

Outpatient Management of Opioid Use Disorder

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Disclosures

- We have no relevant financial relationships to disclose
- We have no disclosures to report

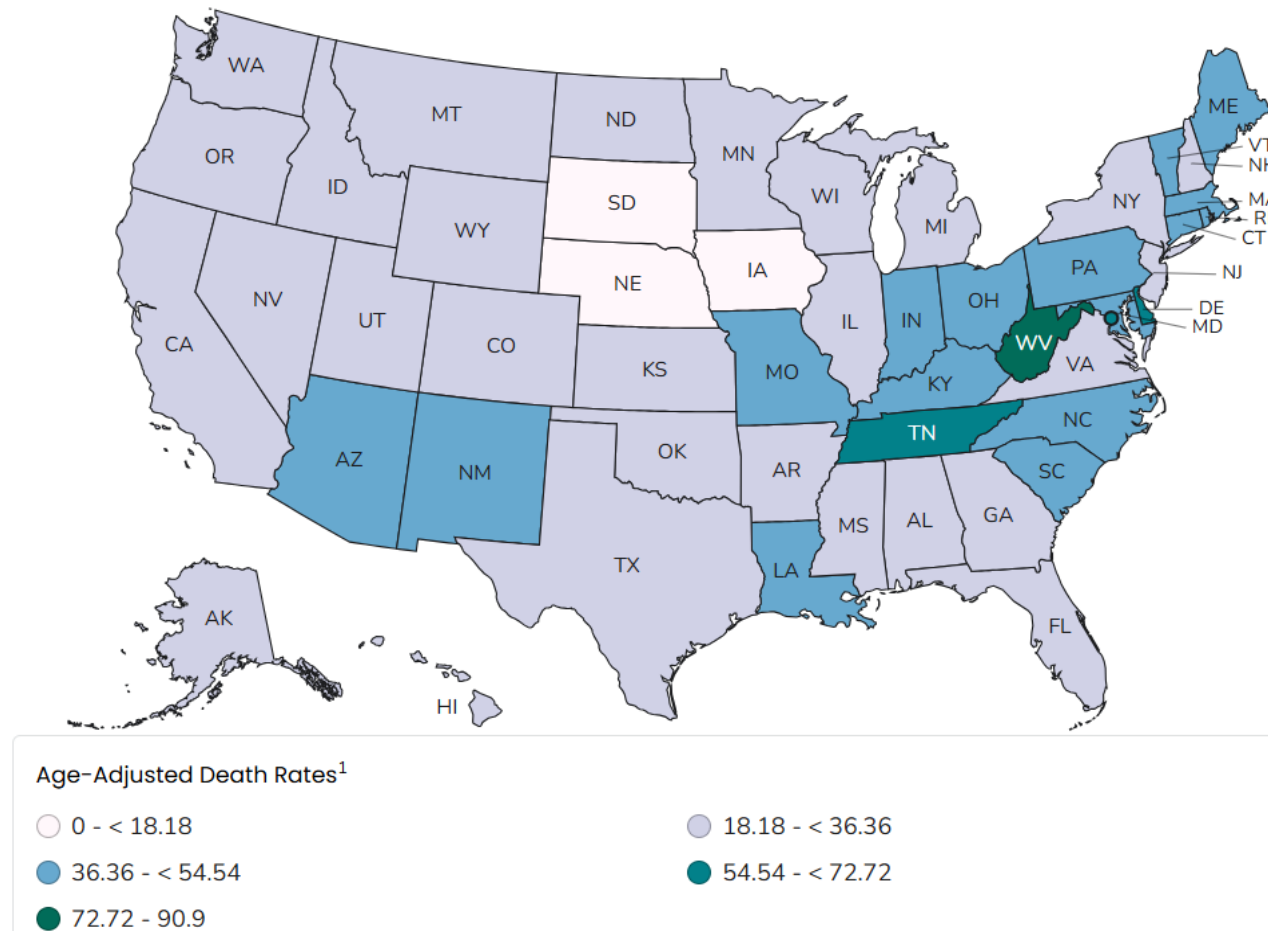
Objectives

- Opioid Use in New Hampshire
- Signs of a Patient in Acute Opioid Withdrawal
- Overview of Medications for Opioid Use Disorder
- Guidelines for Outpatient Initiation of MAT
- Newer practice models on the horizon

Epidemiology

- Prevalence
 - 2024 article published by NIH cited 16 million individuals with OUD worldwide and 2.1 million in the US
 - That is 13% of worldwide OUD in our country alone
- OUD over time
 - CDC data reports 16,849 deaths by drug poisoning involving opioid analgesics or heroin in 1999
 - By 2012 this number was almost 2.5 times higher at 41,502
 - Fast forward to 2024 and provisional data suggests 87,000 overdose deaths
 - Although this is over doubled compared to 2012, there is some encouragement in the fact that there was a 24% decrease compared to 2023

Epidemiology



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Risk Factors - Nature vs Nurture

- Genetics
 - Journal of Clinical Investigation (JCI) in 2024 article noted that for opioid addiction, 38%–61% of the population variability is attributable to genetic factors in twin-based studies and 11%–18% from SNP-based heritability
- Social Determinants of Health
 - The positive.....in addition to risk factors as below, studies did reveal that parental support as well as early childhood education were protective factors in regards to opioid use disorder
 - Studies however revealed several risk factors (common among several studies): negative peer influences, neighborhood instability, unemployment, and involvement in the criminal justice system

Patient Cases – Case 1



A 37 year old female with pmh of OUD presents to discuss medication management.

