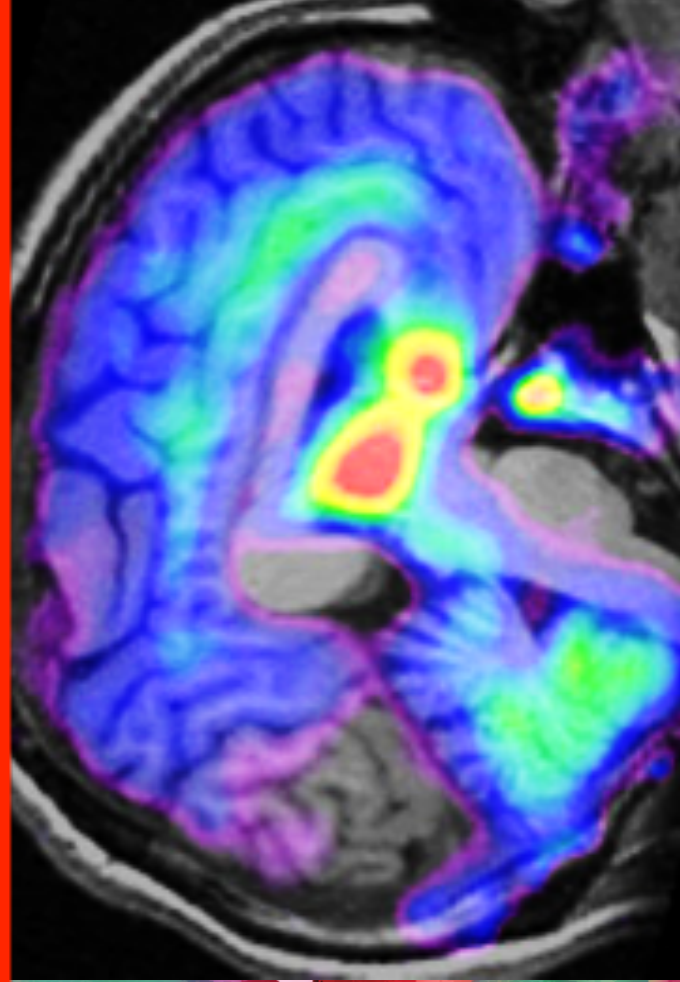


# *Opioids and Cannabis: Myths and Misperceptions*



Nora D. Volkow, M.D.



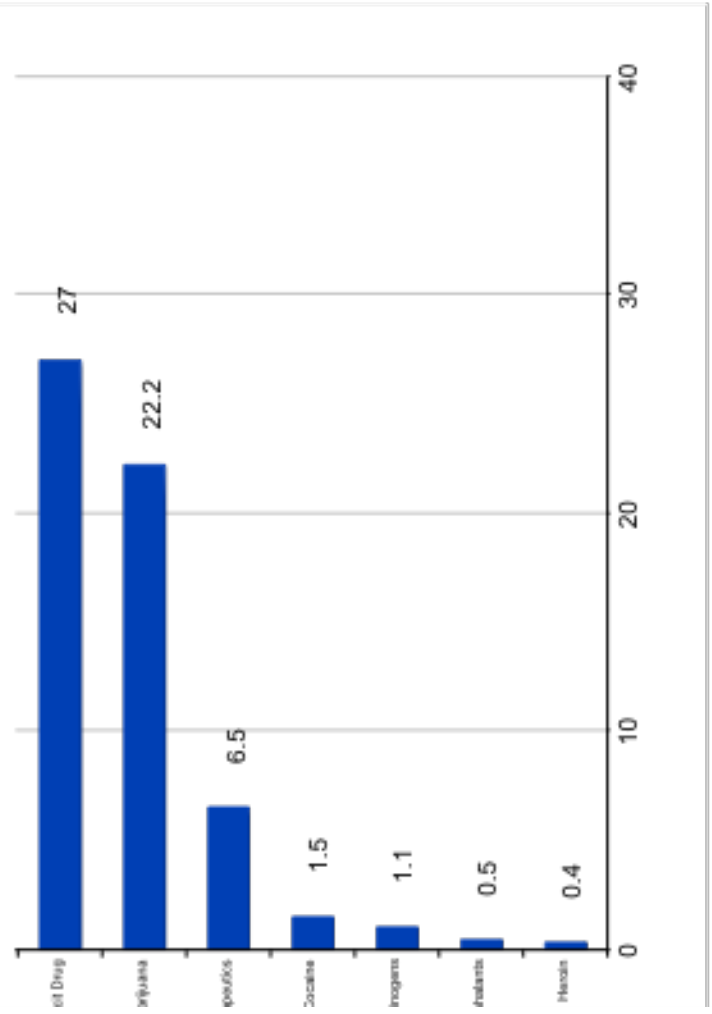
Director  
National Institute  
on Drug Abuse



@NIDAnews

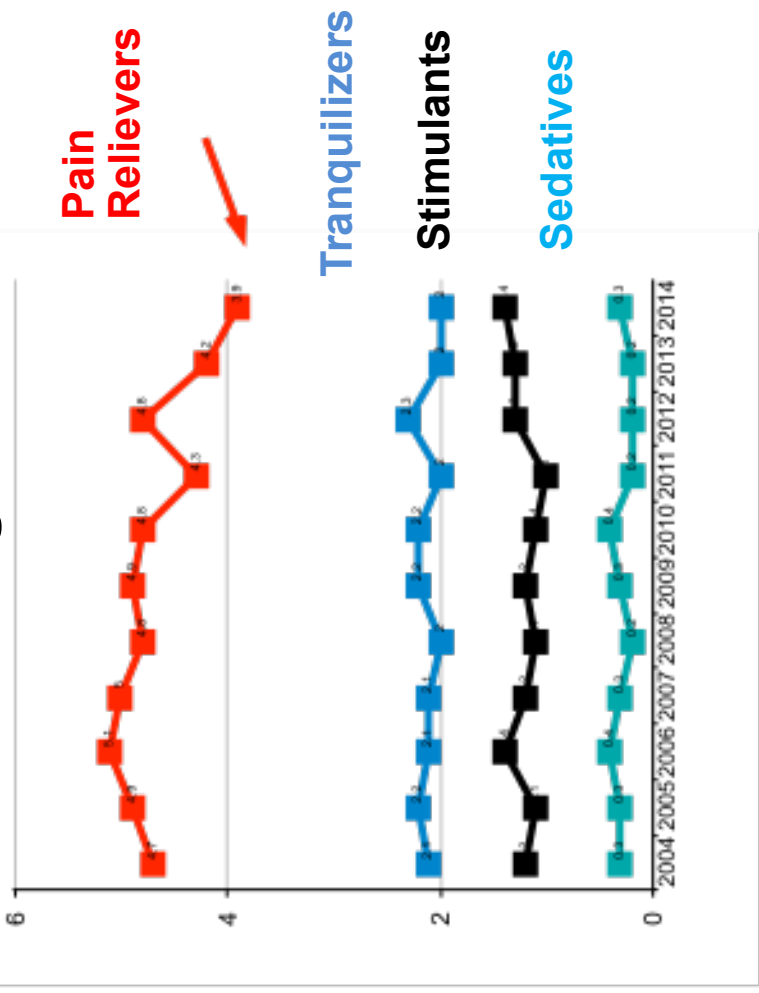
# Prescription Drug Misuse/Abuse is a Major Problem in the US

Current Drug Use Rates in Persons Ages 12+



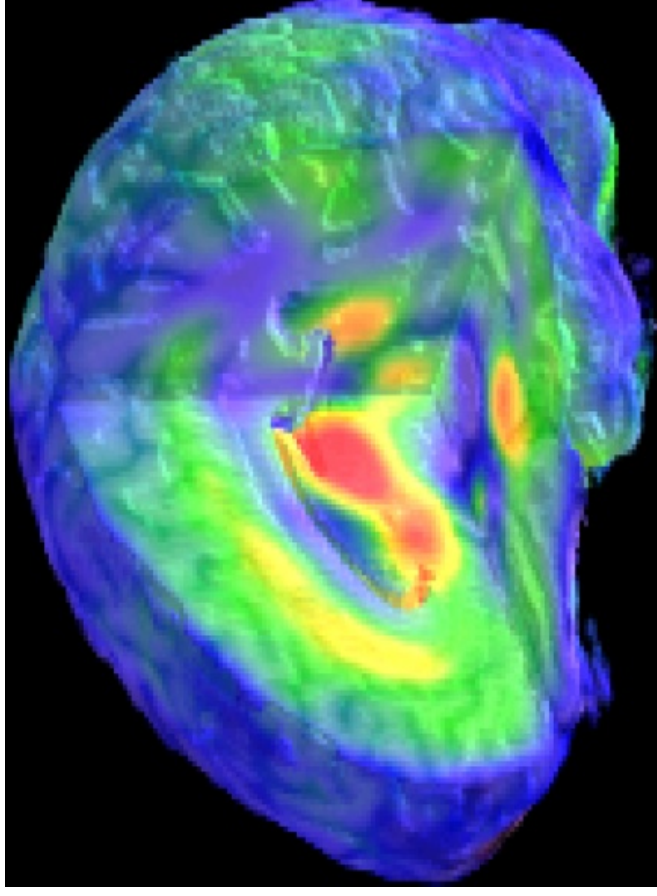
Numbers in Millions

Past Year Nonmedical Use of Psychotherapeutic Drugs Persons Ages 12+



Source: SAMHSA, 2014 National Survey on Drug Use and Health, 2015.

# Analgesic Mechanisms of Mu Opiate Drugs (Heroin, Vicodin, Morphine)



**ACC**  
(pain)

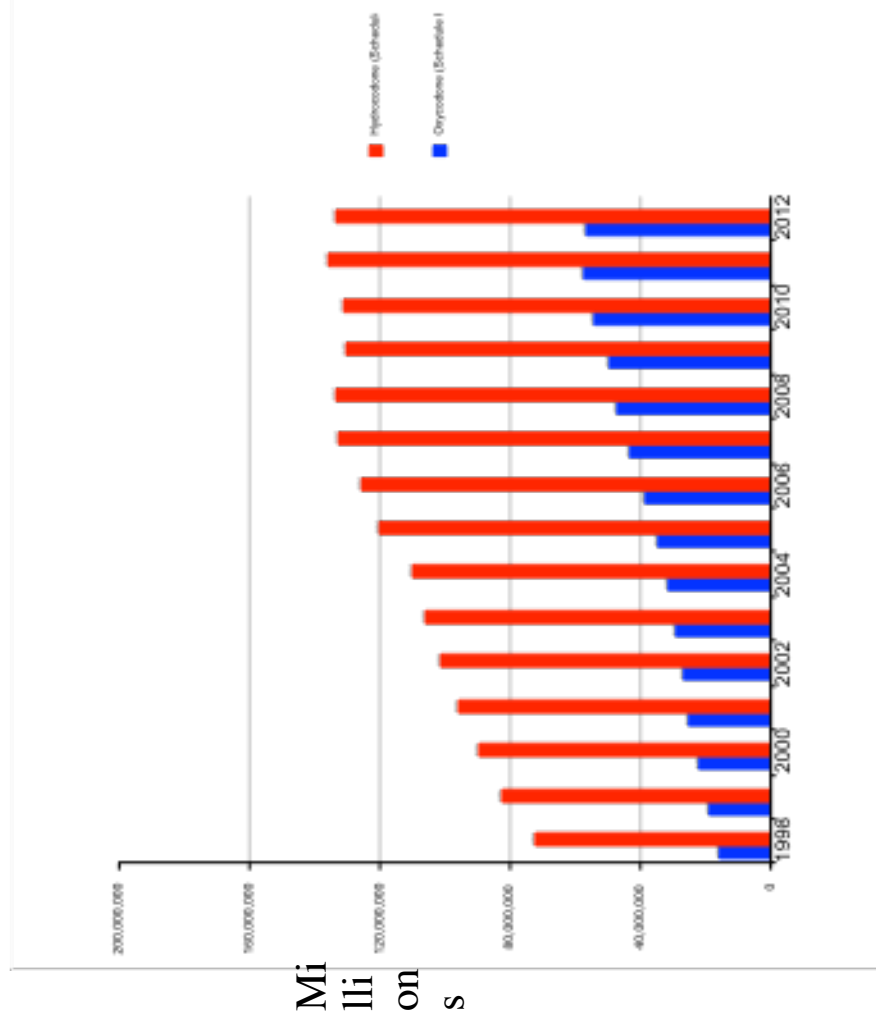
**Accumbens**  
(reward)

