Trends in Opioid Misuse and Abuse

Objectives

- Describe landscape and trends in opioid misuse and abuse
- Identify pharmacology and physiologic effects of opioids
- Discuss consequences of misuse, abuse, and addiction
- Discuss efforts designed to mitigate the risk of opioid use

Opioid Terminology

**Opiate**: Naturally occurring compounds derived from the opium plant (morphine, codeine)

**Opioid**: Broad term to describe all compounds, natural and synthetic, that work at opioid receptors

**Narcotic**: From the Greek word for stupor; considered a legal term and should not be used clinically to describe opioids
**History of Opium**

- **1700s**
  - Morphine discovered; produced by Merck

- **1803-1827**
  - Opium abuse high in China; Opium Wars

- **1840s-1856**
  - British export opium to China

- **1874-1900s**
  - Heroin synthesized from morphine by Bayer

- **1914**
  - Heroin banned by Harrison Narcotics Act

- **1900s**
  - Heroin is widely used in cough medicines and other products

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**Opioid Mechanism of Action and Effects**

- **Central nervous system depressants bind to opioid receptors**
- **Effects**
  - Reduced perception of pain
  - Drowsiness, mental confusion, nausea, constipation, slowed breathing
  - Potential for euphoria

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**Concerns Related to Opioid Therapy**

- **Misuse**
  - Use of medication for purposes other than as directed or indicated
- **Abuse**
  - Use of any illicit drug with intentional self-administration of medication for nonmedical purposes, such as altering consciousness
- **Addiction**
  - A primary, chronic, neurobiological disease with genetic, psychosocial & environmental factors influencing its development and manifestations; characterized by one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving
- **Diversion**
  - Intentional removal of medication from legitimate distribution and dispensing channels for illicit sale or distribution

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Illicit Drug Use (2017)

**Past Month Users, Age 12 or older (Millions)**

- Heroin: 0.5
- Inhaling: 0.6
- Methamphetamine: 0.8
- Hallucinogens: 1.4
- Cocaine: 2.2
- Psychotherapeutics: 6
- Marijuana: 28
- Any illicit drug: 30.5

Use of psychotherapeutics is greater than cocaine, hallucinogens & heroin combined

3.2 million nonmedical users of prescription pain relievers, second only to marijuana among specific abused substances

Past Year Nonmedical Use of Rx Opioids and Heroin (2014)

Past Year Nonmedical Use of Rx Opioids and Heroin (2017)

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Number (Millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocodone</td>
<td>6.3</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>3.7</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>245,000</td>
</tr>
<tr>
<td>Heroin</td>
<td>324,000</td>
</tr>
</tbody>
</table>

11.4 Million People with Opioid misuse (4.2% of Total Population)

11.5 Million People with Past Year Pain Reliever Misuse
- 542,000 People with Past Year Pain Reliever Misuse and Heroin use (4.9% of Opioid Misusers)
- 860,000 People with Past Year Heroin Use Only (7.8% of Opioid Misusers)

10.5 Million People with Pain Reliever Misuse Only
- 6.3 Million Rx Hydrocodone
- 3.7 Million Rx Oxycodone
- 245,000 Fentanyl

Heroin Use and Heroin Deaths

- Number of Heroin Users doubled
- Number of Heroin Deaths 7.7 times higher

Contributing Factors

- Prescription opioid regulation
- Demand
- Accessibility
- Purity
- Cost

Seizures of heroin up 81%

Four out of five recent heroin initiates previously abused prescription pain relievers

Heroin

- Chemical Name: Diacetylmorphine
- Schedule I in US
- Typically injected but may also be snorted or smoked
- Street Names:
  - Smack
  - Dope
  - Junk
  - Mud
  - Skag
  - Brown Sugar
  - Brown
  - "H"
  - Big H
  - Horse
  - Charley
  - China White
  - Boy
  - Harry
  - Mr. Brownstone
  - Dr. Feelgood
- Speedball = heroin + cocaine
Effects of Heroin

- **Acute Effects:** Euphoria, skin flushing, dry mouth, heavy extremities, impaired mental function, slowed breathing
- **Long-Term Effects:** Collapsed veins, abscesses, infections, liver disease, lung complications


Onset

- IV: 7-8 seconds
- IM: 5-6 minutes
- Smoked or Snorted: 10-15 minutes

Who Is Using?

