

Session 2:

Easy Buprenorphine Prescribing for Everyone, presented by Sarah Spencer, DO Advanced Buprenorphine Prescribing, presented by Sarah Spencer, DO

These presentations were part of the one-day Fairbanks Syndemic Clinical Training: Addressing the Syndemic of Substance Use Disorders and Related Disease States held on April 9 and April 10,2025.



ANTHC Syndemic Conference Fairbanks, AK April 2025 Sarah Spencer, DO, FASAM

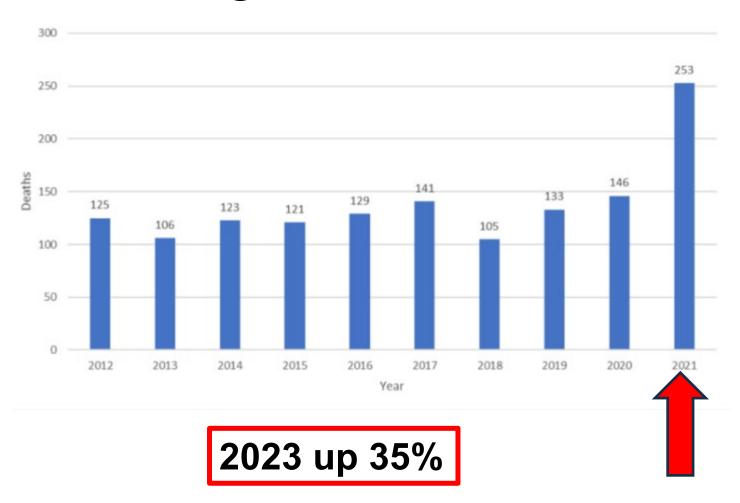
# Easy Buprenorphine Prescribing for Everyone



## 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.

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



Alaskan NativesOD rate 77/110K

WhiteOD rate 28/100K

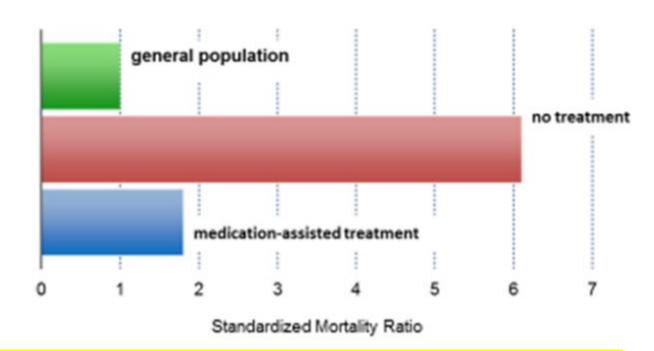
Meth OD up 150%

Fentanyl OD up
 150%

## Benefits of MAT: Decreased Mortality

#### **Death rates:**

Increased overdose risk after leaving treatment



MOUD can reduce death rates by >60%

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



### "Detox" is not a treatment for OUD

# Treating opioid disorder without meds more harmful than no treatment at all

Non-medication-based treatments for opioid use disorder may be more harmful than no treatment at all, a new Yale study finds.

When the researchers calculated the risk of fatal overdose death for each treatment, they found that, compared with no treatment at all, methadone and buprenorphine reduced the risk of death...

"However, non-medication-based treatments increased the risk of death compared to no treatment by over 77%,"

### Reframing the perception of buprenorphine prescribing

#### **OLD**

A high-risk medication requiring specialized training and integrated behavioral health to prescribe

#### **NEW**

A very safe lifesaving medication that is the gold standard treatment for a deadly disease, that all providers should be comfortable prescribing

This is why the X-waiver was eliminated



## The Waiver is Gone!!!

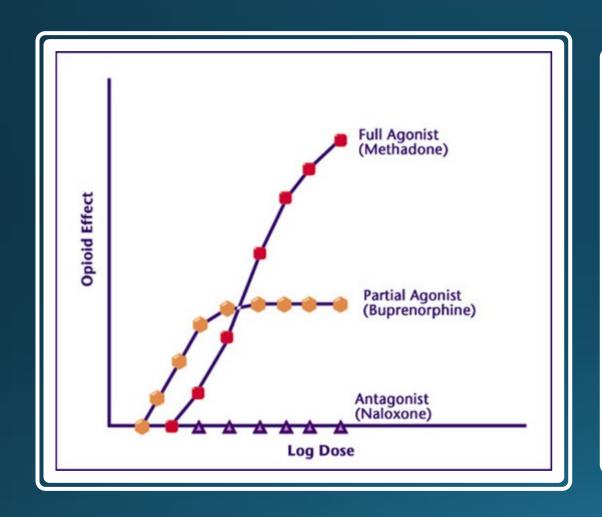
- All prescribers authorized to Rx Schedule 3 can prescribe buprenorphine for OUD or pain
  - No limits on dose or formulation of BUP
    - No limits on numbers of patients
  - No requirement to refer for counseling
    - No educational requirements
    - 8-hour waiver course meets the

DEA MATE act requirements

NO EXCUSE NOT TO PRESCRIBE THIS LIFESAVING MEDICATION!

# Every day of BUP treatment is helpful

- All providers should be comfortable in the basics of MOUD
- Lack of follow-up arrangements are not a contraindication to prescribing BUP
  - Warm handoff always preferred when possible
- Aways provide SLBUP Rx on discharge (minimum 1 week) or administer XRBUP before discharge
- Every day that a patient takes BUP reduces their risk of overdose
- Not prescribing MOUD is NOT following standard of care guidelines and results in worse outcomes!!!

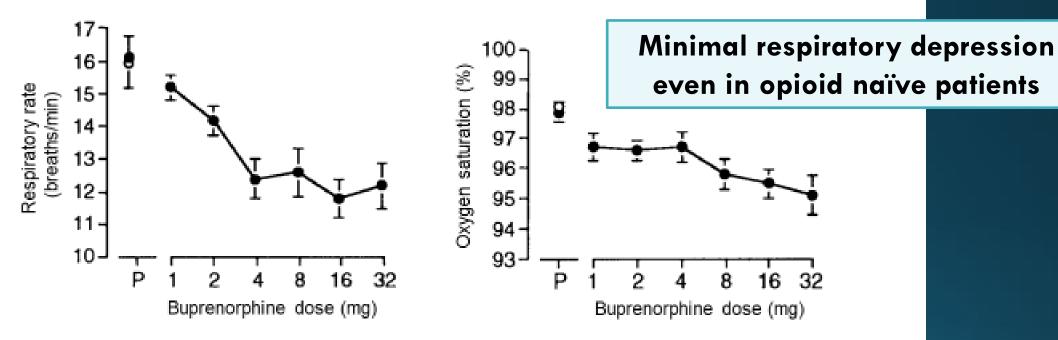


# Properties of Buprenorphine, a $\mu$ -Opioid Partial Agonist

- Ceiling effect on respiratory depression
- High affinity for μ-opioid receptor
- Slowly dissociates from μ-opioid receptors
- Ameliorates withdrawal once underway
- Can precipitate withdrawal if given in temporal proximity to full agonist opioids

## Buprenorphine Dosing: Safety

Cognitive and psychomotor effects appear to be negligible



Nearly all fatal poisonings involve multiple substances

### FORMULATIONS OF **BUPRENORPHINE**



Buprenorphine/naloxone SL/buccal films (Generic/brand, many strengths)



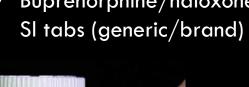
Brixadi Weekly/monthly SQ injection, various doses



Buprenorphine SL tab (2 & 8mg) (Subutex)

Long-Acting **Injectables** 

Buprenorphine/naloxone SI tabs (generic/brand)







**Combo-SL Products** 





IV Buprenorphine

(Transdermal and Buccal Buprenorphine products used for Chronic Pain (Butrans/Belbuca) are general considered too low dose and not legal to treat OUD)

# Naloxone is included in SL buprenorphine as an Abuse Deterrent

Is has minimal absorption and no clinical effect when used as directed sublingually (it does NOT alter the effectiveness of the medication, cause precipitated withdrawal or block opioids)

It only has action if the product is misused (IV/snorted/smoked can trigger PW or partially block BUP effect)

Prescribing this combination product may reduce misuse risk 3-6-fold compared to plain buprenorphine products (limited data)

Intolerable side effects to combo product may be an indication to switch to mono product or XRBUP (Nausea/HA 1 hr after dose)

# Formulations of Buprenorphine NOT allowed for OUD/WD outpatient

- Butrans (transdermal, pain only)
- Belbucca (buccal, pain only)
- IV BUP

• It is illegal to use any other opioid agonist to treat opioid withdrawal in the outpatient setting (including methadone and tramadol)

 ALL forms of BUP and ALL opioid agonists may be used in the inpatient/ED setting to treat withdrawal

### **Initial Assessment**

- A patient history: medical and psychiatric history
- Social History:
  - Substance use history: type, route, quantity, treatment hx
  - Family and psychosocial supports, children, living situation, employment, transportation, legal issues
- Access the patient's prescription drug history through the state's Prescription Drug Monitoring Program (<u>PDMP</u>) to detect unreported use of other medications, such as sedative-hypnotics or alcohol, that may interact adversely with the treatment medications.

