MEDICATIONS FOR OPIOID USE DISORDER

AMERICAN ACADEMY OF FAMILY PRACTICE
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OUTLINE

- The disease of addiction
- The neuroscience of addiction
- Opioid overdose
- Medication Assisted Treatment (MAT)
- Medications for Opioid Use Disorder (MOUD)
- MOUD and pregnancy
- Benefits of MOUD
- Take home points

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THE DISEASE OF ADDICTION

- Addiction is a chronic, often relapsing brain disease that causes compulsive drug seeking and use, despite harmful consequences to the addicted individual and to those around him or her
  - Drugabuse.gov June 30, 2016
- Like diabetes, cancer and heart disease, addiction is caused by a combination of behavioral, environmental and biological factors

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THE DISEASE OF ADDICTION

- Addiction is similar to other chronic medical problems
  - Treatment can remove or reduce the symptoms but does not affect the root cause of the disease
  - Treatment requires significant changes in lifestyle and behavior on the part of the patient to maximize the benefit
  - Relapses are likely
  - Treatment should involve regular monitoring of medication adherence as well as encouragement and support of pro-health changes in lifestyle

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THE GENETICS OF ADDICTION

- Genetic risk factors account for about half of the likelihood that an individual will develop addiction
  - National Center on Addiction and Substance Abuse 2017
- Children of addicts are 8 times more likely to develop an addiction
  - Prescott, C.A., & Kendler K.S., Genetic and environmental contributions to alcohol abuse and dependence in a population-based sample of male twins. Am J Psychiatry, 1999. 156(1): p. 34-40

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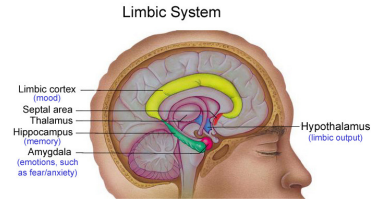

NEUROCHEMISTRY OF ADDICTION

LIMBIC SYSTEM CONTAINS THE BRAIN'S REWARD CIRCUITRY

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LIMBIC SYSTEM

- Responsible for our perception of emotions, both positive and negative

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LIMBIC SYSTEM

Controls and regulates our ability to feel pleasure which motivates us to repeat behaviors that we need to survive

Activated by healthy, life-sustaining activities but also drugs of abuse

Dopamine is the key neurotransmitter in the limbic system

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DOPAMINE

- Dopamine regulates movement, emotion, motivation and feelings of pleasure
- Drugs of abuse target the brain's reward system by flooding the circuit with dopamine producing euphoria
- When the reward circuit is activated, the brain triggers a memory and teaches us to repeat that behavior

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DOPAMINE

Average brain – 50 ng/dL daily of dopamine

Sex – 125 ng/dL

Tobacco – 450 ng/dL

Marijuana – 650 ng/dL

Heroin- 975 ng/dL

Methamphetamine – 1100 ng/dL

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DOPAMINE

With continued exposure to high levels of dopamine the brain downregulates the number of receptors and natural dopamine release

Less receptors means that the person's ability to experience any pleasure is reduced

This leads to ongoing drug abuse in order to try and increase the levels of dopamine

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OPIOID WITHDRAWAL

- The withdrawal from any substance is the opposite of the intoxicating effects
- Acute opioid withdrawal – agitation, anxiety, muscle aches, increased tearing, insomnia, runny nose, sweating, yawning, abdominal cramping, diarrhea, dilated pupils, goose bumps, nausea, vomiting, increased heart rate and blood pressure, tremor
- Subacute opioid withdrawal – depression, anhedonia, insomnia, fatigue, anorexia, cravings, impaired concentration, sleep disturbance
- Severity of the withdrawal contributes to the ongoing use – use just to avoid being sick
- Tolerance increases which leads to increasing doses

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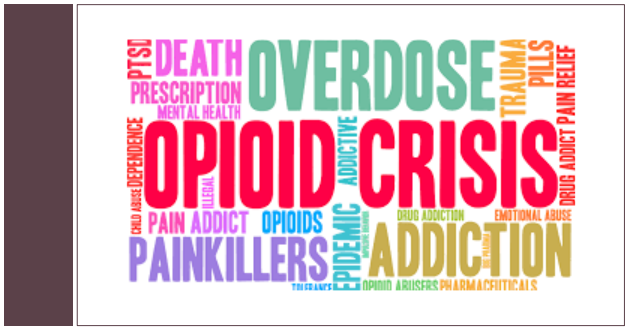

