

# Buprenorphine for Opioid Use Disorder

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# Disclosures

**No conflicts of interest or relationships to disclose.**

# Disclaimer

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# DATA CONSIDERATIONS

*Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.*



To Learn More:

<https://www.cdc.gov/minorityhealth/racism-disparities>

# LEARNING OBJECTIVES

1. To identify the role of buprenorphine as a medication for opioid use disorder (MOUD).
2. To describe approaches to counseling patients on MOUD options.
3. To outline practical considerations for buprenorphine initiation for OUD.

# SUBSTANCE USE DISORDERS AND HIV

- Addressing substance use disorders in people with HIV is important for several reasons.
- Substance use can:
  - Drive transmission of HIV infection (e.g. injection drug use)
  - Increase high-risk sexual behaviors
  - Reduce HIV treatment adherence
  - Worsen neurologic and other complications of HIV infection
  - Increase viral load, further disease progression, and increase mortality in people with HIV even if on ART regimen (Dash 2015)
- Treating SUD can:
  - Reduce risk of HIV acquisition and transmission
  - Improve HIV and other medical treatment adherence

# King County Fatal Overdose Dashboard

Source: King County Medical Examiner's Office  
As of 5/10/2023

## 2023 Summary

Confirmed Drug Overdose or Alcohol Poisoning	435
Possible (unconfirmed) Overdose	5
Probable (unconfirmed) Overdose	58

# of Overdose Deaths YTD in 2023 that Involved:

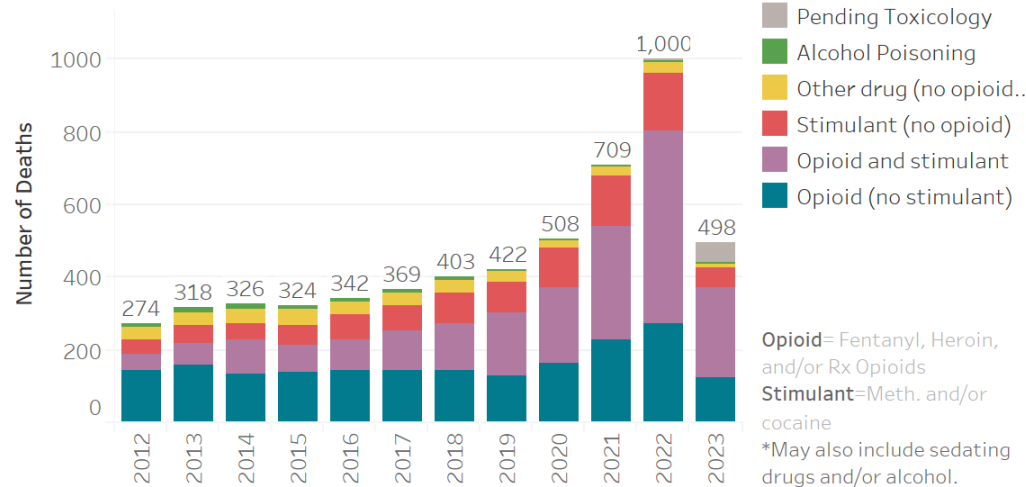
Opioids	372	Fentanyl	359	Methamphetamine	235
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# of Overdose Deaths in 2022 that Involved:

Opioids	802	Fentanyl	712	Methamphetamine	528
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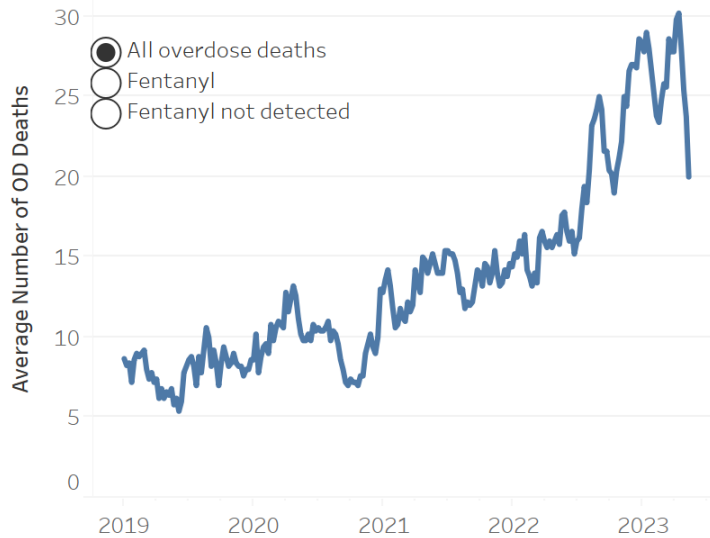
## Drug & Alcohol Poisoning Deaths, King County

(Note: Bar chart can be viewed in terms of counts or rates; each decedent with an overdose death is represented once.)



