The Opioid Epidemic

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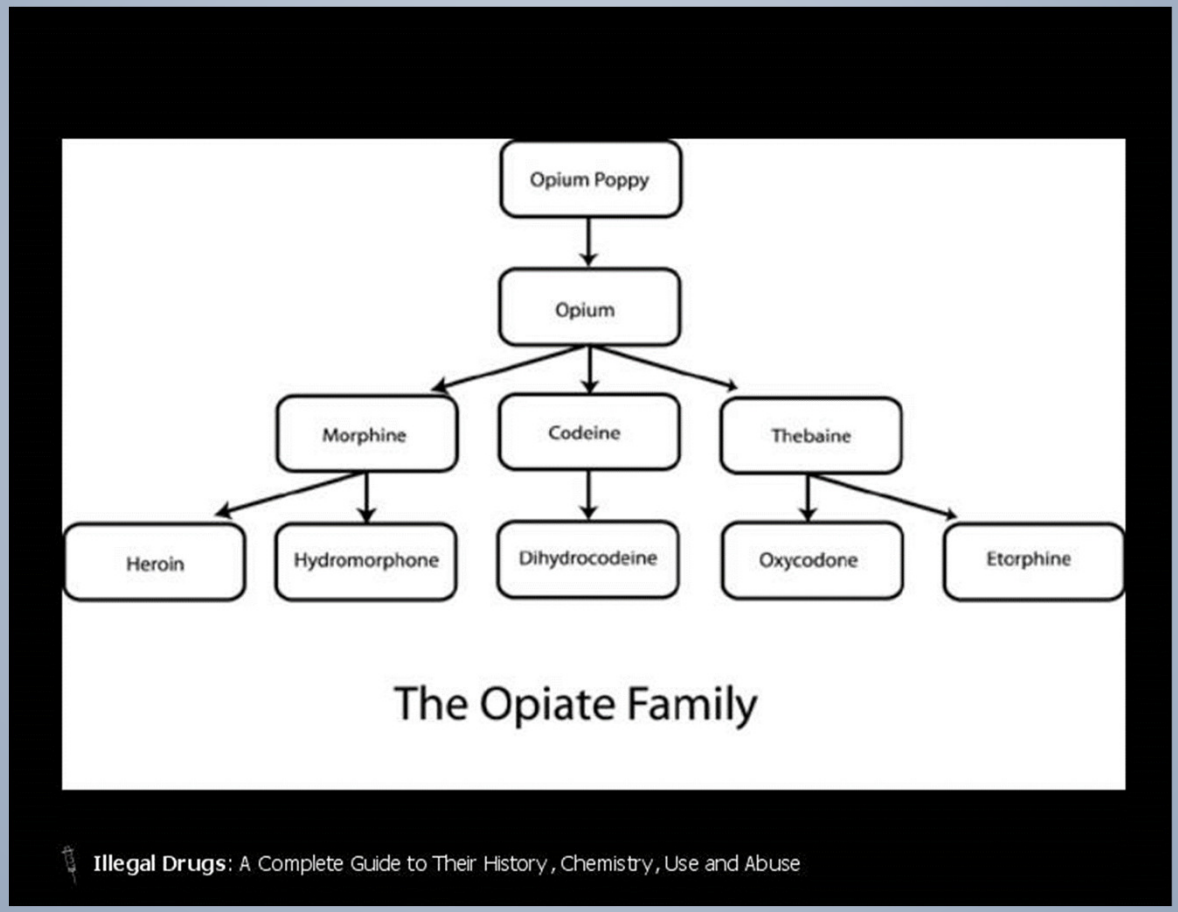
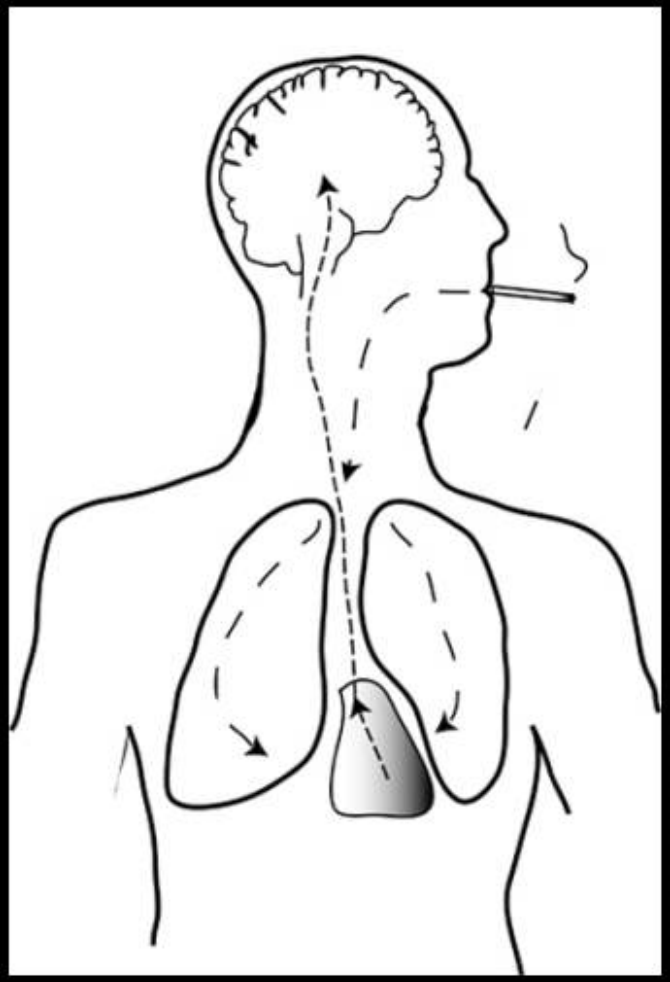


