



# Cutting Through Confusion: MOUD Management in Surgery Patients

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# Disclosures

The planner(s) and speaker(s) have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

# Learning Objectives

At the end of this session, learners should be able to:

- Review the agents utilized for the treatment of opioid use disorder, including their mechanism of action and place in therapy.
- Differentiate between guideline-recommended perioperative pain management strategies for patients with opioid use disorder.
- Develop acute pain plans for post-surgical patients on medications for opioid use disorder (MOUD) therapy.

# Outline

- Review the medications utilized to treat opioid use disorder (OUD).
- Review current guideline recommendations for perioperative management.
- Address common challenges and concerns surrounding OUD management during the perioperative period.
- Compare MOUD agents and their perioperative considerations.
- Apply principles through a mock post-surgical MOUD plan.

# Abbreviation Key

- ASAM – American Society of Addiction Medicine
- BUP – buprenorphine
- ER – extended release
- FDA – U.S. Food and Drug Administration
- IM – intramuscular
- MOR – mu-opioid receptor
- MOUD – medication for opioid use disorder
- NPO – nothing per orem
- NSAID – nonsteroidal anti-inflammatory drug
- OUD – opioid use disorder
- OTP – opioid treatment program
- PET – positron emission tomography
- SAMHSA – Substance Abuse and Mental Health Services Administration
- SL – sublingual
- TDD – total daily dose
- UDS – urine drug screen
- VA – Veterans Affairs

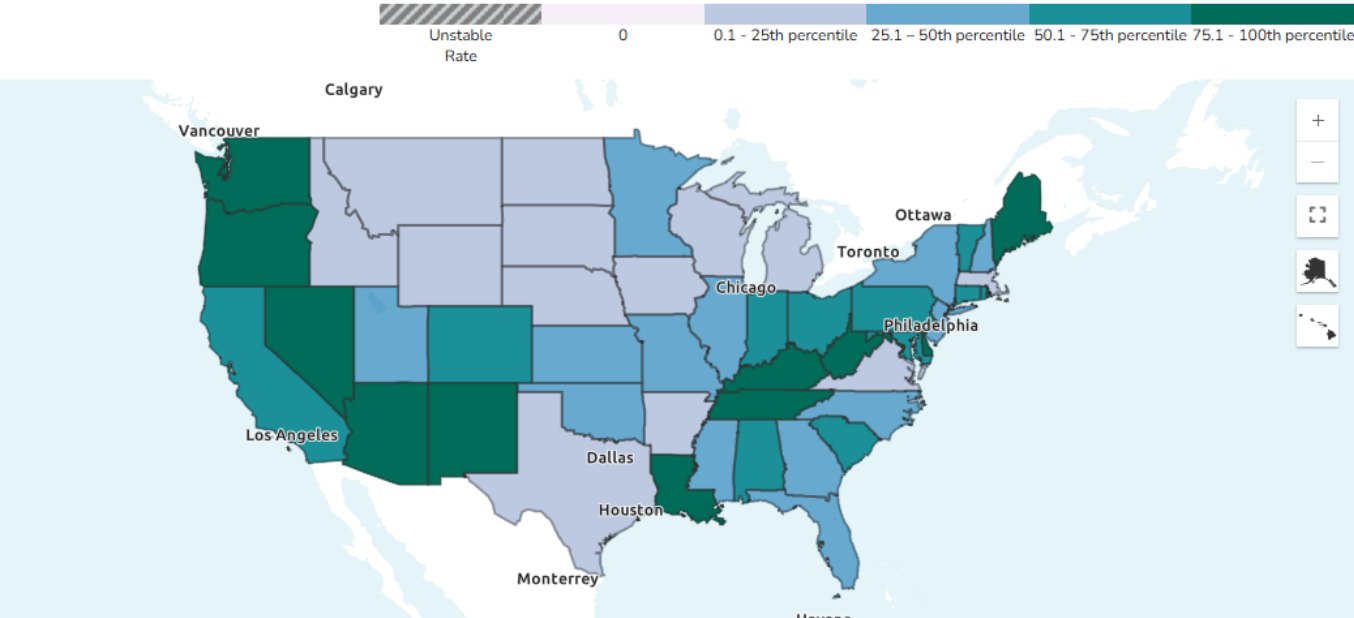
# Background: Opioid Epidemic and MOUD

# Key Definitions

- Medication for opioid use disorder (MOUD) refers to the use of medication specifically FDA approved for the treatment of opioid use disorder (OUD).
- OUD: chronic medical condition characterized by compulsive opioid use despite harmful consequences to health, social life, or responsibilities at work or home.

