Addressing the Opioid Epidemic:  
A Primer on Opioid Addiction, Overdose Management, and Medications for Opioid Use Disorder
Learning Objectives

As a result of participating in this session, learners will:

• Understand the factors that led to the US opioid crisis
• Know the proper uses of naloxone for overdose reversal
• Recognize the signs of opioid use disorder
• Debunk commonly held myths and beliefs about treatment for opioid use disorder
• Understand the key role of MOUD (Medications for Opioid Use Disorder) in enhancing outcomes
The Opioid Epidemic

Opioid Use Disorder as a Disease

Overdose Management

Medications for Opioid Use Disorder
What are Opioid Drugs and what are their Effects?

- Bind to the opioid receptors; in the brain, spinal cord, and gastrointestinal tract
- Opioids are:
  - Opiate drugs (derived from opium from the poppy plant), e.g., morphine, heroin
  - Semi-synthetic and synthetic drugs (man made with chemicals), e.g., hydrocodone, oxycodone and fentanyl

- Used to treat pain, cough
- Side effects include: euphoria, sedation, nausea, constipation, itching
- Creates tolerance, the need to take higher doses for same effect, and craving or withdrawal symptoms in its absence
- Overdose danger: respiratory depression

Source: Samhsa.gov
Not a New Problem

Industrial Revolution
Commercialization of morphine

1861

Civil War
"Soldier's Disease"
Shift from Medical to Moral/Criminal

1900

Temperance Movement

Harrison Act
Illegal to prescribe opioids for people with addiction

1914

Vietnam War
Heroin

1972

Methadone Clinics
Legalization of maintenance clinics for opioid users

1990

Change in Prescribing
Increased opioid use for non cancer pain
Record high of 93,331 drug overdose deaths in 2020

More than 60% = synthetic opioids

During 2020, 28 states saw drug overdose deaths ↑ > 30%, amid the social isolation and economic stress of the pandemic

Social, Economic and Cultural Issues Contribute to Substance Use Patterns

Overlap in Regions with High Opioid Pain Medication Use and Unemployment (around 2010)

SOURCE: Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 2010
US Drug Overdoses 2015-2019

New Jersey

Second Highest Group of States with Drug Overdoses per 100k population

~ 11/day

~ 3000/ year

NJ OD Deaths Increasing in African Americans And 55 and Older
Still More than 10 Million People in US with Opioid Misuse
Vast Majority of those with Opioid Misuse = Prescription Pain Relievers

10.1 MILLION PEOPLE WITH OPIOID MISUSE (3.7% OF TOTAL POPULATION)

- 9.7 MILLION Rx Pain Reliever Misusers (96.6% of opioid misusers)
- 745,000 Heroin Users (7.4% of opioid misusers)
- 5.1 MILLION Rx Hydrocodone
- 3.2 MILLION Rx Oxycodone
- 269,000 Rx Fentanyl
- 404,000 Rx Pain Reliever Misusers and Heroin Users (4.0% of opioid misusers)

4X higher ~ 3 M

Modest decline overall for each opioid category except prescribed fentanyl (no change)

Rx = prescription.
Opioid misuse is defined as heroin use or prescription pain reliever misuse.

PAST YEAR, 2019 NSDUH, 12+

SAMHSA
Substance Abuse and Mental Health Services Administration
How did this epidemic happen?
ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients, Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

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“The risk of addiction is much less than 1%”
Porter & Jick, NEJM 1980

Cited more than 900 times
(Google Scholar)
Oxycodone vs Oxycontin

- **Oxycodone** (Roxycodone)
  - Immediate release
  - Acute pain
  - 4-6 hrs duration of action
  - Tabs (30mg), liquid

- **Oxycodone CR** (Oxycontin)
  - Controlled release
  - Chronic pain; already tolerant to opioids
  - 12 hrs duration of action (BID dosing)
  - Tablets (80 or 160 mg)
  - Long acting oxycodone; Delayed absorption “abuse-resistant”
Crush, sniff, and inject

Powerful high > eight hrs

Euphoria ~ heroin
Commercial Triumph, Public Health Tragedy

$1 Billion sales within 5 years of FDA approval
Marketed aggressively to PCPs for non-cancer pain
Purdue sued by 48 states for fueling the crisis
What is the most common way(s) that individuals who abuse prescription opioids obtain them?
Most get Prescription Opioids from Family/Friends

Sources Where Pain Relievers Were Obtained for Most Recent Misuse among People Who Misused Prescription Pain Relievers

