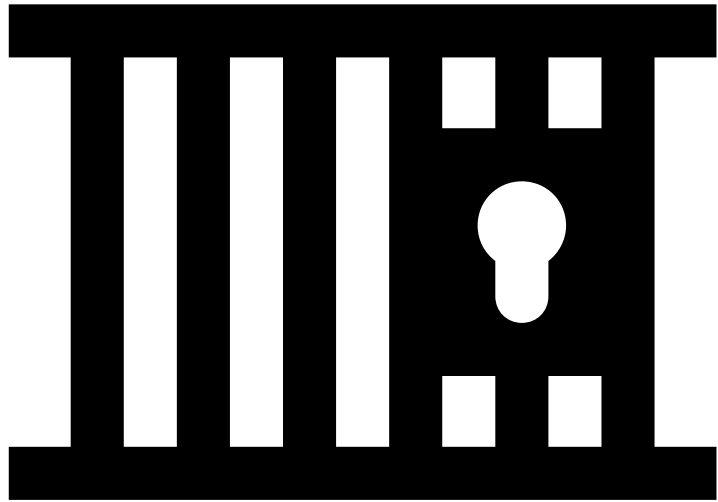


OPIOIDS, ADDICTION, AND THE BRAIN

Presenters:

- Dr. Miriam Harris, Assistant Professor of Medicine and Addiction Medicine Fellow, Boston University School of Medicine; Department of Internal Medicine, Boston Medical Center
- Lisa Newman Polk, Esq. LCSW, lawyer and social worker



Opioids, Addiction, and the Brain

Miriam Harris, MD, MS

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Fellow Boston University School of Medicine

Instructor of Medicine University of British
Columbia

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@miriamh_harris

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- Dr. Lipi Roy presentation and slide inspiration
- Dr. Alexander Walley
- Professor Leo Beletsky

Conflicts of
interest

None to report



Objectives

1. Define addiction as a chronic medical disease & disease of the brain and how this relates to the criminal justice system
2. Understand how opioids work
3. Understand the pharmacokinetics and pharmacodynamics of opioid overdose
4. Define how social dynamics of drug use are related to overdose
5. Identify overdose prevention and response strategies

Outline



Addiction – Definition, Neurobiology



Opioid use disorder, and overdose prevention and response



Intersection of addiction and criminal justice system



Role of the Legal Community



Resources

Substance Use Disorder



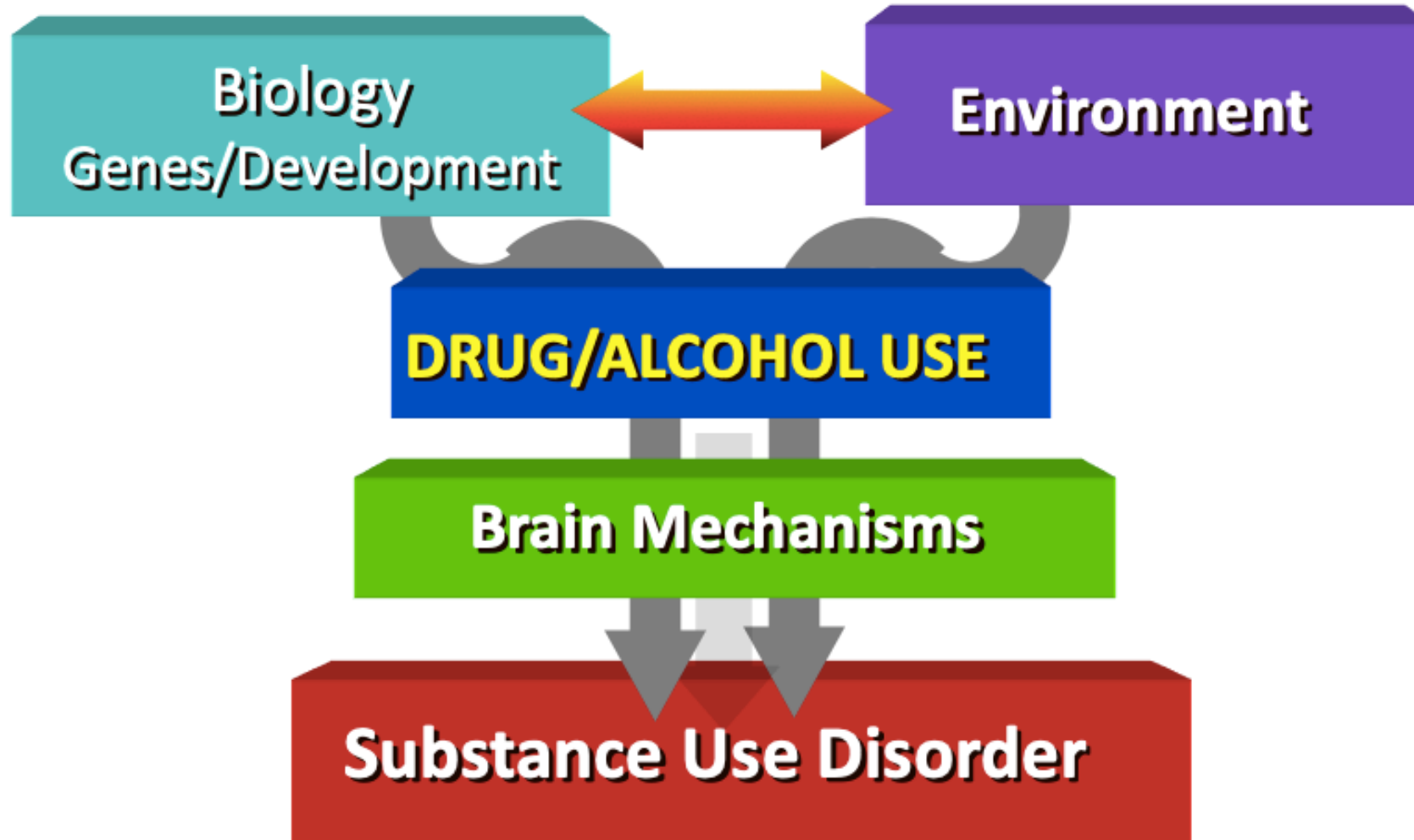
Substance Use Disorder a diagnostic term in DSM-5 defined as the recurrent use of alcohol or other drugs causing significant impairment, such as health problems, disability and failure to meet major responsibilities

