



A Salient History of Narcotics and the Current Opioid Epidemic

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United
Healthcare

| **Optum** Health Education™



‘Narcotic’

*From ancient Greek (Galen of Pergamon,
Greek physician 129-216 A.D.)*

‘norko’

“to make numb”

*referred medically to any psychoactive
substance that affects mood or behavior.*



The 'Original' Narcotic





History

The poppy has been cultivated throughout the history of civilization and opium has been used widely to treat a variety of ailments

- *~3400 BCE – Mesopotamia, Sumerians – “joy plant”*





Opium

*Source - Papaver
somniferum*

Three main psychoactive constituents

Morphine: 8-19 %

Codeine (methyilmorphine): 1-3 %

Thebaine (raw material for semi-synthetic opioids): 2-5 %



Paracelsus (1493-1541)

‘The Founder of Toxicology’

***“Only the dose makes the
poison...”***

Laudanum (1527) – Tincture of Opium

(10% opium in alcohol)

Analgesic and paregoric



“War on Drugs”

1729 *China* - *first of several opium prohibitions*

1839-42 *First Opium War* -

Qing Emperor ordered > 1000 tons opium destroyed, fought British East India Company for compensation in silver. British had swift victory with trade restored.

1857-58 *War continued with ultimate resultant increase in opium trade.*





The 'New and Improved' Narcotics





Opiates and Opioids

Natural Opiates

Morphine, Codeine, Thebaine

Semi-synthetic Opioids

Morphine: *diacetylmorphine (Heroin), hydromorphone (Dilaudid)*

Codeine: *hydrocodone (Norco), oxycodone (Percocet)*

Thebaine: *buprenorphine, oxymorphone, naloxone*

Synthetic Opioids

Fentanyl, methadone, meperidine (Demerol), Tramadol

Endogenous Opioids

Endorphins, Enkephalins, Dynorphins, Endomorphins

1973 *Drs. Candice Pert and Solomon Snyder (Johns Hopkins)*
– *elucidation of μ opioid receptor using ^3H -naloxone*



Morphine

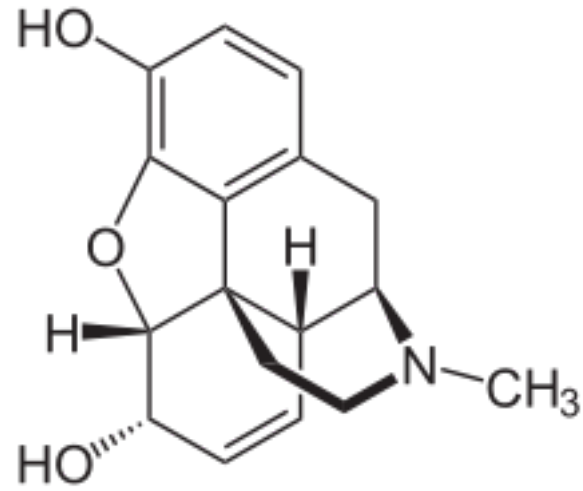
Morpheus – Greek God of Dreams

1805 first alkaloid isolated from opium poppy by Fredrich Serturner (German pharmacist)

1827 Merck Chemical Company first marketed the drug commercially

2013 523,000 kilograms produced

45,000 kilograms for severe pain management





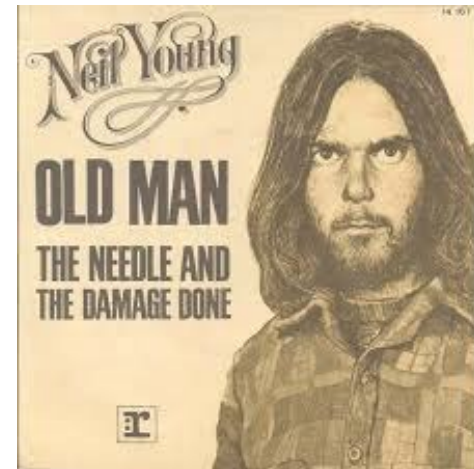


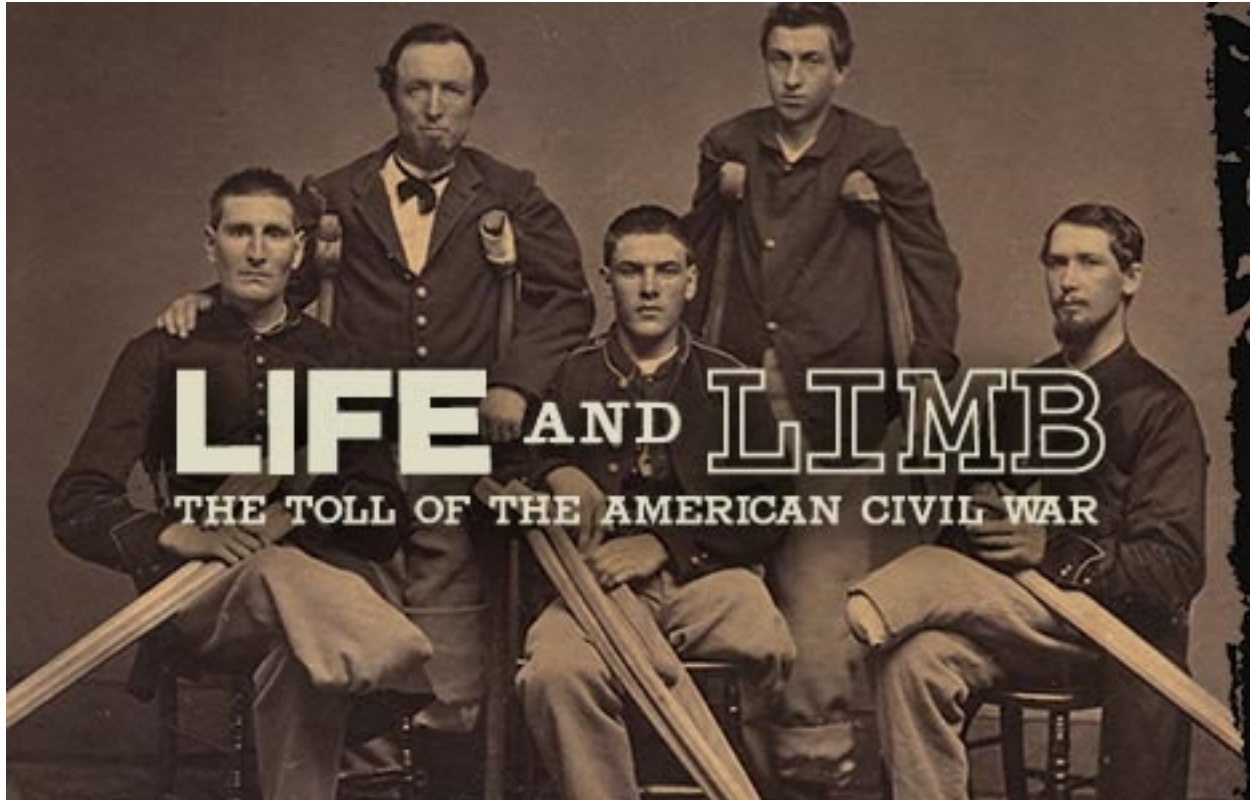
Development and refinement of hypodermic needle/ syringe

1844 Drs. Francis Rynd, Dublin, Ireland

1853 Alexander Wood, Scotland

***- revolutionized drug delivery,
and accelerated narcotic addiction
(and disease transmission!) around the
world***





1861-65 American Civil War



~1 MM casualties (3% of population!)