**PAG**  
(pain)

**Thalamus**  
(pain)

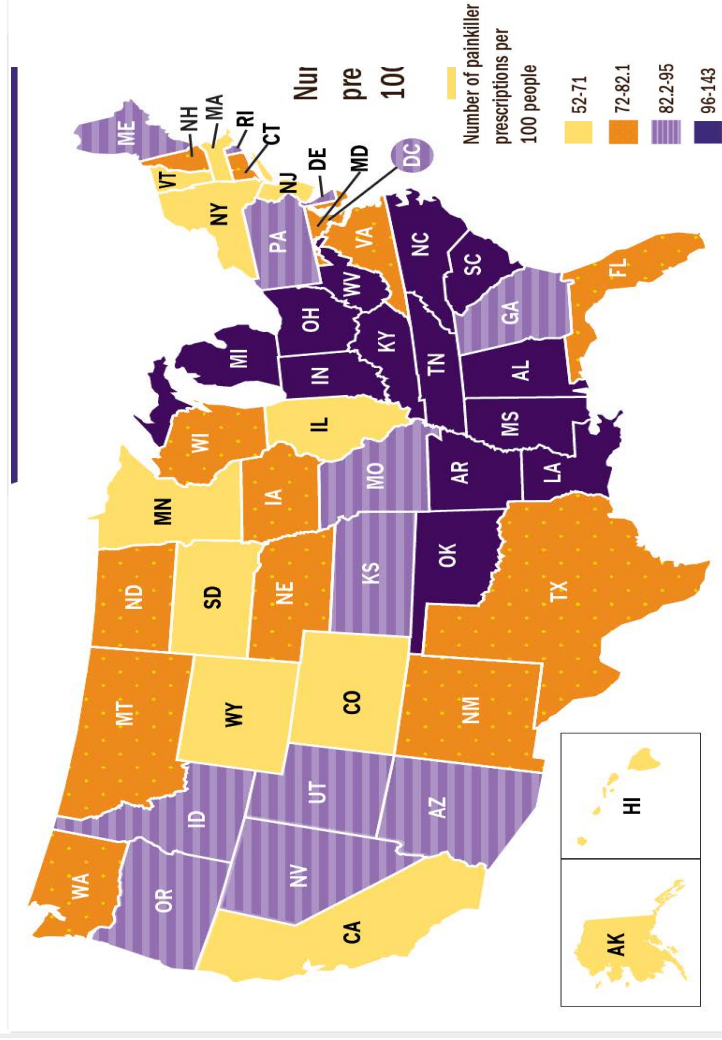
# Opioid Prescriptions have Quadrupled since 1999

Oxycodone & Hydrocodone Prescriptions



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

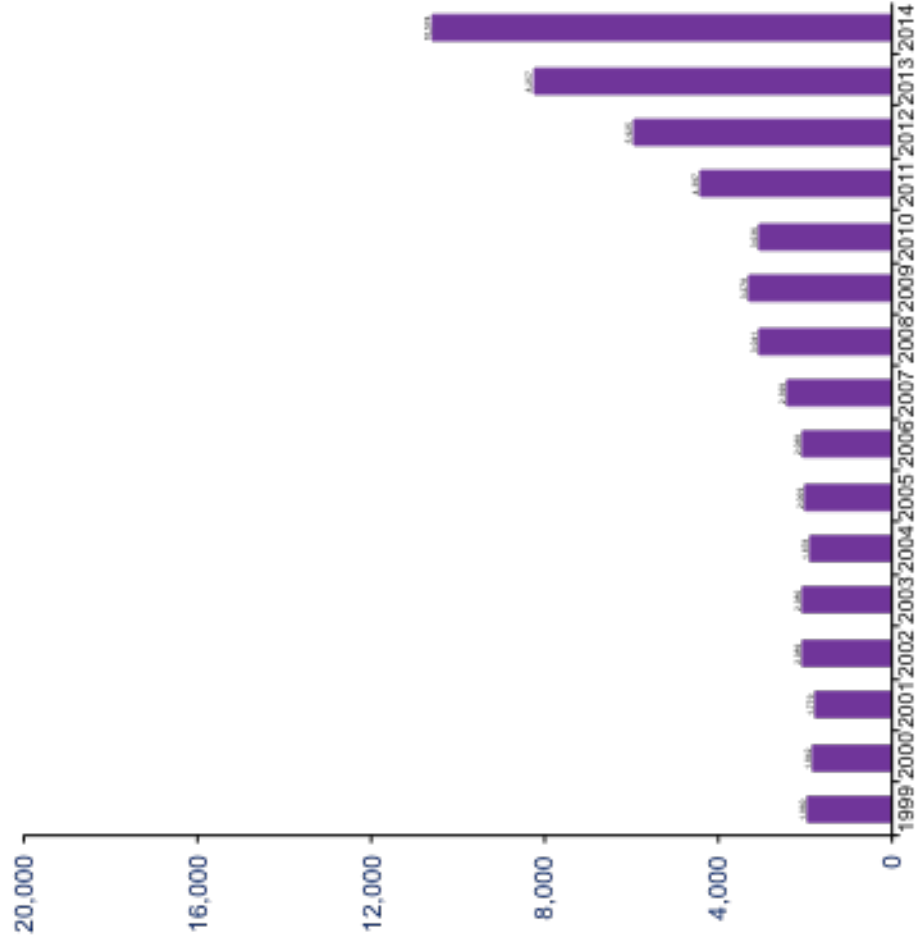
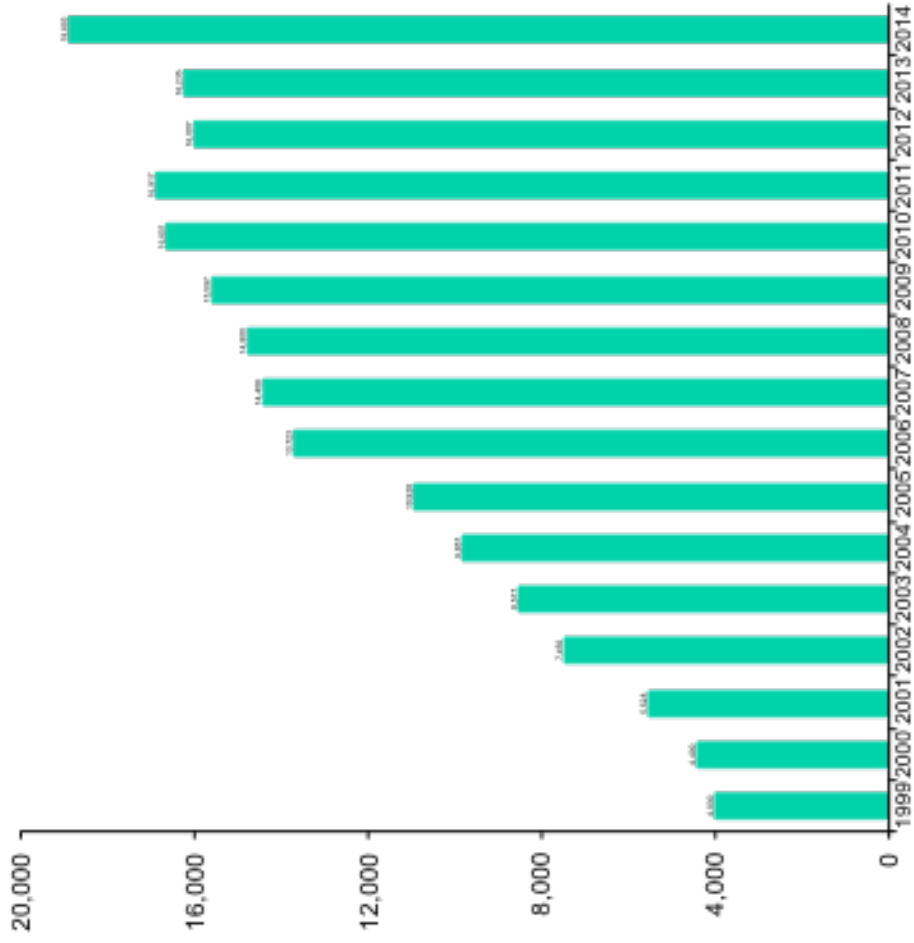
# Opioid Prescribing Rates Are 3x Higher In Some States Than Others



Source: MMWR Vital Signs, July 2014.

Source: IMS, National Prescription Audit (NPATM), 2012.

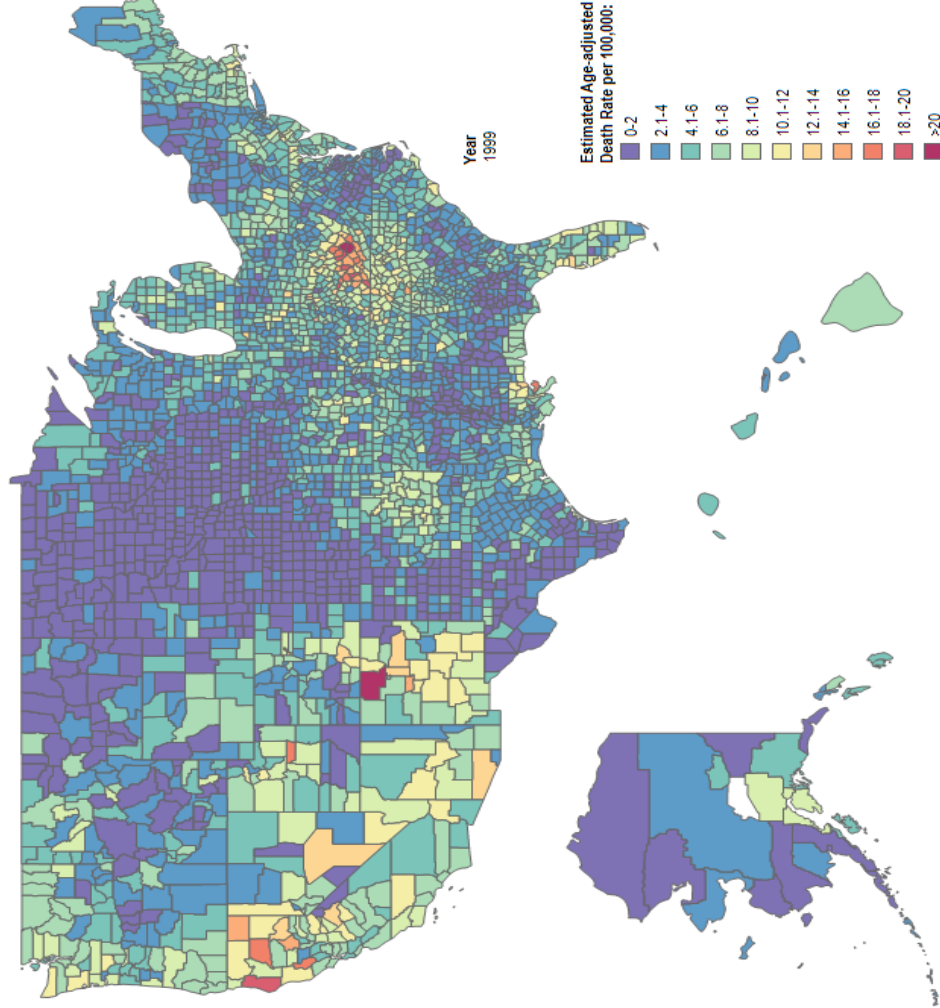
### Heroin Overdose Deaths in the USA



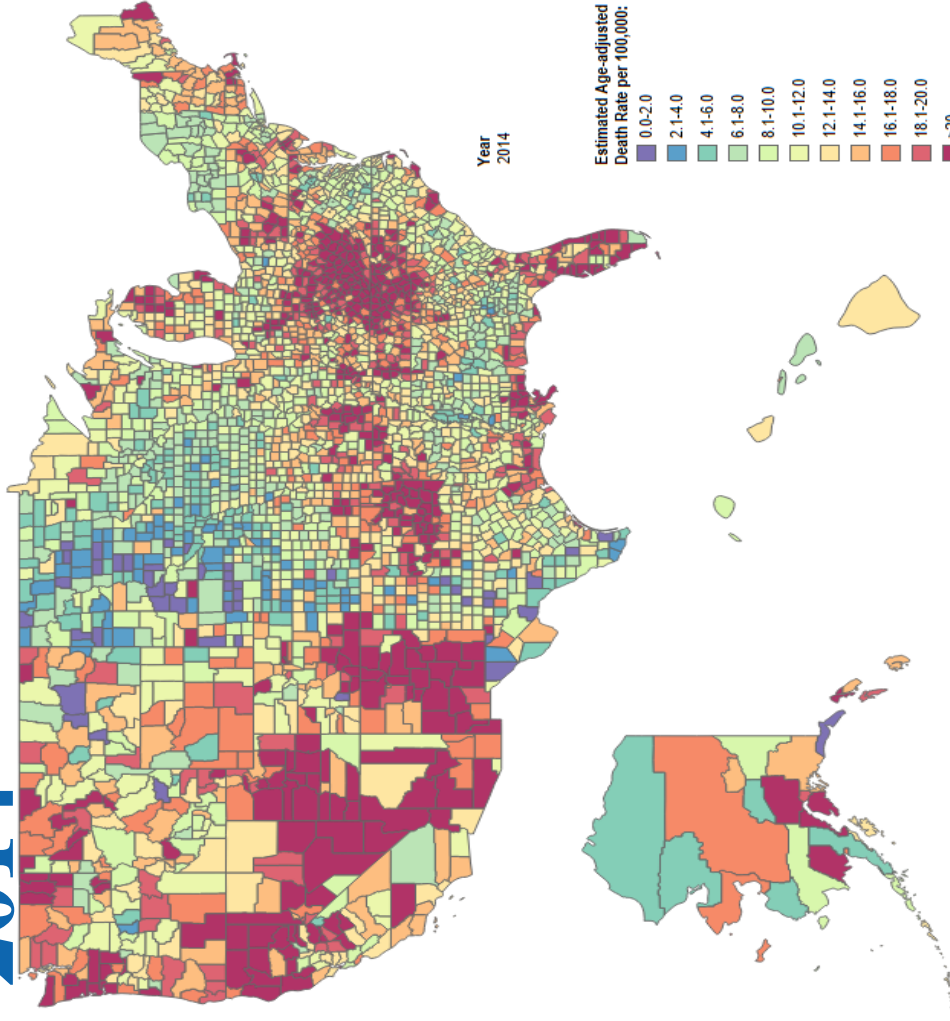
Centers for Disease Control and Prevention. Wide-ranging Online Data for Epidemiologic Research (WONDER), Multiple Cause-of-Death file, 2000–2014. 2015 ([http://www.cdc.gov/nchs/data/health\\_policy/AADR\\_drug\\_poisoning\\_involving\\_OA\\_Heroin\\_US\\_2000-2014.pdf](http://www.cdc.gov/nchs/data/health_policy/AADR_drug_poisoning_involving_OA_Heroin_US_2000-2014.pdf))

