The Nature and Extent of the Opioid Epidemic

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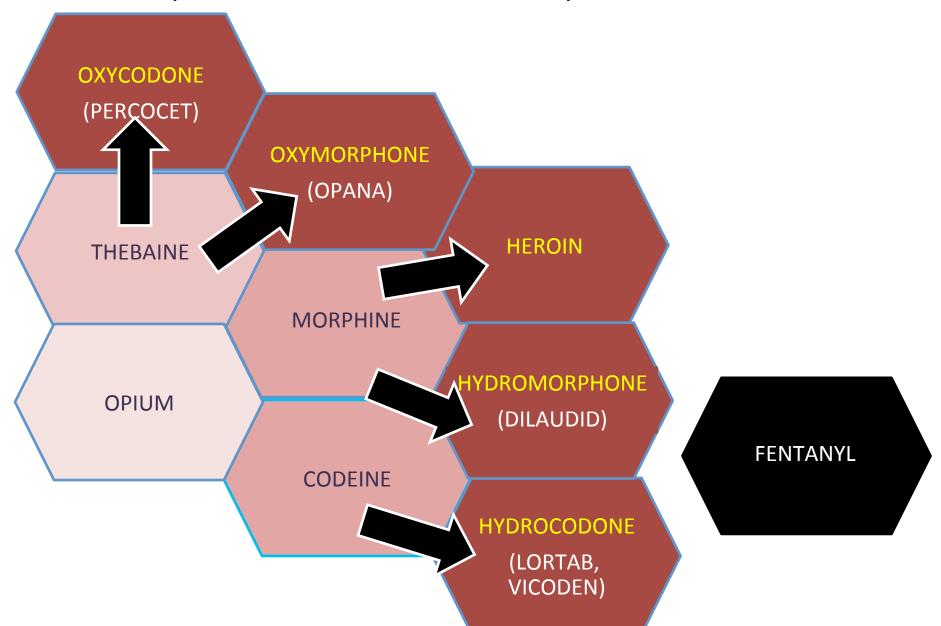
Presentation at the 2019 Fulbright Student Symposium
Combating Addiction and Addressing the Opioid Crisis
Buffalo, New York
April 25, 2019

The Unfolding of an Epidemic

- The nature of opiates
- The nature and origin of the epidemic
- The popular narrative
- Questioning the popular narrative
- The epidemic unfolded



OPIUM, OPIUM COMPOUNDS, AND DERIVATIVES



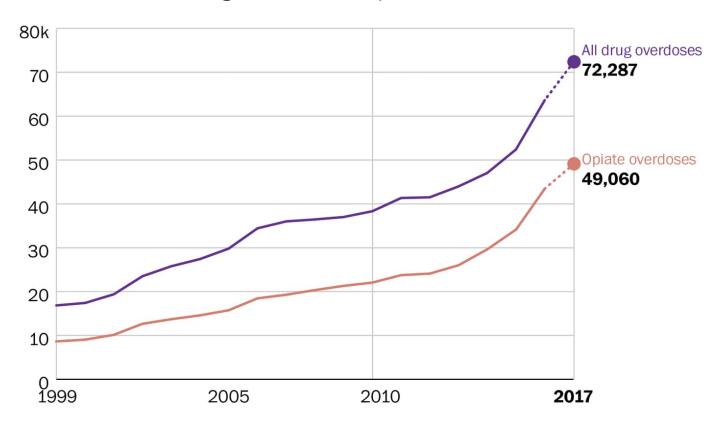
Additional Opioids Used for Treatment of Addictions

- Naloxone
- Naltrexone
- Buprenorphine
- Morphine

Death rates from drug overdoses in the U.S. 1999-2017

Overdose deaths hit record high in 2017

Annual deaths from all drug overdoses and opiate overdoses



Note: 2017 figures are provisional

Source: Centers for Disease Control and Prevention

Origins of the Epidemic

 Porter J, Jick H. Addiction rare in patients treated with narcotics 1980 NEJM

Full text of the Porter and Jick letter

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 no 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.

Origins of the Epidemic

- Porter J, Jick H. Addiction rare in patients treated with narcotics 1980 NEJM
- American Pain Society pushes pain as the 5th vital sign 1990s
- Oxycontin approved by FDA as less appealing to drug abusers and aggressive marketing by company

Origins of the **Epidemic**

FREEDOM FROM PAIN

Extra strength pain relief free of extra prescribing restrictions.



Up to five refills in 6 months No triplicate Rx required

Excellent patient acceptance.

In 12 years of clinical experience, nausea, sedation and constipation have rarely been reported.1

COMPARATIVE PHARMACOLOGY OF TWO ANALGESICS						
	Consipation	Florgerstory Depression	Sedaton	Enesis	Physical Dependence	
HYDROCODONE		x		1 - /	X	
OXYCODONE	XX	XX	XX	xx	XX	

Blank space indicates that no such activity has been reported. Table adapted from Facts and Compa 1991 and Catalano RB. The medical approach to management of pain caused by cancer. Semin Oncol 1975; 2, 379-92 and Reuler JB, et. al. The chronic pain syndromer misconceptions and management. Ann

The heritage of VICODIN; over a billion doses prescribed.2

- VICODIN ES provides greater central and peripheral action than other hydrocodone/acetaminophen combinations.
- Four to six hours of extra strength pain relief from a single dose
- The 14th most frequently prescribed medication in America²



