Washington State Health Care Authority

Opioid Use Disorders &Medication Treatment

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Washington State Health Care Authority

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Learning Objectives:

1) Review recent trends and consequences of the current opioid epidemic
2) Describe the ‘science’ of opioid use disorder to better treat patients suffering from opioid use disorder
3) Discuss medication treatment

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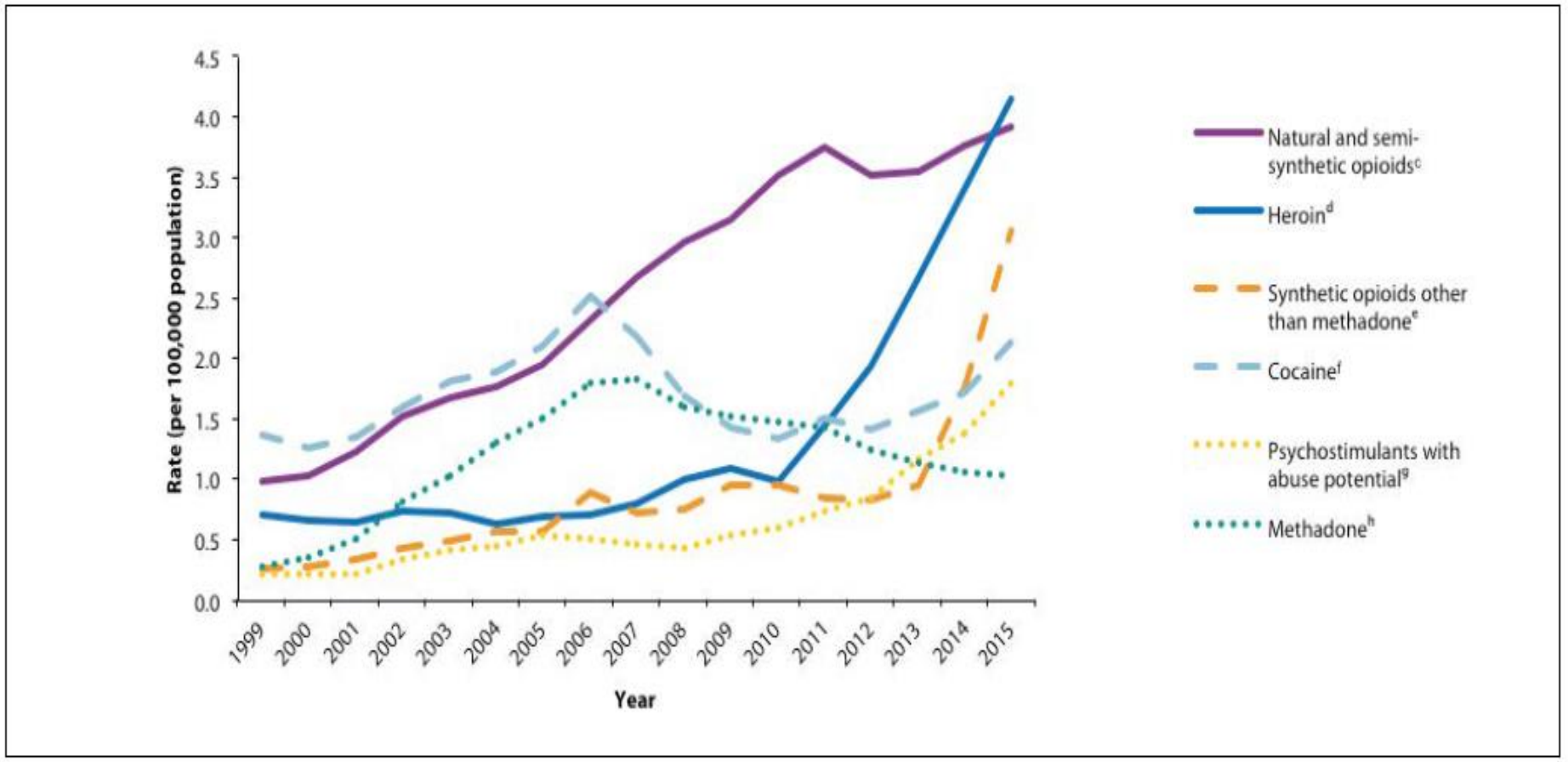
Age-adjusted drug overdose deaths by drug



Source: National Vital Statistics System, Mortality File, CDC WONDER.

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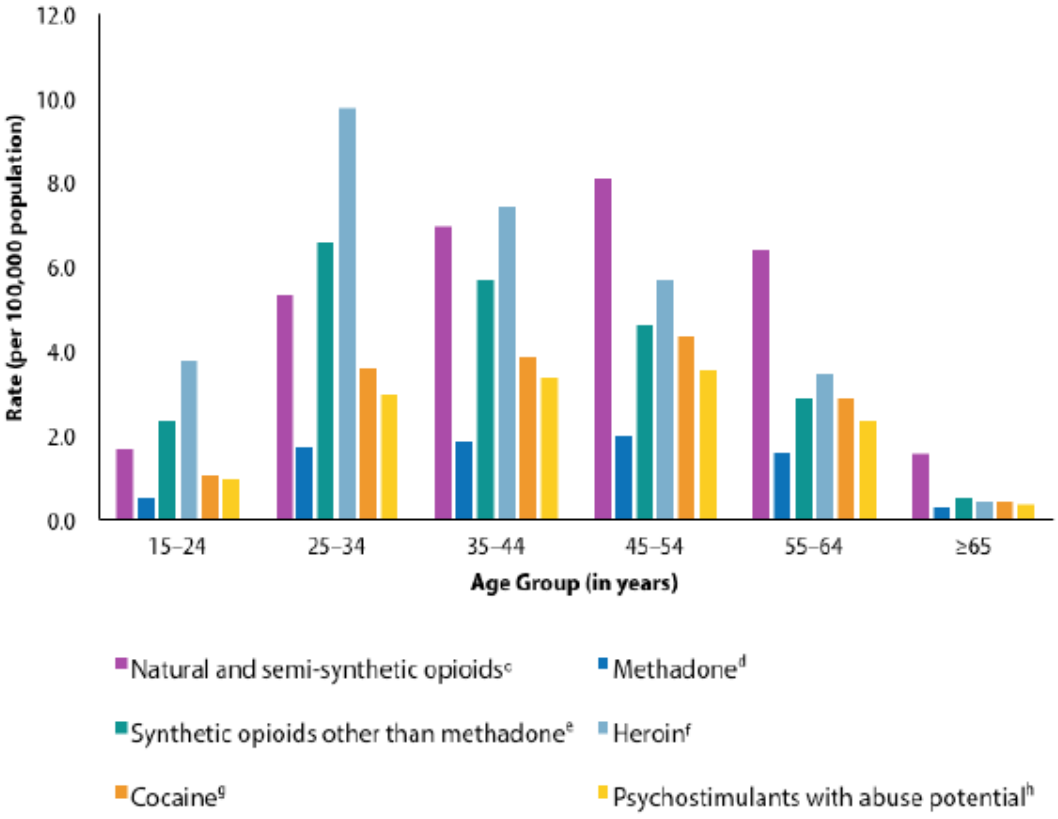
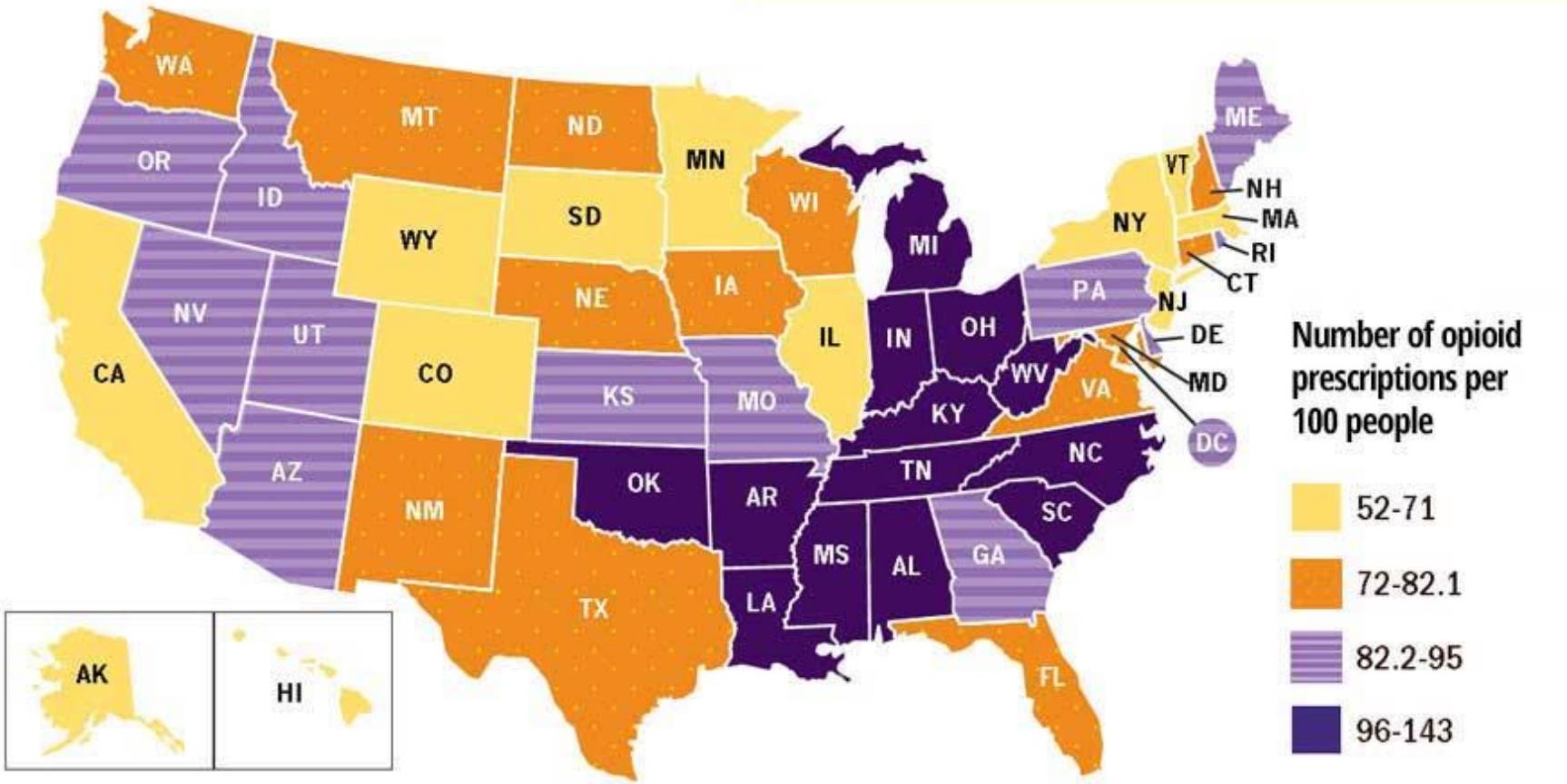
Age-adjusted drug overdose deaths by age



Source: National Vital Statistics System, Mortality File, CDC WONDER.

Some states have more opioid prescriptions per person than others.



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

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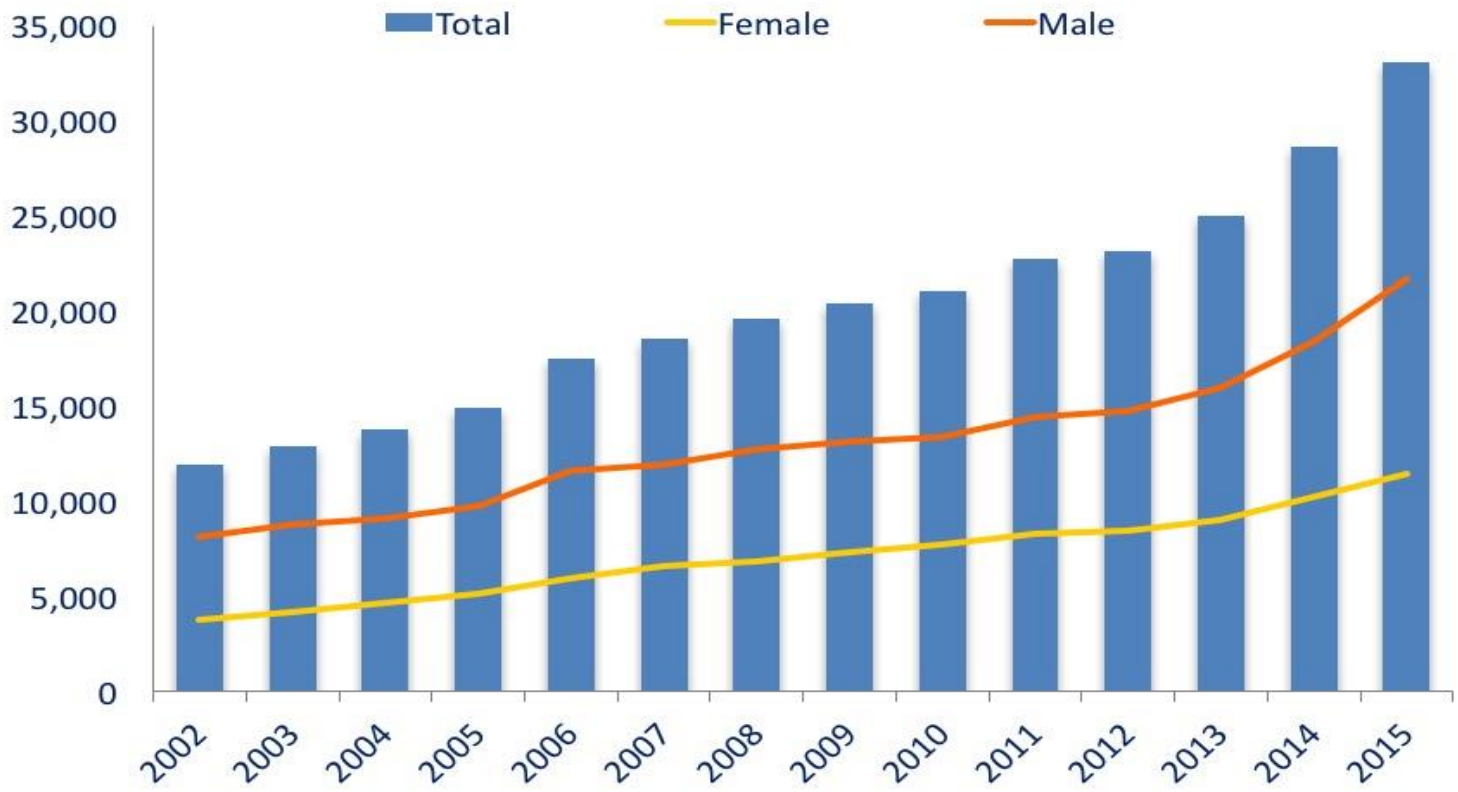
NIH National Institute on Drug Abuse

National Overdose Deaths

Number of Deaths Involving Opioid Drugs



Source: National Center for Health Statistics, CDC Wonder

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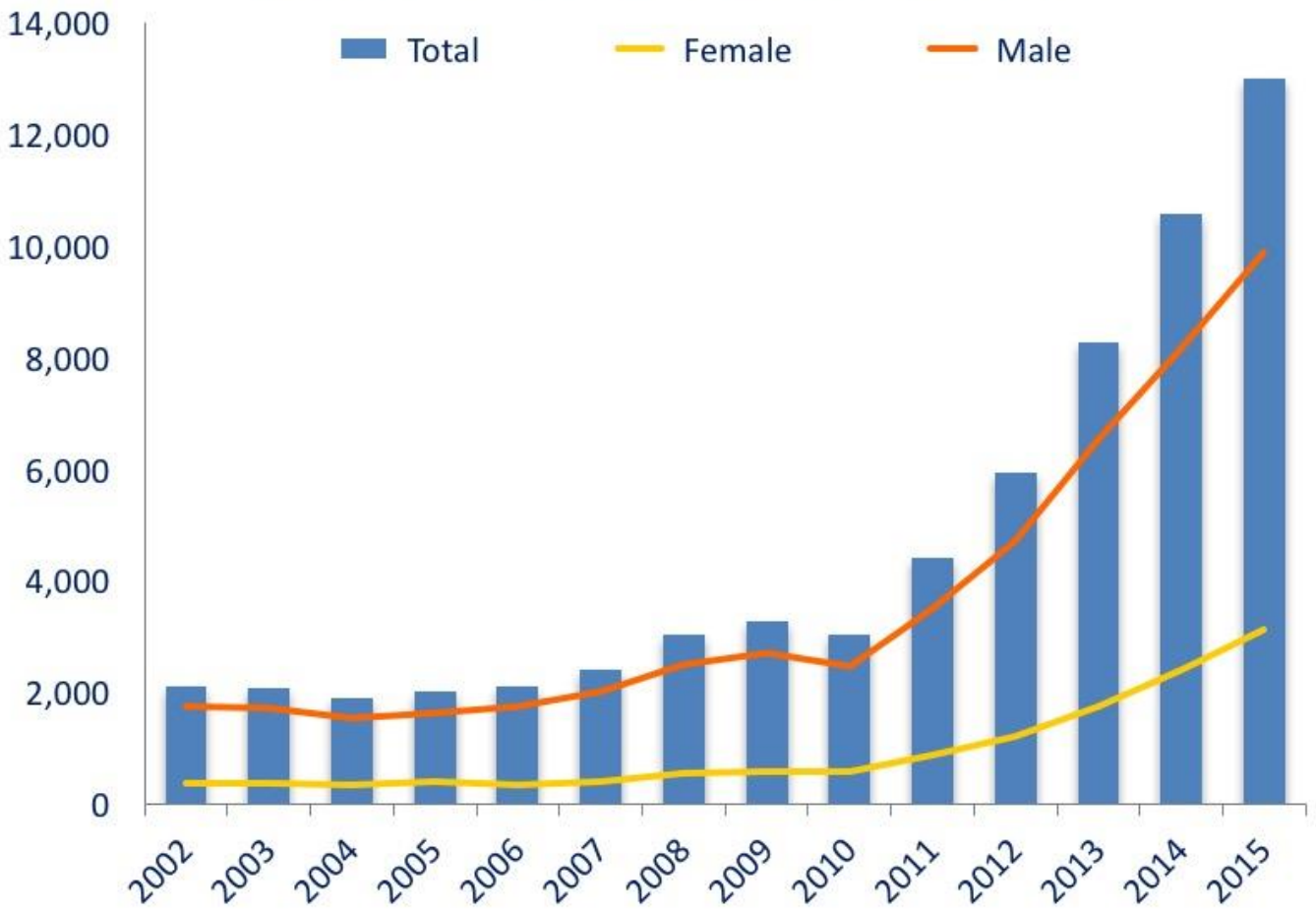
NIH National Institute on Drug Abuse