She has been on methadone for 15+ years, managed by a local methadone clinic. She has been attempting to wean off of methadone for many years but has been unable to due to withdrawal symptoms when trying to go below 15mg of daily methadone.

Her goal of treatment is to be weaned off opiate therapy all together.

What are her options?

A Patient in Withdrawal

- Lacrimation/Rhinorrhea
- Piloerection
- Myalgia
- N/V/D
- Pupillary Dilation
- Photophobia
- Insomnia
- Autonomic hyperactivity

Symptoms of Opiate Withdrawal

Symptoms In First 24 Hours	Runny nose	Inability to sleep	Yawning very often	Lacrimation (eyes tearing up)
	Restlessness	Muscle aches	Anxiety	Excessive sweating
Symptoms After Day Or So	High blood pressure	Nausea and vomiting	Abdominal cramping	Rapid heart rate
	Diarrhea	Goosebumps on the skin	Dilated pupils and possibly blurred vision	

Things to Consider

- Concurring Conditions
 - Alcohol Use Disorder
 - Stimulant Use Disorder
 - Psych Conditions
- Method of Use
 - Does it matter?
- Medications
 - Acute symptoms vs maintenance
 - More to come

Withdrawal Package

- Standard Meds
 - Clonidine, Loperamide, Hydroxyzine, Promethazine, Dicyclomine, Ibuprofen
- Sleep
 - Sleep is an important consideration in patients both in withdrawal and in recovery
 - Some meds above can help, but often times more is necessary (ie trazodone)
- Pros and Cons of Gabapentin
 - Something you can give the patient to allow partnership and their trust in you
 - A lot of patients get it and take it from external sources, prescribing it could help to keep them away from those influences
 - Negative side is that it does potentiate effects of opioids, and they can sell it themselves so it's a double edged sword

Treatment Options

- In patients with physical dependence, first line treatment is done with pharmacologic management. (Naltrexone, Buprenorphine, Methadone)
- Psychosocial therapy is used as an adjunct to pharmacologic therapy. This is typically recommended to all patients, although participation is not required to continue treatment.

Agonist vs Antagonist Therapy

- For initial treatment of patients with moderate-severe OUD, opioid agonist therapy (Buprenorphine or methadone) is preferred.
- For patients who cannot tolerate, or will not take agonist therapy, opioid antagonist therapy (naltrexone) is a reasonable alternative.

**Patients will need to undergo medically supervised withdrawal prior to initiating naltrexone.

Methadone Vs Buprenorphine

- Methadone (older)
 - Preferred in certain situations. (access to methadone, poor response to buprenorphine or diversion, or higher level of physical dependence)
 - Methadone requires access to a licensed opioid treatment program. (OTP)
 - Generally harder to wean/come off from (stay tuned for methods to transition)
- Buprenorphine
 - Lower risk of death with overdose, greater accessibility, and fewer drug-drug interactions.

Comparison of advantages and disadvantages of buprenorphine and methadone for treatment of opioid use disorder

Feature	Buprenorphine*	Methadone [†]
Treatment retention ^[1-3]	Appears lower	Appears higher
Accessibility ^Δ	Can be prescribed in private offices	Requires licensed OTP
Suppression of nonprescribed opioid use ^[4]	Appears comparable	Appears comparable
For patients with a high level of physical dependence		May be preferable
For patients with fentanyl use		May be preferable
Drug-drug interactions	Potentially lower	
Overdose-related mortality from the treatment medication ^[5]	Likely lower	Likely higher
All-cause mortality ^[2]	Appears comparable	Appears comparable
Induction difficulty	Risk for precipitated withdrawal when initiating	Need for slow titration to avoid potential iatrogenic overdose
Availability of wraparound services	May be available	Counseling availability required in OTP settings in the United States; other services may be available
Cardiac conduction effects	No evidence of cardiac conduction effects	May cause QTc prolongation if other risk factors and/or very high doses used

LAI Buprenorphine

- Common formulations : Sublocade , Brixadi
- Dosing is typically monthly, potential increase in compliance
- Less concern around abrupt stop of medication, making it easier for patients to wean off/stop.
- Comparing the two
 - Sublocade: FDA approved as of 2017, monthly injections, at least 8mg daily dosing
 - Brixadi: FDA approved in 2023, weekly vs monthly, offers an option for patients taking less than 8mg daily

The Future of Injectable Buprenorphine

- Recently FDA approved Rapid Initiation with injectable buprenorphine (Sublocade)
 - Previously guidelines were that a patient would have to be stable on a dose of buprenorphine for at least 7 days
 - Begins with initial dose (4mg) of transmucosal buprenorphine. If they tolerate it well after 1 hour, proceed with LAI in office setting. (300mg)

Case #1 Continued

- A 37 year old female with pmh of OUD presents to discuss medication management. She has been on methadone for 15+ years, managed by a local methadone clinic. She has been attempting to wean off of methadone for many years, but has been unable to wean off completely. This is due to withdrawal symptoms when trying to go below 15mg of daily methadone.
- Her goal of treatment is to be weaned off opiate therapy all together.
- We discussed this case with both the patient and our MAR team. The decision was made to follow the Bernese Method to transition to buprenorphine.