# National Overdose Statistics/Prevalence of OUD

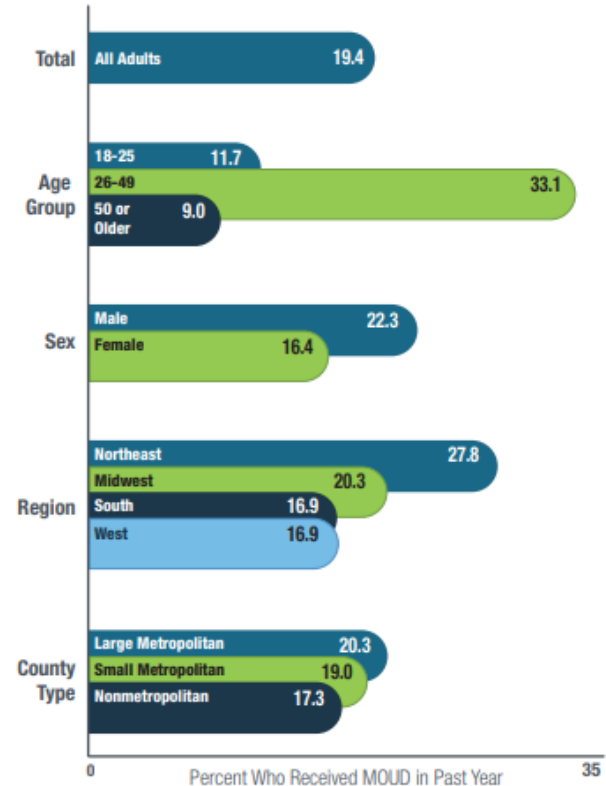
Unintentional Drug Overdose Death Rate per 100,000 People by State, July 2024 – June 2025 (Provisional Data)



# MOUD Statistics

- About 1 in 5 (19.4%) of the 5.0 million adults who had an OUD in the past year, received MOUD in that period.
- 17,000+ substance use disorder facilities in the US.

Receipt of MOUD: Among Adults Aged 18 or Older Who Had an OUD in the Past Year, 2022-2024



# MOUD Agents

# Medication Treatment for OUD

Agent	Mechanism	FDA Approved Formulations for OUD	Therapeutic Dose Range	Success Rate
<b>Buprenorphine ± Naloxone</b>	Partial MOR agonist	<b>Bup with Naloxone:</b> SL tablets (Zubsolv <sup>®</sup> , Suboxone) SL film (Cassipa <sup>®</sup> , Suboxone <sup>®</sup> ) Buccal film (Belbuca <sup>®</sup> , Bunavail <sup>®</sup> ) <b>Bup without Naloxone:</b> SL tablets (Subutex <sup>®</sup> ) ER injection (Brixadi <sup>®</sup> , Sublocade <sup>®</sup> )	12-32* mg/day	Up to 80% retention rate Decreases risk overdose by 59% Decreases risk opioid-related death by 38%
<b>Methadone</b>	Full MOR agonist	Oral solution Dissolvable tablet	80-120+ mg/day	Up to 85% retention rate Decreases risk overdose by 59% Decreases risk opioid-related death by 59%
<b>Naltrexone</b>	MOR antagonist	ER IM Injection (Vivitrol <sup>®</sup> ) Oral tablets	380 mg monthly	Up to 55% retention rate No association with reduction in risk overdose or opioid related death

Laroche MR, et al. *Ann Int Med*. 2018;169(3):137-145.

Wakemake SE, et al. *JAMA* 2020;3(2).

Krupitasky E. et al. *Lancet*. 2011;377(9776):1506-1512

Smith K, et al. *J Clin Pharmacol*. 2022;62(4):449-462.

Kohan L, et al. *Reg Anesth Pain Med*. 2021;46(10):840-859.

National Institute on Drug Abuse. National Institute of Health. 2021.

