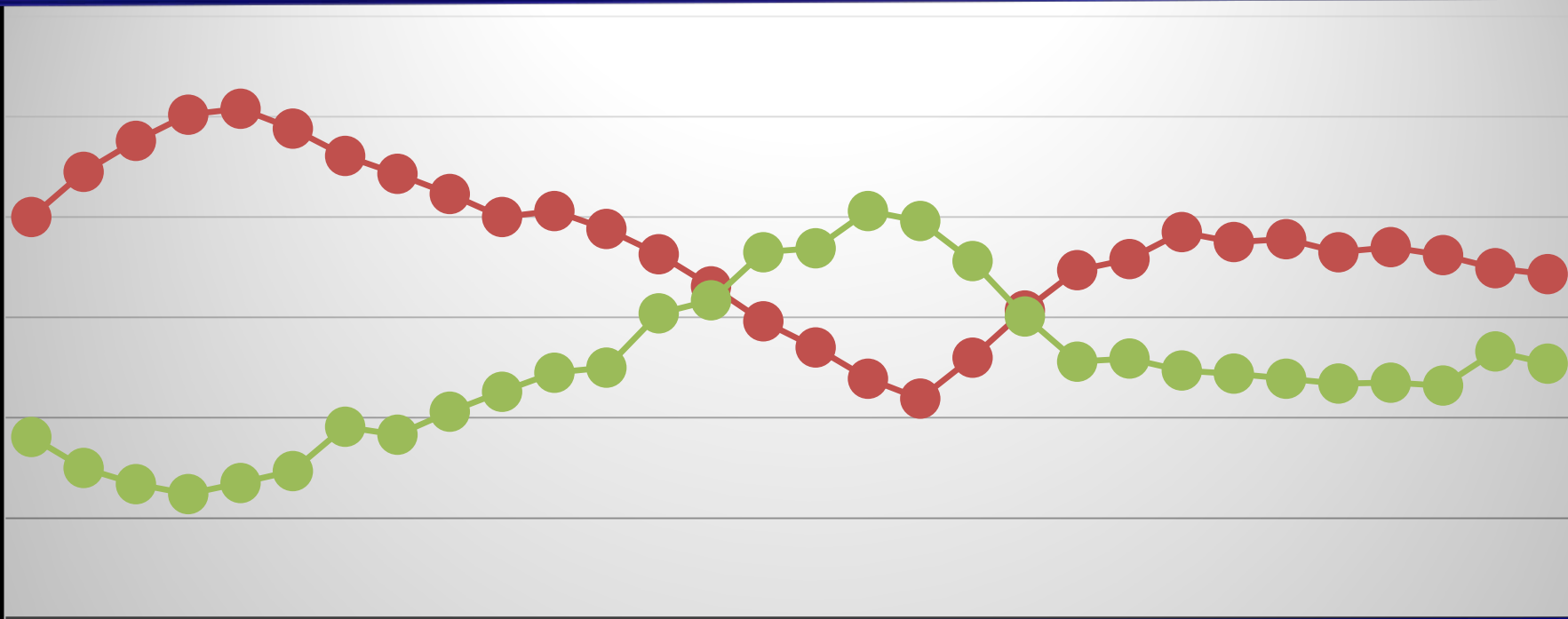
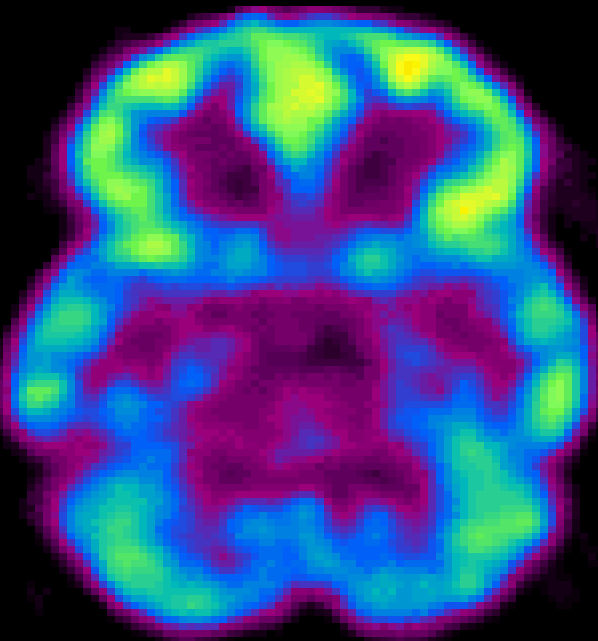


# *Science = Solutions*



**Kathy Etz, Ph.D.**

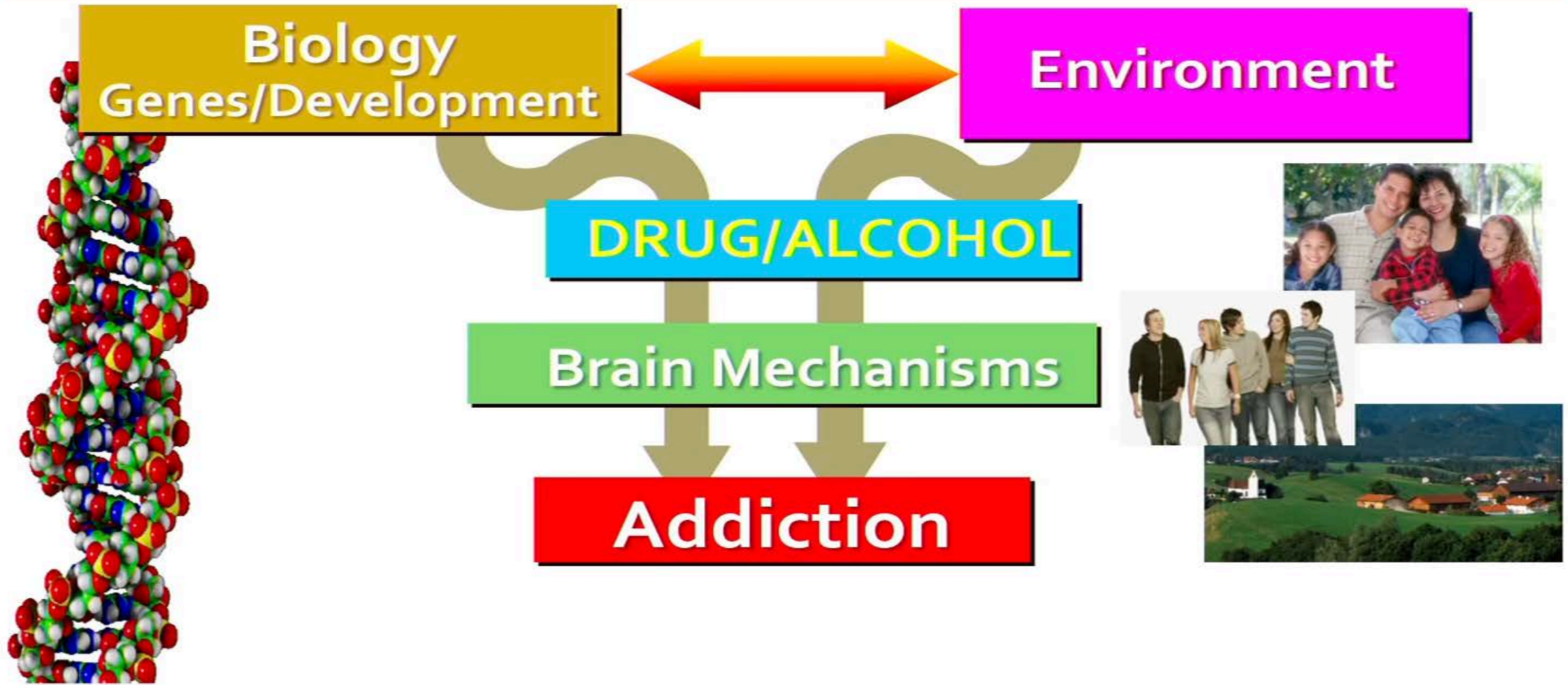
Director, Native American Program

Program Director

National Institute on Drug Abuse

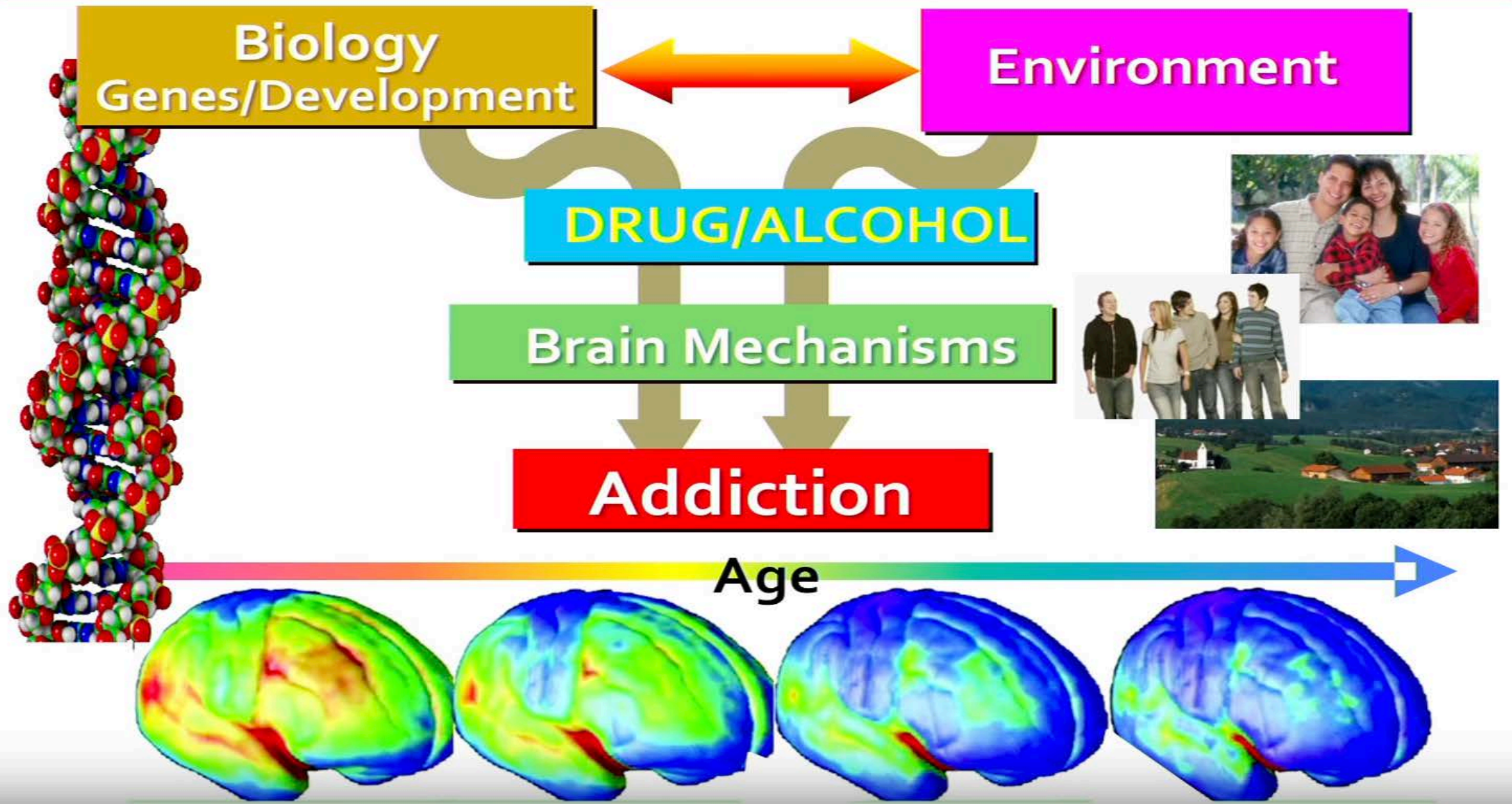


# ADDICTIONS as Diseases of *Gene-Environment-Development*





# ADDICTIONS as Diseases of *Gene-Environment-Development*



# Three Major Addiction Themes Where *Science is Needed* to Inform Policy

---

- **MARIJUANA:** The shifting legal landscape suggests possible population impacts