- Prescriptions from More Than One Doctor (1.1%)
- Stole from Doctor's Office, Clinic, Hospital, or Pharmacy (0.8%)
- Prescription from One Doctor (35.7%)
- From Friend or Relative for Free (37.0%)
- Got through Prescription(s) or Stole from a Health Care Provider¹ (37.5%)
- 83.8% of the friends or relatives were prescribed the pain reliever by a single doctor
- Some Other Way (5.5%)
- Bought from Friend or Relative (9.2%)
- Bought from Drug Dealer or Other Stranger (6.2%)
- Took from Friend or Relative without Asking (4.6%)

9.7 Million People Aged 12 or Older Who Misused Prescription Pain Relievers in the Past Year
Overdose Death Rates Involving Opioids, by Type, United States, 2000-2017

- Wave 1: Prescription
- Wave 2: Heroin
- Wave 3: Fentanyl

Fentanyl = U.S. Cannot Control Supply

- Schedule II synthetic opioid
- 100 times stronger than morphine
- Well suited for the internet age
- Cheap, mass-produced
- Innovations in “cooking” from precursors
- Easy to ship (tiny amount)
- Encrypted online/ monetary services
- Counterfeit pills, cocaine supply
- Lack of international controls on precursors

Pardo et al., RAND Corp, 2019
Fentanyl Increasing in Heroin and Pills in NJ

15-20 types of fentanyl analogs by 2017

Fentanyl in 21% of pills seized by law enforcement

Suspected Heroin Submissions Containing Fentanyl (98% in 2022 in NJ)
• Step 1: Put a small amount (at least 10mg) of your drugs aside in a clean, dry container.
• Step 2: Add water to the container and mix together. Please note: For most drugs, you need ½ teaspoon of water. If you are testing methamphetamines, use 1 full teaspoon.4
• Step 3: Place the wavy end of the test strip down in the water and let it absorb for about 15 seconds.
• Step 4: Take the strip out of the water and place it on a flat surface for 2 to 5 minutes.
Changing Patterns

Xylazine

- Veterinary tranquilizer (Rompun)
- Not controlled substance
- Similar to antipsychotic (Chlorpromazine)
- Potentiates high- raises risk of OD
- Causes skin necrosis
- “tranq” or “tranq dope”

Fentanyl Sudden Death

- Worse hypoxia (lack oxygen)
- Hypothermia (low body temperature)
- Chest Wall Rigidity (no breathing)

Cocaine and Stimulant ODs

- Increasingly, especially in Northeast
The Opioid Epidemic

Opioid Use Disorder as a Disease

Overdose Management

Medications for Opioid Use Disorder
Substance Use Disorders = Chronic Medical Conditions

- Genetic susceptibility
- Chronic pathophysiologic/functional changes
- Risk factors influenced by choices
- Similar treatment goals & strategies
- Similar clinical outcomes
Addiction is a brain disease
Risk Factors for Opioid Use Disorder

• 10-20% of opioid users at risk (licit/illicit)

• Higher Risk
  – Co-occurring psychiatric (Depression / Attention deficit disorder)
  – Family history substance use
  – Prior substance use disorder
  – Men > women
  – Native Americans
  – Trauma exposure
DSM 5 Criteria for Substance Use Disorder

- **Loss of Control**
  - Larger amounts, longer time
  - Inability to cutback
  - More time spent, getting, using, recovering
  - Activities given up to use
  - Craving

- **Physiologic**
  - Tolerance
  - Withdrawal

- **Consequences**
  - Hazardous use
  - Social or interpersonal problems related to use
  - Neglected major roles to use
  - Continued use after significant problems

A substance use disorder is defined as having 2 or more of these symptoms in the past year.

Severity is related by the number of symptoms.

- Tolerance and withdrawal alone don’t necessarily imply a disorder.

