

How to Implement Low Dose Buprenorphine Initiation in Your Practice: A Case-Based Workshop

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ASAM 2022 April 1, 2022



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Disclosure Information

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◆ No disclosures



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Melissa Weimer DO MCR FASAM

- ◆ Path CCM, Inc, Monetary Compensation, Medical Advisory
- ◆ CVS Health, Monetary Compensation, Medical Advisory



Learning Objectives

- ◆ Describe low-dose buprenorphine initiation and clinical indications for its use
- ◆ Summarize how to engage in shared decision-making with patients about the risks and benefits of low-dose buprenorphine initiation
- ◆ Understand how to initiate low-dose buprenorphine in different clinical situations in both the inpatient and outpatient setting

Resources/Pre-reading



JAM Narrative Review and Practical Guide



1 Page Outpatient Guide



Shared Decision Making tool

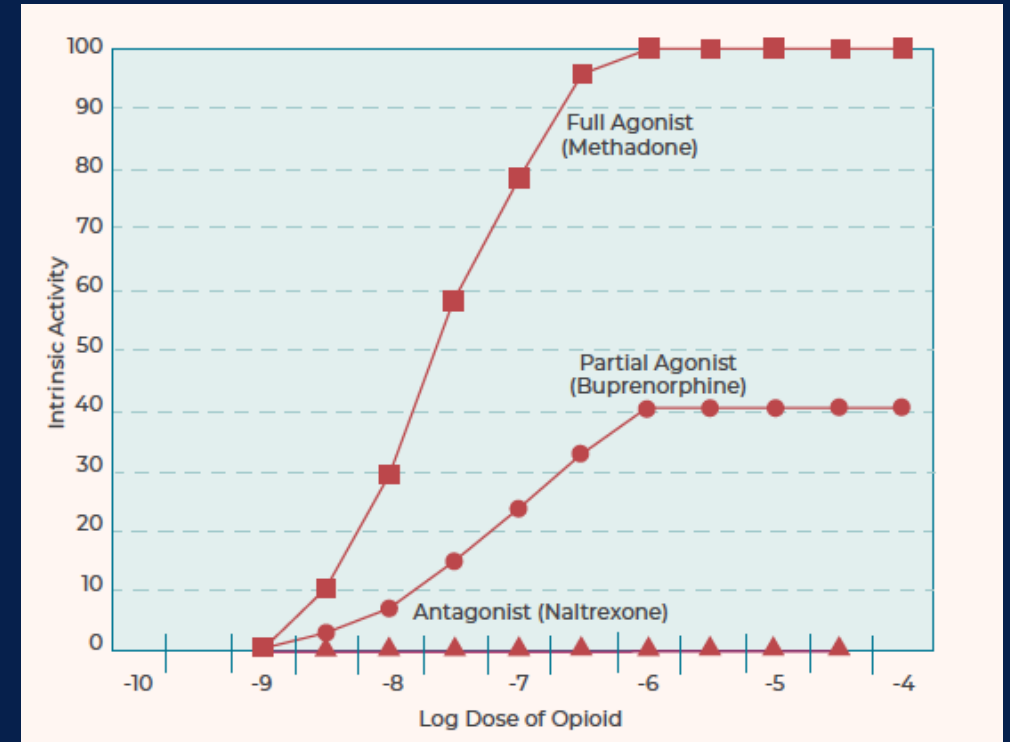
A minute on terminology: “LOW-DOSE” vs “MICRO-DOSE”

- ◆ Accuracy & connotation of terms are important, especially as we grow as a field
- ◆ In pharmacology and translational science, “micro-dose” refers to non-medical use
 - ◆ Connotation with LSD use
- ◆ We prefer “Low dose,” “ultra low dose,” or “Bernese method”
- ◆ If you can’t shake “micro,” we recommend “micro-induction”

