Pharmacologic Treatment of Opioid Use Disorder

Kate Marshall, MD, FASAM
Ehsan Seyedhossini, PharmD

Disclosure Statement

Kate Marshall and Ehsan Seyedhossini have no relevant financial relationships to disclose.

A note on language

- In this presentation we will make an effort to use person-first, morally-neutral language and ask that you consider your language when discussing people with substance use disorders
- Evidence shows that using appropriate language in care (avoiding *addict*, *abuser*, *dirty* etc.) improves quality of care for our patients and helps them heal!

NIDA: Words Matter: Preferred language for talking about addiction.

Learning Objectives

After this presentation attendees should be able to:

- Describe key moments in the history of pharmacologic treatment for opioid use disorder and the current regulatory status of methadone and buprenorphine
- Name several clinical benefits of pharmacologic treatment for opioid use disorder
- Differentiate between the mechanisms of action of methadone, buprenorphine and naltrexone
- Counsel a patient on safe and effective use of sublingual buprenorphine
- Describe indications for providing a naloxone rescue kit

Primary care office

Joe

- Age 65, cisgender male (he/him)
- Retired anesthesiologist
- Previously using diverted fentanyl, now dependent on illicitly obtained fentanyl
- Requests a prescription for methadone in order to prevent withdrawal and treat his use disorder
- Unwilling to be treated in methadone clinic
- Not interested in counseling

Knowledge check

Q: Which of the following best describes current regulations around methadone in the outpatient setting?

a. Methadone may be prescribed for opioid use disorder but not for chronic pain.

b. Methadone may be prescribed for pain but not for opioid use disorder.

c. Methadone may not be prescribed for either pain or opioid use disorder.

d. An emergency supply of 1 week of methadone may be dispensed at any pharmacy to prevent withdrawal in someone enrolled with a methadone clinic.

Milestones in OUD treatment

1919 Supreme Court rules that prescribing an opioid to treat opioid withdrawal or cravings is not medically appropriate

1974 Controlled Substances Act creates an exception – methadone may be used for this purpose in a federally-regulated manner and with a separate DEA registration (methadone clinics are born)

2000 DATA-2000 creates a second exception – may use approved schedule III narcotics for this purpose with separate DEA registration (X-waiver)

2016 X-waiver eligibility opened to NPs and PAs

2023 MAT Act eliminates separate DEA registration to prescribe buprenorphine

Milestones in OUD treatment

- *Any* opioid may be used in the hospital setting to treat opioid cravings or withdrawal
- Another exception for methadone: practitioners may request an exception to dispense up to 72 hours of medication as a bridge to ongoing treatment

SAMHSA DEA 2022.

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Primary care office

Joe
- "So what are my options?"

Knowledge check

Q: Which of the following best pairs the medication with its primary mechanism of action?

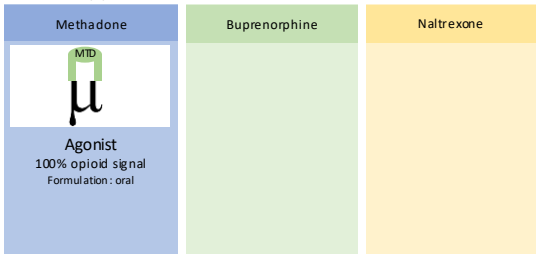
a. Buprenorphine: opioid antagonist
b. Naltrexone: partial opioid agonist
c. Methadone: opioid agonist
d. Naloxone: partial opioid agonist

FDA-approved medications for OUD

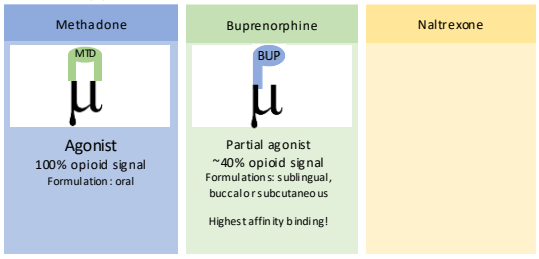
Methadone	Buprenorphine	Naltrexone

NIDA.

