

The Opioid Epidemic:

Understanding and responding to the worst public health crisis in a generation

J. Nile Barnes, PharmD
Stoddard Davenport, MPH

NOVEMBER 2019



Presenters



J. Nile Barnes, PharmD
jbarnes@uiwtx.edu
210-883-1089



Stoddard Davenport, MPH
stoddard.davenport@milliman.com
303-672-9007

Agenda:

- Understanding substance use disorders
- How did we get here?
- Far-reaching impacts
- Where do we go from here?
- Questions?

Understanding opioid use disorder



Nociception and pain

- **Nociception:** the nervous system's response to potentially noxious or damaging stimuli (e.g. hot, cold, sharp, crushing, chemical, etc.)
- **Pain:** a subjective feeling that results from higher brain center processing of nociception in sentient beings
- **Suffering:** the experience of pain, hardship, or distress
 - Physicians take an oath to reduce suffering – but not all suffering results from nociception and pain

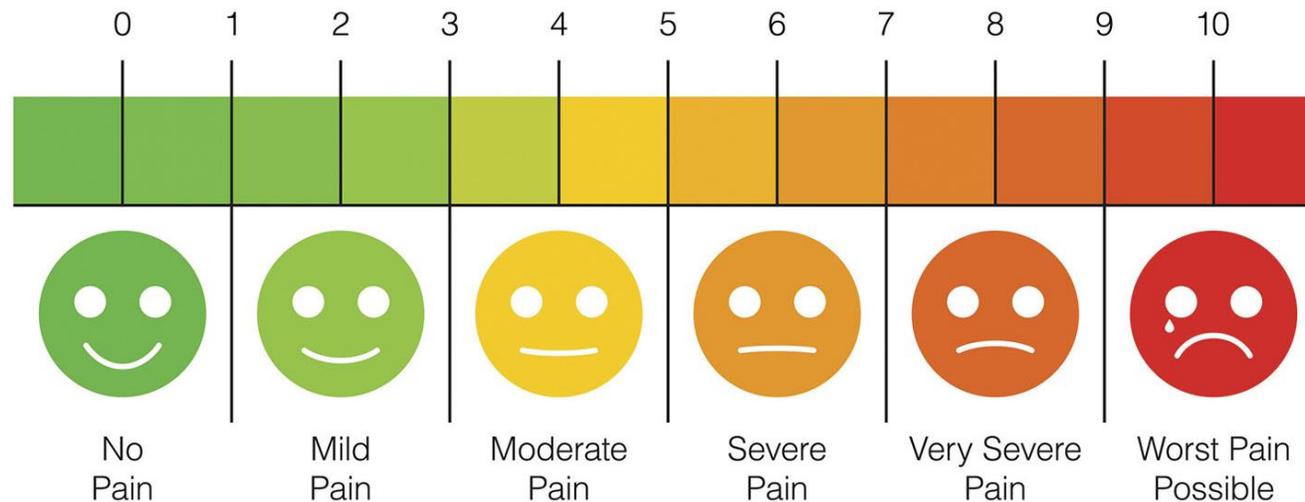


Image: © EgudinKa/Getty Images

Types of opioids

Source

- **Endogenous opioids**
 - Enkephalins and endorphins, made in the brain to regulate nociception by binding to the opioid receptors
- **Exogenous opioids**
 - Naturally derived (opiates) or synthetically produced (opioids)

Effect

- **Full agonists**
 - Activate the opioid receptors in the brain, resulting in full opioid effect (e.g. heroin, oxycodone, methadone, hydrocodone, morphine, opium, etc.)
- **Antagonists**
 - Attaches to the opioid receptors without activating them and blocks full agonists (e.g. naltrexone, naloxone)
- **Partial agonists**
 - Activates the opioid receptors, but does not produce the full opioid effect, and blocks other agonists (e.g. buprenorphine)

Opioid strength

- Strength measured in Morphine Milligram Equivalents



Tramadol (0.1/mg)
Hydrocodone (1/mg)
Morphine (1/mg)
Opium (1/mg)

Hydromorphone (3/mg)
Oxymorphone (3/mg)

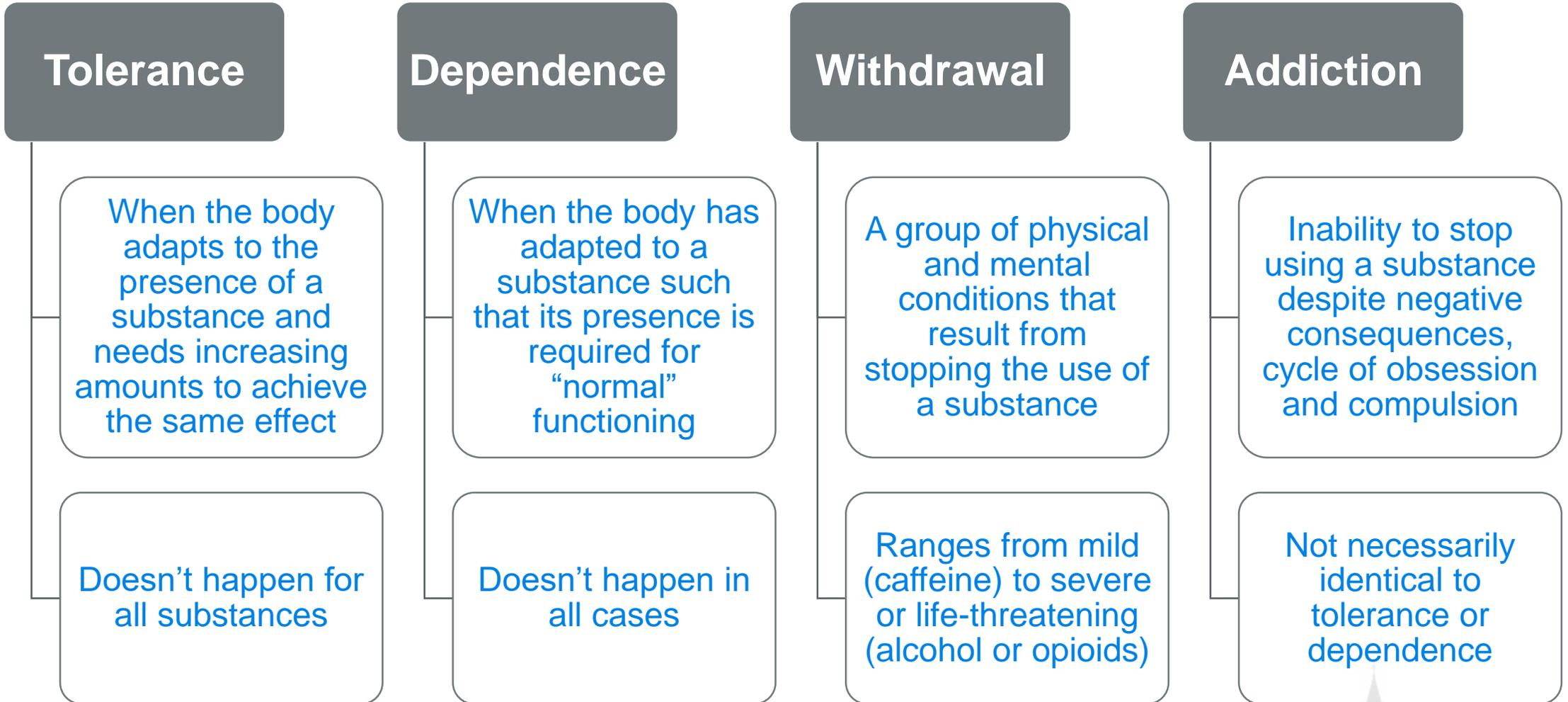
Fentanyl patch (7.2/mcg)



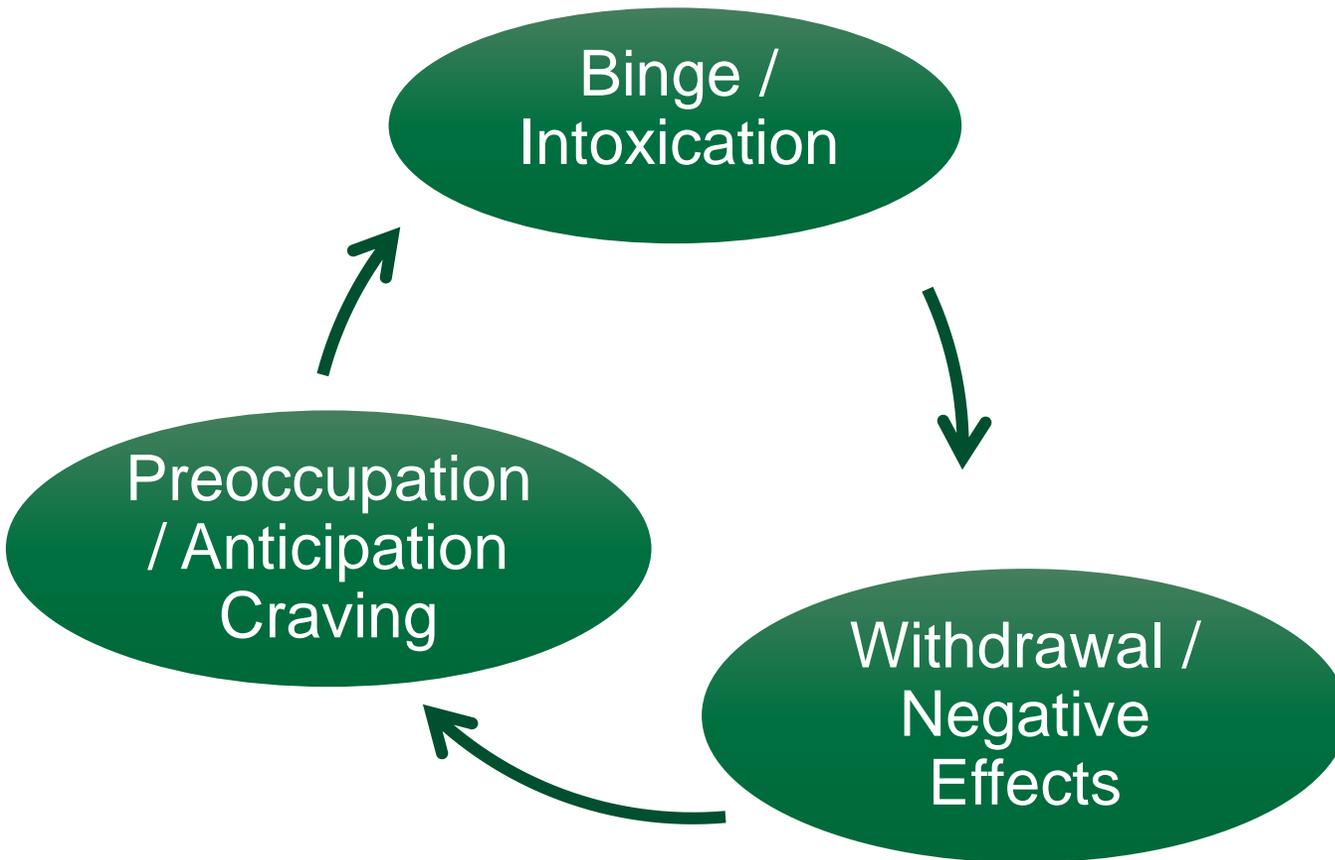
A lethal dose: 2mg of fentanyl

Image credit: [DEA](#)

Process of addiction



Addiction as a disease: dysregulated pleasure pathway

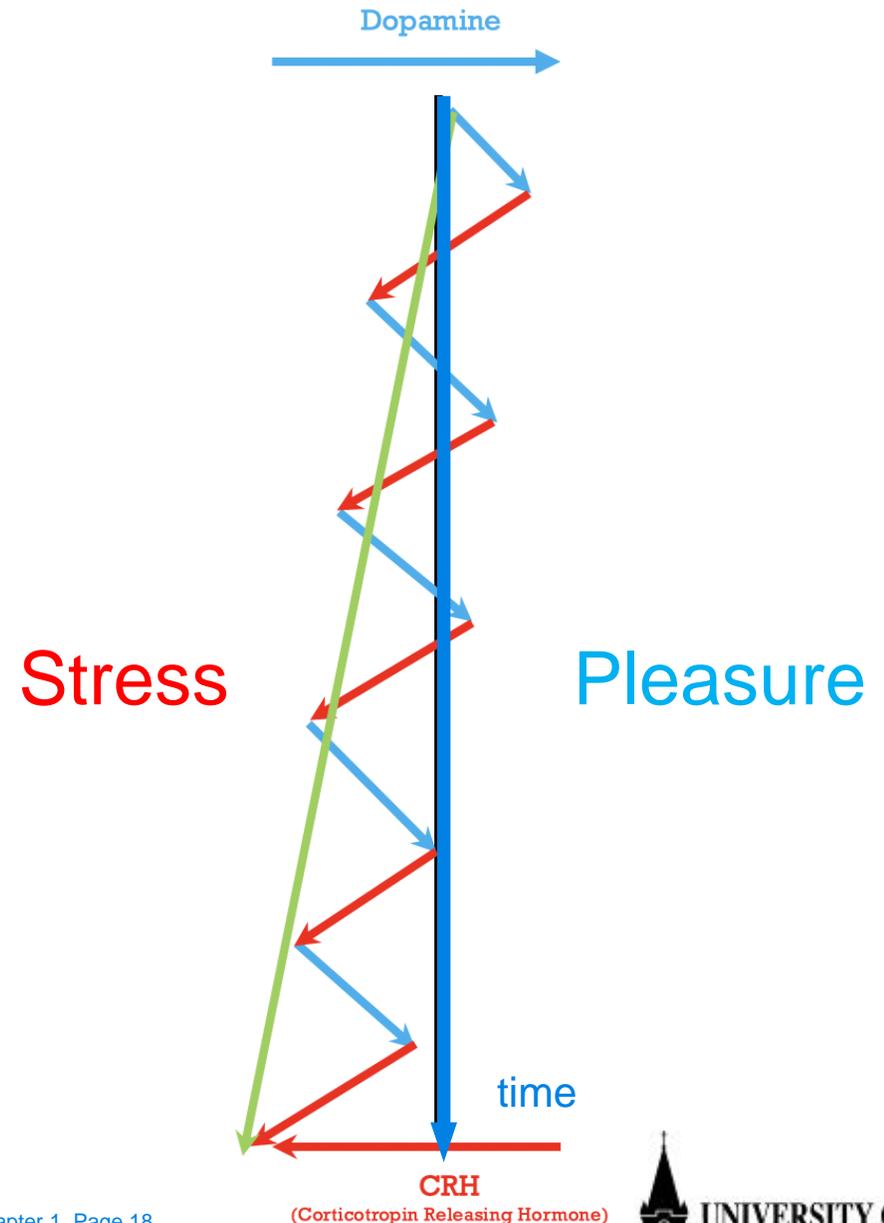


- Mesolimbic System(s)
- Multiple neurotransmitters
- Dependence varies
- Up to 23% of heroin users become dependent → 72% do not

Neuropsychopharmacology. 2010 Jan; 35(1): 217–238.

