Historical Trends and Emerging Patterns of Substance Use Disorders: 1819 - 2019

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Phases of a Substance Use Disorder Epidemic

- **Incubation**
- **Expansion**
- **Plateau**
- **Decline**

Users & Problems X 1000

Year 1 to Yr 10

# of Users & Problems

Time
Contributing Factors of a Drug Epidemic

Supply Vectors

Demand Vectors

Phases of a Drug Epidemic:
- Incubation
- Expansion
- Plateau
- Decline

# of Users & Problems

Time
Contributing Factors – Supply Vectors

• Production
• Patterns of Trafficking
• Price
• Purity
• Profit
• Availability
• Poisonous Contamination
Contributing Factors – Demand Vectors

• Attitudes:
  • Perceived Harmfulness
  • Perceived Wrongfulness
  • Acceptance by others

• Desired Effects

• Withdrawal – “Dope Sick”

• Public Consensus

• Cost

• Rapid Onset of Action

• Access
Cycles of Change

Reoccurring Patterns of Substance Use Disorder Epidemics 1880 – 2019
Reoccurring Patterns of Opioid Epidemics: 1880 - 2019

1880 - 1900

- Morphine & Heroin

1955 - 1970

- Heroin

1990 - 2019

- Rx Opioids
- Heroin & Fentanyls
History of Opioids

• Opium the first drug from early agricultural civilizations
  • Assyrians invented slicing the poppy pod
  • Sumerians - The “Joy Plant”
  • Egyptians first produced opium as a drug – Thebaine
  • Greeks
  • Indian Subcontinent
  • Medieval Trade spread the drug

• 1804 German pharmacist first isolated Morphine
  • Named after the Greek god of sleep and dreams, Morpheus

• 19th Century 330 Wars forced production of Morphine
  • Used in US Civil War
History of Opioids in the U.S.

• In 1874, Heroin was created in Germany and sold in the United States as a “safe, non-addictive” substitute for morphine.

• From the late 1800’s to the 1900’s, drug companies sold over-the-counter drug kits containing glass barreled hypodermic needles and vials of morphine or heroin.

• Heroin, morphine and other opiates were sold legally in the U.S. until controlled by Harrison Narcotic Tax Act in 1914 and made illegal in the 1920’s

• 200,000 heroin addicts in the U.S. by 1925
History of Opioids in the U.S.
History of Opioids in the U.S.

• 1950’s – Drug Advertising and Direct Marketing to Physicians – antibiotic Terramycin

• 1960’s – Valium becomes first $100 million drug

• 1980’s – *NEJM* Porter and Jick Letter to Editor
  Purdue Pharma releases MS Conti
  WHO Ladder of Pain treatment

• 1996 - Purdue Pharma releases OxyContin
  Nation’s first Pill Mill South Shore, KY
  American Pain Society – Pain as 5th Vital Sign
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
Sources of Origin for Wholesale-Level Heroin Seizures In the United States: 2000 -20016

Shift From South American To Mexican

Source: DEA
DREAMLAND
The True Tale of America’s Opiate Epidemic

SAM QUINONES

WITH A NEW AFTERWORD BY THE AUTHOR
Fentanyl: A Potent Opioid

- Schedule II synthetic opioid
  - 100 times more potent than heroin
- Introduced into medical use in the 1960s and approved for medical use
- μ-opioid receptor agonist
- Short duration of effects
- Similar to oxycodone in its effects

How Rogue Chemists Are Creating the Deadliest Wave of the Opioid Epidemic
Regional Trends In Fentanyl Crime Lab Reports (Rates per 100,000): 2014-2017

**Source:** NIDA-NDEWS and DEA-NFLIS
Past Year Heroin Use among People Aged 12 or Older: 2002-2018

Heroin Use Down 2014 to 2018

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Note: Estimates of less than 0.05 percent round to 0.0 percent when shown to the nearest tenth of a percent.

