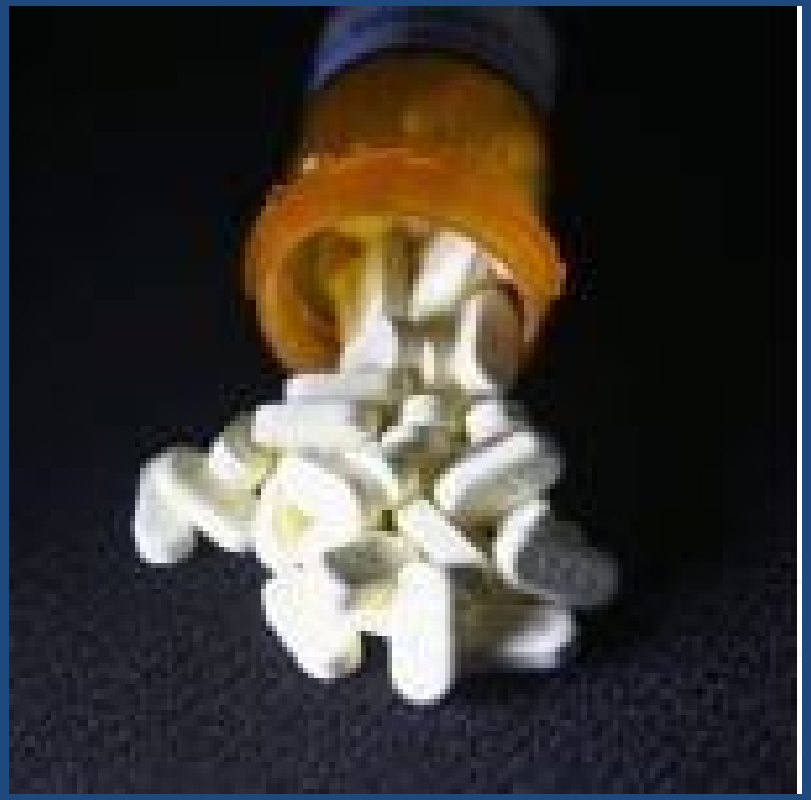
The U.S. Opioid Epidemic: Occupational Health Perspectives



John Howard, M.D.
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services

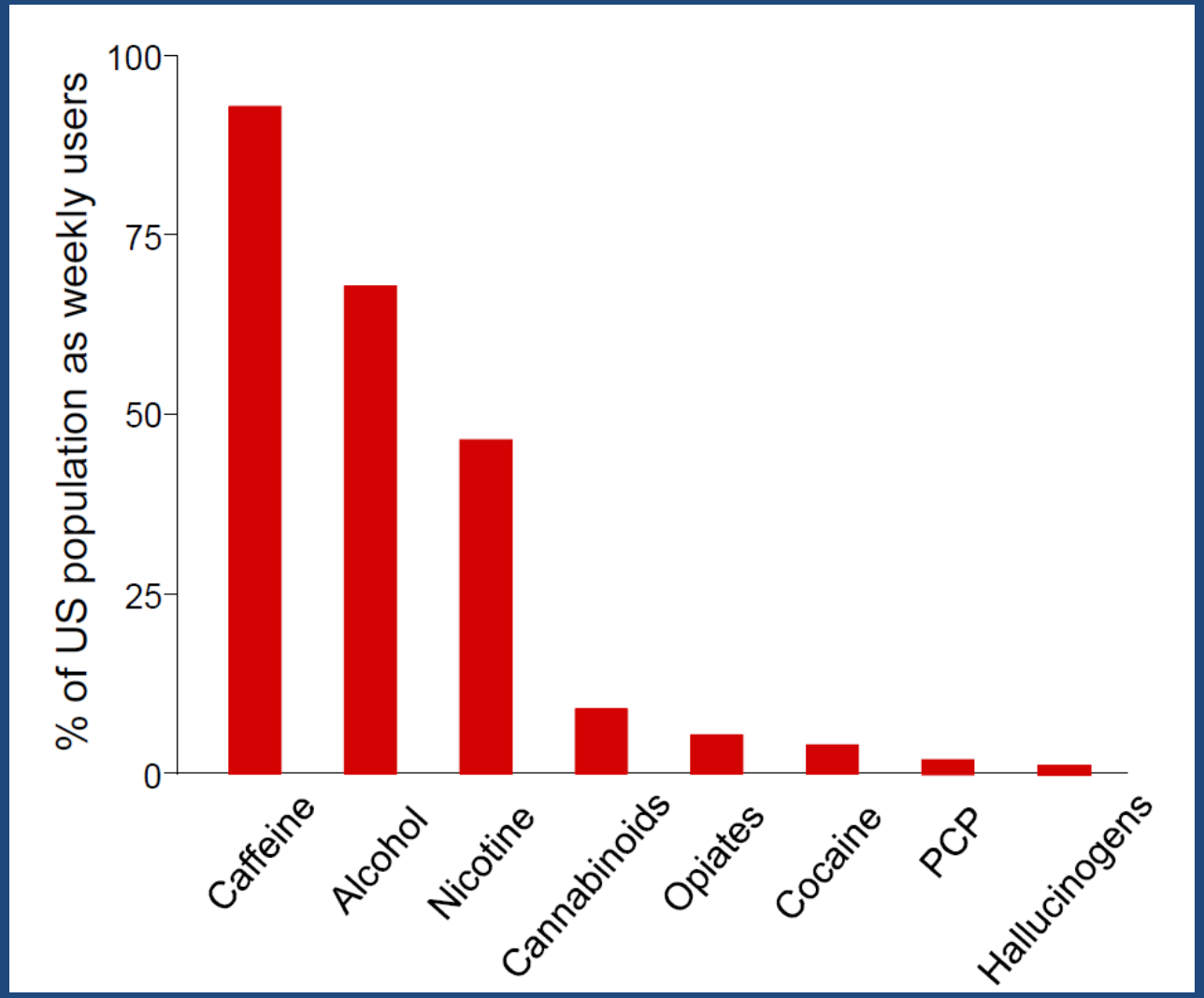
4 December 2019

California Industrial Hygiene Council
Mark Hopkins Hotel
San Francisco, CA

Why Do People Take Substances of Abuse?

NIDA, 2007

- To feel good
- To feel better
- To do better
- Because others are doing it



Overview of the Opioid Epidemic

- Terminology, Pharmacology, History
- Prescribing Epidemic
- Opioid Use Disorder
- Neurobiology of Addiction
- Illicit Epidemic
- Workforce
- Public Policy

Papaver somniferum

- Opium is processed from the latex sap of the opium poppy, *Papaver somniferum*.

- One of the oldest herbal medicines, has been used as analgesic, sedative, and antidiarrheal drug for 5,000 years.

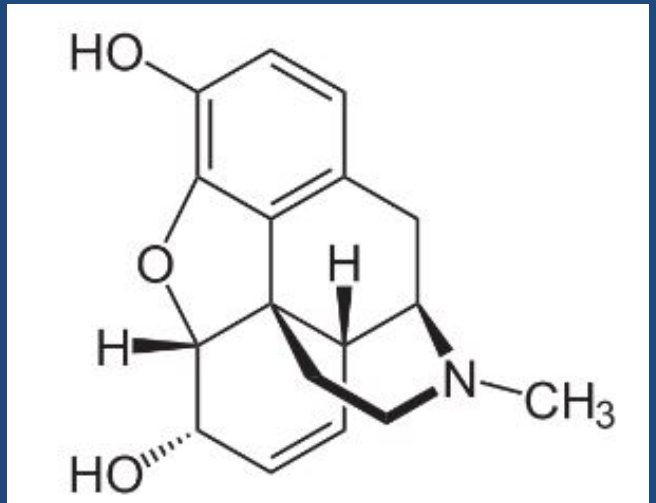
Opiate *vs* Opioid

- **Opiates**
  - Chemical compounds that are “*extracted*” or “*refined*” from natural plant matter (poppy sap and fibers).
  - Opium, morphine, codeine

- **Opioids**
  - Chemical compounds that generally are <u>not</u> derived from natural plant matter.
  - Most opioids are "made in the lab" or "*synthesized*."

3 Categories of Opioids

- **Natural-occurring opioids**
  - Morphine and codeine
- **Semi-synthetic opioids**
  - Hydrocodone, oxycodone, heroin
- **Synthetic opioids**
  - Methadone, demerol, tramadol
  - Fentanyl
    - 50x to 100x more potent than morphine
  - Fentanyl analogues (>2000)
    - Carfentanil
      - Used in veterinary medicine for sedating elephants
      - 10,000x more potent than morphine



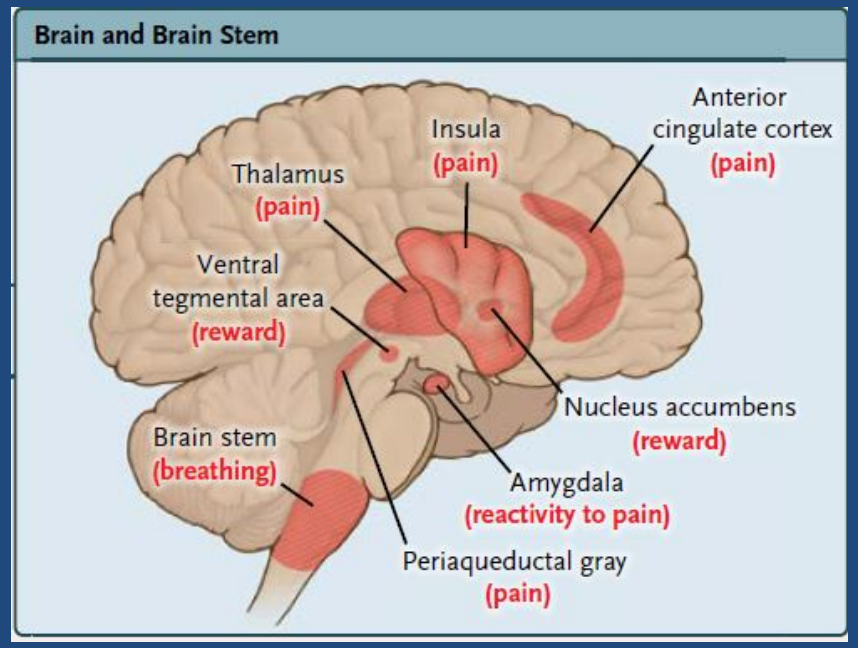
Morphine - chemical structure

Pathophysiology

- Opioids increase activity at mu (**μ**), kappa (**κ**), and delta (**δ**) opioid receptors.
- Opioid receptors are activated by both *endogenous* (endorphins) and *exogenous* (opioids) compounds.
- Mu receptors are responsible for most of the clinical effects:
  - Regulate the perception of pain (***analgesia***)
  - Regulate the perception of pleasure (***euphoria***)
- Rewarding effects of opioids are accentuated mostly when the drugs are delivered *rapidly* to the brain through intranasal or intravenous routes

Location of Mu-Opioid Receptors

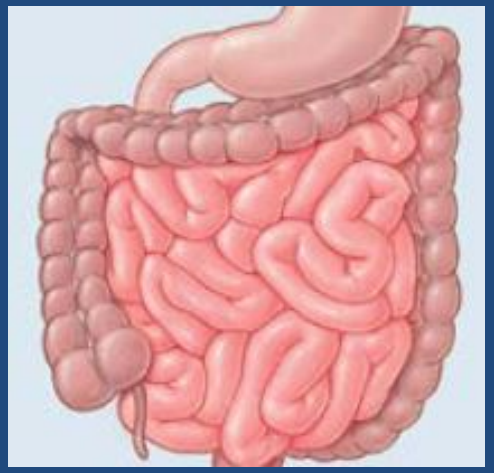
- **Brain and Brain Stem**
  - High concentration in the thalamus, periaqueductal gray, insula, and anterior cingulate (regions involved with **pain perception**), in the ventral tegmental area and nucleus accumbens (regions involved with **reward**), in the amygdala (a region involved with emotional **reactivity to pain**), and in the locus ceruleus of the brain stem (nuclei that regulate **breathing**).

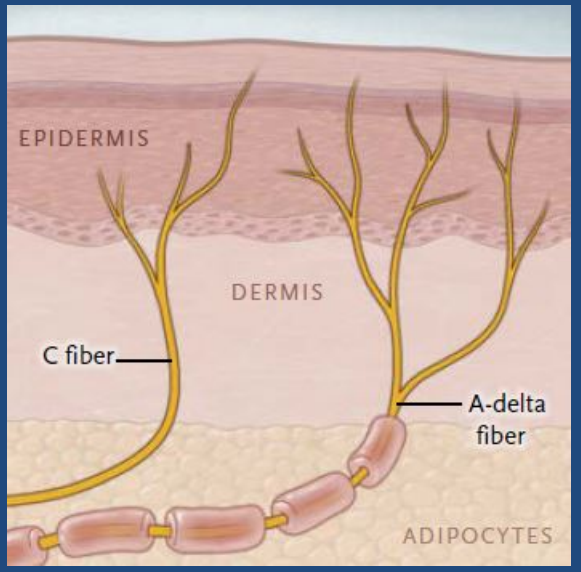


- **Spinal Cord**
  - High concentration of mu-opioid receptors located in the dorsal horn.

- **Peripheral Nervous System**
  - Modulate the perception of pain.

- **Intestine**
  - Regulates gut motility.





Clinical Manifestations of Overdose

- Essential sign is **respiratory depression**

- Individual with a respiratory rate of 12 breaths/minute or less:
  - Who is not in physiologic sleep
  - Suggests acute opioid intoxication particularly when accompanied by **miosis** or **stupor.**

Opioids in the United States—A History

Post-Civil War Era

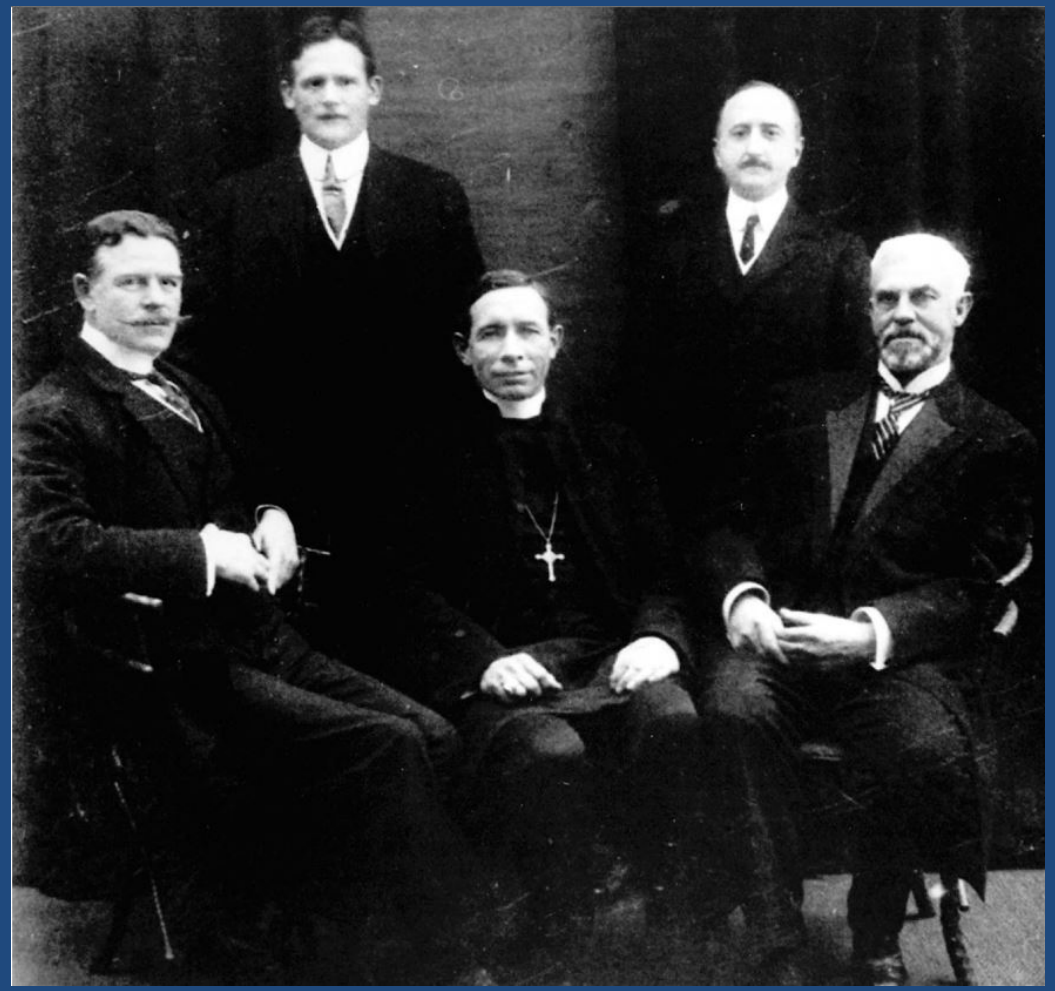
- Morphine first extracted from opium in pure form in 19th century.
- In decades after Civil War, U.S. developed a narcotics habit when disabled veterans became addicted to morphine.
- Later, genteel “society ladies” dosed up with *Laudanum* — a tincture of alcohol and opium first prepared in the 16th century by Paracelsus.

Tincture of Laudanum

- Sold as “elixirs” and “syrups”
- Widely used for in children for “teething,” as a cough suppressant, and an anti-diarrhea medication

“The Greatest Drug Fiends in the World”

Miroff, N. *Washington Post* (2017) quoting *Hamilton Wright* in 1908



U.S. delegation to the *International Opium Conference* at The Hague in 1911.
America’s first Opium Commissioner, Hamilton Wright, is at left.

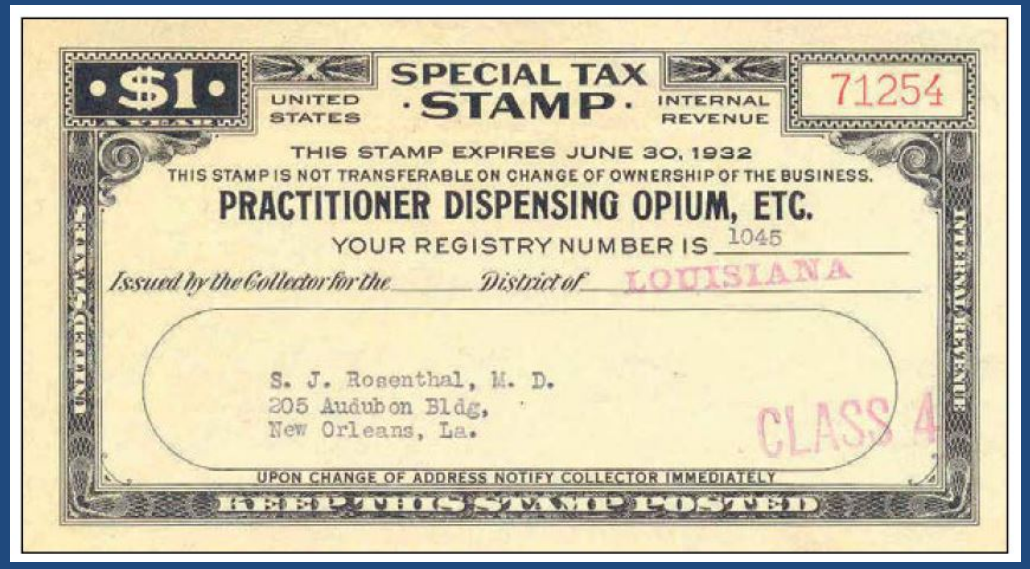
Government Reacts to Opium Use

- **1890—**U.S. government begins taxing *opium*.
- **1905—**U.S. bans *opium*.
- **1906—***Pure Food and Drug Act* forced manufacturers to disclose the contents of their products, so consumers wary of *opium* would know if it was in their children's cough syrup.
- **1909—***Opium Exclusion Act* bans import of opium for *smoking*.

