - Know the resources in your community and how to assist with warm handoff (behavioral health, social services, Harm reduction)
- Spread the word, no wrong door (ED, shelters, criminal justice, child welfare)
- Don't reinvent the wheel:
  - Bridge to treatment: practical tools, algorithms, patient education

Case Study Discussion

- A 25 yo NA female at 16 WGA with first pregnancy, is referred to your addiction specialty clinic from a local primary care practice to take over her buprenorphine prescribing. She has been intermittently taking prescribed buprenorphine but has moved between 3 different practices in the past 2 months due to chaotic life circumstances. She frequently no-show for visits and has many gaps in medication continuity. She reported to her PCP last week that she has been struggling to take her SLBUP daily and has continued to use fentanyl pills most days and it also using about 6mg/day of non-prescribed alprazolam as well as methamphetamine. She has had 2 attempts at admitting to withdrawal management but has left AMA on day 1 both times. The nearest OTP is 200 miles away and she refuses residential treatment.

Case questions

- How can we reduce immediate risks (overdose, withdrawal, infection) to herself and her fetus?
- How can we engage her in care and encourage a stable therapeutic relationship?
- Is she a candidate for XRBUP?

- Naloxone, not using alone, fentanyl test strips, injection supplies
- XRBUP
- Trauma informed/safe, judgement free space
- Benzo taper
- Stimulant use treatment (CM, BH)
- Prenatal care
- Counsel on child welfare involvement
- MI for higher level of care

Final Takeaways/Summary

- Patients who use methamphetamine with fentanyl are at an increased risk of overdose death, while also having multiple barriers to accessing and retaining on MOUD
- XRBUP has a high patient satisfaction rating and a unique pharmacology resulting in an excellent blockade of fentanyl induced respiratory depression that can extend beyond the cessation of medication which may reduce overdose risk.
- Harm reduction based low-threshold access to XRBUP may help patients stay on buprenorphine longer. OBOT programs should work to reduce barriers to access this medication.

Resources

- Bridge to treatment: practical tools, algorithms, patient education https://bridgetotreatment.org/tools/resources/
- SAMHSA Buprenorphine Quick Start Guide https://www.samhsa.gov/sites/default/files/quick-start-guide.pdf
- ASAM Clinical Considerations: Buprenorphine Treatment of Opioid Use Disorder for Individuals Using High-potency Synthetic Opioids https://journals.lww.com/journaladdictionmedicine/Fulltext/9900/ASAM_Clinical_Considerations__Buprenorphine.212.aspx
- AK Native Tribal Health Consortium's Harm Reduction Toolkit https://www.iknowmine.org/wp-content/uploads/2021/01/ANTHC_Harm-Reduction_Toolkit.pdf
- National Harm Reduction Coalition https://harmreduction.org/

Sarah Spencer DO, FASAM
Addiction Medicine Specialist & Consultant

Ninilchik Traditional Council Community Clinic
Ninilchik, Alaska
Cell 907-299-7460
sarahspencerak@gmail.com