

- March 8, 2023
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Objectives

- Discuss how the limbic system and dopamine play a role in Substance Use Disorders (SUD)
- Recognize the benefits of Medications for Opioid Use Disorder (MOUD)
- Compare the different medications for Opioid Use Disorder

Outline

Addiction 101

How opioids are different

Mortality of opioids

Recovery

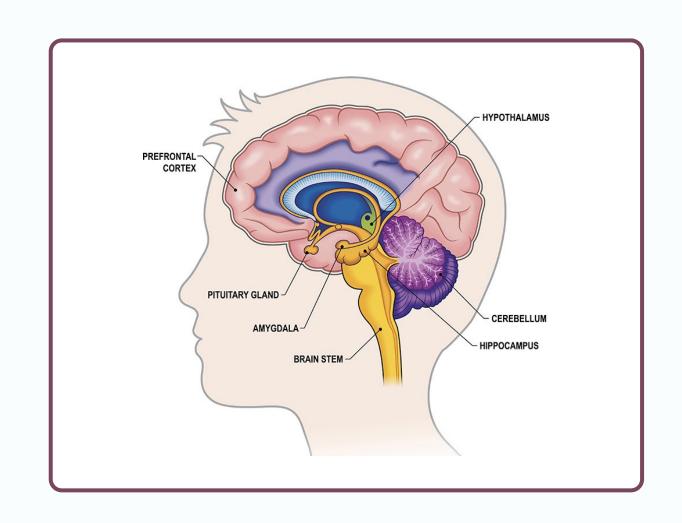
Medications for Opioid Use Disorder

Impact of MOUD

Questions??

Neurochemistry of Addiction

Limbic system contains the brain's reward circuitry







Limbic system

Responsible for our perception of emotions, both positive and negative



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



- 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

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



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

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

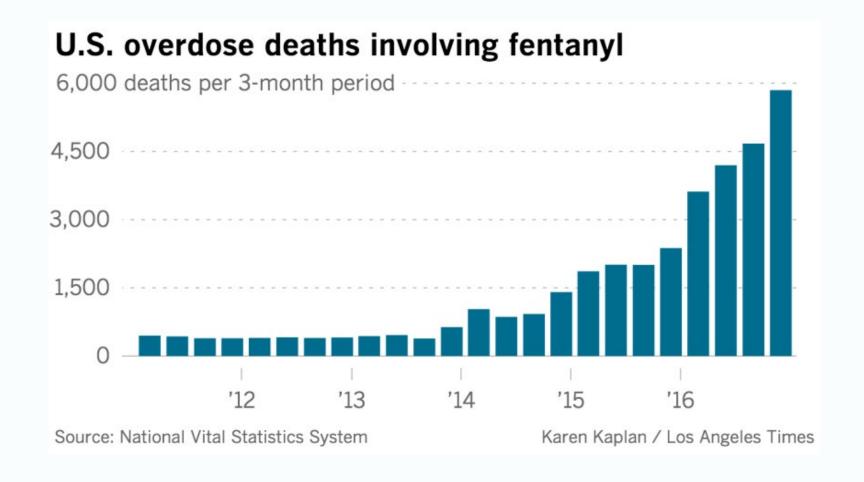
Three Waves of the Rise in Opioid Overdose Deaths 16 **Any Opioid** 15 14 Deaths per 100,000 population 13 **Other Synthetic Opioids** 12 (e.g., Tramadol or Fentanyl, 11 prescribed or illicitly manufactured) 10 Heroin **Commonly Prescribed Opioids** (Natural & Semi-Synthetic Opioids and Methadone) 2006 2015 2016 2017 2009 2018 2003 2004 2005 2007 2008 Wave 1: Rise in Wave 3: Rise in Synthetic Wave 2: Rise in Heroin **Prescription Opioid Opioid Overdose Deaths Overdose Deaths Overdose Deaths** Started in 2013 Started in 2010 Started in 1999 SOURCE: National Vital Statistics System Mortality File.