1914—Harrison Narcotics Tax Act

- Required anyone who imported, produced, sold, or dispensed "narcotics" to register, pay a nominal tax, and keep detailed records.
  - *Linder v. U.S.* (1925)

- With such records, officials could better enforce existing laws, such as those requiring sale by prescription only.



Controlled Substances Act of 1970

- Federal statute prescribing U.S. drug policy under which the manufacture, importation, possession, use and distribution of certain chemical substances is regulated.

- Passed by Congress as Title II of the *Comprehensive Drug Abuse Prevention and Control Act of 1970* and signed into law by President Nixon.

- CSA created 5 Schedules in a hierarchy of production, prescribing and dispensing controls.

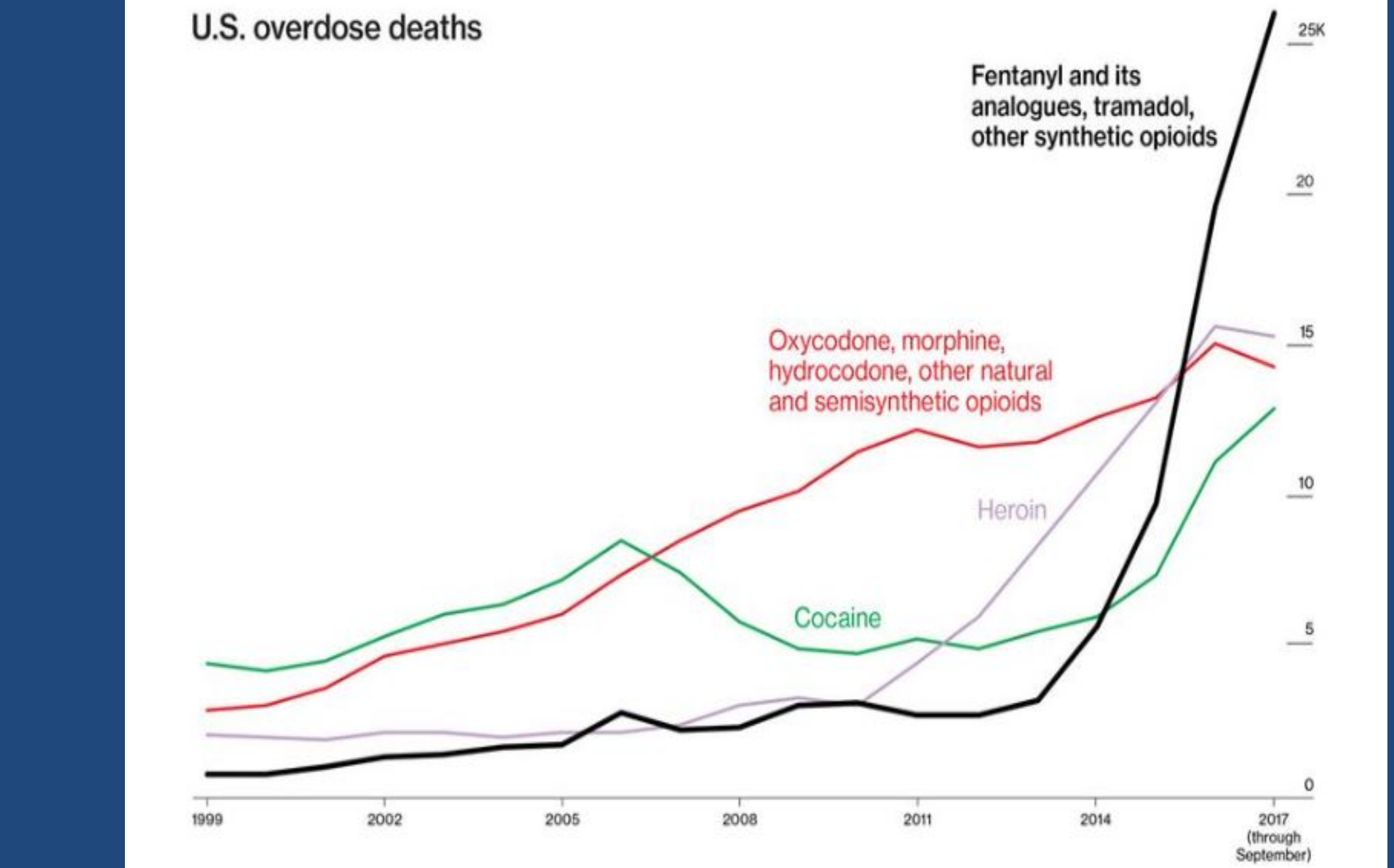
Schedule 1	Drugs with no currently accepted medical use and a high potential for abuse. They are the most dangerous drugs of all the drug schedules with potentially severe psychological or physical dependence.	- Heroin - Lysergic acid diethylamide (LSD) - Marijuana (Cannabis) - Methylenedioxymethamphetamine (Ecstasy) - Methaqualone - Peyote
Schedule 2	Drugs with a high potential for abuse, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous.	- Combination products with less than 15mg of hydrocodone per dosage unit (Vicodin) - Cocaine - methamphetamine - Methadone - Hydromorphone (Dilaudid) - Meperidine (Demerol) - Oxycodone (OxyContin) - Fentanyl - Dexedrine - Adderall - Ritalin
Schedule 3	Drugs with a moderate to low potential for physical and psychological dependence. Schedule 3 drugs abuse potential is less than Schedule 1 and Schedule 2 drugs but more than Schedule 4.	- Products containing less than 90mg of codeine per dosage unit (Tylenol and codeine) - Ketamine - Anabolic steroids - Testosterone
Schedule 4	Drugs with a low potential for abuse and low risk of dependence.	- Xanax - Soma - Darvon - Darvocet - Valium - Ativan - Talwin - Ambien - Tramadol
Schedule 5	Drugs with lower potential for abuse than Schedule 4 and consist of preparations containing limited quantities of certain narcotics. Schedule 5 drugs are generally used for antidiarrheal, antitussive, and analgesic purposes.	- Cough preparations with less than 200mg of codeine per 100ml (Robitussin AC) - Lomotil - Motofen - Lyrica - Parepectolin

Cannabinoids with FDA approval:

Marinol (synTHC)
Syndros (synTHC)
Cesamet (nabilone)
Epidiolex (cannabidiol)

Fast Forward to Present—3 Epidemic Curves

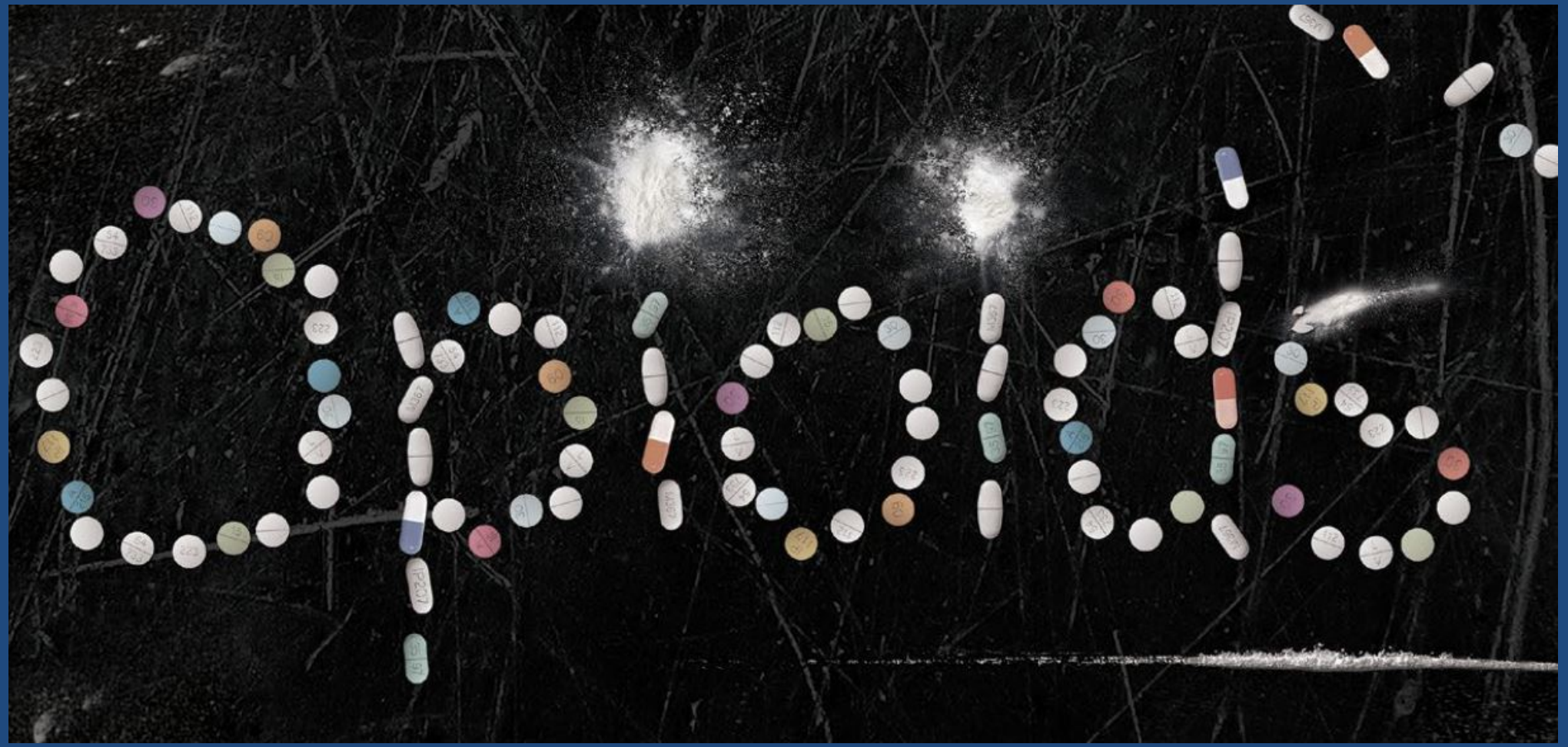
- **1990 to 2013**
  - Physician prescribing practices
- **2010**
  - Abuse-deterrent reformulation of OxyContin (making it difficult to crush or dissolve) led to quadrupling of heroin deaths (Evans et al., 2019) and 222% increase in hepatitis C infections (Powell et al., 2019).
- **2013 to Present**
  - U.S. opioid overdose deaths increased 90% from 25,052 to 47,600
  - Driven by illicitly manufactured fentanyl or fentanyl analogs mixed with heroin, sold as heroin, or pressed into counterfeit prescription pills.


U.S. overdose deaths
Fentanyl and its analogues, tramadol, other synthetic opioids
Oxycodone, morphine, hydrocodone, other natural and semisynthetic opioids
Heroin
Cocaine
25K
20
15
10
5
0
1999
2002
2005
2008
2011
2014
2017 (through September)
Source: Centers for Disease Control and Prevention
Bloomberg

Lifetime odds of death for selected causes, U.S., 2017

Cause of Death	Odds of Dying
Heart Disease	1 in 6
Cancer	1 in 7
Chronic Lower Respiratory Disease	1 in 27
Suicide	1 in 88
Opioid overdose	1 in 96
Motor Vehicle Crash	1 in 103
Fall	1 in 114
Gun Assault	1 in 285
Pedestrian Incident	1 in 556
Motorcyclist	1 in 858

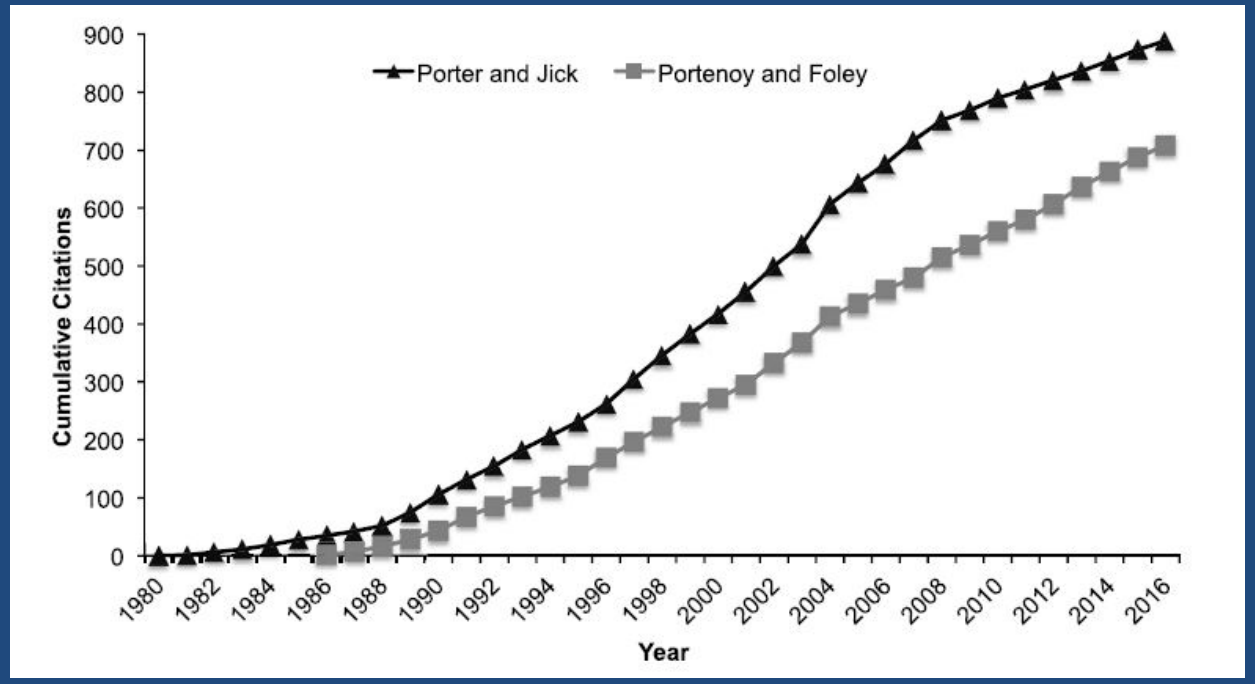
Prescribing Epidemic



Contributors to Physician Practices

- **1980**
  - **Porter & Jick** (*NEJM* 1980;302:123)
    - Letter suggested very low (0.03%) addiction rates in hospitalized patients treated with opioids for acute, non-recurrent pain.

- **1986**
  - **Portenoy & Foley** (*Pain* 1986;25:171-186)
    - 2/38 patients (5.3%) with history of substance abuse developed opioid issues.



Contributors to Prescribing Epidemic

- **1986**
  - **World Health Organization Cancer Pain Relief Guidelines**
    - Included opioids for the first time and recognized treatment of pain as a universal right.

- **1990s**
  - Hospitals begin patient/customer surveys
  - *Was your pain adequately relieved during your hospital stay?*

- **1996**
  - **American Pain Society**—adopts pain as the 5th vital sign.
  - **FDA** approves *Oxycontin*® (oxycodone extended release).
    - Marketed aggressively with claim addiction was very rare.
    - 2010—reformulation of *Oxycontin*® lead to wave of heroin overdose deaths

Contributors to Prescribing Epidemic

- **1998**
  - **Veterans Health Administration**
    - Launches National Pain Management Strategy (pain as the 5th vital sign)
  - **Federation of State Medical Boards**
    - Physicians would *not* receive excessive scrutiny if prescribing notable amounts of opioids.
- **2000**
  - **JCAHO** mandates pain assessment and treatment programs by 2001.
  - **DEA** adopts a "balanced policy" examining physician prescribing practices.

- **2007-2012**
  - **Excessive shipments to pharmacy dispensers**
    - 224,260,980 oxycodone shipped to West Virginia, 2007-2012
    - 555,808,292 hydrocodone shipped to West Virginia, 2007-2012
    - 433 opioid pills for every man, woman and child in West Virginia

Virginia Doctor Sentenced to 40 Years For Illegally Prescribing Thousands of Opioid Doses

Smithers was convicted in May of more than 800 counts of illegally distributing opioids, including oxycodone and oxymorphone that caused the death of a West Virginia woman.