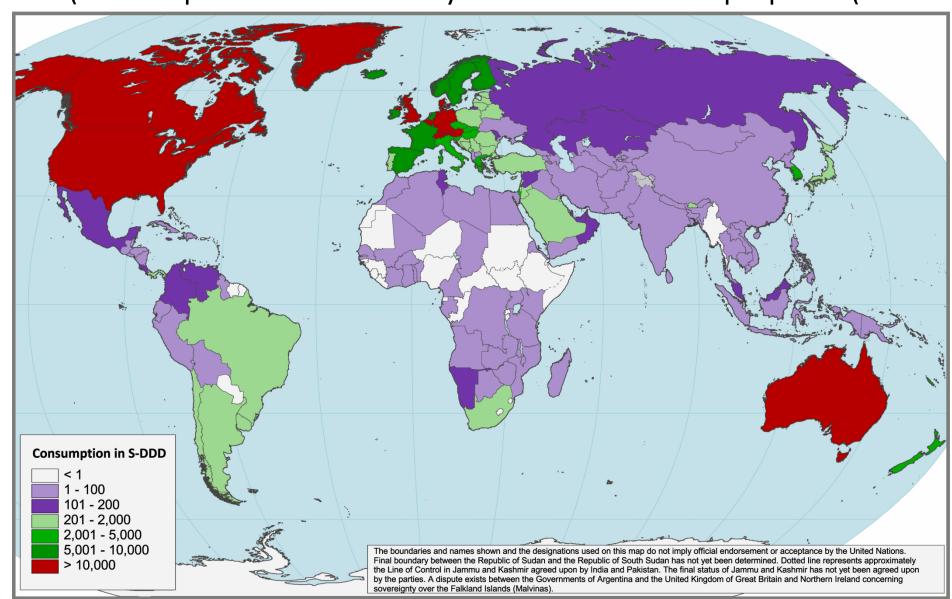
Tablet for tablet, the most potent analgesic you can phone in.

⁽hydrocodone bitartrate 5 mg [Warning: May be habit forming] and acetaminophen 500mg)

Data on Ne. Knoll Pharmaceuticals
 Standard inclusing new prescription audit

Availability of opioids* for pain management (2010-2012 average)

(Consumption in defined daily doses for statistical purposes (S-



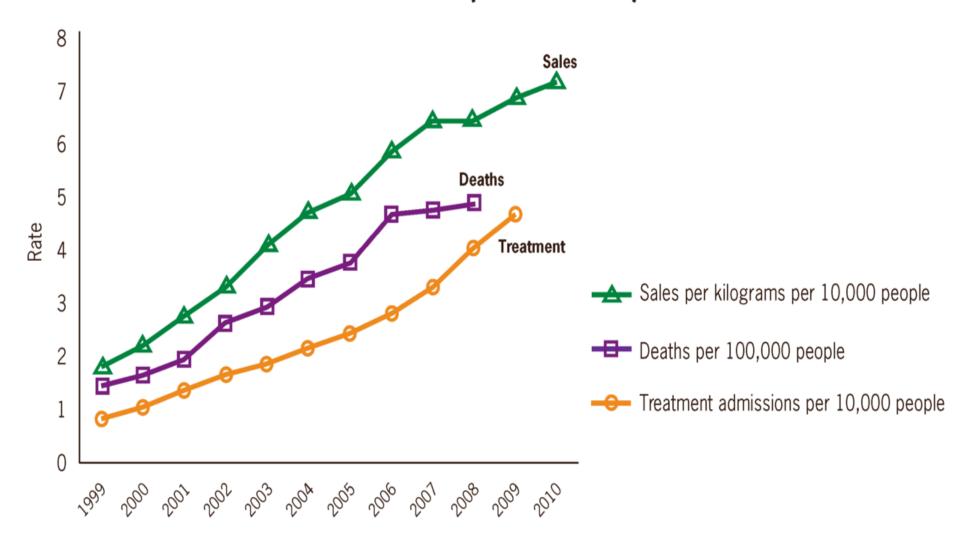
For First Time, Pharmaceutical Distributor Faces Federal Criminal Charges Over Opioid Crisis

The charges against the wholesaler, Rochester Drug Cooperative, and two of its former executives marked a new tactic for prosecutors in tackling the epidemic of addiction to prescription painkillers. Laurence F. Doud III, who had served as chief executive of Rochester Drug Cooperative, surrendered to Drug Enforcement Administration agents on Tuesday.

