OPIOIDS
A Comprehensive Look
TOPICS OF DISCUSSION

- Definitions
- Opium Poppy
- History of Opium
- Effects of Opioids
- Opiates vs. Opioids
- Rx Opioids and Heroin Abuse Trends in US
- Addiction Treatment
- New Drug Trends
- Testing for Opiates/Opioids
DEFINITIONS

- **Opiates** – alkaloids derived directly from the poppy plant

- **Opioids** – broader class of drugs that are capable of either producing opium like effects or binding to opioid receptors

- **Semisynthetic opioid** – created by the chemical modification of an opiate

- **Synthetic opioid** – a chemical compound not derived from an opiate, that is capable of binding to an opioid receptor and producing opioid effects clinically
POPPY PLANT
POPPY PLANT

- **Papaver somniferum**
  - Annual herb growing to be about 100 cm
  - Origin is possibly the Eastern Mediterranean, extensive cultivation and introduction of the species throughout Europe has obscured its origins

- **Opium**
  - The dried latex produced by the seed pods
  - Contains a class of naturally occurring alkaloids known as opiates
    - Morphine
    - Thebaine
    - Codeine
    - Papaverine
    - Noscapine
    - Oripavine
HISTORY OF OPIUM
**EARLY HISTORY**

<table>
<thead>
<tr>
<th>3400 B.C.</th>
<th>1300 B.C.</th>
<th>400 A.D</th>
<th>1300’s</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Earliest Reference</strong></td>
<td><strong>Passing It On</strong></td>
<td><strong>China Bound</strong></td>
<td><strong>Taboo</strong></td>
</tr>
<tr>
<td>• Cultivated in Mesopotamia</td>
<td>• Sumerians</td>
<td>• Introduced in China by Arab traders</td>
<td>• Disappears from European historical records for 200 years</td>
</tr>
<tr>
<td>• Sumerians called it <em>Hul Gil</em>, “joy plant”</td>
<td>• Assyrians</td>
<td></td>
<td>• During Inquisition it was taboo</td>
</tr>
<tr>
<td></td>
<td>• Babylonians</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Egyptians</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Enter the trade routes to Europe</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The British East India Company assumes control of Bengal and Bihar, opium-growing districts of India. British shipping dominates the opium trade out of Calcutta to China.

China's emperor, Kia King, bans opium completely, making trade and poppy cultivation illegal.

The Chinese emperor, Yung Cheng, issues an edict prohibiting the smoking of opium and its domestic sale, except under license for use as medicine.

The British East India Company establishes a monopoly on the opium trade. All poppy growers in India were forbidden to sell opium to competitor trading companies.

The British East India Company's import of opium to China reaches a staggering two thousand chests of opium per year.

The import of opium into China becomes a contraband trade. Silver was smuggled out to pay for smuggling opium in.

Friedrich Serturner of Germany discovers the active ingredient of opium by dissolving it in acid then neutralizing it with ammonia. The result: morphine. Physicians believe that opium had finally been perfected and tamed. Morphine is lauded as "God's own medicine" for its reliability, long-lasting effects and safety.

The Dutch export shipments of Indian opium to China and the islands of Southeast Asia; the Dutch introduce the practice of smoking opium in a tobacco pipe to the Chinese.

The Dutch export shipments of Indian opium to China and the islands of Southeast Asia; the Dutch introduce the practice of smoking opium in a tobacco pipe to the Chinese.

The Dutch export shipments of Indian opium to China and the islands of Southeast Asia; the Dutch introduce the practice of smoking opium in a tobacco pipe to the Chinese.
OPIUM WARS

• China’s attempt to suppress the opium trade

• Stop illegal exporting of opium into China
  ▪ Widespread addiction
  ▪ Social and economic disruption

• Two Wars
  ▪ 1839-42: China and Britain
  ▪ 1856-60: Britain and France against China

• China lost both wars
OPIUM DENS

- Site to buy and sell opium
- Chinese immigrants came to US in mid-1800s to work for the railroads and Gold Rush
- They brought the habit with them and opium dens began opening up across the country

https://www.deamuseum.org/ccp/opium/history.html
LAWS

• **1890:** U.S. Congress, in its earliest law-enforcement legislation on narcotics, imposes a tax on opium and morphine.

