TREATING OPIOID USE DISORDER WITH MEDICAL ASSISTED THERAPIES

Mary J. Wade, MS, MSN, CRNP
CANPA Annual Conference Meeting
February 1, 2020

Financial Disclosure

There are no financial disclosures to report as I do not have a financial agreement or affiliation with any organization that could be perceived to be a conflict of interest.

Objectives

At the end of this presentation, the participant will be able to:

1. Discuss the etiology of OUD
2. Describe the impact on the individual, families & society
3. Discuss tolerance, dependence, vs. addiction & the reward system
4. Discuss the use of medical assisted therapies as a treatment – its advantages and management issues
5. Discuss use of the CDMP, BTOD/REMS office based appropriate use and maintenance checklists

Opioid Use Disorder (OUD): a DMS-5 Dx

- Anyone can become dependent on opioids
- More common than most think
- Not a bad person
- Alterations in the brain
  - Synaptic Dopamine increases in Nucleus Accumbens → perception is rewarding/reinforcing
  - New neural connections made & activity is repeated with automatic behaviors & associations that become triggers
  - Prefrontal cortex becomes less active → less control, less motivation
  - More drug needed (tolerance) for reward or steady state
- Genetics – 50% influence but not pre-determined
- Psych diagnosis means DSM &HIPA rules are more strict

Risk Factors/Patients

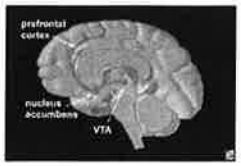
- Past or current substance abuse
- Untreated psychiatric disorders
- Social environments that encourage misuse
- Family environments that encourage misuse
- H/o overdose
- 2 million patients
- Less than 50% are treated
- Lack of desire for treatment by many patients

Opiates and Opioids

- Opiates – present in opium products (morphine, codeine, thebaine)
- Opioids are manufactured
  - Semi-synthetic – derived from an opiate (e.g., heroin from morphine)
  - Completely synthesized & function similar to natural opiates (methadone, fentanyl, meperidine)
- Bind to Mu receptors in the brain → acute changes in neuronal excitability, increased release of GABA

Reward System

- Reward Pathway –
  - Ventral Tegmental Area (TGA)
  - Nucleus Accumbens with projections to Prefrontal Cortex
  - Dopaminergic System



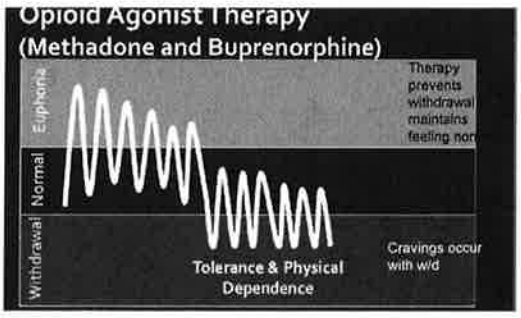
Neurobiology of Drug Addiction, NIH

- VTA neurons contain neurotransmitter dopamine, released to Nucleus Accumbens then Prefrontal Cortex
- Natural rewards include eating, drinking, procreating, being nurtured
- External – opiates/opioids, alcohol, gambling, etc.

Opioid Tolerance, Physical Dependence vs. Addiction

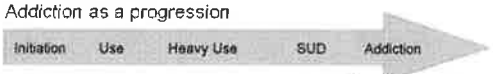
- Physiologic adaptions to chronic opioid exposure
  - Tolerance: increased dosage needed to produce specific effect
    - Develops rapidly to reduce CNS & respiratory effects
  - Physical Dependence: signs & symptoms of withdrawal by abrupt cessation, rapid dose reduction or administration of an antagonist
- Addiction: not a physiologic adaption – behavioral syndrome of compulsive use despite negative consequences
  - **ASAM definition**: 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. (http://www.asam.org/docs/publicy-policy-statements/1definition_of_addiction_short_4- 11.pdf?sfvrsn=0)
  - Addicted brain has altered function and there are changes in behavior and decision-making associated with these alterations.
  - Distress or difficulty functioning is part of the diagnosis.

