Opioid Response Network

Low-threshold Care for patients who use Stimulants with Fentanyl

OAFP COnference, September 2023

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Opioid Response Network

Learning Objectives

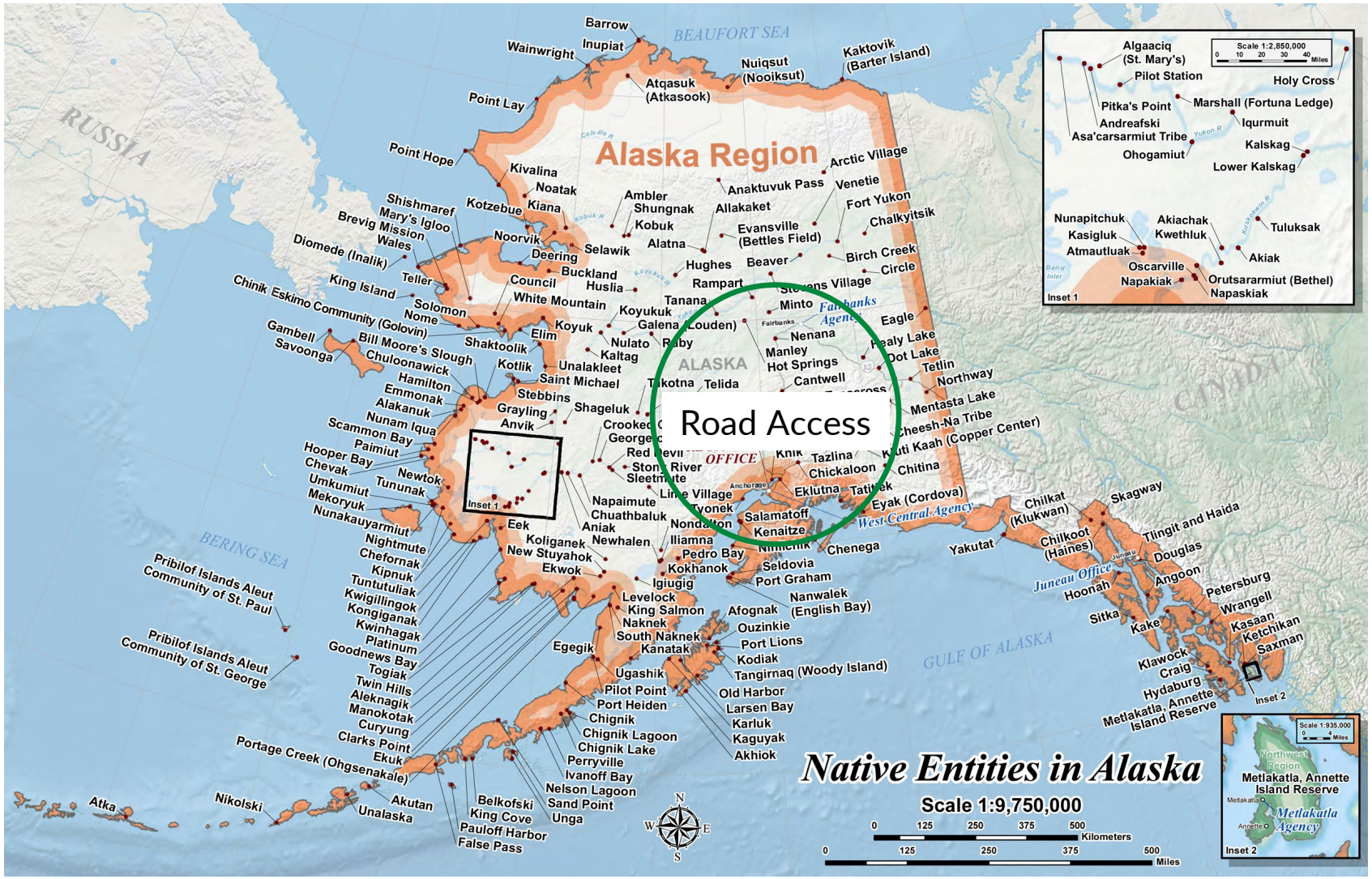
- **Participants will be able to describe the interaction of opioid and stimulant use.**
- **Participants will demonstrate understanding of treatment considerations when working with people with co-occurring opioid and stimulant use.**
- **Explore Harm reduction techniques for comorbid stimulant and opioid 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.



