

# The North American Opioid Crisis: Origins, Current State, and the Path Forward

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# Opium



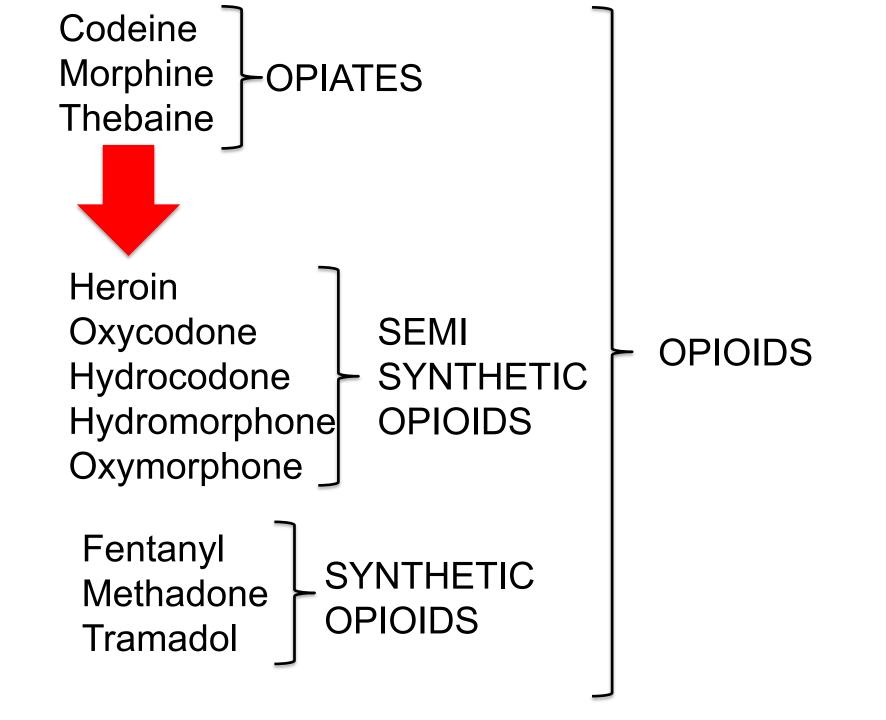
# Opium



Codeine Morphine Thebaine



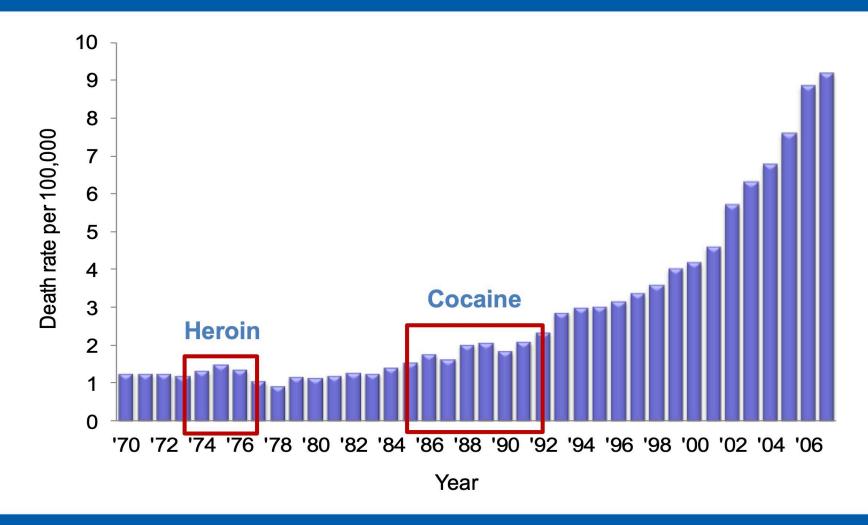
Heroin
Oxycodone
Hydrocodone
Hydromorphone
Oxymorphone



### Why Opioids Are Highly Addictive

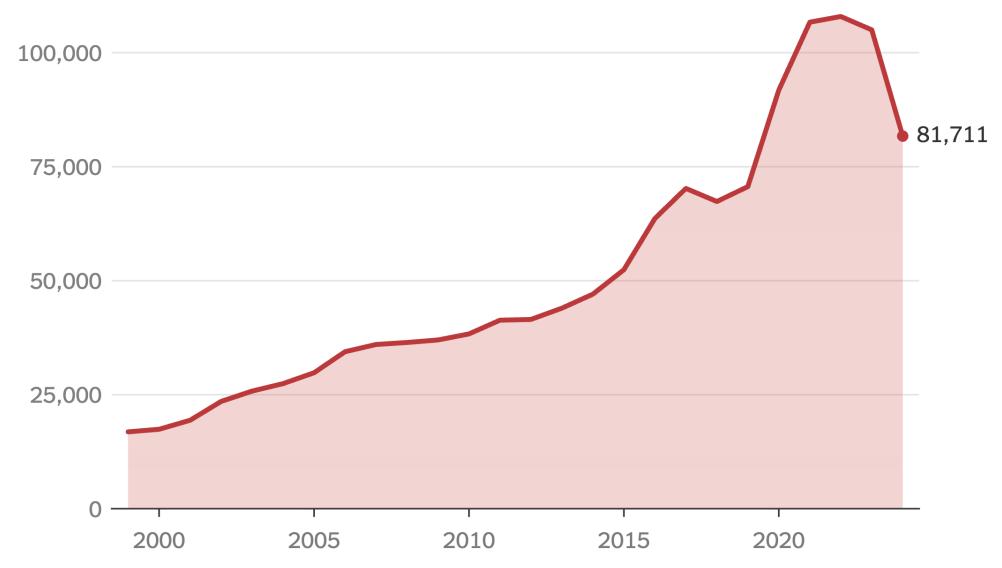
- Taking an opioid produces positive effects: euphoria and/or pain relief.
- Once dependence sets in, stopping opioids produces negative effects: dysphoria and/or pain

