

Opioid Crisis: The challenges and opportunities to change the course of the epidemic

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Outline

- **Historical aspects**
- **Current state of heroin addiction**
- **Current state of prescription opioid addiction (POA)**
- **Opioid OD deaths**
- **Management of opioid addiction**
- **Challenges**

THE MRI SHOWS THAT YOUR BRAIN HAS BEEN HIJACKED BY DOPAMINE PIRATES.



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ARE YOU WRITING ME A PRESCRIPTION?

NO, I'M BUYING STOCK IN THOSE COMPANIES.





Historical aspects

HEROIN

“It’s not hypnotic and there is no danger in acquiring a habit!”

– Boston Medical and Surgical Journal 1900



COUGH

The Suits of Chronic Expectoration Designated Glyco-Heroin (Smith) as a Respiratory Sedative Superior to All Remedies in the Preparation of Croup, Whooping Cough and Other Nervous and Irritable Coughs of the Infant or Debilitating Effects which characterize the latter when given in doses sufficient to reduce the reflex irritability of the bronchial, tracheal and laryngeal mucous membranes.

THE PROBLEM
of establishing a cough in great distress, with little or no fever, and of the most irritating kind, in the most delicate child.

HAS BEEN SOLVED BY
the pharmaceutical compound known as

GLYCO-HEROIN (Smith)

The results obtained with Glyco-Heroin (Smith) in the short time and with a few doses are attested by numerous clinical studies. But have appeared in the medical journals within the past few years.

Scientifically Compounded, Scientifically Conceived, GLYCO-HEROIN (SMITH) simply stands upon its merits before the profession, ready to prove its efficacy to all who are interested in the advances in the art of

BAYER

PHARMACEUTICAL PRODUCTS.

We are now sending to Physicians throughout the United States literature and samples of

ASPIRIN

The substitute for the Salicylates, agreeable of taste, free from unpleasant after-effects.

HEROIN

The Sedative for Coughs,
HEROIN HYDROCHLORIDE
Its water-soluble salt.

You will have call for them. Order a supply from your jobber.

Write for literature to
FARBENFABRIKEN OF ELBERFELD CO.
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THE NEW YORK MEDICAL JOURNAL 99

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ASPIRIN
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The anti-malarial

HEROIN
The sedative for coughs

FERRO-SODIUM
The iron salt

HEMICRANIN
The specific for malaria

LYCETOL
The uric acid solvent

SONATOSE
The most soluble salt

PHENACETIN
The analgesic

TRIONAL
The diuretic

SALOPHEN
The antirheumatic and antineuralgic

EUROPHEN
The soluble uric acid solvent

HEROIN-HYDROCHLORIDE
The ready for coughs

SYCOSE
The soluble for coughs

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Opioid epidemics in modern US history

- First epidemic was early 1900s
 - Opioid maintenance started with Morphine clinics
- Second epidemic was post WW II
 - First methadone clinic opened in NY City in 1972
- This is our third opioid epidemic



Current state of heroin addiction

Scope of Heroin Use in the US (National Survey of Drug Use and Health, NSDUH)

- NSDUH: Past year heroin use

- 2016: 948,000

- 2014: 914,000

- 2012: 669,000

- 2007: 373,000

- NSDUH: Past month heroin use

- 2016: 474,000

- 2015: 591,000

- 2014: 435,000

- 2012: 335,000

- 2007: 161,000

This increase has been seen in....

- Men
- Non-Hispanic whites
- Ages 18-25 years
- Living in the North East
- Suburban and rural communities
- Household income less than \$20,000 per annum
- People addicted to prescription opioid drugs/cocaine/alcohol/marijuana
- People without insurance

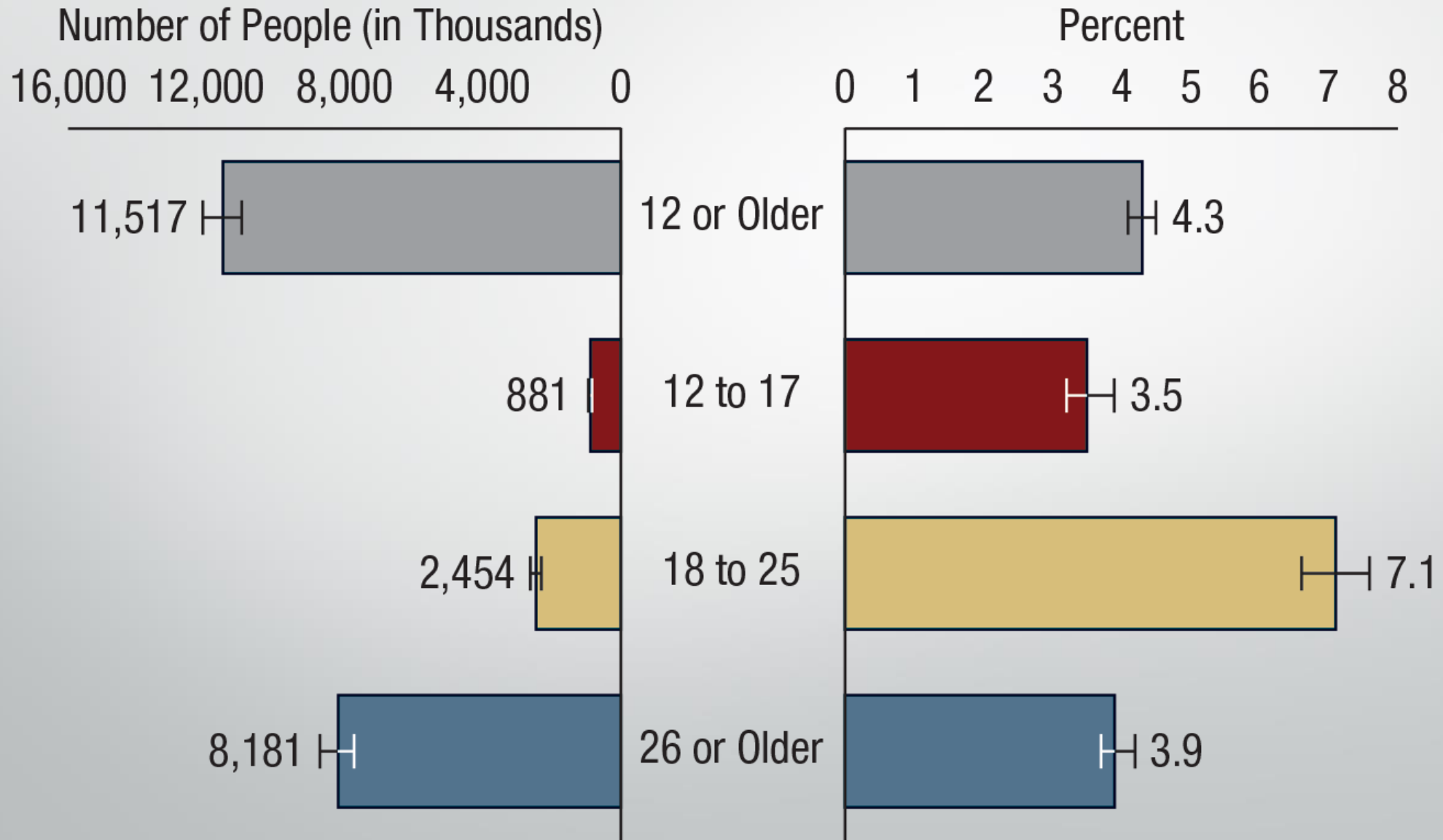
Heroin Use Has INCREASED Among Most Demographic Groups

