ADDICTION POLICY FORUM

American College of Emergency Physicians®
ADVANCING EMERGENCY CARE

E·QUAL | EMERGENCY QUALITY NETWORK

Opioid Initiative Wave I

History & Pharmacology

Presenter

Jeanmarie Perrone, MD, FACMT

The Evolving Opioid Epidemic: History and Pharmacology

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What is The Epidemic?

Prescription Drugs

/

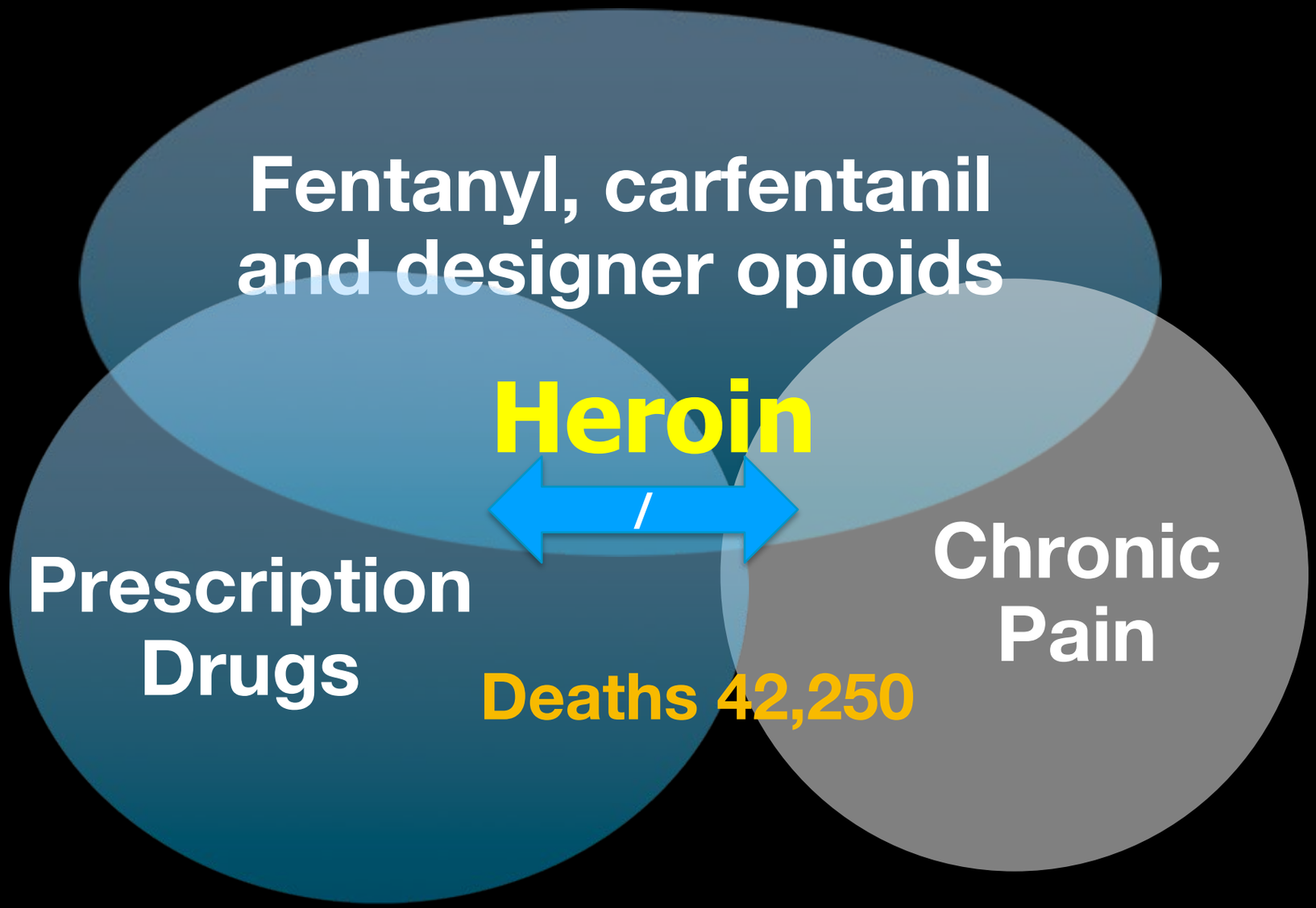
Deaths (27,000)
Addiction
534 billion dollars

Chronic Pain

100 million

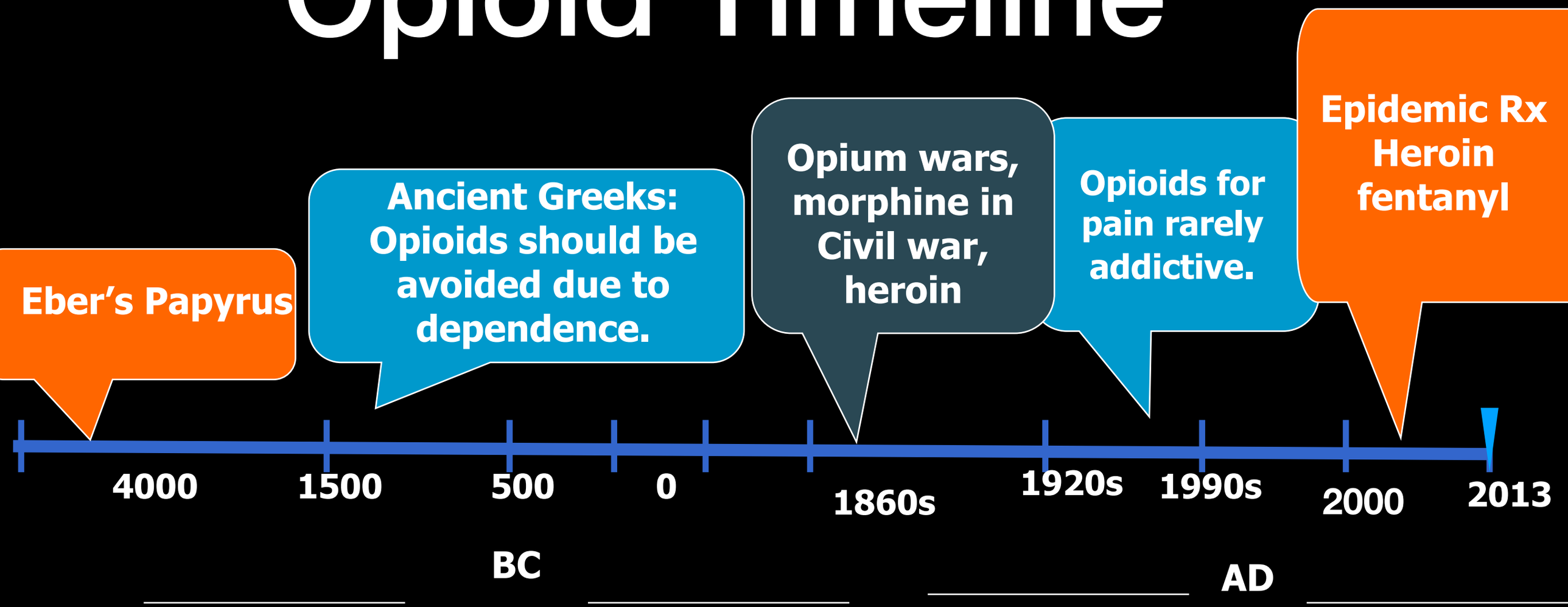
CDC Grand Rounds: January 2012

The Epidemic Now



CDC 2016

Opioid Timeline



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 patients[1] 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.

JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug
Surveillance Program
Waltham, MA 02154 Boston University Medical Center

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.

