CareOregon:
MOUD: medications, maintenance, and myths

Thursday, June 5th – 7:30 am – 10:00 am Pacific Time

Session focuses on increasing comfort and awareness around MOUD treatment, while helping eliminate lingering myths.

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Approved for CME & CEU Credit Hours:

American Academy of Family Physicians – Prescribed credits – American Medical Association (AMA) Physician's Recognition Award (PRA) Category 1 Credits 2.5 hours	Oregon Board of Pharmacy – Recognizes credits to toward CE hours requirements for license renewal! 2.5 hours
National Association of Social Workers – Clinical CEU credits – 2.5 hours	

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Topic – Approximate Timing	Presenters
2 hours – 7:30am start 1 hour – 7:30 am – 8:30 am 30 mins – 8:30 am – 9:00 am 30 mins – 9:00 am – 9:30 am	**Eleasa Sokolski, MD (she/her) – Assistant Professor of Medicine and Psychiatry – Oregon Health & Science University** Dr. Sokolski specializes in the treatment of people with substance use disorders and psychiatric disorders. She chose these areas of focus after recognizing the need for increased access to both addiction and mental health services and the often-intertwined nature of these conditions. She enjoys building relationships with her patients to understand their experience and empower them in their recovery. Her professional interests include medical education and the application of psychotherapy interventions to the hospital setting. **Emily Skogrand, PharmD – Clinical Pharmacist – Oregon Health & Science University** Emily Skogrand is a clinical pharmacist at Oregon Health and Science University in Portland, Oregon. She primarily works with the inpatient Internal Medicine department with a special interest in optimizing care and reducing stigma for patients with substance use disorders. **Session Learning Objectives:** • Review how to initiate and maintain patients on buprenorphine for the treatment of opioid use disorder. – **7:30 am – 8:30 am** • Define best practices for managing patients who use multiple substances while on medication for opioid use disorder. – **8:30 am – 9:00 am** • Learn how to incorporate long-acting injectable buprenorphine into clinical practice settings. – **9:00 am – 9:30 am**
30 minutes – 9:30 am – 10:00 am	**Audience Q&A** Questions to be solicited from enrolled attendees via chat.

Housekeeping

- CMEs & CEUs
- Chat function
- Q&A at end of session

Objectives

1. Review how to initiate and maintain patients on buprenorphine for the treatment of opioid use disorder.
2. Define best practices for managing patients who use multiple substances while on medications for opioid use disorder.
3. Learn how to incorporate long-acting injectable buprenorphine into clinical practice settings.

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MOUD: Medications, Maintenance and Myths

Eleasa Sokolski, MD
Emily Skogrand, PharmD
June 5, 2025

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Medication for OUD Saves Lives

In the year after non-fatal overdose, compared with no medication for OUD:

- Methadone maintenance was associated with DECREASE in all-cause mortality (aHR 0.47 [CI 0.32-0.71])
- Buprenorphine associated with DECREASE all-cause mortality (aHR 0.63 [CI 0.46-0.87])

MOUD is associated with a larger mortality reduction than any antihypertensive, diabetic agent, or statin, and more than aspirin after STEMI!

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...But Patients aren't Getting Treatment

- **87% of patients with OUD do not receive evidence-based treatmen**t, including life-saving medications.
- Rates of prescribing are increasing, largely driven by office-based buprenorphine, but not fast enough to keep up with treatment need.

Krawczyk. Int J Drug Policy. 2022

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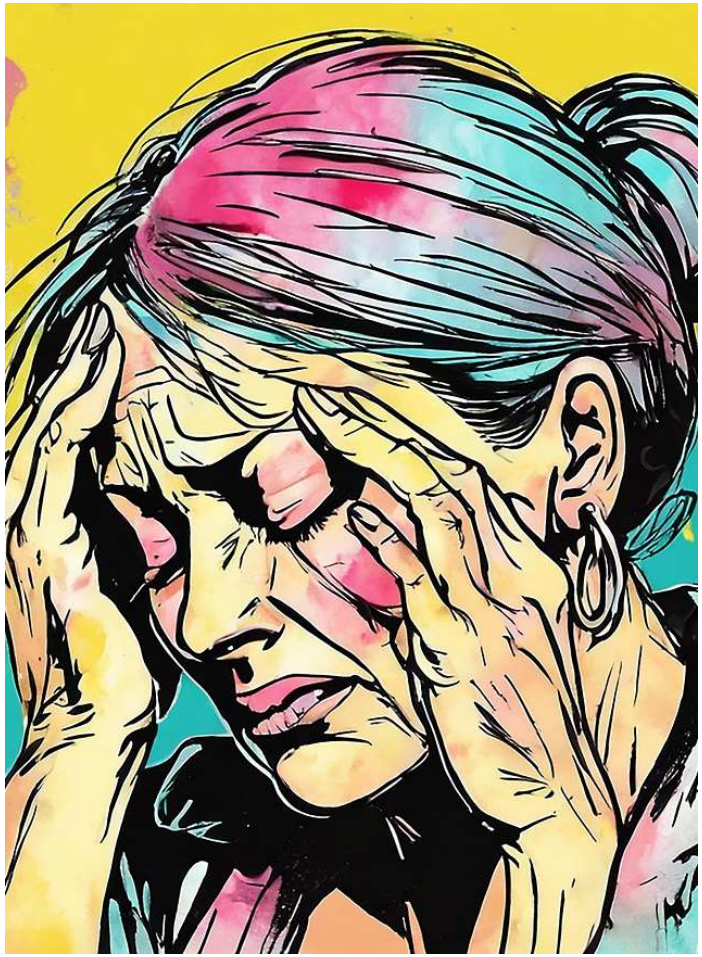
- Jane is a 59 yo female who presents to your office asking for help stopping fentanyl use.
- She previously used heroin but transitioned to fentanyl 3 years ago.
- She had 5 years of abstinence from heroin when taking buprenorphine in the past.
- Since she began using fentanyl, she "just can't get on buprenorphine!"



