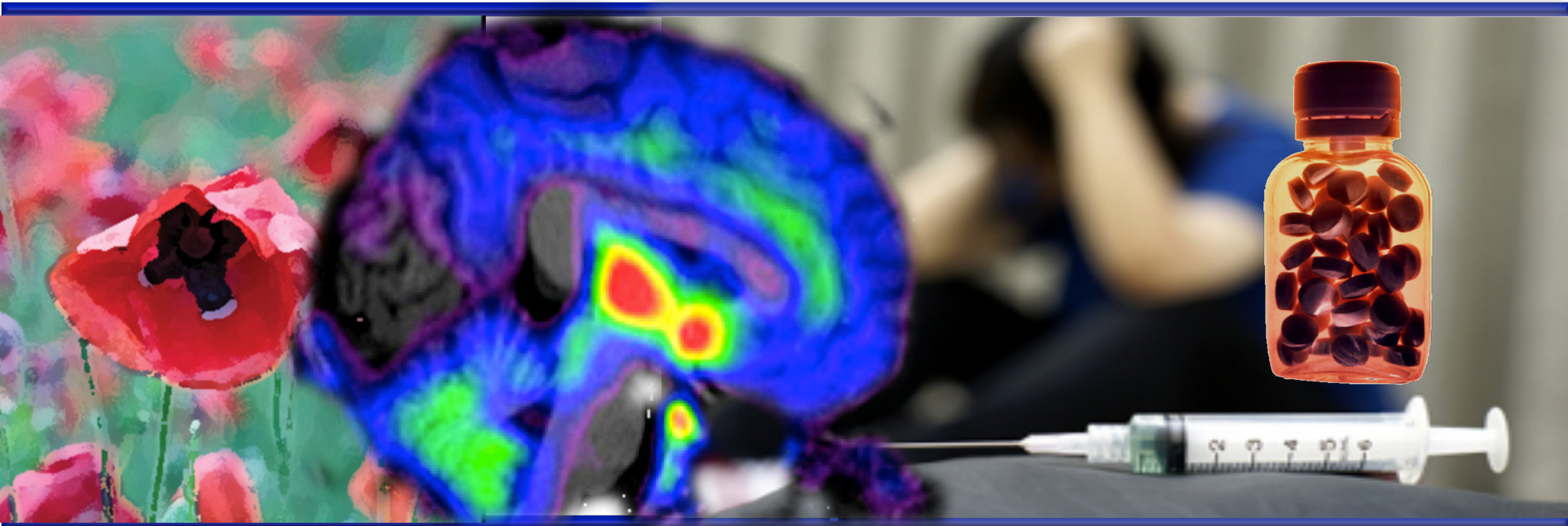


Science = Solutions: Improving the Treatment of Opioid Use Disorders



Wilson M. Compton, M.D., M.P.E.
Deputy Director
National Institute on Drug Abuse



Key Drug Abuse Public Health Crisis

The NEW ENGLAND JOURNAL *of* MEDICINE

REVIEW ARTICLE

Relationship between Nonmedical Prescription-Opioid Use and Heroin use

Wilson M. Compton, M.D., M.P.E., Christopher M. Jones, Pharm.D, M.P.H.

and Grant T. Baldwin, Ph.D., M.P.H.

January 14, 2016

Opioid Crisis: *Prescription Opioids AND Heroin*

JAMA

The Journal of the
American Medical Association

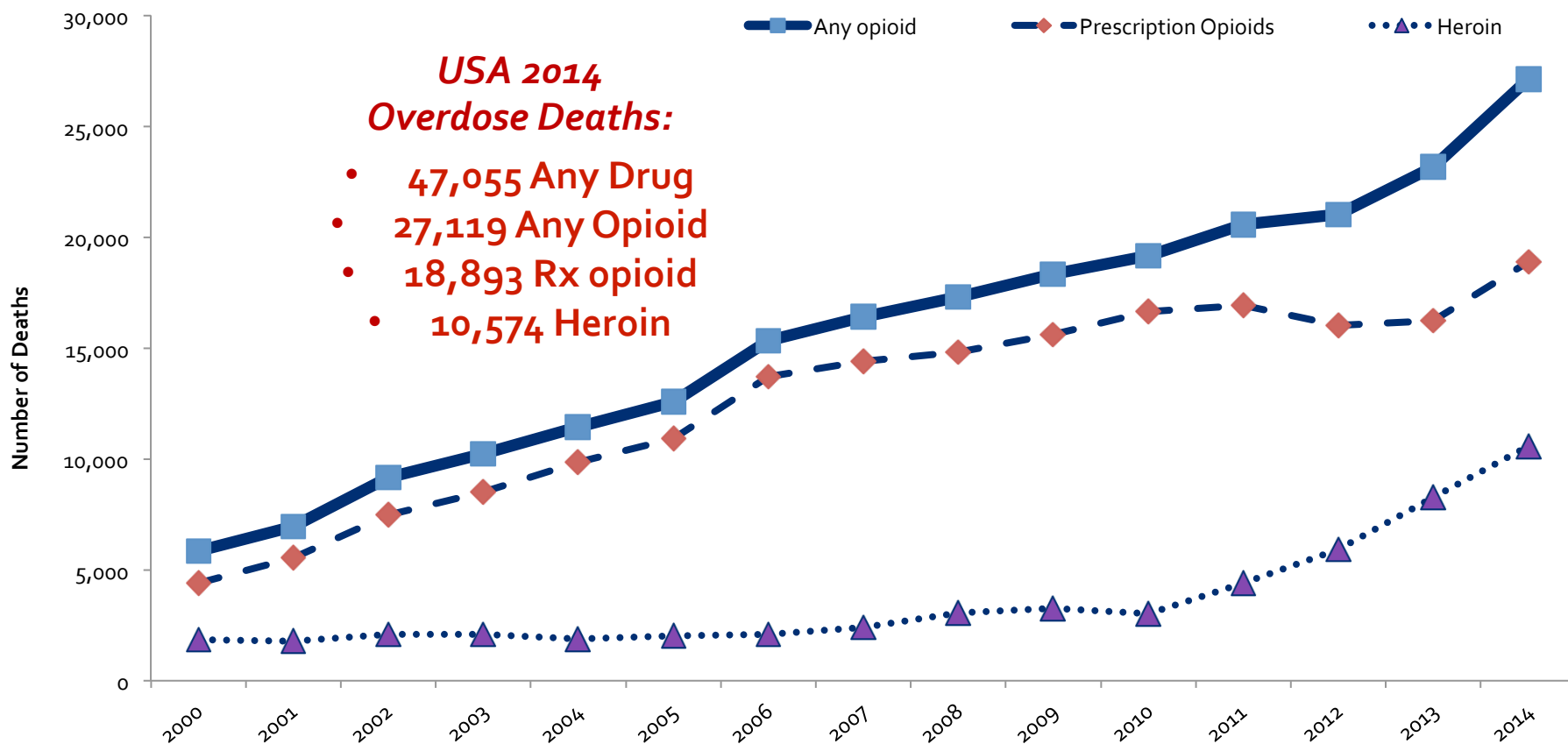
Original Investigation

Nonmedical Prescription Opioid Use and Use Disorders Among Adults Aged 18 Through 64 Years in the United States, 2003-2013

Beth Han, MD, PhD; Wilson M. Compton, MD, MPE; Christopher M. Jones, PharmD, MPH; Rong Cai, MS
October 13, 2015, Vol 314, No. 14

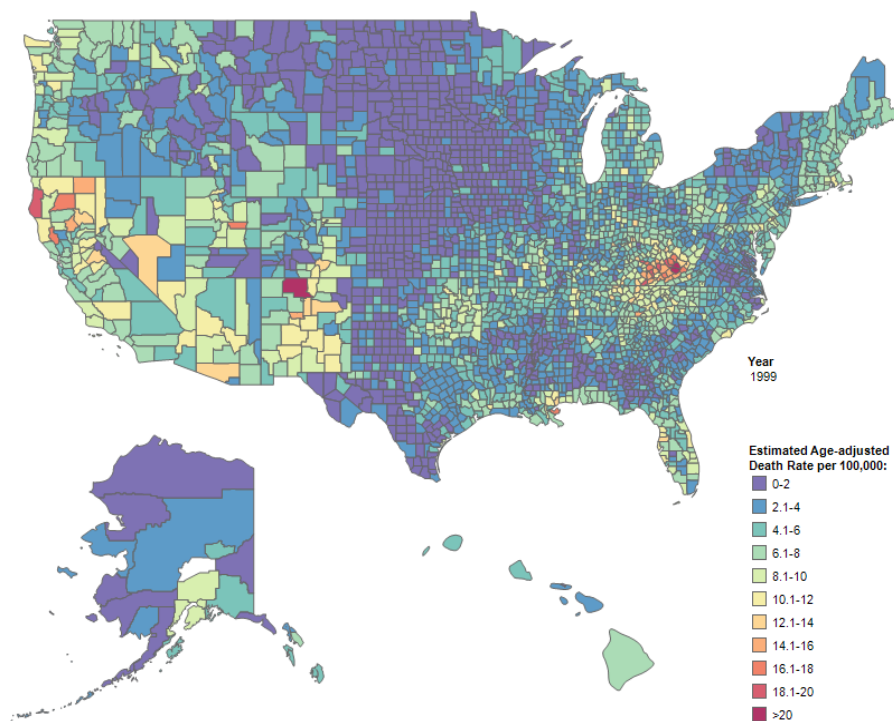
Science = Solutions

Marked *Increases in Prescription Opioid and Heroin Overdose Deaths* in the USA 2000 to 2014

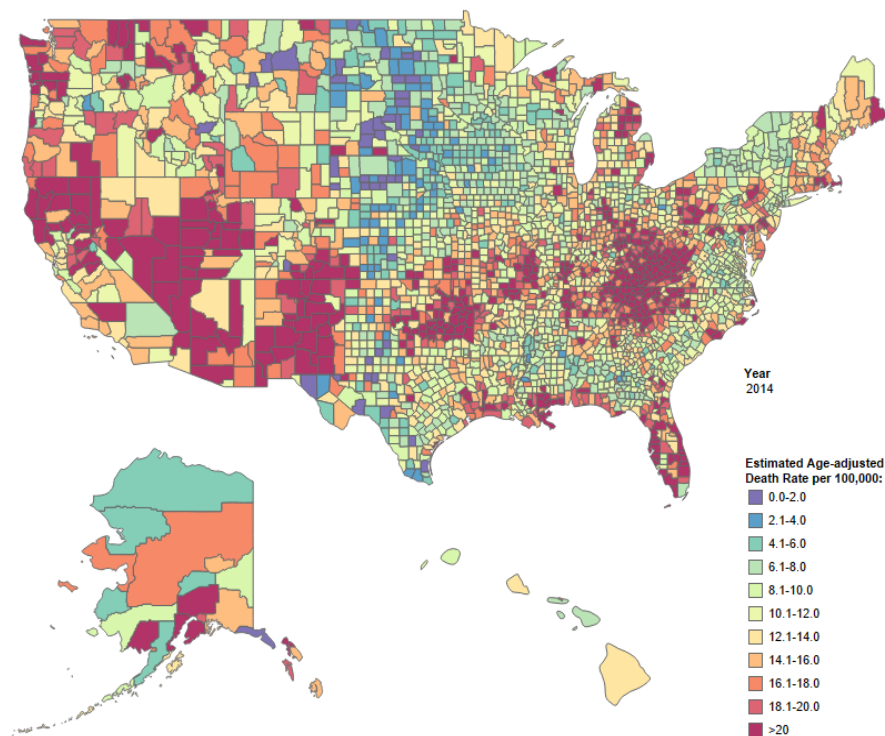


Source: CDC, NVSS 2000-2014

Marked *Geographic and Temporal Variation in Mortality* : *Estimated Age-adjusted Death Rates for Drug Poisoning by County*



