Medication Assisted Treatment (MAT)

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June 19, 2019

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MAT – Learning Objectives

Learning Objectives

At the end of this educational activity, participants should be able to:

1. Discuss the epidemiology and the scope of drug addiction with reference to the "opioid epidemic."
2. Analyze the biology of addiction and recognize addiction as a disease process of the brain.
3. Explain how social and psychological factors impact the development and maintenance of addiction.
4. Define evidence-based practices for medication-assisted treatment (MAT) and its value in the treatment of opiate-use disorders (OUD) and alcohol-use disorders (AUD).

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General References and Resources –SUD and MAT

1. **U.S. Department of Health and Human Services (HHS), Office of the Surgeon General, *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health*. Washington, DC: HHS, November 2016.**

2. ***National Institute on Drug Abuse*. NIDA. (2018, January 17). Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition). Refer to https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/evidence-based-approaches-to-drug-addiction-treatment/pharmacotherapies**

3. ***Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence*. World Health Organization. Dept. of Mental Health and Substance Abuse. ISBN 978 92 4 154754 3 (NLM classification: WM284), 2009 – Refer to: http://www.who.int/substance_abuse/publications/opioid_dependence_guidelines.pdf**

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General References/Resources -Addiction and Medication Assisted Treatment (MAT)

- *SAMHSA - Substance Abuse and Mental Health Services Administration* - **Refer to: https://www.samhsa.gov/medication-assisted-treatment**
- **SAMHSA – National Survey on Drug Use and Health https://nsduhweb.rti.org/respweb/homepage.cfm**
- *PCSS – Providers Clinical Support System – https://pcssnow.org/about/ - multiple opportunities via WebEx*
- *Training Resources are many – some of the best include*
  - *AAAP – American Academy of Addiction Psychiatry Annual Review Course – December every year*
  - *ASAM – American Society of Addiction Medicine*
  - *Waiver Course to be able to prescribe Buprenorphine– 8 Hour Course for physicians; 24 hours for PAs and NPs*
  - **Harvard Medical School Addiction course (McLean Hospital, Course Director Roger Weiss, MD.) - This is one of the best courses in Addiction Psychiatry/Addiction Medicine, is cutting edge, and is repeated annually in Boston.**

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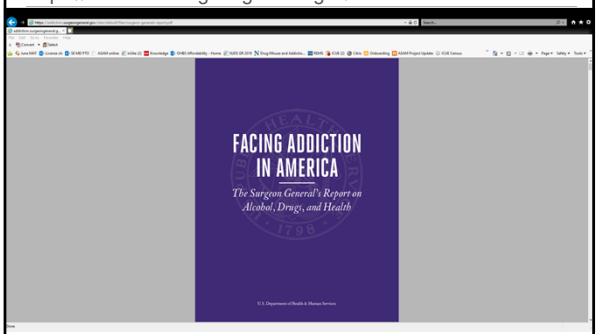
2016 U.S. Surgeon General's Report https://addiction.surgeongeneral.gov/



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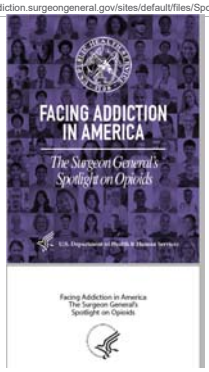
References – https://addiction.surgeongeneral.gov/sites/default/files/Spotlight-on-Opioids_09192018.pdf



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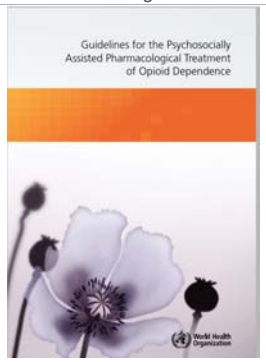
References – World Health Organization 2009 Report



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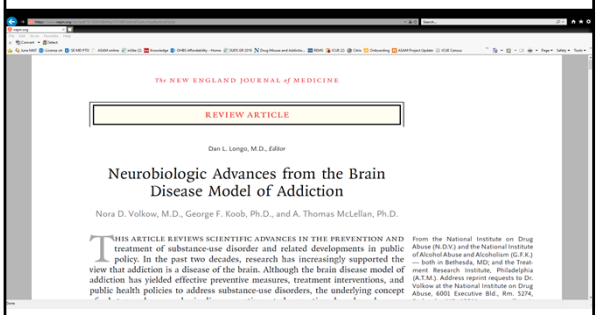
References – NEJM Article by Nora Volkow, et al 2016



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Neurobiologic Advances from the Brain Disease Model of Addiction

Nora D. Volkow, M.D., George F. Koob, Ph.D., and A. Thomas McLellan, Ph.D.