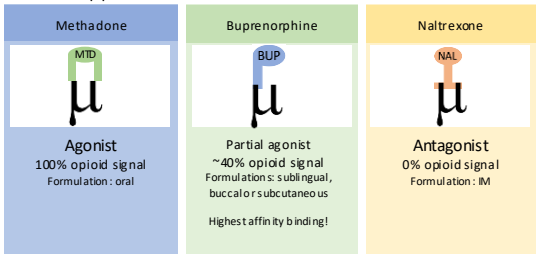
FDA-approved medications for OUD



FDA-approved medications for OUD



FDA-approved medications for OUD



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Primary care office

Joe
- "What's the evidence on these?"

Knowledge check

Q: Which of the following best describes the evidence around use of methadone or buprenorphine as a treatment for opioid use disorder?

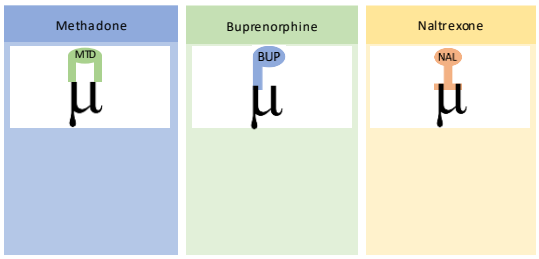
a. Both methadone and buprenorphine have been shown to reduce all-cause mortality in people with opioid use disorder.

b. Behavioral therapy may be as effective in preventing return to use as methadone or buprenorphine.

c. Evidence shows that buprenorphine is best used short-term in order to avoid substituting one drug for another.

d. Most patients who use diverted buprenorphine use it for the purpose of achieving euphoria or "getting high".

Let's compare to non-medication treatment



Hser, et al., 2014; Clark, et al., 2015; Dupouy et al., 2017; Soyka et al., 2017; Kelty et al., 2020.

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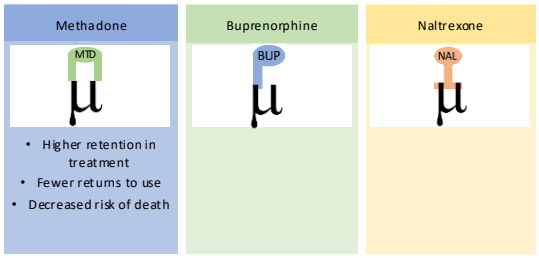

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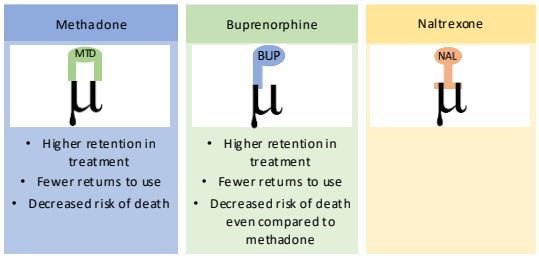

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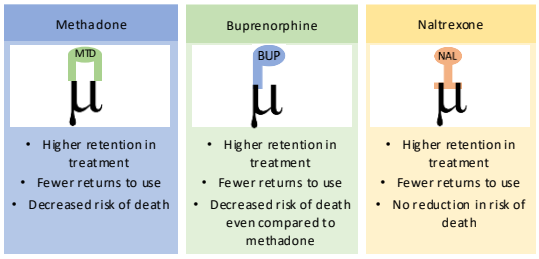

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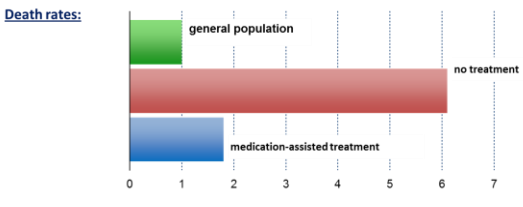
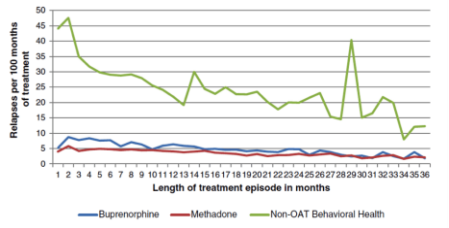
Methadone or buprenorphine *vs* detoxification alone



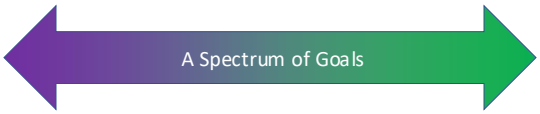
Dupouy et al., 2017; Sordo et al., 2017.