Authorities say Smithers prescribed more than 500,000 doses of opioids to patients from Virginia, Kentucky, West Virginia, Ohio and Tennessee while based in Martinsville, Virginia, from 2015 to 2017.

https://www.nytimes.com/2019/10/02/us/opioids-doctor-sentenced-joel-smithers.html

Opioid Use Disorder

DSM5

Opioid use disorder

2-3: mild

4-5: moderate

6+: severe

Tolerance

Withdrawal

Using larger amounts than intended

Persistent desire and inability to cut down

Can't stop despite knowledge of harm

Spending a lot of time using/obtaining/recovering from substance use

Cravings

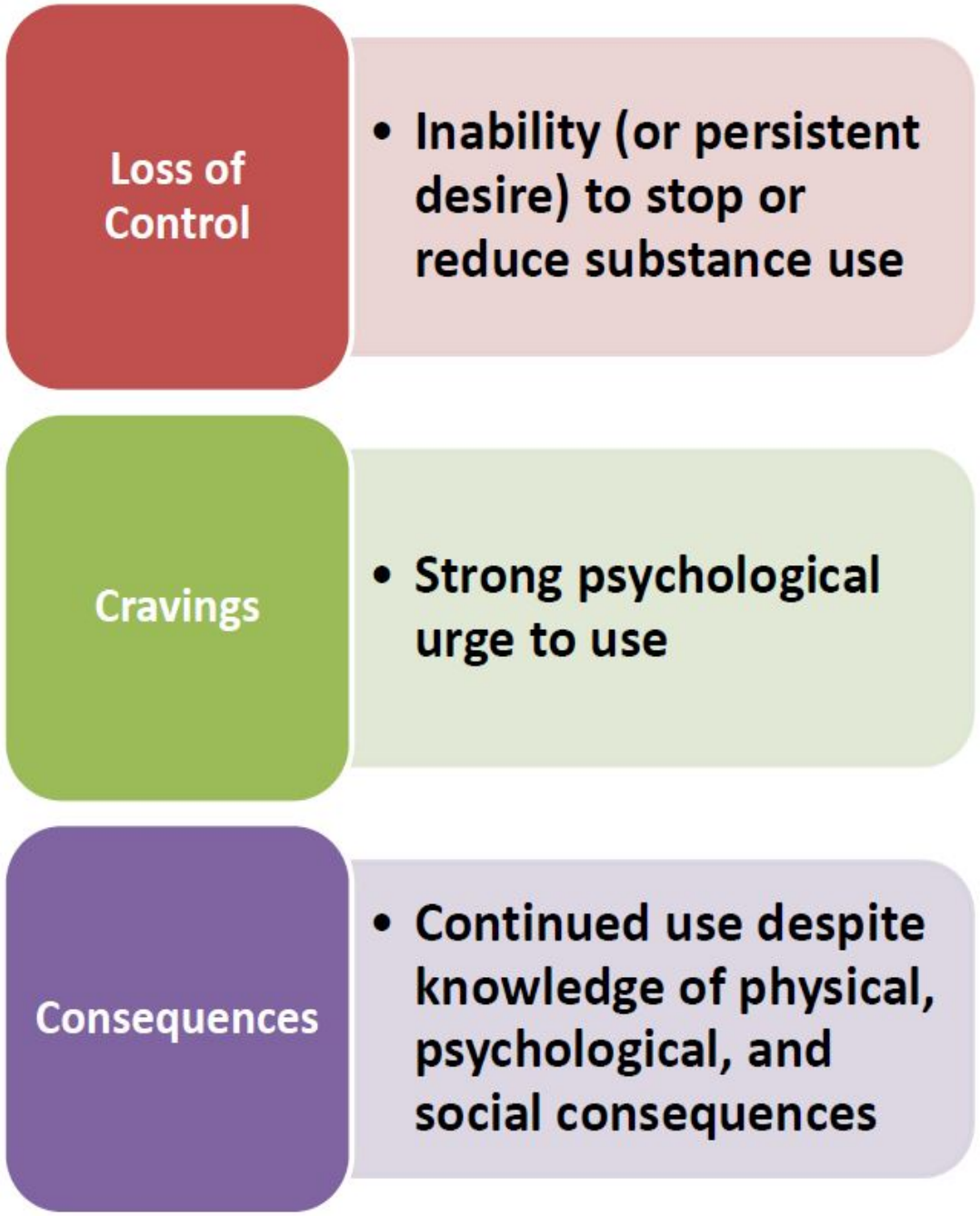
Using the substance in Dangerous situations

Important social and other activities are given up for drug use

Failed role obligations

Social conflict

The Three C's of Addiction



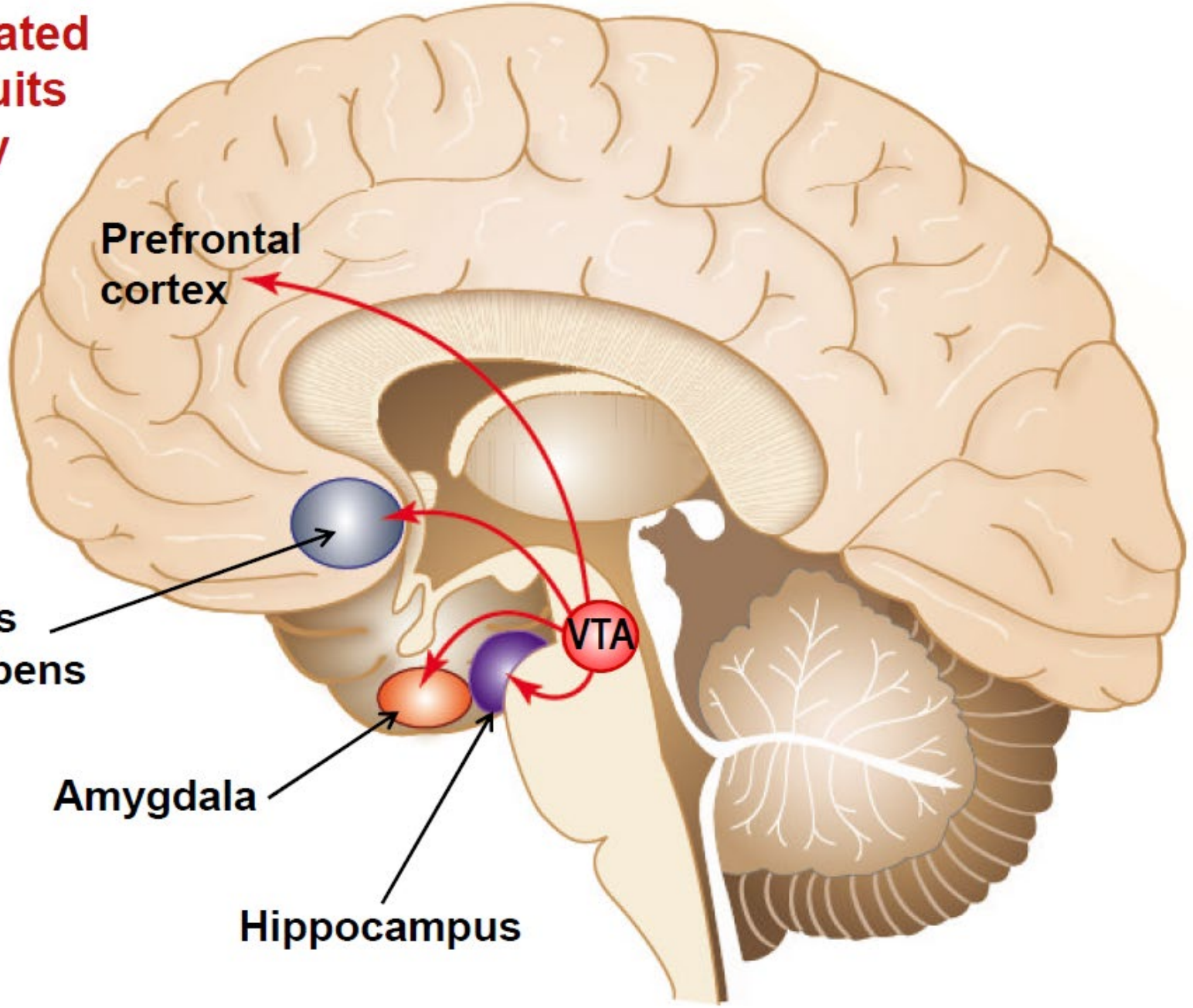
Explanatory Models of Addiction

- Moral → wrong
- Spiritual → empty
- Psychological → impulse control
- Behavioral → habit
- Medical → disease

Neurobiology of Addiction—

An Acquired Brain Disease

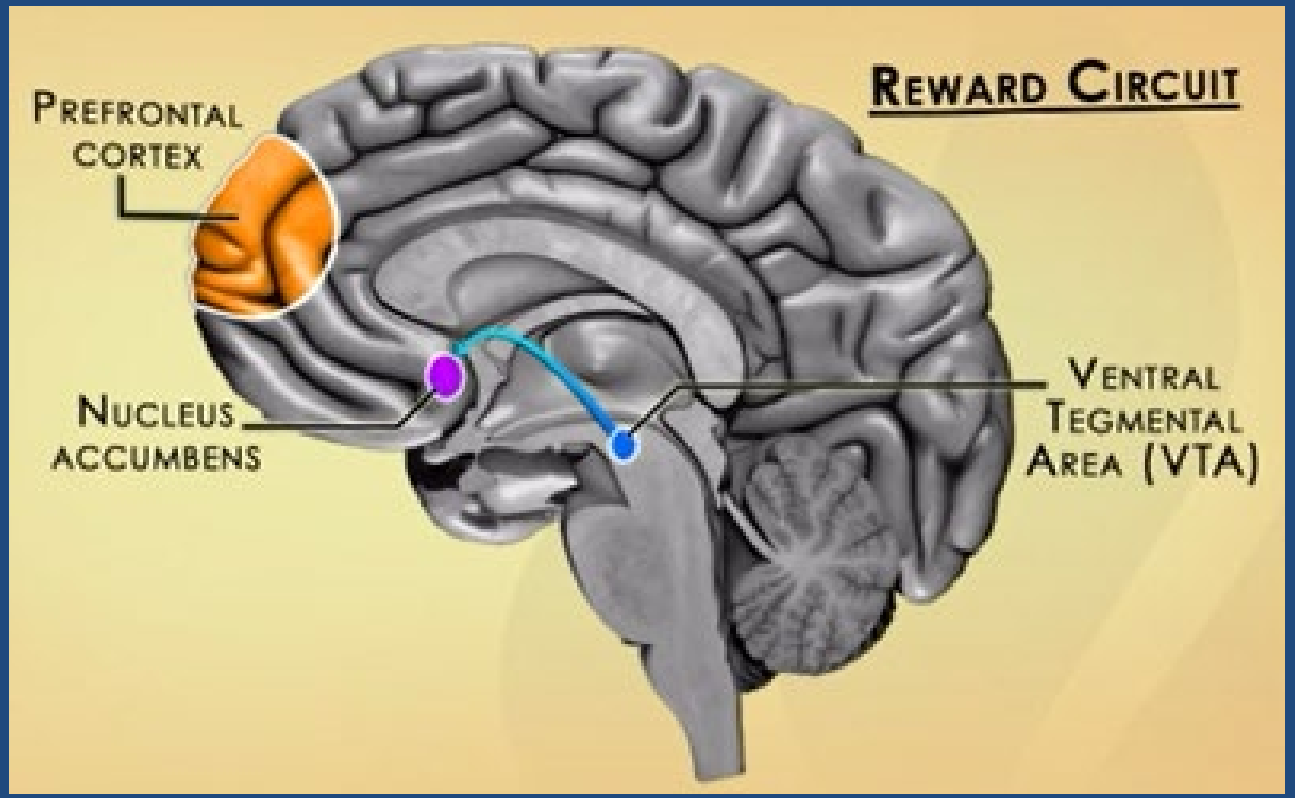
Highly integrated "limbic" circuits innervated by dopamine neurons in the VTA.



Neural Changes in Addiction

Volkow et al., *NEJM*. 374(4):363-371 (2016)

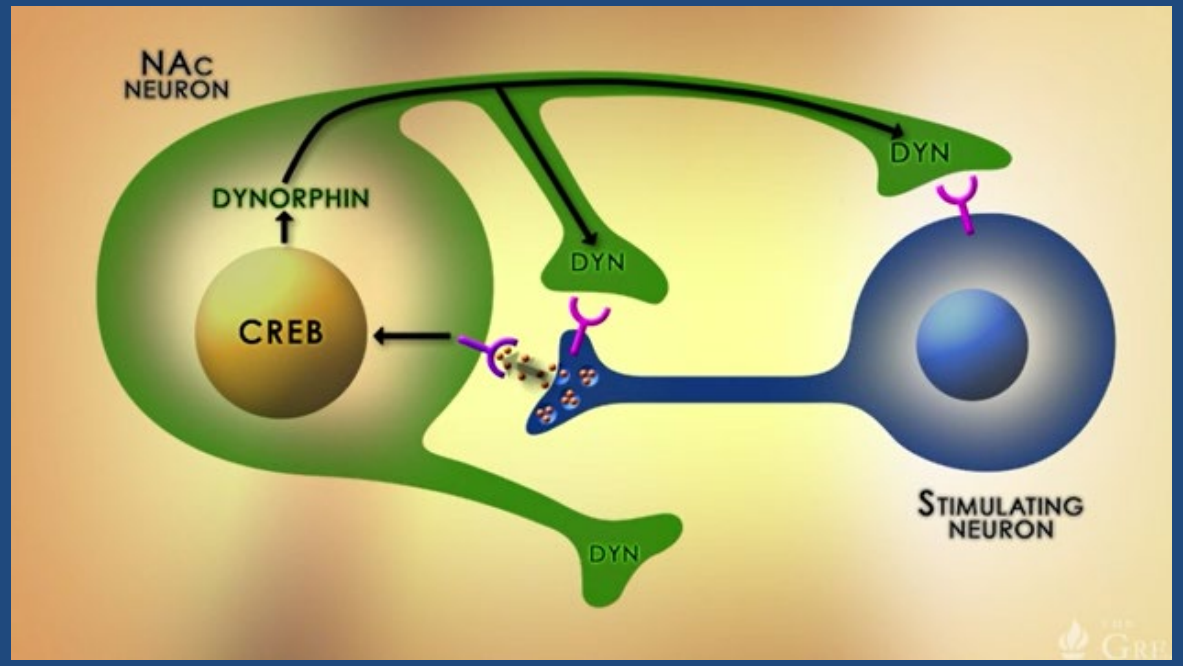
- Desensitization of the pleasure response in the *nucleus accumbens*
  - Tolerance
- Sensitivity to environmental cues leads to cravings
  - Dependence
- Weakened inhibition from pre-frontal cortex
  - Relapse



1. Numbed Pleasure Response—Tolerance

Volkow et al., *NEJM*. 374(4):363-371 (2016)

- NAcc overstimulation produces CREB
  - cAMP response element-binding protein
  - CREB transcribes *dynorphin* which then inhibits NA.



- Person feels less pleasure from drug
  - Requires more drug to feel same pleasure
  - Less sensitive to all types of pleasures.

- Drug then becomes the ONLY way to feel good
  - Tolerance develops

2. Increased Cravings

Kosten & George (2002); Volkow et al. (2016)

- How much a drug user ***likes*** the drug declines over time, but how much user ***wants*** the drugs does not decline

- During periods when the drug is not available, cravings get stronger because the brain remembers the drug

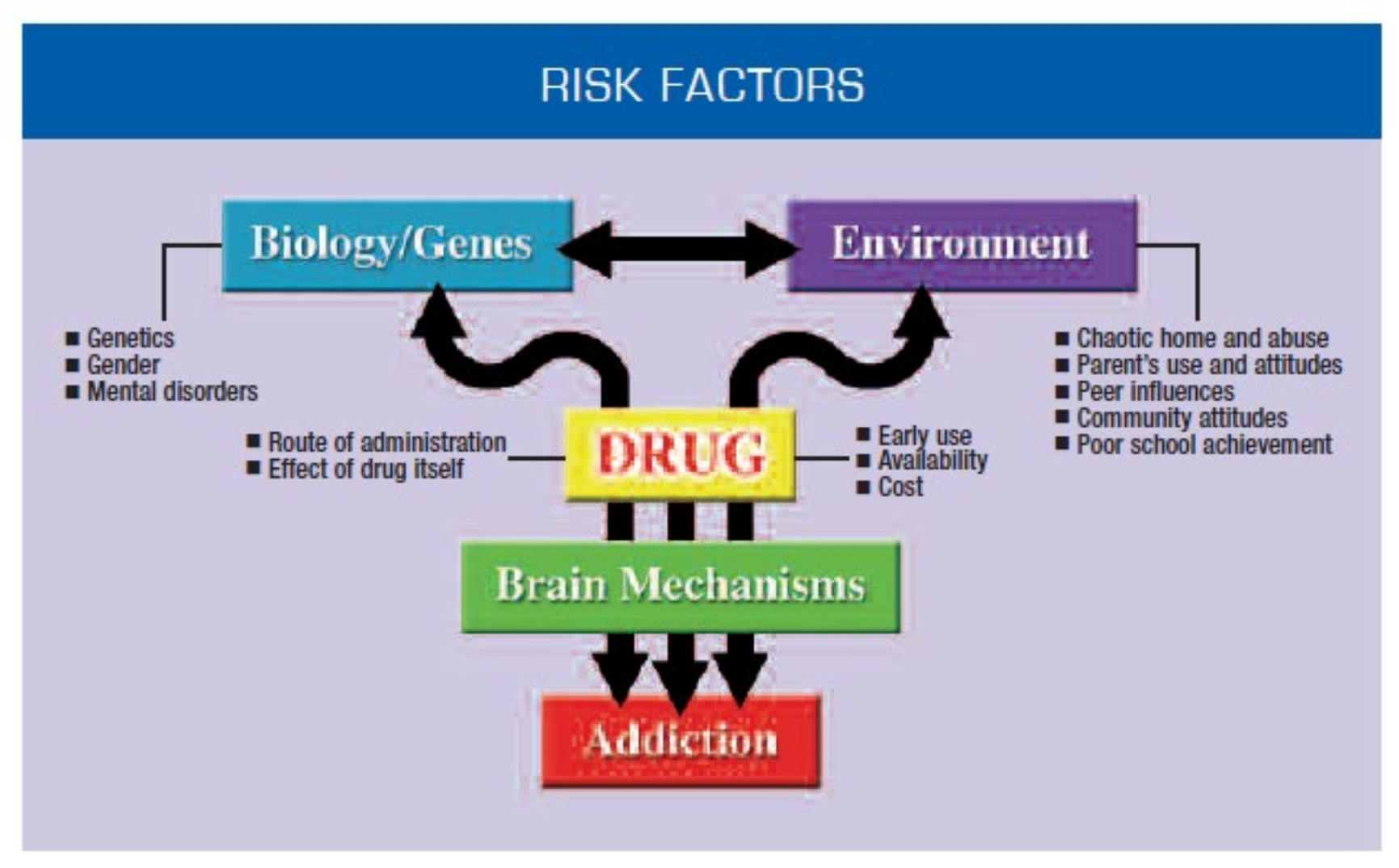
- Cravings may represent increased activity of the cortical excitatory (glutamate) neurotransmitters which drive the resting activity of dopamine-containing VTA neurons.

3. Reduced Self-Control

Volkow et al., *NEJM*. 374(4):363-371 (2016)

- Pre-frontal cortex (PFC) inhibits more primitive reward circuitry
- Accumulating evidence suggests chronic drug use impairs prefrontal cortex anatomy and function
- Neuroimaging in chronic drug users shows:
  - Reduced pre-frontal cortex *activity* and *volume*
- Drug users exhibit cognitive changes
  - Perform poorly on tasks of working memory and decision making
  - Perform poorly on tasks that require sustained attention

No single factor determines whether a person will become addicted to drugs.



CDC Guideline—2016

GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

IMPROVING PRACTICE THROUGH RECOMMENDATIONS

CDC's *Guideline for Prescribing Opioids for Chronic Pain* is intended to improve communication between providers and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder and overdose. The Guideline is not intended for patients who are in active cancer treatment, palliative care, or end-of-life care.