Exp Clin Psychopharmacol. 1994 2(3) 244-268 & Erickson 2007

Opponent-Process overlaid with Neurotransmitter levels



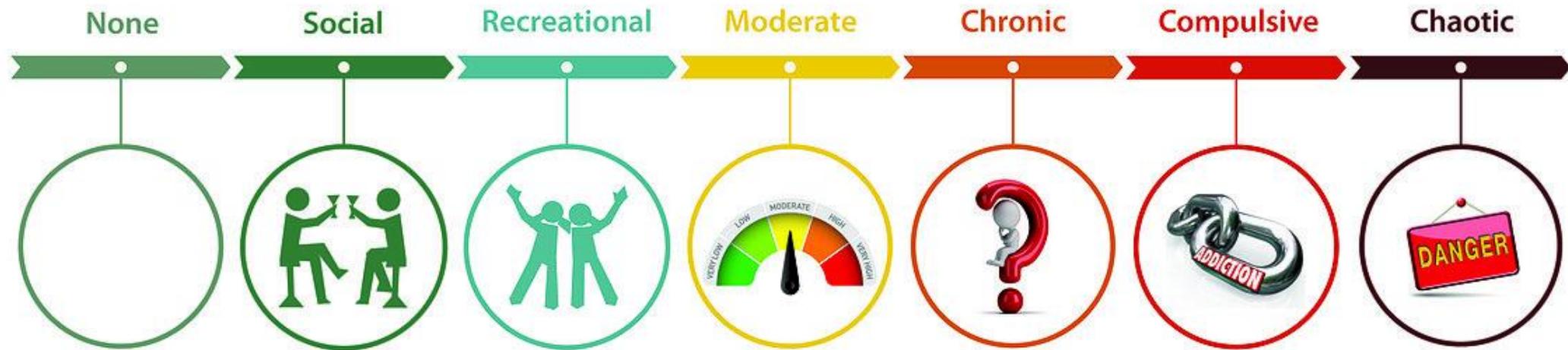
DSM 5 criteria for substance use disorder

To meet *DSM-5* criteria for the diagnosis of SUD, at least two of the following must occur within a 12-month period:

- Larger amounts or longer period than was intended
- Persistent desire or unsuccessful efforts to cut down
- A great deal of time is spent obtaining, using, or recovering
- Craving, or a strong desire or urge to use
- Failure to fulfill major role obligations at work, school, or home
- Continued use despite having persistent or recurrent problems
- Important activities are given up or reduced
- Recurrent use in physically hazardous situations
- Use is continued despite knowledge of having a persistent or recurrent problem
- Tolerance: either a need for increased amounts or diminished effect with use of the same amount
- Withdrawal: withdrawal symptoms or the substance is taken to relieve or avoid withdrawal symptoms

Harm Reduction Continuum

— Substance use and behaviors occur along a continuum from no use to chaotic use



Adapted from Patt Denning's book "Practicing Harm Reduction Psychotherapy"

LivingMoreFully.com

How do people die from opioids?

- Block respiratory center activity
- Respiratory depression
(decreased breathing rate & depth)
- Hypoxia
(low oxygen levels in tissues)
- Heart rate slows
- Cells die
early deaths for sensitive cells (neurons)

- Naloxone can unblock
- Ventilation can substitute
- CPR can temporarily substitute



Stigma

- Oxford Dictionary definition:
- A mark of disgrace associated with a particular circumstance, quality, or person.
- Despite progress, stigma is still widely considered to be among the most significant barriers to treatment
 - Decreases willingness of policymakers to allocate resources
 - Decreases willingness of providers to screen for and address substance use problems
 - Decreases willingness of individuals to seek treatment
 - Increasingly seen as a form of discrimination

Words matter

- The language we use shapes our implicit and explicit biases
- Use language that is patient-supportive
- Recognize difference between clinical processes and personal attributes

- Clean implies dirty as the alternative
 - In recovery vs. not in recovery
- Clean vs. dirty drug screen
 - Negative vs. positive drug screen
- User, misuser, or abuser
 - Non-medical use

Recovery Dialects	Mutual Aid Meetings	In Public	With Clients	Medical Settings	Journalists
Addict	✓	STOP	STOP	STOP	STOP
Alcoholic	✓	STOP	STOP	STOP	STOP
Substance Abuser	STOP	STOP	STOP	STOP	STOP
Opioid Addict	✓	STOP	STOP	STOP	STOP
Relapse	✓	STOP	STOP	STOP	STOP
Medication Assisted Treatment	STOP	STOP	STOP	STOP	STOP
Medication Assisted Recovery	✓	✓	✓	✓	✓
Person w/ a Substance Use Disorder	✓	✓	✓	✓	✓
Person w/ an Alcohol Use Disorder	✓	✓	✓	✓	✓
Person w/ an Opioid Use Disorder	✓	✓	✓	✓	✓
Long-term Recovery	✓	✓	✓	✓	✓
Pharmacotherapy	✓	✓	✓	✓	✓

Language matters but can change depending on the setting we are in. Choosing when and where to use certain language and labels can help reduce stigma and discrimination towards substance use and recovery.



SOURCE: Ashford, R. D., Brown, A. M., & Curtis, B. (2018). Substance use, recovery, and linguistics: The impact of word choice on explicit and implicit bias. *Drug and Alcohol Dependence*, 188, 131-138.

How did we get here?

Chronic pain affects 20% of U.S. adults

Nearly 20 million experienced “high-impact” chronic pain in 2016

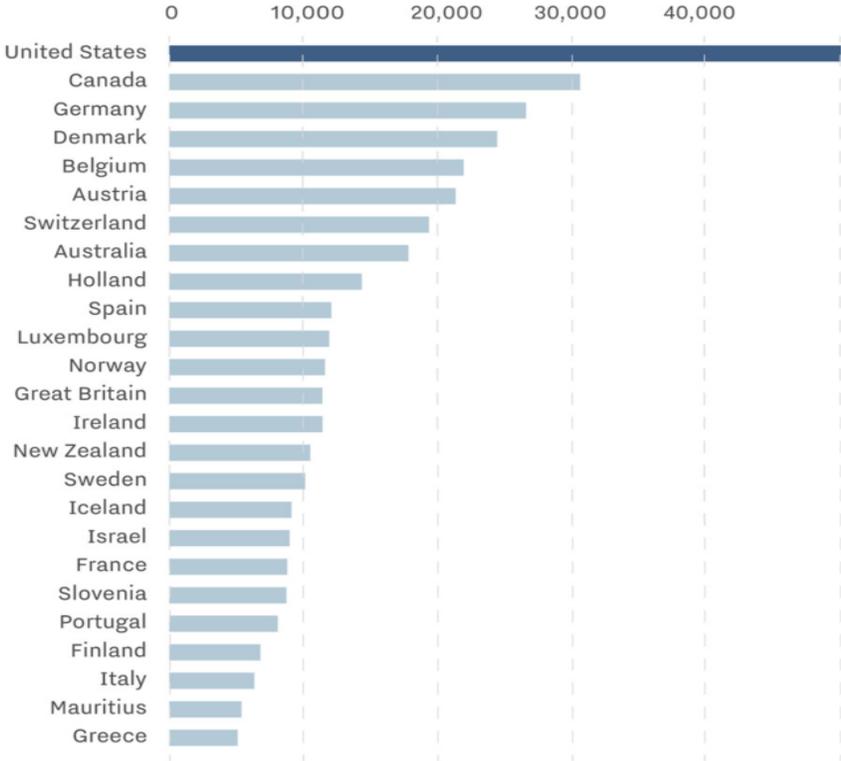
- Undertreatment in the ‘90s
- Pain becomes the “fifth vital sign”
- Pendulum swings to overtreatment
- Early belief that opioid pain management solutions weren’t addictive
- Transition from prescriptions to illicit

Sources:

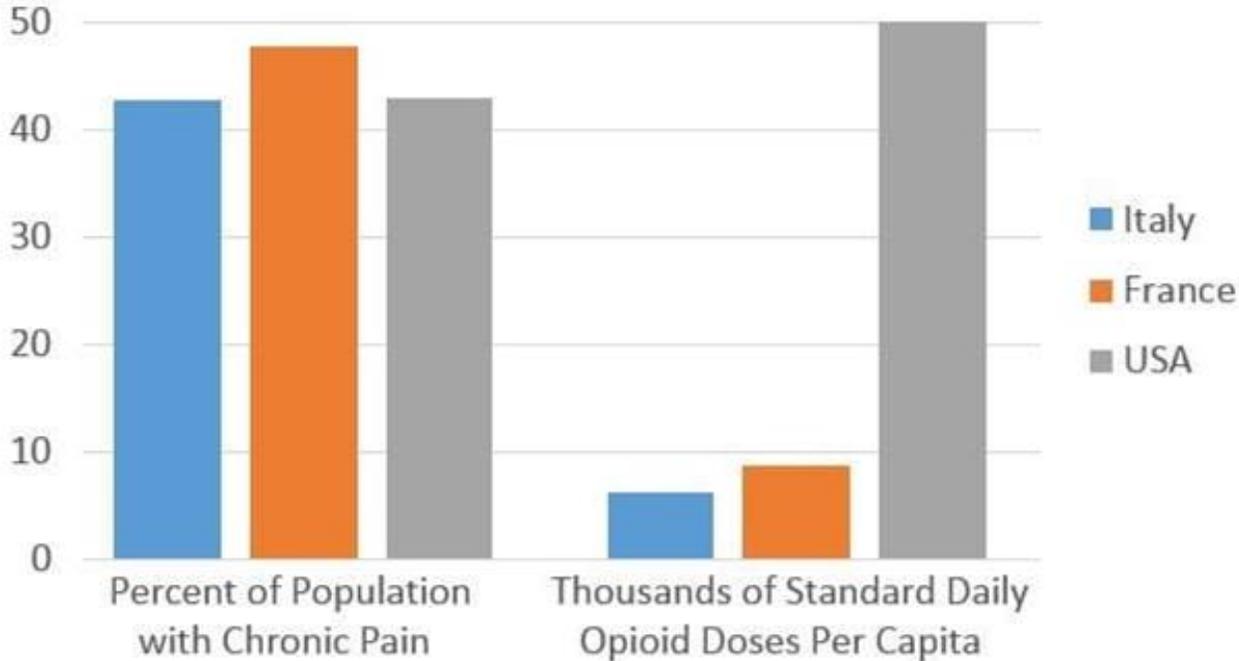
- <https://www.cdc.gov/mmwr/volumes/67/wr/mm6736a2.htm>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5993682/>
- <https://www.ncbi.nlm.nih.gov/pubmed/18602869>

The U.S. consumes more opioids than any other country – 30% of world’s supply

Standard daily opioid dose for every 1 million people

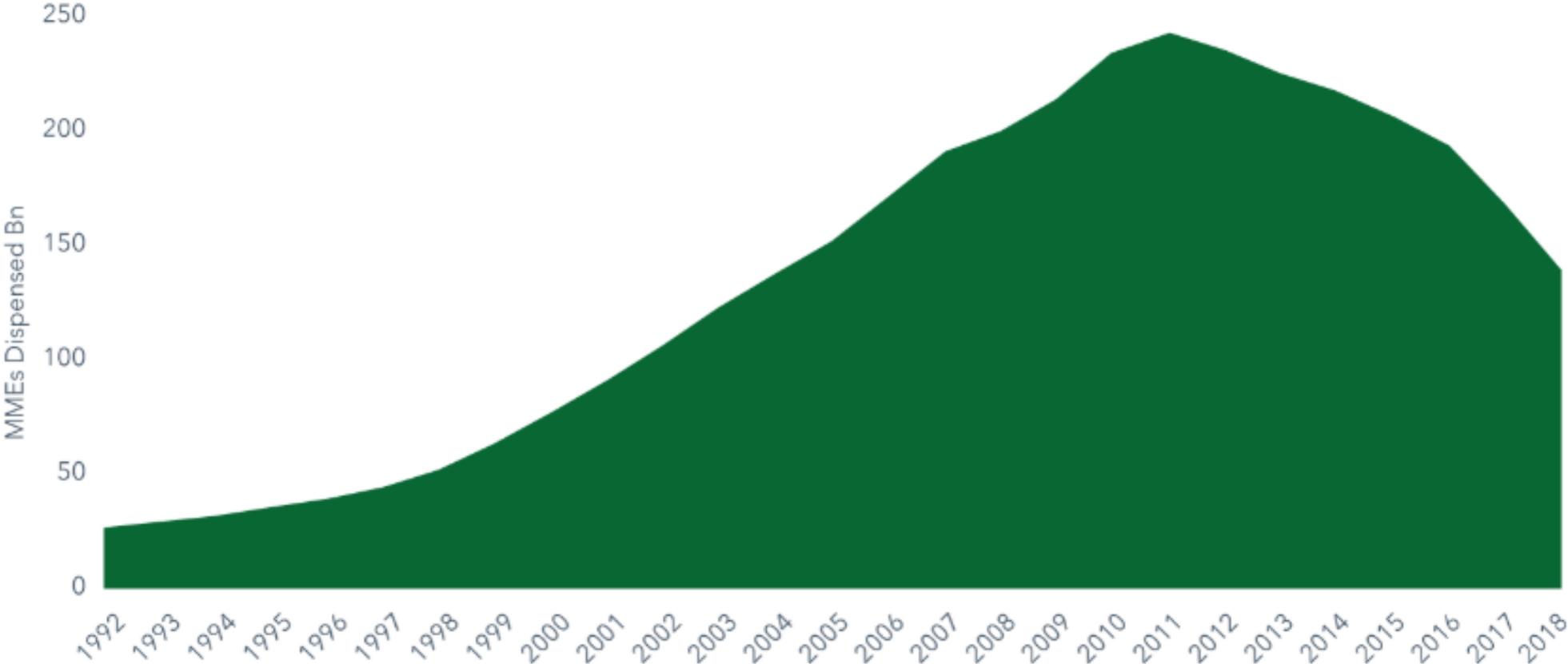


Source: United Nations International Narcotics Control Board
Credit: Sarah Frostenson



- Sources:
- [a-better-america.com/2018/01/27/opioid-use-in-the-us-blows-other-countries-away/](https://www.better-america.com/2018/01/27/opioid-use-in-the-us-blows-other-countries-away/)
 - <https://www.vox.com/science-and-health/2017/8/3/16079772/opioid-epidemic-drug-overdoses>
 - [Graphic from The Washington Post - https://www.washingtonpost.com/news/wonk/wp/2018/03/23/americans-take-more-pain-pills-but-not-because-theyre-in-more-pain/?noredirect=on&utm_term=.8ab4a7cc315c](https://www.washingtonpost.com/news/wonk/wp/2018/03/23/americans-take-more-pain-pills-but-not-because-theyre-in-more-pain/?noredirect=on&utm_term=.8ab4a7cc315c)
 - https://www.incb.org/incb/en/narcotic-drugs/Technical_Reports/narcotic_drugs_reports.html

Opioid prescriptions dispensed by U.S. retail pharmacies (billions of MMEs)



Source: IQVIA National Prescription Audit, Dec 2017; IQVIA Xponent, Feb 2019
Report: Medicine Use and Spending in the U.S. – A Review of 2018 and Outlook to 2023. IQVIA Institute for Human Data Science, May 2019

