



**UW PACC**

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

# **LOW-THRESHOLD EXTENDED-RELEASE BUPRENORPHINE AS A TOOL TO REDUCE OVERDOSE RISK FOR PEOPLE WHO USE STIMULANTS AND FENTANYL**

**SARAH SPENCER DO, FASAM**

**NTC/ANTHC**

**JUNE 2023**



# FINANCIAL DISCLOSURES

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 SAP in Homer



# LEARNING OBJECTIVES

## Review

Review the epidemiology of co-morbid stimulant and opioid use disorders and associated overdose risk

## Review

Review the pharmacology of extended-release buprenorphine (XRBUP)

## Explore

Explore tactics to reduce barriers to care for accessing XRBUP

## Explore

Explore how low-threshold XRBUP may affect retention and OD risk in patients with co-morbid stimulant and OUD



**Over 200 Alaska Native tribes/villages**  
**Spread over 660,000 mi<sup>2</sup>**  
**Most off the road system**

# BARRIERS TO MOUD ACCESS IN RURAL AK



Travel/Transportation/Gas

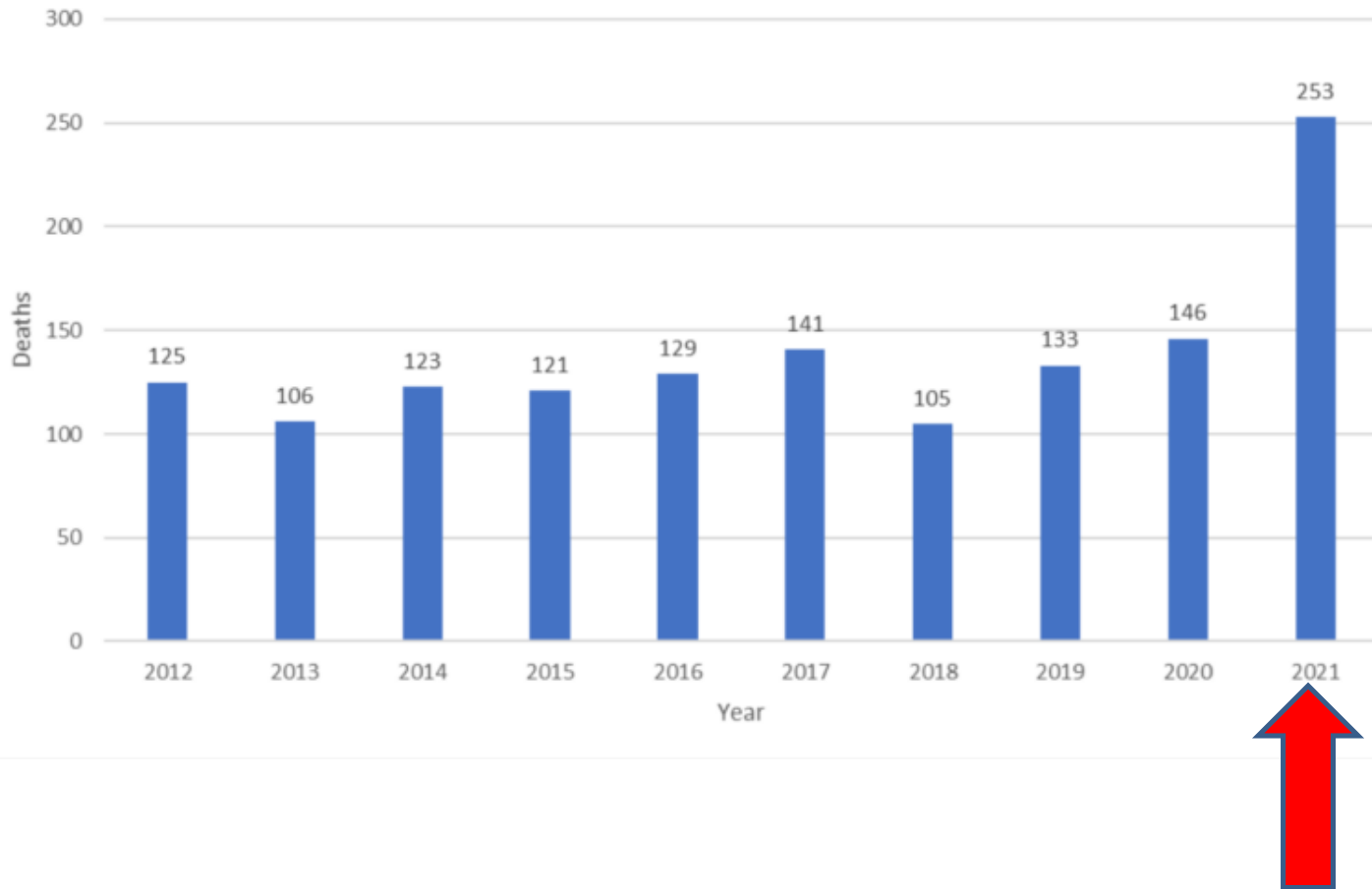
Weather Holds/ Rx delayed in the Mail

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%

**Illicit Fentanyl:** DEA analysis has found counterfeit pills ranging from .02 to 5.1 milligrams (more than twice the lethal dose) of fentanyl per tablet (42% of seized pills contain at least 2mg)