It replaces the DSM-IV categories of **substance abuse** and **dependence** into a single disorder measured on a continuum from **mild, moderate, or severe**

Major Tannate of Addiction is “Use Despite Harm”

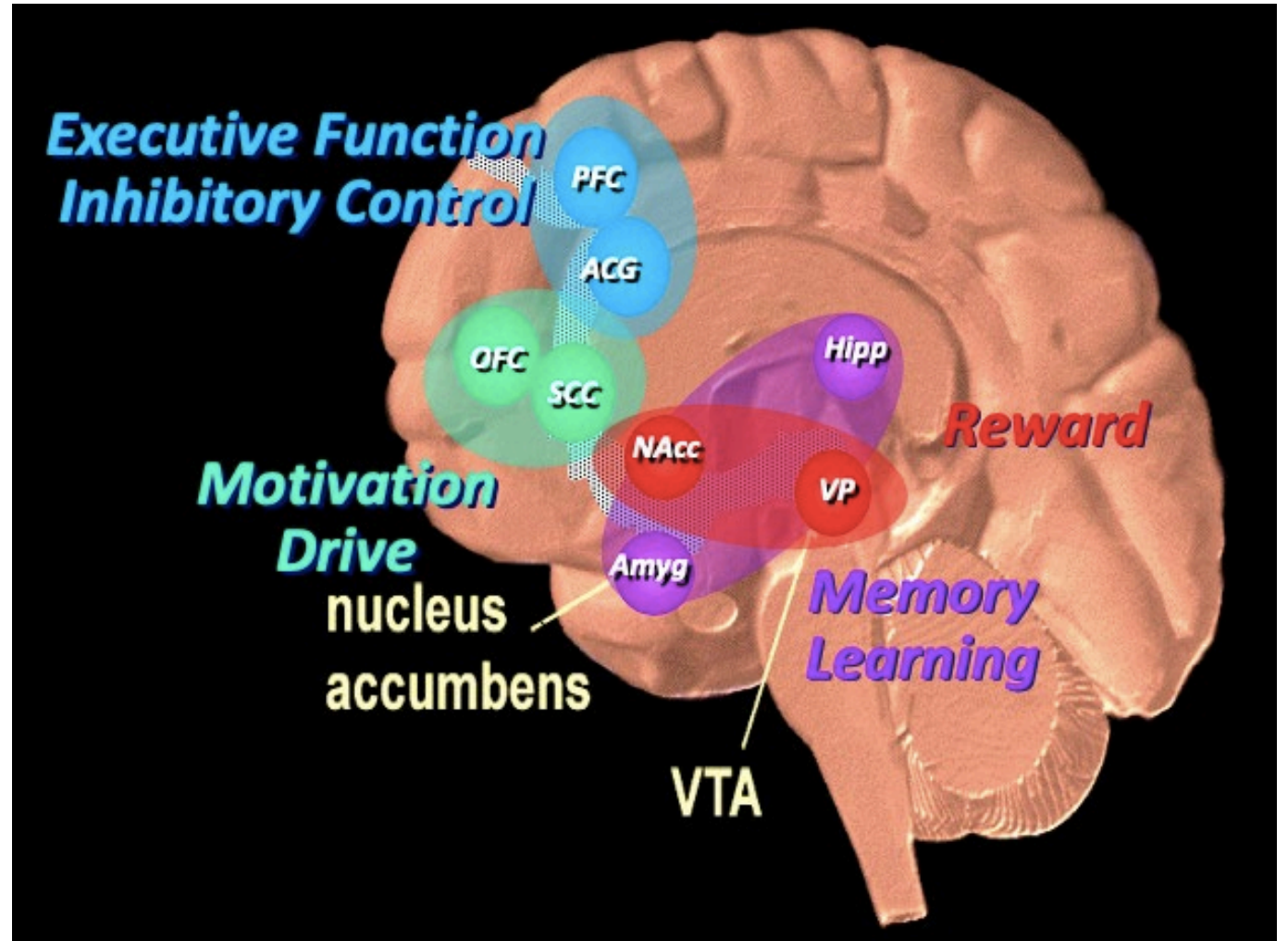
“We have this idea that if we just are cruel enough and mean enough and tough enough to people with addiction that they will suddenly wake up and stop. And that is not the case. Addiction is actually defined by the DSM and by NIDA as compulsive behavior that continues despite negative consequences. That's the definition of addiction. So therefore, if punishment, which is just another word for negative consequences, worked to fight addiction, addiction actually wouldn't exist.” – Maia Szalavitz

