Acute Pain and Perioperative Management in Opioid Use Disorder: **Pain control in patients on buprenorphine, methadone, or naltrexone**

Overview:

Patients admitted for surgery or acutely painful illnesses frequently have comorbid opioid use disorder (OUD).[1] These patients may be on medications including buprenorphine, methadone, or naltrexone. In the inpatient setting clinicians can legally order buprenorphine or methadone if the patient is admitted primary for another medical reason.[2] As with all patients presenting with acutely painful conditions, it is unlikely that they will be pain free during their hospital stay, however pain should be manageable and much improved with the interventions below. Patients with OUD may have a higher pain experience and higher opioid tolerance, therefore if opioids are required they may need higher doses than other patients. The following guidelines apply to adults who are not pregnant and are already receiving these medications in the outpatient setting.

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SHOUT SUPPORT FOR HOSPITAL OPIOID USE TREATMENT

Disclaimer:

These clinical practice guidelines do not set a standard of care, rather they are an educational aid to practice. They do not set a single best course of management, nor do they include all available management options. They were developed by an interdisciplinary team based on published evidence and expert opinion; as the literature develops best practices may change. They should never be used as a substitute for clinical judgement. Individual providers are responsible for assessing the unique circumstances and needs of each case. Adherence to these guidelines will not ensure successful treatment in every situation. This information is intended for healthcare providers and subject matter experts, it is not intended for use by patients and the general population.

This guideline applies to patients in inpatient medical settings. If any of the following points are different for pregnant patients, it is noted in each segment of the following document.

Patients on outpatient buprenorphine or methadone

1. **Importance of continuing home medications for OUD**
   A. Patients should be continued on these medications in the setting of acute pain or surgical intervention. See induction/maintenance guidelines for full instructions on how to do this.
      - This applies to preoperative and postoperative periods, including the day of surgery (and throughout labor for ***Pregnant Only*** patients). Continuing these mediations improves pain control, reduces use of additional opioid pain medicine, and reduces the risk of relapse post discharge.[3,4,5]
      - Although it was previously believed that buprenorphine blocked the effects of full opioid agonists in the setting of acute pain, it is now known that the continuation of buprenorphine does not prevent adequate analgesia from opioids.[6,7] Naloxone present in combination products is not bioavailable and does not block analgesia.
      - Though it is *not recommended*, if buprenorphine is tapered off prior to surgery (or labor in ***Pregnant Only*** patients), it must be done gradually over weeks, as rapid tapers increase the risk of relapse.[8]
      - Discontinuing buprenorphine in the perioperative period or during acute pain episodes (including labor for ***Pregnant Only*** patients) is strongly discouraged as it may increase risk of relapse and increase discomfort during re-induction.
   B. Do not dose reduce these medications prior to surgery, labor, or in the setting of pain.[9,10] Consider dose reduction for recent missed doses or somnolence—see maintenance guidelines for details.
      - Dose reduction prior to surgery is not supported by available evidence, however if necessary dose can be lowered to 12 mg 2-3 days prior to surgery then increased back to their prior home dose before discharge.

2. **How to dose home medications for OUD**
   A. Verify patient's home dose
      - Verify methadone dose with opioid treatment program. If the dose cannot be immediately verified, a low doses (20 mg) can be given safely. See the separate guidelines for methadone induction and maintenance for further detail.
      - Verify buprenorphine or buprenorphine/naloxone dose through the outpatient pharmacy, the CURES system, or the patient's outpatient medical record.
      - Confirm with the patient that they have been taking their home dose as prescribed. Explain that if they have not been taking the buprenorphine, they may experience sudden withdrawal when they restart. Patients tend to disclose non-adherence when they understand the potential for precipitated withdrawal. See the separate guidelines for buprenorphine induction and maintenance for further detail.
   B. Provide the patient's home dose as baseline pharmacotherapy for OUD
      - Note that in some hospitals only buprenorphine monoproduct, not buprenorphine-naloxone combination product is available in the inpatient setting. This is a good substitute at the same dose of buprenorphine.