• **1905:** U.S. Congress bans opium.

• **1909:** The first federal drug prohibition passes in the U.S. outlawing the importation of opium.

• **1914:** The passage of Harrison Narcotics Act which aims to curb drug abuse and addiction. It requires doctors, pharmacists and others who prescribed narcotics to register and pay a tax.
CONTROLLED SUBSTANCES ACT

• 1970 – part of the Comprehensive Drug Abuse Prevention and Control Act

• Schedule I
  ▪ The drug or other substance has a high potential for abuse.
  ▪ The drug or other substance has no currently accepted medical use in treatment in the United States.
  ▪ There is a lack of accepted safety for use of the drug or other substance under medical supervision.

• Schedule II
  ▪ The drug or other substance has a high potential for abuse.
  ▪ The drug or other substance has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions.
  ▪ Abuse of the drug or other substances may lead to severe psychological or physical dependence.
DRUG SCHEDULING

• Schedule III
  ▪ The drug or other substance has a potential for abuse less than the drugs or other substances in schedules I and II.
  ▪ The drug or other substance has a currently accepted medical use in treatment in the United States.
  ▪ Abuse of the drug or other substance may lead to moderate or low physical dependence or high psychological dependence.

• Schedule IV
  ▪ The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule III.
  ▪ The drug or other substance has a currently accepted medical use in treatment in the United States.
  ▪ Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule III.
DRUG SCHEDULING

• Schedule V
  - The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule IV.
  - The drug or other substance has a currently accepted medical use in treatment in the United States.
  - Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule IV.
EFFECTS OF OPIOIDS
Opioid Receptors

**μ (mu) receptor:** produce central depression – analgesia, respiratory depression, miosis, euphoria, reduced gastrointestinal motility, hypothermia, bradycardia, physical tolerance and dependence

**Κ (kappa) receptor:** produce spinal analgesia, sedation, miosis, diuresis, mild respiratory depression and low addiction liability

**δ (delta) receptor:** spinal analgesia, dysphoria, delusions, hallucinations, and respiratory and vasomotor stimulation
AGONIST AND ANTAGONIST

• Opioids are classified into three groups

  ▪ **Full agonist**: compounds that have an affinity for opioid receptors of a certain type

  ▪ **Mixed agonist-antagonist**: compounds with an agonistic effect at one class of receptor and an antagonistic effect at another

  ▪ **Full antagonist**: compounds that inhibit agonist binding of other compounds; have reduced analgesic effect and are primarily used for the treatment of opioid intoxication
EFFECTS

Central Nervous System

- Nervous
  - Euphoria
  - Analgesia
  - Sedation
  - Mental clouding and mood swings

- Pulmonaryary
  - Respiratory Depression
  - Decreased Responsiveness

- Gastrointestinal
  - Nausea
  - Vomiting

- Other
  - Cough suppression
  - Miosis
  - Truncal rigidity
  - Flushing and warming of the skin
  - Sweating and itching
EFFECTS
Central Nervous System

- Psychological
  - Drowsiness
  - Sedation
  - Lethargy
  - Dizziness
  - Mental clouding and mood swings
  - Depressed reflexes
  - Altered sensory perception
  - Stupor
  - Coma

- Physiological
  - Analgesia
  - Headache
  - Dry mouth
  - Facial flushing
  - Nausea
  - Constipation
  - Respiratory depression
  - Muscle flaccidity
  - Pupil constriction
  - Low blood pressure
  - Low pulse
  - Droopy eyelids
  - Low body temperature
EFFECTS

Human Performance

- Driving
  - Slow driving
  - Weaving
  - Poor vehicle control
  - Poor coordination
  - Slow response to stimuli
  - Delayed reactions
  - Difficulty following instructions
  - Falling asleep at the wheel
WARNING

MAY CAUSE DROWSINESS
ALCOHOL COULD INTENSIFY THIS EFFECT
USE CAUTION WHEN OPERATING A CAR
OR DANGEROUS MACHINERY.