Methadone or buprenorphine *vs* counseling alone



RE Clark et al., 2015.

Let's talk about **harm reduction**



Ongoing use at current amount and frequency

Reduced amount, frequency, or number of substances

Complete abstinence from substances

Addressing false beliefs

Addiction is a choice

- *Addiction arises when a individual made vulnerable by genetics and prior life experiences is exposed to a substance with high reward value*

Restrictive policies promote good behavior in SUD treatment

- *Low barrier treatment is as effective, or more effective, than more structured/restrictive programs*

Diverted buprenorphine increases risk of opioid overdose in the community

- *Most diverted buprenorphine is used to relieve withdrawal and avoid use of more harmful substances*
- *Diverted buprenorphine may actually reduce overdose deaths in a community where it occurs*

American Society of Addiction Medicine. Martin, et al., 2018; Chilcoat, et al., 2019; Adams, et al., 2023.

Changing paradigms

Table. Buprenorphine Care: Previous Approaches Compared With New Findings and Recommendations

Previous Approach	New Findings and Recommendations
A medical setting is needed for induction.	Home induction is also safe and effective (6).
Benzodiazepine and buprenorphine coprescription is toxic.	Buprenorphine should not be withheld from patients taking benzodiazepines (5).
Relapse indicates that the patient is unfit for buprenorphine-based treatment.	Relapse indicates the need for additional support and resources rather than cessation of buprenorphine treatment (43).
Counseling or participation in a 12-step program is mandatory.	Behavioral treatments and support are provided as desired by the patient (6).
Drug testing is a tool to discharge patients from buprenorphine treatment or compel more intensive settings.	Drug testing is a tool to better support recovery and address relapse (56).
Use of other substances is a sign of treatment failure and grounds for dismissal from buprenorphine treatment.	Buprenorphine treatment does not directly affect other substance use, and such use should be addressed in this context (43).
Buprenorphine is a short-term treatment, prescribed with tapered dosages or for weeks to months.	Buprenorphine is prescribed as long as it continues to benefit the patient (6).

Martin, et al., 2018.

"'Isn't harm reduction just enabling?' You know what, it is enabling. It's enabling people to be healthier. It's enabling people to be connected to other people. It's enabling people to get access to healthcare. So we use this term 'enabling' with substance use disorders as a negative term. But honestly, I think enabling people to be healthier, happier, and less-dead, is a wonderful goal."

- Haven Wheelock

Knowledge check

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Primary care office

Joe
- "Buprenorphine sounds like the way to go. How do I get started?"

Knowledge check

Q: Which of the following is true with regards to buprenorphine therapy?

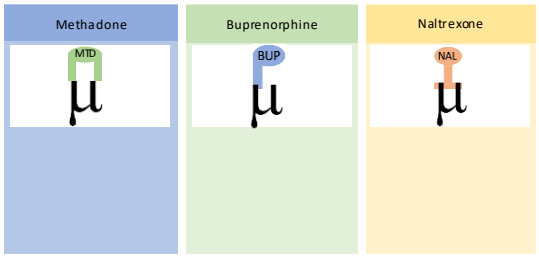
a. It is the naloxone component of the sublingual buprenorphine-naloxone combination product that causes precipitated withdrawal if the product is taken too soon after other opioids

b. When taken as directed, no naloxone is absorbed into the bloodstream from administration of the sublingual buprenorphine-naloxone combination product

c. Patients should be instructed to hold sublingual buprenorphine under their tongue until the film or tablet is completely dissolved

d. Pharmacy-level barriers are not a significant concern for access to buprenorphine therapy

Timing is everything!