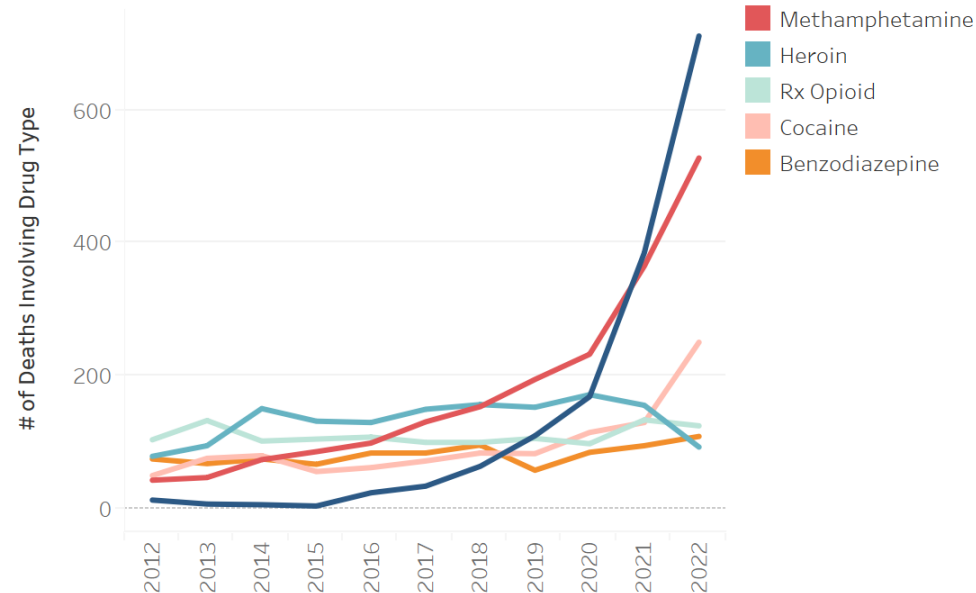
## Fentanyl Overdose Trends

Switch data view: Overdose deaths by week (rolling average)



## Drugs Involved in Confirmed Overdose Deaths

(Note: A decedent may be represented in multiple lines)