Over 200 Alaska Native tribes/villages

Spread over 660,000 mi²

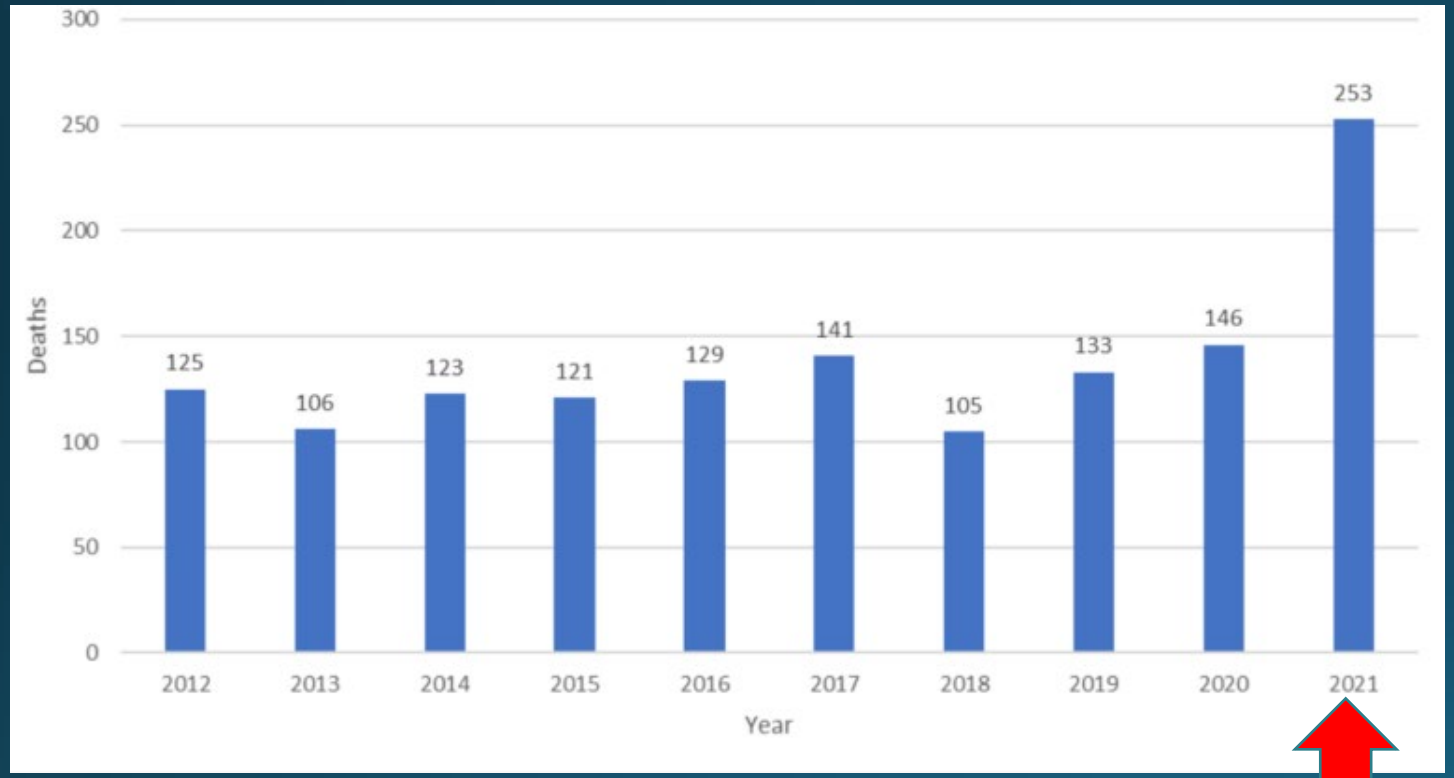
Most off the road system

What barriers do 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**

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

Use of stimulants with opioids has been increasing nationwide

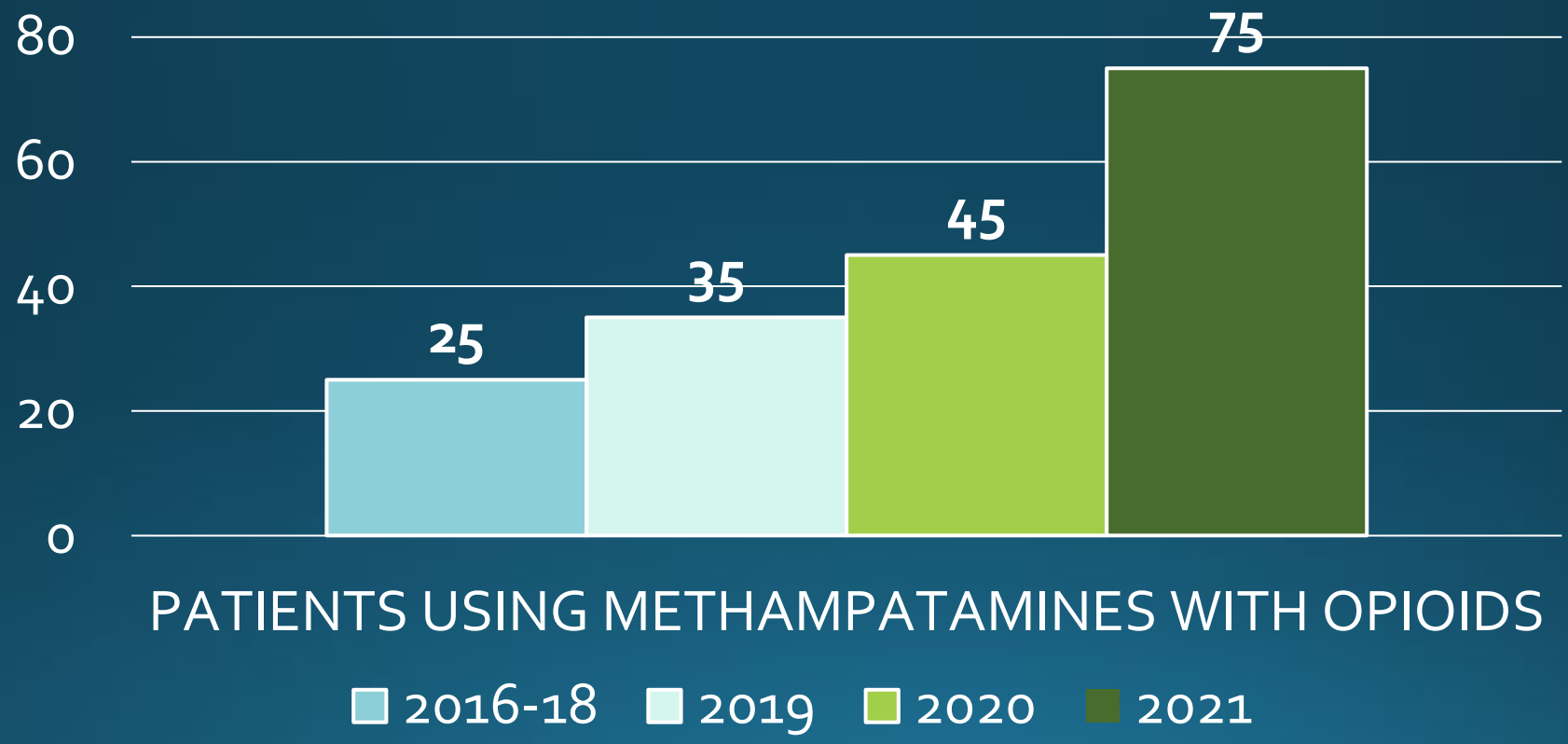
Past month methamphetamine use by people who use heroin

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

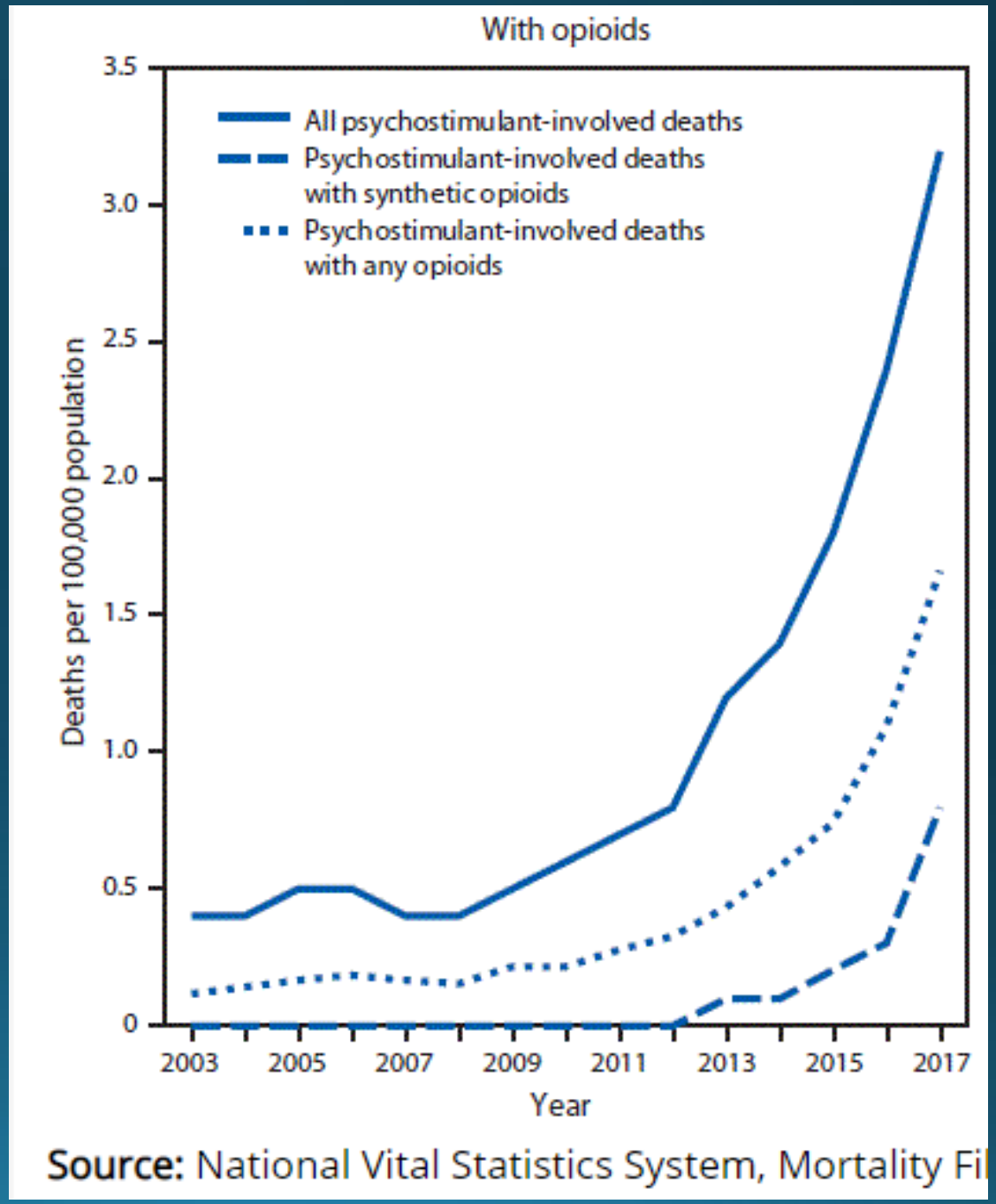
% NTC PATIENTS USING METHAMPHETAMINES WITH OPIOIDS ON OBOT ADMISSION



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



Why do people use stimulants with opioids?

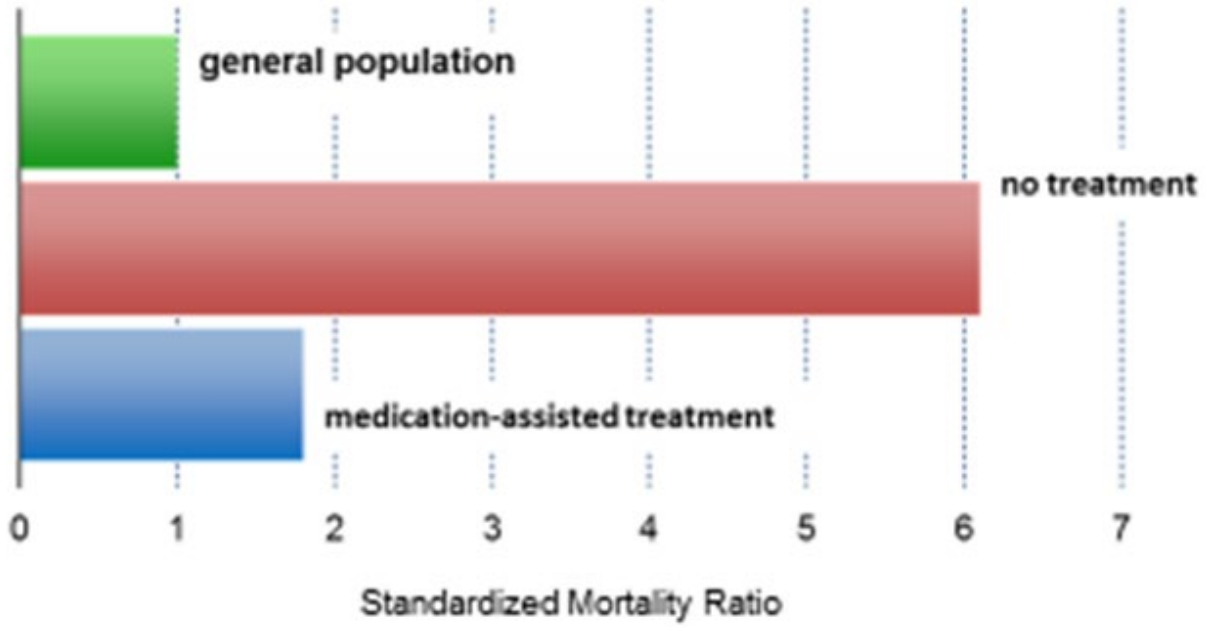
- To prolong the effects of fentanyl
- To counteract the negative effects of opioids (reduce the chance of "nodding out")
- To foster energy and enhance euphoria