Video on Webinar Recording

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

A 1980 Letter on the Risk of Opioid Addiction

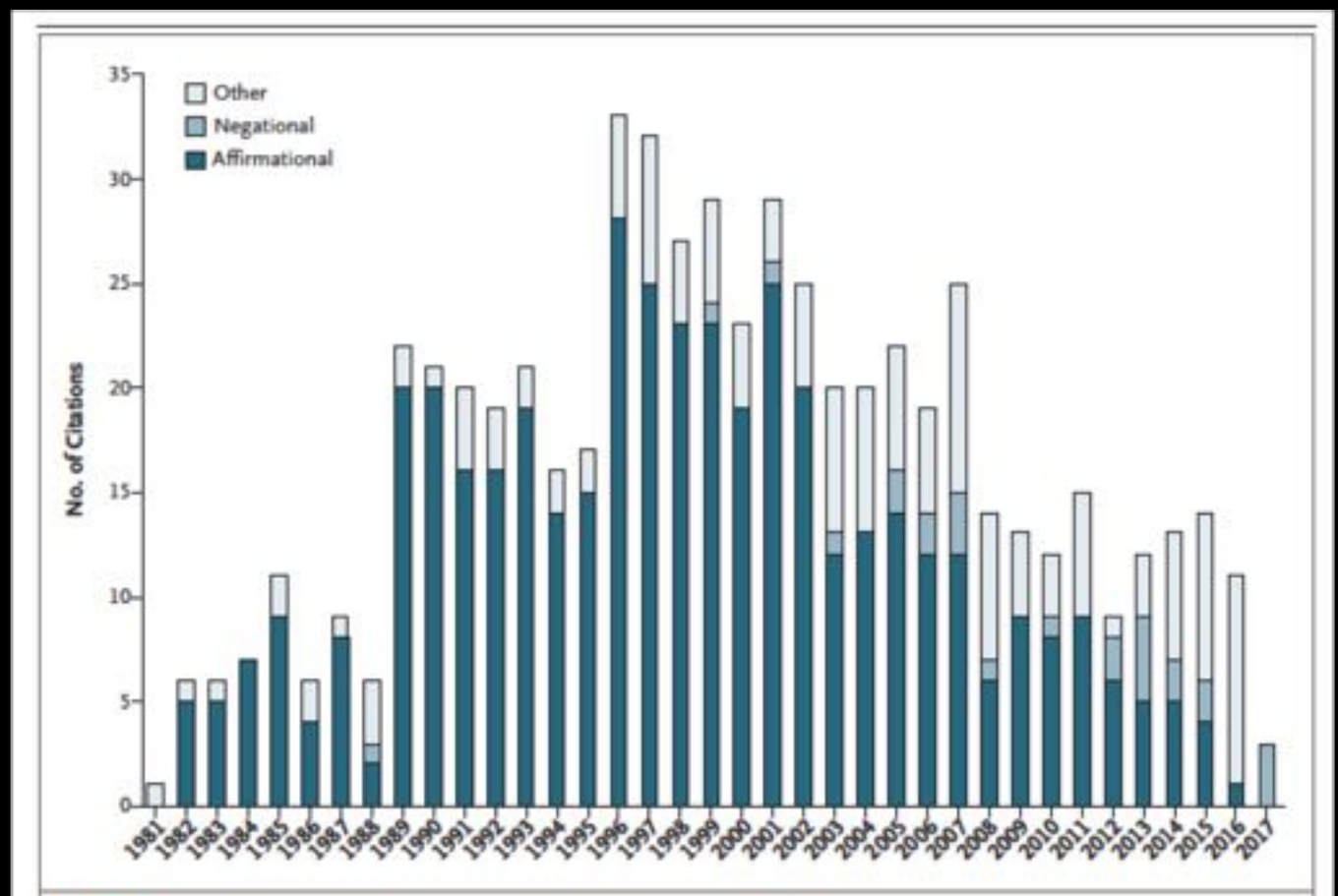


Figure 1. Number and Type of Citations of the 1980 Letter, According to Year.

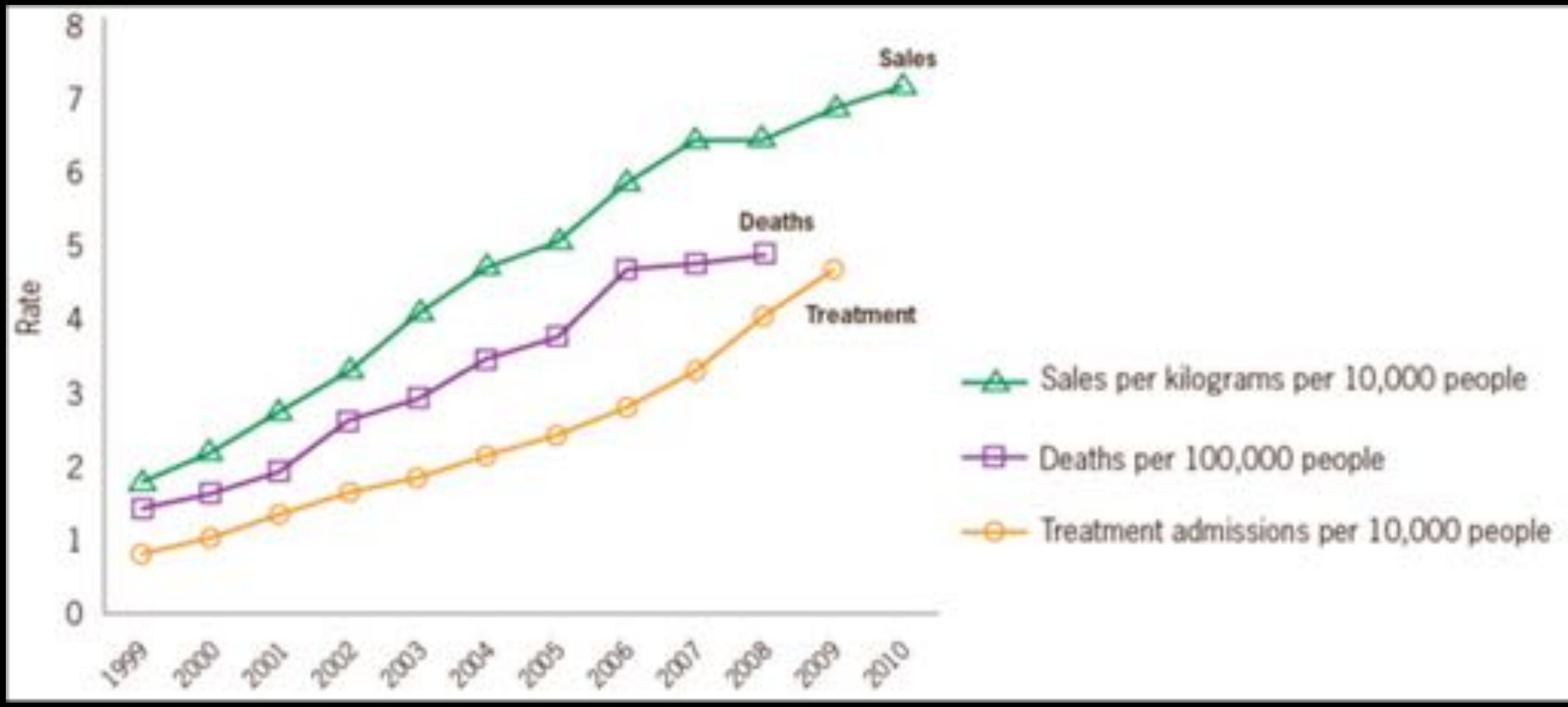
Leung, Juurlink NEJM 2017; 376:2194-2195 June 1, 2017

Factor 1

Prescribing increased as physicians were convinced
addiction risk low
Nearly 100% develop tolerance
5-26% of patient on chronic opioid therapy

Boscarino JA. Addiction 2010;105:1776-1782

Opioid sales quadrupled 1999-2010



Paulozzi L. MMWR. Nov 2011

Factor 2: Pain scores

VIEWPOINT

JAMA®
The Journal of the American Medical Association

Patient Satisfaction, Prescription Drug Abuse, and Potential Unintended Consequences

Aleksandra Zgierska, MD, PhD
Michael Miller, MD
David Rabago, MD

PATIENT-CENTERED CARE CAN IMPROVE TREATMENT outcomes, and its implementation has become the focus of national and local efforts to optimize health and health care delivery. Patients' satisfaction with care is one of the pillars of patient-centered care.[1] As such, results from patient satisfaction surveys (ie, patient experience of care measures) can be a driving force behind changes in health care delivery—with institutions and individual clinicians hoping for and actively seeking optimal survey scores. Although such initiatives generally promote improvements in practice that are responsive to patients' expressed needs, they may paradoxically promote prescribing of opioids and other addictive medications.

haviors. Medical quality committees and even licensure boards can determine that care is substandard if clinicians exclude these components. Before prescribing opioids, clinicians may be expected to recommend nonopioid interventions and refer patients to consultants even if what the patient wants is an opioid prescription. Combined with overall poor treatment outcomes in chronic pain and difficulties reported by most clinicians regarding issues surrounding prescription drug abuse, it is not surprising that clinicians' satisfaction and comfort level with management of care for patients with opioid-treated chronic pain are low.[7] This general picture sets a stage for the following considerations.

