How to Treat Opioid Use Disorder in the General Hospital Setting

Learning Objectives:

1) Diagnose Opioid Use Disorder, Opioid Intoxication, and Opioid Withdrawal
2) Determine whether a patient would benefit from Medication Assisted Treatment (MAT) initiation
3) Incorporate special considerations, metabolic profile, and any contraindications when choosing MAT

Step 1: Determine if Patient is in Acute Opioid Intoxication or Withdrawal (Table 1)

- Prioritize clinical stabilization of acute intoxication or withdrawal prior to doing an assessment for Opioid Use Disorder (see Table 1 for diagnosis of intoxication or withdrawal).
- If patient in active withdrawal, assess severity of withdrawal with clinical instruments such as the Clinical Opiate Withdrawal Scale (COWS), initiate medication-assisted management to ease withdrawal symptoms (see Step 4 and 5).
- If patient is acutely intoxicated:
    - Do not initiate treatment of MAT until patient more stable clinically. Monitor patient for onset of withdrawal symptoms.
    - Consider administration of naloxone, an opioid antagonist, if there are concerns of opioid overdose (see Table 1).

Table 1: Diagnoses of Opioid Intoxication and Opioid Withdrawal (Integrating DSM5 Criteria)

Opioid Intoxication	Opioid Withdrawal
A. Recent use of opioids B. Clinical level behavioral and psychological alterations become apparent during or shortly after use of an opioid. C. Pupils will become constricted and will be accompanied by one of the following during or shortly after use of an opioid (indicative of decreased responsiveness): 1. Somnolence or loss of consciousness 2. Speech articulation will be slurred. 3. There will be deficits in attention or memory. • Urine toxicology is positive for most opioids such as morphine, heroin, codeine, oxycodone, fentanyl, for 12 to 36 hours after use. Methadone and buprenorphine will not be detected in usual urine opioid tests, and they must be specifically tested. • Administer intranasal or initiate IV naloxone at 0.4 mg to 0.8 mg IV if patient has signs of overdose, including diminished consciousness w/difficulty	A. Sudden cessation or reduction of normal opioid dose, OR opioid antagonist given after opioid use B. Three (or more) of the following, developing within minutes to several days after Criterion A: • dysphoric moods • nausea or vomiting • muscle aches • lacrimation or rhinorrhea • pupillary dilation, • piloerection or sweating • diarrhea • yawning • insomnia • autonomic hyperactivity (tachypnea, hyperreflexia, tachycardia, sweating, hypertension, hyperthermia) • The COWS can be used to determine level of withdrawal severity. Score is between 0 to 47 • mild withdrawal (5 to 12) • moderate withdrawal (13 to 24) • moderately severe withdrawal (25 to 36) • severe withdrawal (greater than 37) C. The symptoms in Criterion B cause clinically

arousing, hypopnea or apnea, choking/gurgling, cold/clammy/discolored skin, poor muscle tone.	significant distress or impairment in social, occupational, or other important areas of functioning.
D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.	

Step 2: Familiarize Oneself with the Diagnosis of Opioid Use Disorder (OUD)

- Diagnosis of Opioid Use Disorder in the inpatient setting is useful for linkage to ongoing treatment in the outpatient setting and engaging a patient with Medication-assisted Treatment (MAT). Initiating MAT in the inpatient setting has been shown in studies to improve relapse prevention.
- The DSM 5 defines Opioid Use Disorder as a problematic pattern of opioid use leading to problems or distress, with at least two of the following occurring within a 12-month period:
    - Opioids are often taken in larger amounts or over a longer period than was intended.
    - There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
    - A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
    - Craving, or a strong desire or urge to use opioids.
    - Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
    - Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
    - Important social, occupational, or recreational activities are given up or reduced because of opioid use.
    - Recurrent opioid use in situations in which it is physically hazardous.
    - Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
    - Tolerance, as defined by either of the following:
        - A need for markedly increased amounts of opioids to achieve intoxication or desired effect
        - A markedly diminished effect with continued use of the same amount of an opioid (Note: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.)
    - Withdrawal, as manifested by either of the following:
        - The characteristic opioid withdrawal syndrome
        - Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms. (Note: This criterion is not considered to be met for those individuals taking opioids solely under appropriate medical supervision.)
- Severity: mild = 2–3 symptoms; moderate = 4–5 symptoms; severe = 6 or more symptoms

