EVMS Emergency Medicine Journal Club

Resident: Larry Newton **November 29, 2021**

Herring AA et al., Managing Opioid Withdrawal in the Emergency Department With Buprenorphine. Ann Emerg Med. 2019 May;73(5):481-487.

Strayer RJ et al., Management of Opioid Use Disorder in the Emergency Department: A White Paper Prepared for the American Academy of Emergency Medicine. J Emerg Med. 2020 Mar;58(3):522-546. https://www.aaem.org/UserFiles/file/AAEMOUDWhitePaperManuscript.pdf

What Is BUPRENORPHINE?

Buprenorphine is a semisynthetic derivative of thebaine, developed in 1978 to treat chronic pain conditions. In the United States, buprenorphine is approved to treat OUD and moderate/severe chronic pain. Buprenorphine is a unique m-opioid receptor partial agonist with minimal euphoric reward and a ceiling effect on both sedation and respiratory depression both of which are extremely unlikely. It has a very high affinity and will displace other opioids from mu-receptors.

The high receptor affinity blocks co-administered opioids from binding, effectively limiting the risk of overdose or the euphoria of full agonist opioids while a patient is therapeutic on buprenorphine; this is called ***buprenorphine blockade***.

The slow dissociation of buprenorphine from the receptor allows for an extended half-life ranging from between 6-12 hours for low doses (< 4 mg) and between 24-72 hours (or even longer) for higher doses (> 16 mg), which allows for convenient sublingual daily dosing

What are the current dosing strategies for BUP?

There is currently no definitive approach to the ED dosing strategies for buprenorphine Office-based clinical guidelines for induction are not practical for ED however: In general, patients in the ED can be expected to require buprenorphine at least 8 mg SL to achieve substantive relief, and the majority of patients markedly improve with a 16-mg SL total dose; the maximum is 32 mg SL.

A common induction target dose before ED discharge is 16 mg SL, which may be comfortably increased as provider experience and judgment increase. An initial prescription for 16 mg/day (one buprenorphine 8 mg sublingual tab or one buprenorphine/naloxone 8/2 mg sublingual tablet or strip BID for 1-2 weeks) can be provided as a bridge to outpatient management

