Alcohol and Opioid Use Disorders: Assessment, Diagnosis, and Treatment

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Objectives

01

Diagnose patients with a substance use disorder

02

Discuss initiation and long- term management of medications for alcohol and opioid use disorder with patients

03

Describe the mechanism of action, efficacy, advantages, and disadvantages of medications for the treatment of alcohol and opioid use disorder

Mr. White

- 54 year old man with a history of hypertension and smoking admitted to a skilled nursing facility after a prolonged hospitalization for a trauma in a motor vehicle collision. He was intoxicated at the time of the accident.
- Recently, nursing staff became concerned after they found a bottle of liquor hidden under the patient's pillow.
- Mr. White was embarrassed by this incident and asks for help as he has been having strong cravings for alcohol since hospital discharge.

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How do you diagnose a Substance Use Disorder?

- Does any use of a substance indicate a substance use disorder?
- What about alcohol?
- What screening questions can you ask?

Starting the conversation

- We are doctors and health care providers, not police, judges, or investigators
- Normalizing
- Accepting patient autonomy

Single Item Alcohol Screening Questionnaire (SASQ)

Do you sometimes drink beer, wine, or other alcoholic beverages?
(Followed by the screening question)

1. **How many times in the past year have you had...**
   - ❑ *5 or* more drinks in a day *(men)*
   - ❑ *4 or* more drinks in a day *(women)*

A Positive Screen is any report of the above episodes

NIAA 2007

TABLE 1 Summarized DSM-5 diagnostic categories and criteria for opioid use disorder

Category	Criteria
Impaired control	• Opioids used in larger amounts or for longer than intended • Unsuccessful efforts or desire to cut back or control opioid use • Excessive amount of time spent obtaining, using, or recovering from opioids • Craving to use opioids
Social impairment	• Failure to fulfill major role obligations at work, school, or home as a result of recurrent opioid use • Persistent or recurrent social or interpersonal problems that are exacerbated by opioids or continued use of opioids despite these problems • Reduced or given up important social, occupational, or recreational activities because of opioid use
Risky use	• Opioid use in physically hazardous situations • Continued opioid use despite knowledge of persistent physical or psychological problem that is likely caused by opioid use
Pharmacological properties	• Tolerance as demonstrated by increased amounts of opioids needed to achieve desired effect; diminished effect with continued use of the same amount • Withdrawal as demonstrated by symptoms of opioid withdrawal syndrome; opioids taken to relieve or avoid withdrawal

Mild: 2-3, Moderate 4-5, Severe 6+

Brenzig, Psychiatric Times, 2015

SECTION B: Diagnosing AUD

Once you have identified that your patient might have AUD through the AUDIT or the AUDIT-C, then the DSM-5 criteria can be used to diagnose your patient.

DSM-5 Criteria for AUD [21]

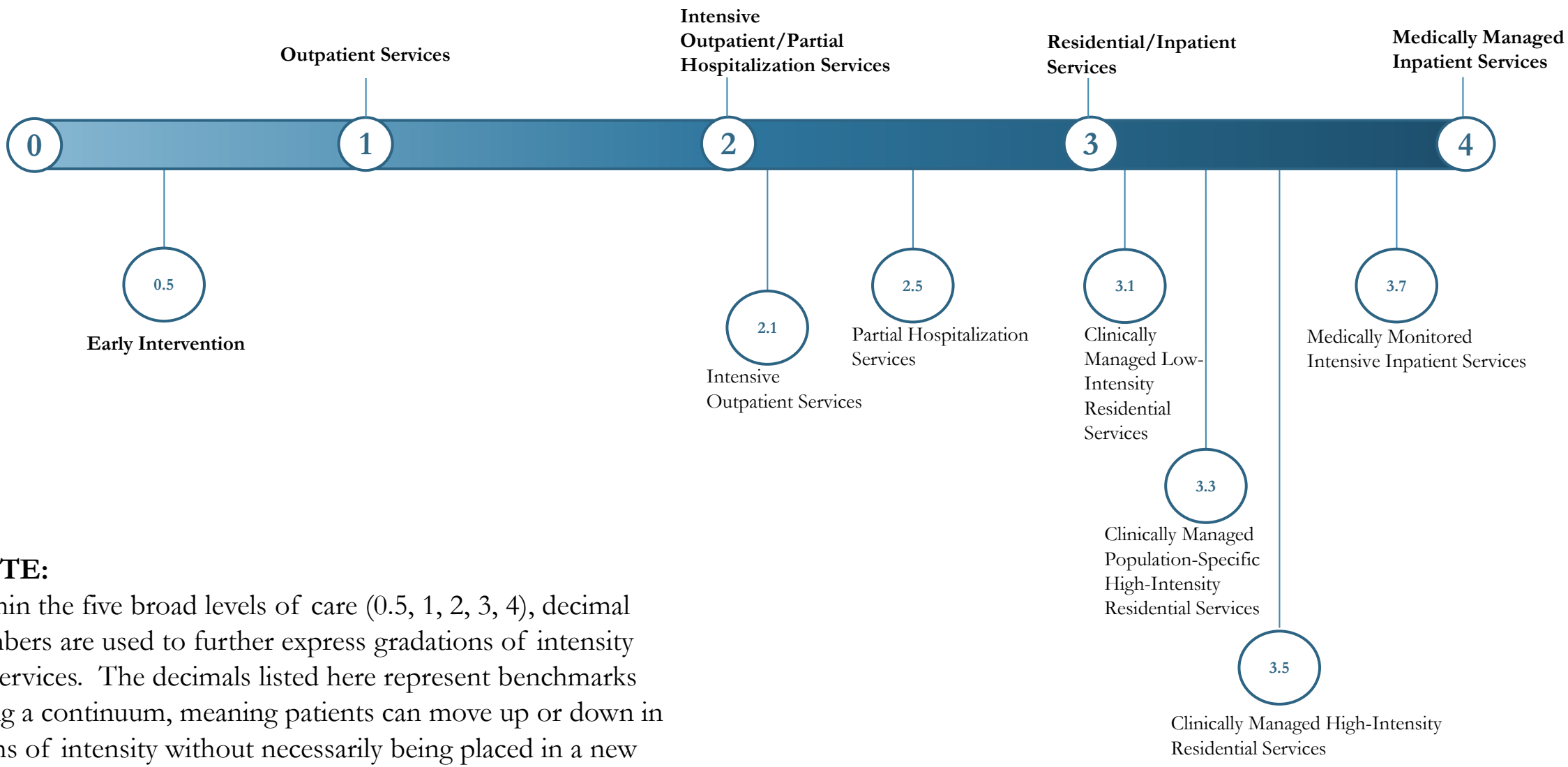
To confirm a diagnosis of AUD, at least two of the following criteria need to be met. Ask your patients, in the past 12-months have you:

- ☐ Had times when you ended up drinking more, or longer than you intended?
- ☐ More than once wanted to cut down or stop drinking, or tried to, but couldn't?
- ☐ Spent a lot of time drinking? Or being sick or getting over the after effects?
- ☐ Experienced craving — a strong need, or urge, to drink?
- ☐ Found that drinking — or being sick from drinking — often interfered with taking care of your home or family? Or caused job troubles? Or school problems?
- ☐ Continued to drink even though it was causing trouble with your family or friends?
- ☐ Given up or cut back on activities that were important or interesting to you, or gave you pleasure, in order to drink?
- ☐ More than once gotten into situations while or after drinking that increased your chances of getting hurt (such as driving, swimming, using machinery, walking in a dangerous area, or having unsafe sex)?
- ☐ Continued to drink even though it was making you feel depressed or anxious or adding to another health problem? Or after having had a memory blackout?
- ☐ Had to drink much more than you once did to get the effect you want? Or found that your usual number of drinks had much less effect than before?
- ☐ Found that when the effects of alcohol were wearing off, you had withdrawal symptoms, such as trouble sleeping, shakiness, irritability, anxiety, depression, restlessness, nausea, or sweating? Or sensed things that were not there?

___ /11 **Severity of AUD is based on the number of criteria met.**

https://cep.health/clinical-products/alcohol-use-disorder/

REFLECTING A CONTINUUM OF CARE



NOTE:
Within the five broad levels of care (0.5, 1, 2, 3, 4), decimal numbers are used to further express gradations of intensity of services. The decimals listed here represent benchmarks along a continuum, meaning patients can move up or down in terms of intensity without necessarily being placed in a new benchmark level of care.

Adapted from ASAM

Modalities of Care

- Addiction Counseling
- Psychotherapy
- Pharmacotherapy
- Mutual help groups (ex: Alcoholics or Narcotics Anonymous)

Any combination of the above may be recommended to patients with the EXCEPTION of recommending medication-assisted treatment be part of treatment for opioid use disorder

Virtual Self-Help Groups

- Virtual AA Meetings
  - https://aa-intergroup.org/
- Virtual NA Meetings
  - https://virtual-na.org/
- SMART Recovery Meetings
  - https://meetings.smartrecovery.org/meetings/

- Do not recommend self-help as the ONLY treatment modality
- Be aware that self-help groups have differing opinions on the use of MAT

Treatment-Resistant Patients

Respect for patient autonomy and their stage of change

Assurance of your continued care for them

Brief intervention

- Elicit permission
- Provide Feedback and Enhance Motivation
- Elicit Response and Set Goals and Follow up

Consider harm reduction strategies

- Prescribing naloxone
- Referral to needle exchange

The use of medications, in additional to psychosocial/behavioral therapies, in the treatment of substance use disorders

Not "replacing one addiction for another," but providing standard of care treatment of a chronic disease which is safe, efficacious, and well-tolerated

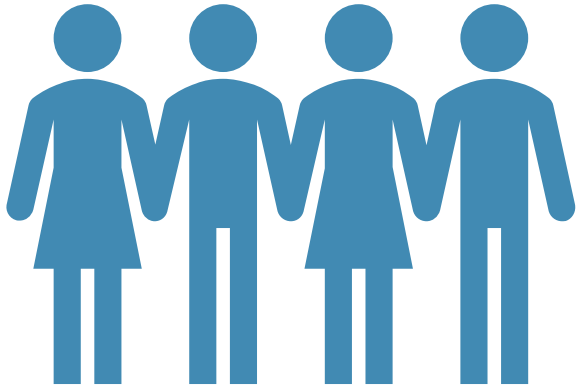
What is Medication-Assisted Treatment (MAT) [New terminology- MAUD, MOUD]

Who is a candidate for medications for substance use disorders?

- Any patient with a moderate to severe substance use disorder

- Patients who are not currently using substances, but who continue to experience strong craving

- Patients who would experience a significant negative consequence of recurrent substance use (ex: medical or legal issues)



Before Starting MAT

Comprehensive history and physical exam including lab work with assessment of kidney and liver function

Mutual goal-setting

Assessment of risk for withdrawal and consideration for medically-supervised withdrawal

Recommend psychosocial treatment

What are the FDA-Approved Medications?

Alcohol Use Disorder

- Naltrexone
- Acamprosate
- Disulfiram

Opioid Use Disorder

- Buprenorphine
- Methadone
- Naltrexone

Mr. White

- 54 year old man with a history of hypertension and smoking admitted to a skilled nursing facility after a prolonged hospitalization for a trauma in a motor vehicle collision. He was intoxicated at the time of the accident.
- Recently, nursing staff became concerned after they found a bottle of liquor hidden under the patient's pillow.
- Mr. White was embarrassed by this incident and asks for help as he has been having strong cravings for alcohol since hospital discharge.