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

1 OPIOIDS ARE NOT FIRST-LINE THERAPY

Nonpharmacologic therapy and **nonopioid pharmacologic therapy** are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

2 ESTABLISH GOALS FOR PAIN AND FUNCTION

Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

Nonpharmacologic therapies and nonopioid medications include:

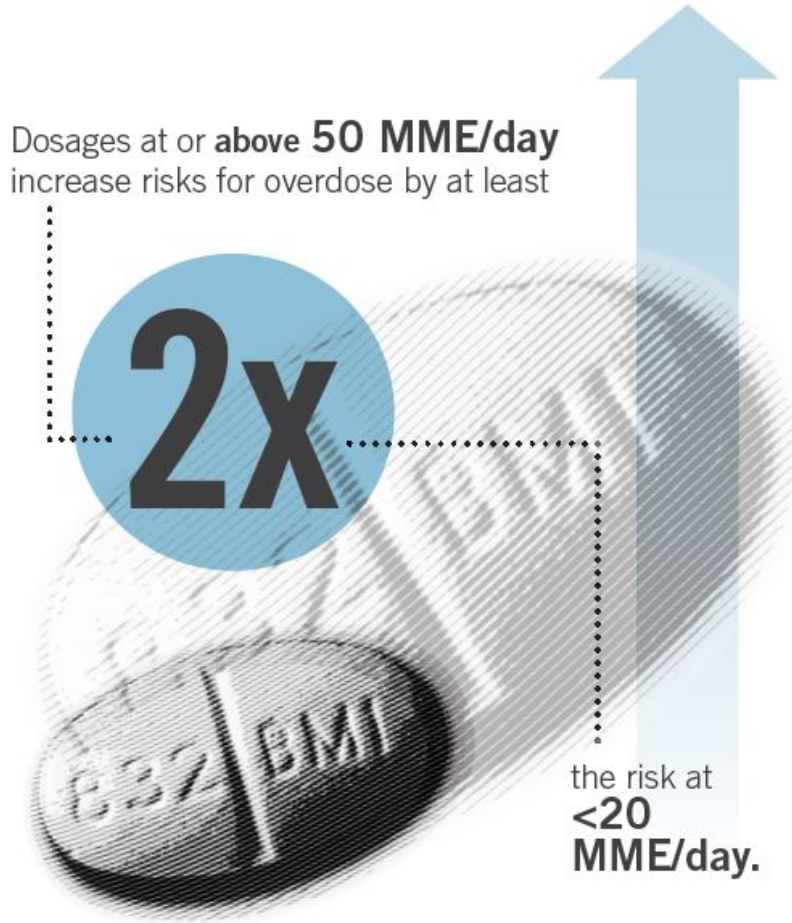
- Nonopioid medications such as acetaminophen, ibuprofen, or certain medications that are also used for depression or seizures
- Physical treatments (eg, exercise therapy, weight loss)
- Behavioral treatment (eg, CBT)
- Interventional treatments (eg, injections)

3 DISCUSS RISKS AND BENEFITS

Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Higher Dosage, Higher Risk.

Higher dosages of opioids are associated with higher risk of overdose and death—even relatively low dosages (20-50 morphine milligram equivalents (MME) per day) increase risk. Higher dosages haven't been shown to reduce pain over the long term. One randomized trial found no difference in pain or function between a more liberal opioid dose escalation strategy (with average final dosage 52 MME) and maintenance of current dosage (average final dosage 40 MME).



WHY IS IT IMPORTANT TO CALCULATE THE TOTAL DAILY DOSAGE OF OPIOIDS?

Patients prescribed higher opioid dosages are at higher risk of overdose death.

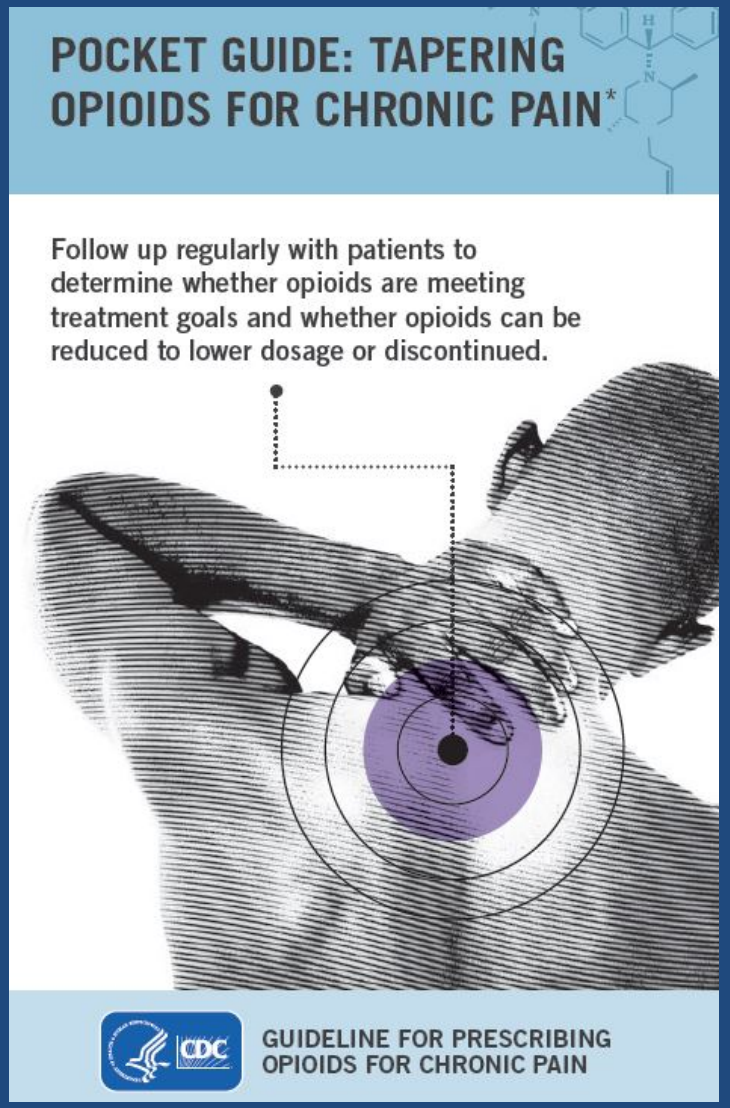
In a national sample of Veterans Health Administration (VHA) patients with chronic pain receiving opioids from 2004–2009, **patients who died** of opioid overdose were prescribed an average of **98 MME/day**, while **other patients** were prescribed an average of **48 MME/day**.

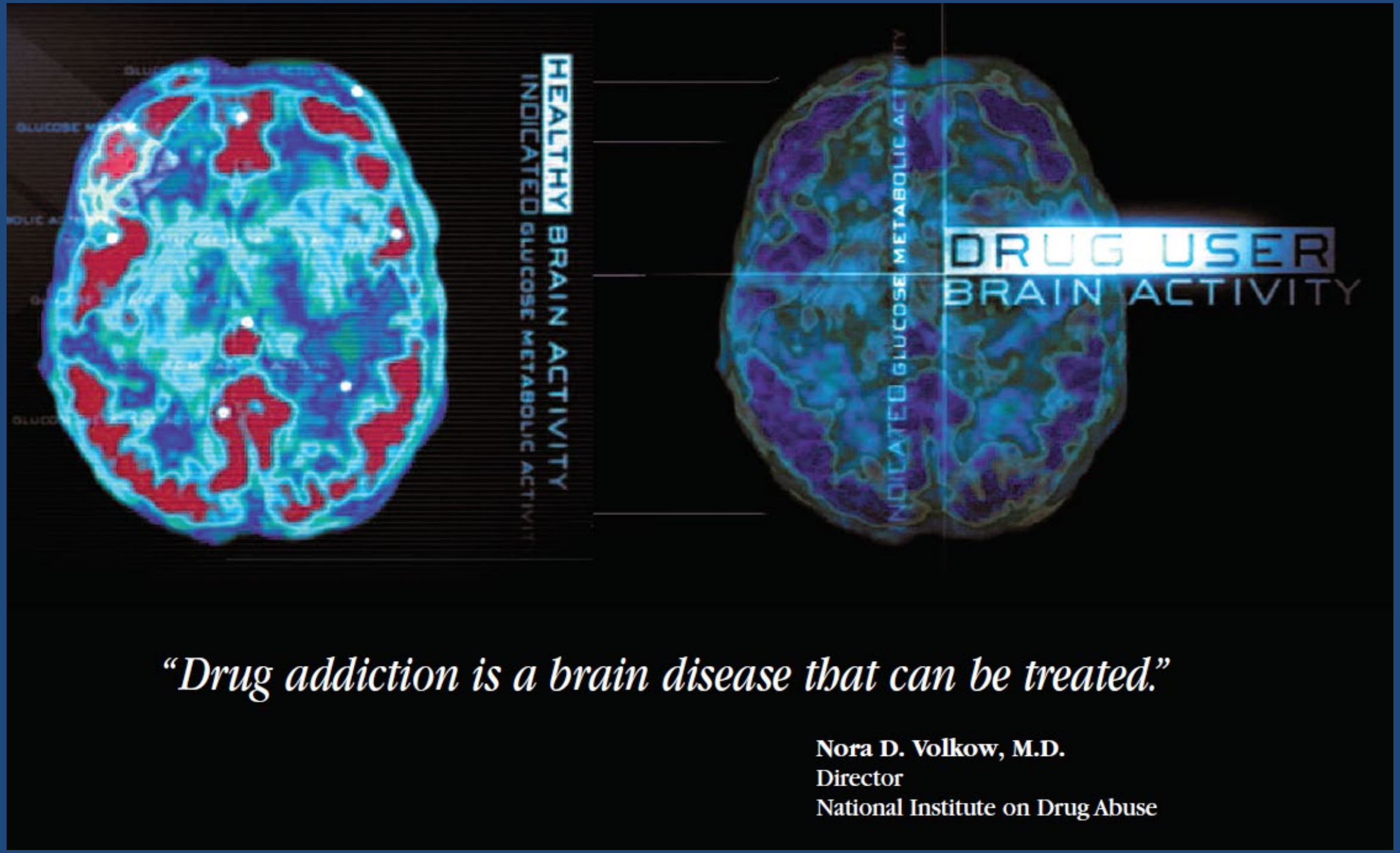
Calculating the total daily dose of opioids helps identify patients who may benefit from closer monitoring, reduction or tapering of opioids, prescribing of naloxone, or other measures to reduce risk of overdose.

Evidence-Based Prescribing Practices

Badu et al. *NEJM* 2019;380:2246-2255; Chou et al. *Ann Intern Med*. 2015;162(4):276-86

- Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.
- Avoid dose escalation co-prescribe naloxone
- Decrease other sedating medications
  - Benzodiazepines—27% vets receiving both opioids and benzos, overdose death rate nearly 4 times as high as those not receiving both (Park, *BMJ,* 2015)
  - Muscle relaxants, Gabapentinoids, and CNS depressants
- **Taper** from high doses
- **Wean** off opioids
- **Transition** to medication-based treatment





"Drug addiction is a brain disease that can be treated."

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse

Similar to Management of Diabetes or HIV

- No cure
- Goal is to prevent acute and chronic complications
- Individualized treatment plans and goals
- Treatment includes:
  - Medication
  - Lifestyle changes
  - Regular monitoring for complications
  - Behavioral support

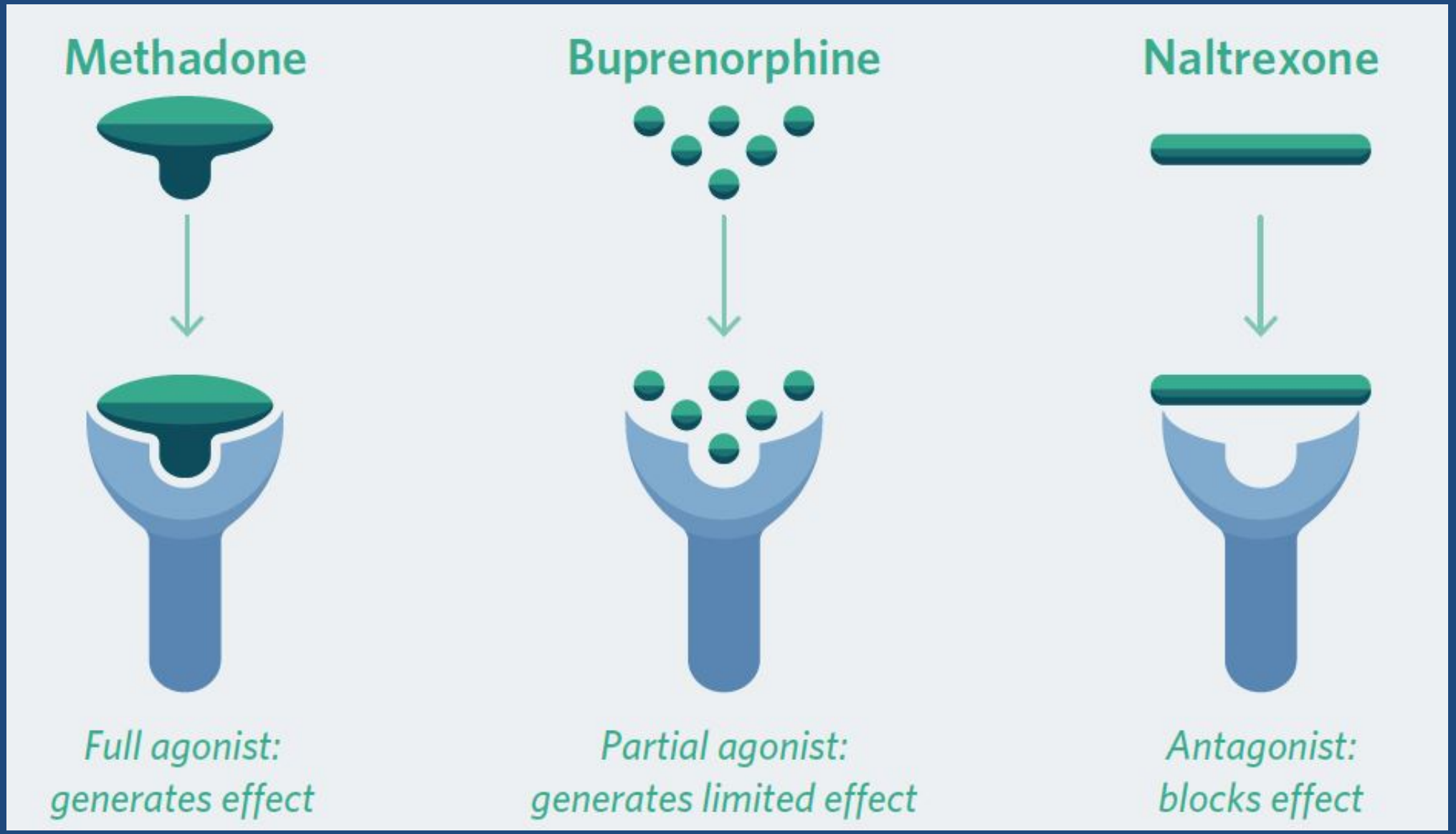
Medication-Based Treatment

https://www.samhsa.gov/medication-assisted-treatment/treatment

- Medication-Based Treatment is the use of medications, in combination with counseling and behavioral therapies, to provide a “whole-patient” approach to the treatment of substance use disorders.

- Research shows that a combination of medication and therapy can successfully treat these disorders, and for some people struggling with addiction, MBT can help sustain recovery.

Chronic, Treatable, Relapsing Brain Disorder



Characteristic	Methadone	Buprenorphine	Naltrexone
Brand Names	Dolophine, Methadone	Subutex, Suboxone, Zubsolv	Depade, ReVia, Vivitrol
Class	**Agonist**	**Partial agonist,** tight affinity for mu receptor. Produces diminished response even with full occupancy	**Antagonist**
Use and effects	Oral daily	Oral/sublingual daily. Often co-formulated with Naloxone to deter injection use	Oral or injection
Advantages	High strength and efficacy as oral dose, slows brain uptake and reduces euphoria	Adherence results in decreased mortality. Waiver is required to prescribe for OUD—8 hours training for physicians.	Not addictive, no sedation or dependence. Depot injection—**Vivitrol**—eliminates need for daily dosing.
Disadvantages	Available through approved outpatient treatment programs. Daily visits required.	Subutex abuse liability. Suboxone diminishes risk by including naloxone—which causes W/D if injected.	Initiation requires 7-day abstinence. Lofexidine approved for 14 days to mitigate withdrawal

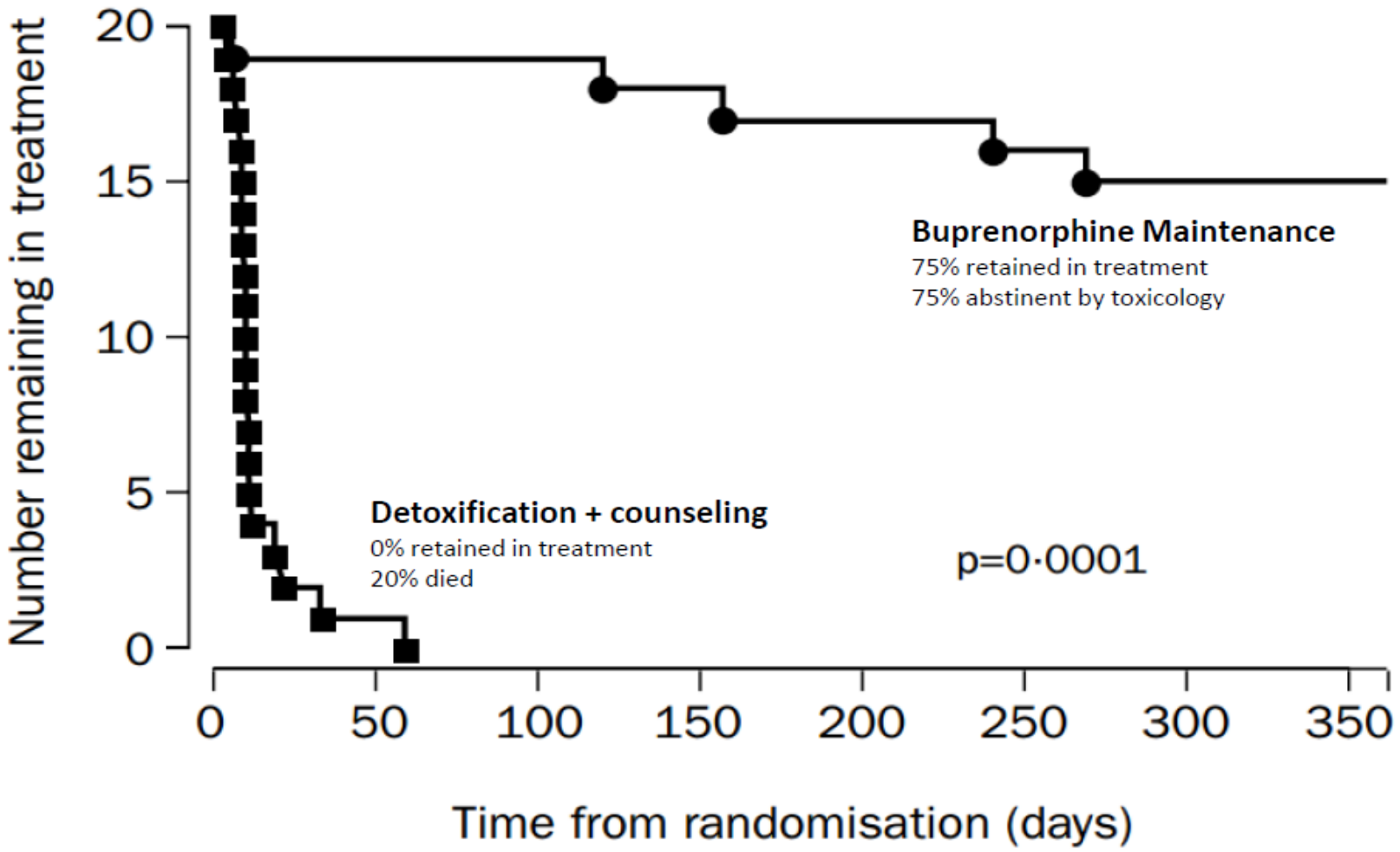

Progress
expected
actual
Time

Abstinence *vs* Medication-Based Treatment

- Research shows that staying in recovery and avoiding relapse for at least a year is more than twice as likely with medications and counseling as without them.
    - https://www.samhsa.gov/medication-assisted-treatment/treatment

- Currently, there is limited access to MBT:
  - Too few addiction recovery specialists;
  - Insurance coverage is limited
  - Abstinence treatment center and 12-step programs do not support idea that a person with an OUD can recover by drug substitution.

