Medication Assisted Treatment
Claudie H. Jimenez MD MS
Objectives

Define
- Define Medication Assisted Treatment

Describe
- Describe Medications Used for Treatment

Understand
- Understand how Medication Assisted Treatment fits into a patient’s recovery from Addiction
Background

Alcohol Use

- 6% of Adult population reports heavy drinking use
- 17% of Adult population reports binge drinking

COST Indiana:

$4,468,200,000

Division of Population Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention
Background
Indiana Opioid Overdose Deaths 1999-2017

The Drug Overdose Epidemic in Indiana: Behind the Numbers Data Brief, Published April 3rd, 2019 https://www.in.gov/isdh/27393.htm
Background: Patients with SUD (including alcohol) That Received Treatment 2015

21.7 million people aged 12 or older needed substance use treatment

19.3 million did not receive substance use treatment at a specialty facility (89%)

2.3 million received substance use treatment at a specialty facility (11%)

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health (NSDUH), 2015.
Definition of Addiction

From the American Society of Addiction Medicine:

"Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors."
Addiction: A Chronic Brain Disease

"Chronic"
Requires a wholistic approach to helping people manage their illness

"Brain"
People must fight stigma and moral blaming

"Disease"
Medical approach can be effectively used for treatment
Addiction Is a Brain Disease, and It Matters

Alan I. Leshner

Scientific advances over the past 20 years have shown that drug addiction is a chronic, relapsing disease that results from the prolonged effects of drugs on the brain. As with many other brain diseases, addiction has embedded behavioral and social-context aspects that are important parts of the disorder itself. Therefore, the most effective treatment approaches will include biological, behavioral, and social-context components. Recognizing addiction as a chronic, relapsing brain disorder characterized by compulsive drug seeking and use can impact society’s overall health and social policy strategies and help diminish the health and social costs associated with drug abuse and addiction.

Dramatic advances over the past two decades in both the neurosciences and the behavioral sciences have revolutionized our understanding of drug abuse and addiction. Scientists have identified neural circuits that subsume the actions of every known drug of abuse, and they have specified common pathways that are affected by almost all such drugs. Researchers have also identified and cloned the major receptors for virtually every abusable drug, as well as the natural ligands for most of those receptors. The drug user or, worse, an addict. The most beneficent public view of drug addicts is as victims of their societal situation. However, the more common view is that drug addicts are weak or bad people, unwilling to lead moral lives and to control their behavior and gratifications. To the contrary, addiction is actually a chronic, relapsing illness, characterized by compulsive drug seeking and use (1). The gulf in implications between the “bad person” view and the “chronic illness sufferer” view is tren-
DSM V Criteria Substance Use Disorder

1. Taking ____________ in larger amounts and for longer than intended
2. Wanting to cut down or quit but not being able to do it
3. Spending a lot of time obtaining the ____________.
4. Craving or a strong desire to use
5. Repeatedly unable to carry out major obligations at work, school, or home due to use
6. Continued use despite persistent or recurring social or interpersonal problems caused or made worse by opioid use
7. Stopping or reducing important social, occupational, or recreational activities due to opioid use
8. Recurrent use in physically hazardous situations
9. Consistent use despite acknowledgment of persistent or recurrent physical or psychological difficulties from using
10. Develop tolerance as defined by either a need for markedly increased amounts to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount. (Does not apply for diminished effect when used appropriately under medical supervision)
11. Develop withdrawal symptoms manifesting as either characteristic syndrome or the substance is used to avoid withdrawal (Does not apply when used appropriately under medical supervision)
Risk Factors

- Genetics
- Exposure
- Stress
Addiction: A Biopsychosocial Illness

- Biological
- Psychological
- Social
- Use

Brain Switch

Addiction

Relapse

1. Stress
2. Triggers (Cues)
3. Exposure (Primers)
Biological Pleasure Response

- It's all about Dopamine
Addiction changes the Brain

Decreased Dopamine Transporters in a Methamphetamine Abuser
Medication Assisted Treatment

- Any treatment that includes a medication as part of that treatment
- Substance Use disorders with FDA approved Medication for Treatment:
  - Alcohol Use Disorder
  - Opioid Use Disorder
  - Nicotine Use Disorder
Basis for Medication Use