National Overdose Deaths

Number of Deaths from Heroin



Source: National Center for Health Statistics, CDC Wonder

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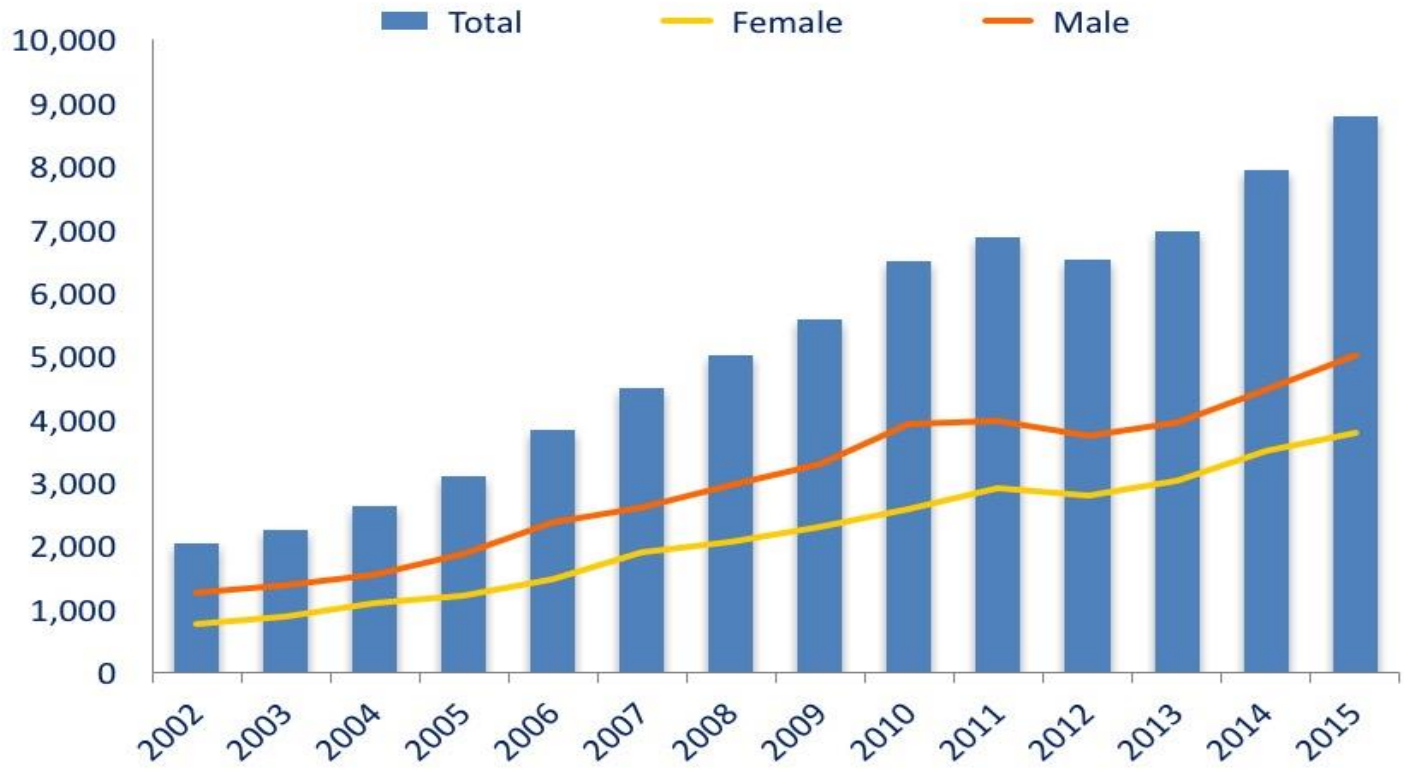
NIH National Institute on Drug Abuse

National Overdose Deaths

Number of Deaths Involving Benzodiazepines



Source: National Center for Health Statistics, CDC Wonder

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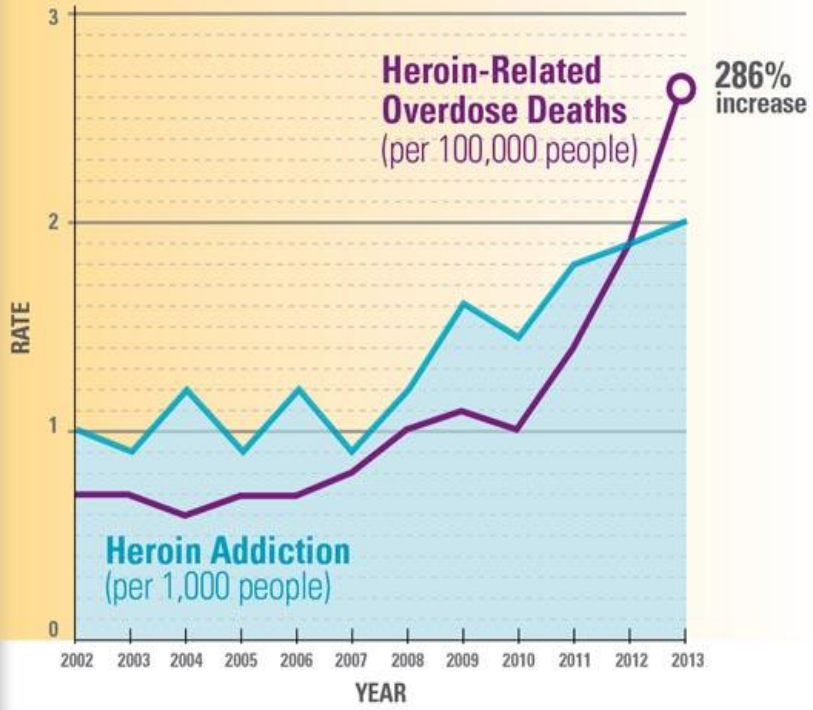
Heroin Use Has INCREASED Among Most Demographic Groups

	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%

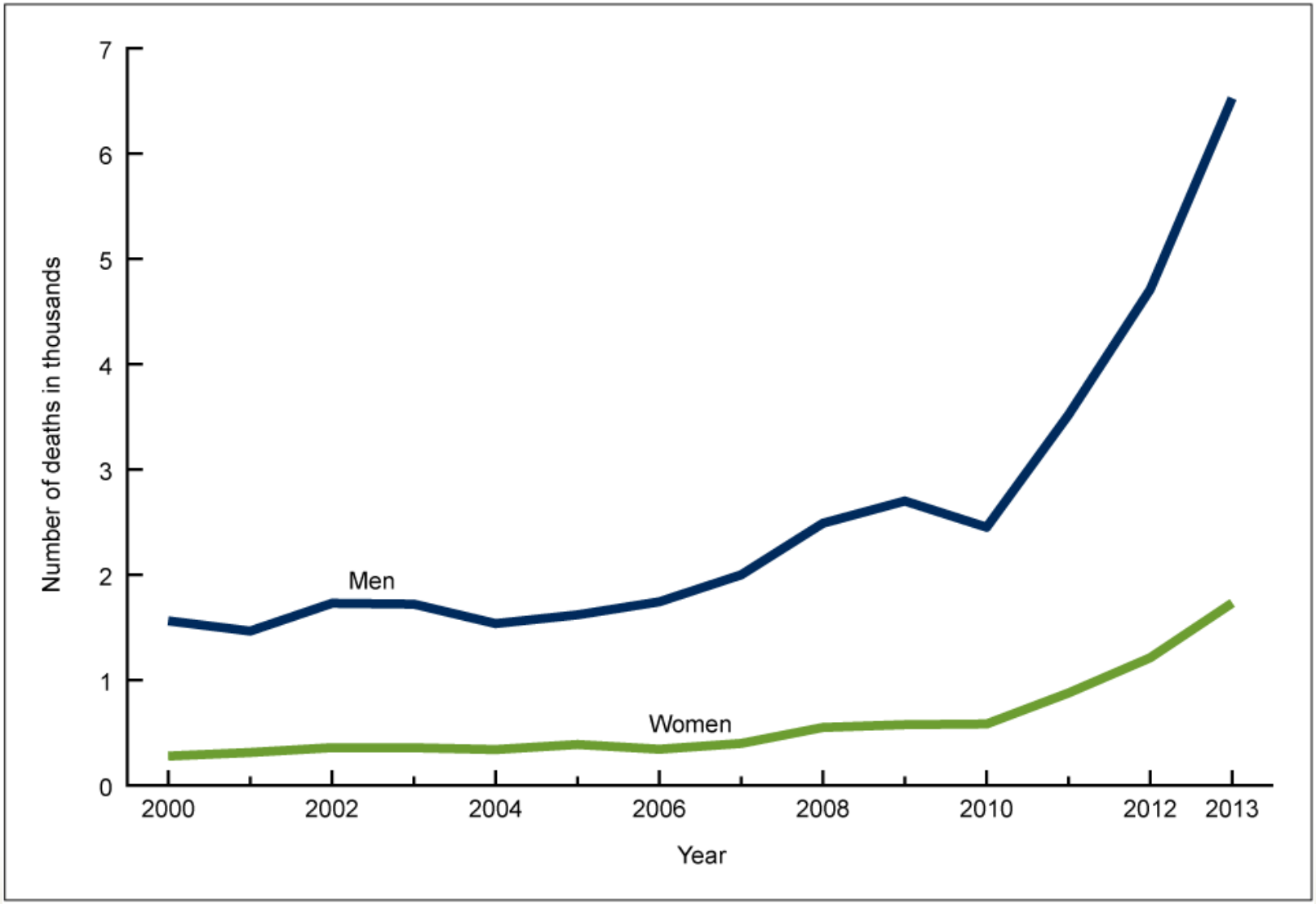
Heroin Addiction and Overdose Deaths are Climbing



SOURCES: National Survey on Drug Use and Health (NSDUH), 2002-2013.
National Vital Statistics System, 2002-2013.

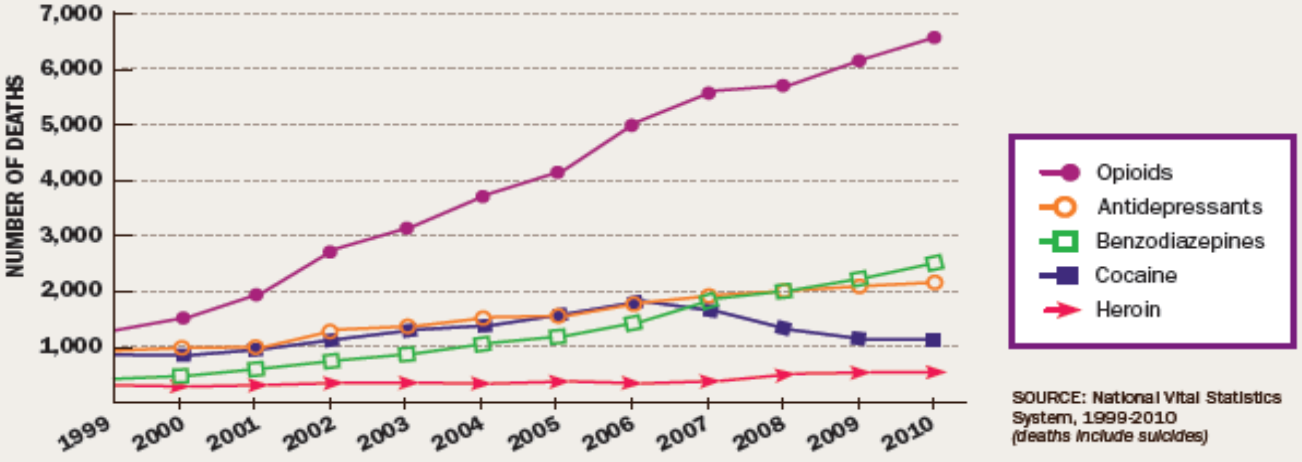
http://www.cdc.gov/drugoverdose/data/heroin.html

Figure 2. Number of drug-poisoning deaths involving heroin, by sex: United States, 2000–2013



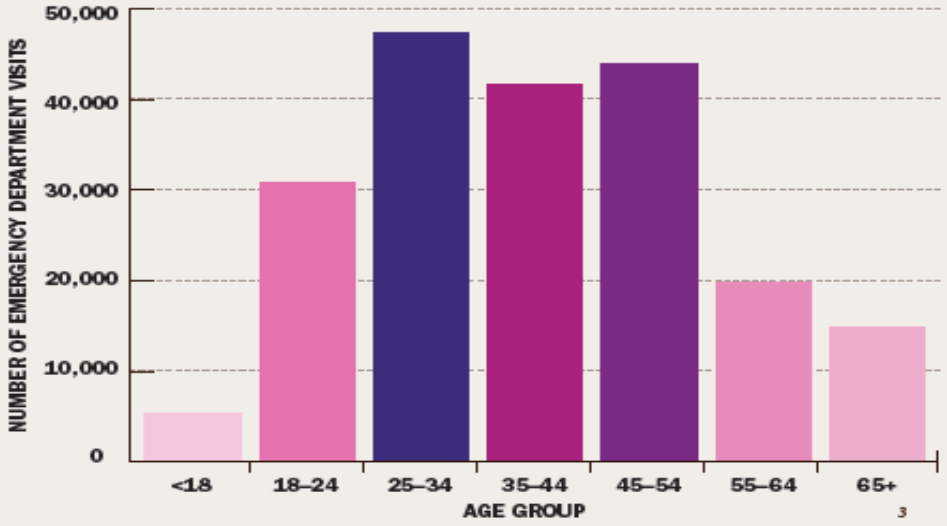
NOTE: Access data table for Figure 2 at: http://www.cdc.gov/nchs/data/databriefs/db190_table.pdf#2.
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality.

Prescription painkiller overdose deaths are a growing problem among women.



Women between the ages of 25 and 54 are most likely to go to the emergency department because of prescription painkiller misuse or abuse.

SOURCE: Drug Abuse Warning Network, 2010. (Suicide attempts are included for the cases (.03% of total) where opioids were combined with illicit drugs in the attempt.)



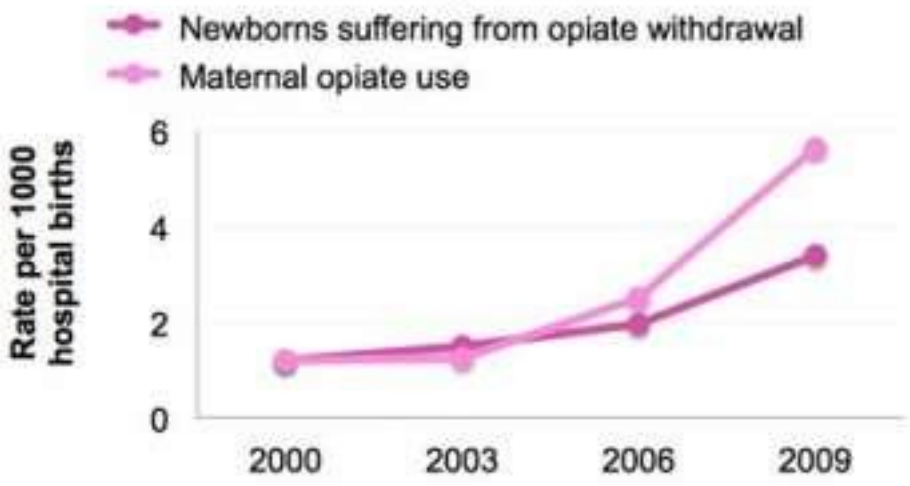
Every hour,

1 BABY

is born suffering from opiate withdrawal.

Average length or cost of hospital stay

NAS and maternal opiate use on the rise



Source: Patrick et. al., JAMA 2012

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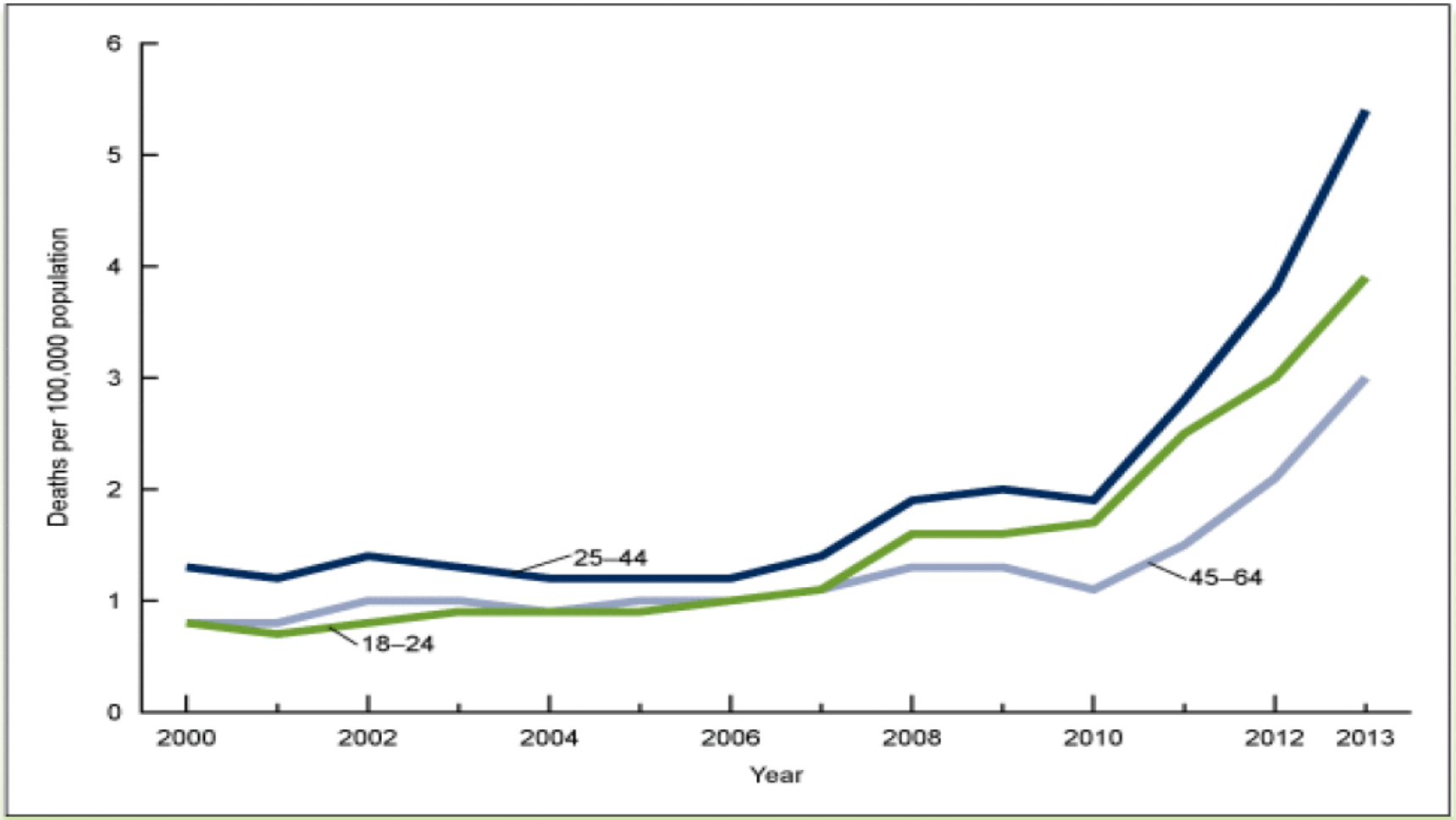
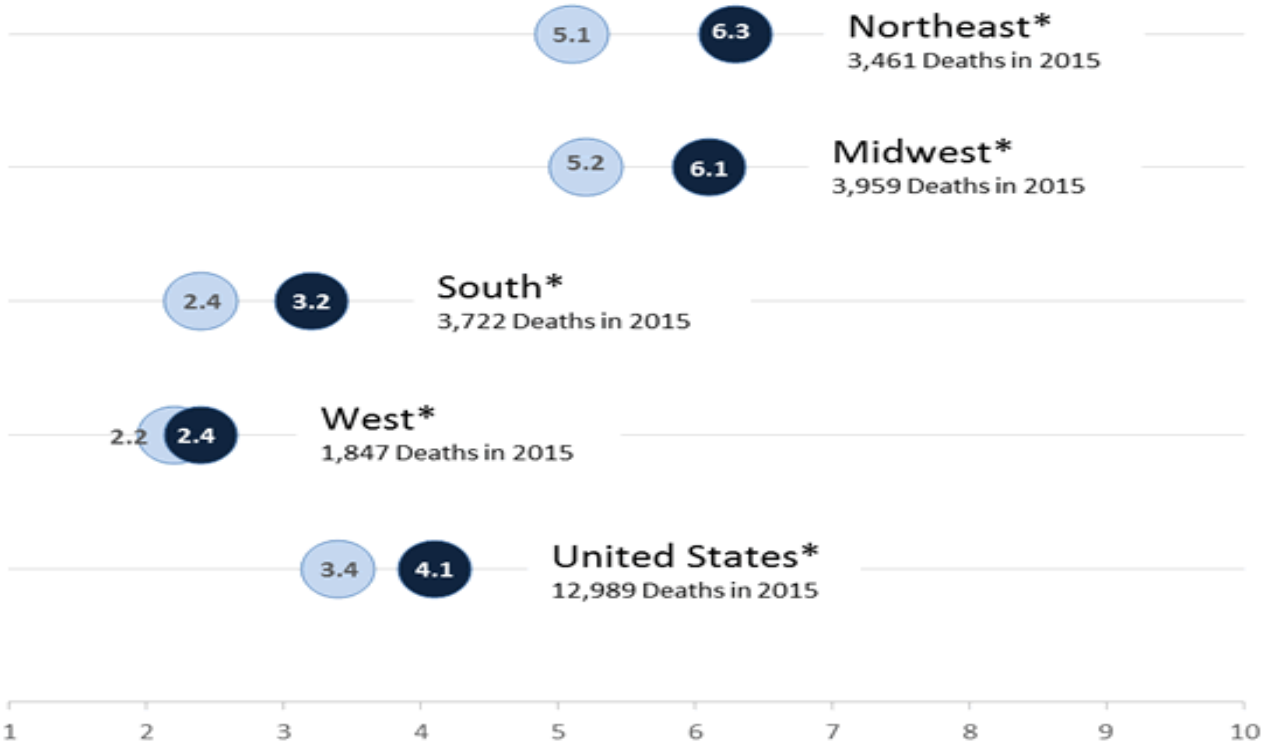
U.S. Heroin Related Overdose Deaths



Rates for drug-poisoning deaths involving heroin, by selected age groups: United States, 2000–2013
Courtesy CDC

Heroin Overdose Death Rates

Age-adjusted deaths per 100,000 population for heroin from 2014 to **2015**, by census region of residence



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/.