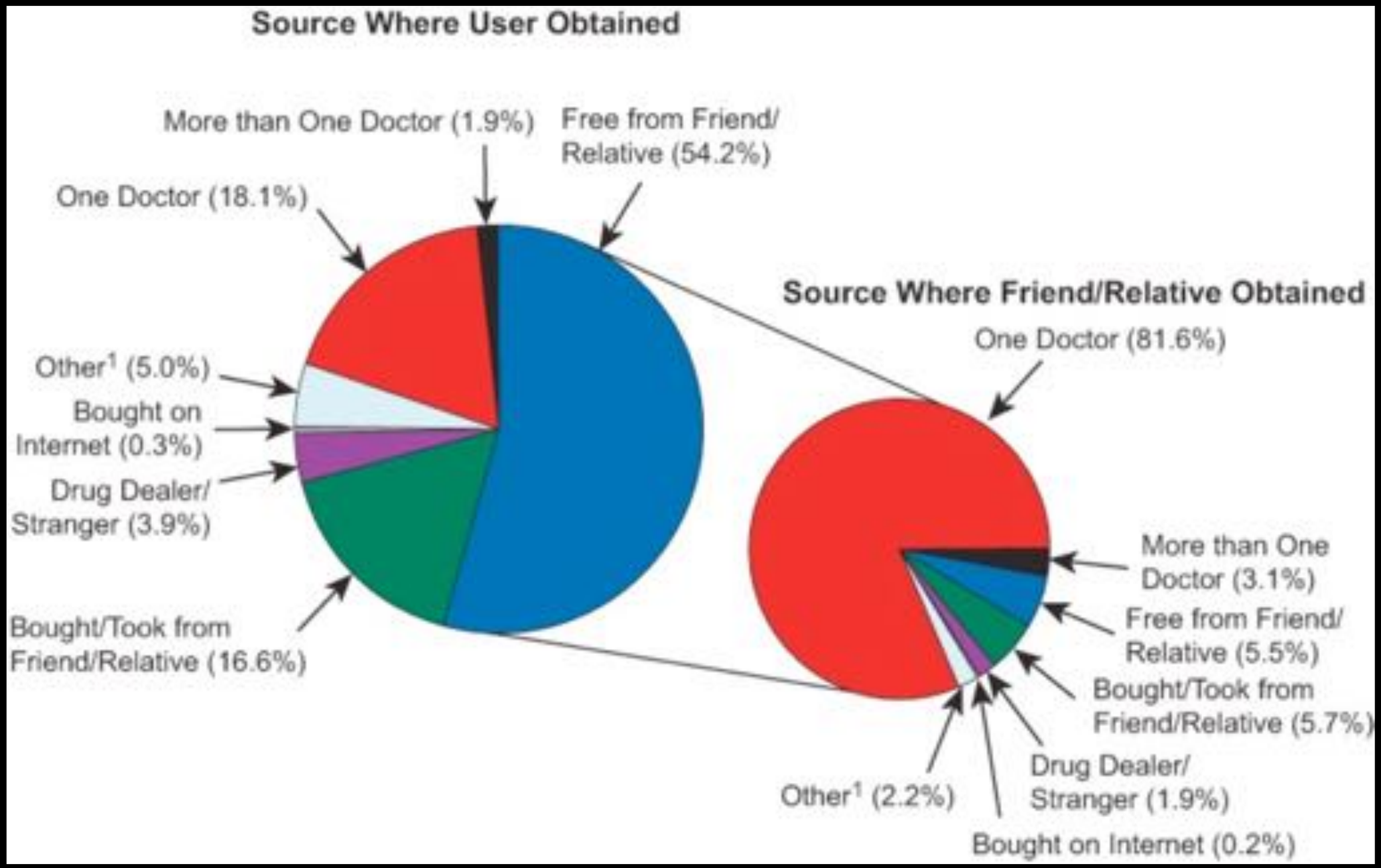
First, office visits in primary care are brief, and the pressure on clinicians to maximize "through-put" to meet patient volume benchmarks has intensified. In the context of these time pressures, how should a clinician respond to the patient's request for inappropriate opioid pain medication? Guidelines[3] suggest discussion of treatment alterna-

Zgierska A et al. JAMA 2012 4;307:1377-8

Factor 3
Escalating doses

As prescribing increased, patients were prescribed these drugs RTC for chronic pain; dependence and tolerance occurred so escalating doses became the norm…

More drugs for diversion



National Household Survey Drug Use Health SAMHSA

Factor 4

Once initiated, opioids are hard to stop…

Risk of Prolonged Opioid Use Among Opioid-Naïve Patients Following Common Hand Surgery Procedures

Shepard P. Johnson, MBBS,* Kevin C. Chung, MD, MS,† Lin Zhong, MD, MPH,†

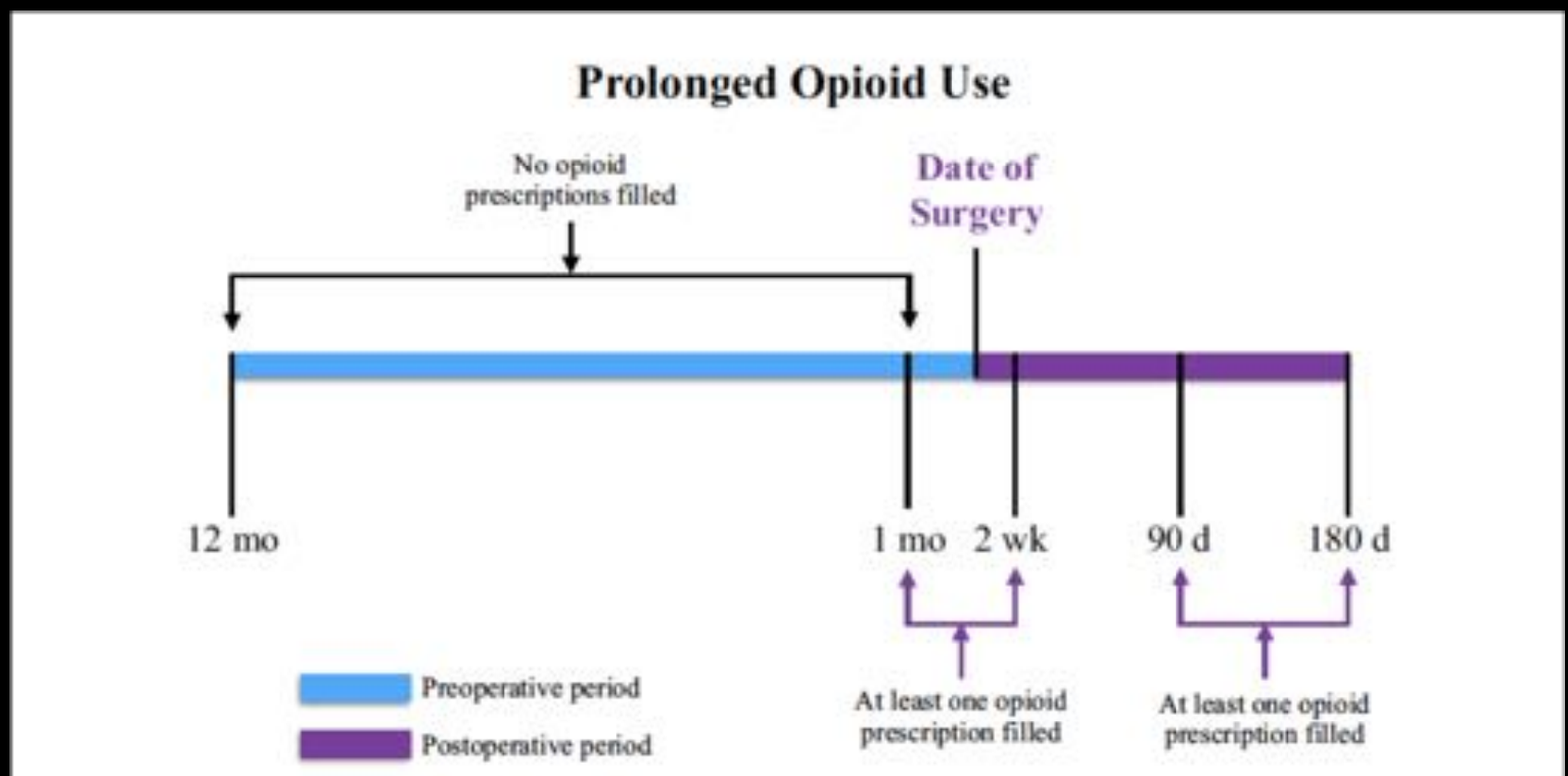


FIGURE 1: Prolonged opioid use was identified when patients filled one or more perioperative opioid prescriptions (ie, between 30 days before surgery and 2 weeks after surgery) and one or more opioid prescriptions between 90 and 180 days after surgery.

13% of opioid-naïve patients *continue* to fill opioid Rx 90-180 days

J Hand Surg Am. 2016;41:947e957.