Development of substance use disorder involves multiple factors



Reward system

- Substances engage systems in the motivation pathways of the brain



Outline



Addiction – Definition, Neurobiology



Opioid use disorder and risk



Intersection of addiction and
criminal justice system



Role of the Legal Community



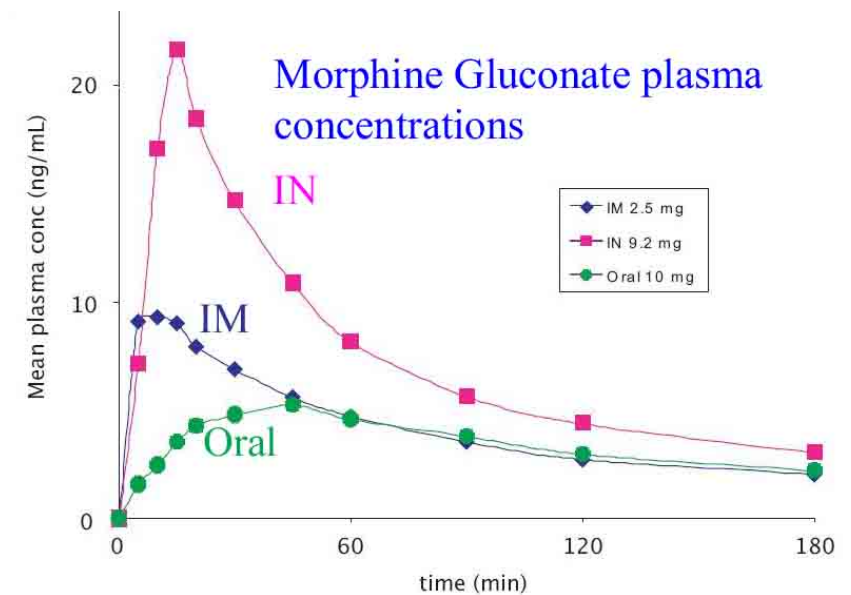
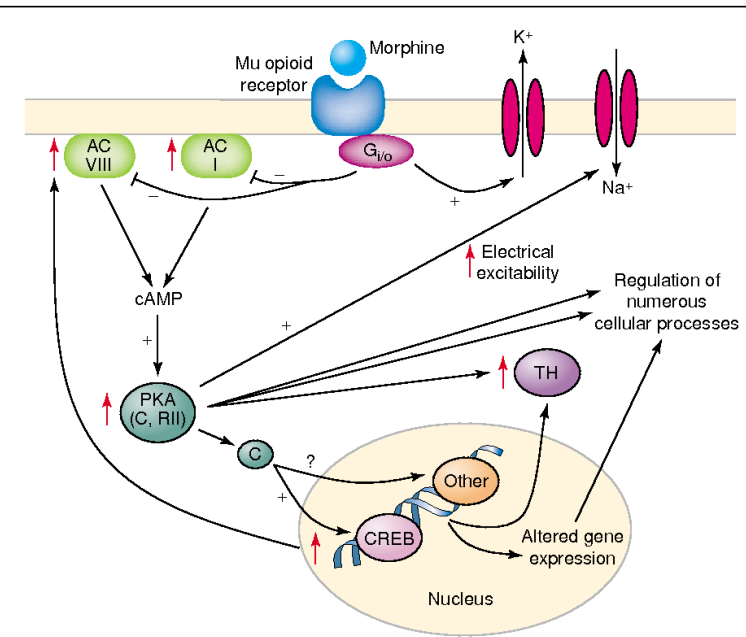
Resources

Opioid Use
Disorder
(OUD)

