Medication-Assisted Treatment (MAT) for Opioid Use Disorders

Christina M. Delos Reyes, MD
Medical Consultant, *Center for Evidence-Based Practices at Case Western Reserve University*
Associate Professor, *Department of Psychiatry University Hospitals Cleveland Medical Center*

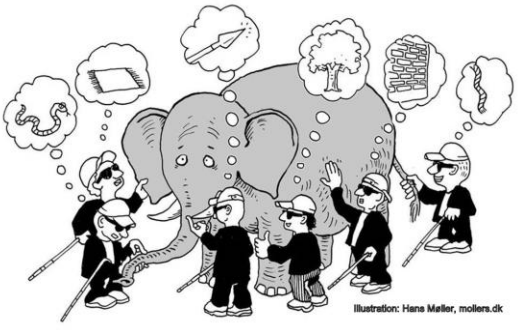
Portage County Opiate Conference: 10.31.17
Rootstown, Ohio

University Hospitals
Cleveland | Ohio

Learning Objectives

- Describe the impact of opioid use disorders on the brain, using the medical model of addiction
- List and review three medications that can be used to treat opioid use disorders
- Dispel common myths about medication-assisted treatment

Part 1: Opioid Use Disorders and the Brain



Explanatory Models of Addiction

- Moral → wrong
- Spiritual → empty
- Psychological → impulse control
- Behavioral → habit
- Medical → disease

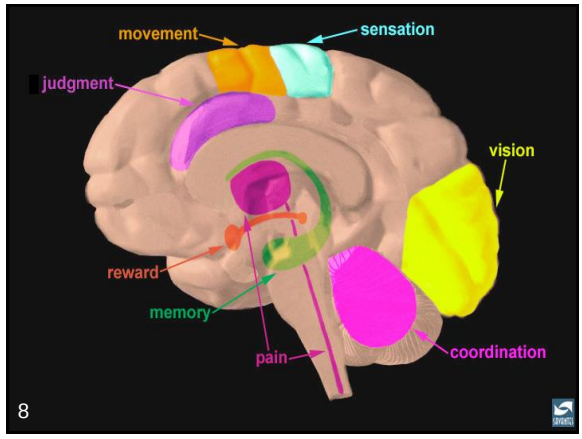
Medical model of addiction

- Sick person seeking wellness
- SUDs as chronic diseases
  - Biological basis
  - Identifiable signs and symptoms
  - Predictable course and outcome
- Treatment improves outcomes
- Lack of treatment may lead to morbidity and mortality

Medical model of addiction

- A chronic relapsing disease of the brain
  - Drugs change brain structure and function
  - Brain changes can be long lasting and lead to harmful behaviors
- Characterized by compulsive drug seeking and use despite harmful consequences

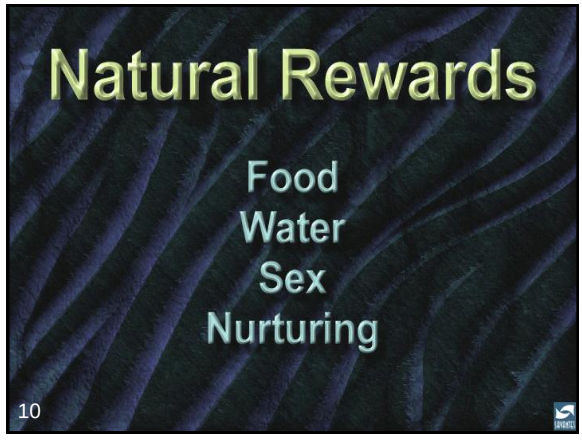
University Hospitals Cleveland | Ohio



Drugs and Pleasure: Dopamine

- All drugs of abuse directly or indirectly flood the brain's reward circuit with dopamine
- Dopamine has many functions
  - Regulation of movement, emotion, cognition, motivation and feelings of pleasure
- Overstimulation of the reward system produces euphoria and teaches the repetition of using behavior

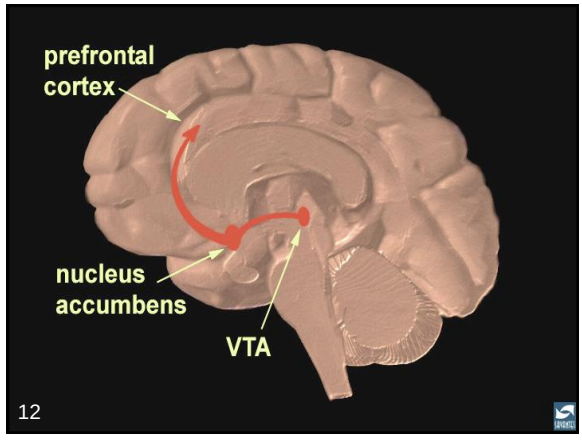
University Hospitals Cleveland | Ohio



Why are drugs more addictive than natural rewards?