DEA illustration of 2 milligrams of fentanyl, a lethal dose in most people



DEA



Use of stimulants with opioids has been increasing nationwide

Past month methamphetamine  
use by people who use heroin

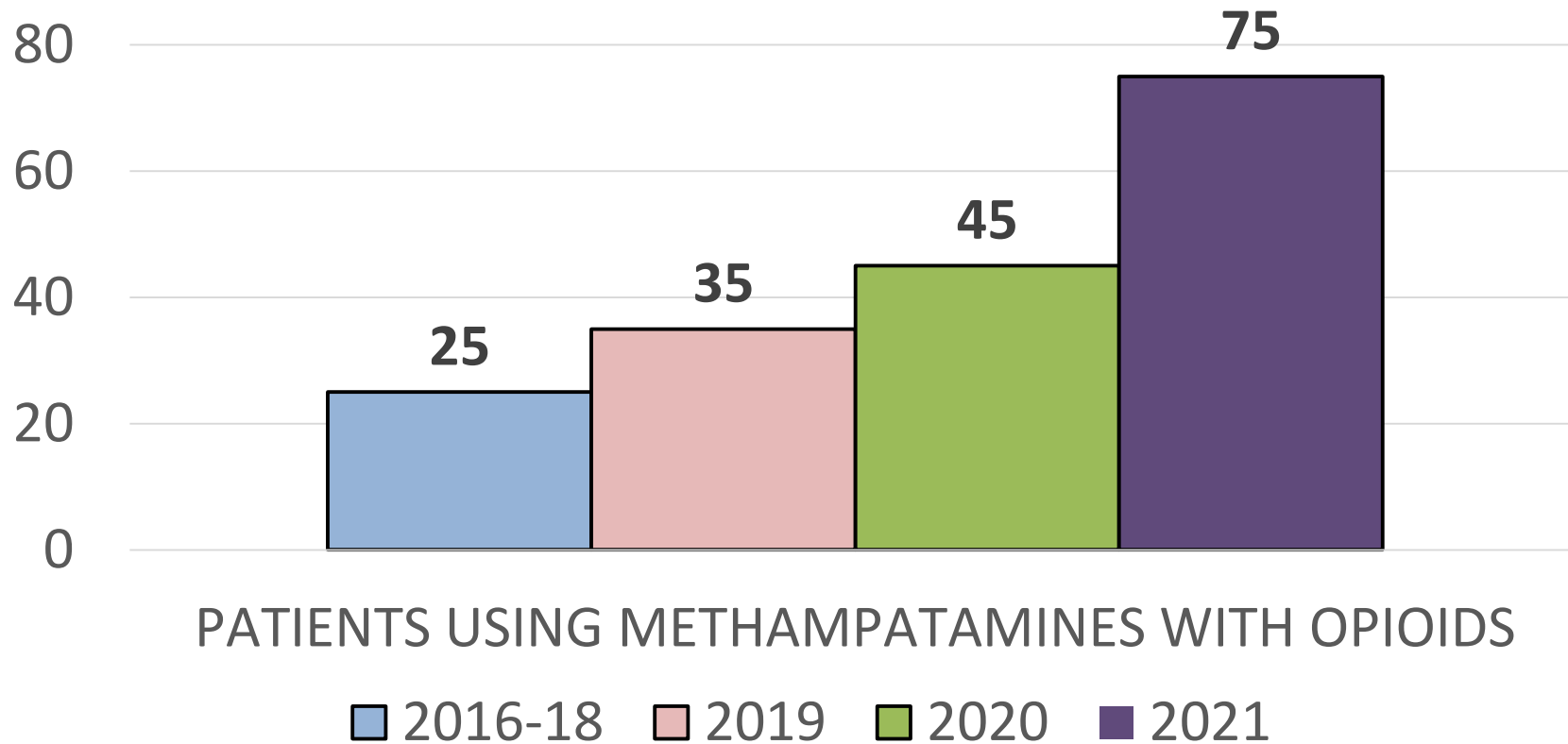


**9.0% to 44.0%**

from 2015-2019

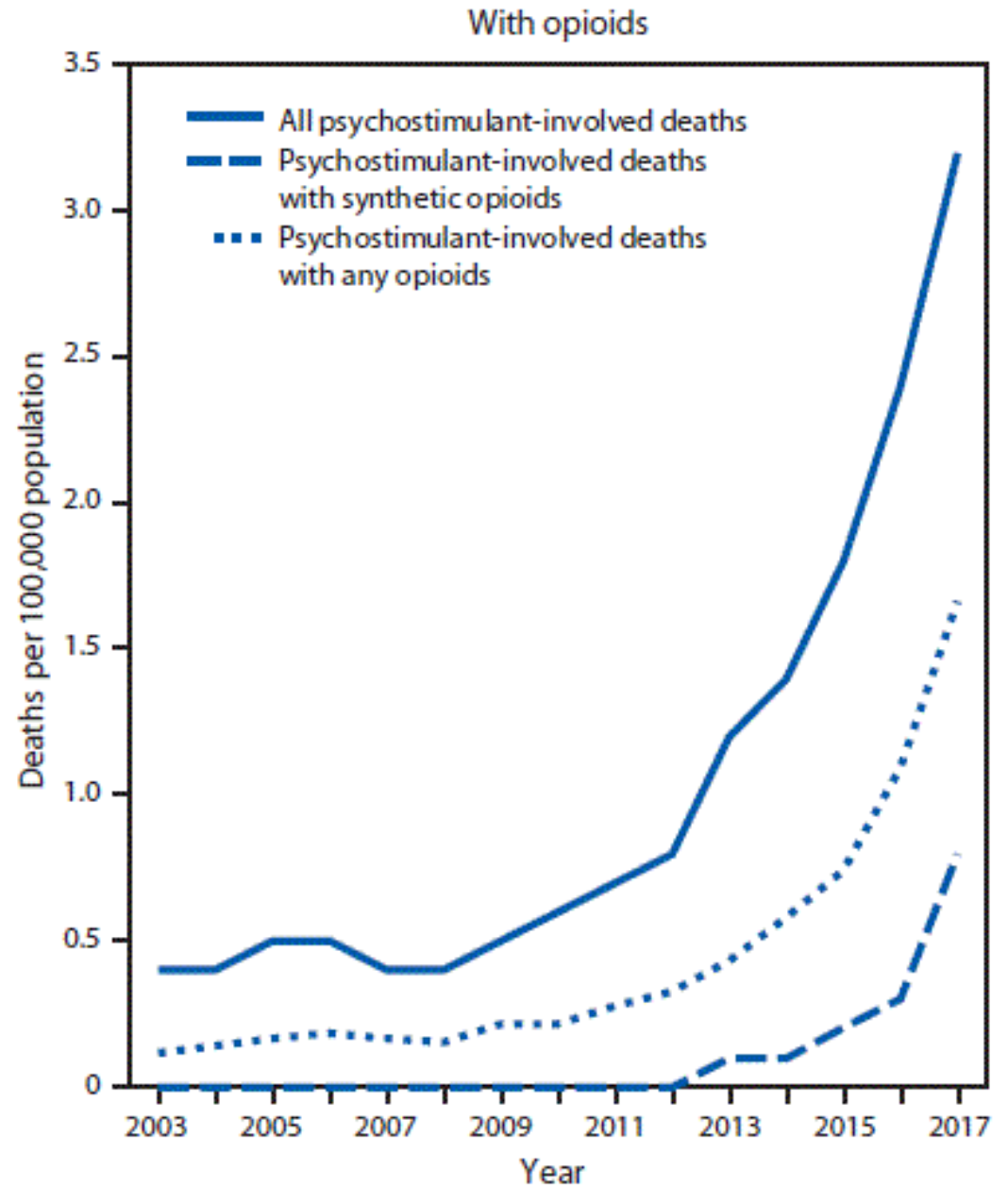


