

## Overview of the Opioid Crisis Where We Are and Where We Need to Go

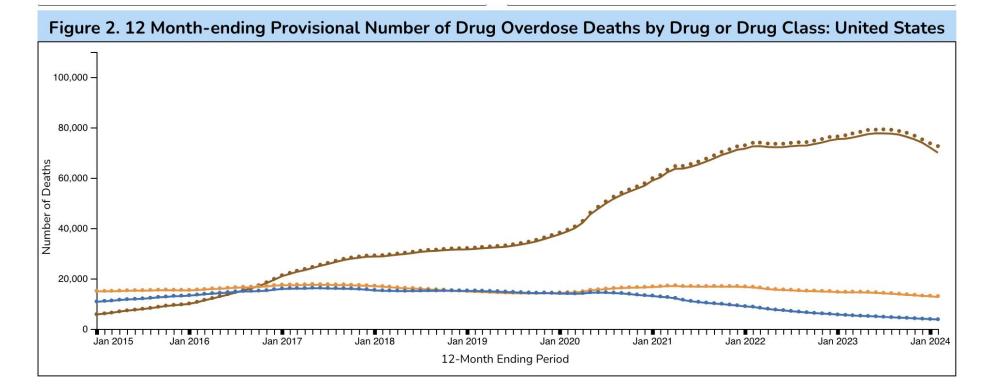
#### Andrew Kolodny, MD

Medical Director, Opioid Policy Research Collaborative Heller School for Social Policy and Management Brandeis University President, Physicians for Responsible Opioid Prescribing



#### 12 Month-ending Provisional Number of Drug Overdose Deaths by Drug or Drug Class

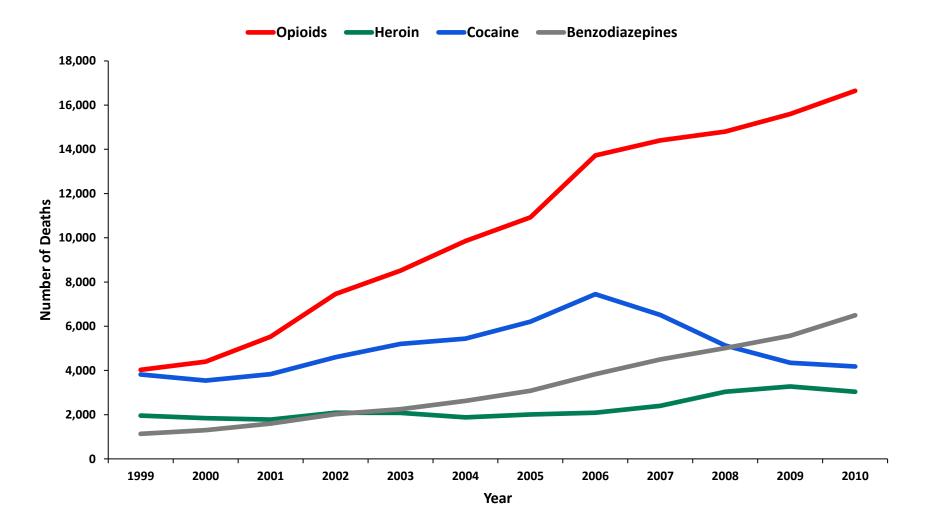
#### Based on data available for analysis on: July 7, 2024



#### Legend for Drug or Drug Class

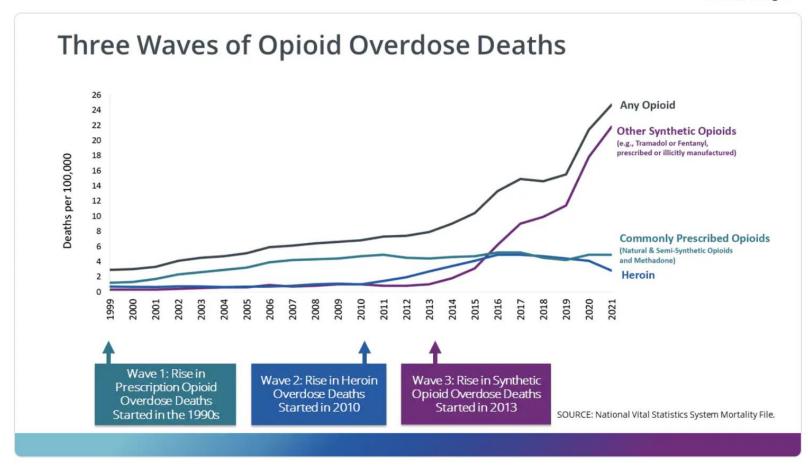
.1)
emi-synthetic opioids, incl. methadone (T40.2, T40.3)
pioids, excl. methadone (T40.4)
emi-synthetic o

### Drug Overdose Deaths by Major Drug Type, United States, 1999–2010



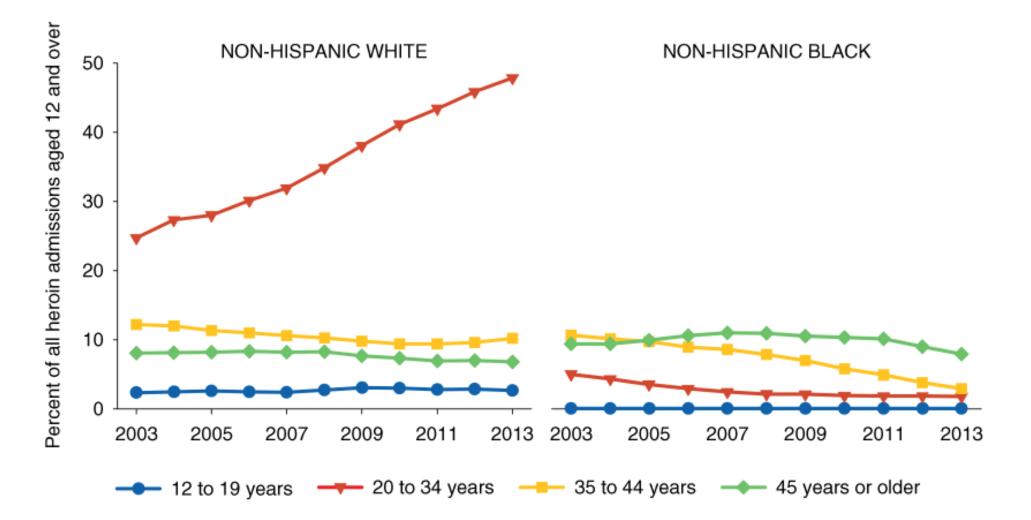
### Three waves of opioid overdose deaths