# Unintentional Drug Overdose Deaths United States, 1970–2007



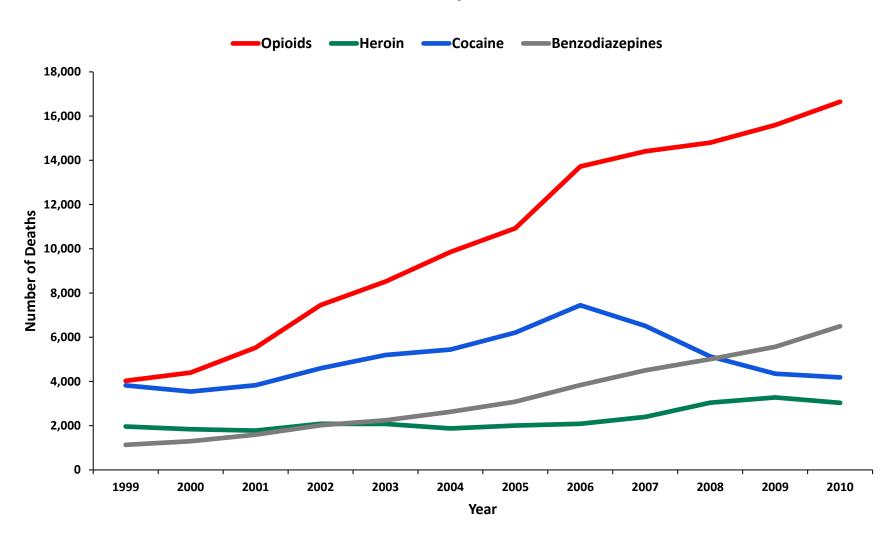


### U.S. Drug OD deaths 1999-2024

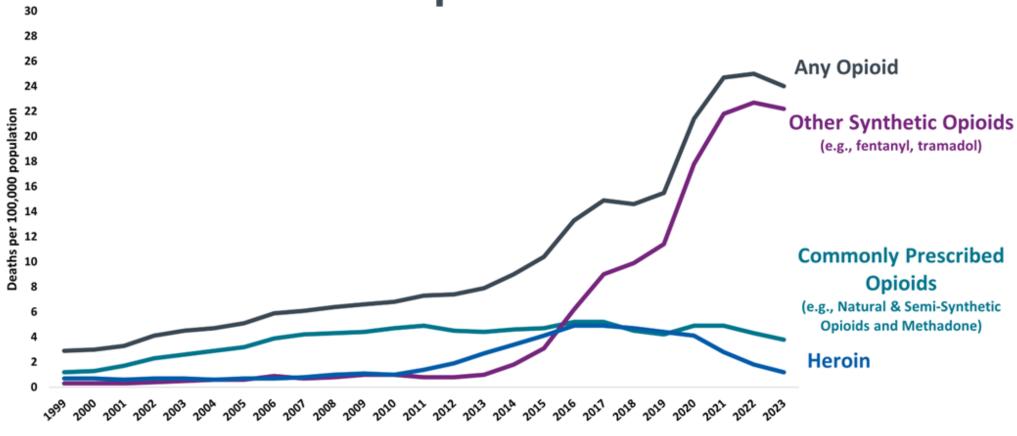


Source: CDC Vital Statistics

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



### Three Waves of Opioid Overdose Deaths



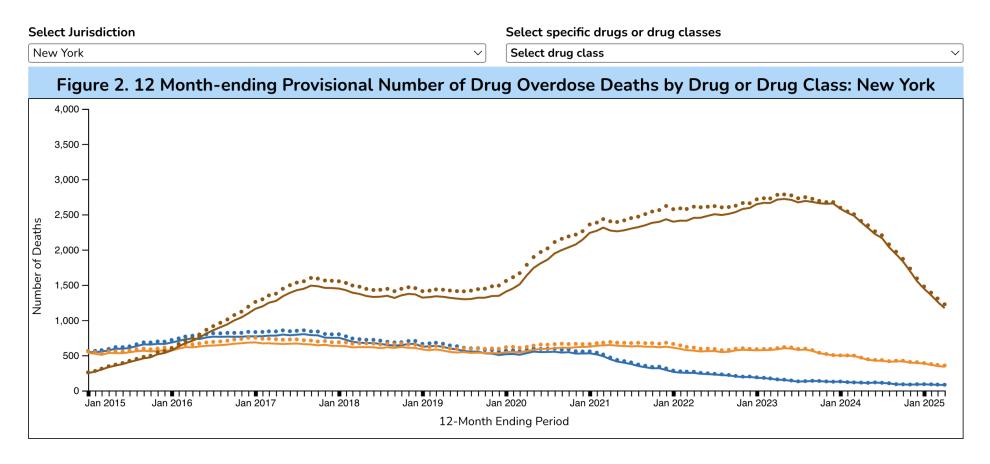
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2024. https://wonder.cdc.gov/.



