Medication Addiction Treatment for Opioid Use Disorders

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Educational Objectives

- Identify 3 types of MAT for the treatment of Opioid Use Disorders (OUDs)
- Identify pros and cons of each modality
- Be familiar with treatment plans with objective monitoring of sobriety for each modality

» Slides Courtesy of Arthur Robin Williams, M.D.; Assistant Professor of Clinical Psychiatry

Overview: Medication Assisted Treatment

- "MAT" is as a term for using medications to treat opioid use disorders (OUDs)
- More recently, instead of using the term "assisted" treatments, move towards addiction treatment- Wouldn't say antipsychotic medication for schizophrenia is "assisted" treatment
- These medications are LIFE-SAVING and should be first-line treatments
- MAT is provided in addition to intensive psychosocial and behavioral therapy
- MAT for OUDs refers to the use of methadone, buprenorphine, or naltrexone
- There is no evidence for a pre-determined length of treatment for MAT
  - Longer Retention = Better Outcomes

Background: Addiction Neurochemistry

- Opioids activate opioid receptors in the brain
- Without opioids, unstable receptors lead to:
  - Withdrawal symptoms
  - Intense cravings
- Receptors are stabilized with MAT medications
- Patients on MAT:
  - Experience fewer and less intense cravings
  - Use drugs at much lower rates

Background: MAT for OUDs

- "Opioids" include synthetic pain pills and heroin
- "Opiates" are natural opioids like opium or morphine
- Unlike other addictive drugs, opioids carry greater risks, such as overdose death
- Injection drug use adds risks such as infectious disease (HIV, Hepatitis C) and injuries

Background: MAT for OUDs

- **MAT is the gold standard for OUD treatment:**
  - **Reduces drug use**
  - **Protects against overdoses**
  - **Prevents injection behaviors**
  - **Reduces criminal behavior**

Background: MAT for OUDs

- MAT includes 3 modalities:
  - Methadone (schedule II)
  - Buprenorphine (schedule III)
  - Naltrexone (not controlled)
- Each modality should be provided in addition to intensive psychosocial and behavioral therapy
- Patients benefit from MAT for >1-2 years of sobriety before attempting to taper, with dosing reassessments every 6 months

Background: MAT for OUDs

- Each MAT modality requires a different induction process for stabilizing the patient
- Each modality has different logistical and financial requirements
- Each modality has different pros and cons
- Patients may respond better to one modality
- As a result, all three options should be available to every patient

Methadone (approved 1972)

- Invented in 1960s; President Nixon heavily funded methadone to treat Vietnam War veterans
- Highly restricted and provided through licensed *programs* that initially require daily attendance
- Methadone fully activates the opioid receptor but lasts for 24 hours, smoothing out highs and lows
- Methadone maintains opioid tolerance, lowering relapse and overdose rates if patients use opioids
  - Higher doses (>60mg) improve these outcomes

Fullerton et al 2014

Methadone: Pros and Cons

- **Pros**
  - Easy induction from active use
  - Lower medication costs but program fees vary
  - Best medication for retaining patients in treatment at 12 months (~80%)
  - Lowers drug use and criminal activity
  - Treatment of choice for pregnant women

Friedman et al 1994; Lund et al 2013

Methadone: Pros and Cons

- **Cons**
  - Requires early morning daily dosing
  - Many states and rural areas have limited access
  - Programs are targeted by drug dealers
  - Patients often combine benzodiazepines and other medications to get "high" on a regular dose
    - i.e. patients "nodding out"
    - Can lead to overdose (esp. first 2 weeks)
  - Can cause medical complications (arrhythmias)
  - Patients face more stigma

Methadone: Monitoring

- Programs are heavily regulated at federal level
- Often have additional state-level restrictions
- Patients are directly observed taking doses
- Patients are frequently drug tested in the program
- Patients are only allowed "take home doses" once stable in recovery with negative urines
- Often program physicians refuse to prescribe benzodiazepines but patients find them anyway

Buprenorphine (approved 2002)

