

ECHO IDAHO

Substance Use in Idaho

Low Dose Induction & Long-Acting Injectables

2/12/26

Todd Palmer, MD

Full Circle Health

None of the planners or presenters for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



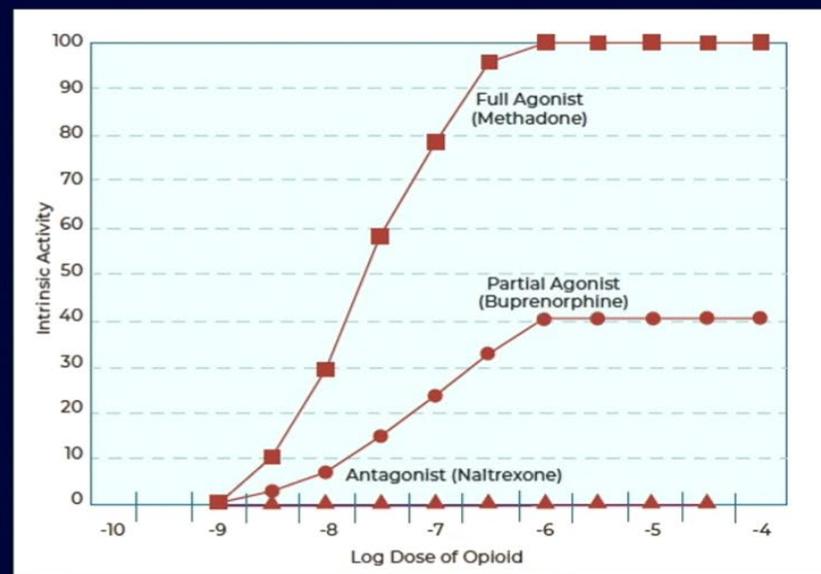
Learning Objectives

- ▶ 1) Understand the general concepts of low dose inductions
- ▶ 2) Be familiar with different low dose inductions regimens
- ▶ 3) Be familiar with the possible advantages and disadvantages of low dose inductions
- ▶ 4) Be familiar with the unique situations with Fentanyl

Buprenorphine: KEY characteristics



High Affinity



Partial Agonist

Issues with converting to Buprenorphine

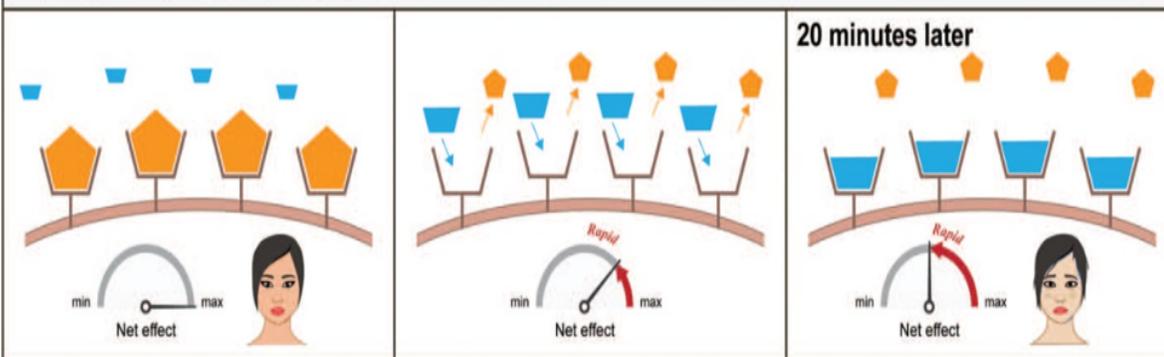
- ▶ Replacing methadone which is a full agonist with Buprenorphine a partial agonist with higher receptor affinity will knock methadone off of the receptor and precipitate sudden withdrawal.
- ▶ Some risk factors for this are high Methadone dose, short time to conversion, and female gender

Can take as much as 96 hours off of Methadone to get to a level of where this does not happen.

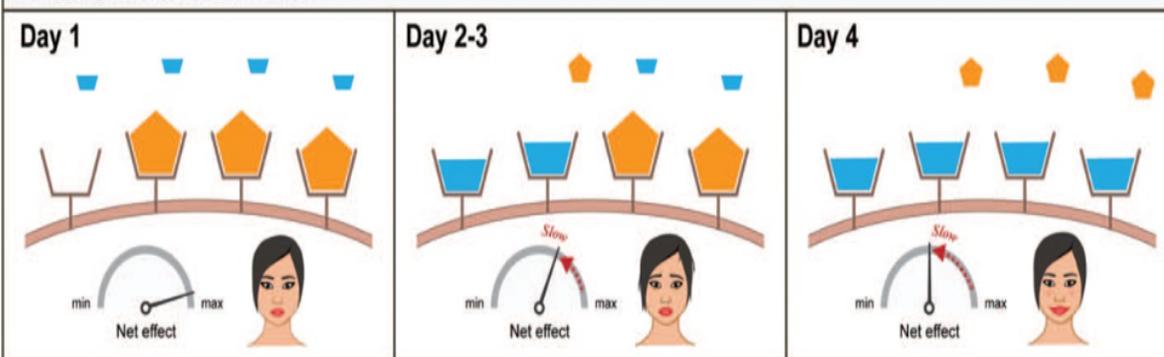
We can do this gradually with low dosing and “bridging”

- ▶ This consists of starting off with very low doses of Buprenorphine with gradual increases and allowing it to take over the Mu receptors.
- ▶ Eliminate patients having to go through withdrawal.
- ▶ Can help prevent an increase in pain during the induction phase.
- ▶ Can be done with much higher doses of Methadone. Typically we like to get patients down to 30 or maybe 40 before doing typical induction.

Precipitated Withdrawal Mechanism



Bridging at Molecular Level



Full agonist opioid
Buprenorphine

FIGURE 1

Mechanism behind precipitated withdrawal mechanism as well as bridging: Partial agonist opioid with high affinity for μ -receptors replaces the full opioid agonist rapidly over a short period of time causing a massive change in the net μ -receptor activation leading to rapid precipitated withdrawal. This can be mitigated by bridging, where the gradual introduction of higher affinity partial agonist opioids can help minimize withdrawal symptoms.

Source

[A Review of Novel Methods To Support The Transition From Methadone and Other Full Agonist](#)

Let's look at different induction methods

- ▶ What we've typically done:
 - ▶ Taper Methadone dose to 30 mg or less (or maybe 40)
 - ▶ 36-72 hours off of methadone with patient presenting in withdrawal
 - ▶ Start induction with small doses of Buprenorphine and titrate upwards to alleviate withdrawal symptoms and/or pain.
 - ▶ Typically, this involves 4 mg of Buprenorphine with a repeat of 4 mg on day 1. Fentanyl situation can be different.
 - ▶ Day 2 this might be 8 plus 4 plus 4, with further titration up on subsequent days if needed.
 - ▶ Works best for methadone doses less than 40 and least well if over 60.
 - ▶ Surprisingly, there was a trend for more successful transfer completion when buprenorphine was given in first 24 hours when only mild withdrawal and better transfer when starting doses were less than 4mg.
 - ▶ Tapering people down to 30 is a dangerous time where bad things can happen and 30 sub therapeutic.

Different ways to use low doses during an induction.

- ▶ There are many regimens out there now-not widely validated yet, but the principles are all the same. Buprenorphine gradually takes over the Mu receptors and eventually saturates them with little or none of the original opioid being bound.
- ▶ Best to leave on the full dose of full mu agonist while going up on the Bup, and then stop on the last day.
- ▶ Low dose bup allows for recovery from tolerance. Stabilizes the mu receptors.