Opioid overdose

Opioid Overdose -Fentanyl

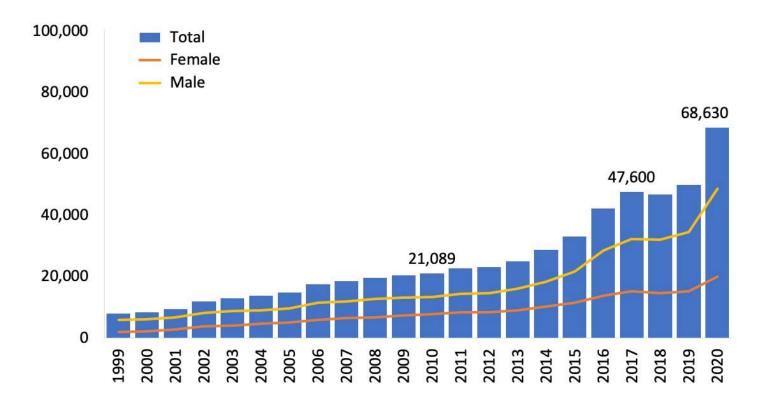
- 50 to 100 times more potent than morphine
- In March 2015, DEA issued a nationwide alert identifying fentanyl as a threat to public health and safety
- Between 2013 and 2019, overdose deaths involving synthetic opioids, such as illicitly manufactured fentanyl, increased by more than 11-fold
 - Fine, et al. Drug Overdose Mortality Among People Experiencing Homelessness, 2003-2018. JAMA Network. January 7, 2022.





Fentanyl overdose

Figure 3. National Overdose Deaths Involving Any Opioid, Number Among All Ages, by Gender, 1999-2020

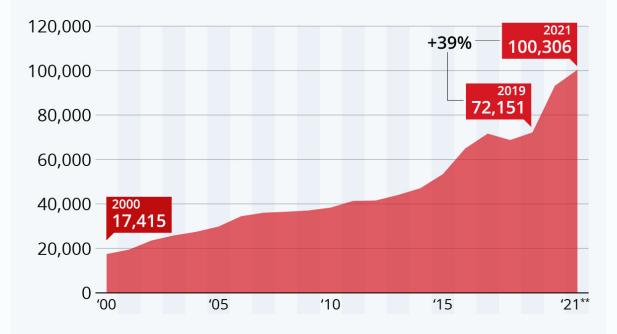


^{*}Among deaths with drug overdose as the underlying cause, the any opioid subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2), methadone (T40.3), other synthetic opioids (other than methadone) (T40.4), or heroin (T40.1). Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.

Opioid Overdose

U.S. Drug Overdose Deaths Spike Amid the Pandemic

Number of drug overdose deaths in the United States*



* Estimates for 2020 and 2021 are based on provisional data.

** 2021 estimate refers to 12-month period ending April 2021 Source: Centers for Disease Control and Prevention





COVID and Overdose

Opioid Overdose

70-80% of drug overdoses are related to opioids

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

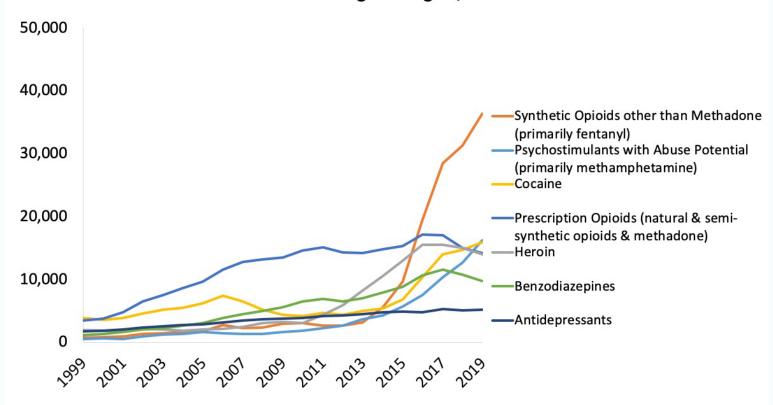
The US claims 27% of the worlds drug overdose deaths

United Nations Office on Drugs and Crime

Opioid Overdose

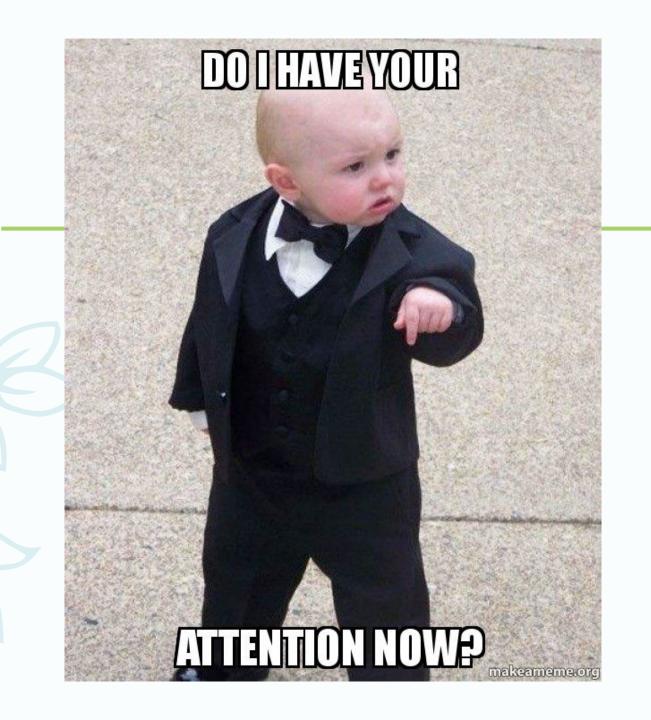
- National Institute of Health reported more than 80,000 people died of opioid OD in 2021 (>71,000 involved Fentanyl)
 - 58,200 US troops died in Vietnam War between 1955 and 1975
 - 43,000 people died due to HIV/AIDS during that epidemic's peak in 1995
 - 2,996 people died in 9/11