- Amount of dopamine release
  - Depending on the drug of abuse, 2 to 10 times the amount of dopamine can be released vs. natural rewards
- Onset and duration of dopamine release
  - Can happen immediately or very quickly and can last much longer than natural rewards
- Drug abuse is something the brain learns to do very very well!

University Hospitals Cleveland | Ohio



Long-term effects on the brain

- Brain must adjust to overwhelming surges in dopamine→ makes less dopamine, fewer receptors
- As a result, the ability to experience any pleasure is reduced
- Now, drugs are needed in larger amounts (tolerance) to feel high
- Eventually, drugs no longer make the individual high and are needed "just to feel normal"

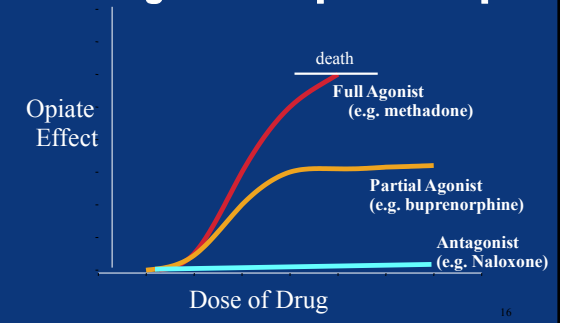
Part 2: 3 Medications to Treat Opioid Use Disorders

Benefits of Medication-Assisted Treatment

Methadone, buprenorphine, and naloxone have been proven to help patients recover from opioid addiction. These medications are:

- **Safe**
- **Cost-effective**
- **Reduce the risk of overdose**
- **Increase treatment retention**
- **Improve social functioning**
- **Reduce the risks of infectious disease transmission**
- **Reduce criminal activity**

Antagonist *vs.* Full Agonist *vs.* Partial Agonist at Opioid Receptor



16

Oral Naltrexone = REVIA

- Blocks opioid receptors that are involved in the rewarding effects of opioids (AND alcohol!)
- Blocks effect of opiates
  - May precipitate opiate withdrawal in opiate abusers
  - Therefore must be opiate-free for 7 to 10 days before taking
- Risk for hepatotoxicity
  - Baseline liver enzymes: don't start if AST/ALT are more than 3X the upper limit of normal
  - Monitor liver enzymes regularly

Injectable Naltrexone = VIVITROL

- Given as a deep muscle gluteal injection Q 4 weeks
- Dosage = 380 mg IM
- May have injection site reactions
- May "wear off" after week 3

CAUTION with Naltrexone

- When clients have had opiate receptors blocked for some time, their tolerance is "reset"
- Returning to drug use at the same levels they were previously using [prior to blockade] puts the client at **INCREASED RISK for OD/death** due to lowered tolerance
- This information needs to be shared with all clients

Naltrexone

- ***Advantages:***
  - Opiate receptor blocker has no abuse potential
- ***Concerns:***
  - Non-compliance is the main barrier to success
    - Most useful for highly motivated patients w/ external circumstances→ medical professionals, lawyers, pilots; parolees, probationers, etc
  - Injection is expensive and requires shipping/refrigeration
  - Increased risk for overdose and perhaps suicide

Methadone

- Opiate agonist to treat opiate dependence
- Well-studied and effective treatment
  - Normalizes function/return to work, decreases crime/violence, reduces HIV exposure
- Doses > 70mg/day generally better than low doses
- Enhanced services = improved outcomes
  - Counseling, medical, social/vocational services, etc
- No contraindication in SMI, though not well studied

Methadone

- Usually taken once a day to suppress withdrawal for 24 to 36 hours
- Usually given in liquid form by Opiate Treatment Programs
- Induction phase—no more than 30 to 40 mg on the first day of treatment
- Dosage changes usually occur once a week
  - *More rapid dosage increases can cause overdose*
- Maintenance phase—usually 80-120mg daily