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Naltrexone: Mechanism of action

- Opioid antagonist
- Decreases cravings and pleasurable effects of alcohol by decreasing opiodergic dopamine release and beta endorphins
- Available in a daily oral formulation and monthly long acting injectable formulation

Naltrexone: Efficacy

- **Oral naltrexone**
  - Efficacy established in multiple meta analyses and systematic reviews
  - NNT return to any drinking: 20
  - NNT reduction of heavy drinking 12

- **Long-acting injectable**
  - Associated with a decrease in heavy drinking, but less evidence for return to any drinking

Naltrexone: Advantages

- Once daily dosing or LAI form
- Works well for patients with significant **craving**

Naltrexone: Disadvantages

- Most common side effects: Rare, generally well-tolerated. Include headaches, nausea, vomiting, fatigue, dizziness.
- Rare but serious: hepatotoxicity. Avoid in decompensated cirrhosis or when transaminases are >5 times the upper limit of normal. Monitor liver enzymes.
- Contraindications: current or planned opioid use

Acamprosate: Mechanism of Action

- Poorly understood
- Inhibition of neuronal hyperexcitability, particularly with glutamate at the NMDA receptor
- Administered orally three times daily (standard dose 666 mg tid)

Acamprosate: Efficacy

- Found to be effective in multiple meta analyses and systematic reviews
- NNT return to any drinking = 12
- NNT reduce heavy drinking = 9

Acamprosate: Advantages

May be particularly helpful in the immediate post-withdrawal period due to management of neuronal hyperexcitability

Acamprosate: Disadvantages

- Generally safe, well-tolerated, and no drug-drug interactions
- Rare diarrhea
- Caution with renal failure (reduce dose or avoid use)
- Three times daily dosing

Table 2: Comparative Effectiveness and Strength of Evidence for Acamprosate and Naltrexone as Treatment for AUD

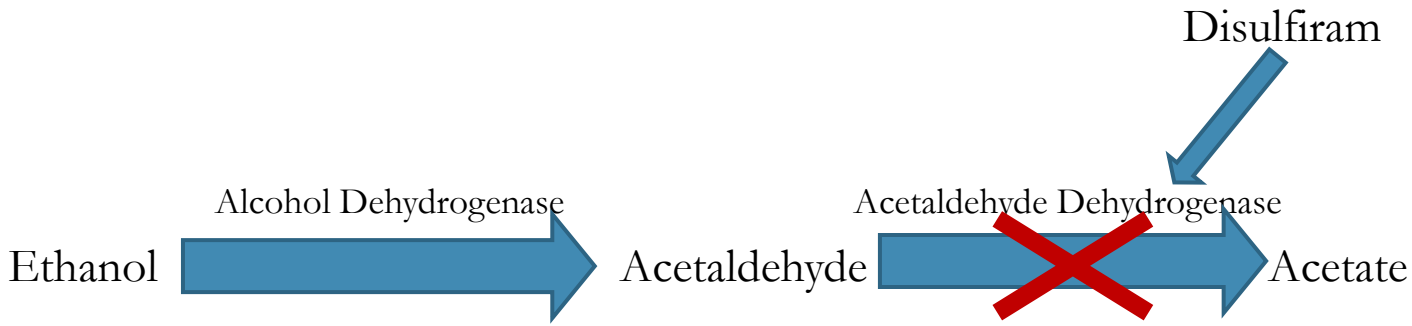
Medication	Outcome	N Studies[a]	N Subjects	Finding	SOE
Acamprosate vs. naltrexone	Return to any drinking	3	800	Not significant[a]	●●○
	Return to heavy drinking	4	1,141	Not significant[a]	●●○
	Percentage of drinking days	2	720	Not significant[a]	●○○

[a]The 95-percent confidence interval was not statistically significant.

COMPARING NALTREXONE AND ACAMPROSATE

Disulfiram: Mechanism of Action

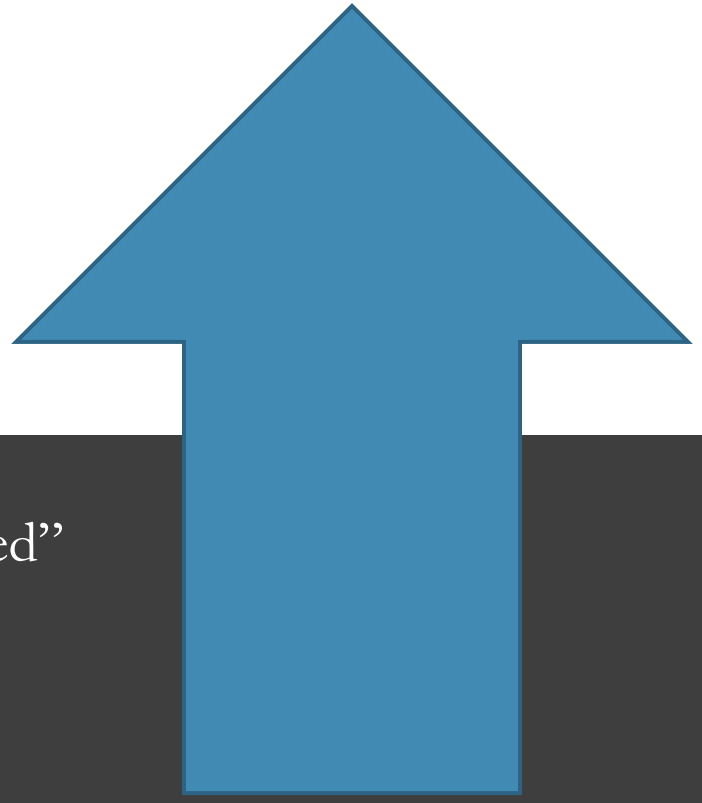
- Inhibits aldehyde dehydrogenase → build up of acetaldehyde and the disulfiram reaction (flushing, sweating, tachycardia, nausea)
- Does not affect the desire to drink alcohol
- Once daily oral dosing