- Notify the outpatient buprenorphine or methadone provider of admission and any potential procedures.
- In patients who are NPO, buprenorphine can be administered sublingually as usual. Methadone can be administered via NG tube or as sublingual liquid. Both medications do come in IV formulations. Discuss dosing intervals and IV vs PO bioavailability with pharmacy prior to use.

3. Monitor and treat for withdrawal

A. Withdrawal is common in this population and can be painful. Patients may not be able to differentiate between withdrawal symptoms and pain. Use the COWS scale to assess for symptoms of withdrawal (see addendum).[11]

B. Treat withdrawal by giving the patient's home dose of buprenorphine or methadone as above before and during treatment of acute pain. If patient continues to exhibit symptoms of withdrawal, their MAT dose may not be adequate. See separate induction/maintenance guidelines for details on dose titration, and contact the outpatient buprenorphine/methadone provider if dose adjustments are made.

4. Manage acute/preoperative pain

Please note that continuing OUD pharmacotherapy alone is generally not sufficient for pain control. Additional pain management should be provided to the patient. Of note, as methadone is a major risk factor for sleep apnea, patients should be closely monitored under anesthesia. Consider pain service consultation.

A. For very mild pain, splitting home doses of buprenorphine or methadone TID is sometimes sufficient for treating acute pain. The analgesic effects of the medications are less than 24 hours, so doses must be split to provide analgesia. [12,13]

B. For mild-moderate pain, as with all patients, use non opioid medications as first line agents.

- Consider NSAIDs, acetaminophen, or topical analgesics (***Pregnancy Only***: NSAIDS are contraindicated)
- In patients with neuropathic pain, consider gabapentin, TCAs or SNRIs
- In patients with spastic pain, consider tizanidine, baclofen or cyclobenzaprine (***Pregnancy Only***: tizanidine is NOT used)
- In patients with anxiety, consider SNRIs or sedating SSRIs (***Pregnancy Only***: consider sertraline or SNRIs)
- Consider Nitrous Oxide for labor pain (***Pregnancy Only***)

C. If opioid analgesics are needed for adequate pain control, it is appropriate to provide opioids to these patients. They will likely require higher than typical doses of opioids.[5] As with all patients on opioids, these patients should be monitored closely, and naloxone should be used if there is respiratory depression or severe oversedation. If pain control is inadequate, increase opioids, consider additional modalities, or consult pain specialists.

D. Consider neuraxial, regional, and local anesthesia when possible. Rarely, and only in consultation with specialty services, consider non-opioid adjunctive treatments like ketamine or dexmedetomidine in severe pain. ***Pregnancy Only:*** Consider regional and local anesthesia when possible. Rarely, and only in consultation with OB anesthesia, consider non-opioid adjunctive treatments like ketamine or dexmedetomidine in severe pain.

E. Avoid using mixed agonists/antagonists such as butorphanol and nalbuphine as they may cause precipitated withdrawal.

5. Manage postoperative pain

Postoperative pain in patients taking maintenance pharmacotherapy for OUD can be managed using multiple modalities, just as in patients without OUD. Patients continued on their maintenance doses of medication postoperatively have been shown to have a lower requirement for PCA-delivered opioid than those whose pharmacotherapy is discontinued.[3]

A. Continue home buprenorphine or methadone.

B. Manage similarly to routine postoperative care, however may need higher opioid dosing (see #4 above for specific suggestions).

Pregnancy Only: Consider maintaining epidural analgesia in the post-partum period in consultation with OB anesthesia.

Pregnancy Only: Only consider NSAIDs in the postpartum period

6. Preparing patients for discharge

Arrange for the patient to receive their maintenance pharmacotherapy for OUD after discharge.

A. If the patient is being discharged to a Skilled Nursing Facility, discuss the patient's need for OUD treatment with the facility to ensure the patient receives their regular medication. SNF's may need to coordinate with methadone or buprenorphine provider to determine how to provide the medication during their stay.