* Statistically significant at p<0.05 level.

www.cdc.gov
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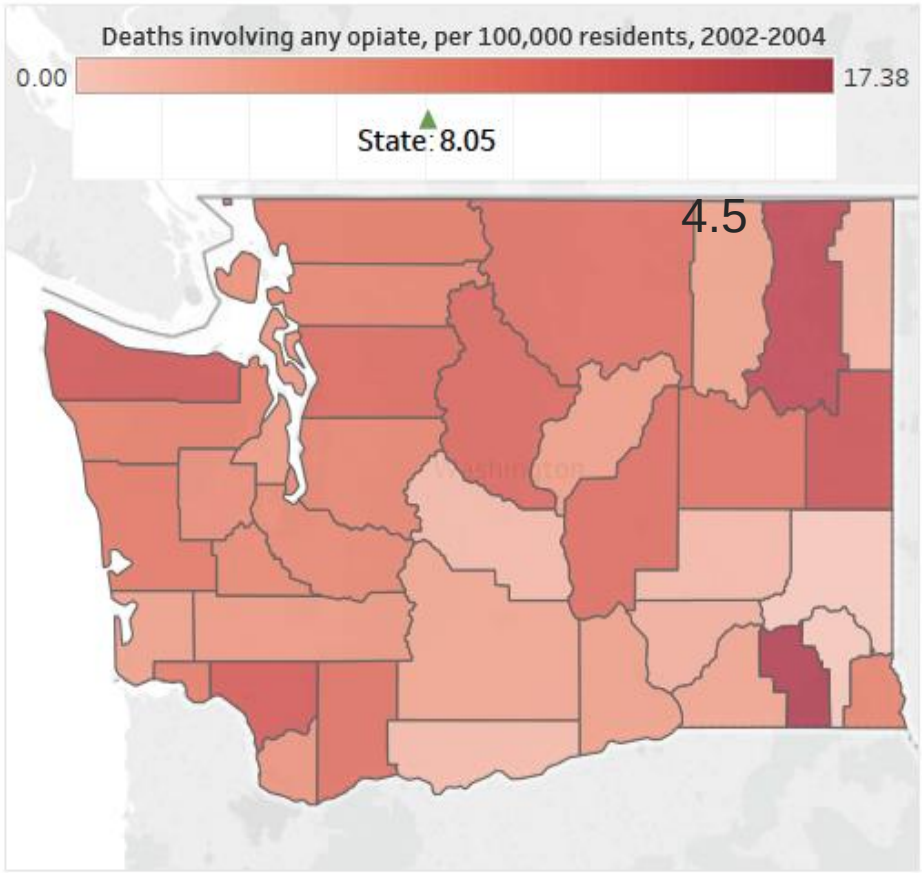
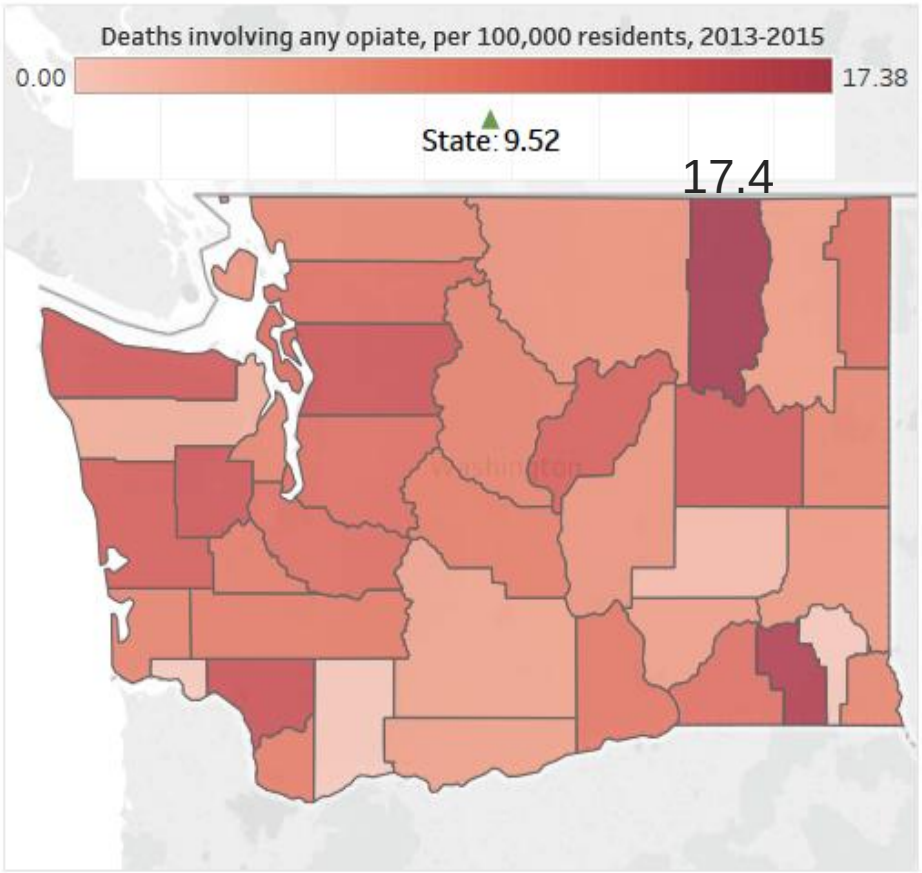
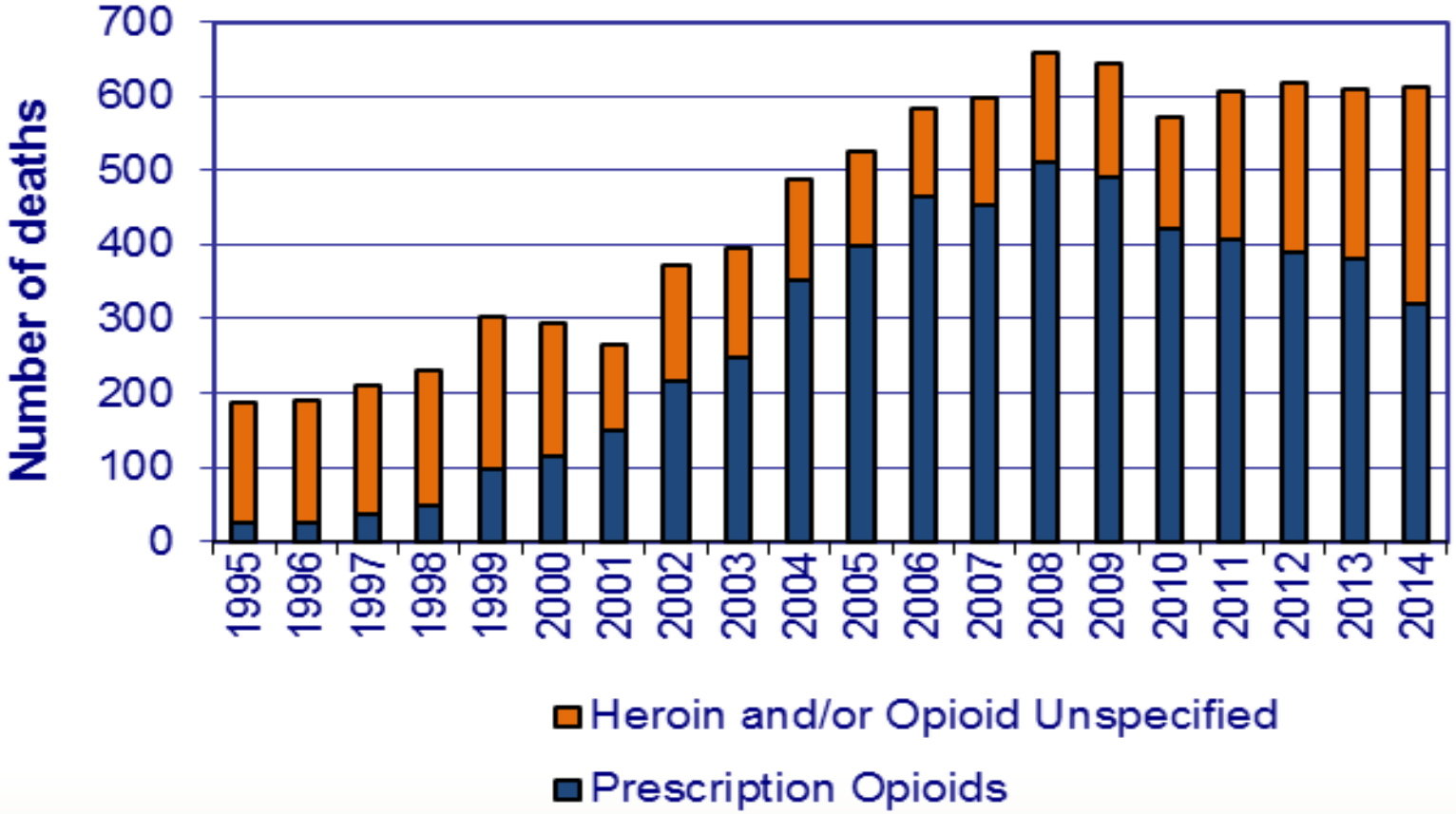
Opioid Overdose Deaths





https://adai.washington.edu/WAdata/deaths.htm

Unintentional Opioid Overdose Deaths Washington 1995-2014



Source: Washington State Department of Health, Death Certificates

Figure 2. Fentanyl-related, Opioid and Heroin Overdose Deaths, 2006-2016, Washington State

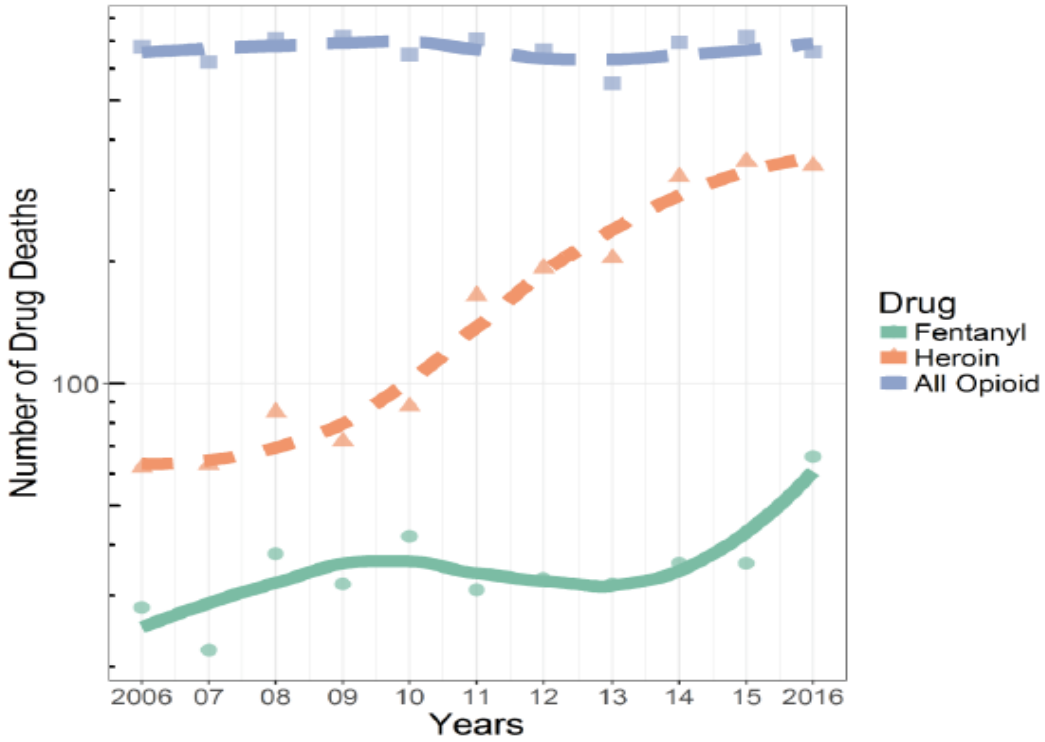


Figure 2 displays the trends in fentanyl-related, heroin and all opioid overdose deaths from 2006-2016 in Washington State. While overall opioid overdose deaths in Washington State have remained stable during this time period, heroin overdose deaths increased starting in 2010, and fentanyl-related overdose deaths increased starting in 2016.

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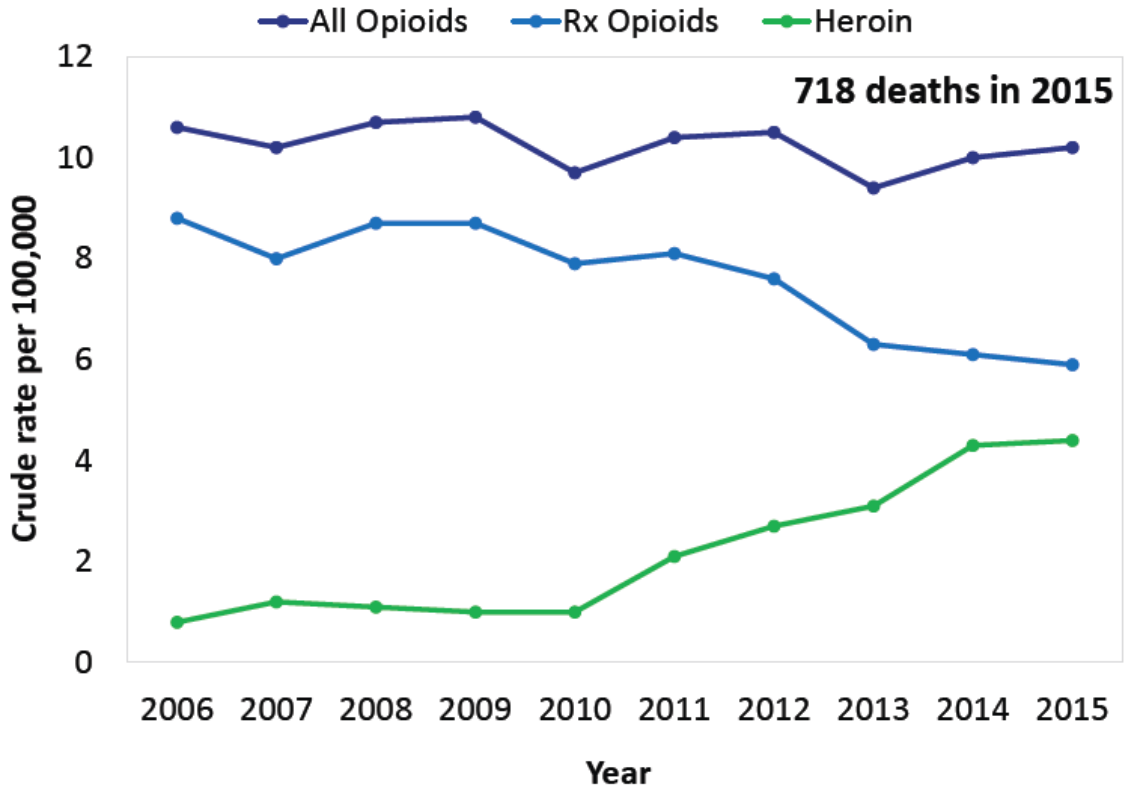
Rx opioid deaths are decreasing while heroin overdoses have risen sharply

Trends in WA state 2006-15, excluding falls



Source: Department of Health death certificates

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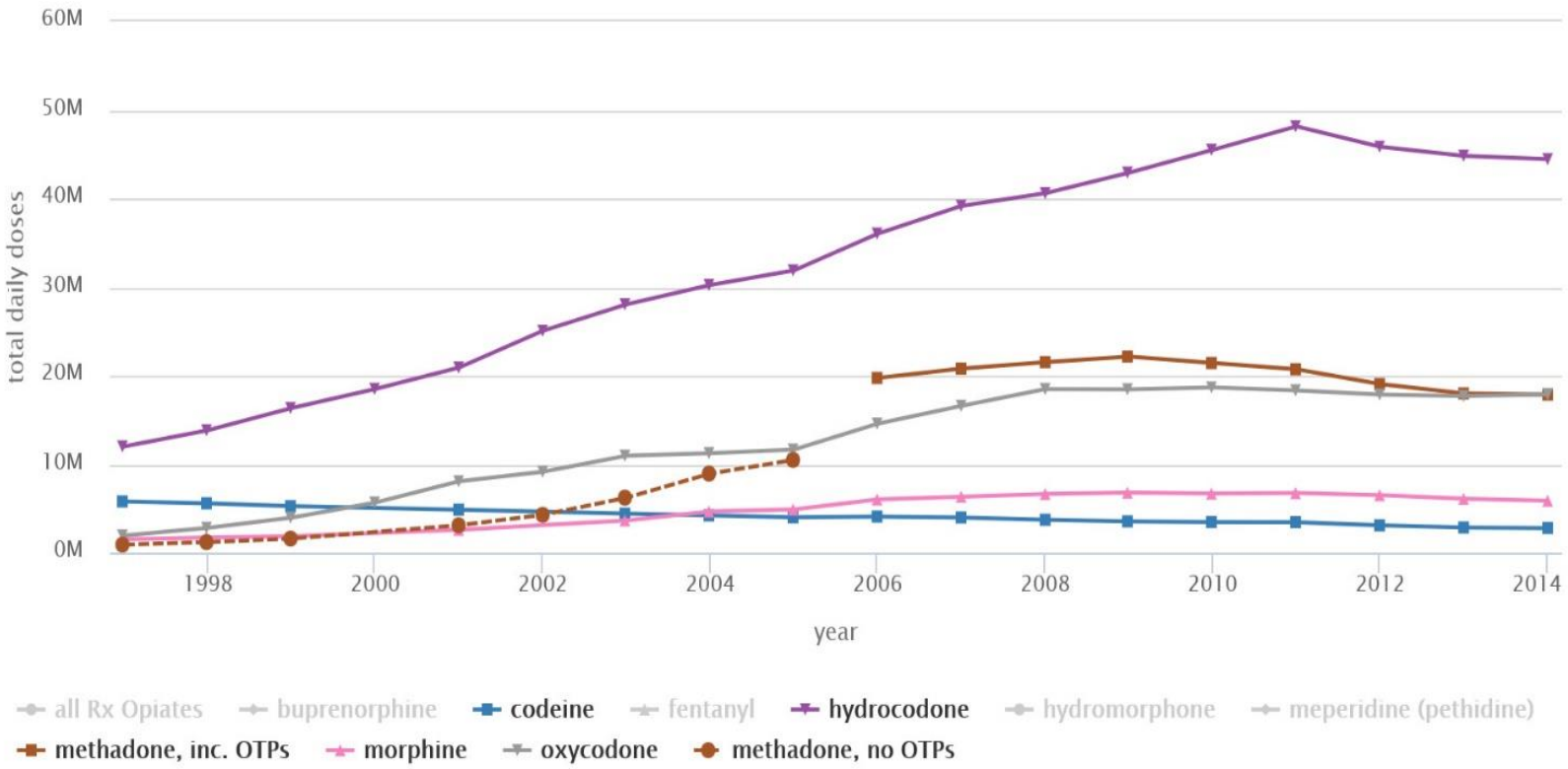
Opioids distributed in WA State (DEA ARCOS)