# Overdose Death Rates

1999

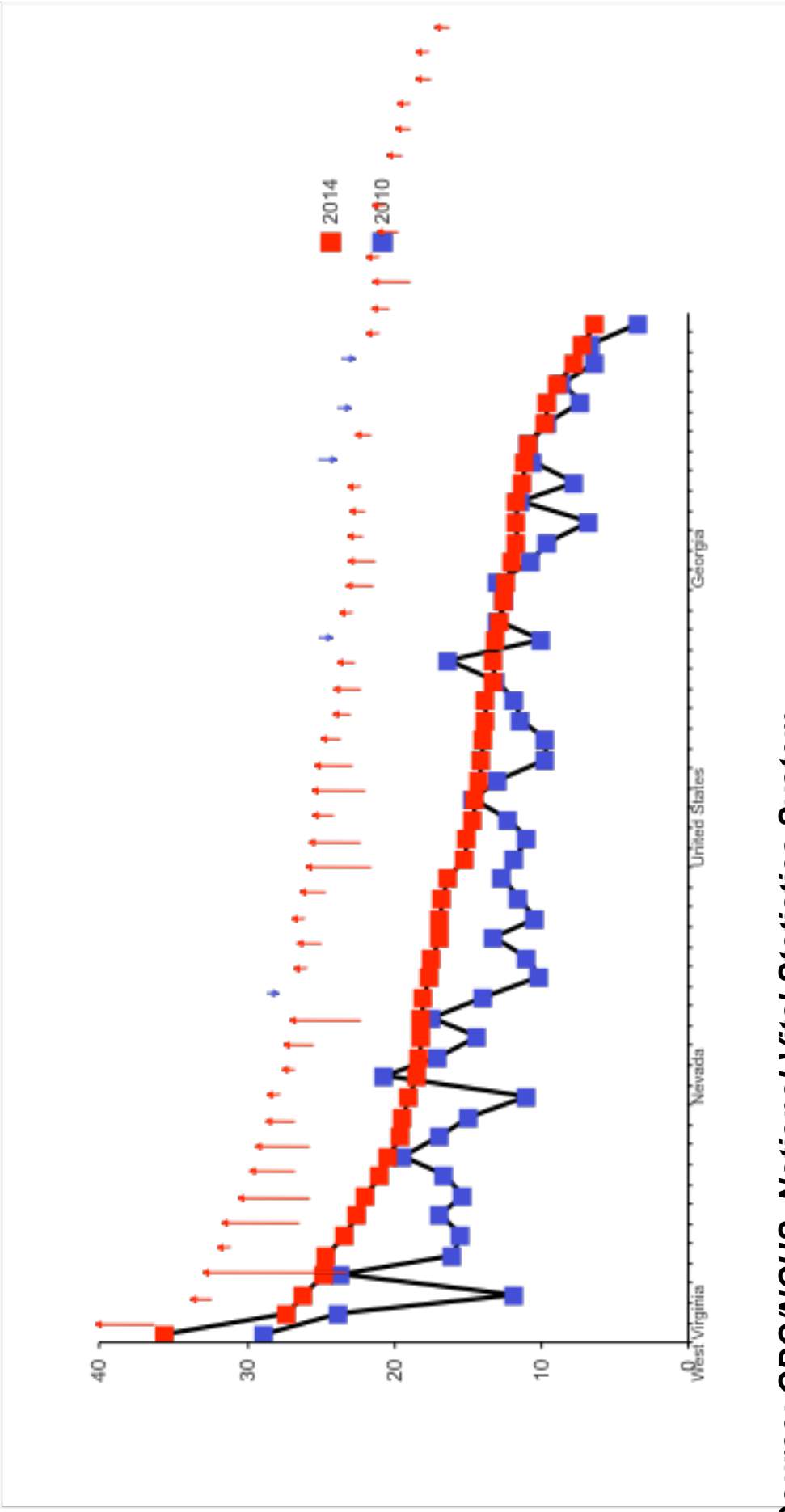


2014



Designed by L. Rossen, B. Bastian & Y. Chong. SOURCE: CDC/NCHS, National Vital Statistics System

# Drug Poisoning Death Rates Have Increased In Almost Every State

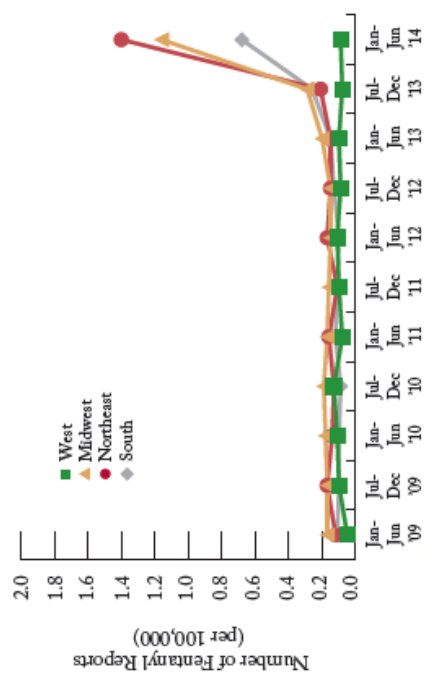


Source: CDC/NCHS, National Vital Statistics System.

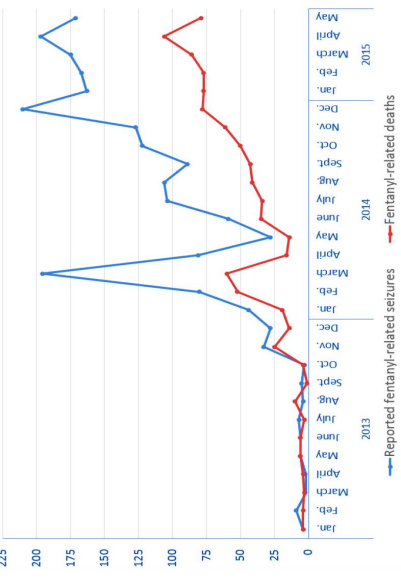
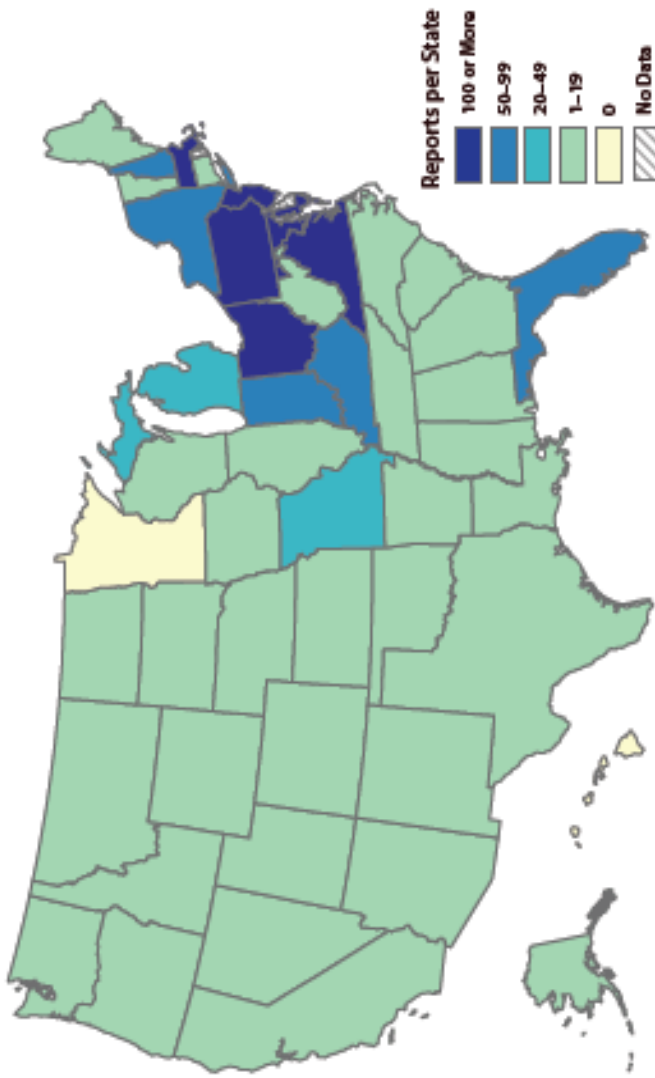


# Fentanyl Seizures Have Been Increasing Particularly in the Northeast

**Figure 3** NFLIS regional trends in fentanyl reported per 100,000 persons aged 15 or older, January 2009–June 2014



**Figure 6** Fentanyl reports in NFLIS, by State, January–June 2014



## Fentanyl seizures mirror fentanyl-related deaths (Ohio)



# Improving Treatments for Pain: Safer Analgesics

## *Opioid deterrent formulations*

### Pro-drugs



### Tamper resistant formulation



### Drug combinations with adverse effects if injected



### Non-Opioid based analgesics

Cannabinoids;  
Inflammatory mediators;  
Ion channel blockers

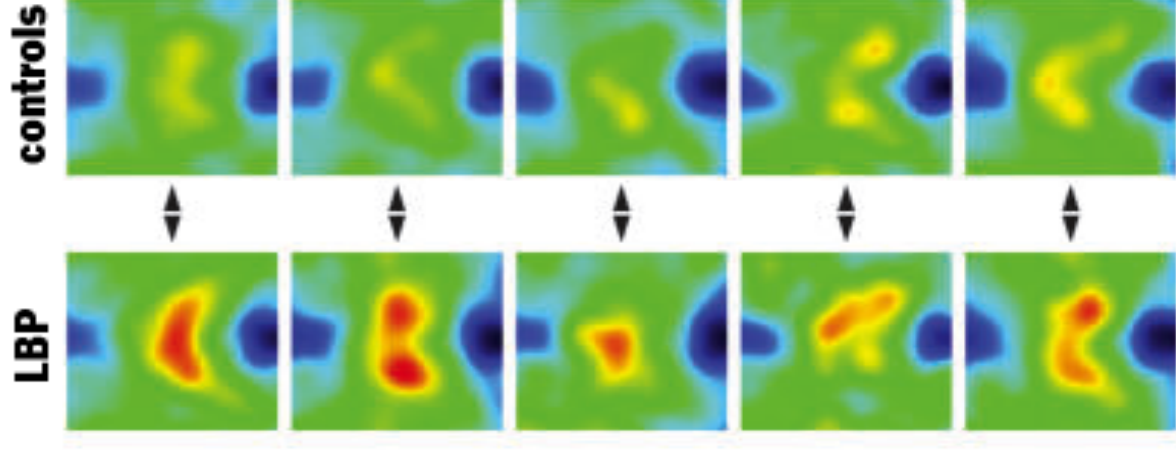
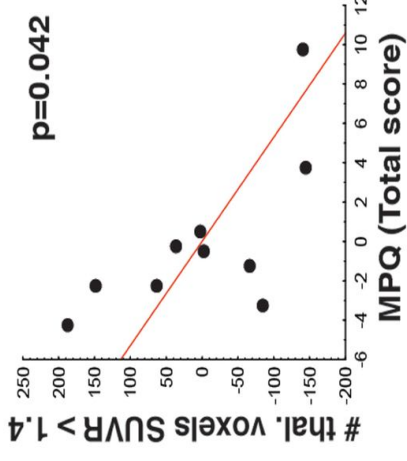
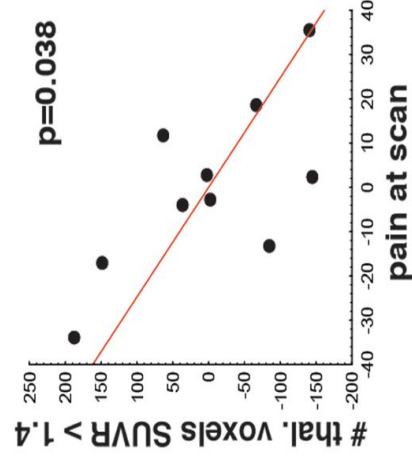
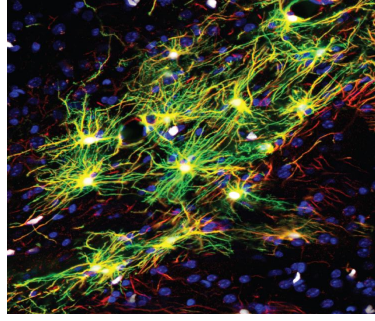
### Non-pharmacological mechanisms and treatments