Step 3: Assess the Patient for OUD Treatment

- Distinguish whether a patient has OUD using diagnostic criteria above versus whether the patient is appropriately using prescribed opioid prescriptions.

    - Be aware of any implicit biases you may be experiencing in assuming a patient has opioid use disorder, and be open to understanding their experience of opioid use.
    - Note that physical tolerance does not equal psychological tolerance and opioid misuse.
- An assessment for OUD Treatment should include:
    - A medical and psychiatric history, a full substance use history, and an evaluation of family and psychosocial supports
    - Frequency of opioid use and route of administration (e.g., oral, intravenous, intranasal) can help gauge likelihood of severe withdrawal or possible infections, which will influence further testing.
    - Prescription opioid use history checked through the state's Prescription Drug Monitoring Program (PDMP), where available, to detect unreported use of other controlled medications, such as benzodiazepines or other opioid medications, that may interact adversely with the treatment medications
    - Previous attempts to stop using opioids, type of medication and non-medication strategies used, and response to treatments
- Review patient labs as part of the assessment:
    - Test urine for opioids, alcohol, and other drugs, such as benzodiazepines.
    - Conduct a complete blood count (especially if any signs of bacterial infection such as endocarditis).
    - Assess for hepatitis B/C and HIV for those who inject intravenously.
    - Offer vaccination for patients who inject drugs and have negative hepatitis B serology
    - Consider testing for syphilis and tuberculosis if indicated.
    - Assess liver and kidney function with liver enzyme, serum bilirubin, and serum creatinine blood tests to adjust MAT dosing or defer from initiation (in case of liver failure/significant cirrhosis).
    - Pregnancy testing for women of reproductive age

Step 4: Determine Best MAT Option for Patient and Initiate Treatment (see Table 2)

- General Considerations for MAT
    - Buprenorphine and naltrexone can block the effects of other opioids taken concurrently and thus can induce opioid withdrawal.
    - Naltrexone should not be given until withdrawal is complete, and buprenorphine should be initiated after patient is in mild to moderate withdrawal (as per COWs scale).
    - Methadone and buprenorphine can be used for medically supervised withdrawal and continued for maintenance treatment.
    - All three medications have evidence for reducing cravings.
    - Naltrexone should not be prescribed in pregnancy.
- Consider structural disparities for vulnerable populations when initiating MAT
    - Studies demonstrate existing stigma that medical providers have towards patients with OUDs and towards MAT. Be aware of your own implicit biases and colleagues' biases. Initiate conversations with colleagues if you notice unwarranted obstacles in place for initiating MAT for a patient.
    - Be aware of existing structural disparities that impact access to MAT for structurally vulnerable populations, including people of color, LGBTQ+ populations, and different