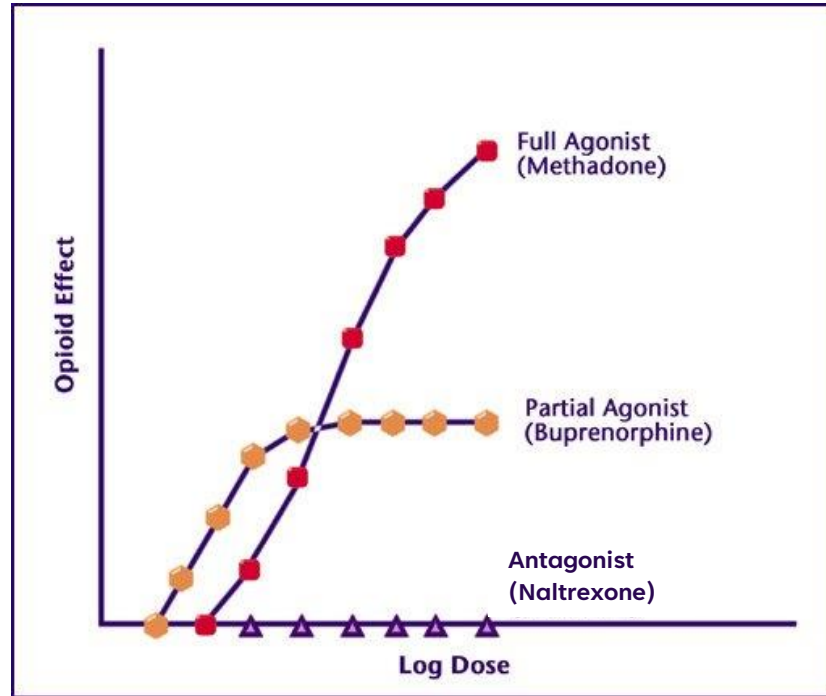
\*expressed in SL bup equivalents

# Mu-Opioid Receptor (MOR) Affinity

Low Affinity ( $K_i > 100\text{nM}$ )		Moderate Affinity ( $K_i 1-100\text{nM}$ )		High Affinity ( $K_i < 1\text{nM}$ )	
Drug	$K_i(\text{nM})$	Drug	$K_i(\text{nM})$	Drug	$K_i(\text{nM})$
Tramadol	12486	Hydrocodone	41.58	Oxymorphone	0.4055
Codeine	734.2	Oxycodone	25.87	<b>Naltrexone*</b>	<b>0.4</b>
Meperidine	450.1	<b>Methadone</b>	<b>3.378</b>	Hydromorphone	0.3654
		Fentanyl	1.346	<b>Buprenorphine</b>	<b>0.2157</b>
		Morphine	1.168	Sufentanil	0.1280

\*Only MOR antagonist included due to use in OUD

# MOUD Mechanism of Action



# Provider Concerns with MOUD

Uncertainty/lack of  
experience  
managing MOUD

Fear of causing  
overdose when  
providing  
additional opioids

Concern for  
MOUD  
interference with  
effective analgesia

# Patient Concerns with MOUD

Fear  
of inadequate  
pain control

Anxiety  
surrounding  
procedures

Exposure to  
potential  
relapse triggers

Worry about  
stigma or being  
labeled "drug-  
seeking"

# Clinical Challenges with MOUD

Disruption of  
treatment for  
OUD

Interference  
with full opioid  
agonists

Complex pain  
control needs

# Risks of Uncontrolled Pain & MOUD Discontinuation

50-90% chance of OUD relapse if MOUD is discontinued

Abrupt cessation while supplementing with opioids misused in the past can trigger relapse

May lead to illicit substance-seeking behavior

Increased risk of overdose

# Perioperative Management of MOUD

# General Principles

- Goal: balance continuation of MOUD with effective post-operative pain control.
- Utilize multimodal analgesia: NSAIDs, acetaminophen, ketamine, regional blocks, gabapentinoids, etc.
- Supplemental opioids may be used but often require higher doses in patients on MOUD.
- Prevent relapse: ensure rapid resumption of MOUD post-op and clear follow-up plan.
- Emphasize interdisciplinary collaboration across surgery, anesthesia, pain, and addiction teams.

# General Principles

- Recommendations to hold buprenorphine and methadone during perioperative period are outdated.
- Every effort should be made to continue buprenorphine and methadone in this setting.

# Use and Outcomes of MOUD Among Patients With OUD Undergoing Surgery (2025)

<b>Design</b>	<ul style="list-style-type: none"><li>• Retrospective cohort study.</li><li>• Evaluated patients 18-64 years old undergoing both major and minor surgical procedures.</li><li>• Compared surgical patients with OUD to those without OUD and examined outcomes among OUD patients with vs without MOUD.</li></ul>
<b>Outcomes</b>	<ul style="list-style-type: none"><li>• Perioperative opioid prescribing patterns</li><li>• Persistent opioid use</li><li>• 30-day readmissions</li><li>• Emergency department visits</li></ul>
<b>Results</b>	<p>Among patients with OUD (MOUD vs no MOUD):</p> <ul style="list-style-type: none"><li>• Lower perioperative opioid use (53.7% vs 82.9%), <math>p &lt; 0.0001</math></li><li>• Lower persistent opioid use (13.8% vs 56.7%), <math>p &lt; 0.0001</math></li><li>• Fewer ED visits (18.3% vs 22.3%), <math>p &lt; 0.0001</math></li><li>• Lower readmission rates (4.8% vs 7.2%), <math>p &lt; 0.0001</math></li></ul>
<b>Conclusions</b>	<ul style="list-style-type: none"><li>• <b>Continuation of MOUD in surgical patients is associated with improved perioperative outcomes.</b></li><li>• Reduction of persistent postoperative opioid use highlights MOUD's role in preventing relapse and prolonged opioid exposure postoperatively.</li></ul>