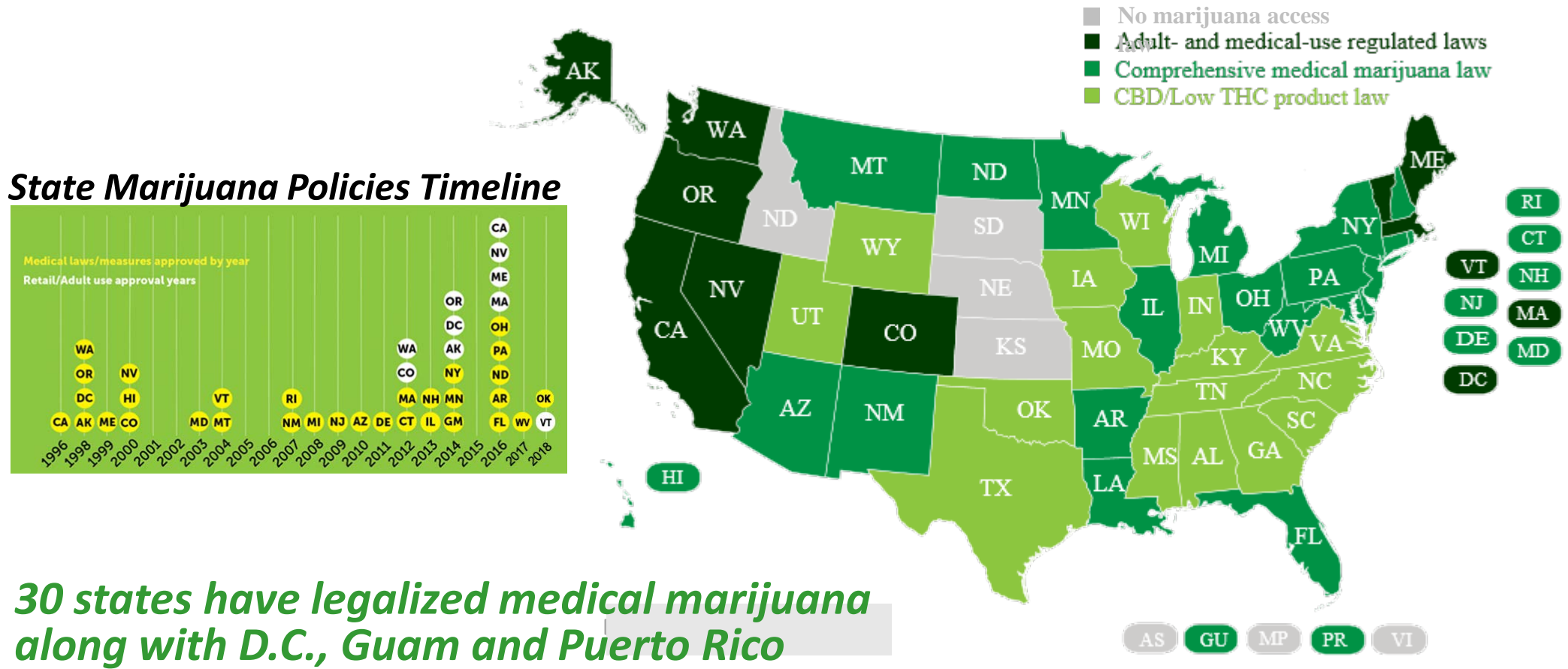


- **E-CIGARETTES:** Both potential promise for established tobacco users and concern for increasing adolescent use

- **OPIOIDS:** Impacts on public health in the USA starting with over-exposure to prescription opioids



# CANNABIS LAWS IN THE U.S.



**30 states have legalized medical marijuana along with D.C., Guam and Puerto Rico**

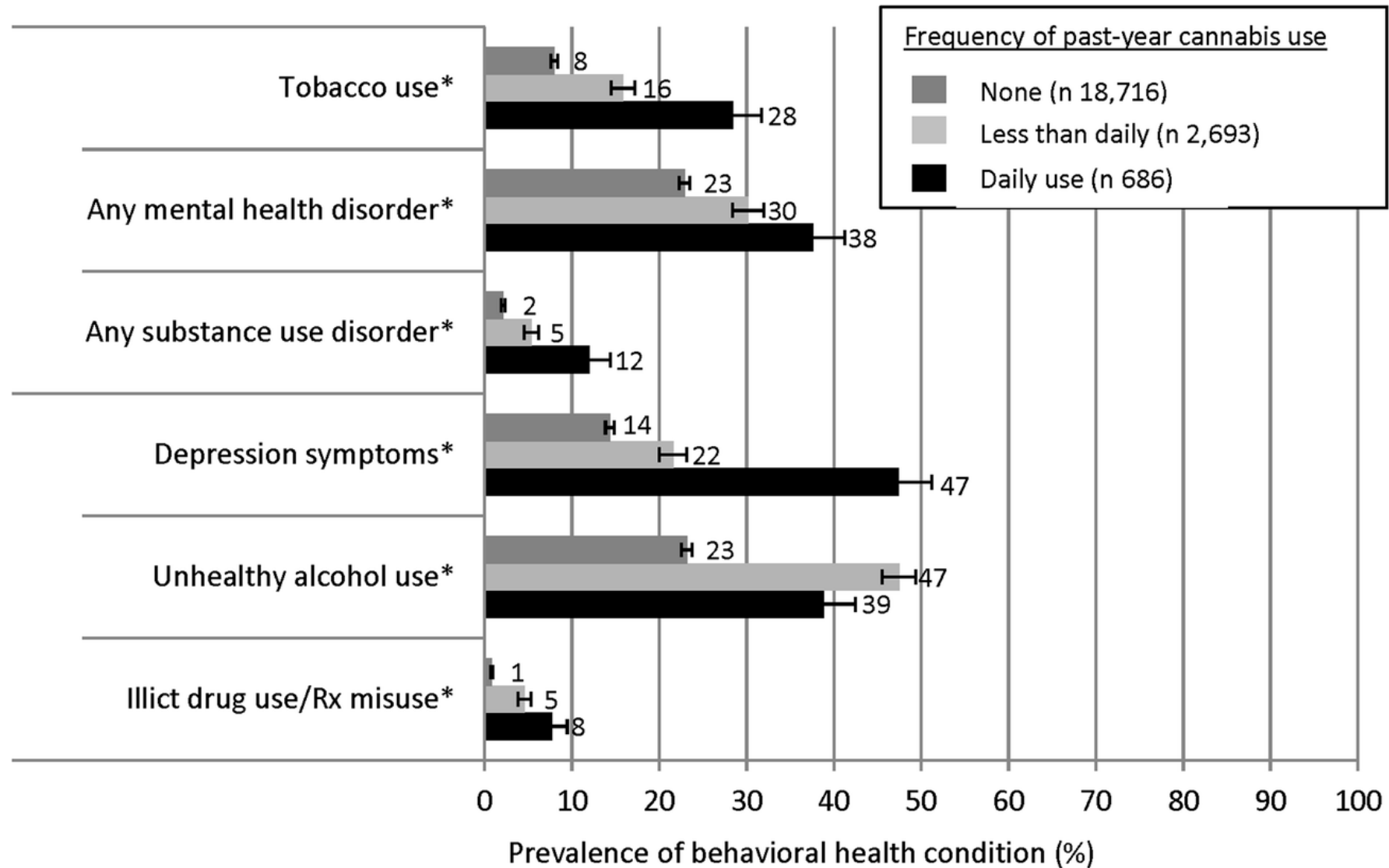
**States with MML vary on:**

- Allowable conditions and routes of administration.
- Dispensaries/home growth and registries.
- Testing, regulatory requirements.

**States with Recreational Laws vary on:**

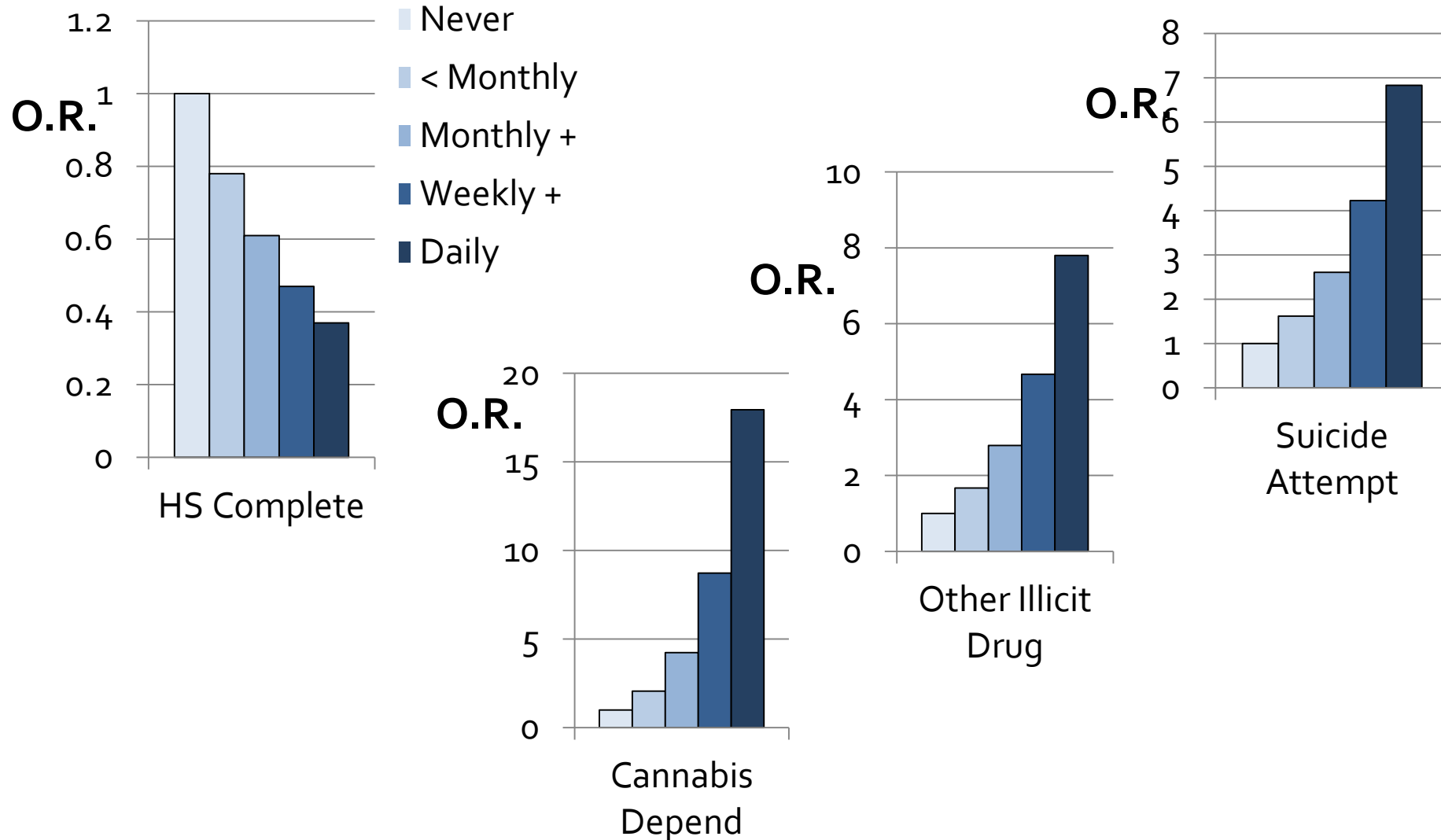
- Marketing, product labeling, distribution (home growth).
- Taxation.