* Difference between this estimate and the 2018 estimate is statistically significant at the .05 level.
Past Year Prescription Pain Reliever Misuse among People Aged 12 or Older: 2015-2018

Non-Medical Use Rx Pain Relievers Down 2014 to 2018

### Age

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Past Year Opioid Misuse among People Aged 12 or Older: 2018

9.9 Million People with Pain Reliever Misuse (97.1% of Opioid Misusers)

506,000 People with Pain Reliever Misuse and Heroin Use (4.9% of Opioid Misusers)

808,000 People with Heroin Use (7.9% of Opioid Misusers)

9.4 Million People with Pain Reliever Misuse Only (92.1% of Opioid Misusers)

302,000 People with Heroin Use Only (2.9% of Opioid Misusers)

10.3 Million People Aged 12 or Older with Past Year Opioid Misuse

Note: The percentages do not add to 100 percent due to rounding.
Percent Change in Drug Overdose Deaths Between 12 months ending in February 2018 and February 2019

Source: CDC - National Center for Health Statistics
National Opioid Crisis in Early Stage of Remission

Yet at High Risk of Relapse

October 2019 Update
Reasons for the declining numbers of drug overdose deaths include:

- Expanded availability & use of **Naloxone** to reverse effects of opioid overdose,
- The adoption of **Medicated Assisted Treatment** to reduce cravings of relapse among individuals receiving addiction therapy and those in Recovery,
- Increased **Public Awareness** about the Opioid Crisis,
- Thousands of local **Community-Based Initiatives** responding to the Crisis across the country
- **Partnerships of Public Health and Criminal Justice** systems working together,
- **Reduced Prescribing of Opioids** as per CDC Prescribing Guidelines,
- A 16-percent **decline in number of past year Rx opioid users** between 2016 and 2018, and
- An **11-percent decline** in the number of **first-time misusers of RX opioids** and
- A **31-percent decline in the number of first time Heroin users** between 2016 and 2018.
Critical Issues contributing to high levels of drug overdose deaths and threats to future progress include:

- Non-Pharmaceutical Clandestine Fentanyl Analogues are the number 1 killer,
- Polysubstance Overdose Deaths involved in 74 percent of all Opioid Deaths,
- Lack of Handoff to Treatment for Hospital Emergency non-fatal Overdose Patients,
- Undiagnosed and Untreated Psychological Trauma linked to Opioid Use (i.e., Adverse Childhood Experiences [ACE] and Post-Traumatic Stress Disorder [PTSD]),
- Slow Transition to Medicated Assisted Treatment by many Treatment Providers,
- A 25-percent Increase in Number of Methamphetamine Users between 2017 and 2018, and
- Polysubstance Deaths with Stimulants (74 percent of Cocaine deaths and 50 percent with Methamphetamine deaths).
National Drug Overdose Deaths Involving Cocaine, by Opioid Involvement
Number Among All Ages, 1999-2017

Cocaine with any Opioid

With Fentanyl Analogues

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

Reoccurring Patterns of Stimulant Epidemics: 1880 - 2019

- Cocaine

# of users and level of consequences

1880 - 1920

1975 - 2019
Cocaine – The Origin

• Since 15th Century – Andean South American native people chewed coca leaves to relieve hunger and dispel fatigue

• 1859 – Alkaloid cocaine isolated by German pharmacist, Albert Niemann

• Dr. Theodore Aschenbrandt - Bavarian Army cocaine water solution for exhausted collapsed soldier who cheerfully resumed the march

• Dr. Sigmund Freud: “a magical drug”
  * recommended to friends and colleagues

• Because of numbing effects became a standard treatment for eye disorders and local anesthetic for minor surgery and dentistry

• By 1863 Vin Mariani – coca leaves and Bordeaux wine
“Fortifies and Refreshes Body and Brain”
Restores Heath and Vitality
The First Cocaine Epidemic 1880 -1920

Introduction Phase - the Drug Rapidly Gains Acceptance

• 1884 – Purified cocaine commercially available in USA

• Wholesale cost very high $5-10 per gram but fell to 25 cents a gram until WW I compared to average wage at 20 cents per hour. Retail price $2.50 per gram

• Popular in the US: sold from drug and grocery stories, saloons and patent-medicine vendors
The First Cocaine Epidemic 1880 -1920

Introduction Phase

• Freud published 5 papers about Cocaine

• Some physicians believed cocaine reduced cravings for opiate addicts and alcoholics

• Encouraged by medical authorities and entrepreneurs as an elixir for the masses

• Touted as a panacea for melancholia, neuralgia, hysteria and nervous afflictions
The First Cocaine Epidemic 1880-1920

Middle Period - Use Spreads, Adverse Effects Revealed

- 1885 – John Pemberton registers a trademark for: “French Wine Coca - Ideal Nerve and Tonic Stimulant”
- 1886- Renamed as “Coca-Cola”
- 1887 – Noted neurologist William Hammond’s cocaine wine 2 grams/pint instead of ½ gram in Vin Mariana

![Image of spoon with 2 grams of cocaine] + ![Image of bottle of Coca-Cola]
The First Cocaine Epidemic 1880-1920

The Repressive Stage 1900 -1920

Cocaine Becoming Most Feared of All Illicit Drugs

- **1903** - Commission on the Acquisition of the Drug Habit declared cocaine, once favored by upper-class professionals, was being used mostly by "bohemians, gamblers, prostitutes, burglars, racketeers, and pimps."