Disulfiram: Efficacy

- Efficacy limited by tolerability and adherence (adherence in unsupervised settings as low as 20%)
- Mixed results in meta analyses

Disulfiram: Advantages



May be most effective in a directly observed setting or for “as needed” use

Disulfiram: Disadvantages

- No alcohol consumption for 24 hours prior to administration
- Warn patients about expected reaction and avoidance of alcohol-containing items such as mouthwash and cooking with alcohol
- Avoid in patients with heart disease
- Common side effects: rash, headache, fatigue, and metallic or garlic taste
- Rare but serious side effects: optic neuritis, peripheral neuropathy, and hepatitis (including cholestatic and fulminant hepatitis and hepatic failure).
- Drug interactions

Off label "Double Dip" Medications

Medication	Evidence	+/-	Special considerations	Dosing
Gabapentin	Mixed efficacy, appears to reduce heavy drinking days	Useful for symptom management in the withdrawal and post w/d period or for anxiety/sleep management	• Addictive potential • "Double dip" for chronic pain	900-3600 mg dosing daily, in divided doses
Topiramate	Strong evidence for increased abstinence and decrease in heavy drinking	Side effects are limiting (cognitive impairment, fatigue)	• "Double dip" for migraines, obesity, seizure disorder	Begin at 25 mg daily and titrate up to goal 100-200 mg daily
Baclofen	Limited evidence, studied in patients with cirrhosis	Sedation effect is limited in patients with AUD	• Can use in advanced liver disease	30 mg daily in divided doses (consider starting at lower doses)

Choosing a Medication

- Naltrexone and Acamprosate are first line FDA- approved medications
- Consider the patients' other medical conditions and medications
- Cost/Insurance issues
- Ease of administration

Mr. White

- 54 year old man with a history of hypertension and smoking. He has normal kidney and liver function.
- He meets 8 criteria for AUD (severe)
- He reports strong craving for alcohol since leaving the hospital, but has a strong desire to be abstinent from alcohol. He is interested in substance use counseling and peer support groups. He is interested in medications for treatment of his alcohol use disorder.

- **What treatment recommendations do you have for Mr. White?**

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Duration of Treatment

- Ideal duration not established
- Generally minimum 6-12 months or until risks outweigh benefits of continuing treatment
- A decision to discontinue therapy may be appropriate in patients who have maintained abstinence, have diminished cravings, and who are engaged in ongoing recovery activities

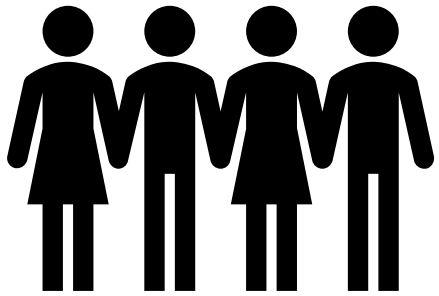
Special Populations

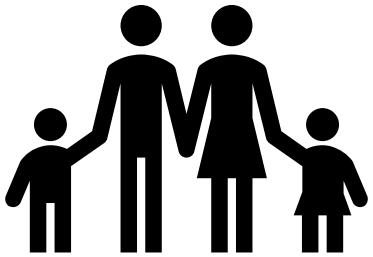
Elderly patients

Same pharmacotherapy as younger adults with caution to choose therapy based on existing conditions and monitor for side effects

Pregnant patients, nursing mothers, and adolescents

Should always be treated in an expert setting with experience in these populations





Mr. Brown

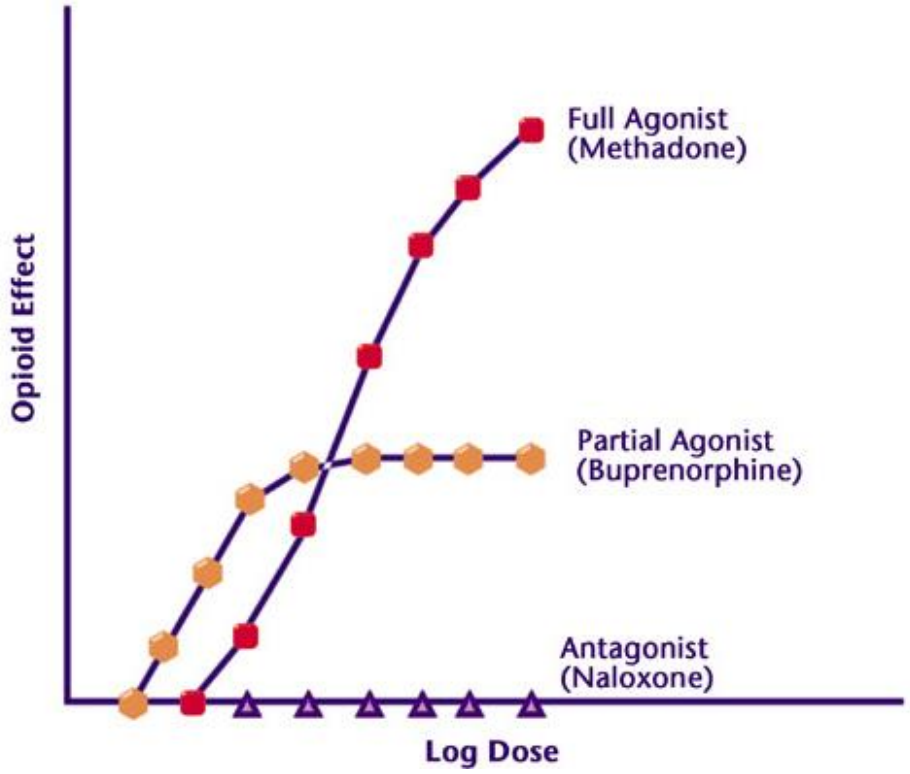
- 26 year old man with a history of opioid use disorder presenting to inpatient physical rehab after a construction accident resulted in trauma with several fractures requiring surgery. He has been progressing in his physical and occupational therapy, but has required oral hydromorphone for pain control.
- Before admission, he was using IV fentanyl and heroin daily for 5 years. He is interested in treatment of opioid use disorder.
- He reports his pain is improving over time.