Methadone

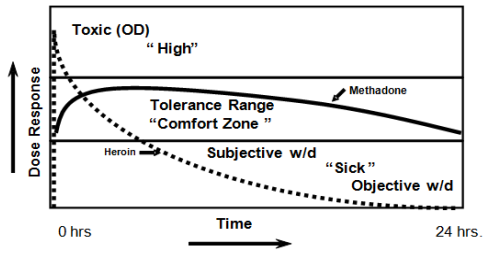
- Common side effects
  - Sweating, constipation, abnormal libido, sleep abnormalities, mild anorexia, weight gain, water retention
- Adverse effects
  - Prolongation of QTc (usually seen with very high doses, mean of 350mg daily)

Methadone: "Addicting patients to another drug?"

- Difference between PHYSICAL DEPENDENCE vs. ADDICTION (or Substance Use Disorder in DSM-5)
- Pharmacology of methadone prevents highs and lows common with short-acting drugs and normalizes patient functioning
- The patient is PHYSICALLY DEPENDENT on methadone but is no longer displaying the behaviors associated with addiction

Heroin vs. Methadone: How It Works

Figure 3.2. Methadone Simulated 24 Hr. Dose/Response At Steady – State in a Tolerant Patient



J. Thomas Payte, MD

Buprenorphine

- Opioid partial agonist
  - ↓ risk of overdose and ↓ abuse potential
- May precipitate withdrawal in individuals using opioids regularly MUST BE IN MILD to MODERATE OPIOID WITHDRAWAL ("dope-sick") before starting it!!
- But what about the naloxone?
  - When taking sublingually, the naloxone is INACTIVE
  - Naloxone is there to prevent abuse by intravenous injection
- Approved in U.S. (2002) as office-based treatment for opioid use disorder vs. OTPs

Buprenorphine

- Maintenance phase: usually 8 to 16 mg daily of SUBOXONE; FDA max dose = 24 mg
- Adverse side effects: Increased LFTs, cytolytic hepatitis
- Common side effects: generally mild
  - Constipation; dizziness; drowsiness; headache; nausea; sweating; vomiting

Buprenorphine Formulations

- Buprenorphine/Naloxone combination = oral tablets, ZUBSOLV tablets, SUBOXONE FILM, BUNAVAIL BUCCAL FILM
- Buprenorphine only = oral tablets, SUBUTEX
  - Suggested use in pregnant patients
- Buprenorphine subdermal implant = PROBUPHINE

4 rods [26 mm x 2.5mm] in upper arm q 6 months;

- **ONLY for patients stable on 8mg or less buprenorphine (oral) daily**

Buprenorphine: Special considerations

- When prescribing buprenorphine **TO TREAT ADDICTION**, physician must have a DATA 2000 Waiver, also called an "X-DEA number"
- DATA 2000 Waiver can be obtained by **any physician** by taking an 8-hour online course
- Allows you to treat 30 patients with buprenorphine in year 1, and 100 patients starting in year 2
- As of 8/2016, specific providers can treat 275 patients/year
- As of 1/2017, NPs and PAs can also prescribe buprenorphine after taking 24-hour online training

20-year Review of Buprenorphine

A nearly 20-year review of buprenorphine published in 2014 clearly demonstrated that buprenorphine:

- Improves treatment retention
- Reduces illicit opioid use
- Associated with improved outcomes during pregnancy
- May afford fewer adverse outcomes than methadone in certain populations
- Clearly provides greater access to care than methadone

– Thomas, C. P., Fullerton, C. A., Kim, M., Montejano, L., Lyman, D. R., Dougherty, R. H., ... & Delphin-Rittmon, M. E. (2014). Medication-assisted treatment with buprenorphine: assessing the evidence. Psychiatric Services, 65(2), 158-170.

Buprenorphine: the Baltimore Experience

- **Found an association between increasing availability of MAT (methadone and buprenorphine) and an approximately 50% decrease in the number of fatal heroin overdoses between 1995 and 2009**

- Schwartz RP, Gryczynski J, O'Grady KE, et al. Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995-2009. *Am J Public Health* 2013;103:917- 22.

Underuse of Medication-Assisted Treatment

- Of the 2.5 million Americans 12 years of age or older who abused or were physically dependent on opioids in 2012, **fewer than 1 million** received MAT. (1)
- Despite their benefits, MATs have been adopted in **less than half** of private treatment programs. (2)
- Even in programs that do offer MAT options, **only about a third** of patients receive them. (2)

(1)Substance Abuse and Mental Health Services Administration, Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-46, HHS Publication No. (SMA) 13-4795. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013.
(2) Knudsen HK, Abraham AJ, Roman PM. Adoption and implementation of medications in addiction treatment programs. J Addict Med 2011;5:21-7.

