OPIOIDS, ADDICTION, AND THE BRAIN

Presenters:

- Dr. Miriam Harris, Assistant Professor of Medicine and Addiction Medicine Fellow, Boston University School of Medicine; Department of Internal Medicine, Boston Medical Center
- Lisa Newman Polk, Esq. LCSW, lawyer and social worker
Opioids, Addiction, and the Brain

Miriam Harris, MD, MS
Assistant Professor & Addiction Medicine Fellow Boston University School of Medicine
Instructor of Medicine University of British Columbia
Miriam.harris@bmc.org

@miriamh_harris
Acknowledgements

• Some of these slides are adapted from the “Chief Resident Immersion Training (CRIT), Improving Clinical and Teaching Skills for Generalists. CRIT is funded by the National Institute on Drug Abuse (R25DA013582)

• Dr. Lipi Roy presentation and slide inspiration

• Dr. Alexander Walley

• Professor Leo Beletsky
Conflicts of interest

None to report
Objectives

1. Define addiction as a chronic medical disease & disease of the brain and how this relates to the criminal justice system
2. Understand how opioids work
3. Understand the pharmacokinetics and pharmacodynamics of opioid overdose
4. Define how social dynamics of drug use are related to overdose
5. Identify overdose prevention and response strategies
Outline

- Addiction – Definition, Neurobiology
- Opioid use disorder, and overdose prevention and response
- Intersection of addiction and criminal justice system
- Role of the Legal Community
- Resources
Substance Use Disorder

Substance Use Disorder a diagnostic term in DSM-5 defined as the recurrent use of alcohol or other drugs causing significant impairment, such as health problems, disability and failure to meet major responsibilities

It replaces the DSM-IV categories of substance abuse and dependence into a single disorder measured on a continuum from mild, moderate, or severe

American Psychiatric Association DSM-5 (2013)
Major Tannate of Addiction is “Use Despite Harm”

“We have this idea that if we just are cruel enough and mean enough and tough enough to people with addiction that they will suddenly wake up and stop. And that is not the case. Addiction is actually defined by the DSM and by NIDA as compulsive behavior that continues despite negative consequences. That's the definition of addiction. So therefore, if punishment, which is just another word for negative consequences, worked to fight addiction, addiction actually wouldn't exist.” – Maia Szalavitz
Development of substance use disorder involves multiple factors
NEGLIGENCE

TRAUMA

emotional abuse

SEXUAL ABUSE

physical abuse

Spiritual abuse

ANGER

RESENTMENT

LIES

SHAME

FEAR

PEARE

HOPELESSNESS

Despair

Anxiety

Resent

Lost

Lost

Innocence

Violent

Abuse
• Substances engage systems in the motivation pathways of the brain
Outline

- Addiction – Definition, Neurobiology
- Opioid use disorder and risk
- Intersection of addiction and criminal justice system
- Role of the Legal Community
- Resources
Opioid Use Disorder (OUD)
Opioid actions

• Orally < intranasally < intravenously used – IV peak 1 min

• Different opioids have different strengths (or binding affinity) and kinetics (length of action)

• Opioid receptors found throughout central nervous system

Jordi Camí, N Engl J Med 2003;349:975-86
Risk factors for fatal overdose

- **Drug**
  - Polysubstance use (alcohol, benzos)
  - Fentanyl

- **Set**
  - Physiological health + mind set

- **Setting**
  - Post detox/incarceration (130X)\(^1\)
  - Using alone: Isolation

1. Larochelle MR, Drug Alcohol Depend. 2019;204:107537
Polypharmacy Overdoses are the Norm, Not Exception

Figure 9. Opioid Overdose Deaths by Number of Drugs Involved, 2014

Harm Reduction

- Aim to lesson negative social/physical consequences associated with drug and/or alcohol use
Overdose Prevention and Response Strategies

• Do not use alone (use in networks is protective)
• Drug checking
• “Start low, go slow”
• Recognize overdose & administer naloxone if overdose occurs
• Seek professional help
• Medications reduce OD risk by > 50%¹,²
• Isolation and stigma kill

What actually prevents OD deaths in the era of synthetic opioids?