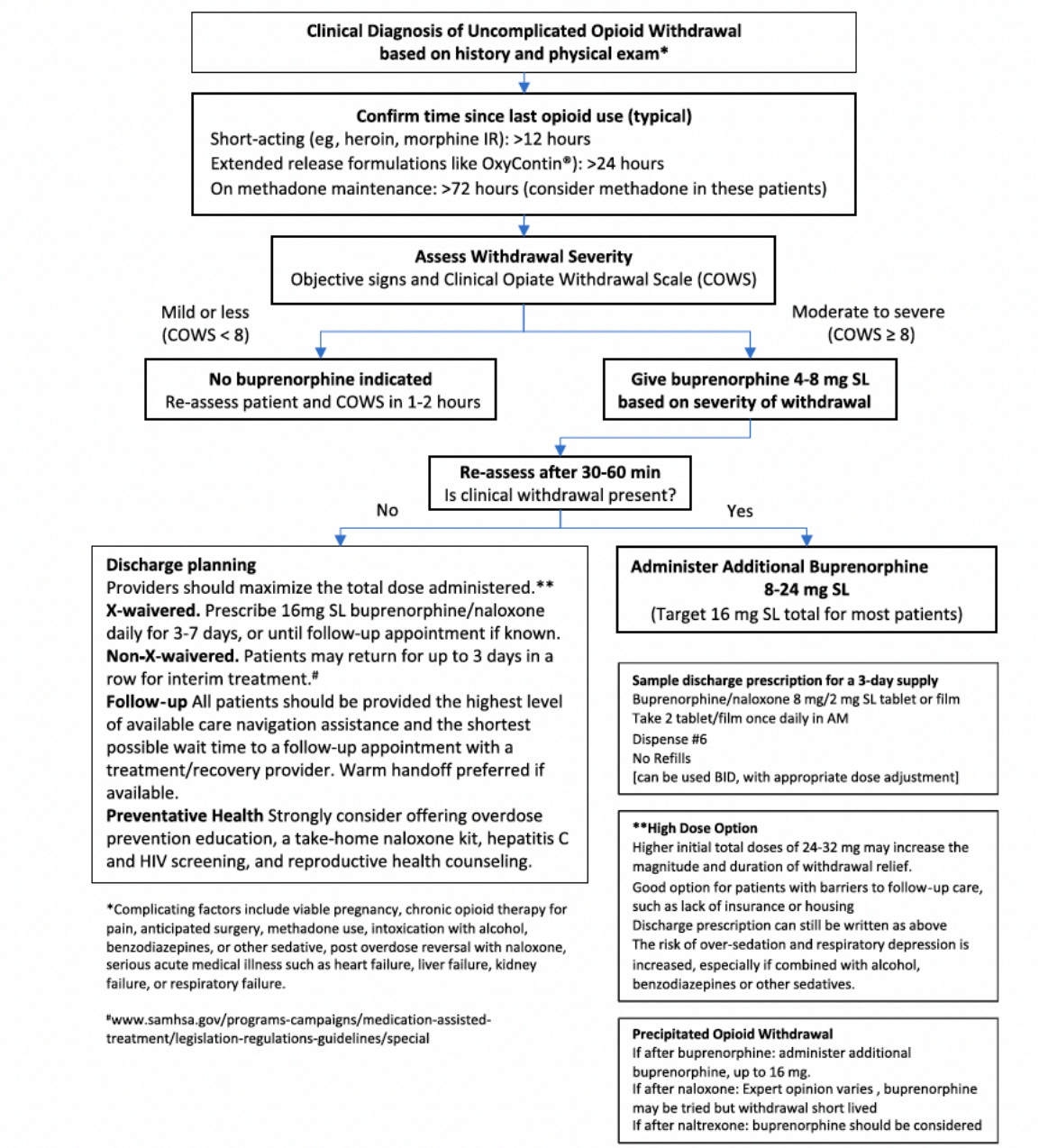


Figure 1. Algorithm for treatment of opioid withdrawal. *BID*, Twice a day.

Any major concerns when initiating buprenorphine treatment in the ED?

An immediate concern with initiating buprenorphine is the displacement of a full agonist by a partial agonist that can result in precipitated opioid withdrawal.

Particular caution should be taken with patients receiving methadone; most guidelines recommend waiting at least 48 hours since last use and until objective signs of

withdrawal are present as BUP will cause precipitous withdrawal in methadone dependent patients. Same for patients on opioids who do not demonstrate evidence of clinical withdrawal.

Buprenorphine predominantly causes harm in two ways: buprenorphine-precipitated withdrawal (BPW) and buprenorphine toxicity. BPW is more likely in patients with insufficiently severe opioid withdrawal and in patients who take long-acting opioids, especially methadone (**Q21**). Patients with opioid withdrawal who are on methadone maintenance should generally be treated with methadone rather than buprenorphine.

As a rule of thumb, patients who use short acting opioids (e.g. heroin) should wait 8-12 hours since last use; patients who use extended-release opioids (e.g. Oxycontin, MS-contin) should wait 24 hours, and patients who use methadone should wait >72 hours

Though buprenorphine is unlikely to cause dangerous respiratory depression in otherwise healthy adults when taken even in very high doses, harmful toxicity may occur when buprenorphine is used in combination with other sedatives (eg, alcohol, benzodiazepines), in the very young, the very old, or the frail.

Buprenorphine is safe during pregnancy, and a 2017 American Congress of Obstetricians and Gynecologists (ACOG) opinion statement supported the use of buprenorphine during pregnancy to treat OUD.[18] Additionally, both ACOG and the American Academy of Pediatrics (AAP) support buprenorphine use for OUD during breastfeeding, regardless of the maternal dose

What is the COWS Score when assessing opioid withdrawal in the ED?

A validated 11-item rating system that can be completed within two minutes by a trained observer and can track opioid withdrawal as differentiated from opioid toxicity through serial measurements.

Score interpretation:

- <5 - no active withdrawal
- 5-12 - mild withdrawal
- 13-24 - moderate withdrawal
- 25-36 - moderately severe withdrawal
- >36 - severe withdrawal

A Clinical Opiate Withdrawal Scale score of 8 is a suggested minimum for initiation by some guidelines, at least one objective sign of opioid withdrawal indicates readiness to initiate buprenorphine. More conservative guidelines suggest withholding buprenorphine until the Clinical Opiate Withdrawal Scale score is 13.

What is the 3-day rule?

Under this rule, discharged patients may return to the ED daily to receive the medication for up to 72 hours. Short-term treatment with direct administration of any opioid approved for use in maintenance or detoxification treatment (typically buprenorphine or methadone) is permitted under the "3- day rule" (Title 21, Code of Federal Regulations, Part 1306.07) https://law.lis.virginia.gov/admincode/title18/agency85/chapter21/section150/

How should emergency clinicians manage patients maintained on buprenorphine who have acute pain from illness or injury?

It is reasonable to supplement the patient's divided daily dose with additional 2-8 mg sublingual buprenorphine every 1-2 hours. The best strategy is to maximize non-pharmacologic and non-opioid analgesic modalities such as NSAIDs, acetaminophen, and local/regional anesthesia techniques where applicable. This can progress to parenteral non-opioids such as intravenous lidocaine, dexmedetomidine, and especially analgesic-dose ketamine, which has demonstrated effectiveness in severe acute pain