age groups**.** Use knowledge of these disparities and practice cultural humility when assessing a patient and when offering specific MAT.
    - Example 1: Despite similar rates of OUD, Black American patients are less likely to be offered MAT, and even when offered, are much less likely to receive buprenorphine prescription than their White American counterparts (even in a study controlling for age, sex, and type of payment).
    - Example 2: LBGTQ patients have special medical considerations in MAT initiation including whether they are taking Prep for exposure prophylaxis, whether they may be living with HIV and taking antiretroviral therapy (ART), and whether they are on hormone therapy. Interactions with these medications should be assessed and conversations around appropriate clinical follow up are important.
  - Engage patient with open, nonjudgmental questions around their beliefs around MAT. Patients may have their own biases around MAT and OUD; if discovered, offer nonjudgmental psychoeducation while validating their concerns.
  - Make sure to offer interpreters for conversations if needed for evaluation and MAT discussion.
  - Assess for structural vulnerabilities that may impact a patient's access to ongoing MAT and incorporate those obstacles when pursuing resources for a patient after discharge.
  - When initiating MAT, coordinate with case management to connect patients with appropriate level of continued OUD treatment services on discharge that incorporates patient cultural, language, and social preferences.
  - Be aware of limitations in different MAT choices.
    - Methadone is only prescribed in structured opioid treatment programs (OTPs).
    - In OTPs, patients initially must be seen daily; over time they may be able to get take-home doses. OTPs can be useful for patients requiring structure and easy access to substance use counseling; however, they can be harder to access for patients living in rural areas and for those with limited transportation options due to socioeconomic factors.
    - Buprenorphine can be induced faster than methadone and can be more accessible if there are certified providers in patient's area. It is available in OTPs and office settings, and no longer requires a waiver for prescribing.
- Whether or not MAT is initiated, offer supportive measures to ameliorate symptoms of opioid withdrawal, including anxiety, insomnia, nausea/vomiting, diarrhea, pain, and autonomic symptoms (see Table 3).

Table 2: MAT Options and Initiation for Opioid Use Disorder

Medication	Methadone	Buprenorphine	Naltrexone
Mechanism of Action	Mu opioid receptor agonist Weak NMDA agonist	Partial mu opioid receptor agonist	Mu opioid receptor antagonist
Uses	Medically supervised withdrawal, maintenance MAT	Medically supervised withdrawal, maintenance MAT	Prevention of relapse to opioid misuse, following medically supervised withdrawal
Formulations and Typical Dose range	Oral: 20-200 mg daily	Sublingual tablet: 2-32 mg daily Sublingual film, tablet (in combination with naloxone): 2/0.5-32/8 mg daily Subcutaneous injection and Subcutaneous implant – not typically started in hospital	Oral: 50 mg daily Intramuscular injection: (Vivitrol) 380 mg every 28 days
Possible Adverse Effects	Most common: Constipation, sedation, hyperhidrosis, dizziness, nausea and vomiting Concerns: respiratory depression, QT prolongation, sexual dysfunction, orthostatic hypotension and syncope, misuse potential, neonatal abstinence syndrome As a full opioid agonist, risk of overdose symptoms if titrated too quickly. Check drug interactions given Cy3A4 metabolism.	Most common: Constipation, nausea and vomiting, hyperhidrosis, insomnia, blurred vision, Concerns: peripheral edema, respiratory depression (particularly combined with benzodiazepines or other CNS depressants), misuse potential, neonatal abstinence syndrome Implant: Nerve damage during insertion/removal, accidental overdose, or misuse if extruded, local migration or protrusion Subcutaneous Injection: Injection site itching or pain,	Most common: Nausea and vomiting, anxiety, insomnia, headache elevated LFTs, muscle and joint cramps Concerns: precipitated opioid withdrawal, hepatotoxicity, depression, suicidality, anorexia /decreased appetite, or other appetite disorders Intramuscular: Pain, swelling, induration, insomnia
Patient already on MAT admitted to hospital	Verify outpatient methadone dose with OTP program, continue if verified unless medically contraindicated	Verify outpatient dose, consider transition to methadone if patient requiring acute pain management/sedation with opioids, otherwise continue unless medically contraindicated	Discontinue if patient will require opioid medication for pain/sedation, monitor for withdrawal precipitation
Initiation	"Start low go slow" Day 1: 10 to 20 mg total, MDD 30 mg Day 2+. Increase slowly by 5 mg every few days in response to symptoms of opioid withdrawal and level of sedation at the peak plasma level 2 to 4 hours after dosing. Stabilization after 4-5 weeks	Initiate while patient is in mild-moderate withdrawal. Day 1: start at 2-4 mg buprenorphine (tab, film), MDD 8mg. Day 2-3: Increase additional 2 to 4 mg every 2 hours up to approximately a 16 mg total daily dose to treat continuing opioid withdrawal. Stabilization after several days	Patients have completed withdrawal and are opioid free for 7 days (short acting) and up to 14 days (long acting). Better evidence for injection vs daily oral