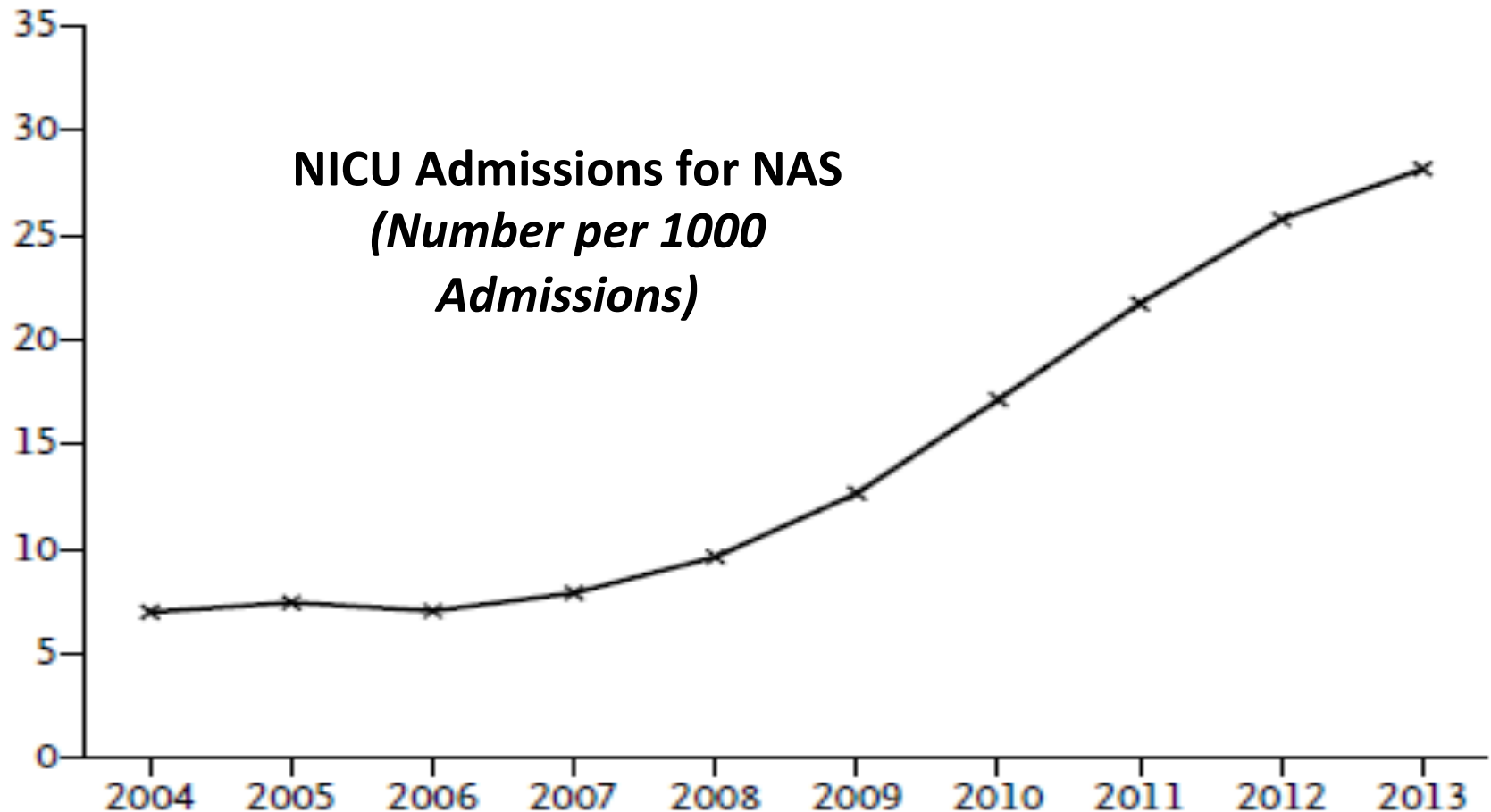
1999



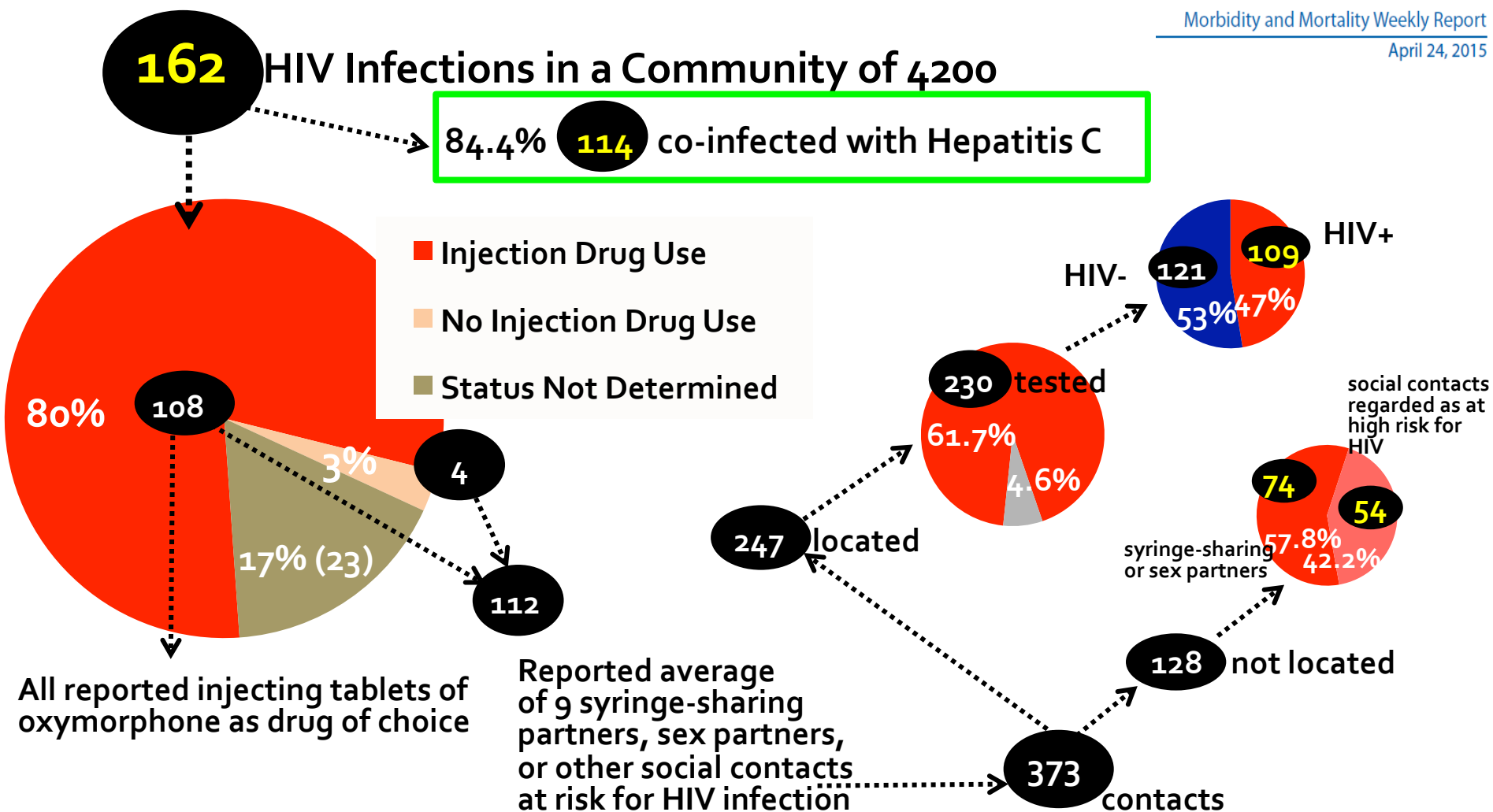
2014

Designed by L. Rossen, B. Bastian & Y. Chong. SOURCE: CDC/NCHS, National Vital Statistics System; Tom Frieden Presentation at the Opioid Summit, Atlanta, April 2016

Increasing *Neonatal Abstinence Syndrome*



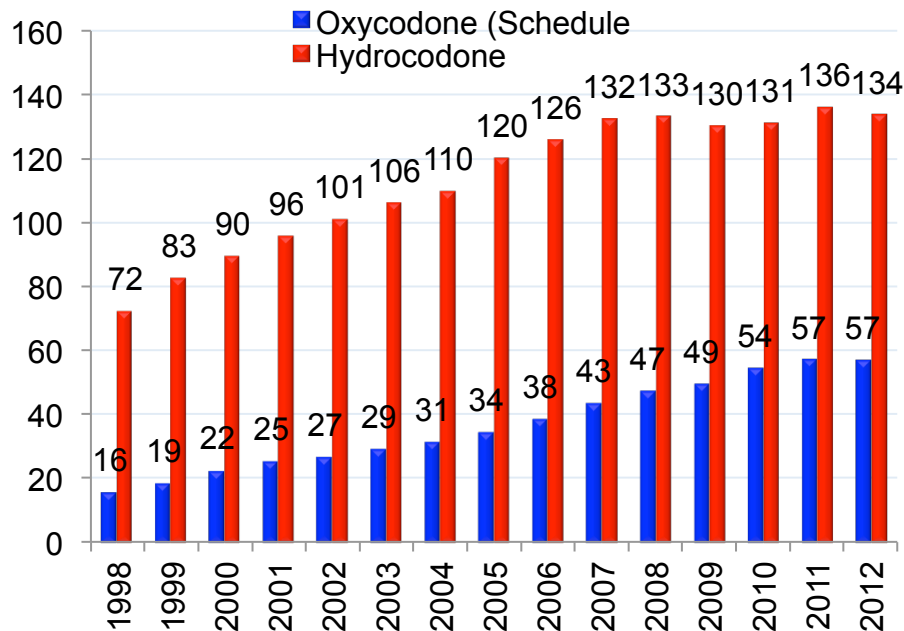
Outbreak of **HIV** Linked to IDU of Oxymorphone in Indiana, 2015



High Levels of Opioid Prescriptions have Facilitated Diversion and Contributed to Overdose Deaths

Opioid Prescriptions have nearly Tripled since 1999

Oxycodone & Hydrocodone Prescriptions



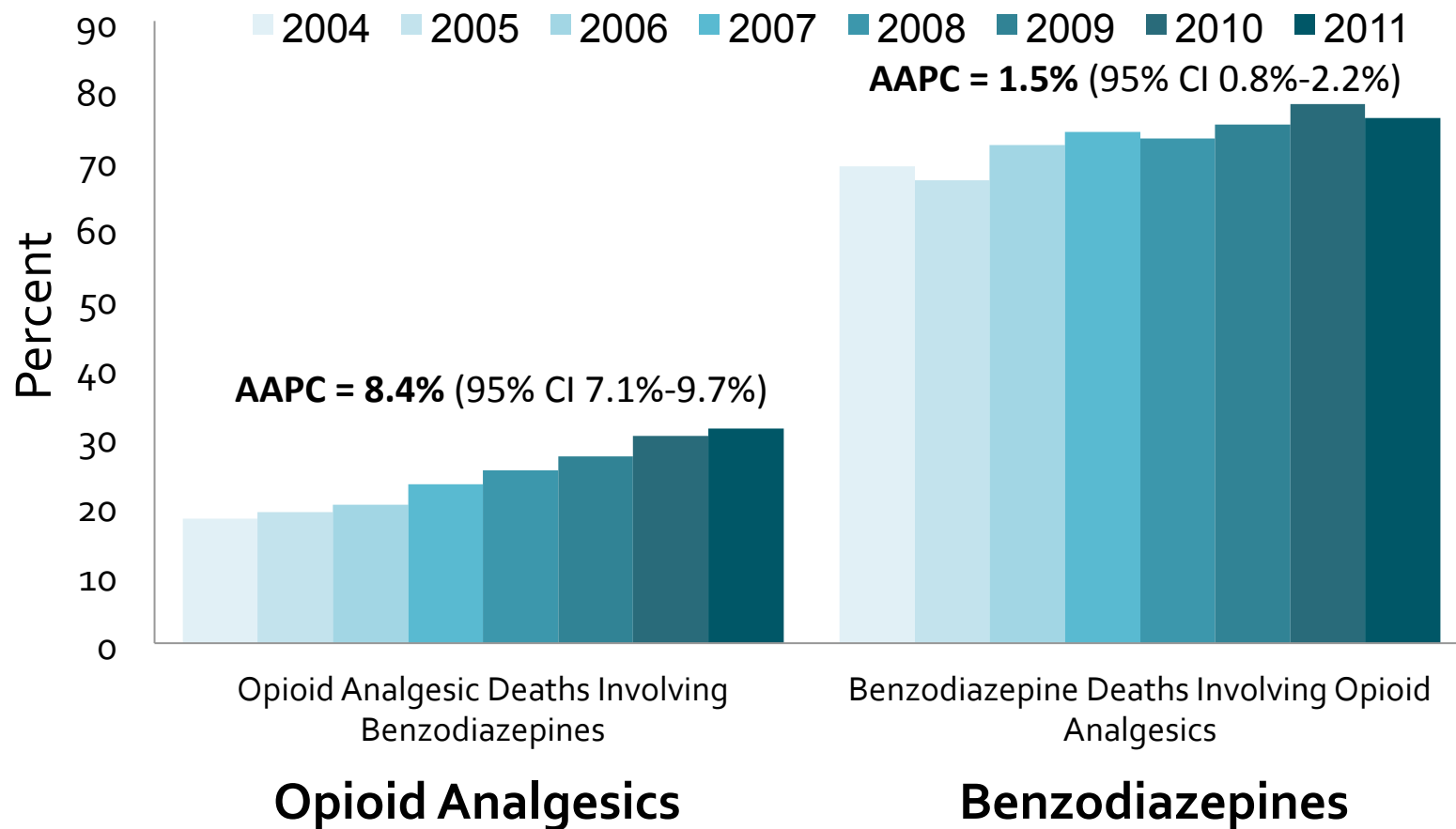
Total Rx Opioid Tablets Dispensed in Retail Pharmacies in the USA:

- **2013** **15,972,304,698**
- **2014** **15,606,882,755**

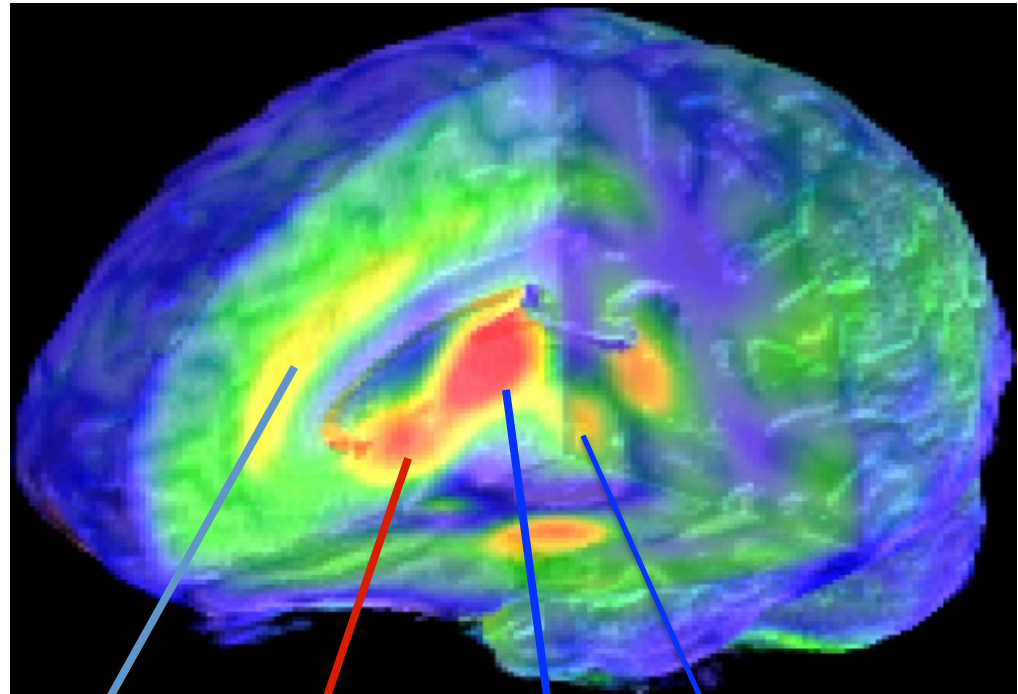
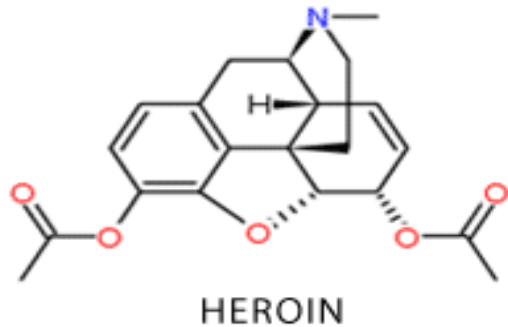
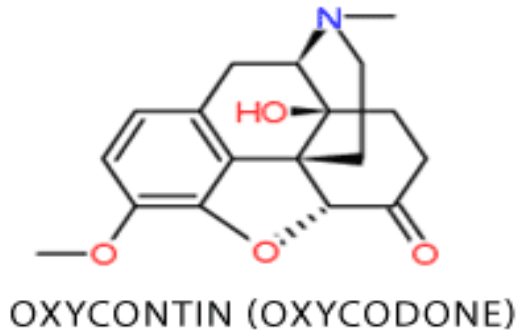
Source: Jones CM, et al. *JAMA Internal Medicine* 2016: doi: 10.1001/jamainternmed.2015.7799

Overlap of *Benzodiazepines and Opioids*

Opioid Analgesic ED Visits and OD Deaths Involving Benzodiazepines & Benzodiazepine ED Visits and OD Deaths Involving Opioids



Similarities of Illicit & Prescription *Opioids*



ACC
(pain)

Accumbens
(reward)

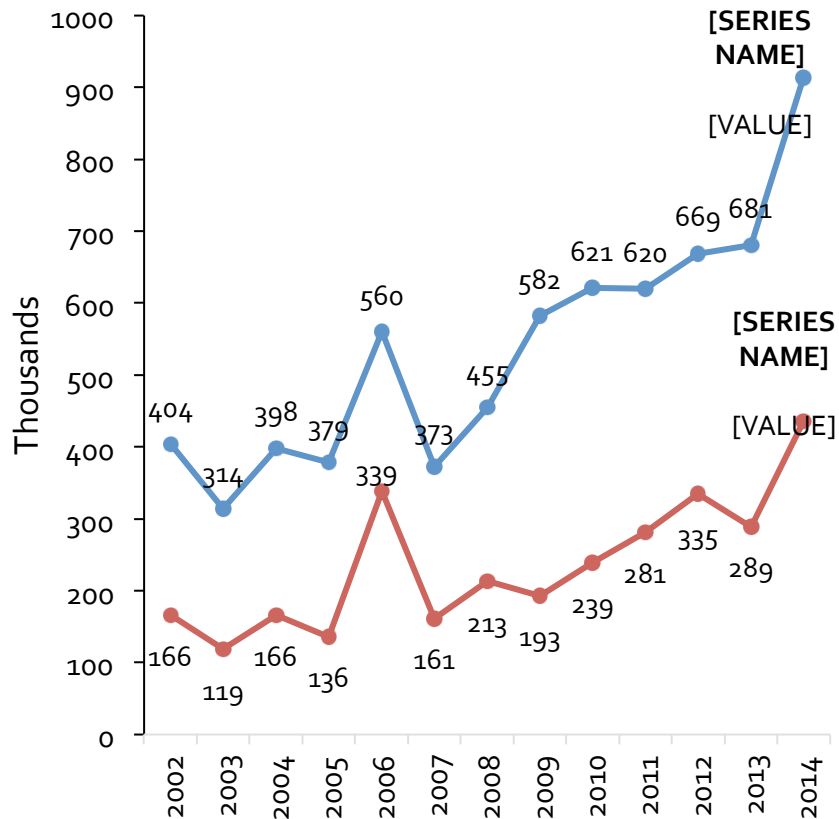
Thalamus
(pain)

PAG
(pain)

Science = Solutions

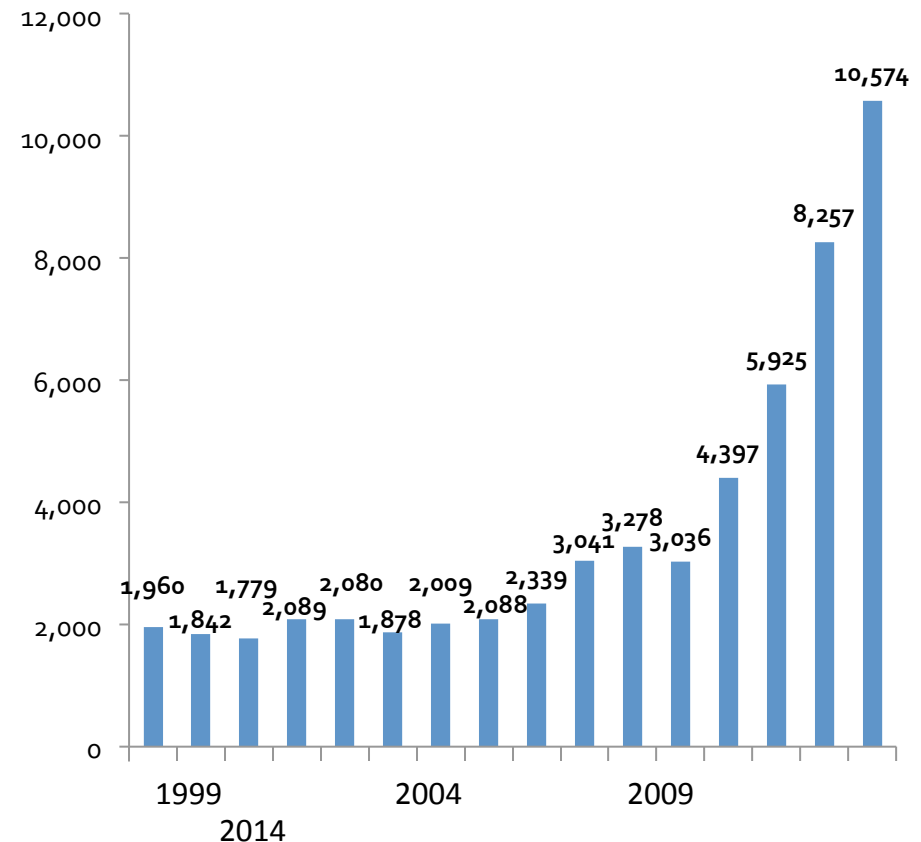
Abuse of Opioid Medications has led to a Rise in *Heroin Abuse and Associated Deaths* from Overdoses

Past Month & Past Year Heroin Use Persons Aged 12 or Older



SAMHSA, 2013 National Survey on Drug Use and Health, 2014.

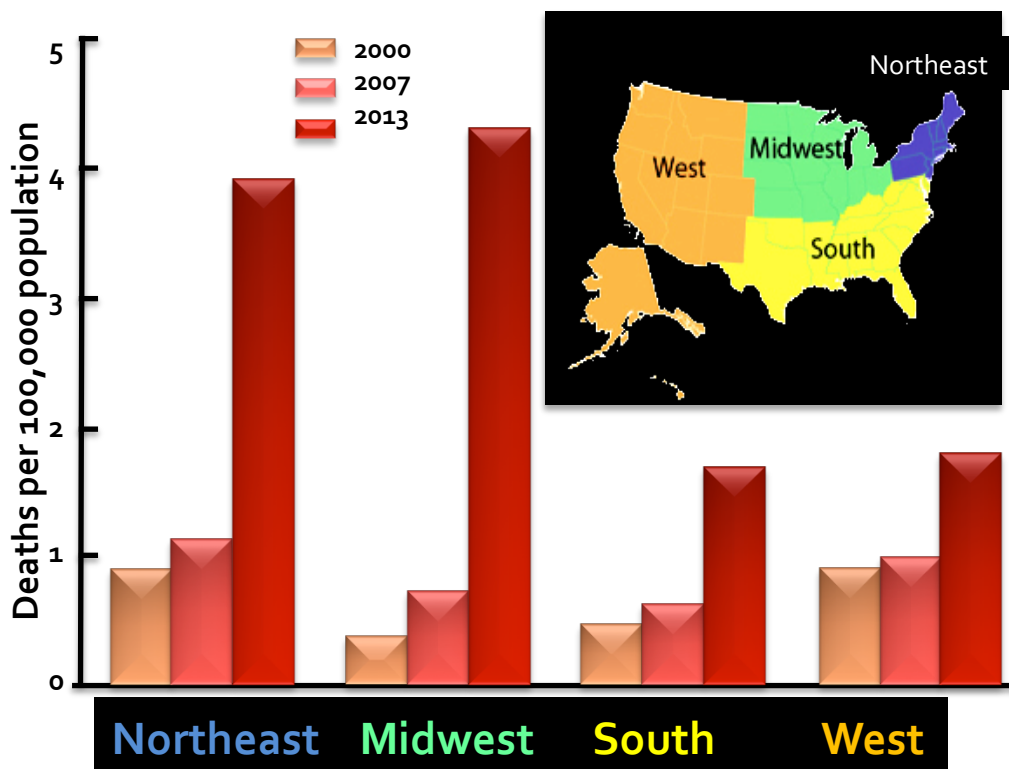
Heroin Overdose Deaths



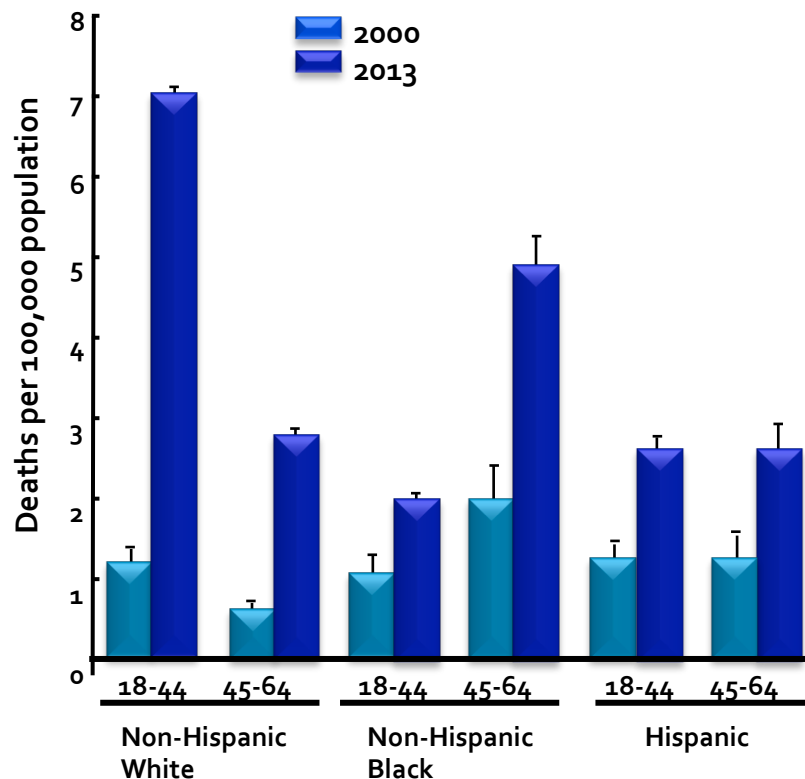
CDC/NCHS, National Vital Statistics System, Mortality File

Increases in All Regions, Especially Northeast and Midwest: Age-Adjusted Rates for Heroin Drug-Poisoning Deaths

Increases for All, Especially Non-Hispanic Whites: Heroin Drug-Poisoning Deaths by Subgroups



CDC, NCHS Data Brief, No 190, March 2015.



CDC, NCHS Data Brief, No 190, March 2015.