THIS ARTICLE REVIEWS SCIENTIFIC ADVANCES IN THE PREVENTION AND treatment of substance-use disorder and related developments in public policy. In the past two decades, research has increasingly supported the view that addiction is a disease of the brain. Although the brain disease model of addiction has yielded effective preventive measures, treatment interventions, and public health policies to address substance-use disorders, the underlying concept

From the National Institute on Drug Abuse (N.D.V.) and the National Institute of Alcohol Abuse and Alcoholism (G.F.K.) — both in Bethesda, MD; and the Treatment Research Institute, Philadelphia (A.T.M.). Address reprint requests to Dr. Volkow at the National Institute on Drug Abuse, 6001 Executive Bld., Rm. 5274,

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Epidemiology and scope of drug addiction- NSDUH

The National Survey on Drug Use and Health (NSDUH) measures:

1. use of illegal drugs, prescription drugs, alcohol, and tobacco
2. mental disorders, treatment, and co-occurring substance use and mental disorders

The data provides estimates of substance use and mental illness at the national, state, and sub-state levels, and helps identify the extent of substance use and mental illness among different sub-groups. It estimates trends over time and is used to determine the need for treatment services.

SAMHSA Substance Abuse and Mental Health Services Administration (U.S. Dept HHS)

https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

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Scope of the Opioid Epidemic

Information is from CDC WONDER*

- From 1999-2017 > 700,000 people have died from a drug overdose
- About 2/3 of the 70,200 drug overdose deaths in 2017 involved an opioid
- 2017 – the # of OD deaths involving any kind of opioid was 6 times higher than it was in 1999, with an average of 130 deaths daily from an opioid overdose.

CDC WONDER is a public service menu driven online database developed and operated by the Centers for Disease Control and Prevention, an agency of United States federal government.

The public web site at http://wonder.cdc.gov is **in the public domain**, and only provides access to public use data and information. You may access the information freely, and use, copy, distribute or publish this information without additional or explicit permission. Please do provide a citation to credit the authors and/or data providers. When referring to a written article or document, please cite the item as you would any other document on the world wide web.

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the Opioid Epidemic - A Deadly Problem

- Drug overdose deaths continued to increase in the United States through 2017. In October 2017 President Trump formally declared the opioid crisis to be a public health emergency in the United States which meant it moved to top priority of all health departments, in all states, and local governments
- Deaths from drug overdose had risen among both men and women, all races, and adults of nearly all ages. There is some evidence that total opioid deaths may be coming down since 2017 but remains high
- Rise in overdose deaths from *ANY* opioid (heroin, fentanyl, prescription opioids) rose dramatically
  - In 1999- there were over 8,000 opioid overdose deaths
  - By 2017 this had risen to over 47,000 opioid overdose deaths – about 130 such deaths every day -- mainly driven by synthetic opioids other than methadone
- Two out of three drug overdose deaths involve an opioid.
- However, for context → Overall mortality from Alcohol and Tobacco related disorders exceed opioid deaths.

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From the CDC – Trends in Heroin Use in the U.S.

- Rates are highest among males 18–25 years old with annual incomes <$20,000, living in urban areas, and having either no health insurance or Medicaid.
- However, rates increased significantly across almost all study groups.
- The greatest increases in heroin use occurred in demographic groups that historically have had lower rates of heroin use: doubling among women and more than doubling among non-Hispanic whites.
- *The rate of heroin abuse or dependence* from 1999-2017nearly doubled and there has been a *sharp increase in heroin-related overdose deaths reported since 2010.*

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Trend in Heroin Use in the U.S. – From the CDC

- ***Heroin abuse is not occurring in isolation.*** **Alcohol, marijuana, cocaine, and opioid pain reliever abuse are significant risk factors for heroin abuse**
- ***poly-substance use is a risk factor for overdose death; most overdose deaths involve multiple drugs***
- ***Abuse or dependence on opioid pain relievers was the strongest risk factor for heroin abuse or dependence.***

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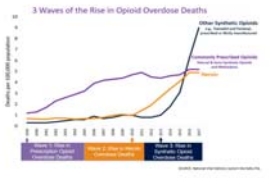

From National Vital Statistics System Mortality File and CDC

Wave 1 – 1999-2009 – Rx Opioids

Wave 2 – 2010 – rapid rise in heroin involved deaths

Wave 3 – 2013 – significant increase in OD deaths involving synthetic opioids, esp illicitly manufactured Fentanyl

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Impact of Comorbid MI and SUD

Co-Occurrence of SUD with other psychiatric disorders is high
- 18.9% US age 18 or older had a mental illness
- 7.8% US age 18 or older had a SUD
- ***3.4% US age 18 or older have both a mental illness and a Substance Use Disorder***

This is about 11 Million Americans

The standard of care in 2019 is to treat both disorders simultaneously. However, the 2017 NSDUH estimated that only 7.7% of adults with any mental illness plus a SUD received any treatment for both disorders.