# % NTC PATIENTS USING METHAMPHETAMINES WITH OPIOIDS ON OBOT ADMISSION



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



Source: National Vital Statistics System, Mortality File

# Why do people use stimulants with opioids?

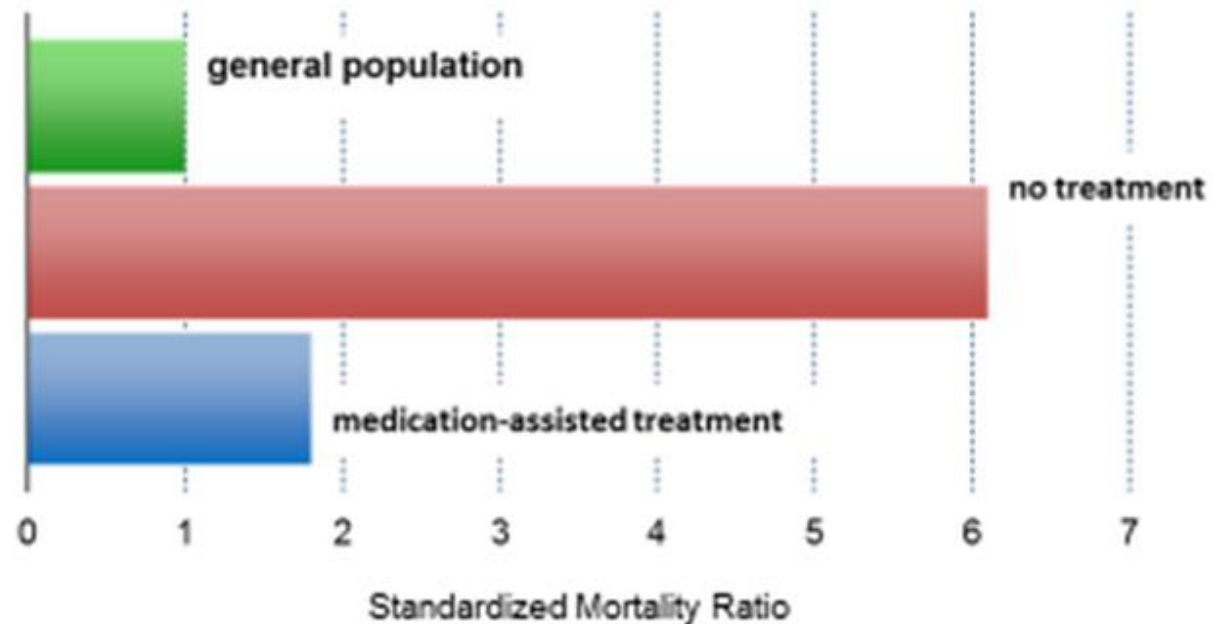
- To prolong the effects of fentanyl
- To counteract the negative effects of opioids (reduce the chance of “nodding out”)
- To foster energy and enhance euphoria