# Prevalence Of Behavioral Health Conditions Across Frequency Of Cannabis Use Among Adult Primary Care Patients In Washington State



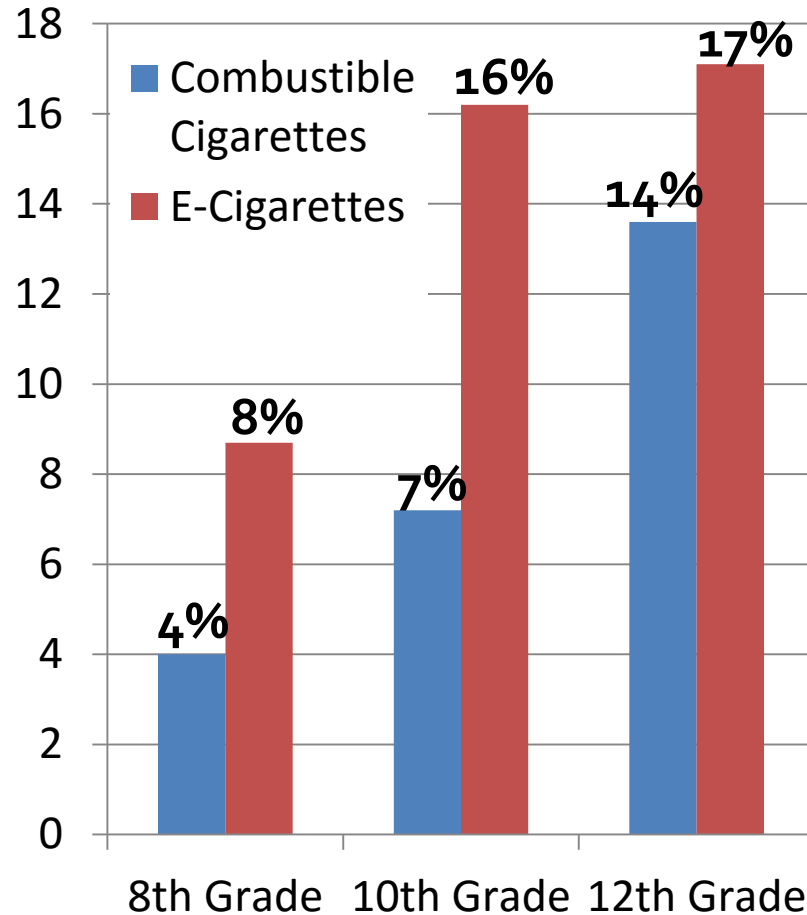


# More Teenage Use of Marijuana Associated with **Worse Outcomes** in 20's (3 Australia/New Zealand Studies)



# More U.S. Youth Use E-Cigs Than Combustible Cigs

2014 Past Month E-Cig vs. Combustibles in USA Students



Monitoring the Future Study 2014,  
University of Michigan

In a prospective study of 14 year old students, **E-Cigarette use predicting onset** of:

- Any combustible 2.75 AOR
- Combustible cigs 1.73 AOR

Leventhal, et al. *JAMA* 2015;314(7):700-707.

2012-2013 U.S. study of 12-17 year olds (n=13,561), **first tobacco product was flavored** among users:

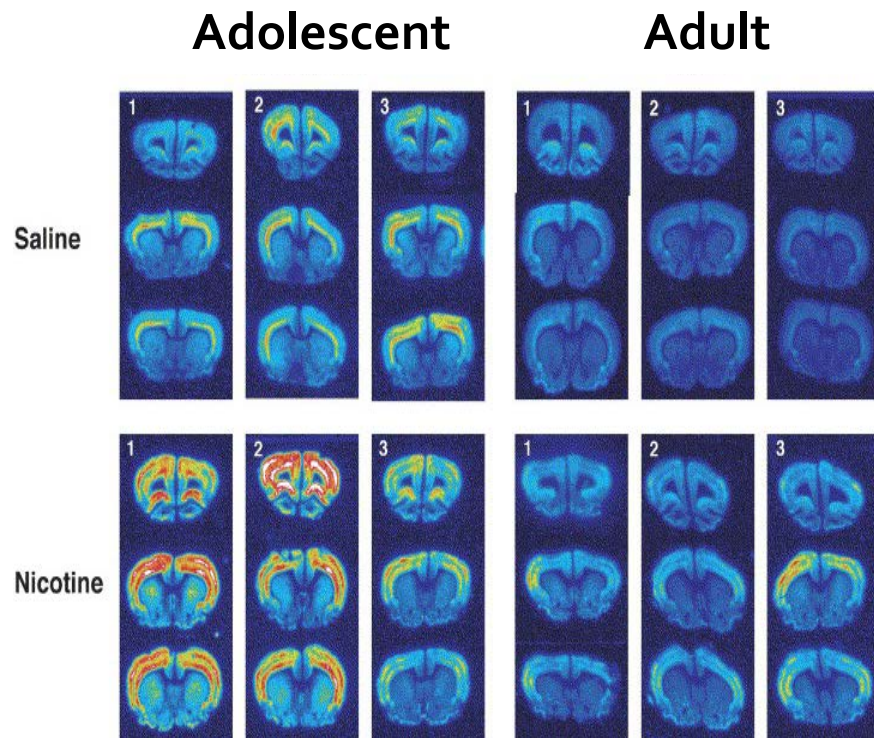
- Cigarettes 50%
- Smokeless 69%
- E-Cigarettes 81%

Ambrose, et al. *JAMA*, 26 October 2015



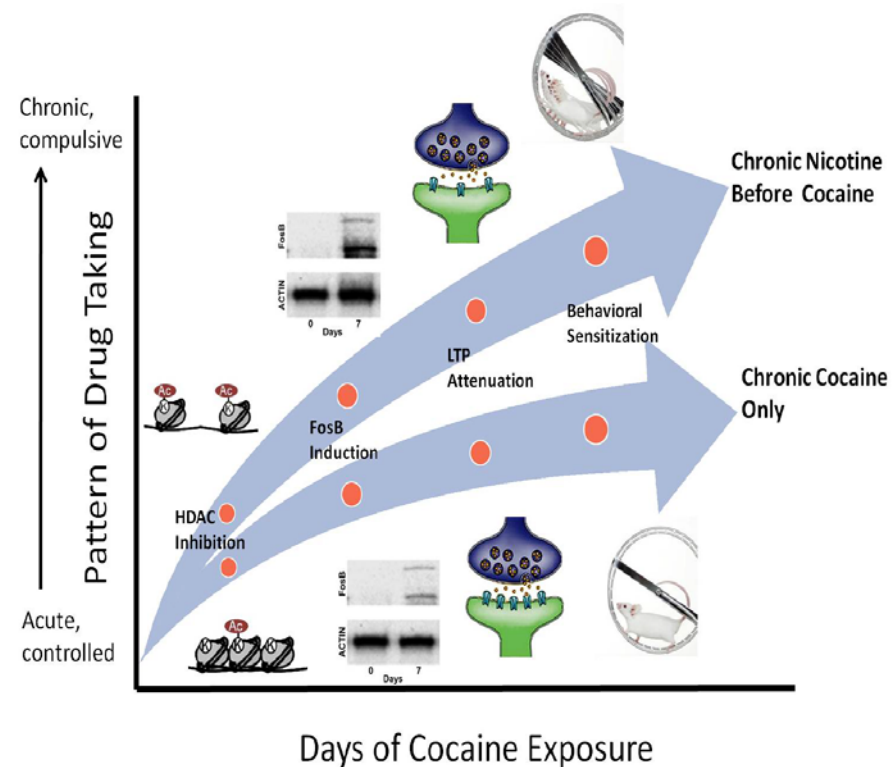
# Nicotine Effects Particularly Impacts *Adolescent Brain*

*Nicotine up-regulates arc*  
(involved in synaptic plasticity)  
*in adolescents but not*  
*adults (rodent models)*



Schochet AE, et al. Neuroscience 135 (2005) 285–297

*Nicotine enhances*  
*response to cocaine in*  
*adolescents but not*  
*adults (rodent models)*



Levine A. et al., Sci Transl Med. 2011

# Adolescent Brain Cognitive Development (**ABCD**) Study

---

*Ten year longitudinal study of 10,000 children from age 10 to 20 years to assess effects of drugs on individual brain development trajectories*



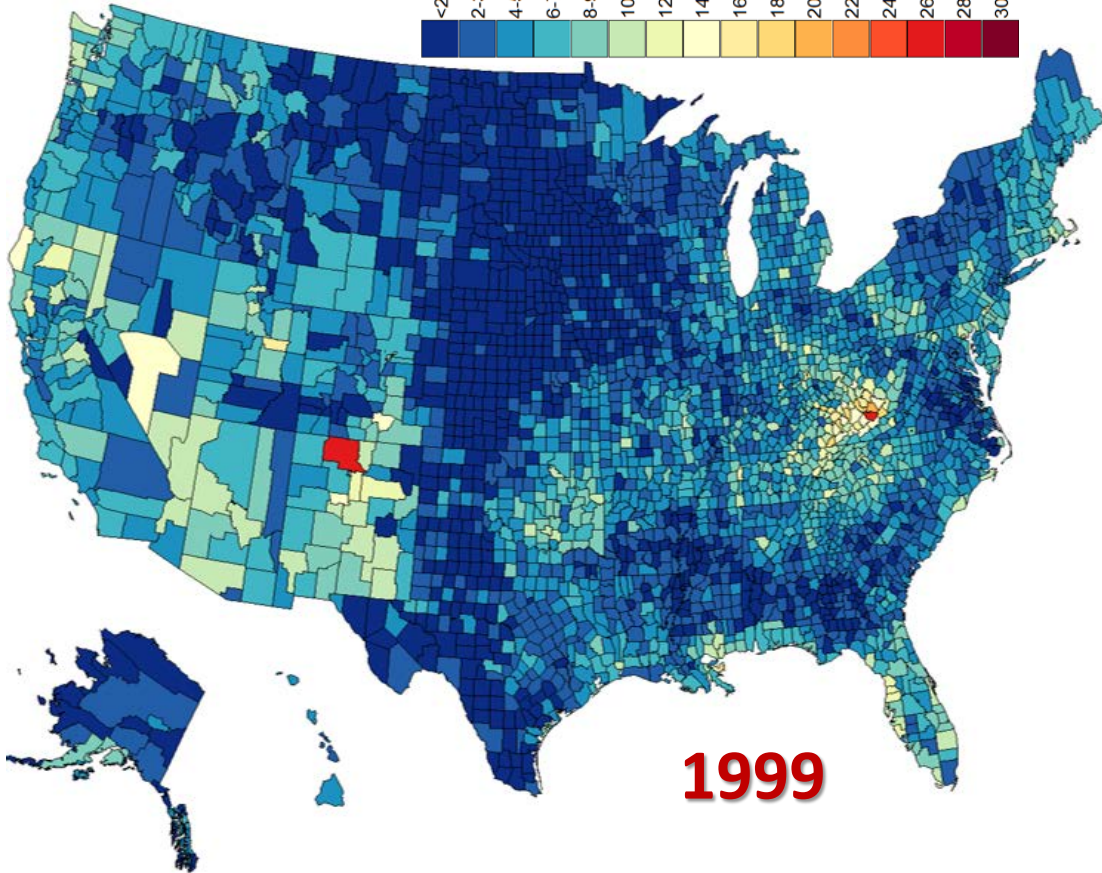
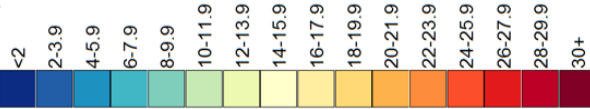
An NIH Collaboration: NIDA, NIAAA, NCI, NIMH, NIMHD, NICHD, NINDS, OBSSR