Compared to Adults without a Mental Illness 18 year olds and older in the U.S. ***with*** a Mental Illness are:
- Twice as likely to use illicit drugs
- Three times as likely to abuse opioids
- Five times as likely to use heroin

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Suicide and Opioids

People with a SUD are 5x more likely to have suicidal thinking/plans/attempts than those with no SUD

Suicide rate in the general population in the U.S. is 14/100,000

With Opiate Use Disorder (OUD) suicide rate rises 16 times to 87/100,000

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Overview of Alcohol Use in U.S.

Substance Abuse and Mental Health Services Administration (SAMHSA). 2015 National Survey on Drug Use and Health (NSDUH)

86.4% of those in the U.S. who are age 18 or older drink alcohol at some point in their life

Alcohol Use Disorder (AUD) in the United States: 15.1 Million people ages 18 and older

Only ~7% percent of adults with AUD in the past year received treatment for it.

An estimated 623,000 adolescents ages 12–17 (2.5 percent of this age group) had AUD.

BUT ONLY ~ 5% of teenagers with AUD in the past year received treatment.

Defining Heavy Drinking

>4 standard drinks/d or 14-15 drinks a week for men; >3 standard drinks/d or 7-8 drinks a week for women

Binge drinking is consuming 4 drinks for women and 5 drinks for men within 2 hours

26.9% of those age 18 or older reported binge drinking in the past month and 7% reported that they engaged in heavy alcohol use

Heavy alcohol use is defined as binge drinking 5 or more days in the past month.

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Overview - Alcohol Use in U.S.

Substance Abuse and Mental Health Services Administration (SAMHSA). 2015 National Survey on Drug Use and Health (NSDUH)

Alcohol-Related Deaths: Per CDC an estimated 88,000 people die from alcohol-related causes annually, making alcohol the third leading preventable cause of death in the U.S. The first is tobacco, and the second is poor diet and physical inactivity.

Globally, alcohol misuse was the fifth leading risk factor for premature death and disability in 2010. Among people between the ages of 15 and 49, it is the first. In the age group 20–39 years, approximately 25 percent of the total deaths are alcohol attributable. World Health Organization (WHO). *Global Status Report on Alcohol and Health*. p. 57. 2014 ed. http://www.who.int/substance_abuse/publications/global_alcohol_report/msb_gsr_2014_1.pdf?ua=1

Family Consequences: More than 10 percent of U.S. children live with a parent with alcohol problems, according to a 2012 study. Substance Abuse and Mental Health Services Administration (SAMHSA). *Data Spotlight: More than 7 Million Children Live with a Parent with Alcohol Problems*, 2012. http://media.samhsa.gov/data/spotlight/Spot061ChildrenOfAlcoholics2012.pdf.

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PolySubstance Dependence is Part of The Trend

This growing issue also means that an opioid overdose often includes the use of more than one drug at once.

From 2010-2016, there were significant increases in overdose deaths involving synthetic opioids that also involved prescription opioids, heroin, and all other illicit or prescription drugs. Among synthetic opioid–related overdose deaths in 2016, almost 80 percent involved another drug or alcohol, like another opioid, heroin, cocaine, prescription opioids, benzodiazepines, alcohol, psychostimulants, and antidepressants.

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Children and Adolescents –

Substance Use has spread to younger and younger populations in the past few generations

Why is this such a problem compared to adult onset substance abuse?

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Substance Abuse can interfere with normal development of the Adolescent Brain

- Adolescence is associated with more impulsivity and poorer judgment seen in higher levels of binge drinking and experimenting with drugs.
- Adolescence is a critical time in brain development, especially for cortical development related to Executive Function, including Self Control (Impulse and Emotional), Flexibility, Planning, Prioritizing, Organization and others
- Adolescent brain undergoes a lot of physical changes in neurogenesis, cortical synaptic remodeling, neurotransmitter receptors and transporters.
- Frontal cortical development occurs later in adolescence and is not complete until the early to mid 20s

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The Adolescent Brain - The ABCD Study (ABCDStudy.org)

The ABCD study is the largest long-term study of brain development and child health in the United States.

The ABCD Research Consortium consists of a Coordinating Center, a Data Informatics and Analysis Center, and 21 research sites across the country (see map), which will recruit approximately 10,000 children ages 9-10 and following them into early adulthood.