Cycle of Euphoria, Normalcy, Withdrawal



Progression to Addiction

- Substance Use – usually by prescription or obtaining from a friend or family member (diversion)
- Abuse patterns develop → increase from use to heavy use & progresses to
- Substance Use Disorder (SUD) – e.g.
  - Opioid Use Disorder
  - Heroin Use Disorder
- Addiction as a progression

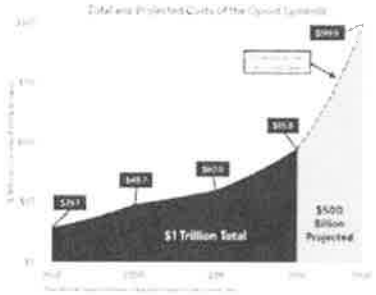


- Influenced by genetics and environment (family history, social support systems, etc.)

Collateral Effects

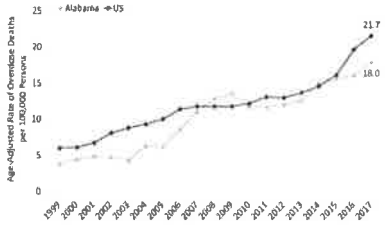
- Drug seeking behaviors
  - Confining & limit other activities (family, work, social)
- Stigma to individuals (barrier to treatment & recovery)
- Economics - $600 billion annually
  - Loss of productivity
  - Incarcerations – up to 20% of prisoners for drug offenses
  - Health care – 14K treatment facilities in US (costly), medications; 100k self-help groups; Neonatal Abstinence Syndrome (NAS), Hep C & HIV treatments
- Loss of significant other, parent, etc. have significant societal effects with >91K children in foster care
- Clinician attitudes

Projected Costs of Opioid Epidemic



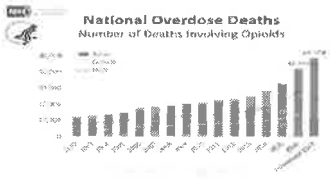
Drug Overdose Deaths

Rate per 100,000 persons, in the U.S. and Alabama.
Source: CDC WONDER.



National Burden of Disease

- 2 million people in the US diagnosed with opioid use disorder
- > 50,000 deaths annually



Legislation

- Drug Addiction Treatment Act (DATA) of 2000
- Allows for prescription of an opioid for treatment of an opioid addicted person
- Prescriber must be certified in addiction medication, addiction psychiatry, participated in clinical trials or completed 8 hr training for physician or 24 hrs for NP or PA
- Obtain X-number in addition to DEA for prescribing buprenorphine or buprenorphine/naloxone for Addiction (schedule III; methadone is schedule II)
  - 30 patients first year
  - 100 patients thereafter
  - 275 patients upon request – physicians only as amended by DATA 2016
    - Patients remain on census until last Rx has run out

Practice Guidelines

- First steps in the medical management of opioid addiction include 1) use of validated screening tools to identify patients who may have a problem with opioid use and 2) further assessment to clearly delineate the scope of the problem when opioid addiction is identified. Consideration must be given to the appropriate treatment approach when treatment is indicated. Assessment should also identify complicating or comorbid emotional or medical conditions. Complete assessment may take several days but it is not recommended that initial treatment be delayed (SAMHSA, 2004).
- Thorough assessment will assist in confirmation of the diagnosis. It is designed to determine need for treatment, develop a treatment plan, and establish a baseline measure for evaluating progress. The assessment should encompass all of the following:
  - Confirmation of an opioid use disorder diagnosis;
  - Establishment of current opioid use;
  - Documentation of substance use history;
  - Identification of any need to require medically supervised detoxification from opioids as well as benzodiazepines, alcohol, or other sedatives;

Practice Guidelines

- Determination of where and when detoxification should be accomplished (inpatient, clinic, home)
  - Detox is NOT treatment!
- Identification of comorbid psychiatric and medical conditions and disorders
  - Prioritization and coordination of their management
- Screening for infectious diseases that place opioid users at elevated risk such
  - Hepatitis C, Hepatitis B, HIV/AIDS (SAMHSA, 2015)