- 2016-2017 estimated 3030 (2900–3240) death events averted
- 1580 (1480–1740) averted by take-home naloxone
- 230 (160–350) by overdose prevention services
- 590 (510–720) were averted by opioid agonist therapy

Irvine MA. Addiction. 2019;114(9):1602-13
Natural History of Opioid Use Disorder

Alford DP. http://www.bumc.bu.edu/care/
Detoxification

Quickly weaned off opioids (usually with some form of pharmacotherapy)

Relapse rate (88%)\(^1\)
Detox w/out tx associated with increased risk of fatal overdose\(^2\)

Treatment

Started on pharmacotherapy + counseling/psychosocial supports

Relapse rate (40-75%)\(^3\)
Tx associated with 50% reduction in mortality\(^4\)

---


---
OAT Treatment Outcomes

**Patient outcomes**

- Increases treatment retention
- Decreases illicit opioid use
- Decreases mortality
- Decreasing harms associated with use

**Public Health**

- Decreases hepatitis and HIV seroconversion
- Decreases criminal activity
- Increases employment

Treatment Gaps Large & Overdose deaths Continue to Rise

Figure 2. National Drug Overdose Deaths Number Among All Ages, 1999-2017

Despite Consequences and Disease Burden, Treatment Gaps Remain Vast

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on COC WONDER Online Database, released December, 2018

SAMHSA (2018), NSDUH 2017
Outline

- Addiction – Definition, Epidemiology, Neurobiology
- Opioid use disorder
- Intersection of addiction and criminal justice system
- Role of the Legal Community
- Resources
Incarceration in the US
US leads the world in incarceration

Lifetime Likelihood of Imprisonment of U.S. Residents Born in 2001

- All Men: 1 in 9
- White Men: 1 in 17
- Black Men: 1 in 3
- Latino Men: 1 in 6

- All Women: 1 in 56
- White Women: 1 in 111
- Black Women: 1 in 18
- Latina Women: 1 in 45

International Rates of Incarceration per 100,000

- United States: 655
- El Salvador: 618
- Rwanda: 464
- Russia: 383
- Brazil: 333
- Australia: 172
- Spain: 127
- China: 118
- Canada: 114
- France: 104
- Germany: 77
- Denmark: 63
- Sweden: 59
- India: 33


https://www.sentencingproject.org/criminal-justice-facts/
Crime, Incarceration and SUDs are linked

• 65% percent of the United States prison population has an active SUD\(^1\)

• Additional 20% were under the influence of drugs or alcohol at the time of their crime\(^2\)

• Providing comprehensive substance use treatment to criminal offenders while incarcerated is effective\(^3\) & not treating associated with relapse and fatal overdose post release\(^4\)

• WHO 2005: Opioid agonist medications are on the list for essential medications that should be available for ALL prisoners with OUD

1. Abuse and America’s Prison Population, February 2010
4. Larochelle MR. Drug Alcohol Depend. 2019;204:107537
Outline

Addiction – Definition, Epidemiology, Neurobiology

Opioid use disorder

Intersection of addiction and criminal justice system

Role of the Legal Community

Resources
Sally Friedman

“This case should serve as a wake-up call for states and localities across the country. The common practice of denying MAT in correctional settings not only increases illicit drug use, overdose, and death, but is illegal,”
Review and “Pearls”

• Addiction is a **chronic relapsing and remitting medical disease**, a disease of the brain (**NOT a moral failing**) 

• **Punishing** people who use drugs is a **futile strategy to address addiction** 

• The criminalization of addiction perpetuates stigma, interrupts treatment, and **incarceration is linked with increased fatal overdose** 

• Overdose is driven by isolation and barriers to help-seeking 

• **Take home naloxone, harm reduction, and medications are standard of care and can prevent overdose** 

• Lawyers & the entire legal system play an integral role in enhancing addiction treatment
Objectives

1. Define addiction as a chronic medical disease & disease of the brain and how this relates to the criminal justice system
2. Understand how opioids work
3. Understand the pharmacokinetics and pharmacodynamics of opioid overdose
4. Define how social dynamics of drug use are related to overdose
5. Identify overdose prevention and response strategies
Resources

• American Society of Addiction Medicine (ASAM)
• Centers for Disease Control and Prevention (CDC)
• Center for Court Innovation
• Centre for Addiction and Mental Health (CAMH)
• Drug Policy Alliance (DPA)
• Harm Reduction Coalition (HRC)
• Legal Action Center (LAC)
• Legal Services Corporation (LSC)
• National Academy of Sciences, Engineering & Medicine (NASEM)
• National Center for State Courts – Judicial Opioid Task Force
• National Institute of Drug Abuse (NIDA)
• Open Society Foundations (OSF)
• Providers’ Clinical Support System (PCSS)*
• Substance Abuse and Mental Health Service Administration (SAMSHA)
• U.S. Surgeon General’s Report 2016
• Vera Institute of Justice
Additional Materials, References, and Slides
How did we get here?