Bernese Method and methods that led to it

- ▶ Divide up Buprenorphine pills into eights or quarters and do slow titration. Like starting with .2 mg q 6 hours.
- ▶ An example of a regimen would be:
 - ▶ Day 1: $\frac{1}{4}$ of 2 mg pill (.5mg)
 - ▶ Day 2: $\frac{1}{4}$ of 2 mg pill (.5mg) bid
 - ▶ Day 3: $\frac{1}{2}$ of 2 mg pill (1mg) bid
 - ▶ Day 4: 1, 2 mg pill bid
 - ▶ Day 5: 2 of the 2 mg pill (4mg) bid
 - ▶ Day 6: 2 of the 2 mg pill (4 mg) tid
 - ▶ Day 7: 8 mg bid and stop the full agonist Or you might do this after day 6 at 12 mg and titrate up to 16 later as needed.
- ▶ Can pause for a day or 2 along the way if withdrawal symptoms occur and give body change to equilibrate.

Another very similar one I've used, although I would continue the full agonist through day 7

Buprenorphine Microdosing

- ☀ Day 1 = Bup 0.5mg DAILY, cont. methadone, oxycodone 30mg q6h
- ☀ Day 2 = Bup 0.5mg BID, cont. methadone, oxycodone 30mg q6h
- ☀ Day 3 = Bup 1mg BID, cont. methadone, oxycodone 30mg q6h
- ☀ Day 4 = Bup 2mg BID, cont. methadone, oxycodone 30mg q6h
- ☀ Day 5 = Bup 4mg BID, cont. methadone, oxycodone 30mg q6h
- ☀ Day 6 = Bup 8mg DAILY last day of FULL OPIOID AGONIST
- ☀ Day 7 = Bup 12 mg DAILY
- ☀ Day 8 = If needed, increase to buprenorphine 16 mg TDD

More tips

- ▶ You want people on a predictable dose of their full agonist before doing this. Like if they are having acute pain after surgery and dose of full agonist varies, not a good time.
- ▶ Don't forget about adjunctive meds for withdrawal if you need them, but hopefully won't, e.g. Clonidine, Ibuprofen, Loperamide, antiemetics.
- ▶ You can pause the induction and keep same doses going for more than one day.

Slightly different, same principle. 12 given on day 7.

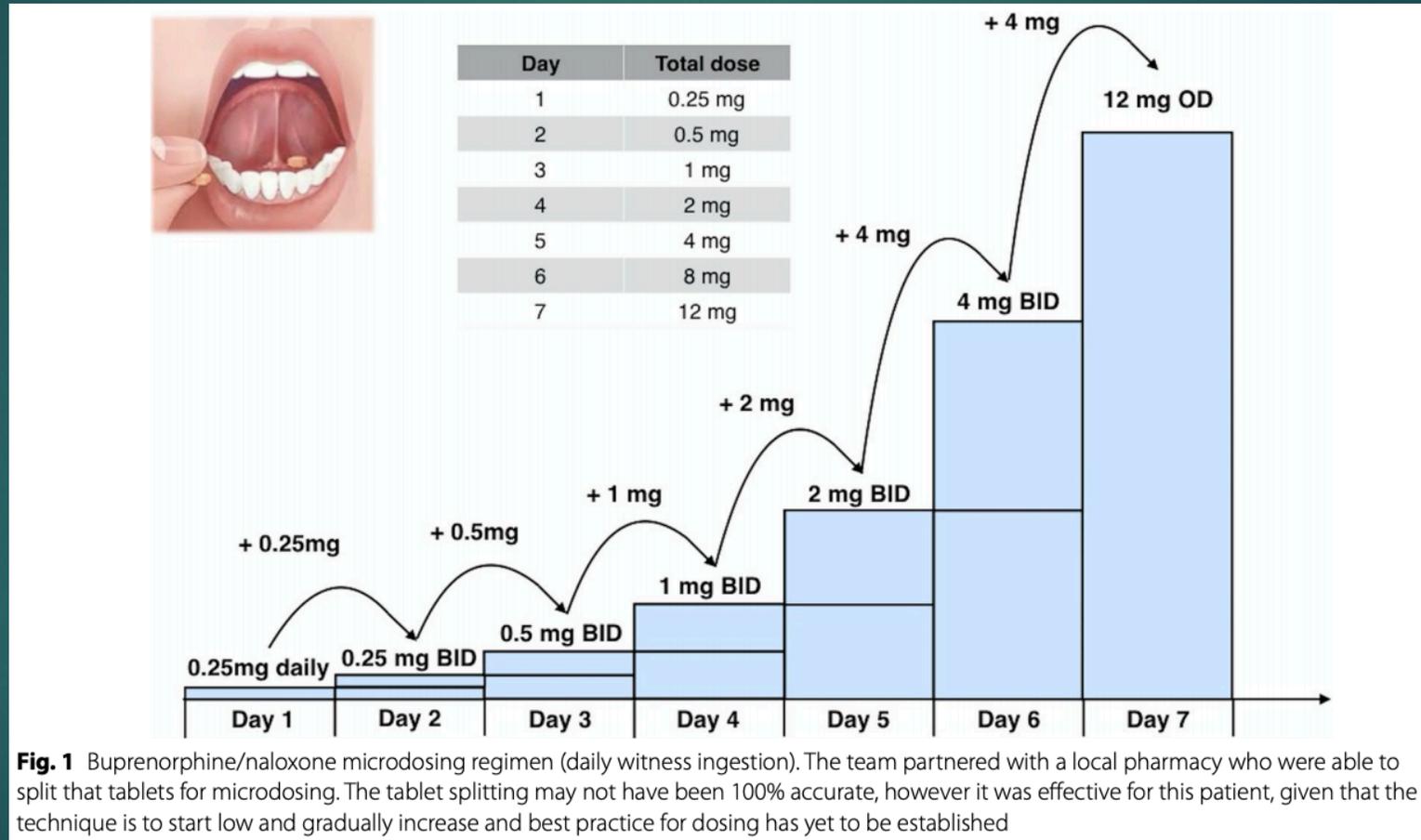


Fig. 1 Buprenorphine/naloxone microdosing regimen (daily witness ingestion). The team partnered with a local pharmacy who were able to split that tablets for microdosing. The tablet splitting may not have been 100% accurate, however it was effective for this patient, given that the technique is to start low and gradually increase and best practice for dosing has yet to be established

Or a more rapid induction which you might consider for hospitalized patient.

- ▶ 5 mg Bup q 3 hours on day 1
- ▶ 1 mg q 3 hours on day 2

2 mg prn.