Illegal Drugs: A Complete Guide to Their History, Chemistry, Use and Abuse

Types of Opiates

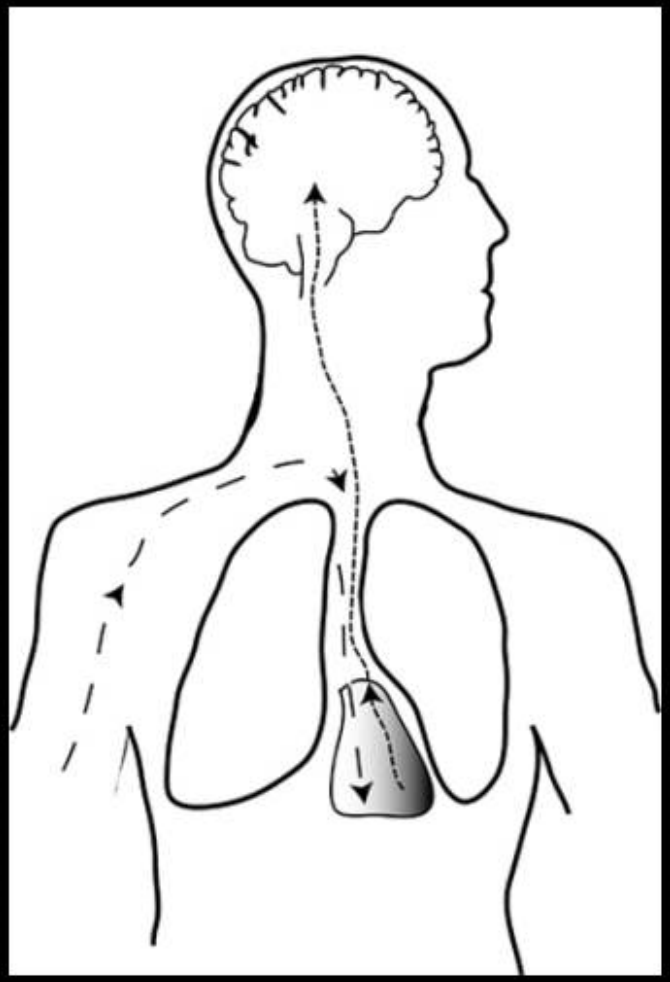
Opioids

Drug	Mechanism of action	Indication	Notes
Heroin	Strong μ agonist	**Manage pain, suppress cough, antimotility for diarrhea** Contraindication: phenothiazine, MAO inhibitors, and tricyclic antidepressants (depressant effects); alcohol and benzodiazepine (respiratory effects); hepatic metabolism	Often abused IV; not legal in US;
Morphine	Strong μ agonist		Prototypical opioid; various routes of admin
Fentanyl	Strong μ agonist		**Rapid onset and offset** with small doses; CV stability; 100x more potent than morphine
Methadone	Strong μ agonist		Also used for opioid/heroin withdrawal; racemic mixture of NMDA antagonist and mu agonist
Meperidine	Strong μ agonist		No biliary SE, doesn't constrict sphincter of Oddi; seizures
Codeine	Moderate μ agonist		Less potent morphine
Hydrocodone	Moderate μ agonist		Most prescribed opiate; often combined with NSAIDs/acetaminophen