- Middle Age Adults (45-54 yrs old)
- Males > females
- Non-Hispanic Whites

- Young Adults (20-34 yrs old)

Public Health Consequences

- HIV, Hepatitis B and C and other blood borne pathogens
- Increased utilization of healthcare, lost productivity and crime
- Treatment center admissions
- Overdose
- Death
While prescription fentanyl rates have fallen, the drug supply of illicitly manufactured fentanyl identified by law enforcement has risen sharply.
Fentanyl and Fentanyl Analogues

- Fentanyl: 50-100 times more potent than morphine
- Fentanyl Analogues (e.g. carfentanil, furanyl fentanyl, acetyl fentanyl): up to 10,000 times more potent than morphine
- Street Names: Apache, China White, Dance Fever, Goodfella, Jackpot, Murder 8, TNT, and Tango and CashChina


U-47700

- Schedule I synthetic opioid
- 7.5 times the potency of morphine
- Responsible for at least 80 deaths in 2016
- Street names: U4, Pink, or Pinky


Prevention and Treatment Strategies

- Responsible opioid prescribing
- Substance use disorder treatment access and research
- Overdose prevention measures
- Education and social awareness
Illicit Drug Use (2017)
Past Month Users, Age 12 or older (Millions)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin</td>
<td>0.5</td>
</tr>
<tr>
<td>Inhalants</td>
<td>0.6</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>0.8</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td>1.4</td>
</tr>
<tr>
<td>Cocaine</td>
<td>2.2</td>
</tr>
<tr>
<td>Psychotherapeutics</td>
<td>6</td>
</tr>
<tr>
<td>Marijuana</td>
<td>20</td>
</tr>
<tr>
<td>Any Illicit drug</td>
<td>30.5</td>
</tr>
</tbody>
</table>

Use of psychotherapeutics is greater than cocaine, hallucinogens & heroin combined

3.2 million nonmedical users of prescription pain relievers, second only to marijuana among specific abused substances

Nonmedical Opioid Misuse Source¹

53.1% of People who Misused Pain Relievers Obtained them from a Friend or Relative

Drug Dealer/ Stranger 5.7%
One Doctor...
More than One Doctor...
Bought from Friend/Relative...
Stole from Doctor’s Office...

Nonmedical Opioid Misuse: Breakdown of Source

Source Where Friend/Relative Obtained

Responsible Opioid Prescribing

Risk Evaluation/Stratification
- Patient history & physical including assessment for risk factors for addiction
  - Stratify into low, medium, or high risk

Manage & Mitigate Risk
- Informed Consent
- Treatment Agreement
- Goal Setting & Medication Trials

Consultations, Referrals, Exit Strategy
- Objective
- Informed Consent
- Treatment Agreement
- Goal Setting & Medication Trials

Monitoring
- Patient Exam
- Aberrant Behaviors
- PDMP, UDT, Pill Counts
- Clinical Documentation

Goals:
- Manage & Mitigate Risk
- Informed Consent
- Treatment Agreement
- Goal Setting & Medication Trials

Aberrant Behaviors
- UDT, PDMP, Pill Counts
- Clinical Documentation

Evolution of Urine Drug Testing

FORENSIC Model of UDT
- Workplace drug testing
- Focus on illicit use
- Qualitative
- Immunoassay
- Confirm only positive results

CLINICAL Model of UDT
- Monitoring of prescribed medications and/or substance use
- Therapeutic incentivizing
- Quantitative
- Laboratory-based testing
Clinical Settings

Urine Drug Testing is utilized in numerous settings:
- Pain Management/Chronic Opioid Therapy (COT)
- Substance Use Treatment
  - Office-Based Treatment
  - Addiction Treatment Facilities
- Primary Care
- Psychiatry
- Obstetrics

Urine Drug Testing (UDT) Rationale

UDT helps clinicians to:
- Monitor and support decisions about medication therapy, particularly controlled substances
- Identify recent use of prescription medications, non-prescribed medications, and illicit substances
- Detect medications that may result in drug-drug interactions
- Advocate for and communicate with patients about individual treatment plans
- Identify possible illicit drug or medication abuse, misuse, or diversion