# Buprenorphine ± Naloxone

# Pharmacologic Considerations

# MOR Affinity

- Human-carfentanil positron emission tomography (PET) utilized to provide direct insight into MOR occupancy and availability at various buprenorphine doses.
  - Dose range where buprenorphine has additive analgesic effects when used with full opioid agonist.
  - Time intervals between buprenorphine and full agonist administration to optimize receptor availability.

# Dose Related MOR Availability

Trial	Measure	Results	
Zubieta et al (2000)	Reduction in MOR availability	2mg: 36-50% 16mg: 79-95%	
Greenwald et al (2003)	Reduction in MOR availability	2mg: 41% 16mg: 80% 32mg: 84%	
Greenwald et al (2007, 2014)	Availability of MOR	1mg: 71-85% 2mg: 53-72% 4mg: 36-55% 8mg: 11-22%	12mg: 13-24% 16mg: 9-20% 24mg: 4-15% 32mg: 2-12%

Quaye et al. Pain Med. 2019;20(7):1395-1408.  
 Malinoff et al. Am J Ther. 2005;12(5):379-384.  
 Greenwald et al. Drug Alcohol Depend. 2014;144:1-11.  
 Zubieta et al. Neuropsychopharmacol. 2000;23(3):326-334.  
 Greenwald et al. Neuropsychopharmacol. 2003;28(11):2000-2009.  
 Greenwald et al. Biol Psychiatry. 2007;61(1):101-110.

# Surgical Considerations

# Surgical Considerations

## Urgency of procedure

- Non-emergent
- Emergent

## Severity of expected pain

- Dictates anticipated opioid requirements post-operatively

# Severity of Expected Pain by Procedure

## Low Anticipated Opioid Requirements

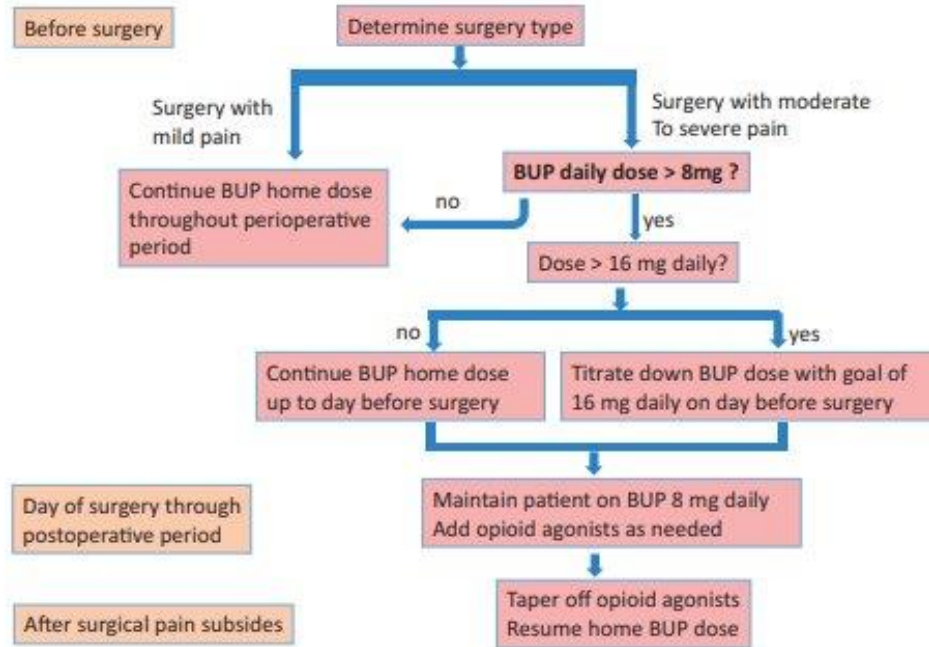
- Invasive non-surgical procedures
- Outpatient procedures
- Laparoscopic procedures
- Distal extremity orthopedic surgery

## Moderate-High Anticipated Opioid Requirements

- Major surgical procedures
  - Thoracotomy
  - Open-abdominal procedure
  - Major spine surgery