60,000 amputations (1 in 13 veterans!).

opium and morphine used extensively

*2.88 MM ounces opium tincture/
morphine powder*

John Pemberton, 000 pills consumed

Wounded, becomes morphine addict...

~400,000 soldiers addicted! – “soldier’s disease”



1863 Vin Mariani

Angelo Mariani

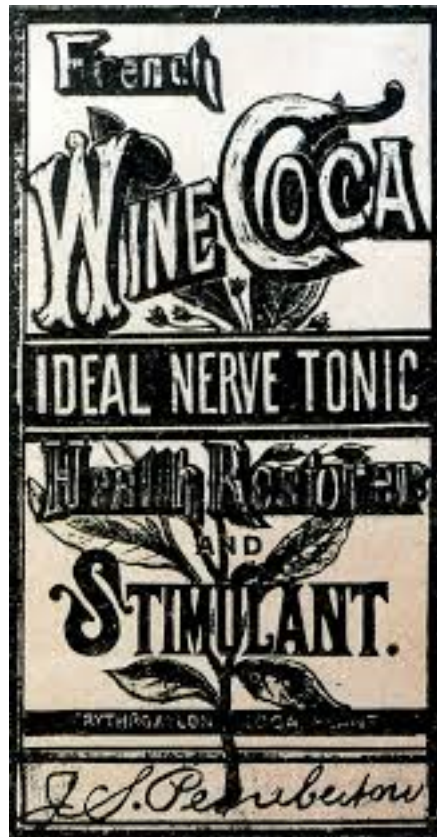
Parisian chemist

Bordeaux wine and coca leaves



 1860s French Wine Coca John Pemberton

“a most wonderful invigorator of sexual organs”



1800s - Temperance Movement

- promoting the temperance or complete abstinence from the consumption of alcoholic beverages.



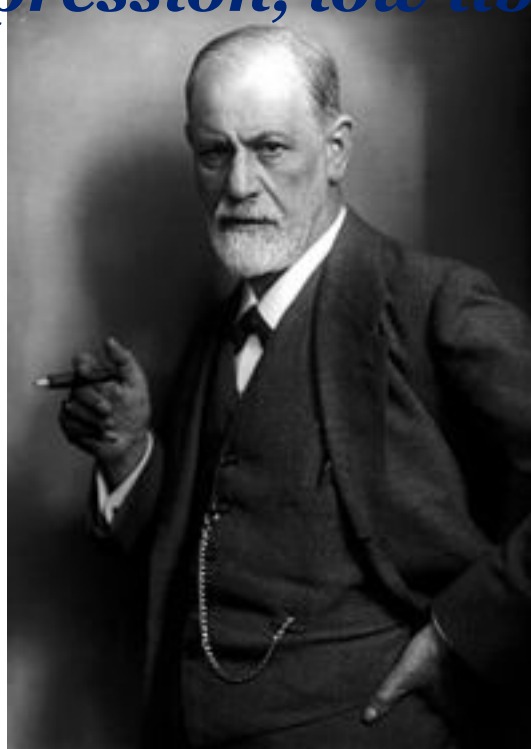
Carry Nation, Activist



1884 Cocaine Champion!? Sigmund Freud

Austrian neurologist, ‘Father of Psychoanalysis’

“Cure for alcoholism, opium addiction, depression, low libido...”

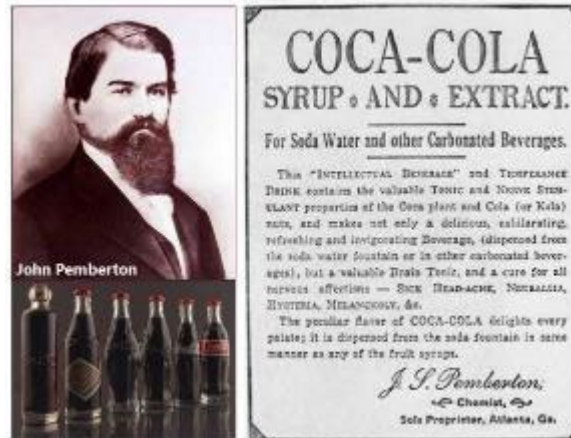




1886 Inventor of Coca Cola!

***John Pemberton, pharmacist/
chemist***

***Forced to remove alcohol from French Wine
Coca by Temperance Movement***





Coca-Cola

ISA
DELIGHTFUL
PALATABLE + HEALTHFUL
BEVERAGE
IT RELIEVES FATIGUE AND IS INDISPENSABLE
FOR
BUSINESS AND PROFESSIONAL **MEN** STUDENTS WHEELMEN ATHLETES
It relieves mental and physical exhaustion
IS THE FAVORITE DRINK FOR
LADIES
WHEN
THIRSTY + WEARY
DESPPENDENT

CUT THIS OUT
AT BOTTLED LINES

SOLD AT
FOUNTAINS
5c

*The most refreshing
drink in the world*

SOLD IN
BOTTLES
5c

MADE IN ATLANTA



Coca-Cola

The Great Temperance Beverage

AMONG modern business men, and with the rising cult of younger men, the most marked tendency of the day is toward *strict temperance*.

In this connection Coca-Cola admirably fills the universal American demand for a strictly temperance beverage, which is at once delicious, refreshing and absolutely harmless; *and which stands for those truly American traits—healthy activity of mind and body!*

It has been repeatedly analyzed by chemists of National reputation and declared to be as harmless as tea or coffee.

Carbonated in bottles
On draught at founts **5c**



1903 Cocaine taken out of Coca Cola!

1914 Cocaine made illegal nationally!


***Coca-Cola Co. vs. Koke Company
U.S. Supreme Court (1920)***



Koke syrup label, circa 1910.



COCAINE
TOOTHACHE DROPS
Instantaneous Cure!
PRICE 15 CENTS.
Prepared by the
LLOYD MANUFACTURING CO.
219 HUDSON AVE., ALBANY, N. Y.
For sale by all Druggists.
(Registered March 1890.) See other side.



ONE NIGHT
TRADE MARK
COUGH SYRUP

EACH OUNCE CONTAINS

ALCOHOL, (less than 1%)	4/16m
CANNABIS INDICA, F.E.,	4/16m
CHLOROFORM,	2 1/2m
MORPHIA, SULPH.,	1/8gr

SKILLFULLY COMBINED WITH A NUMBER OF OTHER INGREDIENTS

DIRECTIONS
DOSE: One-half to one full teaspoonful three



BABY EASE
TRADE MARK

THE
World's
Best Baby Medicine

6-
PRAISED BY MOTHERS,
RECOMMENDED BY PHYSICIANS
FOR ALL BOWEL COMPLAINTS
TEETHING TROUBLES ETC.

FAC-SIMILE SIGNATURE OF
J.P. Marshall
ON EVERY BOTTLE
25¢ & 50¢ AT ALL DRUG STORES

For Sale by



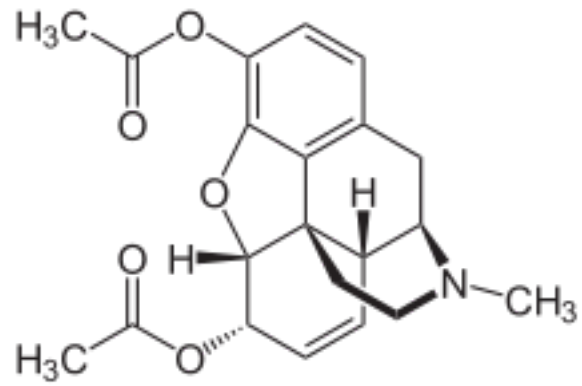
Heroin

'diamorphine' 2-4x more potent than morphine

1874 *C.R. Alder Wright (chemist)
synthesizes by acetylation*

1888 *Bayer markets heroin as
analgesic*

1924 *U.S. banned importation, sale
and manufacture*





1895-1910 Bayer markets heroin world-wide

1912 Opium is made illegal in the U.S.

BAYER
PHARMACEUTICAL PRODUCTS.