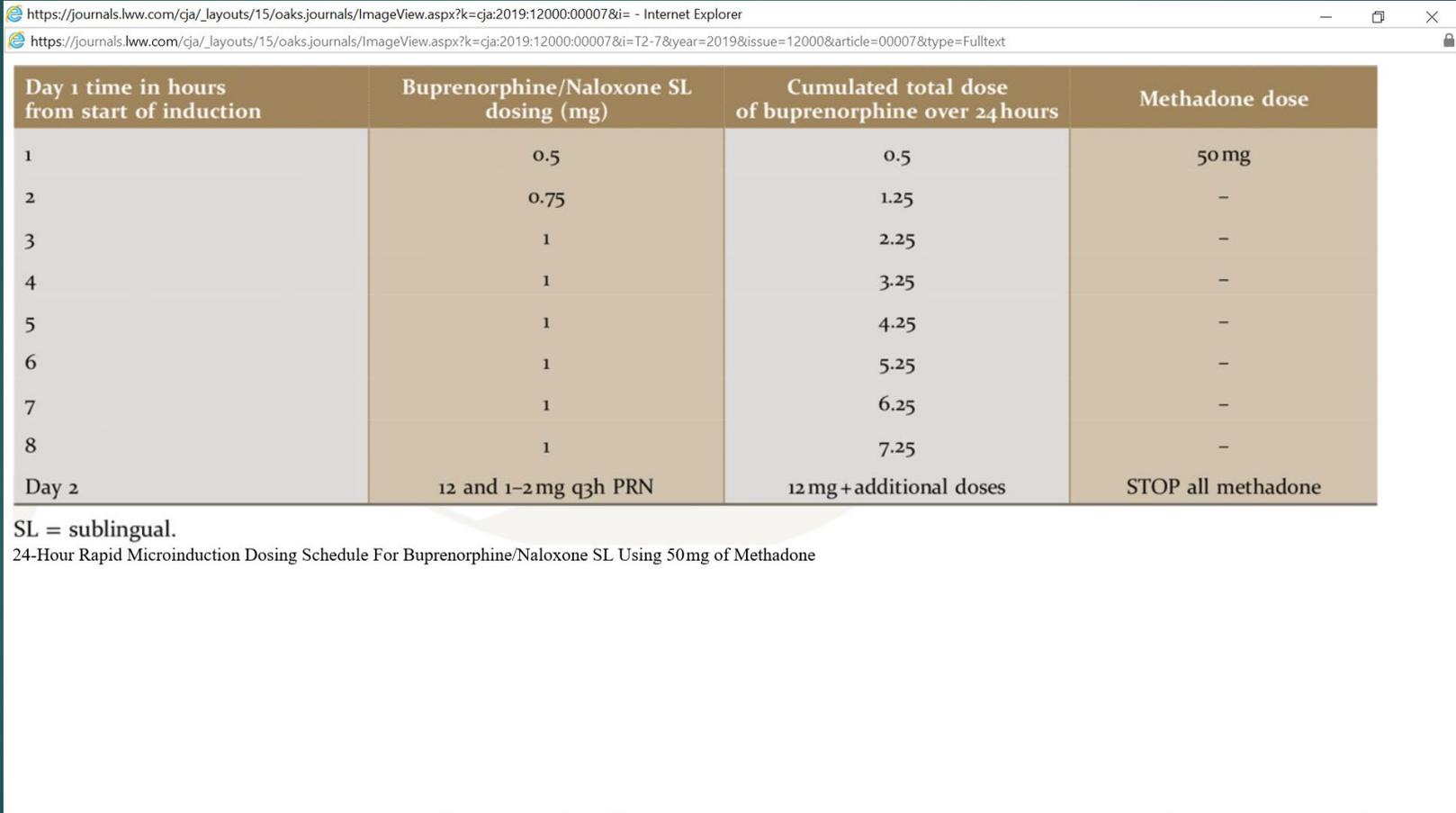
More rapid low dose transitions

- ◆ Takes advantage of rapid onset of action of sublingual, IV, or buccal buprenorphine
 - ◆ Frequent dosing – every 3-6 hours
- ◆ Only published experience in hospital
- ◆ No data for transitions from methadone

	Buprenorphine/Naloxone*		Hydromorphone	
	Dosing	Total Daily Dose	Dosing	Total Daily Dose
Day 0	N/A		3 mg PO q4h regular 2-4 mg PO q4h PRN	24 mg
Day 1	0.5 mg SL q3h	2.5 mg	3 mg PO q4h regular 2-4 mg PO q4h PRN	26 mg
Day 2	1 mg SL q3h	8 mg	3 mg PO q4h regular 2-4 mg PO q4h PRN	24 mg
Day 3	12 mg SL daily	12 mg	Discontinued	



Or over 24 hours (not totally sure about this)



The image shows a screenshot of a web browser window displaying a table from a journal article. The browser's address bar shows the URL: https://journals.lww.com/cja/_layouts/15/oaks.journals/ImageView.aspx?k=cja:2019:12000:00007&i=T2-7&year=2019&issue=12000&article=00007&type=Fulltext. The table is titled "24-Hour Rapid Microinduction Dosing Schedule For Buprenorphine/Naloxone SL Using 50mg of Methadone".

Day 1 time in hours from start of induction	Buprenorphine/Naloxone SL dosing (mg)	Cumulated total dose of buprenorphine over 24 hours	Methadone dose
1	0.5	0.5	50 mg
2	0.75	1.25	-
3	1	2.25	-
4	1	3.25	-
5	1	4.25	-
6	1	5.25	-
7	1	6.25	-
8	1	7.25	-
Day 2	12 and 1-2 mg q3h PRN	12 mg + additional doses	STOP all methadone

SL = sublingual.
24-Hour Rapid Microinduction Dosing Schedule For Buprenorphine/Naloxone SL Using 50mg of Methadone

But it can be difficult to break the pills-
this is where the transdermal patch or
buccal form can help.

- ▶ Peak plasma volume from patches occurs at 48 hours.
- ▶ Patch 20 mcg = 0.5mg SL daily
- ▶ Cost significantly limits this approach

Literature guide

Buprenorphine Formulation	Starting dose	Sublingual equivalent	Advantages	Disadvantages	Reference
Sublingual film	0.5mg	0.5mg	Simplest Allows frequent dosing	Hospitals may restrict splitting	Terasaki et al
Buccal film	225mcg	0.5mg	Rapid onset(~4hrs) Allows frequent dosing	Inpatient only (for OUD)	Weimer et al
Intravenous	0.15mg	0.5mg	Rapid onset Allows frequent dosing	Inpatient only	Thakrar et al
Transdermal patch	20mcg	0.5mg	Gradual onset	Expensive Inpatient only (for OUD)	Ghosh et al

Weimer, *J Addict Med*, 2021 Thakrar, *J Addict Med*, 2021 Ghosh, *CMAJ*, 2019
 Hickey, *Med Clin North Am*, 2022 Terasaki, *Pharmacotherapy*, 2019

#ASAMAnnual2022



Sample Transdermal regimen

- ▶ Day 1: Place 20 mcg bup transdermal patch
- ▶ Continue both long and short-acting opioids
- ▶ For short-acting, can start SL bup/nlx at 24 hours; for long-acting, wait 48 hours. But do you really need to wait?
- ▶ Begin SL dosing with 1 mg BID (1/2 tab).
- ▶ Day 2: 1 mg BID
- ▶ Day 3: 2 mg BID
- ▶ Day 4: 4 mg BID.
- ▶ Day 5: 6 mg BID
- ▶ Day 6: 8 mg BID Stop full Mu agonist.
- ▶ Stop patch a couple of days into it.
- ▶ I am assuming that you can do the same sort of regimen with the Buccal preparation (225 mcg) for day one or longer if need to.

Fastest protocol: Lembke & Raheemullah in JAMA March 2019

- ▶ Day 1, place 20 mcg bup patch for 24 hours
- ▶ Day 2, give 2 mg SL bup/nlx + 2-4 mg prn doses q 2-4 hours for maximum dose of 8 mg.
- ▶ Day 3, + 2-4 mg prn doses q 2-4 hours for max dose of 16 mg.
- ▶ Remove patch after 48 hours (after day 2). Discontinue full agonists by end of day 3.