# Guideline Recommendations and Supporting Literature

# Massachusetts General Protocol



# Massachusetts General Protocol

<b>Design</b>	<ul style="list-style-type: none"><li>• Retrospective observational study</li><li>• Patients on buprenorphine undergoing major surgical procedures</li></ul>
<b>Methods</b>	<ul style="list-style-type: none"><li>• Comparison of perioperative continuation versus holding buprenorphine<ul style="list-style-type: none"><li>○ Post-anesthesia care unit (PACU) pain scores</li><li>○ Postoperative outpatient dispensing</li></ul></li></ul>
<b>Exclusion Criteria</b>	<ul style="list-style-type: none"><li>• Minor procedures</li><li>• Transdermal buprenorphine patches</li><li>• Buprenorphine for chronic pain management</li><li>• Emergent surgery</li></ul>

# Massachusetts General Protocol

<b>Data Collection</b>	Outpatient opioid utilization: <ul style="list-style-type: none"><li>• Number of full MOR agonist prescriptions filled</li><li>• Total amount of full MOR agonist dispensed (in MME)</li></ul> Postoperative buprenorphine adherence: <ul style="list-style-type: none"><li>• Number of buprenorphine prescriptions filled</li></ul> Postoperative pain level: <ul style="list-style-type: none"><li>• Pain scores in PACU (0-10)</li></ul>		
<b>Baseline Characteristics</b>	<b>Mean buprenorphine dose (mg):</b> <ul style="list-style-type: none"><li>• Continued: 17.7</li><li>• Held: 15.1</li></ul> <b>Age (years):</b> <ul style="list-style-type: none"><li>• Continued: 50.3</li><li>• Held: 51.1</li></ul>	<b>Surgical Type (%)</b>	
		Orthopedic <ul style="list-style-type: none"><li>• Continued: 50</li><li>• Held: 53</li></ul> Abdominal <ul style="list-style-type: none"><li>• Continued: 21</li><li>• Held: 18</li></ul>	Cardiothoracic <ul style="list-style-type: none"><li>• Continued: 11</li><li>• Held: 12</li></ul> Urology/gynecology <ul style="list-style-type: none"><li>• Continued: 8</li><li>• Held: 18</li></ul>

# Massachusetts General Protocol

<b>Results</b>	<p>N = 55 (continued (38): held (17))</p> <ul style="list-style-type: none"><li>• Opioids prescriptions dispensed outpatient<ul style="list-style-type: none"><li>○ 53% continued vs 82% held (p = 0.011)</li></ul></li><li>• MME of full MOR agonist dispensed<ul style="list-style-type: none"><li>○ Mean 229 continued vs 521 held (p = 0.033)</li></ul></li><li>• Buprenorphine continued postoperatively<ul style="list-style-type: none"><li>○ 91% continued vs 88% held (p = 0.324)</li></ul></li><li>• PACU pain score<ul style="list-style-type: none"><li>○ Mean 2.9 continued vs 7.6 held (p &lt; 0.001)</li></ul></li></ul>
<b>Conclusions</b>	<ul style="list-style-type: none"><li>• Significantly less full MOR agonist use in postoperative continuation group.</li><li>• Effect pain control can improve when buprenorphine is continued perioperatively.</li></ul>
<b>Impact</b>	Evidence to support the continuation of buprenorphine at a moderate dose
<b>Limitations</b>	<ul style="list-style-type: none"><li>• Single-center, nonrandomized.</li><li>• Patients in held group may have more difficult to control pain.</li><li>• Did not account for regional anesthetic use.</li></ul>