Buprenorphine: KEY characteristics



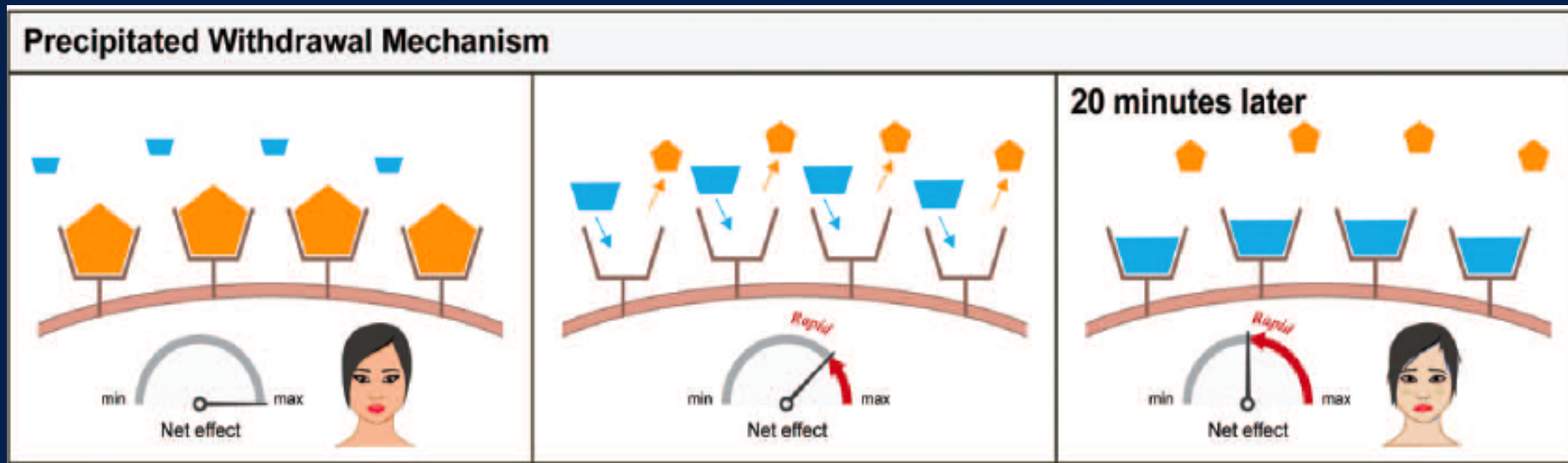
High Affinity





Partial Agonist

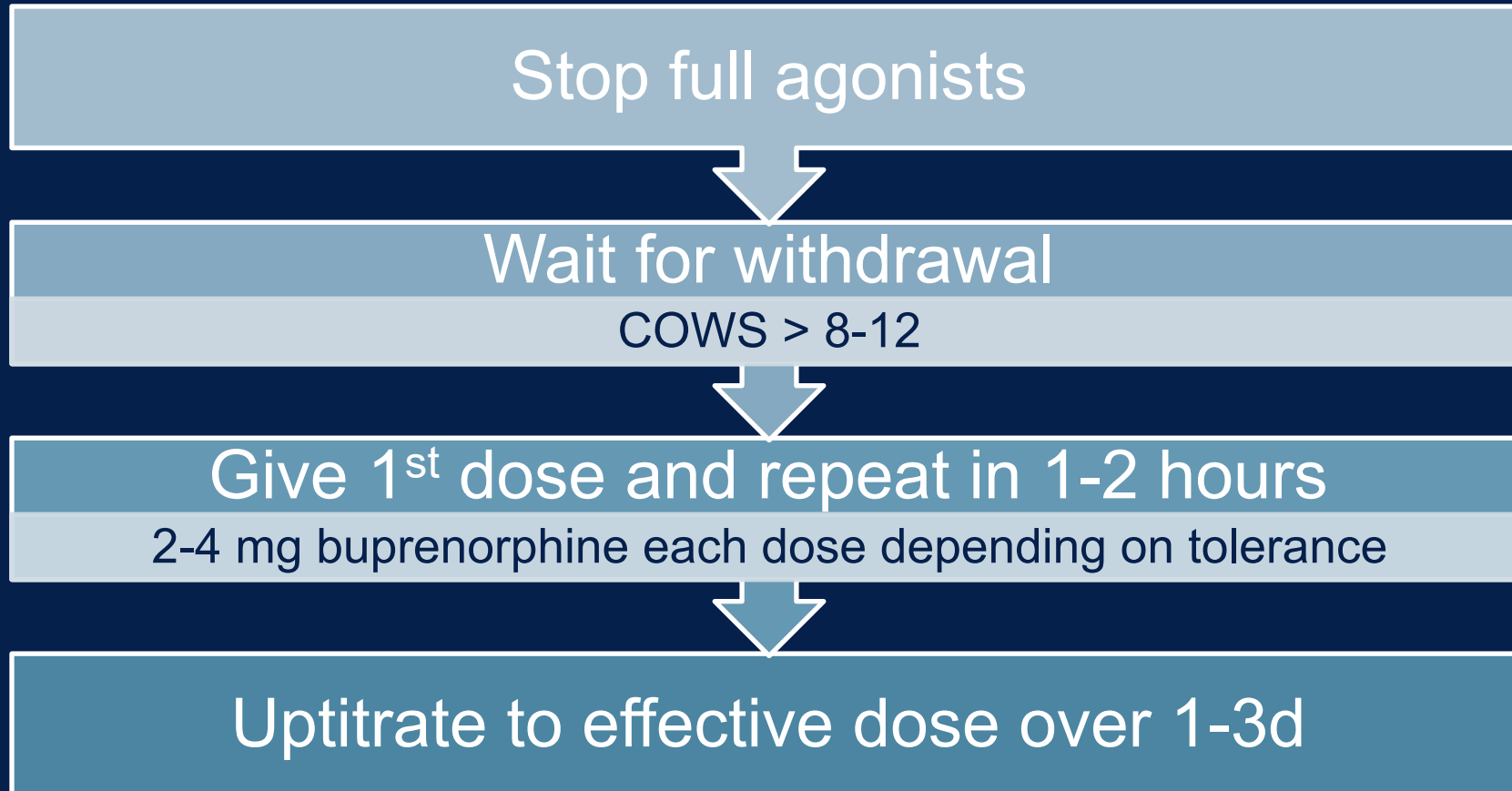
Precipitated opioid withdrawal

- ◆ Partial opioid agonists can cause opioid withdrawal symptoms when introduced to full opioid agonists



 Full agonist opioid
 Buprenorphine

“Classic” Buprenorphine Initiation

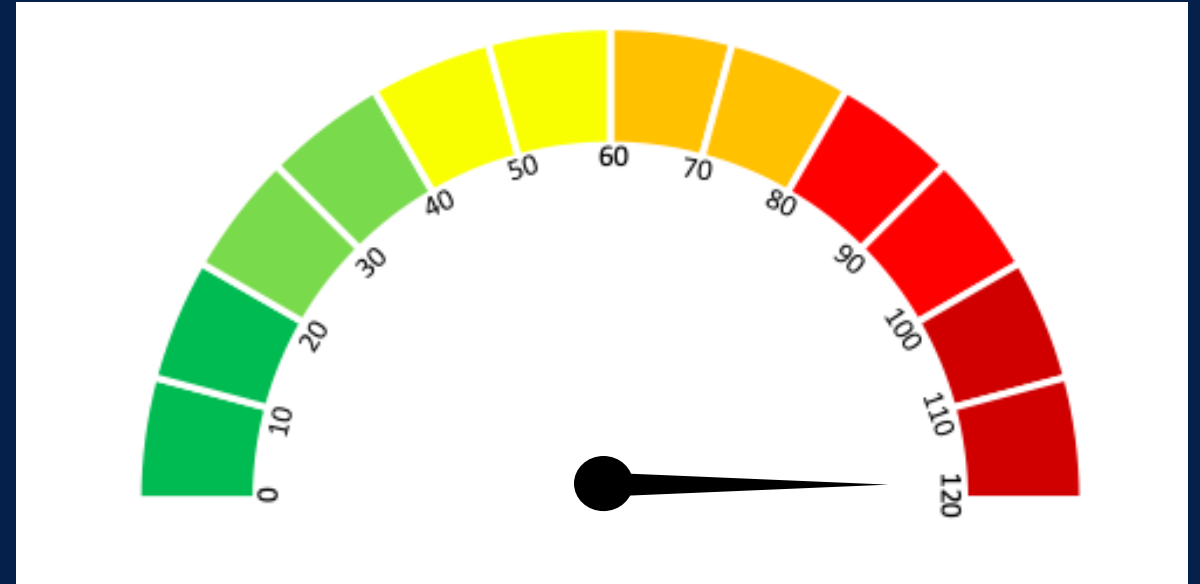
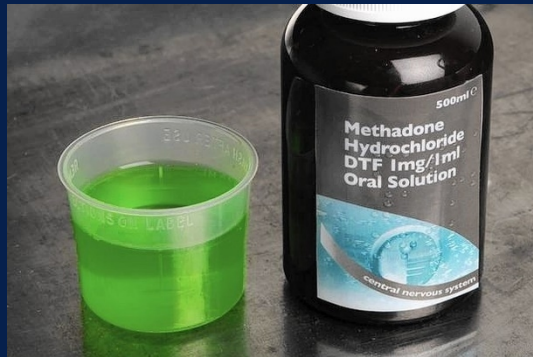