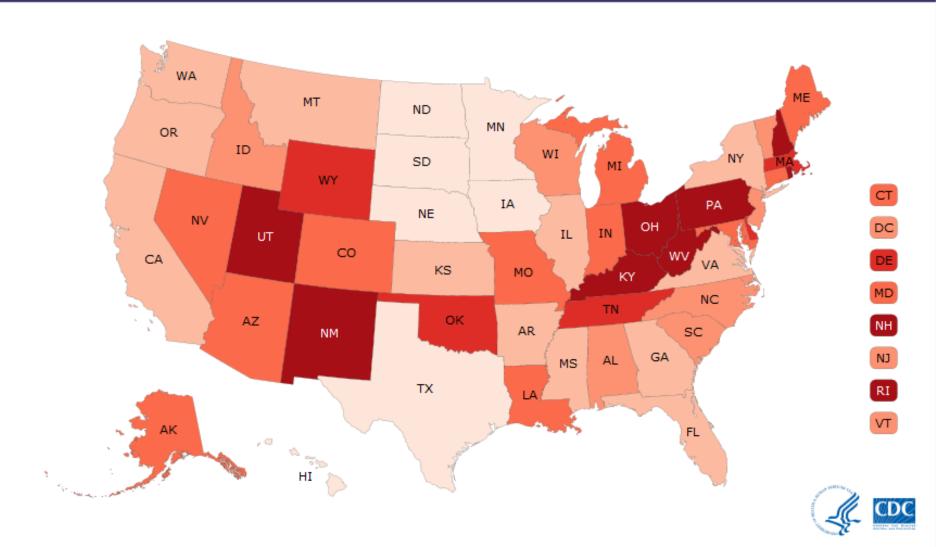


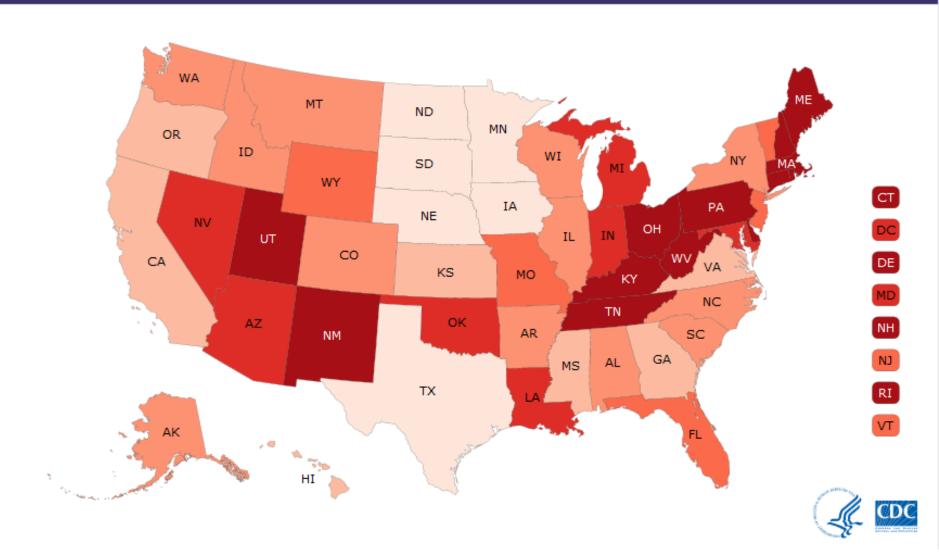
Credit Dave Sanders for The New York Times Image

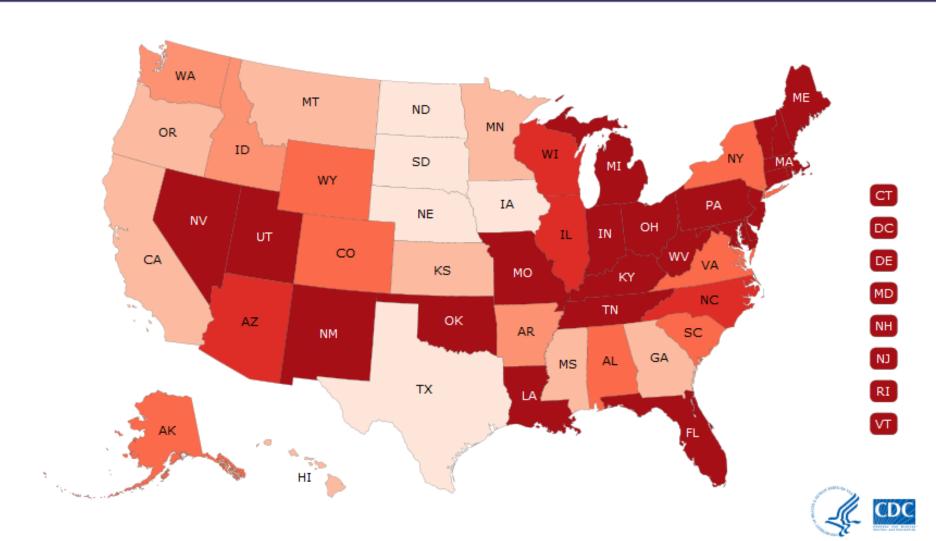
Rates of prescription painkiller sales, deaths and substance abuse treatment admissions (1999-2010)

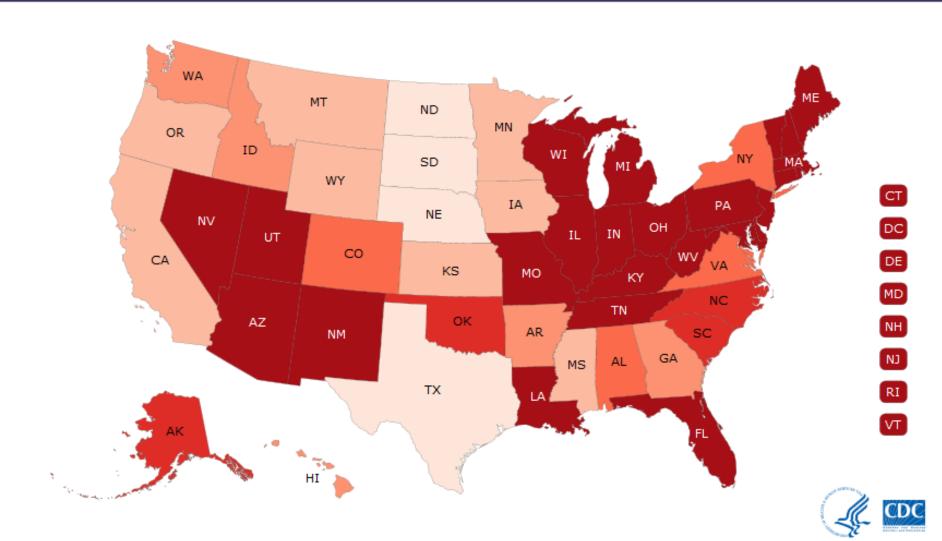


SOURCES: National Vital Statistics System, 1999-2008; Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 1999-2010; Treatment Episode Data Set, 1999-2009