- As use of cocaine increased so did abuse.

- Chronic abuse led to paranoid delusions, insomnia, malnutrition and nasal septum ulcerations.
The First Cocaine Epidemic 1880-1920

The Repressive Stage 1900 -1920

Cocaine Becoming Most Feared of All Illicit Drugs

- **1903** - Coca-Cola removes cocaine as an ingredient
- **1906** – Pure Food and Drug Act only required cocaine listed as an ingredient in Over-the-Counter remedies
- **Cocaine becomes target of the** Temperance Crusade
The First Cocaine Epidemic 1880-1920

The Repressive Stage 1900 -1920

Cocaine Becoming Most Feared of All Illicit Drugs

• 1914 - All 48 States had anti-cocaine laws

• The journal Medical Record reported: "There is no such thing as an occasional or moderate cocaine user. The line is very sharply drawn between the total abstainer and the fiend...."

• The Harrison Act passed, Nation's first major anti-narcotic law
  Cocaine classified as a narcotic, along with opium, morphine and heroin. Permitted sale of cocaine only by prescription. Banned any trace of cocaine in patent meds.
US Drug Policy 1919 vs. 2019
Driven by Stigma of Addiction

1919
• Medical Maintenance Debate
• Control by Dept. of Treasury
• Eve of Alcohol Prohibition
• No Effective Treatment
• Red Scare

2019
• Medicated Assisted Treatment
• Control by Criminal Justice
• Cannabis Legalization in selected states
• No Clear Consensus Treatment Protocols
• “Build the Wall”
The Calm Between Epidemics: 
1950s

Nonmedical Use of Cocaine Nearly Non-Existent

- 1950s - Antidrug laws increased in severity: Era of drug intolerance
- Cocaine use dwindled reaching 50,000 by the late 1950s
- Personal knowledge of a "dope fiend" was unusual for the vast majority of Americans during the 1950s.
- Cocaine Prohibition worked because of strong public consensus
- Cocaine: A problem we used to have and has now been almost eliminated
Cocaine in the early 1980’s

- Chic
- Expensive
- “Non-addictive”
- Relatively “Safe”
- ...But really expensive

July 1981
Hurricane Crack

- The Ether Factor
- Coca Paste – “basuco”
- Netherlands Antilles and Caribbean Trafficking Nations
- Benzine-Washed Cocaine
- “baking soda base” introduced to Caribbean populations in South Florida

Crack accelerates all the consequences of cocaine abuse and escalates the cocaine epidemic
Cocaine in the mid 1980s

- Killer Cocaine
- Addiction from Hell
- Crack Monsters
- Nation’s #1 Drug Problem
- By 1986: Nation’s #1 Problem
Past Year Cocaine Use among People Aged 12 or Older: 2002-2018

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Past Year Cocaine Initiates among People Aged 12 or Older: 2002-2018

Past Year Initiates (in Thousands)

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Reoccurring Patterns of Stimulant Epidemics: 1880 - 2019

Pharmaceutical Stimulants

1929 - 1970

1994 - 2019

# of users and level of consequences

Pharmaceutical Amphetamines

• 1887 – First produced in Germany

• 1919 – Japan makes more powerful version: methamphetamine

• 1929-1945 - First US Epidemic generated by pharmaceutical industry and medical profession

• Gordon Alles seeking substitute for ephedrine as a decongestant and bronchodilator focused on activity of beta-phenyl-isopropylamine (soon to be known as amphetamine)

• 1933 - Smith, Kline and French (SKF) patented amphetamine
  SKF marketed it as the Benzedrine Inhaler (325 mg of oily amphetamine base). Sold as OTC until 1948
Pharmaceutical Amphetamines

1937 AMA “Seal of Approval” for Benzedrine Sulfate amphetamine tablets for narcolepsy, Parkinsonism, and minor depression (first antidepressant)

“...if the individual is depressed...”