WHEN TAKING THIS MEDICATION
DO NOT DRINK
ALCOHOLIC BEVERAGES

www.drugrehab.com
OPIATES VS. OPIOIDS

Classification
OPIATES
ALKALOIDS DERIVED DIRECTLY FROM THE POPPY PLANT

• Opium
  ▪ Morphine, Thebaine, Codeine, Papaverine, Noscapine, Oripavine
  ▪ Schedule I

• Morphine
  ▪ Extracted from opium, 1803
  ▪ Named after Morpheus, the god of dreams
  ▪ Strong μ agonist, weak δ and κ agonist
  ▪ Analgesic Potency = 1
  ▪ Anesthetic supplement, injuries, musculoskeletal, pain management
  ▪ Schedule II/III

• Codeine
  ▪ Extracted from opium, also derived from methylation of morphine
  ▪ Weak μ agonist, weak δ agonist
  ▪ Analgesic Potency = 0.1
  ▪ Injuries, musculoskeletal, cough
  ▪ Schedule II/III
SEMISYNTHETIC OPIOIDS

- **Hydrocodone**
  - Derived from Codeine
  - \( \mu \) agonist
  - Analgesic Potency = 1-2
  - Injuries, musculoskeletal, pain management, cough
  - Schedule II

- **Hydromorphone**
  - Derived from Morphine
  - Strong \( \mu \) agonist
  - Analgesic Potency = 7-10
  - Injuries, musculoskeletal, pain management
  - Schedule II

- **Oxycodone**
  - Derived from Thebaine
  - \( \mu \) agonist
  - Analgesic Potency = 1-2
  - Injuries, musculoskeletal, pain management
  - Schedule II

- **Oxymorphone**
  - Derived from Thebaine
  - Strong \( \mu \) agonist
  - Analgesic Potency = 8-15
  - Injuries, musculoskeletal, pain management
  - Schedule II
SEMISYNTHETIC OPIOIDS

• Heroin
  ▪ Derived from Morphine, 1874
  ▪ Sold as a pharmaceutical until abuse was rampant
  ▪ Strong μ agonist
  ▪ Analgesic Potency = 1-5
  ▪ 6-AM metabolite is 4 times more potent than morphine
  ▪ Schedule I

• Buprenorphine
  ▪ Derived from Thebaine
  ▪ μ agonist, κ agonist
  ▪ High affinity to receptors producing longer-lasting morphine-like analgesia
  ▪ Analgesic Potency = 25-30
  ▪ Detoxification and maintenance in heroin dependence, pain management
  ▪ Schedule III

https://www.deamuseum.org/ccp/opium/history.html
SEMISYNTHETIC OPIOIDS

• Nalorphine
  ▪ Derived from morphine
  ▪ Strong κ agonist, μ antagonist
  ▪ Not used as an analgesic due to unpleasant side-effects
  ▪ Reverse the effects of opioids, overdose treatment
  ▪ Schedule III

• Nalbuphine
  ▪ Derived from oxymorphone
  ▪ Strong κ agonist, δ agonist, μ antagonist
  ▪ Analgesic Potency = 0.5-1
  ▪ Pre-/postoperative, anesthetic supplement
  ▪ Not scheduled
SEMISYNTHETIC OPIOIDS

• Naloxone
  - Derived from Oxymorphone
  - Strong $\mu$ antagonist
  - Reverse the effects of opioids, overdose treatment
  - Not scheduled

• Naltrexone
  - Derived from Oxymorphone
  - Strong $\mu$ antagonist
  - Reverse the effects of opioids, overdose treatment
  - Not scheduled
SEMISYNTHETIC OPIOIDS

• Others
  ▪ Butorphanol – treat migraine and labor pain
  ▪ Dextromethorphan – cough suppressant
  ▪ Levorphanol – treat pain
  ▪ Nalmefene – antagonist, treat alcohol dependence
  ▪ Pentazocine – treat pain
SYNTHETIC OPIOIDS

• Fentanyl
  ▪ Strong µ agonist
  ▪ Analgesic Potency = 100-200
  ▪ Pre-/postoperative, anesthetic supplement, pain management
  ▪ Schedule II

