American Addiction: The Opioid Epidemic
Mark Garofoli, PharmD, MBA, BCGP

Live Activity Handout
2 slides per page
American Addiction: The Opioid Epidemic

ACTIVITY DESCRIPTION
Approximately every 15 minutes in our country, a person dies from prescription drug overdose, while a child is also born approximately every 30 minutes dependent upon opioids. How did we get to this point? Are we the only country in the world with this problem of epidemic proportion? How do we end this epidemic, or at least, how do we as healthcare professionals contribute to the progress of society in the right direction? In this presentation, we will discuss the history of just how we, as a country, ended up in the ‘Opioid Epidemic’ and we will review efforts being made by numerous healthcare professionals to improve the lives of many suffering from the consequences of it. Substance Use Disorder (DSM-V), more commonly referred to as addiction, directly and indirectly affects countless lives every day. Just what is one going through when experiencing addiction, and even further, how can we as humans, and healthcare professionals, better understand our patients in recovery? We will discuss the medication-assisted therapies of methadone and buprenorphine, and review naloxone, the opioid overdose reversal agent. We will also discuss appropriate over-the-counter (OTC) treatments for patients in recovery experiencing common medical symptoms. Unlike opioids, this presentation is sure to open your eyes and possibly even elevate your blood pressure and/or heart rate!

TARGET AUDIENCE
The target audience for this activity is pharmacists, pharmacy technicians, and nurses in hospital, community, and retail pharmacy settings.

LEARNING OBJECTIVES
After completing this activity, the pharmacist will be able to:
• Describe the pathophysiology behind substance use disorder, commonly referred to as addiction.
• Identify proper treatment selections, dosages, and key patient counseling points for the most common medication assisted therapies of methadone and buprenorphine.
• Identify appropriate Over-the-Counter (OTC) treatments of common medical conditions and scenarios for a patient in recovery.

After completing this activity, the pharmacy technician will be able to:
• Recognize what patients with substance use disorder are commonly experiencing in life.
• Identify the most common medication assisted therapies and how to assist a pharmacist in helping patients receiving those.
• Identify opportunities to assist patients with substance use disorder regarding requests for appropriate Over-the-Counter (OTC) treatments of common medical conditions.

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ABOUT THE AUTHOR
Dr. Mark Garofoli graduated from the University of Pittsburgh earning a PharmD in 2004, and later went on to earn an MBA from Strayer University in 2008. Mark is certified in Geriatric Care (BCGP), Immunizations, Medication Therapy Management (MTM), and Weapons of Mass Destruction (WMD) Response. He resides with his lovely wife, Dr. Gretchen Garofoli (also a FreeCE.com presenter), in Morgantown, WV where he is an assistant professor at the West Virginia University School of Pharmacy, Director of the Safe & Effective Management of Pain Program, and Coordinator of the West Virginia Expert Pain Management Panel, which developed the West Virginia Safe & Effective Management of Pain (SEMP) Guidelines available at the www.sempguidelines.org website.

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Learning Objectives

• Describe the pathophysiology behind substance use disorder, commonly referred to as addiction.

• Identify proper treatment selections, dosages, and key patient counseling points for the most common medication assisted therapies of methadone and buprenorphine.

• Identify appropriate Over-the-Counter (OTC) treatments of common medical conditions and scenarios for a patient in recovery.
Introduction

American Society of Addiction Medicine Statistics

• *Drug* overdose is the leading cause of accidental death in the US.
• In 2015, there were just over 33K *opioid* overdose deaths in the US (Rx & illicit).
• Various studies show between 75-80% of new heroin users having started out misusing legal prescription painkillers.