Table 4: Common Supportive Measures for Symptoms of Opioid Withdrawal

Symptoms	Medication	Dosing	Notes
Autonomic Symptoms	Clonidine	Day 1: 0.1–0.2 mg every 4–6 h with a maximum dose of 1.2 mg Day 2 onward: taper by 0.1–0.2 mg per day Dose as needed if patient on MAT	▪ May also treat anxiety, restlessness, pain ▪ IV administration and 7-day patch available ▪ Monitor for hypotension, sedation
	Lofexidine	Day 1: 0.54–0.72 mg every 6 h (total daily dose 2.16–2.88 mg) Day 2 onward: decrease each dose by 0.18 mg every 1–2 days Dose as needed if patient on MAT	▪ No generic in US so can limit accessibility ▪ Monitor for hypotension, sedation ▪ Dose-dependent QT interval prolongation; use with caution (eg, monitor baseline and post-dose electrocardiogram)
Anxiety, irritability, restlessness	Diphenhydramine	50 to 100 mg orally every 4 to 6 hours as needed (maximum 300 mg daily)	▪ May also treat nausea, insomnia ▪ Use reduced dose in hepatic impairment ▪ IV and IM administration available
	Hydroxyzine	25 to 100 mg orally every 6 to 8 hours as needed (maximum 400 mg daily)	▪ May also treat lacrimation, rhinorrhea, insomnia ▪ Use reduced dose (50%) in renal or hepatic impairment ▪ IM and solution administration available
Abdominal cramping	Dicyclomine	10 to 20 mg orally every 6 to 8 hours as needed (maximum 160 mg daily)	▪ IM administration available (lower doses are used) ▪ Use with caution and reduce dose in renal or hepatic impairment
Diarrhea	Bismuth	~524 mg orally every 30 to 60 minutes as needed (up to 4200 mg daily)	▪ Monitor for dehydration and maintain fluid levels with oral and/or IV hydration
	Loperamide	4 mg orally followed by 2 mg after each loose stool (maximum 16 mg daily)	
Nausea/vomiting	Ondansetron	4 to 8 mg orally or IV every 12 hours as needed (maximum 16 mg/day)	▪ Monitor for dehydration and maintain fluid levels with oral and/or IV hydration ▪ Dose-dependent QT interval prolongation; use with caution (eg, monitor baseline and post-dose electrocardiogram)

			▪ Use caution and reduced dose (50%) in severe hepatic impairment
	Prochlorperazine	5 to 10 mg orally three times daily before meals or every six hours as needed (maximum 40 mg/day)	▪ Monitor for dehydration and maintain fluid levels with oral and/or IV hydration ▪ Use with caution in mild to moderate hepatic impairment; avoid in severe hepatic impairment ▪ IV and rectal administration available
	Promethazine	12.5 to 25 mg orally every 4 to 6 hours as needed (maximum 50 mg/day)	▪ Monitor for dehydration and maintain fluid levels with oral and/or IV hydration ▪ Use with caution in mild to moderate hepatic impairment; avoid in severe hepatic impairment ▪ IM and rectal administration available
Insomnia	Trazodone	25 to 100 mg orally at bedtime	▪ May titrate nightly up to 300 mg at bedtime if needed ▪ Use with caution in severe hepatic or renal impairment
	Doxepin	3 to 25 mg orally at bedtime	▪ Use with caution and reduce dose in severe hepatic impairment
Muscle aches joint pain, headache	Ibuprofen	400 mg orally every 4 to 6 hours as needed (maximum 2400 mg daily)	▪ Patient should be well hydrated and without significant kidney disease ▪ Use with caution in mild to moderate hepatic or renal impairment ▪ Avoid all NSAIDs in severe renal impairment or cirrhosis; avoid in patients on lithium
	Acetaminophen	650 to 1000 mg orally every 4 to 6 hours as needed (maximum 4000 mg daily, 3000 mg for age >65)	▪ Appropriate analgesic for most patients ▪ Use reduced dose (ie, 2000 mg daily) or avoid in hepatic impairment or if malnourished