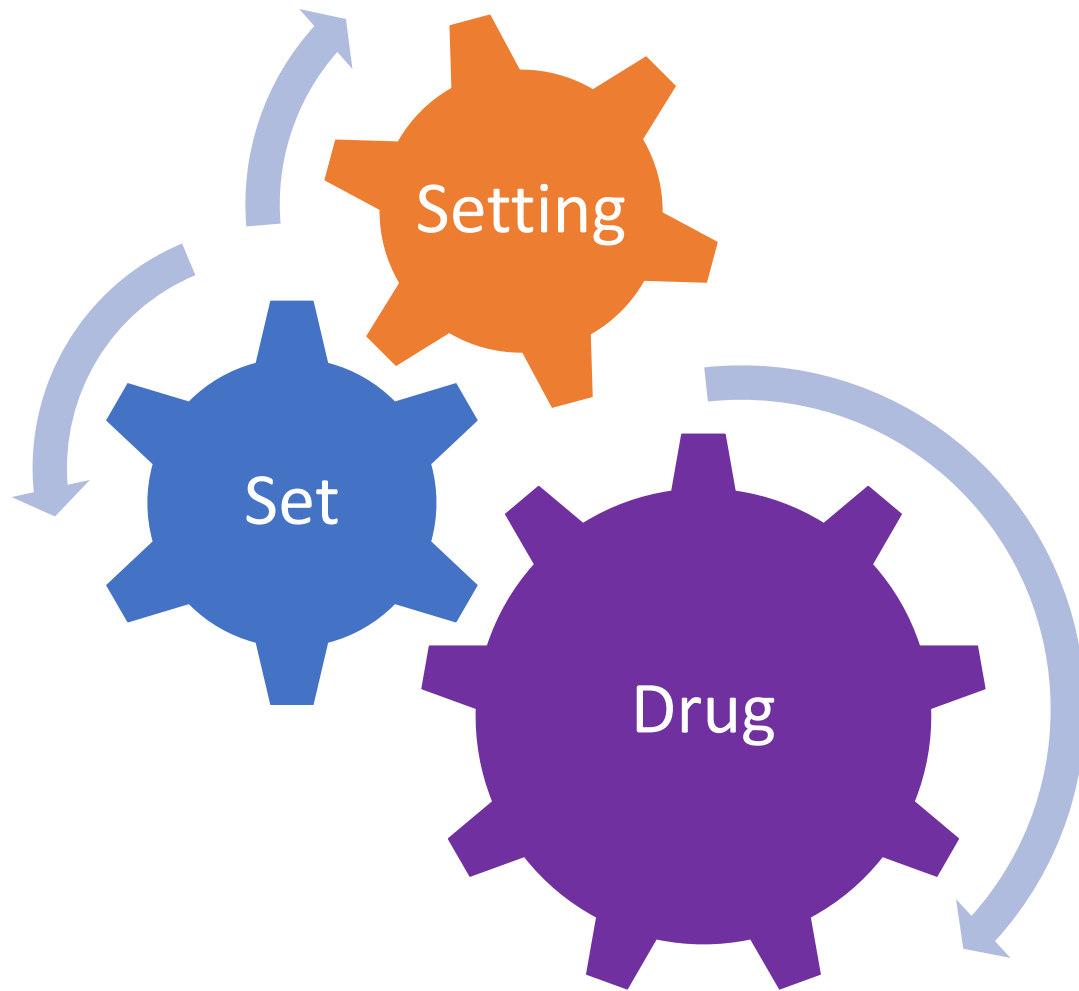


Opioid actions

- Orally < intranasally < intravenously used – IV peak 1 min
- Different opioids have different strengths (or binding affinity) and kinetics (length of action)
- Opioid receptors found throughout central nervous system



