Medication-Assisted Treatment (MAT) for Opioid Use Disorders

Sybil Marsh MA MD FASAM
Department of Family Medicine and Community Health
Case Western Reserve University/UHCMC
Learning Objective 1

• Following this presentation, participants will be able to name 3 medications useful in the treatment of opiate use disorder, and describe for each:
  • indications
  • mechanism of action
  • dosing
  • common side effects
  • effectiveness
Learning Objective 2

• Review some fears and misconceptions about medication-assisted treatment (MAT) that can interfere with its appropriate use.

• Appreciate evidence for the statement that “opioid substitution treatment is effective in suppressing illicit opioid use and reducing all cause an overdose mortality” (Sordo, BMJ, 2017).
Learning Objective 3

• Discuss strategies to more fully integrate MAT into existing mental health, medical and substance use disorder services
Epidemics of unintentional drug overdoses in Ohio, 1979-2008\textsuperscript{1,2,3}

Prescription Opioid Doses per Capita
Ohio’s Automated Rx Reporting System - 2013

N = City ranked by # of Medicare Opioid Rx per city inhabitant.
● = Presence of top 25 prescriber to Medicare patients.

Doses Per Capita
- 22.1 - 61.2
- 61.3 - 84.0
- 84.1 - 119.2
Drug overdose death rates by state per 100,000 people (2008)

Ohio needs effective ways to prevent overdose deaths and other costs of OUD
OD deaths- prescription vs other opioids
What does it mean?

• Even though doses of prescribed opioids and overdose deaths related to them have declined over time, the percentage of deaths due to other opioids has increased

• Total deaths by opioid overdose have increased over recent years, and the major source is illicit

• Opioids from every source are deadly

• They’re not going away

• We need to prevent first use and...

• We need effective treatment for people with opioid use disorder, including long-term relapse prevention
Is MAT effective?

• MAT, particularly with opioid agonist medications, has been found to reduce morbidity and mortality, decrease overdose deaths, reduce transmission of infectious disease, increase treatment retention, improve social functioning, and reduce criminal activity. National and international health organizations, such as the American Society of Addiction Medicine (ASAM), and the World Health Organization, consider MAT an evidence-based best practice for treating opioid use disorder. SAMHSA Advisory 2016
Indications for MAT medications

• Methadone and buprenorphine (or buprenorphine/naloxone) are approved to treat opioid dependence
• Extended-release injectable naltrexone is approved for prevention of relapse to opioid use
• Short acting oral naltrexone reduces craving and binging on alcohol
• Naloxone treats opioid overdose (temporarily)
Indications for MAT medications

• Successful use of MAT requires:

  **Medically-assisted withdrawal** for naltrexone and `buprenorphine (“detox”) - NOT for methadone

  Adequate **medical care** for life threatening disease (infections, liver disease, cardiovascular, psychiatric disease)

  **Willingness to engage** in counselling, behavioral therapies, outpatient psychosocial treatment including mutual help groups like NA and AA

  **Resources** that facilitate treatment for as long as necessary

  **Informed consent** as for other medications
Mechanism of MAT medications

• **Methadone**—agonist
  • Fills opiate receptors
  • Same effects as other opiates- but “slower and flatter”, prevents craving, can cause sedation, but not euphoria

• **Buprenorphine**—partial agonist
  • Fills opiate receptors imperfectly
  • Partial opiate effect and a “ceiling” dose-

• **Naltrexone**—antagonist
  • Blocks opiate receptors
  • NO opiate effect
Effect of MAT on Opioid Receptors
Methadone

• Opiate agonist for treatment of severe opiate use disorder
• Well-studied and effective (BMJ, 2017)
• Normalizes function/return to work, decreases crime/violence, reduces HIV and Hepatitis C exposure
• Dose is individualized to stop craving, avoid sedation
• Goal is lowest dose that prevents withdrawal, minimizes craving and blocks “high” caused by opiates
• Not a “stand-alone” but a program of treatment
• Enhanced services improve outcomes
• Counseling, medical, behavioral, social/vocational services, etc.
Figure 3.2. Methadone Simulated 24 Hr. Dose/Response At Steady – State in a Tolerant Patient
Methadone dosing