### **Initial Assessment**

- A physical examination that <u>focuses on physical findings</u> <u>related to addiction</u> and its complications. (heart murmur, track marks, skin infections) <u>Deferred for telemed</u>
- Laboratory testing (Optional)
  - Urine drug screen
  - Pregnancy test
  - Hepatitis B and C (Hep panel), HIV, RPR, CMP, CBC

Providers should not delay treatment initiation while awaiting lab results

### Important Points to Review With the Patient

- Understand that discontinuing buprenorphine increases risk of overdose death upon return to illicit opioid use.
- Know that use of alcohol or benzodiazepines with buprenorphine increases the risk of overdose and death (but is NOT a contraindication to BUP).
- Offer contraception and inform providers if they become pregnant, to provide extra support.
- Tell providers if they are having a procedure or injury that may require pain medication.

#### Buprenorphine

What You Need to Know

September 2020



#### What is buprenorphine?

- Buprenorphine or bup is medicine for people who have chronic pain or addiction to opioids (heroin or pain pills).
   Many people know it by brand names like Suboxone® and Subutex®.
- Buprenorphine helps get rid of cravings and withdrawal, without making you feel high.
- People have less overdoses when they take buprenorphine.
   It is a safe medicine that has been used for 30 years.
- It is not substituting one drug for another—it is a daily medicine that you may need to stay healthy.
- Often buprenorphine and naloxone are taken together in 1 pill. Naloxone is the same as Narcan®, but if you take the medicine under the tongue the naloxone doesn't go in your body and can't make you sick. Naloxone is only there to make sure that people don't crush the pill and inject it—if you do that, the naloxone does go into your body and does make you sick.

#### What is it like to take buprenorphine?

- Many people say that their cravings and withdrawal go away, they feel "clear in the head," and their chronic pain gets better.
- Every morning you put a pill or a film strip under your tongue and let it dissolve—don't swallow it.
- People need to take it every day in most cases, and do feel sick if they stop taking it suddenly.
- Usually there are no side effects, but some people have headaches, stomach upset, or trouble sleeping.
- Many people keep taking it for years, or forever. If you want to stop taking it that is ok, but talk to your medical team first.
- The chance of an overdose on buprenorphine is very low, but if mixed with other drugs or alcohol overdose is possible.
- Some people take buprenorphine as a once a month shot under the skin of the belly. This is a great option if taking a medicine every day is hard for you.

#### Is buprenorphine right for me?

- If you are currently taking methadone, talk to your medical team before switching.
- Before taking the first dose of buprenorphine, most people need to feel some withdrawal. That is important because if you take it while other opioids are in your system, you can get very sick.
- Talk to your medical team to see if buprenorphine is a good medicine for you. There are many good choices for treatment, only you and your team know what is best for you.

#### How do I get buprenorphine?

- You can go to any of the places below to get started. You
  may need to visit more than once before getting the first
  dose. In some clinics (like methadone clinics), you may
  come in every day to pick up your buprenorphine dose.
- Instead of going to a methadone clinic, you can get the medicine from a primary care doctor. At first you may need daily visits, but many people can soon switch to weekly or monthly visits.
- Some telemedicine groups offer prescriptions over the internet/phone instead of in a doctor's office, so you need a phone and internet to use those services.



https://bridgetotreatment.org/reso urce/buprenorphine-what-youneed-to-know/

# Lower dose BUP is NOT better

ASAM 2020 guidelines recommends minimum 16 mg/day for those in early recovery

Doses 16 mg+ have superior retention in treatment and abstinence (evidence that 24-32mg/day is superior)

Fentanyl blockade requires minimum 16mg/day (higher is better)

Review > J Addict Med. 2023 Sep-Oct;17(5):509-516. doi: 10.1097/ADM.000000000001189. Epub 2023 Jun 16.

### **Evidence on Buprenorphine Dose Limits: A Review**

Lucinda A Grande <sup>1</sup>, Dave Cundiff, Mark K Greenwald, MaryAnne Murray, Tricia E Wright,

"Conclusions: In light of established research and profound harms from fentanyl, the Food and Drug Administration's current recommendations on target dose and dose limit are outdated and causing harm. An update to the buprenorphine package label with recommended dosing up to 32 mg/d and elimination of the 16 mg/d target dose would improve treatment effectiveness and save lives."

# Dosing Frequency

Buprenorphine has a slow dissociation rate from the mu opioid receptor, which gives rise to its prolonged suppression of opioid withdrawal and blockade of exogenous opioids (24-48 hours).

- Once daily dosing for control of drug cravings and withdrawal
- Most patient prefer BID-TID
- Relatively short analgesic duration(6 hours)
- QID dosing for pain control

# Dosing instructions

- Wet mouth first, avoid smoking before dose
- Dissolve under tongue for 15-20 mins (tabs or films)
- No talking, eating, drinking, smoking
- Spit out excess saliva (swallowing can increase nausea)
- Rinse and spit after finished (reduce dental exposure)
- Peak effect in 1-2 hours



## Common BUP Side Effects

- Nausea
- Headache
- Sweating
- Oversedation/dizziness
- Constipation (chronic)
- Urinary Retention
- Edema (XRBUP rare)

# Precipitated Withdrawal

- Precipitated withdrawal can occur due to replacement of full opioid receptor agonist (heroin, fentanyl, or methadone) with a partial agonist that binds with a higher affinity (Buprenorphine).
- Typically occurs 30-60 mins after first SLBUP dose
- Rapid onset of severe opiate withdrawal symptoms
- Like Naloxone precipitated withdrawal but lasts longer
- Avoid by ensuring adequate withdrawal before first dose (COWS > 12; Fentanyl may require higher COWS score) or by using microdosing or high dose start.

# 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)







## Illicitly-manufactured fentanyl

- Though prior pharmacokinetic studies of fentanyl report half lives ranging from 1.5-7 hours, these studies generally relied on brief periods of drug administration.
- Fentanyl is highly lipophilic, allowing it to be sequestered in adipocytes in chronic users, similar to THC.

## Some evidence suggests fentanyl withdrawal...

- \*Starts sooner, lasts longer, is more severe (survey of 114 pts)13
- #Is more likely to lead to precipitated withdrawal with bup
  - OR 5.2 for precipitated withdrawal with bup (v. methadone) within 24 hrs of fentanyl use (multi-center survey of 1679 pts)<sup>14</sup>
  - Precipitated withdrawal with bup despite extended (24-48 hrs) periods of abstinence and high COWS (4 pt case series)<sup>15</sup>
- Is harder to relieve with bup:
  - #"24 mg not uncommonly necessary to manage withdrawal"16
  - Only 38% reported bup "completely alleviated" fentanyl withdrawal<sup>14</sup>



# Increasing reports of buprenorphine precipitated withdrawal merit caution

# Most people in withdrawal can start bup without issue

In populations with 25-76% fentanyl use, 0-3% precipitated withdrawal (EMS, multi center NIDA, single site ED, multi site CA Bridge)



Varshneya NB, Thakrar AP, Hobelmann JG, Dunn KE, Huhn AS. Evidence of Buprenorphine-precipitated Withdrawal in Persons Who Use Fentanyl. J Addict Med. 2021 Nov 23. doi: 10.1097/ADM.0000000000000922. Epub ahead of print. PMID: 34816821.

D'Onofrio et. al, unpublished abstract

Hern et al, unpublished data

ZSFG, upublished data

Lesaint, unpublished data

D'Onofrio G, Fiellin D. Emergency Department-INitiated bupreNOrphine and VAlidaTIOn Network Trial (ED-INNOVATION) (NIH HEAL Initiative). Presented at: Second Annual

# Ask about previous experience with BUP

- Helpful for cravings? What dose worked best?
- Initiation well tolerated:
  - Proceed with standard initiation
- Experienced Precipitated withdrawal:
  - How long did they wait?
  - What dose did they take?
  - Did they succeed with initiation?
  - Considér high dose or low dose overlapping start
  - Consider pre-medication with ondansetron 4-8 mg and clonidine 0.2 mg

#### **Determine Withdrawal**

Objective withdrawal signs help establish physical dependence

# Start when COWS>12

The risk with initiating buprenorphine too soon is that buprenorphine has a very high affinity for the mu receptor and will displace any other opioid on the receptor, thereby causing precipitated opioid withdrawal.