Medication Treatment Improves Retention, Abstinence, Survival



Kakko et al. Lancet. 2003 Feb 22;361(9358):662-8

Original Investigation

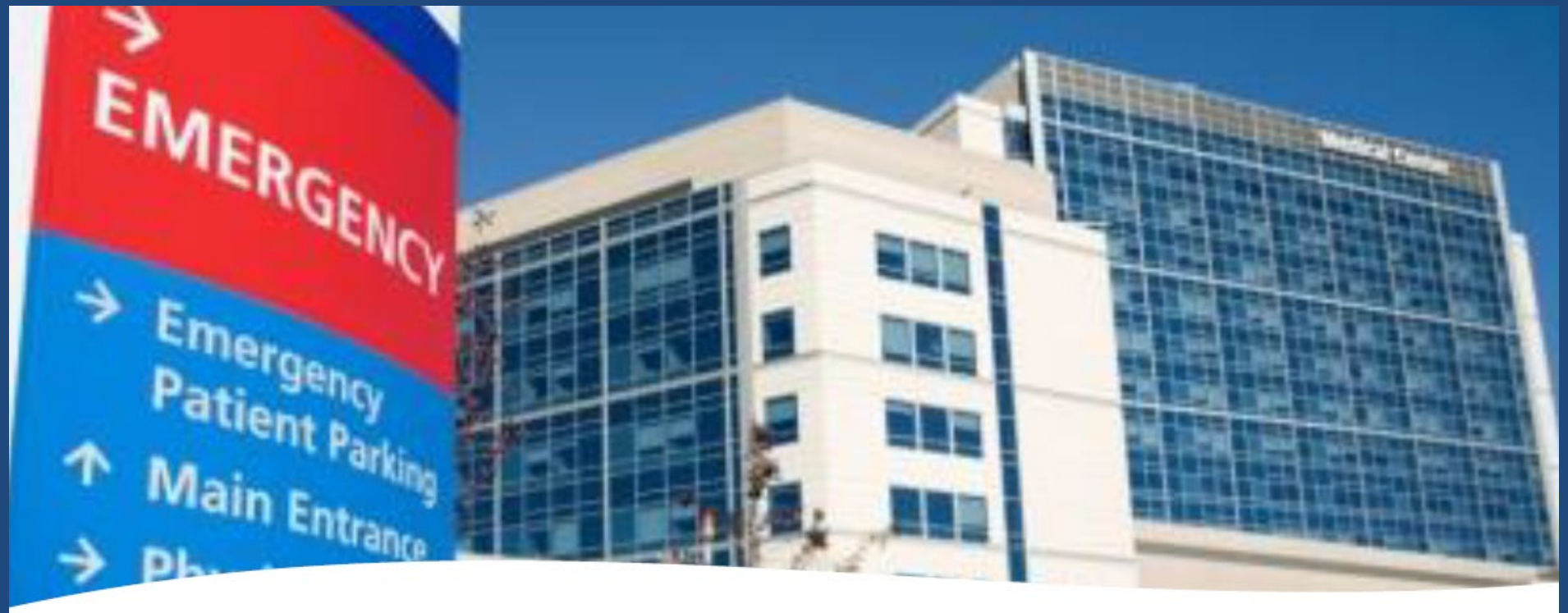
Emergency Department–Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence

A Randomized Clinical Trial

Gail D'Onofrio, MD, MS; Patrick G. O'Connor, MD, MPH; Michael V. Pantalon, PhD; Marek C. Chawarski, PhD; Susan H. Busch, PhD; Patricia H. Owens, MS; Steven L. Bernstein, MD; David A. Fiellin, MD

- Of 329 opioid-dependent patients treated at an ED:
  - 78% in the buprenorphine group
  - 45% in the brief intervention group
  - 37% in the referral group
- were engaged in addiction treatment on the 30th day after randomization.

– D'Onofrio et al. *JAMA*. 2015;313(16):1636-1644



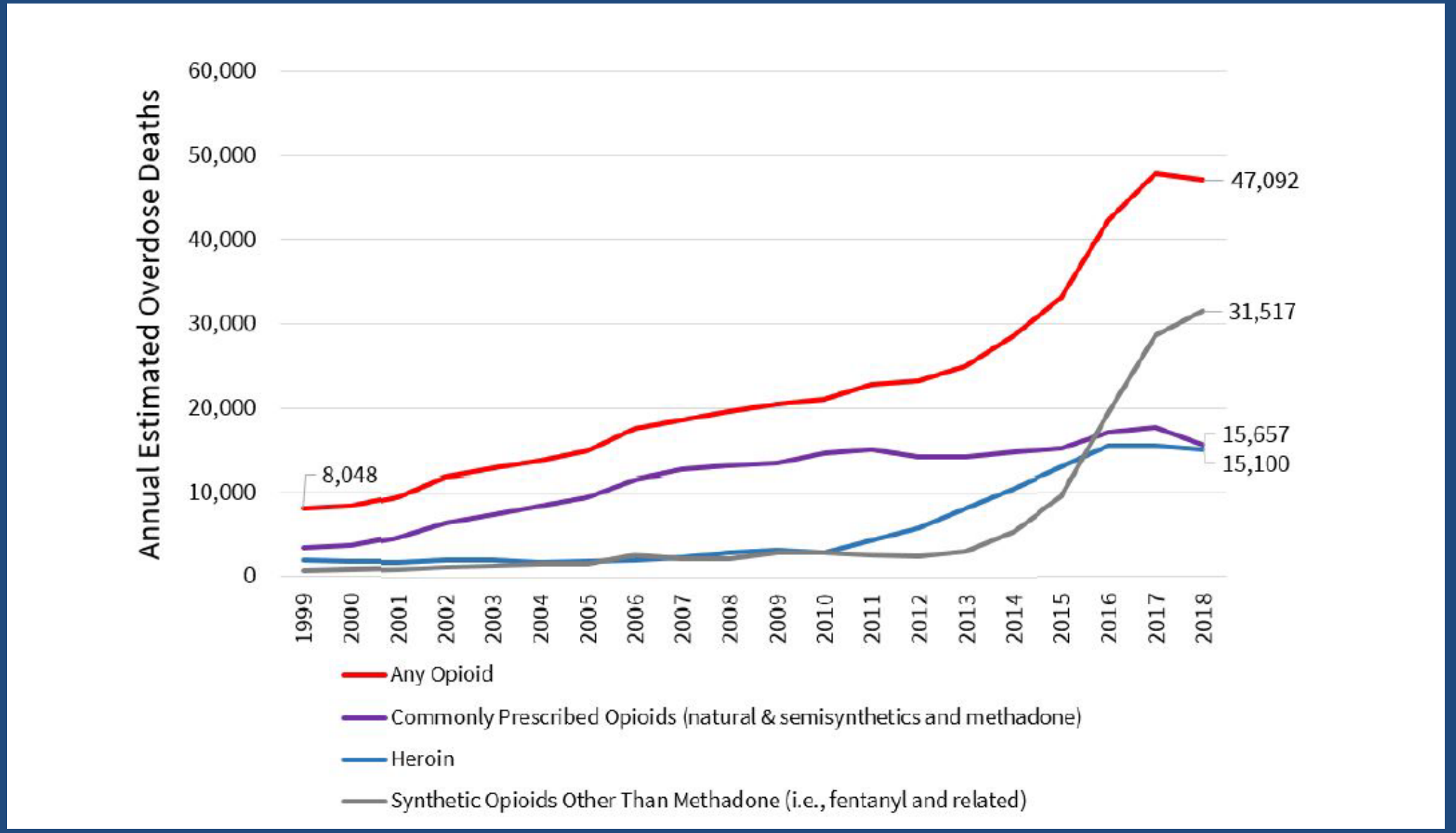
Using Hospitalization as a Reachable Moment

- Initiating methadone in hospital:
  - 82% present for follow-up addiction care
- Initiating buprenorphine vs detox:
  - Bupe: 72.2% enter into treatment after discharge
  - Detox : 11.9% enter treatment after discharge

J Gen Intern Med. Aug 2010; 25(8): 803–808; JAMA Intern Med 2014 Aug;174(8):1369-76.)

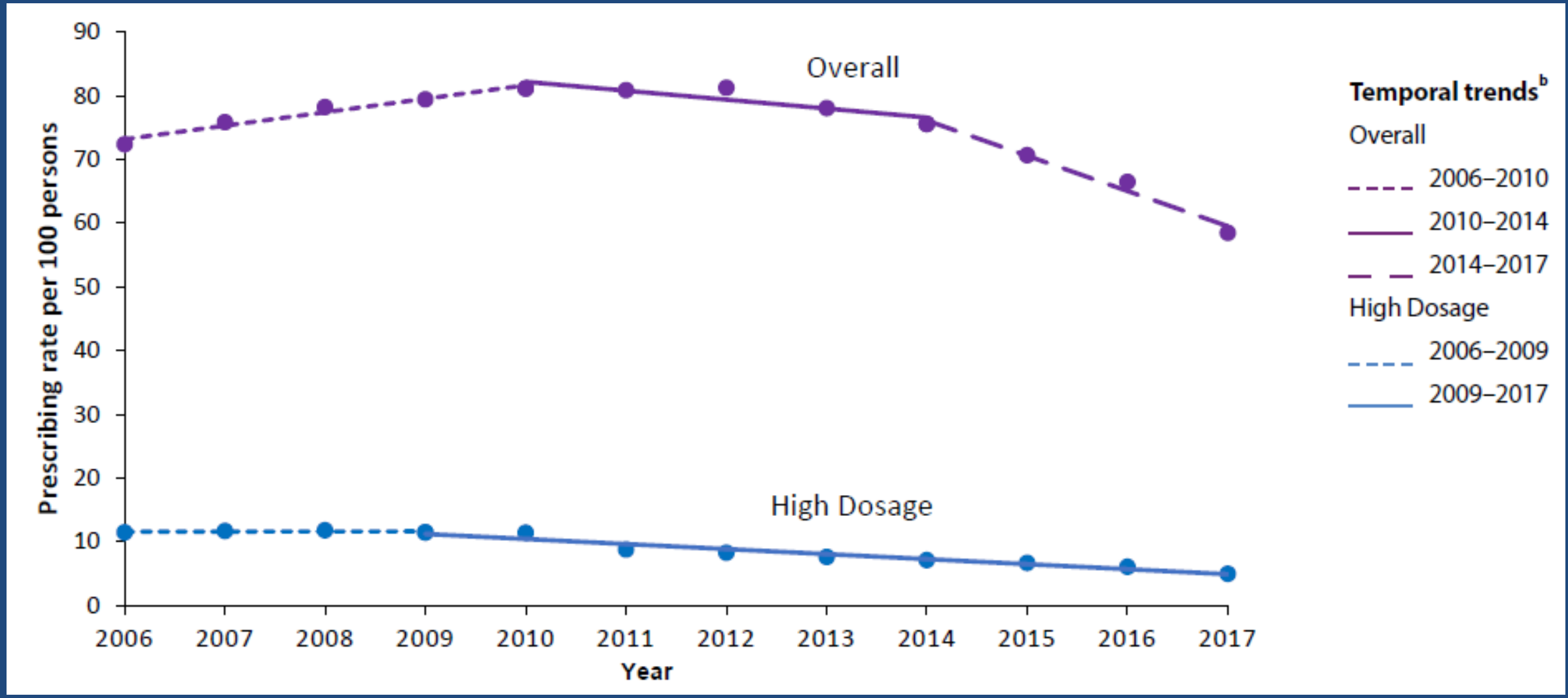
U.S. Opioid Overdose Deaths, 1999 to 2018

National Center for Health Statistics WONDER (1999-2016) and Provisional Drug Overdose Death Counts (2017-2018), National Vital Statistics System, Mortality



Annual Prescribing Rates, U.S. 2006-2017

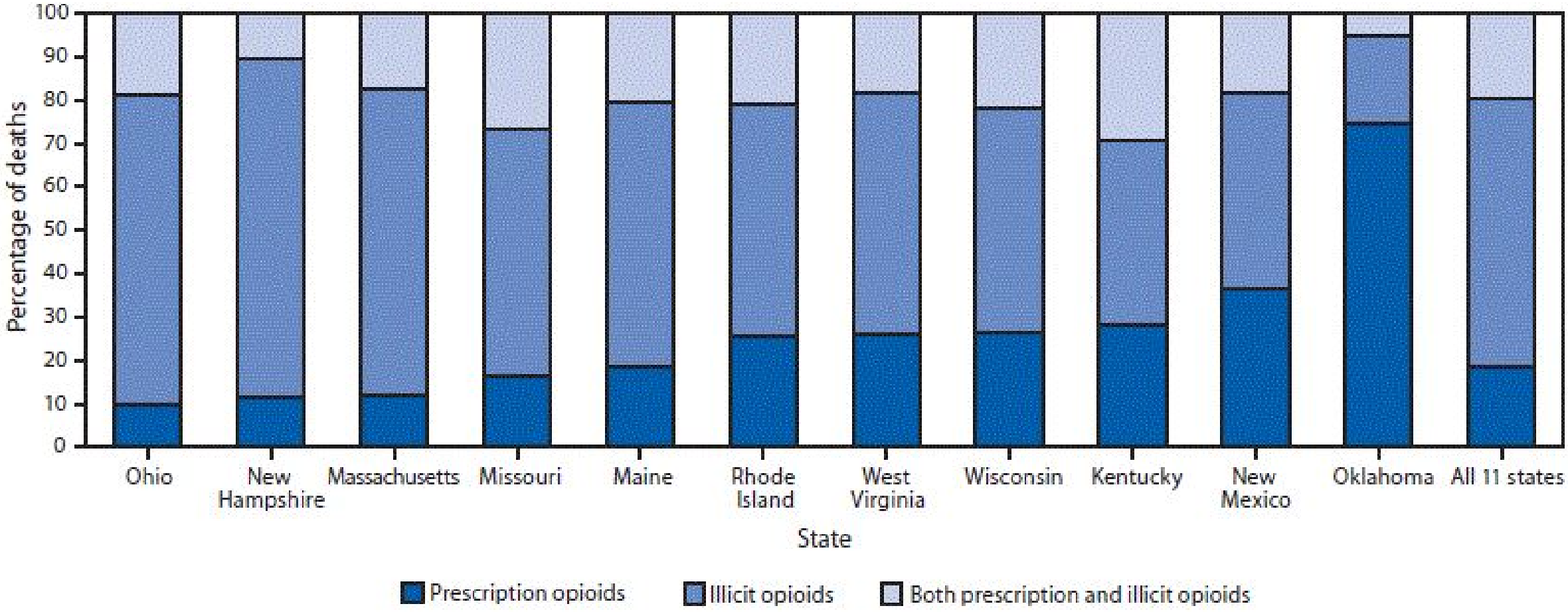
CDC Annual Surveillance Report of Drug-Related Risks and Outcomes (August 31, 2018)