• **Influence of Pharma**
  • Introduced OxyContin in 1995 - Funded >20,000 pain-related educational programs between 1996 and 2002
  • American Pain Society ("Pain is the 5th Vital Sign")

• **Good Intentions Gone Wrong**
  • Late ‘90s: MDs pressured to address “pain as 5th vital sign”
  • Limited education about pain mgmt. during med school
  • Almost no training on addiction

• **Deaths of despair**
  • deindustrialization
  • social safety net cuts
  • mass incarceration
Figure 42. People Aged 12 or Older with a Past Year Substance Use Disorder (SUD): 2018

- **Alcohol**: 14.8M
- **Illicit Drugs**: 8.1M
- **Marijuana**: 4.4M
- **Rx Pain Reliever Misuse**: 1.7M
- **Methamphetamine**: 1.1M
- **Cocaine**: 977,000
- **Rx Stimulant Misuse**: 561,000
- **Heroin**: 526,000

*Rx = prescription.*

Note: The estimated numbers of people with substance use disorders are not mutually exclusive because people could have use disorders for more than one substance.

SAMHSA. (2018). Results from the 2017 National Survey on Drug Use and Health
Why do people use drugs?

To feel good
- To have novel:
  - Feelings
  - Sensations
  - Experiences
  - AND
- To share them

To feel better
- To lessen:
  - Anxiety
  - Worries
  - Fears
  - Depression
  - Hopelessness
  - Withdrawal

Drawings courtesy of Vivian Felsen
The 4 C’s of Addiction:

- Impaired CONTROL over drug use
- COMPULSIVE use
- CONTINUED use despite harm
- CRAVINGS
Campaign by Partnership for a Drug-Free America launched in 1987

Breiter & Rosen, Ann N Y Acad Sci 1999
This is (actually) your brain on drugs

Breiter & Rosen, Ann N Y Acad Sci 1999
Drugs Elevate Dopamine More/Longer
- Desensitized reward circuits → dampened pleasure
- Conditioned responses & stress reactivity → cravings and negative emotions
- Weakened executive function decision making, inhibitory control & self regulation → relapse
## Heritability

<table>
<thead>
<tr>
<th>Trait</th>
<th>Heritability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type II DM</td>
<td>0.3&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Type I DM</td>
<td>0.7&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.3 - 0.5&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Peanut allergy</td>
<td>0.8&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cataract (age-related)</td>
<td>0.5&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>0.6&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>Nicotine</td>
<td>0.5 – 0.6&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cocaine and stimulants</td>
<td>0.4 – 0.8&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td>Heroin and opioids</td>
<td>0.5&lt;sup&gt;9&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cannabis</td>
<td>0.3 – 0.8&lt;sup&gt;10&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>1</sup>Poulsen et al., Diabetologia 1999  
<sup>2</sup>Kyvik et al., BMJ 1995  
<sup>3</sup>Corvol & Jeunemaitre, Endocrine Rev 1997  
<sup>4</sup>Sicherer et al., J Allergy Clin Immunol 2000  
<sup>5</sup>Hammond et al., N Engl J Med 2000  
<sup>6</sup>Goate & Edenberg, Curr Opin Genet Dev 1998  
<sup>7</sup>Sabol et al., Health Psych. 1999  
<sup>8</sup>-10Tsuang et al. 1996; Am J Med Genet. 1996
Adverse Childhood Experiences (ACE) and Illicit Drug Use

• Each ACE increased likelihood of early drug use by 2- to 4-fold
• > 5 ACEs were 7- to 10-fold more likely to report illicit drug use problems

Substance Use Disorder Treatment

Core Treatment
- Intake Assessment
- Treatment Plans
- Group/Individual Counseling
- Residential
- Medications
- Self-Help (AA/NA)
- Monitoring
- Case Management

Support Services
- Financial
- Medical
- Mental Health
- Vocational
- Educational
- Housing & Transportation
- Child Care
- Family
- AIDS / HIV Risks
- Legal

Etheridge, Hubbard, Anderson, Craddock, & Flynn, 1997 (PAB)
Mu Opioid Receptor Activation
Full Agonist, Partial Agonist, Antagonist
Medications for OUD (MOUD)

