Buprenorphine: Managing Opioid Use Disorder

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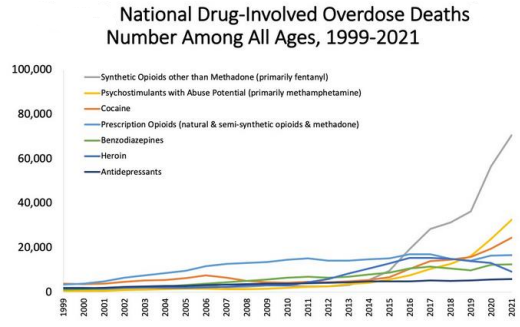
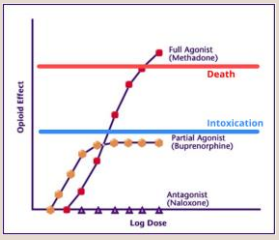
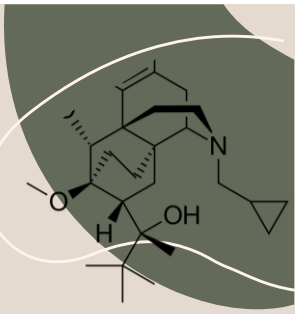


What is buprenorphine?



Regulatory History

- Approved by FDA 2002 to be prescribed for OUD under the Drug Addiction Treatment Act of 2000 (DATA 2000)
- Physicians needed to apply for a DEA waiver after completing an 8-hour course
- Comprehensive Addiction and Recovery Act (CARA) in 2016 extended prescribing authority to NPs and Pas who obtain waiver
- In 2023, Consolidated Appropriations Act eliminated the waiver program
- All providers with DEA registration can now prescribe buprenorphine for OUD



Mono-product vs. Combination Product

- Buprenorphine
- Buprenorphine + Naloxone

Formulations

- Sublingual tablets/films
- Transdermal
- Long-acting injection
- Subcutaneous implant

High Receptor Affinity

+

Partial mu-opioid agonism

⇩

Buprenorphine Precipitated Opioid Withdrawal (BPOW)

7

Managing Withdrawal/BPOW

Joint pain	Nausea/vomiting	Diarrhea	Hot/cold flashes Restlessness	Anxiety
Ibuprofen	Ondansetron	Loperamide	Clonidine	Gabapentin
Acetaminophen				Benzodiazepines
		All of the above		
		Ketamine?		

Assessment

HISTORY
Include substance use assessment, pregnancy test, lab testing including HIV, Hep B and C

URINE DRUG SCREEN
Including fentanyl

CHECK PDMP
Before every refill

SIGNED CONSENT
Include expectations

Diagnosing Opioid Use Disorder (OUD)

- Opioids are often taken in larger amounts or over a longer period of time than 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 to use opioids.

Diagnosing Opioid Use Disorder (OUD)

- Recurrent opioid use resulting in 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 use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.

Diagnosing Opioid Use Disorder (OUD)

- Tolerance, as defined by either of the following:
  - (a) a need for markedly increased amounts of opioids to achieve intoxication or desired effect
  - (b) markedly diminished effect with continued use of the same amount of an opioid
- Withdrawal, as manifested by either of the following:
  - (a) the characteristic opioid withdrawal syndrome
  - (b) the same (or a closely related) substance are taken to relieve or avoid withdrawal symptoms

QUESTIONS TO ASK ABOUT OPIOID USE

1. Type and amount of opioid(s) used recently
2. Route of administration
3. Last use
4. Treatment history
5. Problems resulting from drug use.
6. Experiences with buprenorphine

Opioid Intoxication vs. Withdrawal

Intoxication

- Drooping eyelids
- Constricted pupils
- Reduced respiratory rate
- Scratching (due to histamine release)
- Head nodding

Withdrawal

- Restlessness
- Irritability/anxiety
- Yawning
- Abdominal cramps, nausea, diarrhea
- Dilated pupils
- Sweating
- Piloerection

How should I react to a positive UDS?

- Buprenorphine is a risk reduction strategy
- A positive drug screen in itself should not be a reason to deny/stop treatment
- Drug screens positive for fentanyl or methadone require caution
- Benzodiazepines, barbiturates, and alcohol can increase risk of overdose
- Continued positive UDS on follow-up appointments may require a change in treatment strategy

Induction Steps

- **URINE DRUG SCREEN** — Presence or absence of opioids, fentanyl
- **HOW LONG SINCE LAST USE** — Time to wait depends on drug of choice
- **COWS SCORE** — Should be at least moderate withdrawal
- **GIVE BUPRENORPHINE** — Sublingual
- **WAIT** — Look for BPOW vs. inadequate relief from opioid withdrawal

Clinical Opiate Withdrawal Scale (COWS)