• Usually taken once a day to suppress withdrawal for 24 to 36 hours
• Usually given in liquid form or wafer by MAT Program
• Induction phase—no more than 30 to 40 mg on the first day of treatment
• Dose changes usually occur once a week (every 5-7 days)
  • More rapid dose increases can cause overdose because of rise in blood level with each dose till dose #5
• Maintenance phase—usually 80-120 mg, sometimes less
• Sometimes more for high tolerance, CP 450-inducing medications (like Depakote)
Methadone side effects and hazards

• Common side effects
  • Sweating, constipation, decreased libido, mild anorexia/nausea, weight gain, water retention, dry mouth

• Adverse effects
  • Cardiac rhythm abnormalities
  • Prolongation of QTc (usually seen with very high doses, mean of 350mg daily)
  • Oversedation at excessive dose- different from being “high”
  • Potential interaction with risk of oversedation with ALCOHOL, BENZODIAZEPINES, BARBITURATES
Methadone: “Still an addict?”

- PHYSICAL DEPENDENCE is not SUBSTANCE USE DISORDER/ ADDICTION
- Pharmacology of methadone prevents highs and lows common with short-acting drugs and normalizes patient functioning
- Overuse gives a side effect is sedation, not euphoria
- The patient is PHYSICALLY DEPENDENT on methadone, so might appear to be “drug seeking” to avoid withdrawal but...
- no longer displays behaviors consistent with active opiate use disorder and instead shows evidence of improved quality of life
- Successful methadone treatment results in “Severe Opioid Use Disorder in Remission” not active addiction
- Dr. Bob said it best...
Buprenorphine

• Approved in U.S. (2002) as **office-based treatment (OBOT)** as an alternative to ‘methadone clinics’

• Individual doctors may treat up to 30 patients at a time, using an special DEA number
  • After 1 year, may increase to 100 patients

• Must be addiction medicine/addiction psychiatry certified OR complete 8 hour training

• Must comply with Federal, State and insurance rules and regulations
Buprenorphine mechanism

- Opioid **partial agonist** with a ceiling effect
  - ↓ risk of overdose and ↓ abuse potential
  - May precipitate opiate withdrawal in dependent individuals, so must be started carefully with negative urine drug screen - best started in mild to moderate withdrawal

- Approved for treatment of opiate dependence (severe opiate use disorder)
  - Maintenance dose in the range of 8-16 mg daily, occasionally up to 24 mg

- Sublingual route of administration
  - Buprenorphine only vs. Buprenorphine +naloxone - preferred!
Many variations, same mechanism

Generic buprenorphine
Subutex tabs, films

Generic buprenorphine/naloxone
Suboxone tabs, film
Zubsolv
Bunavail

Not: Butrans patch (chronic pain)
Buprenorphine dosing

• Suboxone, Zubsolv and Bunavail are buprenorphine + naloxone in a 4:1 mixture

• **Treatment agreement**- informed consent

• Not a “stand-alone”, but a “program”- patient should begin a log of counselling, 12 step meetings, other recovery-promoting activities

• Induction phase Day 1: usual dose is 2 mg given every 2-3 hours, up to 8 mg

• Induction phase Day 2: start with 8mg, can go up to 16mg depending on patient symptoms
Buprenorphine- side effects and hazards

• Maintenance phase: usually 8 to 16 mg daily
• This may vary in clinical practice; 16mg dose covers ~95% of opiate receptors
• Adjust dose if necessary- consider craving, tolerance, interactions
• Adverse side effects: Liver abnormality, cytolytic hepatitis
• Common side effects: generally mild
  • Constipation; dizziness; drowsiness; headache; nausea; sweating; vomiting;
• Strategies to manage need for full agonist opiates (surgery etc.)
• Potential interaction with alcohol (avoid), benzodiazepines, barbiturates- (avoid when able, minimize always)
Naltrexone mechanism

• Opiate antagonist to treat opiate dependence
• All effects of opiates are blocked
  • Must undergo medically supervised withdrawal and be opiate-free when starting, or severe withdrawal occurs
• Blocks opioid receptors that are involved in the rewarding effects of opiates (& alcohol!)
• Long term effects on endorphins unknown
• Risk for hepatotoxicity
  • Monitor liver enzymes
Naltrexone- injected, long acting