Prescriptions, misuse, and addiction

2017 Update:

92 million people prescribed opioids in 2015

- Some may be at risk for developing opioid use disorder



55 million

11.5 million reported misusing opioids

- May or may not have discussed their opioid use with a clinician or be ready to begin treatment



11.4 million

1.9 million reported being addicted to opioids

- Many need enhanced care and management for recovery

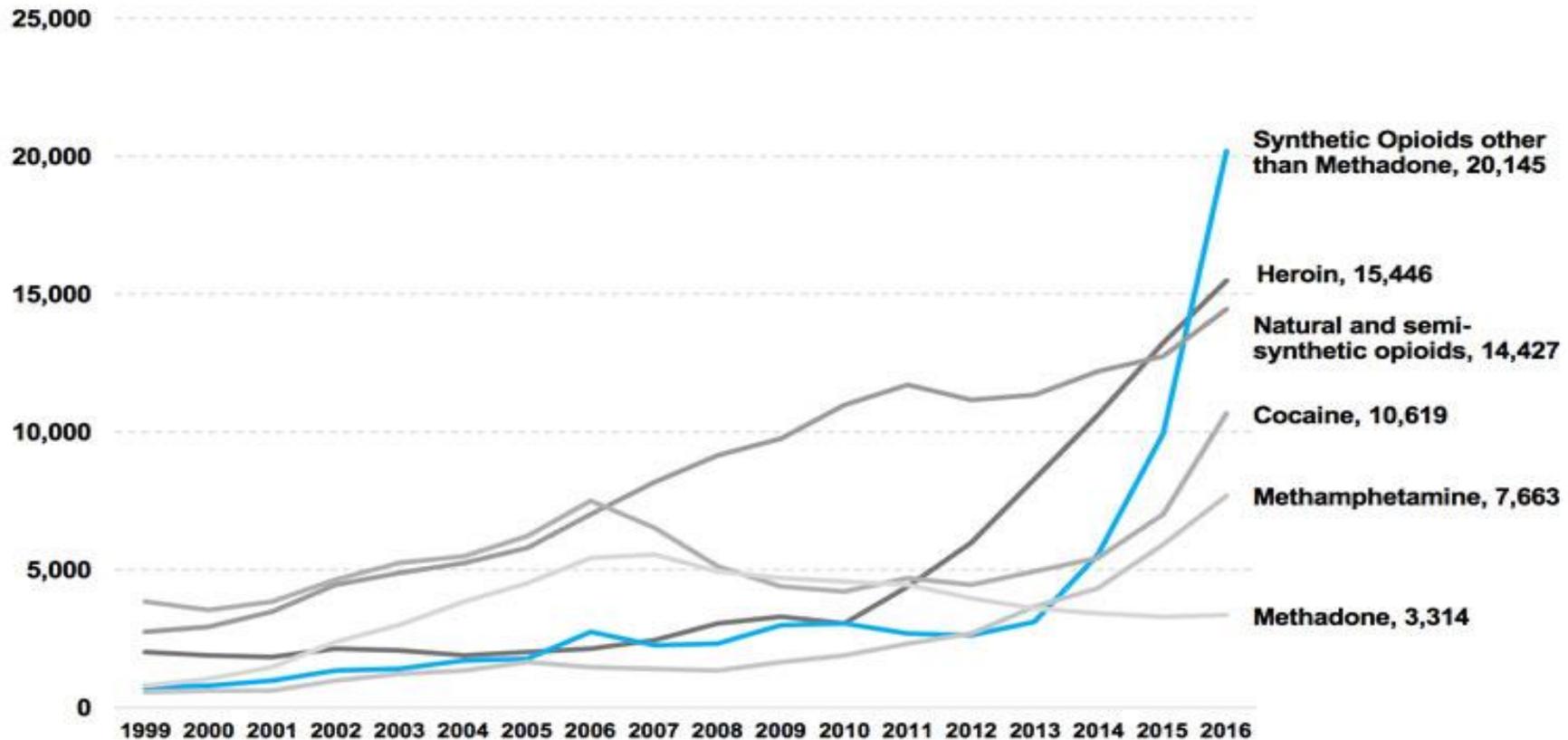


2.1 million

Source: 2015 and 2017 National Survey on Drug Use and Health and CDC - <https://www.cdc.gov/drugoverdose/data/prescribing.html>

Three waves of the epidemic

Drugs Involved in U.S. Overdose Deaths, 2000 to 2016

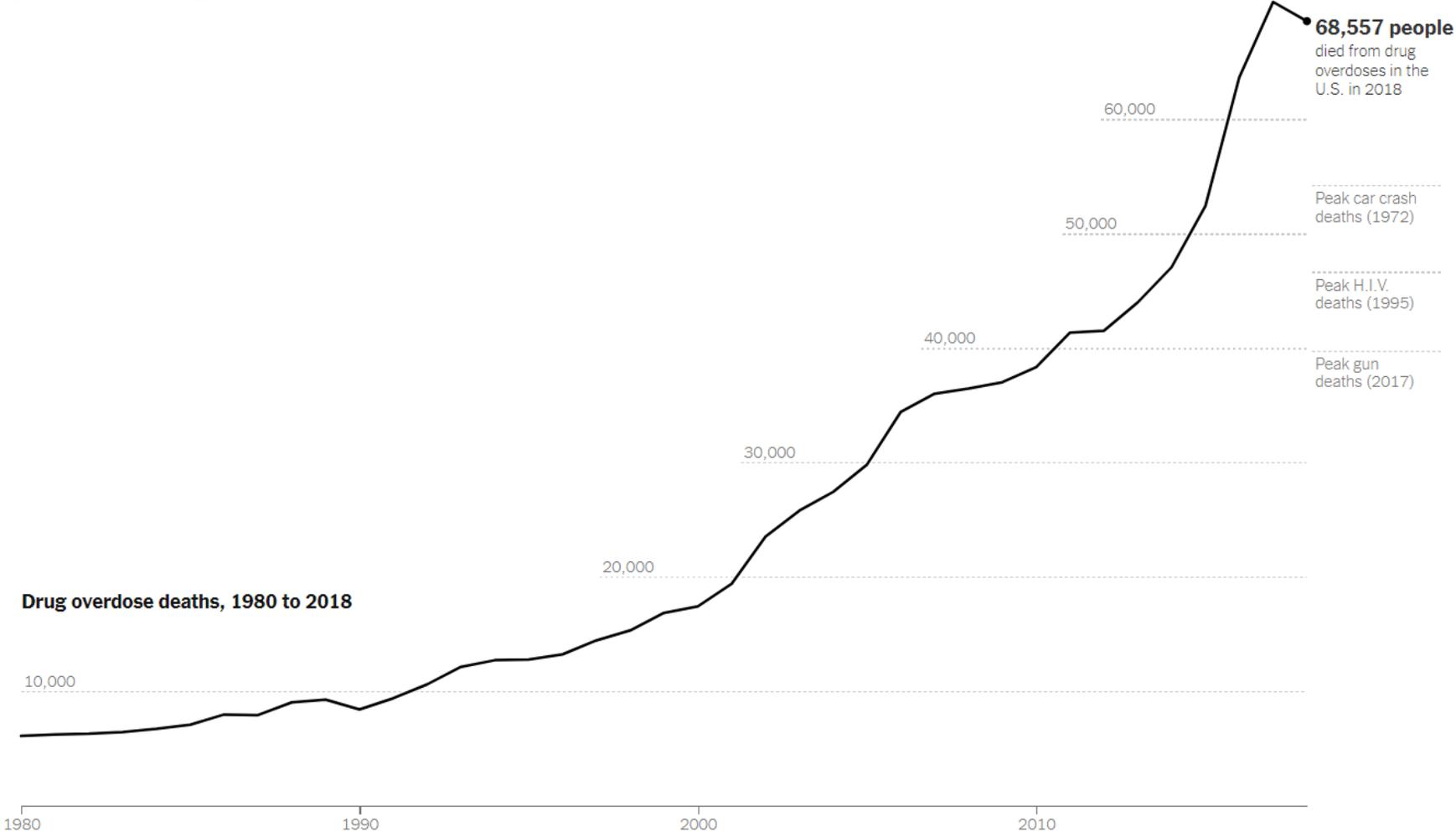


1st wave
Prescription

2nd wave
Heroin

3rd wave
Synthetics

Putting things in perspective



Drug overdose deaths, 1980 to 2018

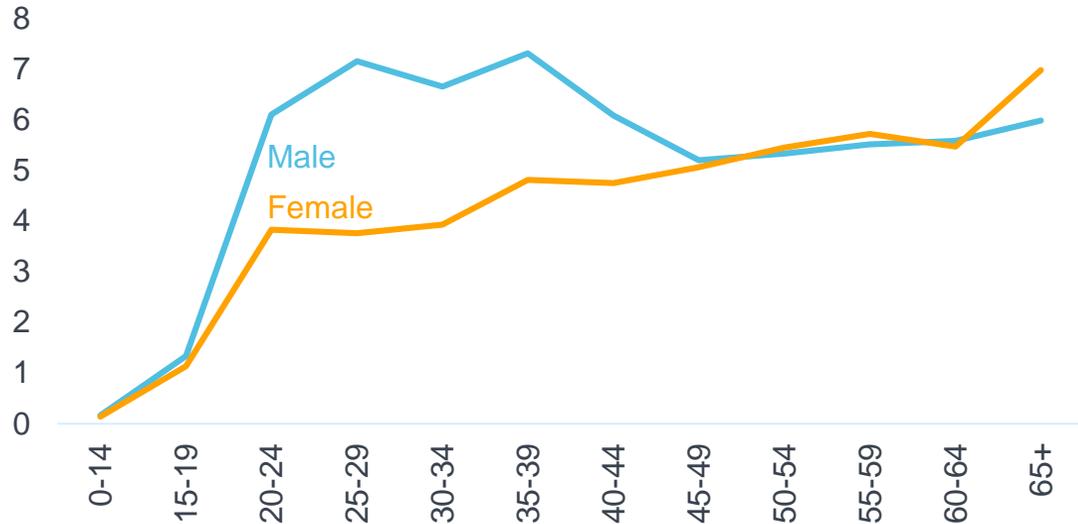
Data through 2017 is based on final reported mortality totals. Data for 2018 is provisional and adjusted to account for delays in drug-death reporting. Source: National Center for Health Statistics, Centers for Disease Control and Prevention

Graphic from The New York Times, July 17, 2019

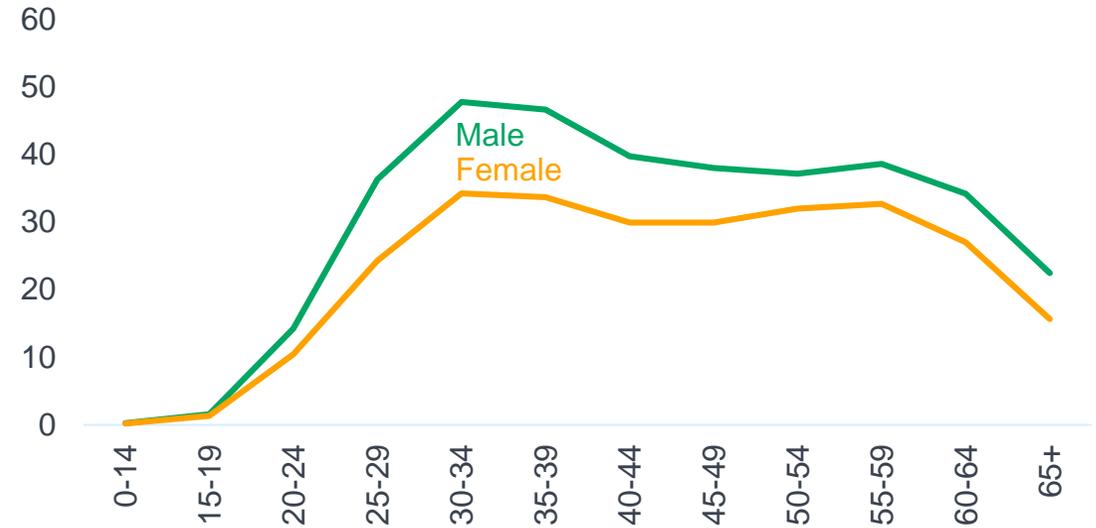
Far-reaching impacts

Nearly 3.7 million with OUD in 2017

Commercial market prevalence by age and sex (per 1,000 population)



Medicaid prevalence by age and sex (per 1,000 population)



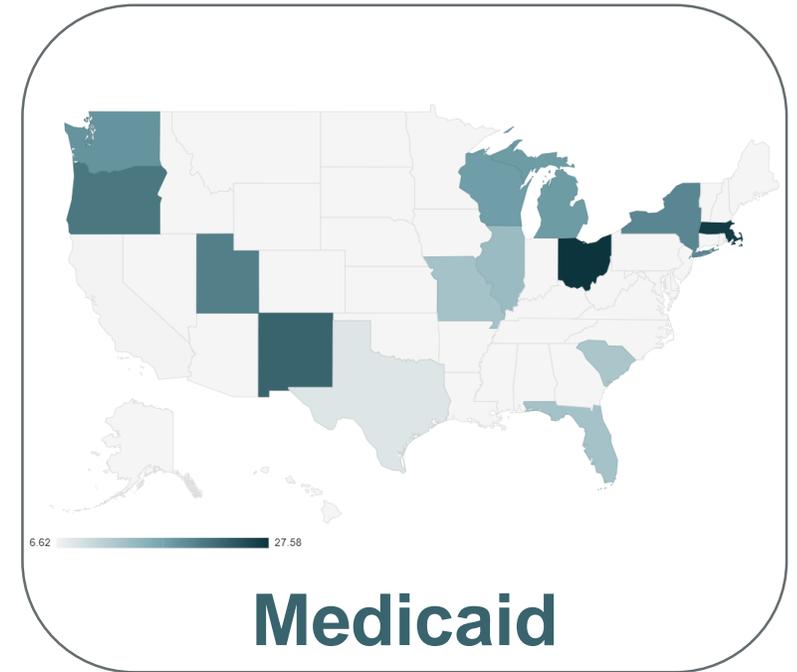
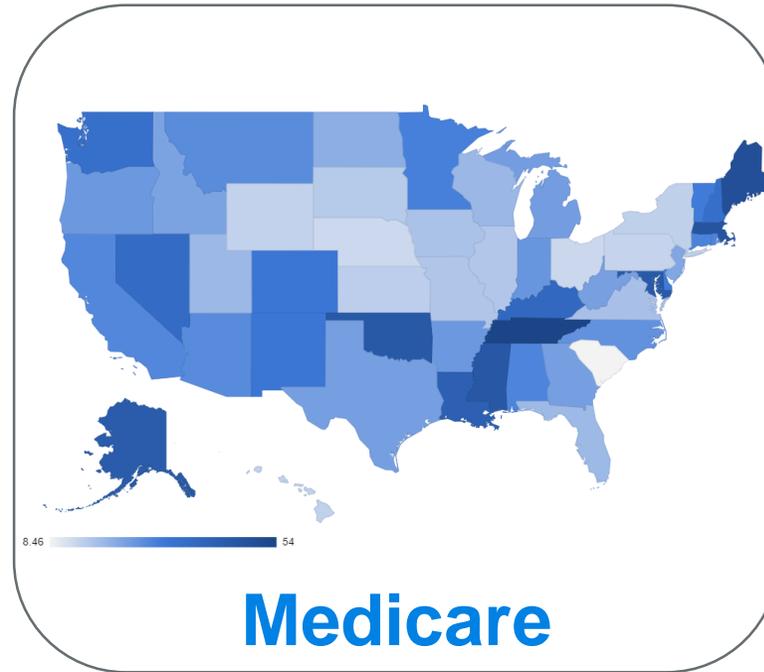
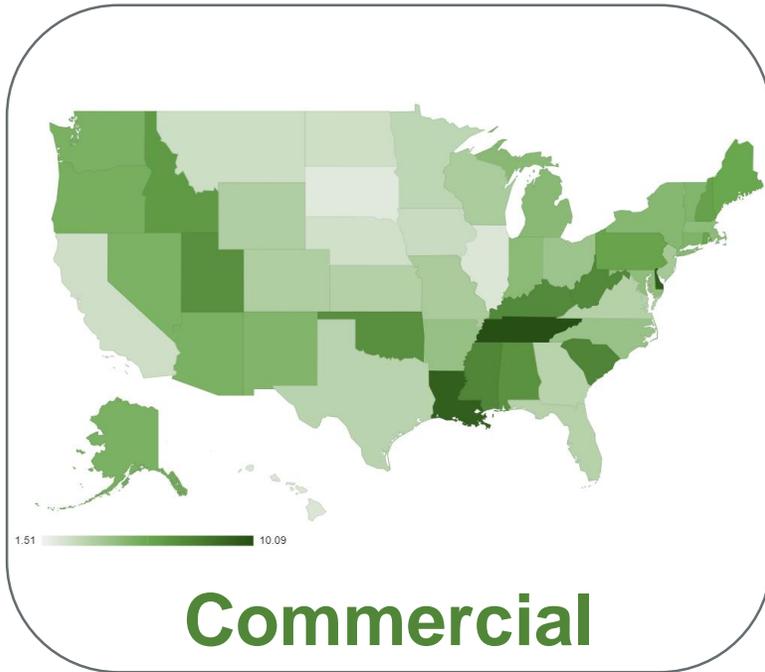
Prevalence by health insurance payer