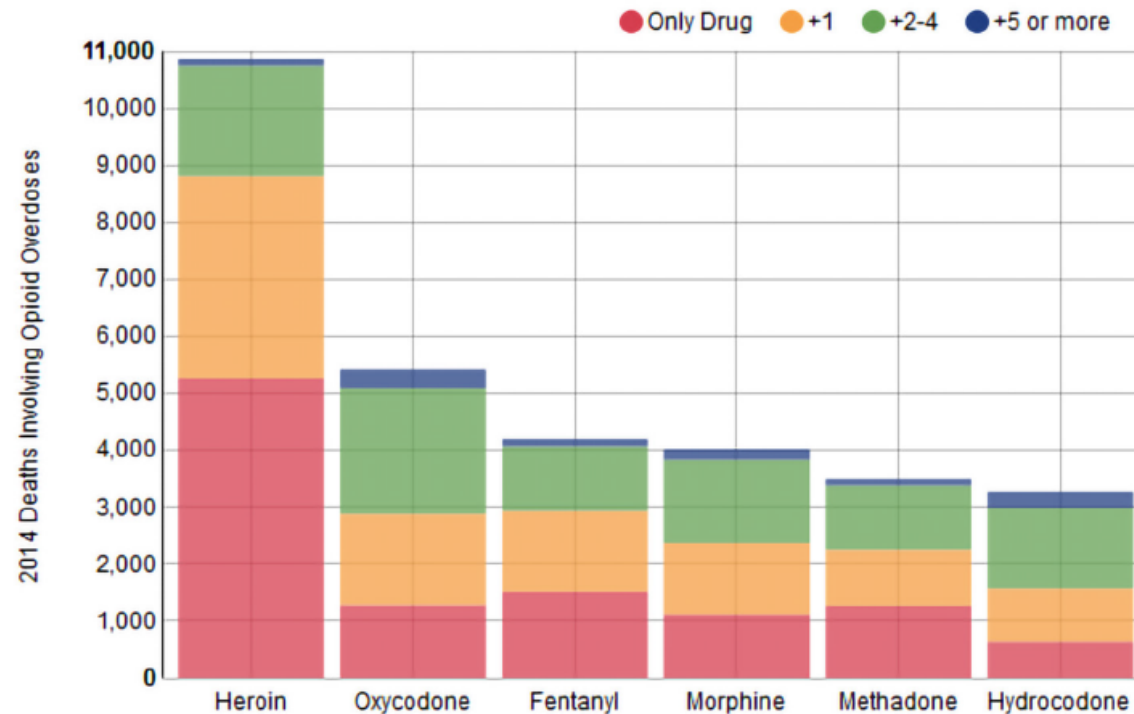
Risk factors for fatal overdose



- Drug
 - **Polysubstance use (alcohol, benzos)**
 - Fentanyl
- Set
 - Physiological health + mind set
- Setting
 - Post detox/incarceration (130X)¹
 - Using alone: Isolation

Polypharmacy Overdoses are the Norm, Not Exception

Figure 9. Opioid Overdose Deaths by Number of Drugs Involved, 2014



Source: CDC, National Vital Statistics Reports, Vol. 65, No. 10, December 20, 2016, Table 5 (https://www.cdc.gov/nchs/data/nvsr/nvsr65/nvsr65_10.pdf). Includes all deaths, unintended or otherwise.



Harm Reduction

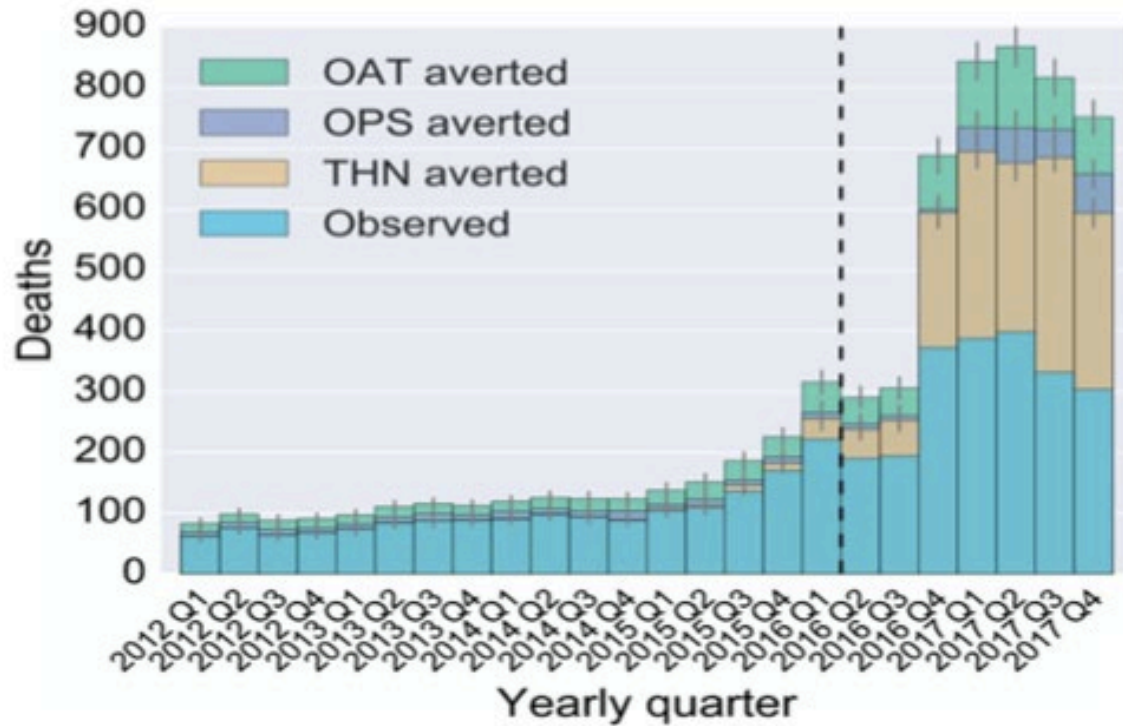
- Aim to lesson negative social/physical consequences associated with drug and/or alcohol use