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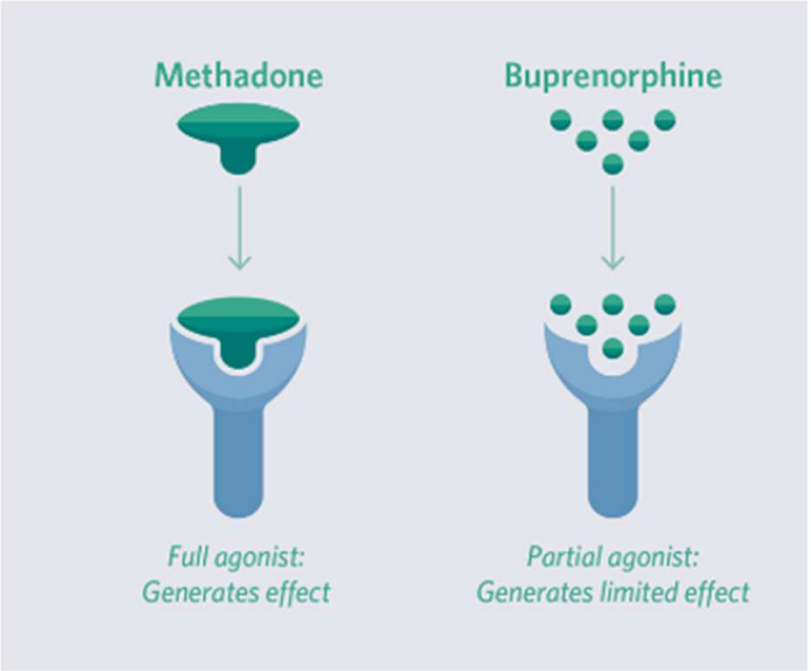
Buprenorphine Basics

- Partial opioid agonist
  - Does not mean partial analgesia!
  - 1 mg of buprenorphine is ~ 30-40 MME
  - Partial applies to sedation, euphoria, constipation
- High affinity at the mu receptor
- Long half life: 24-36 hours
- Bioavailability: 25-55% > formulation dependent
- Peaks: 1-3 hours



Lexi 2024, Pew Chartiable Trusts

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Mu Receptor

- Withdrawal suppression
  - 40-50% mu receptor occupancy
  - >1ng/ml serum level
- Euphoria blockade
  - 70-80% mu receptor occupancy
  - >2-3 ng/ml serum level
- Blockage for high affinity opioids
  - 90% mu receptor occupancy

- Mu receptor occupancy
  - 2 mg SL → 40%
  - 8 mg SL→ 50-60%
  - 16mg SL → 60-80%
  - 24 mg SL→80-90%
  - 32 mg SL→ 90-95%

Greenwald 2014, Greenwald 2003

Fentanyl in Drug Supply

- 50-100X more potent than heroin
- Fentanyl powder, pill form
- **Short acting but highly lipophilic**
  - **Risk of precipitated withdrawal with buprenorphine start due to high affinity**

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Buprenorphine Transition Options

Standard

- Withdrawal occurs
- High risk of causing precipitated withdrawal
- Initial doses are 2 mg
- Longer time to get to therapeutic dosing

High Dose

- Withdrawal occurs
- High risk of causing precipitated withdrawal
- Initial doses are 8-24 mg

Low Dose

- Withdrawal generally does not occur or is not severe
- Complicated dosing instructions
- Full opioid agonist must be used

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Shared Decision Making

Importance acknowledging what is right for the patient!

- Past experiences
  - Which ways worked for them in the past and which did not work
- Support/Resources
  - Safe person and safe place to do transition. Access to bathroom or safe space to sleep
- Dose changes
  - Can they keep track of dosing changes
- Drug supply
  - Do they have access to their same supply
- Withdrawal tolerance
  - What level of withdrawal are they willing to tolerate and for how long

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Shared Decision Making Counseling

- Standard
  - This method waits until you are in moderate-severe withdrawal before starting lower doses of buprenorphine like 2-4 mg. You will continue to take more buprenorphine each hour until you don't feel like you are in withdrawal anymore.
  - I will prescribe comfort medication to help support you to get to as close to 24 hours after your last use as possible.
  - This method will usually take about one day to get to a dose of buprenorphine that makes you feel better.
  - This could be a good method for you if you can tolerate moderate-severe withdrawal for about 24-36 hours.
  - You also need to be able to take buprenorphine multiple times throughout the day so choosing a day without other plans or distractions is important.
  - We will come up with a plan for how you will manage precipitated withdrawal if it happens.

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Shared Decision Making Counseling

- Low Dose
  - Slowest way to transition to buprenorphine but you do not have to be in withdrawal to start.
  - With this method, you continue to use your regular opioids while taking small doses of buprenorphine throughout the day like 0.5-1 mg. Your buprenorphine dose will increase each day until you get to your right dose, then you can stop using opioids.
  - This method might be a good choice for you if you do not want to experience severe withdrawal
  - You will need to follow instructions that will change your dose for the first 3-7 days.
  - You will need access to your regular supply of opioids to complete a low dose induction.

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Shared Decision Making Counseling

- High Dose
  - In this method, you wait until you are in moderate to severe withdrawal, ideally around 24 hours after your last fentanyl use.
  - I will prescribe comfort medication to help support you to get to 24 hours after your last use.
  - You will then take a higher dose of buprenorphine, usually around 16 mg.
  - You can repeat doses every hour until you feel better, up to 32 mg
  - There is a risk of precipitating withdrawal you take your buprenorphine dose too soon.
  - Having a strong support person and access to a bathroom and safe sleeping space is important.
  - We will come up with a plan for how you will manage precipitated withdrawal if it happens.

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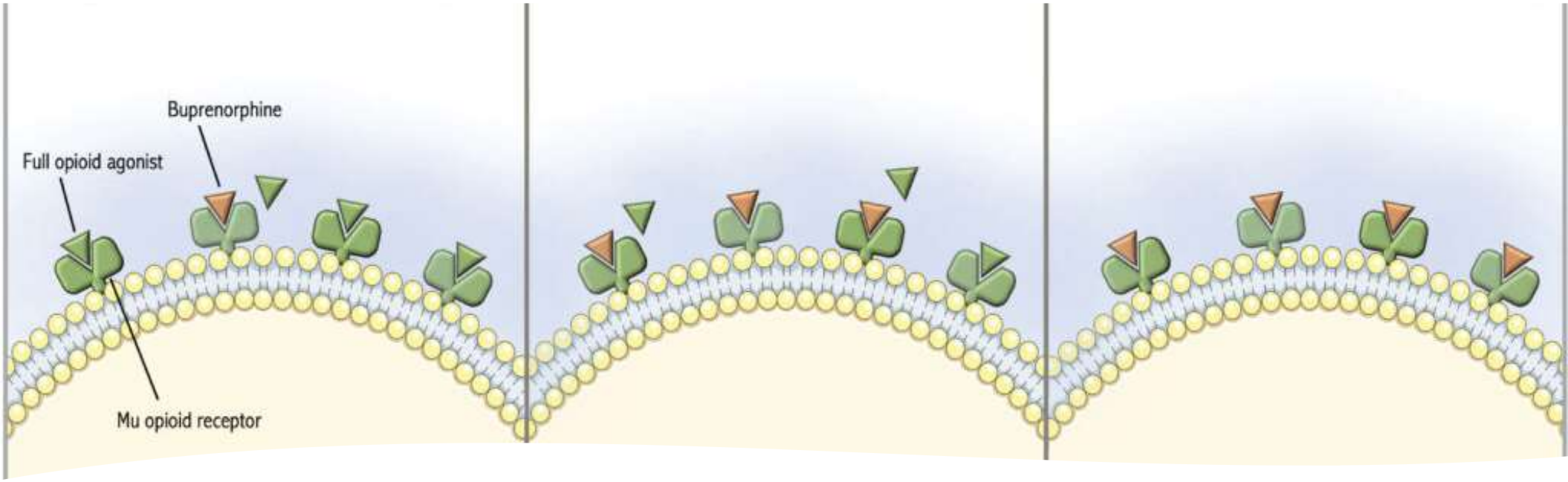
Standard Initiation