Oxycodone	Moderate μ agonist		Similar to hydrocodone
Tramadol	Weak μ agonist		Synthetic codeine; lower addiction risk; can cause **seizures** and **serotonin syndrome**
Buprenorphine	μ agonist; κ antagonist	Analgesic; deterrent, detoxification	High affinity, low efficacy at mu receptor → **partial agonist**
Nalbuphine	κ agonist; μ antagonist	Treats opioid-induced **pruritus**	Originally hoped to be less addictive, less side effects than other opioids → no
Naloxone	μ antagonist (short acting)	Treat opioid addiction, overdose, and toxicity; reverses mu agonist effects; increases respiratory rate within 1-2 min	Better for opioid overdose; half-life is 1 hour
Naltrexone	μ antagonist (long acting)		Treats alcoholism; lasts 24 hours after moderate dose



Smoking

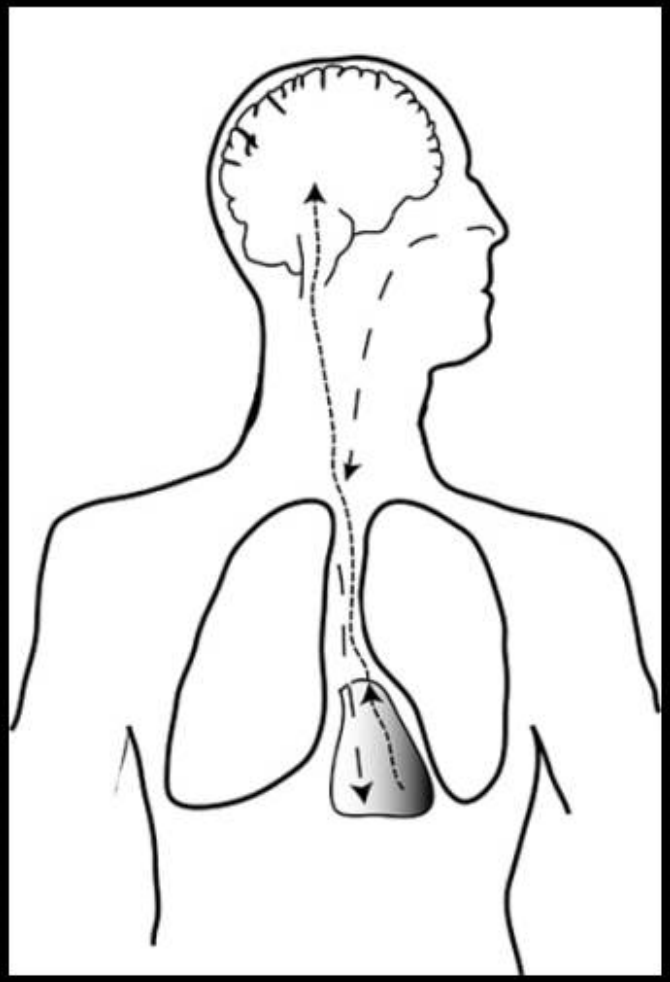
- Time to brain:
  7 to 10 seconds



Injecting

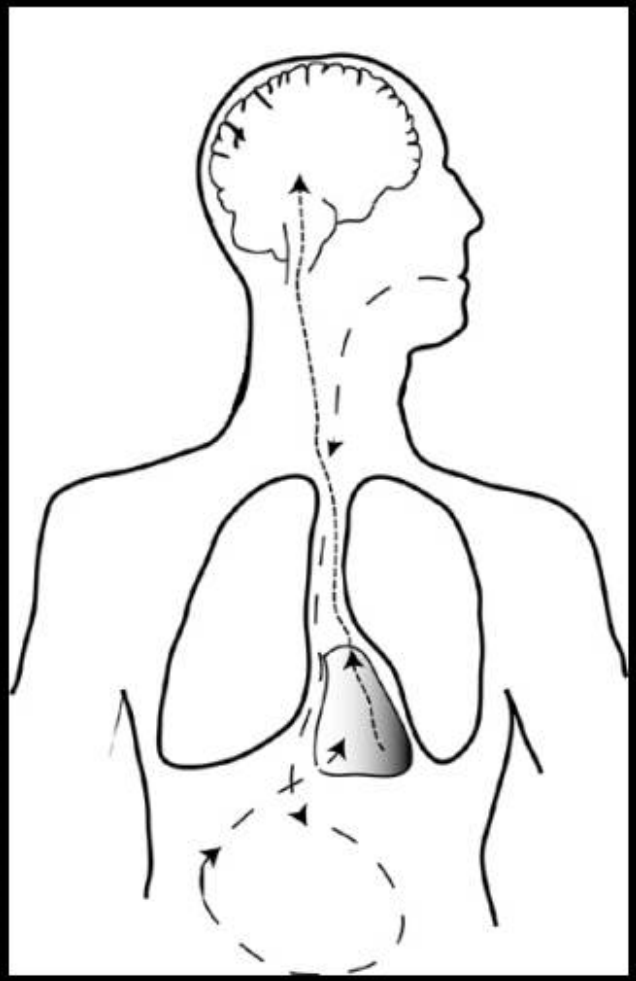
- Time to brain:
  15 to 30 seconds if injected into a vein