Types of UDT

<table>
<thead>
<tr>
<th>Presumptive Immunoassay Screen</th>
<th>Definitive Mass Spectrometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-office Point-of-Care (POC), or Laboratory Qualitative</td>
<td>Laboratory Quantitative (GC-MS or LC-MS/MS)</td>
</tr>
<tr>
<td>Minutes (POC) or days (Lab)</td>
<td>Hours to days</td>
</tr>
<tr>
<td>Drug classes and some select meds/substances</td>
<td>Specific medications, substances, and metabolites</td>
</tr>
<tr>
<td>Guidance for preliminary treatment decisions</td>
<td>Definitive quantitative results</td>
</tr>
<tr>
<td>Higher cutoff levels and cross-reactivity common; more false positives and false negatives</td>
<td>Lower cutoff levels. False positive and false negative results are rare</td>
</tr>
</tbody>
</table>

The clinician must choose testing method based on the needs dictated by the patient's history, presentation, community factors and treatment plan goals. The clinician's rationale for test and the analytes ordered must be documented in the patient's medical record.
**False Negative vs. False Positive**

*Most Common with Presumptive/Immunoassay-based Tests*

**False Negative:** The test fails to detect the presence of the drug or metabolites.

- Primary Reasons Include:
  - Higher cutoffs compared to mass spec.
  - Unable to effectively identify some substances (e.g., lorazepam)

- Potential Adverse Impact on Patient:
  - Undetected illicit use
  - Accused of drug diversion
  - Not receive ongoing meds
  - Drug interactions

**False Positive:** The test incorrectly detects the presence of the drug when none is present.

- Primary Reason:
  - Cross-reactivity

- Potential Adverse Impact on Patient:
  - Discharged from practice
  - Not having access to care
  - Legal decisions – lose family, return to jail

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**Addressing Unexpected Results**

Providers should not always interpret unexpected results as abuse, misuse, or diversion

Numerous factors may contribute to unexpected UDT results:
- Patient medication use
- Time of the last dose
- Undiscovered or unknown over-the-counter or prescription medication use
- Type of testing
- Pharmacogenetics
- Drug-drug interactions

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**Opioid Metabolic Pathways**

- **Codeine** → **M-6-glucuronide** → **M-3-glucuronide**
- **Hydromorphone** → **M-6-glucuronide** → **M-3-glucuronide**
- **Oxycodone** → **M-6-glucuronide** → **M-3-glucuronide**
- **Fentanyl** → **M-6-glucuronide** → **M-3-glucuronide**

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Heroin Metabolism

Heroin Metabolism

Cmax
Tmax

Concentration
Time

“The Abuse Quotient” = Cmax/Tmax
Cmax: maximum concentration
Tmax: time to max concentration

Meet “Michael”

• 28-year-old male, history of heroin use disorder and hepatitis C
• Has received office-based treatment for opioid dependence from Dr. Gibbons for 6 months in addition to counseling
• Current medications:
  o Buprenorphine/naloxone (Suboxone®)
  o Ledipasvir-sofosbuvir (Harvoni®)

Substance Use Monitoring

Urine Drug Testing

• American Society of Addiction Medicine (ASAM) recommends urine drug testing as a key diagnostic and therapeutic tool, useful for patient care and in monitoring the ongoing status of a person treated for addiction
• “Drug use during treatment must be monitored continuously”
  ▪ Awareness of monitoring can be an incentive
  ▪ Monitoring may identify an early indication of a relapse and need to adjust the treatment plan
• Each test should be based on individual patient situation in support of the treatment plan
Case: “Michael”

Per published guidelines, Michael’s physician utilizes urine drug testing to monitor prescribed drug therapy, as well as monitor for illicit and non-prescribed drug use.

In-Office Test Result

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>Negative</td>
</tr>
<tr>
<td>Opiate</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Based on these results, does it appear Michael is taking his medication? What might the opiate positive mean on a urine drug screen?