- Drugs of Abuse work on very specific receptors in the brain and nervous system
- Medications used in the treatment of substance use disorder are used to their effects on these specific receptors in the brain and nervous system
- Medications have very specific efficacy based on their molecular structure
Basis for Medication Use Continued

- Medications have been used for decades in the detoxification process.
- FDA has approved several medications to help manage the disease of addiction.
- MAT is listed as part of CDC recommended strategies to reduce overdose deaths.
- Medications are a prescribed part of a comprehensive treatment plan.
- Medications are used to treat virtually every other medical condition including hypertension and diabetes.
- Science has identified that several changes take place in the brain's chemical structure that are not corrected quickly.
- MAT allows the patient to think more clearly without the physiologic distractions taking away from treatment.
- Most reliable predictor of successful recovery and positive outcomes is length of time in treatment.
  - **MAT keeps patients in treatment longer**
Retention in Treatment MAT vs. Detox

Buprenorphine Maintenance vs Detox

75% retention
75% UTS negative
20% mortality in placebo group

Chronic Disease Adherence to Treatment

- Type 1 Diabetes: 60%
- Hypertension: Less than 40%
- Asthma: Less than 40%
- Substance Use Disorder: 40-60%
Fully Integrated Recovery Home

Case Management/Recovery Management

ER
IC
Clinic
Addiction Medicine MAT-Clinic
Inpatient
Day Tx
IOP
OP
12 Step Programming
Justice System
Sober Housing
Alcohol Use Disorder Medications for Treatment

- Naltrexone (Revia/Vivitrol)
  - Approved for use in Alcohol Use Disorder in 1994
  - Decreases craving for alcohol and relapse to heavy drinking
  - Decreases euphoric effects from alcohol and reinforcing properties
  - Two Forms: Oral and Extended Release Injection (Vivitrol)
    - Better compliance with Injection

- Acamprosate (Campral)
  - Approved for use in Alcohol Use Disorder in 2004
  - Decreases relapse rate
  - Associated with less quantity and frequency of drinking
  - Patients must take 3 pills, 3 times a day which is a challenge for compliance
Alcohol Use Disorder Medications for Treatment (Continued)

- Disulfiram (Antabuse)
  - Approved for use in Alcohol Use disorder in 1949
  - Alcohol Sensitizing agent
    - Make drinking alcohol drinking unpleasurable or even toxic
  - Very poor compliance to medication
  - Lack of evidence showing its effectiveness in relapse prevention

- Other Medications
  - Antidepressants
  - Anti-anxiety (NOT BENZODIAZEPINES)
Effectiveness of MAT for Alcohol

Study #1

- Meta-analysis of naltrexone and acamprosate 2013
- Review of 64 Randomized Controlled Studies from 1970-2009
- Both medications were found to be effective in treating Alcohol Use Disorder
  - Naltrexone had more of an effect on heavy drinking and cravings
  - Acamprosate had a larger size effect on abstinence alcohol
  - Acamprosate became less effective if patient relapsed on to alcohol
  - Both medications were more effective in maintaining abstinence if patient was detoxed prior to starting medication.

Effectiveness of MAT for Alcohol

STUDY #2

- Inpatients admitted for alcohol related disorders
- >100 Patients in study
- Discharge program starting Naltrexone prior to discharge showed significant decrease in hospital readmission and ED visits.

Large Urban Hospital in San Francisco

Results:

- Return to ED within 30 Days: 8.2% (received MAT) vs. 23.4% (did not receive MAT)
- Readmission or ED presentation within 30 days: 12.0% (Received MAT) vs 38.5 % (did not receive MAT)
  - Most presentations in both groups were alcohol related

Wei et al: Treatment and Discharge Planning Protocol for Alcohol Dependence
J Gen Intern Med 30(3):365-70
Effectiveness of MAT for Alcohol Criminal Justice System

- Surprisingly not much in medical literature
- STUDY #2
- Incarcerated population with co-occurring Severe Mental Illness
- Retrospective Study looking at over 5000 patients total
- Used multiple medications including Campral (most utilized), Naltrexone and Disulfiram

Results:
- MAT group: Increased treatment utilization and decreased ED visits compared to Non MAT group
- No statistical difference in recidivism