We are now sending to Physicians throughout the United States literature and samples of

ASPIRIN

The substitute for the Salicylates, agreeable of taste, free from unpleasant after-effects.

HEROIN

The Sedative for Coughs,
HEROIN HYDROCHLORIDE
Its water-soluble salt.
You will have call for them. Order a supply from your jobber.

Write for literature to
FARBENFABRIKEN OF ELBERFELD CO.
40 Stone Street, New York,
SOLE U.S. AGENTS



1919 - 18th Amendment to U.S. Constitution!

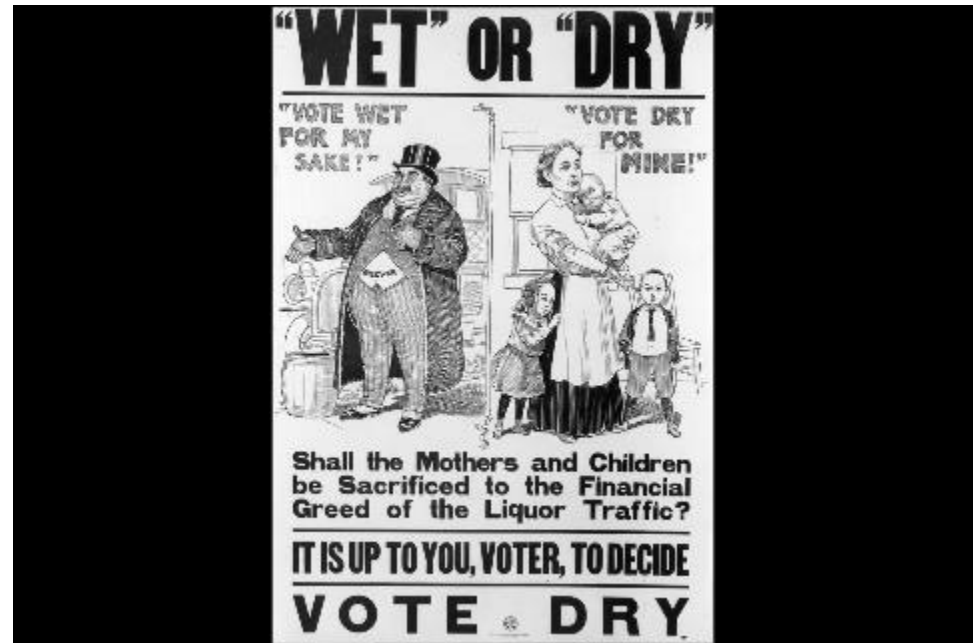
**PROHIBITION of production, importation,
transportation and sale of alcoholic
beverages**





1933 - 21st Amendment to U.S. Constitution!

Prohibition Repealed!





Legislation

1906 Food and Drugs Act

1914 Harrison Narcotics Tax Act

1931 Paris Convention

1938 Federal Food, Drug and Cosmetic Act

1961 Single Convention on Narcotics

1970 Controlled Substances Act



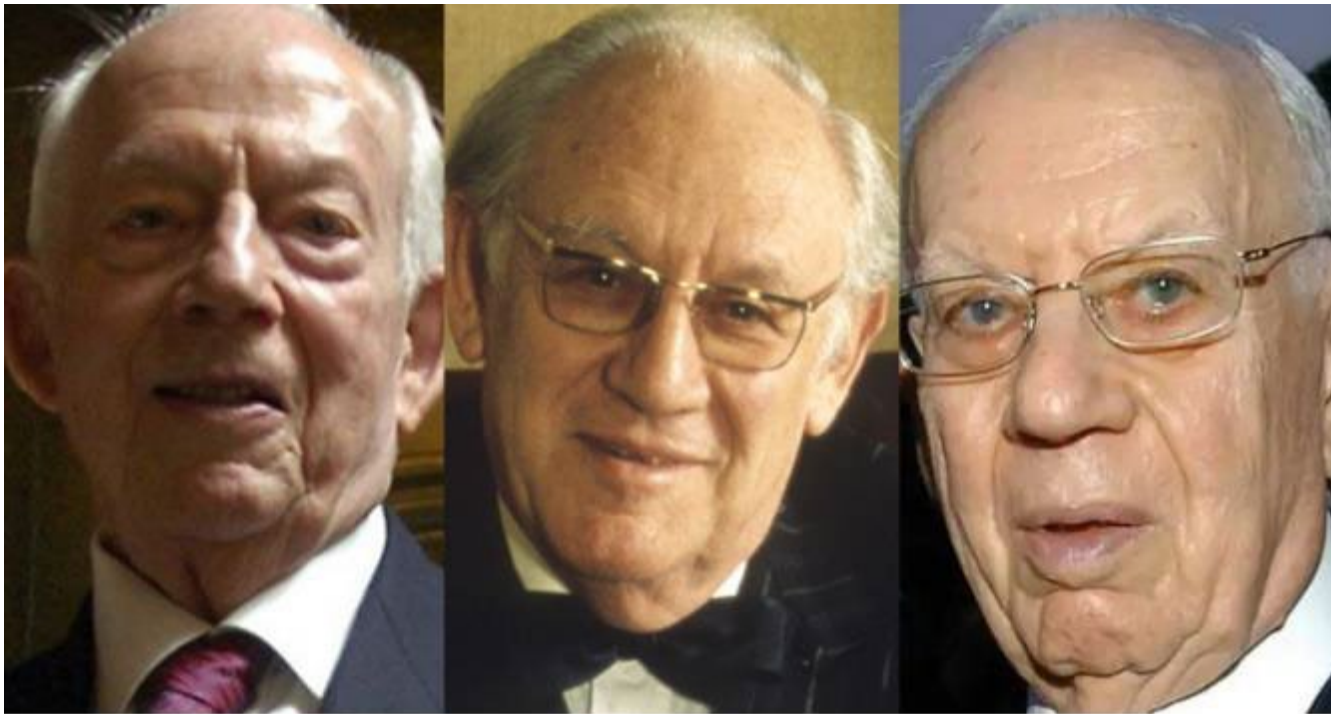
*“Better Things for Better Living Through Chemistry”
DuPont, 1935*





The Sackler Brothers

1952 - Three doctors purchase Purdue Frederick Company,
which grew to become Purdue Pharma (1991)



