KEY ADVANCES
PRACTICE ADVANCE

Medications for Opioid Use Disorder

New August 2025

Why is this topic important?
It is estimated that there are more than 81,000 deaths in the United States annually from drug overdoses involving opioids.(1) Medications for opioid use disorder (MOUD) are an effective treatment that can be started in the emergency department (ED) to reduce opioid-related and all-cause mortality in patients with opioid use disorder (OUD).(2)

How will this change my clinical practice?
Whenever possible, patients with OUD who present to the ED, whether with an opioid-related concern or not, should be offered MOUD and connected to follow-up care.

Synopsis Focus Points:

1. **Initiate MOUD in the ED to reduce opioid-related and all-cause mortality in patients with OUD.**
2. **Use the Clinical Opiate Withdrawal Scale (COWS) score to determine when a patient is in active withdrawal and can be safely started on buprenorphine (BUP), recognizing that patients with a COWS score < 8 are at higher risk of precipitated opioid withdrawal.**
3. **MOUD is most effective in combination with counseling and behavioral therapies.**

Background:

- In 2022, an estimated 8.9 million individuals in the United States misused opioids (3), resulting in more than 81,000 overdose-related deaths.(1)
- One study found that 5.5% of patients treated for opioid overdose ultimately die within 1 year, with the greatest risk (up to 20%) being in the first days to 1 month after their initial ED visit for overdose.(4)
- Craving for the euphoria associated with opioid use and, conversely, the desire to avoid withdrawal are powerful drivers to continued opioid use.
- Although naloxone, a short-acting opioid antagonist, can be lifesaving in the setting of overdose, it can precipitate significant acute withdrawal in patients who are opioid dependent. It is not considered MOUD but rather a rescue strategy.
- Opioid withdrawal is often measured using COWS, which includes a combination of objective and subjective assessments for opioid withdrawal findings. Use of COWS is effective in guiding opioid withdrawal management (see Table 1)

- Although simple symptomatic relief of acute withdrawal (e.g., clonidine and ondansetron) may be effective in the short term, it does not reduce craving, address the effects of long-term withdrawal, or reduce the risk of mortality associated with OUD.
- The greatest likelihood for success and recovery for individuals with OUD comes when MOUD is integrated into holistic addiction treatment programs designed to work in combination with counseling or other behavioral therapies.(5,6)

I. MOUD for OUD:

- MOUD refers to the use of specific US Food and Drug Administration (FDA)–approved medications to treat OUD, beyond those intended for simple symptomatic support.
- MOUD helps reduce cravings and mitigates short- and long-term withdrawal effects.
- Despite MOUD's benefit in reducing opioid-related and all-cause mortality in individuals with OUD (7), only 22% of patients with OUD are receiving MOUD.(8)
- As of 2023, a Drug Enforcement Administration (DEA) X-waiver is no longer needed to prescribe any form of MOUD—only an active DEA registration is required. However, in some states, prescribing ongoing therapy outside of the ED may be subject to additional regulations.

II. FDA-Approved Medications:

The following 3 individual FDA-approved medications have been used for short- and long-term management of OUD: methadone (MTD), BUP, and naltrexone (NTX) (see Table 2).

MTD:

- MTD is a synthetic opioid that acts as a full mu-opioid receptor (MOR) agonist. It occupies and stimulates the MOR, reducing craving and preventing withdrawal, while producing limited euphoria.
- Because it is generally administered orally, MTD has a slow onset of effect, causing less opioid-related euphoria and reward. It has a long half-life, resulting in clinical mitigation of withdrawal that lasts at least 1 day. Both aspects mitigate its potential for misuse.
- Special considerations when choosing MTD for MOUD include:
    - MTD may increase a patient's QT interval, placing patients at risk for life-threatening cardiac arrythmias. Thus, MTD should be avoided in patients with a prolonged QTc interval and should be used with caution in patients taking other QTc-prolonging medications.
    - MTD has a variable half-life and generally requires daily dosing. Thus, in some patients with particularly long half-lives, serum levels can unintentionally build up with repeat dosing, risking oversedation and respiratory depression. This is of greatest concern during the first 2 weeks of dosing, often called the induction period. It is not a concern with a single, appropriate dose, as is typically administered in the ED.
    - As a full MOR agonist, MTD does not have a "ceiling effect," meaning increases in the dose result in increased MOR activation. Thus, while tolerance can develop over time, high doses or rapid dose increases can cause oversedation and respiratory depression.
    - Despite its limited euphoric effect, MTD is still subject to misuse and diversion, increasing the risk of overdose and other adverse outcomes.
    - Due to the significant risk of *respiratory depression*—in addition to oversedation, overdose, and misuse/diversion—long-term dosing of MTD must be done under close supervision in the highly regulated setting of an outpatient treatment program (OTP).
    - No more than 72 hours of bridge dosing (3 doses) can be dispensed from the ED to facilitate the patient's initial linkage to an outpatient treatment clinic.