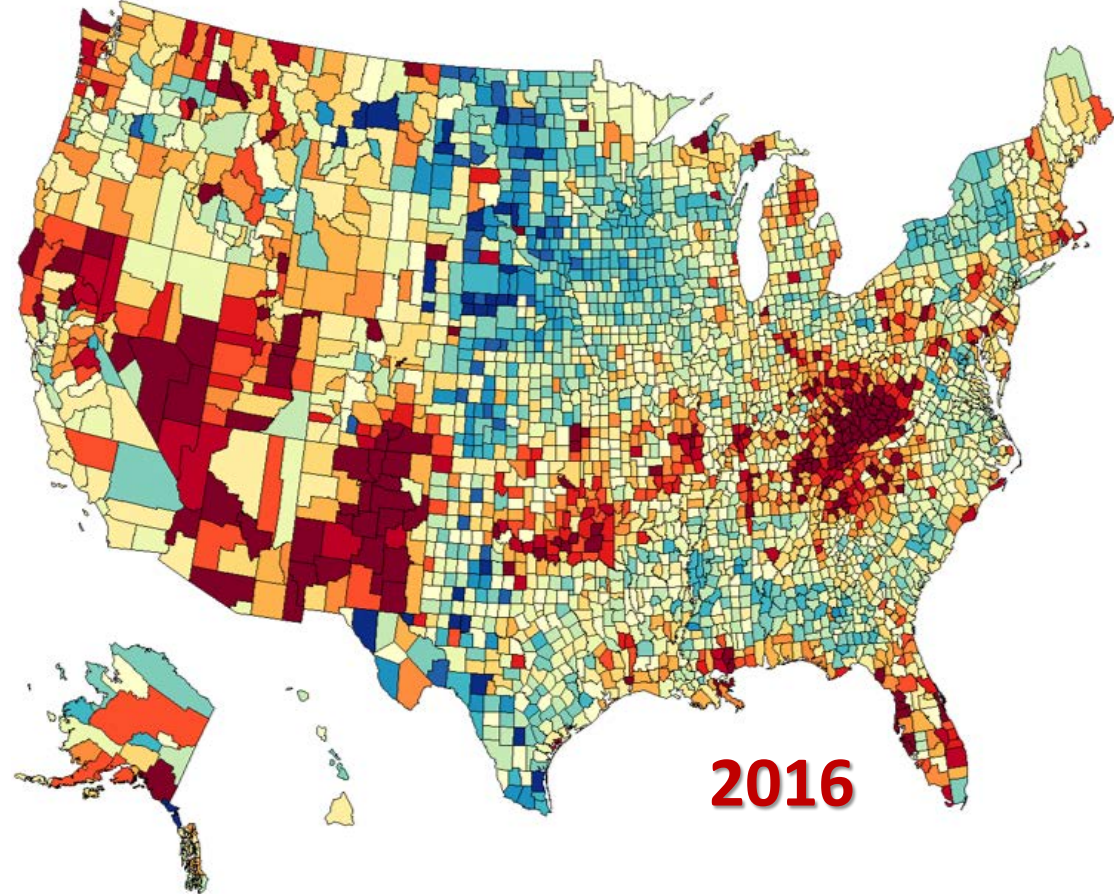
# 63,362 OD Deaths in 2016—42,249 from Opioids (Rx and Illicit)

## Virtually *All of the U.S.* Reports Increased Drug Overdoses:

Estimated Age-adjusted Death Rates per 100,000 for Drug Poisoning by County



1999



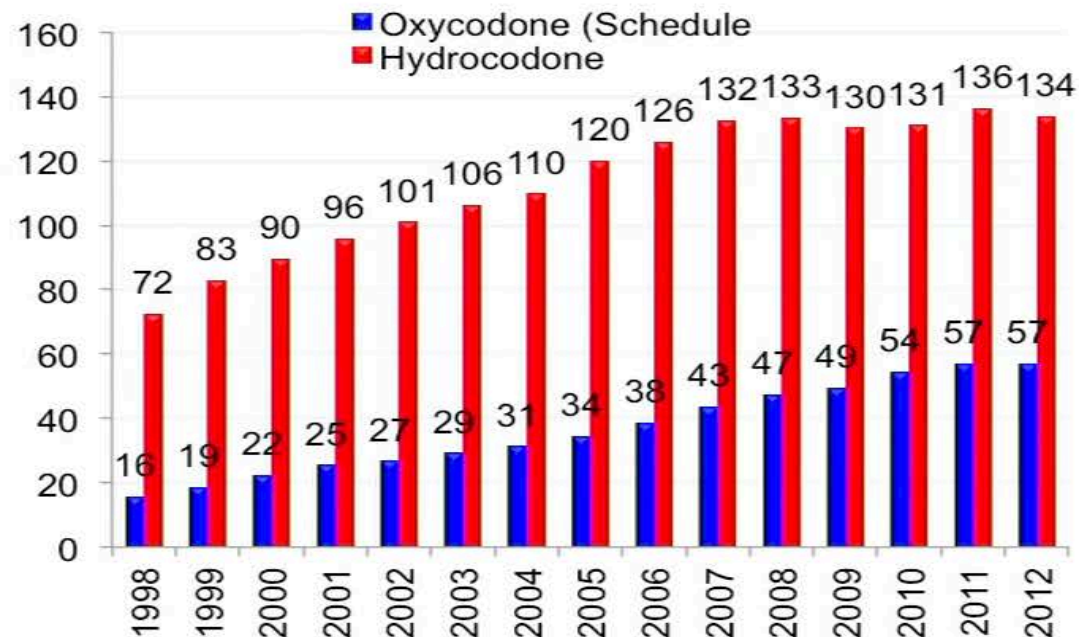
2016

Source: <https://www.cdc.gov/nchs/data-visualization/drug-poisoning-mortality/index.htm>

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

Opioid Prescriptions nearly tripled between 1999 and 2012

## Oxycodone & Hydrocodone Prescriptions



SDI Health, VONA\_02-1-13\_Opioids Schedule II

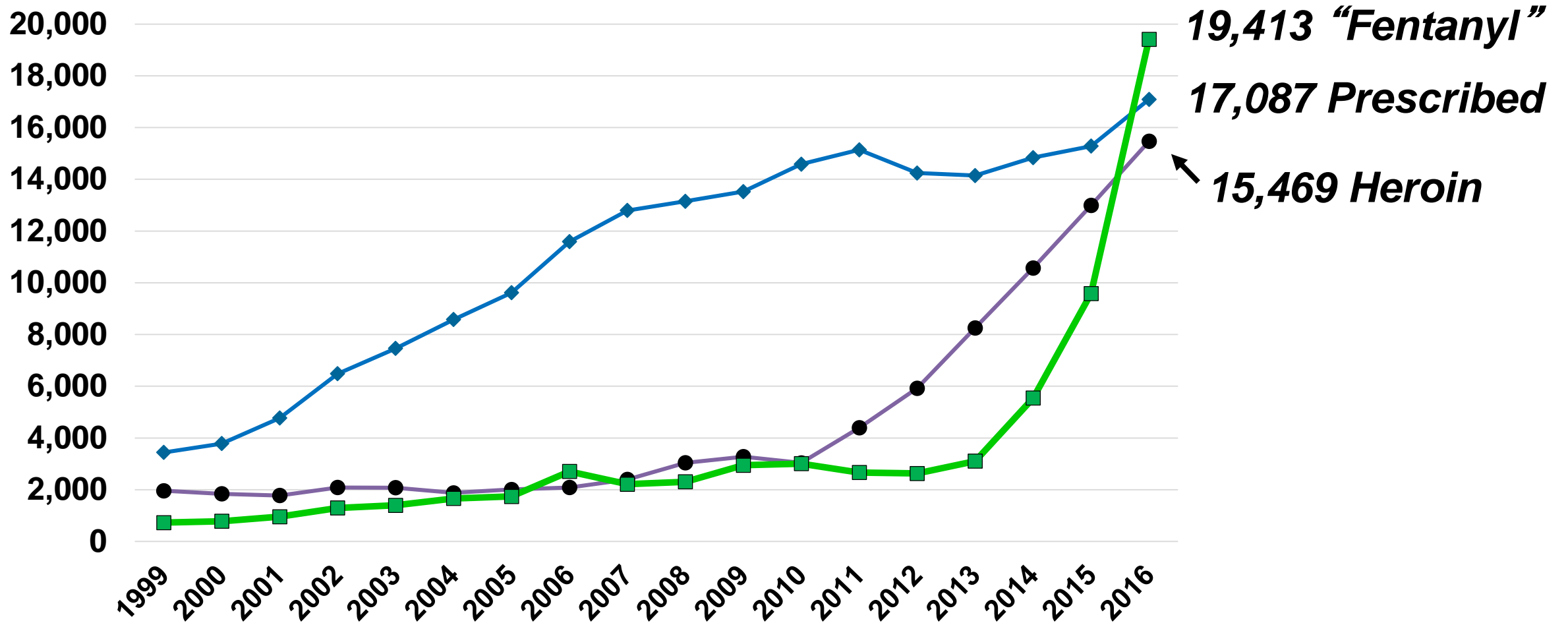
## Total Rx Opioid Tablets Dispensed in Retail Pharmacies in the USA:

- 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



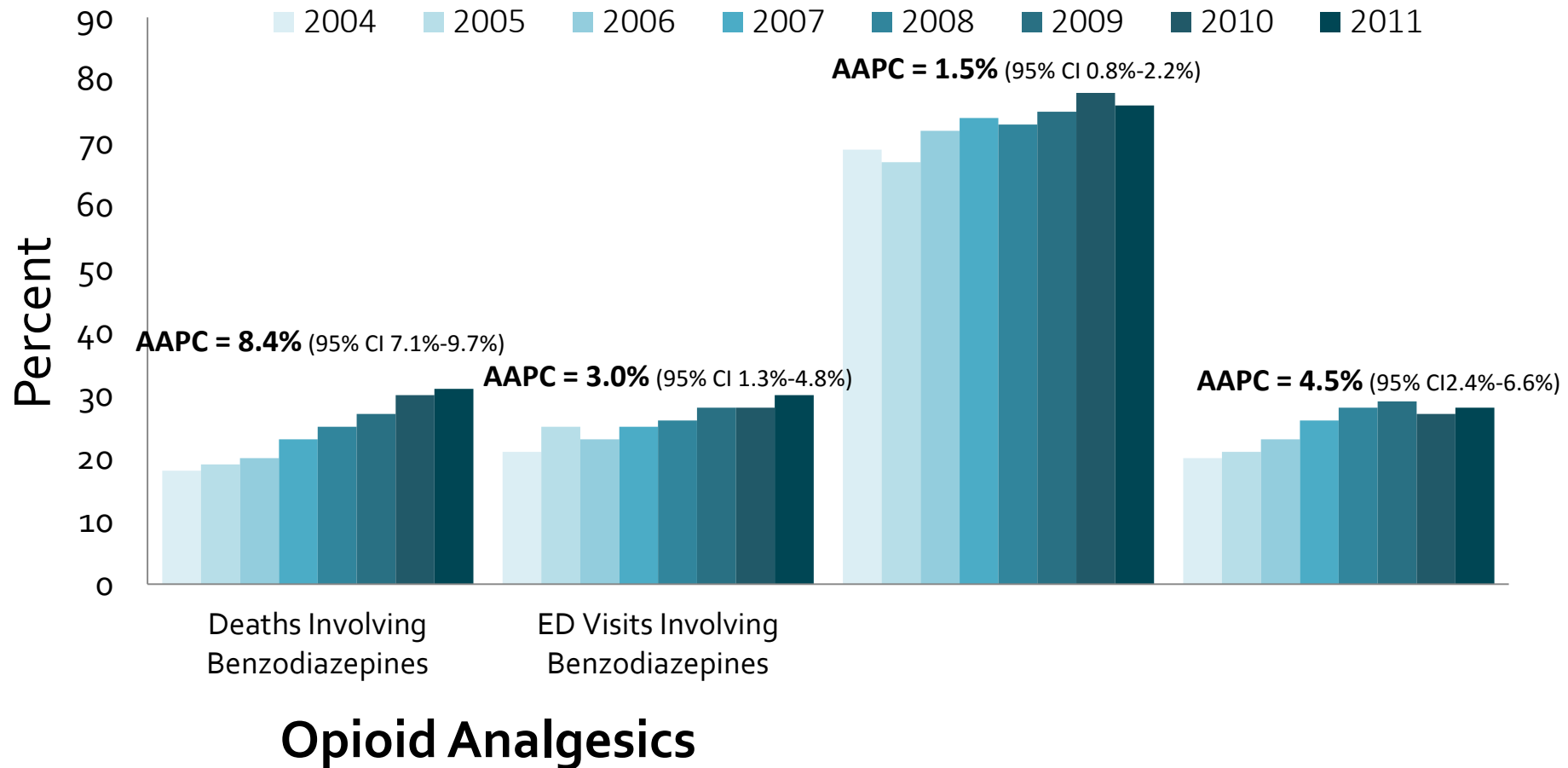
# Evolution of Drivers of Opioid Overdose Deaths: *Opioid Analgesics* ➡ *Heroin* ➡ *Fentanyl*



Source: NCHS WONDER, NCHS Data Brief 294

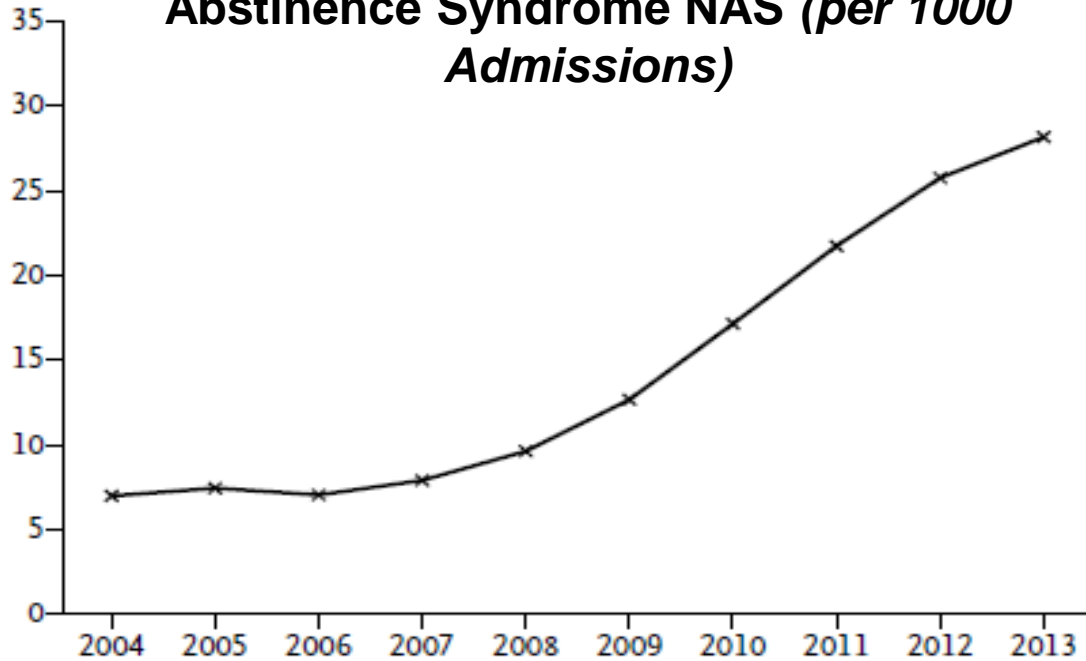
# Overlap of **Benzodiazepines and Opioids**

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



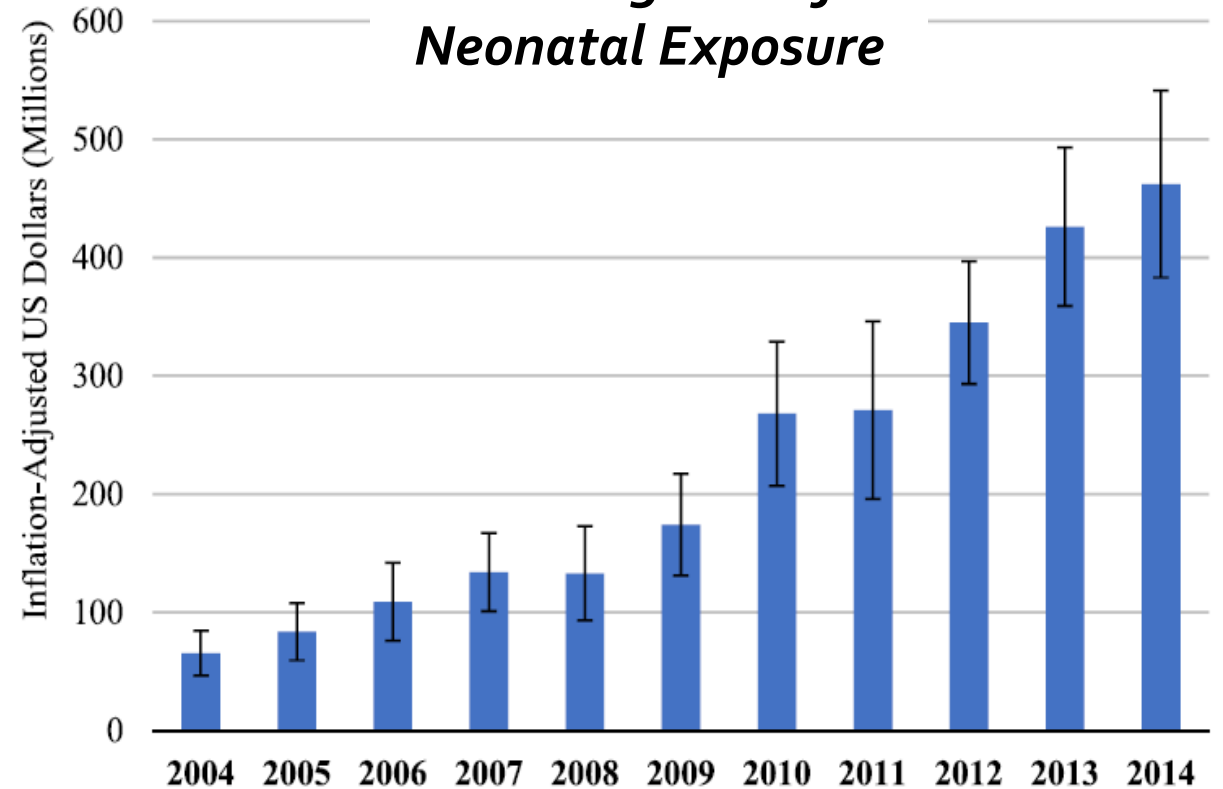
# Opioid Use and Misuse During Pregnancy

**Increasing NICU Admissions for Neonatal Abstinence Syndrome NAS (per 1000 Admissions)**



Source: Tolia VN, Patrick SW, et al., *NEJM* 2015;372:2118-2126.

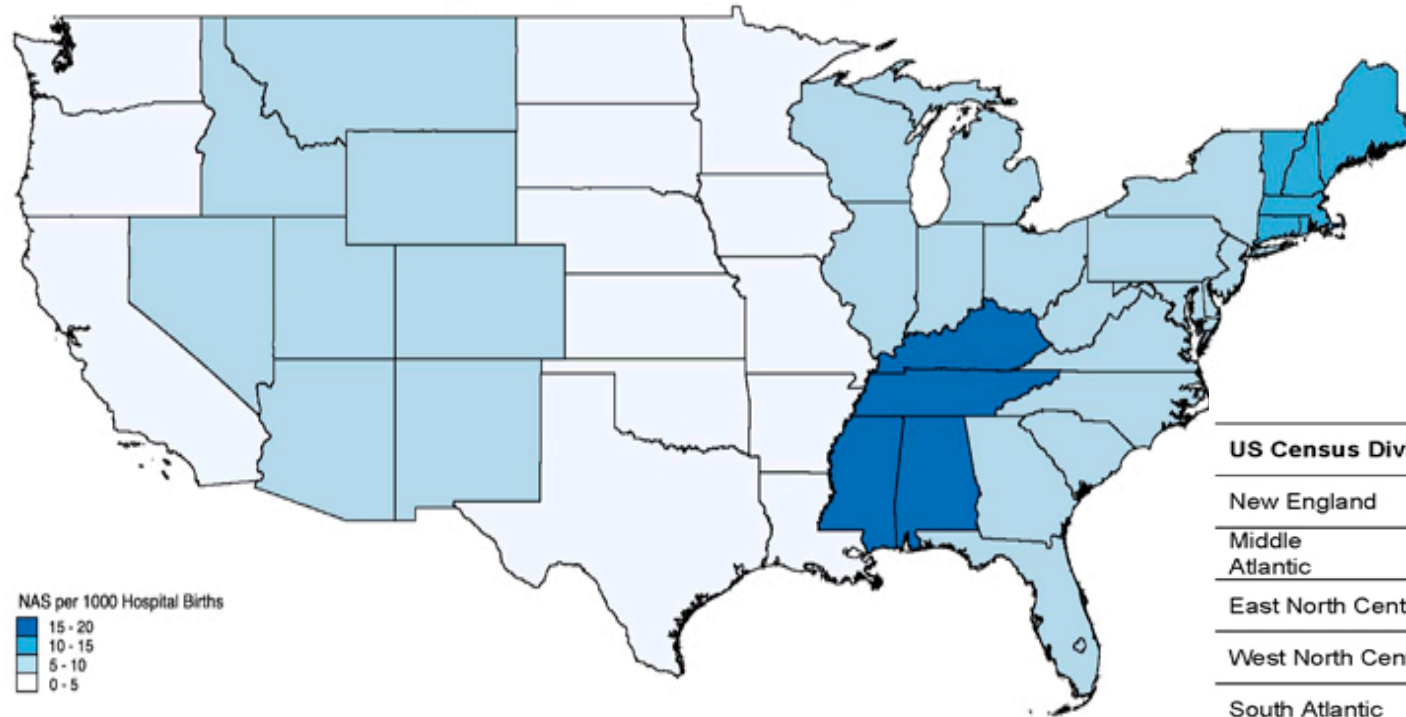
**Increasing Costs for Neonatal Exposure**