Integrating structural and functional brain imaging with genetics, neuropsychological, behavioral, and other health assessments, the ABCD Study will increase our understanding of the many factors that can enhance or disrupt a young person's life trajectory.

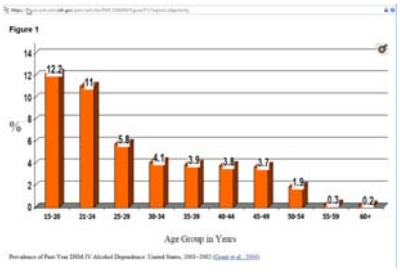
For information go to ABCDStudy.org

What are the BioPsychoSocial Risk Factors for the Development of Substance Use Disorders in Children and Adolescents

1. Genetic Factors account for ~50%
2. Mental Disorders
   a. ADHD
   b. Conduct Disorders
   c. Mood Disorders
3. Traits that increase the risk for SUD
   a. Aggression
   b. Impulsivity
   c. Antisocial
4. Child Abuse
5. Poor Academic Performance
6. Belonging to a Drug Using Peer Group
7. Poverty
8. Parental Drug Use
9. Lack of Adequate Parental Supervision
10. Community Attitudes toward drug use
11. Early Age of onset of drug use
12. Type of Drug Used
13. Route of Administration

Past Year Alcohol Dependence by Age Group

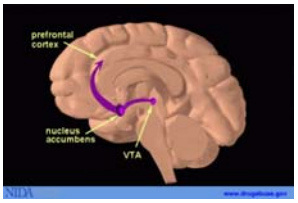
A Proxy For All types of Substance Use



Overview of The Neurobiology of Addiction

What is meant by the Neurobiology of Addiction?

"Dysfunction" and "change" in the Brain's Reward Pathway Accompanies Addiction



Brain reward pathway involves the ventral tegmental area (VTA), the nucleus accumbens, and the prefrontal cortex. When activated by a rewarding stimulus (e.g., food, water, sex), information travels from the VTA to the nucleus accumbens and then up to the prefrontal cortex.

All addicting drugs activate this circuit by mechanisms that release Dopamine. This is a receptor level response → Reward →Conditioned Response (Pavlovian learning associates environmental event with the reward and seeks to repeat it.

from the National Institute on Drug Abuse (NIDA)

Opioid Receptors

Opioid receptors* are widely distributed in the Central Nervous System, peripheral nerves and GI Tract.

When Opioids bind to opioid receptors in the brain reward system stimulation of the reward pathway occurs, which initially is experienced as euphoric and pleasurable

But in the future addicted person it leads to cycles of opioid re-administration leading to tolerance (needing more drug for a euphoric effect), withdrawal symptoms, and the profile of addiction

The Addiction Cycle Has 3 Recurring Stages

- ❖ Binge and intoxication
- ❖ Withdrawal symptoms and associated negative affect
- ❖ Preoccupation and anticipation (or craving).

Neurobiologic Advances from the Brain Disease Model of Addiction" by Nora D. Volkow, M.D., George F. Koob, Ph.D., and Thomas McLellan, Ph.D.. I will cite the names of authors and NEJM (published January 28, 2016.
N Engl J Med 2016; 374:363-371, DOI: 10.1056/NEJMra1511480. https://www.nejm.org/doi/full/10.1056/NEJMra1511480

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Binge and Intoxication

Addictive drugs activate brain reward regions causing increases in Dopamine release. This initially pleasurable experience is a reward signal that triggers classical Pavlovian conditioning

Repeated rewarding experiences become associated with the environmental stimuli that surrounded the drug use.

Dopamine release then occurs in anticipation a drug will be used – simply being where the drug was used, or with whom, and being in a similar emotional state at the time the drug was used can all come to elicit conditioned, fast surges of dopamine release that trigger drug craving and this motivates drug-seeking behaviors and the "binge" use of the drug ensues.

These conditioned responses become deeply ingrained and can trigger strong cravings for a drug long after the use of the drug has stopped - for example, when people are incarcerated or stop using while in a treatment center.

As soon as they return to their prior drug using environment → people, places, things can trigger craving and return to drug use.

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Drug-Induced Neuroplasticity
Long term Structural Changes in the Brain

This drug seeking is to a significant degree biologically based and dopamine plays a large role

physical changes in synapses occur – in other words, communication within the brain changes

With repeated drug use transmission of signals between neurons may increase or decrease.

A number of neurotransmitters and receptors become involved in altering neurotransmission

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Drug-Induced Neuroplasticity
This is Long term Structural Change in the Brain

These "Neuroplastic changes" triggered by drugs have been uncovered in:

the nucleus accumbens (brain-reward region)

the dorsal striatum (encoding of habits and routines)

the amygdala (emotions, stress, and desires)

the hippocampus (memory)

and the prefrontal cortex (self-regulation).