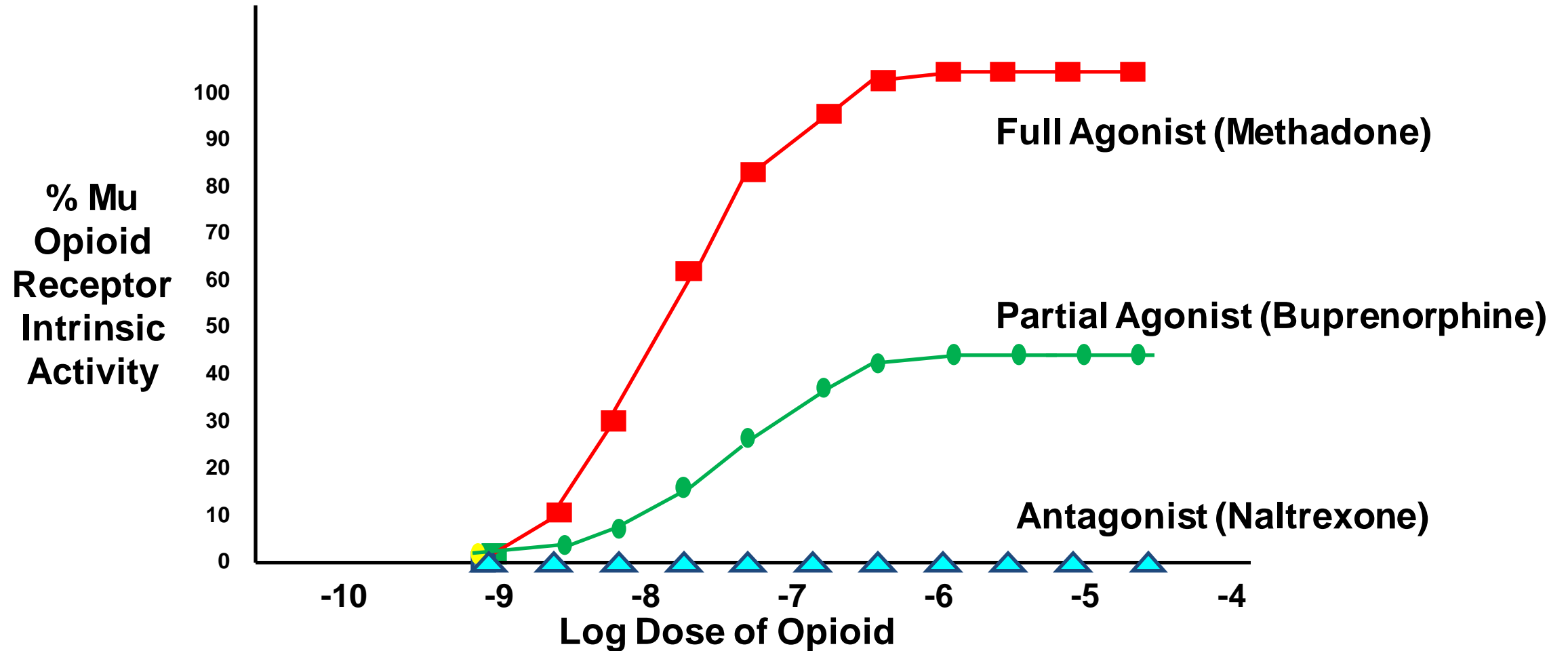
Fentanyl pressed pills ("blues")

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# FDA APPROVED MEDICATIONS FOR OUD (MOUD)



# BUPRENORPHINE

- Partial agonist at mu opioid receptor (MOR)
- Ceiling effect on respiratory depression (lower risk of overdose)
- High affinity for MOR (displaces other opioids)
- Poor oral bioavailability; given sublingually or subcutaneously for OUD (transdermal or buccal for pain)
- Sublingual:
  - Peak level 3-6 hours
  - 24-48 hour duration
  - Half life >24 hours
  - Typical maintenance dose: 16-24 mg daily (typical maximum 32 mg daily)

# BUPRENORPHINE MOUD FORMULATIONS

Formulation	Dosing	FDA-Approved Products
Tablet (Sublingual)	Daily	Generic, buprenorphine-naloxone SL (Suboxone, Zubsolv), buprenorphine (Subutex)
Film (Sublingual)	Daily	Generic, buprenorphine-naloxone (Suboxone)
Extended-Release Injection (Subcutaneous)	Monthly or Weekly	Buprenorphine monthly (Sublocade) Buprenorphine weekly or monthly (Brixadi)

# A NOTE ON BUPRENORPHINE PRESCRIBING...

- Buprenorphine for OUD can now be prescribed by anyone with DEA registration including Schedule III authority as of 1/12/2023. **No X-waiver needed!**
- After 6/27/2023, for new or renewing DEA registrations, a **one-time requirement of 8 hours of training on substance use disorders (SUDs)** is now required
- If you previously got your X-waiver, this counts!

# LEARNING OBJECTIVES

1. To identify the role of buprenorphine as a medication for opioid use disorder (MOUD).
2. To describe approaches to counseling patients on MOUD options.
3. To outline practical considerations for buprenorphine initiation for OUD.

# COUNSELING ON OUD TREATMENT

- Discuss main key components of treatment
  - Medications for opioid use disorder (MOUD)
  - Psychosocial interventions (e.g. counseling, mutual support groups)
- First-line treatment for OUD is medications, with adjunctive psychosocial interventions
- Shared decision-making is key!
- Decreased mortality is associated with opioid agonist treatment (buprenorphine or methadone)

# POSSIBLE REASONS TO CHOOSE BUPRENORPHINE

- Desire to avoid treatment in OTP setting
  - Structured setting
  - Location
  - Need for observed dosing and dispensing at OTP
- Desire to receive care in integrated care setting (e.g. from PCP/OBOT program)
- Methadone side effects or drug-drug interactions
- Dosing schedule and route of administration
  - e.g. Buprenorphine XR injectable form
- Preparation for transition to opioid antagonist treatment (naltrexone)
- **Patient-driven (rather than provider-driven) transitions to buprenorphine are associated with higher rate of success!** (Bhatraju 2022)