  3 to 5 minutes if injected into muscle or skin



Snorting

- Time to brain:
  3 to 5 minutes



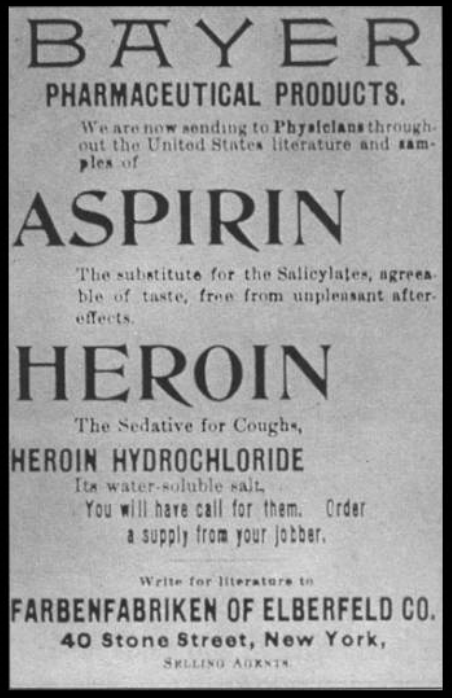
Ingesting

- Time to brain:
  20 to 30 minutes

Timeline

- 1804 – Morphine distilled from opium for the first time
- 1839 – First Opium War breaks out as Britain forces China to sell its India-grown opium, and the British take Hong Kong. A second war erupts in 1957.
- 1853 – The Hypodermic syringe is invented. Inventor's wife is first to die of injected drug overdose
- 1898 – Bayer chemist invents diacetylmorphine, names it heroin

Morphine Syringe (1800's)



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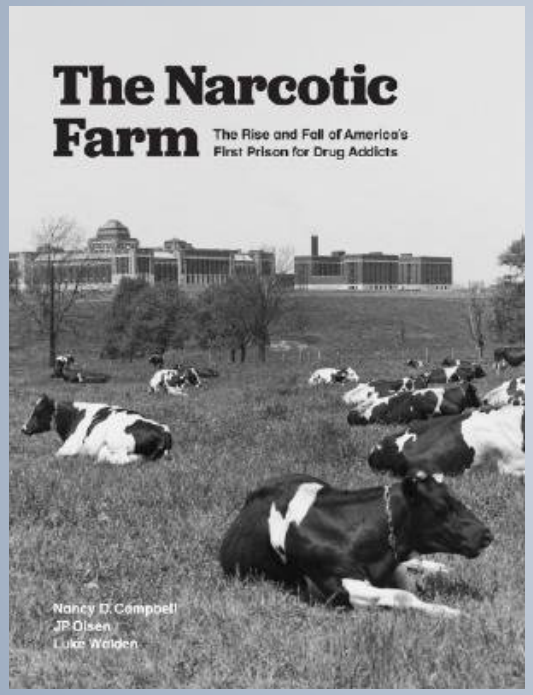
Heroin was first marketed in 1898 by Bayer as a cough treatment

Patent medicines contained opiates and reports of death from overdose were common

Timeline

- 1914- US Congress passes Harrison Narcotics Tax Act
- 1928 – What eventually becomes known as the Committee on the Problems of Drug Dependence forms to organize research in pursuit of the Holy Grail: a nonaddictive painkiller
- 1935 – The Narcotic Farm in Lexington, Kentucky opens as federal prison/drug rehabilitation and research center
- 1951 – Arthur Sackler revolutionizes drug advertising with campaign for antibiotic Terramycin
- 1952 – Arthur, Raymond, and Mortimer Sackler buy Purdue Frederick
- 1960 – Arthur Sackler's campaign for Valium makes it the industry's first $100 million drug

The Narcotic Farm



Newly admitted patients line up for a shot of morphine during detoxification. The second man from the left, with his head bandaged, reportedly injured himself falling out of bed during withdrawal.