	2002-2004*	2011-2013*	% CHANGE
SEX			
Male	2.4	3.6	50%
Female	0.8	1.6	100%
AGE, YEARS			
12-17	1.8	1.6	--
18-25	3.5	7.3	109%
26 or older	1.2	1.9	58%
RACE/ETHNICITY			
Non-Hispanic white	1.4	3	114%
Other	2	1.7	--
ANNUAL HOUSEHOLD INCOME			
Less than \$20,000	3.4	5.5	62%
\$20,000-\$49,999	1.3	2.3	77%
\$50,000 or more	1	1.6	60%
HEALTH INSURANCE COVERAGE			
None	4.2	6.7	60%
Medicaid	4.3	4.7	--
Private or other	0.8	1.3	63%

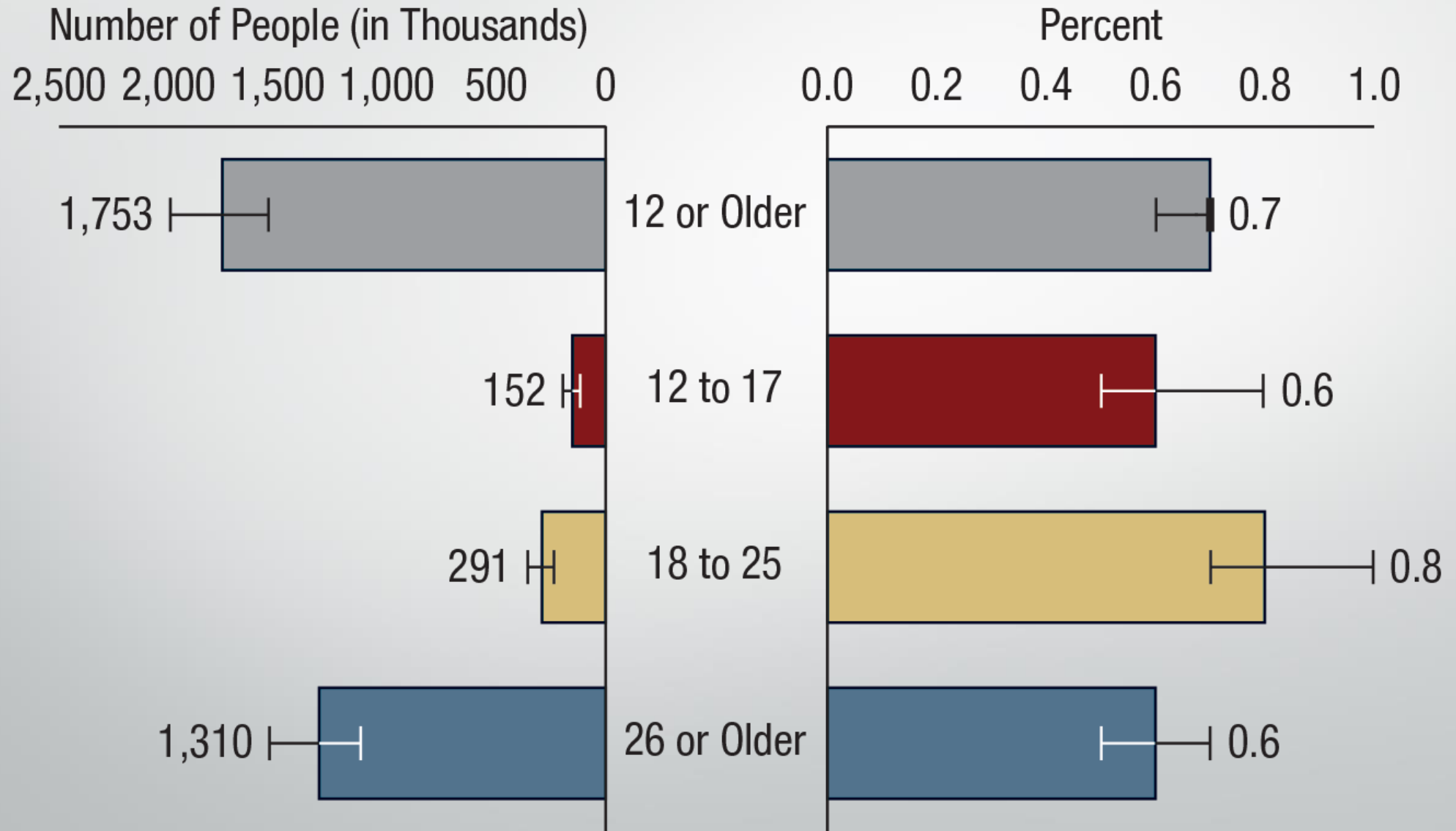


Current state of prescription opioid addiction (POA)

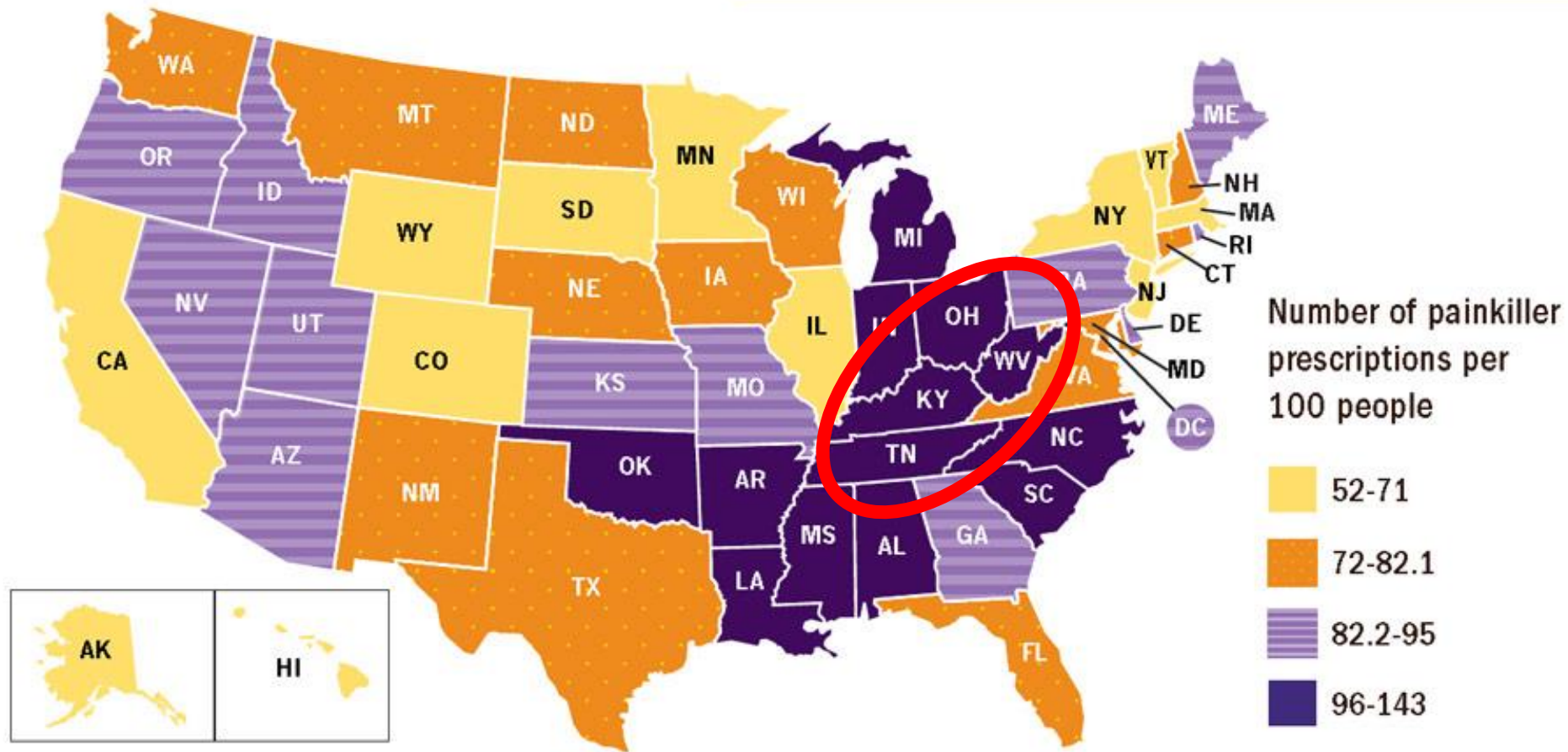
11.5 Million People Misused Prescription Opioid Medication (2016)