Proportion of Opioid Overdose Deaths: 11 States

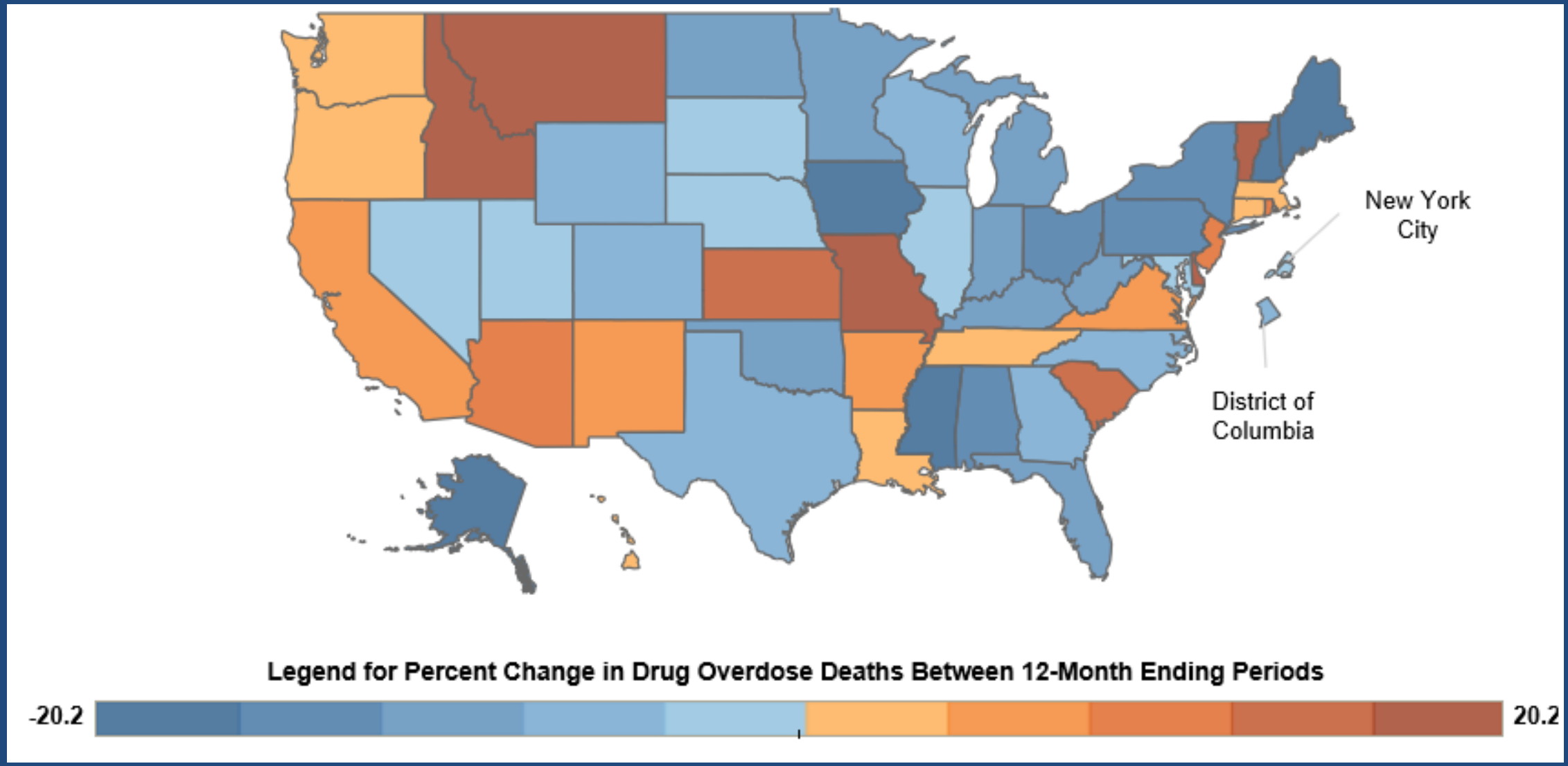
July 1, 2016—June 30, 2017

Mattson CL et al. *MMWR.* 2018;67(34):945-951



Percent Change in 12-month Drug OD Deaths—2018-2019

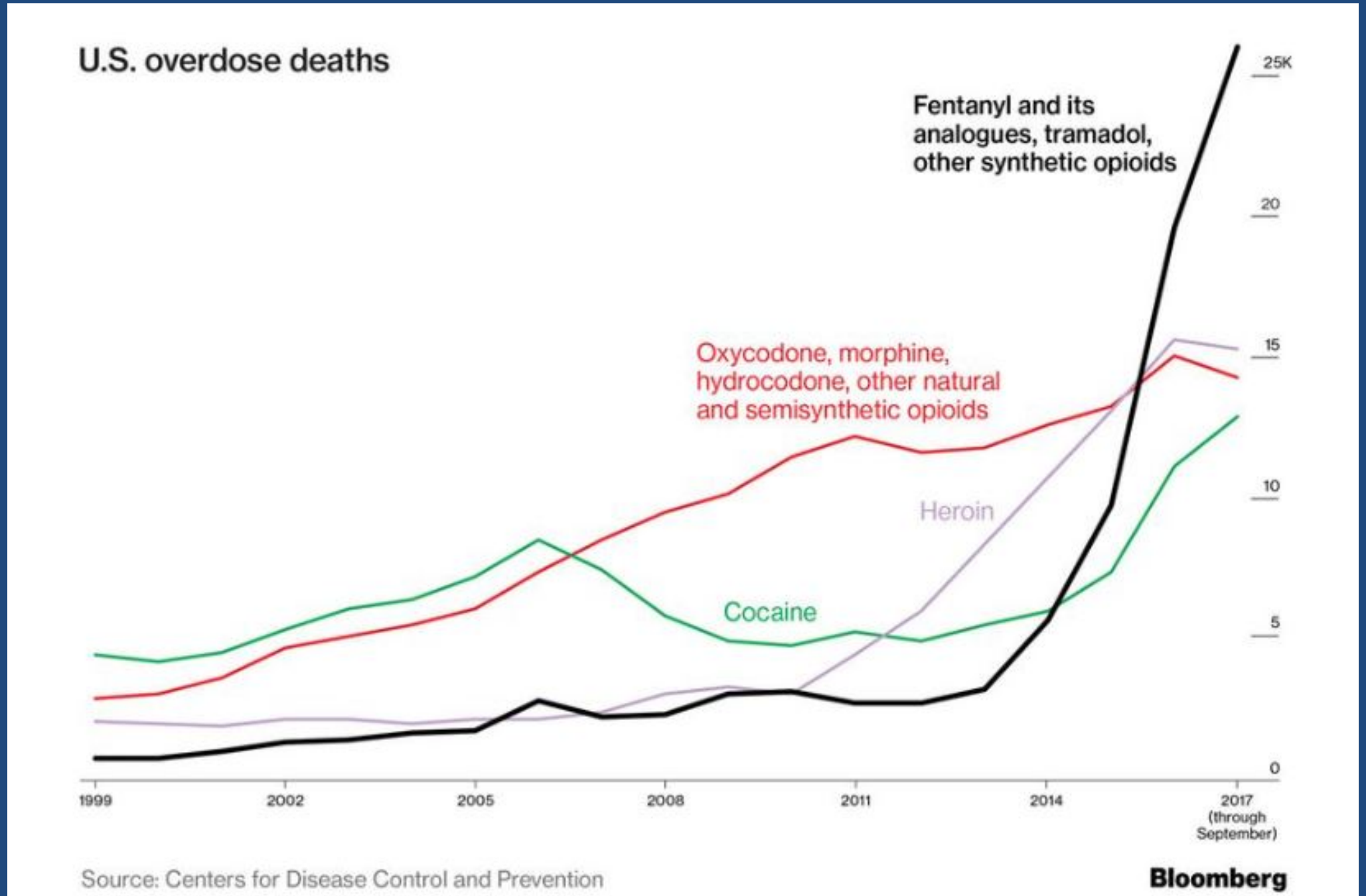
https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm



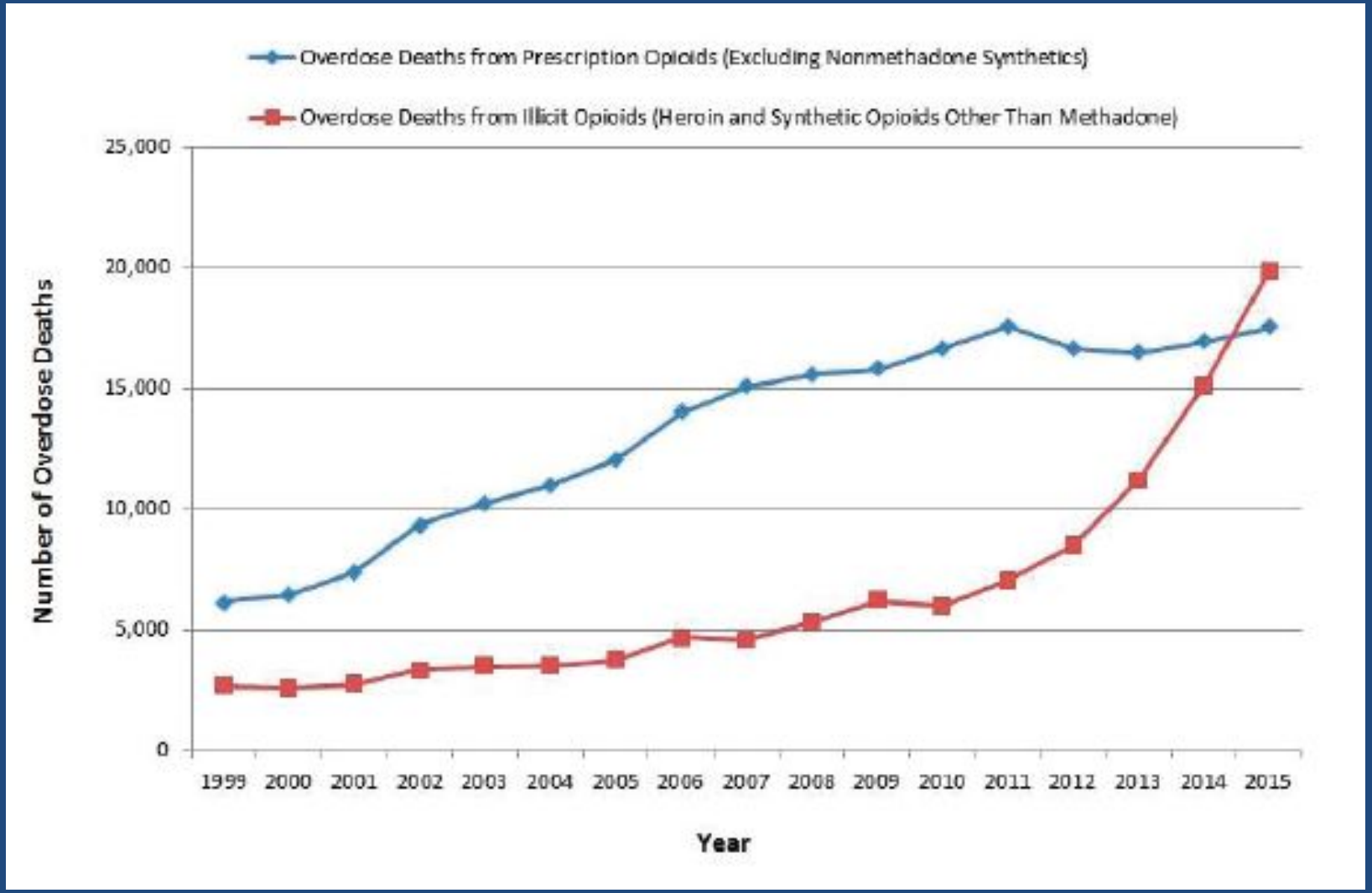
Illicit Epidemic

- Fentanyl 50X to 100X more potent than morphine.
  - ¼ mg can be fatal
  - Low-dose ASA = 81 mg
  - If you were to cut that tablet into 324 pieces, one of the pieces = ¼ milligram

- From 2013 to 2017, the number of opioid-involved overdose deaths (opioid deaths) in the United States increased 90%, from 25,052 to 47,600.* This increase was primarily driven by substantial increases in deaths involving illicitly manufactured fentanyl (IMF) or fentanyl analogs† mixed with heroin, sold as heroin, or pressed into counterfeit prescription pills


U.S. overdose deaths
Fentanyl and its analogues, tramadol, other synthetic opioids
Oxycodone, morphine, hydrocodone, other natural and semisynthetic opioids
Heroin
Cocaine
25K
20
15
10
5
0
1999
2002
2005
2008
2011
2014
2017 (through September)
Source: Centers for Disease Control and Prevention
Bloomberg

Is Licit or Illicit Use Driving the Epidemic?



- National Academies of Sciences, Engineering, and Medicine. 2017. *Pain management and the opioid epidemic: Balancing societal and individual benefits and risks of prescription opioid use*. Washington, DC: The National Academies Press. doi: https://doi.org/10.17226/24781.

History of U.S. Fentanyl Outbreaks

Aspect	Previous Outbreaks	Today's Outbreak
Location	Generally localized	Not localized, although there is regional variation
Duration	Generally short; only one lasted more than two years	Nearly six years
Chemicals	Fewer analogs; no reports of super-potent opioids (e.g., carfentanil)	Fentanyl dominates, but there are many analogs and super-potent opioids
Source	Often labs in the United States, with one exception	Almost all is imported, mostly from China and Mexico
Distribution	Limited, although two employed traditional illicit market actors	More widespread; both traditional illicit market actors and mail or internet order
Sold as	Often heroin, although some noted it showing up in cocaine	Heroin and prescription pills, but an increasing share of cocaine and psychostimulant overdoses mention synthetic opioids

Surge Factors in Recent Fentanyl Use

Pardo B et al. *Future of Fentanyl and Other Synthetic Opioids,* RAND (2019)

- Production location switched from U.S. to China & Mexico
  - Suppliers can avoid U.S. law enforcement.

- Adapted to e-commerce over the Internet
  - Online dissemination of easier synthesis methods unlike earlier where production was limited to a few capable chemists.
  - Potency allows small amounts to be shipped direct to buyer for small fee.
  - International package delivery allows suppliers to bypass traditional drug distribution networks.

Supplier Decisions, Not User Demand

Pardo B et al., *The Future of Fentanyl*, RAND (2019)

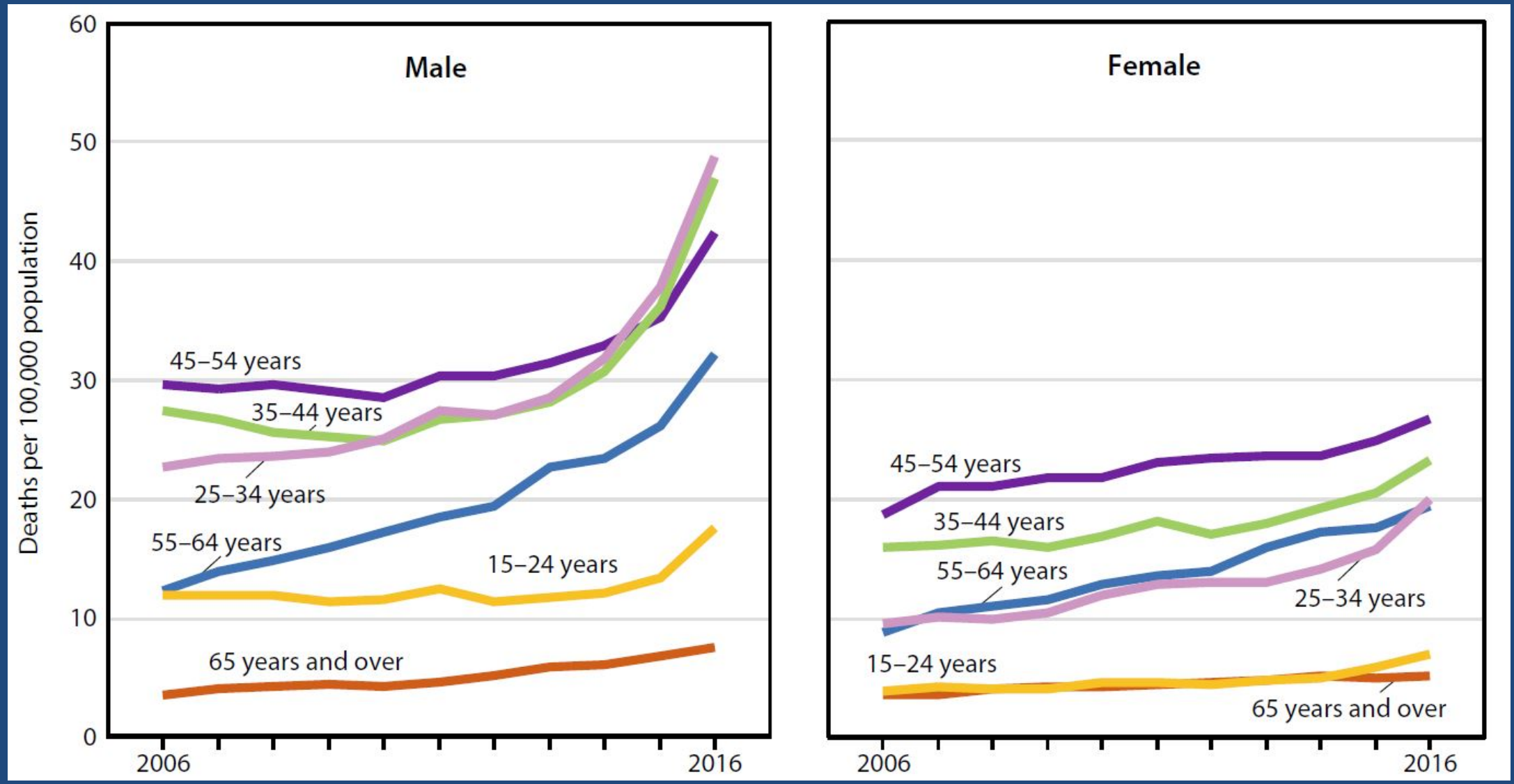
- Previous drug overdose epidemics were spurred by growing demand from users, but fentanyl appears to be a supplier-led issue
  - Surge primarily involves an adulterant, drug users do not seek fentanyl by name.

- Fentanyl is not a drug of initiation; it penetrates the market when suppliers embrace it
  - Few users are looking for fentanyl (initially)
    - Shorter duration, lethality, and unpredictability

Opioids and the American Workforce

95% of Overdose Deaths in Working Age People

U.S. Opioid Overdose Deaths: 2006—2016



Occupational Perspectives

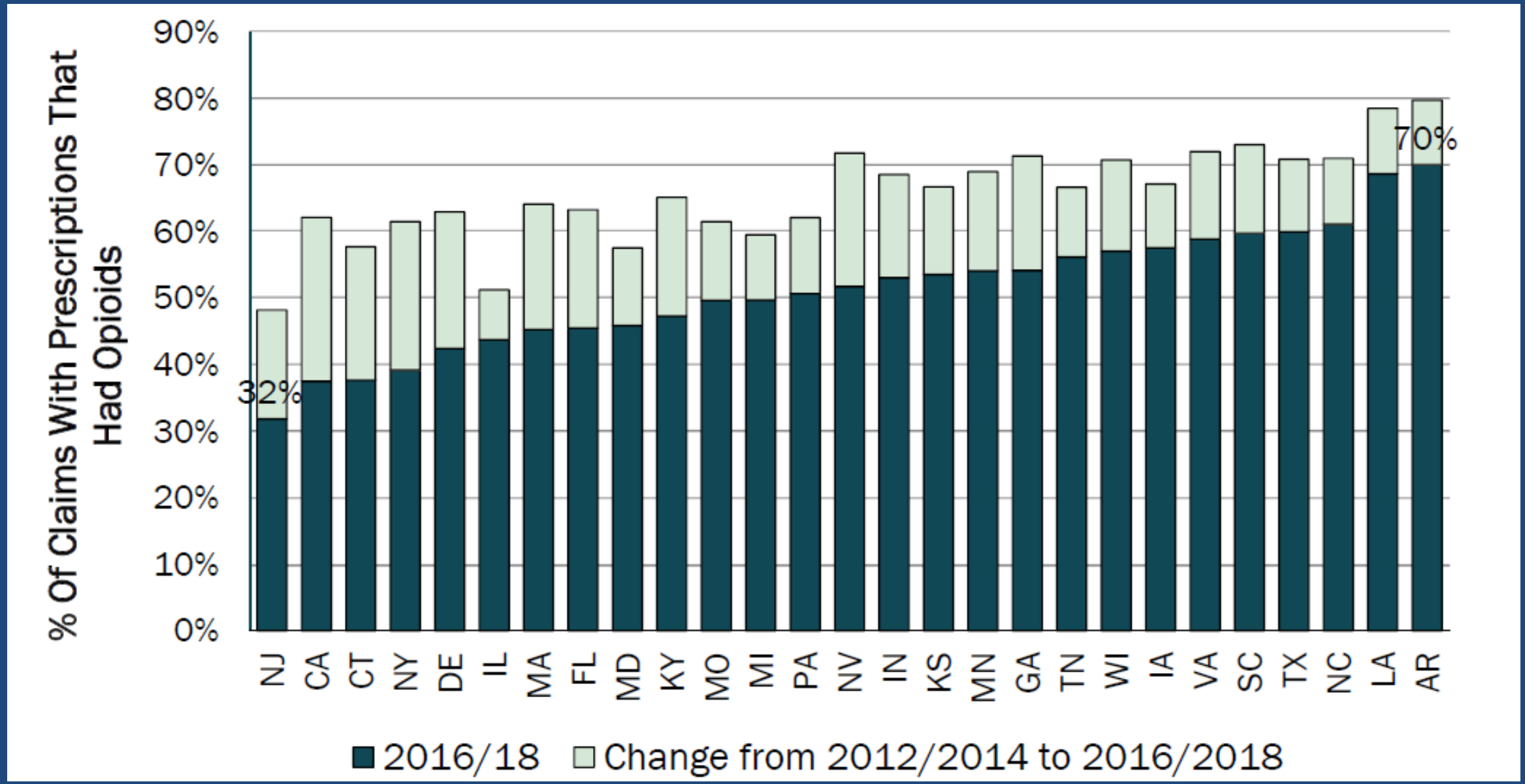
- **Industry & Occupation**
  - Workers' compensation data
  - Public health data
- **Harm Reduction in the Workplace**
- **First responders**
- **Recovery supported workplaces**
- **Drug-free workplaces**

Opioid Dispensing in Workers' Compensation

WCRI, December 2018

- Workers in ***mining and construction*** more likely to receive opioids than workers in other industries and on a longer term basis and at higher doses.
- Workers in ***small firms*** were more likely to receive opioids compared to larger firm workers.
- Workers in ***counties with higher opioid dispensing rates*** and workers in rural counties were more likely to receive opioids.
- Workers with ***neurologic spine pain*** were more likely to receive high-dose and longer term opioids, whereas workers with fractures or carpal tunnel who received opioids did not frequently receive then on a chronic basis or at high doses.
- Workers ***age 40 or more*** were more likely than younger workers to receive opioids.