Timeline

- 1974 – The Narcotic Farm closes and is transformed into a medical center and prison
- 1980 – Jan Stjernsward made chief of the cancer program for the World Health Organization. Devises WHO Ladder of pain treatment
- 1980 – The *New England Journal of Medicine* publishes letter to the editor that becomes known as Porter and Jick
- Early 1980s – First Xalisco migrants set up heroin trafficking businesses in the San Fernando Valley of Los Angeles
- 1984 – Purdue releases MS Contin, a time released morphine painkiller marketed to cancer patients
- 1986 – Drs. Kathleen Foley and Russell Portenoy publish paper in the journal *Pain*, opening a debate about use of opiate painkillers for wider variety of pain.

Porter and Jick Letter

- 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 a 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.
- JANE PORTER
- HERSHEL JICK, M.D.
- Boston Collaborative Drug
- Surveillance Program
- Boston University Medical Center
- Waltham, MA 02154

Xalisco

- Dealers circulate a number around town. An addict calls, and an operator directs him to an intersection or a parking lot. The operator dispatches a driver, who tools around town, his mouth full of tiny balloons of heroin, with a bottle of water nearby to swig them down with if cops stop him. (“It’s amazing how many balloons you can learn to carry in your mouth,” said one dealer, who told me he could fit more than 30.)
- The driver meets the addict, spits out the required balloons, takes the money and that’s that. It happens every day — from 7 a.m. to 7 p.m., because these guys keep business hours.

Timeline

- 1987 – Arthur Sackler dies, having revolutionized pharmaceutical advertising
- Early 1990s – Xalisco Boys heroin cells begin expanding beyond San Fernando Valley to cities across western United States. Their pizza-delivery-style system evolves
- 1996- Purdue releases OxyContin, timed-released oxycodone, marketed largely for chronic-pain patients
- 1996- Dr. David Procter's clinic in South Short, Kentucky, is presumed the nation's first pill mill
- 1996- President of American Pain Society urges doctors to treat pain as a vital sign
- 1998- "The Man" takes Xalisco black tar heroin east across the Mississippi River for the first time, lands in Columbus, Ohio.

Timeline

- 1998- In Portsmouth, Ohio, Dr. David Procter has an auto accident that leaves him unable to practice medicine but still capable of running a pain clinic. He hires doctors who go on to open clinics.
- Late 1990s – Xalisco Boys heroin cells begin to spread to numerous cities and suburbs east of the Mississippi River. Indianapolis is identified as a city with a heroin cell.
- 1998-1999 – Veteran's Administration and JCAHO adopt idea of pain as fifth vital sign
- 2000- Operation Tar Pit targets Xalisco heroin networks – the largest joint DEA/FBI operation and first drug conspiracy case to stretch from coast to coast
- 2001- Injured workers covered under Washington State's workers' comp system start dying of opiate overdoses
- 2002- Dr. David Procter pleads guilty to drug trafficking and conspiracy and serves eleven years in federal prison

Pill Mill Doctor

Pill-mill doctor sentenced to four life terms in prison

By Bill Estep - bestep@herald-leader.com

A doctor convicted of writing prescriptions for pills that contributed to overdose deaths in northeastern Kentucky and elsewhere has been sentenced to four life terms in prison.

Paul H. Volkman, 64, helped run one of the biggest pill-mill operations of the last decade in southern Ohio, improperly writing prescriptions to drug addicts from Kentucky, Ohio, West Virginia and other states in return for cash, prosecutors said in court documents.

U.S. District Judge Sandra Beckwith, who sentenced Volkman on Tuesday in Cincinnati, also ordered him to forfeit $1.2 million.

Volkman worked at Tri-State Health Care and Pain Management in Portsmouth, Ohio, across the Ohio River from Greenup County, and at other locations in the area from April 2003 to early 2006.

He wrote prescriptions for at least 3.3 million pain pills and for an unknown number of anti-anxiety and other types of pills, according to interviews and court records.

At one point, Volkman was the largest buyer of oxycodone in the nation, prosecutors said.

The U.S. Drug Enforcement Administration looked into 34 overdose deaths among Volkman's patients, 19 of them from Kentucky, said James Geldhof, DEA diversion program manager for the region that includes Kentucky.