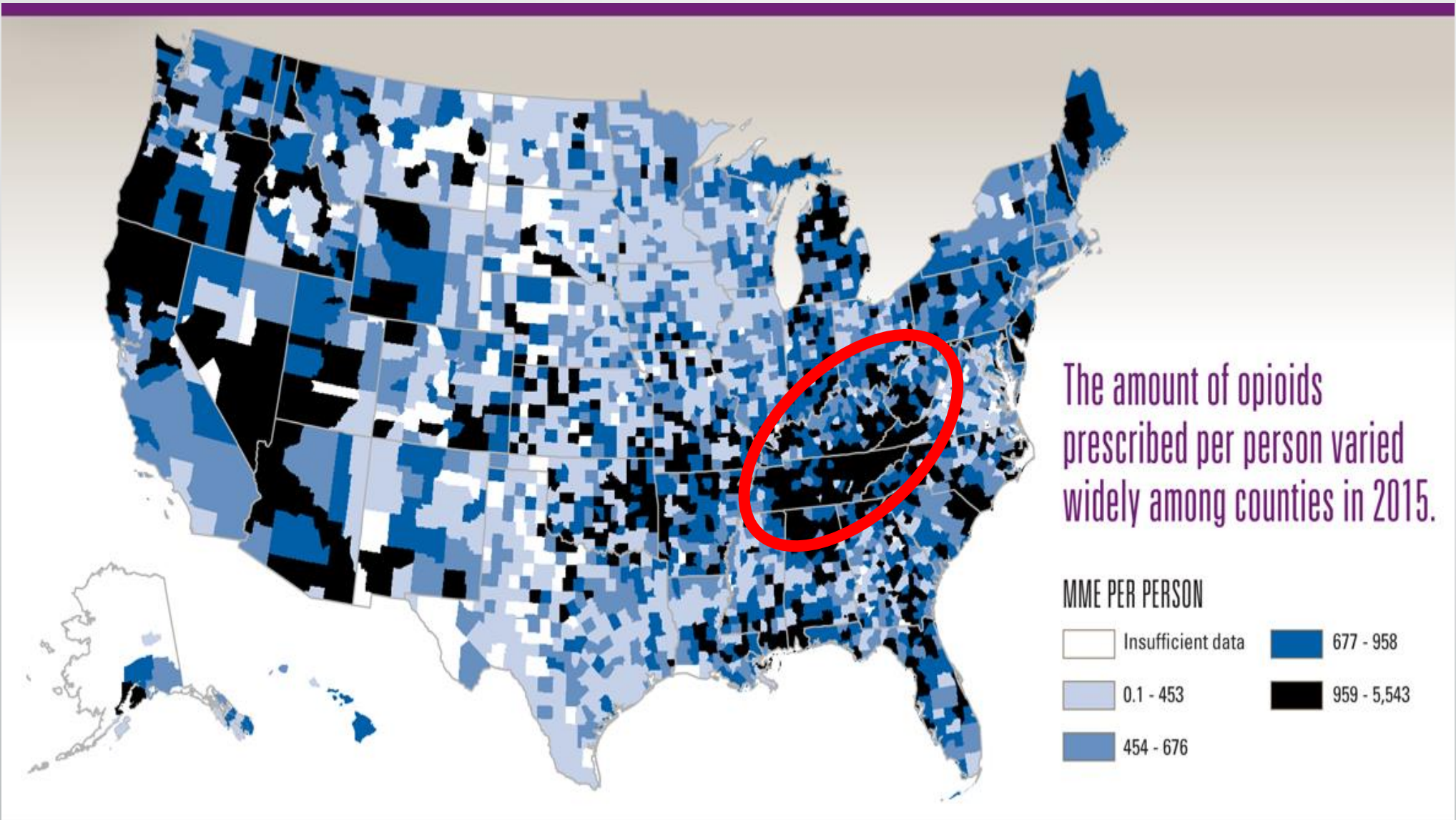
1.8 Million People With Prescription Opioid Addiction (2016)



Some states have more painkiller prescriptions per person than others.



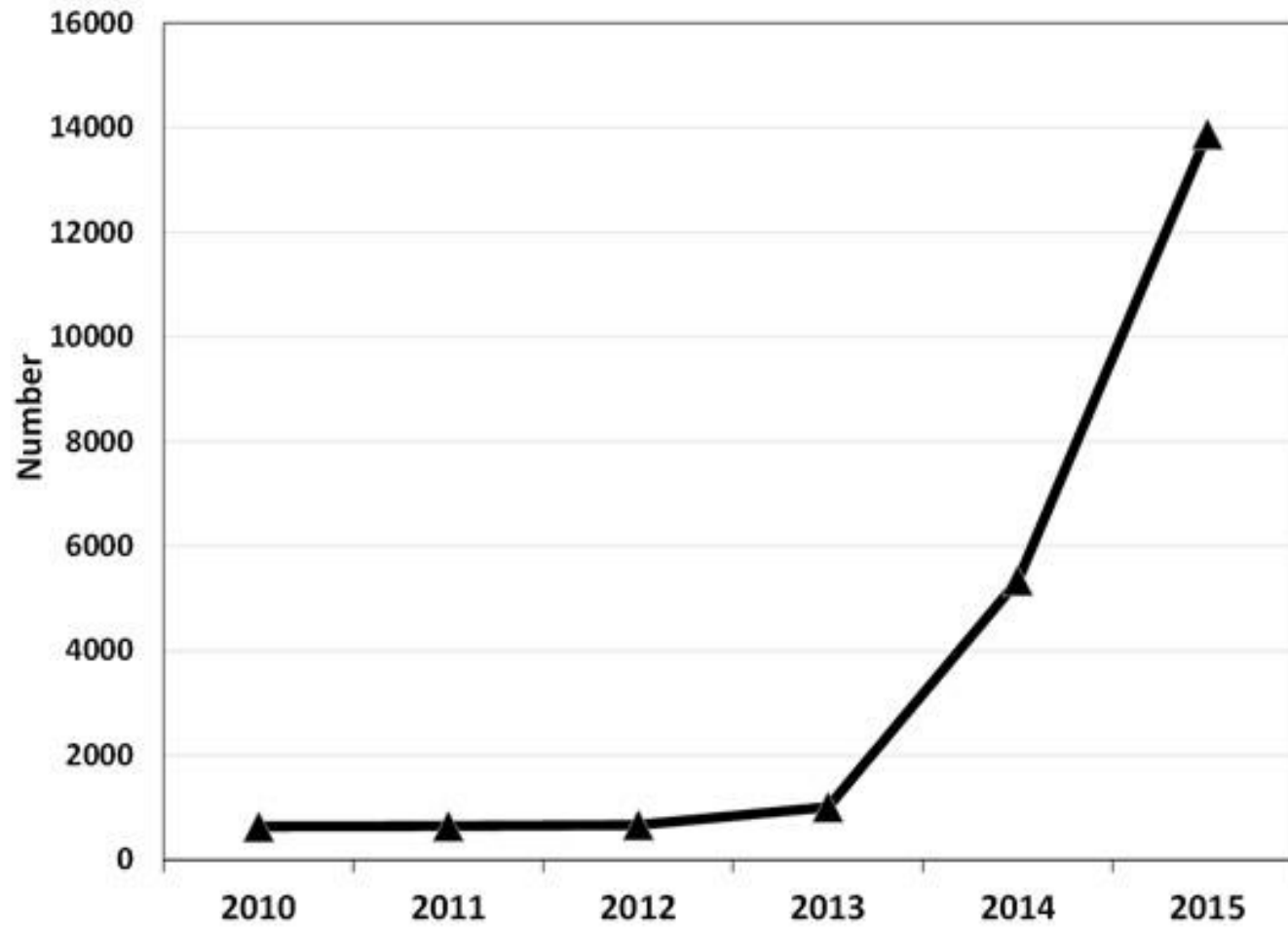
SOURCE: IMS, National Prescription Audit (NPA™), 2012.