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

Benefits of MAT: Decreased Mortality

Overdose risk the first 2 weeks after leaving treatment 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

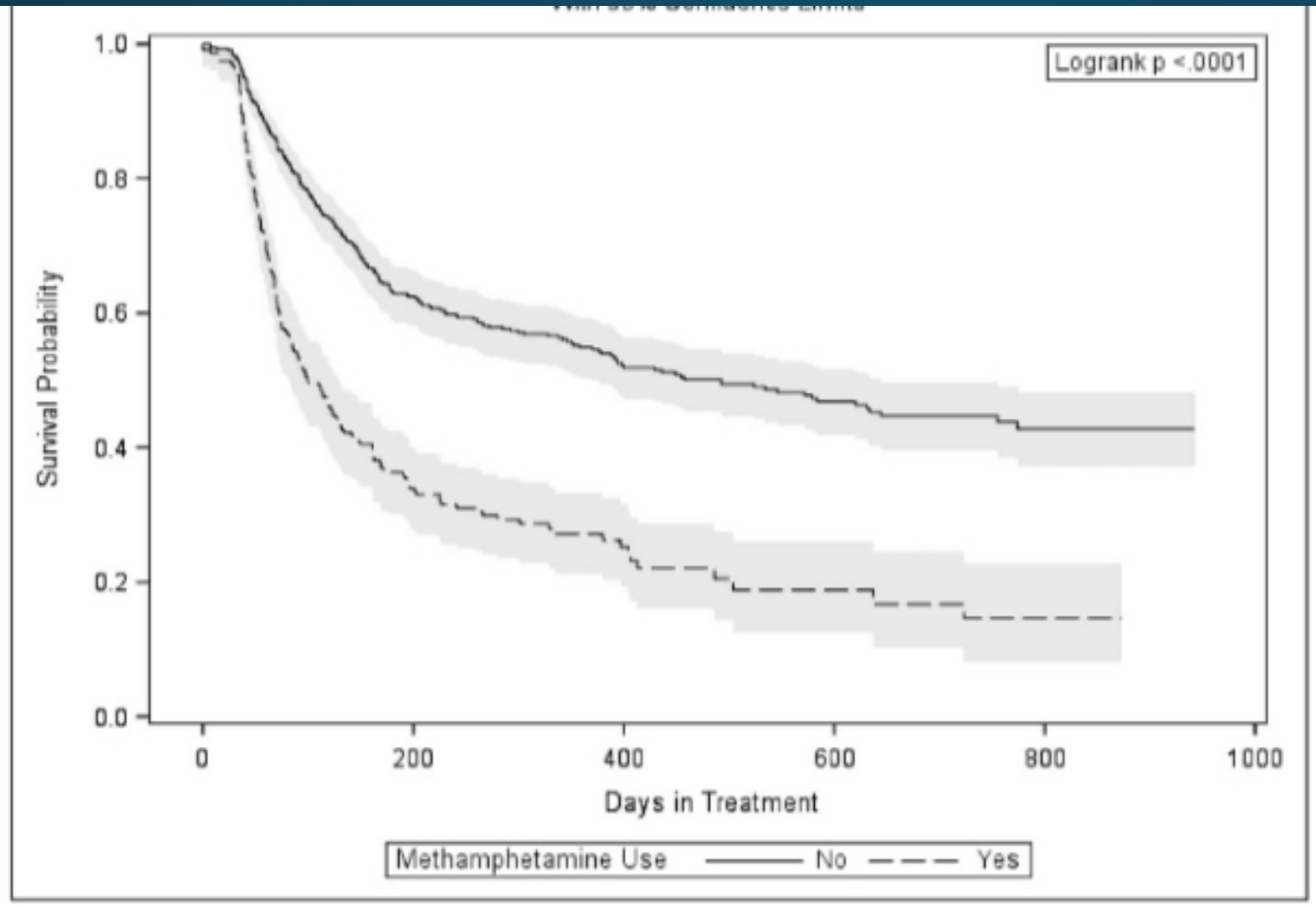


Fig. 1. Kaplan-Meier survival curves for methamphetamine users and non-users with 95% confidence bands (n = 770).

People who use meth 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

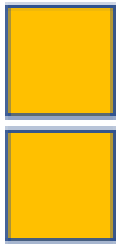
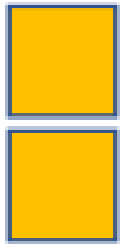
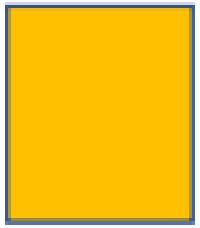
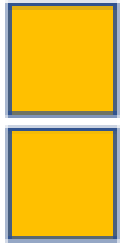
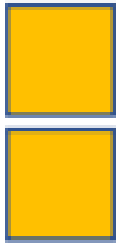
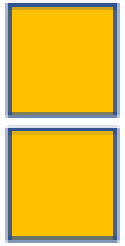
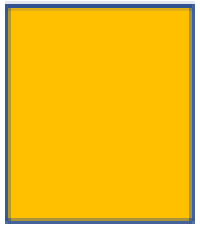
Harm Reduction Based Low Threshold Care (continued)

- 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

Telemedicine Intakes

- First visit via tele-med (same day when possible)
  - Reduces no-show rates
  - Over half via telephone only
- Review treatment options and discuss patient goals
- Provide medication initiation instructions and prescribe supportive meds and naloxone
  - Traditional, low-dose overlapping, high dose starts
- Counsel to come to in person visit even if failed to initiate SLBUP
- XRBUP takes 3-6 days to ship (tele-med 1 week prior to injection appt)

How to

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Buprenorphine dose	0.5mg daily	0.5mg BID	1mg BID	2mg BID	4mg BID	4mg TID	8mg BID
Film size	2mg	2mg	2mg	2mg	2mg	2mg	8mg
Morning dose							
Afternoon Dose							
Night dose							
Full agonist	Continue	Continue	Continue	Continue	Continue	Continue	STOP

CA BRIDGE

Buprenorphine Self-Start

Guidance for patients starting buprenorphine outside of hospitals or clinics

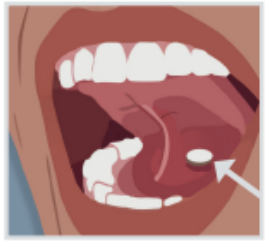
1. Plan to take a day off and have a place to rest.
2. Stop using and wait until you feel very sick from withdrawals (at least 12 hours is best, if using fentanyl it may take a few days).
3. Dose one or two 8mg tablets or strips UNDER your tongue (total dose of 8-16mg).
4. Repeat dose (another 8mg-16mg) in an hour to feel well.
5. The next day, take 16-32mg (2-4 tablets or films) at one time.

If you have started bup before:

- If it went well, that's great! Just do that again.
- If it was difficult, talk with your care team to figure out what happened and find ways to make it better this time. You may need a different dosing plan than what is listed here.

If you have never started bup before:

- Gather your support team and if possible take a "day off."
- You are going to want space to rest. Don't drive.
- Using cocaine, meth, alcohol or pills makes starting bup harder, and mixing in alcohol or benzos can be dangerous.



Place dose under your tongue (sublingual).

If you have a light habit: *(For example, 5 "Norco 10's" a day)*

- Consider a low dose: start with 4mg and stop at 8mg total.
- **WARNING:** Withdrawal will continue if you don't take enough bup.

If you have a heavy habit: *(For example, injecting 2g heroin a day or smoking 1g fentanyl a day)*

- Consider a high dose: start with a first dose of 16mg.
- For most people, the effects of bup max out at around 24-32mg.
- **WARNING:** Too much bup can make you feel sick and sleepy.