**Q** View Larger



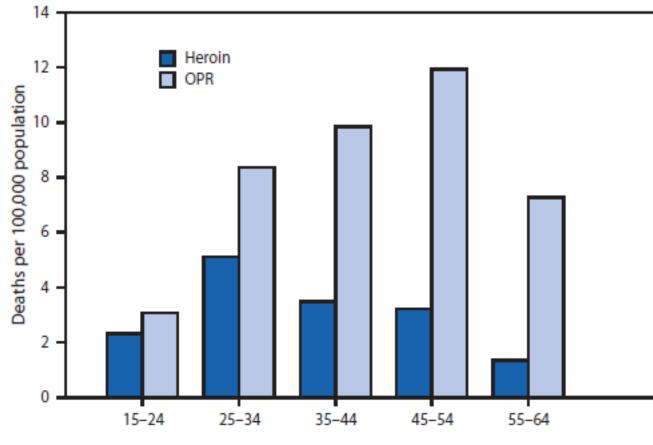
This rise in opioid overdose deaths is shown in three distinct waves.

### Heroin treatment admissions : 2003-2013



SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 01.23.15.

## Death rates from overdoses of heroin or prescription opioid pain relievers (OPRs), by age group

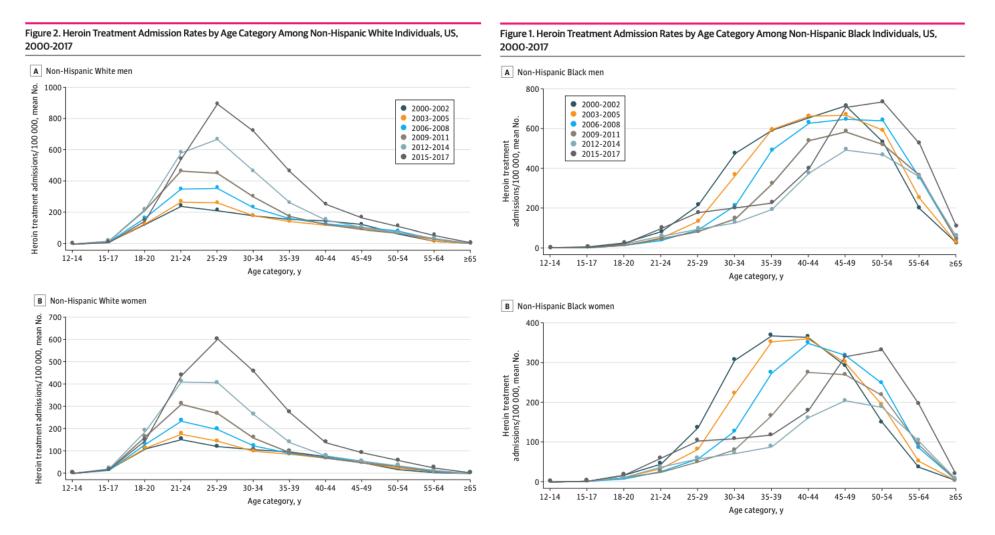


Age group (yrs)

SOURCE: CDC. Increases in Heroin Overdose Deaths — 28 States, 2010 to 2012 MMWR. 2014, 63:849-854

#### **Non-Hispanic Whites**

#### **Non-Hispanic Blacks**



Source: Warren EC, Kolodny A. Trends in Heroin Treatment Admissions in the United States by Race, Sex, and Age. JAMA Netw Open. 2021 Feb 1;4(2):e2036640. doi: 10.1001/jamanetworkopen.2020.36640.

## **Three Opioid-Addicted Cohorts**

- 1. 30-45 y/o, disproportionately white, mainly illicit use, <u>opioid addiction</u> <u>began with Rx use (addicted after 1995)</u>.
- 2. 50 y/o & up, disproportionately non-white, mostly heroin users, <u>opioid</u> <u>addiction began in teen years with heroin use (addicted before 1995)</u>
- 3. 50 y/o & up, Rx opioids for chronic pain, <u>opioid addiction began with</u> <u>Rx use (addicted after 1995)</u>

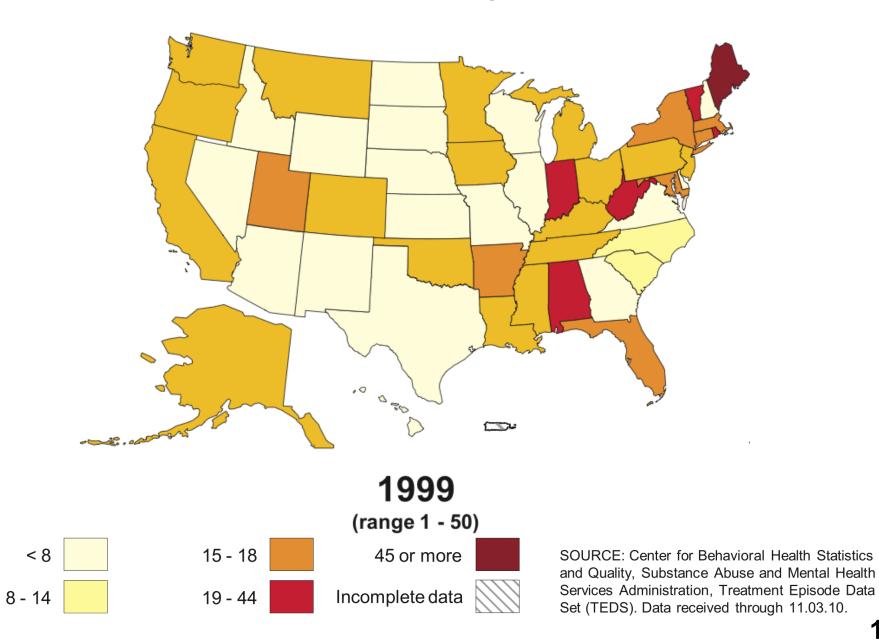
## In one year, drug overdoses killed more Americans than the entire Vietnam War did