Fentanyl encounters

- The number of fentanyl encounters more than doubled in the US from 5,343 in 2014 to 13,882 in 2015
- Extremely high rates were found in Ohio, Massachusetts and New Hampshire
- The steady increase in fentanyl encounters from 2013 to 2015 indicates that the supply of illicitly made fentanyl continues to increase primarily east of the Mississippi river with small increases west of the Mississippi
- Research chemical U-47700 (unscheduled synthetic opioid) found in counterfeit oxycodone pills
- Other synthetic opioids in the market: acetylfentanyl, carfentanil, butyrfentanyl (alveolar hemorrhages), W-18, MT-45 (ototoxic) and AH-7921

Number of Reported Law Enforcement Encounters Testing Positive for Fentanyl in the US: 2010 - 2015



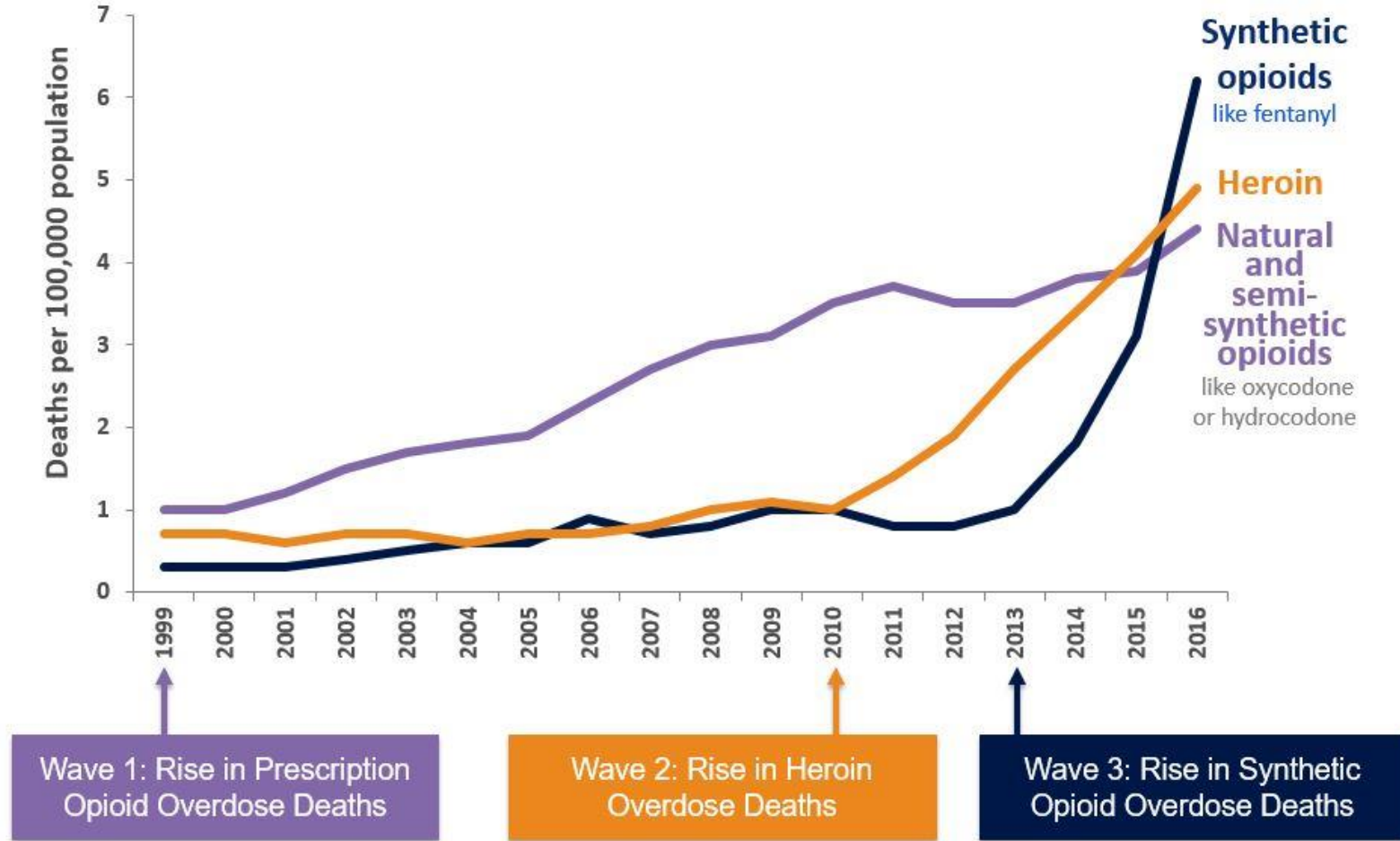


Opioid OD deaths

Opioid OD deaths

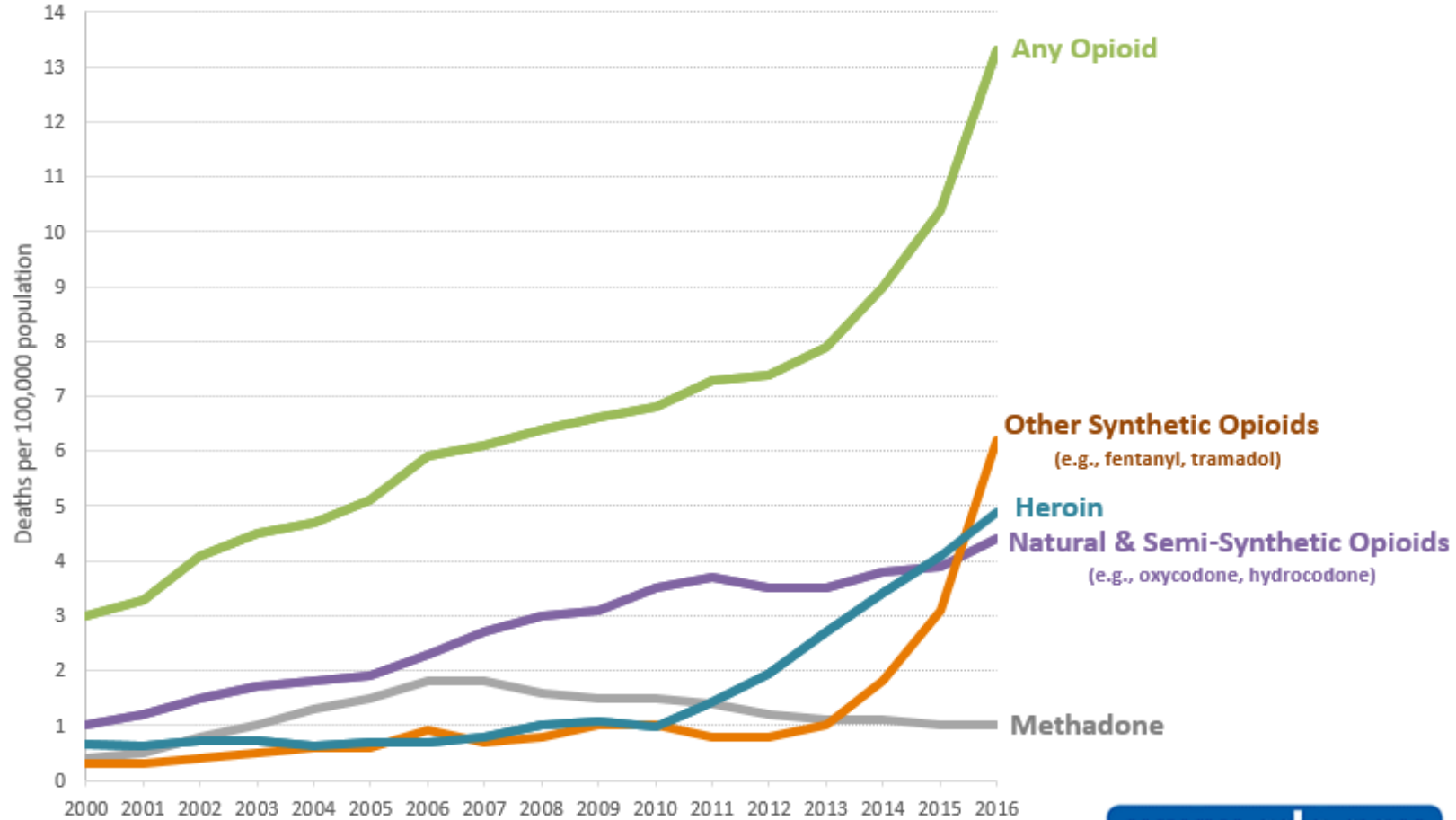
- Opioids were involved in 42,249 deaths in 2016 (Total drug ODs 64,000)
- Heroin was involved in 15,446 deaths in 2016
- Opioid overdose deaths were five times higher in 2016 than 1999
- In 2016, states with the highest rates of death due to drug overdose
 - West Virginia (52.0 per 100,000)
 - Ohio (39.1 per 100,000)
 - New Hampshire (39.0 per 100,000)
 - Pennsylvania (37.9 per 100,000)
 - Kentucky (33.5 per 100,000)