# LIMITATIONS OF BUPRENORPHINE

- Difficulty with tolerating opioid withdrawal
- Risk of return to use when opioid agonist dose is tapered
  - For example, in methadone to buprenorphine transitions
- Precipitated withdrawal if buprenorphine given too soon after stopping opioid agonist (especially with fentanyl)
- Inability to quickly achieve therapeutic effect with buprenorphine



# LEARNING OBJECTIVES

1. To identify the types of medications for opioid use disorder (OUD), with focus on buprenorphine.
2. To describe approaches to counseling patients on MOUD options.
3. To outline practical considerations for buprenorphine initiation for OUD.

# BUPRENORPHINE INITIATION PROTOCOLS

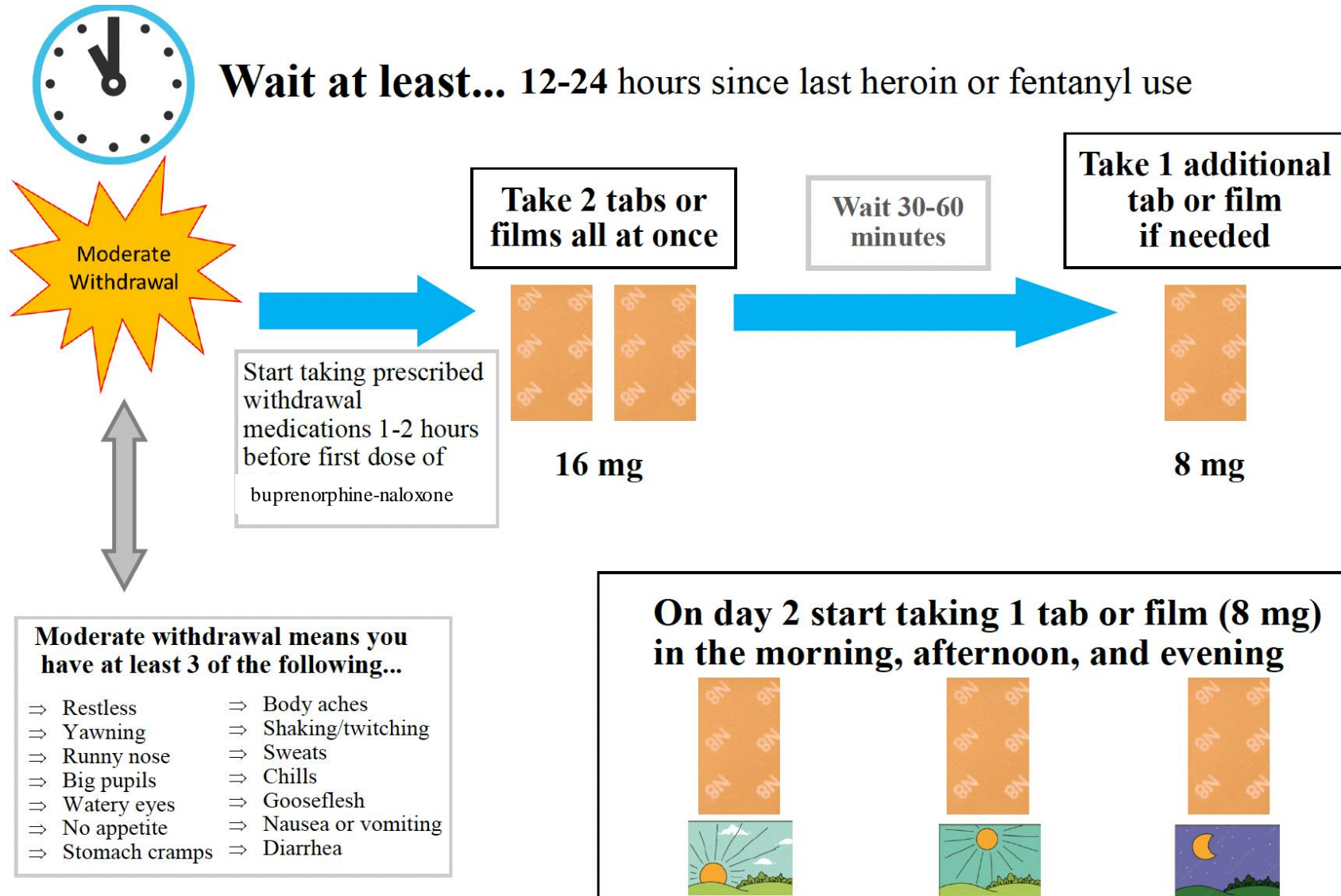
- Standard initiation
- High-dose initiation
- Low-dose initiation
- Practical considerations