Sample Buccal Regimen. Looks like this one would work especially well for someone who is also having pain because of the frequent dosing.

- ▶ 150 mcg every 6 hours on day 1
- ▶ 450 mcg every 6 hours on day two
- ▶ 1 mg orally every 6 hours on day 3
- ▶ 2 mg orally every 6 hours on day 4 then they stay with 8 mg
- ▶ Once the patient is on 8 mg you can try to take off the full mu agonist or leave it on temporarily if they need it for pain.

Another novel idea for getting low dose Bup

We will provide you with a clean 30 ml bottle.

Fill this bottle with clean water until it's full.

Dissolve one of your 8mg Suboxone films (*buprenorphine*) into the water in the bottle. Make sure the film is fully mixed in.

When you need to take a Suboxone (*buprenorphine*) microdose, use the dropper.

One full dropper will give you around 0.25mg of the Suboxone (*buprenorphine*).

Take this dose by placing the liquid from the dropper under your tongue. Let it sit and absorb instead of swallowing it.



1oz
Total Size: 4*1.32 inch



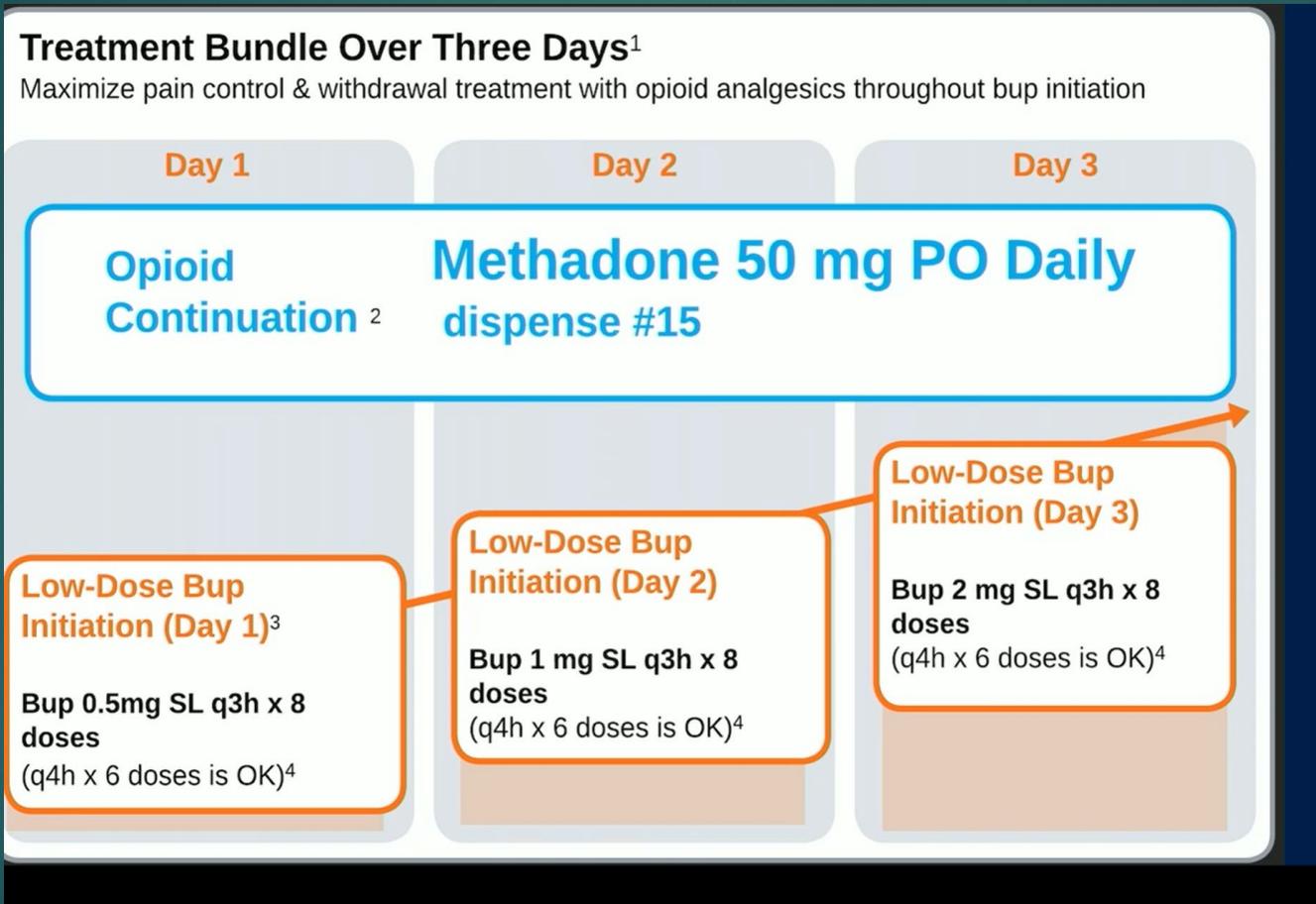
Fentanyl

- ▶ Very lipophilic and renally cleared. Can seep out of tissues for a while. Can have withdrawal even days after last took.
- ▶ How do you do low dose induction with someone using illicit Fentanyl on the street? It's controversial.
- ▶ Can convert to stable dose of Methadone and then do low dose induction, but we can't do that outside of an OTP (opioid treatment program, ie. methadone clinic).
- ▶ If they are having pain, might consider converting to other full mu agonist like MS Contin and then do low dose induction. But, can be risky and you have to have to have reliable patient and good communication with them and any family and friends. You don't want them mixing the MS Contin and fentanyl.
- ▶ What if can't do either. Then shared decision making, but I wouldn't document that you recommend that they continue to use illicit fentanyl. They are choosing to do that after discussing options, but go over safe use: safe needle use, Narcan, never use alone and give never use alone hotline number (see slide at end of presentation), test small batches. If going this way, they need to use same exact dose and form that they were getting before on the street.
- ▶ Consider quicker induction, like 3 days or less.
- ▶ More support the better. May need to admit to hospital.

3 day rule

- ▶ The way things had been: One day's medication may be administered to the person or for the person's use at one time. Such emergency treatment may be carried out for not more than **three days** and may not be renewed or extended.
- ▶ Now practitioners who wish to **dispense** the full three days-worth of medication to patients at one time can make a request to DEA to receive permission to do so. You have to actually email the DEA to obtain the approval. Requests for exception must be emailed to: ODLP@dea.gov under the subject line: "Request for Exception to Limitations on Dispensing for OUD."
- ▶ You can do a rapid low dose induction during this three days.
- ▶ If the patient is in the hospital, you can continue to give opioids for OUD as long as they are there.

Can try 30-60 of methadone a day



Tips to succeed

- ▶ Daily phone calls
- ▶ Dosing guides.
- ▶ Set up pill box
- ▶ Help from pharmacy including blister packs
- ▶ If patient on over 100 of methadone, go really slowly.
- ▶ Have good communication with OTP (Methadone clinic)

Conclusion, pros and cons.

- ▶ Can avoid significant withdrawal
- ▶ Can avoid significant pain
- ▶ Might be more acceptable to patients, especially ones who have failed typical inductions.
- ▶ Works better with patients on higher doses of methadone
- ▶ Better for synthetic opioids with unpredictable clearance, although high dose induction becoming more and more common (ER's).
- ▶ But regimens can seem complicated.
- ▶ Can take longer than typical induction.