3 Waves of the Rise in Opioid Overdose Deaths



SOURCE: National Vital Statistics System Mortality File.

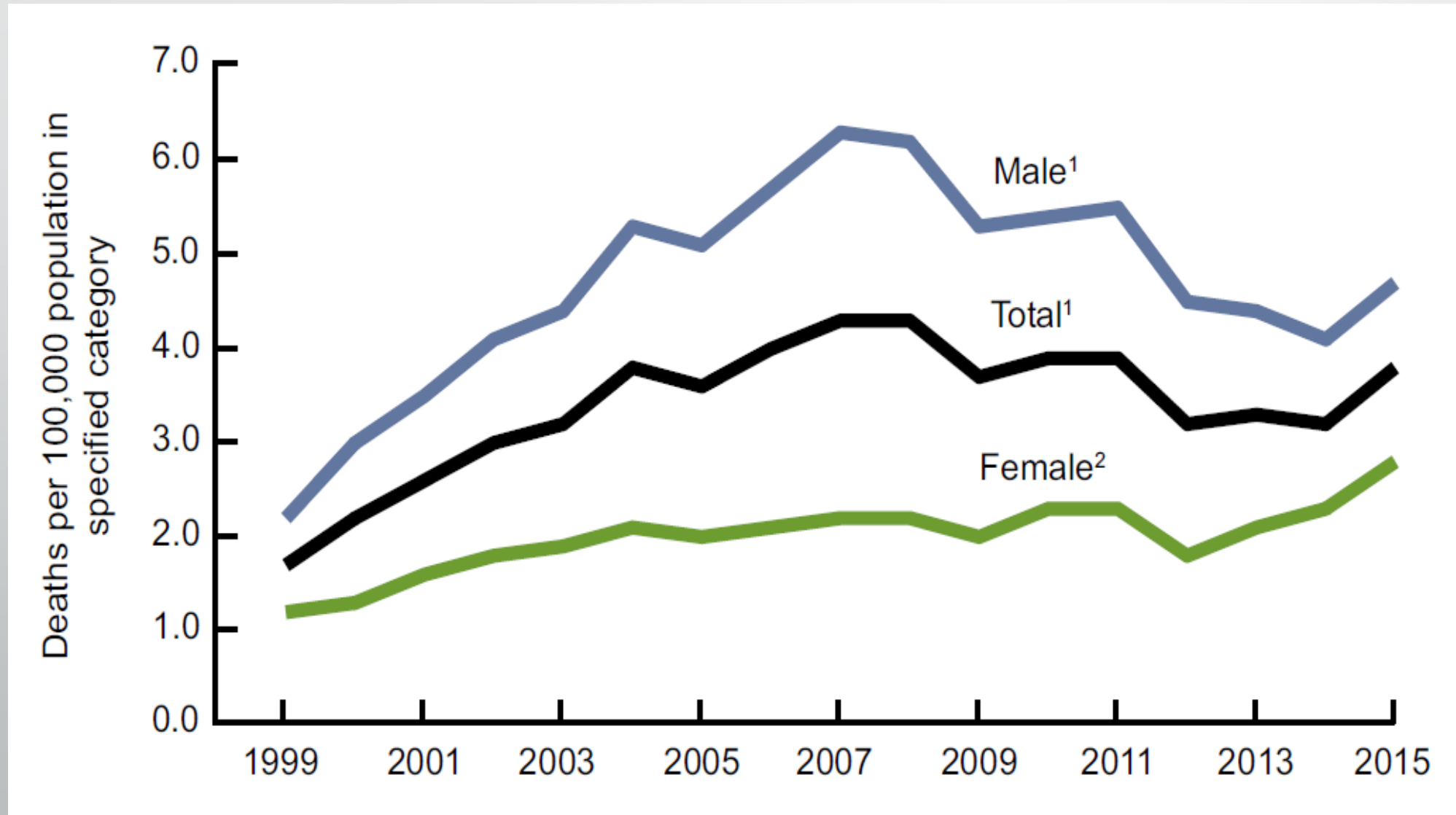
Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2016



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2016. <https://wonder.cdc.gov/>.

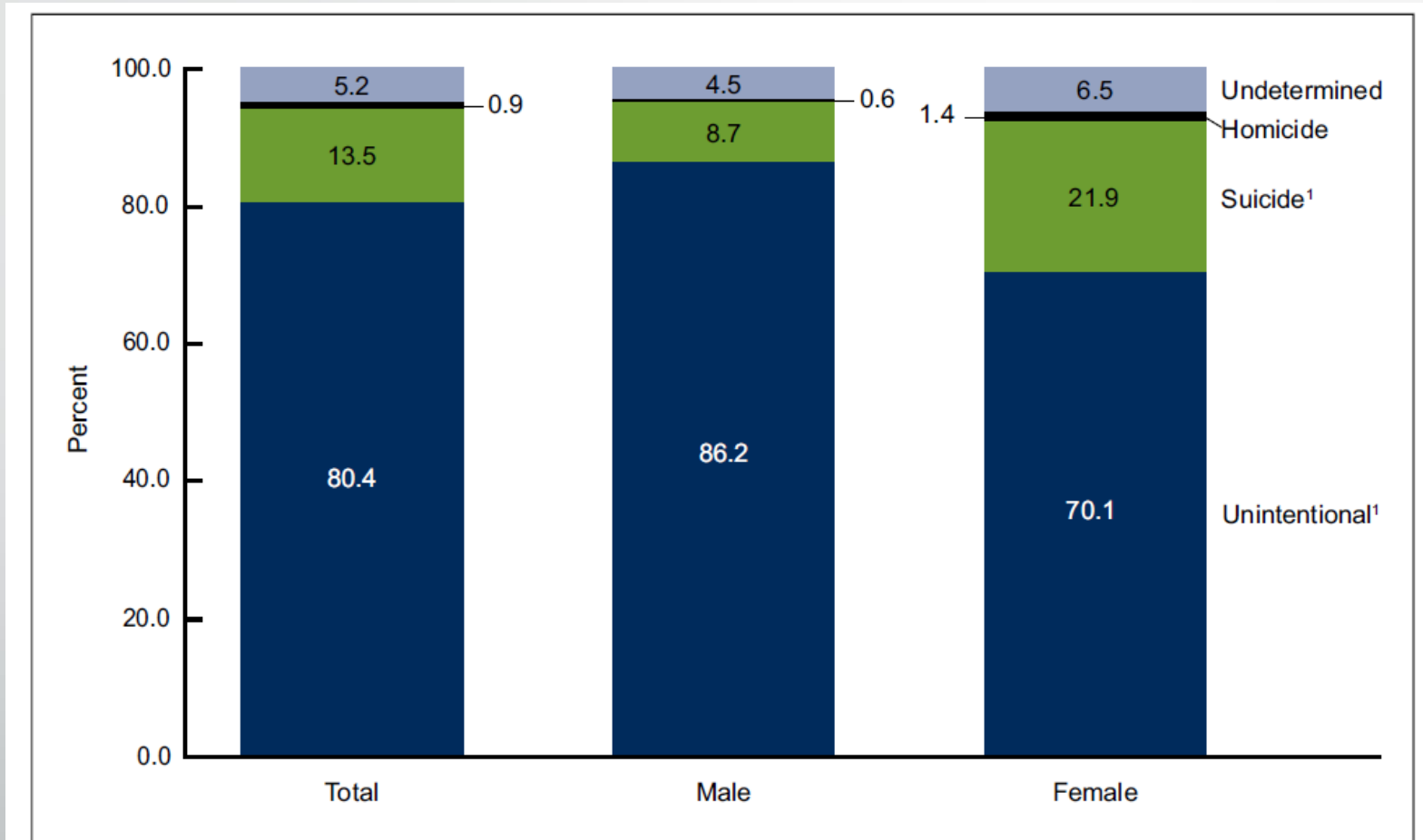
www.cdc.gov
Your Source for Credible Health Information