In Summary

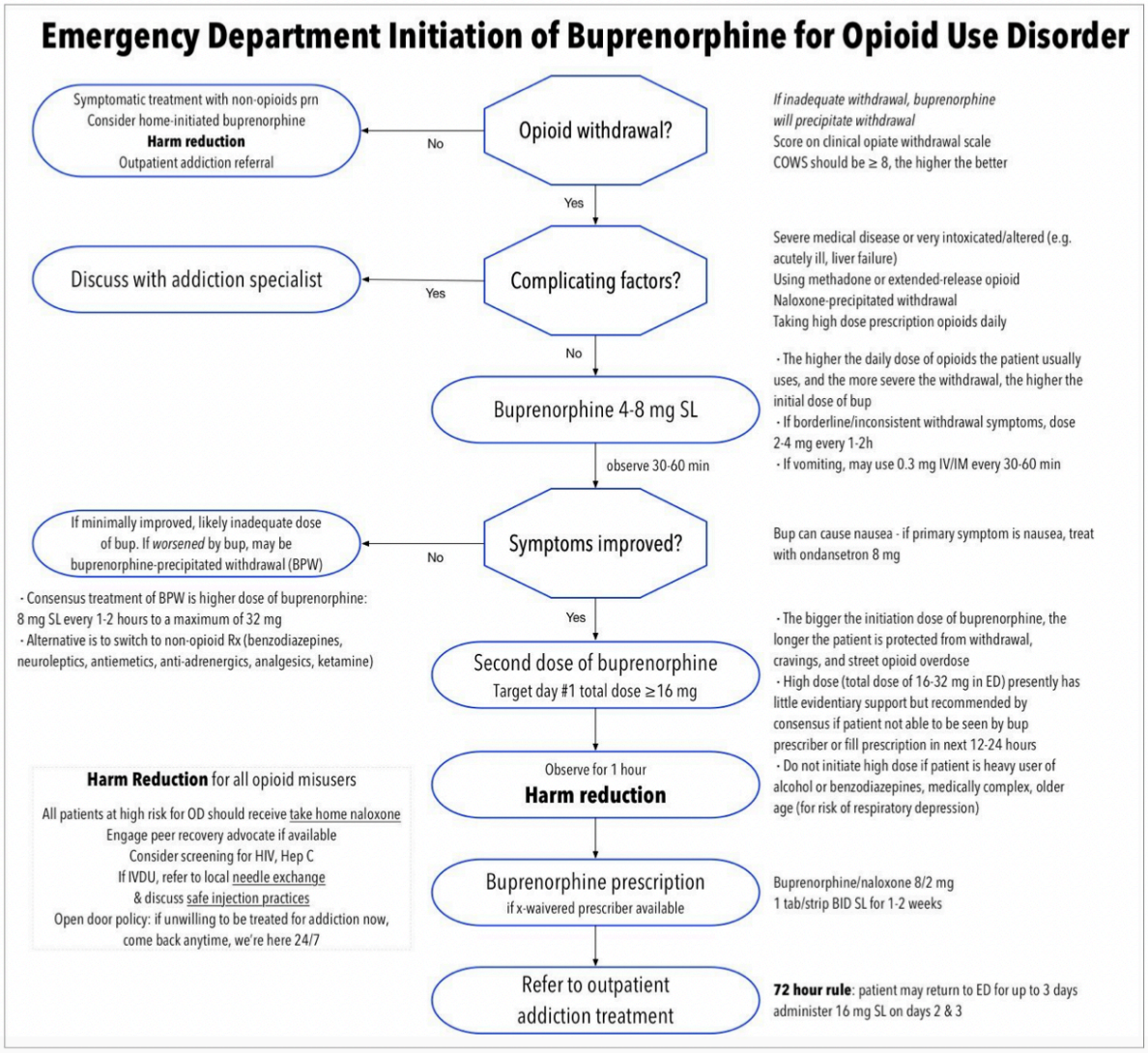
Buprenorphine or methadone treatment reduces or eliminates harms arising from the desperate behavior caused by the fear of running out of opioids and developing withdrawal, as well as the harms associated with using and especially injecting chemicals purchased on the street of uncertain identity and potency.

Patients who request detoxification treatment (often originating from a stigma-based desire to be "drug-free") should be advised of the much higher likelihood of relapse when treatment does not include the use of opioid agonists. Additionally, especially at a time when the street opioid supply has been contaminated with illicit fentanyl and its analogues, patients should be educated about how dangerous relapse is. These conversations may frame buprenorphine as a treatment for addiction similar to insulin as a treatment for diabetes.

If buprenorphine cannot be prescribed (e.g. because no waivered prescribers are available), cannot be filled, or is determined to be inappropriate, patients should be instructed to return to the ED as needed for further administered doses as covered by the 3 day rule .

Providers may be concerned that buprenorphine prescribed or dispensed out of the ED will be sold on the black market. Concerns around buprenorphine diversion should not discourage prescribing. This is because illegally-obtained buprenorphine is primarily used for its intended purpose of preventing opioid withdrawal in patients with OUD and not as an abused substance.

"The history of medicine is, in part, the history of physicians stretching the scope of their practice to answer the pressing needs of their times."



[SAMSHA Waiver Information]