## COWS Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9. Clinical Opiate Withdrawal Scale

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

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

## At home withdrawal assessment

• Wait 12-24 hours after last opioid use

- Wait until you have at least 3-4 WD sxs
  - Rhinorrhea, sweating, tearing, N/V/D, abd cramping, myalgias, goosebumps, restlessness, yawning, anxiety

Wait until you can't wait anymore!

### Common Rx at First Visit

- Buprenorphine/naloxone 8/2 mg tab or film, TID prn dispense #21
- LAIB (Sublocade 300 mg SQ monthly in clinic, Brixadi 128 mg SQ monthly in clinic, Rxs sent to specialty pharmacy)
- Ondansetron 4-8 mg ODT SL tid prn, disp #12
- Clonidine o.1 mg, 1-2 tid prn restlessness and sweating, disp #20
- Naloxone nasal spray kit (refill X3)
- Consider: Trazodone 100 mg qhs for insomnia, Tizanidine 4mg qid for spasms, ibuprofen 800 tid for pain, Imodium 2 qid for diarrhea, hydroxyzine 50 mg tid for anxiety

Wait until in moderate WD

• Start with 8-16 mg
SL (2-4 mg in
patients with low
levels of tolerance)

Repeat 4-16 mg
 every 1-2 hours as
 needed up to 24 32 mg day 1



#### **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 <u>wait</u> until you <u>feel very sick</u> 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.



### Simple Home Start Instructions

https://bridgetotreatment.o g/resource/rapid-guidancefor-patients-startingbuprenorphine-outside-ofhospitals-or-clinics/

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

### If you experience precipitated withdrawal:

- •Immediately take 16 mg of Buprenorphine (2 strips or tablets) dissolve under tongue for 20 mins. You may repeat 8-16 mg of buprenorphine again in 1-2 hours if needed (40+ mg OK)
- Ondansetron 4-8 mg dissolve under tongue for nausea
- •Clonidine 0.1 mg 1-2 tabs every 4 hours for restlessness and sweating

Comfort meds as needed: tizanidine, hydroxyzine, trazodone, NSAIDS, gabapentin, ketamine/benzodiazepines/hydromorphone (inpatient)



# ASAM Clinical Considerations: Buprenorphine Treatment of Opioid Use Disorder for Individuals Using High-potency Synthetic Opioids

Weimer, Melissa B. DO, MCR, DFASAM; Herring, Andrew A. MD; Kawasaki, Sarah S. MD, FASAM; Meyer, Marjorie MD; Kleykamp, Bethea A. PhD; Ramsey, Kelly S. MD, MPH, MA, FACP, DFASAM

Author Information⊗

Journal of Addiction Medicine 17(6):p 632-639, 11/12 2023. | DOI: 10.1097/ADM.000000000001202 @

- 1. What specific clinical situations favor use of low or high-dose buprenorphine initiation strategies?
- 2. What strategies can address patient discomfort, including precipitated opioid withdrawal, if it occurs during buprenorphine initiation?
- 3. After buprenorphine initiation, what range of buprenorphine dosing and/or dosing strategies can be considered during stabilization and long-term treatment?
- 4. What are indications for injectable extended-release buprenorphine for OUD treatment compared with sublingual formulations?
- 5. How do other novel drug components affect buprenorphine initiation and stabilization?
- 6. What are OUD treatment alternatives after repeated unsuccessful attempts at buprenorphine treatment?

# Advantages of Monthly Injectable Buprenorphine In Remote Native 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

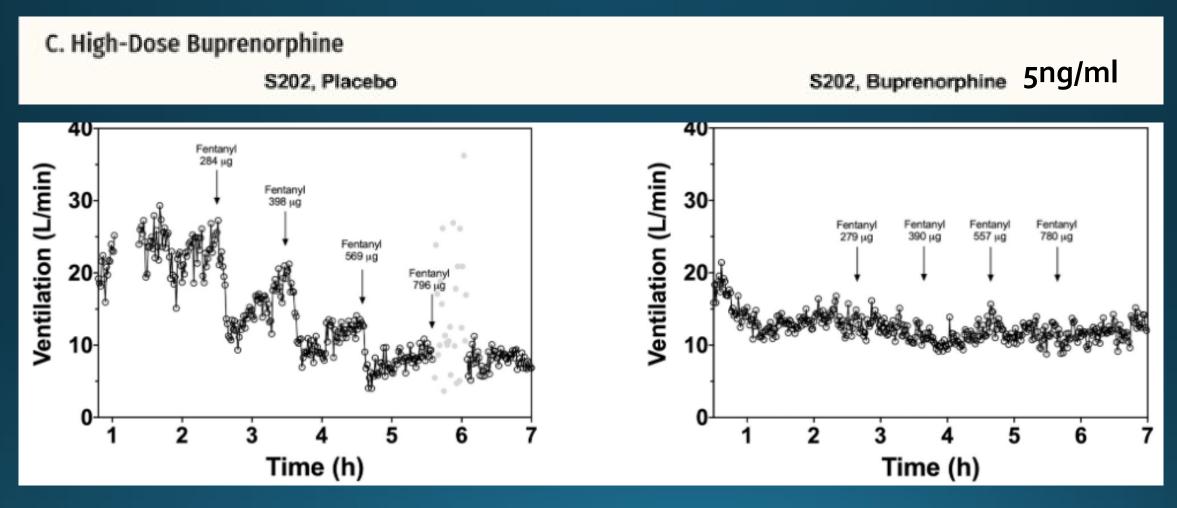
### Excellent and long-lasting opioid blockade

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

The RECOVER™ study found that 75 percent of patients who had received 12 once-monthly doses of SUBLOCADE in a Phase 3 clinical trial were abstinent from illicit opioids for a year after the study ended

# At 12 months 88% of patients reported medication satisfaction

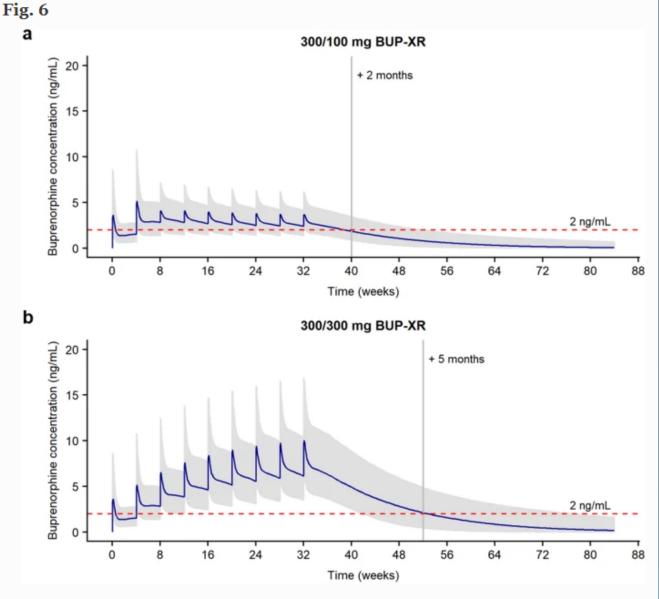
#### High Dose XR Buprenorphine blocks fentanyl induced respiratory depression



Blockade was lost under 2 ng/ml

https://journals.plos.org/plosone/article/figure?id=10.1371/journal.pone.0256752.goo4

# **Extended** opioid blockade after medication cessation



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)

UDS +for 1-2 years

https://link.springer.com/article/10.10 07/540262-020-00957-0

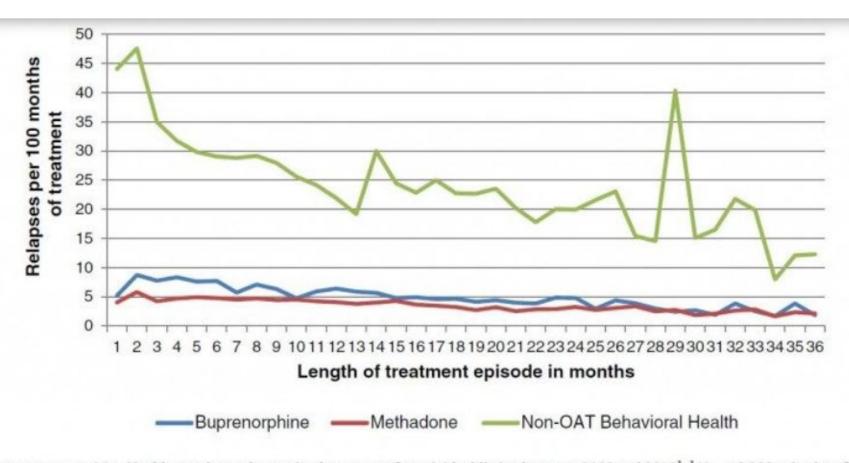
# Maintenance therapy

- Check PDMP regularly to ensure prescriptions are filled, and to check other prescriptions.
- Consider drug testing (UDT) and consider confirmatory testing for unexpected results. UDT can facilitate open communication to change behavior but is not an evidence-based practice and may be a barrier for some patients.
- Ask about how patient is taking their meds
- Discuss cravings and what triggers them
- Discuss side effect management
- Adjust dose as needed to control cravings
- Address co-morbid disorders
- Initial weekly visits until use extinguished, then q2wk, monthly for long term stable patients



## 3 years on MOUD have 2/3 less return to use 5 years on MOUD have 1/2 the return to use rate





**Fig. 1.** Relapses during treatment among MassHealth members who received treatment for opioid addiction between 2003 and 2010<sup>1</sup>. <sup>1</sup> 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.