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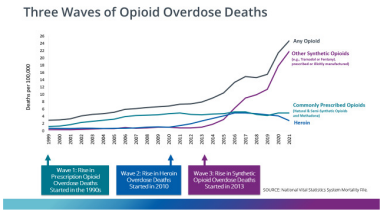
OPIOID OVERDOSE



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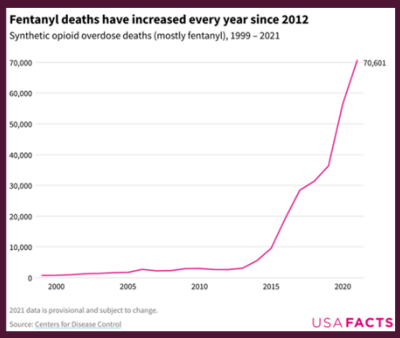

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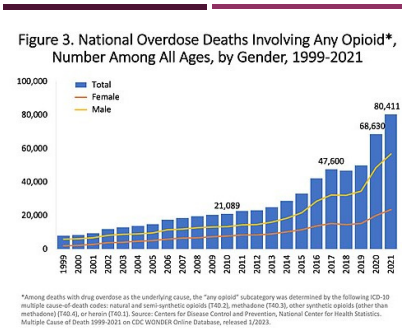

OPIOID OVERDOSE

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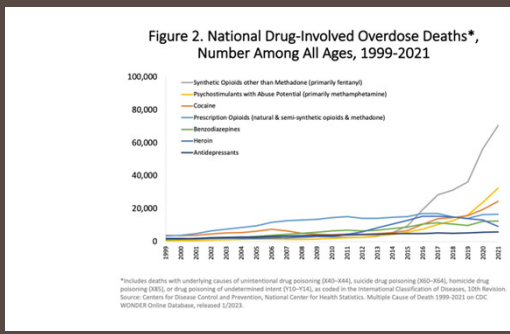

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OPIOID OVERDOSE

70-80% of drug overdoses are related to opioids

295 people die every day from drug overdose (one life every 5 minutes)

The US claims 27% of the worlds drug overdose deaths

- United Nations Office on Drugs and Crime

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OPIOID OVERDOSE

- National Institute of Health reported more than 80,000 people died of opioid OD in 2021(>71,000 involved Fentanyl)
  - 58,200 US troops died in Vietnam War between 1955 and 1975
  - 43,000 people died due to HIV/AIDS during that epidemic's peak in 1995
  - 2,996 people died in 9/11

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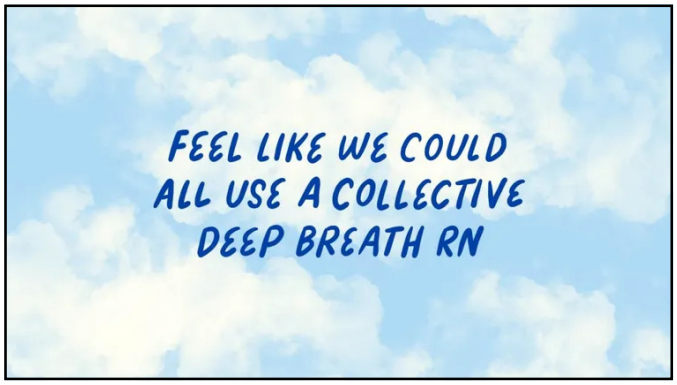

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MEDICATION ASSISTED TREATMENT

- Evidence-based practice that combines pharmacological interventions with substance abuse counseling and social support
- It is NOT
  - Replacing one addiction with another
  - Replacing one drug for another
  - Keeping someone sick in their addiction
  - Keeping someone from finding recovery

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MEDICATION ASSISTED TREATMENT