Myerson, A.—Anhedonia—Am. J. Psychiat., July, 1922,

When this was written—in 1922—the only stimulant drugs employed in the treatment of simple depression were of limited effectiveness.

SMITH, KLINE & FRENCH LABORATORIES, PHILADELPHIA, PA.
Pharmaceutical Amphetamines

World War II

- USA and British military supplied 5-mg Benzedrine tablets
- Germany and Japan supplied methamphetamine
- Increase in use for weight lost during war years not as approved indication but off-brand manufacturers started clinics
- 1945 supply for 1/2 million Americans with 2 tablets daily
- Abused by eating the contents of Benzedrine Inhalers
- Benzedrine abuse was multiplied many times by military exposure
Pharmaceutical Amphetamines

Post World War II

• 1949 AMA approval for weight lost advertisement

• 1952 Food and Drug Administration placed production of amphetamine & methamphetamine salts at nearly 4 times the 1949 estimate

• 1950 SKF intro’s Dexamyl (dextroamphetamine + amobarbital) for mental and emotional distress and weight lost remedy

• In the early 1960s, amphetamines consumed at a higher rate than tranquilizers.

• Largest age group among the medical users were those aged 36 to 45 years, and 85% of all amphetamine patients were women
In the 1950s, competition among pharmaceutical firms boosted amphetamine consumption dramatically, after expiration of the Alles and Smith, Kline and French patent in 1949. Source: Journal of the American Medical Association 147 (1951): 19 (advertising section).
Pharmaceutical Amphetamines

- At the end of the 1950s, monoamine oxidase inhibitors and tricyclic antidepressants were introduced and quickly acclaimed by psychiatrists as superior to amphetamines for depression.

- In the United States, however, prescribing rates for amphetamines did not decline significantly in the 1960s. Mostly prescribed by Primary Care rather than psychiatric specialists.

- By about 1960, widespread consumption had begun to make amphetamine’s negative health consequences more evident.

- Flat retail prescription sales from 1964 to 1970.
Pharmaceutical Amphetamines 1970s

- Early 1970s - BNDD (forerunner of DEA) moves all amphetamine products to Schedule II, including methylphenidate (Ritalin) and the diet drug phenmetrazine (Preludin), both of which had proved attractive to high-dose injection abusers.

- Prescription sales of amphetamines and related drugs shot up when the new restrictions were announced and then plummeted 60% below their original level when they came into effect.

- Only narcolepsy and “hyperkinetic disorder of childhood” (today’s attention deficit disorder, then rare) remained approved usages.

- Because of FDA & BNDD controls, amphetamines became relatively minor drugs of abuse by the late 1970s, while illicit cocaine use exploded
Pharmaceutical Amphetamines

1970s

• The first amphetamine epidemic was created by the pharmaceutical industry and (mostly) well-meaning prescribers

• Current amphetamine resurgence began through a combination of recreational drug fashion cycles and increased illicit supply since the late 1980s.

• Striking similarity between present and past epidemics relates to the role of pharmaceutical amphetamines

• Since 1995, medical consumption of amphetamine-type attention deficit medications, such as Ritalin (methylphenidate) and Adderall (amphetamine) has more than quintupled
Past Year Prescription Stimulant Misuse among People Aged 12 or Older: 2015-2018

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+ Difference between this estimate and the 2018 estimate is statistically significant at the .05 level.
Reoccurring Patterns of Stimulant Epidemics: 1880 - 2019

Illicit Methamphetamine

# of users and level of consequences


1970 - 1995

2008 - 2019
Methamphetamine

• 1919 - Crystallized methamphetamine was first produced from ephedrine using iodine and red phosphorus. Methamphetamine was easier to make than amphetamine and more potent.

• Nazi leaders distributed millions of doses of methamphetamine in tablets called Pervitin to their infantry, sailors and airmen in World War II.
Methamphetamine

• 1938 - **Pervitin** first sold to the German public over the counter and became quite popular. When supplies ran low on the war front, soldiers would write to their families requesting shipments of speed.

• Hitler himself consumed vast quantities of drugs during the war, including cocaine, an early version of oxycodone and crystal meth

• **Stimulants** went a long way toward the Nazi dream of creating super-soldiers.
The Hells Angels acted as security though they were loaded on drugs, cheap red wine and totally uncontrollable.
Methamphetamine

• Early 2000s, meth made from pseudoephedrine, the decongestant in drugstore products like Sudafed, poured out of domestic labs like those in the early seasons of “Breaking Bad.”