• Meperidine
  ▪ Strong µ agonist
  ▪ Analgesic Potency = 0.1
  ▪ Injuries, postoperative pain, obstetrics
  ▪ Schedule II

• Methadone
  ▪ Strong µ agonist
  ▪ Analgesic Potency = 1
  ▪ Detoxification, maintenance, pain management
  ▪ Schedule II

• Propoxyphene
  ▪ µ agonist
  ▪ Analgesic Potency = <0.1
  ▪ Schedule IV
  ▪ No longer sold in US, 2011
SYNTHETIC OPIOIDS

• Tramadol
  ▪ $\mu$ agonist
  ▪ Analgesic Potency = 0.1-0.2
  ▪ Injuries, musculoskeletal, pain management
  ▪ Schedule IV

• Others
  ▪ Diphenoxylate – treat diarrhea
  ▪ LAAM (levacetylmethadol) – treat opiate addiction
  ▪ Loperamide – treat diarrhea
  ▪ Tapentadol – treat moderate to severe pain
CDC PRESCRIBING DATA

• Sales of prescription opioids in the US nearly quadrupled from 1999-2014

• From 2007-2012 the rate of opioid prescribing steadily increased among specialists
  ▪ Pain medicine – 49%
  ▪ Surgery – 37%
  ▪ Rehabilitation – 36%

• Primary care providers account for about half of opioid pain relievers dispensed
CDC PRESCRIBING DATA

- Opioid use varies among subgroups
- More likely to use
  - Older adults (40+)
  - Women
  - Non-Hispanic whites vs. Hispanic person
  - No significant difference between non-Hispanic whites and non-Hispanic blacks
CDC PRESCRIBING DATA

Some states have more opioid prescriptions per person than others.

Number of opioid prescriptions per 100 people

52-71
72-82.1
82.2-95
96-143

Source: IMS, National Prescription Audit (NPA™), 2012.
Sources of Prescription Opioids Among Past-Year Non-Medical Users

- Given by a friend or relative for free
- Prescribed by ≥1 physicians
- Stolen from a friend or relative
- Bought from a friend or relative
- Bought from a drug dealer or other stranger
- Other

Number of Days of Past-Year Non-Medical Use:
- Any
- 1-29
- 30-99
- 100-199
- 200-365

Percent of Users

---

* Obtained from the US National Survey on Drug Use and Health, 2008 through 2011.

* Estimate is statistically significantly different from that for highest frequency users (200-365 days) (P< .05).

* Includes written fake prescriptions and those opioids stolen from a physician’s office, clinic, hospital, or pharmacy, purchases on the Internet; and obtained some other way.

CDC RX OPIOID OVERDOSE DATA

• Nearly half of all US opioid overdose deaths involve a prescription opioid (2015 – 15,000 deaths)
• Most common drugs involved in overdose
  ▪ Methadone
  ▪ Oxycodone
  ▪ Hydrocodone
• Rates highest among people 25-54 years old
• Rates higher among non-Hispanic whites, American Indians including Alaskan Natives
• Men were more likely to die from overdose, but the gap is closing
CDC HEROIN USE DATA

• Use
  ▪ Increasing among men and women, most age groups, and all income levels
  ▪ Greater increase in demographic groups with historically low rates
    ○ Women, privately insured, higher incomes
  ▪ More than doubled in the past decade among young adults aged 18-25 years

• Overdose deaths
  ▪ More than quadrupled since 2010
  ▪ From 2014-2015 death rates increased by 20.6%
  ▪ 13,000 people died in 2015
CDC HEROIN USE DATA

- Risk Factors
  - Past misuse of prescription opioids in the strongest factor
    - Especially if the dependency/abuse occurred within the past year
  - 3 out of 4 new heroin users reported prescription opioid abuse prior to using heroin
  - Increased availability
  - Relatively low prices compared to Rx opioids
OPIOID OVERDOSE DEATHS

Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2015

ARIZONA TAKING ACTION

• January 2015
  ▪ Arizona State University's Walter Cronkite School of Journalism and Mass Communication and the state of Arizona joined forces to shed light on heroin abuse.
  ▪ “Hooked: Tracking heroin’s hold on Arizona.”
  ▪ 30 minute program played on all major Spanish and English stations in Arizona
  ▪ Also played on radio stations.
  ▪ Following the program there was a call center staffed with 100 professionals that could give advice and refer callers to treatment centers.
ARIZONA TAKING ACTION – PART II