BUP:

- BUP is a synthetic opioid that acts as a partial MOR agonist. As such, it occupies the MOR but does not fully stimulate, resulting in reduced opioid-related clinical effects. Due to its high receptor affinity, BUP blocks and/or outcompetes full agonist opioids from occupying and stimulating the MOR.
- Like MTD, BUP has a slow onset of effect and a long duration of action, with similar benefits.
- As a partial agonist, BUP has a ceiling effect at the MOR, whereby, after a certain dose, increasing the dose further does not result in more receptor activation. As such, there is a marked reduction in the risk of respiratory depression, even in patients without opioid tolerance.
- Special considerations when choosing BUP for MOUD include:
    - As a partial agonist, administering BUP to individuals who are opioid dependent with recent opioid use can precipitate opioid withdrawal, which can be severe. Similarly, those in mild withdrawal (COWS score < 8) have an increased risk of developing precipitated withdrawal if the BUP dosing strategy is not optimized. Thus, it is recommended that, without additional training or support, BUP only be used for patients in active withdrawal who have a COWS score ≥ 8.
    - Because of its ceiling effect, BUP is safe for home use and does not require the same degree of supervised utilization as MTD.
    - BUP is associated with a lower risk of adverse neonatal outcomes than MTD, making it the preferred MOUD during pregnancy.(9)

NTX:

- NTX is a long-acting, synthetic MOR antagonist that acts to completely block receptor activity. It has a high affinity for the MOR and can precipitate withdrawal in opioid-dependent patients who still have circulating (i.e., systemic) opioid agonists.
- NTX's main role in MOUD is preventing relapse after complete and sustained withdrawal from opioid use and has a limited to no role in the ED setting.

III. OUD Management in the ED and MOUD Programs:

- Emergency physicians (EPs) should be comfortable treating all aspects of OUD, from acute overdose and withdrawal to management of MOUD and referral to treatment programs.
- EPs use of MOUD is a critical aspect of treatment initiation and leverages a "no wrong door" approach and provides "treatment on demand," whether the ED visit is OUD-related or not.
- Although studies suggest there may be greater treatment retention with MTD, there are no clear data to support recommending one MOUD over another.(6,10,11) Medication selection should be based on the special considerations above and social and practical circumstances that may influence treatment and compliance.
- EPs' use of MOUD is most successful when it is part of holistic addiction treatment programs and coordinated with outpatient treatment clinics.
- Example programs include:
    - Methadone Bridge to Treatment QuickStart
    - BUP Bridge to Treatment QuickStart

Table 1. COWS Score*

Signs or Symptoms	Score
Resting Pulse Rate Measured while patient resting for 1 minute	0 = ≤ 80 beats/min 1 = 81-100 beats/min 2 = 101-120 beats/min 4 = > 120 beats/min
Sweating Not accounted for by patient activity or room temperature	0 = no reports of chills or flushing 1 = subjective report of chills or flushing 2 = flushed or 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 = pinned or normal for room light 1 = possible larger than normal 2 = moderately dilated 5 = only rim of the iris is visible
Bone or Joint Pain Not associated with injury or chronic pain	0 = not present 1 = mild diffuse discomfort 2 = severe diffuse aching 4 = rubbing joints and muscles due to pain
Rhinorrhea or Lacrimation	0 = not present 1 = nasal stuffiness or unusually moist eyes 2 = rhinorrhea or lacrimation present 4 = constant rhinorrhea or tears running down face
Gastrointestinal Upset In past half hour	0 = no gastrointestinal symptoms 1 = stomach cramps 2 = nausea or loose stool 3 = vomiting or diarrhea 5 = multiple episodes of vomiting or diarrhea
Tremor	0 = no tremor 1 = tremor felt but not observed 2 = slight observable tremor 4 = gross tremor
Yawning	0 = no yawning 1 = once or twice 2 = 3 or more times 4 = several times per minute
Anxiety/irritability	0 = none 1 = patient reported 2 = obvious 4 = severe enough to interfere with assessment
Piloerection	0 = skin is smooth 3 = piloerection can be felt or hairs standing up on arms 5 = prominent piloerection

*5-12 = mild, 13-24 = moderate, 25-36 = moderately severe, 36+ = severe.