"He was as bad as any doctor in the country," Geldhof said.

The business was well known to addicts and police in northeastern Kentucky, said Lewis County Sheriff Johnny Bivens.

"We had a litany of people going over to his office," he said. "It was terrible."

Timeline

- 2004- Washington State Department of Labor & Industries Drs. Gary Franklin and Jaymie Mai publish findings on death of injured workers due to overdoses on opiate painkillers
- Mid – 2000s – Xalisco black tar heroin cells are now in at least 17 states. Portsmouth, Ohio, has more pill mills per capita than any US town. Florida's tax regulations make It another center of illicit pill supply.
- 2006- Operation Black Gold Rush, a second DEA operation targeting Xalisco heroin cells across the country
- 2007- Purdue and three executives plead guilty to misdemeanor charges of false branding of OxyContin; fined $634 million
  - Generated $3.1 billion in revenue on the drug
- 2008- Drug overdoses, mostly from opiates, surpass auto fatalities as leading cause of accidental death in the United States

Timeline

- 2011- Ohio passes House Bill 93, regulating pain clinics
- 2013- The College on the Problems of Drug Dependence turns 75 without finding the Holy Grail of a nonaddictive painkiller
- 2014- Actor Phillip Seymour Hoffman dies, focusing widespread attention for the first time on the United States' opiate-abuse epidemic and the transition from pills to heroin in particular
- 2014- The FDA approves Zohydro, a timed-release hydrocodone pain-killer with no abuse deterrent. It also approves Purdue's Targiniq ER, combining timed-release oxycodone with naloxone, the opiate-overdose antidote

Social Impact of the Opioid Crisis

- Enough opioids are prescribed in the U.S. each year to keep every man, woman, and child in the country medicated around the clock for one month.
  - In 2015, an estimated 2.7 million Americans suffered from opioid dependence or addication
  - At risk populations include:
    - Individuals aged 45-64
      - Account for 40% of all drug overdose deaths
        - Majority involved people who received legitimate prescriptions from medical providers
    - Individuals on Medicaid and others living in poverty or with low-income
      - Access and quality of healthcare
      - US Department of Health and Human Services:
        - individuals on Medicaid are more likely to be prescribed opioids, at higher doses, and for longer duration
        - Less likely to have access to evidenced based addiction treatment
      - Environmental and social stresses
        - Scientific Studies show individuals with increased environmental and social stresses are more prone to addiction

Social Impact of the Opioid Crisis

- The Department of Health and Human Services found that nearly three quarters of states saw an unprecedented number of children entering foster care.
  - Parental substance use was cited as the primary reason.
- The Centers for Disease Control reports a record increase in the number of babies born with Neonatal Abstinence Syndrome (NAS).
  - NAS is a drug withdrawal syndrome that occurs shortly after birth, primarily among infants exposed to opioids such as prescription painkillers and heroin while they are in the womb.
  - The number of babies born in the United States with a drug withdrawal symptom has quadrupled over the past 15 years.

Medical Impact of the Opioid Crisis

- Emergency Rooms
  - Role
    - Playing a significant role in crisis
      - Notable source of over prescriptions of opioids
        - Narcotic overdose is the 8th leading cause of death within one week of an emergency room visit
  - Increased services
    - Over 300,000 estimated annual emergency room department visits for opioid overdose
    - https://www.in.gov/isdh/files/CountyProfilesOfOpioidUse2017.pdf
  - New policies
    - Development of opioid dependence screening tools
    - Training to Emergency Department staff on how to address potentially opioid dependent individuals in an ethically neutral manner
    - Expansion of referral sources for outpatient addictions specialty clinics
    - Reduced administrative barriers to becoming and buprenorphine prescriber
    - Development of a financial reimbursement model for prescription opioid screening or treatment in ER settings
    - 21 Century Cures Act and other federal funding to address crisis
    - Stricter policies on prescribing opioids

Financial Impact of the Opioid Crisis

- Fatal Costs and Non-fatal Costs
  - Fatal costs include value of lives lost due to opioid-related deaths
    - Lost earnings due to premature death
    - Other valuable activities in life besides work
  - Non fatal costs include:
    - Workplace costs
      - Medical related Absenteeism
      - Presenteeism
      - Disability costs
      - Lost wages/employment
      - Incarceration (lost wages)
    - Health Care Costs
      - Excess medical and drug sots
      - Substance abuse treatment
      - Prevention and research
    - Criminal Justice
      - Police protection
      - Legal and adjudication
      - Correctional Facilties
      - Property loss due to crime