• January 2017
  ▪ "Hooked Rx: From prescription to addiction"

• HookedRX
ADDICTION TREATMENT
ABSTINENCE SYNDROME

- 8-12 hours
  - Lacrimation
  - Yawning
  - Rhinorrhea
  - Perspiration

- 12-14 hours
  - Irritability
  - Piloerection ("goose flesh")
  - Restless sleep
  - Weakness
  - Mydriasis
  - Tremor
  - Anorexia
  - Muscle twitching
ABSTINENCE SYNDROME

• 48-72 hours
  - Increased irritability
  - Increased heart rate
  - Insomnia
  - Hypertension
  - Anorexia
  - Hot and cold flashes
  - Sneezing

  - Syndrome duration 7-10 days

• Alternating sweating and flushing
  - Nausea and vomiting
  - Piloerection
  - Hyperthermia
  - Hyperpnea
  - Abdominal cramps
  - Aching muscles
MEDICATION-ASSISTED TREATMENT (MAT)

• Methadone
  ▪ Developed in 1964 as a response to post-World War II heroin epidemic
  ▪ Reduces and/or eliminates the use of heroin
  ▪ Reduces the death rates and criminality associated with heroin use
  ▪ Allows patients to improve health and social productivity
  ▪ Potential to reduce the transmission of infectious diseases associated with heroin IV use, like hepatitis and HIV
MAT - METHADONE

• How does it work?
  ▪ Oral effectiveness
  ▪ Moderately long-lasting effect
  ▪ Relieve narcotic craving
  ▪ Suppress the abstinence syndrome
  ▪ Block the euphoric effects associated with heroin
  ▪ Majority of patients require 80-120 mg/d to achieve these effects and require treatment for indefinite amount of time
  ▪ Methadone maintenance is corrective, not curative treatment
MAT - BUPRENORPHINE

- Used as treatment over the last 10-15 years
- Developed for office-based treatment due to a lack of Opioid Treatment Programs
- FDA approved use in 2002 after formal trials proved to be successful
- Office-based treatment does not guarantee the patient is receiving counseling or drug testing
- Doctors are required to go through certification process to prescribe buprenorphine
- In 2010 there was an increase in buprenorphine abuse
MAT - BUPRENORPHINE

- In 2010 there was an increase in buprenorphine abuse

- Suboxone
  - Buprenorphine with naloxone
  - Prevents people from getting high by dissolving and injecting buprenorphine tablets
MAT - NALOXONE

• Opioid Antagonist
• Rapidly reverses opioid overdose
• Three FDA-approved formulations
  ▪ Injectable: professional training required
  ▪ Autoinjectable: EVZIO
    o Once activated device provides verbal instruction to user
    o Injected into outer thigh
    o 2 doses supplied
  ▪ Nasal Spray: NARCAN
    o No assembly required
    o Spray into one nostril
    o 2 doses supplied

www.narcan.com
www.evzio.com
MAT - NALOXONE

• Who can give naloxone?
  - Injectable version is given by medical professional
  - Depending on the state citizens may use the auto injector and nasal spray on someone who has overdosed
  - Some states require a physician to prescribe naloxone
  - In other states pharmacies can distribute naloxone to community without a physician prescription
  - Check the Prescription Drug Abuse Policy System for the laws in your state
    - [http://www.pdaps.org/](http://www.pdaps.org/)
CURRENT TRENDS
KROKODIL

- Desomorphine
- First recognized in Russia in 2002
- Doctors noticed dark and scaly patches of skin on some drug addicts
- Codeine derivative
  - Mixed with chemicals such as paint thinners, hydrochloric acid and red phosphorus
  - Murky yellow liquid with an acrid smell
- Mimics the effect of heroin at a fraction of the cost
- Blood vessels burst at injection site and flesh dies, falling off the bone in large chunks
KRATOM