Opioid Use Disorder Medications

- Methadone
  - Full opioid Agonist
  - Risk for overdose
  - Long acting: Dose once daily
  - No wait time to start treatment
  - Interactions with other medications
  - Can have cardiac side effects
  - Highly regulated and high barrier to treatment (patients must go to clinic for daily dosing)
Opioid Use Disorder Medications

» Naltrexone
- Opioid antagonist
- Patients must be opioid free 5-7 days prior to starting medication
- No risk of overdosing from medication directly
- Decreases cravings for opioids
- Can elevate Liver Function Tests
- Not a controlled substance
- Can be given in an office setting
- Comes in depo injectable form (Vivitrol)
Opioid Use Disorder Medications

- **Buprenorphine**
  - Partial opioid agonist
  - Oral, injectable* and implant available**
  - Lower risk of overdose (respiratory depression ceiling)
  - Controlled Substance
  - Can be given in an office setting
  - Prescriber must have X DEA waiver
  - Less medication interactions
  - Can elevate Liver Function Tests

*FDA approved no studies available showing long term effectiveness
**FDA approved not well integrated into care; multiple practical challenges
<table>
<thead>
<tr>
<th>Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmacological Profile of Methadone, Buprenorphine, and Naltrexone</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Methadone</th>
<th>Buprenorphine</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main effect</strong></td>
<td>Mu full agonist, NMDA antagonist</td>
<td>Mu partial agonist</td>
<td>Mu antagonist</td>
</tr>
<tr>
<td><strong>Bioavailability</strong></td>
<td>70%–80%</td>
<td>50%</td>
<td>&lt; 50% (*100% ER)</td>
</tr>
<tr>
<td><strong>Half-life</strong></td>
<td>28 hours</td>
<td>37 hours</td>
<td>9 hours (4.95 days ER)</td>
</tr>
<tr>
<td><strong>Clinically apparent drug interactions</strong></td>
<td>Rifampin, phenytoin, several ART</td>
<td>Select ART</td>
<td>Opioids NSAIDS (?)</td>
</tr>
<tr>
<td><strong>Active metabolites</strong></td>
<td>None</td>
<td>Non-buprenorphine</td>
<td>6-beta-naltrexol</td>
</tr>
</tbody>
</table>

ART Antiretroviral therapy; NSAID Non-steroidal anti-inflammatory; ER extended release formulation

doi: [10.1080/10550887.2012.694598](http://dx.doi.org/10.1080/10550887.2012.694598)
Full, Partial Agonist, Antagonist Activity Levels

- Full Agonist (e.g. heroin)
- Partial Agonist (e.g. buprenorphine)

% Mu Receptor Intrinsic Activity

- Bupe + Benzo ≠

Maximum opioid agonist effect is never achieved

DRUG DOSE
- no drug
- low dose
- high dose
- ANTAGONIST
### Table 1
Clinical Characteristics of methadone, buprenorphine, and naltrexone

<table>
<thead>
<tr>
<th></th>
<th>Methadone</th>
<th>Buprenorphine</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled substance</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Availability</td>
<td>OTP</td>
<td>OTP or DATA Waived practitioner</td>
<td>Any prescribing practitioner</td>
</tr>
<tr>
<td>1-year retention</td>
<td>60%</td>
<td>60%</td>
<td>20% (53% 6-months ER)</td>
</tr>
<tr>
<td>Direct expense</td>
<td>$</td>
<td>$5</td>
<td>$50–$500</td>
</tr>
<tr>
<td>Dosing frequency</td>
<td>Daily</td>
<td>Daily</td>
<td>Daily or monthly (ER)</td>
</tr>
<tr>
<td>Narcotic blockade</td>
<td>Yes, at steady-state</td>
<td>Yes, at steady-state</td>
<td>Yes</td>
</tr>
<tr>
<td>Can induce withdrawal</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Overdose potential</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Withdrawal upon cessation</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Loss of tolerance on cessation</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Complicates treatment of moderate-severe pain</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

OTP opiate treatment program; DATA Drug Addiction Treatment Act of 2000; ER extended release formulation.
Relapse Rate of Patients on MAT
Background: Patients with OUD that Receive MAT

From 2010 to 2014, Only 11 Percent of Patients With OUD Were Prescribed an MOUD

Of the more than 340,000 patients who carried a diagnosis during some or all of the time during the period from 2010 to 2014, only 11 percent were prescribed MOUD.