## When to Consider Taper?

- Patient Insists (for the right reasons)
- Relapse free for a year
- Stable housing, job, family life
- No major stressors (legal, financial)
- Stable Mental Health
- Actively engaged in strong recovery network

TAPER SHOULD ALWAYS BE PATIENT INITIATED

# We work to counsel patient AGAINST discontinuation:

- During Pregnancy/postpartum
- During high stress times
- During surgery/hospitalization
- Due pressure from family/friends
- Because they "don't need it anymore"



# Advanced Buprenorphine Prescribing

ANTHC Fairbanks Syndemic Conference
April 2025
Sarah Spencer DO, FASAM

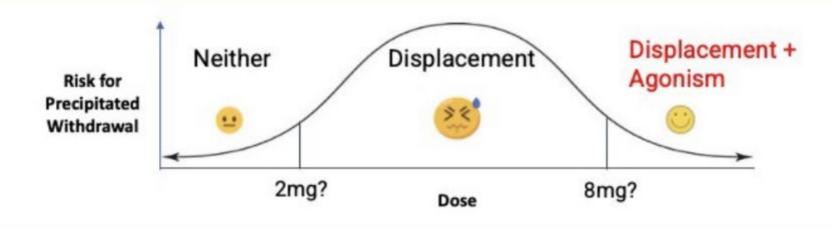
## **Learning Objectives**

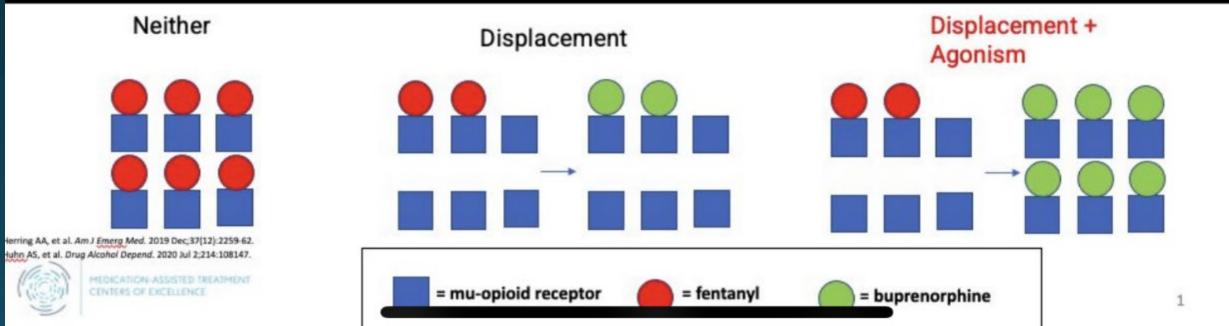
- Identify patients who might benefit from low-dose overlapping start
- Explore the utility of buprenorphine initiation in the ED and hospital
- Troubleshoot problems in early LIAB treatment



# Low Dose Overlapping Buprenorphine Initiation (AKA Micro-dosing)

## Buprenorphine Micro- and Macrodosing Induction Using a Bell-Shaped Curve Framework





# When to consider Micro-dosing?

Transitioning from methadone to buprenorphine

Chronic fentanyl use

Patient with severe acute pain and OUD

Previous failed attempts at induction due to PW

### Basics of Micro-dosing Buprenorphine Induction

- Allow patients to continue the full opioid agonist as starting small doses of buprenorphine
- Start with very small doses of SL buprenorphine (o.5mg) to gradually displace full opioid agonist
- Gradually increase amount of buprenorphine patients receive
- Continue full opioid agonist during induction period
- Stop full agonist as tolerated after buprenorphine maintenance dose achieved (16+ mg)
- Limited evidence, mostly case series reports, commonplace on addiction medicine services

#### Continue to use full agonist (fentanyl, hydromorphone or methadone) on days 1-6

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Buprenorphine dose	0.5mg (1/4 strip) daily	0.5mg (1/4 strip) twice daily	1mg (1/2 strip) twice daily	2mg (1 strip) twice daily	3mg (1 ½ strips) twice daily	4mg (2 strips) twice daily	6mg (3 strips) twice daily
Morning dose							
Night dose							

Day 8+ take 16-32 mg SLBUP daily

Stop using the full agonist on day 7-8 (fentanyl, methadone or hydromorphone)

Can give XRBUP
(Sublocade/Brixadi)
once tolerating 8 mg
SLBUP or anytime if
leaving AMA or for
PW treatment

https://pubmed.ncbi.nlm.nih.gov/34954746/

### 3-day Sublingual Cross Taper Start

#### Prescribe 2 mg buprenorphine films #6, 8 mg buprenorphine films #4 for 3 day supply)<sup>4</sup>

- Day 1: 0.5 mg (1/4 of 2mg strip) SL buprenorphine q3 hours (4 mg total daily dose), continue full opioid agonists
- Day 2: 1 mg (1/2 of 2 mg strip) SL buprenorphine q3 hours (8 mg total daily dose), continue full opioid agonists
- Day 3: 8-16 mg (1-2 8 mg strips) SL buprenorphine once daily and 4 mg SL q6h prn withdrawal (max 32 mg total daily dose), wean or stop full opioid agonists

#### 7-day Sublingual Cross Taper Start

https://bridgetotreatment.org/resource/starting-

buprenorphine-with-microdosing-and-cross-tapering/

- Prescribe 2 mg buprenorphine SL strips # 15, 8 mg buprenorphine SL strips #4 for 7 day supply
  - Day 1: 0.5 mg (1/4 of 2 mg strip) buprenorphine SL daily (0.5 mg total daily dose), continue full opioid agonist
  - Day 2: 0.5 mg (1/4 of 2 mg strip) buprenorphine SL BID (1 mg total daily dose), continue full opioid agonist
  - Day 3: 1 mg (1/2 of 2 mg strip) buprenorphine SL BID (2 mg total daily dose), continue full opioid agonist
  - Day 4: 2 mg buprenorphine SL BID (4 mg total daily dose), continue full opioid agonist
  - Day 5: 3 mg (1+1/2 of 2 mg strip) buprenorphine SL BID (6 mg total daily dose), continue full opioid agonist
  - Day 6: 4 mg (2 of 2 mg strip) buprenorphine SL BID (8 mg total daily dose), continue full opioid agonist
  - Day 7: 6 mg (3 of 2 mg strip) buprenorphine SL BID (12 mg total daily dose), continue full opioid agonist
  - Day 8: 16 mg (2 of 8 mg strip) buprenorphine qday and 4mg (1/2 of 8 mg strip) q6h prn withdrawal (max 32 mg

#### 1-Day Micro-Macro Start

Administer (2) 20 mcg patch, prescribe buprenorphine 8 mg SL film/tablet as needed

- Place 2 x 20 mcg transdermal buprenorphine patch (do not need to wait for withdrawal)
- If patches are not available:
  - Stop full opioids
  - Do not wait for withdrawal
  - Start very low dose of buprenorphine
    - 0.5 mg (1/4 of 2mg strip) SL buprenorphine q3 hours (4 mg total daily dose)

      OR
      - Swallow 2mg SL buprenorphine q3 hours (6 mg total daily dose)
- Wait until the development of moderate to severe withdrawal. Patients should report feeling sick from withdrawals. (COWS 8 or ≥7/10 severity rating by patient)
  - 6-12 hours typically but can be much longer depending on the person and the drugs they have been consuming.
  - Some patients may wait 24-72 hours
  - Patient should stay abstinent and keep microdosing--keep the patches on or keep swallowing the 2mg tablets q3 hours (6 mg total daily dose) until they feel sick from withdrawal

Once withdrawal has become intolerable, take 16mg SL bup in one dose.