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

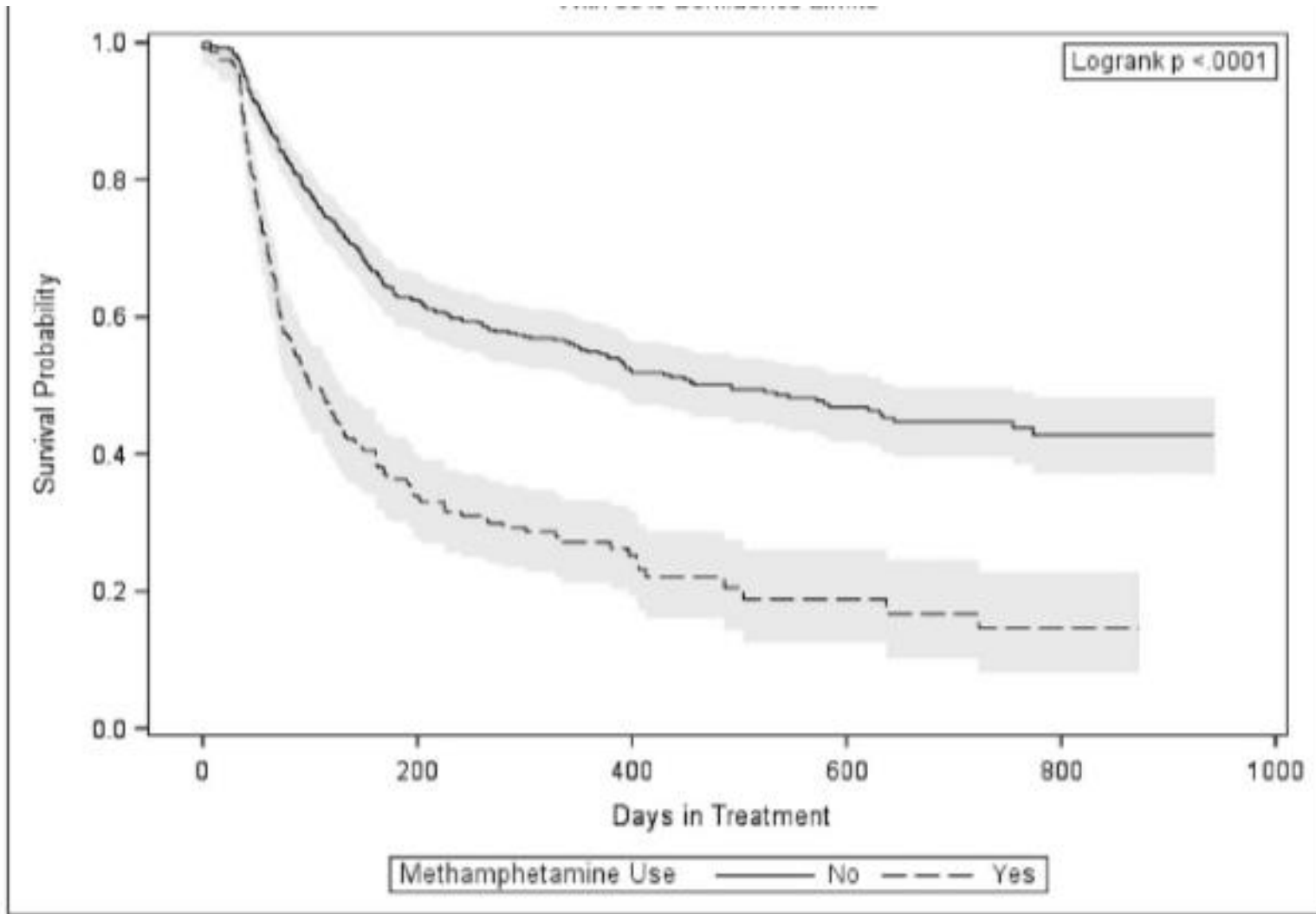
# Benefits of MAT: Decreased Mortality

## Death rates:

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



**MOUD can reduce death rates by 80%**



**People who use meth may have poorer retention in MOUD programs**

**But those who stay in treatment may reduce their use**

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

# Low Threshold Care

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