Overdose Prevention and Response Strategies

- Do not use alone (use in networks is protective)
- Drug checking
- “Start low, go slow”
- Recognize overdose & administer naloxone if overdose occurs
- Seek professional help
- Medications reduce OD risk by > 50%^{1,2}
- Isolation and stigma kill

1. Schwartz R et al. Am J Public Health 2013

2. Jones CM et al. Am J Public Health. 2015

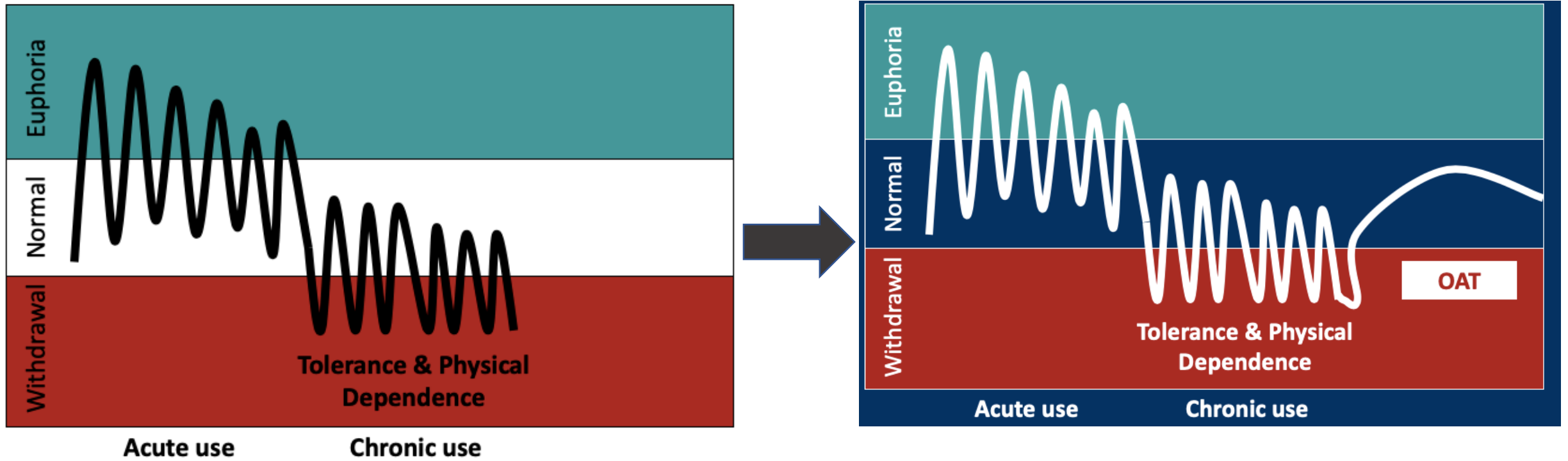


† Total provincial annual deaths observed and averted broken down by each intervention. THN = take-home naloxone; OAT = opioid therapy; OPS = overdose prevention site. [Colour figure can be viewed at wileyonlinelibrary.com]

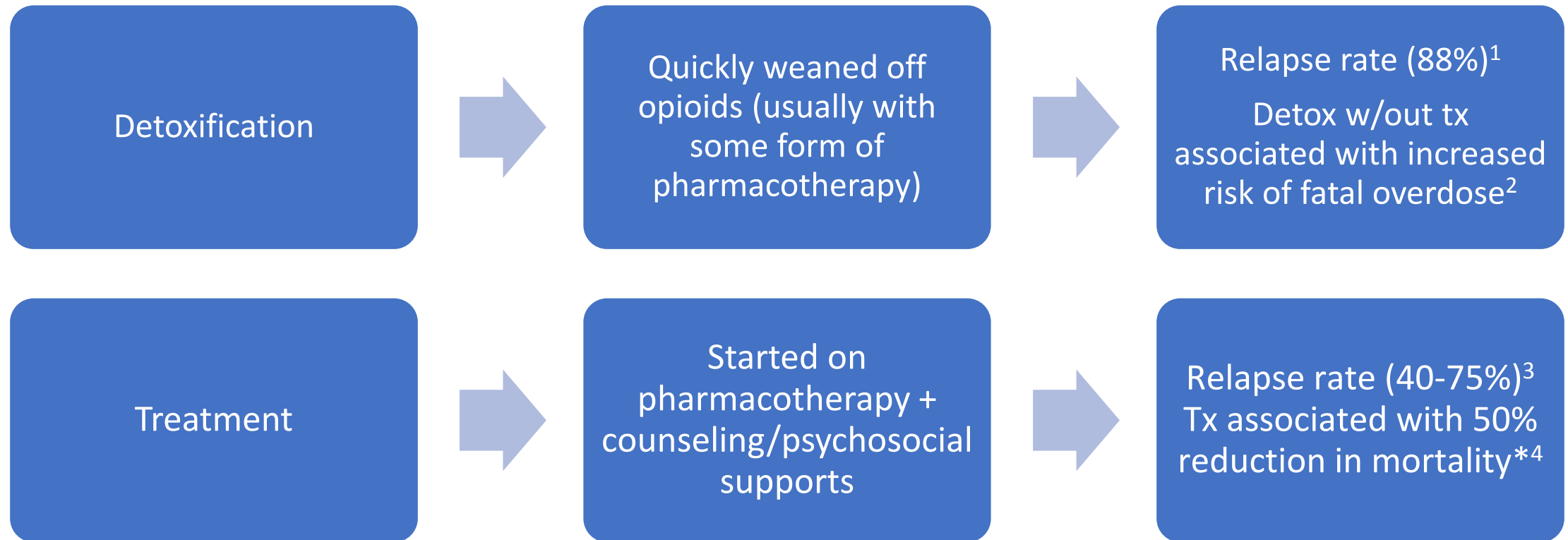
What actually prevents OD deaths in the era of synthetic opioids?