# STANDARD BUPRENORPHINE INITIATION

- Stop opioids and wait until patient is in opioid withdrawal (COWS > 10 typically), usually after:
  - Short-acting opioids (heroin, hydrocodone, oxycodone): 12-16 hr
  - Intermediate-acting opioids (e.g. oxycodone ER): 17-24 hr
  - Long-acting opioids (e.g. methadone, fentanyl): 36+ hours
- Buprenorphine-naloxone started, uptitrated until withdrawal resolves (usually 1-3 days)
- Typically no more than 8-16 mg bup total on day 1
- Pro: less complex protocol
- Cons:
  - Risk for return to use after stopping opioids
  - May take days to achieve therapeutic buprenorphine level

# HIGH-DOSE INITIATION

Like conventional initiation, but higher buprenorphine dose on day 1 (16-32 mg)



# HIGH-DOSE INITIATION

- Like conventional initiation, but higher buprenorphine dose on day 1 (16-32 mg)
- Advantages
  - Less complex protocol than low- or standard-dose start
  - Could be more effective in achieving therapeutic dose while minimizing withdrawal period
- Limited evidence in literature (for now)
  - Retrospective studies from ER setting
  - Very few cases of precipitated withdrawal, even with fentanyl use (Snyder 2023, Herring 2021)

# LOW-DOSE BUPRENORPHINE INITIATION

- Start buprenorphine at low doses while continuing full agonist (i.e. methadone)
- Intention is to minimize precipitated withdrawal
- Pros:
  - May be more acceptable if negative prior experiences with standard buprenorphine initiation
  - Minimizes withdrawal symptoms
- Cons:
  - More complex instructions
  - Limited evidence in outpatient setting

# OUTPATIENT LOW-DOSE 1-WEEK INITIATION EXAMPLE

Day	Actual Dose/Day	Fraction of bup-nal Film (or SL tablets)	Full Opioid Agonist Dose
Day 1	0.5 mg daily	¼ (2/0.5 mg) film once daily	Continue current dose
Day 2	0.5 mg BID	¼ (2/0.5 mg) film twice daily	Continue current dose
Day 3	1 mg BID	½ (2/0.5 mg) film twice daily	Continue current dose
Day 4	2 mg BID	1 (2/0.5 mg) film twice daily	Continue current dose
Day 5	2 mg TID	1 (2/0.5 mg) film three times daily	Continue current dose
Day 6	4 mg BID	2 (2/0.5 mg) films twice daily	Continue current dose
Day 7	4 mg TID	2 (2/0.5 mg) films three times daily	STOP opioid
Day 8+	8 mg BID (can titrate up to 32 mg total daily dose)	1 (8/2 mg) film twice daily (can titrate up to 4 films daily)	