Difficult situations

- ◆ Transitioning from Methadone to Buprenorphine
- ◆ Patients with severe acute pain and OUD
- ◆ Non Rx fentanyl use
- ◆ Previous unsuccessful attempts at buprenorphine initiation



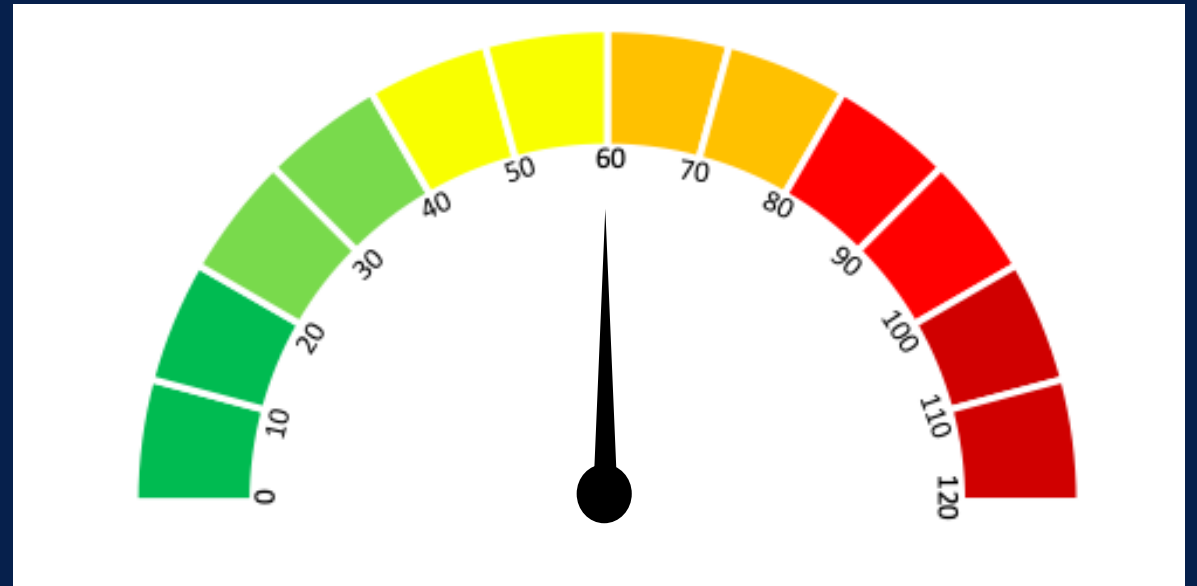
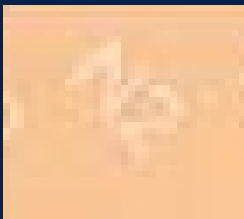
FULL opioid agonist effects



Precipitated Withdrawal

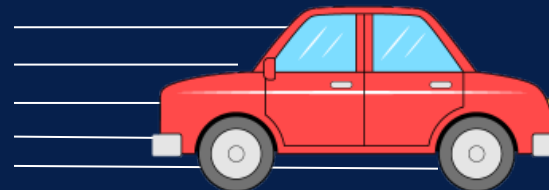
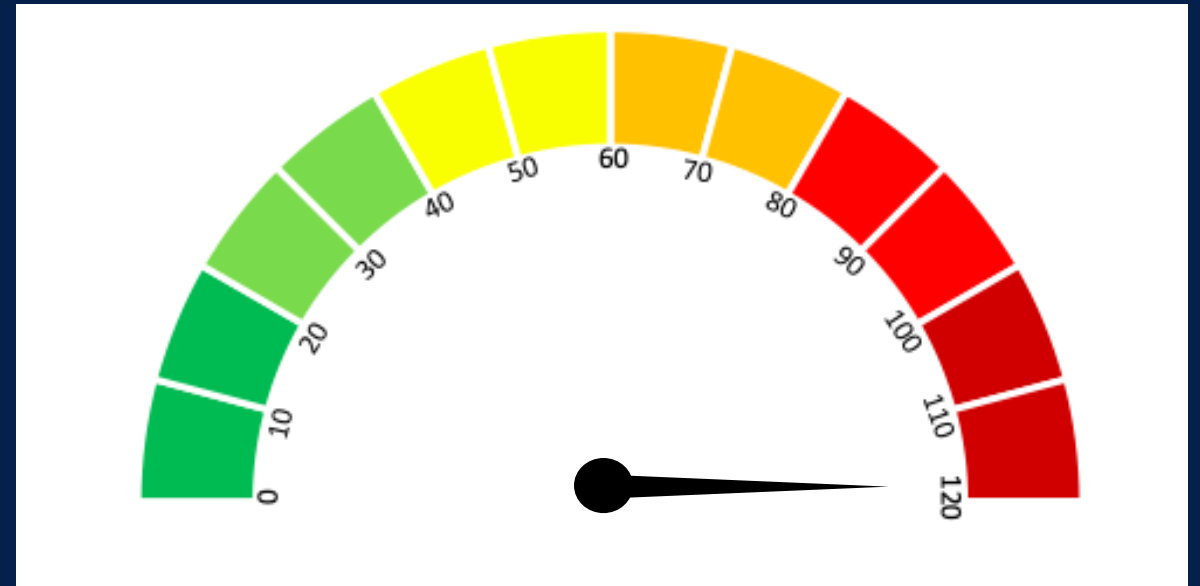