- 2016 -2017 estimated 3030 (2900–3240) death events averted
- **1580 (1480–1740)** averted by take-home naloxone
- **230 (160–350)** by overdose prevention services
- 590 (510– 720) were averted by opioid agonist therapy

Natural History of Opioid Use Disorder



Detox vs Treatment



1. Strain E. C. Comprehensive Textbook of Psychiatry, Lippincott Williams & Wilkins, 9th edition, 2009, O'Connor PG JAMA 2005

2. Chalana H. J Addict. 2016;2016:7620860.

3. Mattick RP. Cochrane Database Syst Rev. 2014(2):Cd002207.

4. Larochelle MR. Ann Intern Med.

OAT Treatment Outcomes



Patient outcomes

Increases treatment retention

Decreases illicit opioid use

Decreases mortality

Decreasing harms associated with use



Public Health

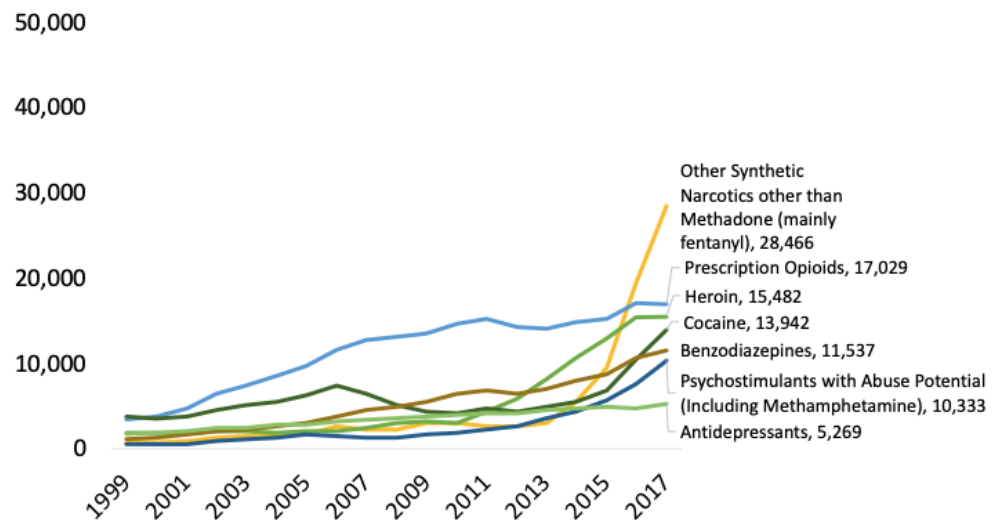
Decreases hepatitis and HIV seroconversion

Decreases criminal activity

Increases employment

Treatment Gaps Large & Overdose deaths Continue to Rise

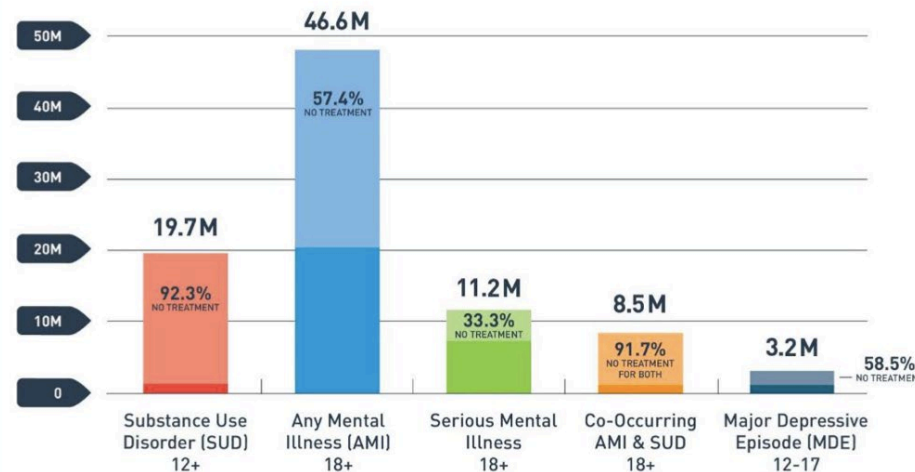
Figure 2. National Drug Overdose Deaths Number Among All Ages, 1999-2017