Resting Pulse Rate: _____beats/minute
Measured after patient is sitting or lying 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 1/2 hour not accounted for by room temperature or patient activity.*
0 no report of chills or flushing
1 subjective report of 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 movements of legs/arms
5 unable to sit still for more than a few seconds

Pupil size
0 pupils pinned or normal size for room light
1 pupils possibly larger than normal for room light
2 pupils moderately dilated
5 pupils so dilated that only the rim of the iris is visible

Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates 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 allergies*
0 not 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 1/2 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 piloerection of skin can be felt or hairs standing up on arms
5 prominent piloerection

Total Score _____
The total score is the sum of all 11 items
Initials of person completing assessment: _____

Source: Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). J Psychoactive Drugs, 35(2), 253–9

Opioid Withdrawal Severity

Severity Category	Associated COWS Range
Mild	COWS < 13
Moderate	COWS 13-24
Moderately severe	COWS 25-36
Severe	COWS > 36

MD+CALC

Induction Settings

INPATIENT FACILITY
- Easiest setting
- Allows constant monitoring
- May be unavailable geographically and may not be affordable

OFFICE
- Original protocols developed for in office
- Has generally been not practical for most ambulatory settings
- Emergency Departments

HOME
- Comfortable for patient
- Requires a lot of education
- Provider not available if BPOW

Home Induction

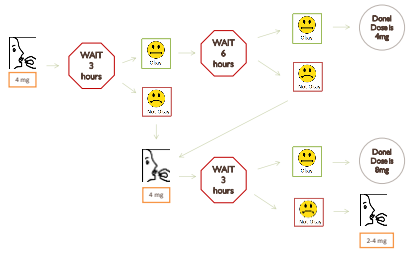
Buprenorphine - Beginning Treatment at Home

Before taking a buprenorphine tablet you want to feel lousy from your withdrawal symptoms. Very lousy! It should be at least 12 hours since you used heroin or pain pills (Roxicet, Vicodin, Lortab, etc.) and at least 24 hours since you used methadone or fentanyl.

Wait it out as long as you can. The worse you feel when you begin the medication, the better it will make you feel and the more satisfied you will be with the whole experience.

You should have a least 3 of the following feelings:
- twitching, tremors or shaking
- joint and bone aches
- bad chills or sweating
- anxious or irritable
- goose pimples
- very restless, can't sit still
- heavy yawning
- enlarged pupils
- runny nose, tears in eyes
- stomach cramps, nausea, vomiting, or diarrhea

Adapted from: Lee JD, Grossman E, DiRocco D, Gourevitch MN. Home buprenorphine/naloxone induction in primary care. *J Gen Intern Med*. 2009;24(2):226-232.



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Typical dosing

- Goal is to eliminate severe cravings that may lead to relapse
- Typical dose 8-16 mg per day
- Dose does not need to be divided, but many patients prefer to take BID or TID
- Doses > 24 mg rarely effective, BUT this may be different with fentanyl
- Suboxone 8/2mg = Zubsolv 5.7/1.4 mg

Always prescribe naloxone

- Available over the counter, but may be expensive
- Free through Vital

https://vitalalabama.com/free-naloxone-and-fentanyl-test-strips/

Contingency Management

- Induction Phase
- Stabilization Phase
  Weekly visits/refills
- Maintenance Phase
  Monthly visits/refills
- Increase intensity of treatment
  Therapy/12 step meeting frequency

Patients can move back to Stabilization Phase when needed

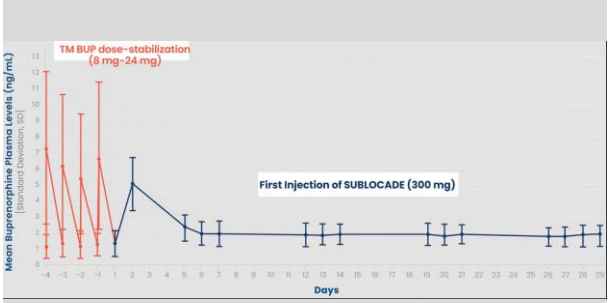
Reducing buprenorphine diversion

Visit Frequency	**Weekly visits/medication fills early in treatment**
Dosing	**Use lowest effective dose**
Drug testing	**Look for buprenorphine and metabolites**
Medication & wrapper counts	**Random call-ins**

Long-Acting Injectible Buprenorphine

Sublocade® (buprenorphine extended-release) injection for subcutaneous use ® 100mg·300mg

Brixadi® (buprenorphine) extended-release injection for subcutaneous use (III)
Weekly 8 • 16 • 24 • 32 mg Monthly 64 • 96 • 128 mg



Pregnant patients

- Buprenorphine is recommended in pregnancy and should be started as early as possible
- Mono-product vs. Combination Product
- Coordinate treatment with OB/Gyn
- Dose may need to be increased during pregnancy – are cravings being controlled?
- Neonatal opioid withdrawal syndrome possible, but not a reason to withhold treatment
- Can (should) continue buprenorphine with lactation

Acute pain & surgery

- Continue usual dose of buprenorphine
- Buprenorphine alone is a very effective pain medication, but in tolerant individuals will not be enough to control acute pain
- Coordinate with surgeon/anesthesiologist
- Add short-acting full agonist opioids in supervised settings until acute pain relief
- Doses of full-agonist opioids may need to be higher than in opioid-naïve patients
- Use adjunctive medications for pain (ibuprofen, acetaminophen, gabapentin)

How long should I treat?