■ Commercial ■ Medicare ■ Medicaid ■ Other Public ■ Uninsured

Significant geographical variation

Prevalence by state and payer, 2017 (per 1,000 population)



Impacts ripple throughout society

Patients

Criminalization of chronic pain patients

Forced tapers

Higher risk of suicide

Organ donor availability

Families

Complicated pregnancies

Neonatal abstinence syndrome

Foster care

Family risk factors

Economy

Labor force participation

High opioid use among unemployed

\$1 trillion cost from 2001-2016

\$500 billion cost in next 4 years

Unexpected victims

Mussels in the Puget Sound

Injured pets

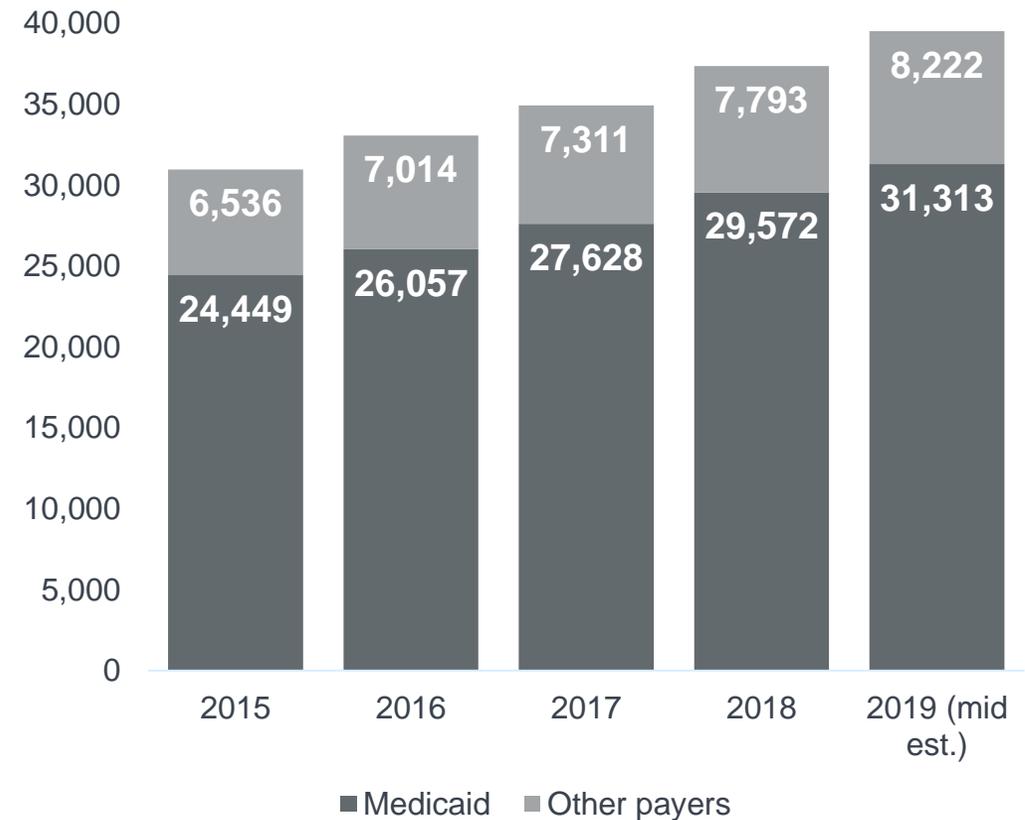
Struggles for Chronic Pain Patients

- Physicians pressured to decrease prescriptions
 - Opioid treatment agreements
 - Tapering
 - Psychological therapies
- Poor management can lead to withdrawal symptoms, even turning to other drugs like heroin
 - Anecdotal evidence suggests that in some places, the rapid decrease in prescription of opioids has led to illicit drugs being cheaper/easier to get than prescription

Family impacts

- Number of pregnant women using opioids grew significantly from 2004 to 2013
- Fivefold increase in newborns with neonatal abstinence syndrome (NAS) over the course of the crisis
- 8% increase in foster children from 2011 to 2015
- Opioid prescriptions are more likely among households already exposed to opioids

Infants born with NAS/NOWS

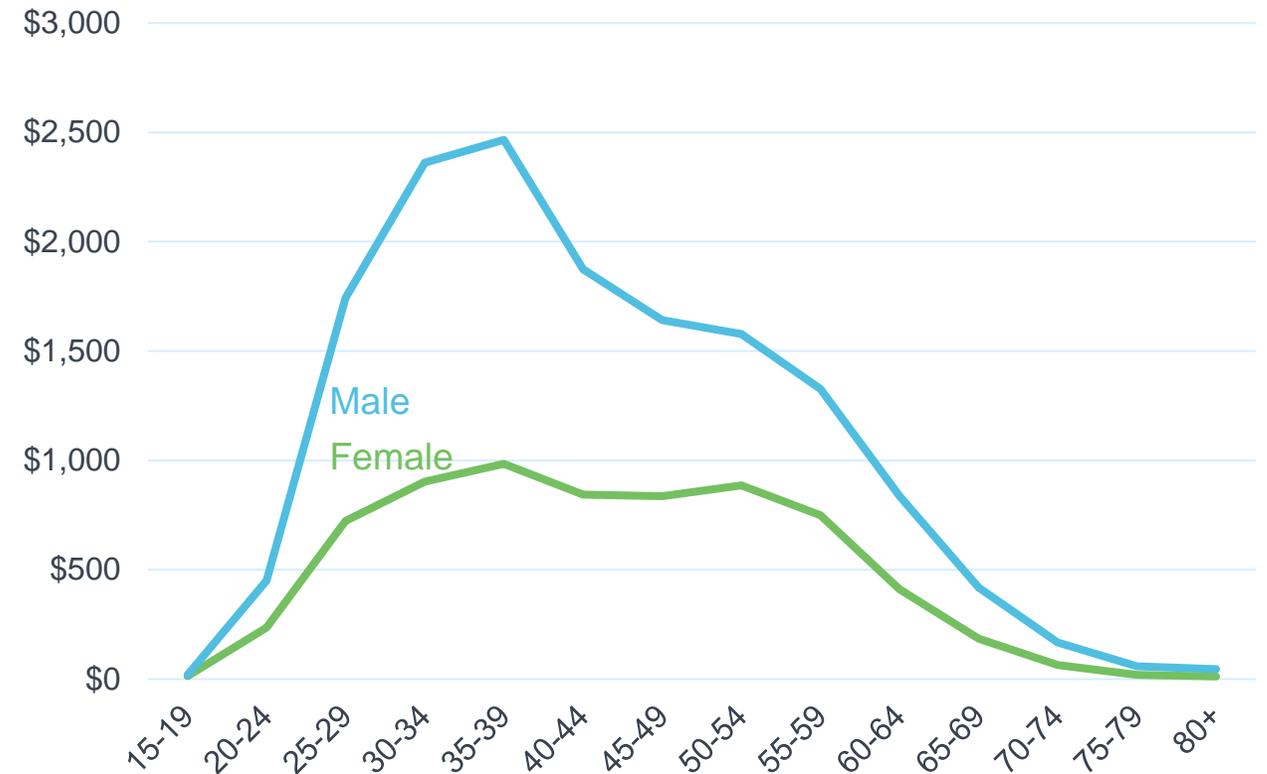


Sources: www.nytimes.com/2018/05/09/magazine/children-of-the-opioid-epidemic.html
www.motherjones.com/politics/2017/07/children-ohio-opioid-epidemic/
www.foxnews.com/health/2017/12/11/opioid-painkiller-prescriptions-may-run-in-families.amp.html
Davenport, S, Weaver, A, Caverly, M. Economic Impact of Non-Medical Opioid Use in the United States. SOA October 2019.
<https://www.soa.org/globalassets/assets/files/resources/research-report/2019/econ-impact-non-medical-opioid-use.pdf>

Impact on labor force

- 20% of drop in American men in labor force attributed to opioid use
- Half of working-age men not in labor force take prescription painkillers daily
- Unemployed are more likely to misuse painkillers
- ~\$96 billion in lost productivity from 2015-2018

Lost productivity by age and sex, 2018 (in millions)



More headlines . . .

By CHRISTINA CAPATIDES / CBS NEWS / May 24, 2018, 5:34 PM

Mussels off the coast of Seattle test positive for opioids

f Share /  Tweet /  Reddit /  Flipboard / @ Email

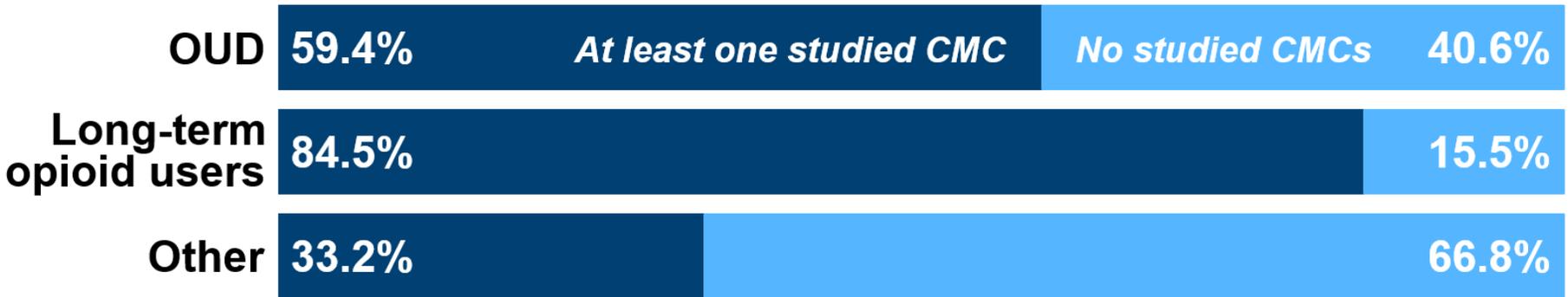
As more and more American communities grapple with **opioid addiction**, the human toll of the **epidemic** has grown in both scope and severity. And now, scientists at the Washington Department of Fish and Wildlife have found evidence that drug's impact has literally flowed downstream to affect marine life, as well.



Complex healthcare needs

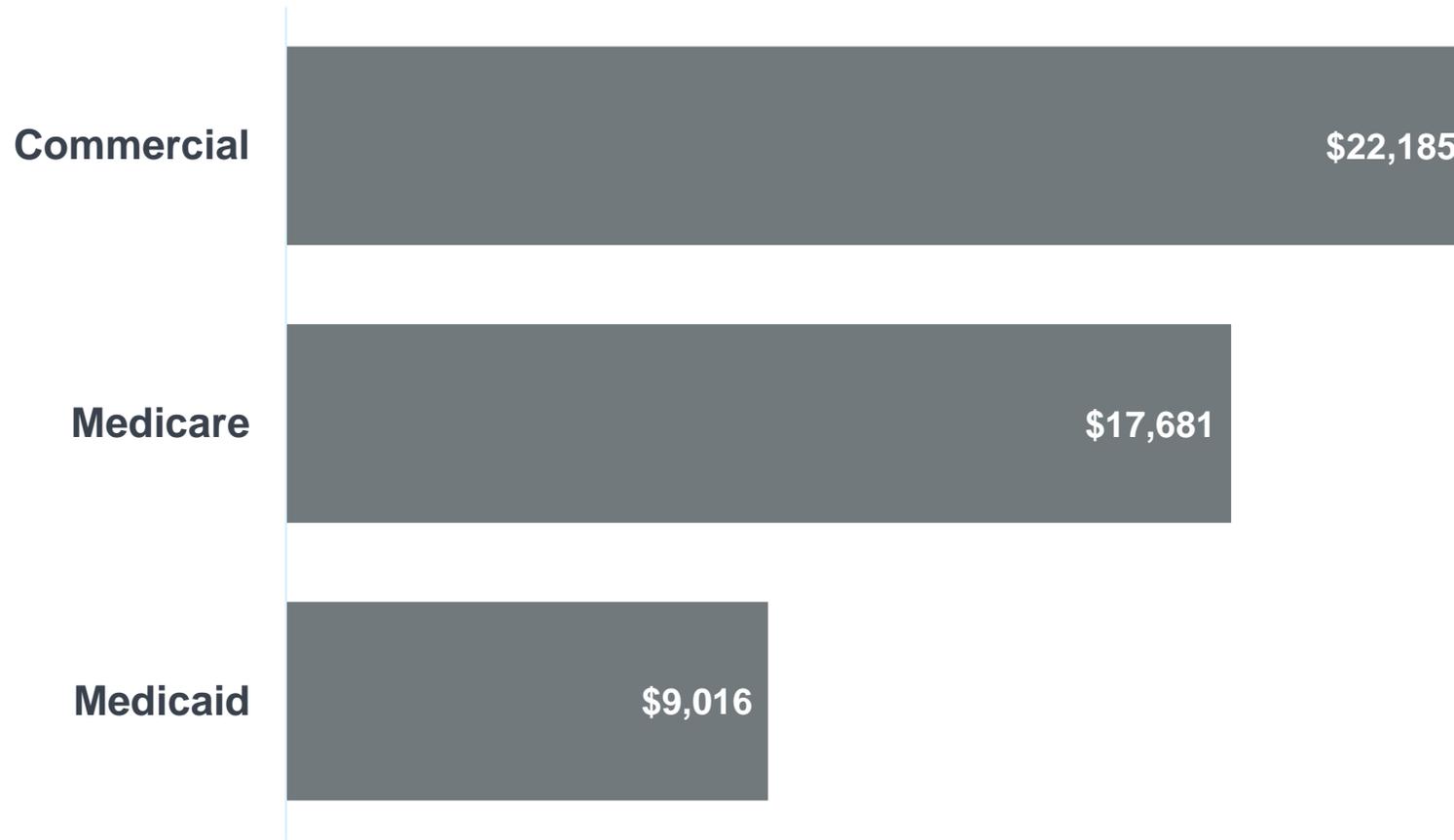
- Patients with OUD were **1.8x** as likely to have at least one of 25 studied chronic medical conditions (CMCs), and long-term opioid users were **2.6x** as likely compared to the general population.