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

#### Based on data available for analysis on: September 7, 2025

After opening the drug class dropdown, click the top of the dropdown menu again to make the checkboxes disappear.



Legend for Drug or Drug Class

Heroin (T40.1)

Natural & semi-synthetic opioids, incl. methadone (T40.2, T40.3)

Synthetic opioids, excl. methadone (T40.4)

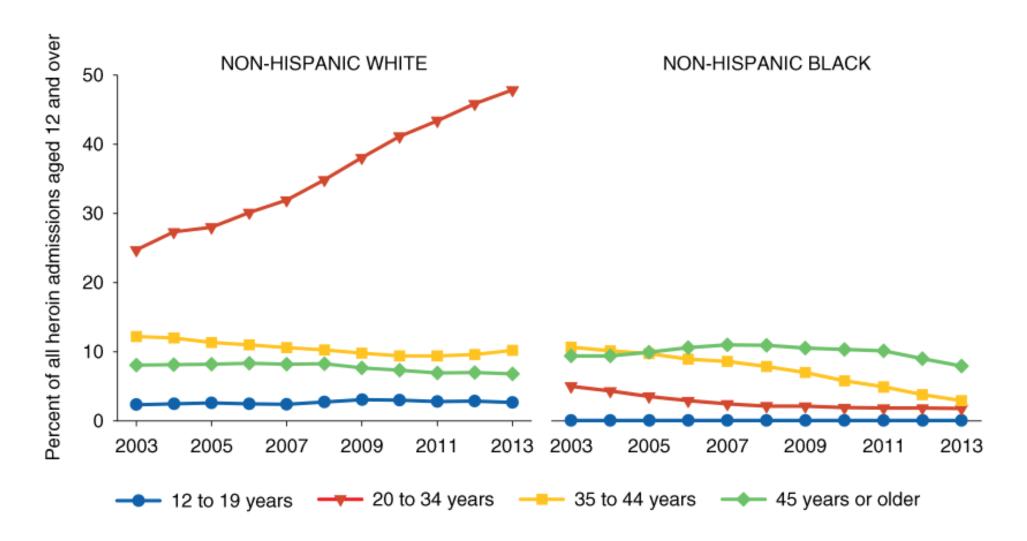
---- Reported Value

O Predicted Value

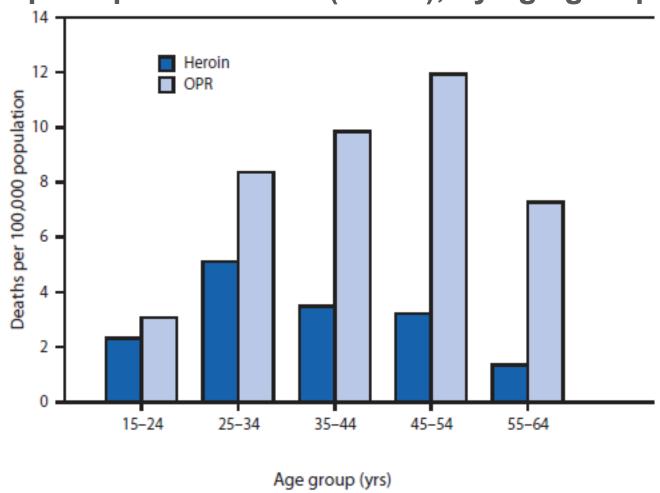
#### **Three Opioid-Addicted Cohorts**

- 1. 30-50 y/o, disproportionately white, significant heroin use, <u>opioid</u> addiction began with Rx use (addicted after 1995)
- 2. 50 y/o & up, disproportionately white, mostly Rx opioids, opioid addiction began with Rx use (addicted after 1995)
- 3. 60 y/o & up, disproportionately non-white, mostly heroin users, opioid addiction began in teen years with heroin use (addicted before 1995)