Drug overdose death rates for adolescents aged 15–19, by sex: United States, 1999–2015



Source: NCHS, National Vital Statistics System, Mortality

Percent distribution of drug overdose deaths for adolescents aged 15–19, by intent and sex: United States, 2015



¹Differences in percentages for males and females were statistically significant; $p < 0.05$.

NOTES: Drug overdose deaths are identified with *International Classification of Diseases, Tenth Revision* underlying cause-of-death codes X40–X44 (unintentional), X60–X64 (suicide), X85 (homicide), and Y10–Y14 (undetermined). Figures may not add to 100 due to rounding. Access data table for

A MOTHER'S KISS



Is Not Half So Soothing to
Baby as

Mrs. Winslow's Soothing Syrup

As Millions of Mothers
Will Tell You.

It Soothes the Child.

It Softens the Gums.

It Allays all Pain.

It Cures Wind Colic.


It is the Best Remedy for Diarrhoea.

It is absolutely harmless and for over sixty years has proved the best remedy for children while teething.

BE SURE YOU ASK FOR

Mrs. Winslow's Soothing Syrup

AND TAKE NO OTHER.



Management of Opioid use disorders (OUD)

- Opioid withdrawal treatment (OWT)
- Opioid maintenance treatment (OMT)
 - *Dispensing and/or prescribing of a full or a partial mu agonist on a long term basis*

OWT

- Extremely high relapse rates > 90%
- High risk for OD upon relapse
- Abstinence based approach is not the best treatment for opioid addiction
- *Treatment outcomes for behavioral interventions alone for opioid use disorders are dismal*
- *Outcomes for better for medication without behavioral interventions, but best for both combined*



Goals of OMT

- Eliminate or reduce illicit opioid use
- Eliminate drug cravings and withdrawal symptoms
- **Decrease HIV/Hepatitis seroconversion**
- Decrease in criminal behavior
- Improve social and occupational functioning & normalize brain functioning

FDA approved treatments

- **Methadone** (Liquid 10mg/ml)
- **Buprenorphine/Naloxone (BUP-NX):**
sublingual films/tablets, buccal film
- **Buprenorphine:** sublingual tablets, XR SQ
monthly preparation
- **Naltrexone:** tablets, IM monthly injection

Naltrexone

- Orally active opioid antagonist
- Half life 10-12hours
- Approved in 1984 for OUD
- Poor compliance with PO Naltrexone for heroin addiction
- In 2010 FDA approved the extended-release Naltrexone (XR-NTX) 380mg monthly IM
- Two recent studies showed that both XR-NTX and BUP-NX were equally safe and effective

Comparative effectiveness of XR-NTX versus BUP-NX for opioid addiction

XBOT (Clinical Trials Network)

- 570 participants, 24 week open label randomized control trial
- n= 283 for XR-NTX
- n= 287 for BUP-NX
- Substantial induction hurdle
 - 72% of XR-NTX successfully initiated compared to 94% for BUP-NX
- Once initiated, both equally safe and effective

Norwegian Study

- 159 participants, 12 week open label randomized control
- n= 80 for XR-NTX
- n=79 for BUP-NX
- XR-NTX was noninferior to BUP-NX as regards to
 - Retention
 - Number of opioid negative drug tests

Methadone

- Full mu agonist
- NMDA antagonist and is an SNRI
- Oral bioavailability 80%
- $T_{1/2}$ 24 hrs, metabolized by CYP₄₅₀ 3A₄, also 1A₂ & 2D6
- Biphasic elimination alpha 8-12 hours and beta elimination 30-60 hours
- Induction does not require patient to be in withdrawal
- Approved for opioid addiction (liquid/wafer) and analgesia (tablets)
- Dose range 60-120mg

Buprenorphine

- Partial mu agonist
- Weak kappa antagonist
- S/L bioavailability 55%
- $T_{1/2}$ 37hrs, metabolized by CYP₄₅₀ 3A₄
- Induction requires patients to be in withdrawal
- Tablets/Film approved for opioid addiction, patch approved for pain (Butrans)
- Dose range 8-16mg

Methadone

- Schedule II
- Dispensed for addiction treatment, prescribed for pain
- Approved in pregnancy
- May prolong QTc
- Limited to people in large metropolitan areas
- *Highly stigmatized treatment*