Goals
- Alleviate physical withdrawal
- Opioid blockade
- Alleviate drug craving
- Normalized deranged brain changes and physiology

Some options
- Naltrexone (opioid antagonist)
- Opioid Agonist Therapy (OAT)
  - Methadone (full opioid agonist)
  - Buprenorphine (partial opioid agonist)
Opioid Overdose Standardized Mortality Ratios Following Touchpoints
(Massachusetts, 2014, n=1,315 opioid-related deaths)

<table>
<thead>
<tr>
<th>Any opioid prescription TP</th>
<th>12.6 (11.1, 14.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dosage</td>
<td>15.1 (12.1, 18.0)</td>
</tr>
<tr>
<td>Benzodiazepine co-prescribing</td>
<td>18.0 (14.9, 21.1)</td>
</tr>
<tr>
<td>Multiple prescribers</td>
<td>10.5 (8.9, 12.1)</td>
</tr>
<tr>
<td>Multiple pharmacies</td>
<td>14.4 (11.8, 17.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Any critical encounter TP</th>
<th>68.4 (62.4, 74.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid detoxification</td>
<td>66.1 (58.0, 74.1)</td>
</tr>
<tr>
<td>Nonfatal opioid overdose</td>
<td>111 (96.7, 126)</td>
</tr>
<tr>
<td>Injection-related infection</td>
<td>54.1 (42.4, 65.8)</td>
</tr>
<tr>
<td>Release from incarceration</td>
<td>30.0 (24.8, 35.3)</td>
</tr>
</tbody>
</table>

Source: Table 1. Larochelle et al. Drug and Alcohol Dependence 2019
Treatment Prevents Opioid Related Death

**Adjusted* hazard for opioid-related mortality**
By monthly receipt of treatment in post-overdose period

- **Buprenorphine**
  - On Treatment: 0.3 (0.2-0.5)
  - Through Discontinuation: 0.6 (0.4-0.9)

- **Methadone**
  - On Treatment: 0.3 (0.2-0.6)
  - Through Discontinuation: 0.4 (0.2-0.7)

- **Naltrexone**
  - On Treatment: 0.5 (0.1-2.1)
  - Through Discontinuation: 1.4 (0.7-2.8)

* Adjusted for: age, sex, depression dx, anxiety dx, incarceration, detoxification, baseline opioid and benzodiazepine rx, and monthly post-overdose receipt of benzodiazepines, opioids, detoxification and short- and long-term residential treatment

Slide from Marc Larochelle
Comparison to current first line OUD Txs

<table>
<thead>
<tr>
<th>First author, year, country</th>
<th>Design</th>
<th>Sample N (% Male)</th>
<th>Medication</th>
<th>Retention outcomes</th>
<th>Retention rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gryczynski, 2013 USA</td>
<td>Prospective cohort, MET vs BUP; secondary analysis of two RCTs</td>
<td>African-Americans entering MAT; 478 (65.2)</td>
<td>MET, BUP</td>
<td>In MAT at 78.1% MET</td>
<td>57.7% BUP</td>
</tr>
<tr>
<td>Pinto, 2010 England</td>
<td>Prospective cohort, MET vs BUP; all received care coordination</td>
<td>Requesting MAT; 361 (75.0)</td>
<td>MET, BUP</td>
<td>In MAT at 69.6% MET</td>
<td>42.5% BUP</td>
</tr>
<tr>
<td>Bounes, 2013 France</td>
<td>Prospective cohort</td>
<td>Treatment settings; 151 (74.0)</td>
<td>MET, BUP</td>
<td>In MAT at 78.0% MET</td>
<td>26.0% BUP</td>
</tr>
<tr>
<td>Serpelloni, 2013 Italy</td>
<td>Retrospective cohort (65 publicly-funded addiction treatment sites)</td>
<td>Patients in MAT in 2010; 8,145 (84.2)</td>
<td>MET, BUP</td>
<td>Days of treatment: M=246.2 (SD=110.1), BUP: M=240.5 (SD=111.7)</td>
<td>85.0% MET for all, 74.3% Jitai for all, MET for BUP, 74.3% Jitai for BUP</td>
</tr>
<tr>
<td>Hao, 2013 China</td>
<td>Prospective cohort, MET vs Jitai tablets; all received psychosocial counseling</td>
<td>Completed detox; 386 (84.4)</td>
<td>MET, Jitai tablets</td>
<td>In MAT at 57.9% overall; retention associated with higher</td>
<td></td>
</tr>
<tr>
<td>Gryczynski, 2014 USA</td>
<td>Prospective cohort; secondary analysis of RCT studying counseling</td>
<td>African-Americans entering MAT; 297 (61.9)</td>
<td>BUP</td>
<td>In MAT at 57.9%</td>
<td></td>
</tr>
</tbody>
</table>