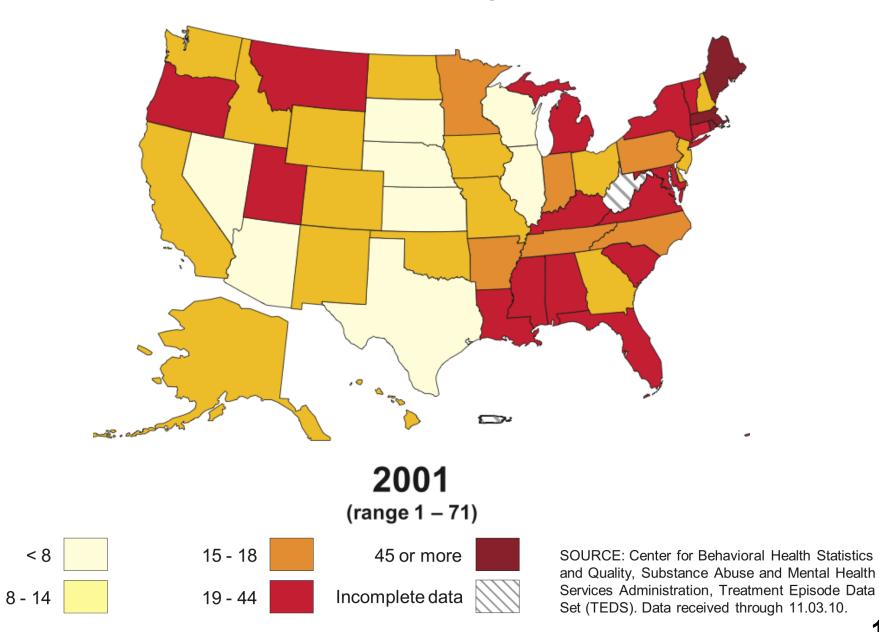
Dramatic Increases in Maternal Opioid Use and Neonatal Abstinence Syndrome

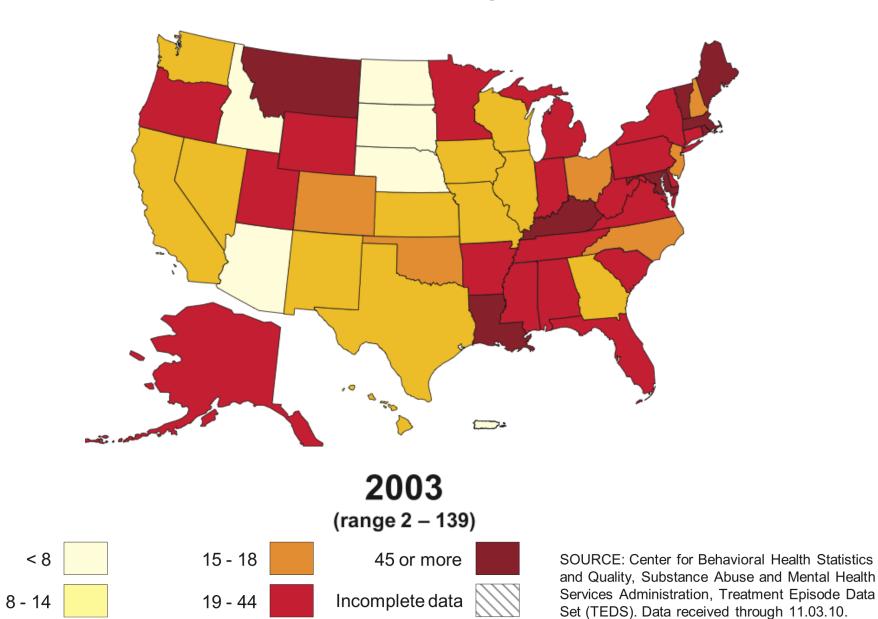
Children of the Opioid Epidemic Are Flooding Foster Homes. America Is Turning a Blind Eye.

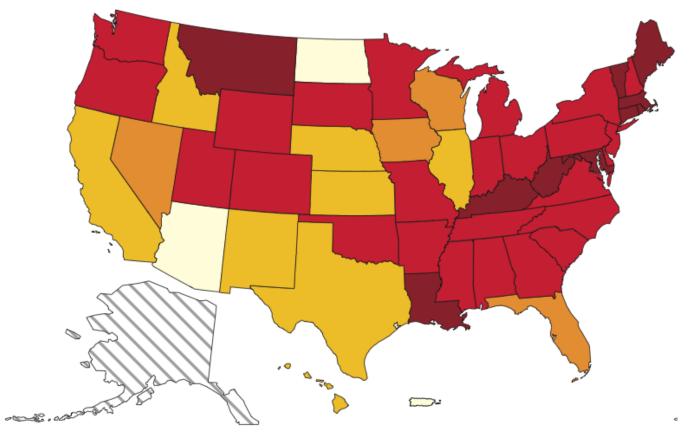
## Drug overdose deaths reach another record with almost 108,000, CDC says