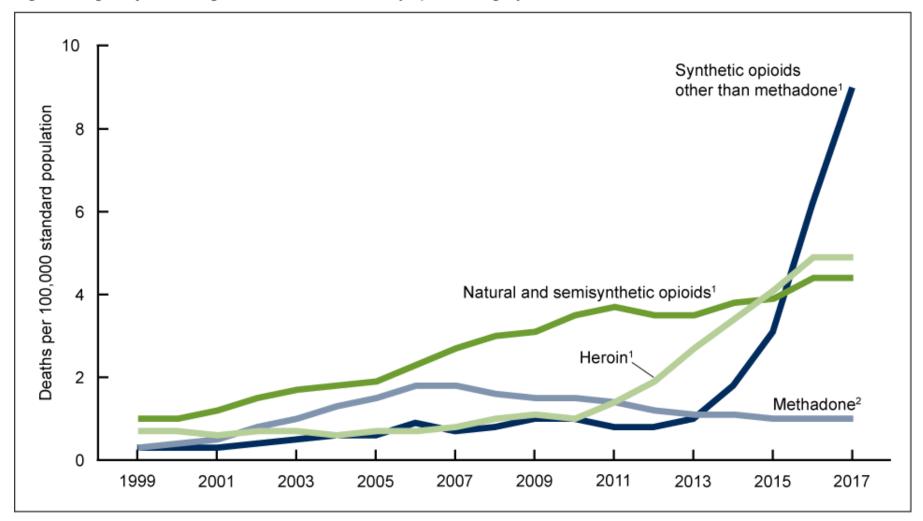






Death rates from opioids, heroin, and fentanyl through 2017

Figure 4. Age-adjusted drug overdose death rates, by opioid category: United States, 1999–2017



¹Significant increasing trend from 1999 through 2017 with different rates of change over time, p < 0.05.

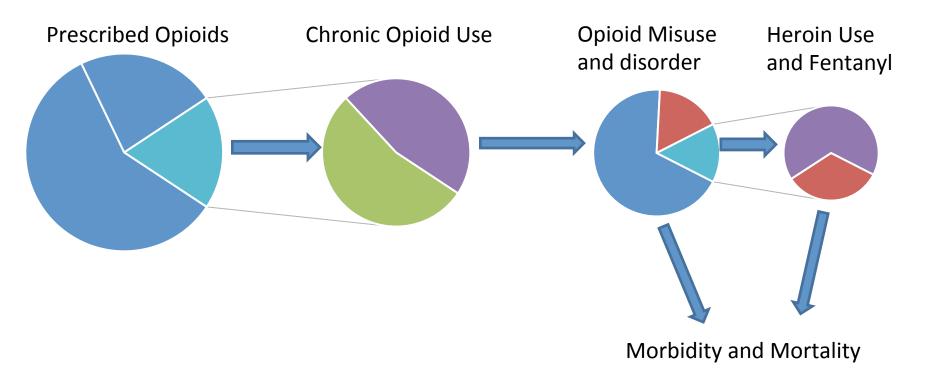
²Significant increasing trend from 1999 through 2006, then decreasing trend from 2006 through 2017, p < 0.05.

Deaths due to opioids- 2017

•	Drug overd	ose deaths	70,237
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- Any opiate overdose deaths 47,600
- Opioid pain med deaths 17,029
- Heroin overdose deaths 15,482
- Fentanyl 28,466

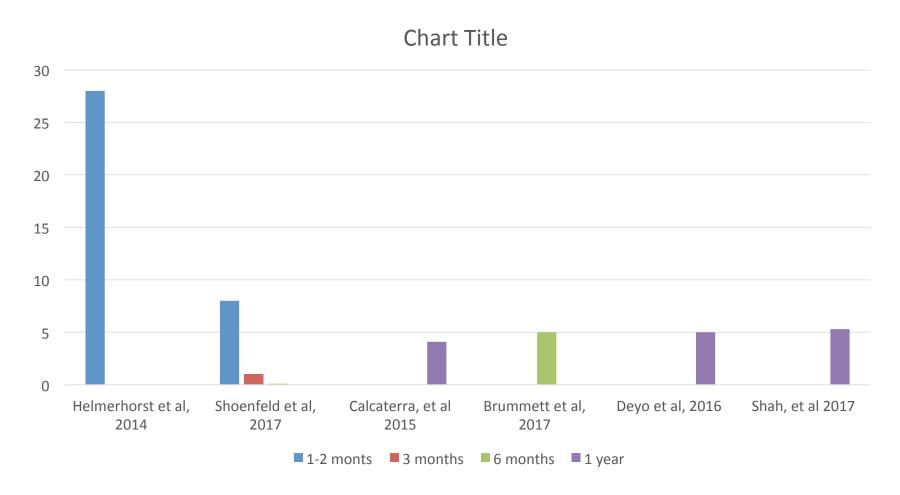
Popular narrative



Key aspects of this narrative

 What is the likelihood of regular use of opioids leading to misuse?