Percent of patients with at least one of the studied CMCs, by opioid use cohort, 2016



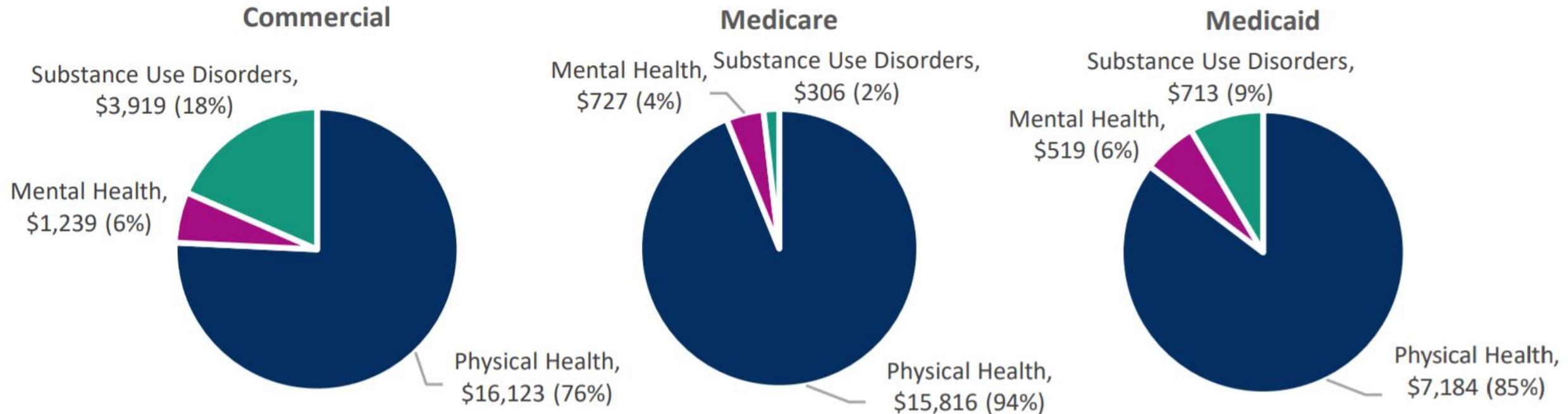
Source: Milliman White Paper – Costs and Comorbidities of Opioid Use Disorder. <http://www.milliman.com/insight/2019/Costs-and-comorbidities-of-opioid-use-disorder/>

Excess healthcare costs for individuals with OUD, 2018



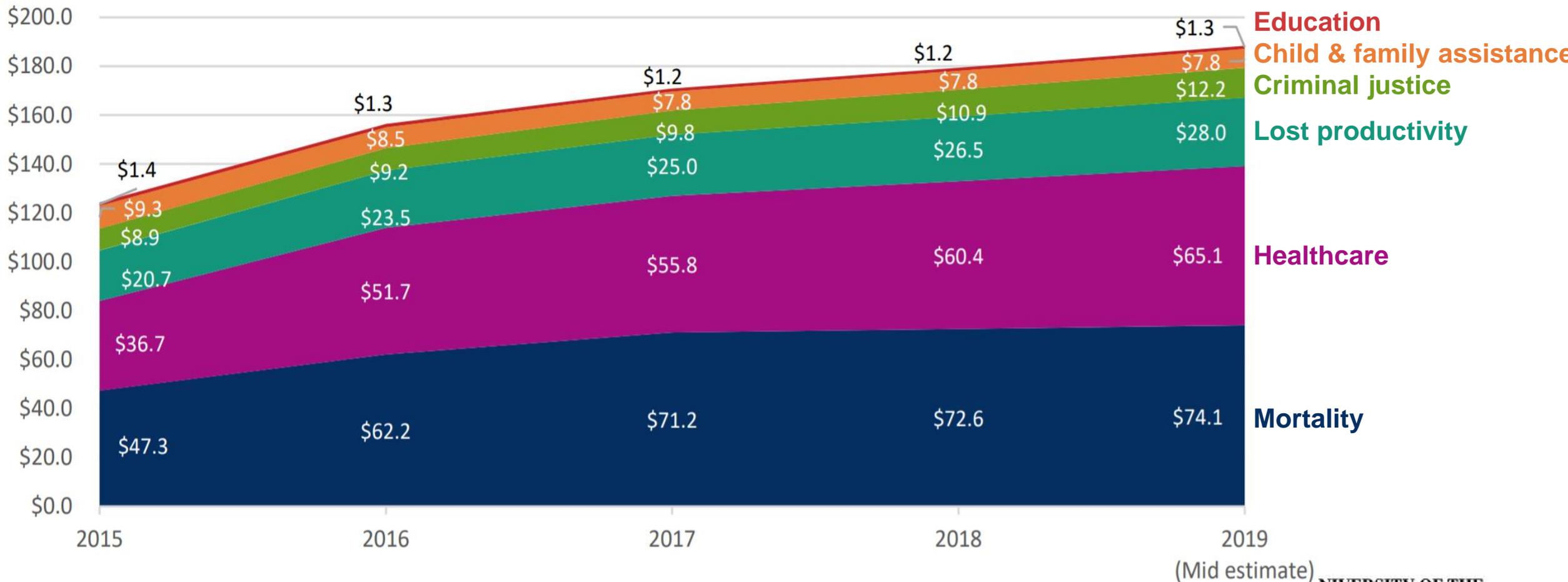
Excess costs go beyond OUD treatment

Distribution of excess costs for patients with OUD, 2015-2016



Economic costs

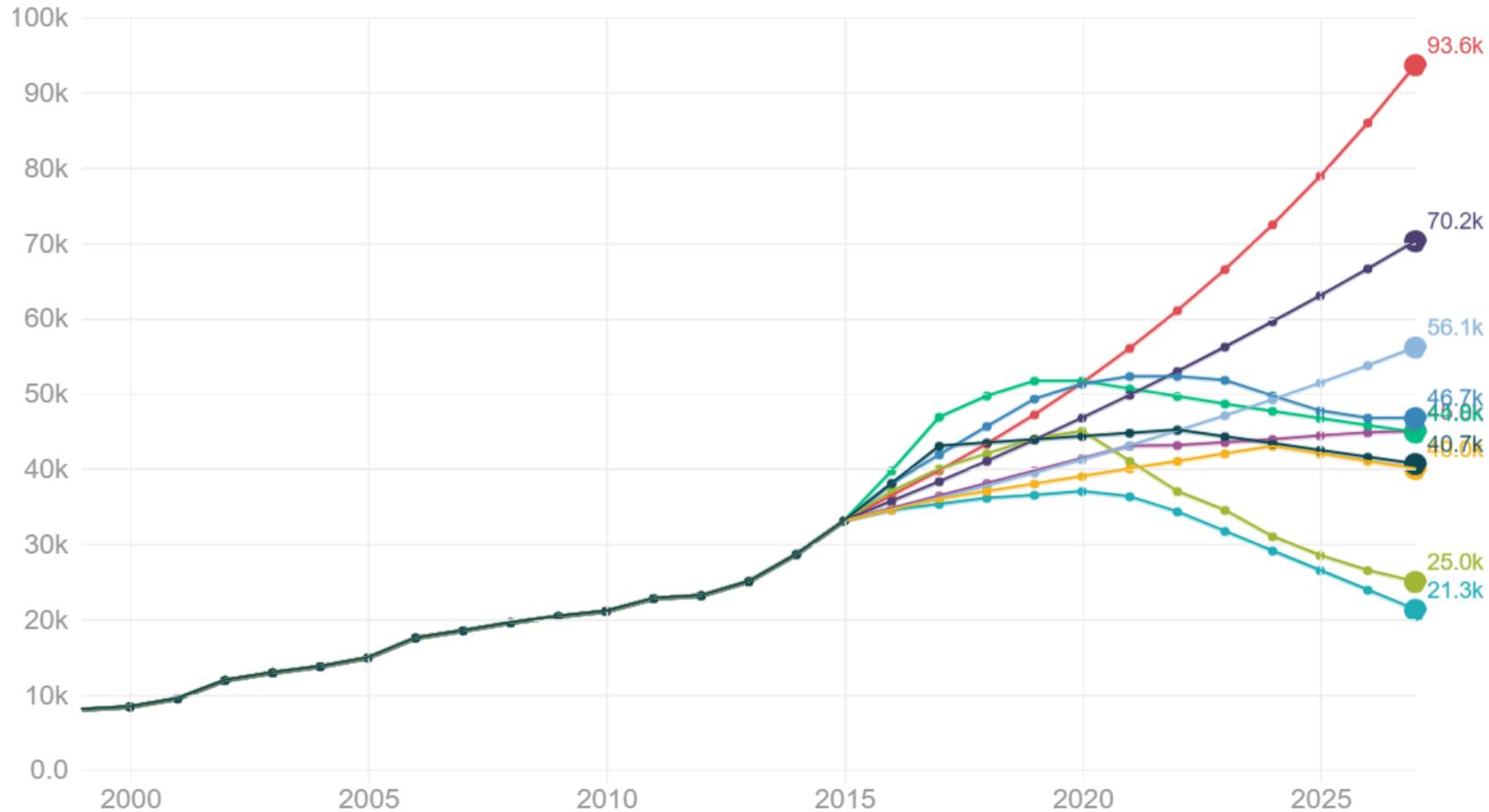
Economic impact of the opioid crisis by category, 2015-2019 (billions)



**Where do we go from
here?**

Ten different experts, ten different futures

Opioid overdose deaths: 10 projected scenarios.



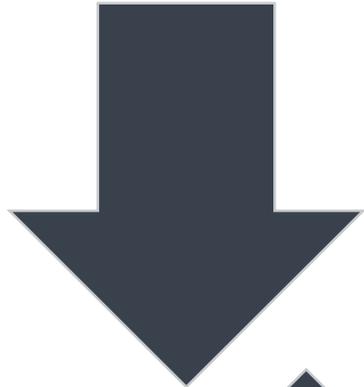
← STATUS QUO

AVERAGE:
500,000 more
deaths in next
10 years

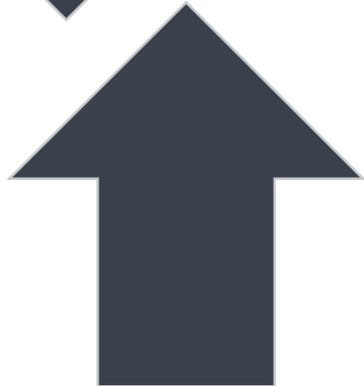
← BEST CASE

Source: <https://www.statnews.com/2017/06/27/opioid-deaths-forecast/>

Encouraging trends



New opioid starts



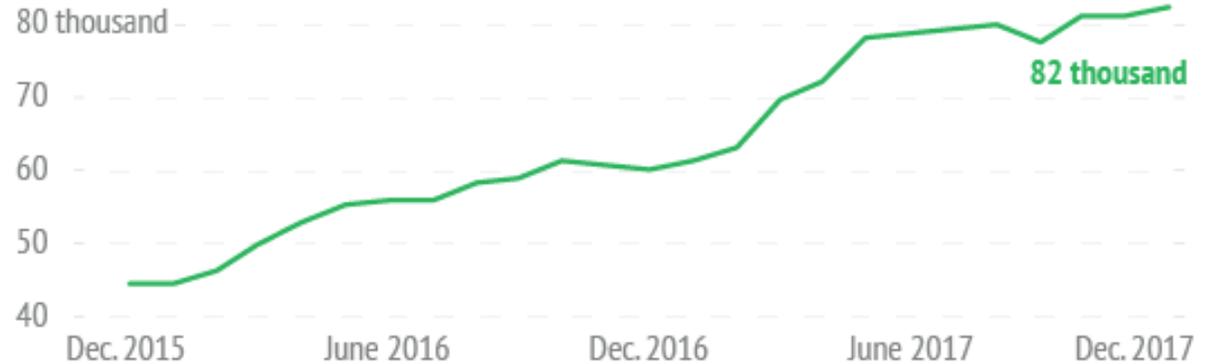
Medication Assisted Treatment

Seeking treatment

Opioid new therapy starts fell to 2.9 million a month at the end of 2017...

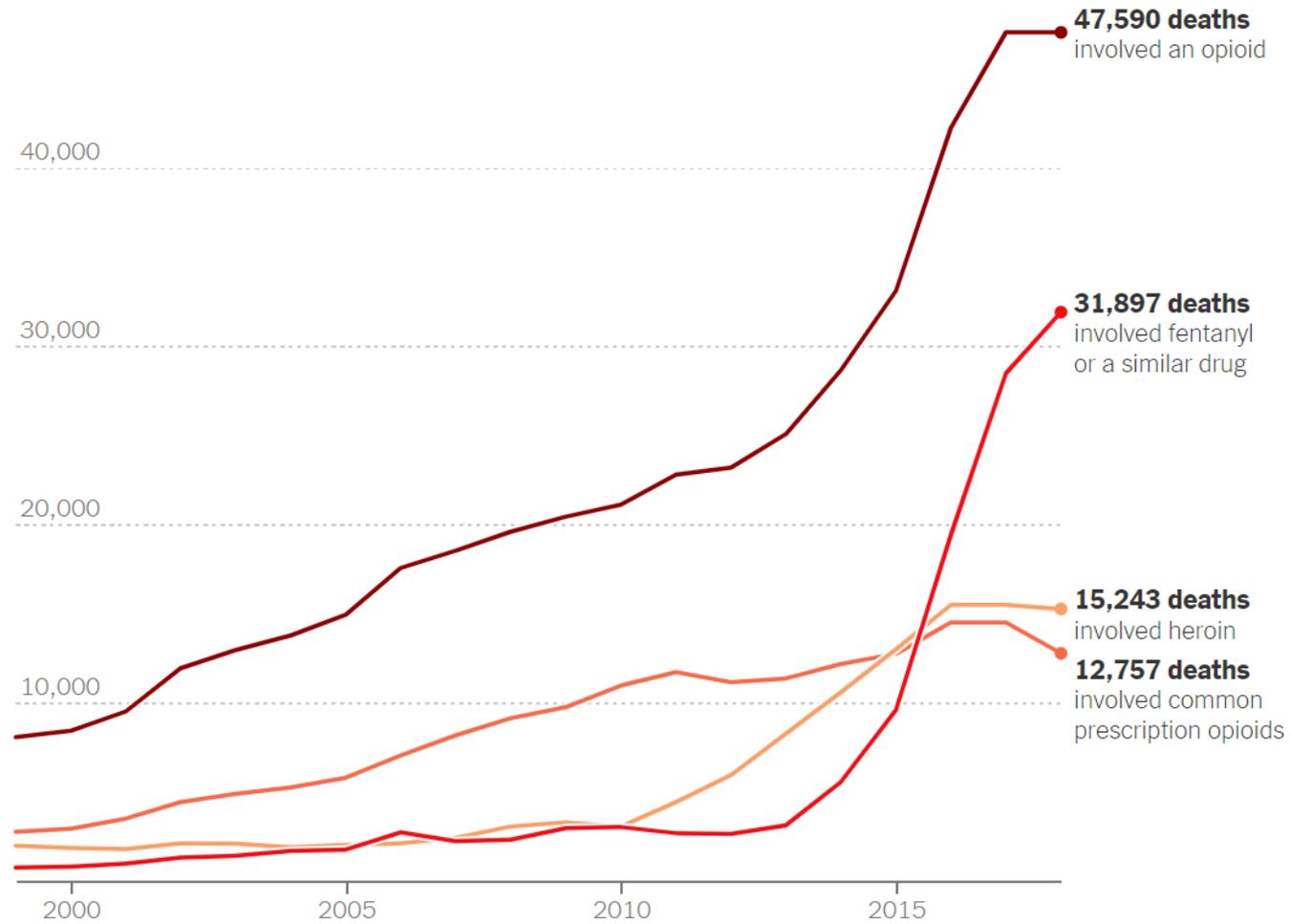


... while medically assisted treatment starts increased.