Most Heroin Users Report *Previous Non-Medical Use* of Prescription Opioids, BUT Only a *Small Proportion of Non-Medical Users* *Progress to Heroin*

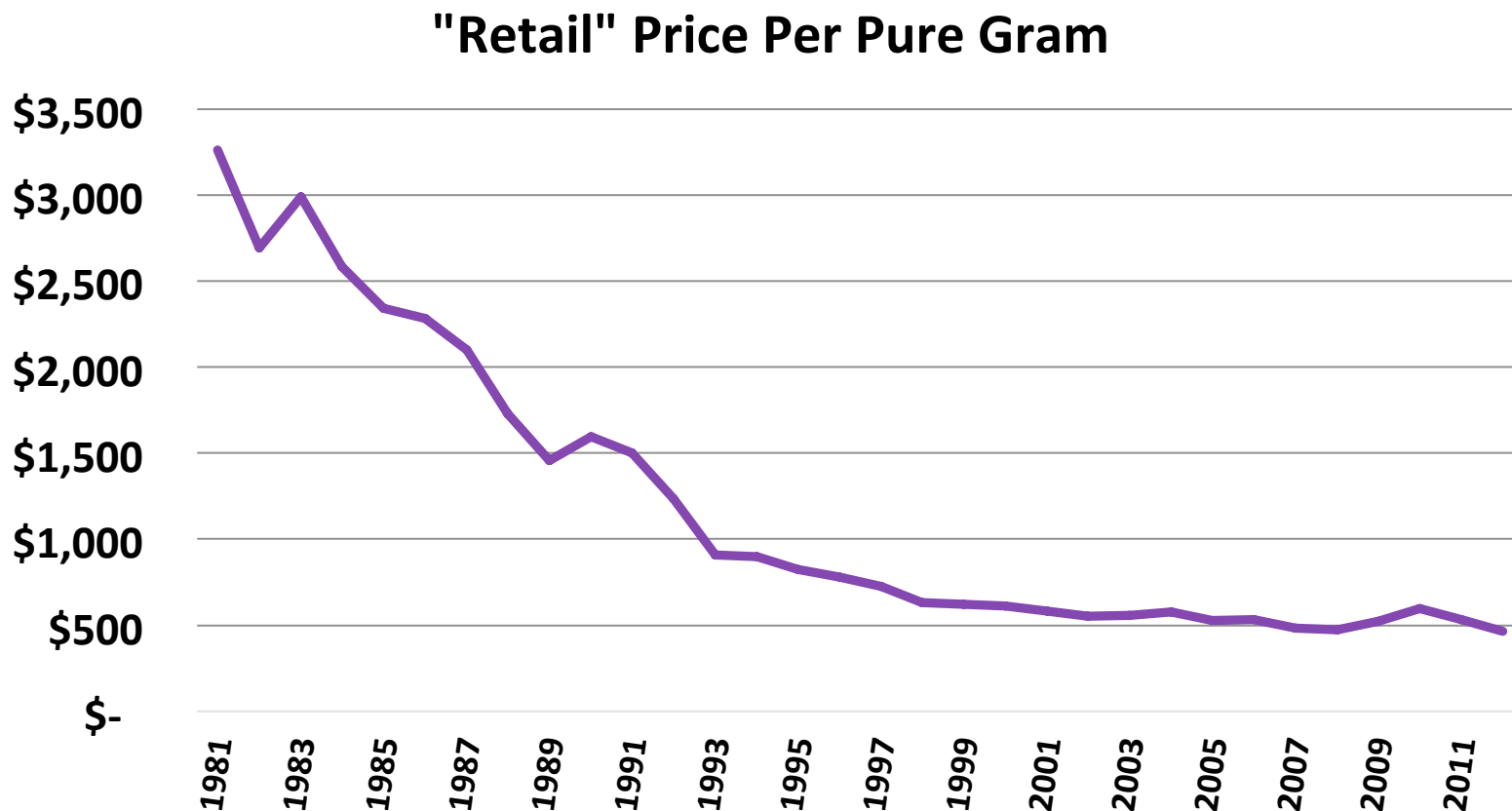
National General Population:

- Within 5 years, 3.6% of non-medical users of opioids progressed to heroin within 5 years (i.e. less than 1% per year) (*Muhuri, Gfroerer, Davies. 2013*)

Local Longitudinal Study of Non-medical users:

- Within 3 years, 7.5% progressed to heroin (i.e. 2.8% per year) (*Carlson, Nahhas, martins, Daniulaityte. 2015*)

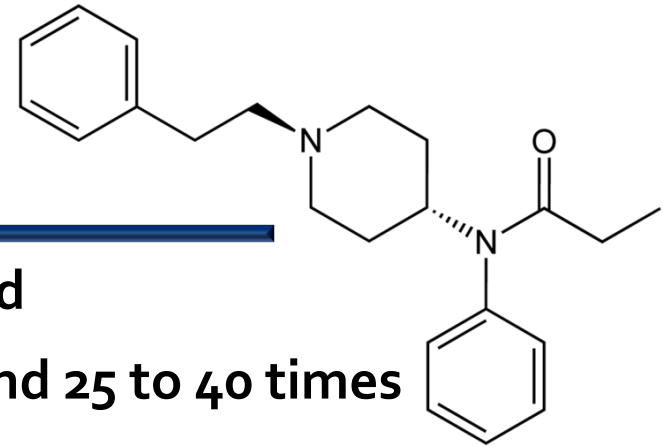
Heroin "Market" Has Changed: Heroin Price Has Been Lower in Recent Years



Source: National Drug Control Strategy--Data Supplement 2014.

https://www.whitehouse.gov/sites/default/files/ondcp/policy-and-research/ndcs_data_supplement_2014.pdf

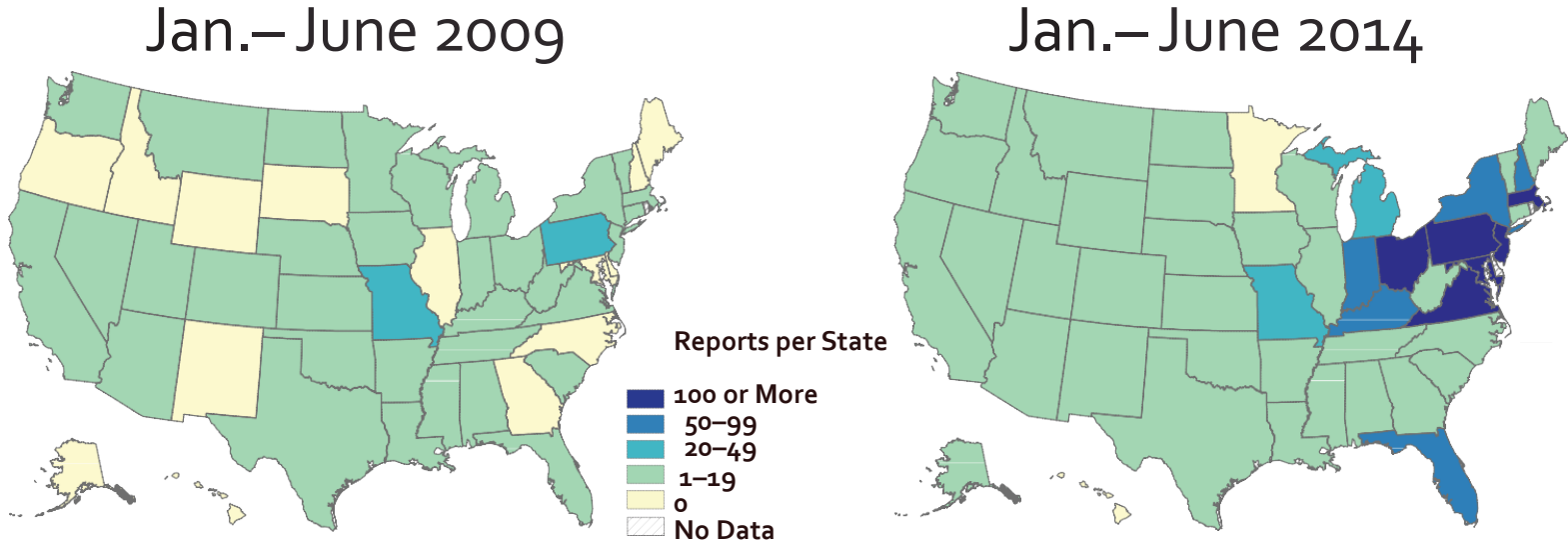
Fentanyl: A Particularly Potent Opioid



- Schedule II synthetic and short-acting opioid
- ~ 80 to 100 times stronger than morphine and 25 to 40 times more potent than heroin
- Introduced into medical practice as an intravenous anesthetic under the trade name of Sublimaze in the 1960s and approved for managing acute or chronic pain associated with advanced cancer
- It is a μ -opioid receptor agonist with a rapid onset and short duration of effects.
- Similar to other μ -opioid receptor agonists (like morphine or oxycodone) in its pharmacological effects

Most overdoses are from non-pharmaceutical fentanyl—manufactured in illicit laboratories

Increases in Fentanyl Reports in Northeast, Midwest and South

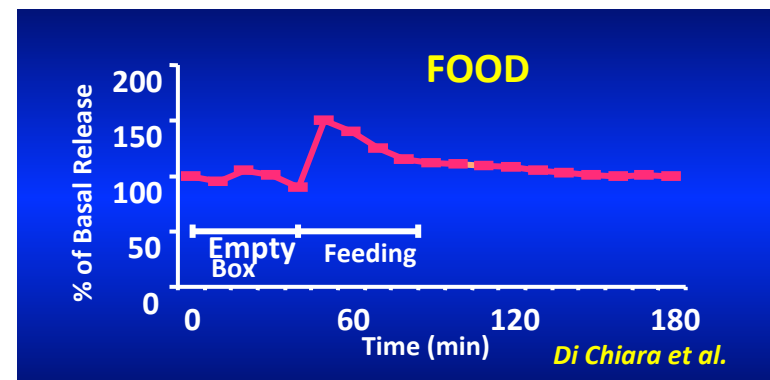
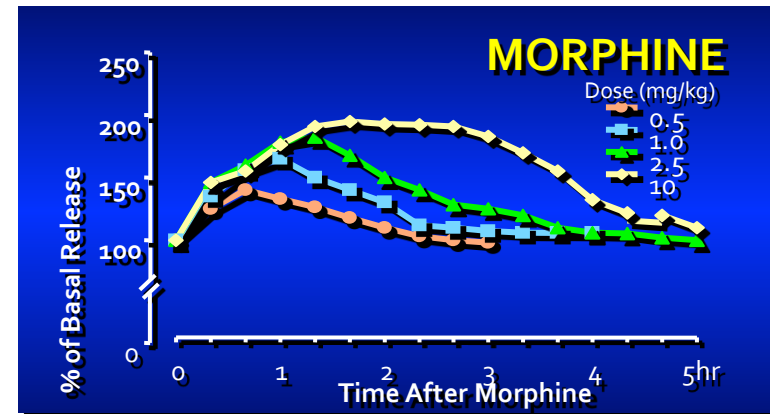
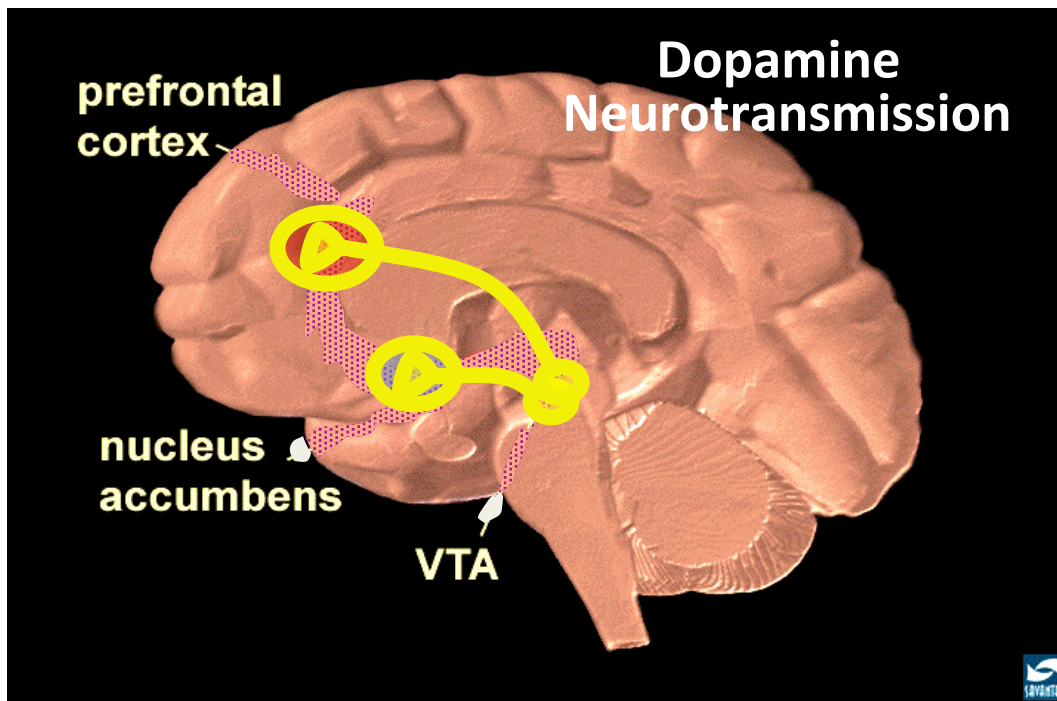


35 States reported analyzing fentanyl during the first half of 2009. No States had more than 49 fentanyl reports. Two States had between 20 and 49 reports.

In the first half of 2014, 46 States reported fentanyl, including 6 with 100 or more reports and 5 States between 50 and 99. Highest numbers mainly in Midwest and Northeast.