How the opioid crisis decimated the American workforce



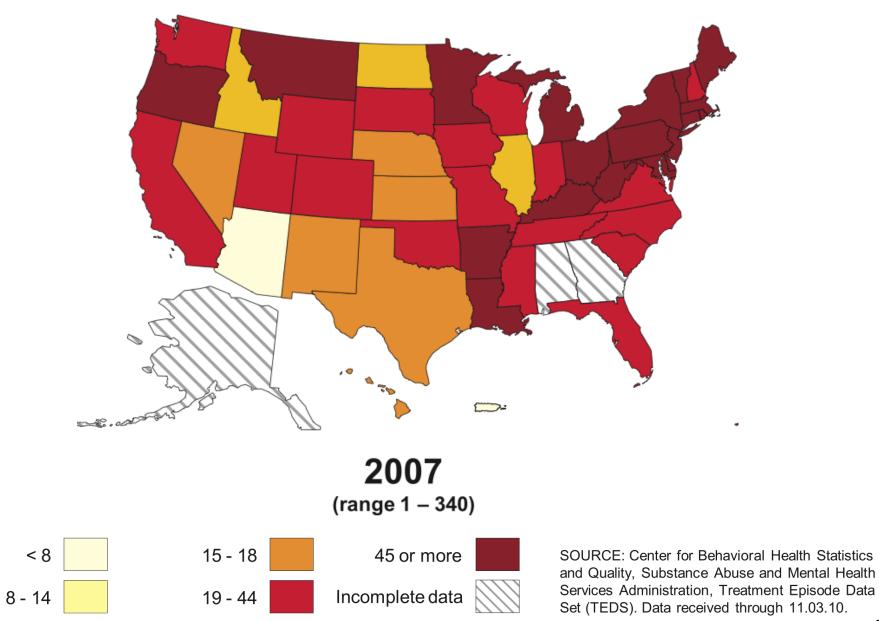


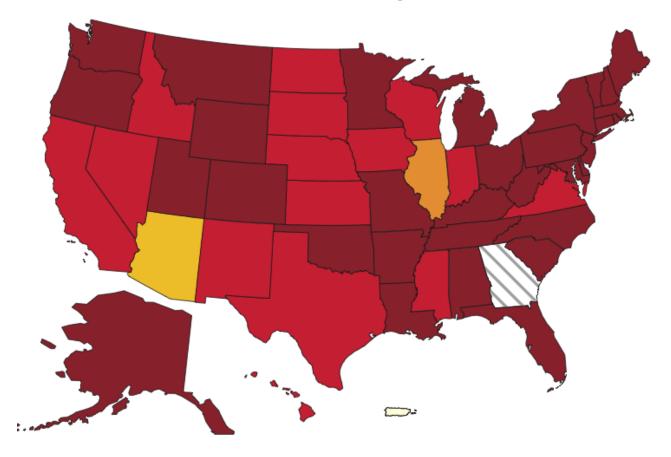




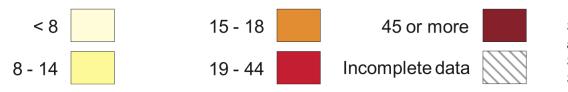
 2005 (range 0 – 214)
< 8</p>
15 - 18
45 or more
8 - 14
19 - 44
Incomplete data

SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.

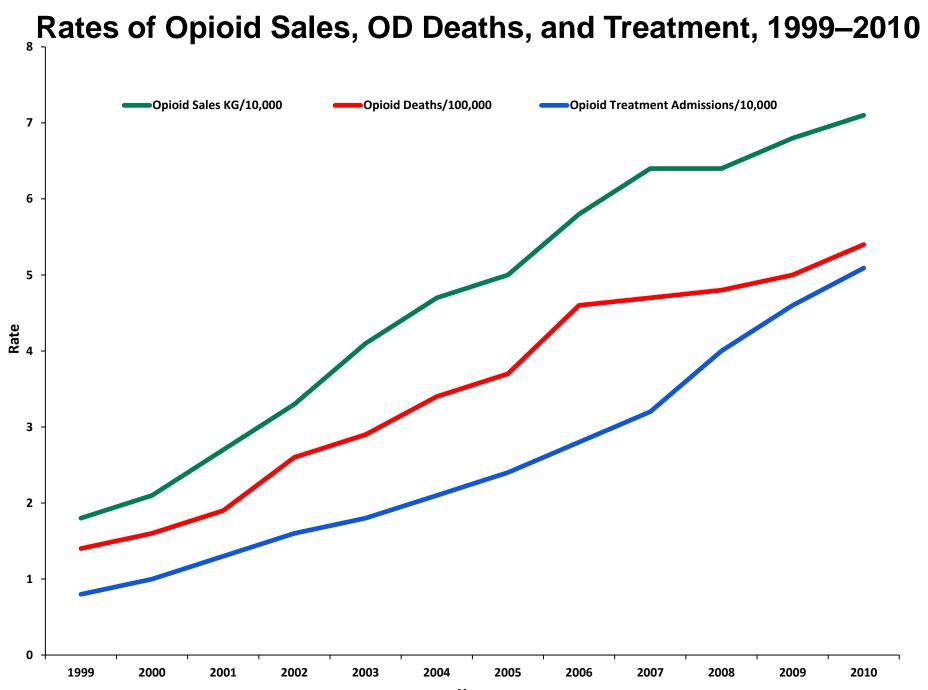


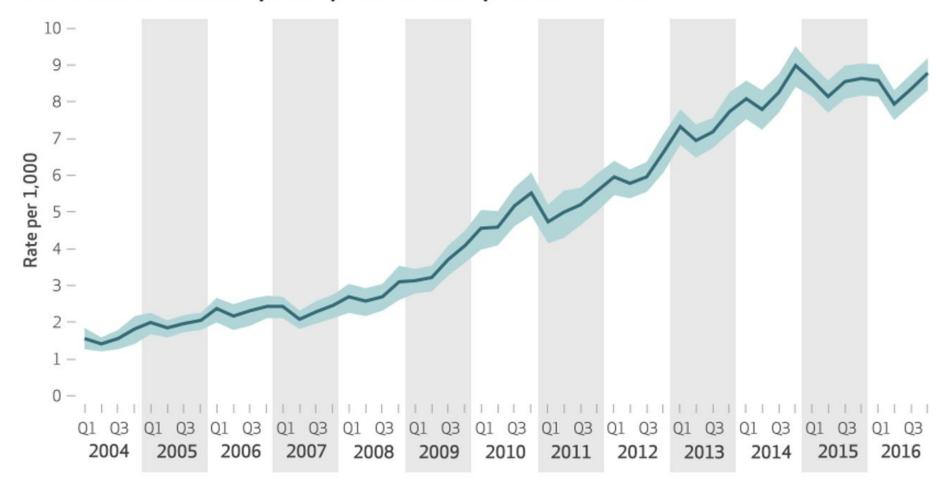


**2009** (range 1 – 379)



SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.

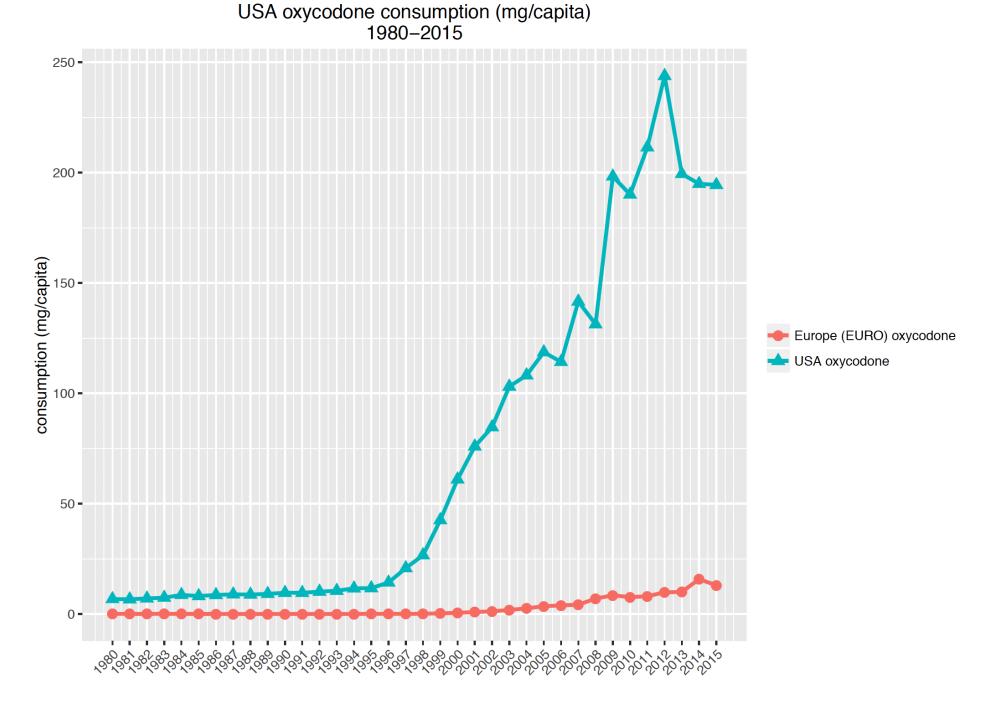




Rates of neonatal abstinence syndrome per 1,000 US in-hospital births, 2004–16

**SOURCE** Authors' analysis of data from the National Inpatient Sample, Healthcare Cost and Utilization Project. **NOTE** The shaded area indicates 95% confidence intervals.