- employment and financial stability
- housing stability
- engagement in mutual-help programs, or involvement in other meaningful activities
- sustained abstinence from opioid and other drugs during treatment
- positive changes in the psychosocial environment;
- evidence of additional psychosocial supports
- persistent engagement in treatment for ongoing monitoring past the point of medication discontinuation

Fentanyl

HIGH POTENCY

- Much greater risk of overdose
- Counterfeit pills
- Fentanyl test strips

HIGH LIPOPHILICITY

- Stays in system much longer than expected
- Greater risk of BPOW

Fentanyl - Prevention of BPOW

48-72 hours	Cross taper from full agonist to buprenorphine	Start 8mg and repeat every 30-60 minutes until comfortable	Low-dose IM ketamine
WAIT	**LOW-DOSE BUPRENORPHINE WITH OPIOID CONTINUATION (LDB-OC)**	**RAPID HIGH-DOSE BUPRENORPHINE (HDB)**	**"MOBILE METHOD"**
Clonidine, gabapentin, etc. to help	Very hard/illegal to do outside of inpatient setting	Hard to do outside of inpatient setting	Suitable for inpatient, ED, possibly office

Cohen SM, Weimer MB, Lexander KA, et al. Low dose initiation of buprenorphine: a narrative review and practical approach. J Addict Med. 2022;16(4):399-406.
Herring AA, Vosoughi AA, Luftig J, et al. High-dose buprenorphine induction in the emergency department for treatment of opioid use disorder. JAMA Netw Open. 2021;4(7):e2117128.

Behavioral Health Crisis Center (BHCC) Protocol AKA "Mobile Method"

AltaPointe Health

ASAM Annual Conference April 2023

LUCINDA GRANDE, MD

- At-home induction
- 8mg oral ketamine when starting to feel uncomfortable
- Up to 32mg during any 8-hour period (for relief from withdrawal symptoms

ANDREW HERRING, MD

- Use in Emergency Department
- 0.5 mg / kg IV target dose

TOM HUTCH, MD

- Potential use in outpatient settings

Potential Mechanisms

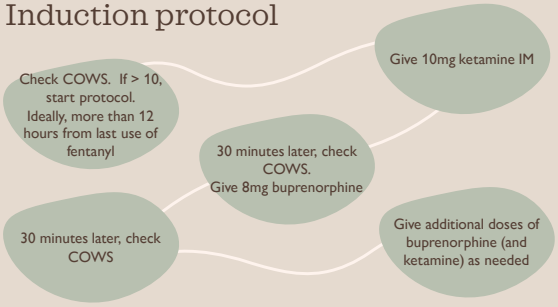
- Direct reduction of opioid withdrawal symptoms
- Potentiates effectiveness of buprenorphine μOR signaling
- Resensitizes μOR in face of fentanyl desensitization
- Inhibits descending pathways of hyperalgesia and central sensitization
- Addresses co-morbid symptoms of depression

- Hallozian C, Luftig J, Lang A, et al. *J Addict Med.* 2022;16(4):483-487.
- Christian NJ, Bumier JL, Evarts MS, Weimer MB. *J Addict Med.* 2023;17(4):488-490.
- Mizobuchi Y, Miyano K, Manabe S, et al. *Biomolecules.* 2022;12(3):426.

Our burning question

Could low-dose intramuscular ketamine assist in preventing BPOW when transitioning from fentanyl to buprenorphine?

Induction protocol



Results

Initial COWS	COWS score 30 minutes after ketamine	COWS score 30 minutes after buprenorphine 8mg	Total buprenorphine given first 4 hours
13.7	5.9	4.0	9.6

INITIAL CONCLUSIONS

Low-dose intramuscular ketamine was well tolerated, safe, and appears to have been successful in decreasing the frequency of BPOW

Transition from Methadone

1. Taper dose to 30mg daily
2. Wait 24-48 hours from last use of methadone (the longer the better)
3. Patient should be in at least moderate withdrawal (COWS>10)
4. Start with 2-4 mg buprenorphine. If withdrawal improves, give additional 2-8 mg until withdrawal symptoms relieved

summary

Buprenorphine is a safe and potentially life-saving medication for individuals with opioid use disorder.

Alabama is in desperate need for more providers to be comfortable prescribing this medication.


thank you
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