Source: Winkelman TNA, Villapiano N, Kozhimannil KB, Davis MM, Patrick SM.. *Pediatrics*. 2018;141(4):e20173520

# Increasing Neonatal Abstinence Syndrome: Incidence & Geography, U.S. 2009-2012

Neonatal Abstinence Syndrome per 1000 Hospital Births by US Census Division, 2012



NAS per 1000 Hospital Births

- 15 - 20
- 10 - 15
- 5 - 10
- 0 - 5

US Census Division	NAS Rate per 1000 Births (95% CI)
New England	13.7 (12.5-14.5)
Middle Atlantic	6.8 (5.9-7.6)
East North Central	6.9 (6.0-7.8)
West North Central	3.4 (3.0-3.8)
South Atlantic	6.9 (6.3-7.4)
East South Central	16.2 (12.4-18.9)
West South Central	2.6 (2.3-2.9)
Mountain	5.1 (4.6-5.5)
Pacific	3.0 (2.7-3.3)

Patrick SW, Davis MM, Lehman CU, Cooper WO. Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012. *J Perinatol.* 2015 Aug;35(8):667. doi: 10.1038/jp.2015.63. PubMed PMID: 26219703.



# Increasing NAS:

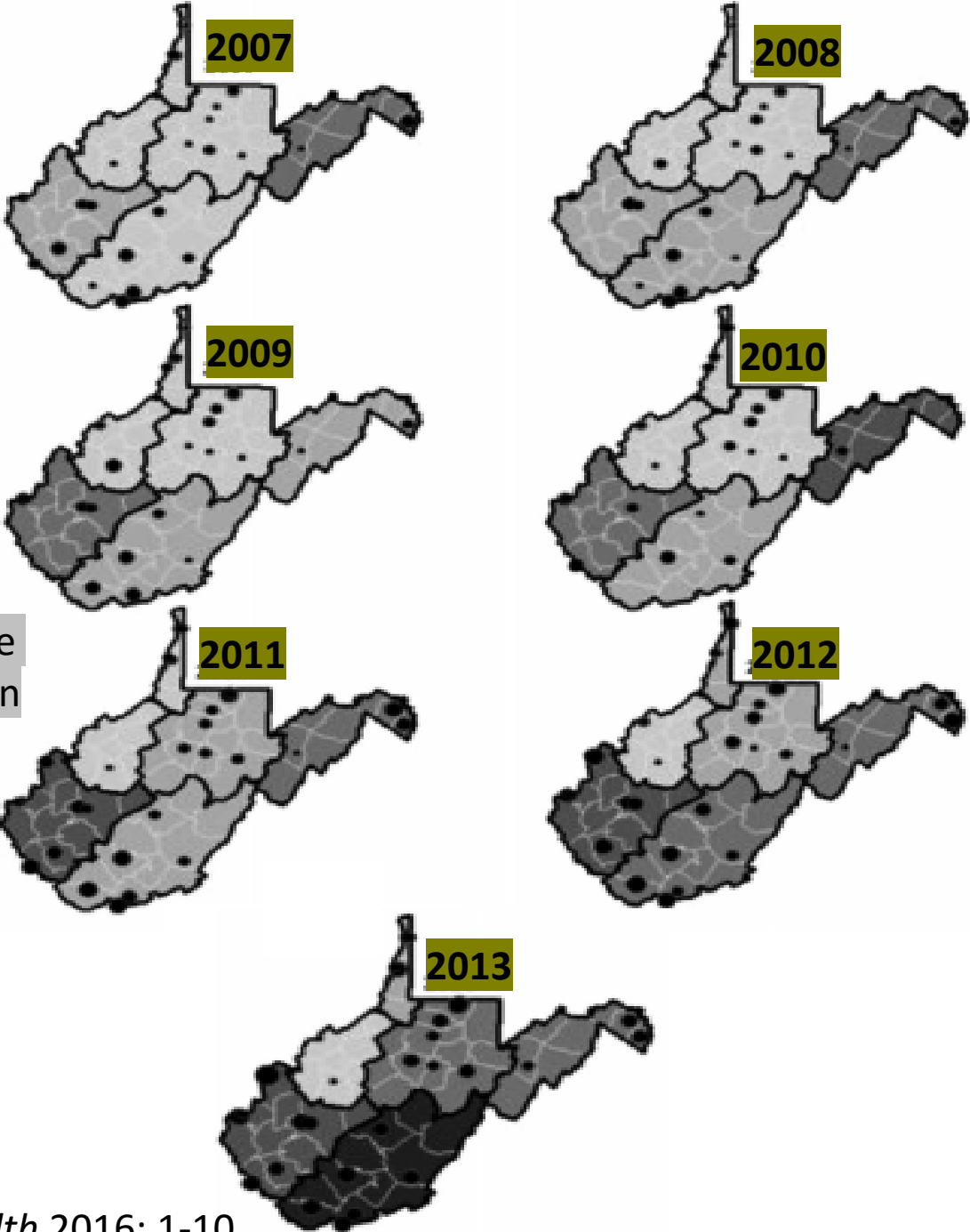
## West Virginia 2007-2013

NAS cases per 1000 live births by hospital

- 0.0 – 1.2
- 1.3 – 13.9
- 14.0 – 27.9
- 28.0 – 74.9
- 75.0 - 100
- 101.0 +

NAS cases per 1000 live births by SAMSHA region

- 0.2 – 10.0
- 10.1 – 20.0
- 20.1 – 30.0
- 30.1 – 40.0
- 40.1 +

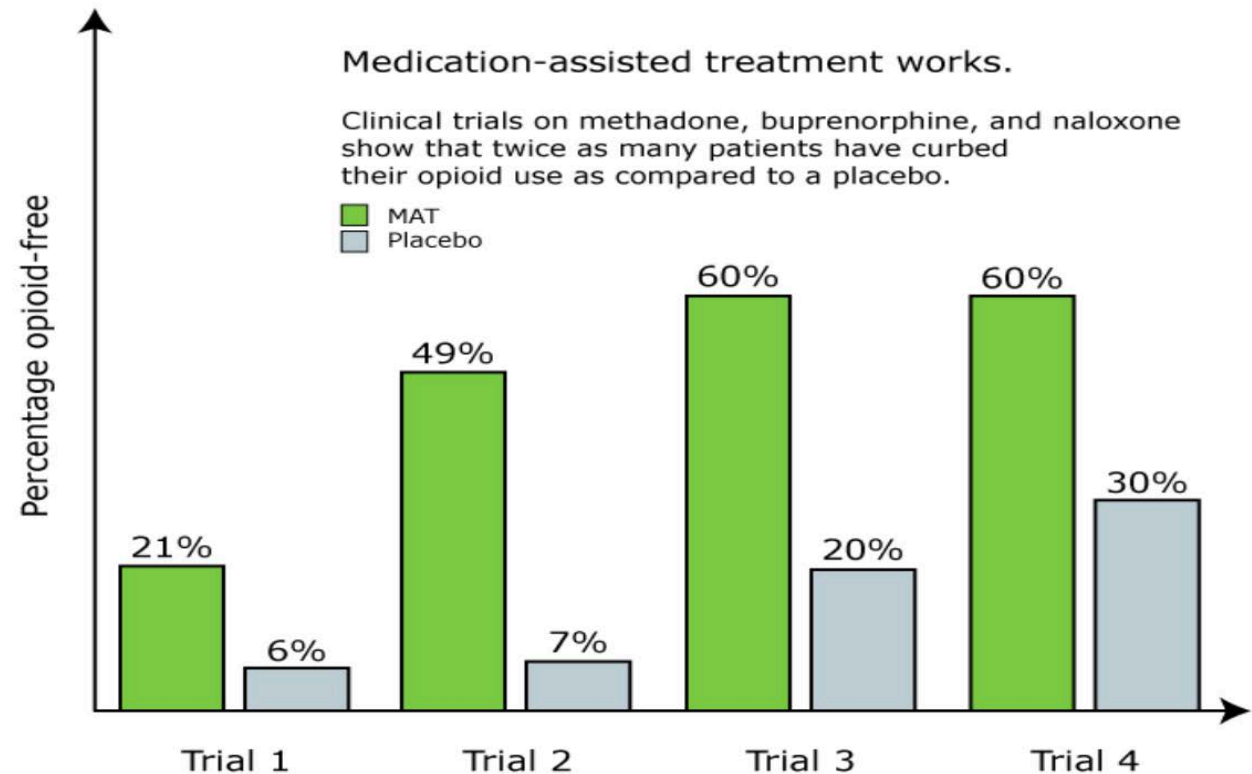


Source: Stabler ME, et al. *Journal of Rural Health* 2016; 1-10

# Medication Assisted Treatment

**Definition:** The use of medications in combination with counseling and behavioral therapies for the treatment of substance use disorders.

- FDA Approved Medications:
  - Methadone
  - Naltrexone
  - Buprenorphine

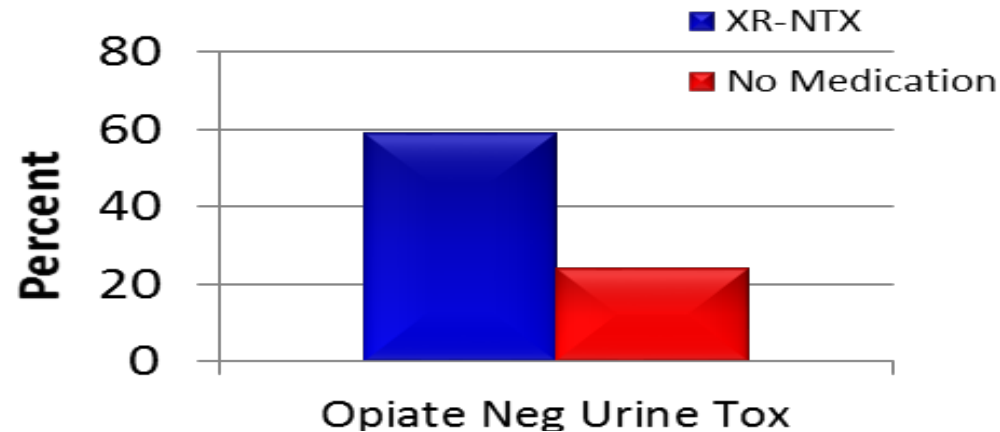


# Improving Outcomes in other than Treatment Settings

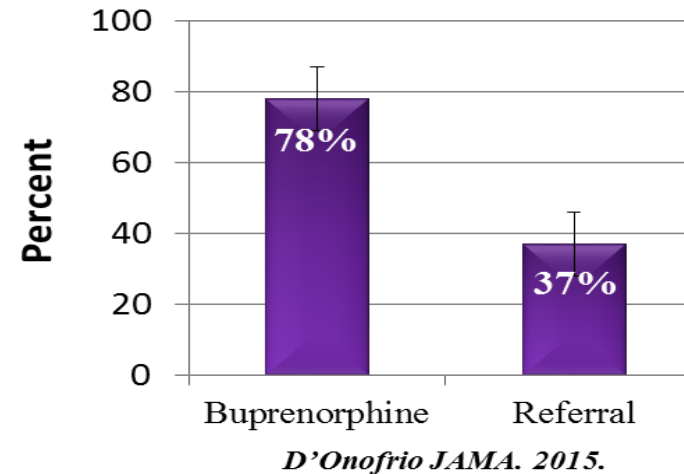
- Initiating buprenorphine treatment in the **emergency department** improves treatment engagement and reduces illicit opioid use
- Extended release naltrexone initiated in **criminal justice** settings lowers relapse rates and overdoses