RAYMOND

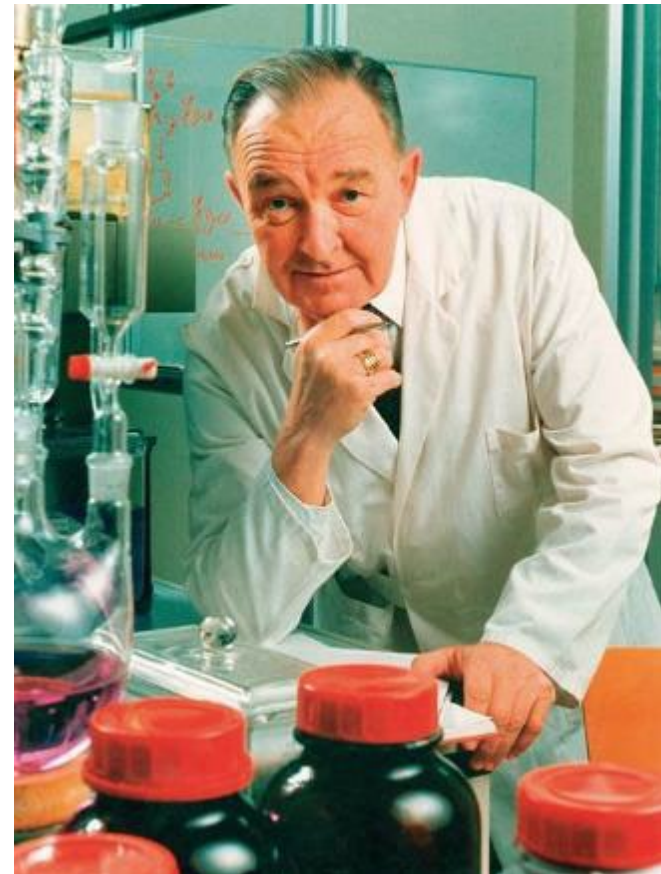
ARTHUR

MORTIMER



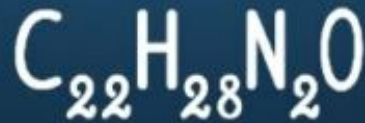
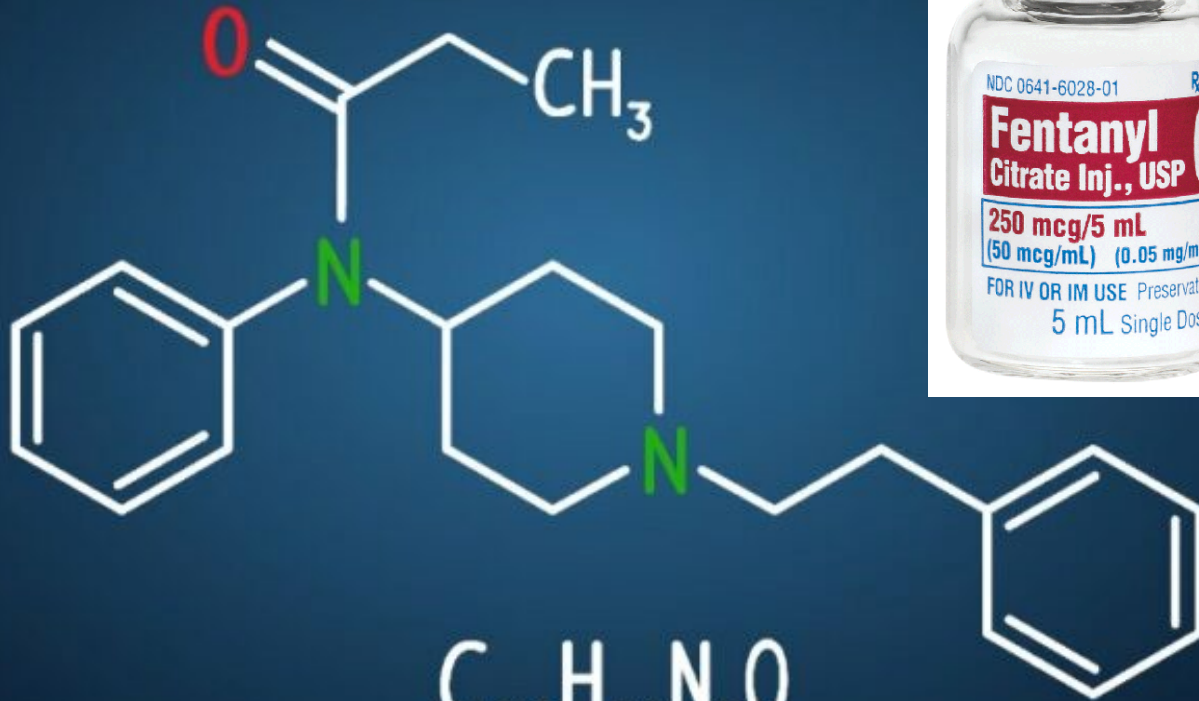
Dr. Paul Janssen

Synthesized Fentanyl – 1960
Founded Janssen Pharmaceuticals,
later acquired by Johnson & Johnson (1961)





Fentanyl





Controlled Substances **Act (1970)**

Schedule classification system

–

***(I, II, III, IV, V) that refined
and expanded previous
legislation (FDA-1930 and
DEA-1973), based on three
main components:
Acceptable medical use***

Abuse or dependency potential

Safety profile



Schedule I

e.g. Heroin, LSD, psilocybin, mescaline, marijuana (THC, CBD), MDMA (Ecstasy), methaqualone, GHB (2000)



NO acceptable medical use

HIGH abuse or dependency potential

Negative safety profile



Schedule II

e.g. morphine, codeine, oxycodone, hydromorphone, hydrocodone (2014), meperidine, fentanyl, cocaine, amphetamine, PCP, methamphetamine, methylphenidate, short-acting barbituates (pentobarbital)

Acceptable medical use

HIGH abuse potential

Abuse may lead to severe psychological or physical dependence



**Potency also makes the
poison!**

Schedule I - Heroin

Schedule II - Fentanyl

***Even though Fentanyl is 50x
more potent than Heroin!***

February, 2018 until May, 2021

***DEA issued temporary order to categorize
Fentanyl as Schedule I***

July 31, 2021

***Janssen Pharmaceuticals, Inc. discontinues
Duragesic Fentanyl transdermal system***



Schedule III

***e.g. anabolic steroids (testosterone),
ketamine, buprenorphine
long-acting barbituates (butalbitol),
marinol (synthetic THC),
paregoric (opium and camphor)***

Acceptable medical use

Abuse potential less than Schedule I or II

***Abuse may lead to moderate or low physical
or high psychological dependence***



Schedule IV

*e.g. benzodiazepines (alprazolam),
benzo-like Z-drugs (zolpidem), long-
acting barbituates (phenobarbital),
tramadol, carisoprodol (2012),
modafanil*

Acceptable medical use

LOW abuse or dependency potential!

*Abuse may lead to **limited** psychological or
physical dependence!*



Schedule IV

Benzodiazepines



e.g. alprazolam, lorazepam, diazepam, chlordiazepoxide, midazolam, temazepam, clonazepam, flunitrazepam

1956 Librium synthesized
1960 FDA approval of Librium
1963 Valium





Schedule V

Antitussive, antidiarrheal, and mild analgesic preparations

e.g. promethazine and codeine, diphenoxyllate (Lomotil), pregabalin (Lyrica)

***Acceptable** medical use*

***LOW** abuse or dependency potential*

*Abuse may lead to **limited** psychological or physical dependence*



Opioids

Schedule I Heroin

*Schedule II Oxycodone, Morphine,
Codeine, Fentanyl*

Schedule III Acetaminophen and Codeine

Schedule IV Tramadol

Schedule V Promethazine and Codeine

1972 *Fentanyl becomes commercially available
for severe pain in cancer patients.*



The Opioid Epidemic

Its Origins

*The How,
Where,
What,*

*When,
Who,*

and Why of it all...





1972 *Contin (continuous drug-delivery system)*

1984 *MS Contin (Morphine Sulfate)*

1996 *OxyContin (Oxycodone)*

1999 *Non-cancer related pain market 86%*

2003 *~50% of OxyContin Rx's from primary care MDs*

1996 *OxyContin Rx's 670,000 2002 6.2 MM*





OxyContin

1996 Sales Revenue \$48 MM

2000 ~\$1.1 BB!

Passing Viagra as the most profitable medication!!