- Day 1
  - Buprenorphine 2 mg SL once COWS greater than 10 and 2 objective withdrawal symptoms
  - Buprenorphine 2-4 mg SL Q1h PRN patient reported cravings or withdrawal
    - Stop using COWS after 1st dose
  - Consider limiting total daily dose to 24 -32mg

- Day 2
  - Total buprenorphine dose given on Day 1 as single dose in morning
  - 2-4 mg SL q1h PRN patient reported cravings or withdrawal



Low Dose Initiation

- Repetitive administration of small doses with sufficient dosing interval should not precipitate opioid withdrawal
- Given long receptor binding time, buprenorphine will accumulate at receptors
- Over time, an increasing amount of full agonist will be replaced by buprenorphine at the opioid receptor

Hammig 2016

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Rapid Low Dose Buprenorphine

Day	Buprenorphine Dose	Full Opioid Agonist
1	0.5 mg SL once*	Continue
2	1 mg TID x 3 doses	Continue
3	1 mg Q3h x 6 doses OR 2 mg TID x 3	Continue
4	8 mg in AM x1 and titrate to cravings/withdrawal up to 24 mg	Stop or continue as needed for acute pain
5	24-32 mg given BID-TID	Continue as needed for acute pain
* 225 mcg film, 20 mcg/hr patch, 0.06 mg IV, ¼ of 2 mg tablet		

Sokolski 2023

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Example Ambulatory Care RX

- Buprenorphine/naloxone (SUBOXONE) 2-0.5 mg SL tablets # 3: Take 0.5-2 mg, SL, QID

Comment: Day 1: take ¼ tablet 4 times daily, Day 2: take ½ tablet 4 times daily then switch to 8 -2mg prescription

AND

- Buprenorphine/Naloxone (SUBOXONE) 8-2 MG SL tablets # 24: Take 1/4-3 tablets, SL, as directed

Comment: Day 3: take ¼ tablet 4 times daily, Day 4: take 1&½ tablets once daily. After taking 1 &½ tablets you may take an additional ½-1 tablet every 4 hours as needed for cravings or withdrawal up to a max of 3 tablets, Day 5+: Take up to 3 tablets per day

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Example Patient Dosing Table

Day	Medication	Directions	Other Opioid Use	Comfort Medications
Day 1	Suboxone 2-0.5mg	Take ¼ tablet four times daily	Continue the same amount of your usual opioid*	Yes
Day 2	Suboxone 2-0.5mg	Take ½ tablet four times daily	Continue the same amount of your usual opioid*	Yes
SWITCH TO 8-2 MG TABLETS				
Day 3	**Suboxone 8-2mg**	Take ¼ tablet four times daily	Last day of your usual amount of opioid	Yes
Day 4	Suboxone 8-2 mg	Take 1&½ tablets in the morning After taking 1&½ tablets you make take an additional ½ to 1 tablet every 4 hours for cravings or withdrawal symptoms. Up to a maximum of 3 full tablets	No opioid	Yes
Day 5+	Suboxone 8-2 mg	Take up to 3 tablets per day	No opioid	

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High-Dose Initiation

- Wait as long as possible to start, at least 24 hours from last use of fentanyl if possible
- Prescribe withdrawal adjuncts while awaiting 24 hours
- Take 8-16mg of buprenorphine, may take additional 8mg every 1-2 hours to max 32mg

Herring, JAMA, 2021
CA Bridge Buprenorphine Self-Start

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CA BRIDGE

Buprenorphine Self-Start

Guidance for patients starting buprenorphine outside of hospitals or clinics

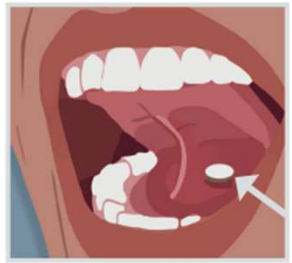
1. Plan to take a day off and have a place to rest.
2. Stop using and wait until you feel very sick from withdrawals (at least 12 hours is best, if using fentanyl it may take a few days).
3. Dose one or two 8mg tablets or strips UNDER your tongue (total dose of 8-16mg).
4. Repeat dose (another 8mg-16mg)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

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Low-to-High Dose Initiation

- Discontinue fentanyl use.
- Start buprenorphine 1mg every 4-6 hours for 24 hours.
- Then when in too much withdrawal, take buprenorphine 16-24mg, may take additional 8mg x1-2 up to max dose 32-40mg.

Adapted from presentation by Jennifer Hartly, MD, PHD, Fentanyl: what to know – what to do – what's coming. 2023

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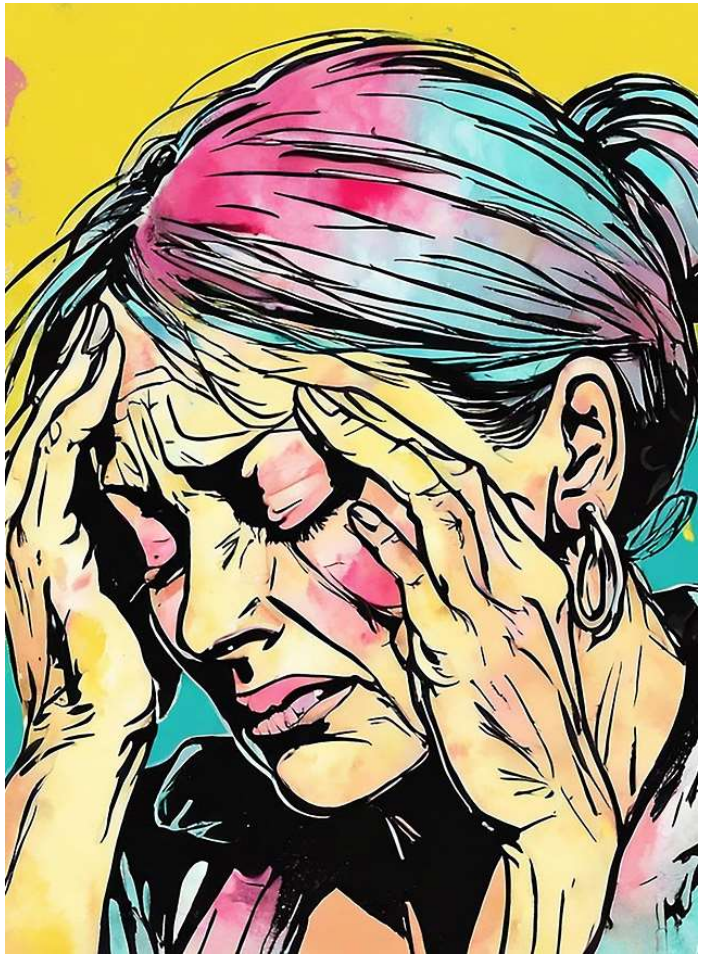
- When you ask Jane about her recent experiences starting buprenorphine, she tells you that she's tried two low dose starts.
- "I had trouble following the directions; the first time I took too much on the first day and felt sick. The second time I used less fentanyl the first two days thinking it would help, but I felt worse!"