#### Adjunctive meds for breakthrough withdrawal symptoms

- Clonidine 0.1mg PO q8 hours PRN opioid withdrawal symptoms not controlled one hour after 2nd dose of buprenorphine. Hold for SBP<90, HR<60</li>
- Acetaminophen 650mg PO every 4 hours PRN headache, musculoskeletal pain
- Ondansetron 4mg PO every 6 hours PRN nausea/vomiting
- Trazodone 100mg PO QHS PRN insomnia
- Lorazepam 1mg PO every 4 hours PRN severe anxiety/agitation (up to 10mg/day)
- Gabapentin 600mg PO TID PRN moderate anxiety/restlessness

# **Buprenorphine in the ED**

# Hospitalization is a high-risk touchpoint

MA statewide study: Residents hospitalized with injection-related infection in 2014 had 54-fold increased risk of fatal opioid overdose compared to general population

OR statewide study: Among adults with OUD hospitalized between April 2015-Dec 2017, 8% died within 12 months of discharge

• Mortality similar to acute myocardial infarction (5-9%)

# Mortality rate after 1<sup>st</sup> Heart attack is about 8% at one year

We would never send a patient home without a statin, which reduces mortality by 25%

Mortality rates after first overdose are 8% at one year

However, patients are routinely sent home without MOUD, which reduces one year mortality by >60%

# Why initiate MOUD via EMS?

- Buprenorphine is an incredibly safe medication
- Quickly control WD symptoms
- Opioid blockade to protect against repeat overdose X 48hrs
- Increased retention in treatment
- >10 states already doing this

https://www.recoveryanswers.org/researchpost/buprenorphine-equipped-ambulances-help-linkoverdose-survivors-addiction-treatment/

#### **Emergency Medical Services**

PERSIST

#### Opioid Withdrawal: Adult Medical Treatment Guidelines



#### ASSESS OPIOID WITHDRAWAL SIGNS & SYMPTOMS ASSESS FOR EXCLUSION CRITERIA OBJECTIVE SIGNS: SUBJECTIVE SYMPTOMS: - Under 18 years of age - Pregnant SIGNS OR Tachycardia - Nausea - Any methadone use within last 10 days Diaphoresis - Stomach/abdominal cramps SYMPTOMS - Altered mental status and unable to give consent Restlessness and/or - Body aches PRESENT Severe medical illness (sepsis, respiratory distress, etc.) aditation - Achy bones/joints Current intoxication or recent use of benzodiazepine, - Restlessness Dilated pupils alcohol, or other intoxicants suspected Rhinorrhea or lacrimation - Hot and cold No clinical opioid use disorder symptoms Vomiting, diarrhea - Nasal congestion Unable to comprehend potential risks and benefits for any Yawning Piloerection Not a candidate for buprenorphine treatment for any NO YES Provide supportive treatment and COWS ≥ 7 Not eligible (Clinical Opioid for prehospital counseling Withdrawal Scale) Assess patient interest in buprenorphine treatment PATIENT PATIENT AGREES TO DENIES TREATMENT TREATMENT . Provide medication for addiction treatment (MAT) brochure Provide naloxone Contact 'Opioid Protocol Physician' for Offer transport buprenorphine administration approval WITH PHYSICIAN APPROVAL 1. Recommend transport to CA Bridge 1. Give water to moisten mucous site or designated overdose receiving IF SYMPTOMS→ membranes IMPROVE 2. Administer 16 mg buprenorphine SL 2. Verify patient contact information 3. Reassess after 10 minutes 3. Inform the patient that the hospital's navigator will initiate contact within IF SYMPTOMS 72 hours to offer additional treatment WORSEN OR

# **EMS** Opioid Withdrawal **Protocol for** Pre-hospital Buprenorphine

- Pending in Alaska
- Useful in long transports

https://bridgetotreatment.org/resource/emerge ncy-medical-services-opioid-withdrawaltreatment-quidelines/





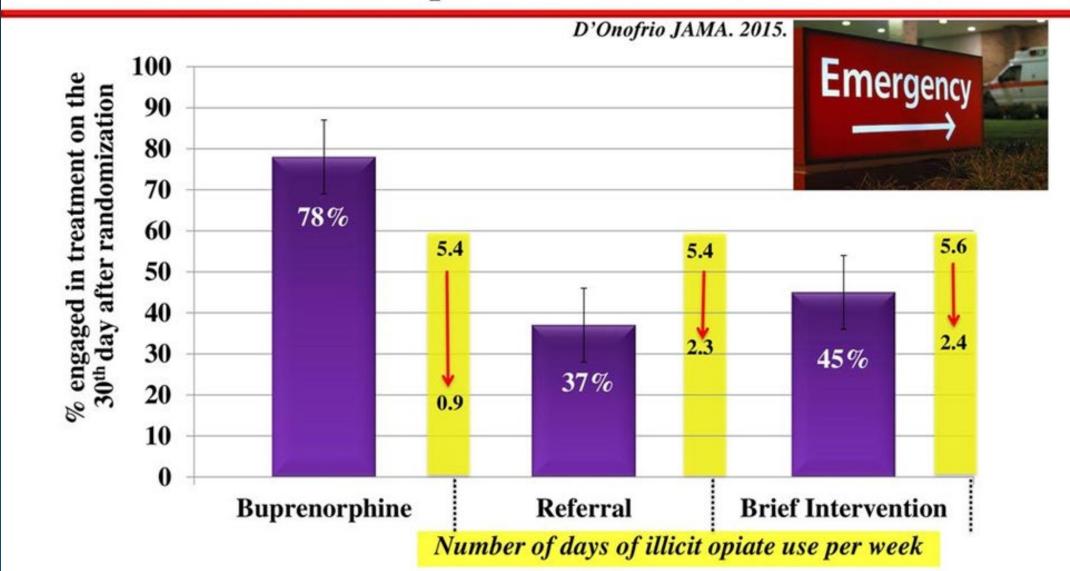
#### Consensus Recommendations on the Treatment of Opioid Use Disorder in the Emergency Department



Kathryn Hawk, MD, MHS\*; Jason Hoppe, DO; Eric Ketcham, MD; Alexis LaPietra, DO; Aimee Moulin, MD; Lewis Nelson, MD; Evan Schwarz, MD; Sam Shahid, MBBS, MPH; Donald Stader, MD; Michael P. Wilson, MD; Gail D'Onofrio, MD, MS

Based on literature review, clinical experience, and expert consensus, the group recommends that emergency physicians offer to initiate opioid use disorder treatment with buprenorphine in appropriate patients and provide direct linkage to ongoing treatment for patients with untreated opioid use disorder.

#### ED-initiated Buprenorphine Increased Engagement In Addiction Treatment, Reduced Self-reported Illicit Opioid Use, & Decreased Use Of Inpatient Addiction Treatment Services



# Buprenorphine administration in the ED reduces cost, return to the ED and admission rates! Average Length of Stay 2.4 hrs!

Evaluation of the use of buprenorphine for opioid withdrawal in an emergency department.

Berg ML, et al. Drug Alcohol Depend, 2007

who received buprenorphine were less likely to return to the same ED within 30 days for a drug-related visit (8%) compared to those who received symptomatic treatment (17%) (p<0.05).

July 15, 2021

#### High-Dose Buprenorphine Induction in the Emergency Department for Treatment of Opioid Use Disorder

Andrew A. Herring, MD<sup>1,2</sup>; Aidan A. Vosooghi, MS<sup>1,3</sup>; Joshua Luftig, PA<sup>1</sup>; et al