1996 - 2001 Total Revenue exceeded \$2.8 BB

In 2001, Purdue Pharma spent \$200 MM on marketing and promotion





1995 FDA-approved Label

“iatrogenic ‘addiction’ to opioids legitimately used in the management of pain is very rare”

“Delayed absorption as provided by OxyContin tablets is believed to reduce the abuse liability of a drug”

2001 Black Box Warning added

These statements were removed!

WARNING:

OxyContin is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.

Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing OxyContin in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

OxyContin Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

OxyContin Tablets are NOT intended for use as a prn analgesic.

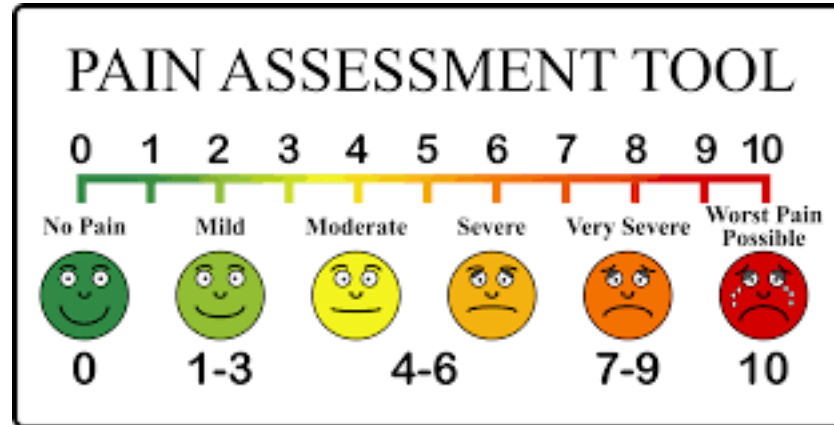
OxyContin 80 mg and 160 mg Tablets ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. These tablet strengths may cause fatal respiratory depression when administered to patients not previously exposed to opioids.

OxyContin TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OxyContin TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.



The 5th Vital Sign

?



Pain!

Hippocrates (460 – 370 BCE)

“Primum non nocere” - First, Do no harm!



1990s *Pharmaceutical Industry* aggressively lobbied the **Diversion Control Division** of DEA to allow for dramatic increases in quotas for importation of raw poppy into U.S. combined with an aggressive marketing campaign promoting opioids for pain management to primary care doctors.

Dramatically changed the ‘culture’ of pain management in the U.S. at many levels of industry, government, law enforcement, and healthcare.



Diversion Control

Division

(DEA, DOJ)

Mission – to prevent, detect, and investigate the diversion of controlled pharmaceuticals and listed chemicals from legitimate sources while ensuring an adequate and uninterrupted supply for legitimate medical, commercial, and scientific needs.



Most Prescribed Medicines in U.S. (2010, in MM Rx)

1. Hydrocodone

131.2

(70.9 in 2018)

2. Simvastatin	94.1	
3. Lisinopril	87.4	
4. Levothyroxine	70.5	
5. Amlodipine		57.2
6. Omeprazole	53.4	
7. Azithromycin	52.6	
8. Amoxicillin	52.3	
9. Alprazolam	48.8	
10. Metformin	48.3	

11. ACEI

47.6



Hydrocodone

#1 prescribed medication in U.S. until 2015!

*October, 2014 – DEA changed Schedule
from **III** to **II***

99% of world's supply consumed in U.S.





Most Abused Medicines in **U.S.**

- 1. Oxycontin**
- 2. Xanax**
- 3. Vicodin**
- 4. Suboxone**
- 5. Adderall**
- 6. Valium**
- 7. Percocet**
- 8. Ambien**
- 9. Fentanyl**
- 10. Klonopin**



Global Poppy Production (2014, in hectares)

1. Afghanistan	224,000
2. Myanmar (Burma)	57,600
3. Australia (Tasmania)	20,631
4. Mexico	15,000
5. India	12,237
6. Laos	6,200
7. Pakistan	2,300
8. Columbia	298
9. Iran	100
10. Turkey	90
11. Thailand	80



Afghanistan

*~2/3 of world's opium
production*

*(also produces 90% of world's
heroin)*

1999 *Taliban prohibits poppy cultivation,*

*production drops by 94 % from **2000-2001** to
8,000 hectares!?*

2001 *U.S. engages Taliban in 'War on Terror'*

2014 *224,000 hectares cultivated for poppy!*



“Opium Island”

Size ~ Ohio

Population ~ 500,000!

***~ 90 % of global legal
poppy production!***

***(~50% thebaine content,
Genetically engineered by J&J)***

~\$100 MM/year!!







The Biggest Players

Production Farmers in Tanzania ('Opium Island')

Manufacture Purdue Pharma, Malinckrodt (generic opioids)

***Distribution Wholesale – McKesson, Cardinal Health,
AmerisourceBergen***

Retail – CVS, Walgreens

Legislation/ Regulation Congress, FDA

Enforcement DEA, DOJ

Prescription Physicians, Surgeons and Dentists

Consumption Patients and the Public



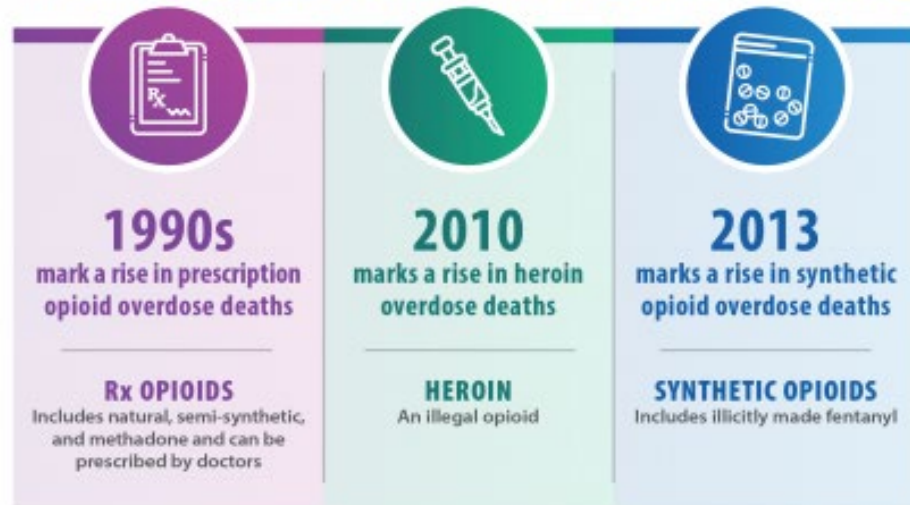
Causes, Consequences, Casualties!

RISE IN OPIOID OVERDOSE DEATHS IN AMERICA

MORE THAN
564,000
PEOPLE DIED FROM AN
OPIOID OVERDOSE
(1999-2020)