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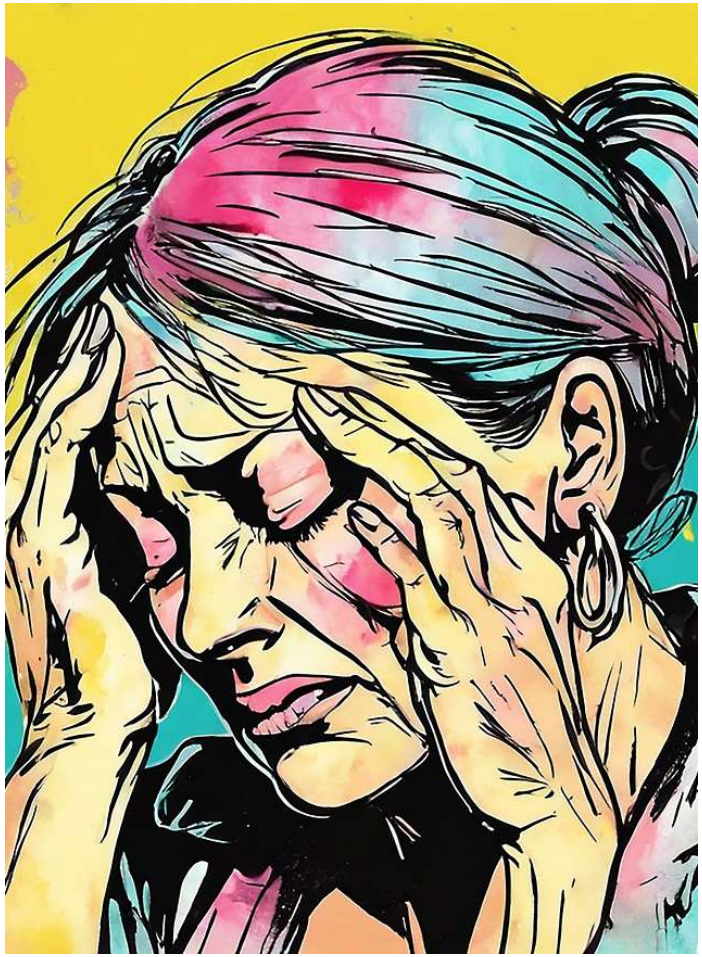
- You go over the different ways to start buprenorphine, and Jane says she'd like to try a high-dose start.
- "I know I'm not going to feel good the first day, but I just want to get this over with!"
- She is interested in adjunctive "comfort" medications that she can take while waiting to start the first dose of buprenorphine.



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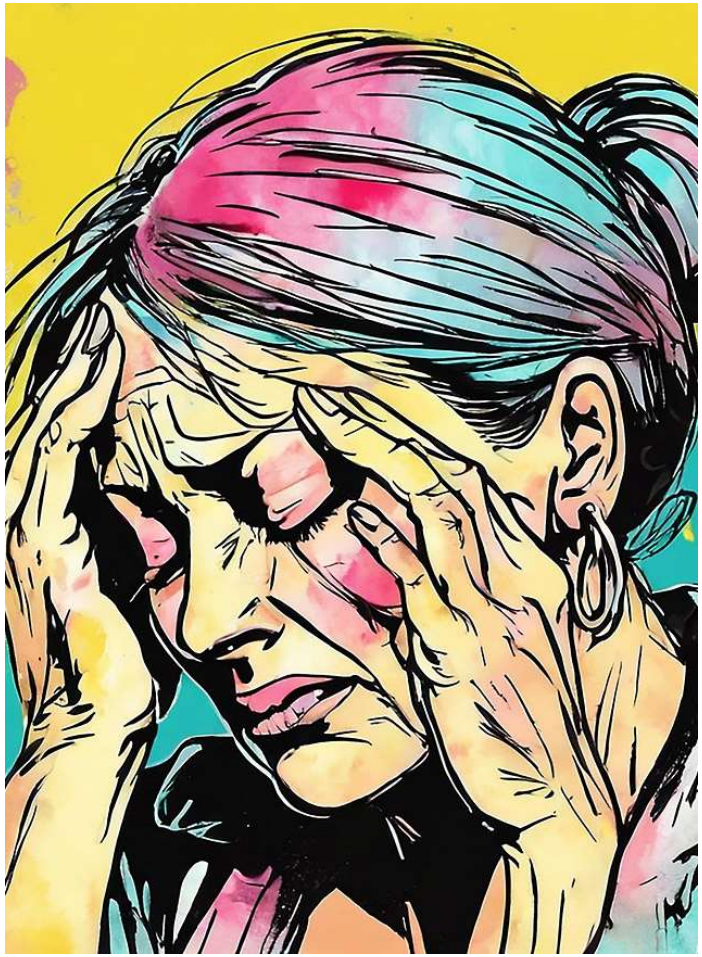
Adjunct Medications for Opioid Withdrawal

Adjunctive Medication	Dose	Indication
Acetaminophen	500 mg every 6 hours as needed	Mild to moderate pain
Clonidine	0.1 mg three times daily as needed	Sweating, anxiety, restlessness, insomnia
Gabapentin	300 mg every 8 hours as needed	Anxiety, restlessness, insomnia
Hydroxyzine	25 mg every 6 hours as needed	Anxiety
Ibuprofen	400 mg every 6 hours as needed	Mild to moderate pain
Loperamide	2 mg every 6 hours as needed	Diarrhea
Melatonin	3 mg at bedtime as needed	Insomnia
Ondansetron	4 mg every 8 hours as needed	Nausea
Tizanidine	2 mg every 6 hours as needed	Muscle spasms

- You see Jane back the next week.
- She was successful in starting buprenorphine and is now on 24mg daily.
- She waited a full 48 hours from her last fentanyl use to start buprenorphine.
- She did not have precipitated withdrawal but did experience moderate opioid withdrawal symptoms while waiting to take the first dose. The adjuncts were helpful.
- She was able to discontinue fentanyl use!