#### Heroin treatment admissions: 2003-2013



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



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

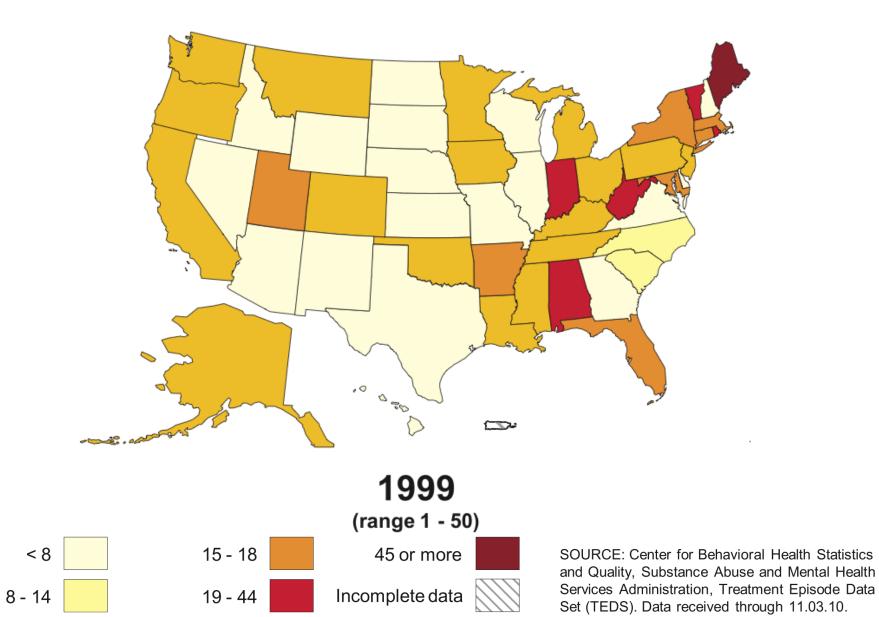
### In one year, drug overdoses killed more Americans than the entire Vietnam War did

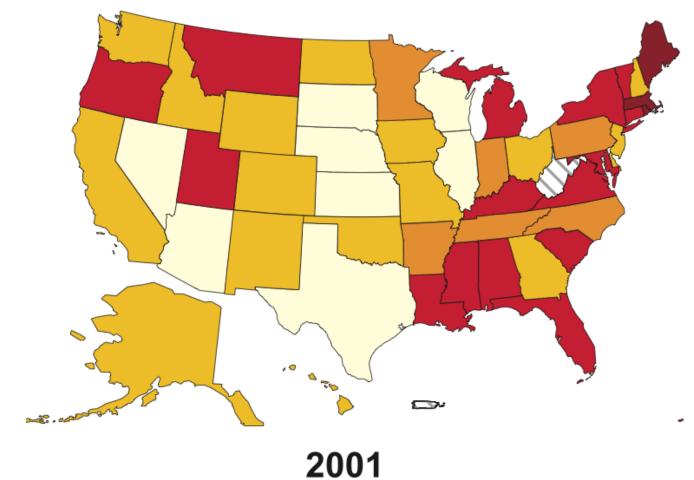
Dramatic Increases in Maternal Opioid Use and Neonatal Abstinence Syndrome

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

Drug overdose deaths jump in 2023 to 105,000, a record high, CDC says

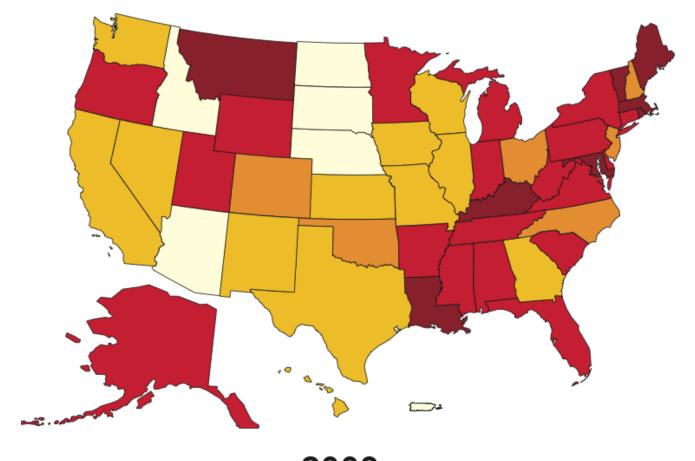
How the opioid crisis decimated the American workforce