### Post Prison-Release Outcomes



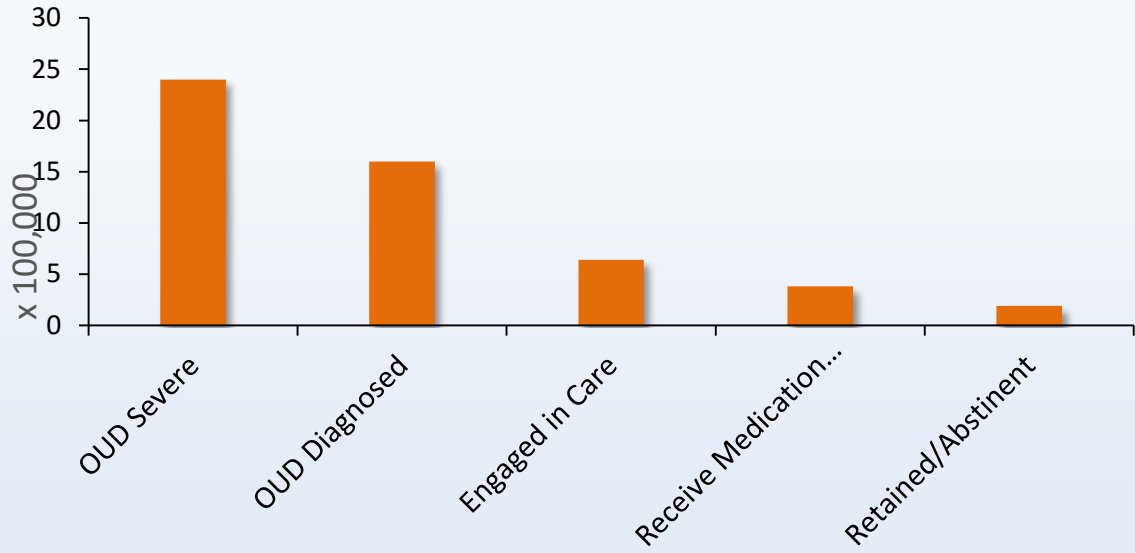
### ED-initiated Buprenorphine Increased TX Engagement



Lee JD, et al., *Addiction* 2015;100:1005-1014  
and *New Eng J Med* 2016;374:1232-1242

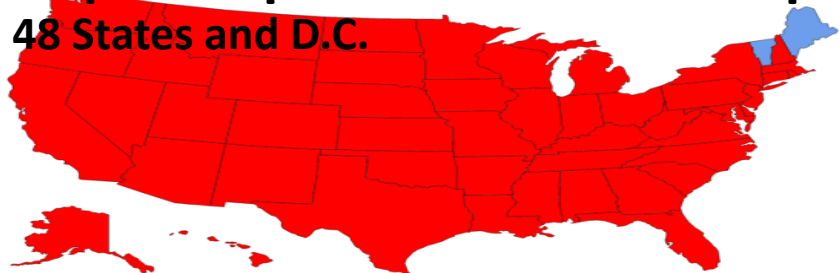
*D'Onofrio JAMA. 2015.*

# Medications are *Underused*



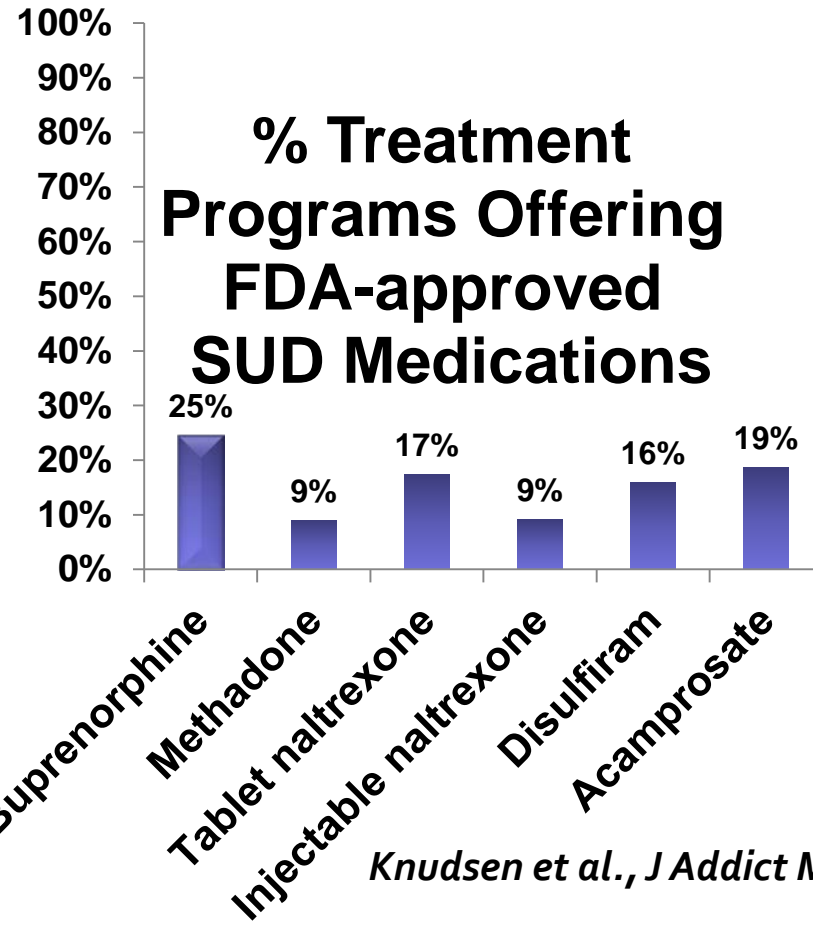
Williams AR, Nunes E, Olfson M. Health Affairs Blog, 2017

**Opioid Use Disorder Rates Exceed Buprenorphine Treatment Capacity – 48 States and D.C.**

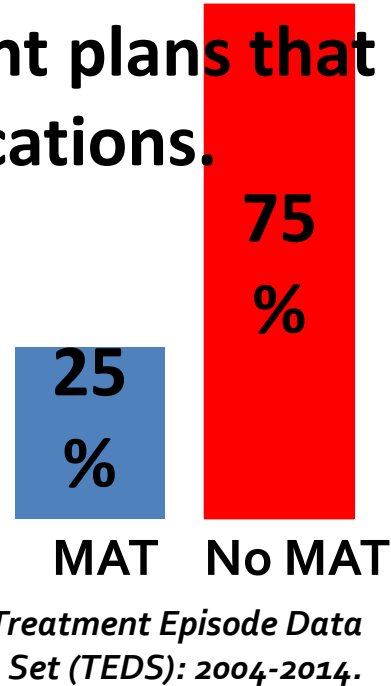


Jones C et al., Am J Public Health 2015.

In 2014, only 25% of opioid admissions had treatment plans that included receiving medications.



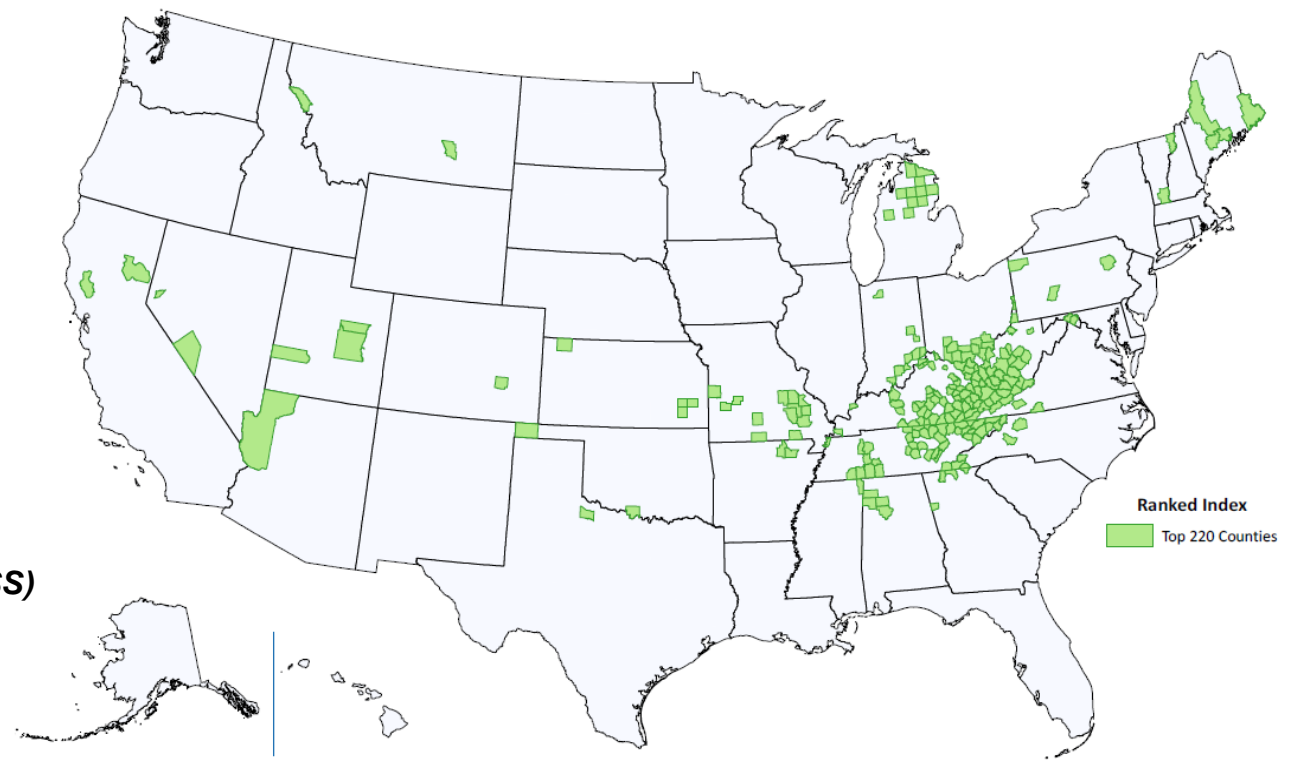
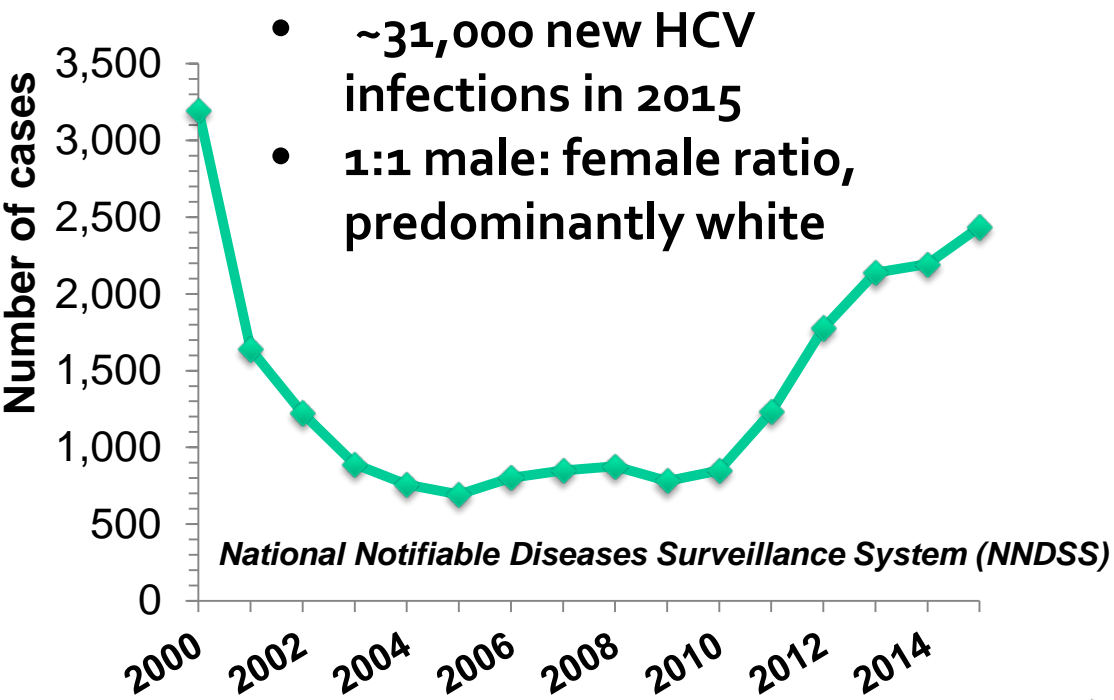
Knudsen et al., J Addict Med 2011