- The American Society of Addiction Medicine (ASAM) announced the release of its National Practice Guideline for the Use of Medications in the Treatment of Addiction involving Opioid Use in early June 2015.
  - PDF version containing full text is available for download at http://www .asam.org/docs/default-source/practice-support/guidelines-and-consensus- docs/national-practice-guideline.pdf#search=%22national%20practice%20guideline%20for%20the%20use%20of%20medi cat%22.
  - The document can also be found in the *Journal of Addiction Medicine*. The Guideline deals with a number of in MAT topics around opioid use such as the role of drug testing in treatment

Screening – DAST 10 Questionnaire

- I'm going to read you a list of questions concerning information about your potential involvement with drugs, excluding alcohol and tobacco, during the past 12 months.
- When the words "drug abuse" are used, they mean the use of prescribed or over-the-counter medications/drugs in excess of the directions and any non-medical use of drugs. • The various classes of drugs may include: cannabis (e.g., marijuana, hash), solvents, tranquilizers (e.g., Valium), barbiturates, cocaine, stimulants (e.g., speed), hallucinogens (e.g., LSD) or narcotics (e.g., heroin). These questions do not include alcohol or tobacco.
- If you have difficulty with a statement, then choose the response that is mostly right. You may choose to answer or not answer any of the questions in this section.

These questions refer to the past 12 months.

0 = No 1=Yes

1. Have you used drugs other than those required for medical reasons?
   0
   1
2. Do you abuse more than one drug at a time?
   0
   1
3. Are you always able to stop using drugs when you want to? (If never use drugs, answer "Yes."
   1
   0

Screening - DAST 10

4. Have you had "blackouts" or "flashbacks" as a result of drug use?
   0
   1
5. Do you ever feel bad or guilty about your drug use? If never use drugs, choose "No."
   0
   1
6. Does your spouse (or parents) ever complain about your involvement with drugs?
   0
   1
7. Have you neglected your family because of your use of drugs?
   0
   1
8. Have you engaged in illegal activities in order to obtain drugs?
   0
   1
9. Have you ever experienced withdrawal symptoms (felt sick) when you stopped taking drugs?
   0
   1
10. Have you had medical problems as a result of your drug use (e.g., memory loss, hepatitis, convulsions, bleeding, etc.)?
   0
   1

Interpreting the DAST 10

In these statements, the term "drug abuse" refers to the use of medications at a level that exceeds the instructions, and/or any non-medical use of drugs. Patients receive 1 point for every "yes" answer with the exception of question #3, for which a "no" answer receives 1 point. DAST-10 Score Degree of Problems Related to Drug Abuse Suggested Action.

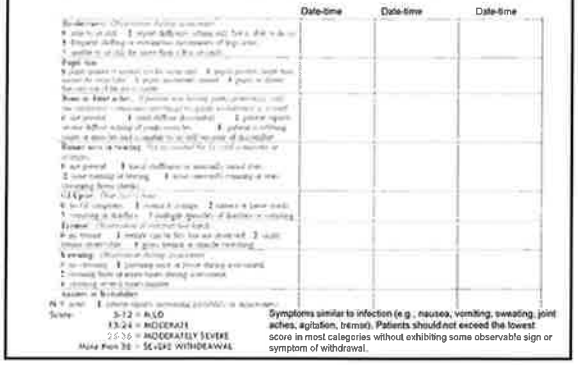
- **Suggested Action**
  - 0 - No problems reported
    - None at this time
  - 1–2 - Low level
    - Monitor, re-assess at a later date
  - 3–5 - Moderate level
    - Further investigation
  - 6–8 - Substantial level
    - Intensive assessment
  - 9–10 - Severe level
    - Intensive assessment

Skinner, H. A. (1982). The Drug Abuse Screening Test. *Addictive Behavior*, 7(4),363–371.