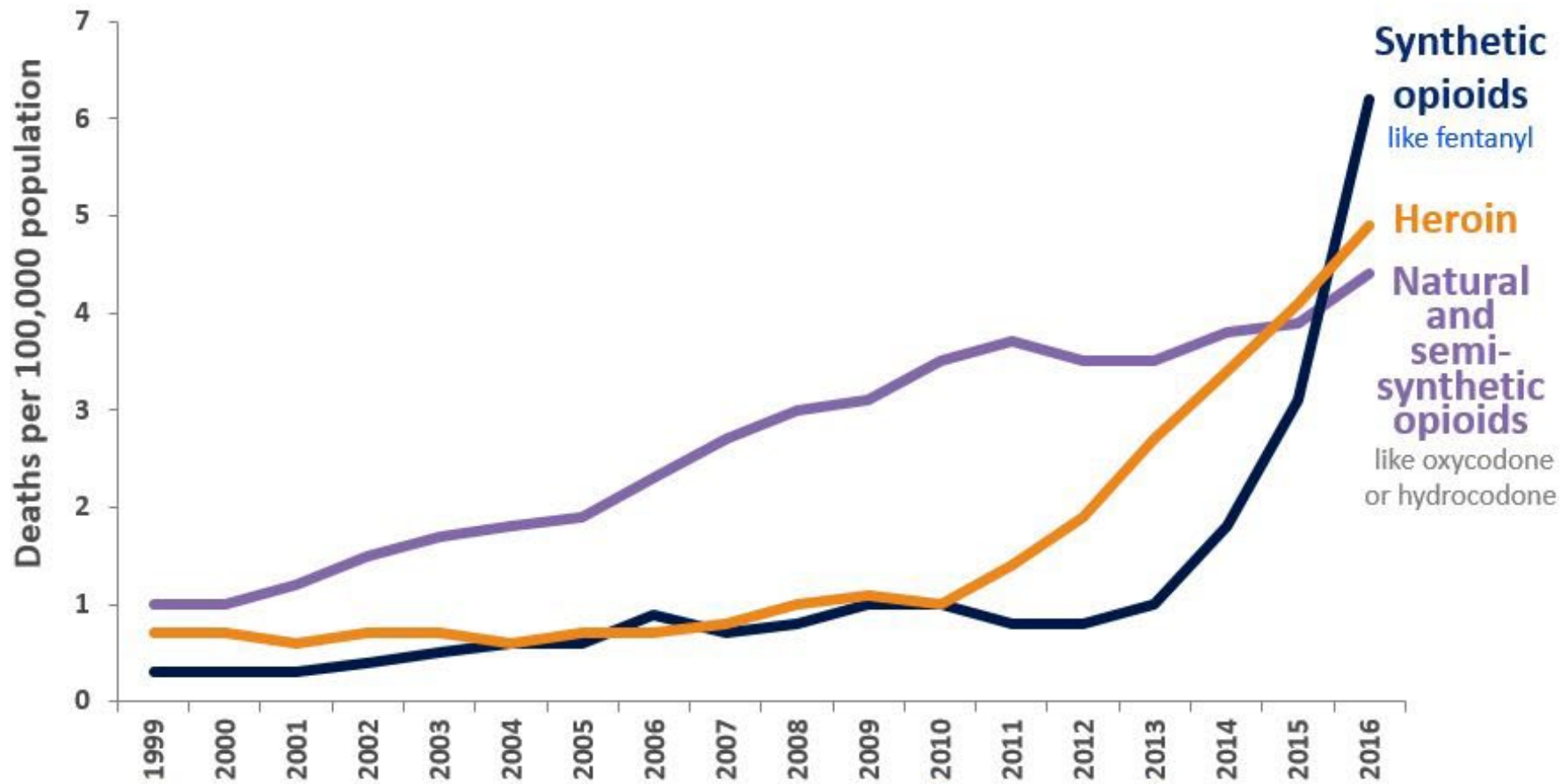
www.cdc.gov

A Multi-Layered Problem in Three Distinct Waves



Learn more about the evolving opioid overdose crisis: www.cdc.gov/drugoverdose

3 Waves of the Rise in Opioid Overdose Deaths



Wave 1: Rise in Prescription Opioid Overdose Deaths

Wave 2: Rise in Heroin Overdose Deaths

Wave 3: Rise in Synthetic Opioid Overdose Deaths



Consumption

1996 – Purdue Pharma introduced

Oxycontin

*Total production quota for oxycodone = 8.3
tons*

2011 TPQ = 105 tons!

1200 percent increase over 14 years!

*2009 - over 500 MM doses of oxycodone
distributed in Florida alone!*



Consumption

2006 – 2014 Over 100 BB opioid pain pills prescribed

In 2012 alone, 259 MM Rxs (\$24 BB)

2015 ~92 MM people use Rx opioids in U.S.





Consequences

1999 - 2014 *>165,000 deaths due to opioid overdoses (CDC).*

2005 *~10 MM adults (3-4 % U.S. population) receive prescriptions for long-term opioid therapy.*

1999 – 2013 *ED visits involving opioid ODs increased 3x!*

2005 *~10K opioid overdose deaths per year*



Consequences

2013 *~2 MM people >12 years old meet DSM IV criteria for opioid use disorder.*

2013 *>22,700 opioid prescription overdose deaths out of a total of almost 44,000 deaths from drug overdose (52 %).*

2015 *>50 adult deaths per day in U.S. due to prescription opioid overdose!*

Contribution



***2007 - Cardinal Health distributed
18 MM doses of Hydrocodone over 9
months through “Internet
Pharmacies”***

April, 2010 – February, 2012

***Walgreens (Jupiter, FL) sent 13.7 MM
doses of oxycodone to SIX
pharmacies***



Collateral

Fines ‘failing to report suspicious orders of controlled substances’

2007 McKesson \$13.2 MM

2008 Cardinal Health \$34 MM

2016 Cardinal Health \$44 MM

“It’s a cost of doing business!”