• Brand name is Vivitrol
• Injection of microspheres provides medication for 30 days
• Approved for alcoholism in 2006
• Approved for opiate dependence Oct 2010
• Given monthly, 380 mg appears to have increased efficacy versus 190 mg
• Reduces craving by occupying receptors and preventing opioid effect
Naltrexone- oral, short acting

- Brand name is Revia (oral tablets)
- Usual dose: 50mg daily
- Efficacy highest in patients who can abstain for 4 to 7 days before initiating treatment
- Not proven better than placebo
- High drop-out rate
- More compliance when the drug involved is alcohol, not opiate
Naltrexone side effects and hazards

- **Side effects** may include anxiety, nervousness, headache, joint pain, nausea- or none of these
- **Injection** requires knowledge of technique to avoid tissue damage
- May not reduce craving as well as agonists **Non-compliance** is the main barrier to success
  - Not taking pills
  - Not showing up for injection
- Most useful for highly motivated patients w/ external circumstances
  - Impaired professionals, parolees, probationers, etc. for whom relapse would bring severe consequences
- Role in relapse prevention for non-dependent opioid users- think younger, newer users with hazardous use pattern, less physical dependence
CAUTION - Naltrexone needs aftercare

• When clients have had opiate receptors blocked for some time, their tolerance is reduced
• Returning to drug use at the same amount they used before blockade by naltrexone puts the client at INCREASED RISK for overdose and death due to lowered tolerance
• This information needs to be shared with all clients, who should get naloxone for emergency use
• Need more research on its long term effects
• Ongoing assessment and after care are needed to ensure continued USE and EFFECTIVENESS
• Most vulnerable time is when naltrexone is stopped because:
  • Client attributes symptoms to it, stops with no back-up plan
  • Client feels (or is told he is) “ready” to get back to “normal life”, is “graduating” and will “NEVER use drugs again”
Naloxone

• Opiate antagonist
• For overdose: Autoinjector, nasal atomizer routes
• Fast acting (2 minutes) with ½ life 1 hour- gone quickly
• Gives enough time to go to ED for naloxone IV drip and other help
• Many recipients REFUSE to go to ED, do not seek treatment, and may have medical and cognitive consequences of their overdose
MAT is MORE than MEDICATION

• **Medications** work on the opioid receptors to relieve craving and prevent withdrawal symptoms.

• **Behavioral treatments** educate patients about the conditioning process and teach relapse prevention strategies.

• Evidence favors using these approaches **TOGETHER**
  • Greater retention
  • Less risk of relapse and overdose
  • More opportunity for **RECOVERY**
Is MAT Recovery?

• Recovery status is best defined by factors other than medication status. Neither medication-assisted treatment of opioid addiction nor the cessation of such treatment by itself constitutes recovery. Recovery status instead hinges on broader achievements in health and social functioning—with or without medication support.

A. Thomas McLellan and William White
Duration of a MAT program - how long?

• AS LONG AS THE PATIENT NEEDS IT
• Mild OUD may respond to behavioral treatment, relapse prevention alone
• Severe OUD is a chronic relapsing lethal disorder and requires chronic effective treatment
• Compare it to “diabetes”
• Bad medicine: “You’ve been on insulin long enough! Time to taper it off! You can do it, just keep going to counselling and use the 12 steps!”
• Bad medicine: “You’ve been in MAT long enough! Time to taper it off! You can do it, just keep going to counseling and use the 12 steps!”
Possible Barriers to using MAT

Fear # 1:
Medication will eventually replace rehabilitation as the treatment of choice for addiction→ “a pill for every ill”

• Response # 1:
  • Medication may be a useful \textit{adjunct} to treatment
  • “Another tool in your toolbox”
  • It increases effectiveness of behavioral treatment because the client can pay attention and participate, and apply lessons without being overpowered by craving
Possible Barriers to using MAT

Fear #2:
Medication will distract from the difficult work needed for recovery from substance use disorder
“makes it too easy to be “clean””

• Response # 2:
• Medication makes withdrawal safer and more humane, and increases retention in treatment
• Medication may allow the process of recovery to begin and continue
• Medication provides a safety net so the patient can take risks to do the “difficult work”
Possible Barriers to using MAT

Fear # 3: Medication will continue an existing addiction

• Rationale # 3:
  • Physical dependence to medication may occur, but addiction behavior will decrease
  • MAT addresses co-occurring use disorders behaviorally or by intensifying treatment
  • Some room for harm reduction
  • 12 step approach to medications is clear and compatible with MAT, though some members’ opinions may not be
Possible Barriers to using MAT