# OUTPATIENT LOW-DOSE 2-WEEK INITIATION EXAMPLE (PATIENT TRANSITIONING FROM METHADONE TO BUP)

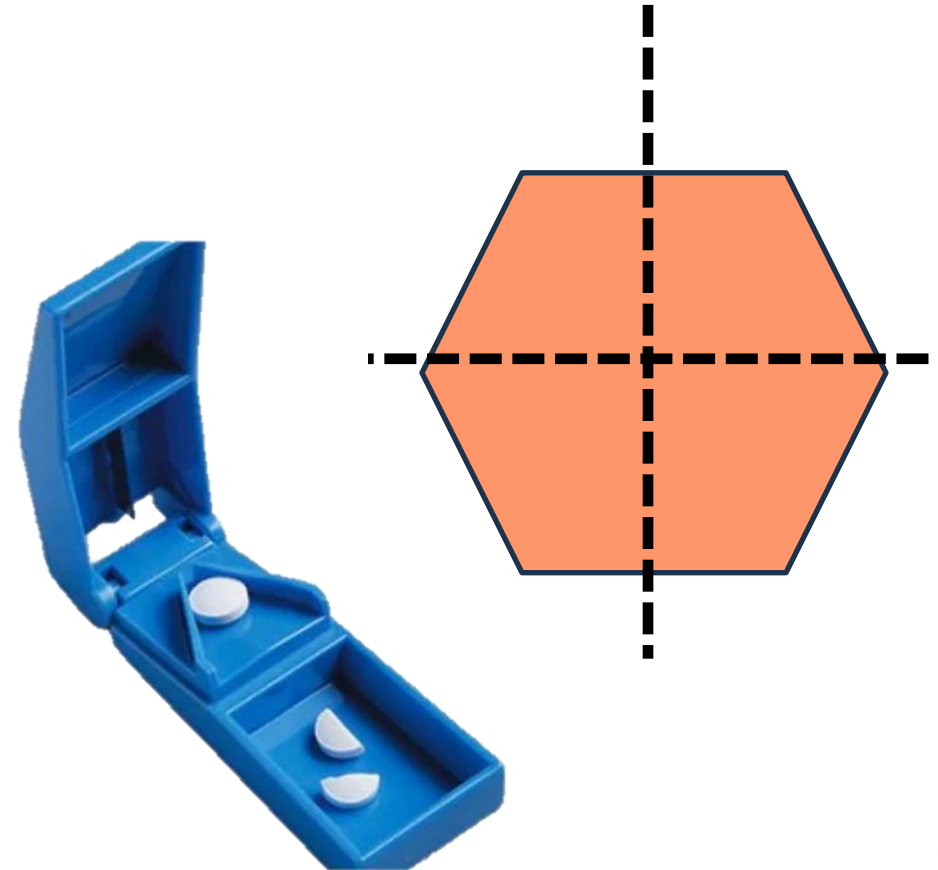
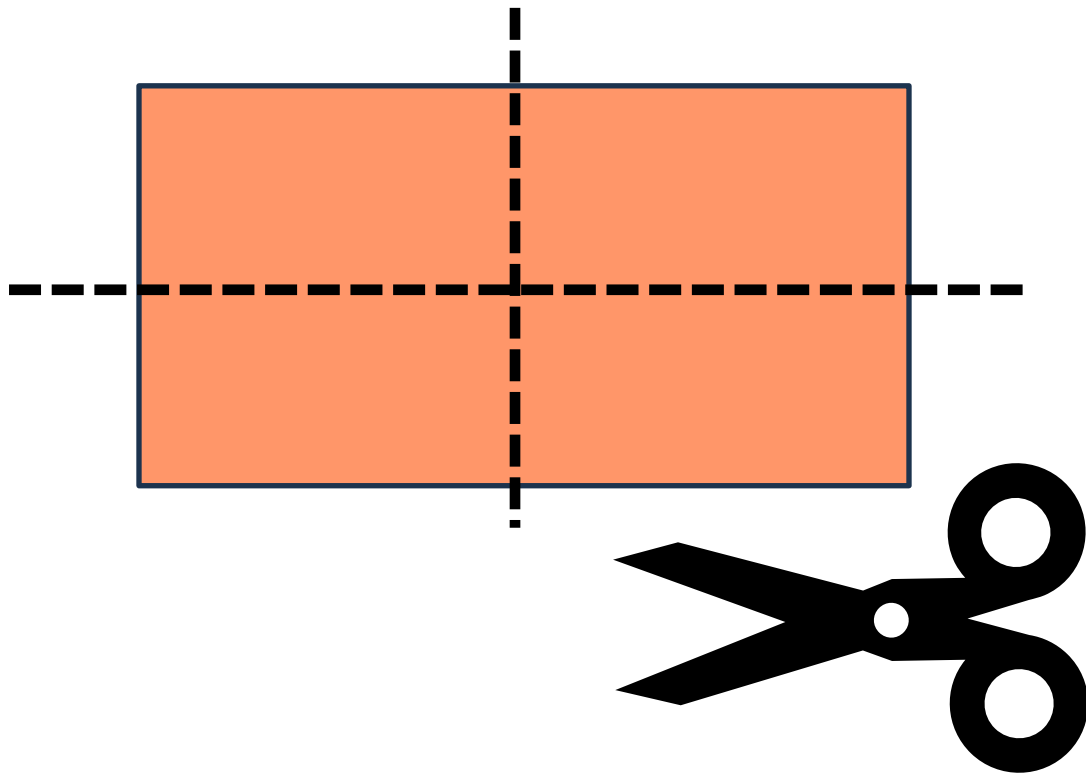
Day	Actual Dose/Day	Film or SL tablets	Methadone Dose	
<b>Buprenorphine/Naloxone Film 2mg/0.5mg</b>				
Day 1	0.5mg	¼ film once daily	Continue current dose	
See ETS Medical Provider on Day 1				
Day 2	0.5mg once daily	¼ film once daily	Continue current dose	
Day 3	1mg once daily	½ film once daily	Continue current dose	
Day 4	1mg once daily	½ film once daily	Continue current dose	
<b>Begin Buprenorphine/Naloxone Tablets for remainder of transition</b>				
Day 5	2mg once daily	1 x 2mg/0.5mg daily	Continue current dose	
Day 6	2mg once daily	1 x 2mg/0.5mg daily	Continue current dose	
Day 7	4mg once daily	2 x 2mg/0.5mg daily	Meet with your ETS medical provider to discuss when to reduce or discontinue methadone dose.	
See ETS Medical Provider on Day 7				
Day 8	4mg once daily	2 x 2mg/0.5mg daily		
Day 9	6mg once daily	3 x 2mg/0.5mg daily		
Day 10	6mg once daily	3 x 2mg/0.5mg daily		
Day 11	8mg once daily	1 x 8mg/2mg daily		
Day 12	8mg once daily	1 x 8mg/2mg daily		
Day 13	12mg once daily	2 x 2mg/0.5mg along with 1 x 8mg/2mg daily		
Day 14	16mg once daily	2 x 8mg/2mg daily	Return to ETS	
See ETS Medical Provider on Day 14				