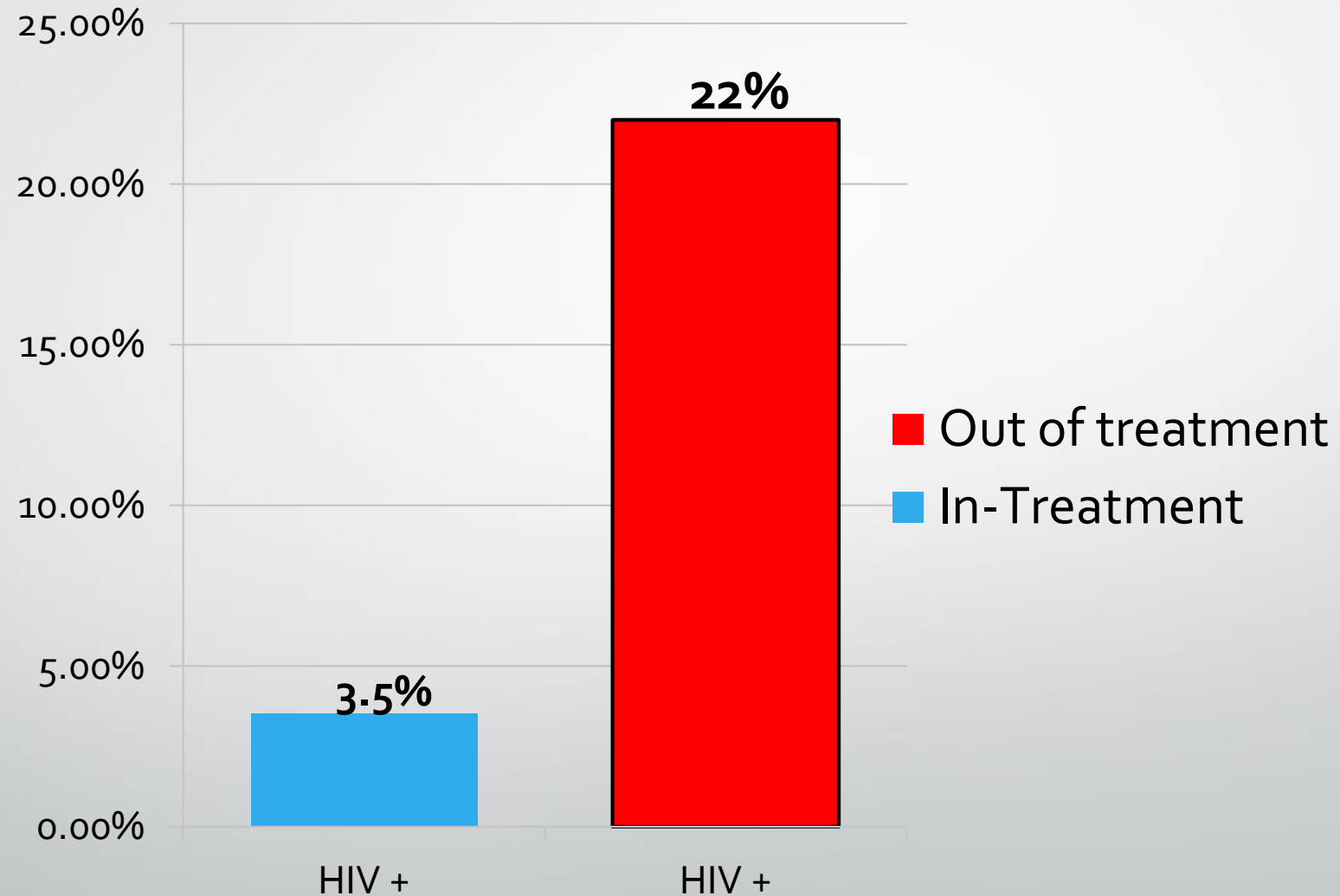
Buprenorphine

- Schedule III
- Prescribed to treat opioid addiction
- Studied in pregnancy (MOTHER Study)
- No cardiotoxicity
- Has increased access to care
- *Less Stigma associated*

Buprenorphine XR preparations

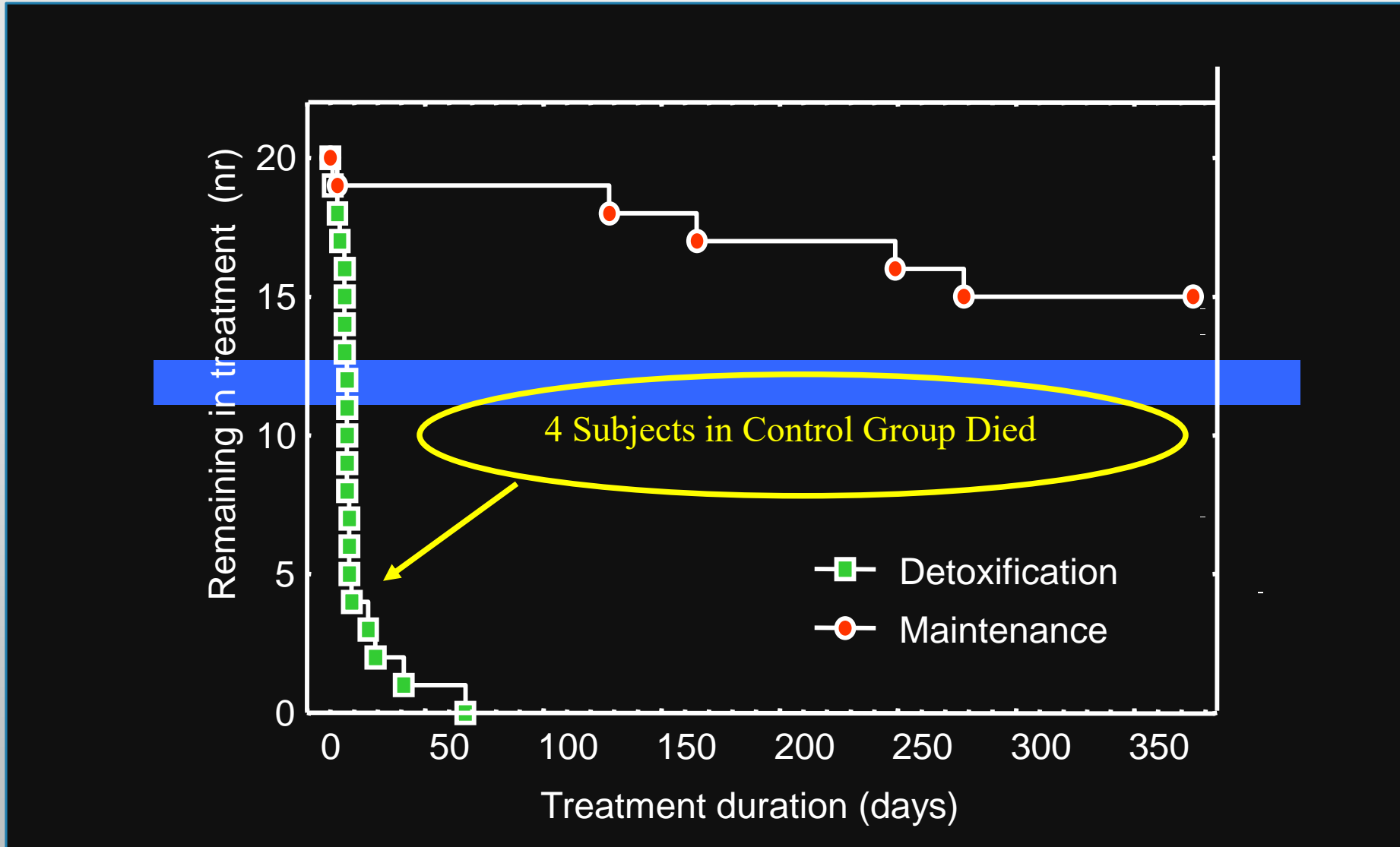
- In November 2017 FDA approved **Sublocade**, the first once-monthly injectable buprenorphine for the treatment of moderate-to-severe OUD
 - Indicated for patients stable on sublingual buprenorphine for at least 7 days
- FDA's Psychopharmacologic Drugs Advisory Committee recommended approval of CAM2038, an investigational buprenorphine weekly and monthly depot injection for the treatment of adults with OUD on November 1, 2017

Methadone Study: 18 Month Follow Up Of HIV- Subjects



(Metzger et al 1993)

Buprenorphine vs. Placebo for Heroin Dependence



Challenges

- Addiction still seen as “**moral failing**”
- We continue to **blame and shame** our patients
- **Stigma** persist against patients as well as approved treatments
 - Families/Friends/ 12 Step Sponsor
 - Providers

- **Access**

- Providers

- ❖ 49,000 waived physicians

- ❖ 48.1% of waived physicians were prescribing to 5 patients or fewer (Sigmon, 2015)