Not going well? Have questions? Contact your Navigator for help!

https://bridgetotreatment.org/resource/rapid-guidance-for-patients-starting-buprenorphine-outside-of-hospitals-or-clinics/

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

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

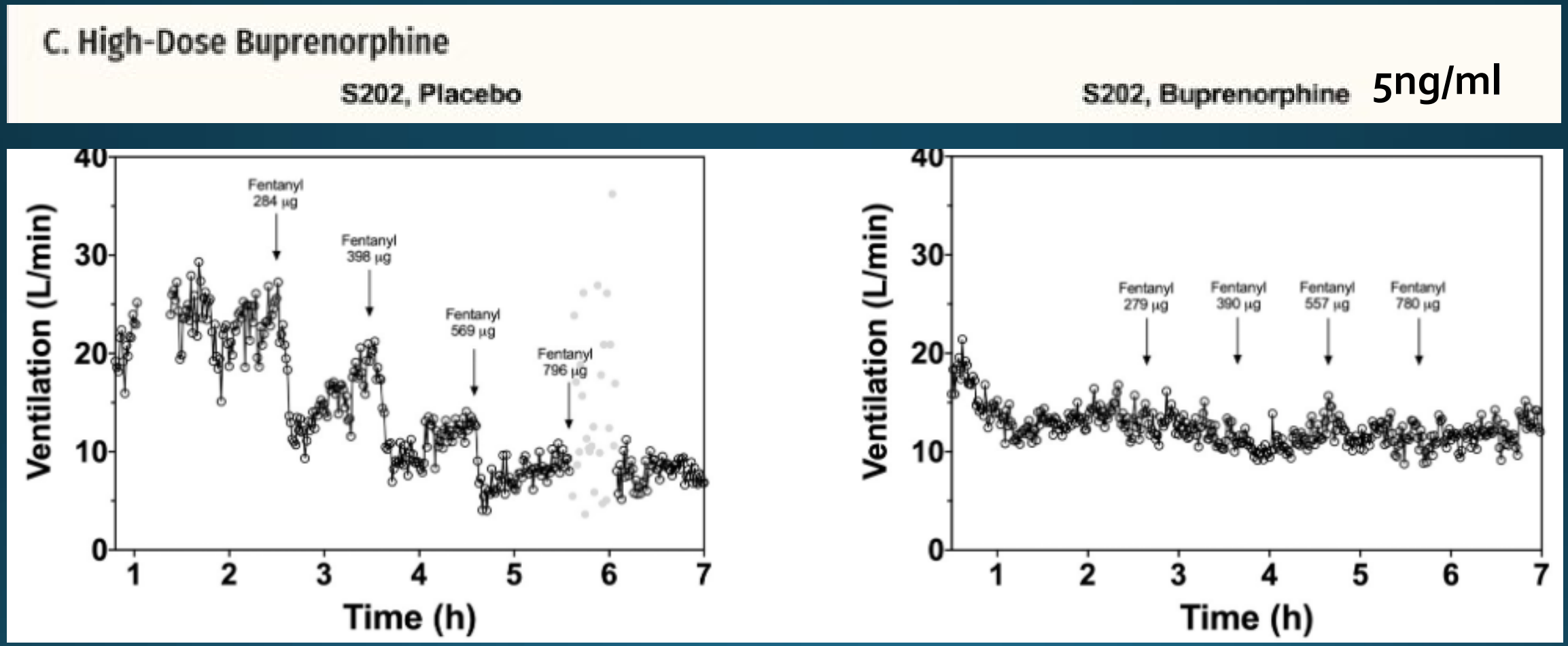
XRBUP
Patient Selection

- 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

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

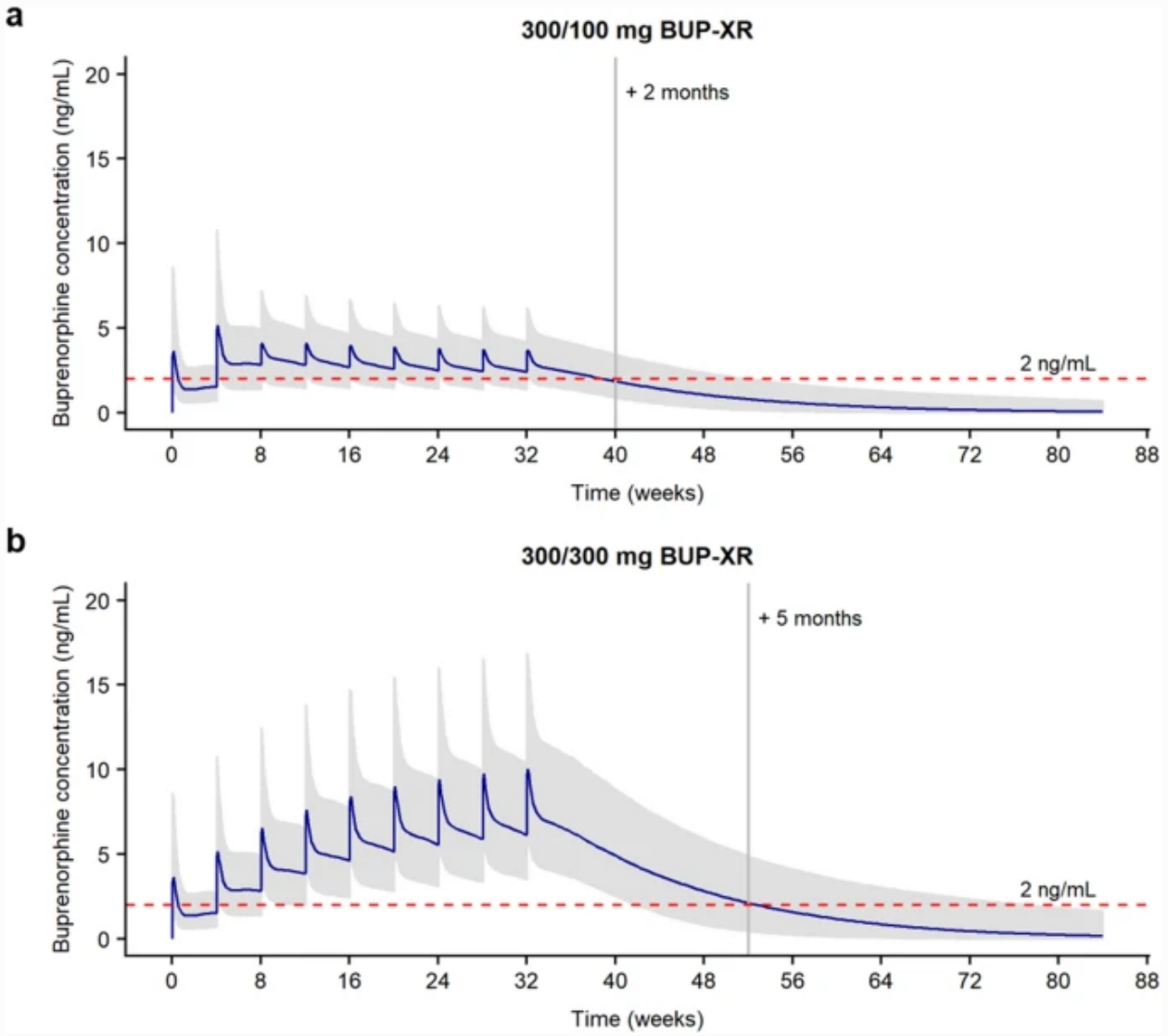
Pharmacokinetic parameters	SUBUTEX daily stabilization		SUBLOCADE		
Mean	12 mg (steady-state)	24 mg (steady-state)	300 mg# (1st injection)	100 mg* (steady-state)	300 mg* (steady-state)
$C_{avg,ss}$ (ng/mL)	1.71	2.91	2.19	3.21	6.54
$C_{max,ss}$ (ng/mL)	5.35	8.27	5.37	4.88	10.12
$C_{min,ss}$ (ng/mL)	0.81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