Examples of Addictive Entities

• Opiates & Opioids
• General Sedatives
  • Benzodiazepines, “muscle relaxers”, hypnotics, Barbiturates, & Ethanol
• Stimulants
  • Cocaine, cathinone, MDPV/Bath Salts, MDMA/Ecstasy, Meth/Amphetamine, Coffee, & Tobacco
• Entheogens
• Dissociants
• Inhalants & Anesthetics
• Anabolic/Androgenic Steroids
• Cannabinoids
• Process
  • Media, relationships, codependency, gambling, performance, compulsive spending, cults, food, sex, & rage/violence
Substance Use Disorder (Addiction)

Choice Theory

Disease/Condition Theory

Organ

Midbrain

Defect

Neurohormone Dysregulation

Symptoms

Craving & Loss of Control

Epigenetics
Abuse → Dependence → Addiction (Progression)

Dopamine

CRH (Corticotropin-Releasing Hormone)

Progression

Heroin
$10/Bag

Hydrocodone Combo Tablets
($5-10/Tab)

Rx to Street Addiction Cycle

Oxycodone Combo Products
($10-15/Tab)

Oxycodone IR Products
$1/mg
Opioid Timeline

1804: Morphine distilled from opium by German RPh apprentice Friedrich Serturner
1839: 1st Opium War (Britain & China)
1853: Hypodermic syringe invented (Alexander Wood, wife 1st to die from injected drug overdose)
1874: Alder Wright synthesized diacetylmorphine, & in 1898: Bayer® reproduced & named it Heroin
1914: U.S. Harrison Narcotic Tax Act
1990's: Increased marketing for and supply of prescription opioid products
2008: Drug overdoses surpass auto fatalities (US accidental death)
Last Decade: Multiple “Big Pharma” settlements involving opioid products
2015: West Virginia state supreme court case (“Prescribers/Dispensers Addiction Liability”)
2015: California doctor guilty of murder for deaths resulting from opioid prescribing habits
2016-17: Multiple drug wholesalers settlements with states

Opioid Supply

*International Narcotics Control Board Report 2014/2015
Most Recent CDC State-by-State Opioid Overdose Death Data

Opioid deaths in 2015
Age-adjusted death rates (per 100,000) for overdose deaths from all opioid drugs

Illicit Opioids

- Laced Heroin
  - Fentanyl, carfentanil, cocaine, clenbuterol
- Krokodil
  - Desomorphine, or di-hydro-desoxy-morphine
- Research Chemicals
  - W18 (Chicklets)
  - U-47700 (Pinks or Pinkies)
- Crunk Juice
  - A carbonated beverage mixed with a Narcotic & Nighttime Cough/Cold Medicine
- Oxy-Crisping
  - Abusing the Abuse-Deterrent OxyContin (the newer “OP” formulation)

Celebrity Opioid Overdoses
Prince, Michael Jackson, Whitney Houston, Philip Seymour Hoffman, Heath Ledger, Amy Winehouse, Anna Nicole Smith, John Belushi, Jim Morrison, Janis Joplin, Elvis Presley, Chris Farley, River Phoenix, & Russell Tyrone Jones (ODB)
As Opioid Sales Rise, Opioid Overdose Deaths Rise (Statistically Parallel)

![Graph showing the correlation between opioid sales and overdose deaths.](https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6043a4.htm)

**Opioid dose and overdose risk**

![Bar chart showing the adjusted hazard ratio for opioid overdose risk at different dose levels.](https://www.fda.gov)

*Opioid overdose defined as death, hospitalization, unconsciousness, or respiratory failure*


Opioid dose and risk of overdose death


Confronting the Opioid Epidemic

Prevention (within healthcare)
- Opioid & Pain Management Guidelines

Treatment
- Therapy & Medication Assisted Therapy (MAT)

Rescue
- Naloxone
Opioid Use Decision
1. Non-Pharm, Non-Opioid, then Opioid
2. Treatment Goals
3. Risk Assessments & Side Effects

Type/Amount/Time of Opioid
4. Immediate Release (IR) not Extended Release (ER)
5. MME > = 50/day: Use caution
   MME > = 90 avoid unless justified
4. Acute pain: Short duration
5. Re-evaluate 1 month, then every 3 months.