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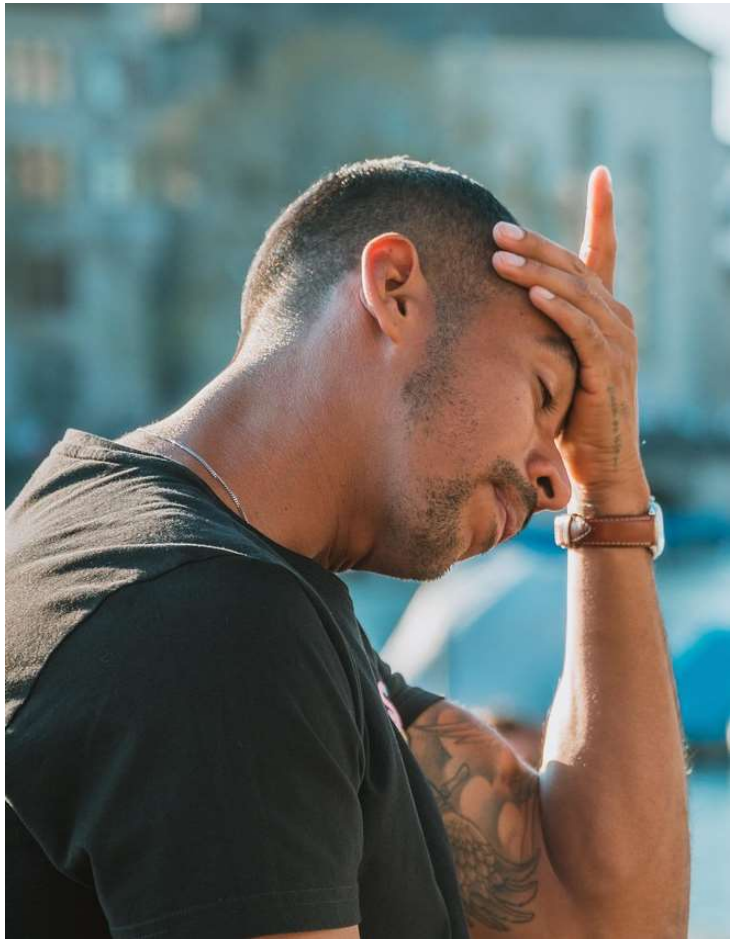
Long Term Dosing

- ASAM National Practice Guidelines recommends titrating dose to alleviate symptoms and to be sufficient to allow for discontinuation of illicit opioid use
- Dosing max of 24 mg has limited evidence
- Dosing of 16-32 mg supports:
  - Improved treatment retention
  - Reduced opioid use
  - Lack of adverse events
- Dosing limits often driven by outpatient insurance

- Sam is a 24 yo male with opioid use disorder who recently started buprenorphine 3 weeks ago.
- Taking 8mg in the morning at 16mg at night.
- He discontinued all fentanyl use.
- Today, he reports persistent chills, night sweats, mild body aches, and insomnia.
- Reports having cravings for opioids.
- He wants to know if he can increase buprenorphine?



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First and foremost:

- You review buprenorphine administration technique to be sure Sam is getting the full dose.
  - Starting with a moist mouth.
  - Not talking while letting the films/tabs dissolve.
  - Holding the tabs or films under the tongue for at least 5 minutes until fully dissolved.
  - Not swallowing the pills or tabs!
  - Avoiding acidic drinks (coffee, fruit juice) or nicotine products 30 min before taking.

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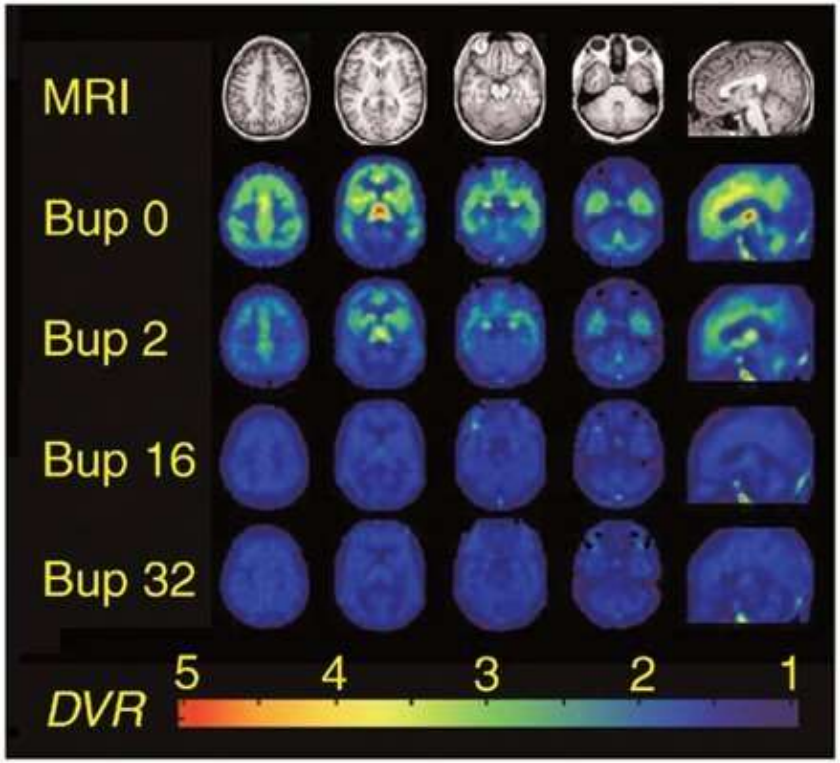
Buprenorphine Dose Limits

- 24mg dose limit is based on data from before the fentanyl era .
- The opioid receptor has 85-92% occupancy at 16mg daily and 94-98% occupancy at 32mg daily.
- Higher receptor occupancy is associated with reduced withdrawal symptoms and cravings.
- A subset of patients do better at 32mg daily!