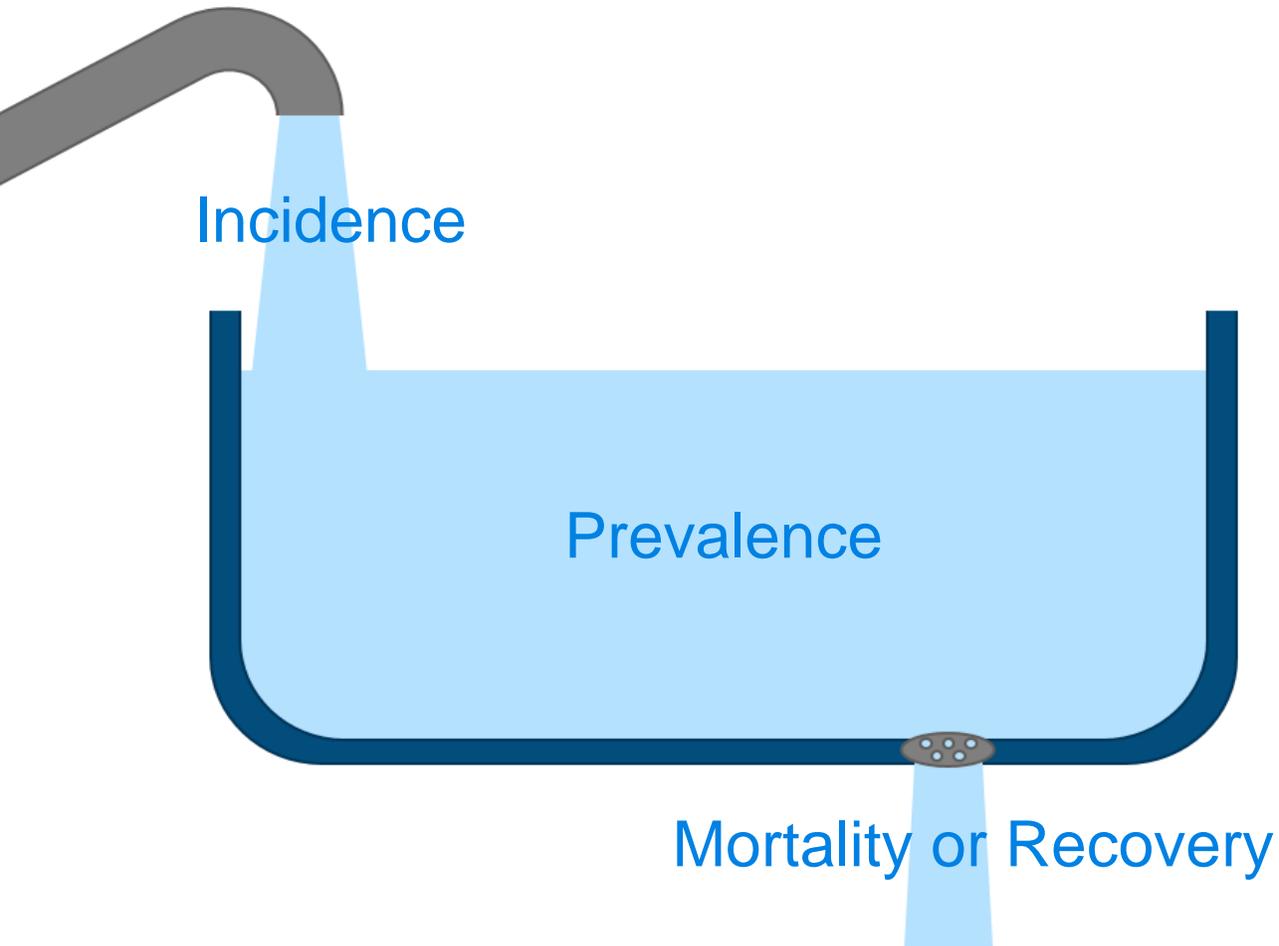
Note: Figures represent three-month moving averages
Source: IQVIA National Prescription Audit

Statistical blip or turning the tides?



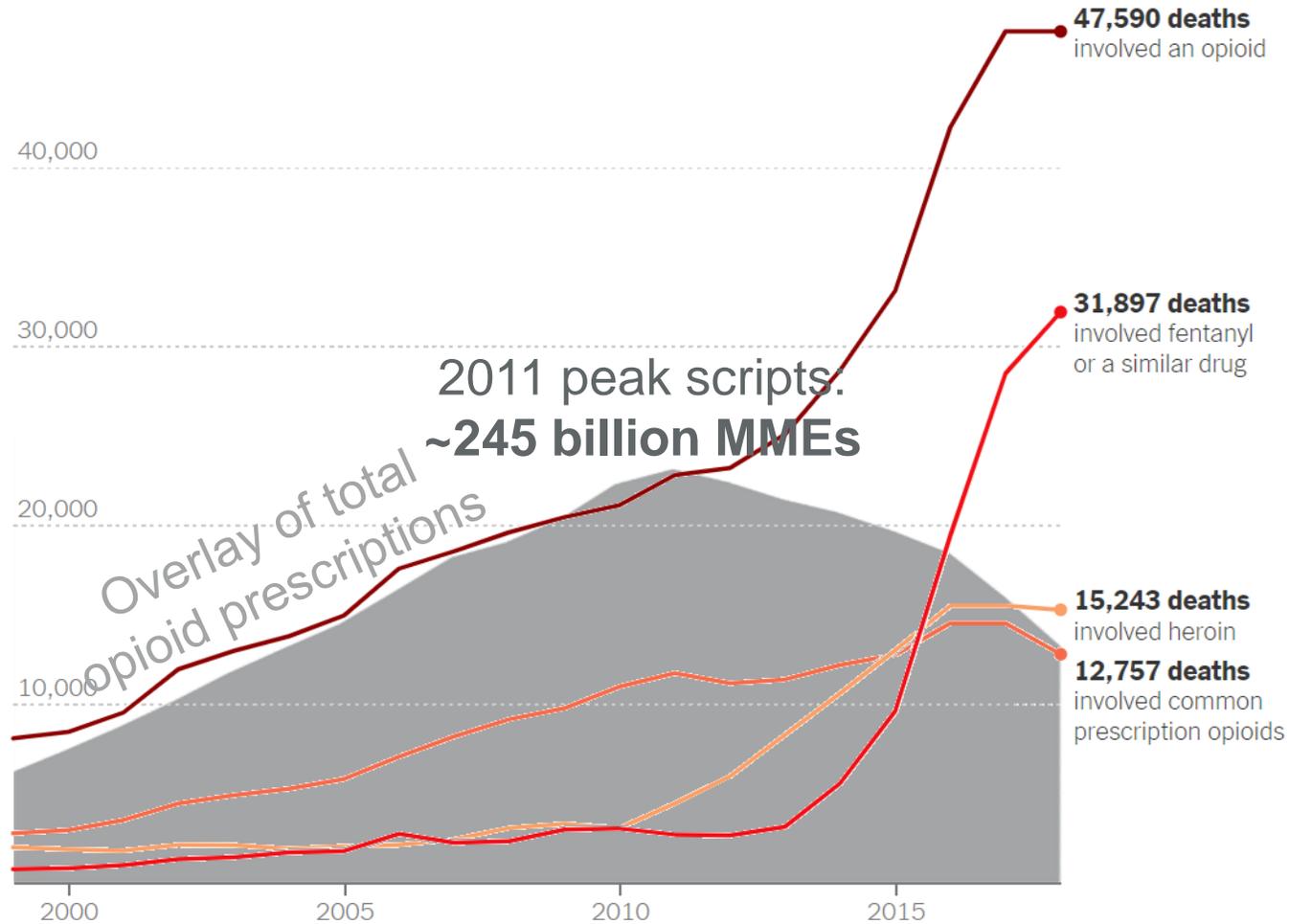
Categories are not mutually exclusive. Deaths often involve multiple drugs. A small portion of the increase in deaths attributable to a specific drug may be due to improved cause-of-death reporting.

Types of responses: Kitchen sink analogy



- Reduce the incidence of new cases
 - Careful prescribing practices
 - Safer drug formulations
 - Address the illicit drug environment
 - Address other risk factors for OUD (socioeconomic, mental health, etc.)
- Help people move towards recovery rather than mortality
 - Improve treatment access
 - Provide evidence-based care
 - Harms reduction strategies

Prescribing guidelines – the full story?



Categories are not mutually exclusive. Deaths often involve multiple drugs. A small portion of the increase in deaths attributable to a specific drug may be due to improved cause-of-death reporting.

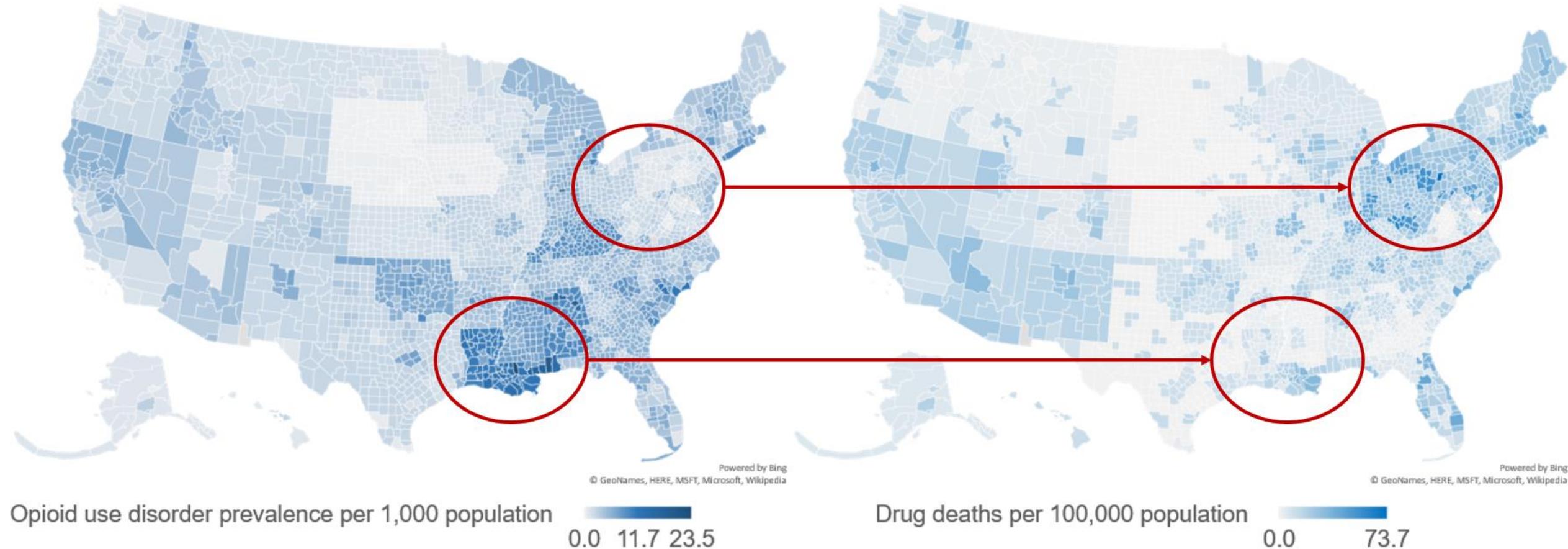
Source: IQVIA National Prescription Audit, Dec 2017; IQVIA Xponent, Feb 2019

Report: Medicine Use and Spending in the U.S. – A Review of 2018 and Outlook to 2023. IQVIA Institute for Human Data Science, May 2019

Graphic from The New York Times, July 17, 2019

Not all opioid use disorder is created equal

Geographic variation in opioid use disorder prevalence and drug overdose death rates

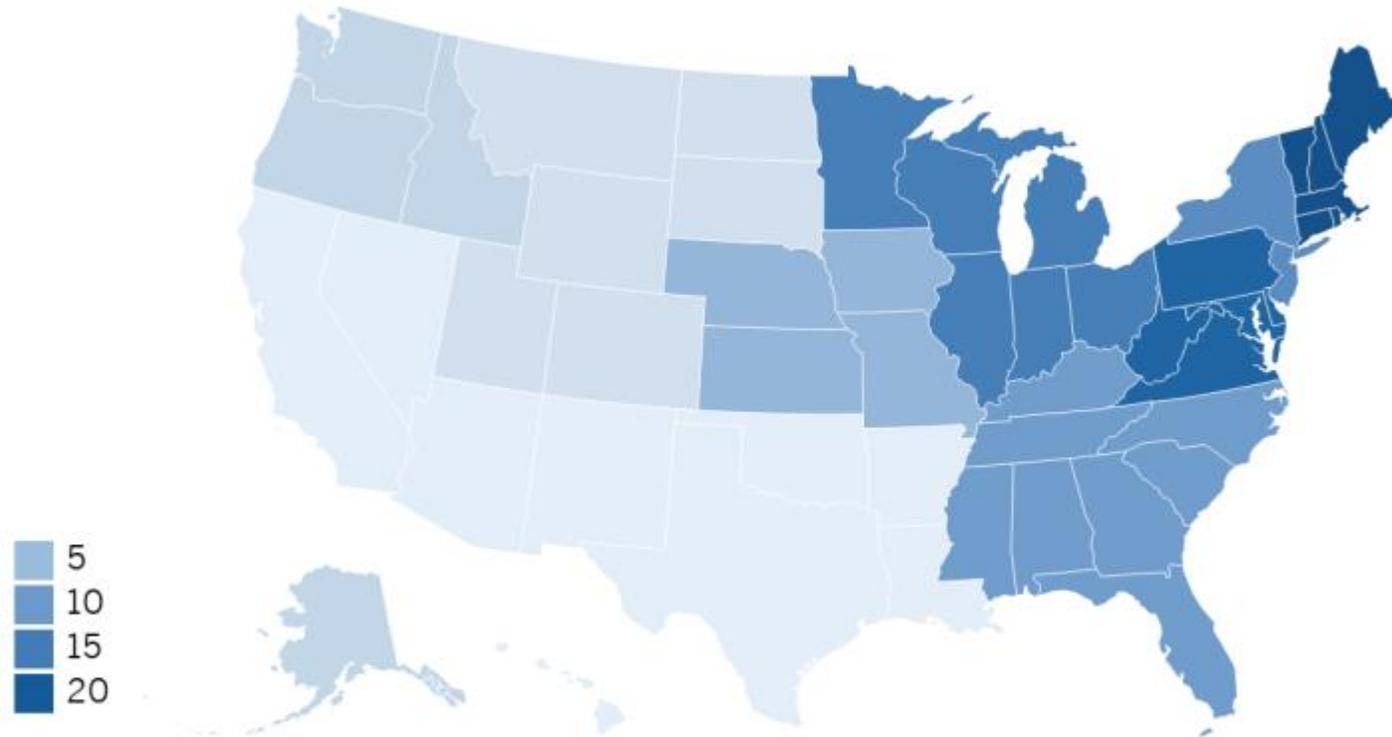


Source: Milliman Analysis, publication pending,
Center for Disease Control, U.S. State Prescribing Rates, <https://www.cdc.gov/drugoverdose/maps/rxstate2016.html>

Westward expansion of fentanyl

Fentanyl overdose deaths

In 2017, fatal overdoses involving fentanyl were most common in the northeast.