- Mitragynine and 7-hydroxymitragynine
  - Extract from tropical tree *Mitragyna speciosa*, native to Southeast Asia
  - Currently not scheduled
    - DEA put a temporary ban in place Fall of 2016, which it lifted
    - DEA asked public to comment on proposed ban, 99% opposed it
    - DEA is currently waiting on FDA analysis on potential harms and health benefits
  - At low doses produces stimulant effect
    - Increased energy, sociability, alertness
  - At high doses produces opioid effect
    - Sedation, pleasure, decreased pain
LOPERAMIDE

- Imodium
- Schedule V
- $\mu$ agonist in the myenteric plexus of the large intestine
- Excessive dosing (10+ times higher than recommended)
  - At high concentrations loperamide can cross the blood-brain barrier
  - Attempt to get high
  - Treat opioid withdrawal symptoms
  - Can fatally disrupt the heart’s rhythm
- Insufflation may be attempted
PINK

- U-47700
- Synthetic opioid
  - First identified in 1978, Upjohn
  - Scientific literature in the early 1980’s reported it behaved like morphine in animal models
  - No approved medical use
  - Not approved for human consumption – FDA
- µ agonist
- Analgesic Potency = 7.5
- DEA temporary Schedule I ban November 2016
  - 46 confirmed fatalities between October 2015-September 2016
  - Temporary ban good for 24 months and can be extended for additional 12 months
PINK

- Drug seizures have resulted in powder form and counterfeit tablets that mimic pharmaceutical opioids
- Abuse often happens unknowingly
- Single substance or mixed with heroin or fentanyl
- Street Names: Pink, Pinky, U4
- Sold online as research chemicals
FENTANYL DERIVATIVES

• Carfentanil (Wildnil)
  ▪ Schedule II
  ▪ Analgesic Potency = 10,000
  ▪ Intended for large-animal use
  ▪ “Heroin laced with elephant tranquilizers”
  ▪ DEA Issues public warning in September 2016
    o 2 mg could be lethal
    o Powder, blotter paper, tablets, spray
    o Can be absorbed through skin or inhaled

• Sufentanil
  ▪ Analgesic Potency = 500-1000
  ▪ Schedule II
DEA WARNINGS

• July 2016
  ▪ Counterfeit Prescription Pills Containing Fentanyls: A Global Threat

• October 2016
  ▪ DEA warns public that drug cartels are selling lethal doses of fentanyl disguised as street heroin and counterfeit OxyContin pills

• Officer Safety Alert – Carfentanil: A Dangerous New Factor in the U.S. Opioid Crisis
I felt like my body was shutting down.
DRUG TESTING FOR OPIOIDS
SCREENING TEST

Looking For
Hydrocodone/Codeine/Morphine
Oxycodone/Oxymorphone
Heroin
Methadone
Buprenorphine (Suboxone)
Tramadol

Test For
Opiates
Oxycodone
Heroin (w/opiate test)
Methadone
Buprenorphine
Tramadol
# GCMS INTERPRETATION

<table>
<thead>
<tr>
<th>Prescription/Drug</th>
<th>Opiate</th>
<th>Parent Drug/Metabolite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin</td>
<td>Diacetylmorphine</td>
<td>6-MAM, Morphine, Codeine</td>
</tr>
<tr>
<td>Tylenol #3, #4</td>
<td>Codeine</td>
<td>Codeine, Morphine</td>
</tr>
<tr>
<td>MS Contin, Roxanol</td>
<td>Morphine</td>
<td>Morphine, Hydromorphone</td>
</tr>
<tr>
<td>Vicodin, Vicoprofen, Tussionex, H-C Tussive</td>
<td>Hydrocodone</td>
<td>Hydrocodone, Hydromorphone</td>
</tr>
<tr>
<td>Dilaudid</td>
<td>Hydromorphone</td>
<td>Hydromorphone</td>
</tr>
<tr>
<td>Oxycontin, Percodan, Percoset, Roxicet</td>
<td>Oxycodone</td>
<td>Oxycodone, Oxymorphone</td>
</tr>
<tr>
<td>Opana</td>
<td>Oxymorphone</td>
<td>Oxymorphone</td>
</tr>
</tbody>
</table>

---

Opioids | 2017

---

64