Shared Decision making tool

Clinician instructions: use with patients who are eligible for low-dose induction based on length of hospitalization

Choosing How to Start Buprenorphine

We want to make it as comfortable as possible for you to start buprenorphine.

Buprenorphine (also known as Suboxone or Subutex) is a long-acting opioid and one of three medications used to treat opioid addiction. It reduces the use of other opioids and lowers the risk of overdose. We recommend it if you have cravings for opioids, if you are struggling to cut back on use, and if you have withdrawal when you stop opioids.

1. What is the issue? If you start the standard dose of buprenorphine while you have other opioids like heroin, fentanyl, or oxycodone in your system, it can put you into immediate withdrawal or make withdrawal worse. We call this "precipitated withdrawal."

2. Why does this matter? You may need opioids for pain OR you may have recently taken another opioid, like fentanyl or methadone, that lasts more than a few hours. It can be hard to stop opioids for many hours or days, especially in the hospital.

3. Have you started buprenorphine before? What did you do that time?

4. What did you like about it and what did you not like about it?

5. What is most important to you? You can check off more than one.

- Continuing my opioid medications (either methadone or opioids for pain)
- Managing pain
- A fast transition to buprenorphine
- Avoiding withdrawal
- Using an approach with the most evidence
- Starting buprenorphine the way I've done it before
- Trying something new
- Other: _____



6. Here are two options to start your buprenorphine:

	<i>What it means:</i>	<i>Reasons to choose:</i>	<i>Reasons NOT to choose:</i>
Standard start	<ul style="list-style-type: none"> • We stop all opioids and wait 8-72 hours for the opioids to wash out of your body before starting buprenorphine • We keep you comfortable with non-opioid medications 	<ul style="list-style-type: none"> • More evidence • Sometimes faster 	<ul style="list-style-type: none"> • Need to stop opioids and wait for withdrawal • Could worsen withdrawal
Low-dose, overlapping start	<ul style="list-style-type: none"> • We continue methadone or opioids for pain • At the same time, we start buprenorphine at a low dose and slowly increase the dose over a few days • Once buprenorphine is built up in your body, we stop other opioids • In our experience, this will not cause withdrawal 	<ul style="list-style-type: none"> • Designed to minimize withdrawal • You continue methadone or opioids for pain at the same time 	<ul style="list-style-type: none"> • Less evidence • Might cause withdrawal, especially if we don't follow the process • Sometimes slower and might mean you stay in the hospital for longer

No matter what you choose, we will monitor you and we can change course if needed.

7. What did we decide today?

- Standard start
- Low dose start
- Continue to discuss and decide later

8. What are the next steps?



Credit to Ashish Thakrar MD for creation, presented at AMERSA 2021

#ASAMAnnual2022

This is still active but has had funding removed by the Trump

English

Never Use Alone

Meeting people where they are, on the other end of the line, one human connection at a time.

[Volunteer](#) [Contact Us](#) [About](#)

NO JUDGEMENT, NO SHAMING, NO PREACHING, JUST LOVE!

(800) 484-3731

If you are going to use by yourself, call us! You will be asked for your first name, location, and the number you are calling from. An operator will stay on the line with you while you use. If you stop responding after using, the operator will notify emergency services of an "unresponsive person" at your location.



[FACEBOOK](#)

[CONTACT US](#)

Moving everything to the website



Privacy - Terms

Why Use it?

- ▶ Compared to SL Bup
 - ▶ Better Adherence
 - ▶ Better retention in care
 - ▶ Better Opioid Abstinence
 - ▶ More consistent Bup levels
 - ▶ Generally higher Bup levels
- ▶ Helps with patient autonomy (more choices)
- ▶ Can be used to taper patients off of Bup
- ▶ Can also help with pain
- ▶ Prevents diversion
- ▶ No Lost meds
- ▶ Harm reduction benefits in the setting of continued use and inconsistent use of SL Bup.
- ▶ If lack place to keep meds (homeless)
- ▶ Dental issues from SL Bup ?
- ▶ Protection from opioid overdose

Contraindications and cautions

- ▶ Don't use if hypersensitive to med or components
- ▶ Liver disease (seems like a bit of a moving target)? Initial and monthly LFT's (drug company recs)?
- ▶ Upcoming major surgery?
- ▶ Caution patient about driving or using heavy machinery until know that sedation not an issue.
- ▶ Can be involved in serotonin syndrome
- ▶ Be aware of concomittant CYP3A4 inhibitors or inducers for over or underdosing.

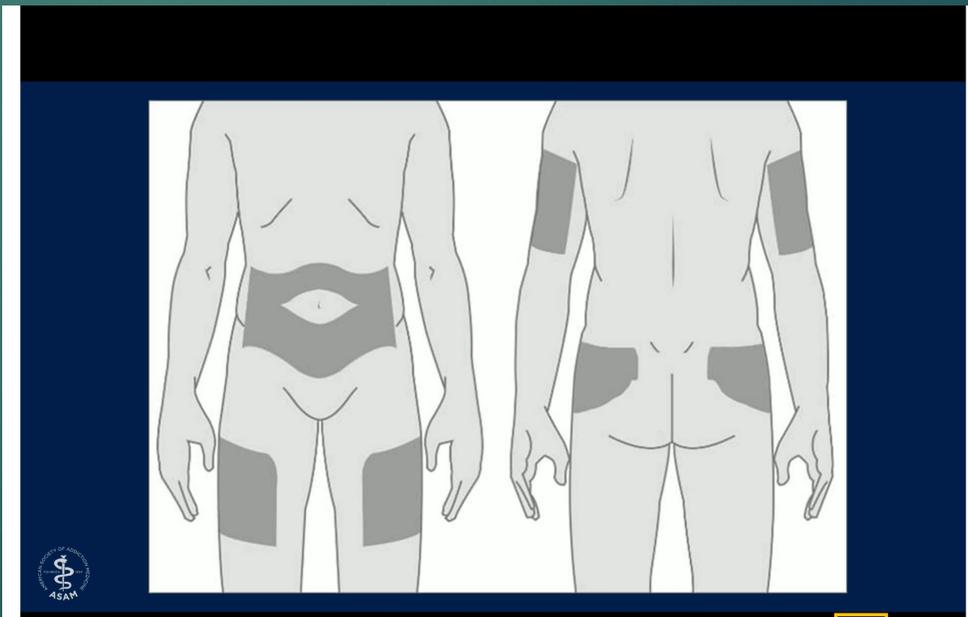
Sublocade and Brixadi, Medicaid pays for both.

Which LAIB to choose?

Feature	Sublocade	Brixadi
Available Doses	100 mg 300 mg	Weekly: 8 mg, 16 mg, 24 mg, 32 mg Monthly: 64 mg, 96 mg, 128 mg
Administration	45-degree angle multiple sites** 19-gauge needle, 0.5-1.5 mL	90-degree angle multiple sites** 23-gauge needle, 0.16-0.64 mL

How to give

- ▶ They both form Polymers which release the medication over time. There are little balls of medication which form with Sublocade which slowly release the medication over time.
- ▶ These can actually be surgically remove if needed within 14 days of placement. Polymers formed by Brixadi are more difficult to feel.