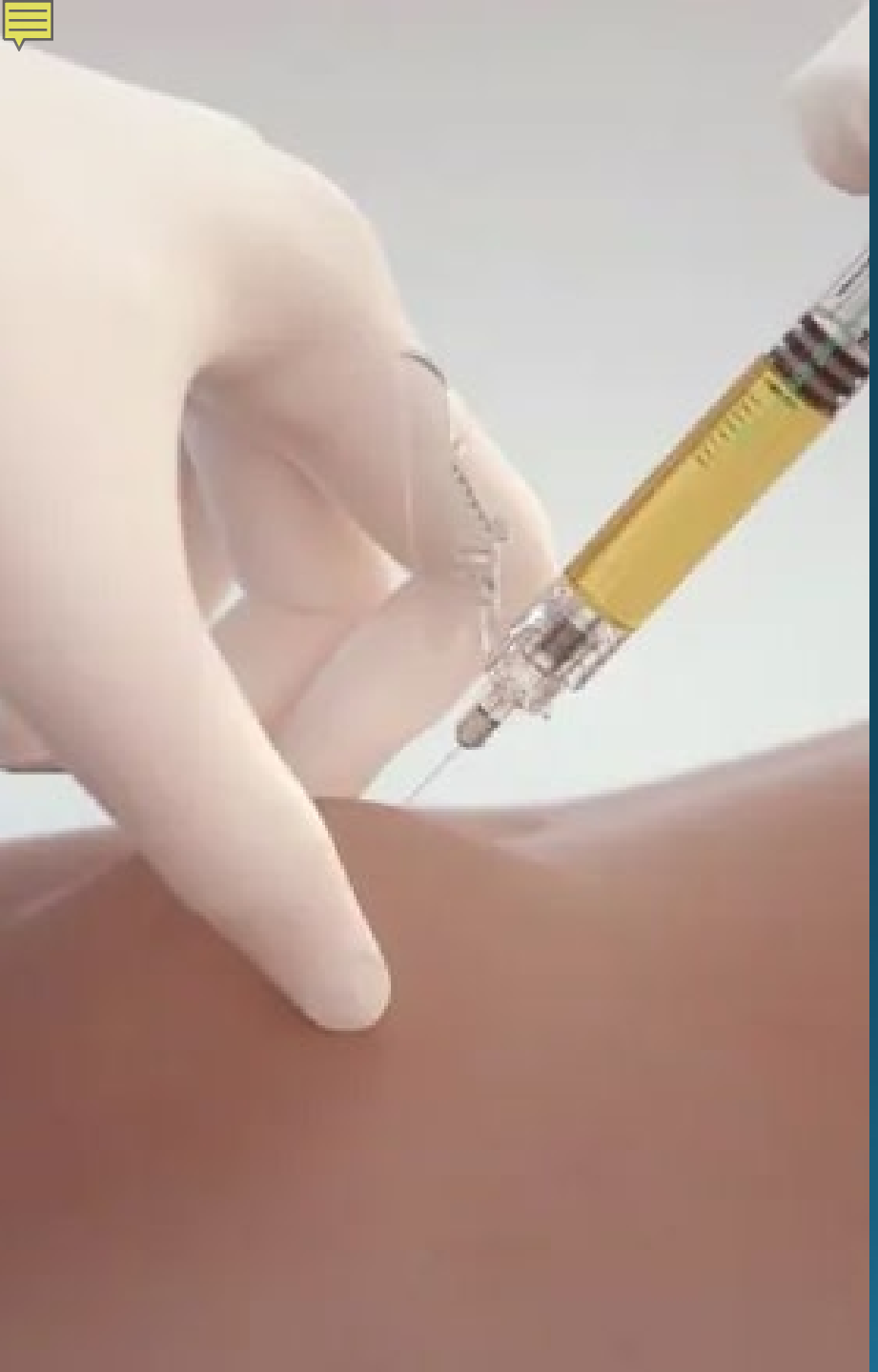


Predicted decrease in buprenorphine plasma concentrations for BUP-XR dosing regimens following treatment interruption. **a** 300/100-mg dosing regimen 2; **b** 300/300-mg dosing regimen. Blue solid lines: median of the simulated data; gray shaded areas: 90% prediction intervals of simulated data. A total 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 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)
- Primary care/harm reduction services

Rapid XRBUP Initiation Studies

Am J Addict. Author manuscript; available in PMC 2020 Jul 27.
PMCID: PMC7383940
Published in final edited form as:
NIHMSID: NIHMS1611380
Am J Addict. 2020 Jul; 29(4): 345–348.
PMID: 32167629
Published online 2020 Mar 13. doi: 10.1111/ajad.13018

Case Series: Rapid Induction Onto Long Acting Buprenorphine Injection for High Potency Synthetic Opioid Users

John J. Mariani, MD,[1,2] Amy Mahony, LMHC,[1] Muhammad N. Iqbal, MD,[1] Sean X. Luo, MD,PhD,[1,2] Nasir H. Naqvi,

Open-label, rapid initiation pilot study for extended-release buprenorphine subcutaneous injection

Howard Hassman, **Stephanie Strafford** ✉, Sunita N. Shinde, Amy Heath, Brent Boyett & Robert L. Dobbins

Received 04 Apr 2022, Accepted 23 Jul 2022, Published online: 24 Aug 2022

Download citation https://doi.org/10.1080/00952990.2022.2106574 Check for updates

Contemp Clin Trials. 2021 May; 104: 106359.
PMID: 33737199
Published online 2021 Mar 16. doi: 10.1016/j.cct.2021.106359

The Design and Conduct of a Randomized Clinical Trial Comparing Emergency Department Initiation of Sublingual versus a 7-day Extended-Release Injection Formulation of Buprenorphine for Opioid Use Disorder: Project ED INNOVATION

Gail D'Onofrio, MD, MS,[1,2] Kathryn F. Hawk, MD, MHS,[1] Andrew Herring, MD,[3] Jeanmarie Perrone, MD,[4] Ethan Cowan,

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."

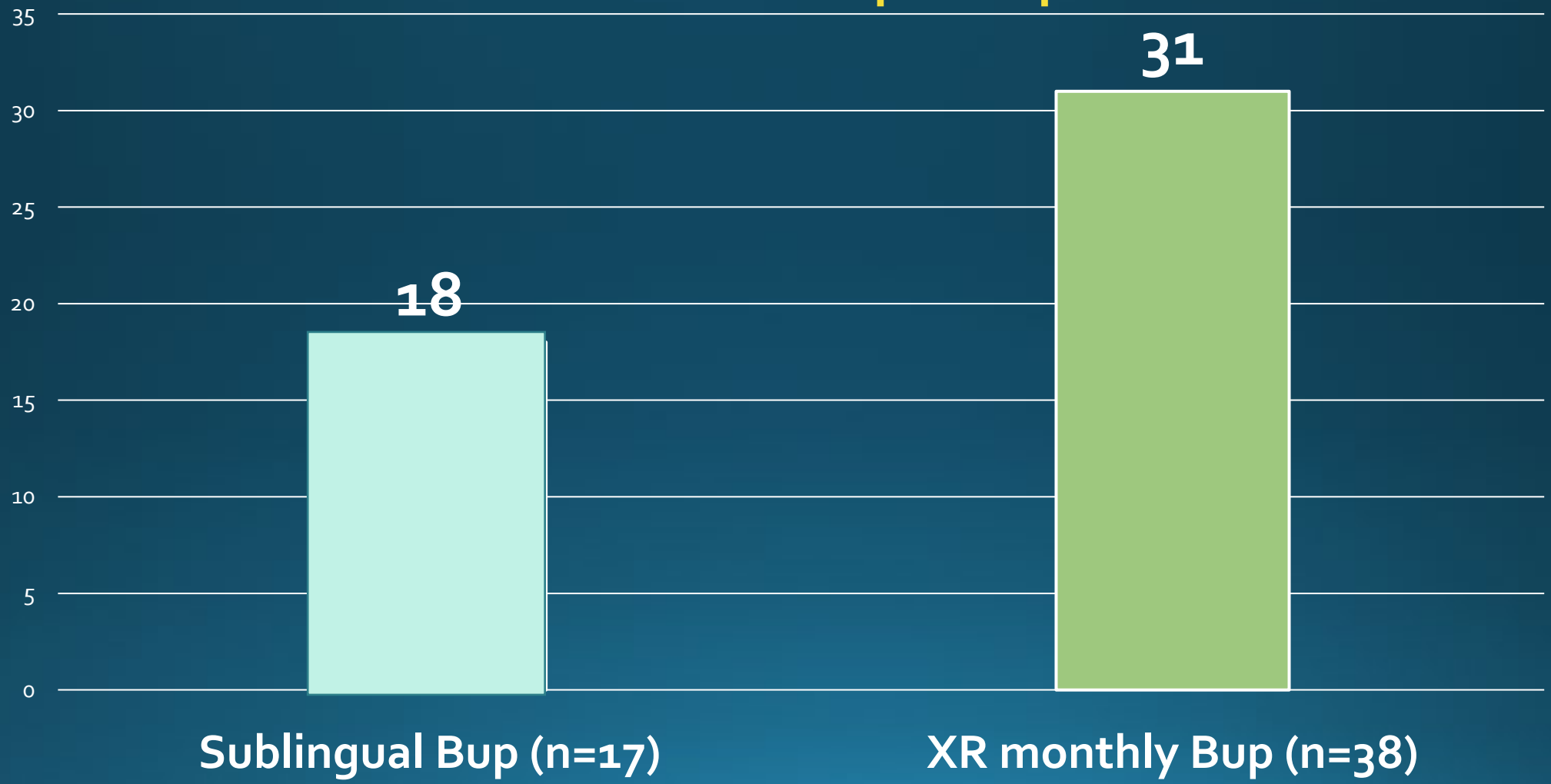
"I tried using heroin and it [my opioid receptors] was totally blocked."