Why Do People Use *Opioids For Pleasure?*

Opioid prescription drugs, like other drugs of abuse (cocaine, heroin, marijuana) raise brain dopamine levels



Science = Solutions

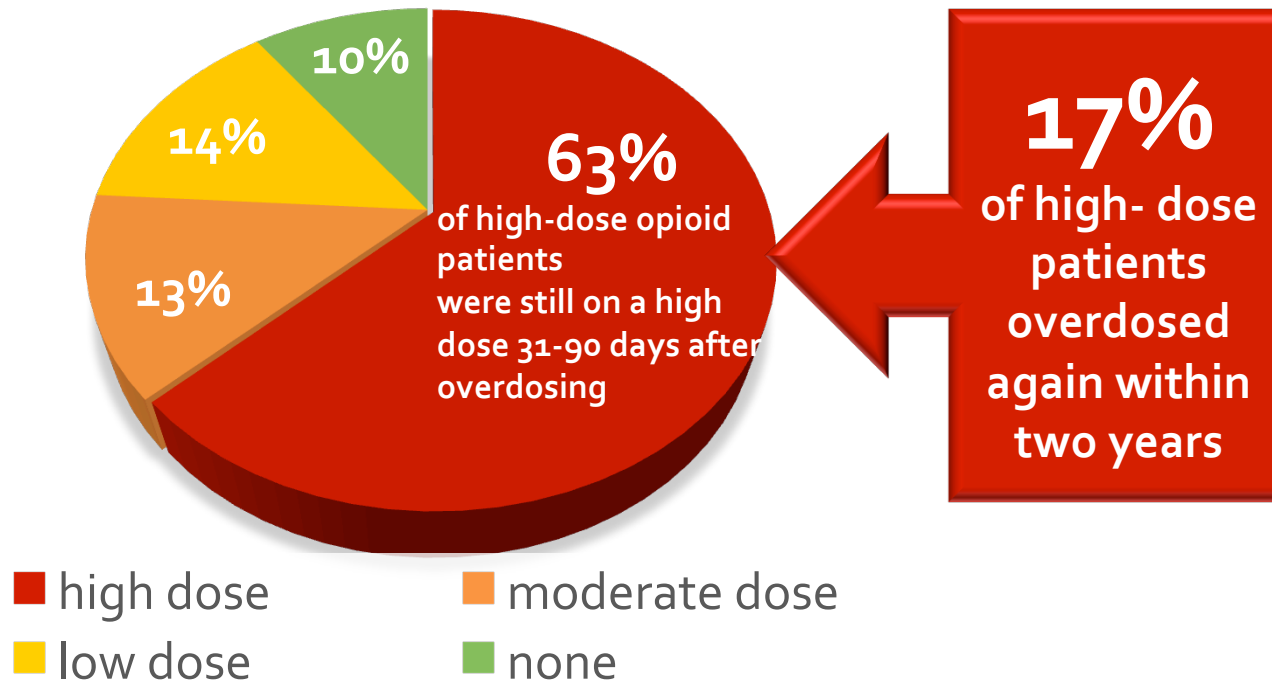
Secretary Burwell's/HHS *Opioid Priority Areas*

- Opioid prescribing practices to prevent opioid use disorders and overdose
- The expanded use of naloxone, used to treat opioid overdoses
- Expanded use of medication assisted treatment (MAT) for opioid use disorders



Doctors Continue to Prescribe Opioids for **Ninety-one Percent** of Overdose Patients

In a **2-year follow-up of 2848 commercially insured patients** who had a **nonfatal opioid overdose** during long-term opioid therapy :



- **33-39% of those with active opioid prescriptions during follow-up also were prescribed benzodiazepines.**

➤ **Recent Landscape for Guidelines:**

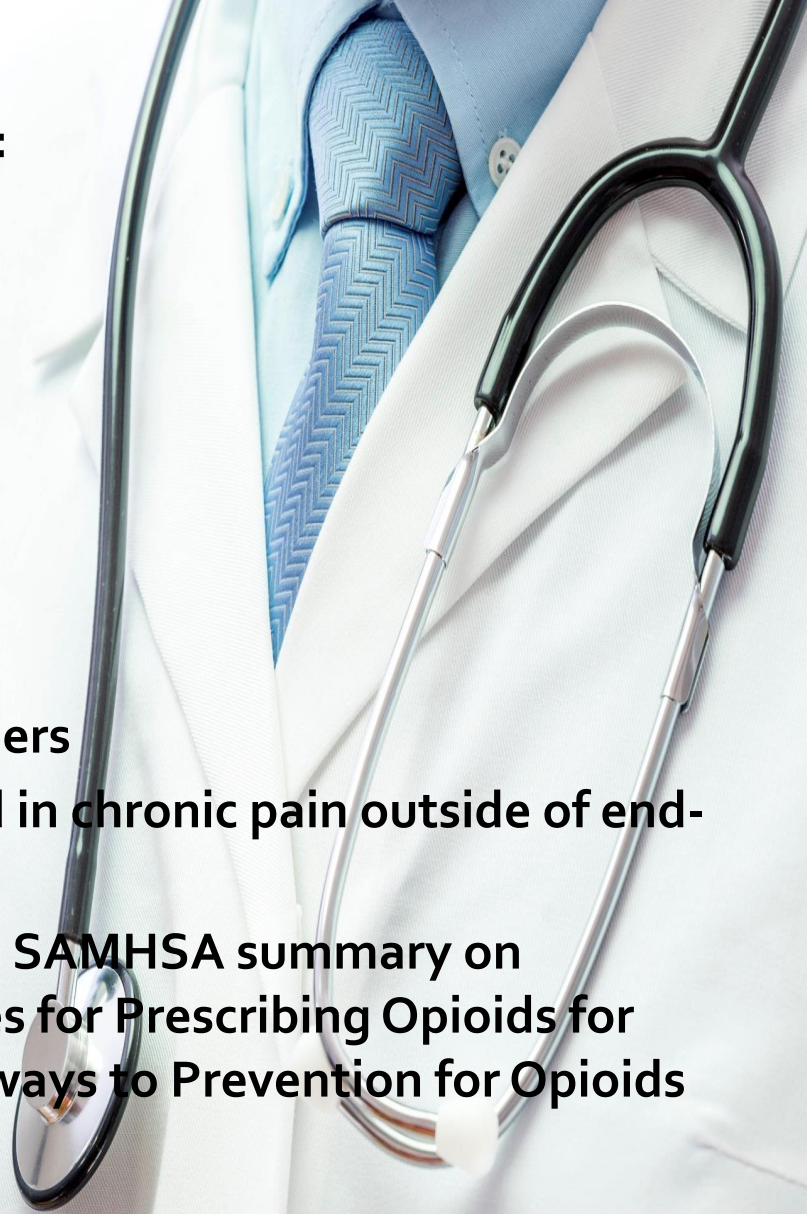
- Small Number
- Outdated
- Not Conflict Free

➤ **Solution....**



***Opioid Prescribing
Guidelines***

- **Intended for primary care providers**
- **Applies to patients >18 years old in chronic pain outside of end-of-life care**
- **Builds on joint CDC, NIDA, ONC, SAMHSA summary on “Common Elements in Guidelines for Prescribing Opioids for Chronic Pain” and the NIH Pathways to Prevention for Opioids in Treating Chronic Pain**
- **PUBLISHED MARCH 15, 2016**



Doctors (and other clinicians) Should Know...

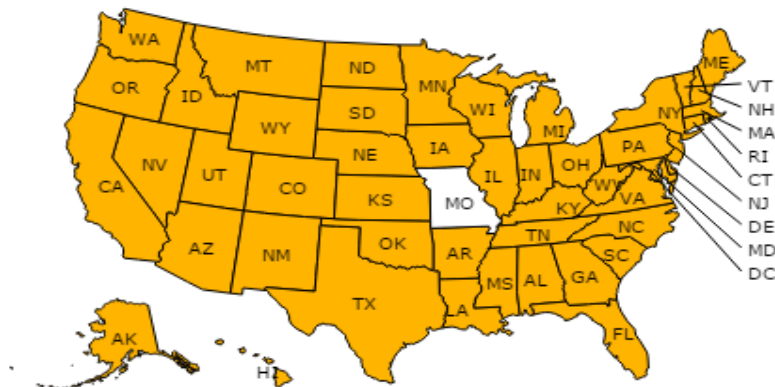
What Prescriptions Have Been Given to Their Patients By Other Practitioners

This information should be:

1. included in the patients' *electronic health care records*
2. accessible through a *Prescription Drug Monitoring Program (PDMP)* that provide immediate information

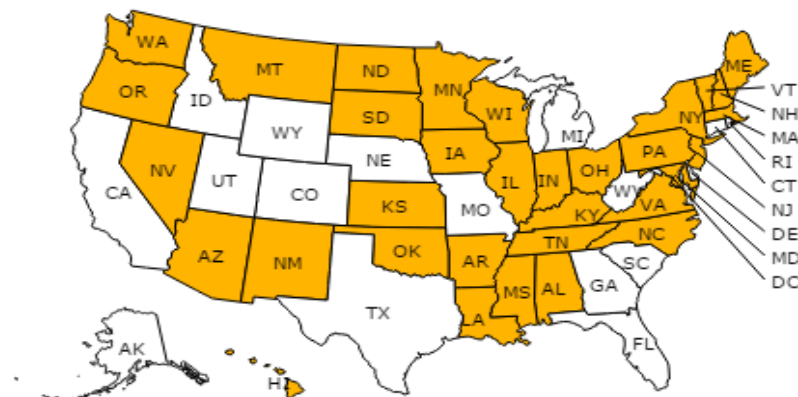


Variation in *PDMP State Laws and Regulations* (as of February 1, 2016)



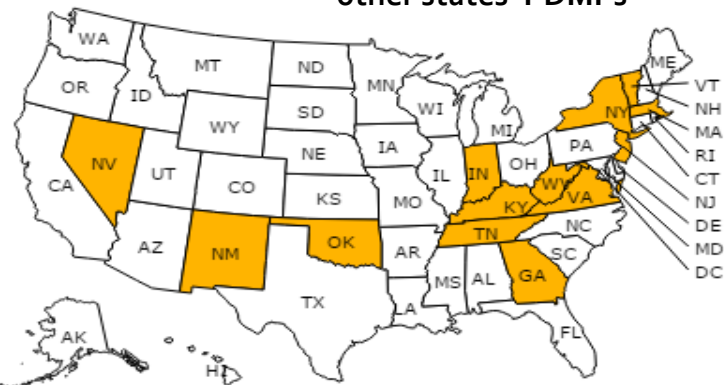
PDMP Authorized

49 states and DC have authorized PDMPs



PDMP Permitted to Share Data with other PDMPs

34 states permit sharing of PDMP data with other states' PDMPs

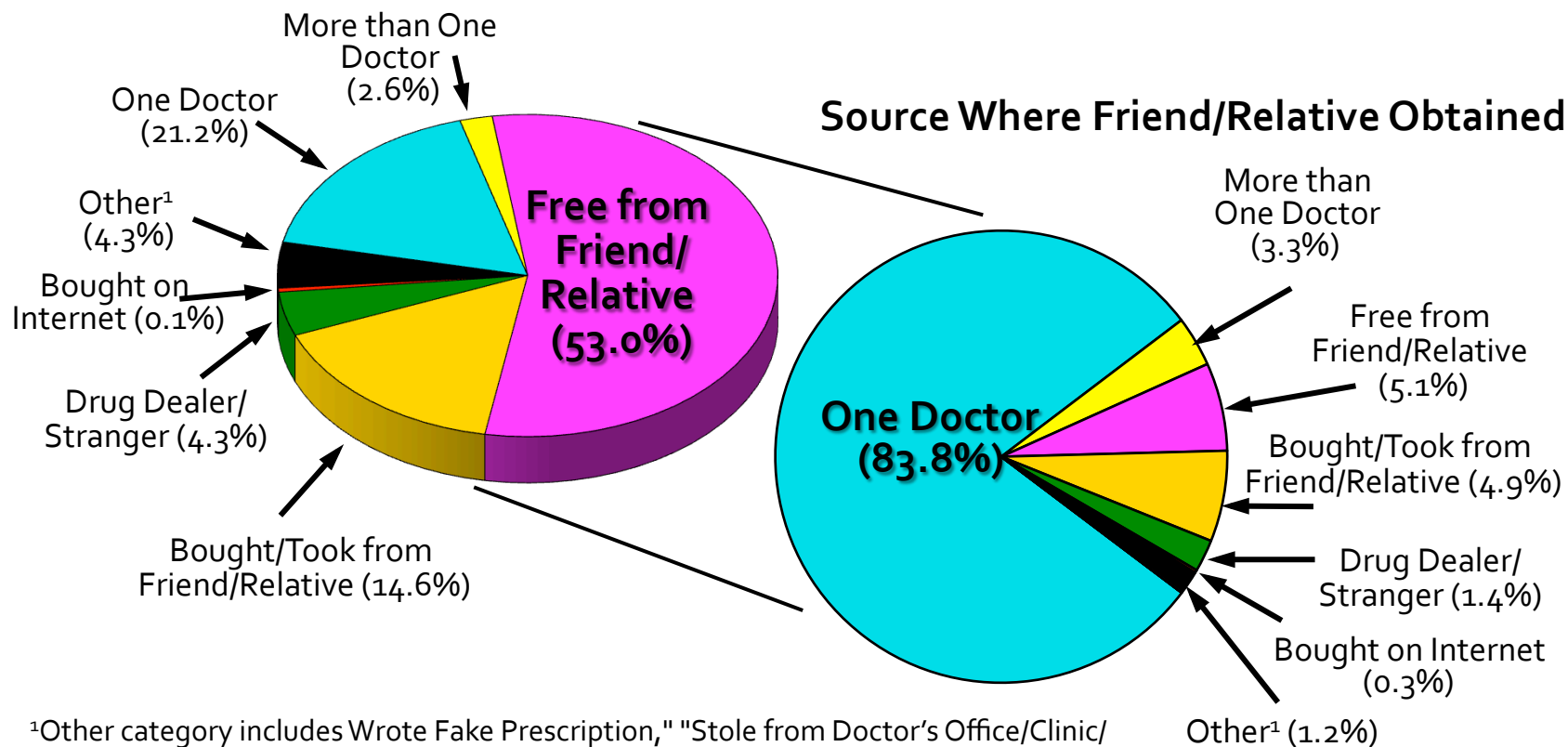


Prescribers Required to Check PDMP

13 states require prescribers to check the PDMP

People Abusing Analgesics *DIRECTLY & INDIRECTLY Obtain Them by Prescription*: Most Recent Pill Source

Source Where Respondent Age 12+ Obtained Analgesics:



Direct *Overdose Intervention*

Naloxone Distribution for opioid overdose victims. The *potential* for direct intervention to save lives.