Age-adjusted death rates are reported per 100,000 people
CDC National Center for Health Statistics



A lethal dose: 2mg of fentanyl

Image credit: [DEA](#)

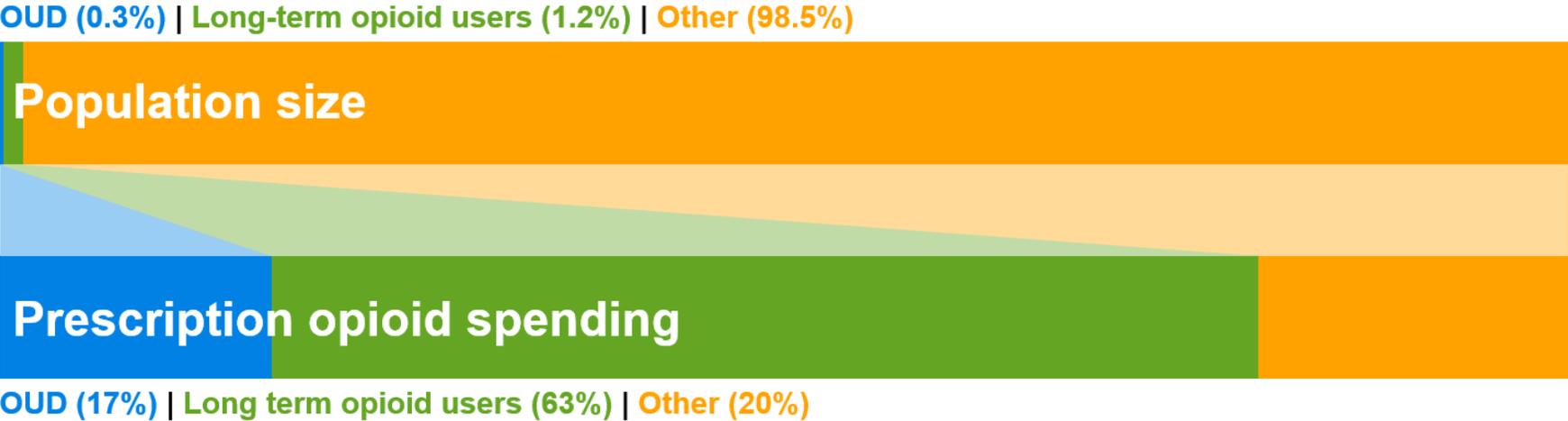
Just last month in CA:
18 pounds seized,
enough for **4 million**
lethal doses

<https://www.cbsnews.com/news/fentanyl-drug-bust-southern-california-enough-to-make-4-million-lethal-doses/>

Who is impacted by opioid prescribing guidelines?

- Among the privately insured, patients with OUD and those with long-term opioid use made up **1.5% of the population** in 2016, but accounted for **80% of spending** on Rx opioids.

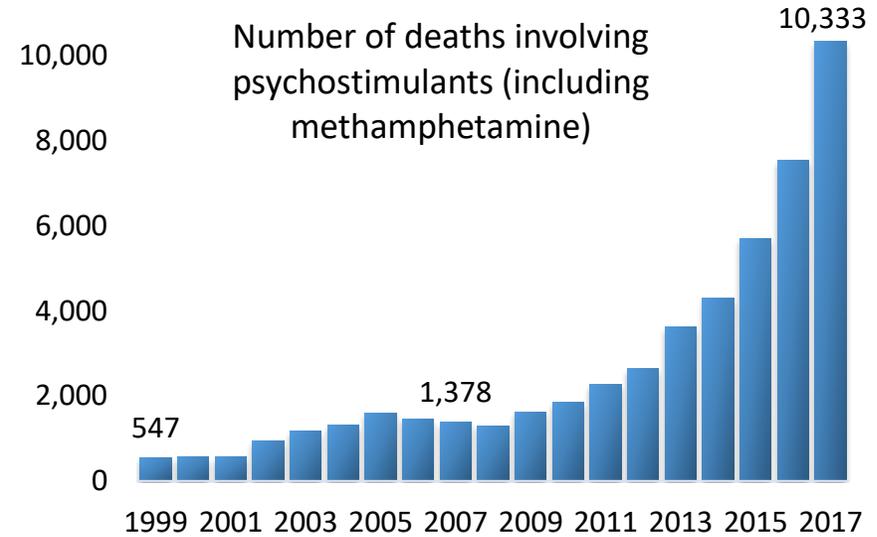
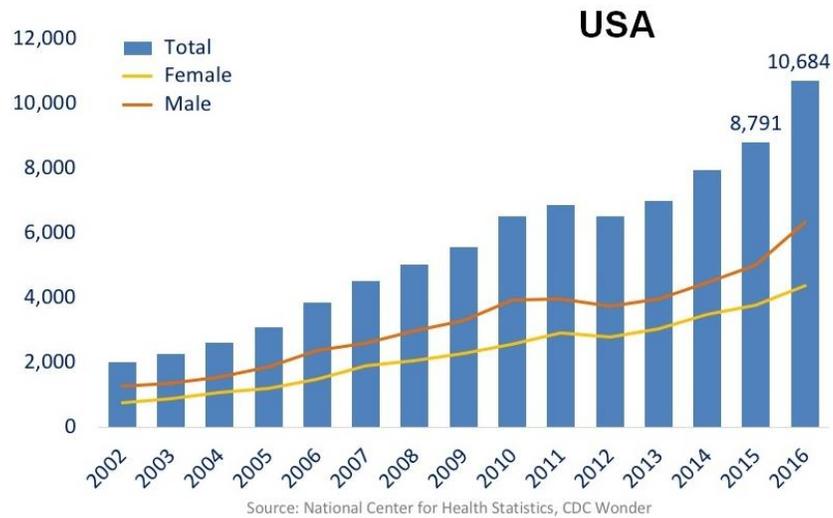
Comparison of population size and Rx opioid spending by opioid use cohort, 2016



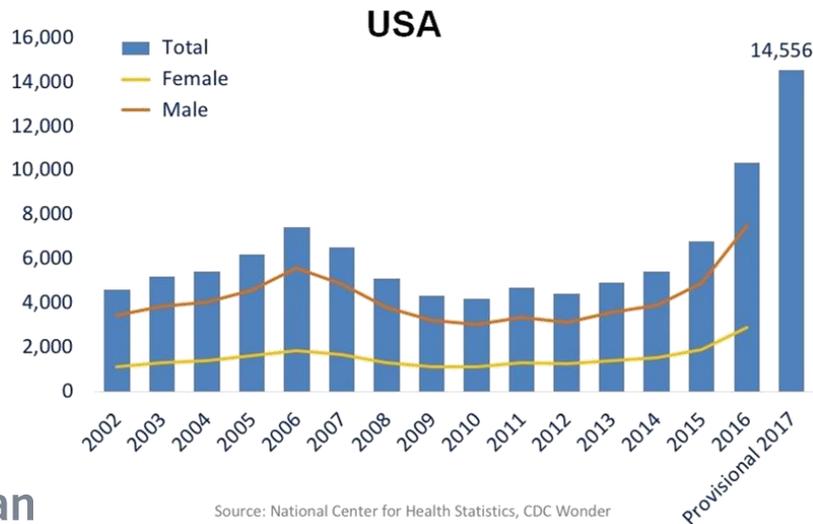
Source: Milliman White Paper – Costs and Comorbidities of Opioid Use Disorder. <http://www.milliman.com/insight/2019/Costs-and-comorbidities-of-opioid-use-disorder/>

Not just an opioid crisis . . .

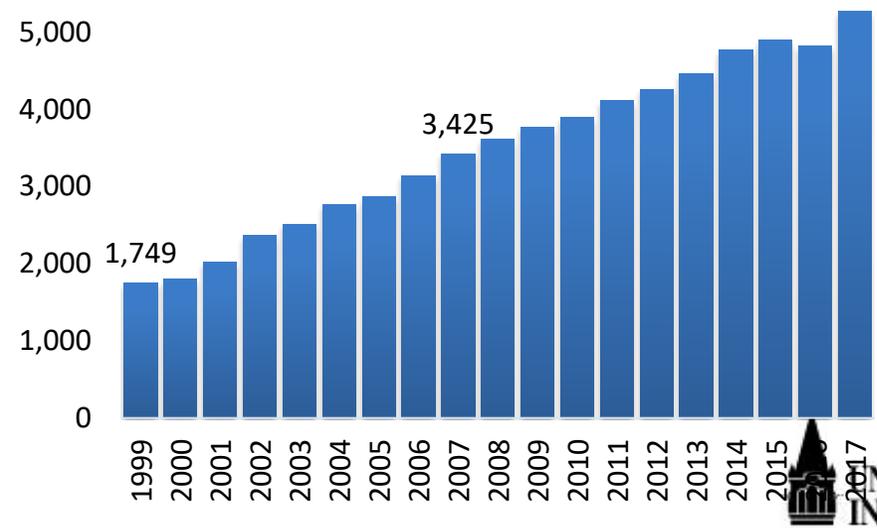
Number of Deaths Involving Benzodiazepines



Number of Deaths Involving Cocaine



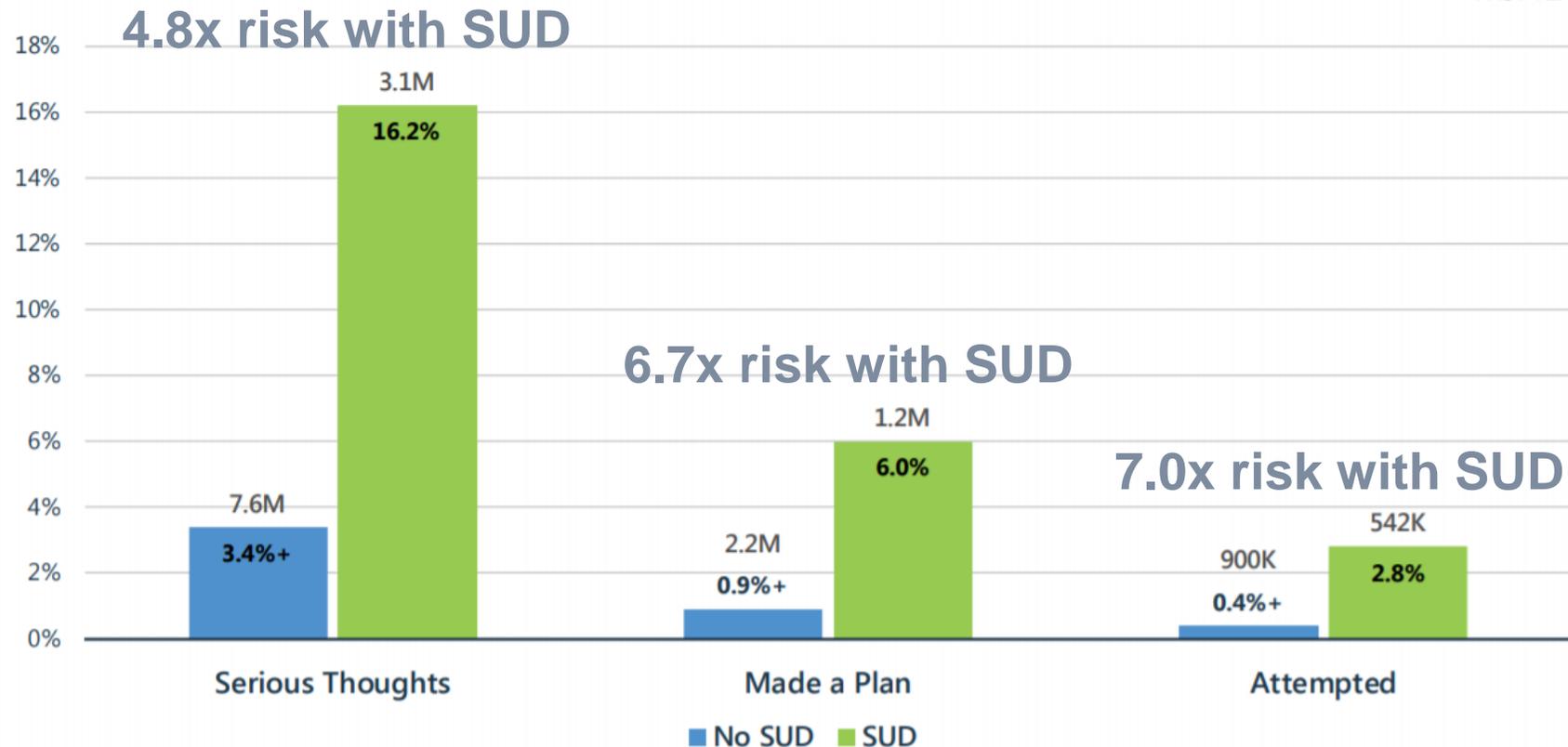
Number of deaths involving antidepressants



Not just an opioid crisis . . .

Co-Occurring Substance Use Disorder (SUD) is Associated with Suicidal Thoughts, Plans, and Attempts among Adults ≥ 18 y.o.

PAST YEAR, 2018 NSDUH, 18+



+ Difference between this estimate and the estimate for adults with SUD is statistically significant at the .05 level.

Competing theories

“Deaths of despair”

- Term popularized by Anne Case and Angus Deaton (Nobel Laureate)
- Idea that increasing deaths due to suicide, alcohol, and drug overdoses are the product of **cumulative socioeconomic disadvantage**
- *Key nuance*: contemporaneous economic conditions are poor explanatory factors, but **worsening opportunities at point of entry to job market** is important

Counterpoint

- NBER working paper finds **no relationship** with employment
- Another finds **only a small relationship** between medium-run economic conditions after controlling for drug environment

Why does it matter?