Risk/Harms of Opioid Use
8. Higher risk → naloxone education/supply
9. PDMP initially + every 1-3 months
10. Urine Drug Screening/Testing initially + annually
11. Avoid combining opioids & sedatives (i.e. benzodiazepines, etc.)
12. Opioid Use Disorder: Offer Medication Assisted Therapy (MAT)

Morphine Milligram Equivalent (MME)

<table>
<thead>
<tr>
<th>Medication</th>
<th>MME Factor</th>
<th>MME Relative Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol</td>
<td>0.1</td>
<td>300mg</td>
</tr>
<tr>
<td>Codeine</td>
<td>0.15</td>
<td>200mg</td>
</tr>
<tr>
<td>Tapentadol</td>
<td>0.4</td>
<td>75mg</td>
</tr>
<tr>
<td>MORPHINE</td>
<td>1</td>
<td>30mg</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>1</td>
<td>30mg</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>1.5</td>
<td>20mg</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>3</td>
<td>10mg</td>
</tr>
<tr>
<td>Heroin (SC diacetylmorphine)</td>
<td>3</td>
<td>10mg</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>4</td>
<td>7.5mg</td>
</tr>
<tr>
<td>Methadone 1-20, 21-40, 41-60, &gt;61 mg/day</td>
<td>4, 8, 10, 12</td>
<td>7.5, 3.75, 3, 2.5mg</td>
</tr>
<tr>
<td>Fentanyl Transdermal (TD) Patch</td>
<td>7.2 (Divide by Days)</td>
<td>12.5mg/hr Patch</td>
</tr>
<tr>
<td>Buprenorphine Patch</td>
<td>12.6 (Divided by Days)</td>
<td>15mcg/hr Patch</td>
</tr>
<tr>
<td>Buprenorphine SL or Buccal</td>
<td>0.03 (for mcg)</td>
<td>1000mcg</td>
</tr>
</tbody>
</table>
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Methadone
- Mu Agonist, SNRI, & NMDA Antagonist
- S-methadone affect K channels → QTc Intervals
- R-methadone is NMDA Antagonist → Analgesia
- Pharmacokinetics: CYP3A4/2B6/2C9/2C19/2D6, & PgP
  - Half-life: 8 to 150 Hours
    - Requires 3-5 days to reach steady state, thus dosage recommendations include:
      - Avoiding frequent/rapid dose adjustments
      - Initial Dosing Max 15mg/day, with increases of 10mg/week
        - Analgesic Effect wears off in hours, Resp Dep Risk lasts ~2 Days
Buprenorphine (+/- naloxone)

- Partial Mu agonist (and Kappa Antagonist)
- C-3 (Controlled Substance Class 3)
  - *DATA-2000 regarding Opioid Use Disorder (OUD)
- CYP3A4 Metabolism
- Ceiling Effect
  - Low dose provides pain relief followed by no feeling of euphoria
- *Very High Affinity for Mu Receptors compared to other Opioids

Buprenorphine ALONE

- **OUD +/- Pain**
  - Subutex® (SL Tablet, 2 mg and 8 mg)
  - Probuphine® (4 rods each containing 74.2 mg injected in upper arm for 6 months)
  - Buprenex® Solution for Injection, 0.3 mg/ml
  - Butrans® (Weekly Transdermal Patch, 5-20 mcg/hr)
  - Belbuca® (Buccal Film, 75-900 mcg)

- **Pain**
  - Suboxone® (SL Tablets)
    - Brand Name tablets are off market, but generic SL tablets are on market
  - Suboxone®/Zubsolv® (SL Films)
  - Bunavail® (Buccal Film, 2x Bioavailability)
    - # side to check, avoid food/liquids until dissolved

Buprenorphine & Naloxone (all for opioid-use-disorder: OUD)

- Suboxone® (SL Tablets)
  - Brand Name tablets are off market, but generic SL tablets are on market
OTCs for Patients in Recovery