Opioid Claims Still High, But Reduced in Most States



Chronic Opioid Use and Weaning Study

California Workers' Compensation Insurance Rating Bureau

- Many states have taken steps to address opioid use

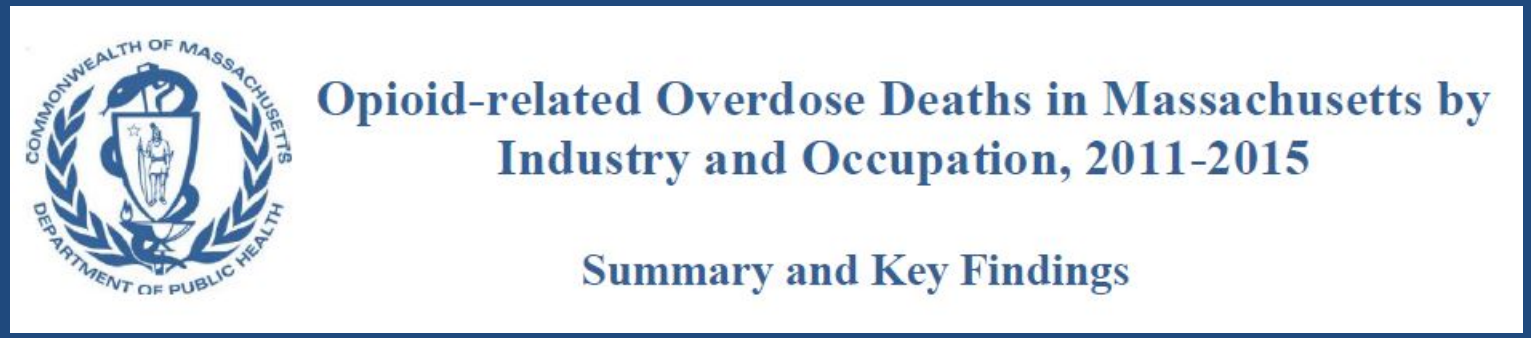
- CA study analyzed injured workers who were chronic opioid users and weaned off of opioids completely and injured workers who did not wean off of opioids.
  - Chronic opioid claimants = workers with prescribed opioids of 50 MME or greater per day for at least 3 consecutive months within the first two years from the date of injury.
  - Weaning was defined as the process of gradual reduction in opioid use after chronic opioid status was achieved.

- **Results**
  - Injured workers reached 50 MME in median of 11 months after injury
  - Mean weaning time = 8 months
  - Cost of claims with opioid use nine times average cost of claims

Opioids Transactions per 100 Claims

https://www.wcirb.com/sites/default/files/documents/study_of_chronic_opioid_use_and_weaning_ca_wc.pdf

Industry and Occupation Data

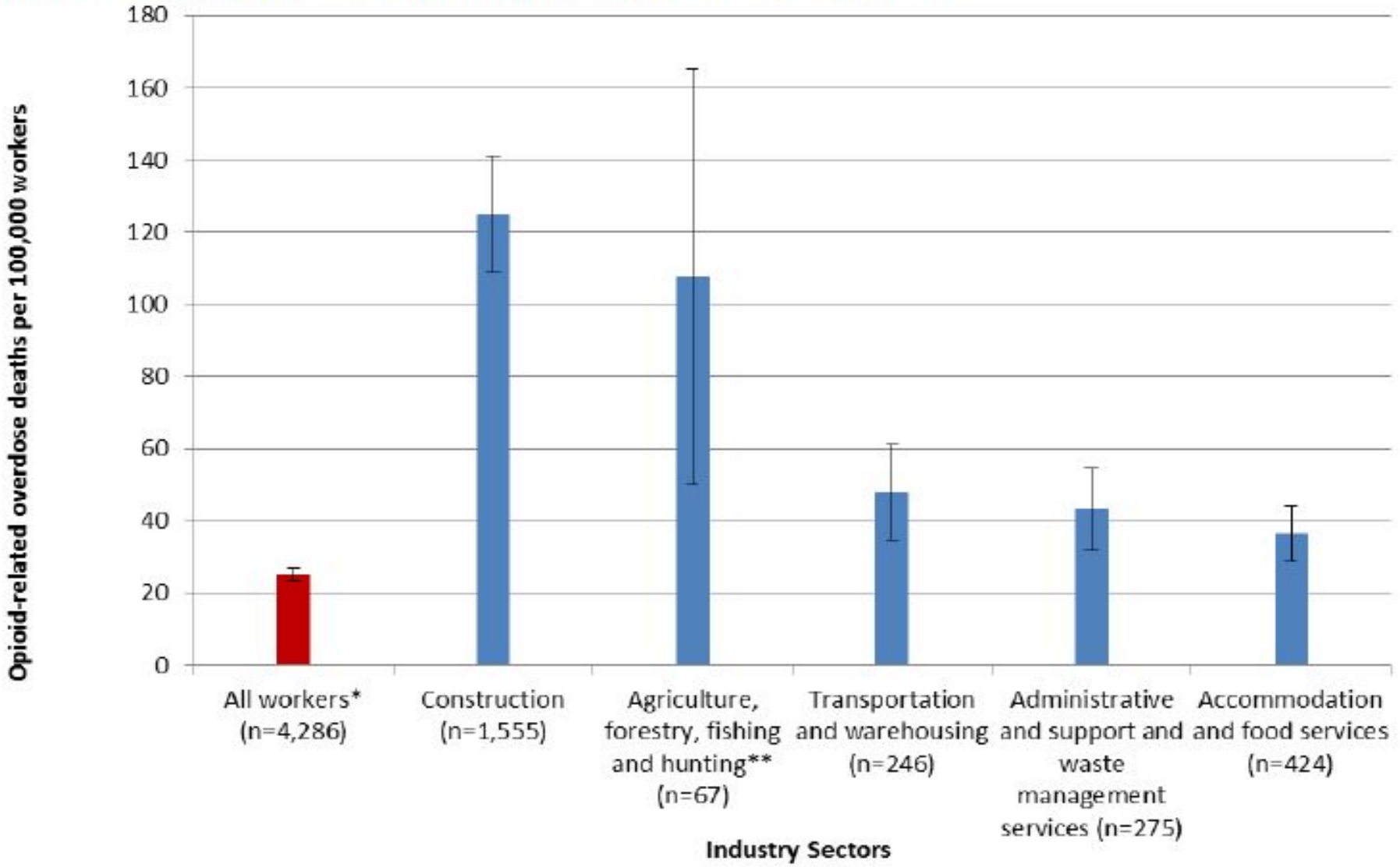


- Construction and extraction workers had both a high rate (150.6 deaths per 100,000 workers) and a high number of opioid-related overdose deaths (n=1,096).

- Opioid-related death rate for those employed in construction and extraction occupation was six times the average rate for all Massachusetts workers (25.1).

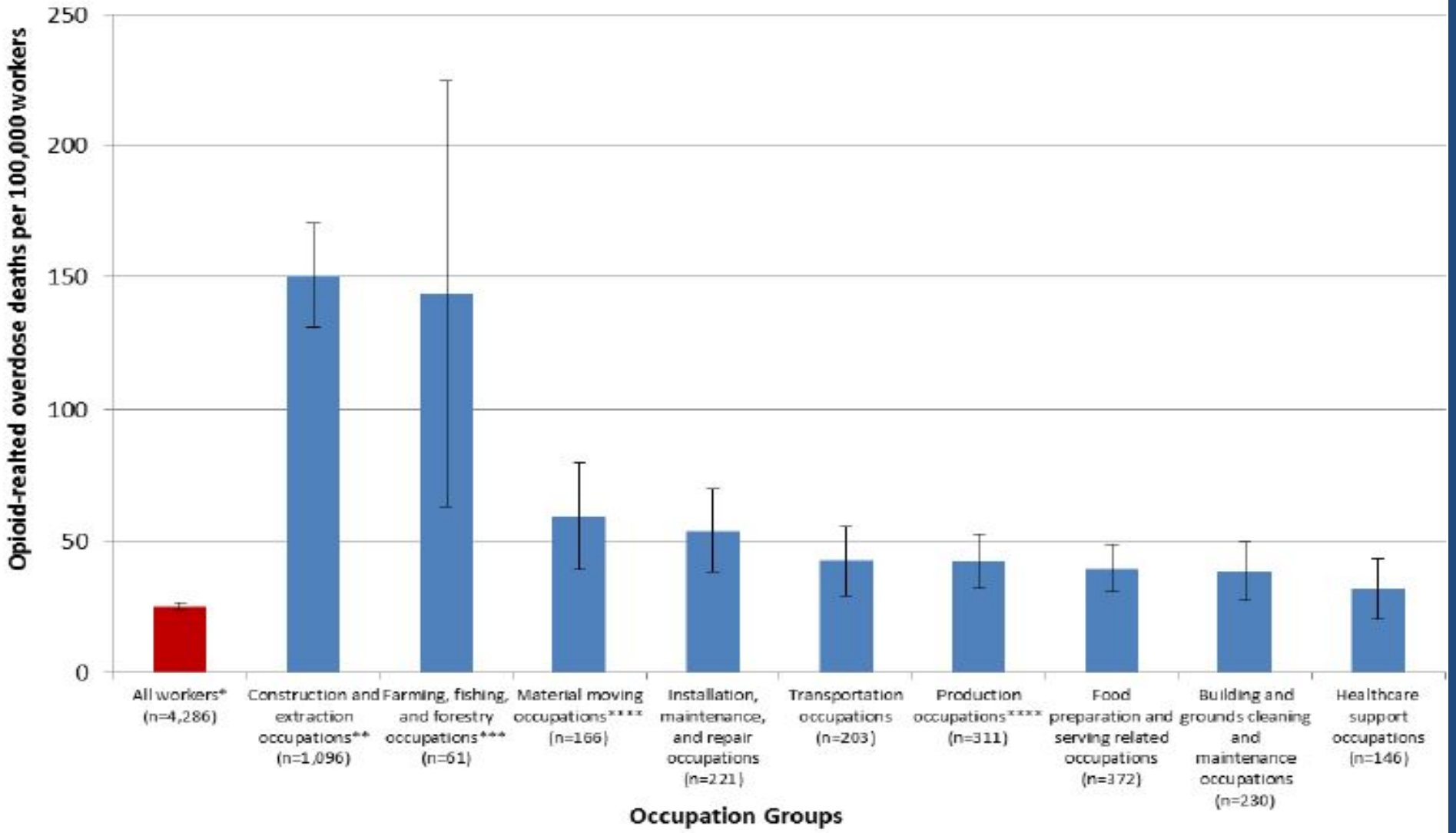
- Construction and extraction workers accounted for more than 24% of all opioid-related deaths among the working population (n=4,302).

Figure 1. Industry sectors with opioid-related overdose death rates significantly higher than the average rate for all workers, Massachusetts workers, 2011-2015, n=4,302



* This category excluded 16 deaths among those working in the military or military specific occupations due to lack of denominator information
** 67.2% of these deaths occurred among workers employed in fishing occupations.
Numerator source: Occupational Health Surveillance Program, 2011-2015
Denominator source: American Community Survey, 2011-2015

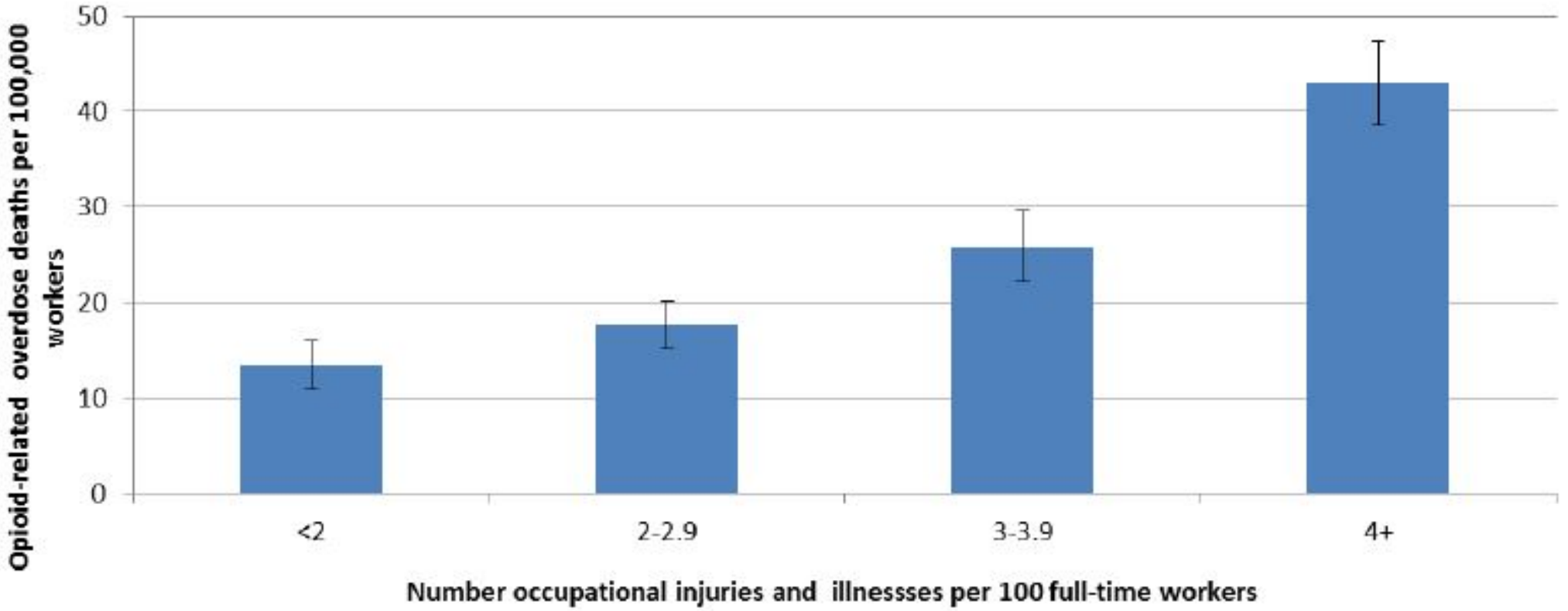
Figure 2. Occupation groups with opioid-related overdose death rates significantly higher than the average rate for all workers, Massachusetts workers, 2011-2015, n=4,302



* This category excluded 16 deaths among those working in the military or military specific occupations due to lack of denominator information.
** At least 97.0% of these deaths occurred among workers employed in construction occupations.
*** 73.8% of these deaths occurred among workers employed in fishing occupations.
**** This category excludes 1 death among a worker employed in the military industry.
Numerator source: Occupational Health Surveillance Program, 2011-2015
Denominator source: American Community Survey, 2011-2015

Opioid-Related Overdose Deaths and Number of Occupational Injury and Illnesses

Figure 4. Rate of opioid-related overdose deaths among Massachusetts workers by industry-specific injury and illness rate category, 2011-2015, n=4,302*



* The figure excludes 16 deaths among those working in the military or military specific occupations and 29 deaths with unknown industry, which lacked corresponding denominators.
Numerator source: Occupational Health Surveillance Program, 2011-2015
Denominator source: Bureau of Labor Statistics, MA Survey of Occupational Injuries and Illnesses, industry, 2015

NIOSH Investigation of Responders Incidents

https://www.cdc.gov/niosh/topics/opioids/fieldinvestigations.html

- Reports of responders experiencing “adverse health effects” during opioid overdose victim incidents

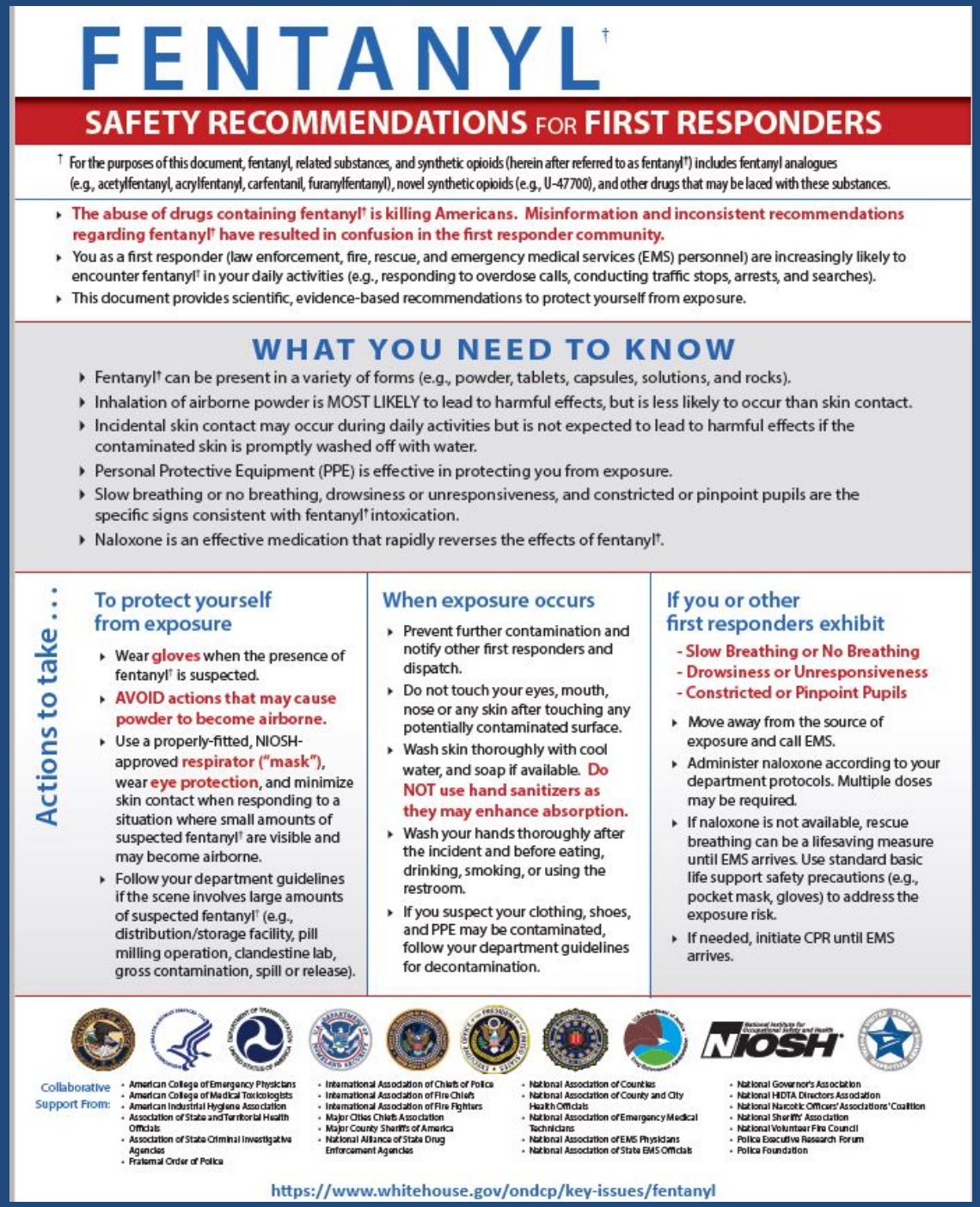
- Health effects are NOT classic opioid overdose symptoms and signs such as apnea, cyanosis, constricted pupils may not occur:
  - Responders report feeling “unwell,” “nauseous,” “lightheaded, “dizzy,” “feeling like I was going-down”

- Some responders given naloxone at the scene with variable responses.