- Case and Deaton argue for long-term investments in expanding economic opportunities
- Others argue that diverting scarce resources to economic development instead of expanding treatment access could be disastrous

Sources:

Case A, Deaton A. Mortality and morbidity in the 21st century. Brookings Pap Econ Act. 2017;2017:397-476.

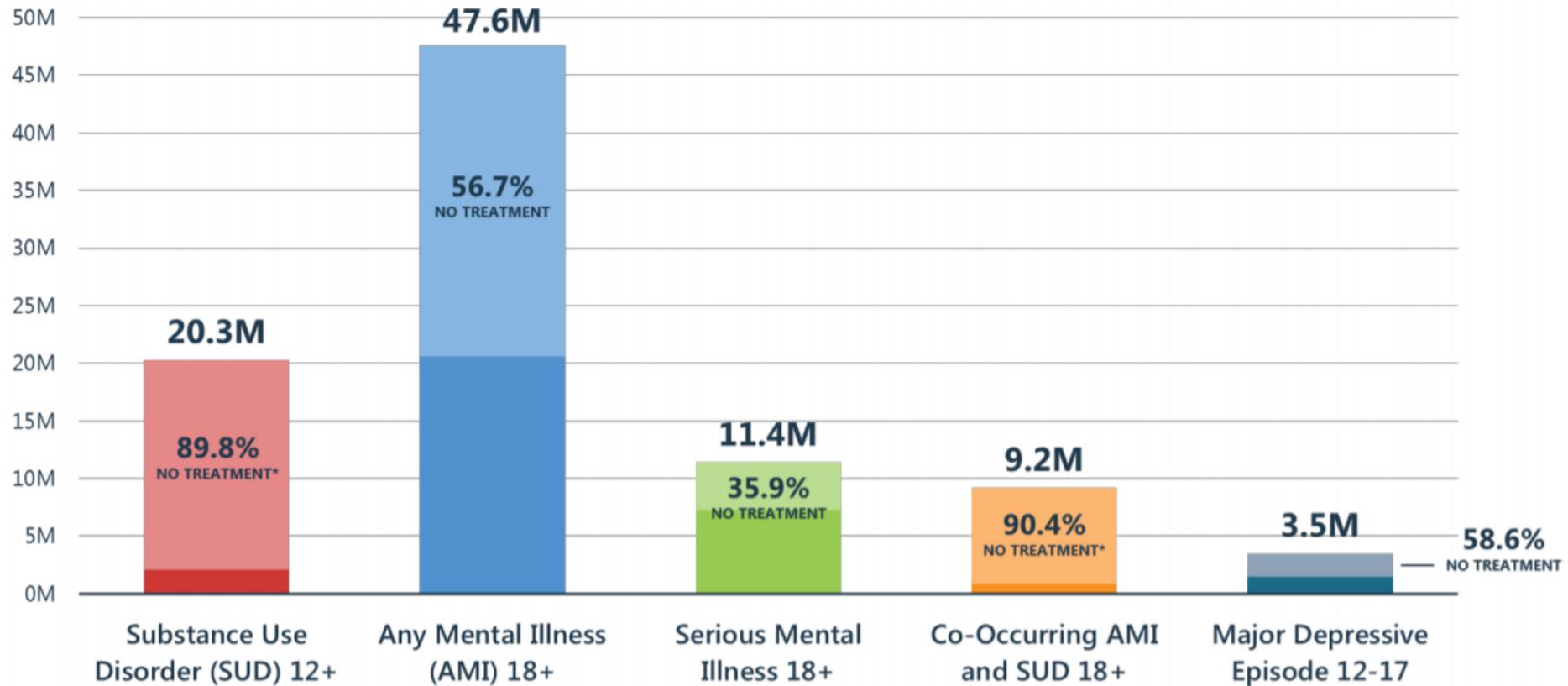
Currie J, Jin JY, Schnell M. U.S. Employment and opioids: Is there a connection? NBER Working Paper Series, no. 24440. Cambridge, MA; 2018.

Ruhm CJ. Deaths of Despair or Drug Problems? NBER Working Paper Series, no. 24188. Cambridge, MA; 2018.

Nearly 90% of those with SUD received no treatment

Despite Consequences and Disease Burden, Treatment Gaps Remain Vast

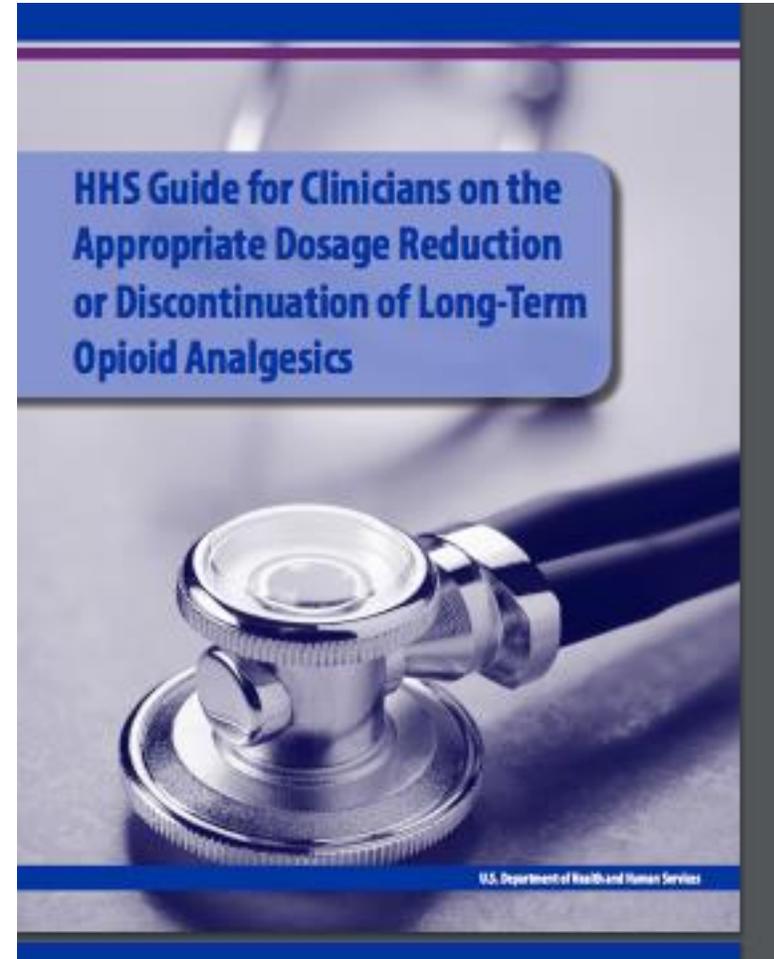
PAST YEAR, 2018 NSDUH, 12+



* No Treatment for SUD is defined as not receiving treatment at any location, such as a hospital (inpatient), rehabilitation facility (inpatient or outpatient), mental health center, emergency room, private doctor's office, self-help group, or prison/jail.

Rational Tapering Guidelines

- Risk of rapid tapering
- Shared decision making
- Individualize taper rate
- Monitor for withdrawal
 - Treat for withdrawal
- Provide Behavioral Health Support
- Consider special populations



New Target for Pain Control

Slide stolen from Wilson M. Compton, M.D., M.P.E., Deputy Director National Institute on Drug Abuse, July 17, 2017

- Congenital analgesia: rare condition, individuals cannot feel pain
 - Mutation identified in gene that encodes for Nav1.7 – sodium channel that regulates pain-sensing neurons
- Targeting Nav1.7 to produce analgesia
 - Several companies now have drugs in pipeline to block channel
- Targeting complications
 - Understanding what happens when Nav1.7 is blocked

nature Vol 444|14 December 2006|doi:10.1038/nature05413

ARTICLES

An *SCN9A* channelopathy causes congenital inability to experience pain

James J. Cox^{1*}, Frank Reimann^{2*}, Adeline K. Nicholas¹, Gemma Thornton¹, Emma Roberts³, Kelly Springell³, Gulshan Karbani⁴, Hussain Jafri⁵, Jovaria Mannan⁶, Yasmin Raashid⁷, Lihadh Al-Gazali⁸, Henan Hamamy⁹, Enza Maria Valente¹⁰, Shaun Gorman¹¹, Richard Williams¹², Duncan P. McHale¹², John N. Wood¹³, Fiona M. Gribble² & C. Geoffrey Woods¹



Cell

157, June 5, 2014

A Monoclonal Antibody that Targets a Nav1.7 Channel Voltage Sensor for Pain and Itch Relief

Jun-Ho Lee,¹ Chul-Kyu Park,² Gang Chen,² Qingjian Han,² Rou-Gang Xie,² Tong Liu,² Ru-Rong Ji,^{2,*} and Seok-Yong Lee^{1,*}

NEUROBIOLOGY

NATURE|Vol 444|14 December 2006

A channel sets the gain on pain

Stephen G. Waxman



Addiction prevention & treatment

Prevention

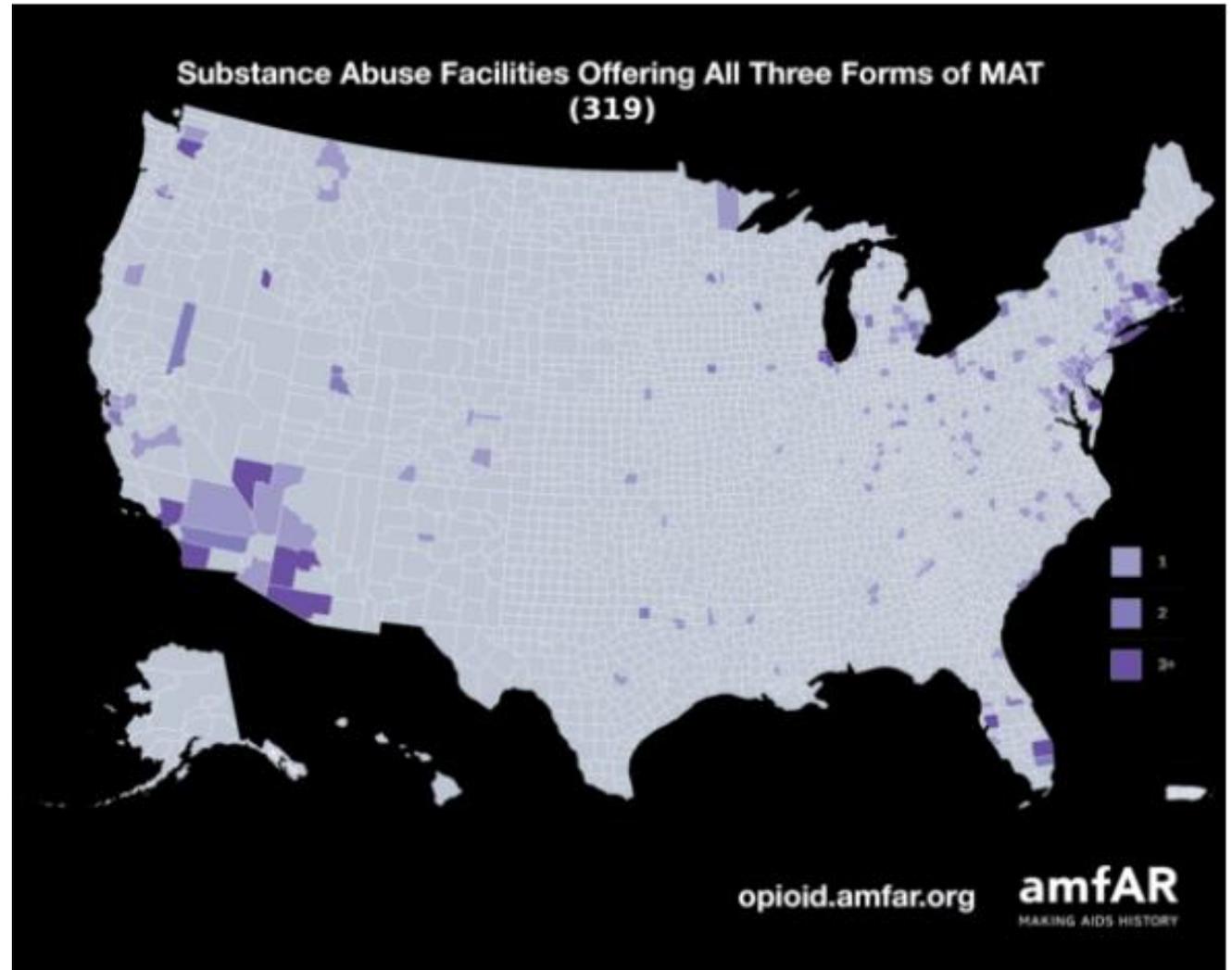
- Stricter prescription guidelines
- Treatment of chronic pain with non-opioid pain management
- Develop stronger opioid antagonist formulas to prevent overdoses
- New non-opioid targets for pain control
- Rationale opioid tapering

Treatment

- Detox, RTF, PHP, IOP, OP, counseling/therapy, MAR
- Expanding access to anti-addiction medication (e.g. naloxone)
- MAT/MAR is gold standard for harms reduction
 - Greater buprenorphine access decreased overdose deaths by 79% in four years in France

Harm reduction possible, but stymied by access issues

- **Medication assisted recovery saves lives and gets people functioning again**
 - **The big three:** Buprenorphine, methadone, naltrexone
 - Buprenorphine credited with cutting France's overdose deaths by 80% after their heroin epidemic in the '90s
- **It's also hard to find and access**
 - DEA waiver process
 - Provider reluctance
 - Lack of financial incentives - insurers cover opioids much more readily than treatments for OUD



Sources: irjci.blogspot.com/2018/01/county-level-map-shows-one-reason.html
www.vox.com/platform/amp/2018/1/10/16872012/opioid-epidemic-medication-addiction-map

Access to Treatment: Insurance

- Parity for addiction treatment is uncommon
 - Often easier to obtain opioids than addiction medication
 - Insurers restrict less-addictive painkillers
 - Prior-approval
 - Termination of coverage on certain non-opioid drugs
 - 85% of US counties have no opioid treatment programs
 - Available treatment is often expensive and uncovered
- Days in residential treatment facilities are often limited to shorter than full courses of treatment

Sources: www.nytimes.com/2017/09/17/health/opioid-painkillers-insurance-companies.html?_r=0
www.washingtonpost.com/opinions/insurers-are-making-it-harder-for-me-to-treat-my-opioid-addicted-patients/2018/04/17/
www.vox.com/policy-and-politics/2018/5/10/17256572/opioid-epidemic-virginia-medicaid-expansion-arts/24/1ed674b0-2090-11e8-8676-54bfff693d2b_story.html?utm_term=.ad2082fcb7fd

Parting thoughts

- Avoid knee-jerk reactions
- Nuance, nuance, nuance!
- Opioid prescribing guidelines matter but are not the full picture
- Need comprehensive support for chronic pain patients, patients with use disorders, and patients in recovery
- Recognize that many non-clinical factors are involved

Questions?



Thank you

J. Nile Barnes, PharmD

jbarnes@uiwtx.edu

Stoddard Davenport, MPH

stoddard.davenport@milliman.com