All these regions of the brain participate in the various stages of addiction, including conditioning and craving. These regions also regulate the firing of dopamine cells and the release of dopamine.

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Withdrawal and Negative Affect

In the addicted person ordinary rewards like food or sex lose power to motivate behavior as the brain reward system becomes conditioned to seek potent dopamine release from drug use

Life becomes more restricted around cues, triggers and drug use.

Repeated drug use over many cycles leads to smaller increases in dopamine levels in the addicted person compared to those who have never used drugs.

This means the brain reward system becomes less sensitive to drug-related rewards. The addicted person no longer gets the same degree of euphoria from the drug as when first used → they will then chase after the euphoria by increasing use of the drug.

They become less motivated by previously important relationships and activities

These changes become deeply ingrained and will not be easy to reversed by the simply stopping the drug, such as going through detoxification.

Neurobiologic Advances from the Brain Disease Model of Addiction" by Nora D. Volkow, M.D., George F. Koob, Ph.D., and Thomas McLellan, Ph.D.. I will cite the names of authors and NEJM (published January 28, 2016. N Engl J Med 2016; 374:363-371, DOI: 10.1056/NEJMra1511480. https://www.nejm.org/doi/full/10.1056/NEJMra1511480

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Preoccupation and Anticipation

The **down-regulation of dopamine** signaling that dulls the reward circuits' sensitivity to pleasure also occurs **in prefrontal brain regions** and their associated circuits, **seriously impairing executive function including the capacity for self-regulation and decision making**, among others.

The modulation of the reward and emotional circuits of prefrontal regions is further disrupted by neuroplastic changes in glutamatergic signaling.

In persons with addiction, the impaired signaling of dopamine and glutamate in the prefrontal regions of the brain weakens their ability to resist strong urges, or to follow through on decisions to stop taking the drug.

This explains why "addicts" can be sincere in a desire and intention to stop using a drug and simultaneously be impulsive and unable to follow through.

In sum, altered brain function in prefrontal regulatory circuits and brain reward circuits impact emotional response

This changes is crucial to development of compulsive addictive behavior and the inability to reduce drug-taking behavior, despite potentially catastrophic consequences.

"Neurobiologic Advances from the Brain Disease Model of Addiction" by Nora D. Volkow, M.D., George F. Koob, Ph.D., and Thomas McLellan, Ph.D.. I will cite the names of authors and NEJM (published January 28, 2016. N Engl J Med 2016; 374:363-371, DOI: 10.1056/NEJMra1511480. https://www.nejm.org/doi/full/10.1056/NEJMra1511480

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Medication Assisted Treatment

Diagnostic Criteria – All Substance Use Disorders

Before turning to MAT – we need to be sure the consumer has a Substance Use Disorder – here are the DSM-5 criteria

1. Social Impairment (Social/Interpersonal Problems related to using)	7. Repeated Attempts to Quit or Control Use
2. Neglect Major Roles and Obligations to use	8. Cravings or Compulsions to Use
3. Give Up Activities to Use	9. Physical/Psychological Consequences/Problems Related to Use
4. Much Time Spent Using	10. Tolerance
5. Hazardous Use (DUI, machinery, etc)	11. Withdrawal
6. Using Larger Amounts or Longer than Intended	

The severity of the Substance Use Disorder is determined by the number of diagnostic criteria that were met within the past 12 months:

Mild (2-3 Criteria)

Moderate (4-5 Criteria)

Severe 6 or more criteria)

Medication Assisted Treatment (MAT) ***INCLUDES:***

- ***Medication plus Counseling*** *– without the structure of counseling a medications only strategy usually will fail.*
- **The most effective counseling/therapies include:**
  - **Motivational Interviewing***
    - **OARS – Open Questions, Affirmations, Reflective listening, Summarizing**
    - **4 Processes –**
      - **Engaging**
      - **Focusing – set Agenda, goals for the session**
      - **Evoking – elicit the person's own motivation – seeks "Change Talk" – why do you want to make a change? Benefit? How might you go about it? Options? First Steps?**
      - **Planning – develop specific plan consumer can agree to**
  - **Motivational Enhancement Therapy**
  - **Contingency Management***
  - **Other Behavior Therapies (e.g, CBT)**

Agonist v Antagonist

The term "Opiate" refers to compounds that occur ***naturally*** and come from the opium poppy plant.