- Are these “mixed drug” effects?

First Responder Guidance

- Interagency group under the direction of the National Security Council.
- Actions first responders can take to protect themselves from exposure.
- Actions first responders can take when exposure occurs.
- Actions first responders can take when they or their partners exhibit signs of intoxication.



FENTANYL†

SAFETY RECOMMENDATIONS FOR FIRST RESPONDERS

† For the purposes of this document, fentanyl, related substances, and synthetic opioids (herein after referred to as fentanyl†) includes fentanyl analogues (e.g., acetylfentanyl, acrylfentanyl, carfentanil, furanylfentanyl), novel synthetic opioids (e.g., U-47700), and other drugs that may be laced with these substances.

- **The abuse of drugs containing fentanyl† is killing Americans. Misinformation and inconsistent recommendations regarding fentanyl† have resulted in confusion in the first responder community.**
- You as a first responder (law enforcement, fire, rescue, and emergency medical services (EMS) personnel) are increasingly likely to encounter fentanyl† in your daily activities (e.g., responding to overdose calls, conducting traffic stops, arrests, and searches).
- This document provides scientific, evidence-based recommendations to protect yourself from exposure.

WHAT YOU NEED TO KNOW

- Fentanyl† can be present in a variety of forms (e.g., powder, tablets, capsules, solutions, and rocks).
- Inhalation of airborne powder is MOST LIKELY to lead to harmful effects, but is less likely to occur than skin contact.
- Incidental skin contact may occur during daily activities but is not expected to lead to harmful effects if the contaminated skin is promptly washed off with water.
- Personal Protective Equipment (PPE) is effective in protecting you from exposure.
- Slow breathing or no breathing, drowsiness or unresponsiveness, and constricted or pinpoint pupils are the specific signs consistent with fentanyl† intoxication.
- Naloxone is an effective medication that rapidly reverses the effects of fentanyl†.

Actions to take . . .

To protect yourself from exposure

- Wear **gloves** when the presence of fentanyl† is suspected.
- **AVOID actions that may cause powder to become airborne.**
- Use a properly-fitted, NIOSH-approved **respirator ("mask")**, wear **eye protection**, and minimize skin contact when responding to a situation where small amounts of suspected fentanyl† are visible and may become airborne.
- Follow your department guidelines if the scene involves large amounts of suspected fentanyl† (e.g., distribution/storage facility, pill milling operation, clandestine lab, gross contamination, spill or release).

When exposure occurs

- Prevent further contamination and notify other first responders and dispatch.
- Do not touch your eyes, mouth, nose or any skin after touching any potentially contaminated surface.
- Wash skin thoroughly with cool water, and soap if available. **Do NOT use hand sanitizers as they may enhance absorption.**
- Wash your hands thoroughly after the incident and before eating, drinking, smoking, or using the restroom.
- If you suspect your clothing, shoes, and PPE may be contaminated, follow your department guidelines for decontamination.

If you or other first responders exhibit

- **Slow Breathing or No Breathing**
- **Drowsiness or Unresponsiveness**
- **Constricted or Pinpoint Pupils**

- Move away from the source of exposure and call EMS.
- Administer naloxone according to your department protocols. Multiple doses may be required.
- If naloxone is not available, rescue breathing can be a lifesaving measure until EMS arrives. Use standard basic life support safety precautions (e.g., pocket mask, gloves) to address the exposure risk.
- If needed, initiate CPR until EMS arrives.

Collaborative Support From:

- American College of Emergency Physicians
- American College of Medical Toxicologists
- American Industrial Hygiene Association
- Association of State and Territorial Health Officials
- Association of State Criminal Investigative Agencies
- Fraternal Order of Police
- International Association of Chiefs of Police
- International Association of Fire Chiefs
- International Association of Fire Fighters
- Major Cities Chiefs Association
- Major County Sheriffs of America
- National Alliance of State Drug Enforcement Agencies
- National Association of Counties
- National Association of County and City Health Officials
- National Association of Emergency Medical Technicians
- National Association of EMS Physicians
- National Association of State EMS Officials
- National Governor's Association
- National HIDTA Directors Association
- National Narcotic Officers' Associations' Coalition
- National Sheriffs' Association
- National Volunteer Fire Council
- Police Executive Research Forum
- Police Foundation

https://www.whitehouse.gov/ondcp/key-issues/fentanyl

Naloxone Availability & Use In The Workplace

https://www.cdc.gov/niosh/docs/2019-101/default.html

Using Naloxone to Reverse Opioid Overdose in the Workplace: Information for Employers and Workers

Introduction

Opioid misuse and overdose deaths from opioids are serious health issues in the United States. Overdose deaths involving prescription and illicit opioids doubled from 2010 to 2016, with more than 42,000 deaths in 2016 [CDC 2016a]. Provisional data show that there were more than 49,000 opioid overdose deaths in 2017 [CDC 2018a]. In October 2017, the President declared the opioid overdose epidemic to be a public health emergency.

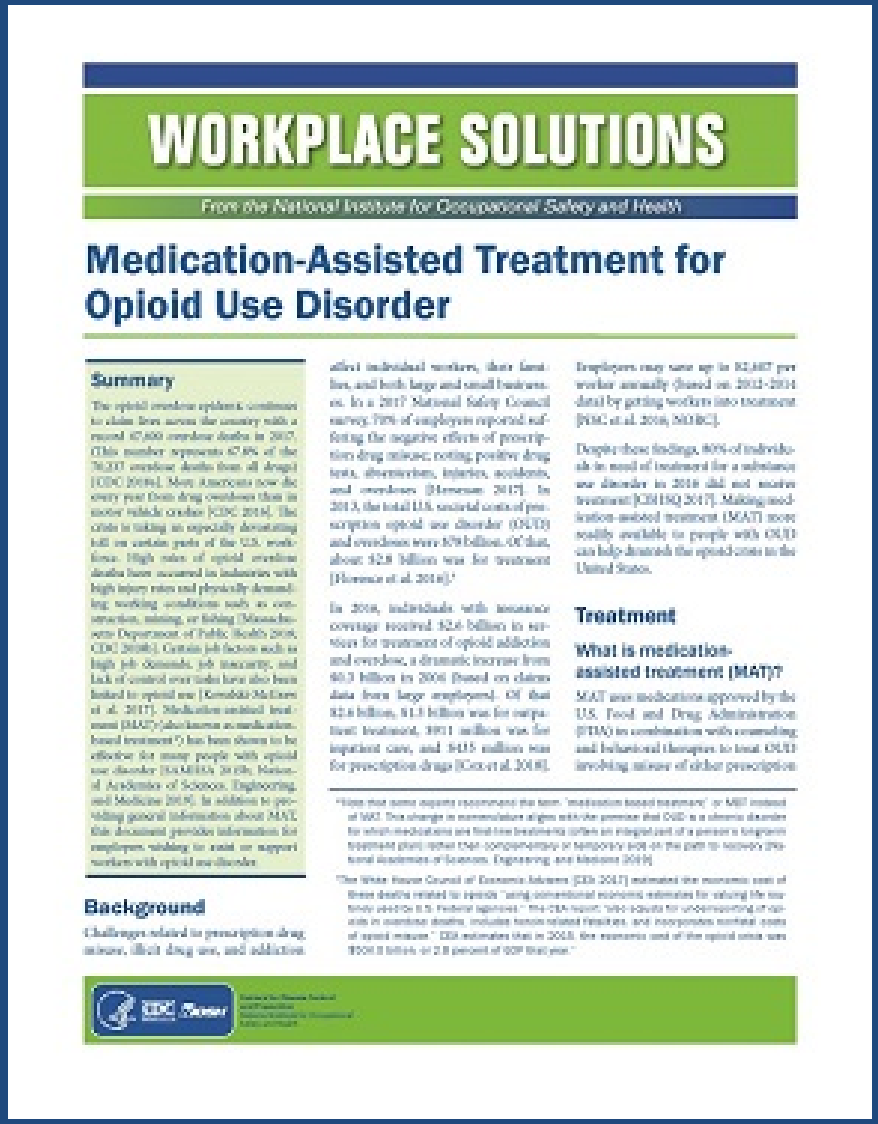
Naloxone is a very effective drug for reversing opioid overdoses. Police officers, emergency medical services providers, and non-emergency professional responders carry the drug for that purpose. The Surgeon General of the United States is also urging others who may encounter people at risk for opioid overdose to have naloxone available and to learn how to use it to save lives [USSG 2018].

The National Institute for Occupational Safety and Health (NIOSH), part of the Centers for Disease Control and Prevention (CDC), developed this information to help employers and workers understand the risk of opioid overdose and help them decide if they should establish a workplace naloxone availability and use program.

Photo by ©Thinkstock

Recovery Supported Employment

- Education and awareness of drug use among workers
- Counseling for scheduled and on-demand recovery support, including tele-counseling in secure room at the worksite
- Peer support groups built into daily schedule
- Support for medication-based treatment
- Onsite drug testing as part of a recovery program
- No automatic termination of employment



WORKPLACE SOLUTIONS

From the National Institute for Occupational Safety and Health

Medication-Assisted Treatment for Opioid Use Disorder

Summary

Background

Treatment

What is medication-assisted treatment (MAT)?

Drug-Free Workplace Act of 1988

- Requires some federal contractors and all federal grantees to agree to provide drug-free workplaces as precondition of receiving federal dollars
- Gave impetus to widespread workplace urine drug testing regimens in the private sector
- Evidence that drug testing uniformly decreases workplace injuries and deters drug use remains unconfirmed.
- Cannabis legalization has some employers abandoning drug testing.
  - Fully legal (11 states and DC) and decriminalized in 15 states and VI

Public Health Interventions

Prescribing and Dispensing

Safe Injection Sites

Research

Prescription Drug Monitoring Programs

- State-run Programs
  - Collect and distribute data about the prescription and dispensation of federally controlled substances.

- Pharmacies dispensing controlled substances and prescribers—pharmacy monitoring programs
  - Required to register with their respective state PMPs
  - Report dispensation of prescriptions to online database.

- All states and the District of Columbia have the drug monitoring databases:
  - Fewer than five require their use; and
  - Less than 20% doctors use the databases when it is not required.

Electronic Prescribing

- Computer-based electronic generation, transmission and filling of a medical prescription, connects the patient, the providers and the dispensers. Helps prevent prescription fraud and drug diversion.

- Federal
  - Prescriptions for all controlled substances covered under Medicare Part D must be transmitted electronically beginning on **January 1, 2021**, with a few exceptions

- States:
  - New York (3/27/2016) for all prescriptions.
  - Maine (7/1/2017) for all controlled substances.
  - Pennsylvania (10/24/2019) for all controlled substances.
  - Michigan (1/1/2020) for all prescriptions.
  - Texas (1/1/2021) for all controlled substances.
  - Indiana (1/1/2021) for all controlled substances.

E-Prescribing—2018 Legislation

- In 2018, eight more **states** passed mandates--Arizona, California, Iowa, Massachusetts, New Jersey, Oklahoma, Pennsylvania and Tennessee—bringing the total number of **states** with EPCS **mandates** to 15.

- California Assembly Bill 2789 will require all health care practitioners who issue prescriptions to prescribe medication electronically and requires that all prescriptions for controlled substances be transmitted electronically (with some exceptions) by **January 1, 2022**.

- Bill also mentions not following the law will be grounds for disciplinary action.

Selected Public Health Measures: Harm Reduction

- Drug Testing Sites
  - Testing for fentanyl contamination
  - Based on a Vancouver, Canada model
    - Only 1% of visits resulted in a drug check, but 80% were positive for fentanyl
      - Karamouzian et al. *Harm Reduc J*.2018;15:46-52.

- Supervised Injection Sites
  - Observation prevents unattended overdoses
  - Relieves first responder and first receiver burden

Fight Drug Abuse, Don't Subsidize It

Americans struggling with addiction need treatment and reduced access to deadly drugs. They do not need a taxpayer-sponsored haven to shoot up.

Aug. 27, 2018

By Rod J. Rosenstein

Mr. Rosenstein is the deputy attorney general of the United States.

Supervised Injection Sites: Philadelphia

https://www.nytimes.com/2019/10/02/us/injection-safehouse-philadelphia-ruling.html

- October 2, 2019, Federal judge rules that a provision of the Controlled Substance Act did not apply to *Safehouse*, in part because the nonprofit group's goal "is to reduce drug use, not facilitate it."

- Congress was not trying to outlaw the facilities proposed by Safehouse when it passed what has commonly been referred to as the act's "crack house" provision in 1986.

- U.S. Department of Justice will appeal.

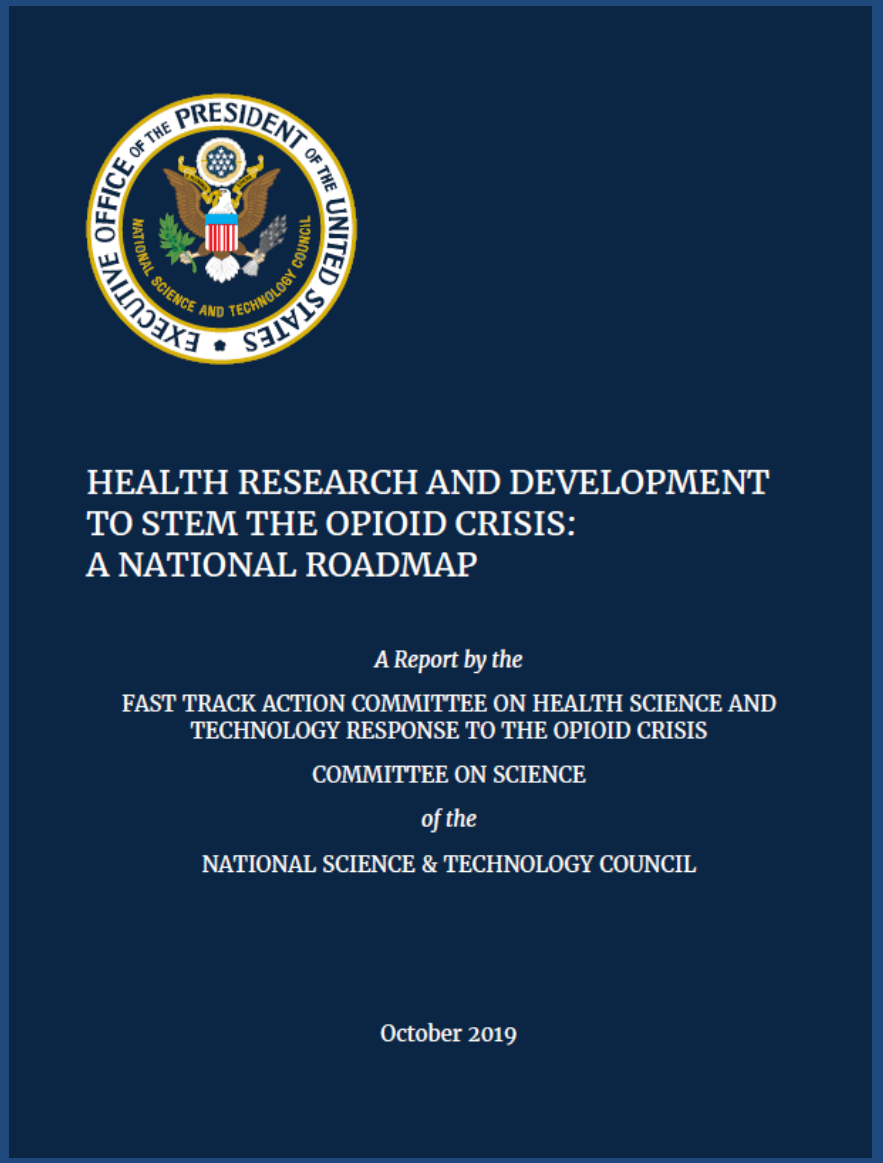
Philadelphia Supervised Injection Site Wins Legal Fight Against Justice Department

A plan to create a space where people can inject heroin and other drugs under medical supervision does not violate a federal law intended to crack down on drug houses, a federal judge ruled.

Research

Volkow & Collins. *NEJM* 2017;377:391-394

- Overdose Prevention and Reversal
  - Stronger opioid antagonist formulations
  - Phrenic nerve stimulation devices
  - Technologies for auto-injection of naloxone
- Treatment of OUDs
  - Vaccines against opioids to prevent brain entry
  - Monoclonal antibodies against synthetic opioids
  - Clinical trials of lofexidine (controls withdrawal symptoms)
- Treatment of Chronic Pain
  - Drugs targeting the endocannabinoid system
  - Nonpharmacologic approaches (rTMS)
  - Drugs that target other opioid receptors than *mu*-receptor



Future

Worse Before Better

Pardo B et al., *Future of Fentanyl and Other Synthetic Opioids*, RAND (2019)

- Synthetic opioids is not yet national epidemic.
- Synthetic opioids now appear in counterfeit prescription meds for other opioids or other drugs—increasing risk of overdose to unsuspecting buyers.
- Fentanyl is not the most potent of synthetic opioid.
    - In 2017, Ohio saw surge in deaths from carfentanil
    - Some analogues have higher affinity for *mu* receptors, requiring higher doses of naloxone for overdose reversal
- Synthetic opioids appear in 50% of postmortems involving cocaine, heroin, and methamphetamine.
    - Stimulant users are not opioid tolerant, increasing risk of opioid overdose

Take Home Messages

- Overdose deaths are the leading cause of death for Americans under age 50—mostly from synthetic opioids.
- Prescribing rates suggest physicians are responding to the prescription-related opioid overdose epidemic.
- Illicit use of synthetic opioids may be a **stronger** driver of the U.S. drug epidemic than the prescription-related opioid use epidemic.
- Opioid use disorder is a chronic, treatable, but relapsing brain disorder.
- Medications are the cornerstone of effective treatment and can be provided in primary care, in emergency rooms, and during hospitalization.
- Attention should be paid to work and occupation as risk factors for opioid use disorder.

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