2-3 = mild
4-5 = moderate
6+ = severe
Why Do People Use / Seek Drugs?
Theoretical Framework for Understanding Addiction and Motivation for Alcohol/Drug Seeking Over the Lifetime

Positive Reinforcement
- Pleasurable Experience

Negative Reinforcement
- Drug withdrawal
- Depression
- Abuse/ Trauma
- Neglect/Poverty
- Social Deprivation

Koob 2013
The Opioid Epidemic

Opioid Use Disorder as a Disease

Overdose Management

Medications for Opioid Use Disorder
Opioid Intoxication

• Euphoria (“high”)
• Constricted pupils
• Slowed breathing
• Low body temperature
• Vomiting
• Constipation
• Drowsiness
• Decreased awareness

Opioid Overdose

• Nonresponsive
• Pinpoint pupils
• No respiration
• Low blood pressure
• Slow heartbeat
• Coma
• Cyanotic
• Flaccid muscles
Opioid Overdose

• Cause of death = respiratory depression
• ~7 non-fatal OD for every fatal OD
• Risks
  – Higher Dose (>50 MME)
  – Recent abstinence (detox, jail)
  – Combination with sedatives (alcohol/ benzodiazepine)
  – Injection User
  – Medical: HIV, liver disease
  – Depression
  – People in household possess
OD Reversal

• Management: Opioid antagonist, naloxone (Narcan)
  – Call 911
  – Rescue treatment

• Intranasal
Naloxone Access

• Free trainings & kits in NJ
  
  Contact Kelley Hamilton, MPH, CHES
  #732-235-4341 khamilton@rwjms.rutgers.edu
  Rutgers Robert Wood Johnson Medical School

• Individuals can obtain at pharmacies without a prescription
  o Approx. $50-150
  o May be covered by insurance
  o Availability varies by pharmacy
Opioid Withdrawal

Not life threatening

- Anxiety
- Yawning
- Sweating
- Tearing
- Runny nose
- Pupils widen (dilate)
- “Goosebumps” / muscle twitching
- Nausea / vomiting
- Diarrhea and abdominal cramps
- Muscle / bone pain
The Opioid Epidemic

Opioid Use Disorder as a Disease

Overdose Management

Medications for Opioid Use Disorder
Recovery is Bio-Psycho-Social-Spiritual

- Biological
  - Withdrawal, craving, medical conditions
- Psychological
  - Depression, trauma, coping
- Social
  - Friends, environment, relationship
- Spiritual
  - Hope, purpose, altruism, forgiveness
MOUD Saves Lives

Medications for Opioid Use Disorder (MOUD)
- Buprenorphine (Suboxone)
- Methadone
- Extended Release Naltrexone (Vivitrol)

Increases Treatment Retention

Saves Lives (Reduces Overdose Deaths)
Rationale for MOUD

• Detoxification and maintenance
• Prevents or lessens withdrawal
• Reduces use (negative urine drug screen)
• More substance free days/weeks
• Reduces crime, infection, HIV
• Greater treatment retention (fewer dropouts) and reduced rate of death
Medication (MOUD) combined with psychosocial therapies and community-based recovery supports is the gold standard for treating opioid addiction.

- Counseling Only/Abstinence only model is Not recommended
- MOUD are substantially more effective than abstinence-based treatment

Only 13% of eligible patients with OUD receive treatment with MOUD

Krawczyk et al., 2022
Barriers to MOUD Access

• Personal
  • Stigma, Misinformation & Beliefs

• Provider Level
  • Stigma, Misinformation & Beliefs
  • Lack of Education

• Systems Level
  • Stigma, Misinformation & Beliefs
  • Lack of / Limited Insurance Coverage
Opioid Use Disorder - Variable Course over 42 Months

Most people with OUD have alternating periods of abstinence and use

Weiss, Drug Alcohol Dep, 2015
Treatment Retention and Decreased Illicit Opioid Use on MOUD

Buprenorphine promotes retention, and those who remain in treatment become more likely over time to abstain from other opioids.

Kakko et al, 2003
Soeffing et al., 2009

From PCSS Waiver Training, 2019.
https://pcssnow.org/medication-assisted-treatment/
Benefits of MOUD: Decreased Mortality

Death rates:

- Dupouy et al., 2017
- Evans et al., 2015
- Sordo et al., 2017

From PCSS Waiver Training, 2019.
https://pcssnow.org/medication-assisted-treatment/
Opioid Classification (mu receptor)

- **Full agonists:**
  - morphine
  - oxycodone

- **Partial agonist:**
  - buprenorphine

- **Antagonists:**
  - naloxone
  - naltrexone
Partial Agonist = partial opiate activity
No Respiratory depression
Limit on analgesia
Prevents opiate withdrawal
Blocks full agonist

Full Agonist = full opiate activity
Respiratory depression
Analgesia

Antagonist = no opiate activity
OD reversal
Complete blockade
Buprenorphine

- Partial mu agonist with ceiling (↓ risk)
  - Lower street value
  - Lower abuse potential
  - No respiratory depression
- Long duration of action
- Strong mu affinity, Displaces other opioids
- Start first dose in mild withdrawal
- Harder induction with fentanyl (low dose)