Figure 2. National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2019



^{*}Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2019 on CDC WONDER Online Database, released 12/2020.

It's not just Opioids!!

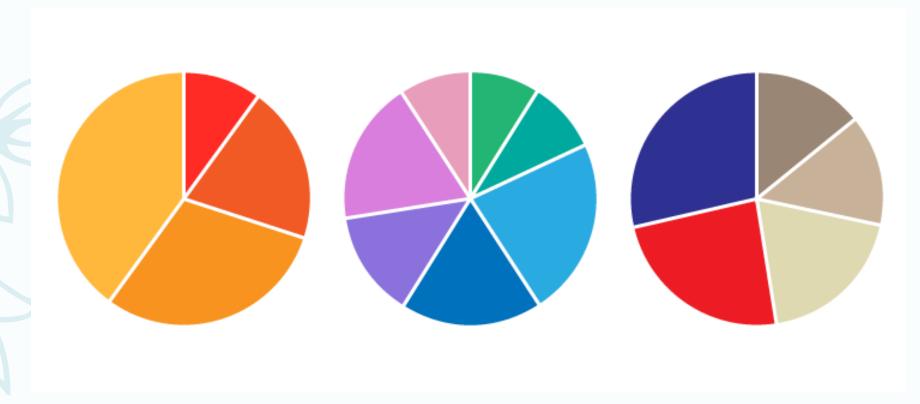




Recovery

 Recovery is a process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential.

If recovery were a pie, no two pies would be alike!



MAT/MOUD

Methadone – full agonist

Buprenorphine – partial agonist

Naltrexone – full antagonist

Naloxone – full antagonist



- Methadone
 - Long-acting synthetic opiate so can be dosed once daily
 - Higher doses are more effective at reducing opioid use.
 - Good outcomes are contingent on length of treatment

Methadone

- Methadone is only available through an Opioid Treatment Program (OTP)
- Wyoming is the only state that doesn't have an OTP
- Clients are required by federal law to see a licensed addiction professional monthly
- 8 urine drug screens are required annually
- Dosed daily out of an OTP take home doses are earned based on compliance with the OTP as well as 8 federal rules

Take-Home Methadone 8 Criteria

- 1. Absence of recent drug and alcohol abuse
- 2. Regular OTP attendance
- 3. Absence of behavioral problems at the OTP
- 4. Absence of recent criminal activity
- 5. Stable home environment and social relationships
- Acceptable length of time in comprehensive maintenance treatment
- 7. Assurance of safe storage of take-home medication
- 8. Determination that rehabilitative benefits of decreased OTP attendance outweigh the potential risk of diversion

Heartview Foundation 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

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	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)

- Subutex buprenorphine alone
- Suboxone combination of buprenorphine and naloxone (antagonist of opioid receptor)
 - Available in tablets or strips
- Zubsolv combination of buprenorphine and naloxone
 (theoretically tastes better than suboxone)
- Sublocade subcutaneous monthly injection

- Buprenorphine
 - Approved by FDA for treatment of opioid use disorder in October 2002
 - Opioid partial agonist able to suppress withdrawal symptoms and less likely to cause euphoric high or lead to death by overdose
 - Lower risk of abuse, addiction and side effects
 - Administered sublingually, intradermally, subcutaneously
 - No evidence of organ damage

- Buprenorphine
 - Heavily regulated by FDA
 - Only recently the rules changed so that any provider can prescribe and there are no limits on the number of patients

- 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 with OUD 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



- 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%

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

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

MOUD and Incarceration

- 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

Take home points

- Addiction is a chronic, relapsing disease of the brain
- Fentanyl is driving the overdose crisis
- Recovery is an individual process that may or may not include MOUD
- MOUD is more effective if combined with psychosocial supports
- MOUD is a lifesaving intervention
- MOUD is vital to our incarcerated population while incarcerated but also upon release



Questions??