Grande. J Addict Med. 2023
Greenwald, Neuropsychopharmacology, 2003

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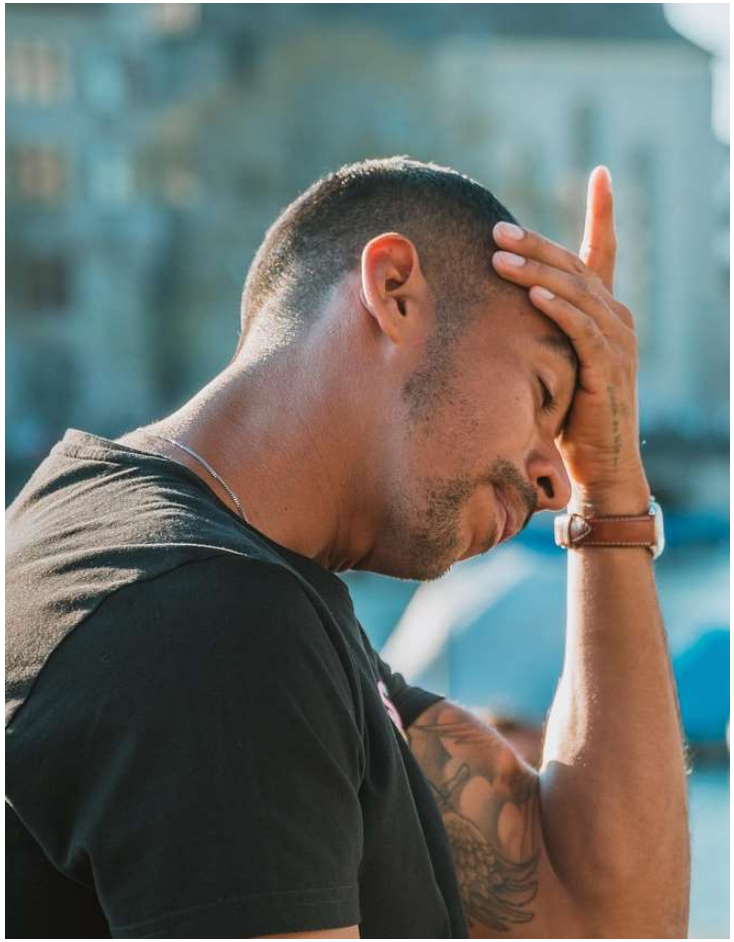
- You increase Sam's dose up to 16mg BID (32mg total daily).
- He comes back to see you a week later and reports improvement in his body aches, chills, and insomnia.
- Cravings for fentanyl are not completely gone but are greatly reduced.
- He is overall feeling much better!



Patients Who Use Multiple Substances

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- Marie is a 45-year-old female with opioid use disorder who has been stable on buprenorphine 24mg daily for the past 8 months. She presents today for routine follow-up.
- She previously used fentanyl daily but has been able to discontinue.
- She completes a point-of-care urine drug screen, which is positive for buprenorphine and benzodiazepines.
- She discloses that she's been taking non-prescribed alprazolam from her friend's prescription.

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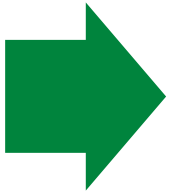
Buprenorphine and Benzodiazepines

FDA Drug Safety Communication

2016: FDA warns about serious risk of death when combining opioids with benzodiazepines



2017: FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressants

FDA 2016, 2017

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Buprenorphine and Benzodiazepines

- Use of benzodiazepines (either prescribed or non-prescribed) is common in those on buprenorphine.
- Increases risk of overdose when taken together, especially if benzodiazepine is used IV or taken at supratherapeutic dose.
- Benzodiazepines can remove buprenorphine's "ceiling effect" on respiratory depression
- Out of 182 people who died by "buprenorphine poisoning" in Finland (2000-2008), in all but one case either a benzodiazepine or alcohol was also found.

Schuman-Olivier, 2013
Hakkinen, 2012

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Buprenorphine and Benzodiazepines

- Among patients in an outpatient buprenorphine treatment program (n=328), those who had a prescription for benzodiazepines were more likely to have accident-related ED visits.
  - Greater risk of ED visits in female patients.
- No influence on treatment retention or illicit opioid use.
- No increase in overdoses and no fatalities occurred during the12-month study.

Schuman-Olivier, 2013

Buprenorphine and Benzodiazepines

- Risk of opioid toxicity is higher with concurrent use of methadone and benzodiazepines.
- Much higher risk when benzodiazepines are used with fentanyl.
  - British Columbia Coroner Services reported BZD+ in 52% fatal fentanyl overdoses in Jan 2022.

Nielsen, 2007
CFSRE, 2022

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Co-Occurring Mental Health Disorders:

- Prevalence of mental health conditions among people with opioid use disorder:
- Depression: 36%
- **Anxiety: 39%**
- **PTSD: 18%**
- ADHD: 21%
- Bipolar disorder: 9%
- OCD: 7%
- Borderline personality disorder: 18%

Santo, Drug and Alcohol Dependence, 2022

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- An unexpected positive urine toxicology for benzodiazepines can open the door to discuss why the are using this substance:
  - Not able to sleep?
  - Uncontrolled worry?
  - Panic attacks?
  - Hyperarousal from PTSD?
  - Euphoric effect?

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"Just simple little things like walking down the street would, you know, really bother my anxiety and now I don't have that feeling anymore, you know? Like I feel like I'm able to do normal things."

"I got prescribed Klonopin and I started taking three a day and then I started buying them so I would end up taking, like, I'd mix Xanax and Klonopins and take them on a high dose of methadone so I would be pretty much high all day."

"I don't take extra. I take them the way I'm supposed to now because I realize taking extra is just screwing myself in the end and if you do take them the right way, they help with what I want them to help with. I don't want the high anymore. I just need the anxiety taken away."

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- Marie reports a long history of anxiety and panic attacks that preceded her onset of opioid use.
- She does not want to take alprazolam but is terrified of having withdrawal symptoms if she stops.
- She is started on sertraline and referred to see a therapist.
- She is prescribed clonazepam with a plan to taper and discontinues use of non-prescribed alprazolam.
- She remains engaged in treatment for OUD with no fentanyl use.

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- Reese is a 21 yo transgender male who presents to clinic to follow-up on OUD.
- He's been taking buprenorphine for 3 months and was successful in stopping all opioid use.
- He continues to smoke methamphetamine daily and is afraid to discuss it as he is worried his buprenorphine prescription will be stopped.

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Buprenorphine and Stimulants

- Stimulant use among those with OUD is extremely common
  - One study of those entering treatment for OUD found that **82.5%** of individuals had been exposed to stimulants in their lifetime.
  - "Twin epidemics"
- Having both an opioid and stimulant use disorder increases the risk of fatal and non-fatal overdose.
- Methamphetamine use is associated with lower treatment retention for OUD.
- Being on medication for OUD is associated with a lower odds of stimulant-related ED visits or hospital admissions.

Ellis, 2021; Palis, 2022; Xu, 2022; Frost, 2021

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- After being reassured that his buprenorphine will be continued, Reese feels more comfortable discussing his methamphetamine use.
- He is not ready to discontinue use but is interested in harm reduction measures which leads to a fruitful discussion.