Buprenorphine 4mg



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FULL opioid agonist effects

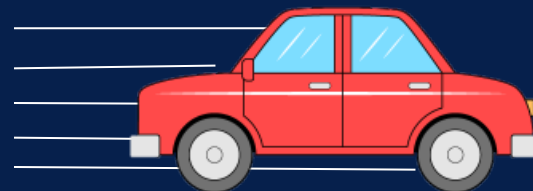
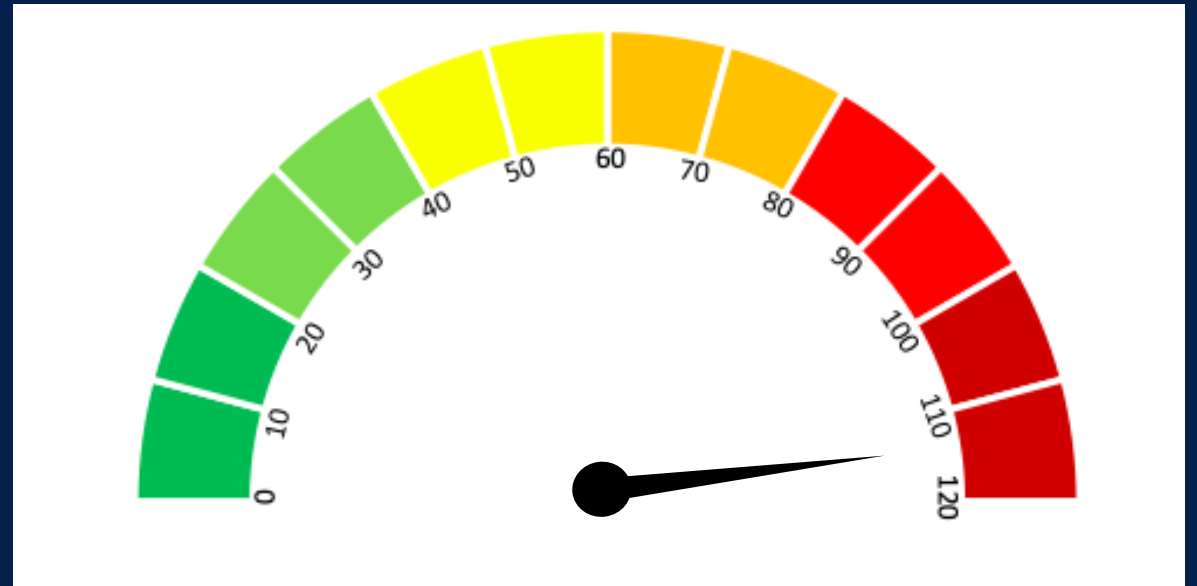


Low dose buprenorphine initiation - day 1



+

Buprenorphine 0.5mg



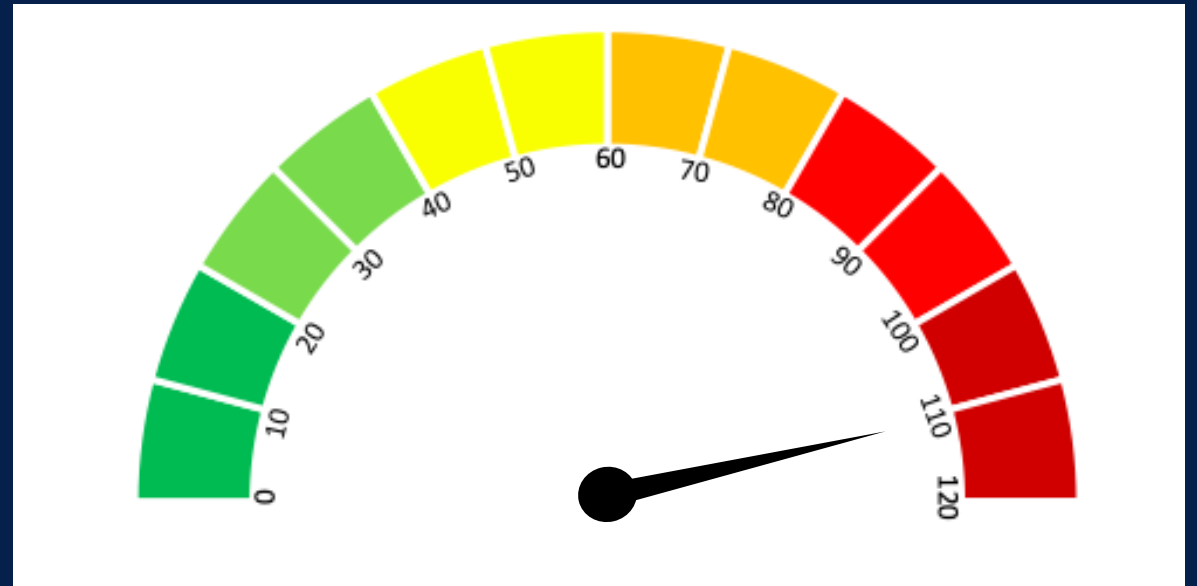
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Low dose initiation - day 2



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Buprenorphine 0.5mg BID



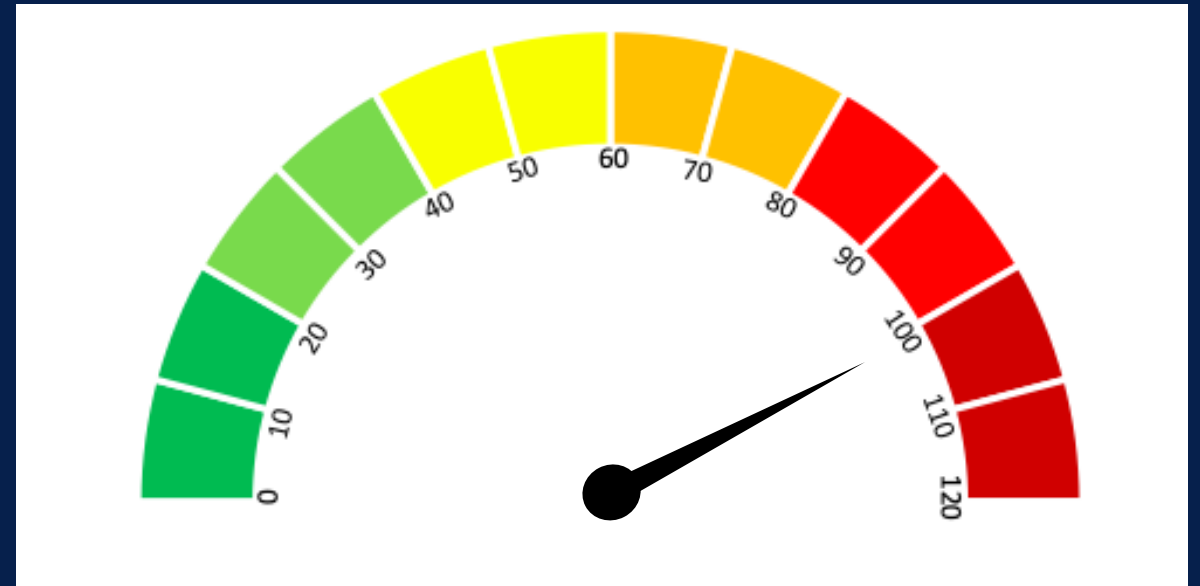
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Low dose initiation - day 3