Rates of continued opioid use after medical procedures



Drug dependence diagnosis according to duration on opioid prescription

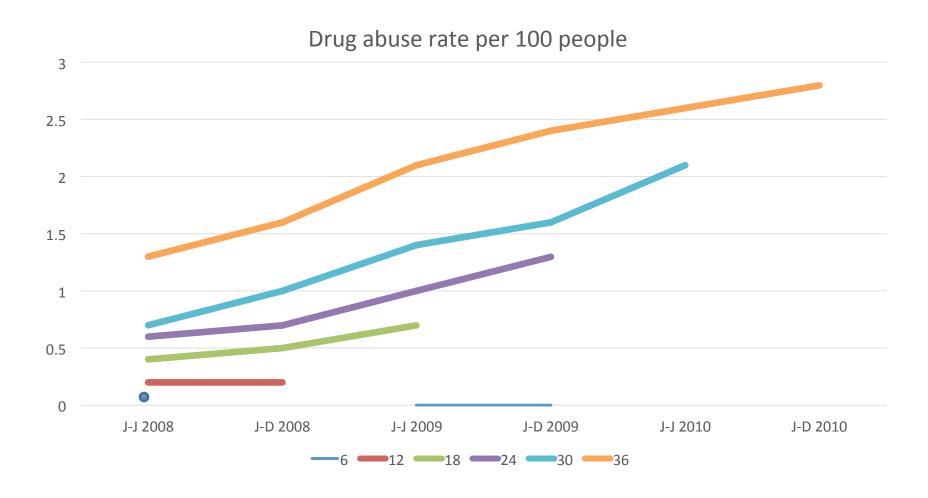


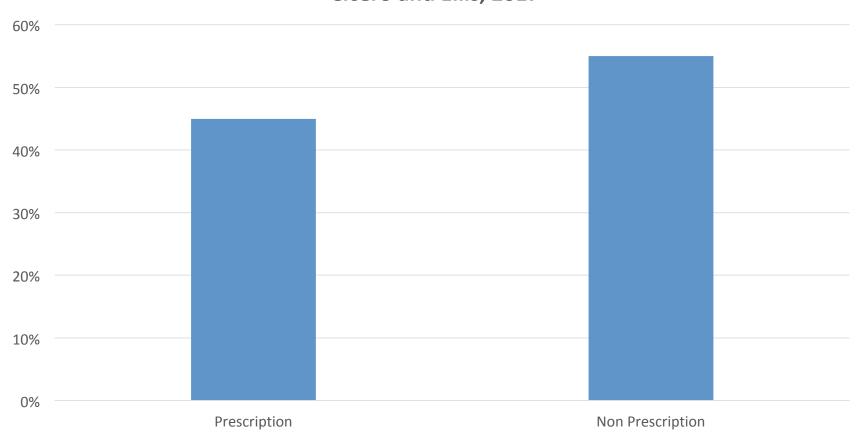
Figure adapted from Paulozzi, Zhang, Jones & Mack, 2014

Key aspects of this narrative

- What is the likelihood of regular use of opioids leading to misuse?
- Are most people who become addicted introduced to opioids through a prescription?

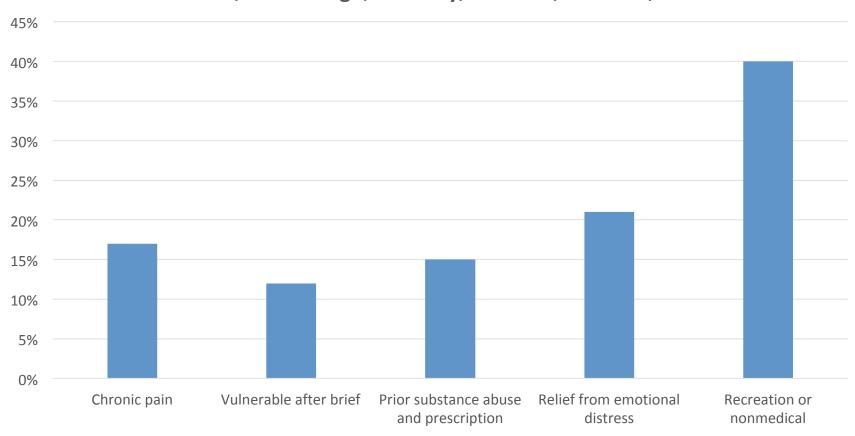
Sources of initial exposure among patients entering treatment for opioid use disorder



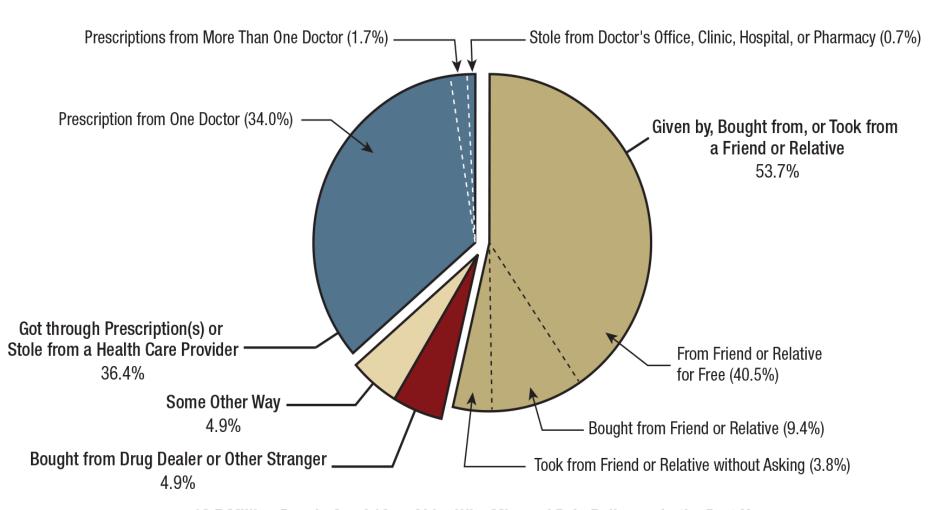


Sources of initial exposure among 121 patients with EMR evidence of opioid dependence