# American Society of Regional Anesthesia and Pain Medicine Recommendations (2021)

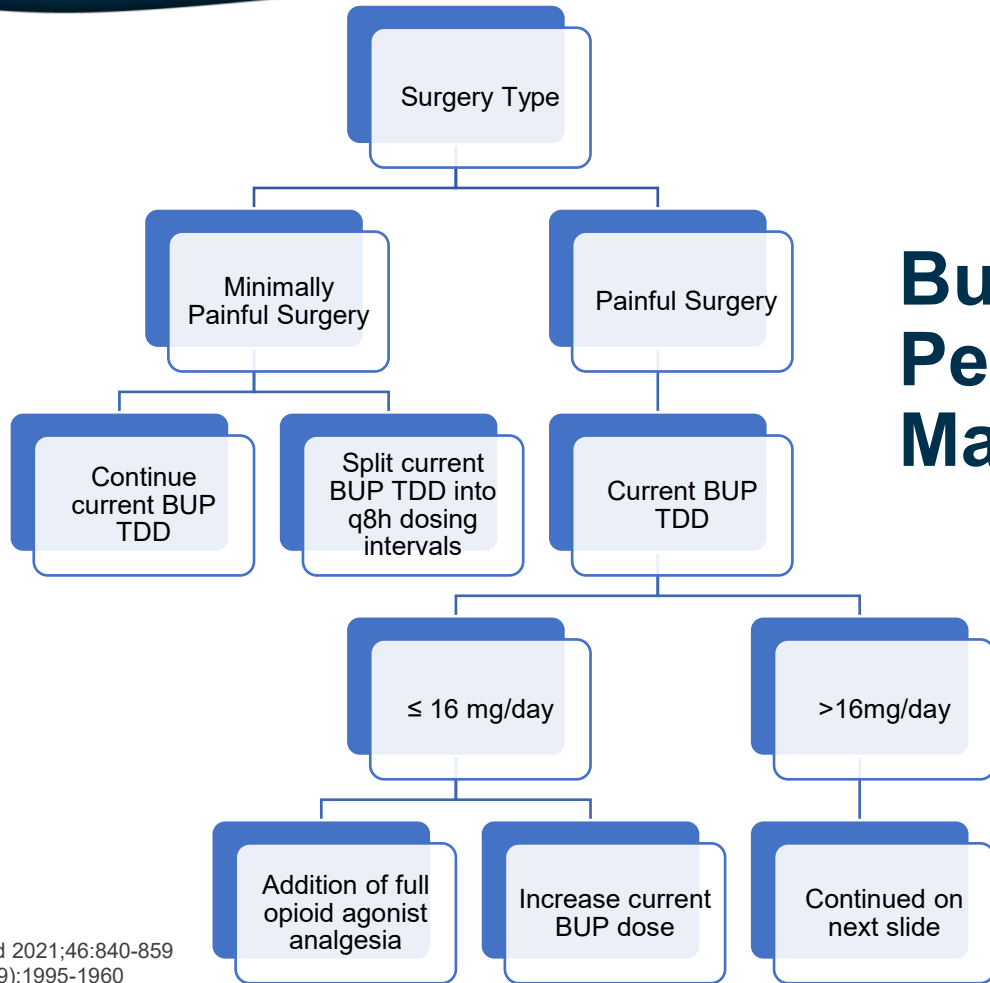
- Avoid routine tapering of buprenorphine preoperatively.
- Continue preoperative dose of buprenorphine unless inadequate pain relief requires a decrease.
- In patients receiving  $> 16\text{mg/day}$  with anticipated high postoperative opioid needs, tapering to  $\leq 16\text{ mg/day}$  may be considered.
- Discontinuation of buprenorphine can increase the risk of OUD recurrence or harm.

# VA Practice Guidelines (2022)

- Buprenorphine treatment should not be routinely discontinued in the perioperative period.
- A buprenorphine taper to  $\leq 16$  mg/day can be considered for patients prescribed higher doses of buprenorphine with anticipated postsurgical pain.
- In situations where a full opioid agonist is needed to adequately control perioperative pain, it is recommended that opioids with similar lipophilicity and binding affinity toward MOR be used.

# MOR Affinity

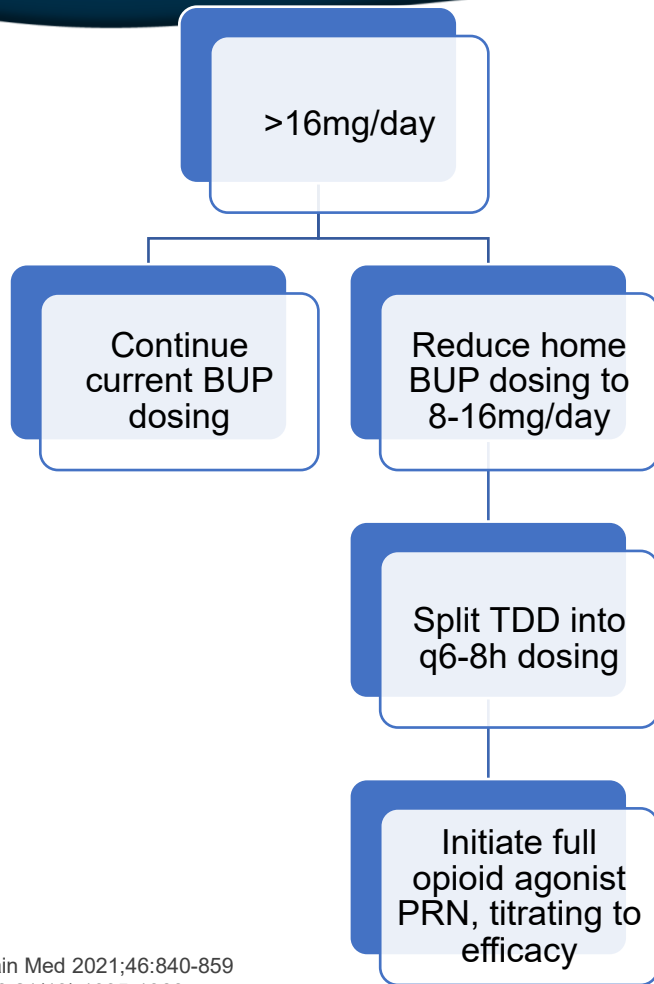
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Drug	$K_i$ (nM)	Drug	$K_i$ (nM)	Drug	$K_i$ (nM)
Tramadol	12486	Hydrocodone	41.58	Oxymorphone	0.4055
Codeine	734.2	Oxycodone	25.87	Naltrexone	0.4
Meperidine	450.1	Methadone	3.378	<b>Hydromorphone</b>	<b>0.3654</b>
		Fentanyl	1.346	<b>Buprenorphine</b>	<b>0.2157</b>
		Morphine	1.168	Sufentanil	0.1280