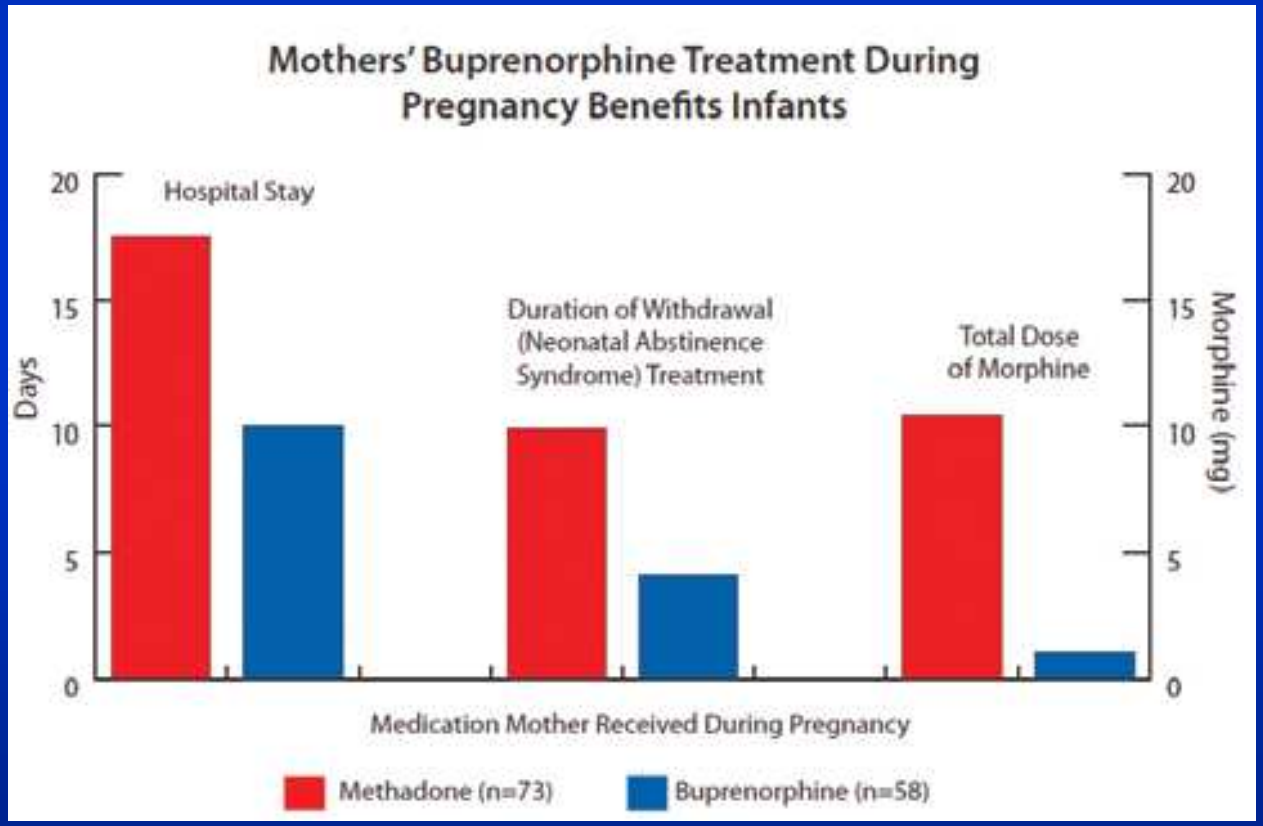
- Used since 1970s for pain
- Developed for addiction treatment more recently
- DATA 2000 Act allows individual physicians to prescribe via an outpatient office
- Physicians must complete 8-hour training and get "waivered" with a DEA "X number" to prescribe
- Can be prescribed with multiple refills
- Often sold as a combo product with naloxone [Suboxone] to deter abuse (i.e. injection)

Buprenorphine: Pros and Cons

- **Pros**
  - Greatly reduces overdose risk
  - Very good pain control when dosed every 6 hours
  - Can be prescribed like any other medication
  - Often monitored in prescription drug monitoring programs (PMPs)
  - Good for pregnancy, better newborn outcomes?
  - Somewhat less stigma (remains controversial)

Buprenorphine: Pros and Cons

- **Buprenorphine may produce better outcomes than methadone for pregnant women and newborns:**



Buprenorphine: Pros and Cons

- **Cons**
  - Patients must be in withdrawal to take first dose
    - Can precipitate withdrawal if taken too soon
    - As a result, some patients struggle to start
  - Physicians need DEA waiver, few prescribe it
  - Has street value and can be sold/diverted
  - Patients can intentionally space out doses and use opioids in between
  - Some people inject it (despite abuse deterrence)