The Washington Post
Democracy Dies in Darkness

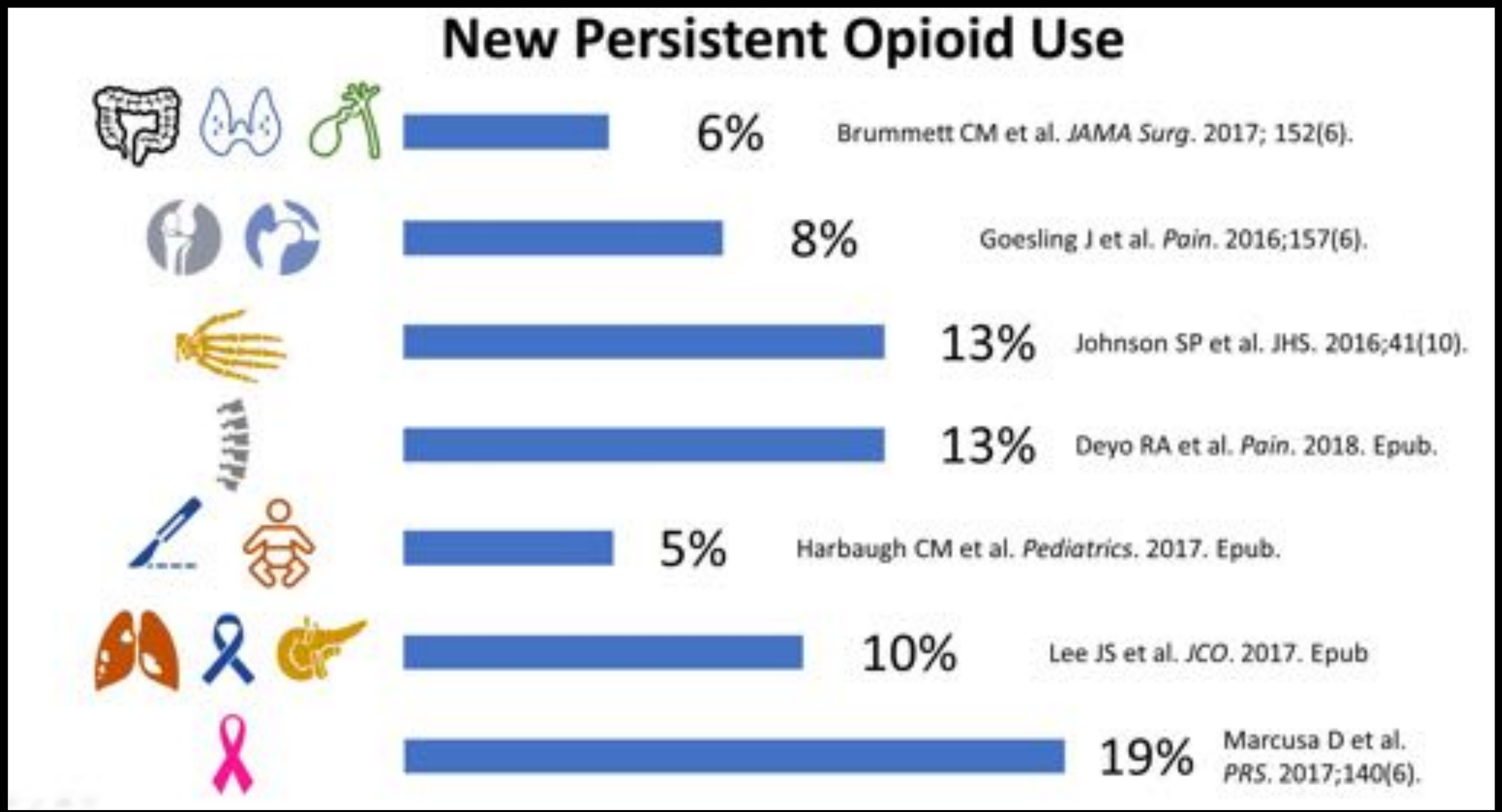
Health & Science

Doctors prescribed me pain meds but couldn't help me get off them

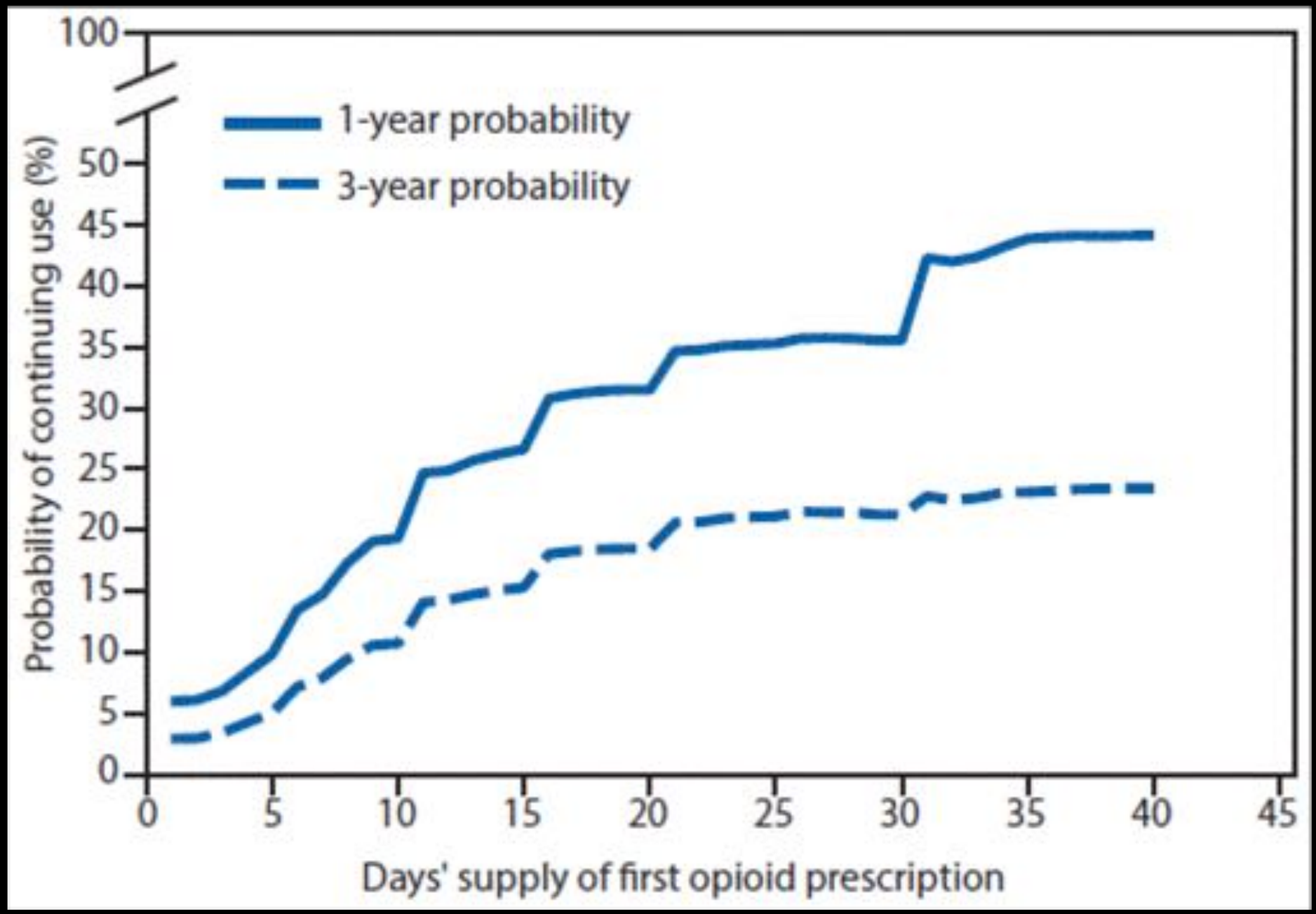
(Brett Ryder/Courtesy of Health Affairs)

By Travis N. Rieder January 22, 2017

Post op opioid prescribing



Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015



MMWR: 66;265–269. March 17, 2017

Annals of Internal Medicine ORIGINAL RESEARCH

Opioid Prescribing After Nonfatal Overdose and Association With Repeated Overdose

A Cohort Study

Marc R. Larochelle, MD, MPH; Jane M. Liebschutz, MD, MPH; Fang Zhang, PhD; Dennis Ross-Degnan, ScD; and J. Frank Wharam, MB, BCh, BAO, MPH

Over a median follow-up of 299 days, opioids were dispensed to 91% of patients after an overdose.

7% (n = 212) had a repeated opioid overdose.
17% cumulative incidence of repeated overdose

Ann Intern Med. 2016;164:1-9.

Kanin

"You should just feel a tiny prick, and then a lifetime of morphine addiction."