- ***"Evzio" naloxone auto-injector***
APPROVED BY FDA, April 3,
2014



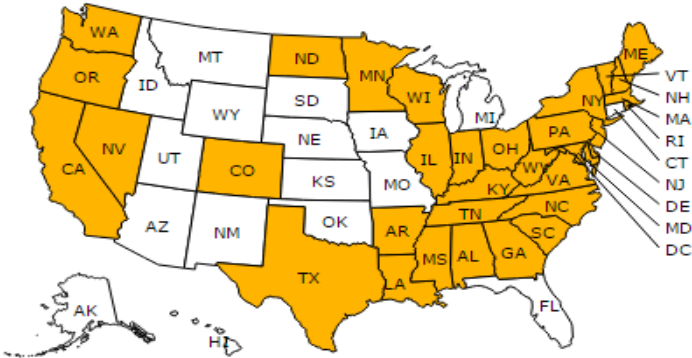
- ***"Narcan Nasal Spray" naloxone***
APPROVED BY FDA, November 18,
2015



Variation in *State Naloxone and Good Samaritan Laws* As of February 1, 2016

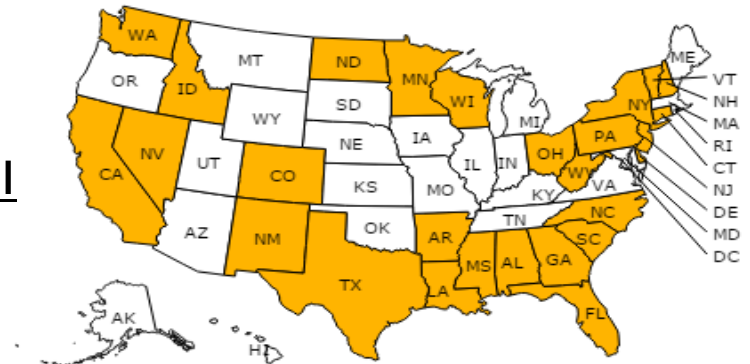
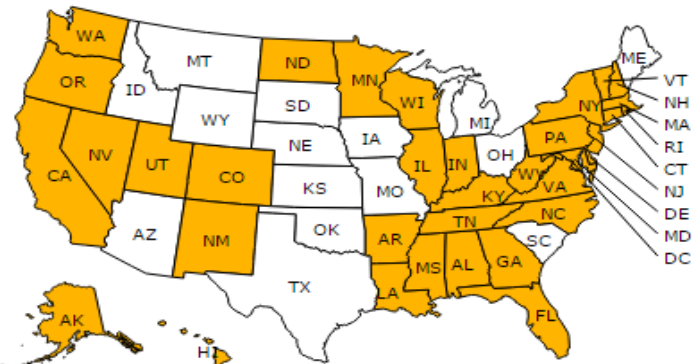
Prescription By Standing Order Authorized

33 states have standing orders to authorize non-medical Personnel to issue naloxone



Prescribers Immune from Criminal And Civil Liability

27 states protect naloxone prescribers from both criminal and civil liability



Good Samaritan Overdose Prevention Law

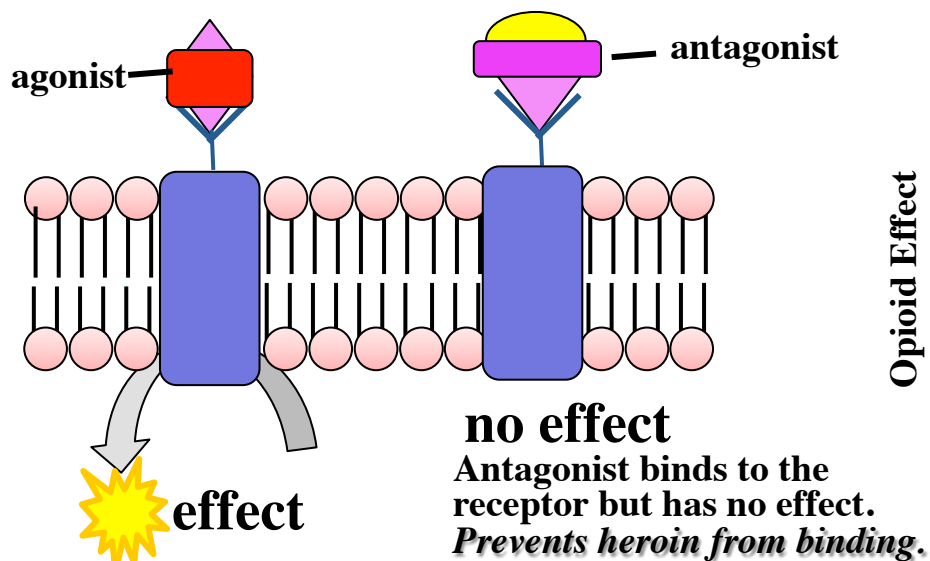
36 states offer legal protections to those who call 911 to report an overdose

Medications for Opioid Addiction

Full Agonist: **Methadone** (daily dosing)

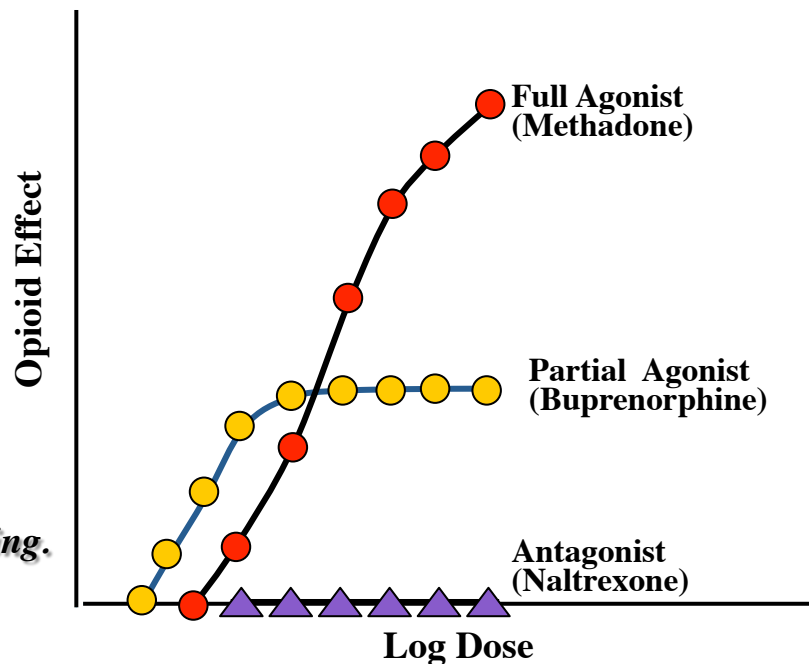
Partial Agonist: **Buprenorphine** (3-4X week, 6 month Implant)

Antagonists: **Naltrexone** (ER 1 month)



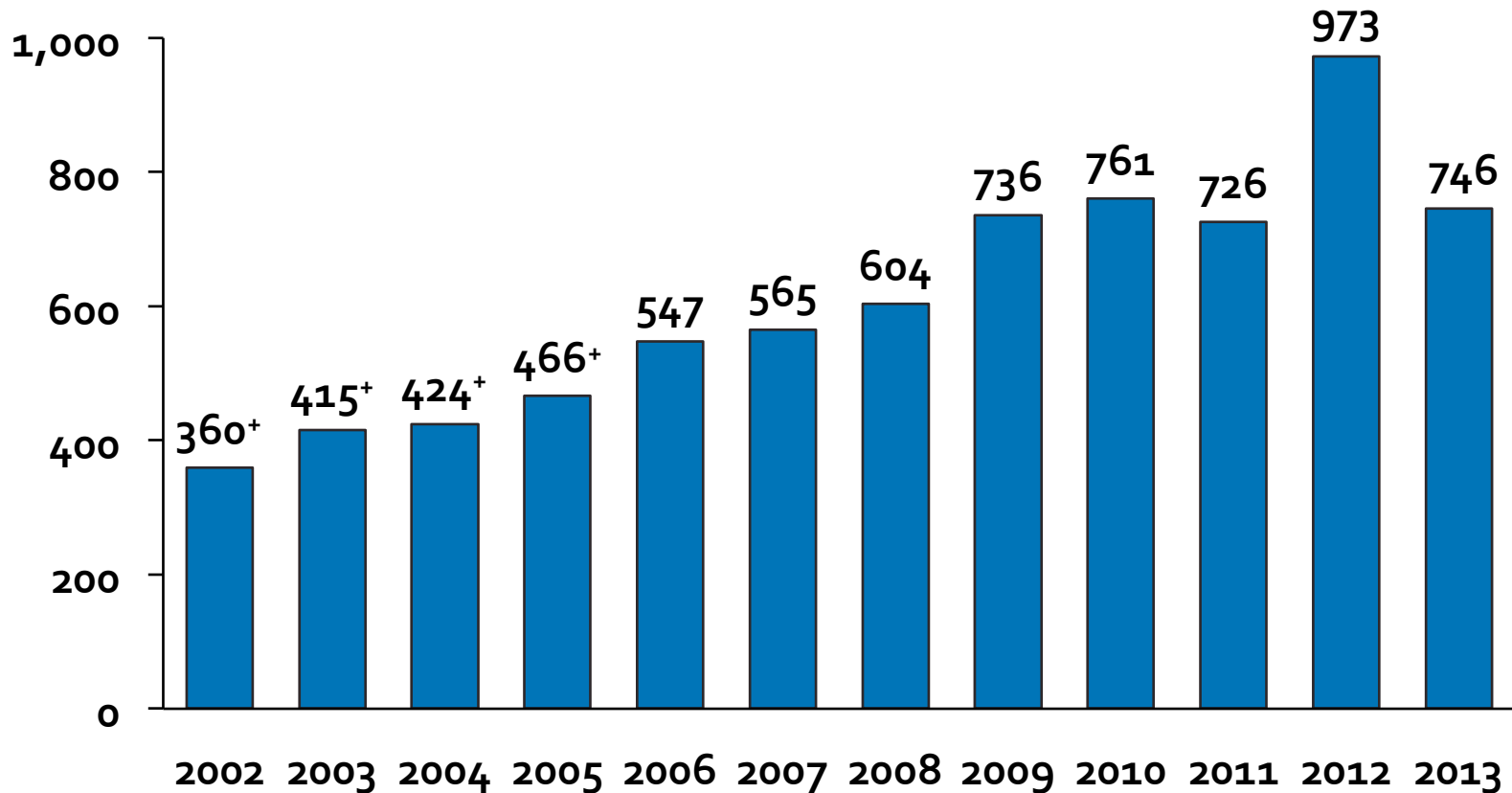
Agonist binds to the receptor and activates it: Full agonists have maximal effect; partial agonist have intermediate effect.

Prevents Heroin from binding.