Buprenorphine/Naloxone Microdosing

- Often referred to as the Bernese Method.
- The goal is to transition patients on to suboxone without them having to undergo withdrawal prior to treatment.
- Repetitive administration of low dose buprenorphine with sufficient dosing intervals (12hr) should not precipitate withdrawal.
- This allows buprenorphine to accumulate at the opioid receptor and slowly replace other opioids at the *u*-receptor

Case #1 Continued

- We used the following microdosing schedule :
 - Day 1: 0.5mg qday
 - Day 2: 0.5mg BID
 - Day 3: 1mg BID
 - Day 4: 2mg BID
 - Day 5: 3mg BID
 - Day 6: 4mg BID
 - Day 7: 4mg BID (stopped methadone)
- She tolerated the micro induction of buprenorphine without any issues, and was able to stop her methadone on day 7.
- She was maintained on 8mg daily buprenorphine for the next couple of weeks.
- Her goal remained to ultimately be maintained off of opiate medications.
- Next steps?

Case #1 continued

- She was transitioned to sublocade from suboxone for less frequent dosing, and with the end goal to wean off buprenorphine. She received 2x doses of 300mg q28 days, followed by one dose of 100mg.
- She was able to fully wean off sublocade after three doses.
- At last contact a few months after completing treatment, she feels well overall, and has had no return to use.
- She has not yet been seen since this visit.
- What would be an appropriate option to consider at this time if she wanted to have pharmacological support for OUD?

Patient Cases – Case 2

36 yo M with h/o fentanyl use who presents to clinic for MAT. He prefers to sniff. He additionally notes sad mood and trouble sleeping and screens positive for severe depression. He is interested in complete abstinence from fentanyl use and does not endorse other drug use at this time.

What additional questions would you ask to clarify the history?
What are his treatment options?

Case #2 continued

Additional SUD Hx:

- Patient has a history of trialing Vivitrol in the past prior to his last relapse, he had a good experience on the medication
- His reported last fentanyl use was 7 days ago
- His current Urine dip was positive for fentanyl

Psych Hx:

- He reports periods of high energy and insomnia lasting multiple days
- He denies AVH/SI/HI
- No psychiatric hospitalizations
- No family psychiatric history

Does this change his treatment options?

What additional POC testing could be considered?

Naltrexone (PO vs LAI)

- Naltrexone effectively blocks the mu-opioid receptor.
 - Available in 2 forms:
 - Long acting injectable (administered monthly)
 - Oral (administered daily)
- Naltrexone hold a few advantages over opioid agonists for mild opiate use disorder
 - Naltrexone does not cause dependence or withdrawal when stopped
 - Naltrexone can easily be switched to agonist therapy
 - Naltrexone blocks the mu-opioid receptor, so if illicit opioids are used during treatment the patient gets no euphoria/effect.

Naloxone Challenge

- Can be used to determine safety of Vivitrol initiation
- If no overt signs of withdrawal, consider a naltrexone challenge to aid in decision of Vivitrol vs Suboxone/Sublocade
- Measure COWS before IM 0.4mg (1 cc) of naltrexone
- If COWS increased by 2 over the next 20 minutes, test is positive and Vivitrol is not recommended at this visit
- Otherwise, patient could continue with Vivitrol initiation

Case #2 continued

Patient declined a naloxone challenge. He was given fentanyl test strips and tested his urine at home until it was negative.

He then followed up for Vivitrol initiation 1 week later. He is still complaining about insomnia and depressed mood.

What are potential next steps?

Suboxone Home Induction

- Abstain from opioid use for 12-18 hours or until withdrawal symptoms present (COWS>16)
- Day 1: Start with 4mg suboxone, re-dose every 1-2 hours until sx resolve for max dose of 16 mg
- Day 2: Maintain dose from yesterday, can increase by 4mg if still having withdrawal sx
- Can increase by 4mg each day, some patient may need an initial dose of 24mg/day before tapering down to 16mg maintenance

Pregnancy

- Opioid agonist therapy (Methadone and buprenorphine) are effective pharmacotherapy for opiate use disorder in pregnancy and have not been shown to be teratogenic.
- Key Points from ACOG
 - MAT is considered safe during breastfeeding and is recommended to be continued postpartum as well
 - In patients with active OUD initiation of MAT as early as possible is recommended
 - ACOG recommends against patients trying to undergo detoxification due to higher rates of relapse

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Thank You