The term "Opioid" includes ***both*** the naturally occuring compounds from the opium poppy plant as well as those compounds made synthetically by man –

****ALL OPIOIDS act by binding to opioid receptors in the body causing them to activate–***

Let's use the term opioid as more general - ALL Opioids are "Agonists"

…this means they work like heroin, hydrocodone, oxycodone, morphine, ***others…if you give an opioid addicted person an "Agonist" it is like you gave them the drug they have been using…in other words it feels like an opioid to them***

An Opioid Antagonist is the opposite…as we will see the main one in MAT is Naltrexone

…antagonists like Naltrexone occupy the opioid receptors and BLOCK or STOP the opioid (ex. heroin) from occupying them --- therefore the opioid cannot activate and produce an opioid effect in the user…

Antagonists like Naltrexone can actually kick the opioid (agonist) off the receptor because it binds more tightly…this can lead to withdrawal effects in the opioid dependent person.

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MAT

The Goal of MAT is to stabilize dysfunctional brain receptors in Opioid Dependent people.

There are TWO approaches:

1 - Block the receptor using the opioid receptor ANTAGONIST Naltrexone

Naltrexone ER (Vivitrol) – a few recent studies show equal efficacy with agonist therapy but this was only in established patients – the trend in treatment centers is to favor the use of Naltrexone but the evidence base is not as solid or longstanding --- YET

2 - Activate the Receptor with an opioid receptor AGONIST – there are 2 AGONIST approaches

A - A PARTIAL Opioid Agonist → Buprenorphine

Transmucosal-SL, Film
Implant – Probuphine 6 months
Abdominal SC – Sublocade monthly

B – A FULL Opioid Agonist → Methadone

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- **All Opiate Agonists produce 4 main effects:**
  1. **Euphoria**
  2. **Analgesia**
  3. **Constipation**
  4. **Respiratory Depression**

- **Buprenorphine is a *Partial Agonist***
  - It will only activate opiate receptors at 25% of their maximal response (this is called a Ceiling Effect)
  - BINDS Opioid receptor very TIGHTLY and will displace a full agonist and precipitate acute withdrawal
  - You need to see opioid withdrawal symptoms (COWS ~ 8) to document the person is actually opioid dependent **AND** to reduce chance of precipitating more acute opioid withdrawal.
  - Because of the ceiling effect it is harder to overdose on Buprenorphine **ALONE**

- **Methadone is a *Full Agonist***
  - Activates opioid receptor at 100% of maximal response –> Respiratory depression→ death.
  - Metabolized by cytochrome P450 system, it is pharmacologically complex with many interactions.
  - Prolongation of the QT interval occurs especially over 100mg a day and can lead to Torsades de pointes, a form of Ventricular Tachycardia that can lead to Ventricular Fibrillation and death.
  - However, other drugs causing QT prolongation include antipsychotics, antidepressants, antibiotics, antihistamines.
  - A QT interval over 500 ms should lead to lowering the dose or discontinuation.
  - Long half-life allows steady occupation of opioid receptor which blocks feeling of being "high" and competes with heroin, etc -- (Note - ***This only occurs with steady and not erratic use)***

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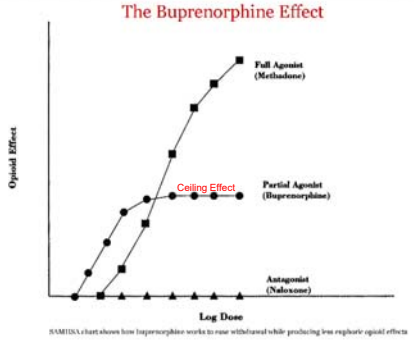
The Buprenorphine Effect



SAMHSA chart shows how buprenorphine works to ease withdrawal while producing less euphoric opioid effects

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What about the worry/argument that you are replacing one drug with another when you use an AGONIST for Medication Assisted Treatment (MAT)

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On Using Opioid Agonists in Opioid Dependent people - MAT IS A HARM REDUCTION STRATEGY

Former FDA Commissioner Scott Gottlieb, MD

- *individuals who successfully transition onto medication-assisted treatment are not swapping one addiction for another.*
- ***Opioid use disorder should be viewed similarly to any other chronic condition that is treated with medication.**"*

National Institute on Drug Abuse (NIDA)

*… **taking these medications as prescribed allows patients to hold jobs, avoid street crime and violence, and reduce their exposure to HIV by stopping or decreasing injection drug use and drug-related high-risk sexual behavior.***

Substance Abuse and Mental Health Services Administration (SAMHSA)

- ***patients receiving MAT for treatment of their opioid use disorder cut their risk of death from all causes in half.***

Elinore F. McCance-Katz, M.D., Ph.D. (Assistant Secretary for SAMHSA)