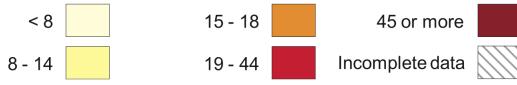


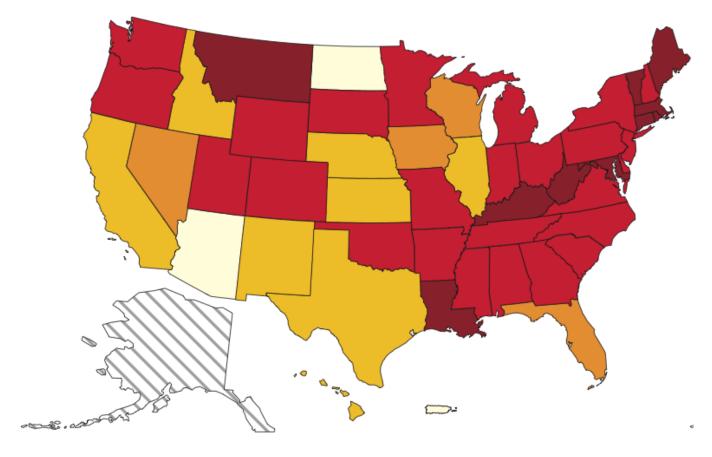




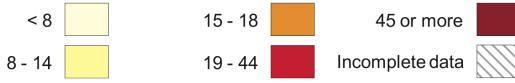


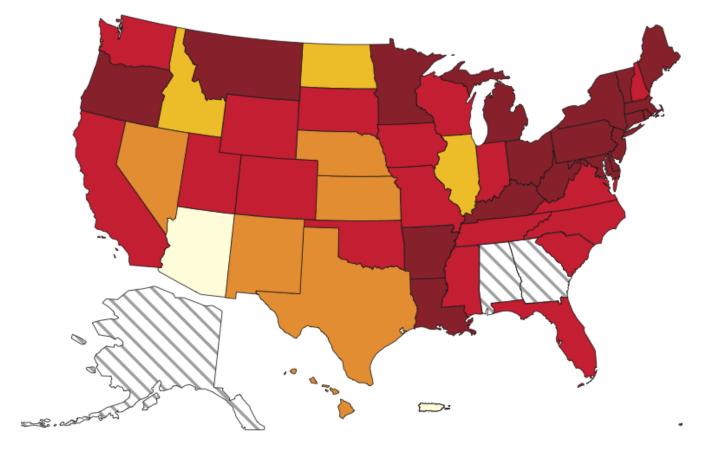
(range 2 - 139)





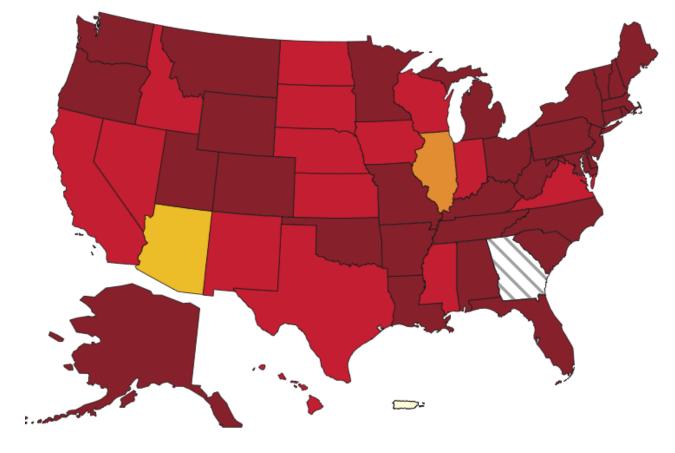




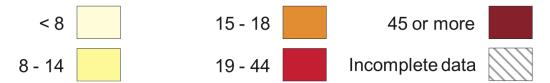


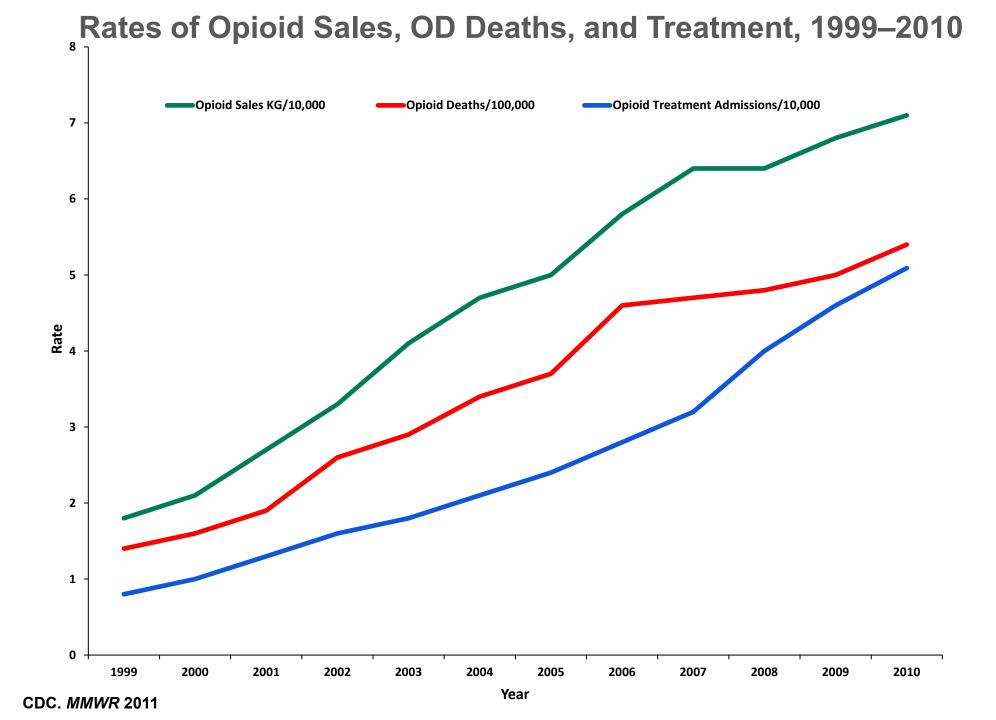
**2007** (range 1 – 340)