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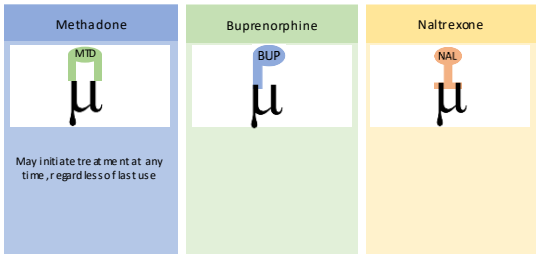

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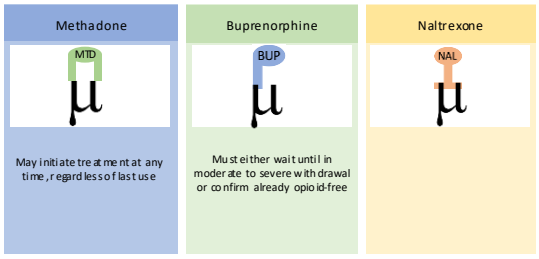
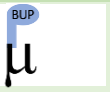
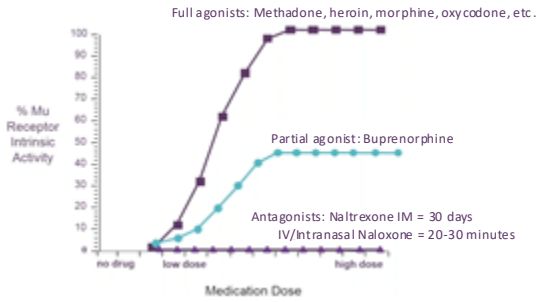
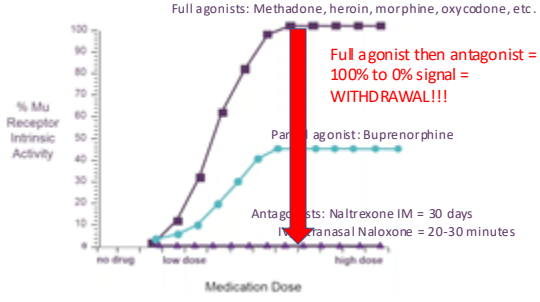
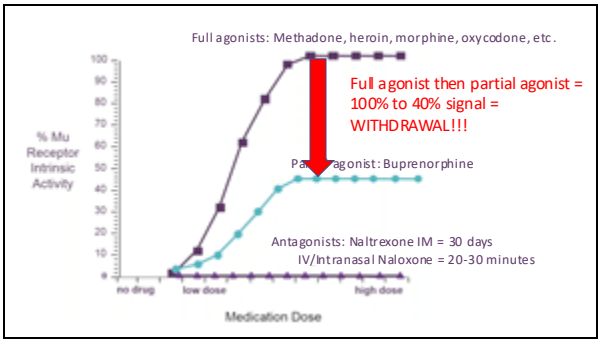


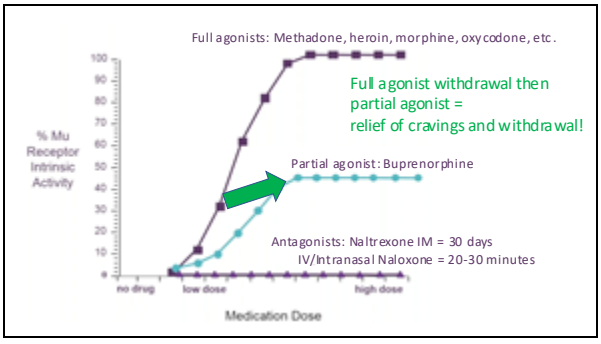
Timing is everything!

Methadone	Buprenorphine	Naltrexone
		
May initiate treatment at any time, regardless of last use	Must either wait until in moderate to severe withdrawal or confirm already opioid-free	Must confirm completely opioid free









Buprenorphine induction strategies

	Traditional	Low Dose (Bernese)	Rapid Low Dose	Macrodose
Transition from:	Short to medium acting (oxycodone, morphine, heroin)	Long-acting (fentanyl, methadone) *or* acute pain present	Fentanyl	Fentanyl
Continue prior opioid?	No	Yes	Optional	No
Comfort meds?	Optional	Optional	Yes	Yes
Directions:	Wait until 12+ hours since last use *and* COWS >10 4mg q2h prn to maximum 16mg day 1	Day 1: ½ mg once Day 2: ½ mg bid Day 3: 1mg bid Day 4: 2mg bid Day 5: 4mg bid Day 6: 6mg bid Day 7: 8mg bid	Day 1: 1mg q6h Day 2: 1mg q3h Day 3: 8mg+ 2-4mg q2h prn to maximum 32mg	Wait until COWS >10 then give 16mg

Opioid withdrawal comfort medications

Clonidine 0.1-0.2mg oral tid prn for sweating/agitation
Tizanidine 2-4mg oral q6h prn for muscle spasms or cramps
Hydroxyzine 25-50mg oral q4h prn for anxiety
Ondansetron 4mg oral q8h prn for nausea
Hyoscyamine 0.125mg oral q6h prn for abdominal cramps
Loperamide 2mg oral qid prn for diarrhea

Benzodiazepines? Opioids?