# Harm Reduction Based Low Threshold Care

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

## Harm Reduction Based Low Threshold Care

- 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





# 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 sx

## 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

- 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



- 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

## XRBUP PATIENT SELECTION (CONTINUED)

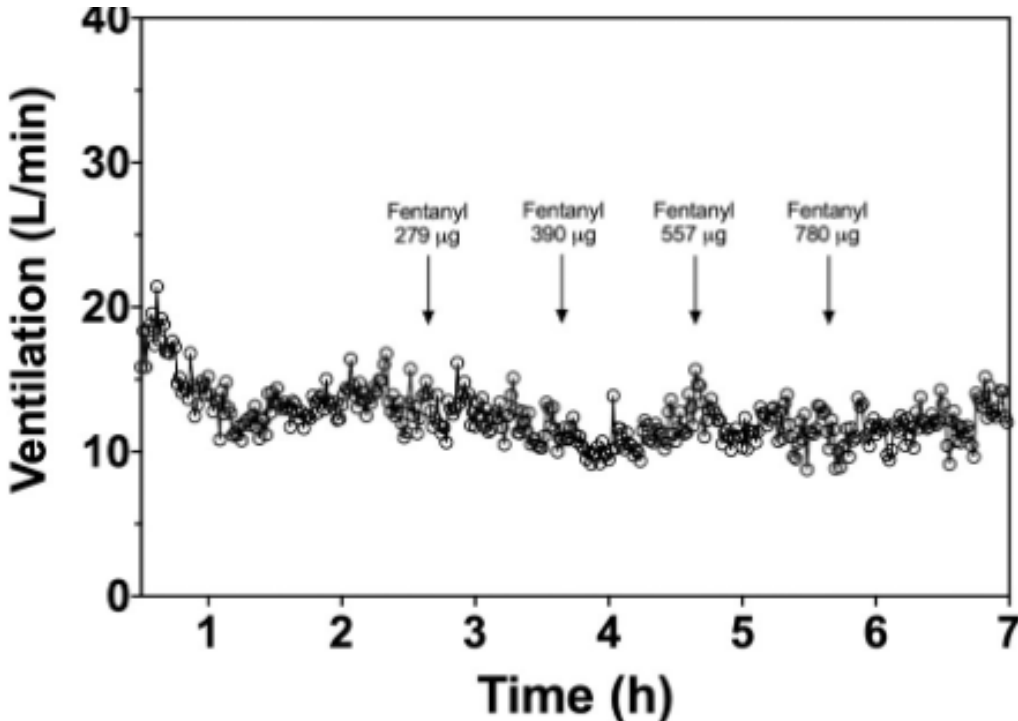
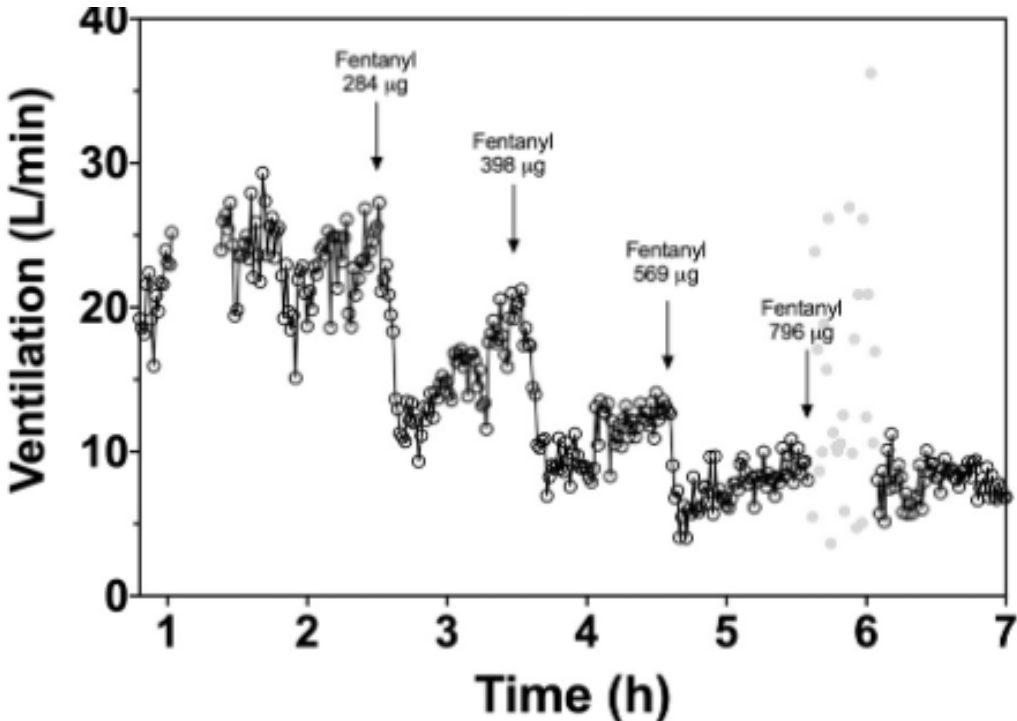