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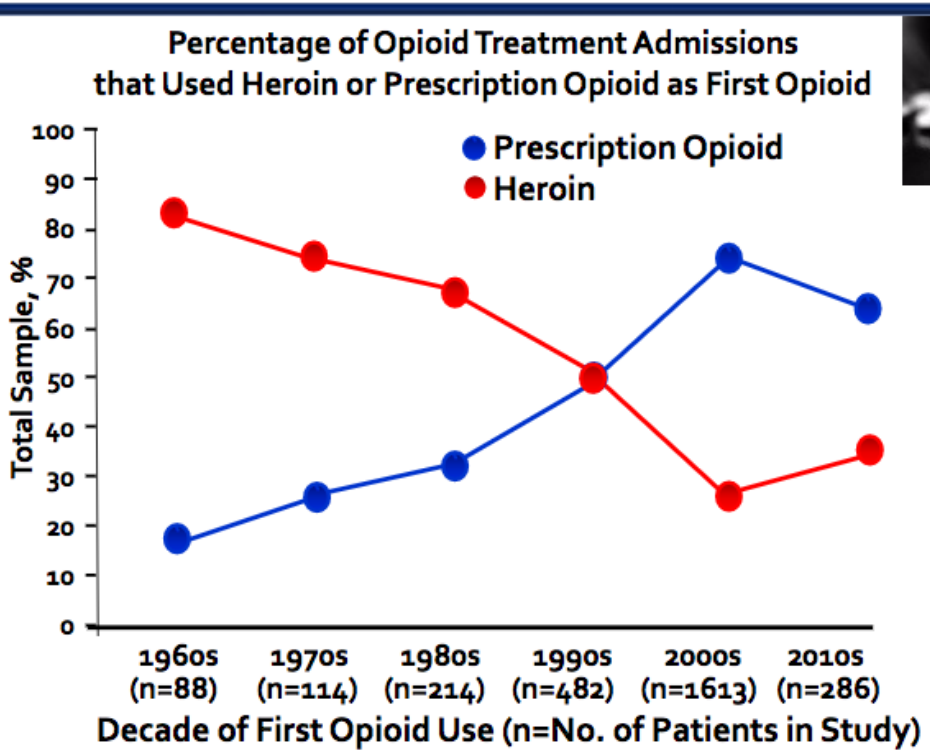
Which Drug is First Opioid in Treatment Seekers?
Shifting Pattern of Heroin vs. Rx Opioid First



Source: Cicero et al. JAMA Psychiatry. 2014;71(7):821-826

1960s: more than 80% started with **heroin**

2000s: 75% started with **prescription opioids**

2010-2013: Increasing initiation with **heroin**

Number of days supplied for opioid prescriptions

DAYS SUPPLIED PER PATIENT DURING THE YEAR
STATE AVERAGE VS. LOWEST AND HIGHEST PATIENT RESIDENTIAL AREAS

FEMALE PATIENTS

Age	Lowest Residential Area		State Avg	Highest Residential Area		High/ Low
2–6	Bellevue	5.5	11.2	19.6	Edmonds	3.5 x
7–11	Bellevue	6.1	11.2	35.0	Vancouver	5.7 x
12–19	Enumclaw	6.3	11.1	45.7	Port Angeles	7.3 x
20–44	Bellevue	27.7	56.0	165.0	Moses Lake	6.0 x
45–64	Pullman	47.7	84.1	156.3	Forks	3.3 x

MALE PATIENTS

Age	Lowest Residential Area		State Avg	Highest Residential Area		High/ Low
2–6	Bellevue	6.0	11.5	22.7	Edmonds	3.8 x
7–11	Bellevue	5.5	9.5	15.7	Port Angeles	2.9 x
12–19	Coupeville	5.5	9.0	20.8	Clarkston	3.7 x
20–44	Toppenish	27.4	51.7	170.1	Aberdeen	6.2 x
45–64	Bellevue	44.7	75.6	161.4	Aberdeen	3.6 x

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Different Regions, Different Care: A Report on Procedure Rate Variation in Washington State

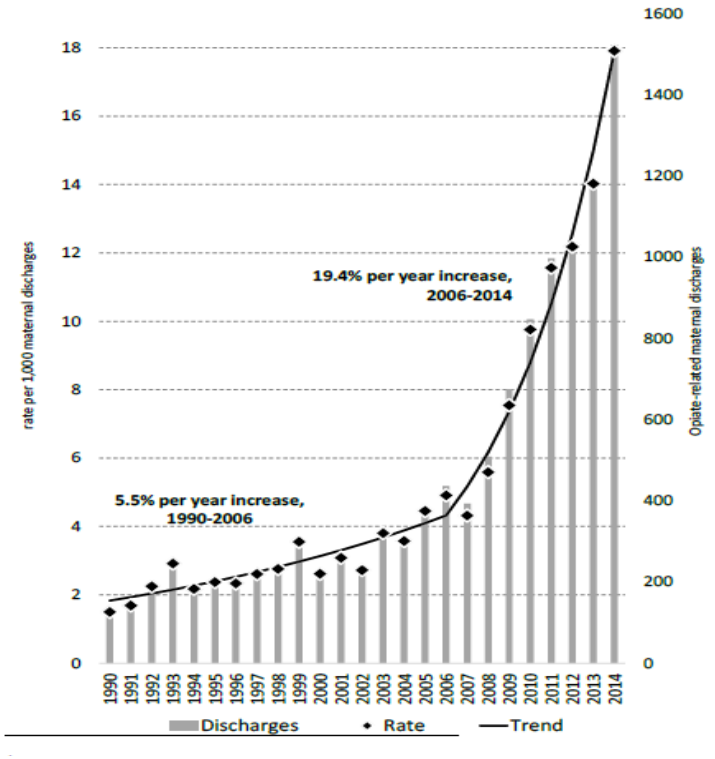
August 2016

(http://wahealthalliance.org/wp-content/uploads.php?link-year=2016&link-month=08&link=2016-different-regions-different-care-report.pdf)

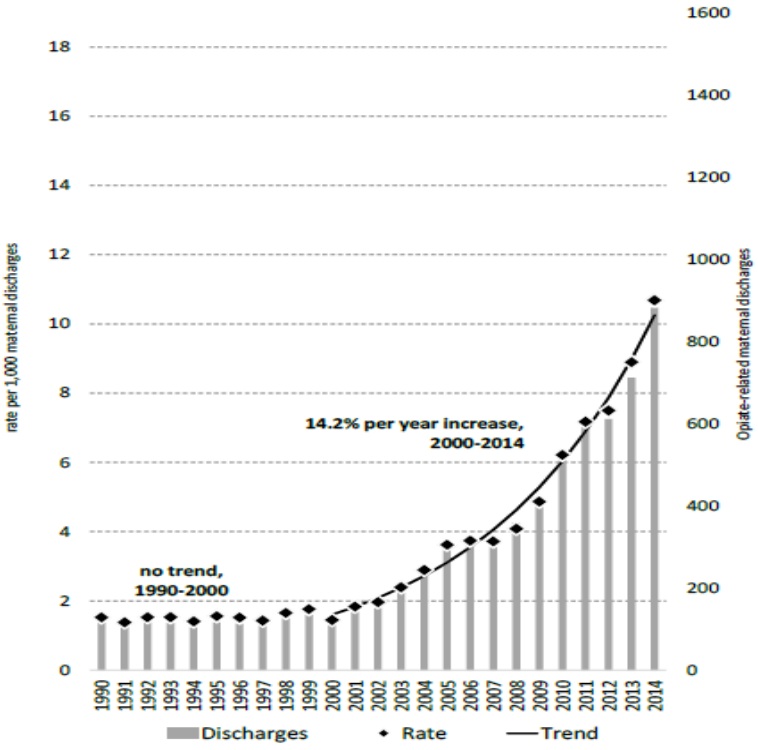
Washington State Department of Health

Maternal and Neonatal Hospitalizations in Washington

Figure 4
Maternal Stays with an Opiate-Related Diagnosis
WA Rates, Trends and Volumes, 1990–2014
WA and OR Inpatient Discharge Data

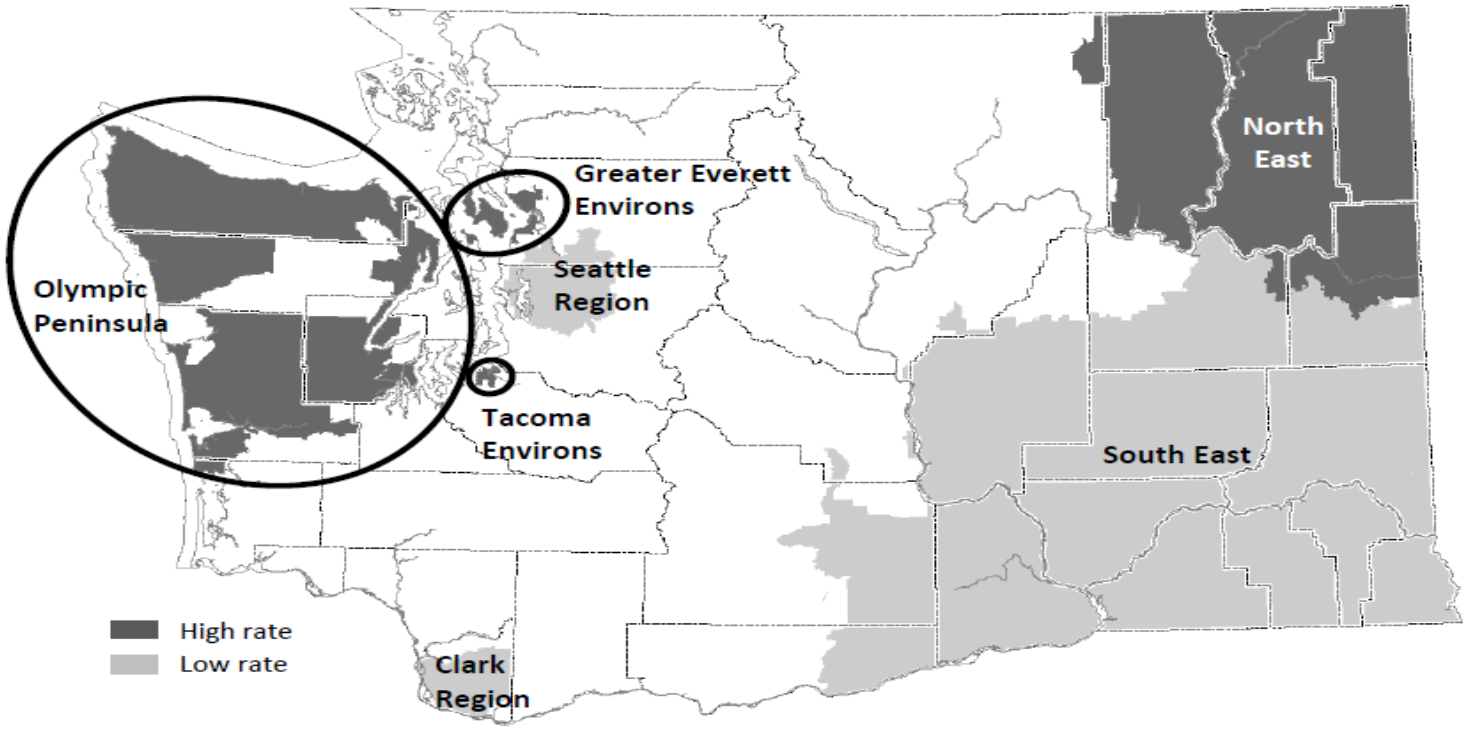


Newborns with Drug Withdrawal Syndrome Diagnosis
WA Rates, Trends and Volumes, 1990–2014
WA and OR Inpatient Discharge Data



Statewide Hot Spots Maternal Opioid Hospitalizations

Figure 8
Maternal Stays with an Opiate-Related Diagnosis: High- and Low-Rate Regions
2012–14 Combined
WA and OR Inpatient Discharge Data



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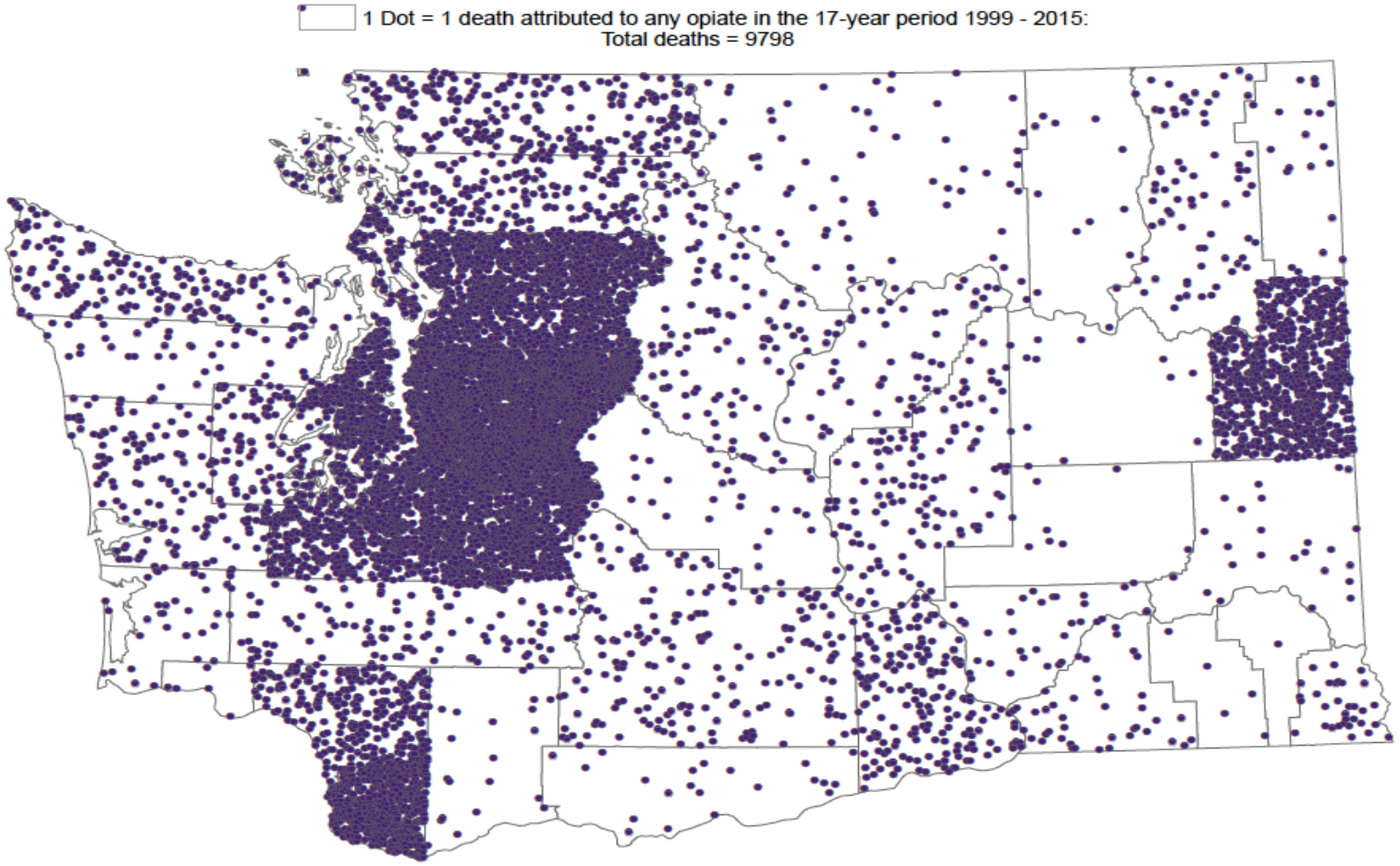
Opioid related overdose deaths in WA 1999-2015



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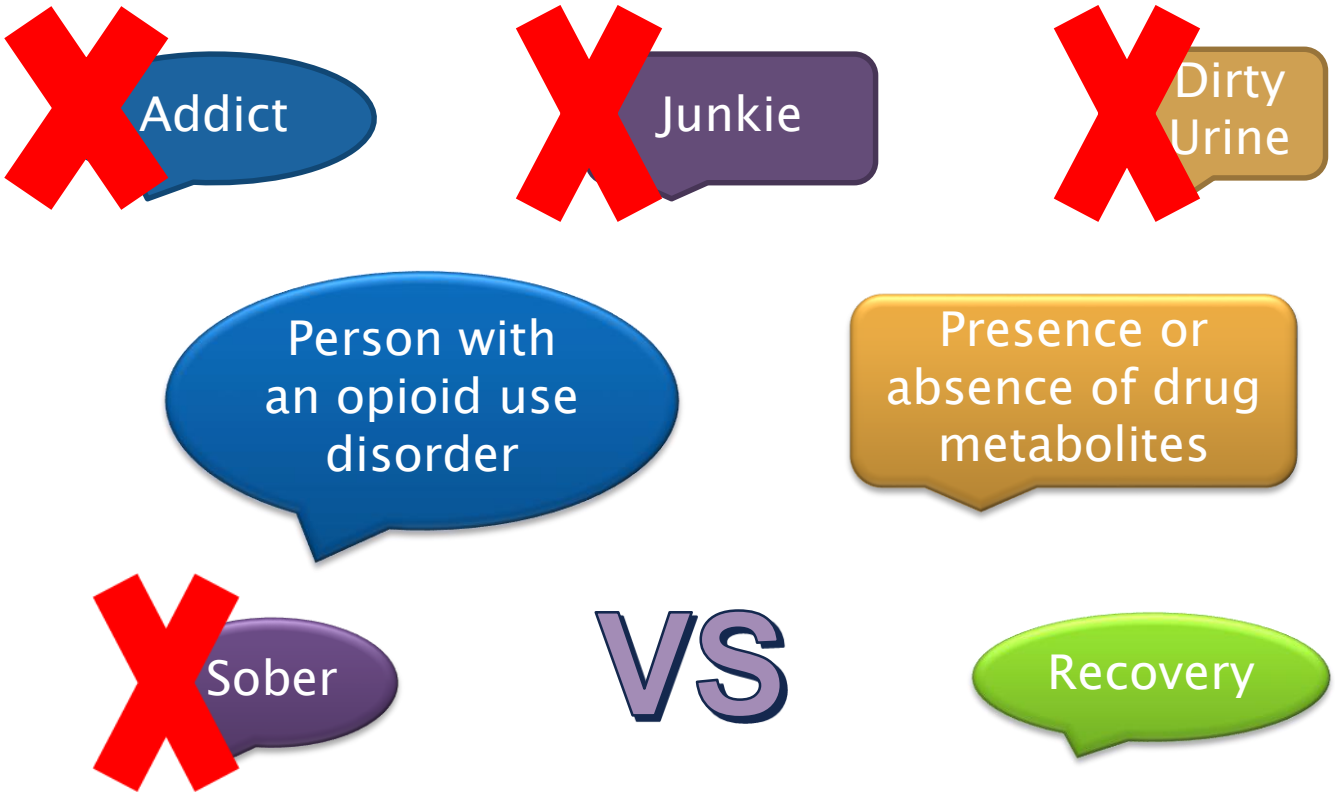
Words Matter



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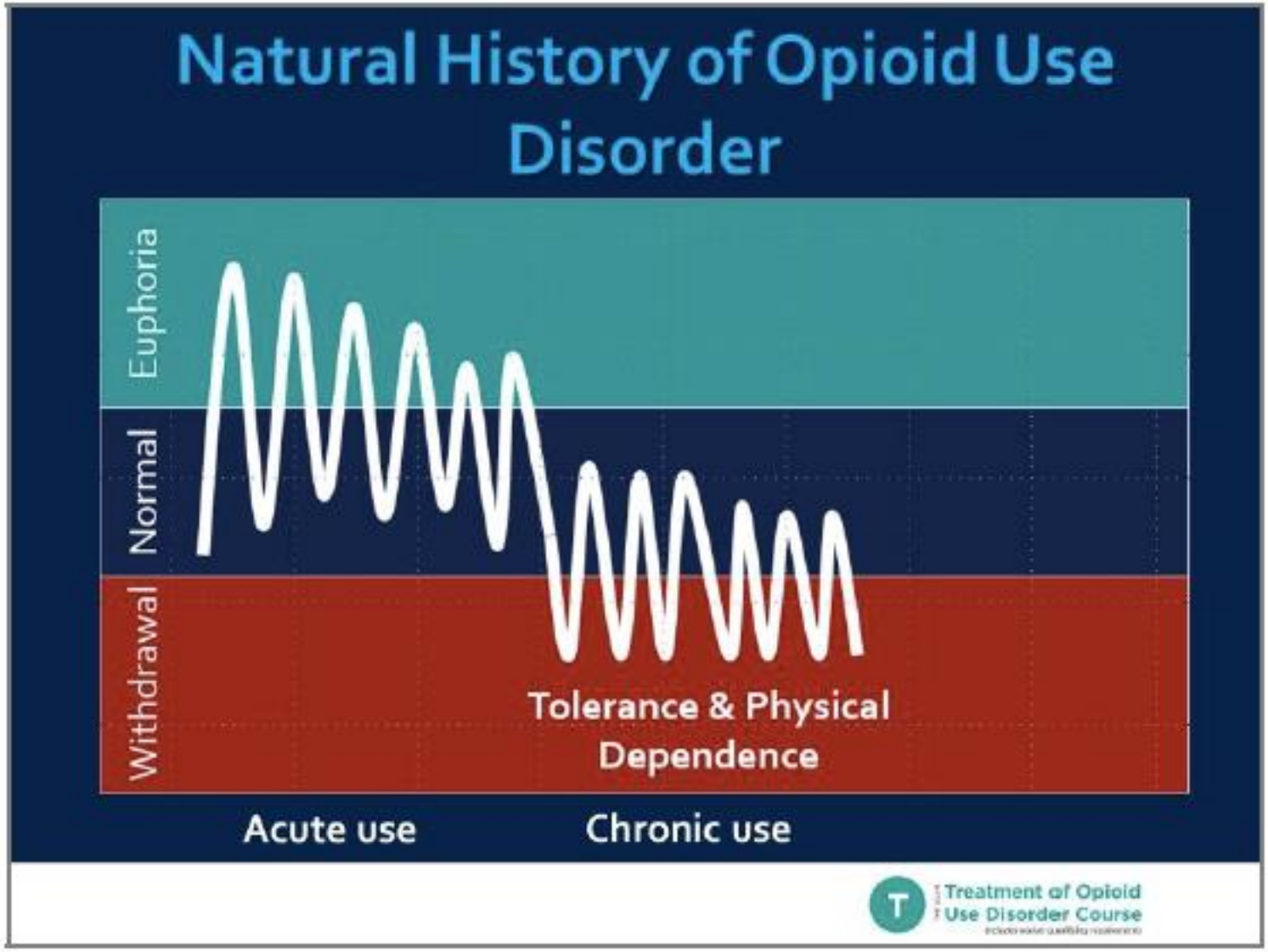
Current Treatment Options