Surgical interventions for pain;  
Neural stimulation technologies for chronic pain; Spinal cord stimulation

# Knowledge of Pain Pathways – New Biomarkers for Pain?

New study assess glial role in human pain

- Patients with low back pain (LBP) versus controls
  - Uses PET to detect levels of glial protein (TSPO)
  - Demonstrates role of glial activation in human pain
  - Possible biomarker
  - May suggest new treatments for chronic pain



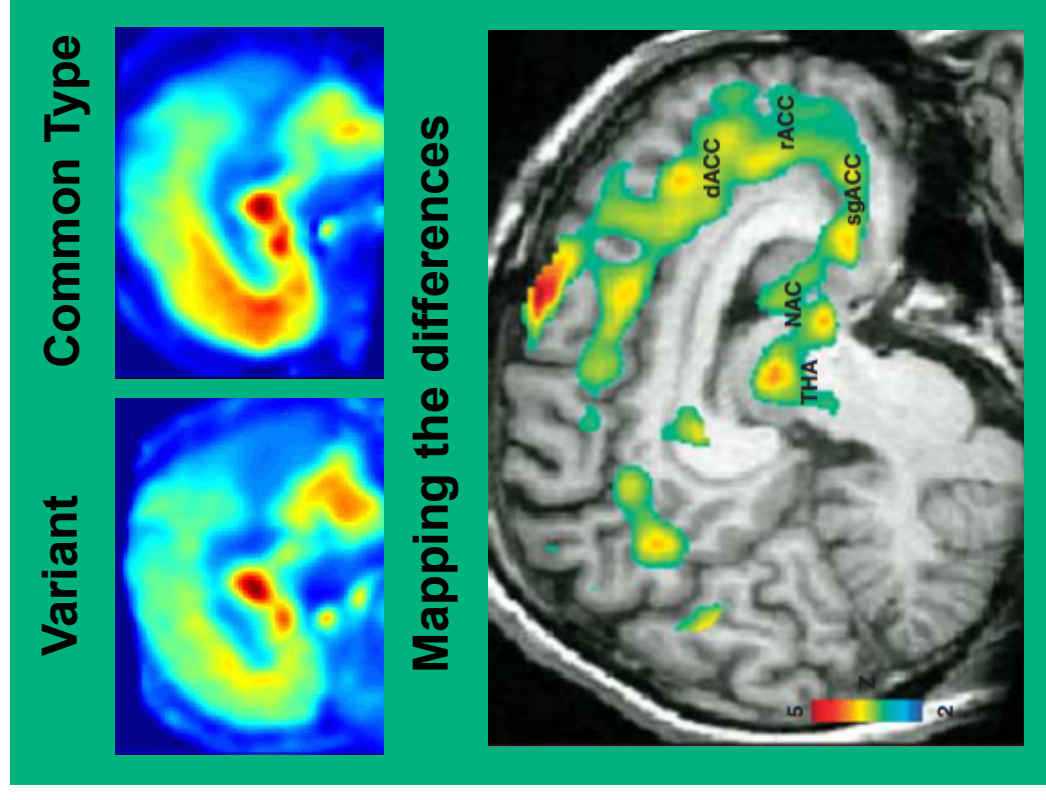
# Limiting Abuse by Predicting Addiction

- *OPRM1* encodes for the target of opioids
- Can variants predict likelihood of addiction?
- *OPRM1* variant
  - Affects receptor levels in brain
  - Associated with increased risk for addiction, overdose severity

Hancock et al., *Biol Psychiatry* 2015; 78.

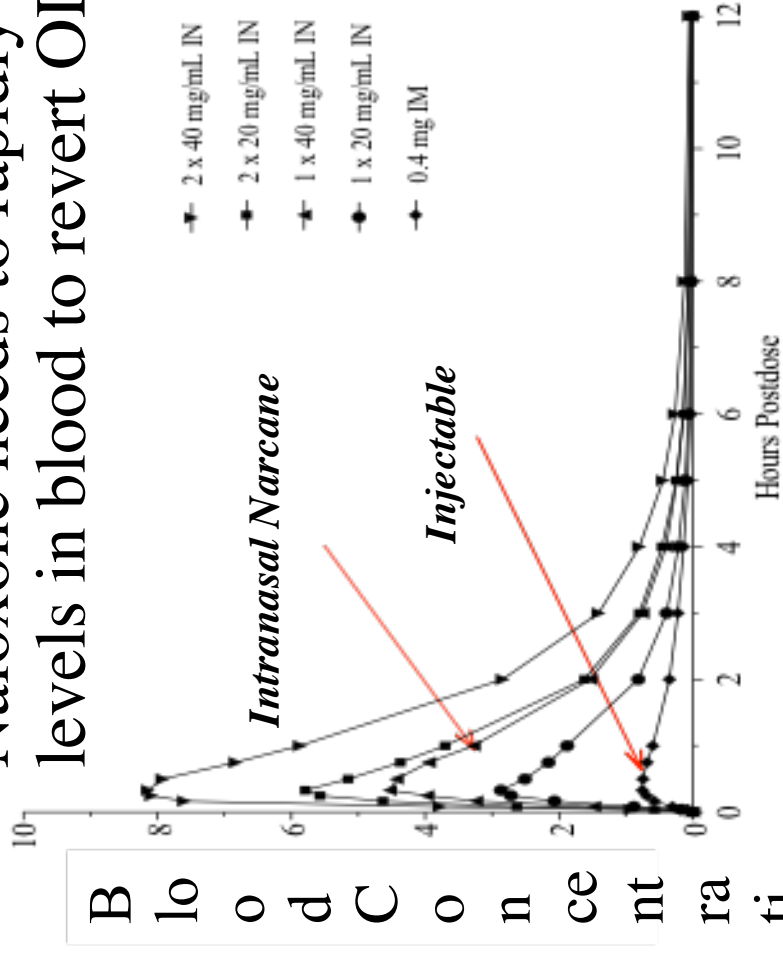
Manini et al., *J Med Toxicol* 2013; 9.

Peciña et al., *Neuropsychopharmacology* 2015; 40.



# Improving Treatments for Overdose: Naloxone

Naloxone needs to rapidly reach high levels in blood to revert OD



- NARCAN Nasal spray device \$37.50 per 4mg
- Approved by FDA, November 2015



Image courtesy of ADAPT Pharma, Inc.

**President Barack Obama**  
**National Prescription Drug**  
**Abuse and Heroin Summit**  
**Atlanta Georgia -- March 29, 2016**

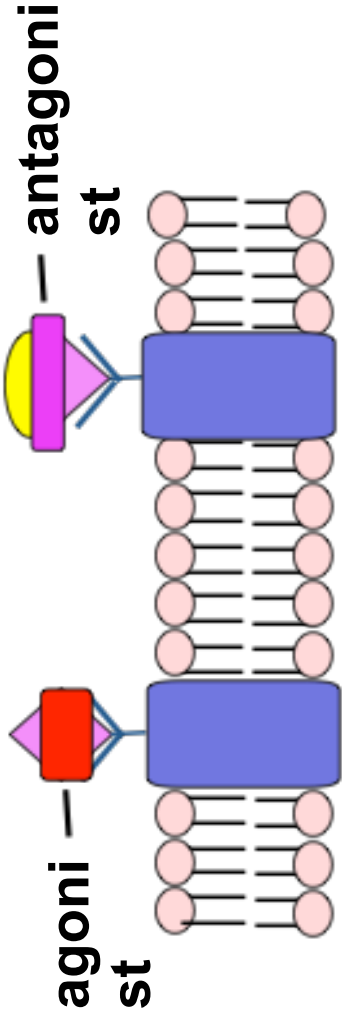


**“ .....we need to recognize that addiction is a disease.  
If we treat addiction like a crime then we’re doing  
something that’s .....ineffective.**

**.... taking parity seriously so that mental health issues  
and addiction issues are treated as a disease in the  
same way that if somebody came in with a serious  
medical illness that it’s treated”**

# Medications for Opioid Addiction

- Full Agonist: Methadone (daily dosing)
- Partial Agonist: Buprenorphine (3-4X week)
- Antagonists: Naltrexone (ER 1 month)



agonist

antagonist

no effect

effect

Binds to receptor but has no effect.

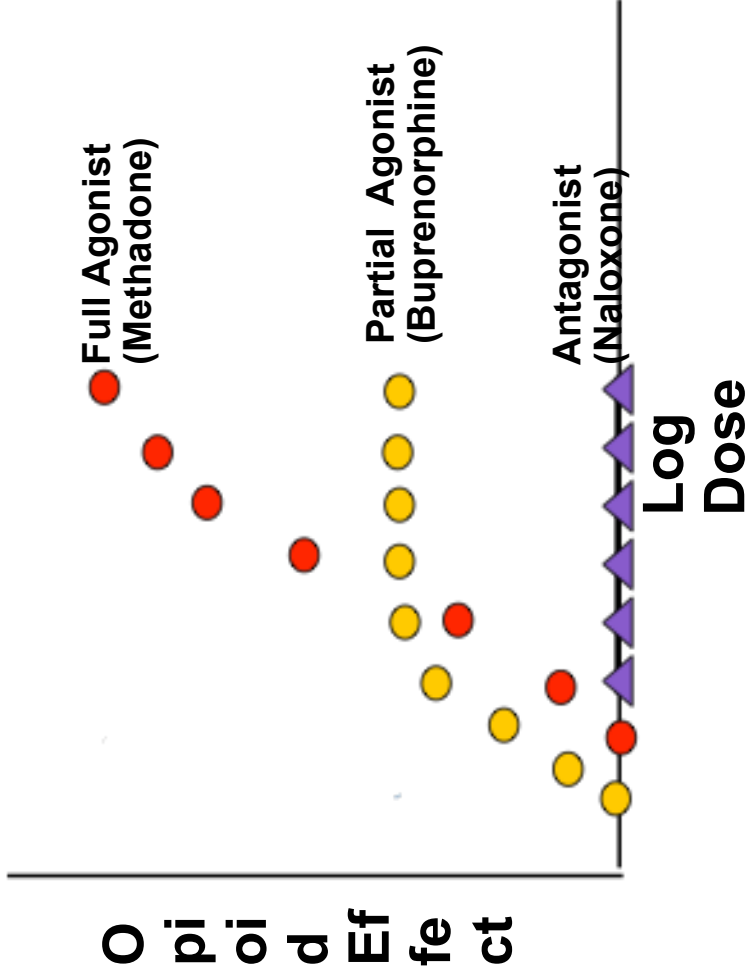
Prevents heroin

from binding and activates it;

**Full agonists have maximal effect**

**Partial agonist have intermediate effect**

**Antagonist prevents Heroin from binding**



Opioid Effect

Full Agonist (Methadone)

Partial Agonist (Buprenorphine)

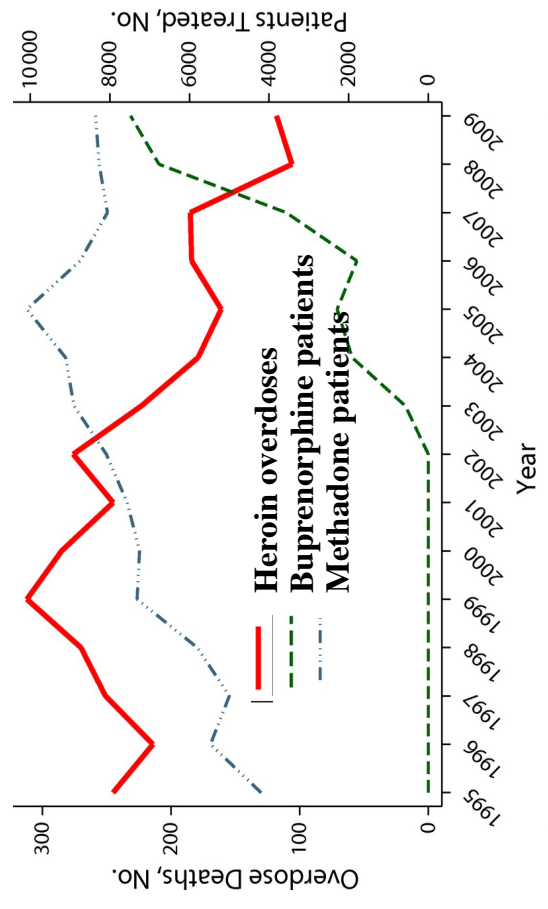
Antagonist (Naloxone)