Addiction is treatable

Relapse is Common in Addiction and Other Complex Chronic Diseases

![Relapse Rates Are Similar for Addiction and Other Chronic Illnesses](image)

Source: McLellan et al., 2000

Treatment Works
Pre- and post-treatment self-reported changes among those in long-term residential TCs

![Treatment Works](image)

Myths about MOUD

**Myth**
- Substituting one addiction for another
- MOUD increases risk of overdose
- Medications will be diverted and create more addiction

**Facts**
- Does not create euphoria; relieves physiological opioid craving & normalizes body’s functioning that were impaired\(^1\)
- MOUD decreases risk of overdose\(^2\)
- Methadone that is diverted mostly from pain treatment not addiction\(^3\), diverted buprenorphine is used for self-treatment\(^4\)

---

1. SAMHSA, 2003
2. Larochelle MR. Drug Alcohol Depend. 2019;204:107537.
3. SAMHSA, 2010
Stigma – attribute, behavior or condition that is socially discrediting

• Major barrier to seeking help

• WHO - addiction is the #1 most stigmatized social problem (more than mental illness)

• Words matter

Stigmatizing/Punitive/Tough

• “Substance/drug abuse”
• “Substance/drug abuser”
• “War on Drugs”
• “Dirty urine”
• “Junkie,” “Addict,” “Cokehead,” “Lush,” “Package,” “Body”

Less Stigmatizing

• “Substance use disorder”
• “Person with substance use issues/disorder”
• “Urine positive for opioids”
Root Causes of Mass Incarceration

Since “tough on crime” and the beginning of the War on Drugs in 1980s the number of people incarcerated skyrocketed and today there are more people behind bars for a drug offense than the number of people who were in prison or jail for any crime in 1980.

Number of People in Prison and Jails for Drug Offenses, 1980 and 2017

- **1980**
  - State Prisons: 19,000
  - Federal Prisons: 4,700
  - Jails: 17,200

- **2017**
  - State Prisons: 190,100
  - Federal Prisons: 78,800
  - Jails: 184,000

[Source: The Sentencing Project](https://www.sentencingproject.org/criminal-justice-facts/)
Safe Supply and Heroin Compassion Clubs

Heroin Compassion Clubs
A cooperative model to reduce opioid overdose deaths & disrupt organized crime's role in fentanyl, money laundering & housing unaffordability

Safe supply: The debate around prescribing opioids to people who use drugs
Date: August 15, 2019    Author: Defne Izenberg & Seema Marwaha
Opioid Death rate 120x higher for individuals with histories of incarceration

Forced Detoxification Disrupts Care

- Methadone continuation (n=114) forced methadone dose taper (n=109)
- Outcomes
  1. Engagement w MMT after release
  2. Time to engagement w MMT
- 106 (96%) of methadone continuation vs 68 (78%) of the forced dose taper re-entered methadone treatment programs (P=0.001)
- 8% of methadone continuation vs 18% of forced dose taper reported opiate use at 1 month (p0.033)

Supervised Consumption Services (SCS)

What are SCS?
Supervised consumption services provide a safe, clean space for a person to use substances under the supervision of a health care professional and to engage in health and social services.

What is OAT?
Opioid agonist treatment suppresses the debilitating symptoms of cravings and withdrawal, better enabling a person to engage in therapy, counselling and support.

Benefits
Supervised consumption services save lives and improve community well-being.

- Less overdose deaths
- Less discarded needles
- Less public drug use
- Reduced sharing of needles
- Less HIV & Hepatitis C transmission
- Increased use of detox & treatment
- Increased access to services
Injectable opioid agonist treatment for opioid use disorder: a national clinical guideline

Nadia Fairbairn MD, Josey Ross MA, Michael Trew MD, Karine Meador MD, Jeff Turnbull MD, Scott MacDonald MD, Eugenia Oviedo-Joekes PhD, Bernard Le Foll MD, Marie-Ève Goyer MD, Michel Perreault PhD, Christy Sutherland MD


Legislation
References