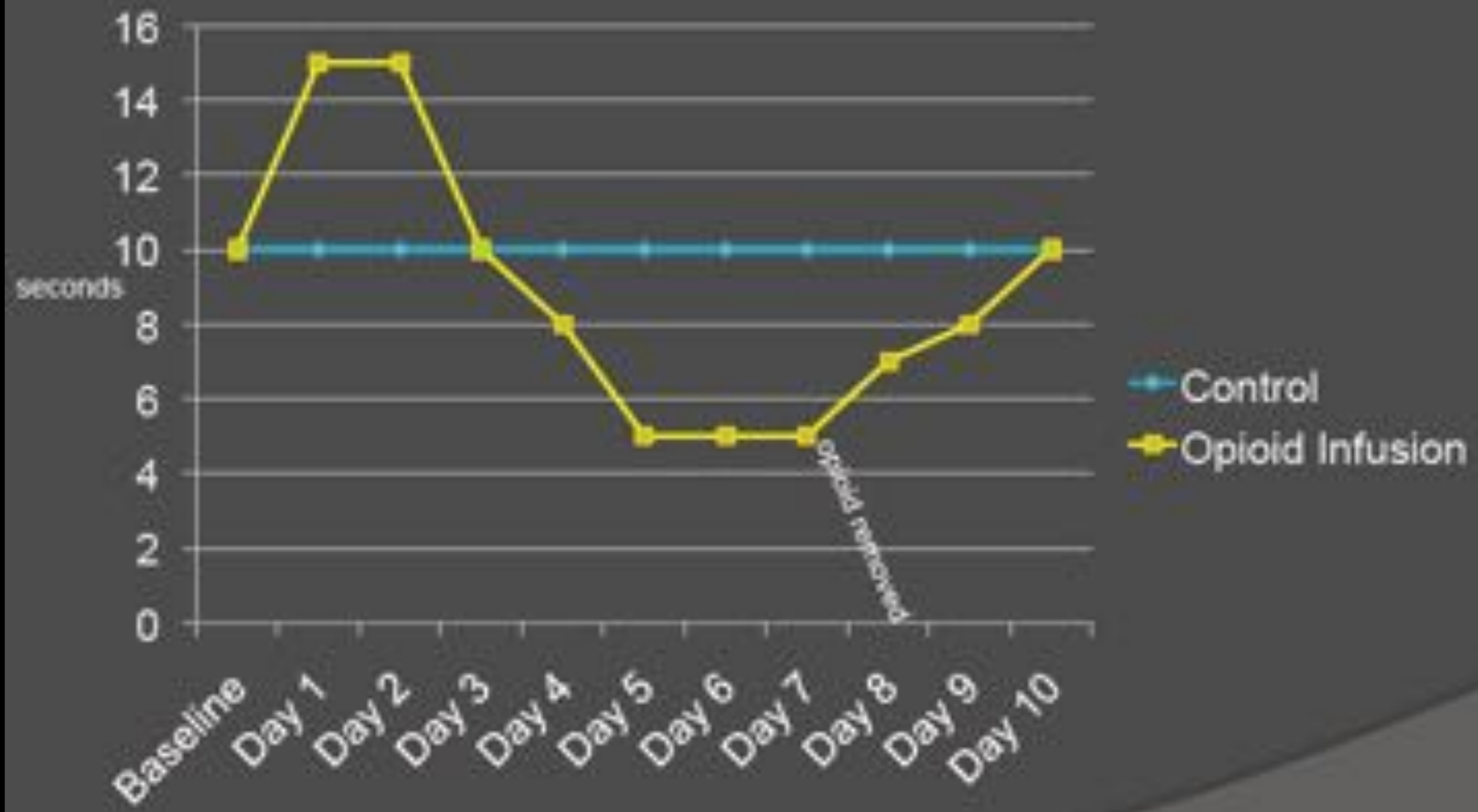
Opioid induced hyperalgesia

A heightened perception of pain in the absence of disease progression or opioid withdrawal.