Financial Impact of the Opioid Crisis

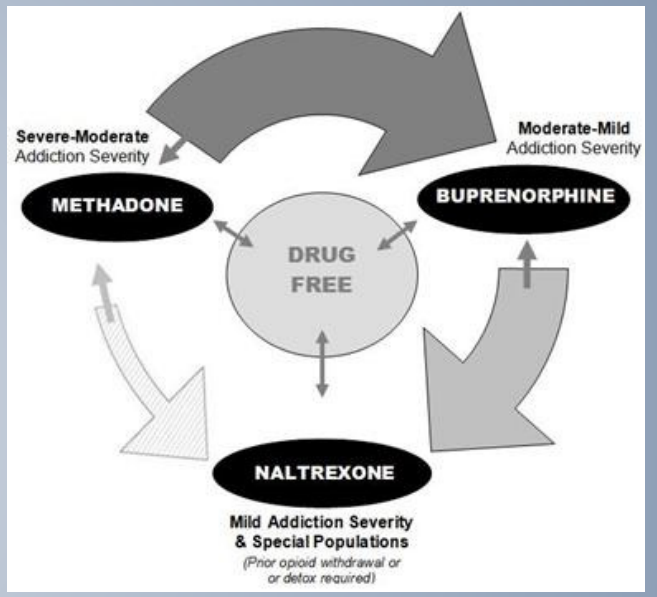
Study	Study Year	Opioids Included	Cost
Birnbaum et al. (2006)	2001	Prescription	$11.5 billion
Birnbaum et al. (2011)	2007	Prescription	$61.5 billion
Florence et al. (2016)	2013	Prescription	$79.9 billion
CEA (2017)	2015	Prescription And illicit	$504.0 billion

Financial Impact of the Opioid Crisis

- US Economy has lost close to 1 million workers to opioid addiction between 1999-2015
  - Ages 25-54
  - Accounts for close to 25% of the total decline in US labor force participation
- Opioid addiction cost workers 12 billion working hours between 1999-2015
- Hollingsworth, Rahm, and Simon (March 2017): For every 1 percent increase in unemployment in the U.S., opioid overdose death rates rose by nearly 4 percent.

Treatment

- Pharmacotherapeutic Medications
  - Methadone
  - Buprenorphine (Subutex)
  - Buprenorphine-naloxone (Suboxone)
  - Naltrexone (Vivitrol)
- Behavioral Health
  - Contingency Management
  - Recovery and Training Self Help (RTSH) for Opioid Use



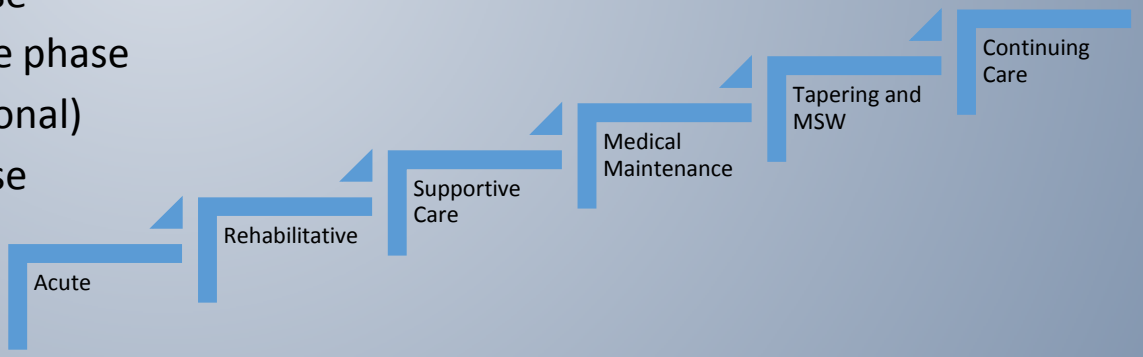
Opiate effect and …	the withdrawal symptoms
Numbness	becomes pain
Euphoria	becomes anxiety
Dryness of mouth	becomes sweating, runny nose
Constipation	becomes diarrhea
Slow pulse	becomes rapid pulse
Low blood pressure	becomes high blood pressure
Shallow breathing	becomes coughing
Pinpoint pupils	becomes dilated pupils
Sluggishness	becomes severe hyper-reflexes
Relaxed muscles	become muscle cramps