# High Dose XR Buprenorphine blocks fentanyl induced respiratory depression

C. High-Dose Buprenorphine

S202, Placebo

S202, Buprenorphine 5ng/ml



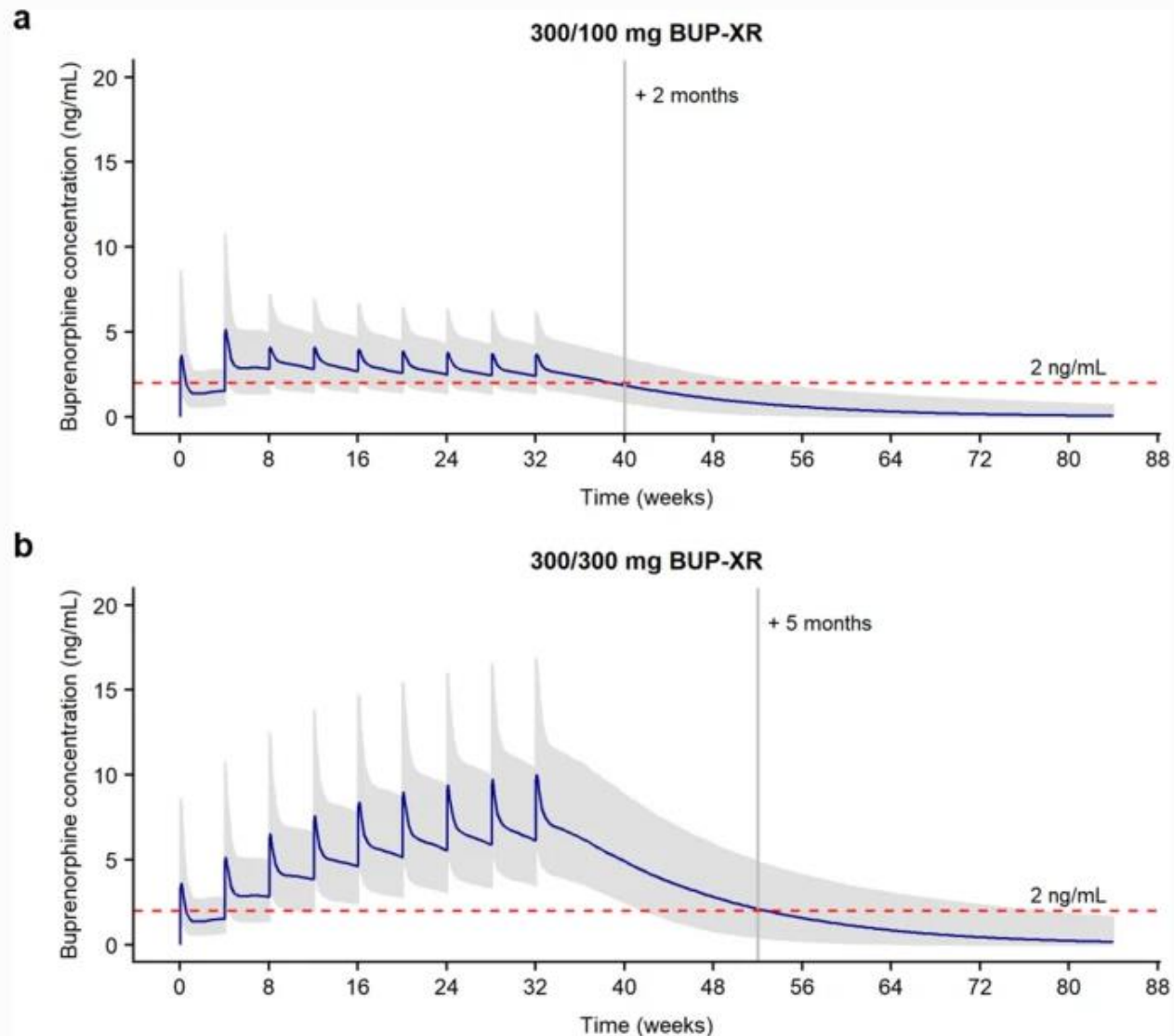
Blockade was lost under 2 ng/ml

| Pharmacokinetic parameters | SUBUTEX<br>daily stabilization |                         | SUBLOCADE                              |                           |                           |
|----------------------------|--------------------------------|-------------------------|--|---------------------------|---------------------------|
|                            | 12 mg<br>(steady-state)        | 24 mg<br>(steady-state) | 300 mg#<br>(1 <sup>st</sup> injection) | 100 mg*<br>(steady-state) | 300 mg*<br>(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**

# Extended opioid blockade after medication cessation

Fig. 6



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)

Predicted decrease in buprenorphine plasma concentrations for BUP-XR dosing regimens following treatment interruption. **a** 300/100-mg dosing regimen; **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

<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<sup>nd</sup>/3<sup>rd</sup> trimester)

# Rapid XRBUP Initiation Studies

[Am J Addict.](#) Author manuscript; available in PMC 2020 Jul 27.