Methods

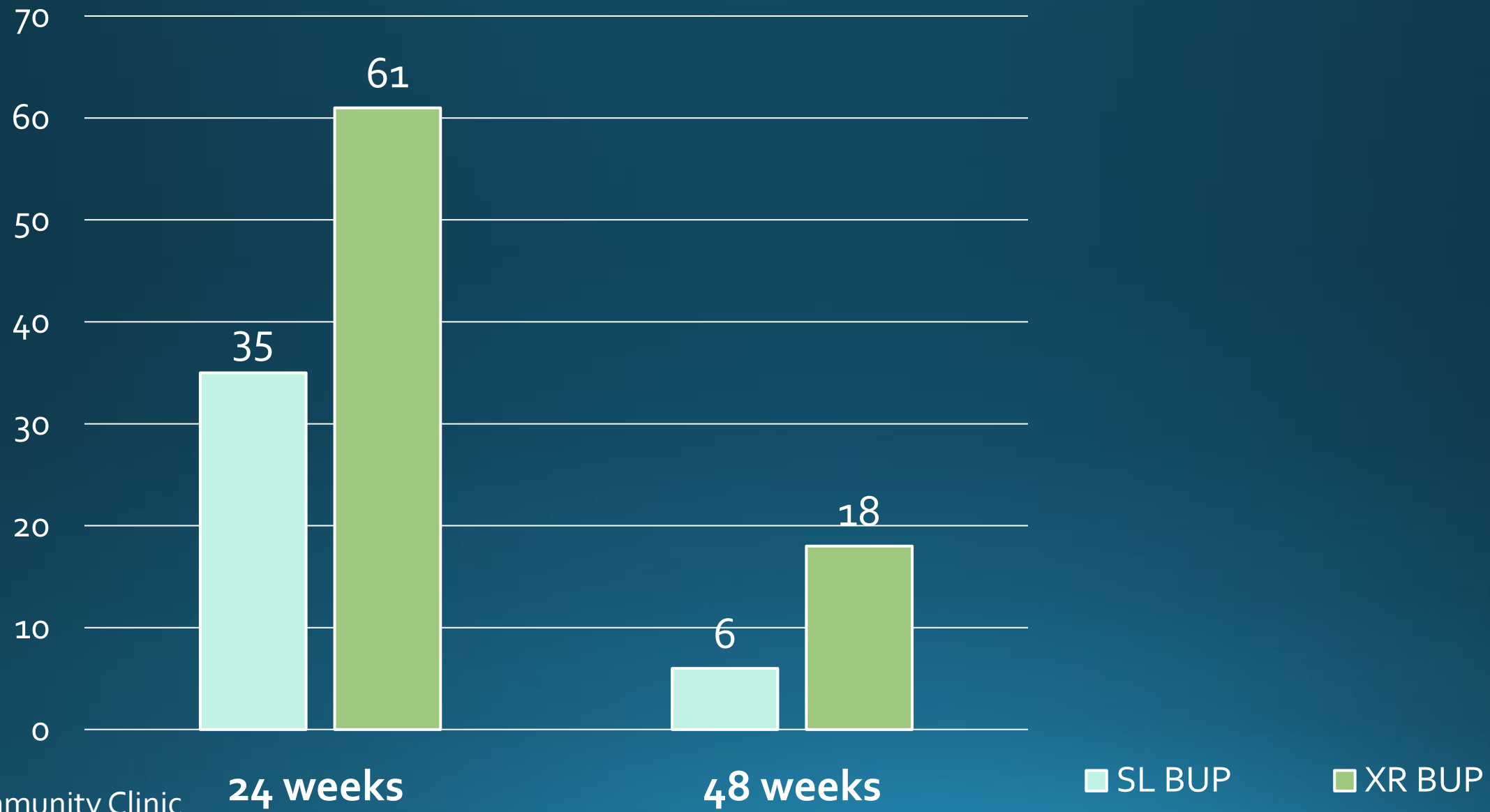
- Reviewed NTC prescriber PDMP records from Jan 2016-Jan 2022
- Identified patients admitted on or after May 2018 and before Aug 2021 who used Methamphetamines with Opioids (n=55)
- Compared retention in treatment (cumulative weeks of buprenorphine therapy)
  - SLBUP vs XRBUP 2018-2022 (at least 1 XRBUP shot)
  - SLBUP 2016-2018 vs SLBUP 2018-2022 (no change)

Treatment Retention SL vs XR Buprenorphine

Cumulative Weeks of Buprenorphine



% Patients with 24 and 48 week cumulative therapy on SL BUP vs XR BUP



Counseling for XRBUP patients

- You won't feel 100% the first month, its normal to have uncontrolled cravings and use, especially the end of the month. Please call us if you need help with withdrawal symptoms and cravings, supplemental SLBUP can be provided for the first 2 months

- Your medication levels will continue to rise for 4-5 months if you stay on high dose XRBUP, so most people find their cravings better controlled the more shots they get

- Nausea, sweating and drowsiness are common the first week after the first shot. Call us if you need more anti-nausea medication. As your body adjusts to the buprenorphine levels the side effects should go away, and most people find each shot is easier.

Counseling for XRBUP patients

- You might not feel the injection wearing off, however if you don't return for your next injection the medication will wear off and most people will have return of cravings and return to use.

- As the shot wears off you may lose your opioid blockade and tolerance and return to use could result in higher risk of overdose. Always keep naloxone on hand, go slow and don't use alone.

- You can always get your injection no matter what drugs you have been using. Don't be afraid to talk with us about your drug use. If you want support to reduce your drug use, we can help.

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 stimulant use dz

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

Contingency Management

What is Contingency Management?

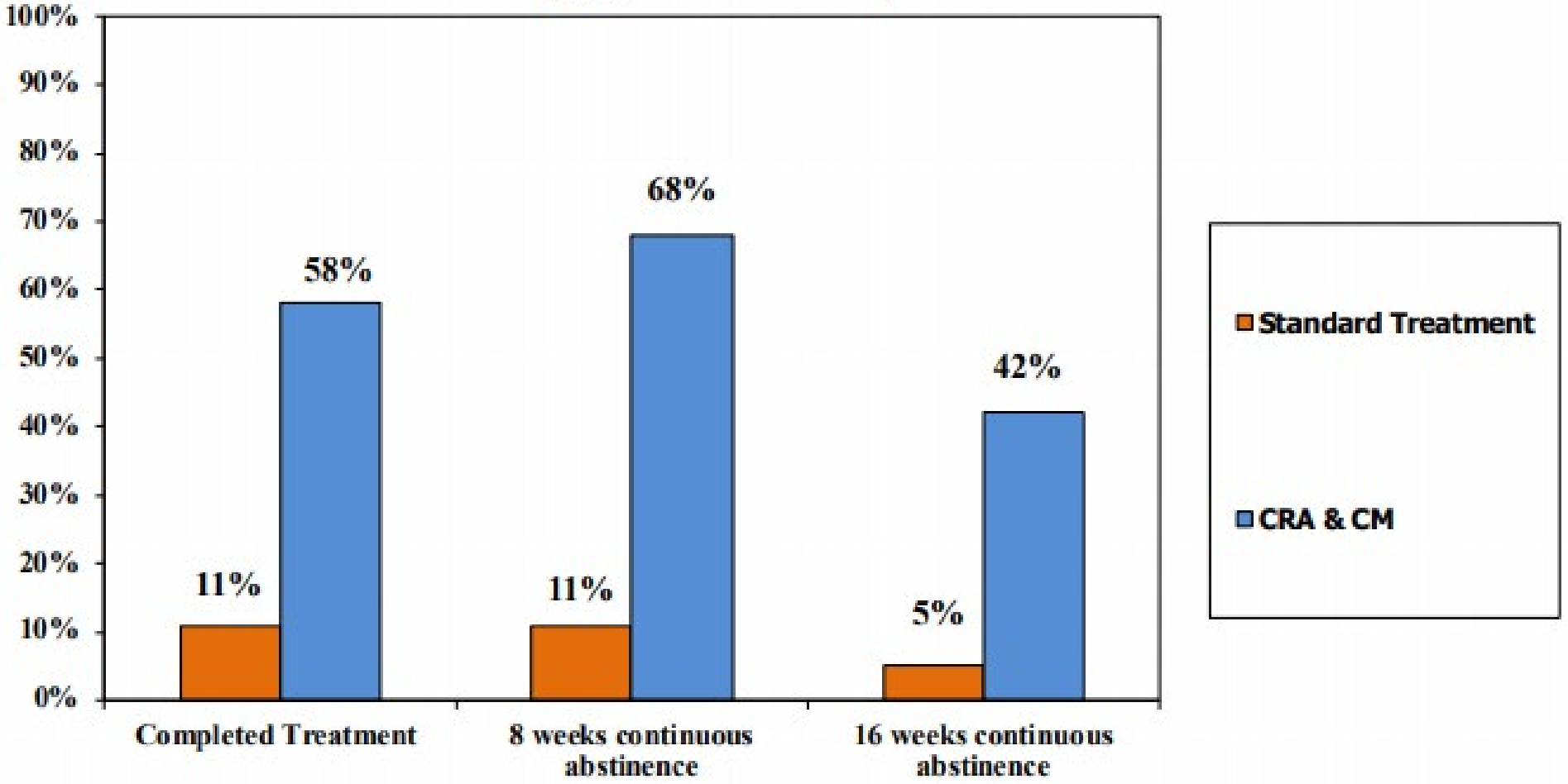
The most effective behavioral health intervention to treat substance use disorders, but also the least utilized.