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Buprenorphine 1mg BID



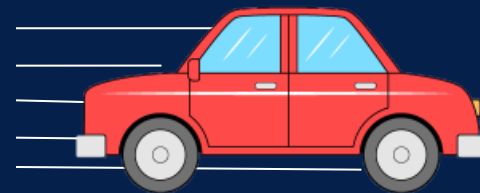
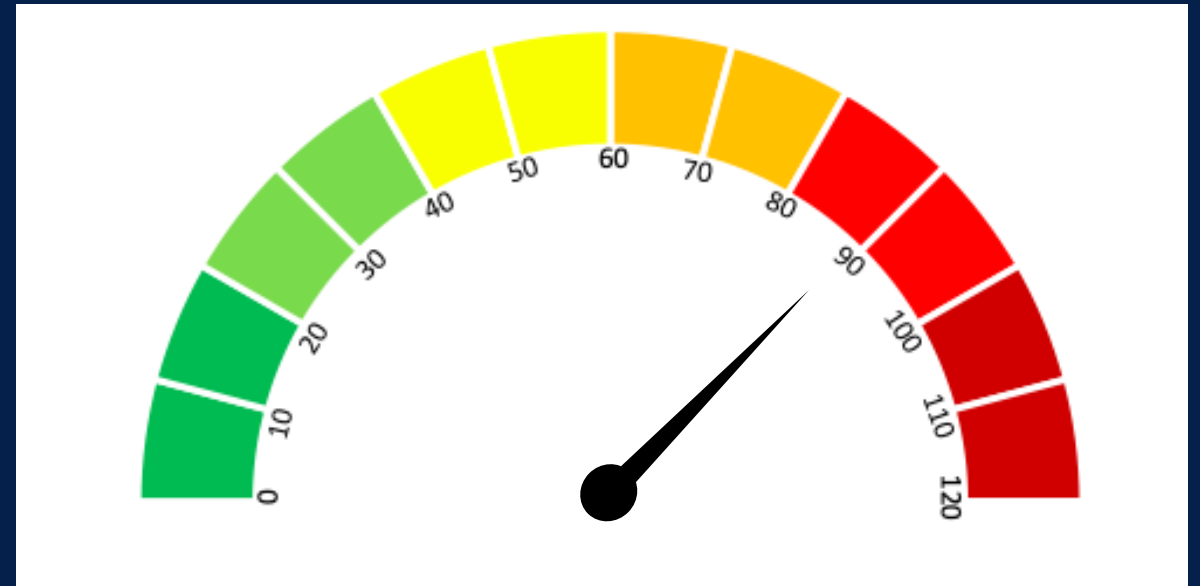
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Low dose initiation - day 4



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Buprenorphine 2mg BID



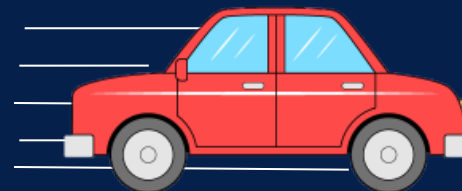
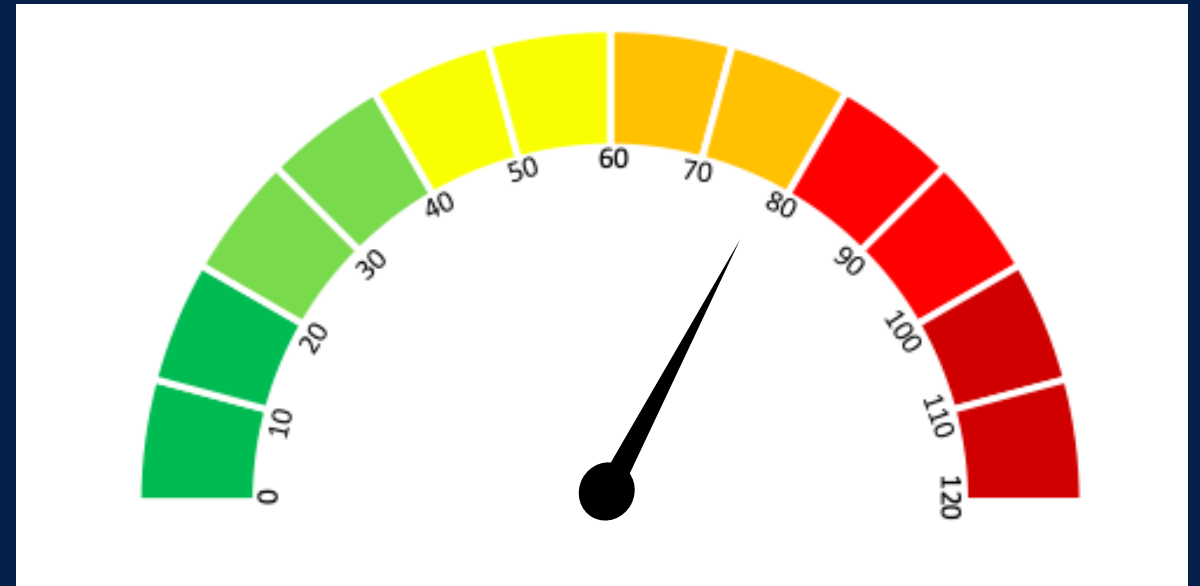
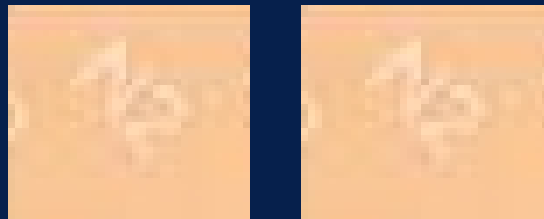
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Low dose initiation - day 5