Buprenorphine Regulations

- Previous DATA (X) Waiver requirement is GONE!
- No patient limit, No specific training requirement to prescribe buprenorphine for OUD (anyone with a DEA license to prescribe schedule III drugs may prescribe)
- MATE Act:
  - New requirement for training for anyone renewing their DEA License (or applying for the first time) to complete 8 hours of training in treating patients with OUD or substance use disorders starting June 2023. One time requirement (not annual)
    - Previous training (X-waiver training) counts
    - Resources:
      - AMA List of Education Resources (many are free) https://edhub.ama-assn.org/course/302
      - DEA MATE Act info: https://www.deadiversion.usdoj.gov/faq/MATE_Act_faq.htm
      - UVA Course: https://www.msv.org/wp-content/uploads/2023/07/UVA-Opioid-Training.pdf

Buprenorphine: Mechanism of Action

- Partial mu-opioid agonist
- Ceiling effect



Buprenorphine: Formulations

1

Combination product- Buprenorphine/ naloxone sublingual tablet and film

- Naloxone only present as a deterrent

2

Monoproduct sublingual tablet (Buprenorphine)*

*only if demonstrated intolerance, <3% of your patients

3

Buprenorphine extended-release subcutaneous injection

- Two approved formulations

4

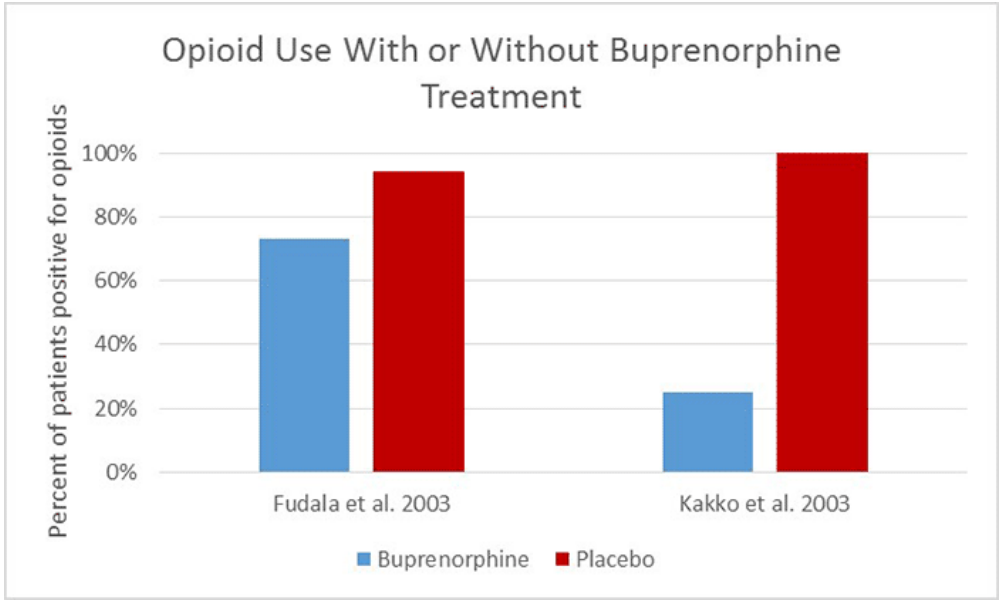
Additional formulations for pain (NOT OUD)

-buccal film (monoproduct)

-transdermal patch

Buprenorphine: Efficacy

- RCT's and meta-analyses show buprenorphine is more effective than placebo in maintaining people in treatment and reducing opioid use, overdose, and death
- Evidence that it can be effective when used in the primary care setting



NIDA

Buprenorphine: Advantages

- Office-based treatment
- Lower risk of side effects and abuse vs methadone
- Long-acting options

Buprenorphine: Disadvantages

- Not more effective than methadone
- Must be in withdrawal to initiate (microdosing protocols are promising)
- Side effects: sedation, constipation, nausea, headache
- Overdose risk- respiratory depression limited by partial activation of mu-opioid receptor, but at risk if taken with other substances

Getting Started

PCSS Providers Clinical Support System

- Education, training
- MENTORSHIP
- 8 hour free training meets DEA MATE requirement
- https://pcssnow.org/medications-for-opioid-use-disorder/buprenorphine-training-for-physicians/

ASAM eLearning

- Buprenorphine Mini Course: Building on Federal Prescribing Guidance
- Free 1 hour course (meets 1 of 8 hours for DEA MATE requirement)
- https://elearning.asam.org/products/buprenorphine-mini-course-building-on-federal-prescribing-guidance

Initiating Buprenorphine: Standard vs Microdosing Induction

- The name of the game is avoiding precipitated withdrawal
- Standard induction is simpler! Can use additional meds for withdrawal (clonidine, ibuprofen, loperamide)
- Microdosing for patients intolerant to withdrawal

Standard Buprenorphine Induction

VCU Health
VCU Medical Center

MOTIVATE Clinic
Division of Addictions
Department of Psychiatry

501 N. 2nd St, #100
Richmond, VA 23219
Office: 804.628.6777

Starting Buprenorphine (Suboxone) at Home

Before beginning, you need to feel very sick from your withdrawal symptoms

It should be at least:

- 12 hours since last use of heroin
- 12-16 hours since last use of pain pills
- 48-72 hours since last use of methadone/ fentanyl

On a scale of 1-10, with 10 being the most sick you have ever felt, you should be at an 8 before starting buprenorphine:

You can take prescribed comfort medications while waiting for these symptoms:

- **Body aches**
- Tremors
- Chills/ sweats
- Irritable, anxious
- Nausea/ **Vomiting**
- **Diarrhea**
- Restlessness
- Runny nose

Once you are ready, follow directions below to start buprenorphine

Day 1:
8-16 mg buprenorphine

Step 1

Take the first 8 mg dose

8 mg

Wait 45 min

- Put the tablet/strip under your tongue
- Keep it there until fully dissolved (about 15 min.)
- Do NOT eat or drink at this time
- Do NOT swallow the medicine

Step 2

Still feel sick?
Take the 2nd 8 mg dose

8 mg

Stop

- Do NOT exceed 16 mg on the first day

Day 2:
8-16 mg

8 mg

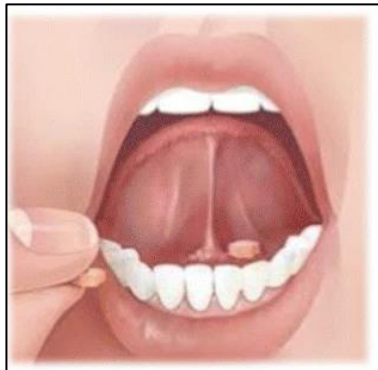
8 mg

-Take 16 mg of buprenorphine
-Most people feel better at 16 mg
-Repeat this dose daily until your next appointment.
-If are still having withdrawal or significant cravings, please call us at (804) 628-6777.

Can use a COWS score of >12 as threshold to initiate

For more information about standard induction, use the **SAMHSA Quick Start Guide**: https://www.samhsa.gov/sites/default/files/quick-start-guide.pdf

Buprenorphine Microdosing Induction



Day	Total dose
1	0.25 mg
2	0.5 mg
3	1 mg
4	2 mg
5	4 mg
6	8 mg
7	12 mg

Most patient with OUD will take **16** (or sometimes up to a max of 24 mg) of buprenorphine daily to control craving and withdrawal

Always give preference to combination (buprenorphine-naloxone) products

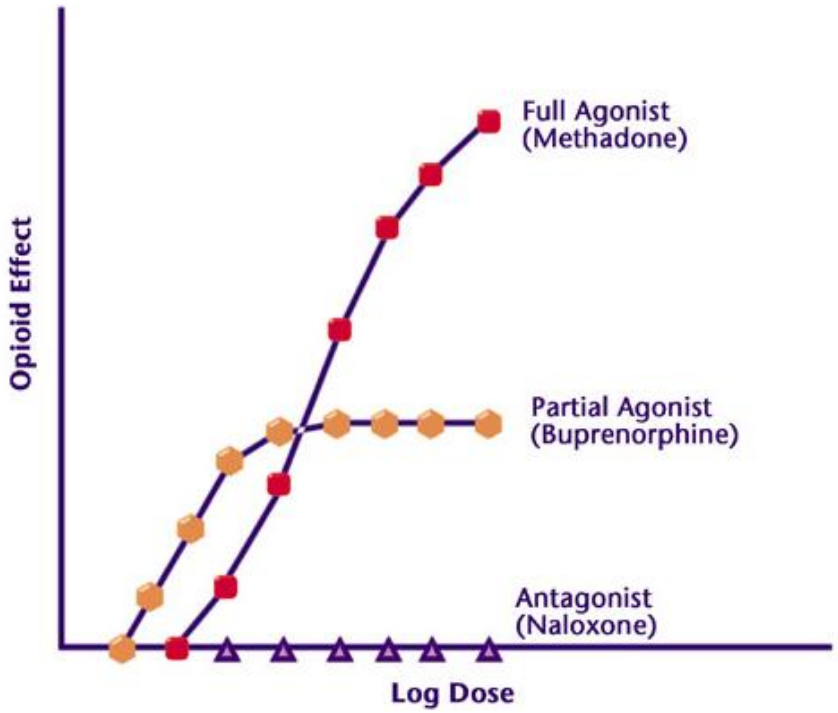
Rozylo J. et al Addict Sci Clin Pract. 2020
https://ascpjournal.biomedcentral.com/articles/10.1186/s13722-020-0177-x/figures/1

Buprenorphine Maintenance

- Most patients should be maintained on 16 mg buprenorphine daily long term
  - Higher dose of 24 mg daily may offer additional pain control (tip: split into multiple doses daily for improved pain management) or rarely for severe continued craving
- Use FindTreatment.gov to locate buprenorphine providers
  - Ensure follow up prior to discharge
  - Give a prescription bridge until follow up (tip: check insurance coverage)
- Consider extended-release injectable!
- Don’t forget to discharge with naloxone rx!