Natural History of Opioid Use Disorder
Euphoria
Normal
Withdrawal
Tolerance & Physical Dependence
Acute use
Chronic use
Treatment of Opioid Use Disorder Course

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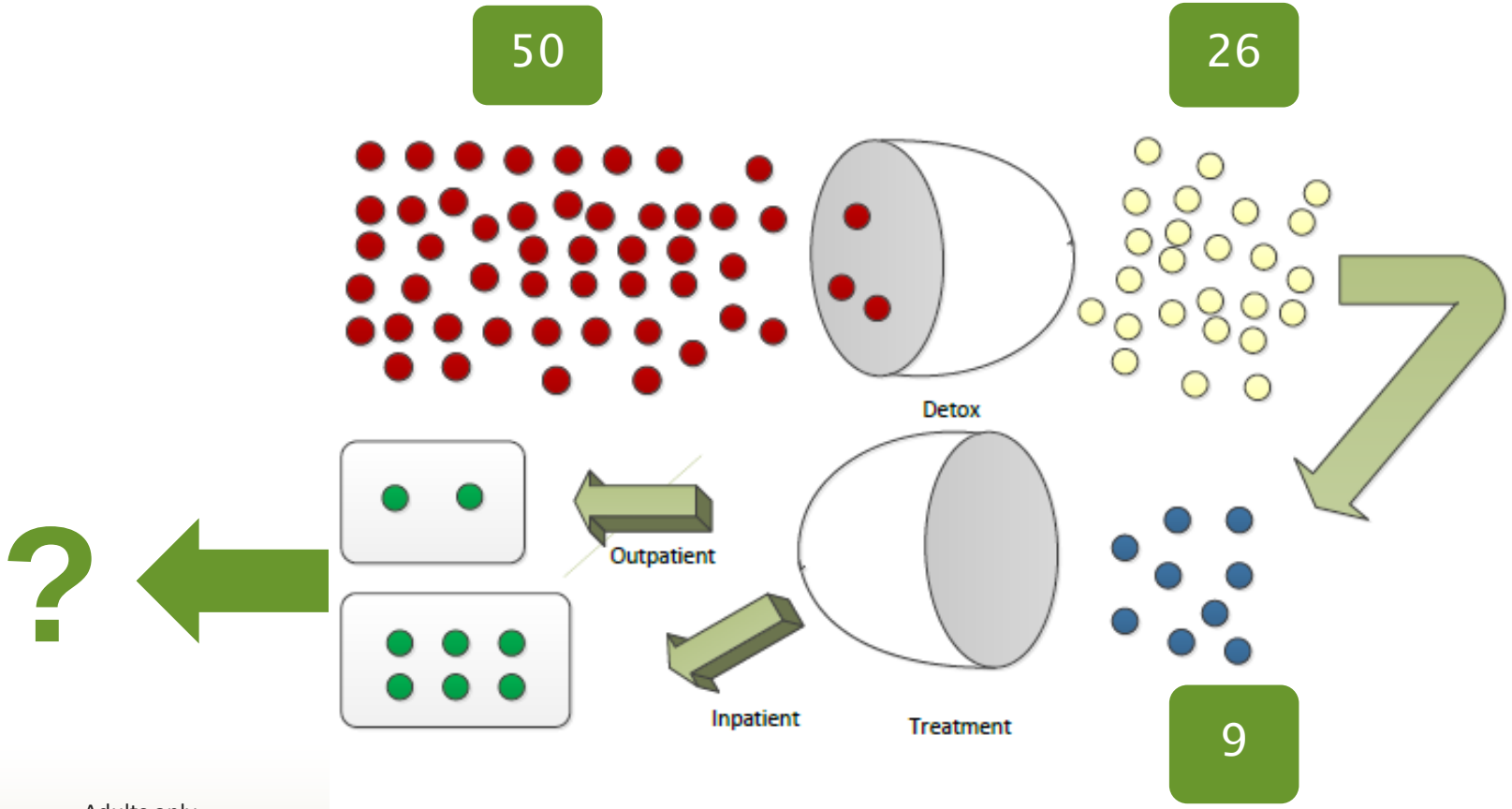
Persons w/Opioid Use Disorder Treated in the Public SUD System



Adults only
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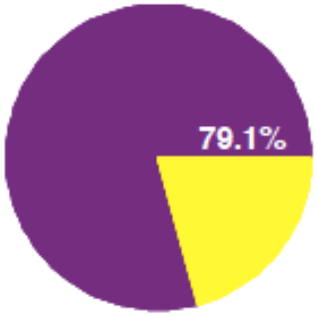
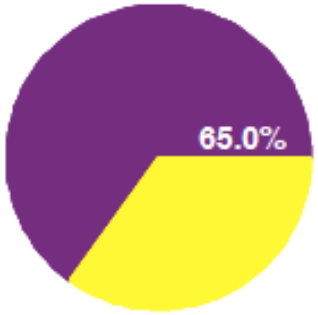
Retention with Opioid Treatment Providers 1/14-12/14

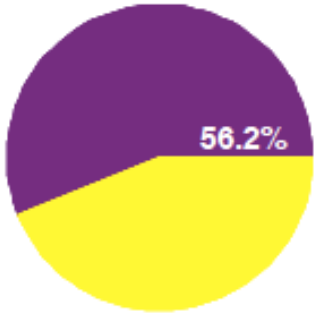
In treatment at least 3 Months



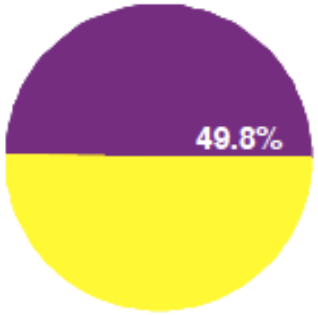
...6 Months



...9 Months



...12 Months



Summary	*In treatment for at least...*			
	3 months	*6 months*	*9 months*	*12 months*
Retention Rate	79.1%	65.0%	56.2%	49.8%
Still in Treatment	3,348	2,751	2,376	2,105
Discharged	882	1,479	1,854	2,125
Total	4,230	4,230	4,230	4,230

Summary Table Notes:

Retention Rate: Still in Treatment/(Still in Treatment + Retention Rate Discharges)

Still in Treatment: the count of clients remaining in treatment at the four time points, derived from admission and discharge dates found in TARGET.

Discharged: count of all discharges through the time four time points.

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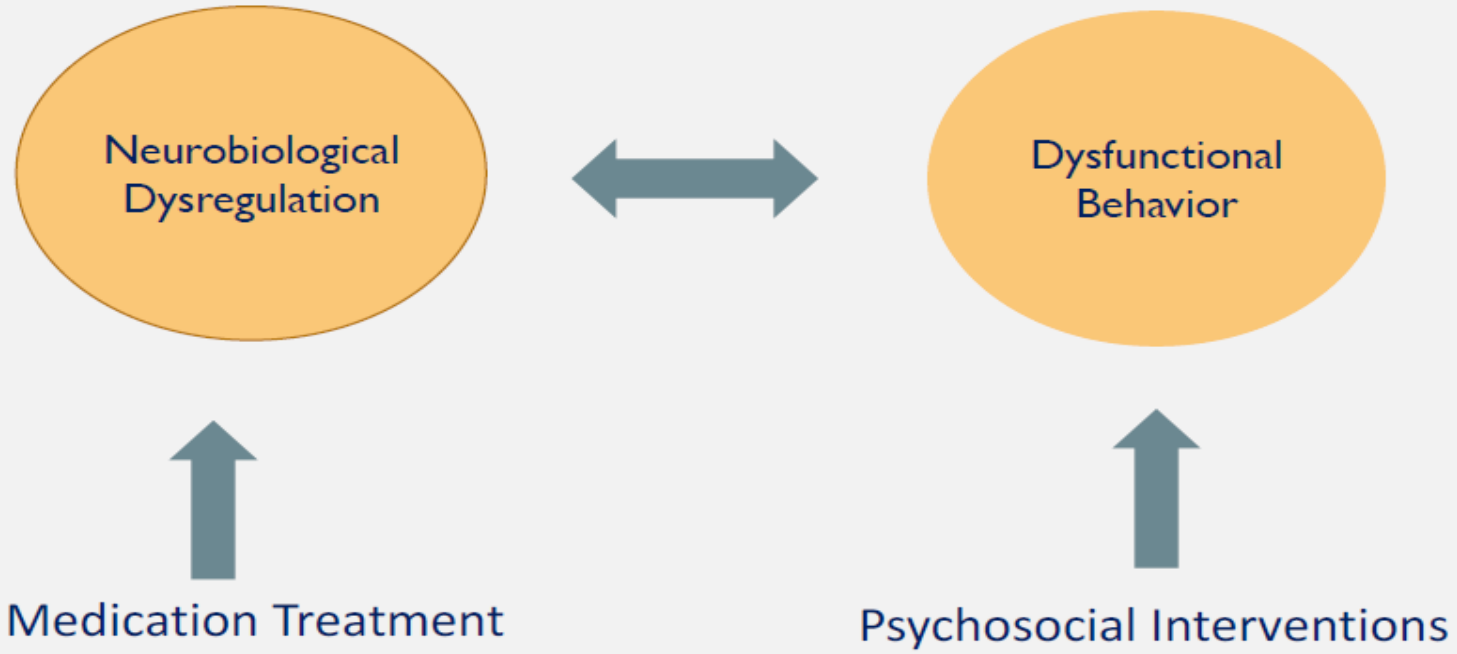
Substance Use Disorders are Chronic Brain Conditions


Neurobiological Dysregulation
Dysfunctional Behavior
Medication Treatment
Psychosocial Interventions

Vulnerability: "Exaggerated Response"

What Did It Feel Like The First Few Times?

- "All My Problems Disappeared"
- "Felt Like I Was Under a Warm Blanket"
- "Thought This is How Normal People Feel"
- "Forgot About All the Abuse"
- "Felt Like the World Was at Peace"
- "Totally Relaxed" "Not Shy"
- "Looking at a Beautiful Sunset"
- "I Was Energized!!"
- *This is a Vulnerability (Liking Opioids)*

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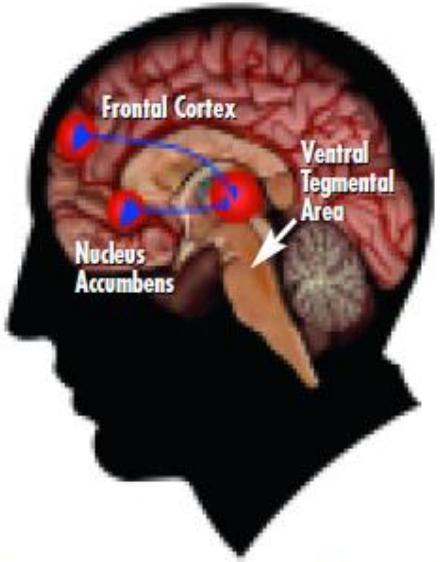
REWARD

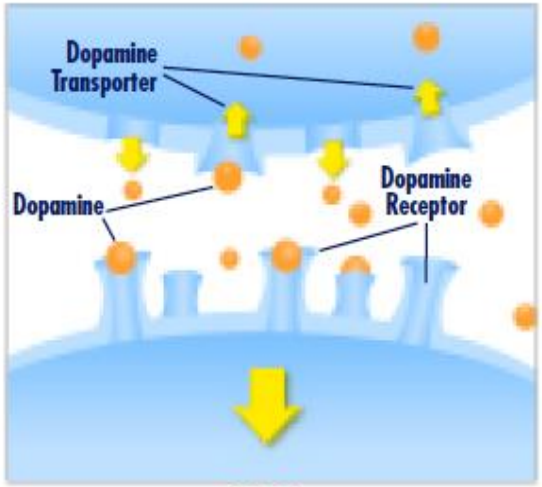
DRUGS OF ABUSE TARGET THE BRAIN'S PLEASURE CENTER

Brain reward (dopamine) pathways

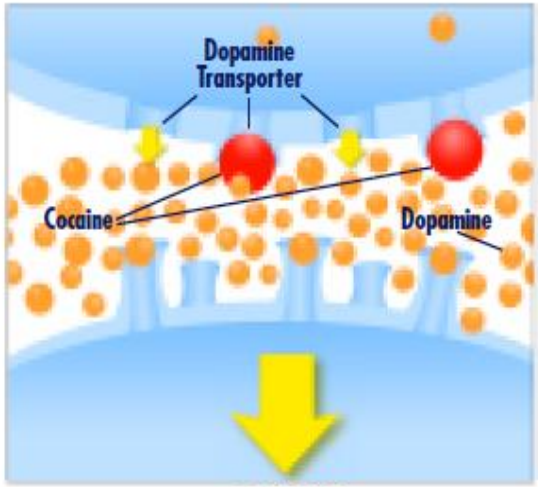


These brain circuits are important for natural rewards such as food, music, and sex.

Drugs of abuse increase dopamine



FOOD



COCAINE

Typically, dopamine increases in response to natural rewards such as food. When cocaine is taken, dopamine increases are exaggerated, and communication is altered.

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REINFORCEMENT

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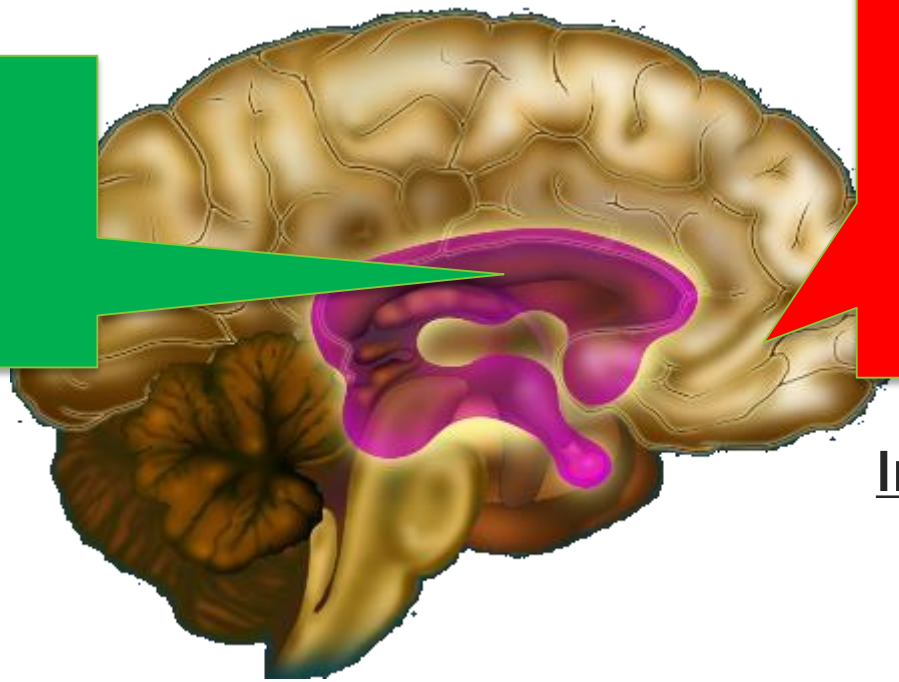
Brain Physiology of SUD treatment

Limbic Region

- **Basic Drives**
- **Experience of Reward & Euphoria**



Cortex

- **Decision making**
- **Thinking**
- **Reasoning**
- **Learning**

Interventions

- Agonist Medications
- Antagonist Medications

Interventions

- Psychosocial Therapies
- 12 Step Programs
- Monitoring
- Contingencies

Source: NIDA Drugs, Brains, and Behavior – The Science of Addiction Website. http://www.nida.nih.gov/scienceofaddiction/brain.html; Fowler JS et al. (2007). Sci Pract Prospect. 3;4:4-16

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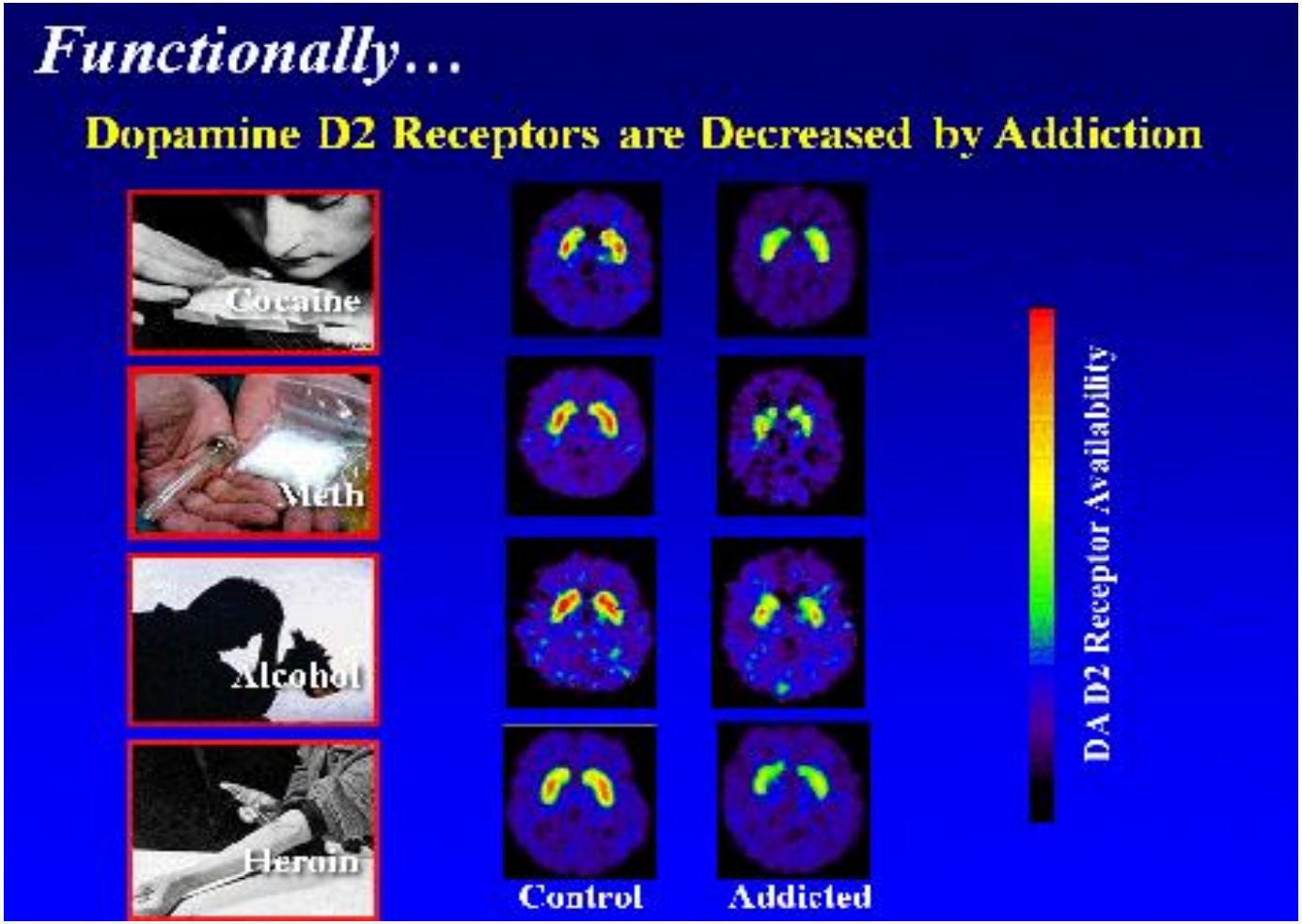
IMPAIRMENT