Stumbo, Yarborough, McCarty, Weisner, & Green, 2017

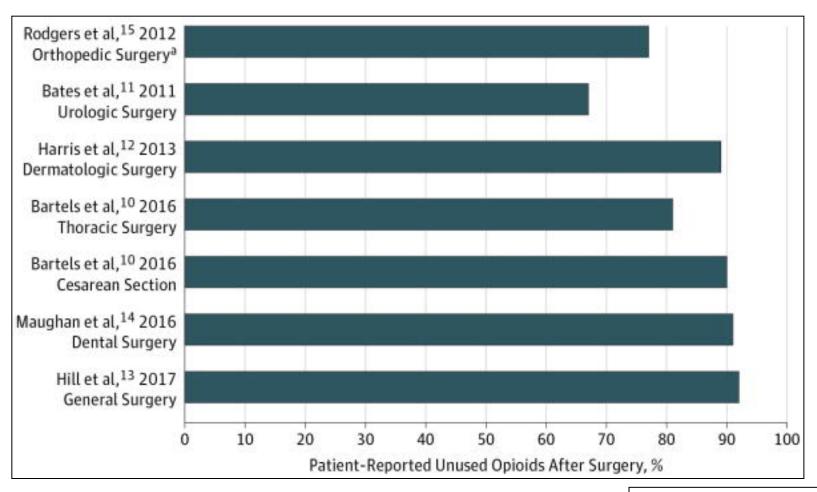


Source of most recent opioid



12.5 Million People Aged 12 or Older Who Misused Pain Relievers in the Past Year

Prevalence of Unused Opioids Prescribed After Surgery



Prevalence of Unused Opioids Prescribed After SurgeryFigure. . aPercentage of patients reporting use of 15 tablets or fewer.

Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review.

Bicket, Mark; Long, Jane; Pronovost, Peter; Alexander, G; Wu, Christopher

JAMA Surgery. 152(11):1066-1071, November 2017. DOI: 10.1001/jamasurg.2017.0831

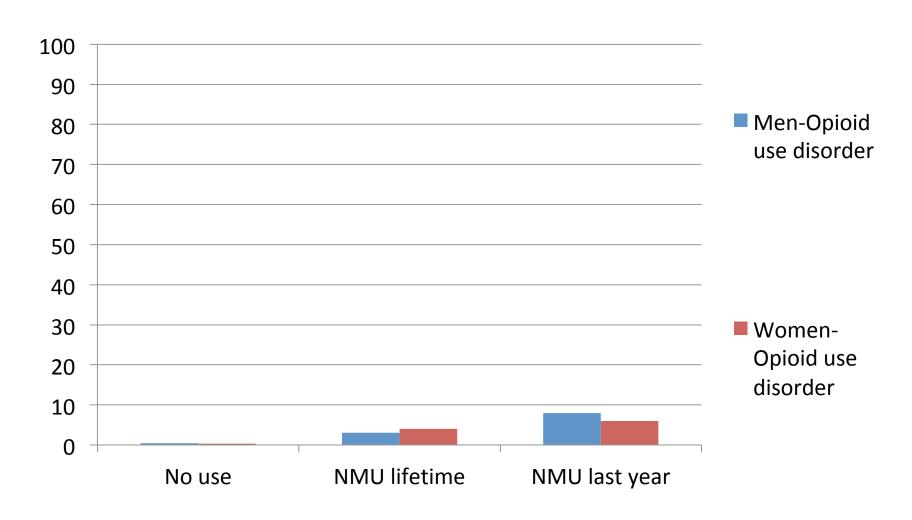




Key aspects of this narrative

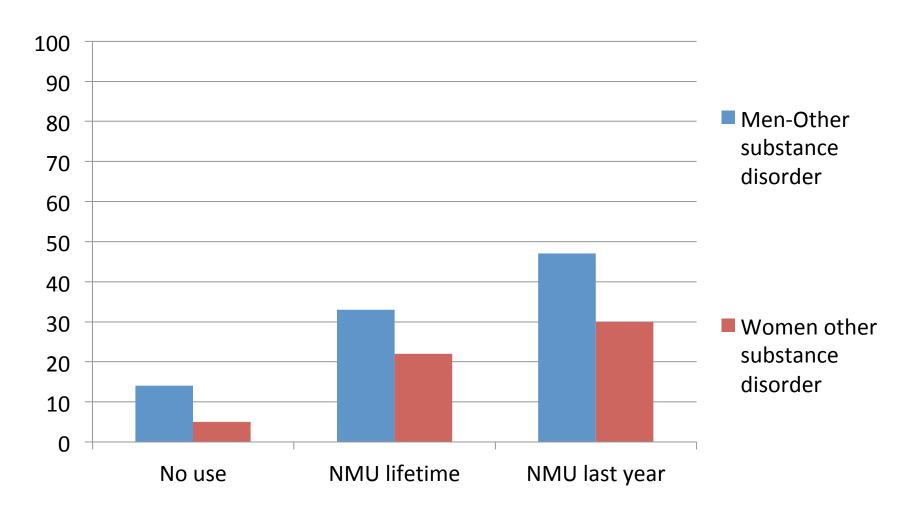
- What is the likelihood of regular use of opioids leading to misuse?
- Are most people who become addicted introduced to opioids through a prescription?
- What is the likelihood of misuse leading to substance use disorders?

Opioid use disorder in 2004-2005 among nonmedical users in 2001-2002



Boyd et al, 2009; NESARC data

Substance Use Disorder in 2004-2005 among non-medical users in 2001-2002



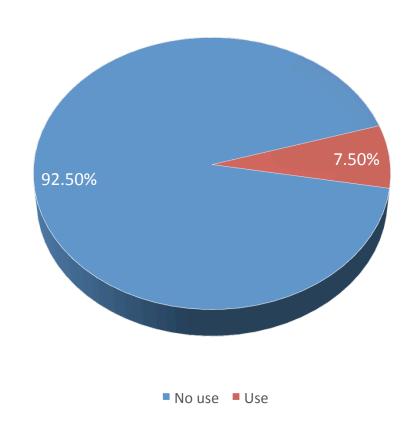
Boyd et al, 2009; NESARC data

Key aspects of this narrative

- Are most people who become addicted introduced to opioids through a prescription?
- What is the likelihood of regular use of opioids leading to misuse or disorder?
- What is the likelihood of misuse leading to substance use disorders?
- What is the likelihood of misuse leading to heroin use?