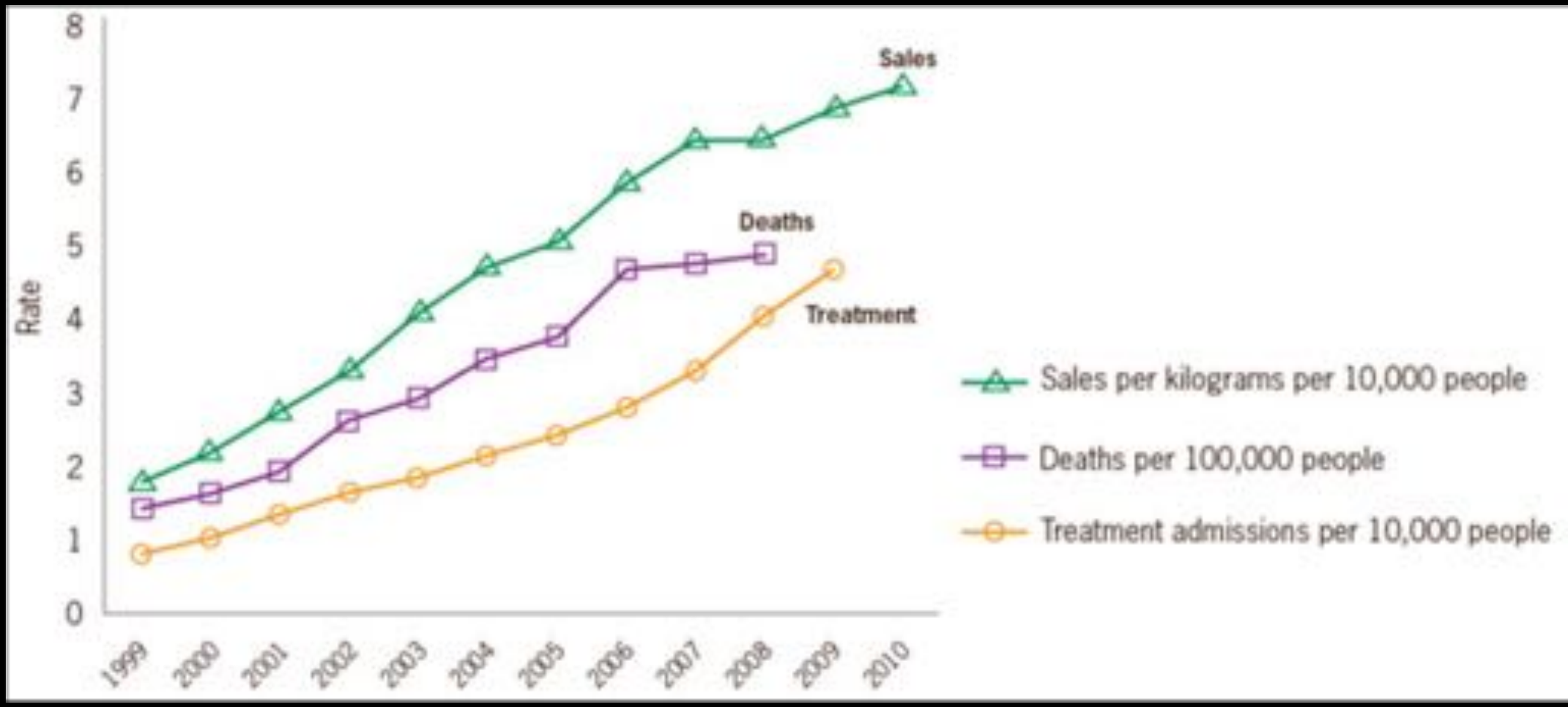
Hyperalgesia: Animal model

The paw withdrawal test

Paw Withdrawal Latency

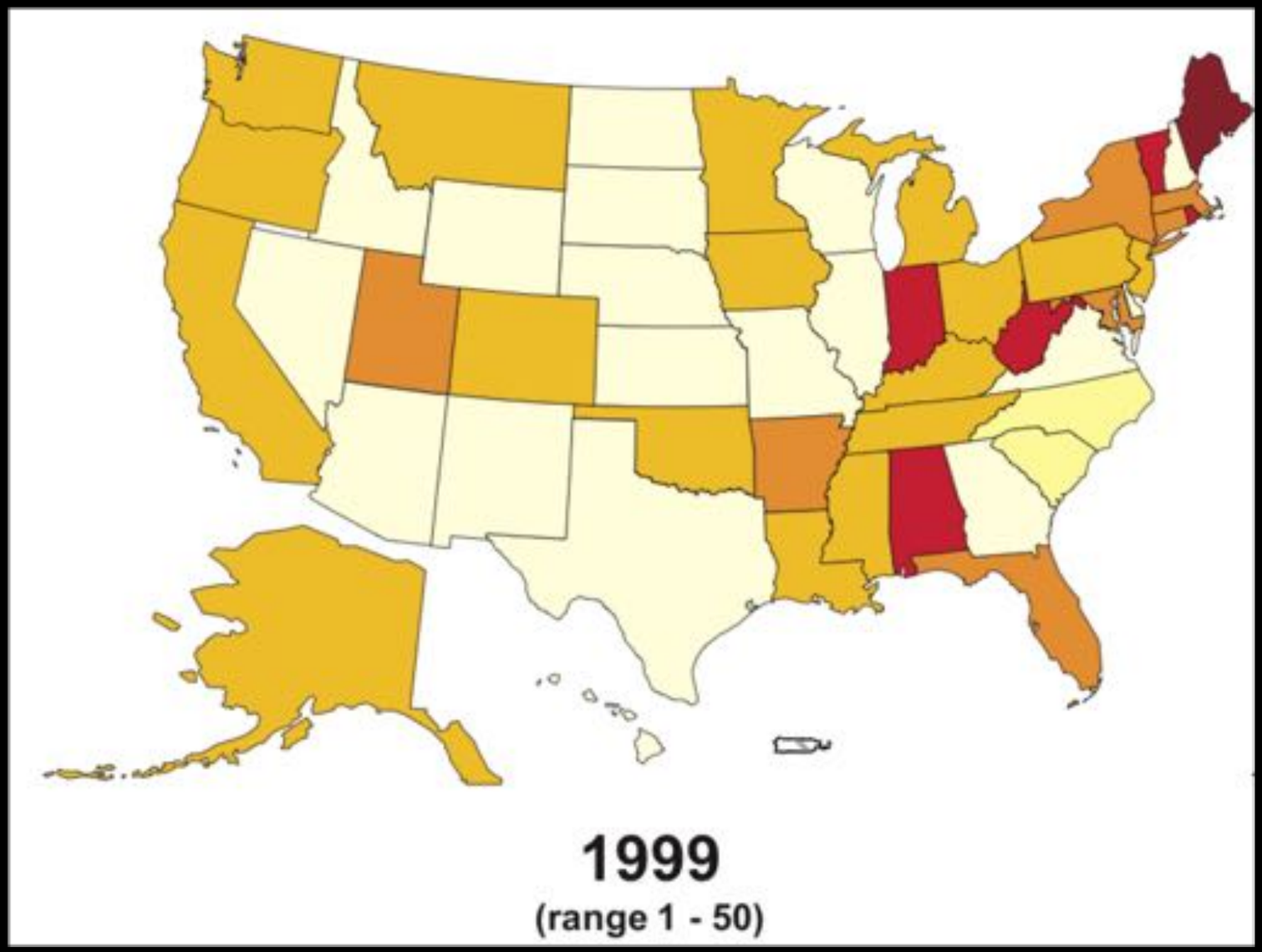


Opioid sales quadrupled 1999-2010



Paulozzi L. MMWR. Nov 2011

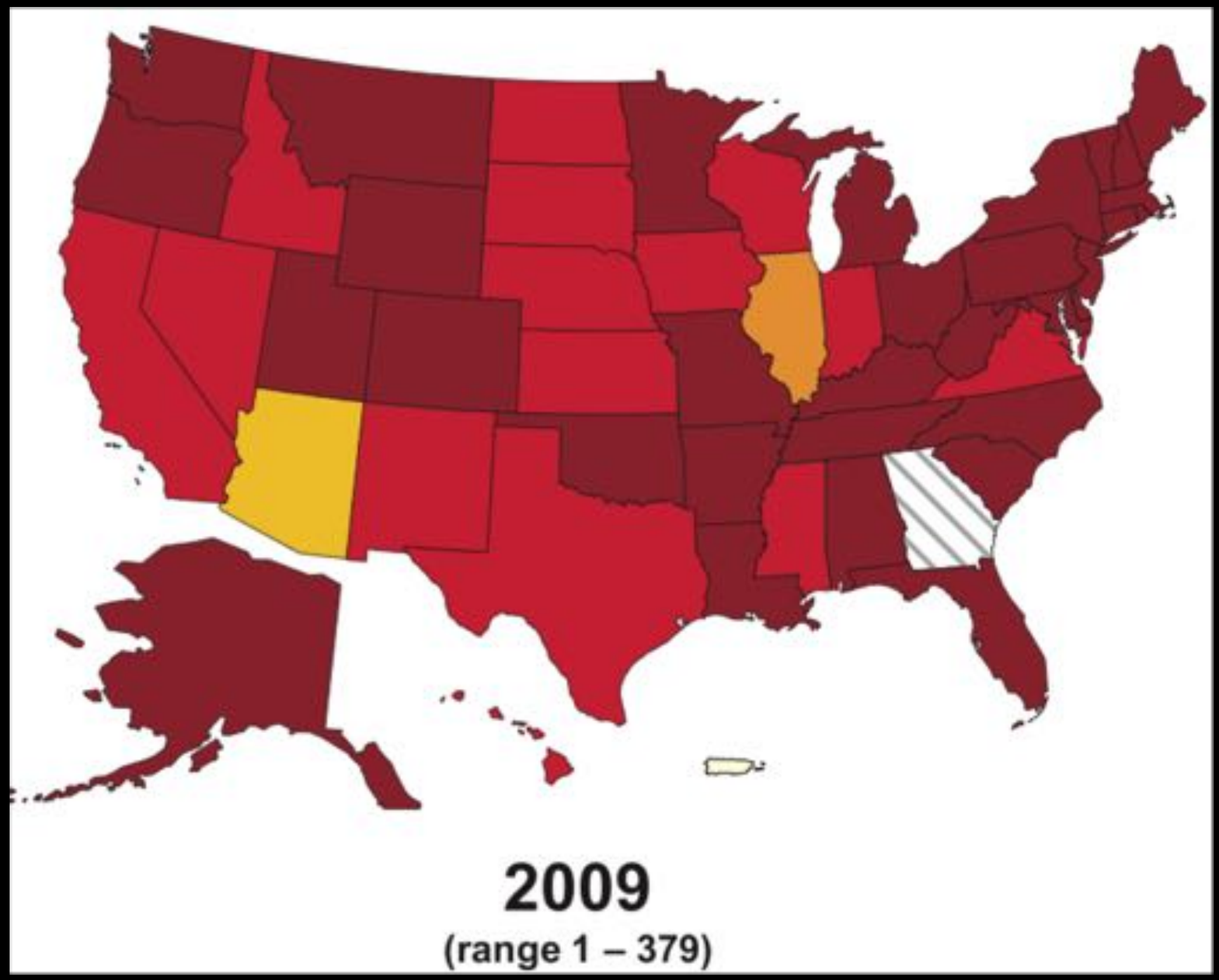
Primary non-heroin opiates/synthetics admission rates, by State (per 100,000 population aged 12 and over)



< 8	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.

Primary non-heroin opiates/synthetics admission rates, by State (per 100,000 population aged 12 and over)



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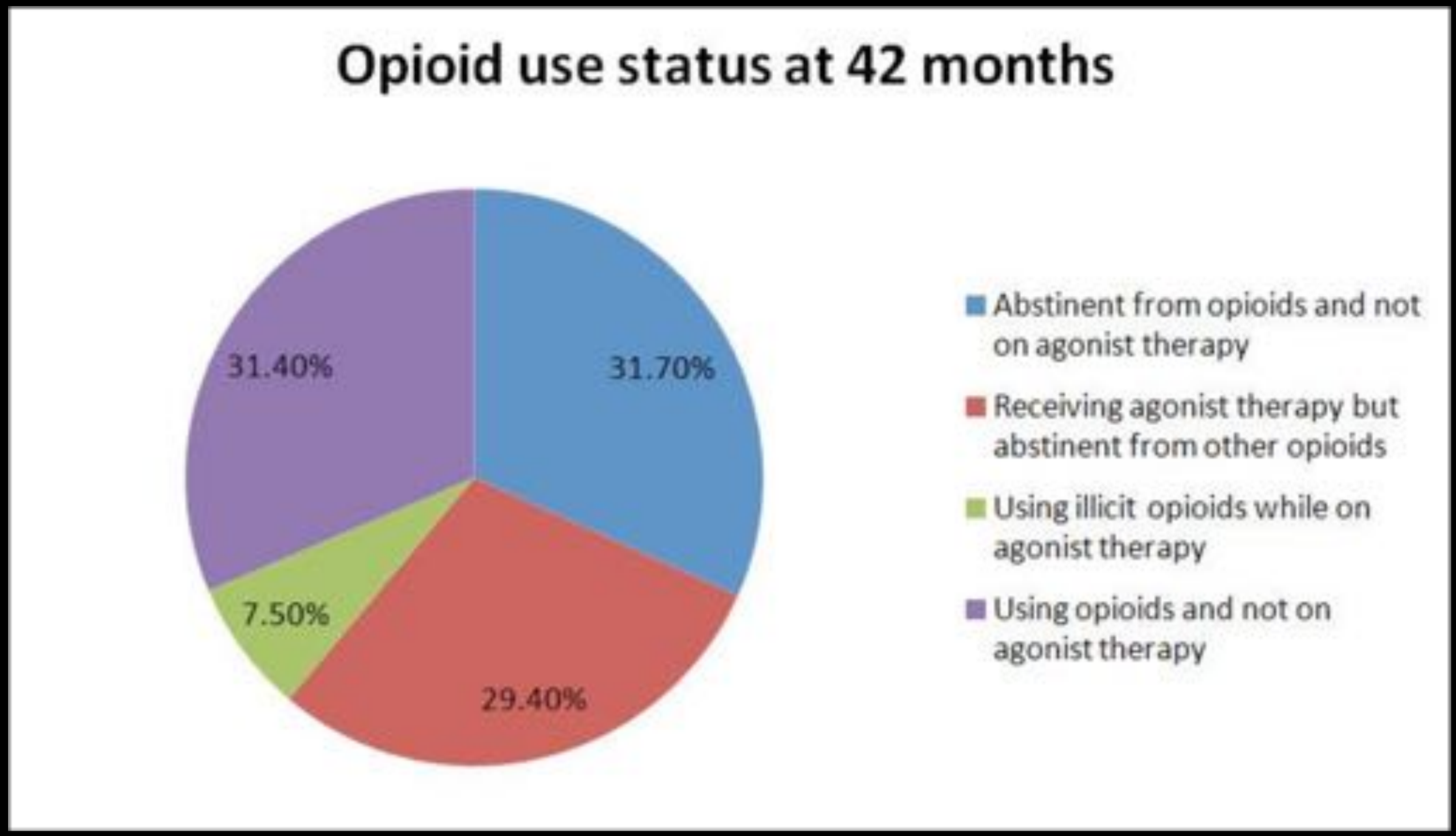
SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.