# Rising rates of HCV

# Counties Deemed Highly **Vulnerable** to Rapid Dissemination of HCV or HIV



Source: Van Handel et al, JAIDS 2016

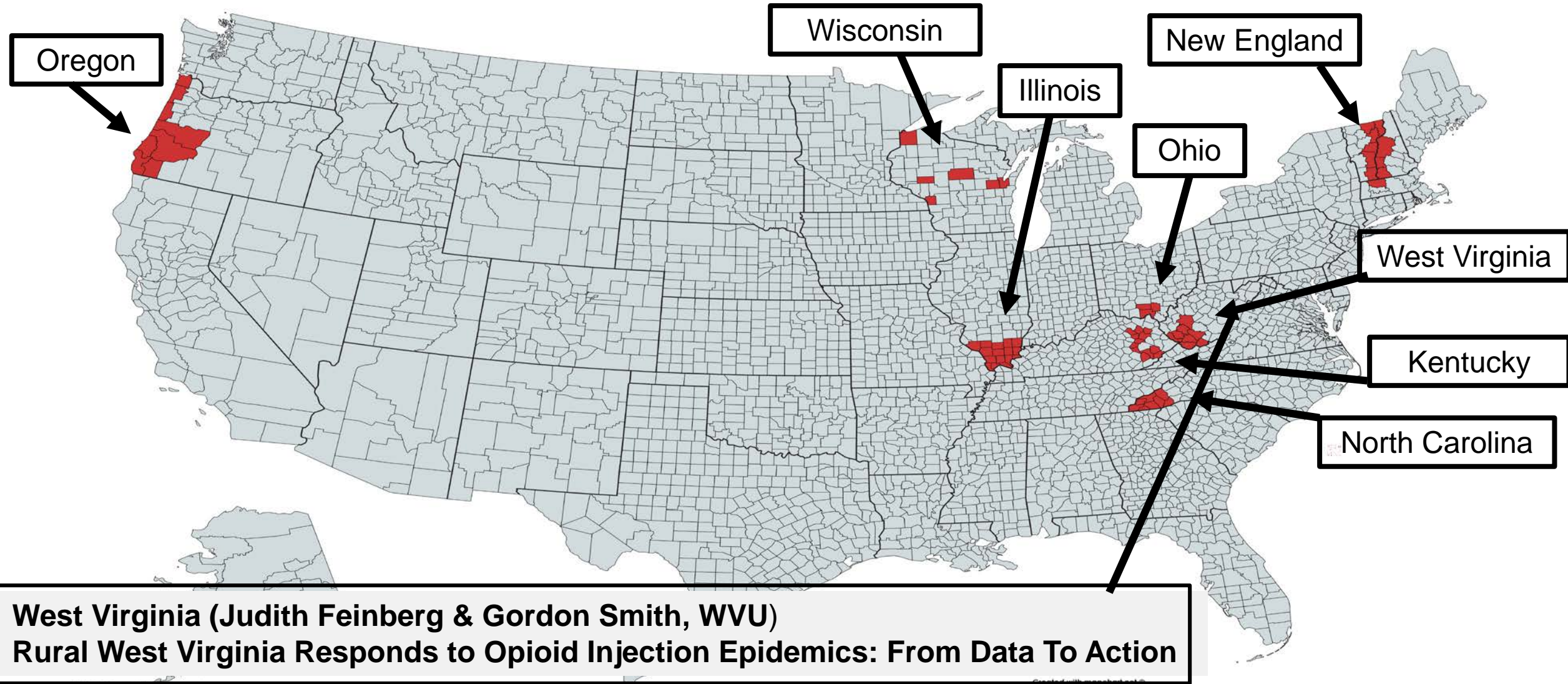
Creation Date: August 27, 2015  
PROJECTION: NAD 1983 Contiguous USA Albers;  
NAD 1983 Alaska Albers, NAD 1983 State Plane Hawaii

## HIV (and Hepatitis C) Outbreak Linked to Oxymorphone Injection Use in Indiana, 2015

Peters et al.

*The New England Journal of Medicine*  
2016;375:229-239

# *Rural Opioid Initiative*: NIDA, CDC, SAMHSA, ARC Partnering to Combat HIV and Viral Hepatitis in Rural Areas



# Project Status

---

## 8 Sites with two stage awards-

UG3: multi-method community assessments---first 2 years

UH3: propose & test implementation of evidence-based practices to address opioid use, HIV/AIDS & related comorbidities in their communities.—next 3 years

Status: Sites are integrating available surveillance data related to opioid use, overdose & infectious disease consequences

- Qualitative & quantitative data from injectors

- Qualitative interviews with stakeholders (providers, law enforcement & judiciary, etc.)

# Examples of West Virginia Projects

---

*Use of wide array of project mechanisms: R01, R21, R03, R36, R00, F30, F31, UG3*

**R00:** Characterization of Menthol's Effect on Nicotine reward and Nicotine Receptor Neurobiology - Brandon Henderson

**R01:** Pharmacy Naloxone Distribution: Assessing A New Tool To Reduce Overdose Mortality - Robin Pollini

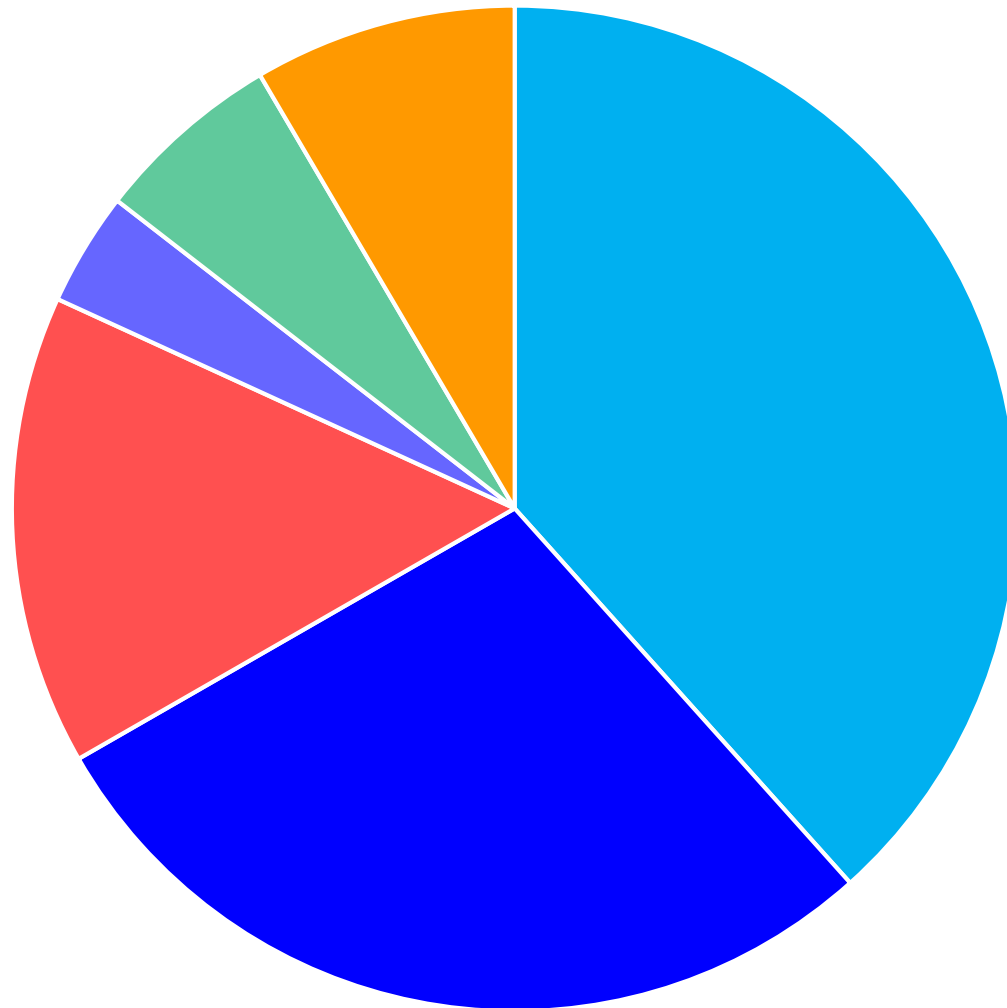
**R21:** Drugs And Driving: Developing A Sentinel Drug\_Fars For Research - Gordon Smith

**R03:** Reducing The Deleterious Effects Of Synthetic Cannabinoid Withdrawal On Emotionality And Motivation - Steven Kinsey

**F30** G-Protein Signaling-12 (Rgs12) In Morphine Modulated Behavior - Shane Kaski

# National Institute on Drug Abuse Portfolio

FY 2017 Actual



- Division of Neuroscience & Behavior -- 38%
- Division of Epidemiology, Services & Prevention Research -- 28%
- Division of Therapeutics and Medical Consequences -- 15%
- Center for the Clinical Trials Network -- 4%
- RMS -- 6%
- Intramural Research -- 8%



# Summary:

---

- Complex biological, developmental and social aspects of substance use and addiction suggest *multipronged responses*.
- Science must continue to focus on *Etiology, Prevention, Treatment, Medications Development, Services, and Neuroscience* to provide the best solutions for drug addiction.