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Buprenorphine 4mg BID



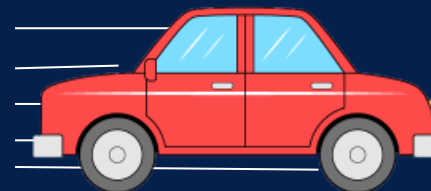
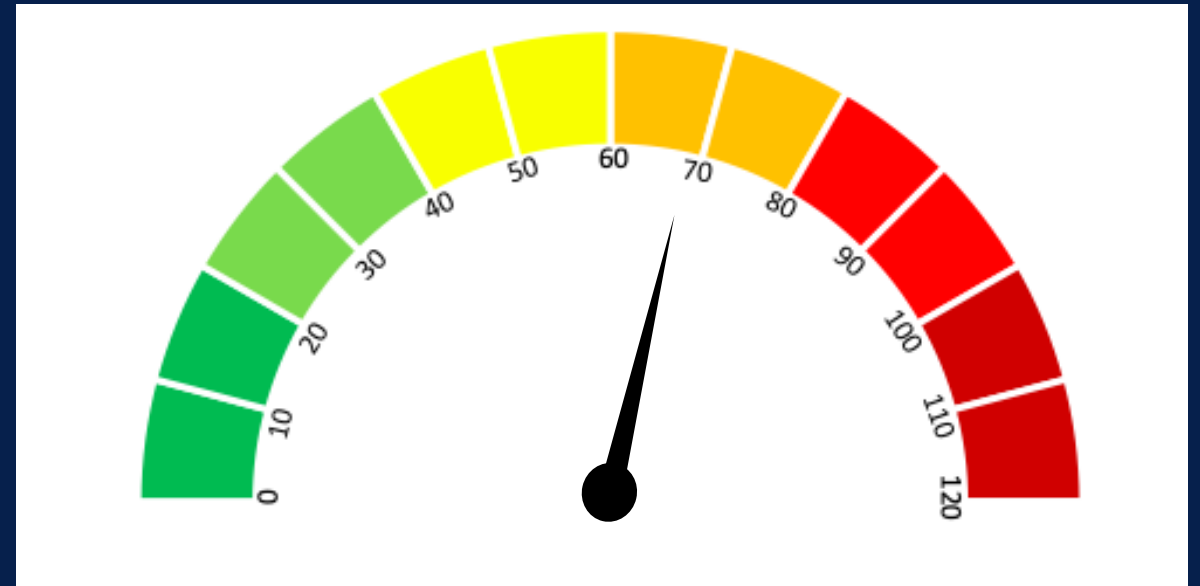
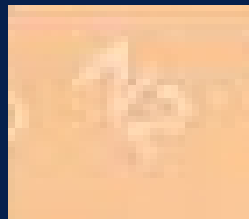
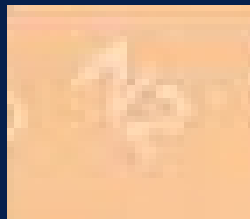
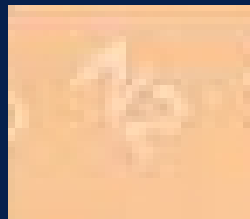
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Low dose initiation - day 6



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Buprenorphine 4mg TID



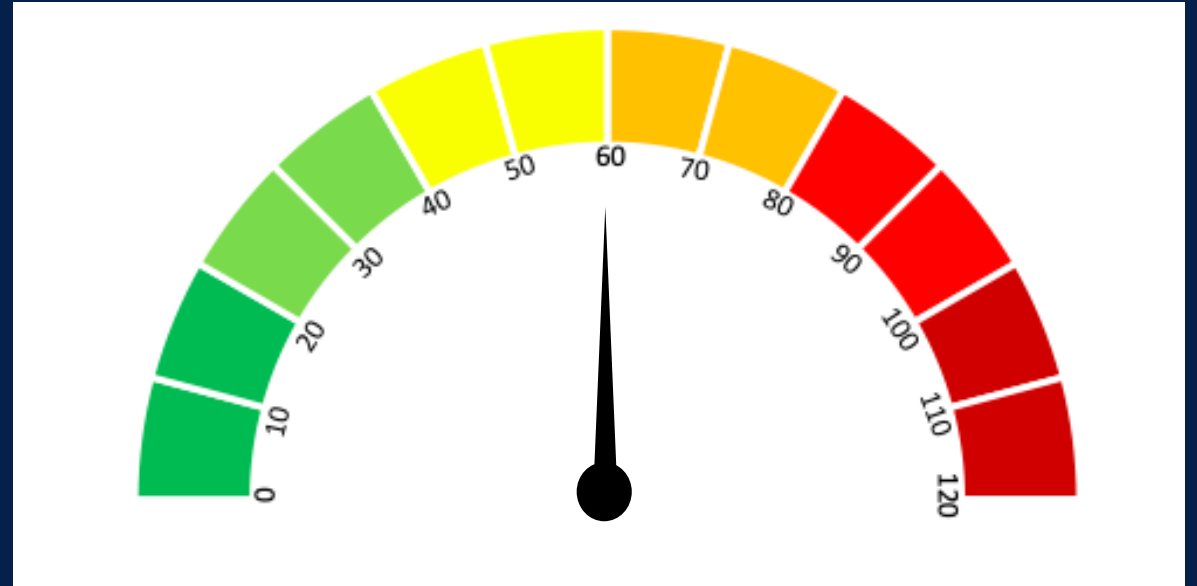
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Low dose initiation - day 7