Provides immediate rewards for meeting goals

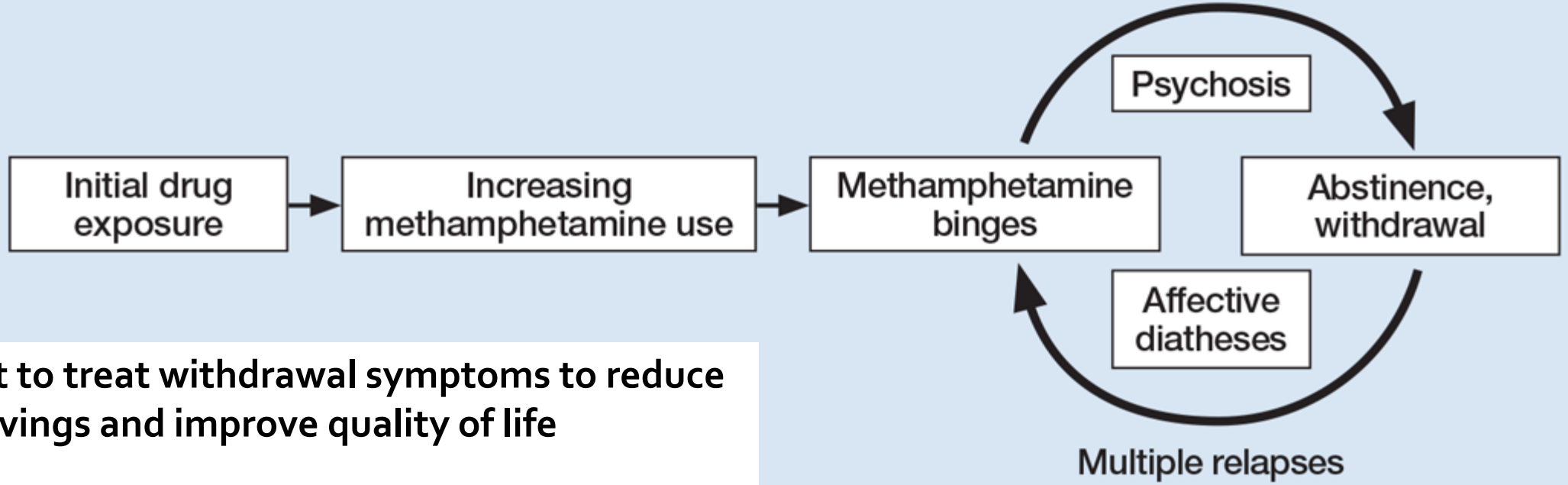
- Negative UDS
- Coming to appointments
- Getting monthly medication injections
- Attending counseling

Example: Gift cards = $100/month

CRA and Contingency Management: Higgins et al., 1993



Cycle of methamphetamine abuse



Its important to treat withdrawal symptoms to reduce cravings and improve quality of life

Provide non-narcotic medications and behavioral health support for:

Depression
Anxiety
Insomnia
Pain
Thought disorders

ASK ABOUT ANXIETY AND DEPRESSION

Treat with non-narcotic medications that may address comorbid conditions

Mirtazapine helps sleep and appetite

Avoid Benzos → try buspirone instead

Consider treating physiological w/d sxs that mimic anxiety with prn clonidine, hydroxyzine, propranolol

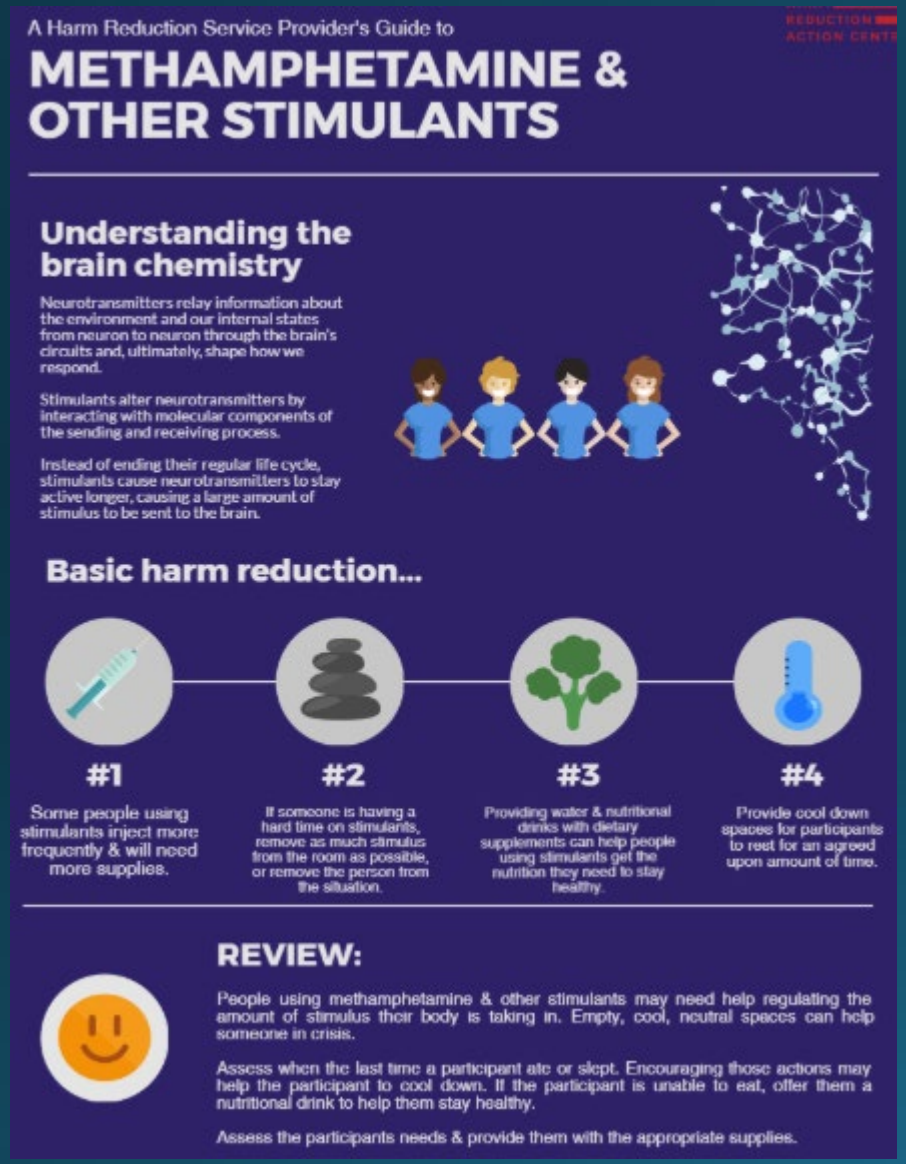
Ask About Sleep

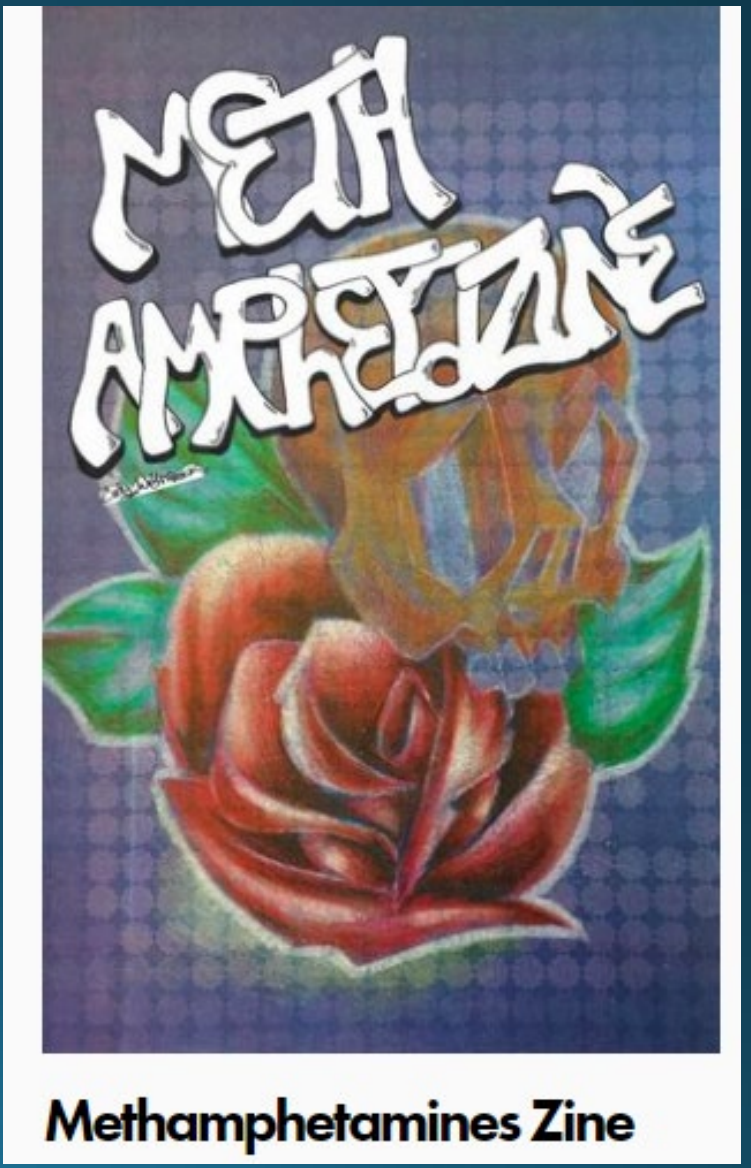
- Make a differential diagnosis to determine whether a client's sleep problems likely stem from protracted withdrawal or are the result of other causes.
- Educate clients about good sleep habits: adopting a regular sleep routine (going to bed and getting up at the same times), exercising early in the day, minimizing caffeine intake, eating well, and avoiding late afternoon naps.
- Utilize non-narcotic meds, consider co-treating comorbid pain/mood disorders: eg TCAs, mirtazapine, trazodone, doxepin, quetiapine (all off label), low-dose melatonin
- Test for sleep apnea (may be central vs obstructive)
- CBTI (free VA app)