• Narcotics squads became glorified hazmat teams.
Methamphetamine

• 2005 Congress passed the **Combat Methamphetamine Act**, which put pseudoephedrine behind the counter. Although some meth makers tried “smurfing,” meth cases plummeted.

• With no more meth lab explosions on the nightly news, the public forgot about the drug.

• Mexican drug cartels stepped in
Methamphetamine

- The market is inundated with so much pure, low-cost meth that dealers have more of it than they know what to do with.

- 2018 - United States border agents seizing 10 to 20 times the amounts they did a decade ago.

- Methamphetamine, experts say, has never been purer, cheaper or more lethal.

- 2012 – 2018 Fentanyl-Contaminated Meth and Cocaine
Past Year Methamphetamine Use among People Aged 12 or Older: 2015-2018

<table>
<thead>
<tr>
<th>Age</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
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<tbody>
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<td>0.6</td>
<td>0.5+</td>
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<td>0.7</td>
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<td>12 to 17</td>
<td>0.2</td>
<td>0.1</td>
<td>0.2</td>
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<td>18 to 25</td>
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<td>0.8</td>
<td>1.1</td>
<td>0.8</td>
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<tr>
<td>26 or Older</td>
<td>0.6</td>
<td>0.5+</td>
<td>0.6+</td>
<td>0.7</td>
</tr>
</tbody>
</table>

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Past Year Methamphetamine Initiates among People Aged 12 or Older: 2015-2018

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<th>Age</th>
<th>2015</th>
<th>2016</th>
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</tbody>
</table>
Number of Drug Crime Lab Reports USA: 2007-2017

Source: NIDA-NDEWS and DEA-NFLIS
Source: DEA-NFLIS
Novel Psychoactive Substances (NPS)

- Buy Online from China
- Worldwide Delivery Services to Your Hometown
MAJOR Synthetic Cathinones

- Cathinones – Synthetic Khat
  - MDPV
  - 4 MEC
  - Methylone
  - Alpha-PVP
  - Ethylone
  - Dibutylone
  - N-Ethylpentylone
  - Others
Molly’s Enigma

• Need for Laboratory Confirmation
• Need for Accurate public information:
  – Content, Purity, Potency
• Forecasted Paradigm Shift in 21st Century Drug Production and Trafficking
• Non-Cartel, mid-level Online Dealers
• Illicitly Manufactured Non-Pharmaceutical Fentanyl Analogues from foreign clandestine labs
Changes in Synthetic Cannabinoid Packaging
Pharmacology of Synthetic Cannabinoids

• Effects almost immediate
• Onset of action is seconds to minutes
• Duration of effects: last 30 minutes – 1 hour
• Tolerance and Dependency develops
  • More drug needed for same effect
• Full and potent agonists at CB₁ Receptors
• Greater receptor affinity than THC (3 - 10 Xs)
• As compared to THC, synthetic cannabinoids produce much more intense responses with smaller amounts of the drug

www.questdiagnostics.com
Kratom

• Large tree indigenous to Thailand and Malaysia
• Leaves are usually chewed but it can be found in a dried form to create powder, tinctures and resins and is sold in the US as a powder, or in capsules, and as liquid.
Kratom Commercial Packaging
Epidemics: 1880 - 2019

- Cocaine
- Pharmaceutical Stimulants
- Methamphetamine
- Opioids

# of users and level of consequences
The National Opioid Epidemic Has Progressed to

The National Addiction Epidemic

Or Simply:

THE EPIDEMIC
The Future?

More Synthetic Drugs: NPS

- More Fentanyl Analogues
- New Synthetic Opioids
- Poisonous Cannabinoids
- Fewer Cathinones
- Direct Delivery to Cartels, small time Dealers, and Users
- Powders, Liquids, and Fake Pills

Contaminated Street Drugs

- Maybe Pure at the Lab
- But Poison when mixed
- Far more profitable to substitute or adulterate
- Deaths and Addiction continue to increase
- Medicated Assisted Treatment for Opioids, but not Stimulants
Cocaine  Pharmaceutical Stimulants  Methamphetamine  Opioids

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Historical Trends and Emerging Patterns of Substance Use Disorders: 1819 - 2019

EPIDEMICS

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