- ***"Medication-assisted treatment combined with psychosocial therapies and community-based recovery supports is the gold standard for treating opioid addiction."***

OPTUM

Benefits of Opioid MAT (Buprenorphine/Methadone)

MAT can double the opioid abstinence rate and this was shown in Clinical Trials ***in the treatment seeking patient*** (important distinction)

- ***Use of MAT likely increases the rate of early abstinence 6-7 fold and***
- **Reduces the risk of overdose during treatment**

MAT is a Harm reduction Strategy – important to communicate to significant others, patients, and providers – ***it has impact beyond the user***

It leads to reduction in crime, medical illness, including HIV, hepatitis C

It leads to improvement in social, family, financial circumstances

OPTUM

- **Current Evidence for Opioid Antagonist Naltrexone ER is mostly for the long acting injection of Naltrexone ER (brand name Vivitrol)**
  - In ***established patients*** it appears to be as effective as buprenorphine/naloxone SL
  - However, it is harder to start, and has a high dropout rate
  - The overdose risk appears to be reduced to a similar extent as with agonist therapies.
- ***ALL 3 MAT choices are considered first line options***

  Agonists = easy to get on, harder to get off
  - Ambivalence is higher in early recovery

  Antagonist = harder to get on, easy to get off
  - ***Have to wait 7-10 days off agonists to start an antagonist – risk is severe withdrawal reaction***
  - At 2 weeks → onset of cravings – these can be persistent – but will improve if can keep the user on the antagonist longer term
  - You can use off label comfort meds to relieve Opiate Withdrawal Syndrome (OWS) and PAWS
  - Lofexidene (similar to clonidine) recently approved by FDA for OWS

OPTUM

Adolescents and MAT

In Adolescents

- **Buprenorphine is the only FDA approved opioid agonist medication for age 16 and older for office based care**
- **You can also use Naltrexone ER (Vivitrol) – important to start treatment earlier in the OUD course of adolescents and to have oversight by parents**

OPTUM

How to choose which MAT medication To Use

- *Comorbid Pain favors using an Agonist (methadone/buprenorphine)*
- *Comorbid Alcohol Use Disorder favors using Naltrexone ER*
- *A need for high intensity monitoring favors Opioid Treatment Program (*OTP) (OTP usually has both methadone and buprenorphine)
- Consumer's occupation may favor Antagonist (e.g., Physician, Pilot, Pharmacist, Nurse, Lawyer, Police officer, Fireman, Truck Driver, etc)

OPTUM

How to choose which MAT medication To Use

- Overdose potential is higher with the agonist Methadone
- There is no overdose potential with the antagonist Naltrexone
- Retention in treatment is better with Methadone than Buprenorphine
- Retention is a problem with Naltrexone – but less if you use contingencies
- Side effects of Naltrexone ER = nausea, vomiting, headaches, and injection site reactions
- With Naltrexone, obtaining analgesia is a problem
- Drug interactions are higher with Methadone than Buprenorphine
- You need a special license called a waiver to prescribe Buprenorphine and there are limits to the number of patients a provider can have on Buprenorphine at any one time to 275

OPTUM

Prescriber requirements/actions in using Buprenorphine

REMS – Risk Evaluation and Mitigation Strategy

1. Verify consumer meets diagnostic criteria for opioid dependence
2. Discuss the risks and side effects of buprenorphine products
3. Do induction under appropriate supervision of consumer
4. Initially only prescribe limited amounts of buprenorphine – enough to last until the next visit
5. Explain safe storage of buprenorphine- **keep out of the reach of children**
6. Schedule appointments commensurate with patient's stability – at least weekly or more frequently in the first month

OPTUM

Prescriber requirements/actions in using Buprenorphine

7. Consider medication counts
8. Determine if consumer is participating in counseling/therapy/psychosocial support and if not, strongly encourage them to do so
9. Assess whether progress is being made toward recovery, including, as appropriate, UDS.
10. Reassess maintenance dosing
11. Reassess and document if the benefits of continued treatment outweigh the risks

OPTUM

Key Messages to consumer to Reduce the Risk of Overdose and Misuse

- Ingestion by a child may cause respiratory depression and can result in death. Medical attention should be sought immediately.
- Warn consumer using Buprenorphine that it is dangerous to use non-prescribed benzodiazepines or other CNS depressants including alcohol.
- Instruct them never to give these products to anyone else
- Because it is an opioid the medication is a target for other users. Keep the buprenorphine in a safe and secure place away from children, and protect it from theft.
- Inform consumers that selling or giving away buprenorphine-containing products is against the law.