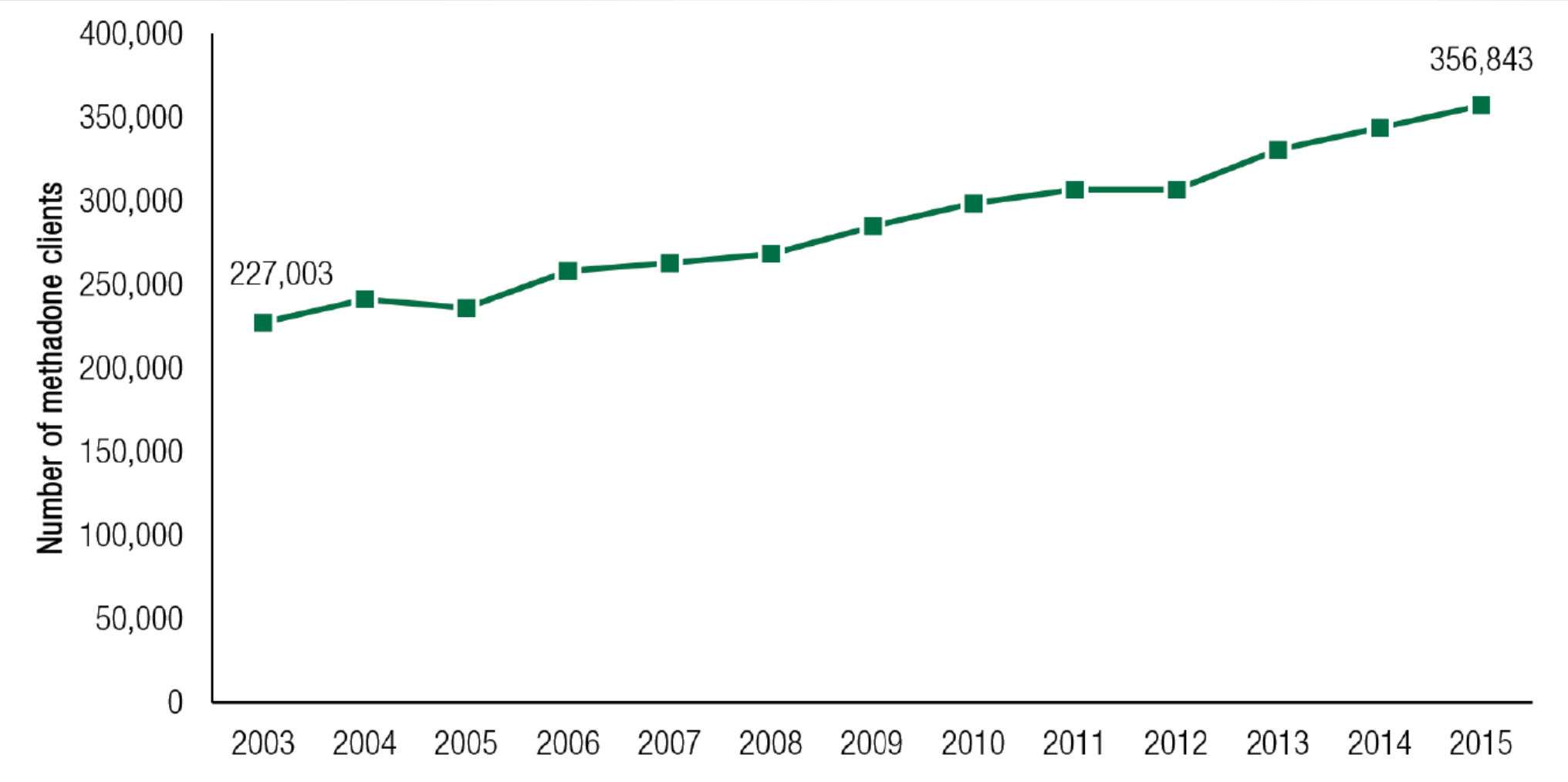
- Psychosocial treatment

- Pharmacological treatment

- Number of children in the Foster Care system

- Patients with chronic pain syndromes

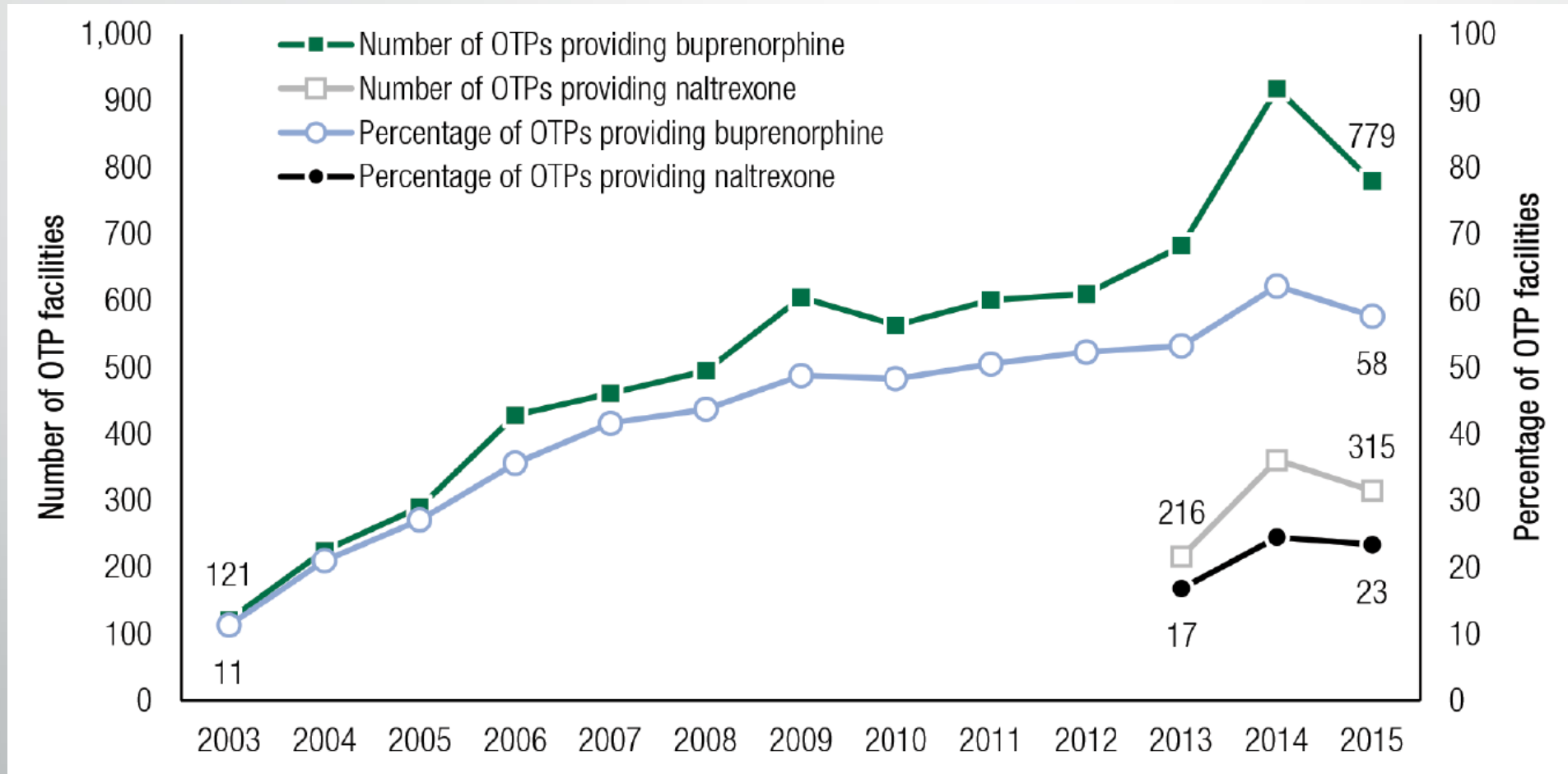
Number of Opioid treatment Programs (OTP) Patients Receiving Methadone: 2003 to 2015



Source: SAMHSA National Survey of Substance Abuse Treatment Facilities (N-SSATS), 2003 to 2015

Note: Patient counts were not collected in 2014; patient counts for 2014 are estimated

Number and Percentage of Opioid Treatment Programs (OTPs) Providing Buprenorphine and Extended Release Naltrexone: 2003 to 2015



Source: SAMHSA National Survey of Substance Abuse Treatment Facilities (N-SSATS), 2003 to 2015

Note: The first year Extended Release Naltrexone data were collected was 2013