<table>
<thead>
<tr>
<th>Chief Complaint</th>
<th>1st Line Medication</th>
<th>2nd Line Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal Congestion</td>
<td>Oxymetazoline</td>
<td>Pseudoephedrine</td>
</tr>
<tr>
<td>Chest Congestion</td>
<td>Guaifenesin</td>
<td></td>
</tr>
<tr>
<td>Seasonal Allergies (eyes/nose)</td>
<td>Loratadine</td>
<td>Fexofenadine</td>
</tr>
<tr>
<td>Pain</td>
<td>Acetaminophen</td>
<td>Ibuprofen/Naproxen</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Melatonin</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>Fiber Laxative</td>
<td>Bisacodyl</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Bismuth subsalicylate</td>
<td></td>
</tr>
</tbody>
</table>


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Naloxone & Naltrexone

Naloxone
- n-allyl derivative of oxymorphone
- Antagonist at mu, kappa, and delta opioid receptors
  - However, does NOT reverse tachycardia/hallucinations from delta receptors in spine
- FDA Approved Products: Nasal Spray, Injection, & Auto-Injector (Nasal Atomizer with syringe also available)

Naltrexone
- Better oral bioavailability & longer duration of action
- PO Tablet (Revia®)
  - FDA Approved in 1984 for Opioid Dependence
  - FDA Approved in 1995 for Alcoholism
- IM Once Monthly (Vivitrol®)
  - FDA Approved in 2006 for Alcoholism
  - FDA Approved in 2010 for Opioid Dependence

Opioid Adverse Reactions
- Sedation, Confusion, & Dizziness
- Constipation, Nausea, & Vomiting
- Itching
- Dry Mouth
- Neuralgia (Hyperalgesia)
- Myoclonus (muscle jerking)
- Bradycardia, Hypotension, & QT Prolongation
- Edema & Urine Retention
- Miosis (pupil constriction)
- Decreased estrogen or testosterone
- Central Sleep Apnea
- Respiration Depression

Naloxone Candidates
- Opioid Rotation
- >50MME
- Opoid-Use Disorder (OUD)
- Recent Overdose
- Personal/Family History of OUD
- Respiratory Condition
- Heavy Alcohol Use
- Concurrent Sedatives
- Rural
- Voluntary Request
Naloxone Administration

SAMHSA Guidelines (Substance Abuse & Mental Health Service Administration)

1. Check for signs of opioid overdose
   - Unconscious and unarousable, gargled/slow/absent breathing, pinpoint pupils, pale clammy skin, blue lips/nails, hypotension, & slow or no heart beat
2. Call EMS to access immediate medical attention*
3. Administer naloxone*
4. Rescue breathe if patient not breathing*
5. Stay with the person and monitor their response until emergency medical assistance arrives. After 2-5 minutes, repeat the naloxone dose if person is not awakening or breathing well enough (10 or more breaths per minute)

*Order depending on the source of guidance.

Help for Healthcare Professionals

Pharmacists Recovery Networks (PRN)
   - [http://www.usaprn.org/](http://www.usaprn.org/)

Healthcare Professional Substance-Use Disorder Treatment
   - Mandated or Voluntary
   - Typically ~5 Years of Monitoring
   - Drug Screenings & Tests
   - Group Therapy
   - Possible Suspended employment until PRN approves (~Setting)
General HELP

SAMHSA Helpline
  • 1-800-662-4357 (1-800-662-HELP)

Veteran’s Crisis Line
  • 1-800-273-8255, Option 1

Narcotics Anonymous (Personal)
  • 818-700-0700

Nar-Anon (Family/Friends)
  • 1-800-477-6291

What Next?

**APhA Institute on Alcoholism and Drug Dependencies**
  • Salt Lake City, Utah (Annually in June)

**APhA Generation Rx Projects**
  • Elementary/Middle School Presentations, Guest Speakers, Drug Take Back Days, Naloxone Training, etc.

**Non-Fiction**
  • Dreamland, Chasing the Scream, Narconomics, American Pain, etc.

**International Overdose Awareness Day** (August 31st)
  • Silver (Awareness Color)
Questions