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- Alexa is a 68 yo woman who has a remote history of OUD and has been on a stable dose of buprenorphine for the past 15 years.
- Now primarily taking buprenorphine for chronic pain.
- Her PCP recently retired, and her new PCP would not refill buprenorphine after her urine drug screen returned (+) for THC.
- She is coming to see you as a new patient to transfer care. She is down to her last tablet of buprenorphine.

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Buprenorphine and Cannabis

- High rates of cannabis use in those with OUD
  - Although rates of use in Oregon are high in general, with 32% of adults reporting past year use in 2022-2023.
- Tetrahydrocannabinol (THC) and cannabidiol (CBD) have no known clinically significant interactions with buprenorphine.
- Cannabis use does not increase the risk of non-medical opioid use in those on MOUD.
- Preliminary evidence suggests that cannabis likely does not improve opioid cravings or withdrawal.

Englander, 2025

- Alexa has been using cannabis daily for the past 5 years to self-manage chronic pain and insomnia.
- You assess for cannabis use disorder (CUD), and she meets mild CUD criteria.
- She does not want to discontinue cannabis use completely but is open to reducing if there are other options to help with her pain and sleep.

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General Approach

- Explore patient perceptions about concurrent substance use
  - Benefits?
  - Harms?
  - Desire to change use / use-pattern?
- Assess for a 2nd substance use disorder
- Treat based on patient's goals – consider a harm-reduction approach for those not ready to discontinue use
- Prioritize continuation of buprenorphine and continued engagement in treatment for OUD.

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Long-Acting Injectable Buprenorphine

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Injectable ER Buprenorphine

Pros

- Doesn't require daily dosing
- Removes concern for lost or stolen medications
- Steady, continuous plasma concentration
- Better OD protection?
- Patient centered outcomes
  - Improved health measures, increase employment, increase medication satisfaction, decrease health care utilization

Cons

- Cost
- Complicated billing
- Availability of administering provider

Ling 2019

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Injectable ER Buprenorphine Options

- Sublocade
  - Monthly

- Brixadi
  - Monthly
  - Weekly

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Sublocade Pharmacokinetics

- Peak: 24 hours
- Half- life: 43-60 days
  - 833 mg of NMP per dose
- Steady state: 4-6 months
- Dosing:
  - 300mg x 2 → 100mg monthly
  - 300mg monthly
  - 300mg q7 days x 2 → 300mg monthly
- Monitoring: baseline and monthly LFTs

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Sublocade Serum Levels

Table 6. Comparison of Buprenorphine Mean Pharmacokinetic Parameters Between SUBUTEX and SUBLOCADE

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

#Exposure after 1 injection of 300 mg SUBLOCADE following 24 mg SUBUTEX stabilization

*Steady-state exposure after 4 injections of 100 mg or 300 mg SUBLOCADE, following 2 injections of 300 mg SUBLOCADE

Sublocade Package Insert

Sublocade Starts

- Stabilized on SL regimen → give injection
  - Peaks in 24 hours so will generally have pt take SL dose on day of injection
  - Can add additional 4-8 mg PRN cravings or withdrawal especially if SL dose is >24 mg
  - Could also add supplemental SL around week 3
- New buprenorphine start
  - Start on SL buprenorphine utilizing whichever method you would use for initiation (low dose, traditional, high dose)
  - Give injection after at least 8 mg or at dose that controls cravings/withdrawal
  - Do not wait 7 days after SL stabilization!
- On Brixadi → give on same day Brixadi was due or up to 7 days before

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Sublocade Updates

- Allowed for additional injections sites
  - Abdomen, thigh, buttocks and upper arm
  - Higher cmax in arm and thigh
- Increases time outside of refrigerator to 12 weeks
- Suggests that maintenance dose of 300mg monthly is appropriate in some patients
- Suggested that 300 mg q2month could sub for 100 mg occasionally
  - Important to recognize much higher peak

Sublocade Updates

- Rapid Dosing
  - 4 mg SL once then 300mg one hour later followed by second dose 1 week later
    - Patients were requested to wait 24 hours from last illicit drug use
    - Higher percentage of fentanyl + patients required supplemental SL buprenorphine on day 1 (maxed at 8 mg)
    - Low rate of precipitated withdrawal
    - Study pending publication
  - Second 300 mg dose can be given as soon as 7 days after initial injection

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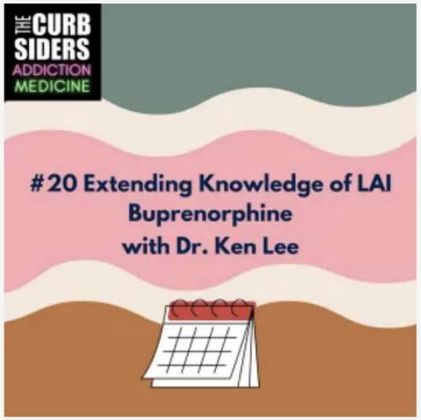
Sublocade Missed Doses

- 4-6 weeks since last injection: planned next dose without SL test dose
- 6-12 weeks since last injection and at steady state: planned next dose without SL test dose
- 6-12 weeks since last injection and NOT at steady state: 8 mg SL test dose
- 12-18 weeks since last injection: if ongoing use or + UA, give 8 mg SL test dose



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Brixadi Pharmacokinetics

- Peak
  - Weekly: 24 hours
  - Monthly: 6-10 hours
- Terminal half life
  - Weekly: 3-5 days
  - Monthly: 19-26 days
- Steady State
  - Weekly: 4 weeks
  - Monthly: 4 months
- Monthly uses N-methyl-pyrrolidine for delivery
  - 57-115 mg NMP per dose
- Weekly uses anhydrous ethanol (0.061g), phosphatidylcholine, glycerol dioleate

Brixadi Package Insert

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Brixadi Serum Levels

Drug product dose			C_{av} (ng/mL)			C_{max} (ng/mL)			C_{trough}[a] (ng/mL)		
SL BPN	Brixadi (weekly)	Brixadi (monthly)	SL BPN *	Brixadi (weekly)	Brixadi (monthly)	SL BPN *	Brixadi (weekly)	Brixadi (monthly)	SL BPN *	Brixadi (weekly)	Brixadi (monthly)
8 mg	16 mg	64 mg	1.2	2.1	2.0 $	4.7	4.3	4.0 $	0.7	0.8	1.3 $
16 mg	24 mg	96 mg	1.8	2.9 $	2.9 $	6.5	5.5 $	6.0 $	1.0	1.4 $	2.0 $
24 mg	32 mg	128 mg	2.5	4.2	3.9	8.2	6.9	11.1	1.4	2.6	2.1

* Average value of two studies

$ Simulated

[a] C_{168h} after 4th dose for BRIXADI (weekly), C_{28d} after 4th dose for BRIXADI (monthly) and C_{24h} after 7th daily dose for Subutex

Brixadi Package Insert

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Dose Titration

- For patients not currently on SL buprenorphine:
  - Weekly formulation
  - 4 mg SL once --> if no precipitated withdrawal --> 16 mg SQ once
  - Assess at 24-72 hours and repeat with an additional 8 mg SQ if needed
  - Re-assess at 24 hours and repeated with an additional 8 mg SQ if needed
  - Max 32 mg per week

- Reality → start patient on SL buprenorphine using whichever method you would normally. Then start the monthly or weekly injections.