# BUPRENORPHINE FILMS AND TABLETS

$\frac{1}{4}$ th of a 2/0.5 mg bup-nal film or tab = 0.5 mg buprenorphine

Can cut the film, or split the tablet, into fourths



# COMPARISONS OF PROTOCOLS

- Most studies are observational case series with heterogeneous populations, methods, and reported outcomes
- Low-dose initiation has more evidence for efficacy
- Most data of low-dose initiation is from inpatient setting; limited generalizability to outpatient setting
- Limited data on high-dose transition from methadone to buprenorphine, but anecdotally some potential benefits to this strategy

# CONVENTIONAL VS LOW-DOSE BUP INITIATION: COLD WATER ANALOGY



# OBOT-BASED BUPRENORPHINE INITIATION: PRACTICAL APPROACH

- Prescribe buprenorphine-naloxone and PRN comfort medications with instructions on home initiation
- Schedule provider visits starting on day 1 of initiation protocol, at least weekly and PRN
- Follow-up via telephone as needed (with RN or other clinic staff)
- If transitioning from methadone to buprenorphine, should collaborate with OTP provider (have ROI signed to allow for communication with OTP)
- If buprenorphine extended-release injectable formulations are available, these have great potential for better adherence to MOUD treatment!

# ADJUNCTIVE MEDICATIONS FOR OPIOID WITHDRAWAL

Symptom	Medication	Typical Dose Range
Anxiety, restlessness, insomnia	Clonidine	0.1-0.2 mg q2H PRN, NTE 1.2 mg daily (avoid if hypotensive), taper by 0.1-0.2 daily
	Gabapentin	300 mg TID PRN
	Hydroxyzine	25-50 mg q6H PRN
Muscle spasms	Methocarbamol	500 mg TID PRN
Muscle aches, joint pain, headache	Ibuprofen	400-800 q6H PRN
	Acetaminophen	500-1000 mg q6H PRN
Nausea, vomiting	Ondansetron	4-8 mg q8H PRN
Abdominal cramping	Dicyclomine	20 mg 4x daily PRN
Diarrhea	Loperamide	2 mg 4x daily PRN

# OTHER PRACTICAL CONSIDERATIONS

- Advise patient to consider reducing work, other obligations as able during initiation (likely 1-2 weeks)
- Ensure clinical support (e.g. access to clinic RN via telephone) available for patient PRN during initiation

# BUPRENORPHINE INITIATION: SUMMARY

- The decision on MOUD depends on various factors
  - **Patient preferences**
  - Risk-benefit discussion
  - Adherence considerations
  - Access
- Risks of buprenorphine initiation include risk of return to use or precipitated withdrawal during transition period
- Low-dose buprenorphine initiation has evidence for efficacy; most evidence comes from hospital setting



# CASE EXAMPLE 1: OBOT PATIENT

38M with history of OUD, ventral hernia, severe vision impairment, unhoused, presenting to low-barrier OBOT clinic for restart of buprenorphine.