Matthew Murphy, DEA

Conversion

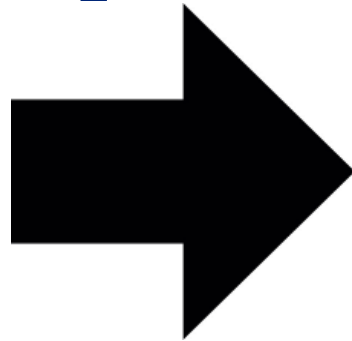


***2012 – 2015 Deaths from heroin surpass
OxyContin***

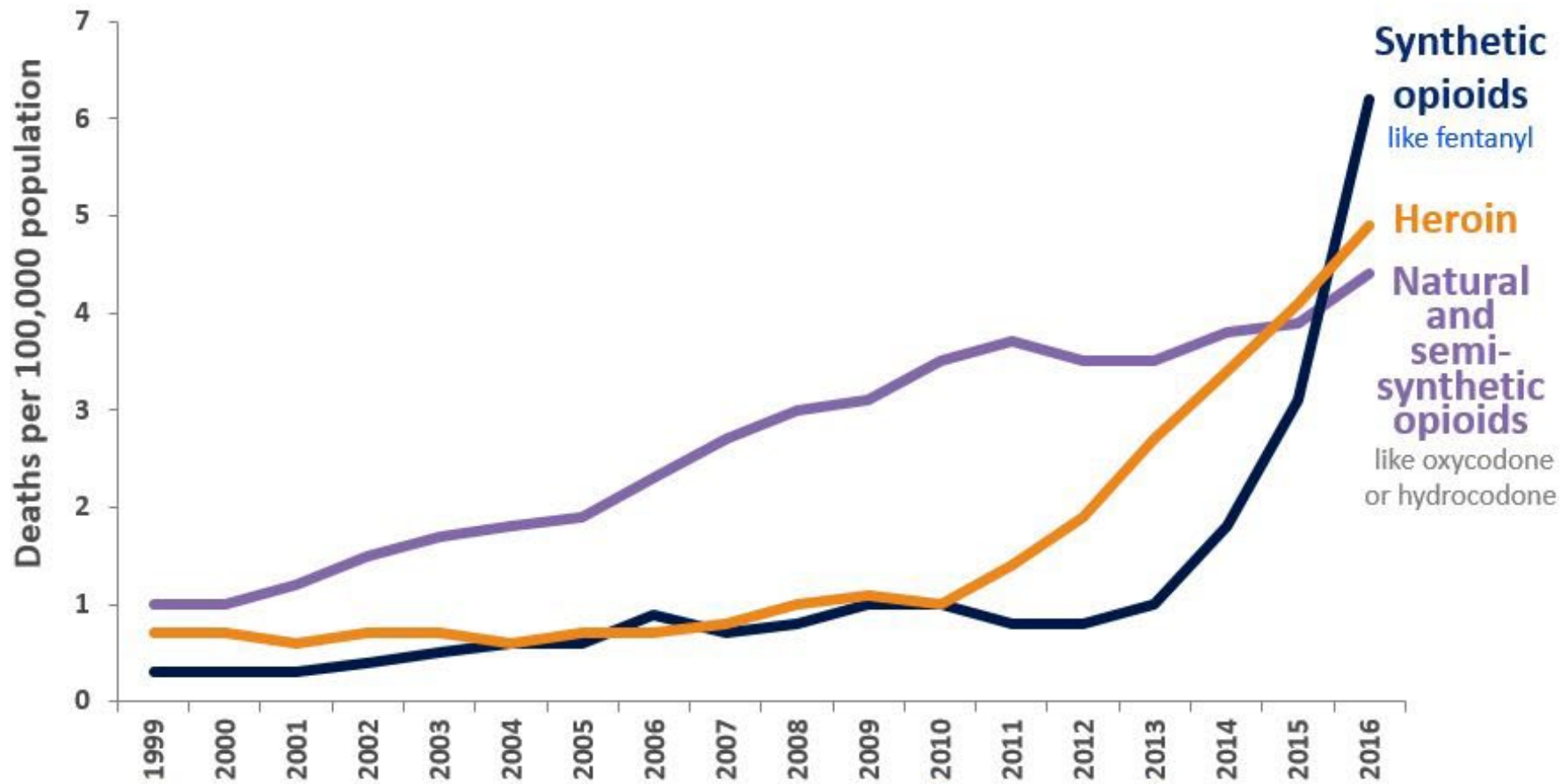
2013 Street use of Fentanyl explodes

2013 - 2016 Fentanyl deaths increase by 540%

***~80% of new heroin users started from Rx
opioids***



3 Waves of the Rise in Opioid Overdose Deaths



Wave 1: Rise in Prescription Opioid Overdose Deaths

Wave 2: Rise in Heroin Overdose Deaths

Wave 3: Rise in Synthetic Opioid Overdose Deaths



Community

***8/26/2016 Huntington, W. Virginia
(population ~50K)***

***27 ODs in four hours from fentanyl-laced
heroin with one death!***

***2011 420,000 ED visits due to opioid
ODs***

2019 ~1 MM ED visits

30% increase during Covid-19 pandemic!



Casualties



**The Artist known as
'Prince'**

Died April 21, 2016

Fentanyl overdose...

“Turn the Tide” campaign

August, 2016

**U.S. Surgeon General plea to 2.3 MM
Healthcare workers and
Public Health leaders**





Convergence

July, 2016 ***‘Ensuring Patient Access
and Effective Drug Enforcement
Act’***

- ***significantly modified the Controlled Substances Act (1970)***
- ***increased the standard of proof required for the DEA to suspend a DEA registration for the distribution of narcotics***

Increased the standard from “preponderance of evidence” to “beyond a reasonable doubt”



Collaboration/ Concession

*From the Controlled Substances Act
(1970)*

the phrase “imminent danger to the public health”

was amended to

“there is a substantial likelihood of an immediate threat that death, serious bodily harm, or abuse of a controlled substance will occur in the absence of an immediate suspension of the registration.”

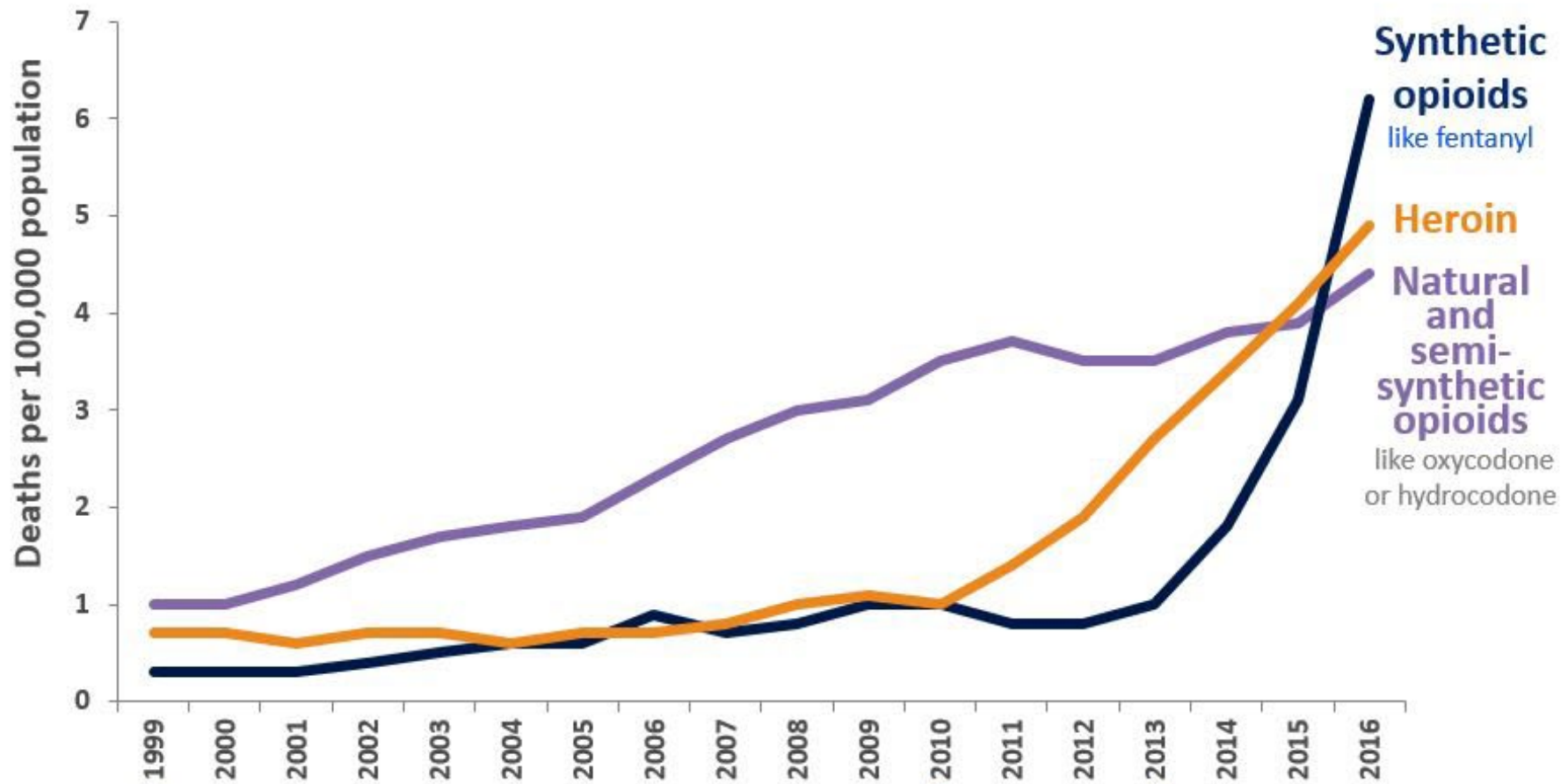


Containment

10/4/2016 Diversion Control Division (DEA) announces reduction in almost every Schedule II opiate and opioid medication that may be manufactured in the U.S. in 2017 by 25 percent or more!

The Aggregate Production Quota (APQ) established by the Final Order of the Federal Register is the total amount of a controlled substance necessary to meet the estimated medical, scientific, research, industrial and export needs for the year, and for the maintenance of reserve stocks.