LC-MS/MS Laboratory Test Results

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Creatinine Normalized Results (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>Negative</td>
<td>0</td>
</tr>
<tr>
<td>Norbuprenorphine</td>
<td>Positive</td>
<td>86</td>
</tr>
<tr>
<td>Naloxone</td>
<td>Negative</td>
<td>0</td>
</tr>
<tr>
<td>6-MAM</td>
<td>Positive</td>
<td>183</td>
</tr>
<tr>
<td>Codeine</td>
<td>Positive</td>
<td>234</td>
</tr>
<tr>
<td>Morphine</td>
<td>Positive</td>
<td>8,536</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Positive</td>
<td>4</td>
</tr>
<tr>
<td>Norfentanyl</td>
<td>Positive</td>
<td>26</td>
</tr>
</tbody>
</table>

How might these test results impact Michael’s treatment?

Number of Treatment Facility Admissions by Primary Substance

<table>
<thead>
<tr>
<th>Year</th>
<th>Heroin</th>
<th>Opiate</th>
<th>Heroin/Opiate</th>
<th>Non-Opiate Opiate</th>
<th>Cocaine</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>207,716</td>
<td>242,463</td>
<td>129,764</td>
<td>126,173</td>
<td>2,036</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>252,290</td>
<td>265,547</td>
<td>131,578</td>
<td>158,210</td>
<td>178,506</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>375,574</td>
<td>317,235</td>
<td>117,254</td>
<td>174,951</td>
<td>107,901</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>367,465</td>
<td>341,304</td>
<td>117,742</td>
<td>178,975</td>
<td>107,845</td>
<td></td>
</tr>
</tbody>
</table>

Illicit Drug and Alcohol Use Disorder Treatment

- In 2017, 20.7 million persons needed treatment for an illicit drug or alcohol use problem (7.6% of the population aged 12 or older)¹
- Of these, only 2.5 million received treatment at a specialty facility (12.2%)

Addiction as a Chronic Disease

<table>
<thead>
<tr>
<th>Addiction</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-60% Genetic</td>
<td>25-50% Genetic</td>
</tr>
<tr>
<td>40-60% Relapse</td>
<td>50-70% Relapse</td>
</tr>
<tr>
<td>Initial choices: alcohol/drug</td>
<td>Initial choices: food, activity</td>
</tr>
<tr>
<td>Potential permanent</td>
<td>Potential permanent</td>
</tr>
<tr>
<td>physiological changes</td>
<td>physiological changes</td>
</tr>
<tr>
<td>Abstinence and medications</td>
<td>Lifestyle changes and medications</td>
</tr>
<tr>
<td>do not reverse disease</td>
<td>do not reverse disease</td>
</tr>
<tr>
<td>&lt; 50% adhere to drug</td>
<td>&lt; 40% adhere to medication, 30% adhere to lifestyle changes</td>
</tr>
<tr>
<td>abstinence 1 year post-treatment</td>
<td></td>
</tr>
</tbody>
</table>

Substance Use Disorder Treatments

- NIDA Principles of Drug Addiction Treatment
  - Behavioral/ Psychosocial
    - In- or out-patient
  - Pharmacological
    - Methadone, Suboxone, AA/NA/Naltrexone, Others in research
Education

- Centers for Disease Control and Prevention – www.cdc.gov
- Drug Enforcement Administration – www.justthinktwice.com
- Partnership for Drug Free Kids – www.drugfree.org

Medical Necessity

Criteria to establish medical necessity must be based on patient-specific elements identified during the clinical assessment and documented in the patient’s medical record by the provider.

Documenting Medical Necessity

- Orders must be individualized
- Tests ordered and reasons for testing must be documented in the patient’s medical record
- Risk assessment and stage of treatment should match testing frequency

Documenting How the Test Results Were Used

- Review of results and use in the treatment plan

Summary

- While drug-poisoning deaths involving opioid analgesics has leveled in recent years, the rate for deaths involving heroin is on the rise
- Heroin is widely available and has become increasingly pure while prices drop
- Young adults have the highest rates of heroin overdose deaths and treatment center admissions
- A combination of strategies are being employed to address opioid misuse, abuse, and diversion
- Understanding the benefits and limitations of the various types of UDT is critical for providers to appropriately apply the results