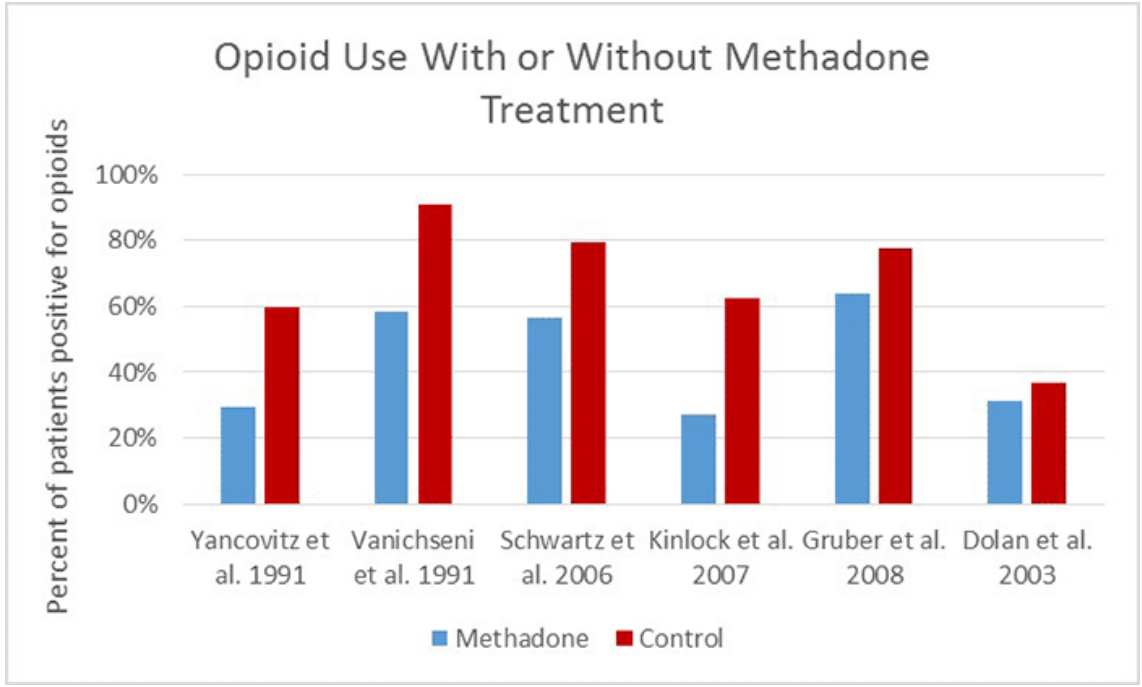
Methadone: Mechanism of Action

- Full mu-opioid agonist
- Long acting
- Maintains a high level of opioid tolerance, limiting euphoric effects



Methadone: Efficacy

- Numerous RCT's and meta-analyses show a decreased number of opiate positive urine
- Patients on Methadone are over 4 times more likely to remain in treatment and have decreased rates of infectious disease transmission and crime compared to placebo with psychosocial treatment



Methadone: Advantages

- No need to be in withdrawal to initiate therapy
- Longest use and best record of efficacy

Methadone: Disadvantages

- Only prescribed at federally-recognized Opioid Treatment Centers (OTP)(not office-based)
- Need for daily dosing in OTP at initiation
- Side effects: constipation, sedation, sweating, medication interactions, cardiac arrhythmias (QT prolongation)
- Higher risk of overdose and side effects vs buprenorphine

Naltrexone

- Efficacy limited by poor adherence to oral and LAI formulations
- When adherence is enforced (ex: court-monitored program), it may be more effective
- Must be free of opioid use and all opioid withdrawal symptoms to safely initiate

Choosing a Therapy for Mr. Brown

- Shared-decision making discussion of the risks, benefits, cost, interactions with other medications or medical conditions, and availability
- Recommend MAT vs psychosocial treatments alone

Duration of Treatment

- Individualized to patient goals and risk for relapse
- Generally, continue for extended periods of time if the benefits continue to outweigh risks
- Weaning agonist therapy is a slow process

Special Populations

Elderly patients

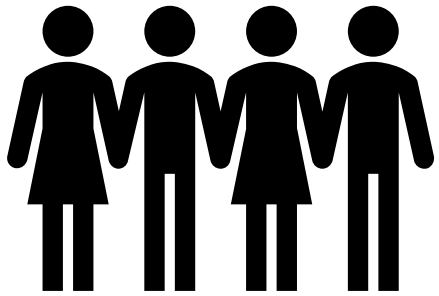
Same pharmacotherapy as younger adults with caution to choose therapy based on existing conditions and monitor for side effects

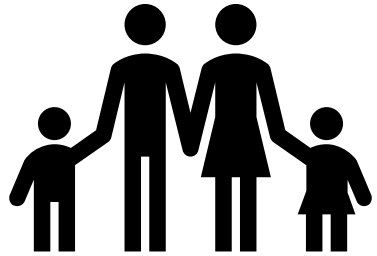
Pregnant patients

All pregnant patients with OUD should be offered MAT with buprenorphine or methadone in an expert setting (more effective than supervised withdrawal)

Adolescents

Candidates for MAT in the expert setting





Conclusions

01

Medication-assisted therapy (MAT) is effective for the treatment of substance use disorders, and should be recommended for all patients with moderate to severe substance use disorders

02

The FDA-approved medications for treatment of Alcohol Use Disorder are Naltrexone, Acamprosate, and Disulfiram

03

The FDA-approved medications for treatment of Opioid Use Disorder are Buprenorphine, Methadone, and Naltrexone

04

Choice of therapy should be based on shared decision-making including discussion of the risks, benefits, cost, and availability of medications

05

MAT should be paired with psychosocial/behavioral treatment for substance use disorders

Resources

- SAMHSA Online Treatment Services Locator
  - https://findtreatment.samhsa.gov/
- CEP Diagnosing a Substance Use Disorder Questions
  - https://cep.health/clinical-products/alcohol-use-disorder
- ASAM Physician Finder
  - https://www.asam.org/publications-resources/patient-resources/fad
- AMA list of OUD/SUD Education for DEA Requirement
  - https://edhub.ama-assn.org/course/302

References

1. ABUSE, S. A. A. M. H. S. A. A. N. I. O. A.; ALCOHOLISM., A. **Medication for the Treatment of Alcohol Use Disorder: A Brief Guide.** Rockville, MD: HHS Publication No. (SMA) 15-4907. Substance Abuse and Mental Health Services Administration 2015.

2. CJ, M. B. A. H. The neurobiology, clinical efficacy and safety of acamprosate in the treatment of alcohol dependence. - PubMed - NCBI. 2018. Disponível em: < https://www-ncbi-nlm-nih-gov.proxy.library.vcu.edu/pubmed/20021295 >.

3. FIELLIN, D. A. et al. Primary care-based buprenorphine taper vs maintenance therapy for prescription opioid dependence: a randomized clinical trial. **JAMA internal medicine**, United States**,** v. 174, n. 12, p. 1947-1954, 2014. ISSN 2168-6114; 2168-6106. Acesso em: Dec.