Symptoms of OUD

- Must have at least two (2) of the following 11 symptoms, occurring together within the past yr.
  - The drug is taken in larger amounts or over a longer period of time than intended.
  - Desire by the user, and usually unsuccessful efforts, to control use of the drug or to cut down on its use.
  - More and more time is spent trying to gain access to the drug, use it, or recover from its use.
  - Activities the person normally enjoys — socially, at work, or for their education — are given up due to use of the drug.
  - Using the drug in situations where it is dangerous or hazardous to do so (e.g., while driving a car).
  - Forgoing major obligations (work, school, or home) due to use of the drug (e.g., unemployment).
  - Continued use despite persistent problems with social, romantic, or interpersonal relationships.
  - Continued use despite persistent problems with a person's physical or psychological health, due to overuse of the drug.
  - Withdrawal symptoms of opioid use, or additional use of the drug to try and stop the withdrawal symptoms.
  - Tolerance—person needs more and more of the drug in order to achieve the same effects, and those effects continue to decline over time with continued use of the drug.

Clinical Opioid Withdrawal Scale (COWS)



Medical Assisted Treatment (MAT)

- Methadone Maintenance Therapy (MMT)
  - Schedule II – physicians only
  - Full agonist
  - Long half-life – no euphoria
  - Dispensed at Methadone Clinics – opioid treatment programs (OTPs) approved by Substance and Mental Health Services Administration (SAMSHA)
    - Liquid, daily & observed
    - Start low – 10-30 mg/day & titrate up slowly → maintenance dose (60-120mg/day, sometimes more)
    - UDS – routine & random
    - Take home privileges once stable
  - Monitor for QTC elongation (ECG on initiation & prn)
  - Counseling & group therapy required
  - Psychiatric referrals for comorbid psych conditions

Opioid Agonists vs. Partial Agonists Antagonists

- Full agonist – binds to & activates receptor site
  - As dose is increased, effect is increased until full effect is achieved (e.g., heroin, morphine, oxycodone, methadone)
  - Up to 100% binding
- Partial agonist – binds to receptor to excite the receptor
  - Plateau reached & **increased dose does not increase effect** (e.g., buphrenorphine → dose increases more than 16-24 mg not effective for treatment
  - E.g., 40% - 60% receptor response
- Antagonist- binds to receptor without causing any activity (e.g., naloxone, naltrexone)

MAT

- Buprenorphine ("designer drug")
  - Binds to Mu receptors as a partial agonist – safer in overdose
  - Long acting - up to 24 hrs; no euphoria
  - Higher binding or affinity for the Mu receptors
  - Blocks other opiates or opioids (This is the blocker)
  - Slow receptor dissociation
  - CNS effects - prevents withdrawal & cravings
  - ENS effects – decreases gastric motility, increases spinchter tone → constipation, etc.
- Outpatient treatment programs
  - COWS score > 7 or 13 (moderate or more severe w/d) prior to initiation
  - Rx provided to be filled at local pharmacy or initiated in office

Induction & Dosing

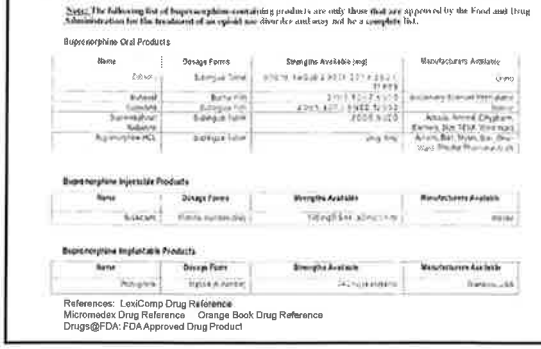
- Give the first dose after discontinuing opioids and some withdrawal symptoms are evident
- Precipitated withdrawal is avoided by giving the first dose of buprenorphine after withdrawal symptoms are displayed
- Dosing
  - Sublingual buprenorphine daily doses of 8 to16 mg has been shown to be equally effective to oral methadone daily doses of 80 to 120 mg (many split their doses to bid or tid).
  - Usually start 8mg bid, 8mg tid for significant IV heroin
  - Buprenorphine maintenance is ideal for people abusing illegal opiates and for those who want to switch from methadone to buprenorphine
  - Methadone dose reduced to 30mg/day before buprenorphine started
- Protocols for treatment can be found in the manual

Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction: a Treatment Improvement Protocol (TIP) 40. Available at: www.samhsa.gov/centers/csat/csat.html