Why is MAT (and specifically Buprenorphine) under-utilized?

- **Stigma**
  - Despite saving many lives, MAT often not accepted by the public
  - Some healthcare providers have a negative opinion of MAT despite medical evidence of its many benefits
- **Lack of access** to opioid maintenance programs
  - Expense
  - Some treatment programs/insurance plans→ limits and regulations on who can be prescribed MAT and for what duration
  - Some treatment programs/insurance plans→ provide too low of a dose or too short of a course of MAT
  - Federal limits on buprenorphine providers
- **Lack of training** for providers (especially in rural areas)

Ohio OBOT Regulations: 4731-11-12 (as of 1-31-2015)

- Visit with MD q month for minimum of 12 months
- Drug screens q month for minimum 6 months, then quarterly
- If no behavioral treatment, must have minimum three 12-step meetings/week for 12 months, with documentation
- No more than 16 mg/day unless specific exceptions are met
- No benzos unless specific exceptions are met
- **Each physician who provides OBOT shall complete at least eight hours of "Category I" continuing medical education relating to substance abuse and addiction every two years**
- http://codes.ohio.gov/oac/4731-11-12

Ohio OBOT Regulations: Senate Bill 319

- Wide-ranging addiction bill which includes this clause about buprenorphine:
- In order to ensure Suboxone is appropriately prescribed and to increase the success of this form of treatment, facilities where prescribers treat 30 individuals or more will now be subject to licensure by the Board of Pharmacy unless the facility is a licensed hospital or is already certified by the state. This reform also requires physician ownership of office-based opiate treatment clinics along with mandatory background checks for the owners and employees of these facilities.
- http://fightingopiateabuse.ohio.gov/Portals/0/PDF/SB%20319%20Fact%20Sheet.pdf

Mortality (per 100,000/yr)

Prescription Opioids: 4.8

Illicit Drugs: 2.8

Methadone Maint: 0.4-0.5

Buprenorphine: 0.1

Clausen et al., Drug and Alcohol Dependence 2008; 94: 151-157
Caplehorn JR, et al. Subst Use Misuse 1996; 31: 177-196
Bell JR, et al. Drug and Alcohol Dep 2009; 104: 73-77

Part 3:
Myths and Facts about MAT

Myth #1:
MAT "substitutes one addiction for another."

Facts:

- When properly prescribed, MAT ↓ drug cravings and prevent relapse without causing a "high"
- Methadone and buprenorphine are opioid-based and result in physical dependence, but are fundamentally different from short-acting opioids such as heroin and prescription painkillers
  - MAT helps patients disengage from drug-seeking and related criminal behavior and become more receptive to behavioral treatments.
- Injectable naltrexone is not opioid based and does not result in physical dependence. (NIDA, 2012)

Myth #2:
Addiction medications are a "crutch" that prevents "true recovery."

Facts:

- Individuals stabilized on MAT can and do achieve "true recovery," as evidenced by not using illicit drugs, lack of euphoria/sedation/other functional impairments, and no longer meeting DSM-5 criteria for addiction, such as loss of control over drug use. (White and Torres, 2010)
- MAT consists not only of medication but also of behavioral interventions like counseling. The medication normalizes brain chemistry so individuals can focus on counseling and participate in behavioral interventions necessary to enter and sustain recovery. (NIDA, 2009)

Myth #3:
MAT should not be long term.

Facts:

- There is no one-size-fits-all duration for MAT. For some patients, MAT could be indefinite. (SAMHSA TIP 43, 2008)
- SAMHSA recommends a "phased approach"
  - Stabilization (withdrawal management, assessment, medication induction, and psychosocial counseling)
  - Medication maintenance and deeper work in counseling
  - Ongoing rehabilitation (patient and provider can choose to taper off medication or pursue longer-term maintenance, depending on the patient's needs)

  (SAMHSA, 2012)

Myth #4:
Requiring people to taper off MAT helps them get healthy faster.

Facts:

- Requiring people to stop taking their addiction medications is counter-productive and increases the risk of relapse. (Day and Strang, 2010)
- Because tolerance to opioids fades rapidly, one episode of opioid misuse after detoxification can result in life-threatening or deadly overdose.
  (Office of National Drug Control Policy, 2012)

Myth #5:
Courts are in a better position than doctors to decide appropriate drug treatment.