Treatment Success

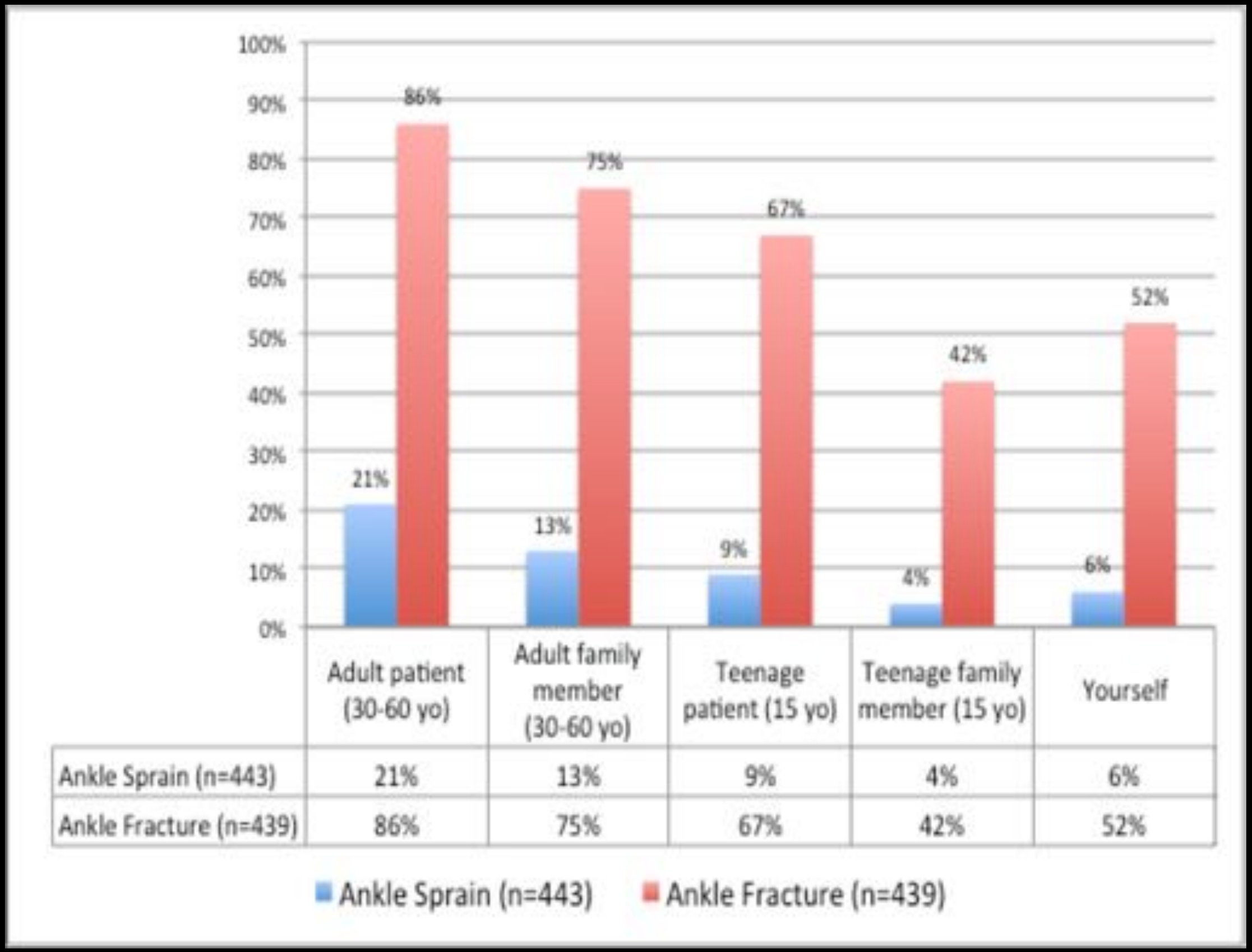


Weiss RD: Long-term outcomes from the National Drug Abuse Treatment Clinical Trials Network Prescription Opioid Addiction Treatment Study 2015. Drug Alcohol Depend, 150, 112-119.

Jeanmarie Perrone MD @JMPerrone... 6d

When considering analgesic Rx "Keep opioid naive patients opioid naive"

October 2015
JAMA Addressing the Opioid Epidemic
Lewis S. Nelson, MD, David N. Juurlink, MD, PhD; Jeanmarie Perrone, MD



	Adult patient (30-60 yo)	Adult family member (30-60 yo)	Teenage patient (15 yo)	Teenage family member (15 yo)	Yourself
Ankle Sprain (n=443)	21%	13%	9%	4%	6%
Ankle Fracture (n=439)	86%	75%	67%	42%	52%

Pomerleau A, Perrone J, Nelson L: West J E Med 2016; 17:791.

How do we scale back?

CDC Guidelines

How Do Physicians Adopt and Apply Opioid Prescription Guidelines in the Emergency Department? A Qualitative Study

Austin S. Kilaru, MD; Sarah M. Gadsden, BA; Jeanmarie Perrone, MD; Breah Paciotti, MPH; Frances K. Barg, PhD; Zachary F. Meisel, MD, MSc*

Kilaru, Perrone, Meisel: Ann Emerg Med 2014 64:482


SORE KNEE, HUH? HAVE YOU TRIED ICING IT?

NON Opioid interventions

Gabapentin
Topicals
NSAIDs
Capsaicin cream
Lidoderm patch
Trigger point injections
Haloperidol
IV lidocaine
US guided regional anesthesia
Cognitive therapy
Heating pads and massage
Ice, Elevation

What else can we do?

Oral preferable to IV

Treat patients with lower risk drugs

Hydrocodone better than oxy

Morphine preferable to hydromorphone

Engage patients and families in risk discussion

What is the oral opioid with the lowest risk of adverse effects?

Which opioid to Rx?

Most Prescribed Opioids 2013*

Total Dispensed Scripts

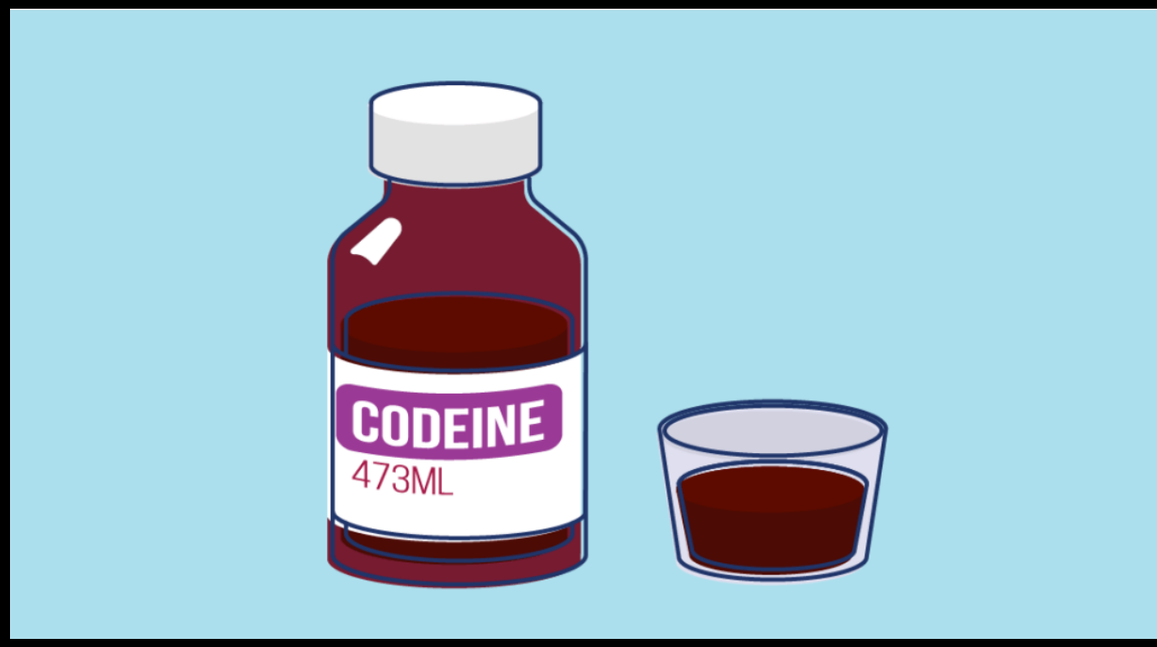
1. **Hydrocodone-combination** (Vicodin) - 127,859,000
2. **Oxycodone with acetaminophen** (generic Percocet) - 32,962,000
3. **Oxycodone HCL** (generic OxyContin) - 16,440,000
4. **Acetaminophen with codeine** - 11,225,000
5. **Morphine sulfate** - 9,658,000
6. **Fentanyl** - 6,468,000
7. **OxyContin** (brand name) - 5,659,000
8. **Methadone** - 3,860,000
9. **Hydromorphone HCL** (generic Dilaudid) - 3,587,000
10. **Oxymorphone HCL, extended release** (Opana ER) - 756,000