- Removal of X Waiver goes into effect June 21, 2023
  No patient limits
Buprenorphine

- Common side effects: constipation, nausea, headache, sweating, dry mouth
- FDA approved > 16
- Taken sublingual (under tongue)
- **Naloxone added** to buprenorphine (↓↓ diversion)
  - When taken orally no effect
  - If crushed, snorted or injected precipitates opioid withdrawal

<table>
<thead>
<tr>
<th>Suboxone (BUP:NAL)</th>
<th>Subutex (BUP)</th>
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<tr>
<td><img src="image1" alt="Suboxone" /></td>
<td><img src="image2" alt="Subutex" /></td>
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Methadone

- Mu receptor agonist
- 50-100mg daily
- Complicated medication interactions
- Lasts a long time in body
- Side effects: constipation, sweating, sexual dysfunction, sedation
- Decades of evidence
  - Reduces and eliminates use of opioids and cocaine
  - Reduces risk of HIV
  - Reduces needle sharing and needle use
  - Reduces crime and incarceration
- Used for opiate use disorder only in a licensed methadone treatment facility. More take home doses since COVID
Methadone Removes Cycle of Intoxication and Withdrawal

Impact of Short-Acting Heroin versus Long-Acting Methadone in Humans

- Functional State (Heroin)
  - "High"
  - "Straight"
  - "Sick"

- Functional State (Methadone)
  - "High"
  - "Straight"
  - "Sick"

Dole, Nysswander and Kreek, 1966
Extended Release Naltrexone (ER-NTX)

• Vivitrol
• FDA approved relapse prevention
• XR-NTX 380mg shot every 4 weeks
• Cannot start until 7 days opioid free
• Works: Greater abstinence, less craving and greater treatment retention vs placebo
• Side effects: Insomnia, injection site reaction, nausea, headache
• Can be expensive ($1500/shot)
Opiate Antagonists
Both = Strong affinity, displace full agonist

Overdose Reversal
Naloxone (Narcan) – shot, intranasal

Relapse Prevention / MOUD
Naltrexone – oral or long acting injection
Longer Duration of MOUD Treatment Reduces Overdose

- 6 months MOUD, 61% less risk of OD (vs stopping)
- Every extra 60 d of MOUD treatment received, reduced risk by another 10%
- Same effect across 11 states
- Medicaid data analysis ~300k
- **Longer treatment is better**

Relative hazard of OD in continued vs stopped MOUD

*Burns et al., Addiction 2022*
Risk for Relapse Following Buprenorphine Discontinuation is High

All Groups High Risk for

- Inpatient Services
- Emergency Services
- Overdose
- Prescription of opioid (full agonist)

6 months after discontinuation

Insurance was not a factor related to duration of treatment

Williams AR et al., AJP, 2020
<table>
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<th>Buprenorphine-Naloxone (Suboxone)</th>
<th>Methadone</th>
<th>ER-Naltrexone (Vivitrol)</th>
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<tbody>
<tr>
<td>Minimal overdose risk</td>
<td>Best retention (better for most severe)</td>
<td>No abuse potential</td>
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<tr>
<td>More access (office based); rural</td>
<td>Easy induction</td>
<td>Complete opioid blockade (pain relief; Less pleasure)</td>
</tr>
<tr>
<td>Better- elderly, complex medical</td>
<td>Most stigma</td>
<td>Induction requires 7 days opioid free</td>
</tr>
<tr>
<td>Less neonatal abstinence syndrome than methadone</td>
<td>Less available</td>
<td>Expensive</td>
</tr>
<tr>
<td>Some pain relief</td>
<td>Complex medical interactions, long half life; cardiac heart arrhythmias</td>
<td>Shots not available everywhere</td>
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MOUD is working if

• Stops using other opioids
• Experiences no craving for opioids
• Has no opiate withdrawal symptoms
• Has no side effects from medications
• Feels that life is no longer out of control
US Crisis: Signs of Progress

Opioid prescribing declining since 2011

Receipt of MOUD from treatment facilities and pharmacies increasing

Increase in naloxone dispensing from US pharmacies
Conclusions

• Several factors including over-prescribing led to the US Opioid Crisis
• Substance use Disorders are chronic brain diseases that warrant recognition and treatment
• Medications for Opioid Use Disorders are effective and underutilized
• 1-844-REACHNJ connects individuals to info and services
  reachnj.gov