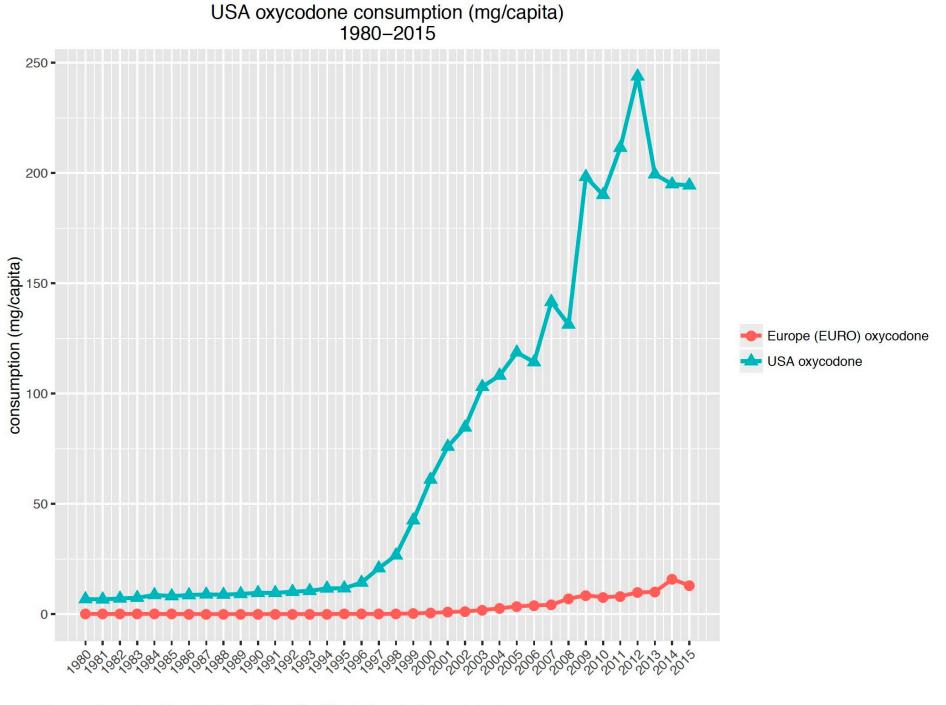




**2009** (range 1 – 379)



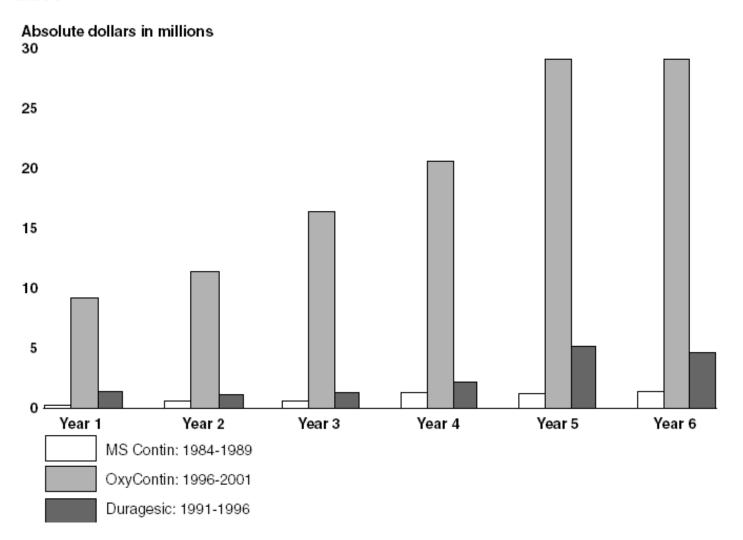




Sources: International Narcotics Control Board; World Health Organization population data

#### **Dollars Spent Marketing OxyContin (1996-2001)**

Figure 1: Promotional Spending for Three Opioid Analgesics in First 6 Years of Sales



Source: United States General Accounting Office: Dec. 2003, "OxyContin Abuse and Diversion and Efforts to Address the Problem."

#### Industry-funded "educational" messages

 Physicians are needlessly allowing patients to suffer because of "opiophobia."

Opioid addiction is rare in pain patients.

Opioids can be easily discontinued.

Opioids are safe and effective for chronic pain.

# Industry-funded organizations campaigned for greater use of opioids

Pain Patient Groups

Professional Societies

The Joint Commission



The Federation of State Medical Boards

# "The risk of addiction from long-term opioid use is much less than 1%"

Porter J, Jick H. *Addiction rare in patients treated with narcotics*. N Engl J Med. 1980 Jan 10;302(2):123

#### N Engl J Med. 1980 Jan 10;302(2):123.

#### ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

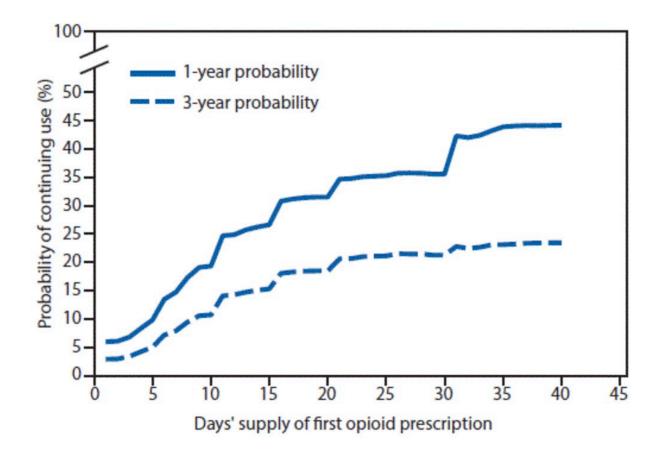
To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients¹ who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,² Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

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HERSHEL JICK, M.D.
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- 1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
- 2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

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



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>				
	Ibuprofen and Acetaminophen <sup>b</sup>	Oxycodone and Acetaminophen <sup>c</sup>	Hydrocodone and Acetaminophen <sup>d</sup>	Codeine and Acetaminophene	P Value <sup>f</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