Published in final edited form as:

[Am J Addict.](#) 2020 Jul; 29(4): 345–348.

Published online 2020 Mar 13. doi: [10.1111/ajad.13018](#)

PMCID: PMC7383940


NIHMSID: NIHMS1611380

PMID: [32167629](#)


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

[John J. Mariani](#), MD,<sup>1,2</sup> [Amy Mahony](#), LMHC,<sup>1</sup> [Muhammad N. Iqbal](#), MD,<sup>1</sup> [Sean X. Luo](#), MD, PhD,<sup>1,2</sup> [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>



[Contemp Clin Trials.](#) 2021 May; 104: 106359.

Published online 2021 Mar 16. doi: [10.1016/j.cct.2021.106359](#)

PMID: [33737199](#)

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,<sup>1,2</sup> [Kathryn F. Hawk](#), MD, MHS,<sup>1</sup> [Andrew Herring](#), MD,<sup>3</sup> [Jeanmarie Perrone](#), MD,<sup>4</sup> [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.”

# Counseling for XRBUP patients

- You won't feel 100% the first month, it's 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

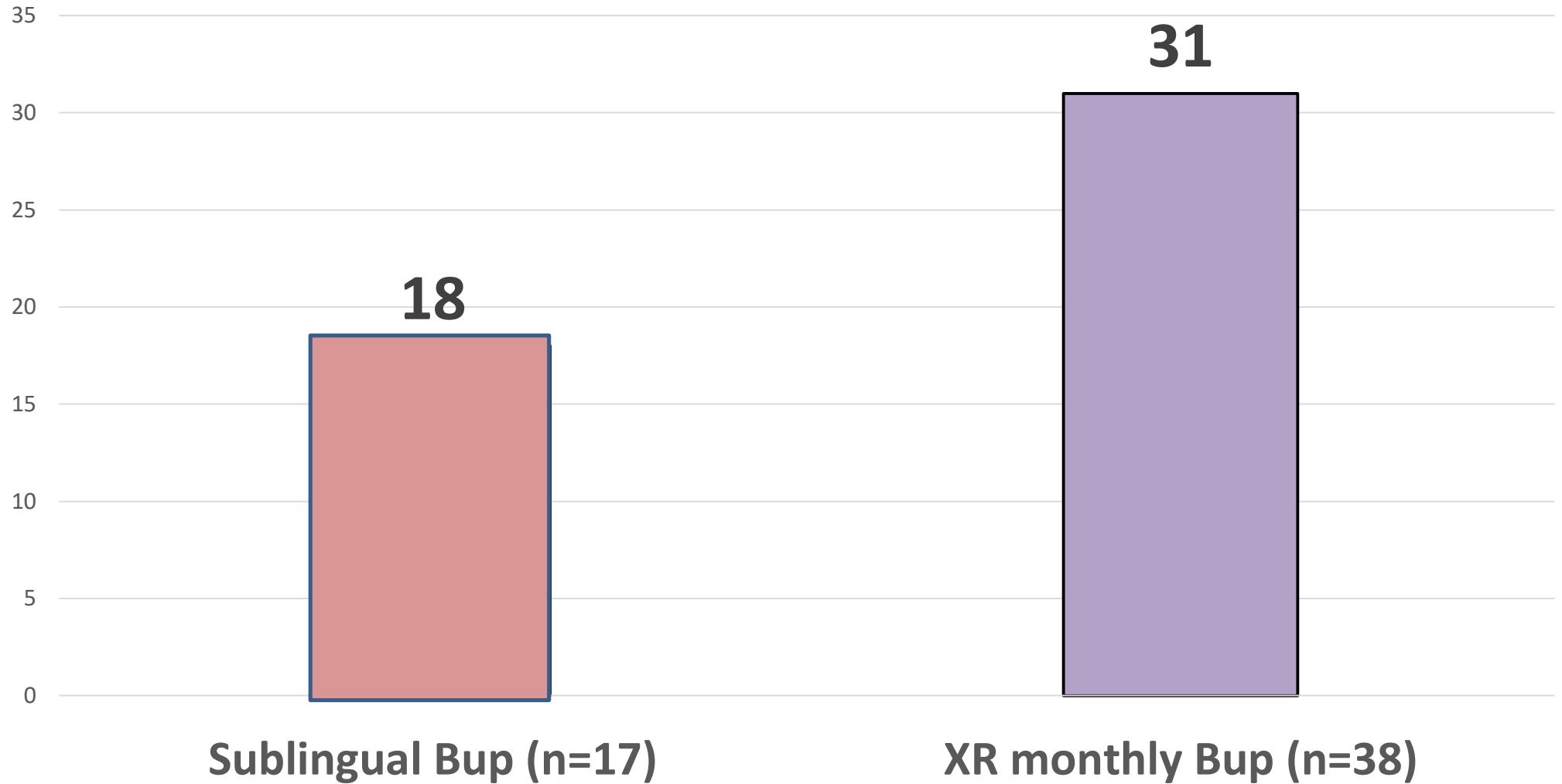
- You might not feel the injection wearing off, however if you don't return for your next injection the medication will wear off and most people will have return of cravings and return to use.
- As the shot wears off you may lose your opioid blockade and tolerance and return to use could result in higher 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.