Minimizing pain

- ▶ Triceps may be less painful and “balls are less visible with Sublocade.
- ▶ The warmer the medication is, the less painful the injections are.
 - ▶ Sublocade can be out of refrigeration for 12 weeks, but if it is in frig, take out and wait 15 minutes to get to room temp. Brixadi does not need to be refrigerated. Can place under arm to warm further.
- ▶ Can Ice the skin for 30-60 minutes before injection.
- ▶ Can have patient use transdermal lidocaine at home before coming in
- ▶ Can use freezing spray on skin
- ▶ Can inject 1 cc of Lidocaine first
- ▶ Both Sublocade and Brixadi can cause pain, but Brixadi generally less because of lower volume, smaller needle, and lower viscosity.

Tips on giving the injection

- ▶ There is going to be air in the syringe. Push it out. Make sure no particulates in injection.
- ▶ Clean skin. Tent it so you go into SQ tissue. Go in 45 degrees with Sublocade and 90 degrees with Brixadi.
- ▶ Document where you injected it. Want to rotate each time.
- ▶ Skin infection and necrosis can happen if go too shallow and don't get into the SQ tissue. Don't want to be subdermal or IM.
- ▶ Getting into a vessel is uncommon but dangerous or lethal because little ball is forming. Always aspirate before injecting. This is why patients can never have this med in their possession, because of the risk of self injection and going into vessel.

Injection tips continued

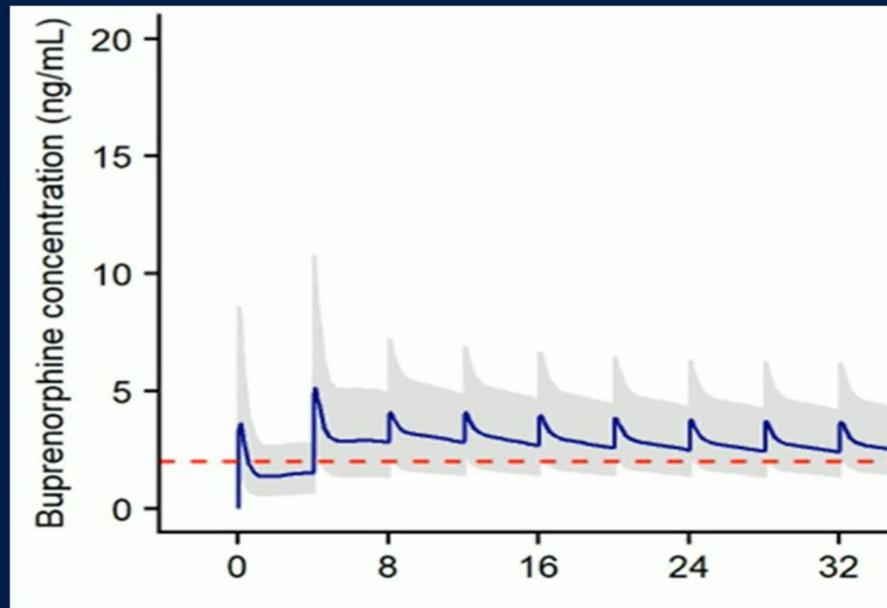
- ▶ Medication leaks out of injection hole. Cover up and place bandaid.
- ▶ Can place ice pack over site.
- ▶ Don't push on the site and tell patient not to mess with it because pressure can flatten out ball and make the medication diffuse faster than wanted. Also don't want belt or tight pants pressing on it.

Let's talk blood levels of medication

- ▶ Two numbers to know:
 - ▶ 2 nanograms/ml: getting above this levels greatly reduces the risk of opioid overdose (unless other drugs like Xylazine are also being used). But I have also heard for very high doses of drugs like fentanyl, may need 5 nanoframs.
 - ▶ 5 nanograms/ml: above this will generally eliminate the “drug liking “ (self-reported measure of pleasurable or hedonic experience-getting high-) which reinforces use and cravings.

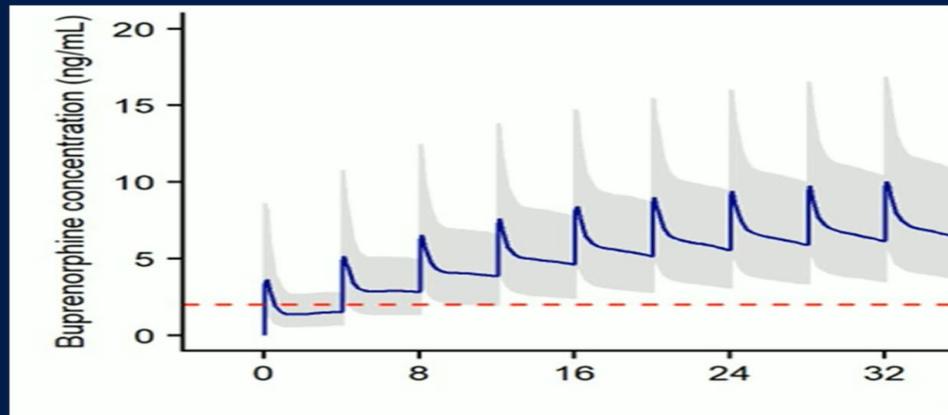
Levels Continued. Levels go up above 2 after the first shot but then quickly come down below 2, so not protected.

Sublocade 300/300/100...



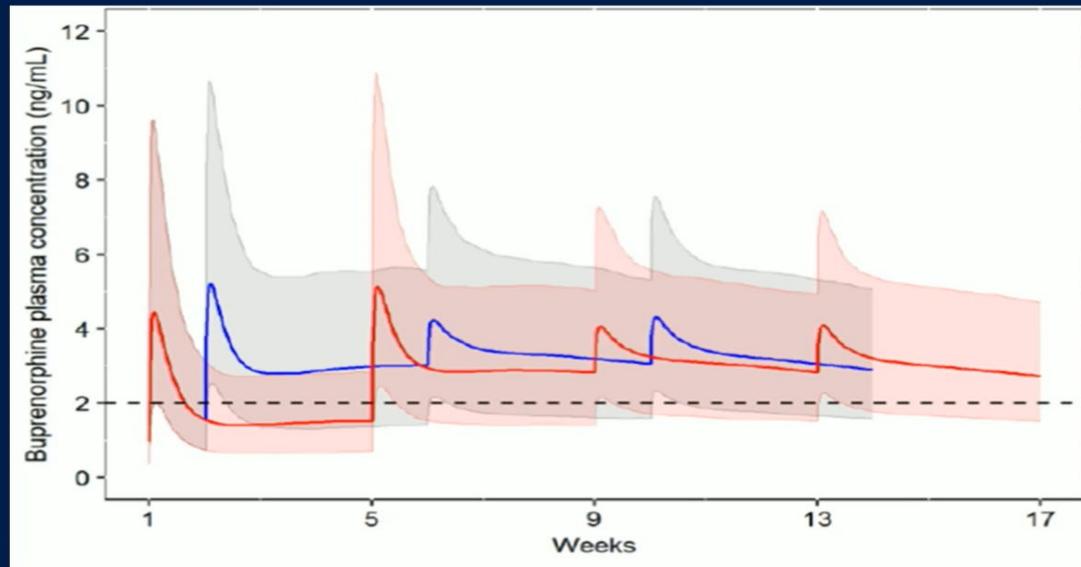
Levels Continued: Also Notice how the 300's every month gets you near or above 5 and gets rid of drug liking, unlike the subsequent 100 mg dosing.

Sublocade 300/300...



Levels continued. So, new regimen is to give second shot one week after first one. Medicaid will pay for this.