*Source: IMS Health

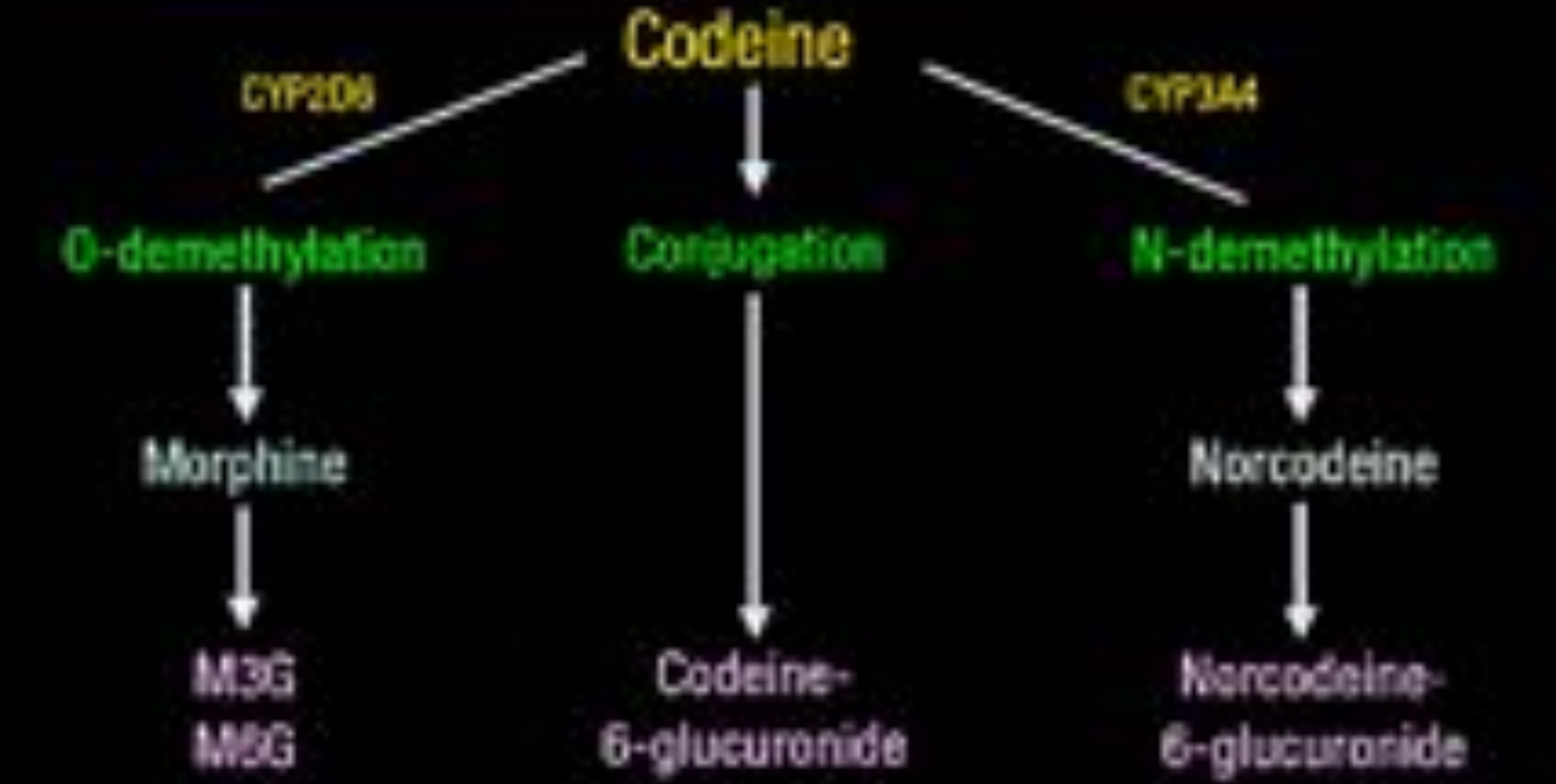
IMS Health 2013

Codeine

- codeine available in 15, 30 and 60mg with APAP and as syrup
- codeine OTC in AZ and some other states
- CYP 2D6 metabolism recognized in children undergoing tonsillectomy



Codeine: Metabolic Pathways



Tramadol is unpredictable

- Tramadol is a codeine derivative- CYP 2D6
- SNRI mechanism leads to increased risk of toxicity
- Small risk of hypoglycemia

Morphine sulfate

- some dysphoria w euphoria
- Can be difficult to fill Rx in some regions
- Rx liquid for lowest dosing

oxycodone/APAP vs hydrocodone/APAP?

Morphine Mg Equivalent

- codeine 15mg
- hydrocodone 1 x 5mg
- tramadol 0.1 x50mg
- morphine sulfate 15mg

Calculating morphine milligram equivalents (MME)

OPIOID (doses in mg/day except where noted)	**CONVERSION FACTOR**
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1-20 mg/day	4
21-40 mg/day	8
41-60 mg/day	10
≥ 61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.

PAIN® 154 (2013) 2639–2648

Factors influencing the selection of hydrocodone and oxycodone as primary opioids in substance abusers seeking treatment in the United States

Theodore J. Cicero[a,*], Matthew S. Ellis[a], Hilary L. Surratt[b], Steven P. Kurtz[b]

Self reported drug use in 3500 patients admitted to 160 treatment centers + qualitative interviews.

PAIN® 154 (2013) 2639–2648

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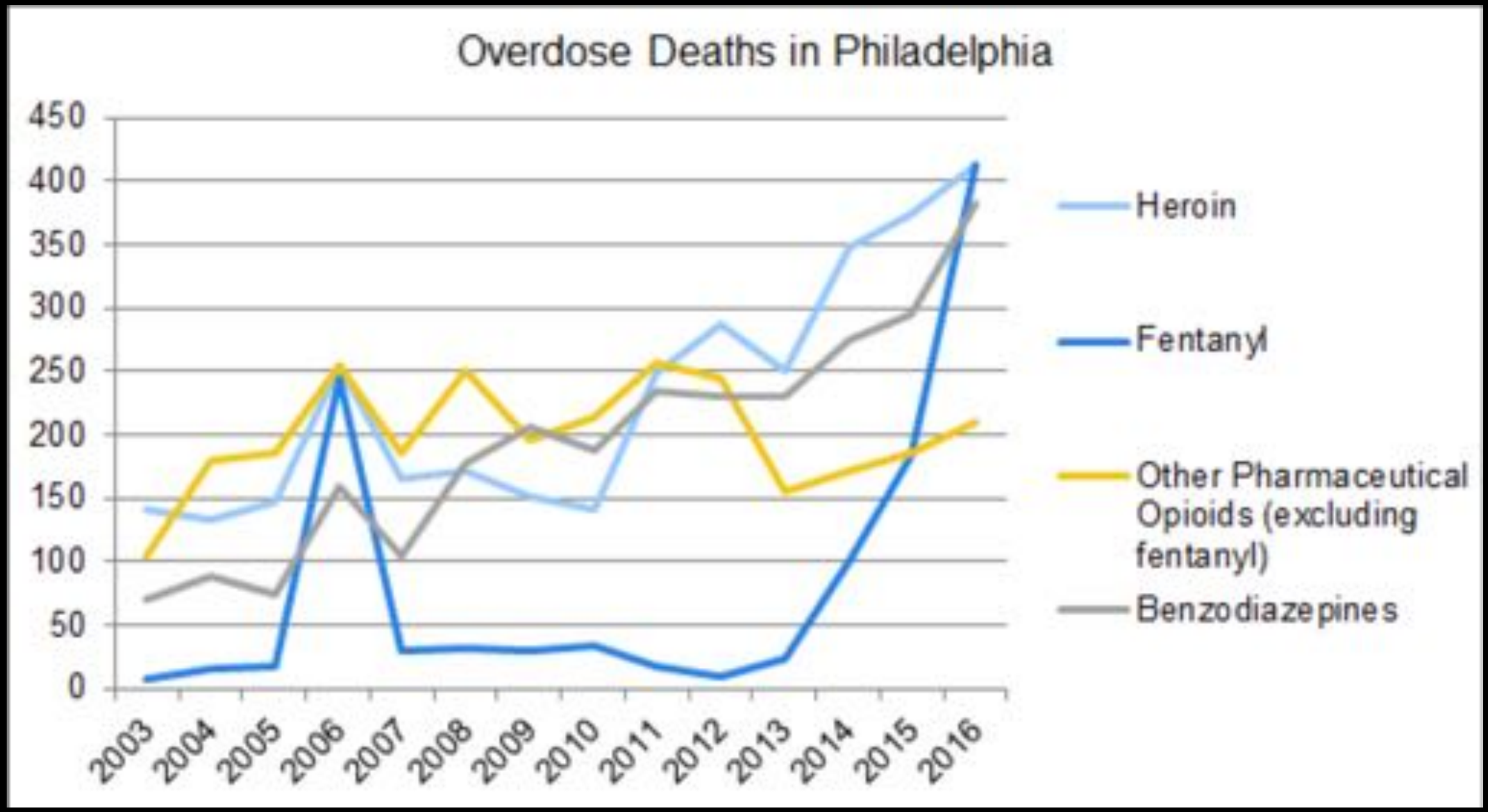
Theodore J. Cicero[a,*], Matthew S. Ellis[a], Hilary L. Surratt[b], Steven P. Kurtz[b]

Oxycodone was the choice of significantly more users (44.7%) than hydrocodone (29.4%)

Reasons cited “quality of the high”
was reported to be much better
54% vs 20% (oxy vs hydro)

The New York Times | ARTS

Prince's Addiction and an Intervention Too Late



Philadelphia Dept. of Public Health, Medical Examiner's Office

Comparing the size of lethal doses of heroin, fentanyl, and carfentanil. The vials here contain an artificial sweetener for illustration. (New Hampshire State Police Forensic Laboratory)

Boston Globe Nov 1, 2017

10 percent revived by Narcan in Mass. died within year, study says

Wiener: ACEP Research Forum 2017

Take home naloxone?

Walley, et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. BMJ. 2013;346:f174.

JAMA October 12, 2017

“Warm handoff”
Treatment access from the ED

D’Onofrio: Emergency Department-Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence: A Randomized Clinical Trial. JAMA 2015

Goals

Be good stewards of opioid use in the future.

Explain risks of opioids with every prescription

Use lowest potency drugs for shortest duration.

Don’t swing the pendulum too far…

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