Table 2. MOUD Chart

MOUD/Withdrawal					
Medication	**Mechanism of Action**	**Use**	**Dose**	**Duration**	**Adverse Effects/Comments**
BUP	Partial MOR agonist	Treatment of OUD; prevention and treatment of opioid withdrawal	Dosing strategies vary*: For COWS score ≥ 8, consider 4-16 mg SL. A second dose may be given up to a maximum dose of 24 mg SL. For COWS score < 4 consider 0.5-1 mg (microdosing)*.	Up to 24 h	Potential for misuse Gastrointestinal upset Precipitated withdrawal Respiratory depression
MTD	Full MOR agonist	Treatment of OUD; prevention and treatment of opioid withdrawal	Typical ED doses are 10-20 mg PO or IM; with repeat doses up to 40 mg maximum in a 24-h period; maintenance doses typically range from 60-120 mg/d, not typically used in the ED, even in patients already in an OTP.	24-36 h	Potential for misuse Respiratory depression Hypotension QT prolongation Serotonin syndrome

IM, intramuscular; PO, per os; SL, sublingual.

***** For complicated cases discussion with a medical toxicologist or addiction medicine physician may be warranted.

References:

1. Hébert AH, Hill AL. Impact of opioid overdoses on US life expectancy and years of life lost, by demographic group and stimulant co-involvement: a mortality data analysis from 2019 to 2022. *Lancet Reg Health Am.* 2024;36:100813.
2. Hawk K, Hoppe J, Ketcham E, et al. Consensus recommendations on the treatment of opioid use disorder in the emergency department. *Ann Emerg Med.* 2021;78(3):434-442.
3. Substance Abuse and Mental Health Services Administration. *Key Substance Use and Mental Health Indicators in the United States: Results from the 2022 National Survey on Drug Use and Health.* Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2023. Accessed May 2, 2025. Available at: https://www.samhsa.gov/data/sites/default/files/reports/rpt42731/2022-nsduh-nnr.pdf
4. Weiner SG, Baker O, Bernson D, et al. One-year mortality of patients after emergency department treatment for nonfatal opioid overdose. *Ann Emerg Med.* 2020;75(1):13-17.
5. Wakeman SE, Larochelle MR, Ameli O, et al. Comparative effectiveness of different treatment pathways for opioid use disorder. *JAMA Netw Open.* 2020;3(2):e1920622. Erratum in: *JAMA Netw Open.* 2024;7(5):e2419798.
6. American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Opioids; Hatten BW, Cantrill SV, Dubin JS, et al. Clinical policy: critical issues related to opioids in adult patients presenting to the emergency department. *Ann Emerg Med.* 2020;76(3):e13-e39.
7. Sordo L, Barrio G, Bravo MJ, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ.* 2017;357:j1550.
8. Jones CM, Han B, Baldwin GT, et al. Use of medication for opioid use disorder among adults with past-year opioid use disorder in the US, 2021. *JAMA Netw Open.* 2023;6(8):e2327488.Suarez EA, Huybrechts KF, Straub L, et al. Buprenorphine versus methadone for opioid use disorder in pregnancy. *N Engl J Med.* 2022;387(22):2033-2044.
9. Degenhardt L, Clark B, Macpherson G, et al. Buprenorphine versus methadone for the treatment of opioid dependence: a systematic review and meta-analysis of randomized and observational studies. *Lancet Psychiatry.* 2023;10(6):386-402. Erratum in: *Lancet Psychiatry.* 2024;11(4):e8.
10. Mattick RP, Breen C, Kimber J, et al. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev.* 2014;6;2014(2):CD002207.

Resources for Additional Learning

ABEM OUD Modules
MEDCalc COWS
California Bridge to Treatment Resources

Notes: Practice Advance synopses should be built from a strong body of evidence that likely includes a systematic review. The synopsis will include a recommendation that should be similar in wording to GRADE (Grading of Recommendations Assessment, Development and Evaluation) recommendations. These should not be controversial recommendations and essentially all emergency physicians should adopt them. The impact or "effect size" should be substantial and no significant harm should be associated with this gain.

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