Log Dose

# Agonist Medications Decrease Heroin OD

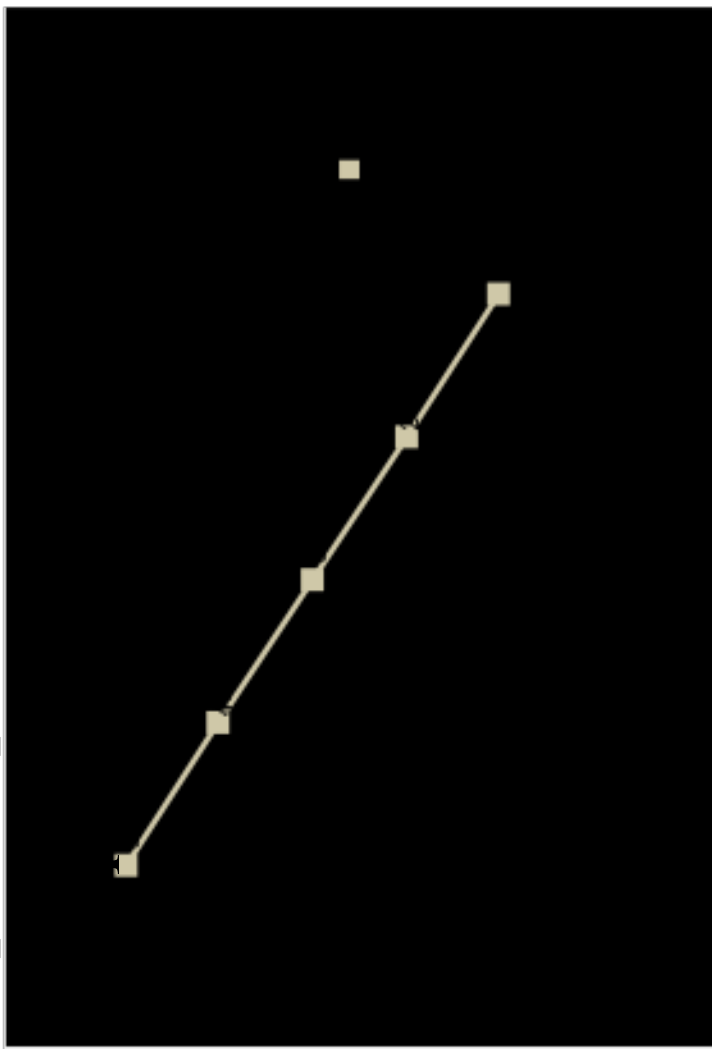
## Agonist Treatment Reduced Heroin OD Deaths

Baltimore, Maryland, 1995-2009



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

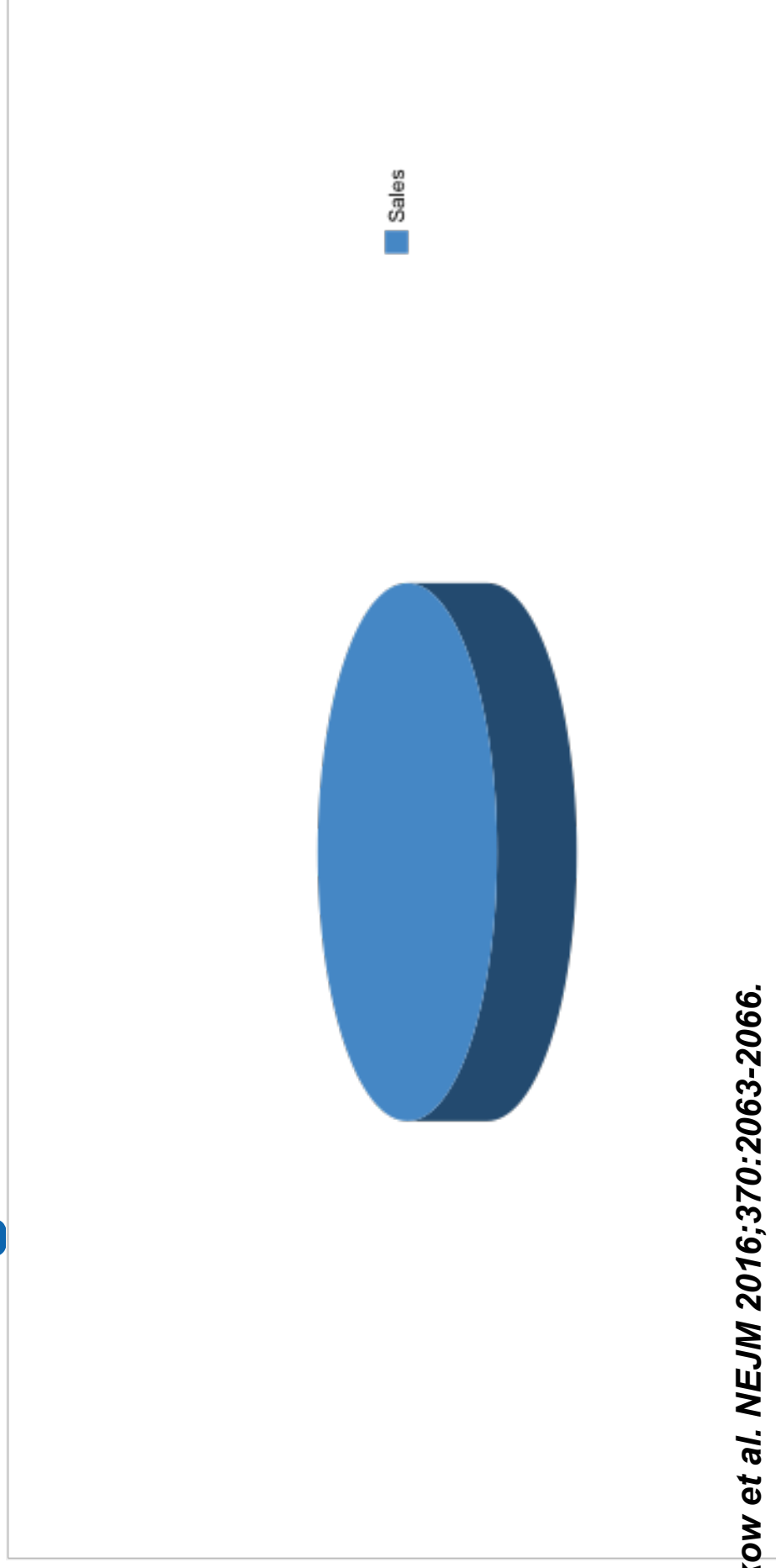
## Buprenorphine Reduced Heroin



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

# Addiction Management & Treatment

**Most people with addiction are not receiving medication-assisted treatment**



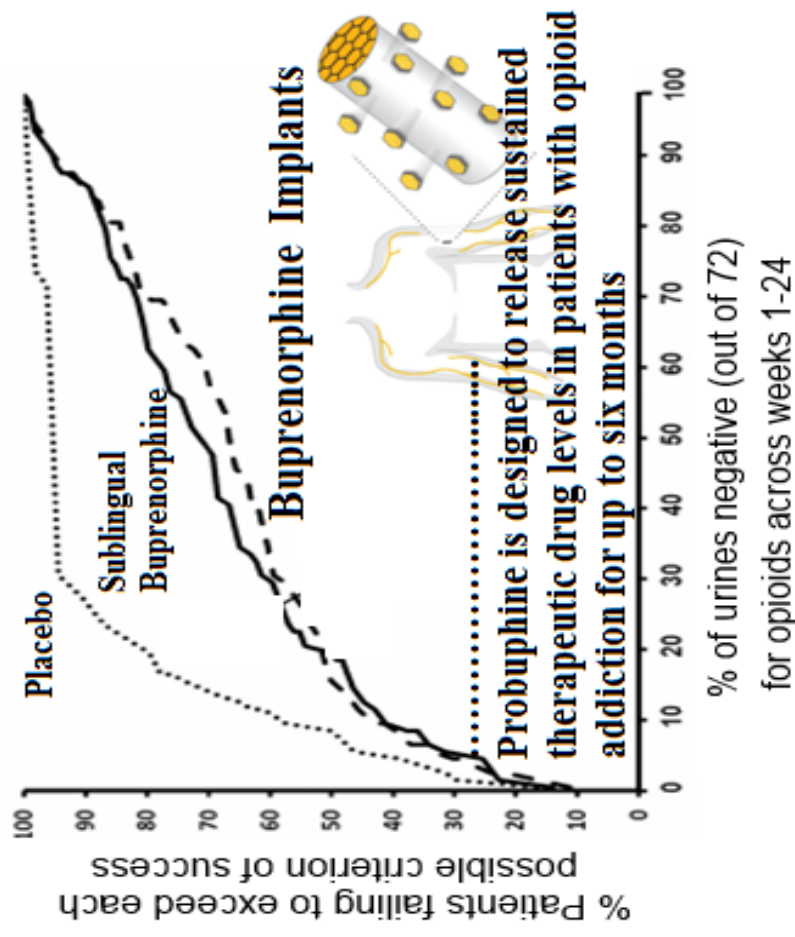
*Volkow et al. NEJM 2016;370:2063-2066.*



# Improving Treatments for Addiction: Extended Release Medications Improve Compliance

- Implanted buprenorphine may improve compliance
  - Trial: buprenorphine implants vs. placebo for 6 months

FDA approval still pending



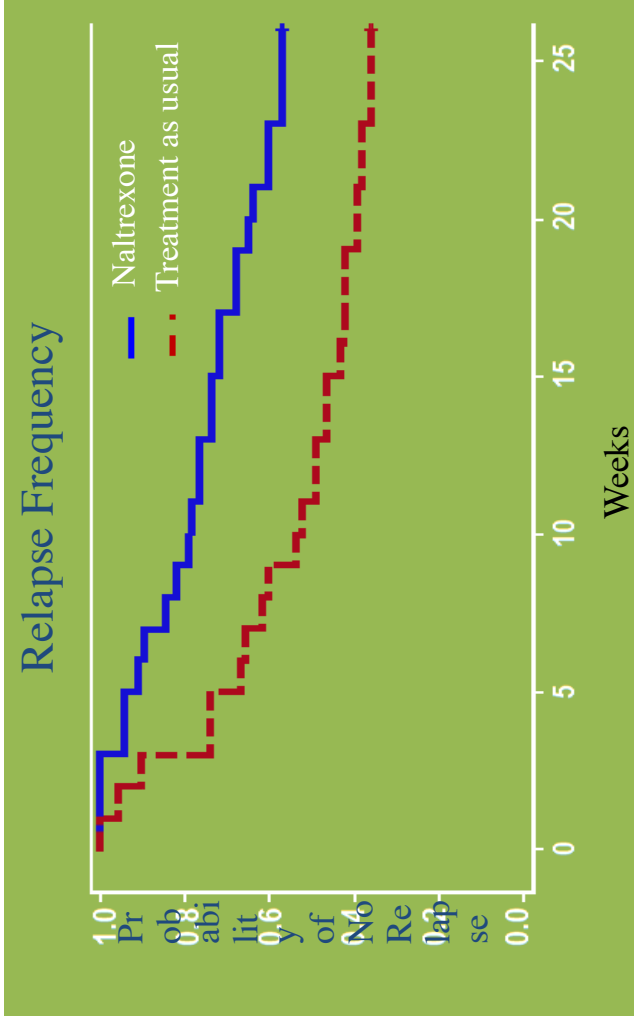
Rosenthal et al., *Addiction* 2013;105.

# Improving Treatments for Addiction:

## Naltrexone Trial in CJ 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)



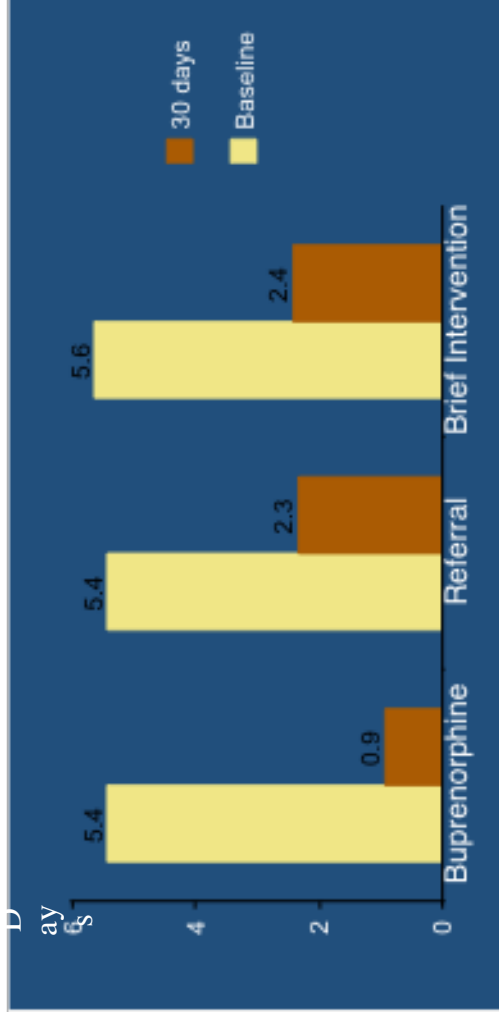
Overdoses in 78 weeks:  
 Control: 7  
 Naltrexone: **0**

Lee et al. *NEJM* March 31, 2016.