OPTUM

Dosing of Buprenorphine

- **Buprenorphine** –
  - Induction Phase – they must be in withdrawal before starting induction. Give 2-4 mg to start – can titrate first day to a maximum of 8 mg. On day 2 and subsequently can add 2 mg a day to target of 12-16 mg. The goal is to stop craving. Most people do not need more than 16 mg, but in some may need 24-32 mg
  - Stabilization Phase – 1-2 months - consumers have stopped using other opioids and cravings have ceased – during this phase consumer may report they tried to use other opioids without euphoria. Drug screens should be negative – no objective signs of opioid use
  - Maintenance Phase – short (<12 months) or up to lifetime – goals = no legal drug related issues, improved family and other support, reintegration into the community employment, other drug/alcohol use.

Safest way to stop Buprenorphine is very gradual dose reduction with close monitoring and counseling

OPTUM

Counseling is critical

- Strongest evidence is for use of contingency management and for Motivational Interviewing
- Main benefit of Counseling is probably that it helps keep the person in treatment
- *Expect a 50% dropout rate at 6 months*
- *Engagement and retention are the target goals of any counseling*
- *The consumer should be educated on all of this*

OPTUM

Using Methadone

- Methadone
  - For Induction give 5-10 mg orally every 4 hours
  - Maximum Dose in the first 24 hours is 40 mg
  - You can then titrate Methadone dose to a target of 60-120 mg over at least a 2 week period with close medical monitoring
  - limit or avoid benzodiazepines/alcohol
  - While it may be safer to switch to buprenorphine if they want to stop agonist therapy you first must reduce Methadone dose to 30 mg a day before attempting to switch them to Buprenorphine.
  - Methadone has a long track record of success back to early 1970s and many of those successful in achieving recovery using Methadone have remained on it for decades

OPTUM

Methadone v Buprenorphine

- Both are associated with a reduction in the use of non-prescribed opioids
- There are no significant differences in mortality
- With Methadone there is greater retention in treatment
- With Buprenorphine there is more opioid use during treatment

REMEMBER THIS IS A HARM REDUCTION STRATEGY – BEST IF USED AS PART OF A LONG TERM STRATEGY – LIKE ANY CHRONIC ILLNESS RELAPSES CAN OCCUR – THESE NEED TO BE MANAGED

PEOPLE SHOULD BE EDUCATED ABOUT MANAGEMENT OF RELAPSES AND SHOULD NOT BE DISCHARGED FROM TREATMENT UNLESS CONTINUED VIOLATIONS OF TREATMENT CONTRACTS OCCUR

OPTUM

Narcan (Naloxone)

Naloxone (Narcan) – IV, IM, SC, Nasal Spray

Use for emergency treatment where opioid overdose is supected – always seek emergency assistance as the opioid the person used may be longer lasting than the Narcan adminstered.

May need repeating every 2-3 minutes if the person does not respond or relapses into unconsciousness or respiratory depression

can take 4 or more doses to resuscitate – and short half-life compared to the agonist on board means they can go into significant respiratory depression again.

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Opioid withdrawal is a big problem in Opioid Use Disorders (OUD)

- Detoxication alone will often fail, especially in those who have a history of multiple treatments or attempts at abstinence
- And after detoxification the person has become **LESS TOLERANT to opioids** and when they relapse they are more likely to overdose and die
- Withdrawal symptoms will occur in the long term management of patients using MAT with Methadone and Buprenorphine if you reduce or stop the drug and this makes discontinuation of MAT more challenging
- Inability to tolerate withdrawal without resumption of the addiction cycle argues for long term maintenance on buprenorphine or methadone -- people can live functional lives with these medications.
- Symptomatic relief of opioid withdrawal using non-opioids by themselves is usually poor
- Opioid withdrawal can be harmful to fetal development in pregnant women

OPTUM

If the person declines MAT

- **Keep on educating them and suggesting it to those with Opioid Use Disorder (OUD), especially refractory cases**
- **The best alternative option may be residential treatment – but for many it is not an option**
- **However, even after extended residential treatment the relapse rate is very high…and since tolerance has been reduced, the chance of a lethal overdose is higher**
- **Educate about relapse risk, overdose prevention, the use of Naloxone, and use of support groups**
- **Consider Naltrexone ER (Vivitrol) in transition back to the community**

OPTUM

Opiate Dependent and Pregnant?

For Pregnant Women with Opioid Use Disorder (OUD) d*etoxification is contraindicated and Agonist maintenance is the standard of care until delivery of the child*

Either Methadone or Buprenorphine can be used in pregnant women

If Buprenorphine is used – use only buprenorphine alone without naloxone

Strongly recommend they discontinue all other substance use including nicotine

After delivery if they remain on an agonist breastfeeding is OK if they are in stable recovery and no other substances are being used

OPTUM