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Buprenorphine 8mg BID

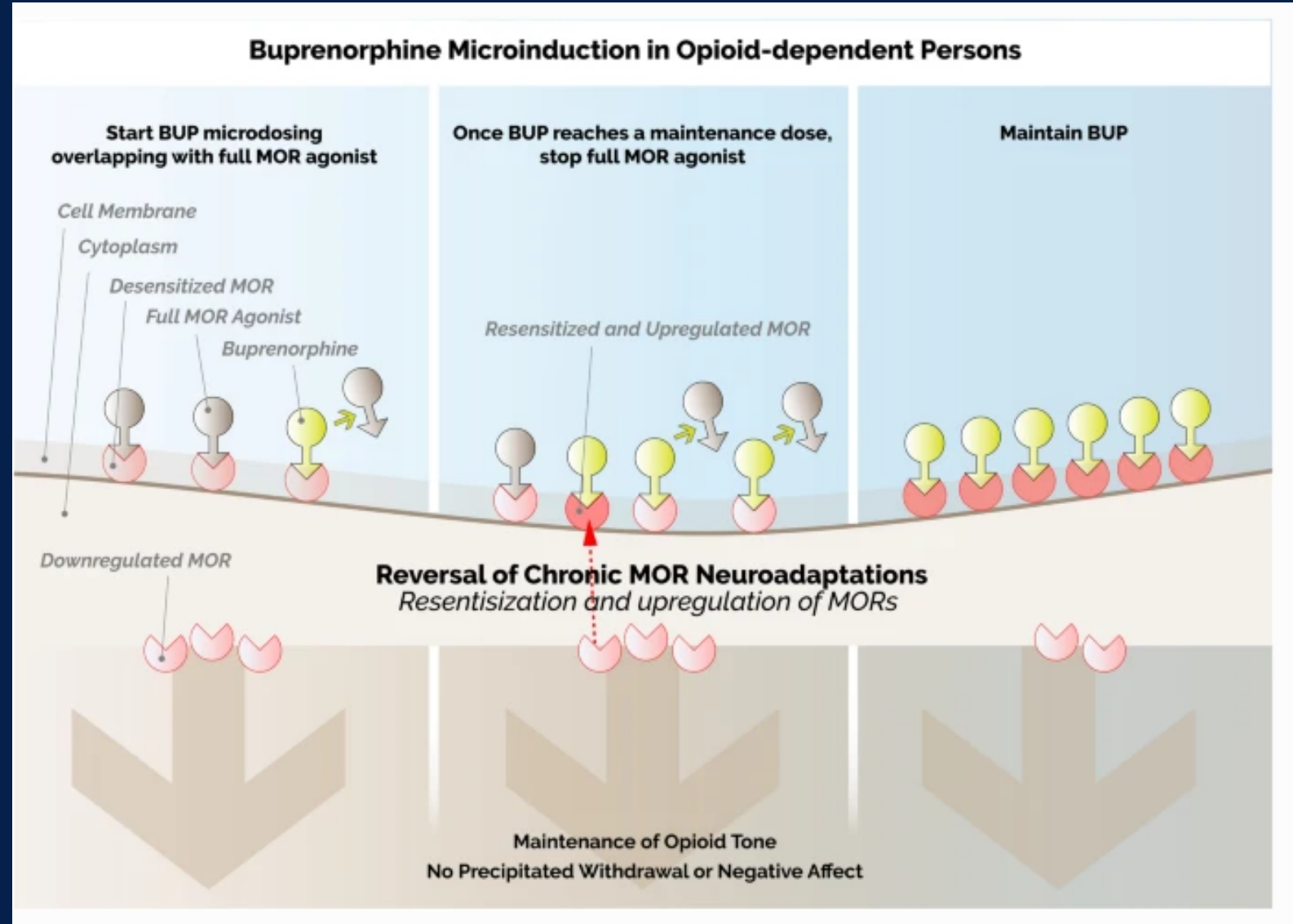


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Low Dose Initiation Theory

Buprenorphine causes “re-sensitization” of the opioid receptors

Low dose approach allows Up-regulation of opioid Receptors to prevent opioid withdrawal



Rationale for Low-Dose Initiation

A **patient-centered** approach that:

- ◆ enables clinicians to start buprenorphine without waiting for withdrawal
- ◆ allows patients to continue full-opioid agonists for pain
- ◆ facilitates faster transitions from methadone
- ◆ May reduce the risk of precipitated withdrawal from synthetic opioids with unpredictable clearance

What's the evidence?

- ◆ Relatively sparse
- ◆ Case reports, series and 2 retrospective chart reviews
 - ◆ ~30 publications
- ◆ Anecdotal success



Principles of low dose buprenorphine initiation



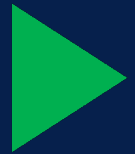
Appropriate clinical situation



Start low



Gradual up titration



Continue the full agonist



Clear and frequent communication



Pause or slow if withdrawal sx



Care coordination is critical

Example Low Dose Initiation regimen

Day	Buprenorphine/naloxone Dose	Strip/tab Strength	Full Agonist Dose
1	0.5mg ($\frac{1}{4}$ strip)	2mg	Continue
2	0.5mg BID ($\frac{1}{4}$ strip)	2mg	Continue
3	1mg BID ($\frac{1}{2}$ strip)	2mg	Continue
4	2mg BID	2mg	Continue
5	4mg BID	2mg	Continue
6	4mg TID	2mg	Continue
7	8mg BID	8mg	STOP

Case 1 - fentanyl

- ◆ 38 year old woman with severe OUD who presents to outpatient clinic with desire to start buprenorphine
 - ◆ Uses fentanyl 2 bundles IV daily
 - ◆ Has had unsuccessful buprenorphine initiations before due to precipitated withdrawal but interested in low dose initiation
- ◆ Question 1: What information is important to gather about her opioid use and past experiences to inform shared decision making about low dose initiation?
- ◆ Question 2: Which harm reduction strategies would you emphasize before starting low dose initiation?
- ◆ Question 3: How can we simplify the low dose initiation process for her?

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.