# Improving Treatments for Addiction: Implementing Medication-Assisted Treatment

- Emergency department-initiated buprenorphine
  - Reduced self-reported, illicit opioid use
  - Increased engagement in addiction treatment; decreased use

of innovation addiction treatment services  
Self-Reported Illicit Opioid Use in the Past 7 Days



JAMA

Original Investigation

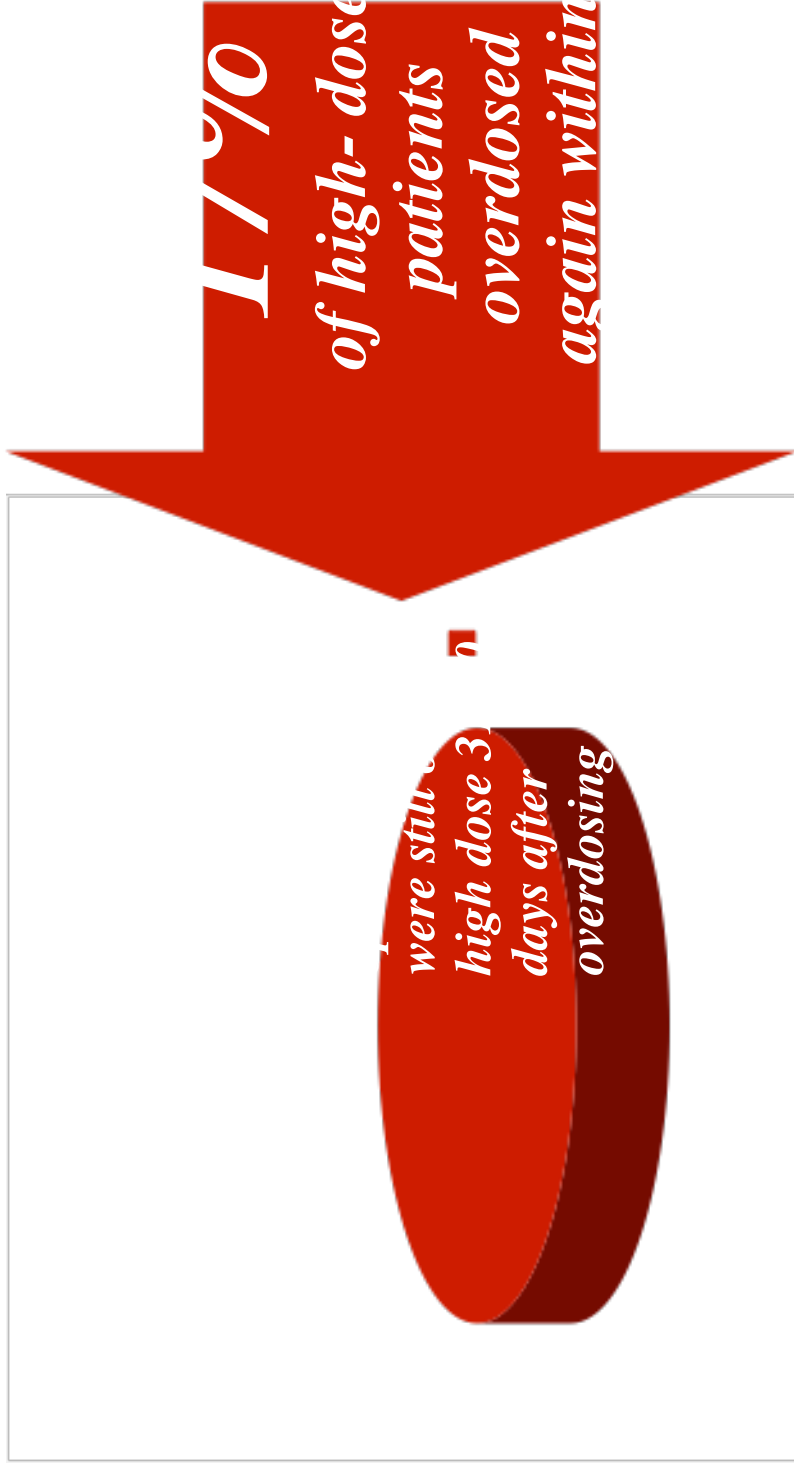
April 28, 2015 Volume 313

Emergency Department–Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence: A Randomized Clinical Trial

Gall D'Onofrio, MD, MS; Patrick G. O'Connor, MD, MPH; Michael V. Pantalon, PhD; Marek C. Chawarski, PhD; Susan H. Busch, PhD; Patricia H. Owens, MS; Steven L. Bernstein, MD; David A. Fiellin, MD

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

In a study of 2848 patients who had a **nonfatal opioid overdose** during long-term opioid pain treatment:

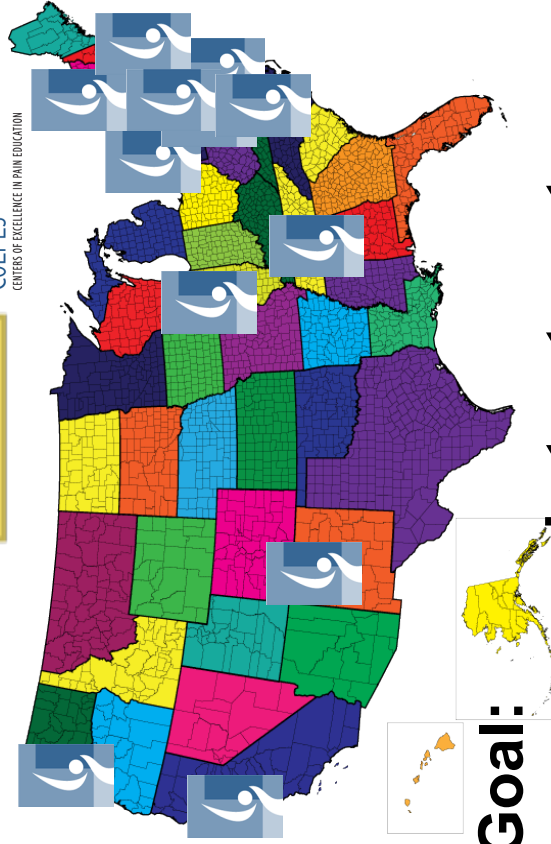


# Education

## PAIN

**NIH Pain Consortium Centers of Excellence in Pain Education**

ORWH NIA  
OBSSR NINR  
NIDA NICHHD  
NIDCR NIAMS  
NINDS NCCIH



**Goal:**  
Improve pain treatment through education

## SUD



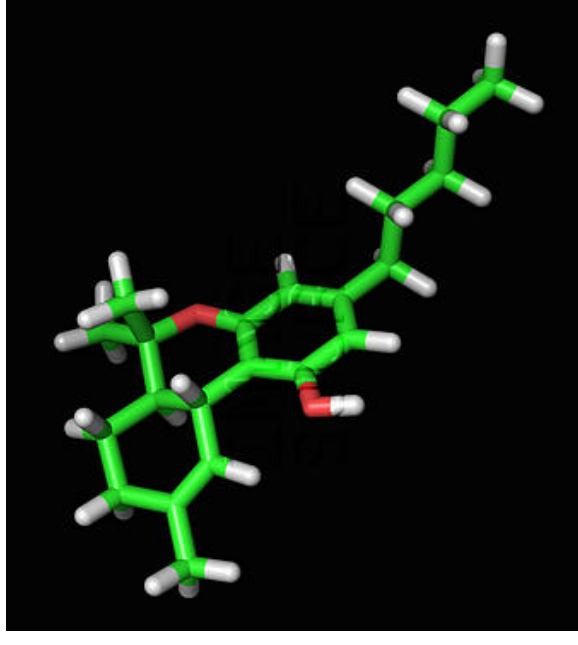
**Goal:**  
Prevent SUD and improve outcomes in addiction through education of health care providers



# *Cannabis is the Most Commonly Used Illicit Drug In the US*



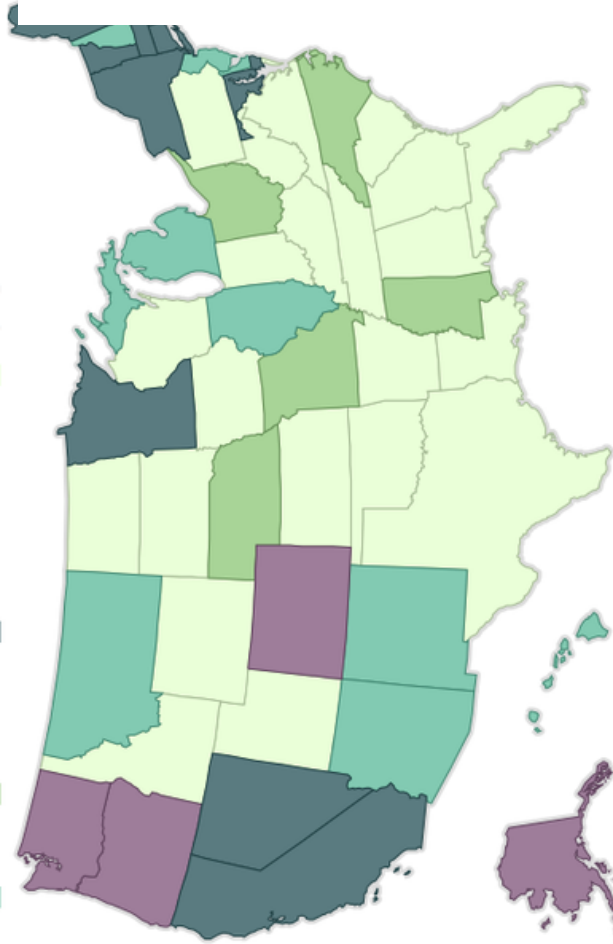
- Over **117 million** Americans have tried it at least once
- An estimated **2.6 million** Americans used it for the first time in 2014



**Tetrahydrocannabinol (THC) Active Ingredient in Cannabis**

# Changes in Cannabis Laws in the US

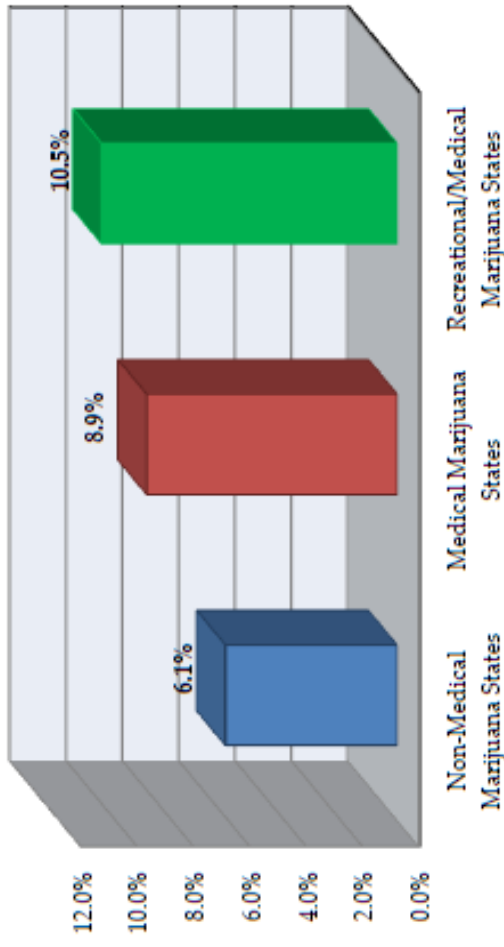
■ Legalized  
 ■ Medical  
 ■ Decriminalized  
 ■ Medical and decriminalized  
 ■ Fully illegal



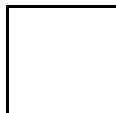
Source: NORML, Drug Policy Alliance, and the Marijuana Policy Project

# Adolescents Cannabis Use is higher in States where it is Legal

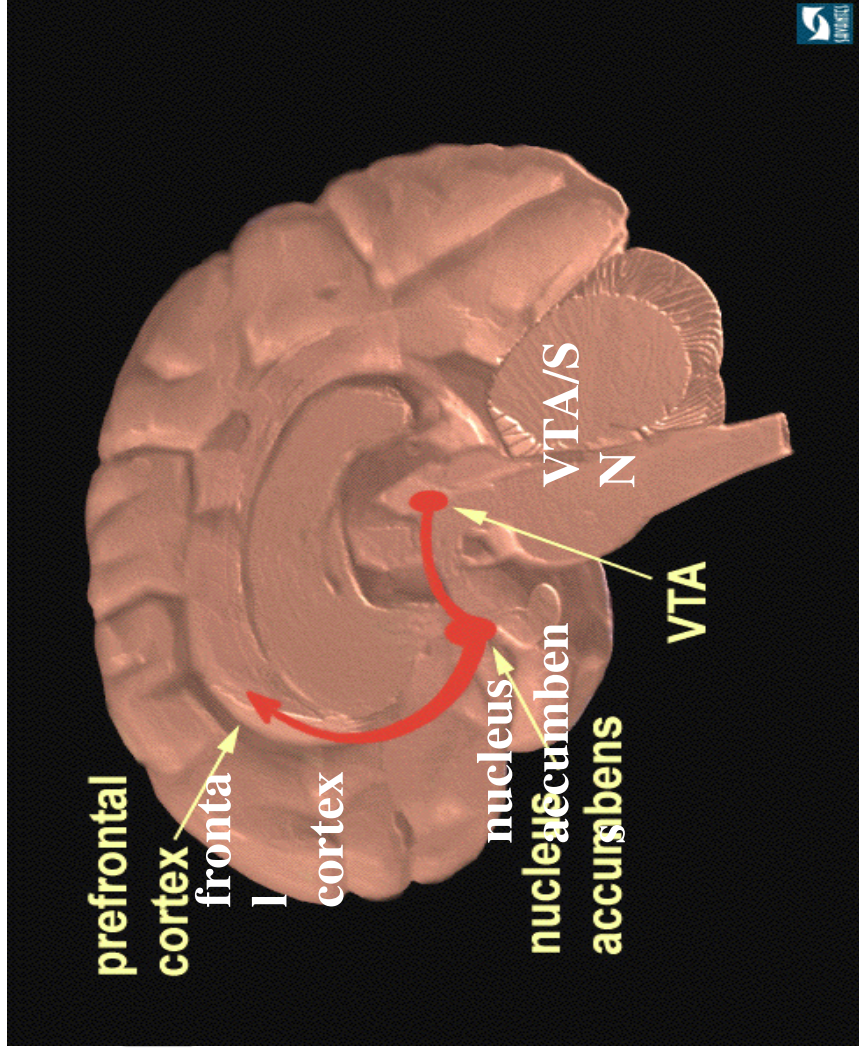
Average Past Month Use by 12 to 17-Year-Olds, 2013