- Has been shown to
  - Improve survival
  - Increase retention in treatment
  - Decrease illicit opioid use
    - Relapse rates without MAT exceed 80%
  - Decrease hepatitis and HIV seroconversion
  - Decrease criminal activities
  - Increase employment
  - Improve birth outcomes for patients and babies

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MEDICATIONS FOR OPIOID USE DISORDER (MOUD)

- Methadone
- Buprenorphine (Subutex, Sublocade, Brixadi)
- Buprenorphine/Naloxone (Suboxone, Zubsolv, Bunavail)
- Naltrexone (Revia, Vivitrol)
- Naloxone (Narcan)

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METHADONE

- Methadone – gold standard for MOUD
  - Only available thru Opioid Treatment Program (OTP)
    - Federally regulated
      - Drug Enforcement Agency
      - Substance Abuse and Mental Health Services Administration
    - State regulated
      - Administrative Rules
      - State Opioid Treatment Authority (SOTA)
    - OTPs in 49 states (not Wyoming)

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METHADONE

- Minot, Fargo, Grand Forks and Bismarck have OTPs
  - Community Medical Services in Minot, Grand Forks and Fargo
  - Heartview Foundation in Bismarck
- State administrative rules require that the OTP be a licensed treatment facility

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METHADONE

- Full mu agonist
- Analgesic half life is shorter than the pharmacologic half life requiring multiple daily doses when used for pain
- Associated with QTc prolongation
- Higher doses are more effective at reducing heroin use – usually 80-120 mg daily

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METHADONE

- Good outcomes are contingent on length of treatment
  - Patients who stay in MAT with methadone for less than three months usually show little or no continued improvement.
  - 80% of people who leave methadone treatment and pursue no additional treatment will relapse

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HEARTVIEW OTP

Heartview Foundation Methadone Patient Outcomes
February 10, 2022

Baseline data (n=305):

- 13.7% (n=42) self-reported having ever tested positive for HIV
- 57% (n=174) self-reported having ever tested positive for Hepatitis C
- 65% (n=198) reported having ever experienced violence or trauma

	Baseline (n=305)	**6 Month Follow-up** (n=190)	**1-year Follow-Up** (n=122)
Employed	32.5% (99)	56% (106)	70.5% (86)
Mean days worked past month	5.88	11.61	12.2
Mean Monthly Income	$452	$886	$863
Fair or Poor mental health	47%	31%	24%
Arrested	90% (lifetime) Ave 10	8% (past month)	4% (past month)
Injected drugs	84% (lifetime)	13% (past month)	9% (past month
Overdose	61% (lifetime)	3.5% (past month)	>.8% (past month)
Treated ED for Alcohol or Drugs	47% (lifetime) Ave 4	4% (past month)	3% (past month)

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MOUD DURING PREGNANCY

- Methadone has been the standard of care for 40 years (Methadone Maintenance Therapy or MMT)
- May produce serious adverse effects
  - Methadone enters fetal circulation via the placenta
  - Fetus experiences withdrawal – Neonatal Abstinence Syndrome (NAS)- hypersensitivity, hyperirritability, tremors, vomiting, respiratory difficulties, poor sleep, low grade fevers
  - NAS may require hospitalization and treatment including morphine taper

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MOUD DURING PREGNANCY

- Enhances chances for a trouble-free pregnancy and a healthy baby compared to ongoing opiate use
  - Lowers risk of developing infectious diseases including HIV and HCV
  - Lowers risk of pregnancy complications including spontaneous abortion and miscarriages
  - Lowers risk of having a child with low birth weight and neurobehavioral problems

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BUPRENORPHINE

- Buprenorphine
  - Approved by FDA for treatment of opioid dependence in October 2002
  - X waiver no longer needed
  - Opioid partial agonist at mu receptor – able to suppress withdrawal symptoms and less likely to cause euphoric high or lead to death by overdose
  - Antagonist at the kappa opioid receptor
  - When administered with a full agonist, it will have an antagonistic effect on the receptors

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BUPRENOPHINE

- Lower risk of abuse, addiction and side effects
- Ceiling effect for respiratory depression enhances safety profile
- Administered sublingually, buccally, subcutaneously
- No evidence of organ damage
- Any provider with a DEA number can prescribe