Drugabuse.org

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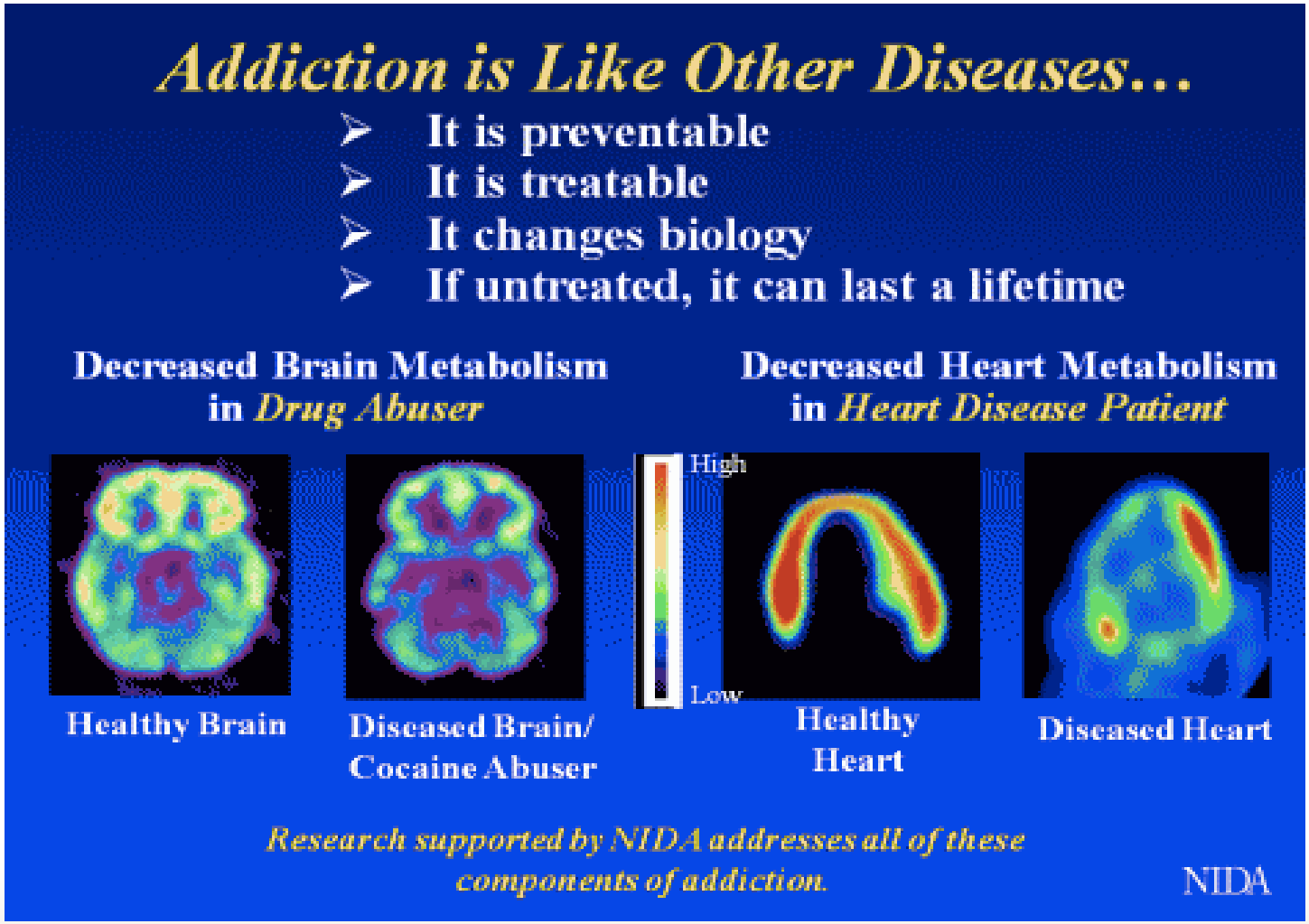
IMPAIRMENT



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CRAVING

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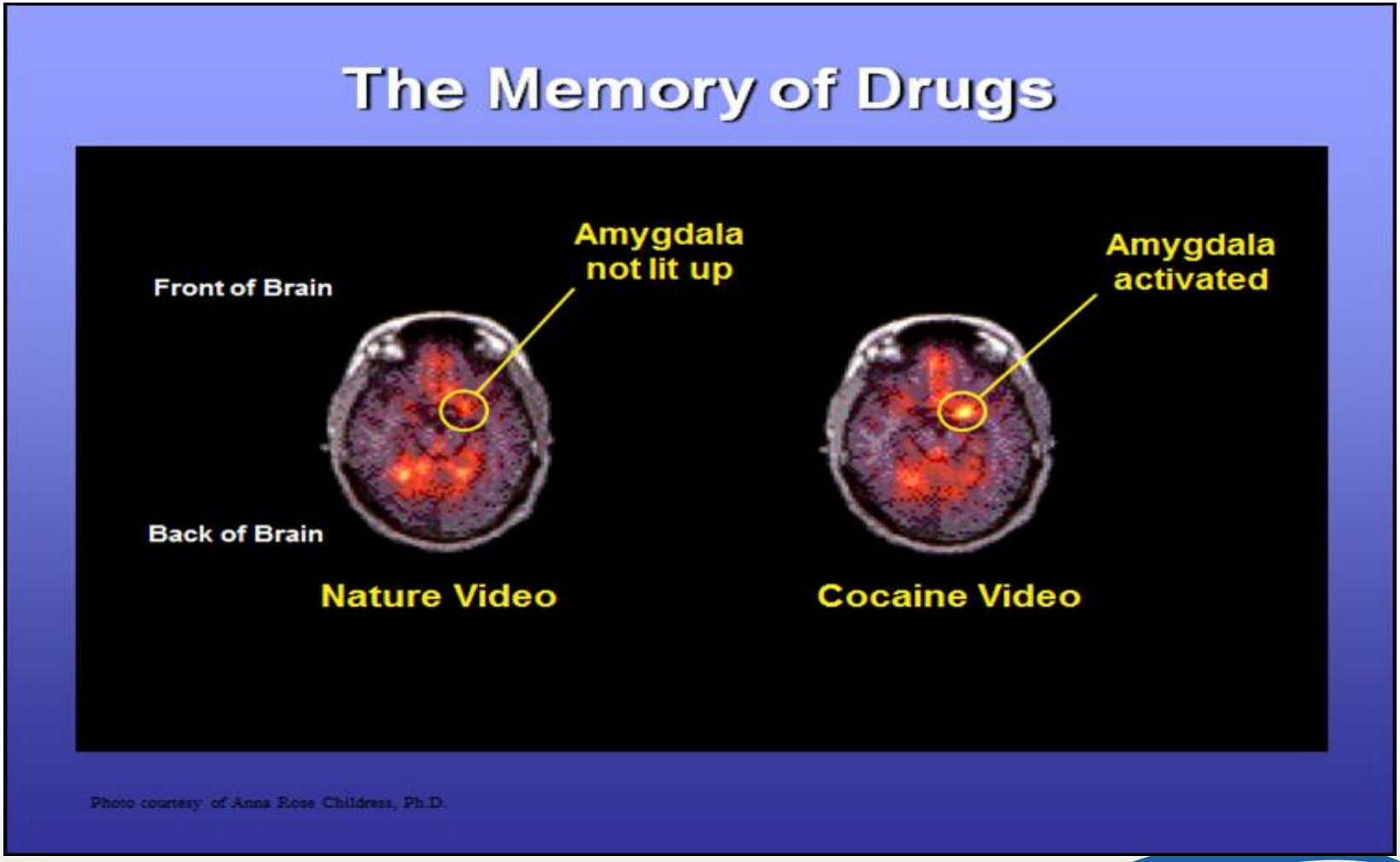
Craving



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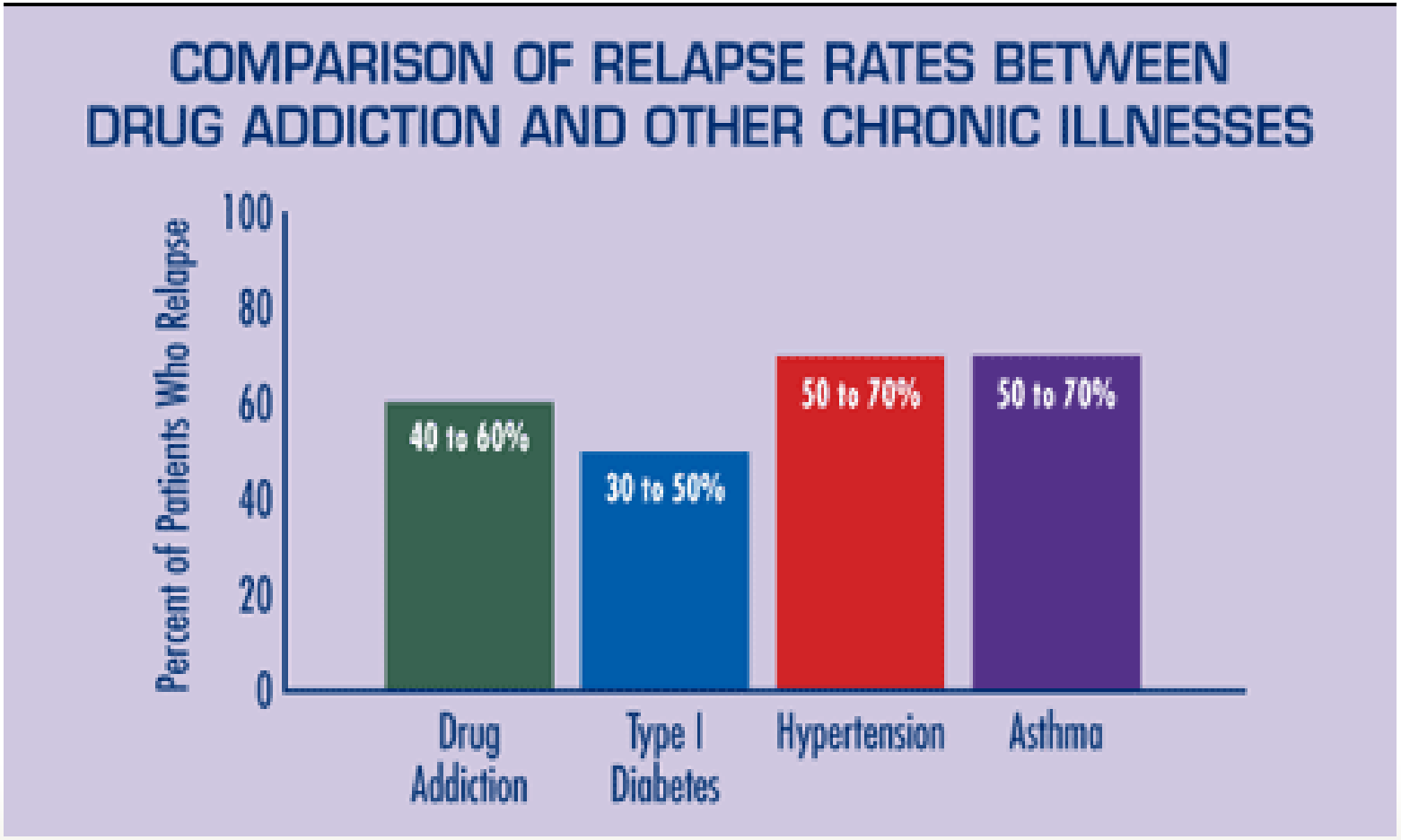
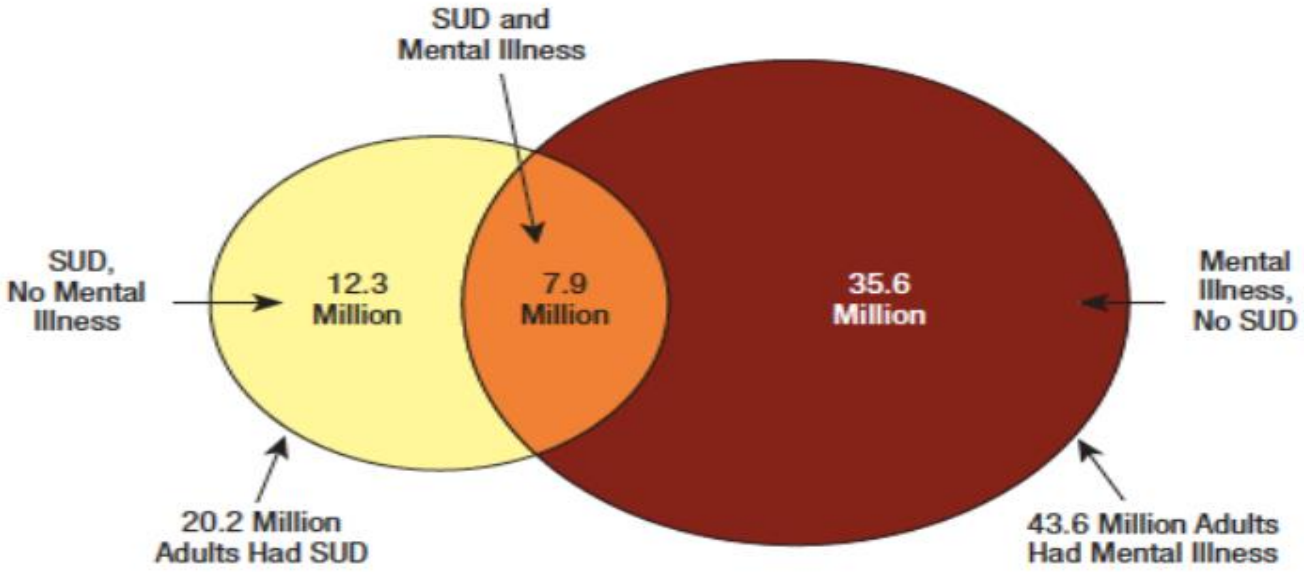
RELAPSE RATES ARE FAMILIAR



Drugabuse.org

Figure 48. Past Year Substance Use Disorders and Mental Illness among Adults Aged 18 or Older: 2014



SUD = substance use disorder.

Behavioral health trends in the United States: Results from the 2014 National Survey on Drug Use and Health

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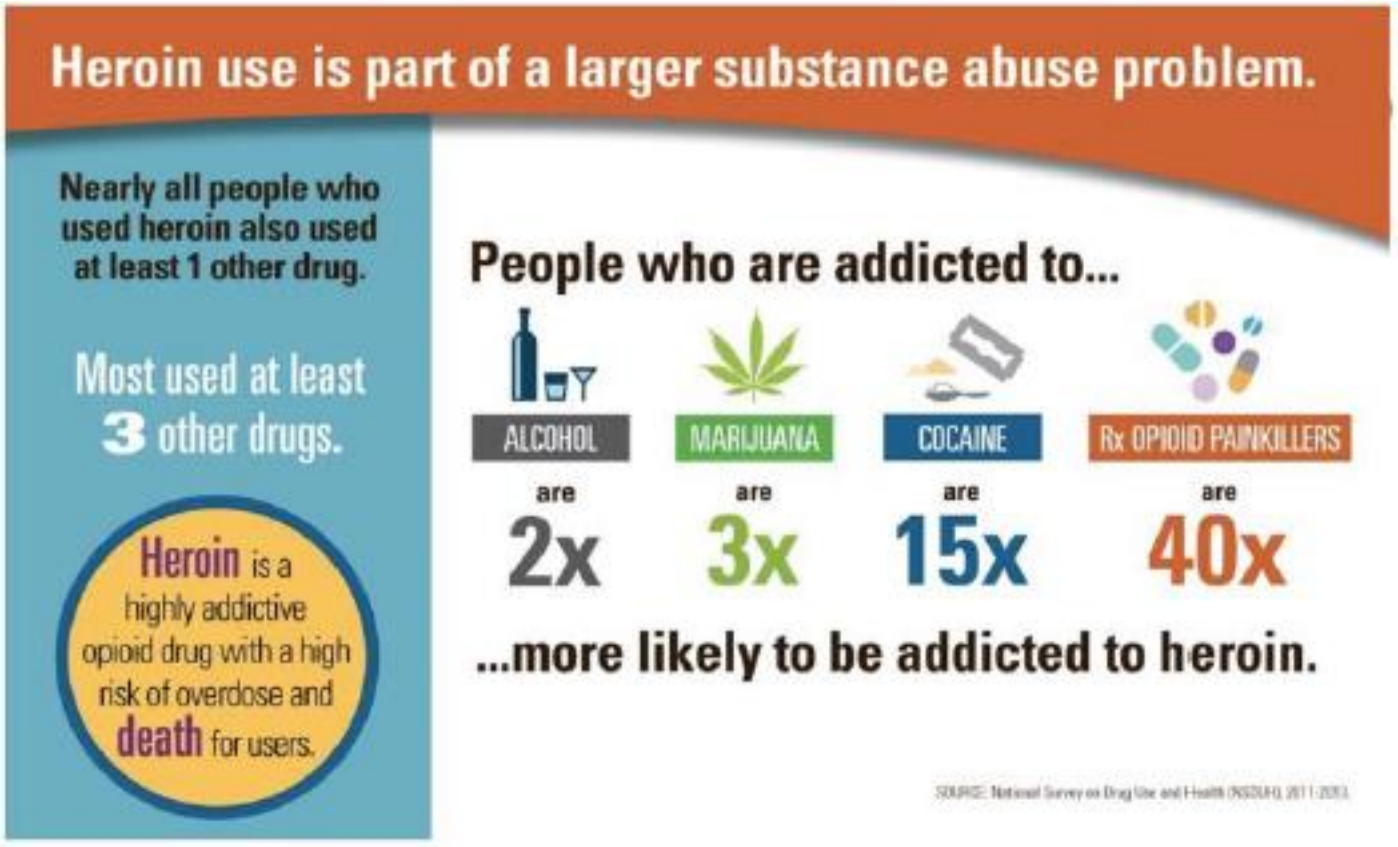
What's our role?