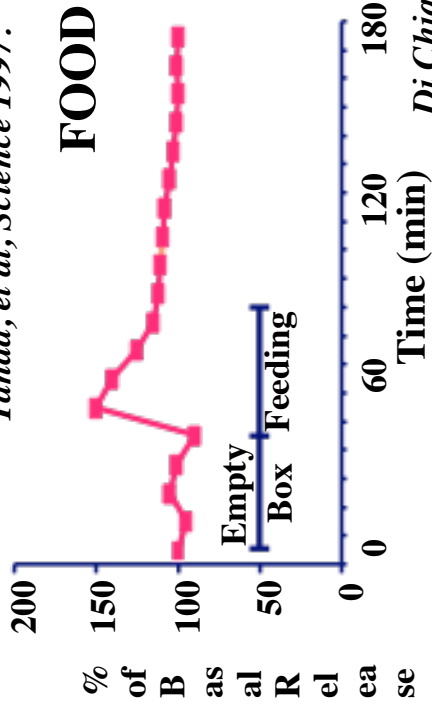
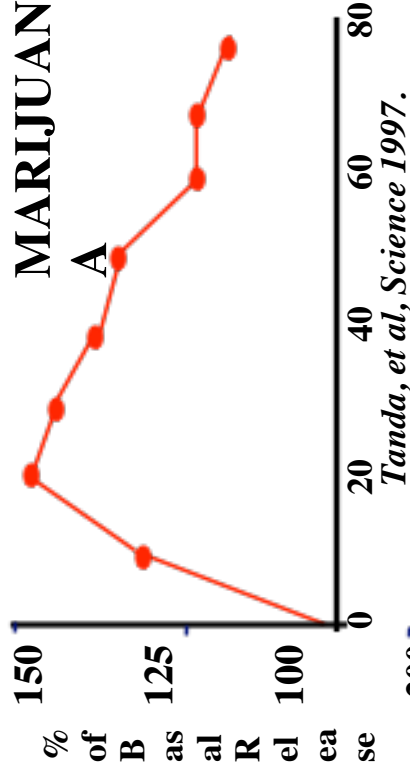
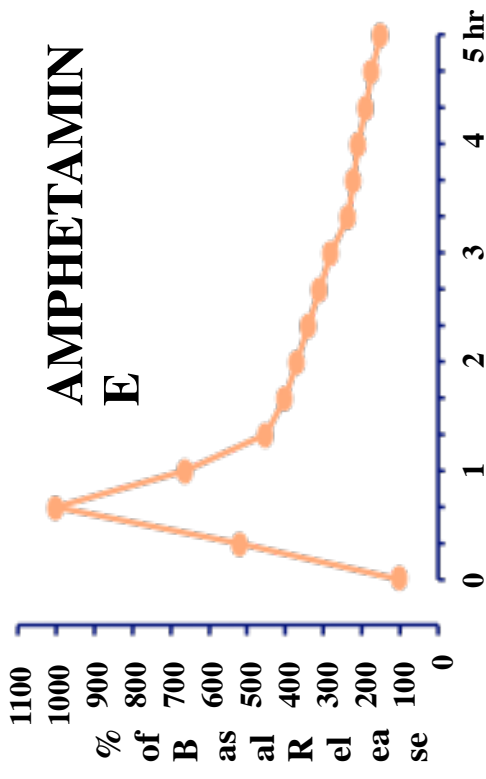
SOURCE: SAMHSA.gov, National Survey on Drug Use and Health 2012 and 2013



# Natural and Drug Reinforcers Increase Dopamine in NAc

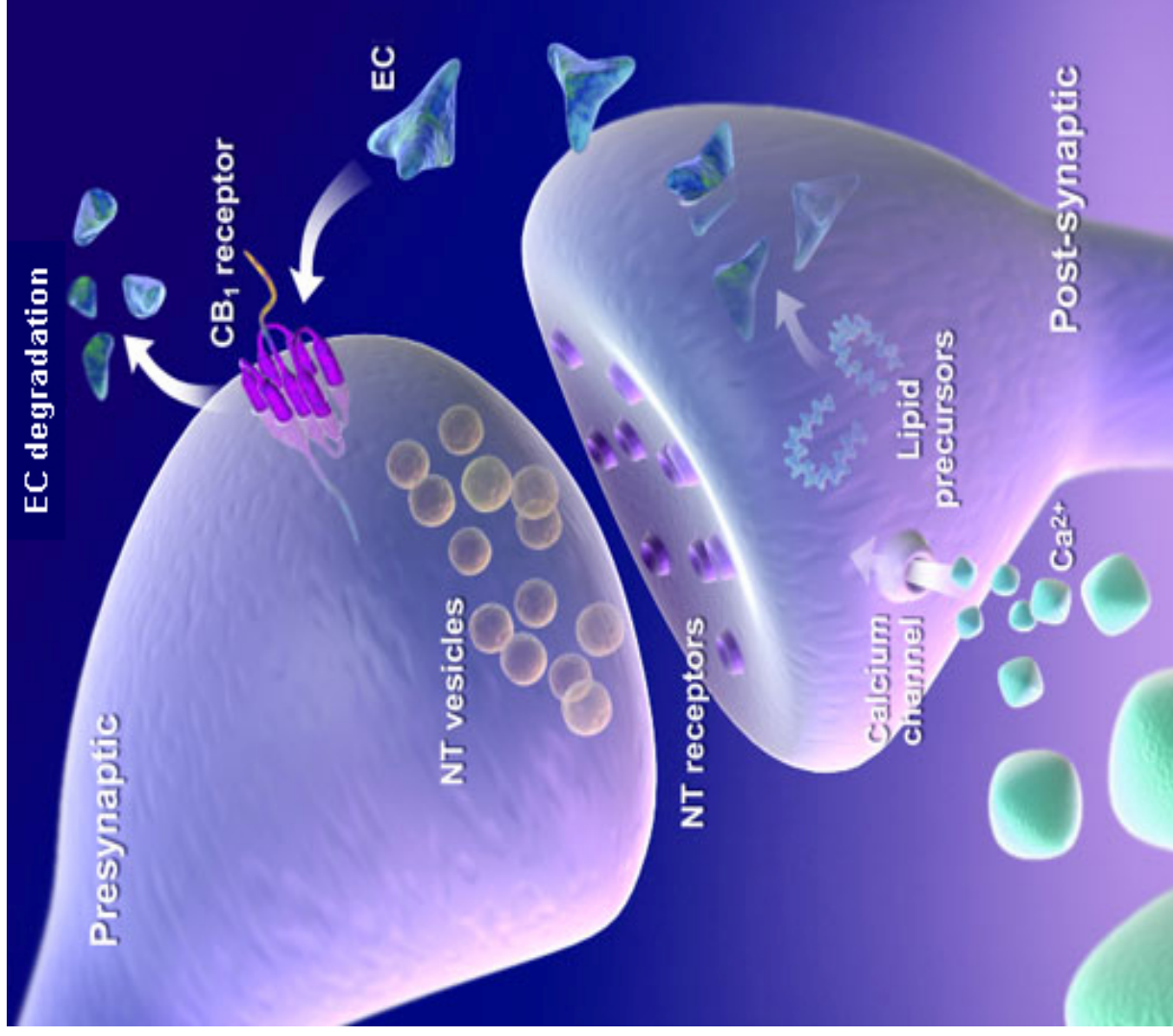
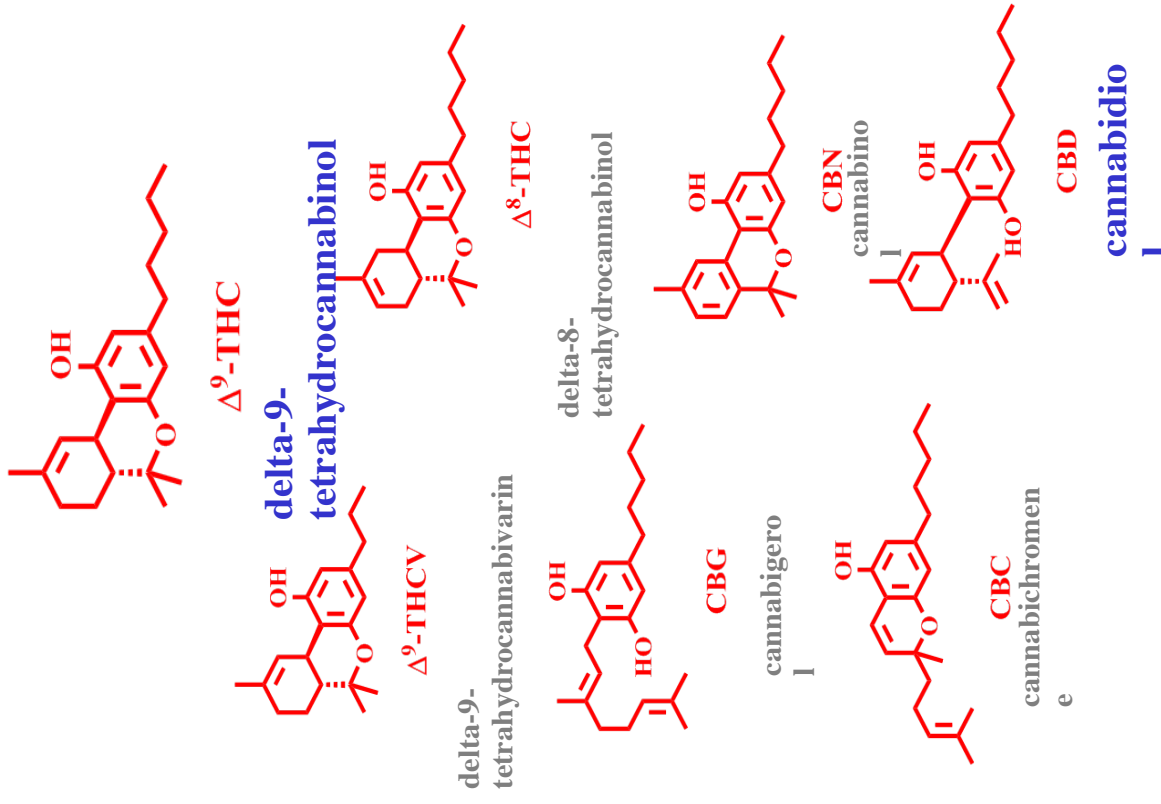