The Substance Abuse and Mental Health Services Administration's (SAMHSA's) Center for Substance Abuse Treatment (CSAT) is developing a Substance Abuse in Brief Fact Sheet on sleep problems

Harm Reduction for Psychostimulant Use

- Overamping prevention (Eat, Hydrate, Sleep)
- Treatment for co-occurring substance use disorders (ex: OUD)
- Naloxone education and distribution
- Exercise
- Dental hygiene supplies
- Syringe services programs, safer injection supplies
- Smoking supplies
- Fentanyl test strips
- Never use alone, Test doses
- Safe sexual practices, condoms, lube
- Hep C treatment





https://www.harmreductionactioncenter.org/new-page

Fentanyl Test Strips

1. Add sterile water to your **empty** baggie or the **cooker you just prepped** – mix well!

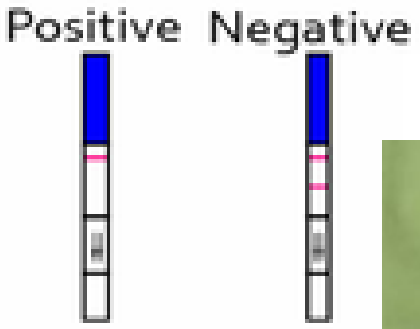
   **Load your shot FIRST! Only test your rinse water!

2. **Dip the test strip** in the water, in up to the first line & **hold for 15 seconds**

3. **Place test strip** on sterile surface or across top of cooker.

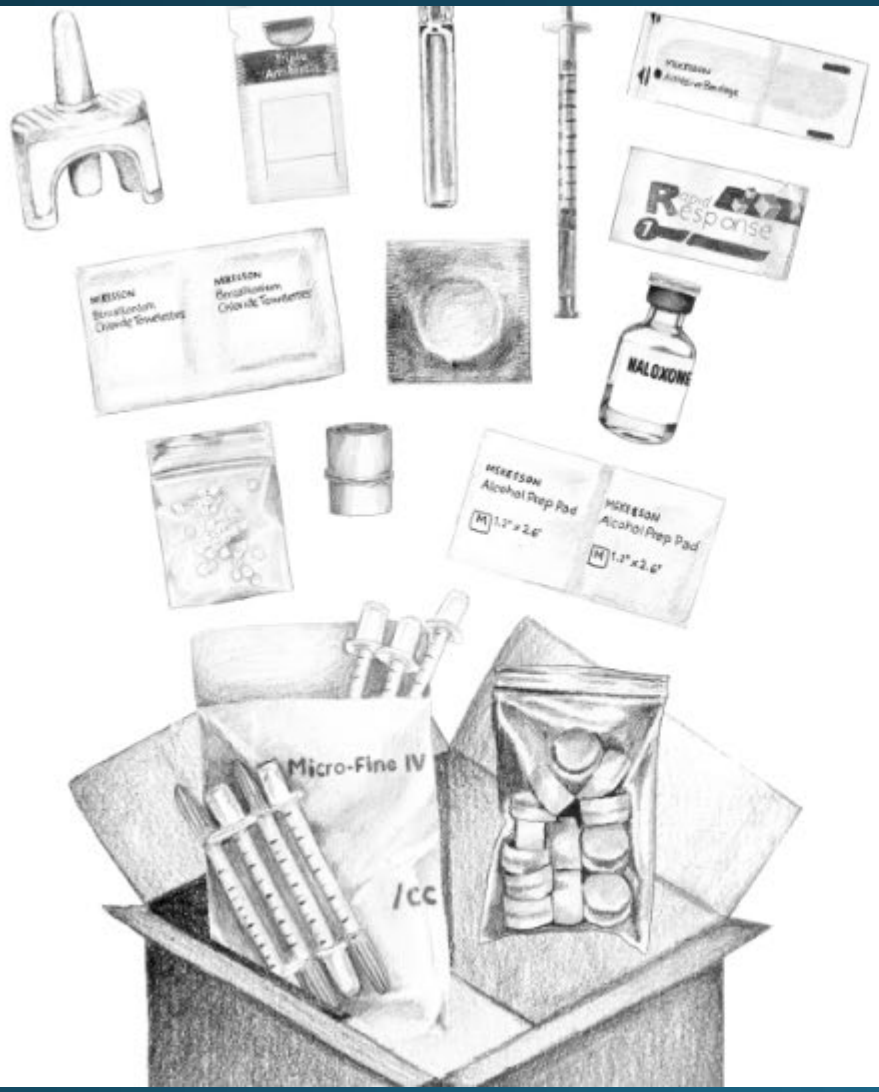
One line POSITIVE

Two lines NEGATIVE



NARCAN RX

- Every patient who receives a prescription for opioids, a new MAT patient, a family member or someone who knows someone who knows uses opioids **should be provided a Narcan® kit.**
- The best way to make Narcan® kits available- hand them out to people who use. They can be the best first responders.
- **Even stimulant users who don't use opioids need a Narcan kit due to fentanyl contamination**



WHAT IS
NEXT Distro?

An online and mail-based **harm reduction service** designed to reduce opioid overdose death, prevent injection-related disease transmission, and improve the lives of people who use drugs.

https://nextdistro.org/

An example of a prescription for syringes

Diabetic syringes

29g, 1/2in *"longs"* *or* ***31g, 5/16in*** *"shorts"*
(ask patient which they prefer)
½ or 1 cc
(ask patient which they prefer, ½ cc is more common)

Dispense #___ boxes of 100 syringes
Refill PRN X 1year

Case #1

- A 35 yo Alaska native male who lives in a roadless village with no local buprenorphine prescribers is seeing you via telemedicine today for a consult to start buprenorphine. He has been smoking 10-15 fentanyl pills “blues” daily for the past year. He wants to get on the XRBUP monthly injection because “the subs make me deathly ill, even when I waited for a day and a half after stopping the blues, I took a half a strip and it made me sicker than a dog. My friend got the shot and said it’s great”. He gets very anxious when you tell him that he will need to take SL BUP prior to getting his injection. “ I have to work, I can’t be home sick all week”. He only has 1 day off work per week available to fly into the clinic for his injection administration. The village receives mail on M,W,F.

Case #1 questions

- How can we assist him in expediting his medication initiation and reducing his barrier to access?
- How to we reduce his days away from home/work?
- How do address his concerns about precipitated withdrawal?

- Telemedicine
- Mail out meds/home initiation
- High dose/low dose start options and comfort meds
- Harm reduction supplies
- Offer rapid XRBUP start
- Find local clinic to send XRBUP to for administration
- Flexible follow up schedule, bridging with SLBUP PRN

Case #2

- 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 #2 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

XRBUP in Pregnancy

Patients presenting to antenatal services who are also receiving treatment with long acting depot buprenorphine

Long acting depot buprenorphine has been approved for the treatment of opioid dependence in Australia

The Therapeutic Goods Administration (TGA) in Australia has approved two long-acting injected depot buprenorphine medications: Buvidal™ and Sublocade™. The Buvidal™ product was listed on the PBS on 1 September 2019.

What does this mean for antenatal, maternity and neonatal health services?

Increasing numbers of patients may present to these health services who are being treated with depot buprenorphine.

These formulations of buprenorphine are administered weekly or monthly

Buvidal™ is a modified release formulation of buprenorphine which is administered via subcutaneous (SC) injection in *weekly* or *monthly* intervals.

Sublocade™ is an extended-release formulation of buprenorphine which is administered via subcutaneous injection in *monthly* intervals.

Depot buprenorphine can be considered for pregnant women

Under the NSW Clinical Guidelines, depot buprenorphine may be considered for pregnant women if the risks of transferring her to sublingual buprenorphine or methadone outweigh the benefits.

https://www.health.nsw.gov.au/aod/resources/Pages/depot-buprenorphine-info-for-non-aod-clinicians-antenatal.aspx

There is a component in the inactive depot gel of XRBUP that has been associated with birth defects in rats. There are no studies in humans. If feasible, XRBUP should be avoided in women planning pregnancy or the first trimester when teratogenic risks are highest. In women who are unable to safely be maintained on SL BUP, XRBUP may be considered for use throughout pregnancy when benefits outweigh risks and the mother consents.

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.

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