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

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

## 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.

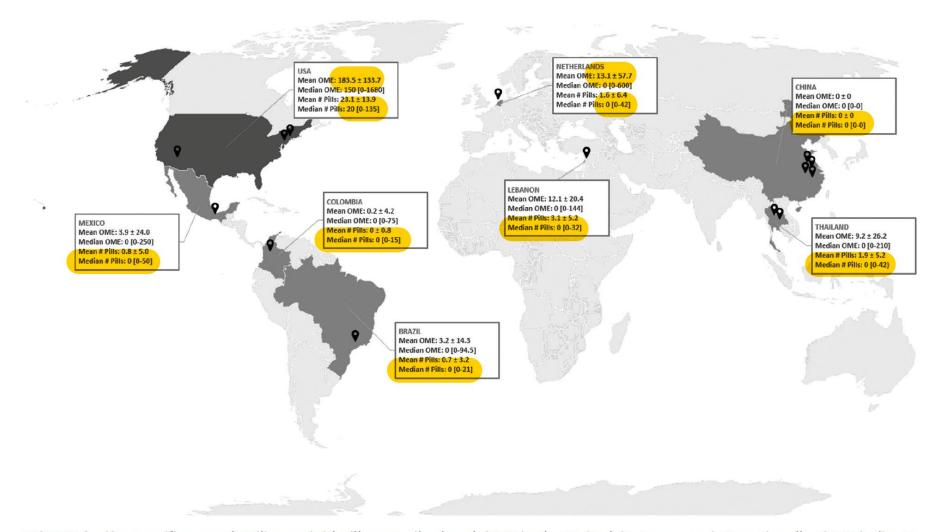
**Results:** A total of 4690 patients were included. The mean age was 49 years, 47% were female, and 4% had opioid use history. Ninety-one percent of US patients were prescribed opioids, compared to 5% of non-US patients (P < 0.001). The median number of opioid pills and OME prescribed were 20 (0-135)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

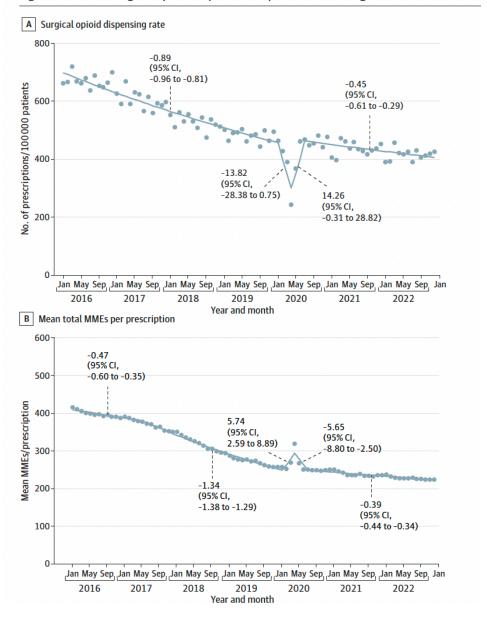
Kaafarani HMA, Han K, El Moheb M, et al. Opioids After Surgery in the United States Versus the Rest of the World: The International Patterns of Opioid Prescribing (iPOP) Multicenter Study [published online ahead of print, 2020 Jul 9]. Ann Surg.



**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.

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



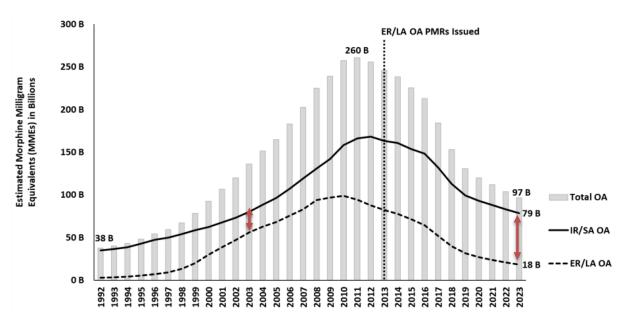
During 2016 to 2022, the rate and size of opioid prescriptions from US surgeons declined.

But these declines
were slower after mid2020 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

## FDA

#### **Trends in Total MMEs**



Nationally Estimated Annual Morphine Milligram Equivalents (MMEs) for Opioid Analgesics Dispensed From U.S. Retail and Mail-Order Pharmacies, Stratified by Formulation, 1992 to 2023. Source: IQVIA National Prescription Audit™, U.S. Launch edition. Data years 1992-2023.