# METHODS

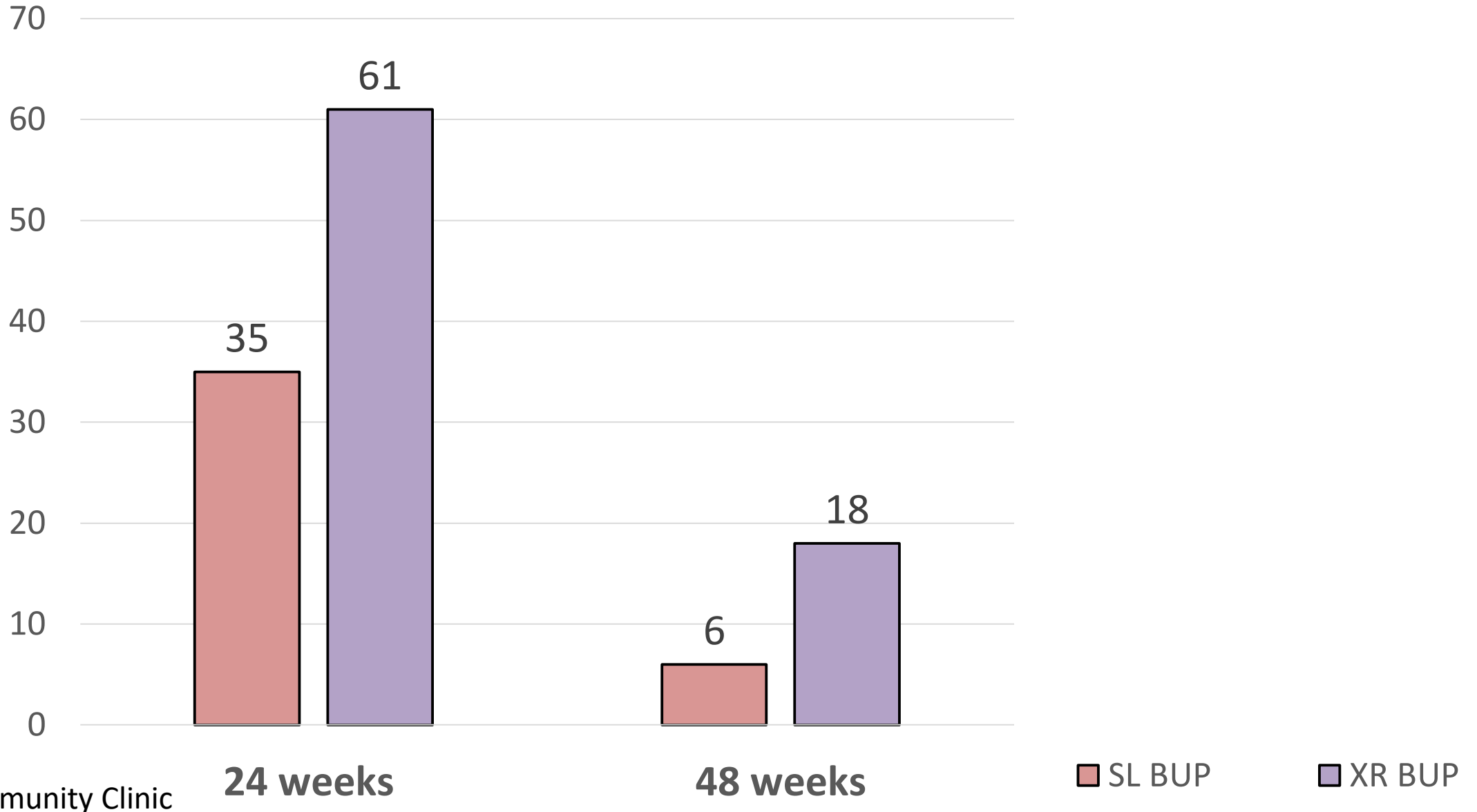
- Reviewed NTC prescriber PDMP records from Jan 2016-Jan 2022
- Identified patients admitted on or after May 2018 and before Aug 2021 who used Methamphetamines with Opioids (n=55)
- Compared retention in treatment (cumulative weeks of buprenorphine therapy)
  - SLBUP vs XRBUP 2018-2022 (at least 1 XRBUP 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



# SUMMARY/TAKEAWAYS

- 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.

Sarah Spencer DO, FASAM  
Addiction Medicine Specialist  
Ninilchik Traditional Council Community Clinic  
Ninilchik, Alaska  
907-299-7460  
[sarahspencerak@gmail.com](mailto:sarahspencerak@gmail.com)