Leech AA, Cooper WO, McNeer E, Scott TA, Patrick SW. Neonatal Abstinence Syndrome In The United States, 2004-16. Health Aff (Millwood). 2020 May;39(5):764-767.



Sources: International Narcotics Control Board; World Health Organization population data

# Industry-funded organizations campaigned for greater use of opioids

• Pain Patient Groups

Professional Societies

• The Joint Commission



• The Federation of State Medical Boards



### Prescription Opioid Use Disorder Among Adults Reporting Prescription Opioid Use With or Without Misuse in the United States

Beth Han, MD, PhD, MPH; Christopher M. Jones, PharmD, DrPH, MPH; Emily B. Einstein, PhD; Deborah Dowell, MD, MPH; and Wilson M. Compton, MD, MPE

#### Abstract

**Objective:** We examined prescriptionrelated opioid use disorder (POUD) prevalence, individual symptoms, severity, characteristics, and treatment by prescription opioid misuse status among adults with prescription opioid use.

Methods: Cross-sectional study using nationally representative data from 47,291 adults aged ≥18 years who participated in the 2021 National Survey on Drug Use and Health. Past-year POUD used *DSM-5* criteria.

**Results:** Among US adults with past-year prescription opioid use, 12.1% (95% CI, 11.1%–13.1%) misused prescription opioids, and 7.0% (95% CI, 6.2%–8.9%) had POUD. Among adults with POUD, 62.0%

(95% Cl. 56.7%–67.2%) reported no prescription opioid misuse, including 49.1% (95% CI, 43.5%-54.7%) with mild POUD, 11.0% (95% CI, 6.5%-15.4%) with moderate POUD, and 1.9% (95% CI, 0.6%–3.2%) with severe POUD. Prevalence of POUD was 4.5 times higher (prevalence ratio = 4.5, 95% Cl, 3.6–5.6) among those reporting prescription opioid misuse (22.0%, 95% Cl. 18.6%–25.8%) than those reporting use without misuse (4.9%, 95% Cl, 4.2%–5.7%). Among adults reporting prescription opioid use without misuse, high POUD prevalence was found for those with  $\geq$ 3 emergency department visits (16.4%, 95% Cl, 11.5%-23.0%), heroin use/use disorder (17.1%, 95% Cl, 5.2%–43.8%), prescription sedative/ tranquilizer use disorder (36.2%, 95% Cl,

23.6%–51.1%), and prescription stimulant use disorder (21.8%, 95% Cl, 11.0%–38.7%).

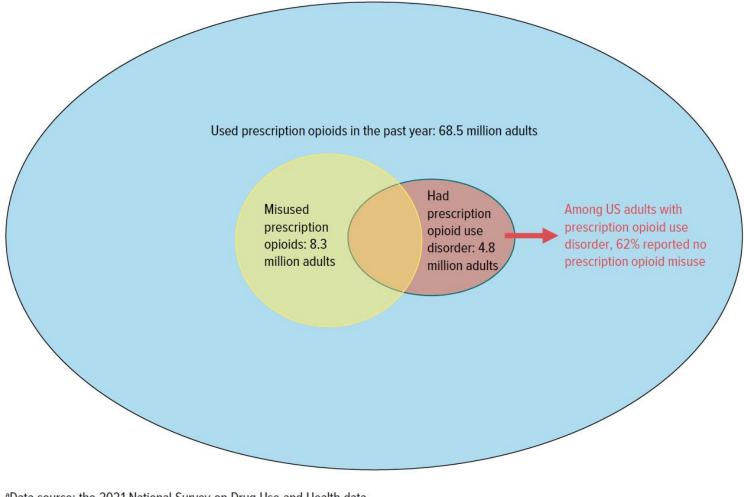
**Conclusions:** Moderate-to-severe POUD is more frequent among adults who report misusing prescription opioids. However, 62% of adults with POUD do not report prescription opioid misuse, suggesting that adults who are treated with prescription opioids and report no misuse could be at risk for developing POUD. Results highlight the need to screen for and treat POUD among adults taking prescription opioids regardless of whether they report prescription opioid misuse.

#### J Clin Psychiatry 2024;85(3):24m15258

Author affiliations are listed at the end of this article.

#### Figure 1.

Overlap of Prescription Opioid Misuse and POUD Among Adults 18 Years and Older With Prescription Opioid Use in the United States in the Past Year<sup>a</sup>



<sup>a</sup>Data source: the 2021 National Survey on Drug Use and Health data. Abbreviation: POUD = prescription-related opioid use disorder. Comparative Effectiveness Review Number 229

#### **Opioid Treatments for Chronic Pain**



### AHRQ Comparative Effectiveness Review on Opioid Treatments for Chronic Pain

#### **Key Messages**

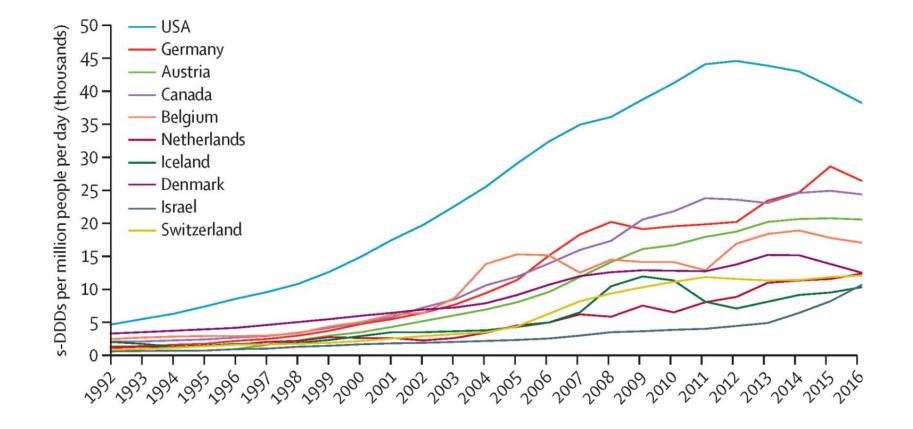
#### **Purpose of Review**

To assess the effectiveness and harms of opioid therapy for chronic noncancer pain, alternative opioid dosing strategies, and risk mitigation strategies