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BUPRENORPHINE INJECTABLE

- Sublocade (Indivior Pharmaceuticals)
  - Buprenorphine only
  - Monthly injectable - 300 mg first two months then 100 mg monthly thereafter
  - Only available through specialty pharmacies
  - Physician must participate in Sublocade REMS
  - Must be stabilized on transmucosal buprenorphine for 7 days prior to injection

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BUPRENORPHINE INJECTABLE

- Brixadi (Braeburn Inc)
  - Buprenorphine only
  - Available in both weekly and monthly injectable
  - Weekly doses are 8 mg, 16 mg, 24 mg, 32 mg
  - Monthly doses are 64 mg, 96 mg, 128 mg
  - Requires participation in REMS

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MOUD

- Buprenorphine and Methadone both raise dopamine to normal levels of 40-60 ng/dL in the brain
- Patients with low dopamine levels have extremely low retention rates for treatment (less than 10%)
- Mortality rate for patients who pursue abstinence-based recovery is 10 times higher than individuals who receive MAT
- MAT combined with psychosocial treatment is superior to drug or psychosocial treatment alone

NATIONAL INSTITUTE ON DRUG ABUSE

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BENEFITS OF MOUD

- Opioid Use Disorder increases the risk of premature death 10-fold compared to the general population
  - 1 in 20 people who survive an opioid OD die within a year – 20% die within the first month
- MOUD is associated with decreased overall mortality by at least 50%

CA BRIDGE

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BENEFITS OF MOUD

- During the first 4 weeks of treatment, buprenorphine is associated with 90% lower mortality rates, Methadone is associated with 80% lower mortality rates and both are associated with 40% lower mortality rates after the first 4 weeks.
- Reduced morality rates associated with buprenorphine hold up when individuals stop receiving pharmacotherapy prescription
- The mean duration of a single treatment episode was 363 days for methadone as compared with 173 days for buprenorphine

RECOVERYANSWERS.ORG

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MOUD AND INCARCERATION

- 15-25% of incarcerated individuals in the US meet criteria for an OUD
- Courts have recently found that denial of MOUD to incarcerated people with an OUD likely violates the 8th Amendment's ban on cruel and unusual punishment and also likely amounts to disability discrimination under the Americans with Disabilities Act
- The risk of unnatural death (including OD, suicide and other preventable causes) was 87% lower for incarcerated people on MOUD compared to incarcerated people not on MOUD
- In the month after release from incarceration an individual is 56-129 times more likely to die of an OD
- MOUD reduces the risk of death from any cause by 85% and the risk of death from an OD by 75% in the first four weeks following release

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NALTREXONE

- Oral Naltrexone (Revia)
  - Opioid antagonist
  - Daily dose of 50-100 mg – hepatotoxicity was seen in obese patients taking 300 mg daily
  - If opioids are in the patient's system, Naltrexone will produce opioid withdrawal.
  - Compliance is an issue

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NALTREXONE

- IM Naltrexone (Vivitrol)
  - Intramuscular shot given every 28 days
  - 380 mg
  - Available through specialty pharmacies
  - Well tolerated
  - Patient must be through their withdrawal before administration

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NALOXONE

- Naloxone (Narcan)
  - Available in community-based programs since 1996
  - Safe, minimal side effects, inexpensive
  - Can be given IV, SQ, IM, IN, IO, PR
  - OTC (IN)

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MOUD

- MOUD is grossly underutilized
  - Less than 10% of patients seeking treatment for OUD receive MOUD
  - Only 23% of publicly funded treatment programs reported offering any FDA-approved medications

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TAKE HOME POINTS

- Addiction is a chronic disease of the brain
- Opioid overdoses are a national and local public health crisis
- Fentanyl is driving the opioid overdose epidemic
- Medications for Opioid Use Disorder is evidenced based and underutilized
- Opioid Treatment Programs are federally and state regulated

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TAKE HOME POINTS

- Methadone is currently available in Minot, Bismarck, Grand Forks and Fargo through Opioid Treatment Programs
  - Methadone is not reported on the PDMP (yet)
- Buprenorphine has a complex mechanism of action
- Buprenorphine is category C in pregnancy
- Naloxone is OTC

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QUESTIONS??

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