Most non medical users of opioids do not become heroin users

Rate of initiation to heroin over 3 years among NMUPO

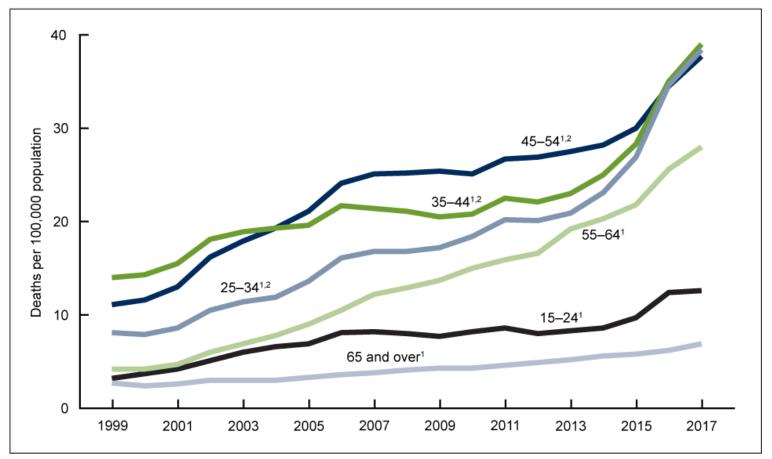


Key aspects of this narrative

- Are most people who become addicted introduced to opioids through a prescription.
- What is the likelihood of regular use of opioids leading to misuse or disorder
- What is the likelihood of misuse leading to substance use disorders?
- What is the likelihood of misuse leading to heroin use?
- What's going on with those who don't start heroin?

Death rates increasing for older population that is less likely to use heroin

Figure 2. Drug overdose death rates, by selected age group: United States, 1999-2017



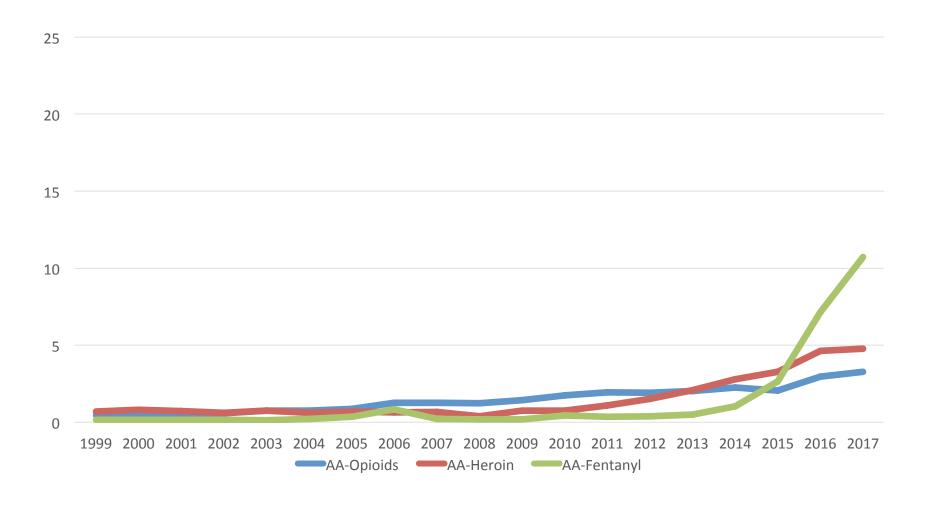
Significant increasing trend from 1999 through 2017 with different rates of change over time, p < 0.005.

²2017 rates were significantly higher for age groups 25–34, 35–44, and 45–54 than for age groups 15–24, 55–64, and 65 and over, *p* < 0.05. The rate for age group 35–44 was significantly higher than the rate for age group 45–54 and statistically the same as the rate for age group 25–34.

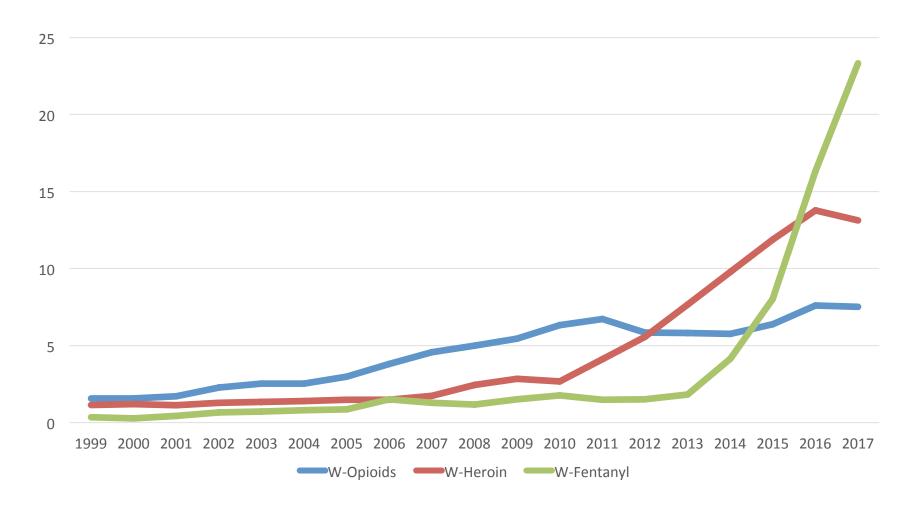
NOTES: Deaths are classified using the *International Classification of Diseases*, 10th Revision. Drug-poisoning (overdose) deaths are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Access data table for Figure 2 at:

https://www.cdc.gov/nchs/data/databriefs/db329_tables-508.pdf#2. SOURCE: NCHS, National Vital Statistics System, Mortality.