#### **Key Messages**

- Opioids are associated with small improvements versus placebo in pain and function, and increased risk of harms at short-term (1 to <6 months) followup; evidence on long-term effectiveness is very limited, and there is evidence of increased risk of serious harms that appear to be dose dependent.
- At short-term followup, evidence showed no differences between opioids versus nonopioid medications in improvement in pain, function, mental health status, sleep, or depression.
- Evidence on the effectiveness and harms of alternative opioid dosing strategies and the effects of risk mitigation strategies is lacking, although provision of naloxone to patients might reduce the likelihood of opioid-related emergency department visits, a taper support intervention might improve functional outcomes compared to no taper support, and co-prescription of benzodiazepines and gabapentinoids might increase risk of overdose.
- No instrument has been shown to be associated with high accuracy for predicting opioid overdose, addiction, abuse, or misuse.

Source: Chou R, et al. Opioid Treatments for Chronic Pain. Comparative Effectiveness Review No. 229. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 20-EHC011. Rockville, MD: Agency for Healthcare Research and Quality; April 2020.



Source: International Narcotics Control Board

### Opioids After Surgery in the United States Versus the Rest of the World

The International Patterns of Opioid Prescribing (iPOP) Multicenter Study

**Objective:** The International Patterns of Opioid Prescribing study compares postoperative opioid prescribing patterns in the United States (US) versus the rest of the world.

Summary of Background Data: The US is in the middle of an unprecedented opioid epidemic. Diversion of unused opioids contributes to the opioid epidemic.

Methods: Patients  $\geq 16$  years old undergoing appendectomy, cholecystectomy, or inguinal hernia repair in 14 hospitals from 8 countries during a 6-month period were included. Medical records were systematically reviewed to identify: (1) preoperative, intraoperative, and postoperative characteristics, (2) opioid intake within 3 months preoperatively, (3) opioid prescription upon discharge, and (4) opioid refills within 3 months postoperatively. The median/range and mean/standard deviation of number of pills and OME were compared between the US and non-US patients.

**Results:** A total of 4690 patients were included. The mean age was 49 years, 47% were female, and 4% had opioid use history. Ninety-one percent of US patients were prescribed opioids, compared to 5% of non-US patients (P < 0.001). The median number of opioid pills and OME prescribed were 20 (0–135) and 150 (0–1680) mg for US versus 0 (0–50) and 0 (0–600) mg for

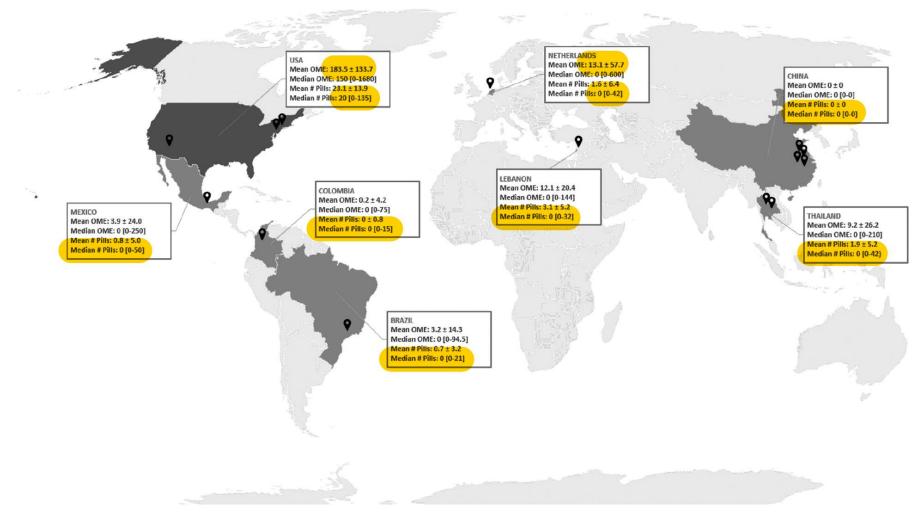
non-US patients, respectively (both P < 0.001). The mean number of opioid pills and OME prescribed were  $23.1 \pm 13.9$  in US and  $183.5 \pm 133.7$  mg versus  $0.8 \pm 3.9$  and  $4.6 \pm 27.7$  mg in non-US patients, respectively (both P < 0.001). Opioid refill rates were 4.7% for US and 1.0% non-US patients (P < 0.001). Conclusions: US physicians prescribe alarmingly high amounts of opioid medications postoperatively. Further efforts should focus on limiting opioid prescribing and emphasize non-opioid alternatives in the US.

Keywords: analgesics, narcotics, opioid, postoperative pain, prescription

(Ann Surg 2020;xx:xxx-xxx)

The United States (US) is in the midst of an unprecedented opioid epidemic. In 2016, drug overdoses (mostly opioids) resulted in 65,000 deaths, a number much higher than that caused by human immunodeficiency disease in 1995, at the peak of that epidemic.<sup>1</sup> The etiology of the opioid epidemic that commenced 2 decades ago is multifactorial and includes misleading marketing strategies by a few pharmaceutical companies that advocated for opioids as a risk-free optimal solution to pain, and a concomitant recognition by the

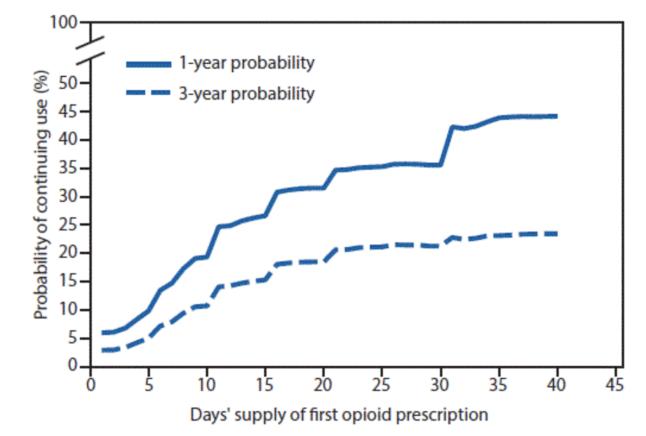
Kaafarani HMA, Han K, El Moheb M, et al. Opioids After Surgery in the United States Versus the Rest of the World: The International Patterns of Opioid Prescribing (iPOP) Multicenter Study [published online ahead of print, 2020 Jul 9]. Ann Surg.