B. If the patient is returning to an outpatient living situation, arrange a plan with patient's buprenorphine provider or methadone clinic so that there is not a gap in care.

- If patient's home dose was decreased or split during hospitalization, dose should be returned to home dosing prior to discharge if it is safe to do so. Provider may contact consult services or patient's clinic provider to discuss re-titration.
- For methadone: call the methadone clinic 1-2 days prior to discharge to ensure that the patient is able to return to the clinic after discharge.
- For buprenorphine:
    - Ensure that the patient has enough buprenorphine or buprenorphine/naloxone at home to last until their next visit with their prescriber.
    - Hospital providers with DEA waiver to prescribe buprenorphine can write a discharge prescription for buprenorphine or buprenorphine/naloxone to last until the patient's next appointment.
    - In some hospitals, patients may return to the emergency room for daily directly observed buprenorphine dosing (not prescription)[14] for up to 3 days as a bridge to the first outpatient appointment.
    - If the patient still has acute pain requiring opioids, hospital prescribers can provide patients with additional prescriptions for opioids on discharge from the hospital, as they would for patients without OUD. A step-down approach is recommended with the goal of returning the patient to pre-hospitalization opioid requirement.[15] As with all patients, the recommendation is to generally prescribe 3 or less days of opioids for acute pain, and rarely greater than a 7 day prescription.[16] This plan should be coordinated with the patient's primary care provider and buprenorphine or methadone prescriber.

Patients on outpatient naltrexone (NOT for pregnant patients)

Naltrexone is not a first line treatment for opioid use disorders, as drop-out rates are much higher than for methadone or buprenorphine. However, it is used in patients who decline agonist therapies, and is often used in alcohol use disorder to decrease cravings. As a full opioid antagonist, naltrexone can limit the analgesic effects of opioids. Patients who have been on naltrexone and no longer have it in their system may have lower opioid tolerances than they did previously, so caution must be used. In the perioperative or acutely painful setting:

1. For elective surgeries where use of opioids is anticipated, hold oral naltrexone for 72 hours prior to presentation[17] and hold IM naltrexone for at least 30 days.
2. Hold naltrexone upon presentation for any acute pain that may require opioids.
3. If naltrexone is still in effect, pain management should center on NSAIDs, acetaminophen, ketamine, and local/regional anesthesia, or conscious sedation with non-opioids as needed.
4. If naltrexone is still in effect and opioids are necessary, high dose opioids can be used to out-compete naltrexone at the opioid receptor. The patient must be closely monitored (e.g. ICU level or pulse oximetry) to ensure that as the naltrexone wears off, oversedation does not occur.
5. If opioids are used, hold naltrexone for 3-7 days from last opioid dose.[18]

Cautions

In the vast majority of cases it is important to continue home pharmacotherapy for OUD. If unsure, please call the outpatient buprenorphine/methadone prescriber or the Substance Use Warmline. Rare situations where you should consider holding medications include:

1. Severe sedation or respiratory depression—if not sedated but receiving additional sedating medications, monitor closely but do not withhold OUD medications
2. QTc>500 on methadone—in perioperative period, acute illness and new medications can change QTc and elevate risk. Consider decreasing dose of QTc prolonging medications, including methadone if QTc is prolonged.
3. Newly decompensated liver disease
4. New medications that increase or decrease methadone levels—monitor for withdrawal or sedation (see below)

Drug Interactions

Some common drugs may have pharmacokinetic or synergistic interactions with methadone. The methadone dose may require adjustment. Please consult with clinical pharmacist for more complete list of interactions.