Dosing of buprenorphine products

- Buprenorphine/naloxone
  - Suboxone (sublingual films): buprenorphine/nalxone
    - 2 mg/0.5 mg; 4 mg/1 mg; • 8 mg/2 mg; 12 mg/3 mg
  - Suboxone (sublingual tabs): buprenorphine/nalxone
    - 2.0 mg/0.5 mg; 8 mg/ 2.0 mg
  - Zubsolv (sublingual tablets): buprenorphine/nalxone
    - 0.7 mg/0.18 mg; 1.4 mg/0.36 m g; 2.9 mg/0.71 mg; 5.7 mg/1.4 mg; 8.6 mg/2.1 mg; 11.4 mg/2.9 mg
  - Buprenorphine mg amount is bioequivalent for the two products
  - Naloxone only active in the formulations if they are injected IV, inhaled or snorted (prevents misuse & initiates immediate w/d)
- Buprenorphine tablets: (Subutex) 2 mg or 8 mg
- Tablet(s) or film should be held under the tongue until completely dissolved.
- Once stable (months to yrs) – can consider slowly titrating dose down but do not consider tapering after a relatively short time

Buprenorphine Containing Products



References: LexiComp Drug Reference
Micromedex Drug Reference Orange Book Drug Reference
Drugs@FDA: FDA Approved Drug Product

Special Considerations

- Relapses: to be expected, continue to treat if at all possible
- Pregnancy:
  - High risk pregnancy referral
  - Treatment not to be discontinued
  - Switch to buprenorphine only products (e.g., Subutex)
  - Neonatal Abstinence Syndrome (NAS) usually avoided
  - Breastfeeding – can be considered
- Benzodiazepines & other sedatives to be avoided (Read *Benzo Blues* by Edward H. Drummand, MD)
- Hepatic impairment: use buprenorphine only products
- Diversion & abuse: monitor for & deal with
  - Check the PDMP

Preventing Diversion & Abuse

- Consider supervised administration initially, esp. if buprenorphine only product
- Short term prescriptions 3-7 days initially & frequent f/u
- Longer term prescriptions once stable & reliable
- Plans for "lost or stolen" medications"
- Drug treatment contract
- Urine drug screening (important to check for buprenorphine metabolite norbuprenorphine)
- Lock all Rx pads & no signed blanks
- Write all numbers (quantity & strength) in both Arabic numbers & letters
- "No" is a complete sentence
- Check the PDMP

Use of Antagonists

- Naltrexone
  - FDA approved for >18 y/o
  - Binds to opioid receptors 24-30 hrs
  - Abstinence from all opioids 7-10 days or immediate w/d
  - Once initiated, no euphoric effects if opiates taken
  - If switching to methadone or buprenorphine, abstinence of 24 hrs for oral & 30 days for injectable
  - Effective for highly motivated persons
- Oral formulations:
  - 25, 50, 100mg tablets
    - Variable dosing dependent on addiction, e.g., 50mg can block 25mg IV heroin for 24 hrs
    - Doubling or tripling dose will extend effects 48-72 hrs

Injectable Naltrexone (Vivitrol)

- Extended release → once a month injection
- IM injection: alternating buttocks by health care professional
- Standard dose: 380mg
- Candidates:
  - Failed methadone or buprenorphine
  - High motivation for abstinence
  - Shorter/less severe hx opioid dependence
  - Intense risk of opioid use relapse (including intense stress)
  - Prefer office based clinic rather than specialty clinic
  - Less time for clinic visits

Vivitrol Precautions

- Wear medical alert ID
- Pregnancy: contraindicated
- Keep safe & locked if PO
- No other opiates
- Not to be taken with other meds that can slow breathing (alcohol, other illicits)

Overdose, etc.