JAMA Netw Open. 2021;4(7):e2117128. doi:10.1001/jamanetworkopen.2021.17128

#### **ADDICTION**



Research Report

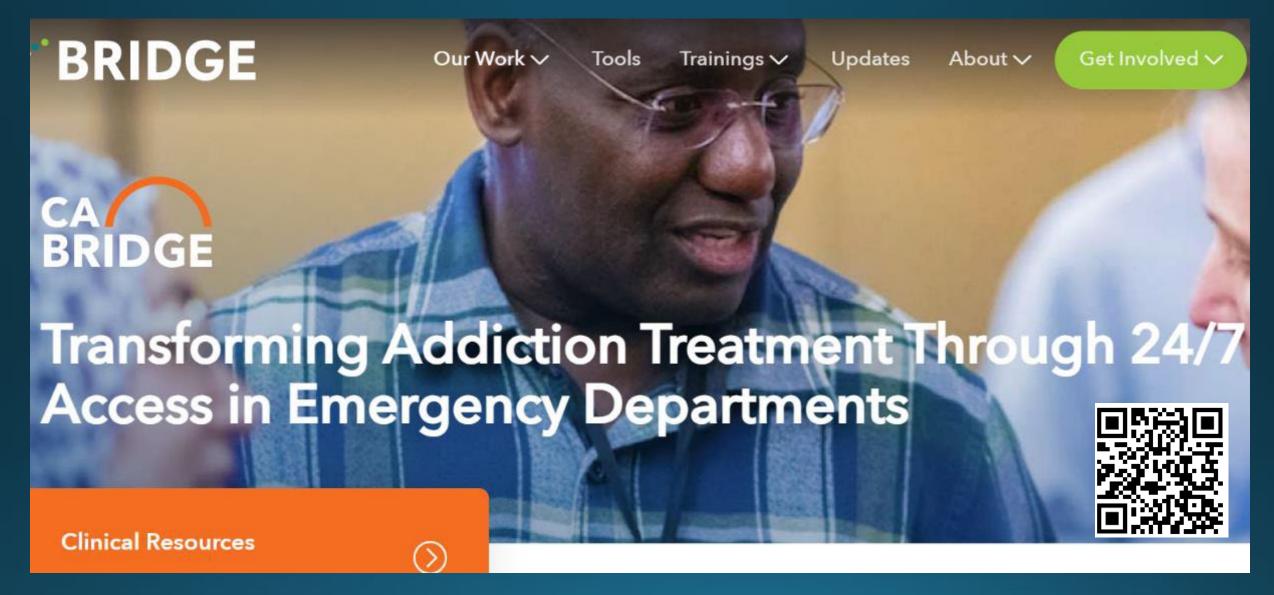
Cost-effectiveness of emergency department-initiated treatment for opioid dependence

Susan H. Busch ⋈, David A. Fiellin,
Marek C. Chawarski ... See all authors →

First published: 16 August 2017

https://doi.org/10.1111/add.13900

Treatment with buprenorphine was the most costeffective treatment option with a mean cost of
\$1,752. The mean cost of a brief intervention
alone was \$1,805 and the mean cost for a referral
alone was \$1,977. The ED-initiated buprenorphine
group was nearly twice as likely to enroll in
addiction treatment and used illicit opioids for
fewer days during the 30 days after their ED visits.
This group also used fewer illicit opioids over the
study period.



An AMAZING free online resource with free protocols and training materials to start utilizing buprenorphine in your hospital ED

https://bridgetotreatment.org/addiction-treatment/ca-bridge/







30-60 minutes

30-60 minutes

Opioid

withdrawal\*

(range 8-24+ mg)

Withdrawal

improved?

Administer 2nd dose

Additional 8-24+ mg SL bup

#### **Emergency Department Buprenorphine (Bup) Quick Start**

Connect with your patient: Accurate diagnosis and treatment requires trust, collaboration, and shared decision making.

# • Rx per "Discharge" box below. If no improvement or worse, consider: Worsening withdrawal

Worsening withdrawal (common): Occurs with lower starting doses and heavy tolerance; improves with more bup (additional 8-16 mg SL).

Rx self-directed start:

· Wait for severe withdrawal

then start with 8-24+ mg SL.

Other substance intoxication or withdrawal: Continue bup and manage additional syndromes.

Bup side-effects: e.g., nausea or headache. Continue bup and treat side-effects with supportive medications.

Medical illness: Continue bup and manage underlying condition.

If sudden & significant worsening, consider precipitated withdrawal (rare): See box below.

#### \*Diagnosis Tips for Opioid Withdrawal:

- Look for at least two clear objective signs not attributable to something else: large pupils, yawning, runny nose & tearing, sweating, vomiting, diarrhea, gooseflesh/piloerection, tachycardia.
- Confirm with the patient that they feel 'bad' withdrawal and they feel ready to start bup. If they feel their withdrawal is mild, it is likely too soon.
- 3. As needed, consider using the COWS (clinical opioid withdrawal scale). Start if COWS ≥ 8 with ≥ 2 objective signs.
- Withdrawal sufficient to start bup typically occurs 24-36 hrs after decreased/stopped use, but can vary from 6-72 hrs. Methadone withdrawal commonly takes longer.

#### \*\*Bup Dosing Tips:

- Respect patient preference. Shared decision making, flexibility, and collaboration are essential.
- Heavy dependence/tolerance (e.g., fentanyl) may need higher doses of bup.
- 3. Low dependence/tolerance may do well with lower doses of bup.
- 4. Starting bup may be delayed or modified if there complicating factors:
  - Altered mental status, delirium, intoxication
  - Severe acute pain, trauma, or planned surgery
  - Severe medical illness
  - Long-term methadone maintenance

Discharge

# Patient Home Start Instructions





#### **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 <u>wait</u> until you <u>feel very sick</u> 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.

When discharging patients not in active withdrawal yet

Always give at least 1 week of SLBUP Rx

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

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

# Precipitated withdrawal

- Bup 16mg SL -AND- PO benzodiazepine x1
- Repeat bup until mydriasis resolves
- If withdrawal persists, ketamine 0.3mg/kg IV slow push every 30 minutes until calm and light sedation. Hold for excessive sedation or dissociative symptoms

# Enhanced Care Practice: Precipitated Withdrawal 90-Minute Emergency Room Bundle

- Carroll GG, Wasserman DD, Shah AA, et al. Buprenorphine Field Initiation of ReScue Treatment by Emergency Medical Services (Bupe FIRST EMS): A Case Series. Prehaspital Emerg Care Off J Natl Assoc EMS Physicians Natl Assoc State EMS Dir. 2021;25(2):289-293. doi:10.1080/10903127.2020.1747579
- Herring AA, Schultz CW, Yang E, Greenwald MK. Rapid induction onto sublingual buprenorphine after opioid overdose and successful linkage to treatment for opioid use disorder. Am J Emerg Med. 2019;37(12):2259-2262. doi:10.1016/j.ajem.2019.05.053
- Herring AA. Postoverdose Initiation of Buprenorphine After Naloxone-Precipitated Withdrawal Is Encouraged as a Standard Practice in the California Bridge Network of Hospitals. Ann Emerg Med. 2020;75(4):552-553. doi:10.1016/j.annemergmed.2019.12.015

## If no improvement or worse consider:

Undertreated withdrawal: Occur with lower starting doses and heavy tolerance; improves with more bup (add'l 8-16 mg SL).

Other substance intoxication or withdrawal: Stimulant intoxication, alcohol/benzo/xylazine/GHB withdrawal. Continue bup; manage additional syndromes.

Bup side-effects: Nausea, headache, dysphoria. Continue bup, treat side-effects with supportive medications.

Other medical/psychiatric illness Anxiety, sepsis, influenza, DKA, thyrotoxicosis, etc. Continue bup manage underlying condition.

If sudden/signficant worsening, consider precipiated withdrawal See box below.

# Buprenorphine Precipitated Withdrawal: Treatment approach by phase

#### **Early**

- 1. Act quickly
- 2. Calm & confident
- Benzo
- High-dose Bup (16mg)

Clonidine Pramipexole Gabapentinoid

#### **Acute**

- Monitored bed
- 2. Bup to 64mg SL
- 3. Ketamine 20 IV q 30
- 4. Fentanyl 200mcg Q 10 min

#### Residual

- 1. Pramipexole 0.5mg
- 2. Clonidine 0.3mg
- Benzo (loraz 1mg IV)
- Pregabalin 100-300mg po

Olanzepine 10mg IM

## goal

#### **XRBUP**



> J Hosp Med. 2022 Sep;17(9):744-756. doi: 10.1002/jhm.12893. Epub 2022 Jul 26.

Management of opioid use disorder and associated conditions among hospitalized adults: A Consensus Statement from the Society of Hospital Medicine

Susan L Calcaterra <sup>1</sup>, Marlene Martin <sup>2</sup>, Richard Bottner <sup>3</sup>, Honora Englander <sup>4</sup>, Zoe Weinstein <sup>5</sup>,

- Assess hospitalized patients with unhealthy opioid use for OUD
- Use shared decision making to initiate medications for OUD
- Offer buprenorphine or methadone as first line agents to treat opioid withdrawal and OUD
- Assess and treat pain in the setting of OUD
- Continue buprenorphine or methadone during hospitalization, including in the setting of acute pain and the perioperative period
- Link patients to a buprenorphine prescriber or an opioid treatment program when they want to continue buprenorphine or methadone following hospital discharge

#### 3 Basic Acute Pain Management Options:

- 1. Divide buprenorphine dose every 6 hours, INCREASE DOSE UP TO 32+ MG/DAY (no known ceiling for analgesic effect, can be given on top of long-acting injectable buprenorphine), add adjunctive meds but do not use additional opioids (minor pain/day surgery)
- 2. Continue buprenorphine maintenance therapy (If desired at lower dose 8-12mg) utilize multimodal analgesia and administer high-dose, potent, short-acting opioid analgesics (hydromorphone or fentanyl), titrate to effect. (mod-severe pain/inpatient surgery),
- 3. Discontinue buprenorphine maintenance therapy and use opioid analgesics (major surgery). Convert back to buprenorphine therapy when acute pain no longer requires opioid analgesics.