Data extracted July 2024. Sources for MME conversion factors: Centers for Disease Control and Prevention, NDC and Oral MME Conversion File, 2019 version,

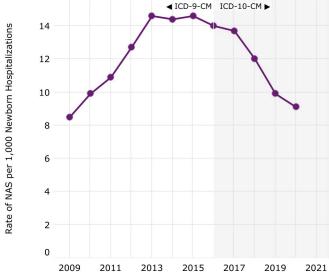
<a href="https://www.cdc.gov/drugoverdose/resources/data.html">https://www.cdc.gov/drugoverdose/resources/data.html</a>. McPherson ML, Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing, 2nd Edition, American Society of Health-System Pharmacists, 2018. Medscape, Opioid Equivalents and Conversions, <a href="https://emedicine.medscape.com/article/2138678-overview">https://emedicine.medscape.com/article/2138678-overview</a>. GlobalRPh, Opioid conversions calc (single agent) equianalgesic, <a href="https://emedicine.medscape.com/article/2138678-overview">https://emedicine.medscape.com/article/2138678-overview</a>. GlobalRPh, Opioid conversions calc (single agent) equianalgesic, <a href="https://emedicine.medscape.com/article/2138678-overview">https://emedicine.medscape.com/article/2138678-overview</a>. GlobalRPh, Opioid conversions calc (single agent) equianalgesic, <a href="https://emedicine.medscape.com/article/2138678-overview">https://emedicine.medscape.com/article/2138678-overview</a>. GlobalRPh, Opioid conversions calc (single agent) equianalgesic, <a href="https://emedicine.medscape.com/article/2138678-overview">https://emedicine.medscape.com/article/2138678-overview</a>. GlobalRPh, Opioid conversions calc (single agent) equianalgesic, <a href="https://emedicine.medscape.com/article/2138678-overview">https://emedicine.medscape.com/article/2138678-overview</a>.

Abbreviations: B, billions; ER/LA OA, extended-release/long-acting opioid analgesic; IR/SA OA, immediate-release/short-acting opioid analgesic; U.S., United States

www.fda.gov

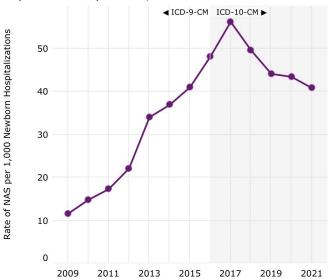
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#### Massachusetts: Rate of NAS per 1,000 Newborn Hospitalizations by All NAS, 2009 to 2020



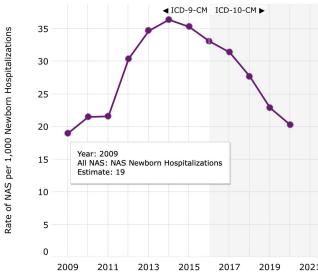
Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) 2009 to 2020 (all available data as of 10/18/2022). Abbreviation: NAS, neonatal abstinence syndrome.

#### 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.

### Controlling the epidemic:



# Controlling the epidemic: Primary Prevention

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

Finding a case early in its course

#### **Strategies include:**

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

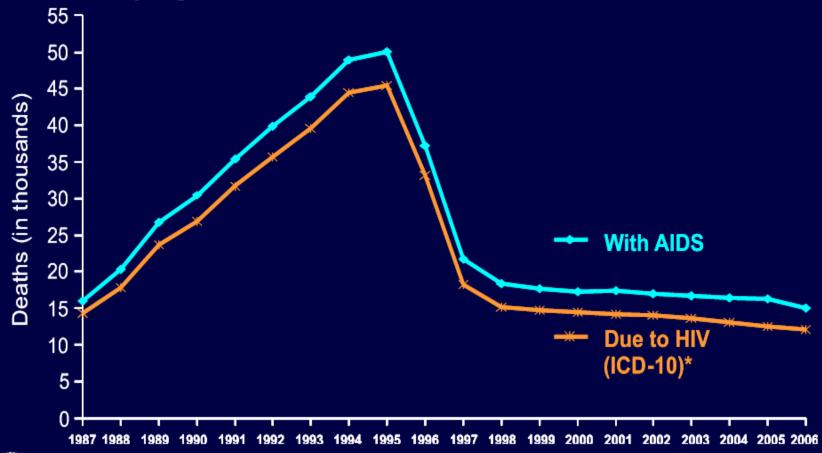
# Controlling the epidemic: Tertiary Prevention

Intervening to prevent the most severe outcomes

#### **Strategies include:**

- Low threshold treatment access
- Syringe exchange
- Naloxone

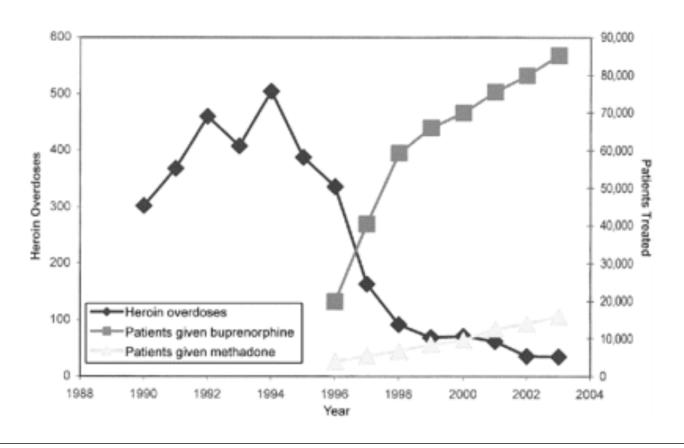
Comparison of Mortality Data from AIDS Case Reports and Death Certificates in Which HIV Disease Was Selected as the Underlying Cause of Death, United States, 1987–2006







# Buprenorphine Use and Heroin Deaths Trends in France, 1988-2004



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

## Summary

 The U.S. is in the midst of a severe epidemic of opioid addiction and overdose deaths, which worsened during Covid.

- 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