- Call 911
- Sternal rub, rescue breathing
- Administer Naloxone IM or intranasal, repeat prn
- Prescriptions for Naloxone for patients, families, etc.
- AL HB208 (2015): immunity for prescribing & administering opioid antagonists (e.g., Naloxone)
- HB379 (2016): State Health Officer or county health officer w authority to write standing order for dispensing naloxone

Prescription Drug Monitoring Programs

- New Patients
  - Review PDMP prior to ALL controlled substance Rx
  - Explore PDMP with the patient
  - Address any concerns with an honest and upfront conversation
  - Multiple Prescribers = RED FLAG
  - Rarely will I give "emergency refills"
- Return Patients
  - Review PDMP EVERY time (staff assistance helpful)
  - Verify PDMP with Rx bottles
  - Contact the pharmacy if necessary
  - Rely on Controlled Substances Agreement
  - Trust but verify

Prescription Drug Monitoring Programs Alabama Requirements

- For 30 MME or less per day, use PDMP in a manner consistent with good clinical practice (what does this mean?)
- For more than 30 MME per day, review the PDMP at least two times per year and document the use of REMS (Risk Evaluation and Mitigation Strategy) in the medical record
- For more than 90 MME per day, review PDMP every time prescriptions are written, on the same day the prescriptions are written, and document use of REMS in the medical record.
- Exemptions: nursing home patients, hospice patients (must indicate hospice on Rx), *active* malignant pain, intra-operative care, in-patient prescribing (in-patient orders *not* discharge Rx)

Special Considerations

- CANNOT put a printed copy in chart but can refer to being checked & result of check
- Multiple prescribers ("doctor shopping")
- Barriers to MAT
  - Not ready
  - Lack of social support
  - Cost
  - Programs or agencies that restrict MAT
  - Incarceration
  - Lack of clinics & prescribers
  - Limit in no. of buprenorphine RXs, esp. NP/PAs
  - Minimal coverage for counseling
  - Workforce misunderstandings & attitudes re: nature & use of MAT

APPROPRIATE USE CHECKLIST

BTOD/REMS: Office Based Buprenorphine Therapy for Opioid Dependences Maintenance Appropriate Use Checklist, October 2018

Maintenance Checklist

BTOD/REMS: Office Based Buprenorphine Therapy for Opioid Dependences Maintenance Checklist, October 2018

Treatment Agreements

- Variable usefulness & efficacy
  - Keep medications locked & safe
  - Take medications as prescribed
  - On time for appointments & notify if otherwise
  - Keep provider informed of other diagnosis and medications
  - No other prescribers for opioids
  - Missing an appointment or losing medication, no more medication until next office visit. May also have to start having supervised buprenorphine dosing.
  - If intoxicated when coming to clinic, the provider will not see me, and I will not receive more medication until the next office visit & may require supervised buprenorphine dosing.

Selling or giving away medication is diversion, is illegal; may result in supervised buprenorphine dosing or a higher level or care

Treatment Agreements

- Violence, threatening language or behavior, or participation in any illegal activity at the office will result in treatment termination from the clinic.
- Random urine drug testing is a treatment requirement. If a urine sample is not provided, it will count as a positive drug test.
- Treatment involves more than just taking medication. Complying with recommendations for additional counseling and/or for help is essential

Summary

- MAT is EFFECTIVE & more so than without
- Pharmacotherapy (MAT) only one aspect of treatment
- Naloxone prevents overdose deaths
- Relapse is to be expected
- At least 50% recover & regain ability to resume normal functioning, stable life
- Treating individuals with OUD is extremely rewarding
- Lower threshold treatment models to increase treatment will save lives!

Sources

- American Society of Addiction Medicine (ASAM)
  - ASAM Buprenorphine Course
  - Federal Guidelines for Opioid Treatment Programs
- American Academy of Nurse Practitioners (AANP) Waiver Training Course (8 hrs & 16 hrs)
- Alabama Department of Public Health & AL Law Enforcement Naloxone Training
- Harvard Medical School (HMS) CE Programs (*Understanding Addiction*, etc.)
- National Institute of Health (NIH): National Institute on Drug Abuse (*Alabama Opioid Summary)*
- Harrison School of Pharmacy at Auburn University: CE Courses on Opiates, etc. (e.g., *Pitfalls of Buprenorphine Prescribing*)
- Tennessee Department of Mental Health & Substance Abuse Services
- Buprenorphine Containing Transmucosal Products for the Treatment of Opioid Dependence (BTOD) Risk Evaluation and Mitigation Strategy (REMS) Program, "Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers, Oct. 2018
- www.PsychCentral: *Opioid Use Disorder Symptoms*, June 20-19s