**FIGURE 1.** Site-specific map detailing opioid pills prescribed and OME in the United States versus internationally. OME indicates oral morphine equivalents.

Kaafarani HMA, Han K, El Moheb M, et al. Opioids After Surgery in the United States Versus the Rest of the World: The International Patterns of Opioid Prescribing (iPOP) Multicenter Study [published online ahead of print, 2020 Jul 9]. Ann Surg.

One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of days' supply\* of the first opioid prescription — United States, 2006–2015



\* Days' supply of the first prescription is expressed in days (1–40) in 1-day increments.

Source: Shah A, Hayes CJ, Martin BC. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015. MMWR Morb Mortal Wkly Rep 2017;66:265–269.

#### Research

#### JAMA | Original Investigation

#### Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency Department A Randomized Clinical Trial

Andrew K. Chang, MD, MS; Polly E. Bijur, PhD; David Esses, MD; Douglas P. Barnaby, MD, MS; Jesse Baer, MD

#### Key Points

**Question** Do any of 4 oral combination analgesics (3 with different opioids and 1 opioid-free) provide more effective reduction of moderate to severe acute extremity pain in the emergency department (ED)?

**Findings** In this randomized clinical trial of 411 ED patients with acute extremity pain (mean score, 8.7 on the 11-point numerical rating scale), there was no significant difference in pain reduction at 2 hours. Mean pain scores decreased by 4.3 with ibuprofen and acetaminophen (paracetamol); 4.4 with oxycodone and acetaminophen; 3.5 with hydrocodone and acetaminophen; and 3.9 with codeine and acetaminophen.

**Meaning** For adult ED patients with acute extremity pain, there were no clinically important differences in pain reduction at 2 hours with ibuprofen and acetaminophen or 3 different opioid and acetaminophen combination analgesics.

#### Table 2. Numerical Rating Scale (NRS) Pain Scores and Decline in Pain Scores by Treatment Group

	NRS Pain Score, Mean (95% CI) <sup>a</sup>				
	lbuprofen and Acetaminophen <sup>b</sup>	Oxycodone and Acetaminophen <sup>c</sup>	Hydrocodone and Acetaminophen <sup>d</sup>	Codeine and Acetaminophen <sup>e</sup>	P Value <sup>†</sup>
No. of patients <sup>9</sup>	101	104	103	103	
Primary end point: decline in score to 2 h	4.3 (3.6 to 4.9)	4.4 (3.7 to 5.0)	3.5 (2.9 to 4.2)	3.9 (3.2 to 4.5)	.053
Baseline score	8.9 (8.5 to 9.2)	8.7 (8.3 to 9.0)	8.6 (8.3 to 9.0)	8.6 (8.2 to 8.9)	.47
Score at 1 h	5.9 (5.3 to 6.6)	5.5 (4.9 to 6.2)	6.2 (5.6 to 6.9)	5.9 (5.2 to 6.5)	.25
Score at 2 h	4.6 (3.9 to 5.3)	4.3 (3.6 to 5.0)	5.1 (4.5 to 5.8)	4.7 (4.0 to 5.4)	.13
Decline in score to 1 h	2.9 (2.4 to 3.5)	3.1 (2.6 to 3.7)	2.4 (1.8 to 3.0)	2.7 (2.1 to 3.3)	.13

### Systematic review of the relative efficacy of non-steroidal anti-inflammatory drugs and opioids in the treatment of acute renal colic

#### Anna Holdgate, Tamara Pollock

**Results** 20 trials totalling 1613 participants were identified. Both NSAIDs and opioids led to clinically important reductions in patient reported pain scores. Pooled analysis of six trials showed a greater reduction in pain scores for patients treated with NSAIDs than with opioids. Patients treated with NSAIDs were significantly less likely to require rescue analgesia (relative risk 0.75, 95% confidence interval 0.61 to 0.93). Most trials showed a higher incidence of adverse events in patients treated with opioids. Compared with patients treated with opioids, those treated with NSAIDs had significantly less vomiting (0.35, 0.23 to 0.53). Pethidine was associated with a higher rate of vomiting.

**Conclusions** Patients receiving NSAIDs achieve greater reductions in pain scores and are less likely to require further analgesia in the short term than those receiving opioids. Opioids, particularly pethidine, are associated with a higher rate of vomiting.

#### What is already known on this topic

Both non-steroidal anti-inflammatory drugs (NSAIDs) and opioids provide analgesia in acute renal colic

NSAIDs have well recognised side effects

#### What this study adds

NSAIDs achieve slightly greater reductions in pain scores than opioids in patients with renal colic

Patients with renal colic are less likely to need rescue analgesia if treated with NSAIDs

BMJ, doi:10.1136/bmj.38119.581991.55 (published 3 June 2004)

Opioids, particularly pethidine, are associated with a higher rate of vomiting and other adverse effects

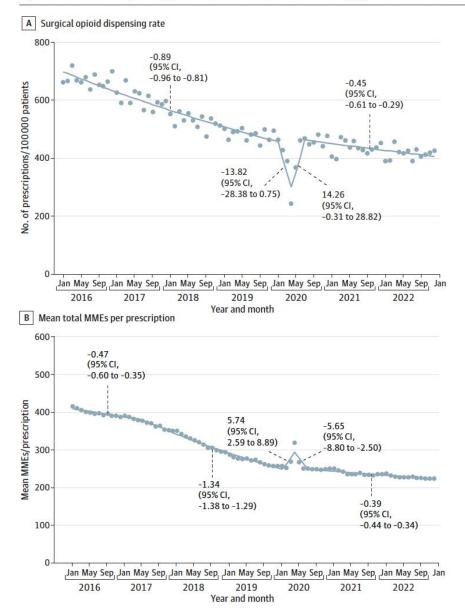
### Pain Management for Third-Molar Extractions

Moore & Hersh Systematic Review (2015)

- Ibuprofen + APAP more effective than either one alone
- Ibuprofen + APAP more effective w/less side effects than opioid combos

Source: Moore PA, Hersh EV. Combining ibuprofen and acetaminophen for acute pain management after third-molar extractions: translating clinical research to dental practice. J Am Dent Assoc. 2013 Aug;144(8):898-908.

Figure. Rate and Dosing of Dispensed Opioid Prescriptions From US Surgeons, 2016-2022



During 2016 to 2022, the rate and size of opioid prescriptions from US surgeons declined.