Pharmacotherapeutic Medications for Opioid Addiction Treatment

- Methadone:
  - most frequently used, long-acting, has many formulations, decreases pain-killing effects of opioids, available in OTPs
- Buprenorphine:
  - Larger doses do not increase effects, has increased margin of safety, administered in doctor's offices and healthcare settings
- Buprenorphine-naloxone:
  - Combination of 2 medications, administered in doctor's offices and healthcare settings
- Naltrexone:
  - does not have abuse potential; blocks effects of heroin, morphine, methadone; can cause withdrawal in non-abstinent patients; administered in OTPs and doctor's offices

Pharmacotherapeutic Medications for Opioid Addiction Treatment

- Phased-Treatment Approach
  - The phased-treatment approach comprises five or six patient-centered phases for planning and providing MAT services and evaluating treatment outcomes in an OTP:
    - Acute phase
    - Rehabilitative phase
    - Supportive-care Phase
    - Medical maintenance phase
    - Tapering phase (optional)
    - Continuing-care phase



Pharmacotherapeutic Medications for Opioid Addiction Treatment

- Variations of Phased Treatment
  - Types and intensity of services vary throughout treatment
  - Most patients need:
    - Intensive treatment services at entry
    - Diversified services during stabilization
    - Fewer intensive services after recovery benchmarks are met
  - Treatment phases are on a dynamic continuum
  - Assessment of treatment should be ongoing
  - Duration of treatment is a team decision based on data and medical experience

Behavioral Health Treatment for Opioid Addiction

- Contingency Management
  - Awards prizes for abstinence and treatment compliance, such as group attendance and healthy behaviors.
  - Based on a construct central to behavioral psychology known as operant conditioning, or the use of consequences to modify the occurrence and form of behavior.
  - Program augments existing, usual care services in community-based treatment settings for adults who primarily abuse stimulants (especially cocaine) or opioids (especially heroin) or who have multiple substance use problems.
  - Over a period of 3 months, urine and breath samples are collected two or three times a week for at least the first 6 weeks and once or twice weekly thereafter.
    - For each sample that tests negative for the target drug, clients can draw slips of paper or plastic chips from a bowl for the chance of winning a prize valued from $1 to $100.
    - Clients may also receive draws from the prize bowl for attending counseling/group therapy sessions and completing weekly activities designed to meet goals related to health (e.g., scheduling or attending a medical or nutritionist appointment, obtaining medications, recording daily medication or food consumption, exercising at a gym), sobriety (e.g., attending 12-step meetings), employment (e.g., creating a resume), and other areas.
    - The number of draws from the prize bowl increases from 1 to as many as 15 with consecutive negative test results and/or attendance at consecutive sessions.
    - A drug-positive sample or an unexcused absence resets the number of draws to one.
    - Bonus draws may be awarded to clients on a predetermined schedule.
  - Although the original trials of Prize Incentives were conducted over 3 months, the intervention can be used with urine and breath samples collected one to three times weekly for longer durations.

Behavioral Health Treatment for Opioid Addiction

- Recovery and Training Self Help (RTSH) for Opioid Use
  - A relapse-prevention program for individuals recovering from opioid use disorder.
    - Conducted in groups
    - Combines cognitive—behavioral, social support, and lifestyle change approaches
    - Aims to reduce the occurrence and frequency of relapse.
  - Based on the idea that, regardless of a person's original reasons for using substances, substance use disorders stem from conditioning due to the reinforcing effects of repeated substance use.
  - Designed to prevent relapse to opioid use and opioid use disorder by teaching and supporting alternative responses to stimuli previously associated with opioid use.
  - Program components were designed to address the clinical concerns of persons with opioid use disorder.
    - The four main components of the RTSH program include recovery training sessions, support group meetings, weekend activities, and a support network. Details for the four components follow.
      - Recovery trainings (23 sessions) focus on recovery-specific situations and obstacles that a recovering person with opioid use disorder might encounter (e.g., dangerous situations, forming new social and romantic relationships, and finding employment).
      - Support self-help group meetings (weekly) are co-led by a therapist (who may or may not be a person in recovery) and by a recovering group leader. During the meeting, participants have the opportunity to share personal impediments, discuss experiences, and solve problems as a group. These meetings create an alliance of support with other adults experiencing similar issues.
      - Weekend recreational activities provide opportunities for participants to interact in substance-free social events.
      - Support networks are made up of individuals with well-established recoveries from an opioid use disorder who frequently connect with group members and offer guidance and continued support. Also, members participate actively in the broader recovery community.

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