Sublingual Buprenorphine Administration

Directions:

- Must be dissolved under the tongue
- Avoid eating/drinking for 30 minutes before and after
- Allow medication to dissolve completely under the tongue, avoiding swallowing if possible
- May swallow saliva or spit
  - spitting may help avoid GI and naloxone side effects
- Rinse mouth after, wait 1 hour before brushing teeth

Gregg, et al., 2023

Let's talk about access

2022 SAMHSA/DEA Town Hall:

- "We're dealing with a very frightened supply chain at this point."
- Manufacturers/distributors apply supply thresholds as part of anti-diversion efforts, pharmacies that surpass these may be cut off from supply, but thresholds are not clear
- Lengthy resolution process for systems that request threshold increase
- Red flags/evolving practice
  - Buprenorphine above usual dose limits
  - Telehealth prescribing
  - Dose changes/early fills
  - Cash purchases
- *As a result, buprenorphine may not be dispensed at all in 20% of Medicaid-participating pharmacies*

https://www.samhsa.gov/sites/default/files/virtual-town-hall-buprenorphine-access-pharmacies.pdf
Freeman, et al., 2024.

Knowledge check

Q: Which of the following is true with regards to buprenorphine therapy?

a. It is the naloxone component of the sublingual buprenorphine-naloxone combination product that causes precipitated withdrawal if the product is taken too soon after other opioids
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Primary care office

Joe

- Prescribed a supply of 2mg SL buprenorphine monoproduct for rapid low-dose initiation at home
- Also prescribed comfort medications to take during the process
- Encouraged to fill or purchase a naloxone rescue kit
- Follow up appointment scheduled in 3 days

Knowledge check

Q: Which for the following would be an evidence-based reason NOT to dispense an opioid overdose reversal medication (OORM/naloxone rescue kit)?

a. The kit is being dispensed to someone who intends to use it on a friend or family member
b. Having a reversal medication available increases risky behavior with drugs
c. The patient is in long-term remission on buprenorphine therapy and states they have no risk of overdose
d. None of the above

Enhancing access to rescue medications

- According to SAMHSA, "everyone should keep an OORM on hand, but especially those who use opioids or other drugs or have friends or family members who use opioids or other drugs."
- There is no evidence that having an OORM on hand increases opioid use or risk of overdose.
- While buprenorphine poses much less risk for overdose compared to full opioids, overdose can occur especially in unintended exposure by a child, opioid-naïve adult, or pet.

SAMHSA Overdose Prevention and Response Toolkit; Tse, et al., 2021; Hayes et al., 2008.

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d. None of the above

Primary care office

Joe

- "That wasn't easy, but I got there."
- At return, taking 24mg buprenorphine daily and ceased use of fentanyl 24 hours ago
- Prescribed 2 week supply of 24mg SL buprenorphine-naloxone daily
- Plan to increase to 1-month supplies once UDS shows fentanyl free and buprenorphine consistently present

Question Break

Conclusion

- Prescribing buprenorphine no longer requires a separate DEA registration, but methadone for OUD may only be dispensed in a federally-regulated opioid treatment program
- Medication treatment for OUD is associated with decreased return to use, increased treatment retention, and decreased risk of death
- Methadone is a full opioid agonist, buprenorphine a partial opioid agonist and naltrexone an opioid receptor antagonist
- Buprenorphine initiation is tricky; attention to dose and timing is critical
- Opioid overdose reversal medications are a critical tool in harm reduction from both prescribed and non-prescribed opioids

Thank you!

Katharine.F.Marshall@kp.org
Ehsan.X.Seyedhossini@kp.org

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