Brixadi Package Insert

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Brixadi Dosing

Daily Sublingual Buprenorphine Dose*	BRIXADI Weekly	BRIXADI Monthly
≤6 mg	8 mg	-
8-10 mg	16 mg	64 mg
12-16 mg	24 mg	96 mg
18-24 mg	32 mg	128 mg

Brixadi Package Insert

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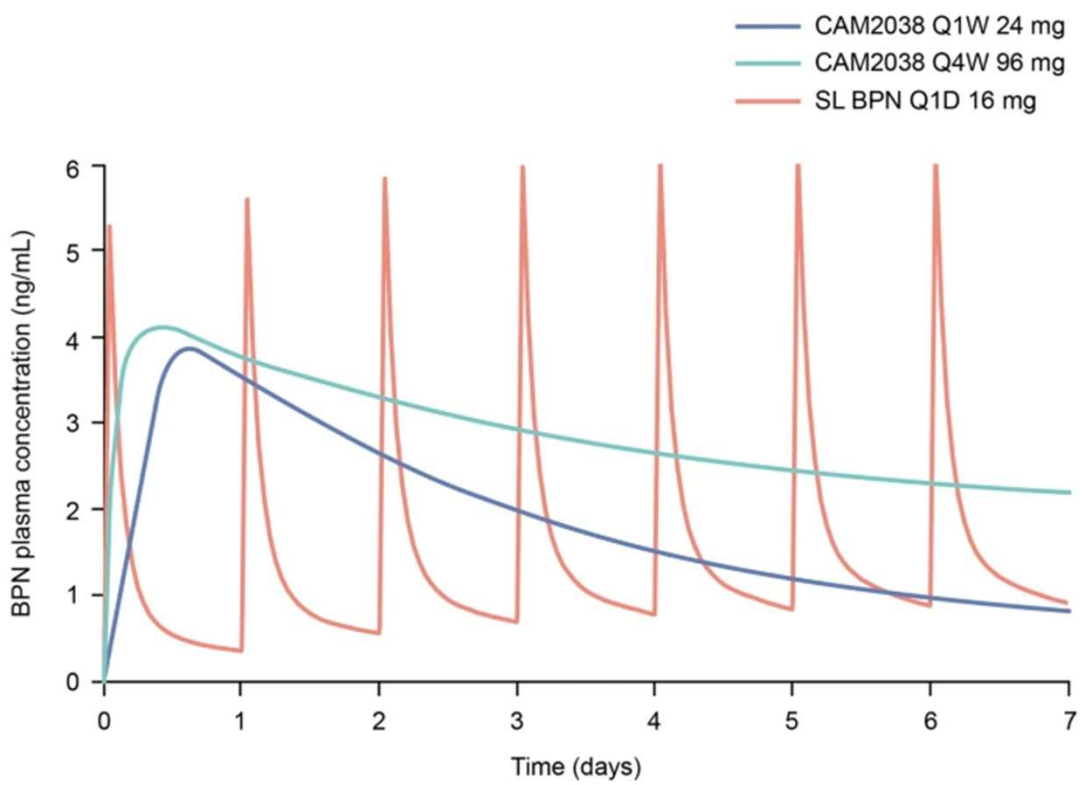
Direct to Inject Brixadi

- Weekly formulation only!
- Evidence in ED and small ambulatory case series
- Slow peak of weekly formulation allows for gradual accumulation
- Low incidence of precipitated withdrawal
- Low COWS score
  - most had COWS <8

Serum Levels

Fig. 4



Brixadi Package Insert

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Direct to Inject Brixadi

- COWS score > 4 and 6-12 hours since last use
  - Risk vs benefit discussion if neither are true
- NO methadone exposure for over 72 hours
- Prescribe/order withdrawal adjuncts
- SQ weekly formulation
  - 24 mg used in ED study
  - Ambulatory case series allowed for 8mg, 16 mg or 24 mg with 24 mg being the most common

Rosenwohl-Mack 2025, D'Onofrio 2024

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Direct to Inject Brixadi

- Counsel patients not to use any other opioids for 6 hours after injection
- Supplemental SL buprenorphine allowed 24 hours after injection
  - 16 mg → 20-24 mg TTD supplemental SL
  - 24 mg → 16-20 mg TTD supplemental SL (4 mg q6h PRN)
- Transition to monthly formulation 48 hours after initial injection

Rosenwohl-Mack 2025, D'Onofrio 2024

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Switching Between Products

Sublocade 300mg monthly

- Avg: 6.54
- Max:10.12
- Min: 5.01

Brixadi 128 mg monthly

- Avg: 3.9
- Max: 11.1
- Min: 2.1

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Switching Between Products

Sublocade 300mg x2 →100mg

- Avg: 3.21
- Max: 4.88
- Min: 2.48

Brixadi 96 mg monthly

- Avg: 2.9
- Max: 6
- Min: 2

Brixadi 128 mg monthly

- Avg: 3.9
- Max: 11.1
- Min: 2.1

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Things to Consider When Choosing Formulation

- Brixadi's T1/2 is shorter→ less forgiving of late doses
- More dosing options with Brixadi so ability to tailor dosing to your patient specific needs
- Less painful injection with Brixadi
- Lower serum levels with Brixadi
- Less NMP in Brixadi
- Should not use Brixadi in patients with soybean allergy

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Injectable to Taper off Sublingual

- Some patient find taper challenging around 8mg
- Consider 100 mg x1 to aid in smoother taper
- Repeat at 4-8 weeks if needed

OR

- Don't taper SL and do 300mg x 2 and then 100mg x 5-6

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Steps to Obtaining in Clinic

1. Apply for facility DEA license
2. Enroll in REMS
3. Develop a storage system (double lock)
4. Develop system for inventory (double staff sign in/out)
5. Develop policy for destruction
6. Find authorized supplier and set up account
    1. Cardinal, Henry Schein, Besse
7. Give injection!

Grayken Center has great guide and example of policy/logs!

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Questions

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Q&A

Submit questions using the Chat feature

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Survey will be emailed to all enrolled participants

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Thank you!

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