# Buprenorphine: Perioperative Management

BUP TDD expressed in SL buprenorphine equivalents

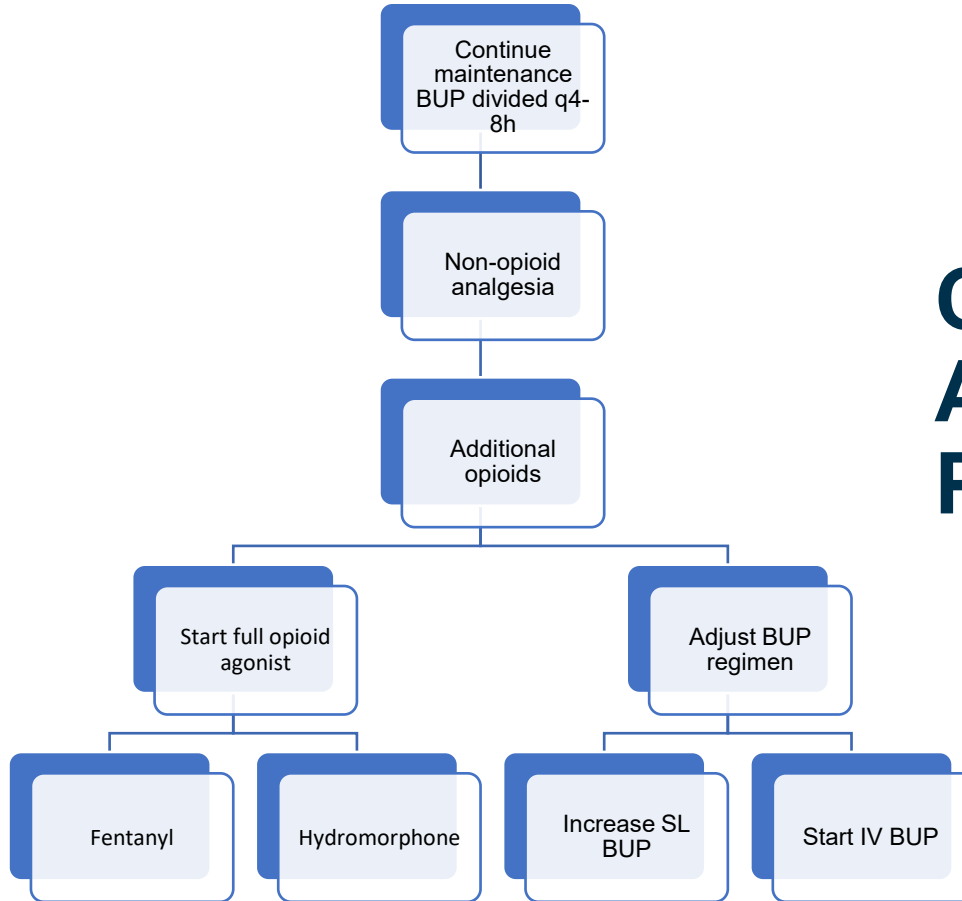




# Buprenorphine: Perioperative Management

BUP TDD expressed in SL buprenorphine equivalents





# CA Bridge Acute Pain Protocol (2019)

BUP TDD expressed in SL buprenorphine equivalents



# Assessment Question #1

A 45 YO man with OUD maintained on buprenorphine-naloxone 16 mg/day is scheduled for an elective laparoscopic cholecystectomy. He has been stable on therapy for 2 years without relapse.

What is the most appropriate recommendation for this patient?