Last seen in OBOT clinic in 2021, prior history of heroin use and started on buprenorphine-naloxone, previously stable on 16 mg daily. Since then, moved to Olympia, began use of fentanyl blues about 1.5 years ago (and stopped heroin). Now taking 15-20 blues daily, occasional fentanyl powder. Has returned to Seattle, staying in tent. Wants to stop fentanyl use. Doesn't have money to continue buying fentanyl.

Tried to quit fentanyl and start buprenorphine-naloxone (purchased from street) but unsuccessful in the last few weeks. Says that prior successful approach to bup initiation (taking 1-2 Suboxone strips [8-16 mg bup] BID about 24 hours after last use of heroin) hasn't been successful with fentanyl, and sent him into precipitated withdrawal, even when waiting 2 days from last use of fentanyl.

Asks for your help with restarting buprenorphine-naloxone.

- **How can you counsel this patient on approaches to starting buprenorphine? What more information might you need?**
- **What are some pros and cons to traditional, low-, and high-dose initiation approaches?**



# CASE EXAMPLE 1: OBOT PATIENT

Buprenorphine Initiation Approach	Pros	Cons
Traditional	Simpler instructions Can stop using opioids right away	Already tried it, didn't work due to precipitated withdrawal
Low-Dose	Minimizes withdrawal risk	Requires continued fentanyl use (\$\$ is a concern) Complex titration instructions, takes a week or more Vision impairment
High-Dose	Simpler instructions Fastest method to get onto bup Can stop using opioids right away	Risk of precipitated withdrawal Patient concerned about GI side effects (with history of ventral hernia) Least evidence/experience

- In the end, patient opted for low-dose buprenorphine-naloxone initiation.
- Buprenorphine-naloxone prescribed, with comfort medications to use PRN (clonidine, gabapentin, ondansetron)
- Naloxone kit given to patient
- Unfortunately did not make it to follow up appointment, outcome not determined

# CASE EXAMPLE 2: HOSPITALIZED PATIENT

- 65M history of OUD, gastric adenocarcinoma s/p resection complicated by severe anastomosis stricture, presenting with recurrent stricture resulting in acute on chronic abdominal pain and malnutrition.
- Smoking 10 fentanyl "blues" daily previously.
- Methadone started at 30 mg daily, increased to 35 mg daily
- However complicated by intermittently prolonged QTc >500
- Risk/benefit discussion with patient:
  - Patient willing to transition to buprenorphine
  - Motivated by desire to travel, felt monthly visits to clinic more feasible than frequent OTP clinic visits
  - Risks of precipitated withdrawal discussed

# CASE EXAMPLE 2: HOSPITALIZED PATIENT

Day	Buprenorphine	Methadone	Notes
0	None	35 mg daily	No withdrawal symptoms
1	Buprenorphine 450 mcg buccal once	35 mg daily	"Irritability"
2	Buprenorphine 450 mcg buccal BID	35 mg daily	No change in symptoms
3	Buprenorphine 900 mcg buccal BID	35 mg daily	No change in symptoms
4	Buprenorphine-naloxone 2-0.5 mg SL BID	35 mg daily	No change in symptoms
5	Buprenorphine-naloxone 4-1 mg SL BID	35 mg daily	Restlessness, rhinorrhea
6	Buprenorphine-naloxone 8-2 mg SL BID	None	Irritability, anxiety, restlessness, rhinorrhea
7	Buprenorphine-naloxone 8-2 mg SL BID	None	Nausea, diarrhea, but otherwise better

Patient ultimately transitioned to XR buprenorphine 300 mg SC injection by day 10  
 Discharged with OBOT clinic follow-up for buprenorphine monthly injections

# Thank you!

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