- Drugs that may INCREASE methadone concentration or effect (okay to use, but monitor the patient): azole antifungals, some SSRI's, tricyclic antidepressants, eryrthromycin, ciprofloxacin, quetiapine
- Drugs that may DECREASE methadone concentration/effect: rifampin, many antiretrovirals, phenytoin, carbamezapine

****CAUTION**** co-administration of CNS depressants such as benzodiazepines may lead to increased sedation and respiratory depression, while co-administration of naltrexone or buprenorphine may lead to precipitated withdrawal

Breastfeeding Guidelines:

Methadone or buprenorphine maintenance for opioid use disorder is not a contraindication for breastfeeding. Patients taking opioid agonist therapies for opioid use disorder who are not currently abusing other substances and who wish to breastfeed should be encouraged to regardless of the dose. Current evidence shows that breastfeeding while on methadone or buprenororphine is beneficial to neonates with neonatal abstinence syndrome (NAS). Neonates receiving breast milk from these patients experience lower NAS scores, require less pharmacologic treatment such as morphine, and have shorter lengths of hospital stay.

Consult Contacts:

UCSF Substance Use Warm-line: 855.300.3595 or https://tinyurl.com/yd4ymyx6 (available M-F, between 10 a.m. and 6 p.m EST)

References:

1. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: Author.
2. Drug Enforcement Administration/Department of Justice, 2017, §1306.07
3. Macintyre, P. E., Russell, R. A., Usher, K. A. N., Gaughwin, M., & Huxtable, C. A. (2013). Pain relief and opioid requirements in the first 24 hours after surgery in patients taking buprenorphine and methadone opioid substitution therapy. *Anaesthesia and intensive care*, *41*(2), 222.
4. Oifa, S., Sydoruk, T., White, I., Ekstein, M. P., Marouani, N., Chazan, S., ... & Weinbroum, A. A. (2009). Effects of intravenous patient-controlled analgesia with buprenorphine and morphine alone and in combination during the first 12 postoperative hours: a randomized, double-blind, four-arm trial in adults undergoing abdominal surgery. *Clinical therapeutics*, *31*(3), 527-541.
5. Sen, S., Arulkumar, S., Cornett, E. M., Gayle, J. A., Flower, R. R., Fox, C. J., & Kaye, A. D. (2016). New pain management options for the surgical patient on methadone and buprenorphine. *Current pain and headache reports*, *20*(3), 1-8.
6. Mercadante, S˙, Villari, P., Ferrera, P., Porzio, G., Aielli, F., Verna, L., Casuccio, A. (2006). Safety and effectiveness of intravenous morphine for episodic breakthrough pain in patients receiving transdermal buprenorphine. *Journal of pain symptom management, 32(2),* 175-179.
7. Jones, HE., O'Grady, K., Dahne, J., Johnson, R., Lemoine, L., Milio, L., Ordean, A., Selby, P. (2009). Management of acute postpartum pain in patients maintained on methadone or buprenorphine during pregnancy. *American journal of drug and alcohol abuse, 35(3),* 151-156.
8. Sigmon , S., Dunn, K., Saulsgiver, K., Patrick, M., Badger, G., Heil, S., Brooklyn, J., Higgins, S. (2013). A randomized, double-blind evaluation of buprenorphine taper duration in primary prescription opioid abusers. *JAMA Psychiatry*, 70(12):1347-54.
9. Mitra, S. & Sinatra, R. (2004). Perioperative management of acute pain in the opioid-dependent patient. *Anesthesiology, 101(1)*, 212-27.
10. Kornfield, H. & Manfredi, L. (2010). Effectiveness of full agonist opioids in patients stabilized on buprenorphine undergoing major surgery: a case series. *American journal of therapeutics 17(5),* 523-528.
11. Wesson, D. R., & Ling, W. (2003). The clinical opiate withdrawal scale (COWS). *Journal of psychoactive drugs*, *35*(2), 253-259.
12. Alford, D. P., Compton, P., & Samet, J. H. (2006). Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Annals of Internal Medicine*, *144*(2), 127-134.
13. Alizadeh, S., Mahmoudi, G. A., Solhi, H., Sadeghi-Sedeh, B., Behzadi, R., & Kazemifar, A. M. (2015). Post-operative Analgesia in Opioid Dependent Patients: Comparison of Intravenous Morphine and Sublingual Buprenorphine. *Addiction & health*, *7*(1-2), 60
14. Substance Abuse and Mental Health Services Administration. (2016). *Special Circumstances for Providing Buprenorphine.* Retrieved from https://www.samhsa.gov/medication-assisted-treatment/legislation-regulations-guidelines/special-circumstances-providing-buprenorphine.
15. McQuay H. Relief of chronic non-malignant pain. 2006:1–27.
16. Centers For Disease Control and Prevention. (2017). *CDC Guideline for Prescribing Opioids for Chronic Pain.* Retrieved from https://www.cdc.gov/drugoverdose/prescribing/guideline.html
17. Vickers, A. & Jolly, A. (2006). Naltrexone and problems in pain management. British medical journal*, 332(7534),* 132-133.
18. World Health Organization. (2009). *Guidelines for the Psychosocially Assisted Pharmacologic Treatment of Opioid Dependence.* Retrieved from http://www.who.int/substance_abuse/publications/opioid_dependence_guidelines.pdf