Adapted from Morgan et al. 2017; permission for use of data provided by Dr. J. R. Morgan
Incarcerated Population

- 24% of prison population meet criteria for Alcohol Use Disorder
- 30% of prison population meet criteria for other Drug Use Disorder
  - Women prisoners up to 50%

- Only 11% of prisoners who meet criteria for any substance use disorder receive any treatment

MAT Use Pre and Post Release Incarceration

- Study #1
- Western MA County Jail
- Forty-seven Patients
- XR-NTX approximately 7 days prior to release,
  - 2 groups Pre and Post Release
  - Rate of retention at week 4 was higher in group with treatment initiation prior to release week 4: 55% versus 25%; week 8: 36% versus 25%; week 24: 21% versus 15%
  - Three patients died from overdose at 3-5 months after release and 2.5 or more months after stopping XR-NTX,
MAT Use Pre and Post Release Incarceration

- Study #2
- Baltimore Jail
- 211 Patients
- Bup/Nal Started upon admission to Jail
  - 2 groups (Bup + Counseling) (Counseling only then referral for bup after release)
  - Present to treatment 47.5% of bup participants entered community treatment, while for the counseling only 33.7% participants entered community treatment. Three patients died from overdose at 3-5 months after release and 2.5 or more months after stopping XR-NTX,
MAT and Incarcerated Populations

- Study #2
- Meta analysis 2019
- Compared Methadone, Buprenorphine and Naltrexone Treatment during and after incarceration delivered in prisons and jails
- Looked at Randomized controlled trial and quasi-experimental studies published through December 2017 that examined induction to or maintenance on methadone (18 studies), buprenorphine (3 studies), or naltrexone (3 studies) in correctional settings
- There were a sufficient number of methadone RCTs
- Too few buprenorphine or naltrexone studies
- Methadone provided during incarceration increased community treatment engagement, reduced illicit opioid use and injection drug use, but did not reduce recidivism
- Individual review of buprenorphine and naltrexone studies showed these medications were either superior to methadone or to placebo, or were as effective as methadone in reducing illicit opioid use post-release.
- More study is needed
MAT for Smoking

- Nicotine Patches
  - Nicotine Replacement
  - Multiple Forms: patches, inhaler, gum

- Bupropion
  - Agonist α4β2 sub-type of the nicotinic receptor
  - Anti-depressant
  - Decreases Cravings for cigarettes

- Chantix
  - partial agonist selective for αβ nicotinic acetylcholine receptor
  - Decreases cravings and pleasurable effects from smoking
  - Can have significant side effects
Other Substances

- **Stimulants: Methamphetamine and Cocaine**
  - Many studies on multiple different medications - nothing has been shown to be effective
  - There are no FDA approved medications
  - Behavioral Treatment is the recommended treatment
    - Contingency Management
    - Cognitive Behavioral Therapy

- **Benzodiazepines**
  - There is no MAT
  - Detox - not effective long term
  - Long taper
  - Cognitive Behavioral Therapy to Manage Anxiety and Insomnia
  - SSRIs can help manage anxiety
MAT as part of a Fully Integrated Recovery Home

Case Management/Recovery Management

- ER
- IC
- Clinic

- Inpatient
- Day Tx
- IOP
- OP

Addiction Medicine MAT-Clinic

12 Step Programming

Justice System

Sober Housing
MAT as part of Comprehensive Support for Communities, Patients and Families

- Incorporate MAT into a comprehensive treatment program for patients and families
- Increase access to Residential Treatment Programs
  - Utilize MAT in Residential Programs
  - Increase the number of beds
  - Provide Reimbursement for Services
- Increase Access to Peer Support
  - Appropriate Reimbursement for Peer Support Services
- Focus on Prevention
  - Education for Providers
    - Formal Addiction Training in Medical School, NP/PA School and Residency Programs
    - Training on Controlled Substance Prescribing—not just opioids
  - Community Education
    - Awareness of using controlled substances including prescriptions
    - Develop Resilience
Thank you!