Doubling of Treatment for Analgesic Use 2002 - 2013: ***Most Recent Treatment in the Past Year for the Use of Pain Relievers among USA Persons Aged 12 or Older***

Numbers in Thousands

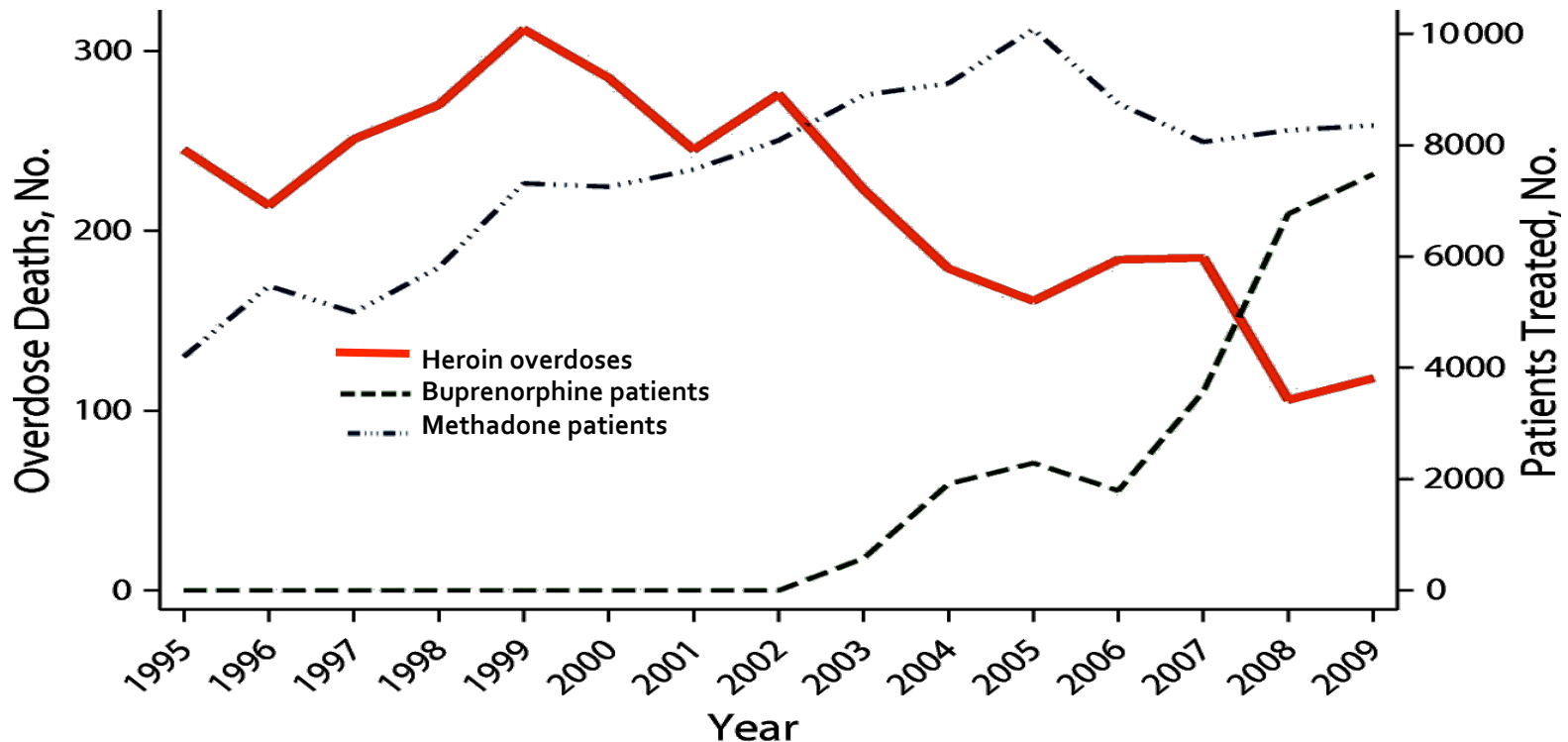


+ Difference from the 2013 estimate is statistically significant at the .05 level.

Source: SAMHSA, 2013 National Survey on Drug Use and Health, released September 2014

Accessing *Medications Can Save Lives*

Opioid Agonist Treatments Decreased Heroin OD Deaths Baltimore, Maryland, 1995-2009

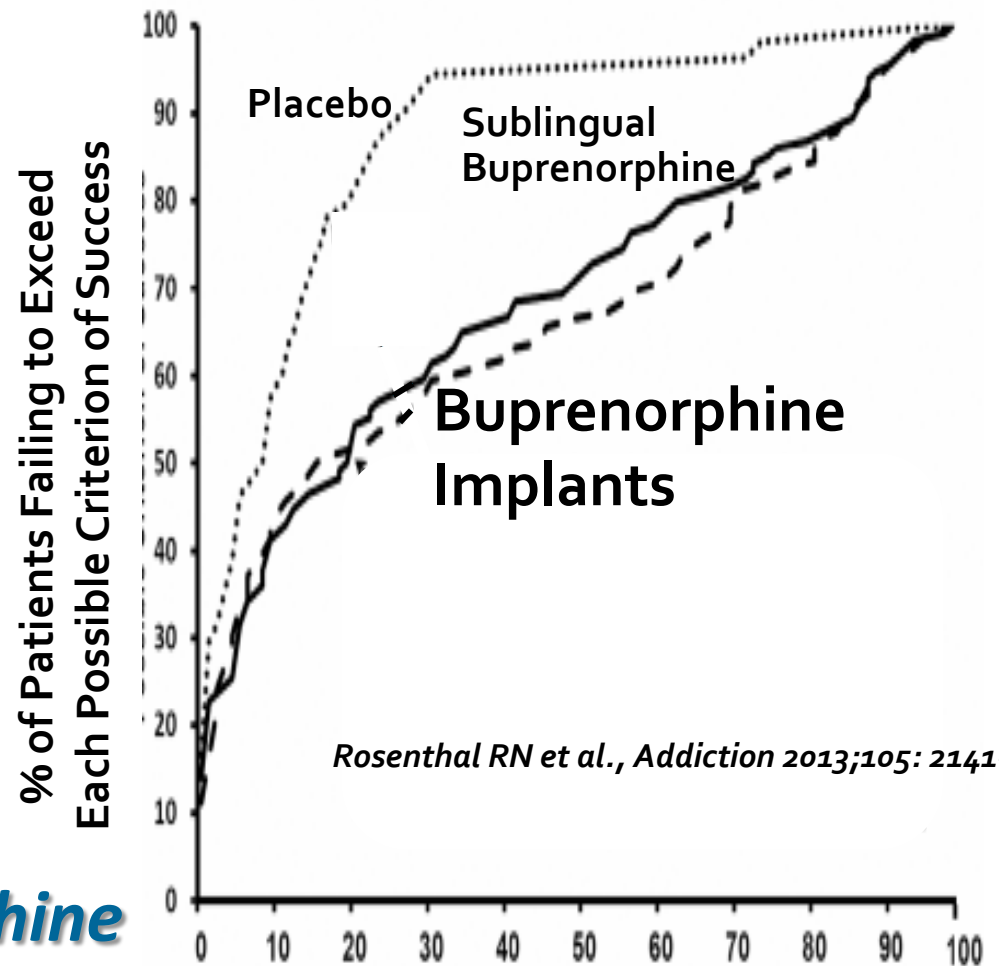


Source: Schwartz RP et al., Am J Public Health 2013; 103(5):917-22.

ADDICTION: *New Medications*

Challenge:
Compliance with
daily intake

Solution: Develop
long acting
medications

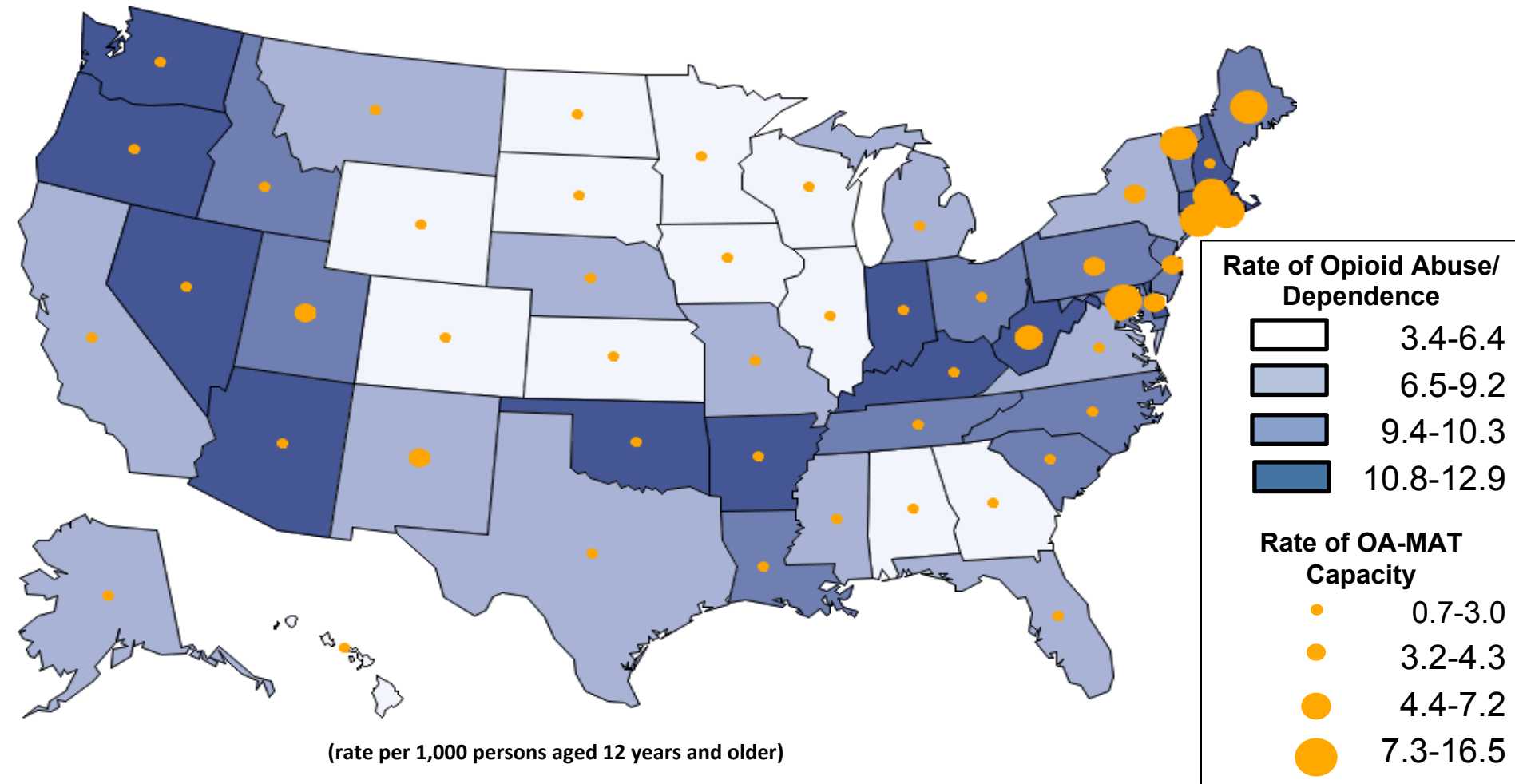


Rosenthal RN et al., Addiction 2013;105: 2141-2149.

***“Probuphine” buprenorphine
implants approved by FDA,
May 27, 2016***

% of Urines Negative (out of 72) for Opioids
Across Weeks 1 to 24

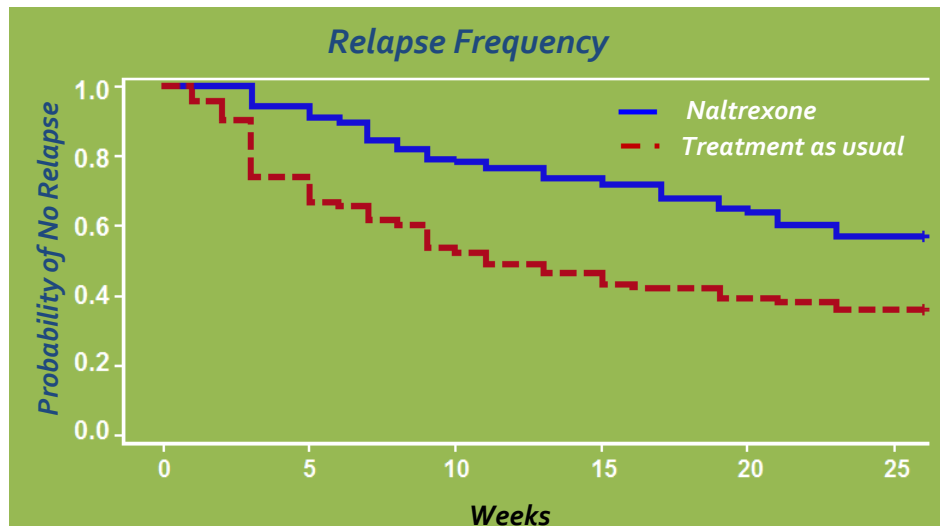
Additional Challenge: *Lack of medication-assisted treatment capacity*



Improving Treatments for Addiction: *Extended Release Naltrexone* in Criminal Justice Involved Populations



- *Participants:* parolees/probationers with opioid addiction – all *volunteers* – received either
 - Monthly injections of extended release naltrexone for 6 months
 - Community treatment, including methadone or Suboxone (encouraged)



Overdoses in 78 weeks:

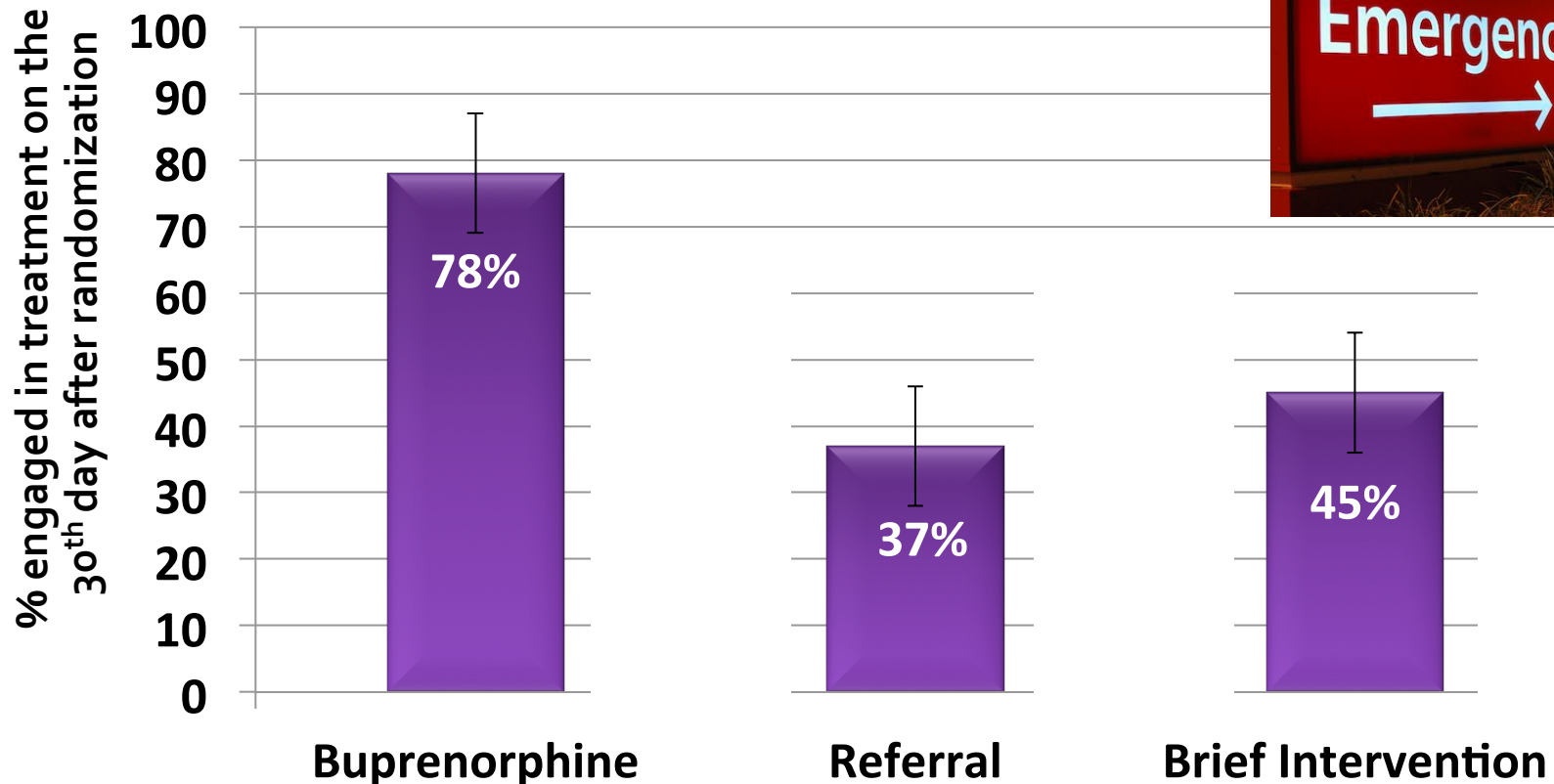
Control: 7

Naltrexone: 0

Source: Lee et al. NEJM March 31, 2016.

Science = Solutions

Treatment: *Access to Buprenorphine in Emergency Department* Increased Engagement In Addiction Treatment & Reduced Self-reported Illicit Opioid Use



Source: D'Onofrio, et al. JAMA. 2015;313(16):1636 . .

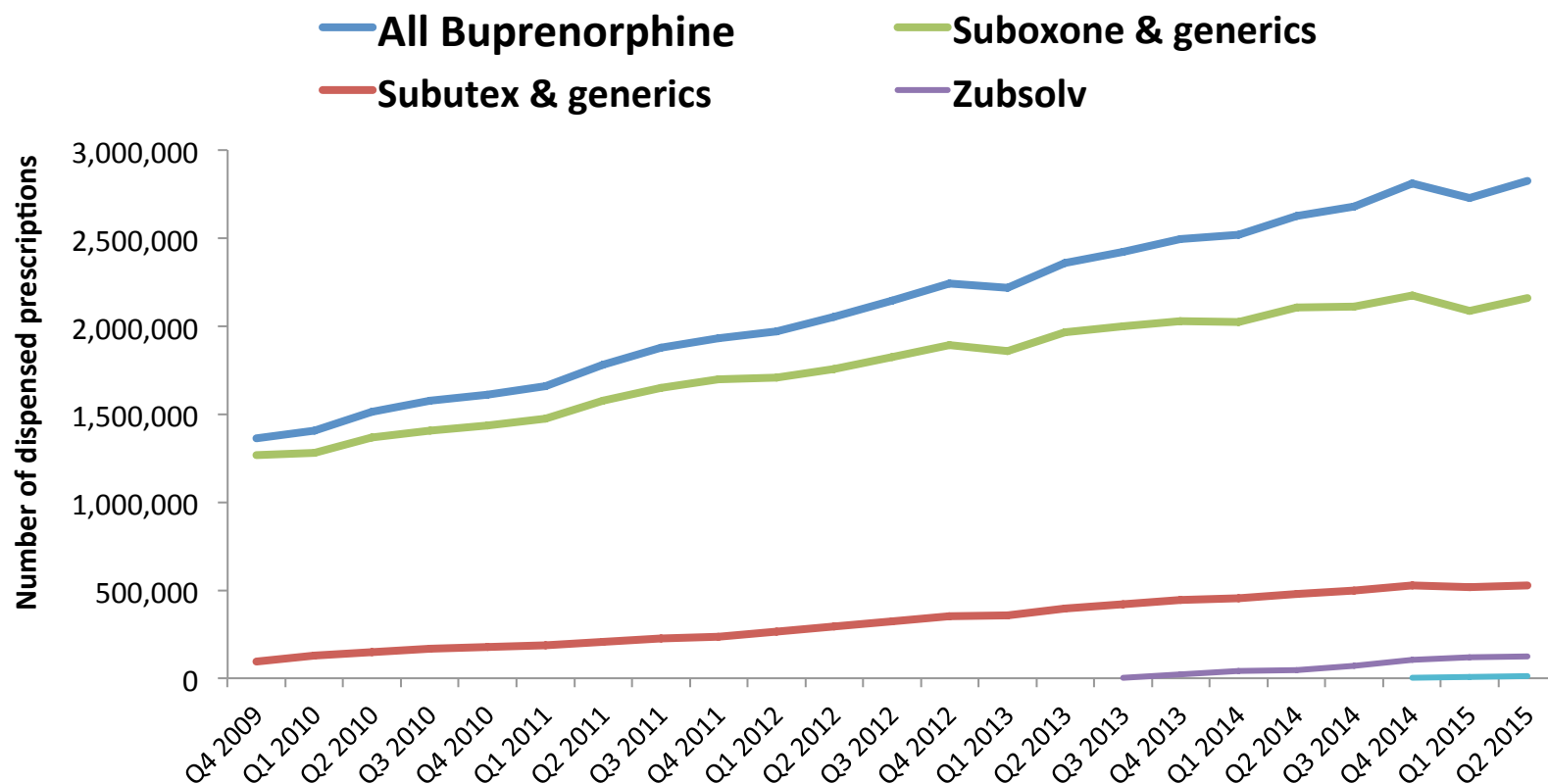
State Successes in *Improving Treatment Capacity*

- **Massachusetts Collaborative Care Model**
Expanded the number of DATA-waived physicians by 375% (from 24 to 114) within 3 years
- **New Mexico Project ECHO**
Initiation of SUD-focused clinic associated with much more rapid growth in waived physicians practicing in traditionally-underserved areas compared with the rest of the US



Sources: LaBelle CT, et al. *J Subs Abuse Treat* 2015., and Komaromy, M. et al. *Substance Abuse* 2016

Increasing Buprenorphine* prescriptions dispensed from US retail pharmacies, Q42009-Q22015



*Does not include Butrans or Buprenex (or generics)

Source: CM Jones. NIDA Webinar 9/1/2015. Based on IMS Health National Prescription Audit (extracted 8/24/2015) Retrieved from <http://www.drugabuse.gov/news-events/meetings-events/2015/09/latest-prescription-trends-controlled-prescription-drugs>.

Science = Solutions: Using Research to Improve HIV and Hepatitis C in Rural Areas

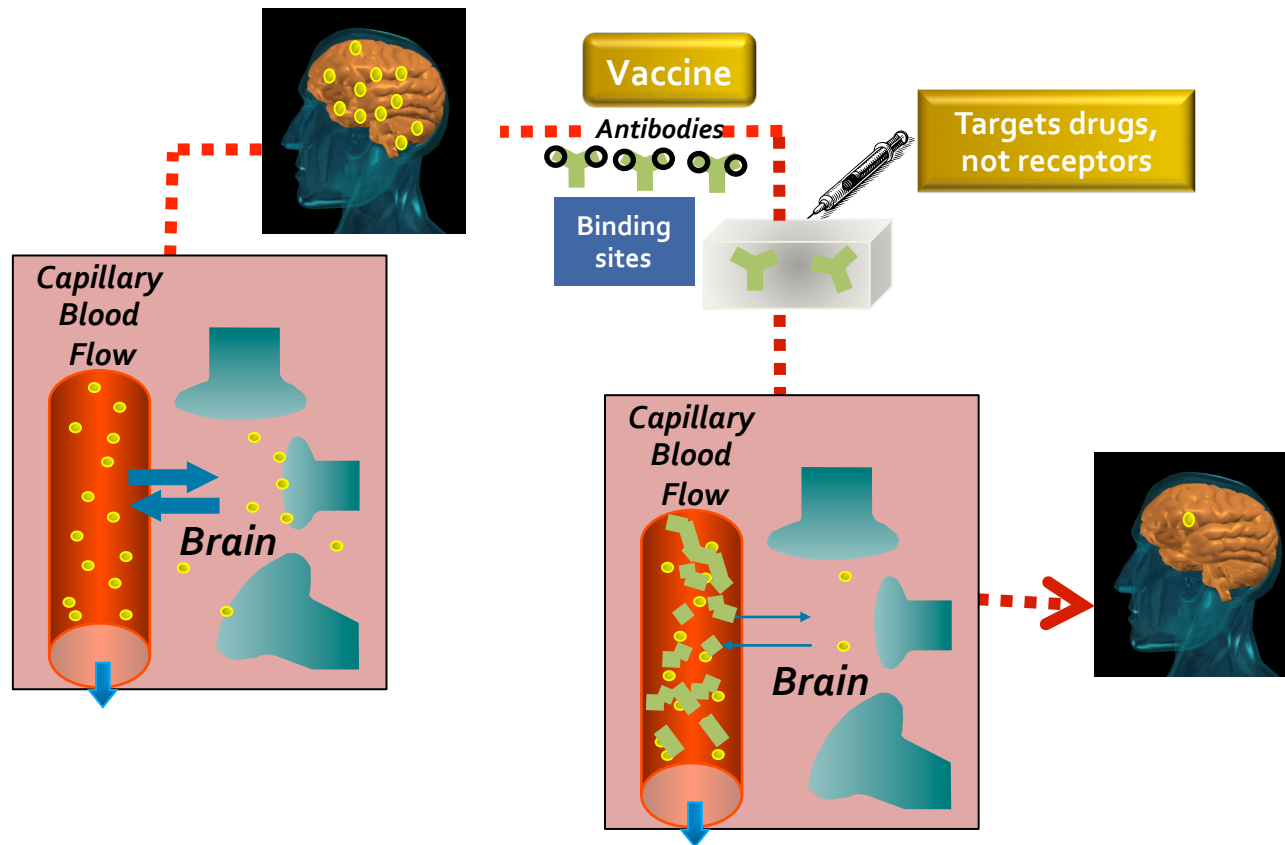


NIH is partnering with the CDC, SAMHSA and the Appalachian Regional Commission (ARC) to conduct research to address increased opioid injection drug use and resulting overdose, HIV and Hepatitis C infection.

- Improve understanding problem's scope; contributing health trends
- Identify resources, obstacles
- Develop intervention approaches to address these health threats

ADDICTION: Immunotherapies (*Vaccines*)

Antibodies (i.e. Vaccines) reduce amount of drug in the brain



Summary

- *Complex biological, developmental and social aspects of substance abuse and addiction suggest **multipronged responses**.*
- *Opioid misuse can be **prevented** and addiction **treated**.*
- ***Science** provides clues and is essential in planning responses.*

The President's Opioid Initiative

Actions across federal, state, local governments and the private sector



IMPROVE PRESCRIBER TRAINING

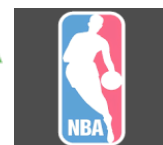
- Train >540,000 health care providers
- Double PDMP registration
- Reach >4M providers with appropriate prescribing practices messaging

IMPROVE ACCESS TO TREATMENT

- Double number of buprenorphine prescribers
- Double number of naloxone providers
- Reach >4M providers with opioid abuse messaging

COMMITMENTS FROM:

- Over 40 provider groups, including physicians, dentists, advanced practice registered nurses, physician assistants, physical therapists and educators
- CVS Health, Rite Aid and several pharmacy and pharmacist organizations (naloxone, PDMPs)
- CBS, ABC, The New York Times, Google, the National Basketball Association, and Major League Baseball will donate media space for PSAs



www.drugabuse.gov

Science = Solutions

The Prescription Opioid Epidemic & Heroin

Research Report Series

National Institute on Drug Abuse

Principles of Drug Abuse
Treatment for Criminal
Justice Populations | A Research-Based Guide

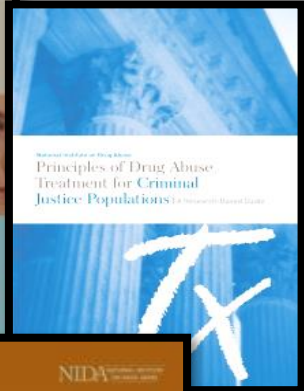
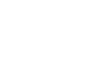
National Institutes of Health
U.S. Department of Health
and Human Services

National Institute on Drug Abuse

SEEKING DRUG ABUSE TREATMENT:
KNOW WHAT TO ASK

U.S. Department of Health and Human Services
National Institutes of Health

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