Fear # 4: Medication will cause new addictions

Response # 4:
- Incidence is low because methadone and buprenorphine are not highly reinforcing- “not worth it”
- Physical dependence is not addiction
Possible Barriers to using MAT

Fear # 4:
Medication will cause new addictions

• Response # 4:
• Incidence is low because methadone and buprenorphine are not highly reinforcing—“not worth it” to use to get high
• Naltrexone not at all reinforcing
• Patient self-care includes education about risks of physical dependence and withdrawal prevention strategies
Other Barriers to MAT?

Financial
- MAT may be an expense and insurance coverage inconsistent

Logistical
- Not enough methadone clinics; not enough slots
- Many physicians are trained to prescribe buprenorphine, but relatively few are actually prescribing
- Why?!?
- Usual treatment settings are not set up to provide MAT
- OBOT (Office Based Opiate Treatment) is time consuming in a primary care office and involves complex decision making
- Buprenorphine can be diverted and misused
- Mixed messages to prescribers about OBOT cause anxiety:
  - We need you!
  - We’re watching you!
Helping clients get access to MAT

• Most patients self refer
• There are not enough treatment providers- waiting lists and travel
• Not all providers accept insurance
• How to help a reluctant client with the idea of starting and staying on MAT?

• Try some Motivational Interviewing:
  • Listening and Reflection
  • “Ask-tell-ask” to correct misinformation
    • “if I take meds, then I am not really sober”
    • “What do you know about?” ....
More Motivational Interviewing

- What are the client’s goals?
- How does medication fit (or not fit) with those goals?
- What are the pros and cons of the medication available?
- What are the patient’s fears about medication?
- Use reflective listening
- What is the patient willing to do right now? Go for assessment? Talk about it some more? Medically supervised withdrawal and IOP or other behavioral interventions while thinking about it?
- Start with antagonist (long long-acting injectable naltrexone), moving to agonist treatment if needed?
False + due to nutritional supplement/stimulant, so he stopped it* CFS system case closed*No mania on Depakote and a higher than average Suboxone dose* Self-pay, decreased drug screening schedule after 3 negative tests*Stopped using heroin and has a job despite chronic pain*In intensive counseling now for mood disorder*Kept her job as a dancer, and her 8 year old son*Recovering from endocarditis* Got a knee replacement without relapsing*Completes treatment for Hepatitis C*Finally getting counseling for life-long anxiety*Breastfeeding her baby*Didn’t relapse when her grandma died and kept taking her meds* Stopping MAT in the spring, with 5 meetings per week*May have thyroid cancer, but hasn’t relapsed* Hopes he’ll be back for reinduction and COPD treatment post incarceration* Went off MAT and died of heroin overdose* Died of an overdose while in a MAT program* Died of cancer while on methadone, but not because of methadone* Lived another day because of MAT*
Discussion

• What strategies can your setting use to help patients/clients who would benefit get access to MAT?
  • Inpatient and Outpatient
  • AOD and MH
  • Physical and Behavioral health
  • Integrative health

• Think of a short-term goals (3 to 6 months) and long-term goals (12 to 24 months) that would improve access, use, or integration MAT services for clients who would benefit from them?

• What further training or support would help your organization meet these goals?
Summary

• MAT is an important tool in the toolkit for treating opioid use disorders- it can be lifesaving!
• Despite internal and external barriers, MAT can be successfully implemented; antagonist treatment presents fewer barriers
• More agonist treatment is needed state-wide to increase choice
• Set short- and long-term goals to support and more fully integrate MAT into your setting
Resources and References

• Center for Evidence Based Practices, Case Western Reserve University, www.centerforebp.case.edu

• BUPRENORPHINE TREATMENT: A TRAINING FOR MULTIDISCIPLINARY ADDICTION PROFESSIONALS
  • www.nida.nih.gov/blending/buptreatment.html

• www.pcss-o.org
Resources and References

• Center for Substance Abuse Treatment. Medication Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) Series 43. DHHS Publication No. (SMA) 05-4048. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2005

• Sordo, Luis et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of covert studies. BMJ, 2017;357:j1550

• SAMHSA Advisory, HHS Publication No. (SMA) 16-4938, 2016