Patient directed only, NOT recommended.

"Given the increased mortality rate immediately after discontinuing buprenorphine-naloxone, we strongly recommend continuing buprenorphinenaloxone preoperatively to ensure overall patient stability and prevent relapse from stopping and restarting the medication."

The perioperative patient on buprenorphine: a systematic review of perioperative management strategies and patient outcomes, Can J Anesthesia, February 2019, Volume 66, Issue 2, pp 201–217

### **Labor and Delivery**

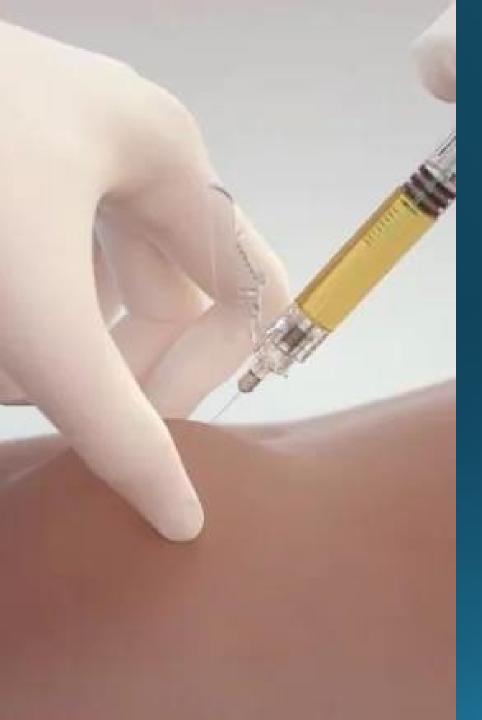
- Epidurals!
- Full Opioid Agonists are still OK!
   Hydromorphone 2-3 times usual dose
- Don't give extra Bup during labor to treat acute pain
- OK to increase Bup dose post delivery
- Don't give nalbuphine, butorphanol (precipitated w/d)
- Schedule NSAIDS/acetaminophen
- Buprenorphine and methadone are safe in breastfeeding

# Opioids + MOUD

- 4-12% Mu receptor availability at 24mg daily dose of buprenorphine
- Hydromorphone serum level of 4ng/ml is associated with lowest level of good pain control
- How Much?
  - Swedish post-Cesarean Protocol: Hydromorphone oral 4-6mg q4h + 4-8mg q4h prn pain
  - 2-3x typical dosing
  - No longer than non-opioid tolerant patients

# Develop a standing order set for patients with OUD leaving AMA

- Administer a high dose of buprenorphine (24-32mg) (If possible, administer XRBUP injection)
- Give at least 1 week Rx for outpatient buprenorphine
- A referral to outpatient MOUD provider with warm handoff/ peer support



### Low Threshold XR-BUP/LIAB

- Given regardless of active drug/alcoholuse
- No required drug testing
- Flexible schedule
- Walk-in appointments for injections
- Single day medication start for opioid tolerant patients (no SLBUP)
- Flexible dose
- SL supplementation available
- Available in pregnancy (2<sup>nd</sup>/3<sup>rd</sup> trimester)



# XRBUP/LAIB Brixadi vs Sublocade

- Does not require refrigeration
- Can be given at alternate sites once stable
- No palpable lump
- Weekly and monthly formulations with various strengths
- Labeled dosing for opioid/BUP naïve patients
- Weekly form likely preferred in pregnancy
- Highest dose monthly 128mg is = 200 mg Sublocade average serum drug levels
- Monthly formulation has shorter half life than Sublocade
- Same REMS/ordering procedure, similar cost (\$100 less)

## Overview of LAIB products

	Monthly injection (RBP-6000: Sublocade®)	Weekly and monthly injection (CAM2038: Buvidal®/Brixadi®)	SL tab (Suboxone®)
FDA Indication	Moderate-severe OUD, tolerating SL bup at 8-24 mg/day for ≥7 days. Counseling & psychological support should be part of tx plan.	Moderate-severe OUD after a single SL dose or already on bup. Counseling & psychological support should be part of tx plan.	Maintenance tx of opioid dependence. Counseing, etc.
C <sub>avg</sub> bup at steady state (ng/mL)	100 mg: 2.87 300 mg: 6.32	Weekly         Monthly           8mg: -         64 mg: 2.0           16 mg: 2.1         96 mg: 2.9           24 mg: 2.9         128 mg: 3.9           32 mg: 4.2	8/2 & 8 mg: 1.19 24 mg: 2.91
C <sub>max</sub> bup after single dose (ng/mL)	100 mg injection: 1.54 300 mg injection: 5.37	Weekly         Monthly           16 mg: 3.08         64 mg: 3.81           24 mg: 3.64         96 mg: 5.47           32 mg: 5.27         128 mg: 6.59	8/2 & 8 mg: 3.00 Generic 16/4 mg: 4.70
Time to peak  Terminal half- life	~24 hours 43-60 days	Weekly Monthly Within 24 hrs Within 6-10 hrs  3-5 days 19-26 days	24-42 hrs
Solvent	N-methyl-2-pyrrolidone (NMP): 278 and 833 mg NMP	Weekly: Ethanol Monthly: NMP 16-61 mgs* 57-115 mg	-

Sublocade OK to continue 300 mg empirically

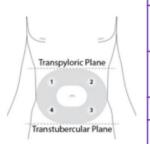
Only advantage of 100 mg shot is smaller bump, less side effects Can give part of a shot (ex 200mg/dose is approx)

Brixadi weekly 8 mg can be given every 2-3 days the first week X3 doses to titrate up pts with low/no tolerance

NEVER give 4 mg test dose of SLBUP (Very high risk of PW)

### Subcutaneous Monthly RBP-6000

\*Injection Transition Doses for Patients whose Disease Symptoms are Controlled (FDA label)

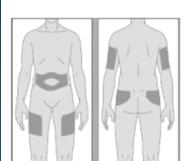


BUP-Sublingual Transition Doses	RBP-6000 Injection #1	RBP-6000 Injection #2	Maintenance Dose
8-18 mg/day*	300 mg (1.5 mL)	100 mg (0.5 mL)	100 mg
20-24 mg/day*	300 mg	300 mg	100 mg
If new- after 7-day lead of <a>2</a> mg daily:	300 mg	300 mg	100 mg

-No < q 26 days, delays up to 2 wks not expected to have neg effect -If on 100 mg and traveling & will miss – consider 300 mg for 2 months

### Subcutaneous Weekly and Monthly CAM2038

BUP-SL dose and approximate equivalent weekly and monthly BUP-XR dose



BUP-Sublingual	CAM2038 weekly (rotate sites)	CAM2038 monthly	
<u>&lt;</u> 6 mg	8 mg (0.16 mL)		
8-10 mg	16 mg (0.32 mL)	64 mg (0.18 mL)	
12-16 mg	24 mg (0.48 mL)	96 mg (0.27 mL)	
18-24 mg	32 mg (0.64 mL)	128 mg (0.36 mL)	
If new to bup	Use arms only after 4 weekly doses. Can initiate on day 1 after a 4 mg SL dose, then 16 mg same day with option of additional 8 mg if needed	-	

Pharmacokinetic parameters	SUBUTEX daily stabilization		SUBLOCADE		
Mean	12 mg (steady-state)	24 mg (steady-state)	300 mg# (1 <sup>st</sup> injection)	100 mg* (steady-state)	300 mg* (steady-state)
C <sub>avg,ss</sub> (ng/mL)	1.71	2.91	2.19	3.21	6.54
C <sub>max,ss</sub> (ng/mL)	5.35	8.27	5.37	4.88	10.12
C <sub>min,ss</sub> (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 sublingual dosing is indicated in patients who experience craving or withdrawal in early treatment

### Switching Patients Stable on SLBUP to LIAB/XRBUP

- Inquire on motivations (convenience, taper)
- Counsel on risk of anxiety related to loss of control of dosing med
- Opioid withdrawal mimics many other conditions (runny nose, sweating, anxiety, insomnia, myalgias)
- High BUP levels can cause sweating, may be intermittent
- Offer BH counseling prior to transition to prepare for and manage anxiety related to loss of ritual and control
- Plan desired approach (stop SLBUP cold turkey or overlap with taper of SLBUP)
- Consider giving second Sublocade dose 1 week after first, especially if dose is >= 24mg/day
- Medication levels peak in 24 hrs, then slowly decline.
- Consider offering SLBUP the last 2 weeks of the month, decreasing daily dose each month
- Consider checking serum Bup levels to clarify symptom correlations with objective levels

> J Addict Med. 2021 May-Jun 01;15(3):252-254. doi: 10.1097/ADM.000000000000738.