4. FUDALA, P. J. et al. Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. **N Engl J Med,** v. 349, n. 10, p. 949-58, Sep 4 2003. ISSN 0028-4793. Disponível em: < http://dx.doi.org/10.1056/NEJMoa022164 >.

5. FULLER, R. K. et al. Disulfiram treatment of alcoholism. A Veterans Administration cooperative study. **Jama,** v. 256, n. 11, p. 1449-55, Sep 19 1986. ISSN 0098-7484 (Print)0098-7484. Disponível em: < http://dx.doi.org/ >.

6. How effective are medications to treat opioid use disorder? , 2018. Disponível em: < https://www.drugabuse.gov/publications/research-reports/medications-to-treat-opioid-addiction/efficacy-medications-opioid-use-disorder >. Acesso em: Feb 5 2019.

7. JONAS, D. E. et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. **Jama,** v. 311, n. 18, p. 1889-900, May 14 2014. ISSN 0098-7484. Disponível em: < http://dx.doi.org/10.1001/jama.2014.3628 >.

8. KAKKO, J. et al. 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomised, placebo-controlled trial. **Lancet,** v. 361, n. 9358, p. 662-8, Feb 22 2003. ISSN 0140-6736 (Print)0140-6736. Disponível em: < http://dx.doi.org/10.1016/s0140-6736(03)12600-1 >.

9. KRUPITSKY, E. et al. Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial. **Lancet,** v. 377, n. 9776, p. 1506-13, Apr 30 2011. ISSN 0140-6736.

10. LAAKSONEN, E. et al. A randomized, multicentre, open-label, comparative trial of disulfiram, naltrexone and acamprosate in the treatment of alcohol dependence. **Alcohol,** v. 43, n. 1, p. 53-61, Jan-Feb 2008. ISSN 0735-0414. Disponível em: < http://dx.doi.org/10.1093/alcalc/agm136 >.

11. MATTICK, R. P. et al. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. **Cochrane Database Syst Rev**, n. 3, p. Cd002207, 2004. ISSN 1361-6137. Disponível em: < http://dx.doi.org/10.1002/14651858.CD002207.pub2 >.

12. Pharmacotherapy for Adults With Alcohol Use Disorder (AUD) in Outpatient Settings | Effective Health Care Program. 2016. Disponível em: < https://effectivehealthcare.ahrq.gov/topics/alcohol-misuse-drug-therapy/clinician >.

13. ROSNER, S. et al. Opioid antagonists for alcohol dependence. **Cochrane Database Syst Rev**, n. 12, p. Cd001867, Dec 8 2010. ISSN 1361-6137. Disponível em: < http://dx.doi.org/10.1002/14651858.CD001867.pub2 >.

14. TREATMENT, C. F. S. A. Incorporating Alcohol Pharmacotherapies Into Medical Practice. 2009 2009. Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/ >.

15. TREATMENT, N. A. O. A. F. B. **Buprenorphine Education: Technical explanation of Buprenorphine mu receptor, affinity of agonist and antagonist** 2019.

References

- NIDA-Modified ASSIST (NM ASSIST) https://archives.drugabuse.gov/nmassist/
- **Christina Brezing, MD, Adam Bisaga, MD,** Opioid Use Disorder: Update on Diagnosis and Treatment, **Psychiatric Times**, Vol 32 No 4, Volume 32, Issue 4, April 30, 2015
- **BRIEF INTERVENTION FOR SUBSTANCE USE: BRIEF INTERVENTION FOR SUBSTANCE USE:A MANUAL FOR USE IN PRIMARY CARE**. World Health Organization (WHO) 2013.
- Community Services Boards. 2019. Disponível em: < http://dbhds.virginia.gov/community-services-boards-csbs >. Acesso em: February 6 2019.
- MCKAY, J. R. et al. Conceptual, methodological, and analytical issues in the study of relapse. **Clin Psychol Rev,** v. 26, n. 2, p. 109-27, Mar 2006. ISSN 0272-7358 (Print)0272-7358. Disponível em: < http://dx.doi.org/10.1016/j.cpr.2005.11.002 >.
- MEE-LEE, D.; AMERICAN SOCIETY OF ADDICTION MEDICINE. **The ASAM criteria : treatment for addictive, substance-related, and co-occurring conditions**. Third edition. Chevy Chase, Maryland: American Society of Addiction Medicine, 2013. xv, 460 pages ISBN 9781617021978
- National Helpline | SAMHSA - Substance Abuse and Mental Health Services Administration. 2018. Disponível em: < https://www.samhsa.gov/find-help/national-helpline >. Acesso em: February 6 2019.
- Olfson M, Zhang V, Schoenbaum M, King M. Buprenorphine Treatment By Primary Care Providers, Psychiatrists, Addiction Specialists, And Others. Health Aff (Millwood). 2020 Jun;39(6):984-992. doi: 10.1377/hlthaff.2019.01622. PMID: 32479224.
- National Institute on Alcohol Abuse and Alcoholism. Helping patients who drink too much: a clinician's guide, 2005 Edition. Bethesda, MD, 2007.
- Rozylo J, Mitchell K, Nikoo M, Durante SE, Barbic SP, Lin D, Mathias S, Azar P. Case report: Successful induction of buprenorphine/naloxone using a microdosing schedule and assertive outreach. Addict Sci Clin Pract. 2020 Jan 15;15(1):2. doi: 10.1186/s13722-020-0177-x. PMID: 31941547; PMCID: PMC6964069.
- Salapenka I, Konakanchi JS, Sethi R. Outpatient Rapid Microinduction of Sublingual Buprenorphine in 3 Days From Methadone for Opioid Use Disorder. Prim Care Companion CNS Disord. 2022 Dec 27;24(6):21cr03150. doi: 10.4088/PCC.21cr03150. PMID: 36584361.