3 Waves of the Rise in Opioid Overdose Deaths



Wave 1: Rise in Prescription Opioid Overdose Deaths

Wave 2: Rise in Heroin Overdose Deaths

Wave 3: Rise in Synthetic Opioid Overdose Deaths



Currently

THE OPIOID EPIDEMIC BY THE NUMBERS

CURRENTLY...



274

People who die every day from opioid-related drug overdoses¹



9.3 m

People who misuse prescription opioids annually⁴



100,306

People who died between April 2020-2021 from overdosing on opioids²



5,480

People who misused prescription pain relievers for the first time today⁴



3 million

People who have an opioid use disorder²



13,516

Deaths attributed to overdosing on prescription pain relievers²



500,000

People who are dependent on heroin²



937,800

Estimated number of people who died from a drug overdose from 1999-2020⁴



66%

Overdose deaths attributed to fentanyl¹



30%

Increase in overdose deaths from 2020-2021²



\$271.5 billion

Annual economic impact of prescription and illicit drug misuse⁵

Sources: ¹ CDC's National Center for Health Statistics, ² NCH Opioid Addiction 2021, ³ CDC / NIDA / US Surgeon General 2021, ⁴ SAMSHA National Report 2020

Updated November 2021. For more information, visit <http://www.hhs.gov/opioids/>





Currently

Opioid Rx revenue ~\$100 BB/ year

~70K opioid OD deaths per year

*Every 25 minutes, a baby is born with
opioid withdrawal in U.S.*



Casualties

2021– 42% of fake, opioid prescription pills contain a potentially lethal dose of fentanyl

2022 – 68%!

2 mg!





Casualties

“One Pill Can Kill!”

2 mg – a potentially fatal dose of fentanyl!



COUNTERFEIT DRUGS

OXYCODONE



REAL

FAKE

ADDERALL



REAL

FAKE

SOURCE: DEA



Contraband

PRESS RELEASE

Fentanyl Seizures at Border Continue to Spike, Making San Diego a National Epicenter for Fentanyl Trafficking; U.S. Attorney's Office Prioritizes Prosecutions and Prevention Programs

Thursday, August 11, 2022

For Immediate Release

U.S. Attorney's Office, Southern District of California





Cash

2022 - DEA seized over 50.6 MM fentanyl-laced fake prescription pills and >10,000 pounds of fentanyl powder, representing nearly 380 MM potentially fatal doses of fentanyl!

2x the amount in 2021!





Crime

~ 50% of ALL incarcerations in the U.S. are drug-related crimes!

'Texas Lawmakers Unanimously Pass Bill That Will Allow Fentanyl Dealers To Be Charged With Murder'

By Cassandra MacDonald
March 17, 2023
The Gateway Pundit





Cartels

“WEAPON OF MASS DESTRUCTION”: Mexican Resident Charged With Possessing **OVER 1 MILLION Fentanyl Pills** Equaling **108 Kilograms** With Intent to Sell in Arizona **AND 2.5 Million+ Pills Seized at The Border Last Week**

By **Jordan Conradson**

Mar. 24, 2023

The Gateway **Pundit**





Consequences

*By 2017, cumulative revenue of
OxyContin*

~\$37 BB!

*‘Purdue Pharma, Sacklers reach \$6
billion deal with state attorneys general’*

March 3, 2022

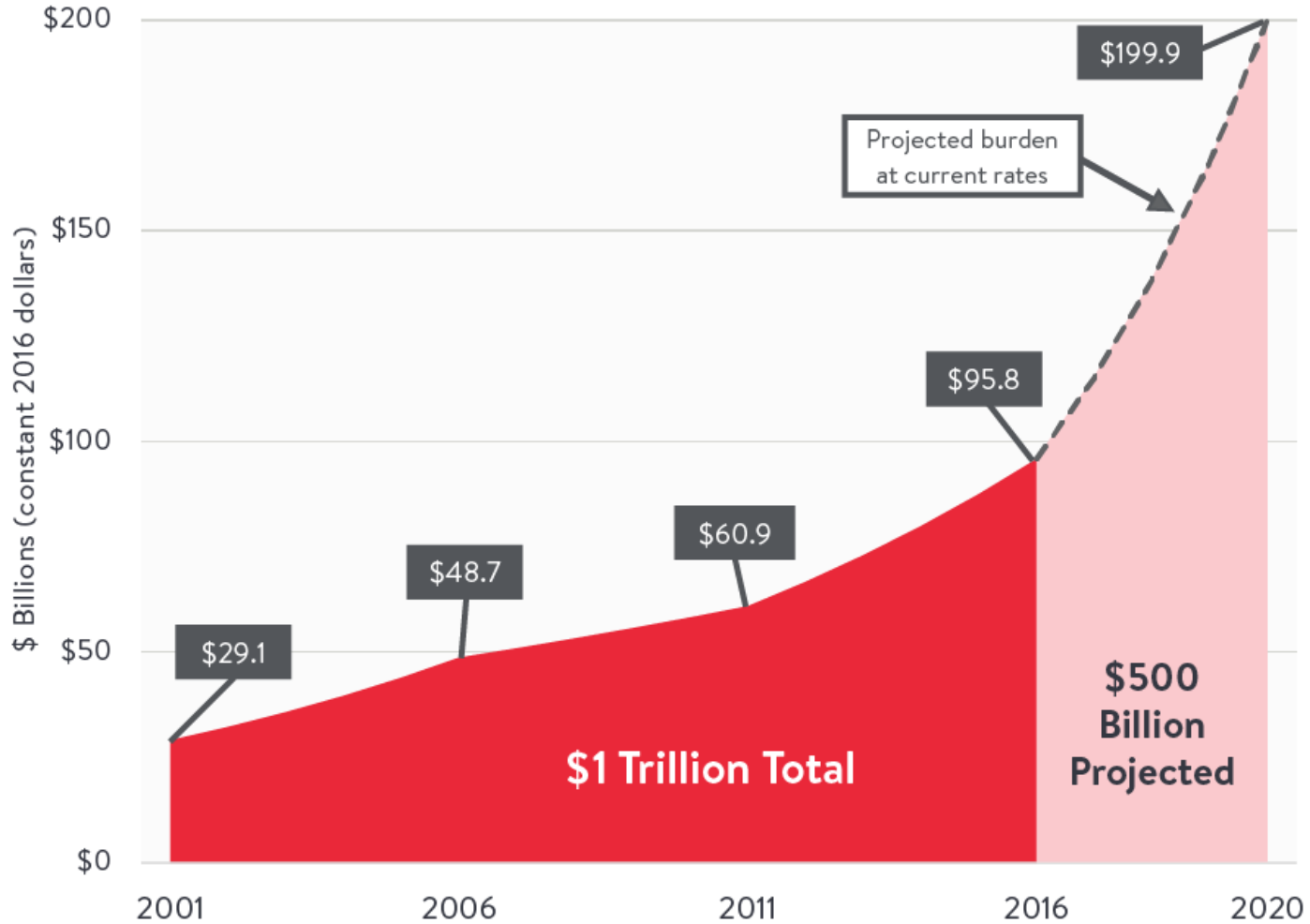
Heard on All Things Considered, PBS

By Brian Mann and Martha Bebinger



Costs

Total and Projected Costs of the Opioid Epidemic



* Data between labeled estimates interpolated using constant growth rates



Crisis!

‘Their toddler took a nap in an Airbnb — and fentanyl killed her’

By Meryl Kornfield and Lisa Rein

The Washington Post

March 3, 2023





Thank You!