But these declines were slower after mid-2020 compared with before 2020

Source:Zhang J, Waljee JF, Nguyen TD, et al. Opioid Prescribing by US Surgeons, 2016-2022. JAMA Netw Open. 2023;6(12):e2346426. doi:10.1001/jamanetworkopen.2023.46426

## Controlling the epidemic: Primary Prevention

Primary Prevention is preventing a disease from occurring

**Strategies for preventing OUD include:** 

- Promoting more cautious prescribing
- Informing public about opioid risks
- Social marketing campaigns to dramatize negative consequences

## Controlling the epidemic: Secondary Prevention

# Secondary Prevention is catching a disease early in its course

**Strategies include:** 

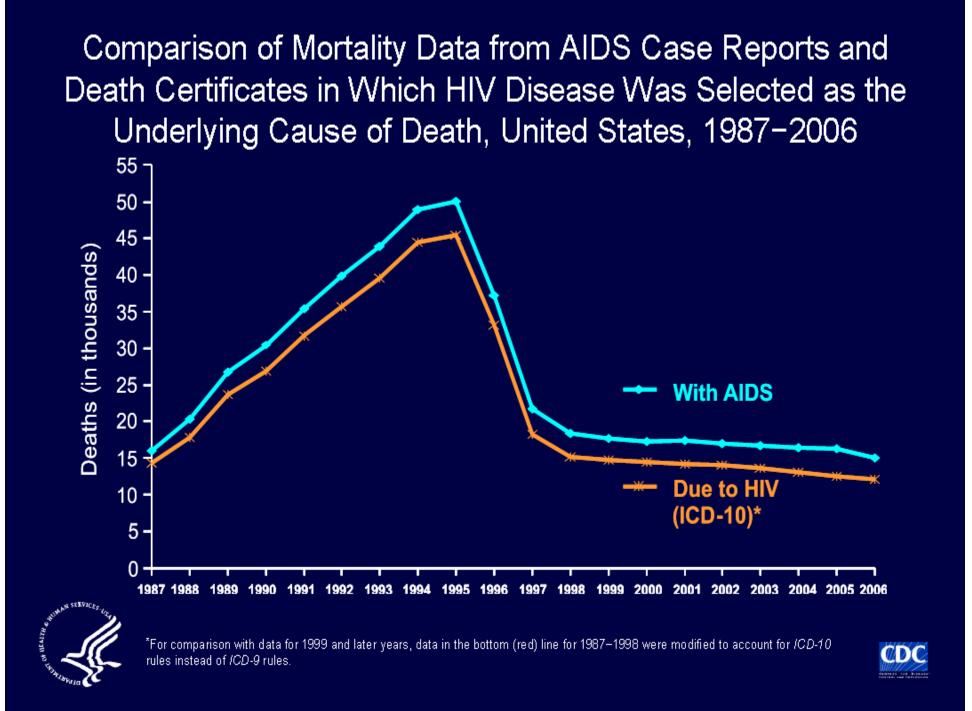
- Screening & active case finding
- Linking people to treatment
- Social marketing campaigns to engage people in treatment

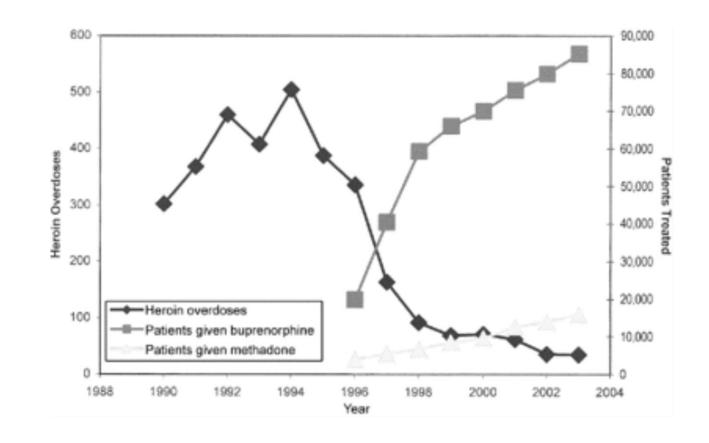
## **Controlling the epidemic: Tertiary Prevention**

# Tertiary Prevention is treatment (and harm reduction) to prevent most severe outcomes

**Strategies include:** 

- Low threshold treatment access
- Syringe exchange
- Naloxone



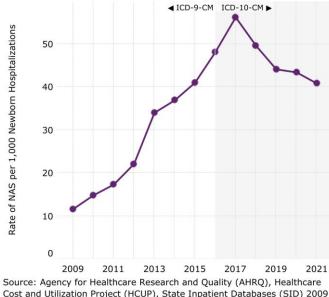


From: Buprenorphine Use: The International Experience Clin Infect Dis. 2006;43(Supplement\_4):S197-S215. doi:10.1086/508184 Clin Infect Dis | © 2006 by the Infectious Diseases Society of America Massachusetts: Rate of NAS per 1,000 Newborn Hospitalizations by All NAS, 2009 to 2020



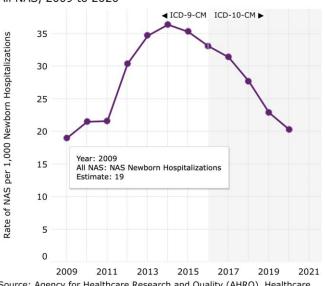
Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) 2009 to 2020 (all available data as of 10/18/2022). Abbreviation: NAS, neonatal abstinence syndrome.

West Virginia: Rate of NAS per 1,000 Newborn Hospitalizations by All NAS, 2009 to 2021



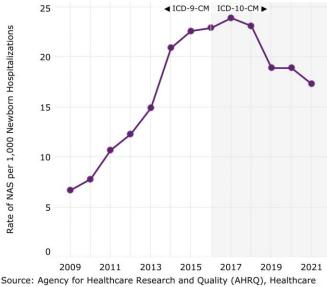
Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) 2009 to 2021 (all available data as of 10/18/2022). Abbreviation: NAS, neonatal abstinence syndrome.

Maine: Rate of NAS per 1,000 Newborn Hospitalizations by All NAS, 2009 to 2020



Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) 2009 to 2020 (all available data as of 10/18/2022). Abbreviation: NAS, neonatal abstinence syndrome.

Kentucky: Rate of NAS per 1,000 Newborn Hospitalizations by All NAS, 2009 to 2021



Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) 2009 to 2021 (all available data as of 10/18/2022). Abbreviation: NAS, neonatal abstinence syndrome.

## Summary

- The U.S. is in the midst of a severe epidemic of opioid addiction and overdose deaths
- To bring the epidemic to an end:
  - We must prevent new cases of opioid addiction
  - We must improve access to treatment for people already addicted