4 of 5 new heroin users started out using prescription opioids
Jones, Drug Alc Dep, 2013

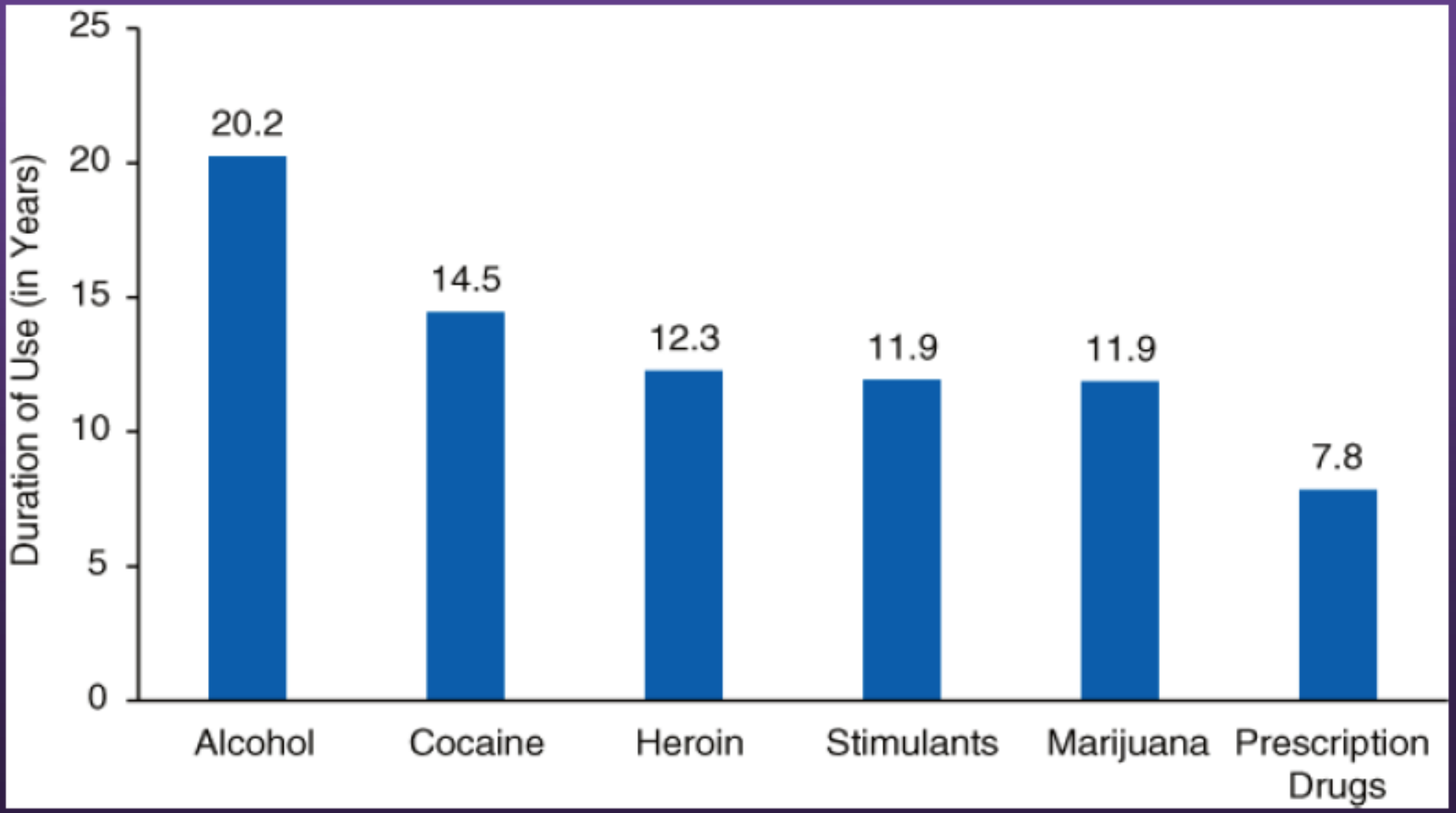
Washington State Interagency Working Plan

Priority Goals

Goal 1: Prevent Opioid Misuse and Abuse	Goal 2: Treat Opioid Dependence	Goal 3: Prevent Deaths from Overdose	Goal 4: Use Data to Monitor and Evaluate
↓	↓	↓	↓
Improve Prescribing Practices	Expand Access to Treatment	Distribute naloxone to people who use opioids	Optimize and expand data sources

Priority Actions

The Average Time Between Onset of Substance Use and First Treatment is 15.6 Years (SAMHSA, 2011)



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The Number of Persons Needing Treatment vs. Placebo to Reduce Acute Pain by 50 %

Drug	NNT	95% CI
ASA 1000 mg	4.2	(3.8–4.6)
Celocoxib 400 mg	2.6	(2.3–3)
60 mgCodeine	12	(8.4–18)
Diclofenac potassium 50 mg	2.1	(1.9–2.5)
Ibuprofen 600 mg	2.7	(2.0–4.2)
Ibuprofen 400 + Codeine 60 mg	2.2	(1.8–2.6)
Ibuprofen 400 + Acetaminophen 1000 mg	1.5	(1.4–1.7)
Ibuprofen 400 + Oxycodone 5mg	2.3	(1.8–2.6)
Naproxen 500 mg	2.7	(2.3–3.3)
Acetaminophen 1000 mg	3.6	(3.2–4.1)
Acetaminophen 1000 + Codeine 60 mg	2.2	(1.8–2.9)
Acetaminophen 1000 + Oxycodone 10 mg	1.8	(1.6–2.2)

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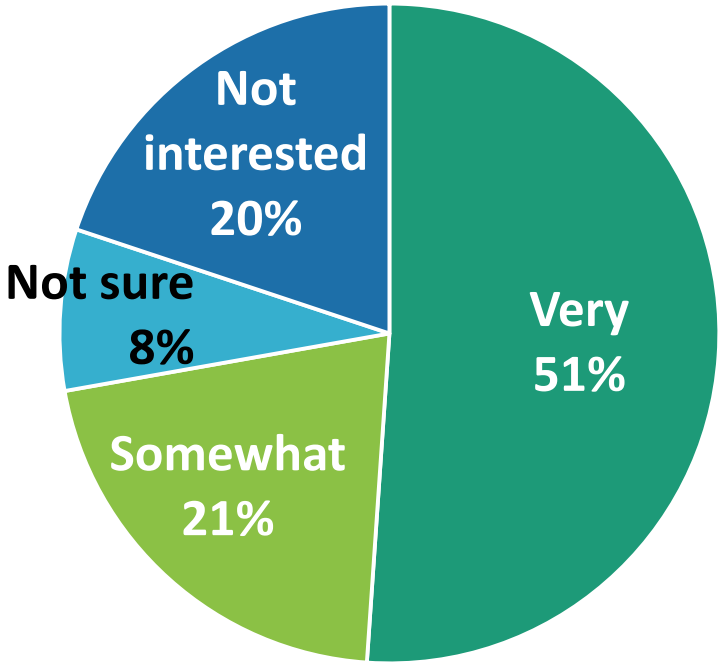
When Prescribing Opioids for Acute Pain:

@

Many people in WA are not getting treatment

How interested are you in reducing or stopping your opioid use?



What types of help would you want if they were easy to get?

- 56% medication treatment
- 39% detox
- 34% individual counseling for addiction

Source: UW Alcohol and Drug Abuse Institute, WA State Drug Injector Health Survey, 2017

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Medication Treatment

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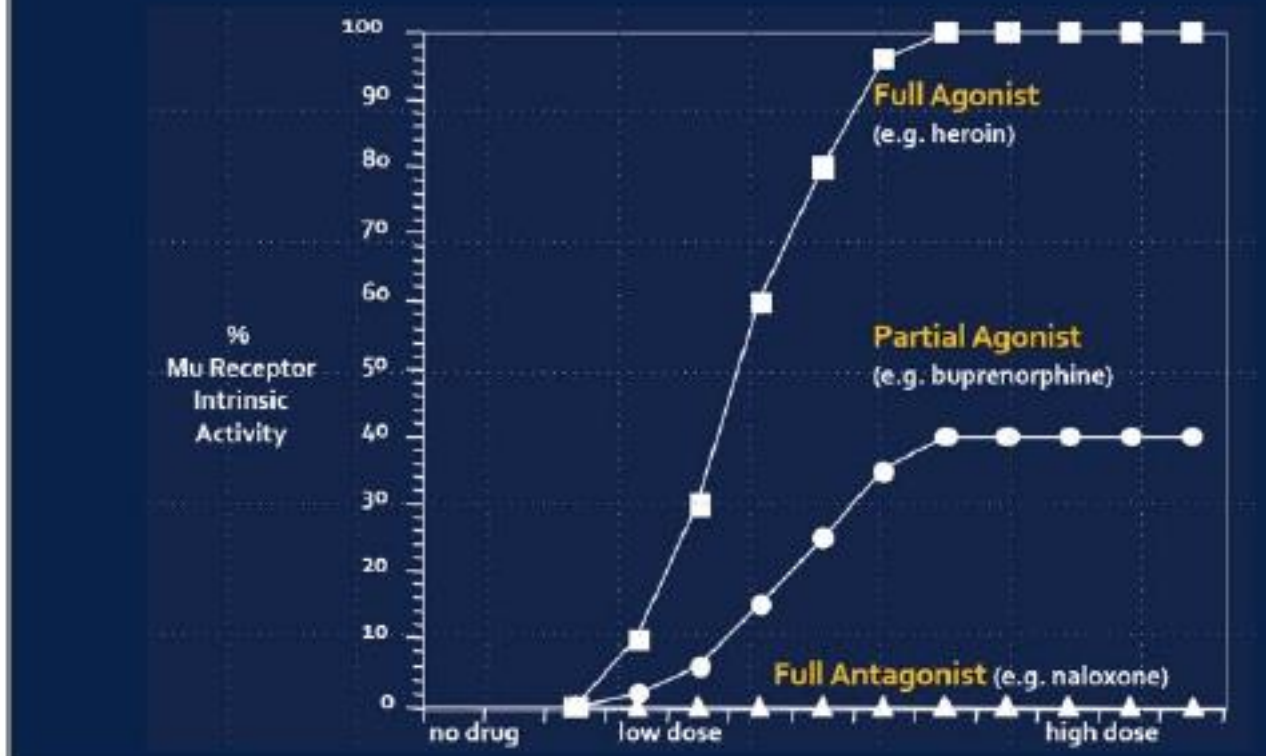
Medication Assisted Addiction Treatment

"**All** Treatments Work For **Some** People/Patients"

"**No One** Treatment Works for **All** People/Patients"

Alan I. Leshner, Ph.D
Former Director NIDA

Opioid Agonists and Antagonists



Treatment of Opioid Use Disorder Course

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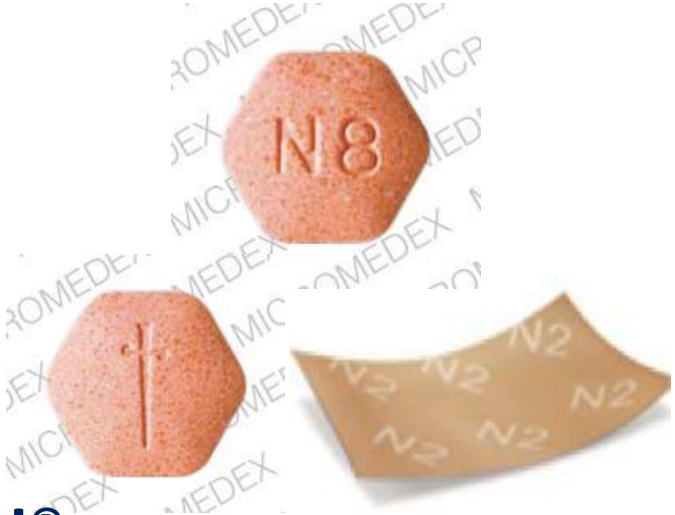
Medications for Opioid Use Disorders

Methadone

Buprenorphine



Naltrexone/Vivitrol®

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Buprenorphine Products

- Schedule III
- Most commonly used in combination w/naloxone
- Monoproduct used in pregancy
- Currently only MDs and DOs are allowed to prescribe
- Submit waiver application to SAMHSA notify DEA
- 8 hours CME

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Buprenorphine

- Partial mu agonist
- Very strong receptor affinity
- Naloxone added for abuse deterrence
- Must not have opioids in system before 1st dose
- Onset 10-30 minutes after dose, don't take with food
- Half-life is 15-56 hours depending on product

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Buprenorphine

- Designed for daily dosing but….
- Usual dose 8 mg-16 mg; some folks need 24+ mg
- Reduces craving & withdrawal; improves treatment retention
- When used alone it has a ‘ceiling’ effect
- Blocks actions of other opioids
- The receptor blockade can be overcome with very high doses of opioids, (needed for trauma, surgery)

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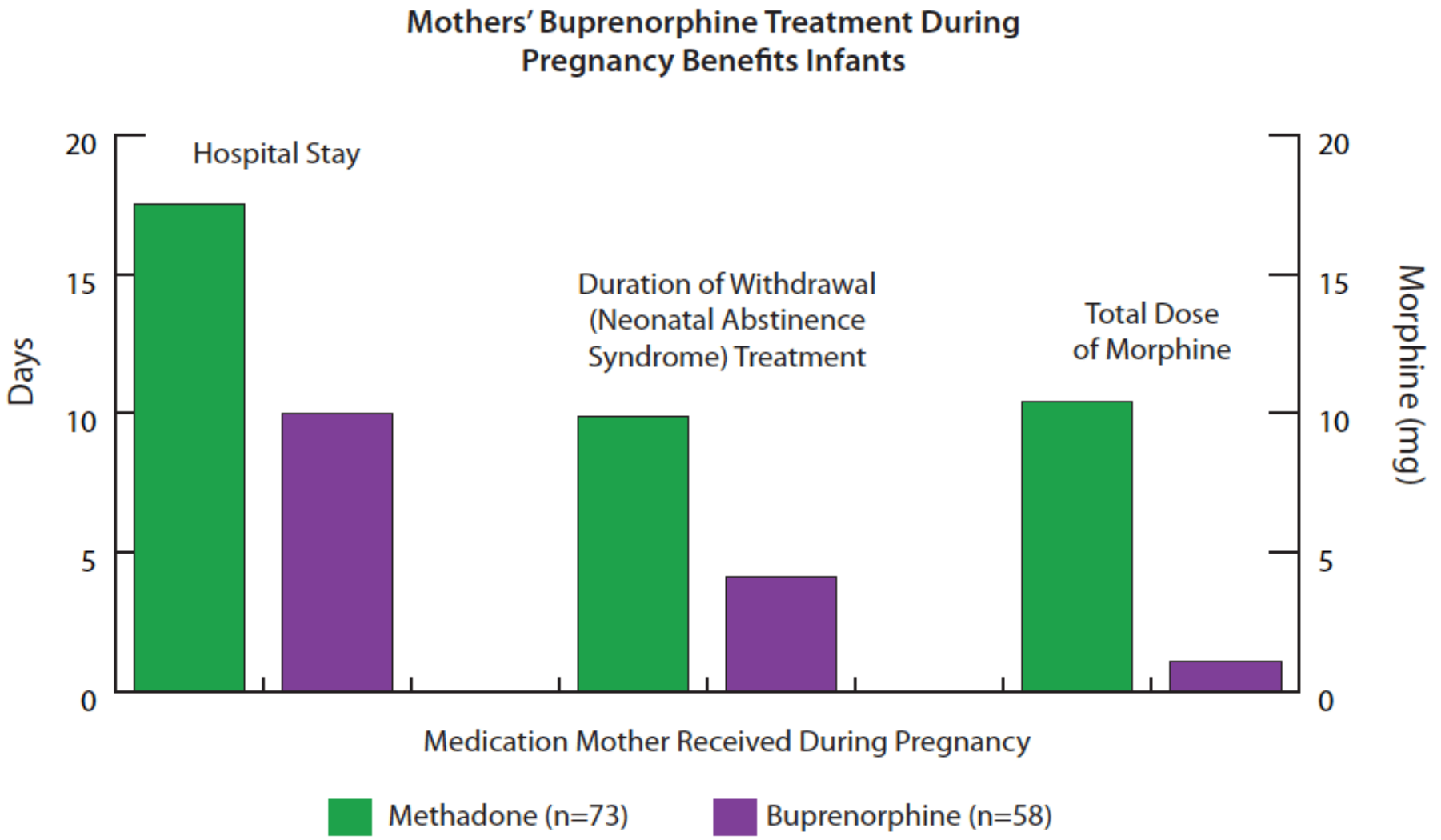
Buprenorphine

- In combination, particularly w/benzodiazepines, deaths have occurred
- Any sedative hypnotic, alcohol, will add to the risk of respiratory depression, overdose and death
- Naloxone reverses its effects
- Can monitor urine samples for its metabolite, norbuprenorphine to see if it is being taken
- Used for treatment of neonatal abstinence
- Short periods of use not as effective

BUPRENORPHINE VS. METHADONE



http://www.drugabuse.gov/news-events/nida-notes/2012/07/buprenorphine-during-pregnancy-reduces-neonate-distress

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Vivitrol®(naltrexone)

- An opioid antagonist
- 380mg IM given every 4 weeks
- When using for opioid use disorder, wait 7-10 days (up to 14 for methadone)
- Most common side effects
  - Nasuea, vomiting, headache, dizziness, fatigue, anxiety, somnolence
- Potential for liver toxicity
- Usual recommendation is for 3 months but can take up to a year

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Vivitrol® (naltrexone)

- Can use intermittently
- Proper injection technique
- Compared to placebo decreased relapse rates during and after short term, less than 12 weeks treatment.
- Reduces craving
- Injection effects can be overcome with high dose opioids
- Tolerance resolves quickly and return to prior doses of opioids can lead to overdose

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Potential Naltrexone Candidates

- Occupational Obstacles: e.g, HCPs
- Not Interested/Failed Agonists
- High Motivation for AA Model of Recovery
- Currently Abstinent: High Risk for Relapse
- ? Younger, Lower Duration of OUD
- Don't want to be Physically Dependent
- Tired of regulations, stigma, and SO pressure

Courtesy Adam Bisaga, M.D.

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Impact of Methadone Maintenance Treatment

- Reduction death rates (Grondblah, '90)
- Reduction IVDU (Ball & Ross, '91)
- Reduction crime days (Ball & Ross)
- Reduction rate of HIV seroconversion (Bourne, '88; Novick '90,; Metzger '93)
- Reduction relapse to IVDU (Ball & Ross)
- Improved employment, health, & social function

Methadone Maintenance Treatment

Limitations

- Limited access
- Inconvenient and highly punitive
- Mixes stable and unstable patients
- Lack of privacy
- No ability to "graduate" from program
- Stigma

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Opioid Detoxification Outcomes

- Low rates of retention in treatment
- High rates of relapse post-treatment
  - < 50% abstinent at 6 months
  - < 15% abstinent at 12 months
  - Increased rates of overdose due to decreased tolerance
  - Walter Ling "Quote"

O'Connor PG JAMA 2005 Mattick RP, Hall WD. Lancet 1996 Stimmel B et al. JAMA 1977

Buprenorphine Efficacy Summary

- Studies (RCT) show buprenorphine more effective than placebo and equally effective to moderate doses (80 mg) of methadone on primary outcomes of:
  - Abstinence from illicit opioid use
  - Retention in treatment
  - Decreased opioid craving

Johnson et al. *NEJM*. 2000.
Fudala PJ et al. *NEJM*. 2003.
Kakko J et al. *Lancet*. 2003.

Overdose Risk Minimal

- Low risk of clinically significant problems
- Pre-clinical studies suggest high doses of buprenorphine should not produce respiratory depression
- No reports of respiratory depression in clinical trials
- Overdose and misuse (e.g., injecting) of buprenorphine combined with other CNS depressants result in respiratory depression and risk overdose
- France experience…
  - IV buprenorphine + high potency benzodiazepines → deaths

Abuse Potential of Buprenorphine

- Euphoria in non-opioid dependent individuals
- Abuse potential less than full opioid agonists
- Abuse among opioid-dependent individuals is relatively low
- Combination product theoretically less likely to be abused by IV route
- Most illicit use is to prevent or treat withdrawal and cravings

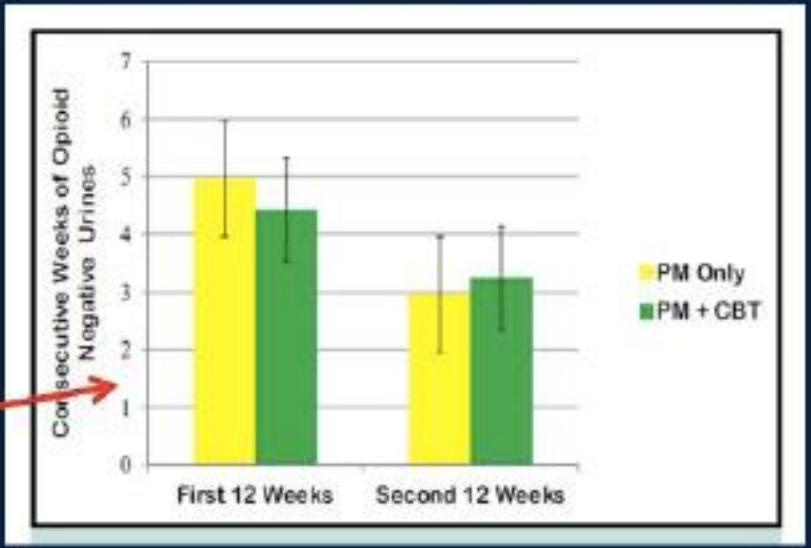
Yokel MA et al. *Curr Drug Abuse Rev.* 2011.
Lofwall MR, Walsh SL. *J Addic Med.* 2014.