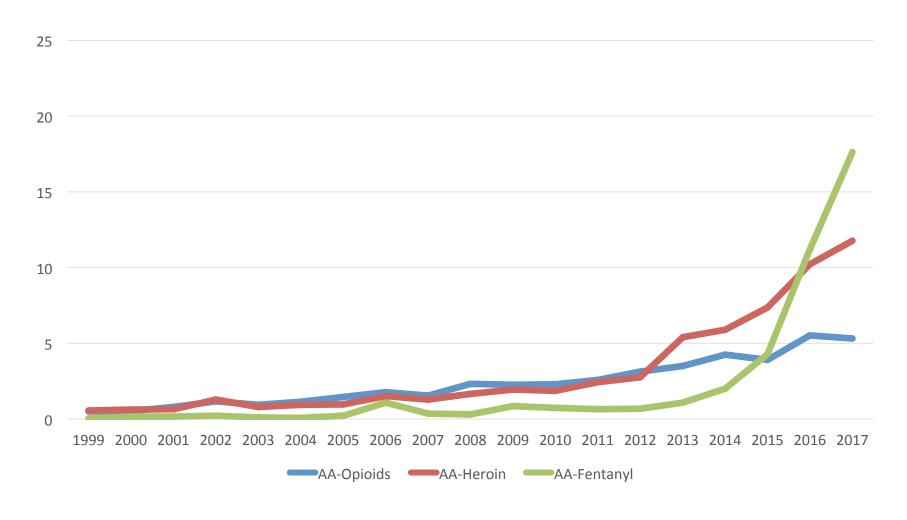
Opioid, Heroin, and Fentanyl deaths in African Americans, age 25-34



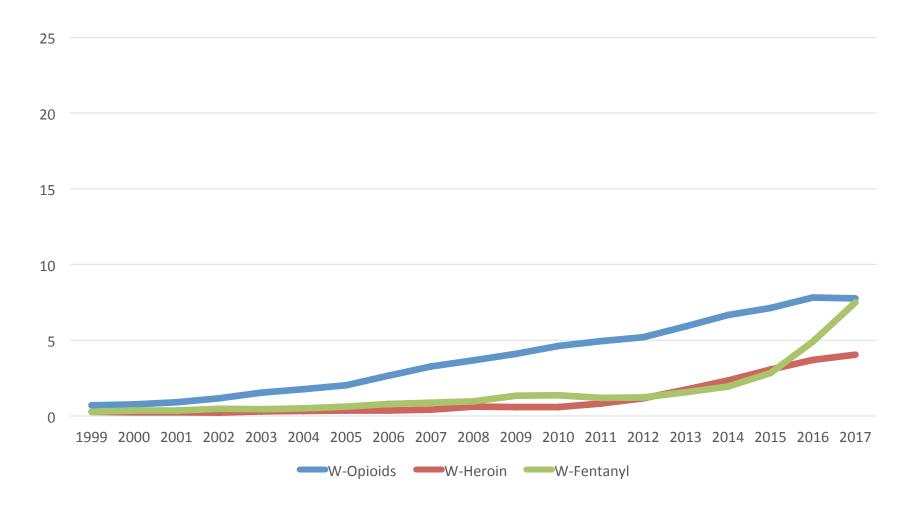
Opioid, Heroin, and Fentanyl deaths among non Hispanic whites age 25-34



Opioid, Heroin, and Fentanyl deaths in African-Americans age 55-64



Opioid, Heroin, and Fentanyl deaths in non Hispanic whites- age 55-64



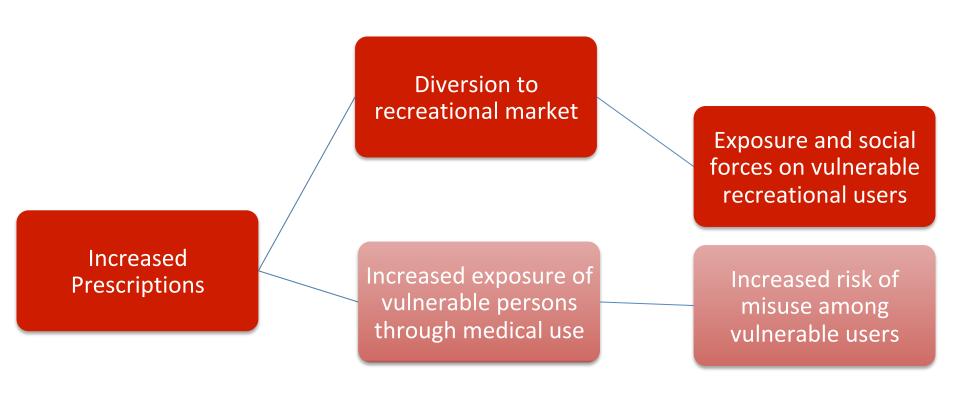
Estimated use, misuse, and disorder in 2015

- Annual use 91,800,000 37.8%
- Opioid Misuse 11,500,000 ~5%
- Opioid Use Disorder 1,900,000 ~.7%
- Heroin Use 828,000 ~.3%
- Drug overdose deaths 53,402
- Any opiate overdose deaths 36,897
- Opioid pain med deaths 13,294
- Heroin overdose deaths 13,150
- Fentanyl 9,803

Increased Prescriptions

Increased exposure of vulnerable persons through medical use

Increased risk of misuse among vulnerable users



Diversion to recreational market

Increased opioid demand, switch to heroin and fentanyl

Exposure and social forces on vulnerable recreational users

Increased Prescriptions

Increased exposure of vulnerable persons through medical use

Increased risk of misuse among vulnerable users

Increased opioid demand, switch to heroin and fentanyl Diversion to recreational market Exposure and social forces on vulnerable recreational users **Increased** Increased exposure of Increased risk of Prescriptions vulnerable persons misuse among through medical use vulnerable users Long term medical Opioid Dependence, use of opioids tolerance to opioid