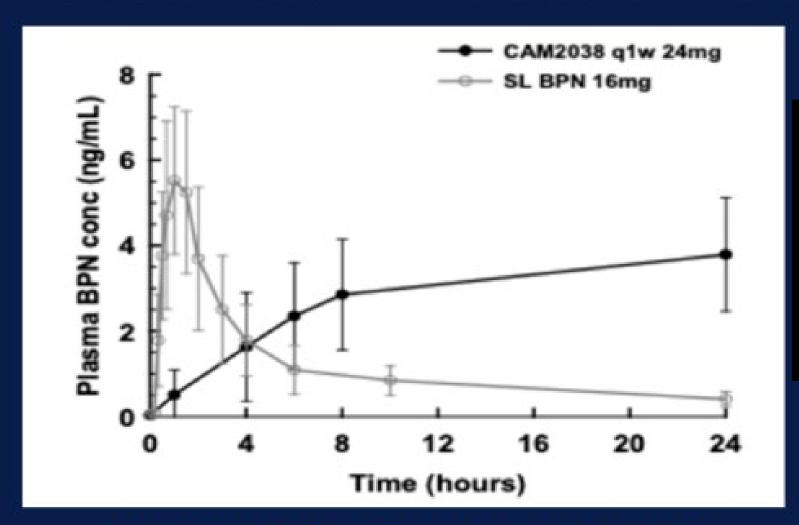
## Using Extended Release Buprenorphine Injection to Discontinue Sublingual Buprenorphine: A Case Series

Alexis D Ritvo 1, Susan L Calcaterra, Jonathan I Ritvo

### Abstract

Buprenorphine is highly effective for the treatment of opioid use disorder and is increasingly being used in the treatment of chronic pain. For various reasons, patients on buprenorphine may request discontinuation of this medication. Tapering off buprenorphine can be challenging due to intolerable withdrawal symptoms, including nausea, malaise, anxiety, and dysphoria. A single dose of extended-release buprenorphine may facilitate discontinuation of buprenorphine by mitigating prolonged, debilitating opioid withdrawal symptoms. We report on three cases of successful transition from low dose sublingual buprenorphine to a single injection of 100 mg extended-release buprenorphine to opioid cessation in patients who had previously been unable to taper fully off buprenorphine. This novel use of extended-release buprenorphine provides a viable alternative to fully transition patients off buprenorphine when they are medically and emotionally ready.

# ED-INitiated BupreNOrphine VAlidaTION Network Trial ED INNOVATION



XRBUP given in ED
1200 patients
9 cases of PW
(0.76%)
Did NOT give SLBUP
prior to shot

https://jamanetwork.com/jou rnals/jamanetworkopen/fullar ticle/2802898

Pharmacokinetics of XR- & SL- Buprenorphine

### Updated Sublocade Prescribing Info 3/2005

SUBLOCADE must be injected into the subcutaneous tissue of the abdomen, thigh, buttock, or back of the upper arm. (SUBLOCADE PI 2.1)

Patients should receive an initial dose (e.g. 4 mg) of transmucosal buprenorphine and be observed for one hour to confirm tolerability before administering the first injection of SUBLOCADE. The recommended starting dose of SUBLOCADE is 300 mg. Monitor patients in a healthcare setting after injection with SUBLOCADE to assess for symptoms of worsening withdrawal or sedation. Patients' symptoms should be stable or improving prior to release from the healthcare setting. On induction day, up to an additional 8 mg of transmucosal buprenorphine could be administered to manage withdrawal symptoms. (SUBLOCADE PI 2.3) (Never give 4 mg test dose prior, give as much SLBUP as needed the first 24 hours to treat PW)

The recommended dose for the second injection is 300 mg. The second injection may be administered as early as 1 week and up to 1 month after the initial injection, based on patient need. (SUBLOCADE PI 2.3)

# Black Bag Exemption

Question: Can a physician transport controlled substances and administer at the patient's home residence (the so-called "black bag exception")? Answer: Yes, with a limit. DEA will permit a physician who is registered with DEA to dispense controlled substances at a particular location in a state to travel to other unregistered locations in the same state to dispense controlled substances on an "as-needed and random basis," so long as the physician does not maintain a principal place of professional practice at any of those unregistered locations. If a physician intends to dispense controlled substances from a particular location several times a week or month, he must first file a separate registration for the location.



### **Mobile MOUD Clinic**

- Saves patients 50-120 miles round trip travel
- MOUD injections
- Harm Reduction supplies
- Comfort Medication Samples
- Rapid Testing
- Outreach
- Medical visits for Treatment of addiction and comorbid conditions





- No gas/car/license (carpool)
- House arrest
- Parents without childcare
- Living with other PWUD
- People needing harm reduction and wound care supplies
- People working 9-5 jobs



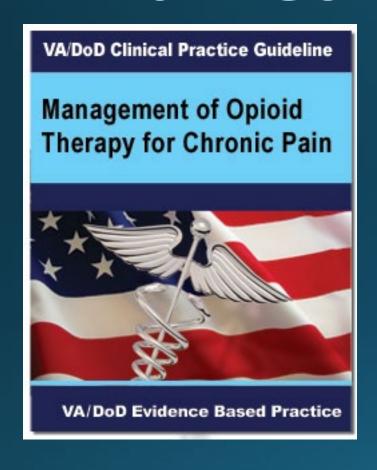
# Buprenorphine for Chronic Pain

# CDC 2022 Opioid Guidelines

Under Recommendation #5

"Emerging evidence suggests that patients for whom risks of continued high-dose opioid use outweigh benefits but who are unable to taper and who do not meet criteria for opioid use disorder might benefit from transition to buprenorphine. Buprenorphine is a partial agonist opioid that can treat pain and opioid use disorder and has other properties that might be helpful, including less respiratory depression and overdose risk than other opioids"

## VA 2022 Guidelines



For patients receiving daily opioids for the treatment of chronic pain, we suggest the use of buprenorphine instead of full agonist opioids due to lower risk of overdose and misuse.

### Which patients on COT may benefit from transition to BUP?

- Patients who find that protracted opioid withdrawal symptoms are unbearable when attempting an opioid taper
- Patients at high risk for opioid/sedative related morbidity or mortality on their current therapy
- Patients with opioid induced hyperalgesia??? Or other current opioid induced symptoms (depression, cognitive impairment, somnolence)
- Patients with opioid use disorder

# Insurance will usually cover SLBUP for Pain with PA indicating medical necessity

Example: Patient with multiple comorbidities on high dose chronic opioids, needing to change/taper for safety concerns (at risk for respiratory suppression) or side effects, but unable to tolerate opioid taper, buprenorphine can reduce overdose risk.

(ASAM 2020 guidelines and HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics 2019)

# Calculating Buprenorphine dose

- There is no verified MME or conversion factor for buprenorphine
  - (some sources online suggest 1 mg SLBUP= 20-30MME, not linear)
- Dosing/therapeutic effect is not linear
- If insurance covers transdermal/buccal, and patient on less than 50-100 MME then start there and follow manufacturers instructions
- If insurance does not cover FDA approved forms or patient on >100-150 MME then start with 2 mg films that can be quartered, prescribe only 1-2 days and be ready to rapidly escalate dosage as high as needed to achieve therapeutic effect (5 days to achieve steady state), insurance will rarely cover more than 24 mg/day

### Amazing FREE algorithms, order sets, patient education materials!



Our Work ✓

Resources

Trainings V

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https://bridgetotreatment.org/tools/resources/

#### Billing for the Community Health Worker Benefit

SITE EXAMPLE: Example site billing system for Community Health Worker (CHW) benefit



#### Blueprint for Hospital Opioid Use Disorder Treatment

TOOLKIT: Implementation guide for hospital-based opioid use disorder treatment programs



#### **Bridge Clinics**

REPORT: Overview of providing low-barrier MAT at an inhospital clinic



### Buprenorphine: What You Need to Know

PATIENT MATERIALS: Information for patients about buprenorphine and what to anticipate upon starting (also available in Spanish, Tagalog, Vietnamese, and traditional and simplified Chinese)

#### Buprenorphine and Pharmacy Frequently Asked Questions

FAQ: Pharmacy related questions on buprenorphine, prescribing, substance use navigators and prescription insurance questions

#### Buprenorphine Emergency Department Quick Start

PROTOCOL: Clinical guide for the treatment of acute withdrawal and opioid use disorder utilizing buprenorphine for ED-based starts Sarah Spencer DO, FASAM Addiction Medicine Specialist Ninilchik Community Clinic Ninilchik, Alaska 907-299-7460

sarahspencerak@gmail.com