**Drugs of abuse increase DA in NAc, which triggers the neuroadaptations that result in addiction**



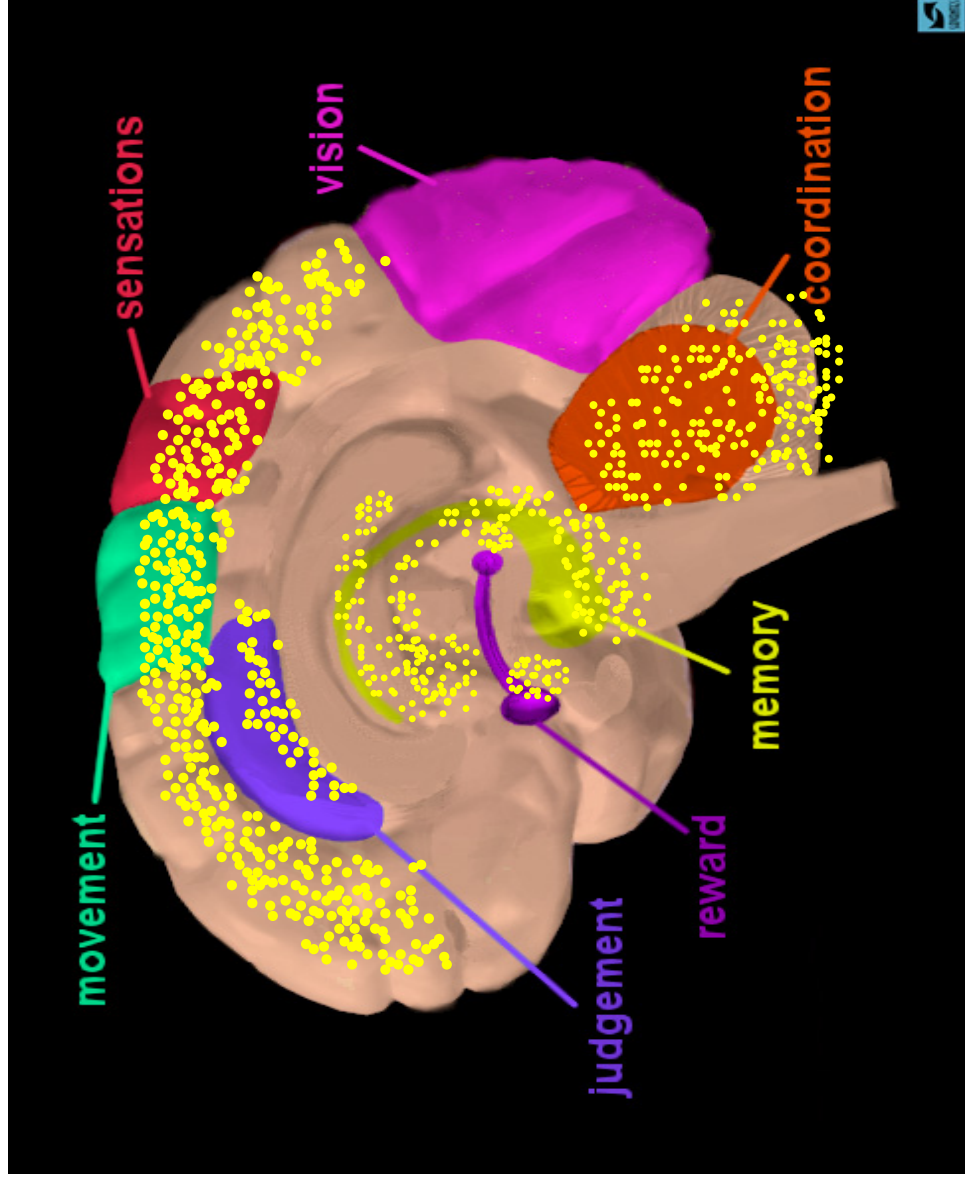


# Cannabis Constituents and the Cannabinoid System



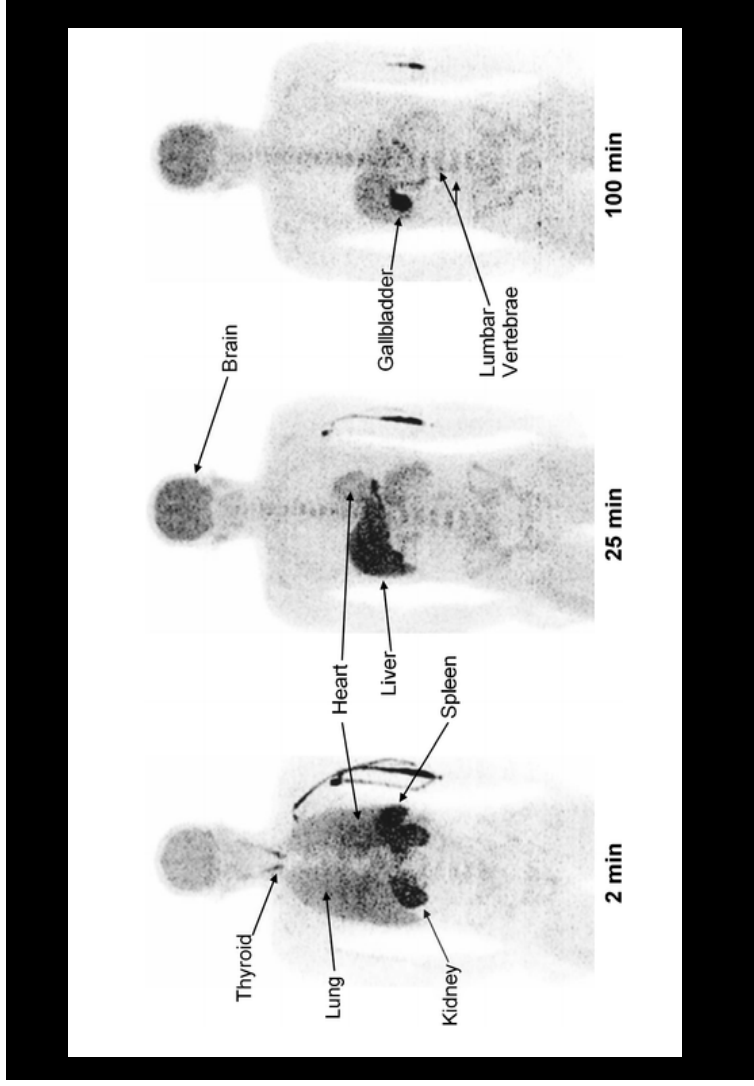
# Cannabinoid Receptors Are Located Throughout the Brain and Regulate:

- Brain Development
- Memory & Cognition
- Motivation & Reward
- Appetite
- Immunological Function
- Stress
- Movement



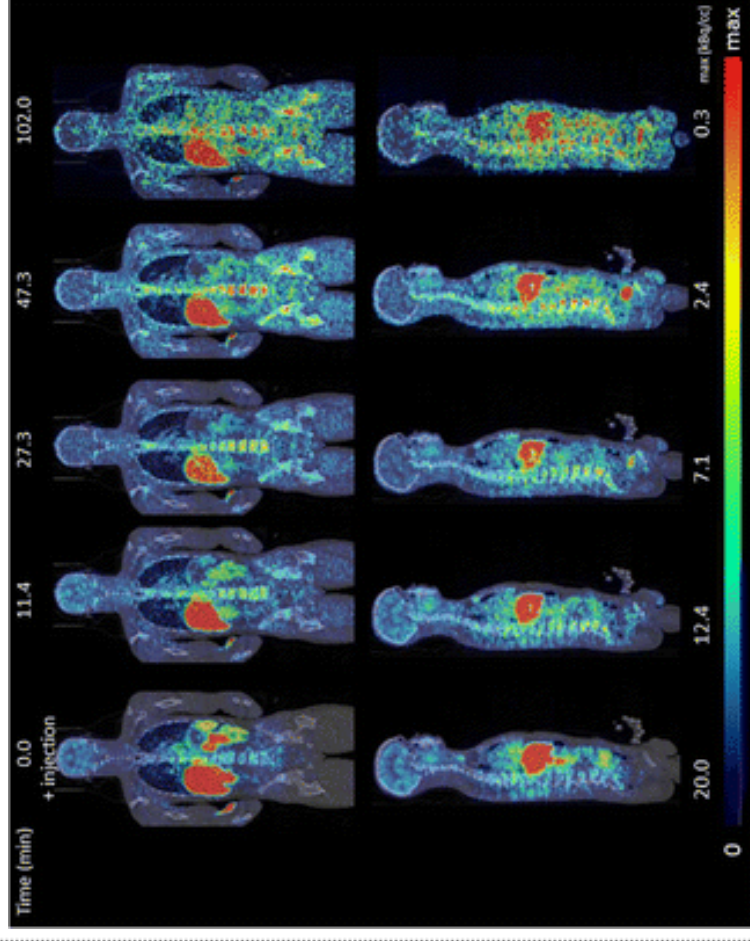
# Cannabinoid Receptors Are Also Located Throughout the Body

Whole Body Distribution of CB1 Receptors (2, 25, and 100 min after injection of  $^{11}\text{C}$ -MePPEP)



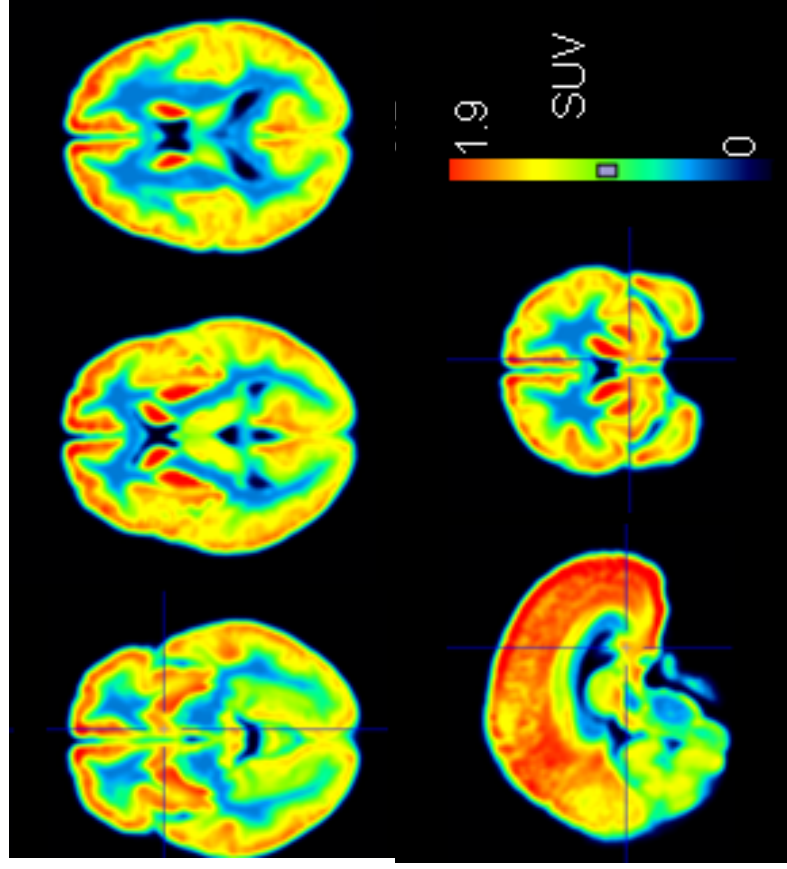
Terry et al., *Eur J Nucl Med Mol Imaging*. 2010.

PET images of  $^{11}\text{C}$ -NE40 (CB2R radioligand)

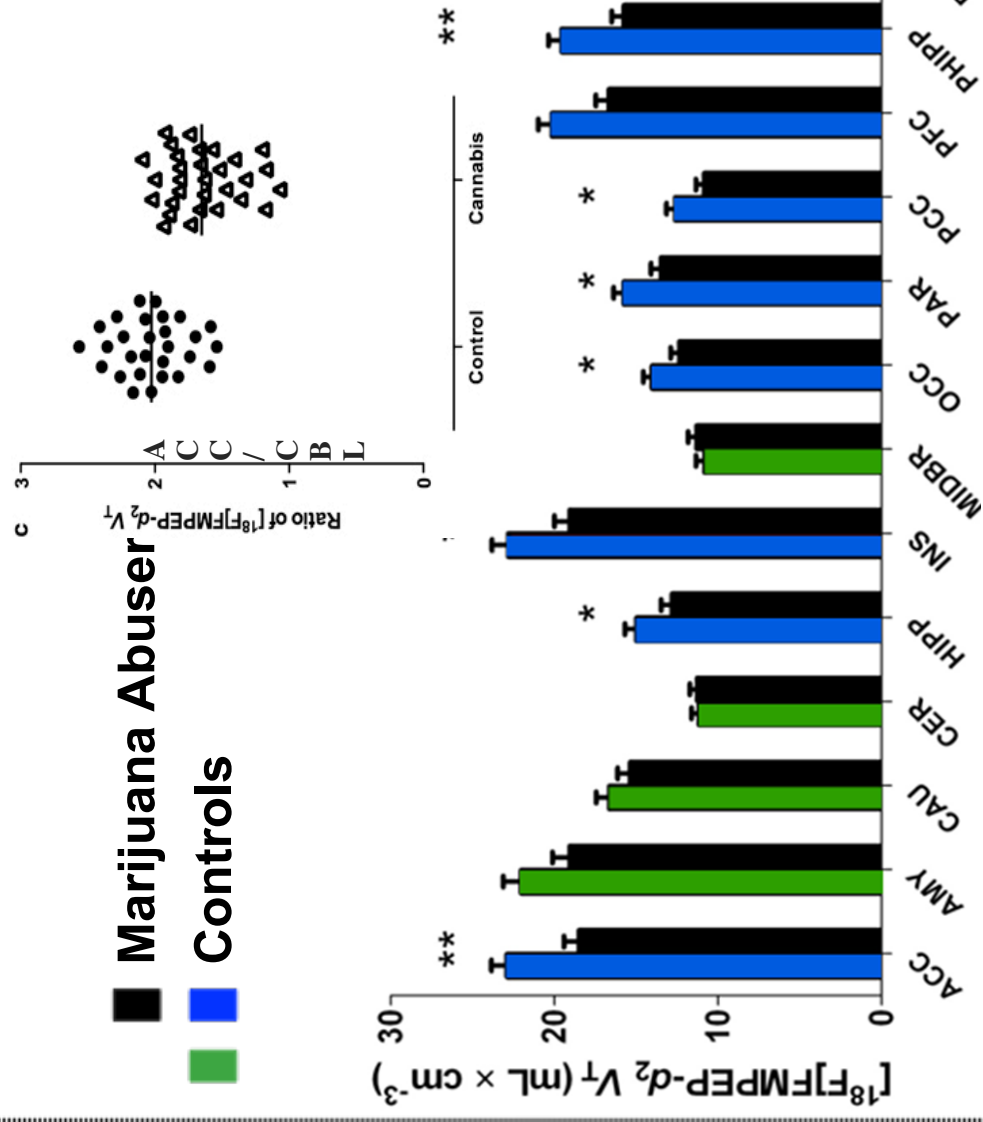


Ahmad et al., *Mol Imaging Biol*. 2013.

# Cannabinoid CB1 Receptors in Human Brain are Downregulated in Cannabis Abusers



Van Loere et al., 2007.



Hirvonen et al., Mol Psychiatry 2013.