Facts:

- Deciding the appropriate treatment for a person with opioid addiction is a matter of physician discretion, taking into consideration the relevant medical standards and the characteristics of the individual patient. (ASAM, 2013)
- Just as judges would not decide that a person should treat her diabetes through exercise and diet alone, and instruct her to stop taking insulin, courts are also not trained to make medical decisions with respect to MAT.

NOW WHAT?? How can I help?

- Increasing access to Buprenorphine
  - Federal regulations
  - State regulations
  - Insurance limitations and prior authorizations
  - DATA 2000 Waiver Training of prescribers
- Decreasing barriers for those on MAT
  - In treatment facilities
  - In recovery housing
  - In 12-step programs
- Increasing education and training about MAT
  - Medicine, pharmacy, nursing, social work, counseling, etc.

National

- Know your Senators' and Representative's general stance on addiction and specific stance on opioid use disorders and MAT
  - Emails, calls, letters, visits to their local offices
- Helpful National Websites
  - http://www.asam.org/ American Society of Addiction Medicine
  - https://www.samhsa.gov/medication-assisted-treatment Substance Abuse and Mental Health Services Administration
  - http://pcssmat.org/ Providers' Clinical Support System For Medication Assisted Treatment
  - http://pcss-o.org/ Providers' Clinical Support System For Opioid Therapies

State

- Know your State Senator's and State Representative's general stance on addiction and specific stance on opioid use disorders and MAT
  - Emails, calls, letters, visits to their local offices
- Helpful State Websites
  - Ohio Department of Mental Health and Addiction Services http://mha.ohio.gov/
  - Ohio Department of Health http://www.odh.ohio.gov/
  - State Medical Board of Ohio http://med.ohio.gov/
  - State of Ohio Board of Pharmacy http://pharmacy.ohio.gov/
  - Governor's Cabinet Opiate Action Team http://fightingopiateabuse.ohio.gov/

Local

- Your county may have a local opiate task force—join it!
- Attend meetings of your county ADAMHS Board—ask how your taxpayer dollars are being used to fight the opiate epidemic
- If you work in the mental health or addiction treatment field
  - Ask your agency leadership what more can be done to integrate MAT and increase access to treatment for Opioid Use Disorders
  - Encourage all patients with Opioid Use Disorders to obtain a naloxone (Project DAWN) kit
  - Teach patients and their family members about MAT

REFERENCES

- Bell, J. R., Butler, B., Lawrance, A., Batey, R., & Salmelainen, P. (2009). Comparing overdose mortality associated with methadone and buprenorphine treatment. Drug and alcohol dependence, 104(1), 73-77.
- Caplehorn, J. R., Dalton, M. S., Haldar, F., Petrenas, A. M., & Nisbet, J. G. (1996). Methadone maintenance and addicts' risk of fatal heroin overdose. Substance use & misuse, 31(2), 177-196.
- Clausen, T., Anchersen, K., & Waal, H. (2008). Mortality prior to, during and after opioid maintenance treatment (OMT): a national prospective cross-registry study. Drug and alcohol dependence, 94(1), 151-157.
- Knudsen HK, Abraham AJ, Roman PM. Adoption and implementation of medications in addiction treatment programs. J Addict Med 2011;5:21-7.
- O'Brien M. Medication-Assisted Treatment for Opioid Addiction: Myths and Facts (2016). http://lac.org/wp-content/uploads/2016/02/Myth-Fact-for-MAT.pdf
- Substance Abuse and Mental Health Services Administration, Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-46, HHS Publication No. (SMA) 13-4795. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013.
- Schwartz RP, Gryczynski J, O'Grady KE, et al. Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995-2009. Am J Public Health 2013;103:917- 22.
- Thomas, C. P., Fullerton, C. A., Kim, M., Montejano, L., Lyman, D. R., Dougherty, R. H., ... & Delphin-Rittmon, M. E. (2014). Medication-assisted treatment with buprenorphine: assessing the evidence. Psychiatric Services, 65(2), 158-170.

Contact Information

Christina M. Delos Reyes, MD

10524 Euclid Avenue, Suite 13-107

Cleveland, Ohio 44106

Christina.DelosReyes@uhhospitals.org

216-844-7661 (Voicemail)

216-844-5833 (Fax)