- a. Discontinue buprenorphine 72 hours before surgery to allow full agonist opioids to work
- b. Continue buprenorphine at the same dose and use multimodal analgesia post-operatively
- c. Convert buprenorphine to methadone one week prior to surgery
- d. Hold buprenorphine the morning of surgery only, then resume on post-op day 1

# Methadone

# Pharmacologic Considerations

$\alpha$ -elimination half-life: 8-12 hours

- Responsible for analgesic effect

$\beta$ -elimination half-life: 30-60 hours

- Responsible for withdrawal suppression

Binds to ~30% of the mu-opioid receptors, allowing additional activity from other opioid agonists

Can cause QTc prolongation

# American Society of Addiction Medicine (ASAM) Guideline Recommendations

Discontinuation before planned surgery is NOT recommended

Doses may be skipped during the NPO period before surgery

- Withdrawal not expected in first 24-48 hours
- IV:PO Conversion 1:2

Dividing home dose into 3-4 daily doses can maximize analgesic properties of methadone

High-potency IV full opioid agonists can be used perioperatively for analgesia

# Substance Abuse and Mental Health Services Administration Guideline Recommendations

Patients should receive their full usual daily dose of methadone, barring contraindications

Contact patient's opioid treatment program (OTP) directly to confirm the outpatient methadone dose

Home methadone dose should not be considered a dose for pain management

Prescribe short-acting opioids scheduled, not as needed. Patients will likely need higher doses of due to opioid tolerance.

# Assessment Question #2

A 56 YO F treated with methadone 90 mg daily for OUD presents for emergency total hip replacement. She received her methadone dose this morning. She reports severe pain (10/10) post-operatively.

What is the best approach to managing her pain?

- a. Withhold methadone post-operatively and switch to PRN IV morphine
- b. Decrease methadone dose by 50% and add hydrocodone-acetaminophen
- c. Continue her full methadone dose and treat acute pain with multimodal analgesia and short-acting opioids
- d. Discontinue methadone and begin a PCA with no basal rate

# Naltrexone

# Pharmacologic Considerations

## Full opioid antagonist

- Causes precipitated withdrawal in patients actively on opioids
- Competitive antagonism allows for MOR blockade to be overcome with high doses of opioids

## Half-life

- Oral tablet: ~ 4 hours
- Intramuscular injection: 5-10 days
  - Gradual decline in MOR blockade over 4 weeks, more easily overcome in weeks 3-4

## Oral formulation used off label for OUD

- Only recommended in select patient groups

# Therapeutic Considerations

- No physical dependence associated with naltrexone use
  - Naltrexone withdrawal is NOT a concern
- Larger place in therapy for alcohol dependence
- Lack of proven mortality benefit in OUD when compared to methadone or buprenorphine
  - Benefit mainly in reducing cravings

# ASAM Guideline Recommendations

## Oral naltrexone

- Should be discontinued 72 hours before surgery if pain management with opioids is anticipated

## Extended-release injectable naltrexone

- Should be discontinued 30 days before anticipated surgery
- Oral naltrexone may be used temporarily until 72 hours prior to surgery

Naltrexone should not be resumed until patient has been off all opioids for 3-7 days

# When IM Naltrexone is NOT Held

Elective/Planned  
Surgery

- Reschedule to allow for recommended discontinuation timeline

Emergency  
Surgery

- Large doses of high-affinity opioids can be used to overcome MOR blockade

# Postoperative Pain Management Considerations

Non-opioid multimodal analgesia should be prioritized over high-dose opioid agonists, particularly when naltrexone cannot be discontinued perioperatively

Doses 6-20 times typical opioids have been needed in animal models to overcome MOR blockade

Patients are still at risk of respiratory depression, so require close monitoring while using high dose opioids

Patients may be more sensitive to opioids if proper discontinuation of naltrexone has occurred

# Assessment Question #3

A 38 YO M on extended-release IM naltrexone 380 mg monthly is admitted for a femur fracture after a car accident. His last injection was 2 weeks ago. He requires urgent orthopedic surgery.

Which of the following are appropriate post-operative pain management strategies?

- a. Use standard opioid doses post-op; naltrexone blockade is minimal at 2 weeks
- b. Use high dose opioids to overcome MOR blockade
- c. Delay surgery until naltrexone fully wears off
- d. Prioritize non-opioid multimodal analgesia and regional anesthesia techniques

# Final Summary

# Conclusions

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There is an increasing population of patients on MOUD

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Achievement of perioperative pain management in patients on MOUD is multifactorial and highly patient specific

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Benefits of continuing methadone and buprenorphine  $\pm$  naloxone perioperatively outweigh the risks

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Higher doses of full MOR agonists and optimization of multimodal analgesics likely required to achieve pain control when MOUD is continued

# Questions?

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