References

1. Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition). 2018. Contract No.: NIH Publication No. 12–4180.
2. American Psychiatric Association. Substance-Related and Addictive Disorders. Diagnostic and Statistical Manual of Mental Disorders (5th Edition). DSM Library. 5th ed. Arlington, VA: American Psychiatric Association; 2013.
3. Avery J, Taylor KE. Calculated Decisions: Clinical opiate withdrawal scale (COWS). Emerg Med Pract. 2019;21(11):CD5-CD6.
4. Button D, Hartley J, Robbins J, Levander XA, Smith NJ, Englander H. Low-dose Buprenorphine Initiation in Hospitalized Adults With Opioid Use Disorder: A Retrospective Cohort Analysis. J Addict Med. 2022;16(2):e105-e11.
5. Girouard MP, Goldhammer H, Keuroghlian AS. Understanding and treating opioid use disorders in lesbian, gay, bisexual, transgender, and queer populations. Subst Abus. 2019;40(3):335-9.
6. Hansen H, Siegel C, Wanderling J, DiRocco D. Buprenorphine and methadone treatment for opioid dependence by income, ethnicity and race of neighborhoods in New York City. Drug and Alcohol Dependence. 2016;164:14-21.
7. Lagisetty PA, Ross R, Bohnert A, Clay M, Maust DT. Buprenorphine Treatment Divide by Race/Ethnicity and Payment. JAMA Psychiatry. 2019;76(9):979-81.
8. Mackey K, Veazie S, Anderson J, Bourne D, Peterson K. Barriers and Facilitators to the Use of Medications for Opioid Use Disorder: a Rapid Review. J Gen Intern Med. 2020;35(Suppl 3):954-63.
9. Madras BK, Ahmad NJ, Wen J, Sharfstein JS. Improving Access to Evidence-Based Medical Treatment for Opioid Use Disorder: Strategies to Address Key Barriers within the Treatment System. NAM Perspect. 2020;2020.
10. Reif S, Acevedo A, Garnick DW, Fullerton CA. Reducing Behavioral Health Inpatient Readmissions for People With Substance Use Disorders: Do Follow-Up Services Matter? Psychiatric Services. 2017;68(8):810-8.
11. Smith K, Wang M, Abdukalikov R, McAullife A, Whitesell D, Richard J, et al. Pain Management Considerations in Patients With Opioid Use Disorder Requiring Critical Care. The Journal of Clinical Pharmacology. 2022;62(4):449-62.
12. Srivastava AB, Mariani JJ, Levin FR. New directions in the treatment of opioid withdrawal. Lancet. 2020;395(10241):1938-48.
13. Substance Use and Mental Health Services Administration. Medications for Opioid Use Disorder. For Healthcare and Addiction Professionals, Policymakers, Patients, and Families. SAMHSA; Treatment Initiation Protocol 63, 2021. p. 1-382.
14. Torres-Lockhart KE, Lu TY, Weimer MB, Stein MR, Cunningham CO. Clinical Management of Opioid Withdrawal. Addiction. 2022;117(9):2540-50.
15. Wang S. Historical Review: Opiate Addiction and Opioid Receptors. Cell Transplant. 2019;28(3):233-8.
16. Weinstein ZM, Englander H. Reachable Moment: Hospital-Based Interventions. In: Wakeman SE, Rich JD, editors. Treating Opioid Use Disorder in General Medical Settings. Cham: Springer International Publishing; 2021. p. 43-56.