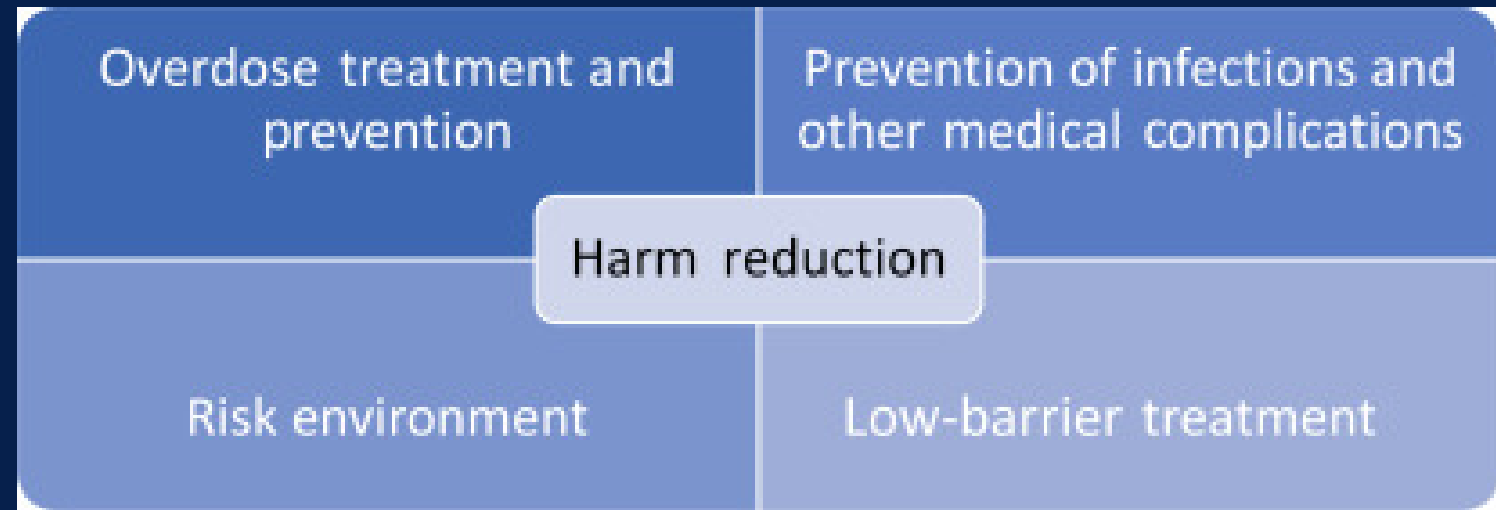
7. *What did we decide today?*

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

8. *What are the next steps?*

Harm reduction counseling














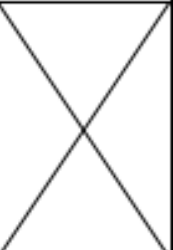







- ◆ Consistent supply
- ◆ Safer Injection techniques
- ◆ Naloxone
- ◆ Avoid using alone



Dosing Guide



1 page
guide

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

Simplifying Dosing

Make medisets together



Partner with a community pharmacy
→ Bubble pack a starter kit



Case 2 - methadone

- ◆ 45 year old man with severe OUD in sustained remission on methadone 100mg presents to your clinic to discuss transition to buprenorphine
 - ◆ Had success with buprenorphine >10 years ago but transitioned to methadone after a period of returning to opioid use
 - ◆ Worried about developing cravings and withdrawal if he has to taper methadone
 - ◆ Interested in low dose initiation
- ◆ Question 1: What would you do with the methadone dose throughout the low dose initiation process?
- ◆ Question 2: What would you do if he develops withdrawal symptoms during the transition?
- ◆ Question 3: How would you coordinate with the OTP? What might cause the OTP to stop methadone during the low dose transition?

Traditional Methadone-> buprenorphine transition

- ◆ High risk for precipitated withdrawal unless down-titrated to 30-50mg
- ◆ Down-titration → risk of opioid use recurrence



Troubleshooting withdrawal symptoms

Prescribe adjuncts



Pause or slow if
withdrawal symptoms



OTP communication

- ◆ Must continue methadone throughout process
 - ◆ Ideally same dose
- ◆ Not informing OTP → risk of stopping methadone → withdrawal, loss of follow up, recurrence of use
 - ◆ May see buprenorphine on PMP or urine



Case 3 – In hospital acute pain

- ◆ 24 year old woman with severe OUD admitted to the hospital with endocarditis now s/p tricuspid valve replacement. Interested in starting buprenorphine.
 - ◆ Currently on hydromorphone 8mg PO q3hr as needed for pain hydromorphone 2mg IV q3hrs for breakthrough as well as other adjunctive pain medication
 - ◆ Cannot stop opioids in post-op setting for traditional initiation
- ◆ Question 1: Your hospital pharmacy says you can't split films/tab in the hospital? What other buprenorphine formulations can you use?
- ◆ Question 2: What would you do if the patient is planned for discharge before completing the transition?

Literature guide

Buprenorphine Formulation	Starting dose	Sublingual equivalent	Advantages	Disadvantages	References
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

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Hickey, *Med Clin North Am*, 2022 Terasaki, *Pharmacotherapy*, 2019



More rapid low dose transitions

- ◆ Takes advantage of rapid onset of action of sublingual, IV, or buccal buprenorphine
 - ◆ Frequent dosing – every 3-6 hours
- 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	

◆ Only published experience in

Final Takeaways/Summary

- ◆ Terminology and language is important in our new field
- ◆ Low dose buprenorphine initiation is an important new strategy in certain clinical situations
- ◆ Low dose buprenorphine initiations should utilize several guiding principles and may be different in different clinical settings
- ◆ Shared decision making with patients is an important component of a successful initiation

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Buprenorphine Dosing Plan - Patch

Day	Buprenorphine Dose	Full Opioid Agonist Dose
1	20 mcg patch	Same
2	1 mg SL BID	Same
3	2 mg SL BID	Same
4	4 mg SL BID	Same
5	6 mg SL BID	Same
6	8 mg SL BID	OFF

Supportive Medications (ondansetron, loperamide, hydroxyzine, tizanidine, clonidine, dicyclomine)



Buprenorphine Dosing Plan - IV

Day	Buprenorphine	Full Opioid Agonist Dose
1	0.15 mg IV q6h x2 doses	Same
1	0.3 mg IV q6h x2 doses	
2	0.6 mg IV q6h x2 doses	Same
2	4 mg SL q6h x2 doses	
3	8 mg SL q6h x2 doses	OFF

Supportive Medications (ondansetron, loperamide, hydroxyzine, tizanidine, clonidine, dicyclomine)

Buprenorphine Dosing Plan - SL

Day	Buprenorphine Dose	Tab	Full Opioid Agonist Dose
1	0.5 mg qd	Quarter of 2 mg tab	Same
2	0.5 mg bid	Half of 2 mg tab	Same
3	1 mg bid	Full 2 mg tab	Same
4	2 mg bid	Two 2 mg tabs	Same
5	4 mg bid*	Half of 8 mg tab	Same
7	8 mg bid	Full 8 mg tab	Off

Supportive Medications (ondansetron, loperamide, hydroxyzine, tizanidine, clonidine, dicyclomine)

*Can repeat days if patient develops withdrawal, achiness



Buprenorphine Dosing Plan – Buccal

Day	Buprenorphine Dose	Buccal Buprenorphine	Full Opioid Agonist Dose
1		225mcg once daily	Same
2		225mcg BID	Same
3		450mcg BID	Same
4	2 mg BID		Same
5	4 mg BID		Same
6	4 mg TID		Same
7	8 mg BID		Off