New Sublocade Prescribing Info



Brixadi

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_{2th} after 7th daily dose for Subutex

Sublocade

Pharmacokinetic parameters	Transmucosal Buprenorphine				SUBLOCADE	
	8 mg	12 mg	16 mg	24 mg	100 mg	300 mg
$C_{avg,ss}$ (ng/mL)	1.37 (40)	1.79 (40)	2.16 (40)	2.84 (40)	2.87 (32)	6.32 (32)
$C_{max,ss}$ (ng/mL)	4.27 (45)	5.60 (45)	6.77 (45)	8.86 (45)	5.10 (33)	11.81 (35)
$C_{trough,ss}$ (ng/mL)	0.66 (63)	0.87 (63)	1.04 (61)	1.37 (62)	2.46 (40)	5.47 (39)

Important things to notice about levels

- ▶ Notice the trough on the SL Bup. All doses below 2.
- ▶ With Brixadi, all trough around 2 and lowest dose below.
- ▶ With Sublocade at 300, all levels above 5.
- ▶ With SL Bup, 8 and 12 average level below 2.

So how much do you give. Also depends a lot on craving and how much bup they were using before

- ▶ Sublocade drug rep would say leave everyone on 300 a month.
- ▶ UTD says for long term bup users (months to years) if taking over 20 mg bup a day, go with 300, 300, then 100 each month. If 8-18, go with 300 times one month then 100 each month. If short term use of Bup (seven days but usually not weeks) 300, 300, then 100 each month.
- ▶ For synthetic opioid users like Fentanyl, 300 every month typically needed. If having withdrawal on the 100 mg dose or continued opioid use or craving, can go with 300 a month.
- ▶ You can also go with doses between the 300 and 100. can squirt out in sink. Document well. 300 and 100 doses cost the same.
- ▶ Except for first two doses, minimal interval between doses, 26 days.

Brixadi

Daily dose of sublingual buprenorphine	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 (weekly)	BRIXADI (monthly)
16 mg	64 mg
24 mg	96 mg
32 mg	128 mg

Supplemental SL Buprenorphine

- ▶ This is common
- ▶ May need early on to get them over the 2 nanogram level, especially if not giving the second Sublocade shot in a week.
- ▶ May need it with the low troughs that we see with certain doses and preparations. And may need when getting started and withdrawing from other opioids
- ▶ Can think of it like nicotine replacement therapy. Have long acting and then supplement for cravings, comfort and other reasons.

What conditions do we need before giving Long acting injectable Bup.

- ▶ It used to be that patients needed to be on at least 8 mg of SL Bup for 7 days.
- ▶ Now FDA is saying that for Sublocade, you give them a 4 mg test dose and if no withdrawal in one hour, proceed with 300 mg SQ. For Brixadi, give 4 mg test dose and if no precipitated withdrawal, give 16 mg of the weekly Brixadi and give additional 8 mg dose in the first 3 days to get to 24. if needed, can give an additional 8 mg in the first week to get to 32, but need to wait 24 hours after the last dose. Base subsequent weekly doses on how much was given in first week, and can make adjustments.

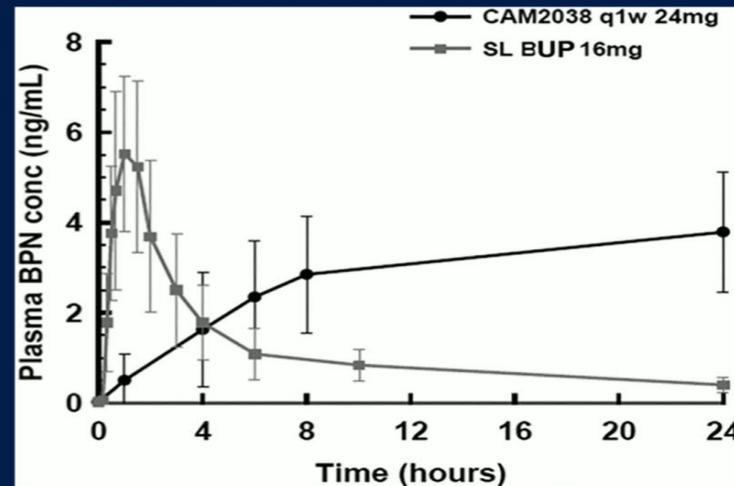
Some problems with this

- ▶ 4 mg is a bit of an odd dose. If using a lot of fentanyl, may not feel comfortable doing this until maybe 36 hours.
- ▶ Peak plasma concentrations can occur within the first hour
- ▶ Hard to watch people for an hour
- ▶ May be higher risk of withdrawal than injecton.

New option using Brixadi

Pharmacokinetics of 7-day Brixadi

- ◆ Reach 1 ng/mL hour 2
- ◆ Peak plasma concentration at 20 hours
- ◆ Closer to what we estimate with a “micro-dose” induction



D'Onofrio 2023



ED Study

Direct to Inject – From ED

JAMA
Network | **Open**...

Original Investigation | Substance Use and Addiction

Extended-Release 7-Day Injectable Buprenorphine for Patients With Minimal to Mild Opioid Withdrawal

Gail D'Onofrio, MD; Andrew A. Herring, MD; Jeanmarie Perrone, MD; Kathryn Hawk, MD; Elizabeth A. Samuels, MD; Ethan Cowan, MD; Erik Anderson, MD; Ryan McCormack, MD; Kristen Huntley, PhD; Patricia Owens, MS; Shara Martel, MPH; Mark Schactman, MHS; Michele R. Lofwall, MD; Sharon L. Walsh, PhD; James Dziura, PhD; David A. Fiellin, MD

- ◆ ED based initiation of Brixadi 24mg without subL
- ◆ High rates of precipitated withdrawal in smaller trial of 100 patients with COWS <8 (COWS 0-3 13.5%, 4-7 3.2%)
- ◆ COWS >8 unpublished, but prelim data is much lower rates of precipitated withdrawal