Buprenorphine: Monitoring

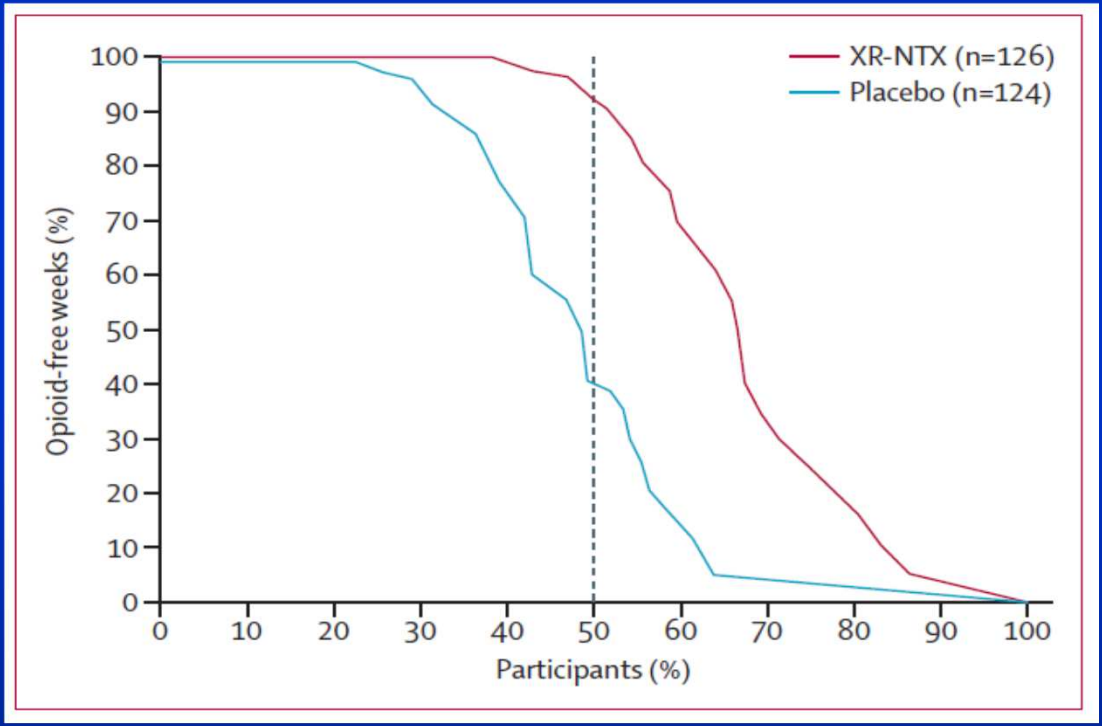
- **Check prescription drug monitoring program (PMP)!**
- **Requires routine urine testing**
  - Urine should be positive for buprenorphine (if negative, suggests diversion)
  - Urine should be negative for opioids and benzodiazepines
- **Aberrant behaviors must be monitored including:**
  - "Losing" prescriptions and/or running out early
    - May need dose increase
    - Prescribe for shorter intervals (i.e. weekly)
  - Requesting dose > 16-24mg (suggests diversion)
    - Use in-office medication counts

Naltrexone (approved 1984, 2010)

- Naltrexone binds tightly to opioid receptors, pushing off all other opioids (whether used before or after taking naltrexone)
- Available as a daily pill or as a monthly injection, "the blocker shot," called xr-naltrexone (Vivitrol)
- Completely protects from overdose for 4 weeks
- Reduces cravings due to activity at opioid receptor
- Does not cause physical dependence and patients lose their opioid tolerance while taking

XR-Naltrexone

- **Monthly injection, "Vivitrol," is an extended release form of naltrexone enhancing outcomes**



XR-Naltrexone: Pros and Cons

- **Pros**
  - Patients no longer fear going into withdrawal
  - Blocks opioid use of any kind
    - ~50% of patients "test" the blockade initially and quickly extinguish use
  - Can be given as monthly injection (Vivitrol) to ensure adherence and block relapse
    - Injection has 2x retention as oral treatment
  - Less stigma

XR-Naltrexone: Pros and Cons

- **Cons**
  - Most difficult induction, requires 3-10 days of abstinence: Patients must fully detox to start, often drop out
  - Hard to find providers
  - Many insurers don't reimburse (costs $1,500/mo)
  - Lowers tolerance: if patients stop medication they could overdose if/when relapsing
  - No pain relief and should be stopped for surgery

XR-Naltrexone: Monitoring

- **Least likelihood of abuse/diversion (no street value)**
- **Injection is directly administered by clinician**
- **Frequent urine testing remains vital to treatment**
- **About half of patients "test" blockade initially; can be therapeutic experience, extinguishing behavior**
- **Patients with protracted withdrawal may require additional treatment**
  - Insomnia common for 1-2 months
  - Anxiety and gastrointestinal distress also common

Tapering

- **Typically patients with continuous sobriety for 1-2+ years have the best outcomes**
  - Treatment <6 months has worse outcomes
- **There is no evidence to support stopping MAT**
  - 95% of methadone patients do not achieve abstinence when attempting to taper off (Nosyk, et al. 2013)
  - Over 90% of buprenorphine patients relapse within 8 weeks of taper completion (Weiss, et al. 2011)
- **Successful patients are commonly maintained on**
  - Methadone for 24+ months
  - Buprenorphine for 18+ months

Tapering

- **Clinical considerations before tapering:**
  - Treatment history (i.e. prior relapse after taper)
  - Addiction history (length/severity)
  - Family history
  - Resilience and personality traits
  - Life stressors, loss, and transitions
  - Patient motivations for tapering

Tapering MAT

- **Methadone and buprenorphine**
  - **Better results with longer taper (over months)**
  - **Methadone programs often "blind" the dose**
  - **May need new medications for symptom relief**
  - **Many patients relapse during this process**
  - **Should only be attempted when clinically indicated (not for insurance or regulation)**
  - **Should not occur during major stressors**
- XR-Naltrexone does NOT require tapering
  - Patients become "unblocked" after 4 weeks

Tapering MAT

- **Overall: longer, slower tapers work better**
  - Tapering some patients from buprenorphine may be more difficult and may require a longer period of time than tapering from methadone
  - Consider following a taper with xr-naltrexone for a year or longer

(Weiss et al., 2011)

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