PATIENT NAME:	DATE OF ASSESSMENT:
PATIENT DATE OF BIRTH:	MEDICAL RECORD NUMBER:

Clinical Opioid Withdrawal Score (COWS)

For each item, write in the number that best describes the patient's signs or symptom. Rate only the apparent relationship to opiate withdrawal. *For example: If heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.*

Enter scores at time zero, 30 minutes after first dose, 2 hours after first dose, etc.	*Time:*	*Time:*	*Time:*	*Time:*
Resting Pulse Rate: Record beats per minute *after patient is sitting or lying down for one minute* • 0 - pulse rate 80 or below • 1 - pulse rate 81–100 • 2 - pulse rate 101–120 • 4 - pulse rate greater than 120				
Sweating: *Over past ½ hour not accounted for by room temperature or activity* • 0 - no chills or flushing • 1 - subjective chills or flushing • 2 - flushed or observable moistness on face • 3 - beads of sweat on brow or face • 4 - sweat streaming off face				
Restlessness: *Observation during assessment* • 0 - able to sit still • 1 - reports difficulty sitting still, but is able to do so • 3 - frequent shifting or extraneous movement of legs/arms • 5 - unable to sit still for more than a few seconds				
Pupil size • 0 - pupils pinned or normal size for light • 1 - pupils possibly larger than normal for light • 2 - pupils moderately dilated • 5 - pupils dilated that only rim of the iris is visible				
Bone or joint aches: *If patient was having pain previously, only the additional component attributed to opiate withdrawal is scored* • 0 - not present • 1 - mild/diffuse discomfort • 2 - patient reports severe diffuse aching of joints/muscles • 4 - patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing: *Not accounted for by cold symptoms or allergy* • 0 - none present • 1 - nasal stuffiness or unusually moist eyes • 2 - nose running or tearing • 4 - nose constantly running or tears streaming down cheeks				
GI upset: *Over last ½ hour* • 0 - no GI symptoms • 1 - stomach cramps • 2 - nausea or loose stool • 3 - vomiting or diarrhea • 5 - multiple episodes of diarrhea or vomiting				
Tremor: *Observation of outstretched hands* • 0 - no tremor • 1 - tremor can be felt, but not observed • 2 - slight tremor observable • 4 - gross tremor or muscle twitching				
Yawning: *Observation during assessment* • 0 - no yawning • 1 - yawning once or twice during assessment • 2 - yawning three or more times during assessment • 4 - yawning several times/minute				
Anxiety or irritability • 0 - none • 1 - patient reports increasing irritability or anxiousness • 2 - patient obviously irritable or anxious • 4 - patient so irritable or anxious that participation in the assessment is difficult				
Gooseflesh skin • 0 - skin is smooth • 3 - piloerrection of skin can be felt or hairs standing up on arms • 5 - prominent piloerrection				
5—12 = mild; *13—24 = moderate;* *25—36 = moderately severe;* *> 36 = severe withdrawal* **TOTAL** OBSERVER INITIALS				

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