Opioid Use Disorder (OUD): Behavioral Treatment Components

- Psychosocial Services: often helpful for treatment of OUD
  - Can be delivered directly by physician and/or by referral when needed
- DATA 2000: "…the practitioner has the capacity to refer the patients for appropriate counseling and other appropriate ancillary services."
- Refer patient as clinically determined to:
  - Individual and group therapy
  - Family therapy
  - 12 Step
  - Higher psychiatric severity patients more responsive to increased services

Is Behavioral Treatment in OBOT Effective?

- Three trials show that additional behavioral therapy (i.e., CBT, drug counseling) does NOT significantly improve outcomes over that achieved by buprenorphine PLUS medical management or "medical counseling"



Weiss RD et al. *Arch Gen Psychiatry*. 2011.
Fiellin DA et al. *Am J Med*. 2013.
Ling W et al. *Addiction*. 2013.

Pregnancy: Benefits of Opioid Agonist Therapy

Maternal Benefits

- 70% reduction in overdose related deaths
- Decrease in risk of HIV, HBV, HCV
- Increased engagement in prenatal care and recovery treatment

Fetal Benefits

- 70% reduction in overdose related deaths
- Decrease in risk of HIV, HBV, HCV
- Increased engagement in prenatal care and recovery treatment

Treatment of Opioid Use Disorder Course

Maternal Dose and NAS Severity

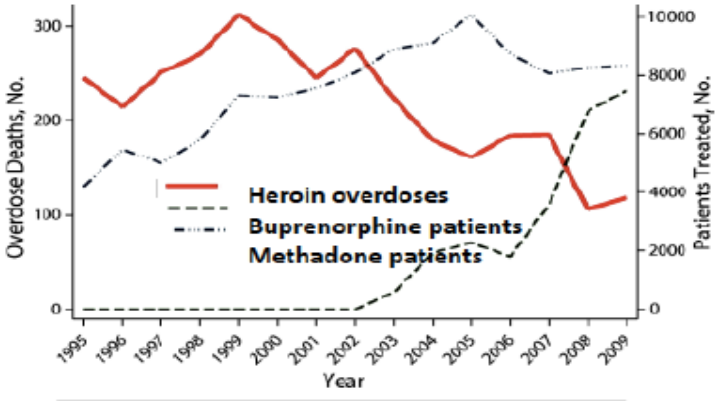
- No correlation between maternal opioid maintenance therapy dose and the duration or severity of NAS
- Women should be encouraged to report any symptoms of withdrawal through her pregnancy without fear a dose increase will affect her baby's hospital stay or need for NAS treatment

Berghella et al. 2003; McCarthy et al. 2005; Cleary et al. 2010; Isemann et al. 2010; Jones et al. 2010; Seligman et al. 2011.

Agonist Medications Decrease Heroin OD

Agonist Treatment Reduced Heroin OD Deaths

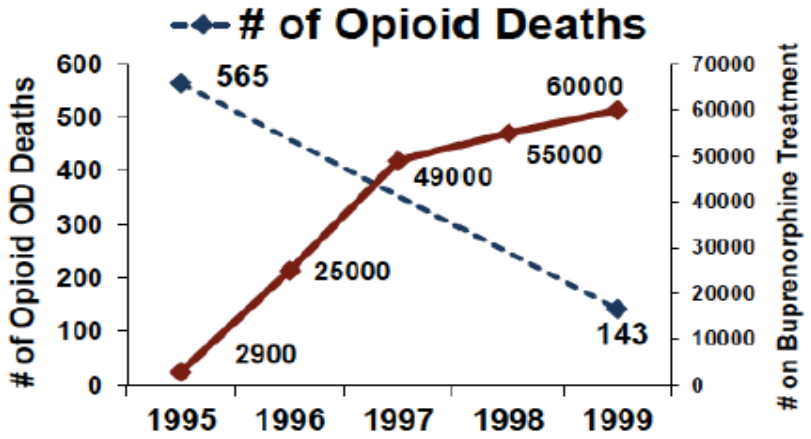
Baltimore, Maryland, 1995-2009



Schwartz RP et al., Am J Public Health 2013.

Buprenorphine Reduced Heroin OD

France 1995-1999 (75% reduction)



Ling et al. J Subst Abuse Tx 2002;23:87-92.
Auriacombe et al. JAMA 2001;285:45.

Medication Treatment Prevents Opioid Related Deaths

- English National Drug Treatment Database
- Followed 151,983 persons over 4 years, 2005-2009
- Compared fatal drug related poisoning across residential, MAT and psychologic support combinations
- During treatment death rate was 2.9/1000 (CI 2.7-3.1) vs. 4.5/1000 (CI 4.3-4.7) when on MAT
- Risk of death was not different between those who completed and didn't complete residential treatment (50-80%) higher

Pierce, et.al. Addiction, 2015; 111:298-308

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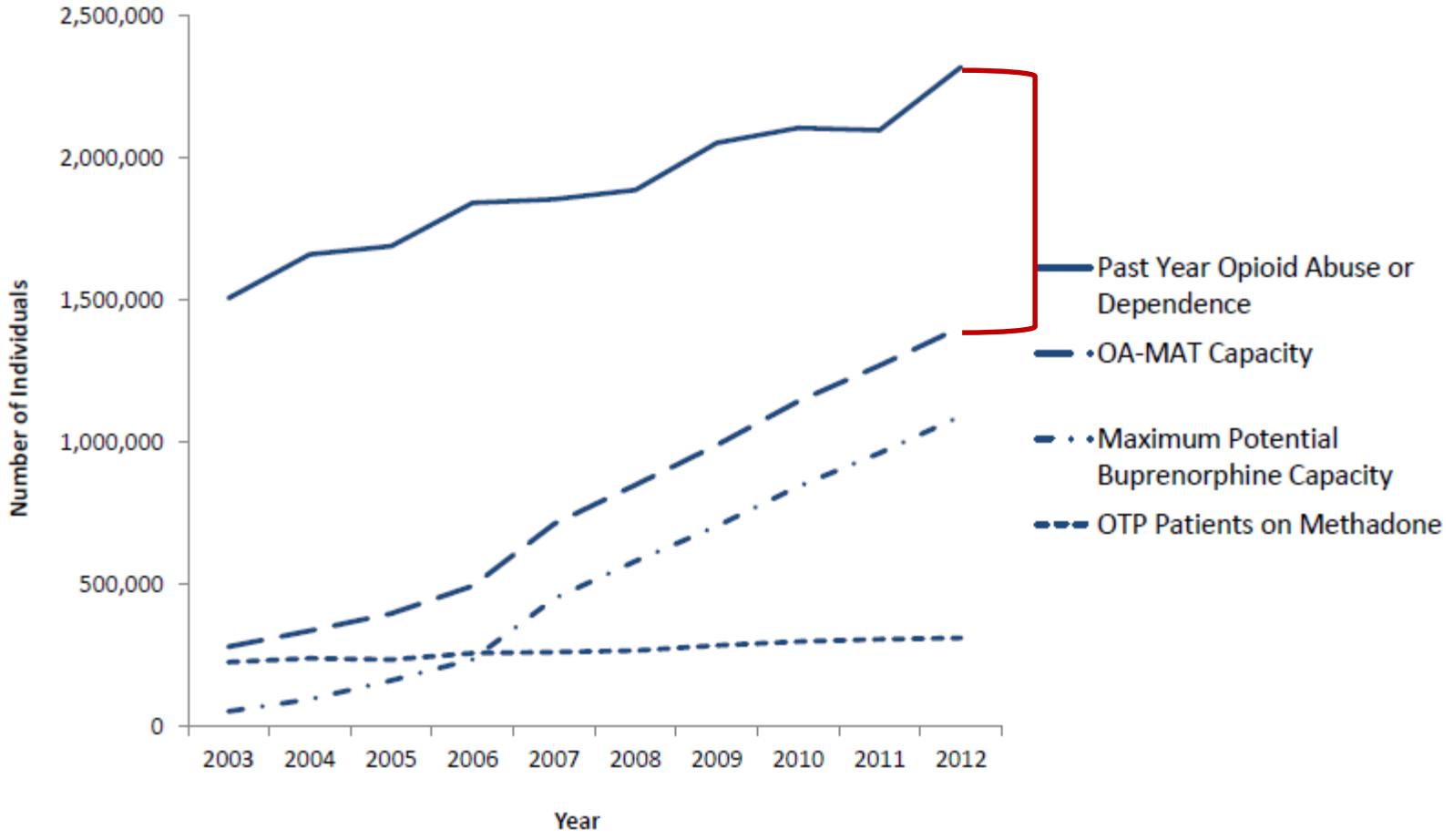
MAT Prevents Opioid Related Deaths

- Risk of treatment being in psychologic treatment alone doubled the risk of death
- 6x higher risk 1st 28 days after DC
- 3.5x higher 1st 28 days after MAT stopped
- THE BOTTOM LINE: MAT SAVES LIVES

Treatment need for opioid abuse or dependence exceeds capacity for opioid agonist medication assisted treatment (OA-MAT) in the US



Source: Jones CM, Campopiano M, Baldwin G, McCance-Katz E. National and state treatment need and capacity for opioid agonist medication assisted treatment. AJPH. 2015

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Prevent Overdose

Potency Equivalents

- MORPHINE: 1
- FENTANYL: 100 X *Chest Wall Rigidity-Rapid IV
- CARFENTANIL: 10,000 X

- Novel Psychoactive Substances:
  Congeners of Fentanyl

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Washington's Good Samaritan Law

- **RCW 69.41.095:** Opioid overdose medication
  - Amended in 2015
  - Licensed health care providers
  - Pharmacists
  - First responders
  - Family members
  - Any person in a position to assist persons at risk of an opioid overdose

http://app.leg.wa.gov/RCW/default.aspx?cite=69.41.095

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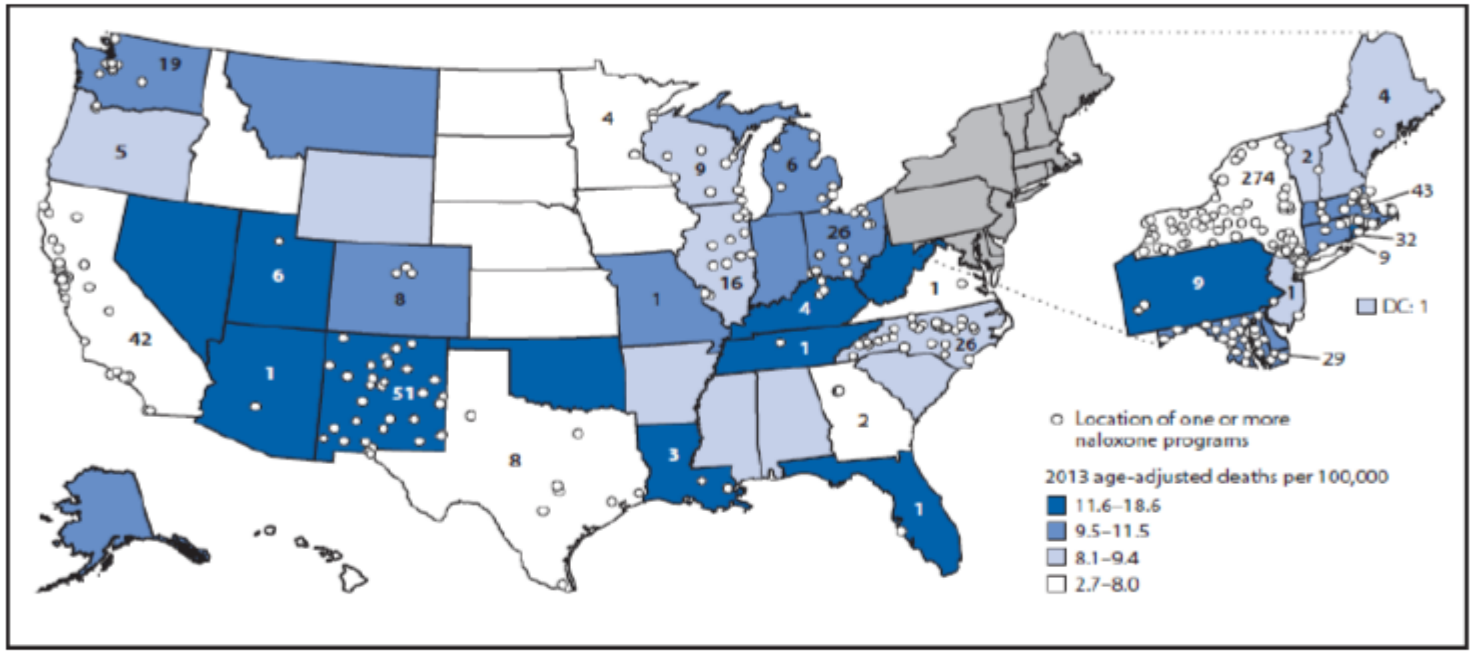
Number* and location of local drug overdose prevention programs providing naloxone to laypersons and age-adjusted drug overdose death rates



Source: Wheeler E, Jones TS, Gilbert MK, Davidson PJ. MMWR 2015

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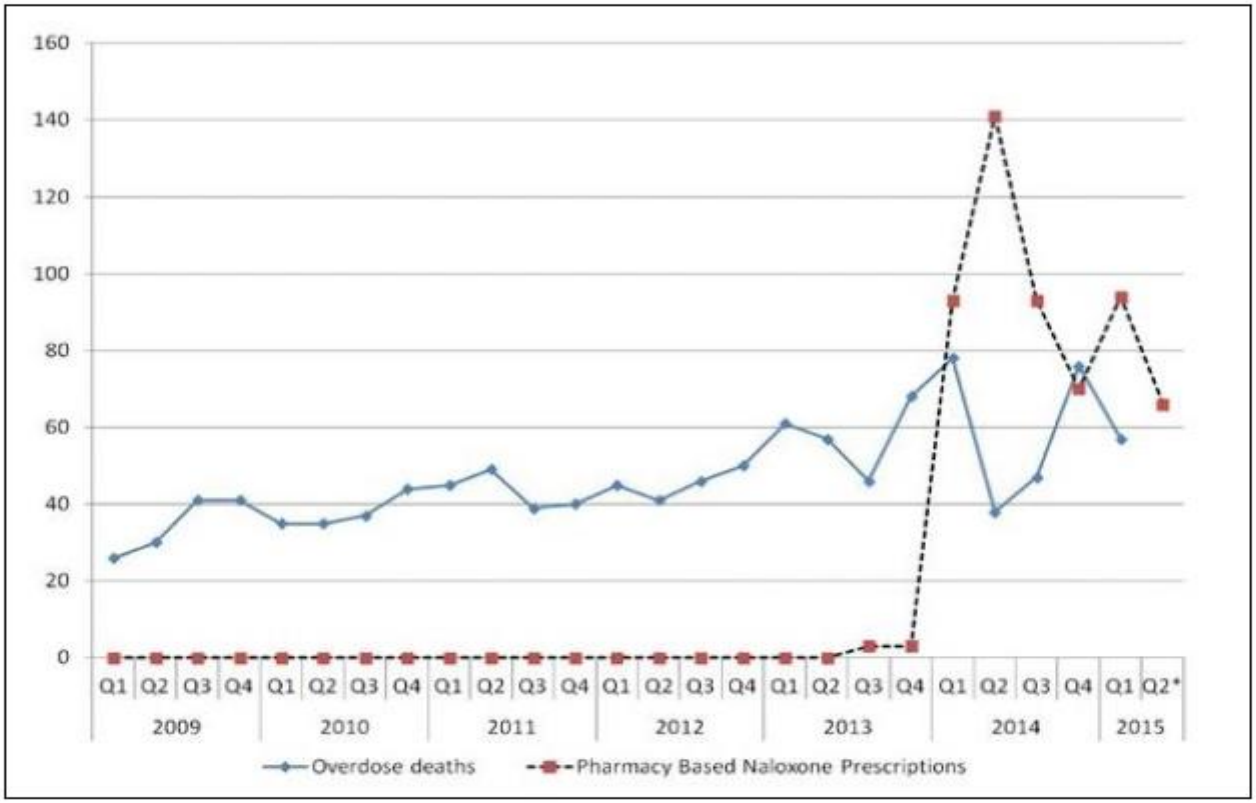
Overdose deaths and pharmacy-based naloxone prescriptions dispensed in Rhode Island



Source: Green TC et al. Orienting patients to greater opioid safety: models of community pharmacy-based naloxone. Harm Reduction J. 2015

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Naloxone Formulations

Injectable

Intranasal

EVZIO® Autoinjector

Narcan ® Nasal Spray

Stopoverdose.org

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Recovery

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Peer Strengths

- Empathic
- Hopeful
- Integrated
- Strength based
- Lived experience
- Health, home, purpose, community

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Peer Recovery Supports

- Reduce the risk of relapse
- Provide hope
- Provide experiential knowledge
- People don’t live in clinics or treatment centers

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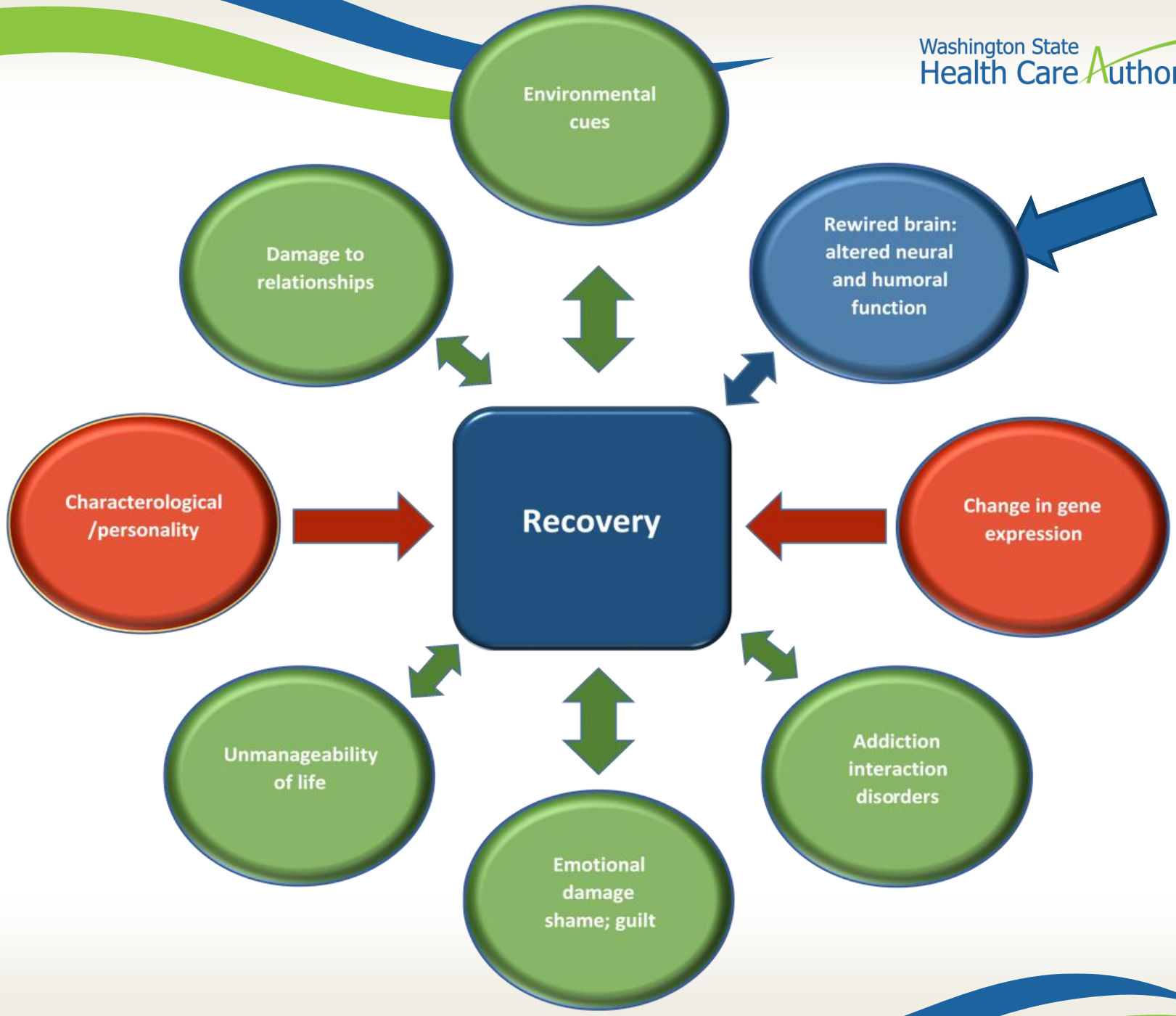

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Questions?