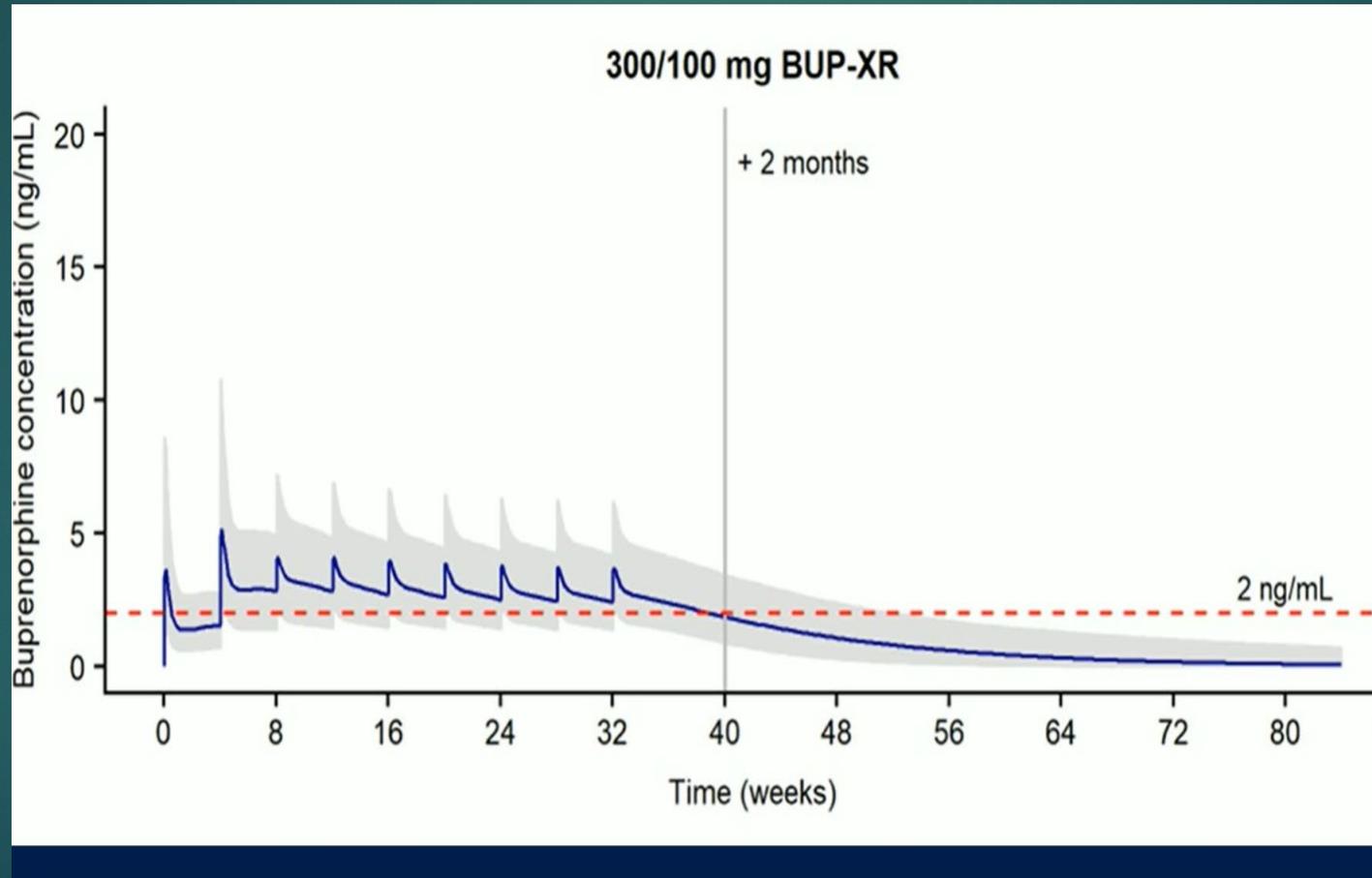
Outpatient study (not ER)-Direct to inject

- ▶ Small study (21 patients)
- ▶ Recorded COWS and used different doses
- ▶ Low COWS on injection, most received 24 mg Brixadi
- ▶ 27 % of patients said process was fine, 59% said unwell but OK, 14 % said really rough.
- ▶ Return to care and retention was really high

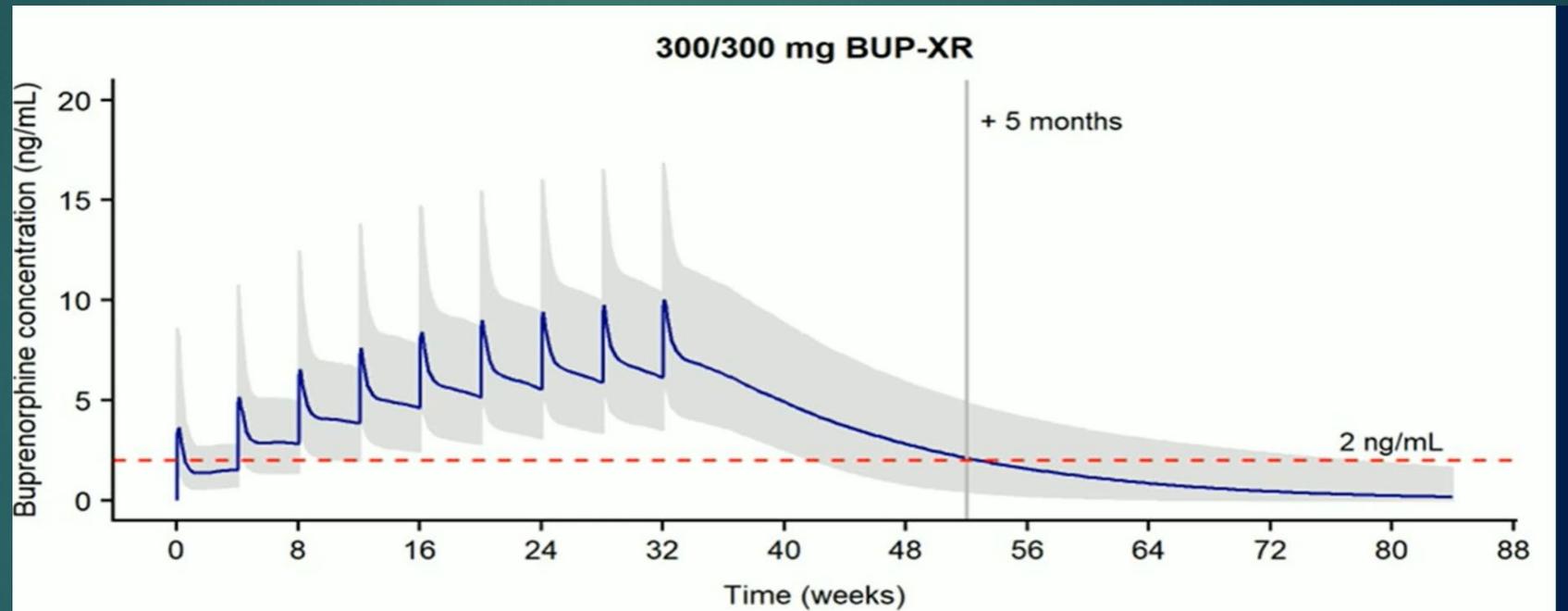
So what do you do for direct to inject?

- ▶ You could give the 4 mg oral test dose as per the FDA recs. Probably what I would do for now.
- ▶ If they have a COWS greater than 8 and at least one objective sign of withdrawal, fairly safe to give Brixadi, especially the 7 day preparation.
- ▶ Can give them low dose induction up to the 4 mg, which can be done over a couple of days.
- ▶ In patients with low COWS and recent use, and highly motivated and willing to risk (about 10%) mild to moderate withdrawal, go ahead and use the Brixadi
- ▶ Use comfort meds (e.g. alpha 2 agonists which can help especially if they have other substances on board like Xylozine)

Using Long Acting Injectable Buprenorphine to taper patients off.



Levels after 300 mg doses



What about treating pain

- ▶ Not much in the literature, but hearing from experience, can be a great option.
- ▶ Get higher levels
- ▶ Can supplement with SL preparation

Logistical concern with administering and storing long-acting injectable Bup

- ▶ Has to be double locked (locked cabinet in locked room}
- ▶ Pharmacies who carry Injectable Bup need to be REM(Risk evaluation and mitigation strategy) certified. Helps prevent direct dispensing to patients. Clinics don't need to unless they are buying it and billing patients.
- ▶ Sublocade can be out of frig for 12 weeks. For Bixadi, no refrigeration required.
- ▶ DEA rules say a provider can only administer long acting injectable Buprenorphine at the site matching the address on their DEA license.

Getting it paid for. In support is for sublocade. Braeburn also has a program for Brixadi. Idaho Medicaid covers both

How will she pay for it?



Medicaid Coverage



“Buy and Bill” approach

Copayment Assistance Programs



inSupport
Copay Assistance



Ross, Addiction, 2024