Source: : Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018

Despite Consequences and Disease Burden, Treatment Gaps Remain Vast

PAST YEAR, 2017



SAMHSA (2018), NSDUH 2017

Outline



Addiction – Definition, Epidemiology,
Neurobiology



Opioid use disorder



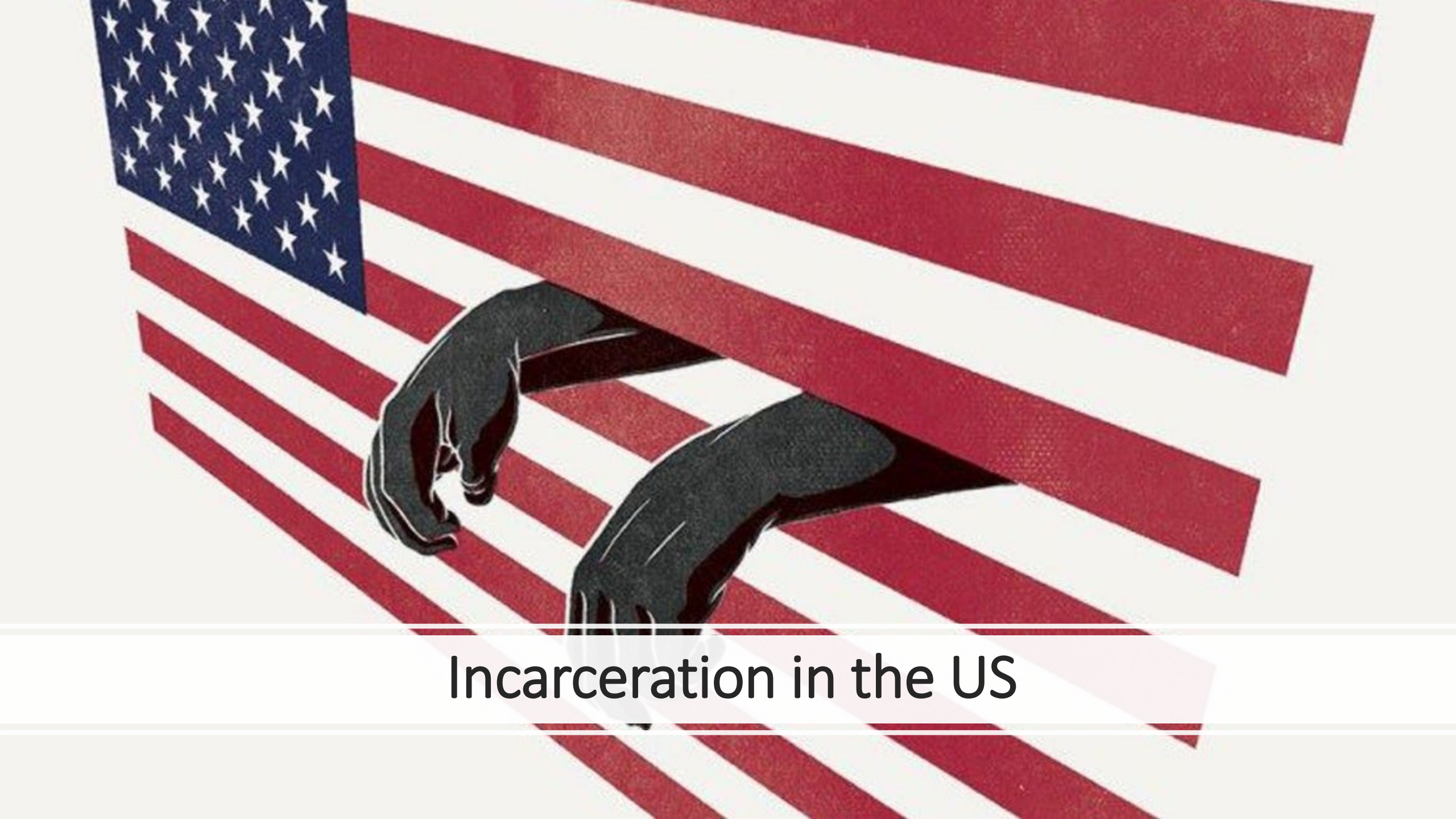
**Intersection of addiction and criminal
justice system**



Role of the Legal Community



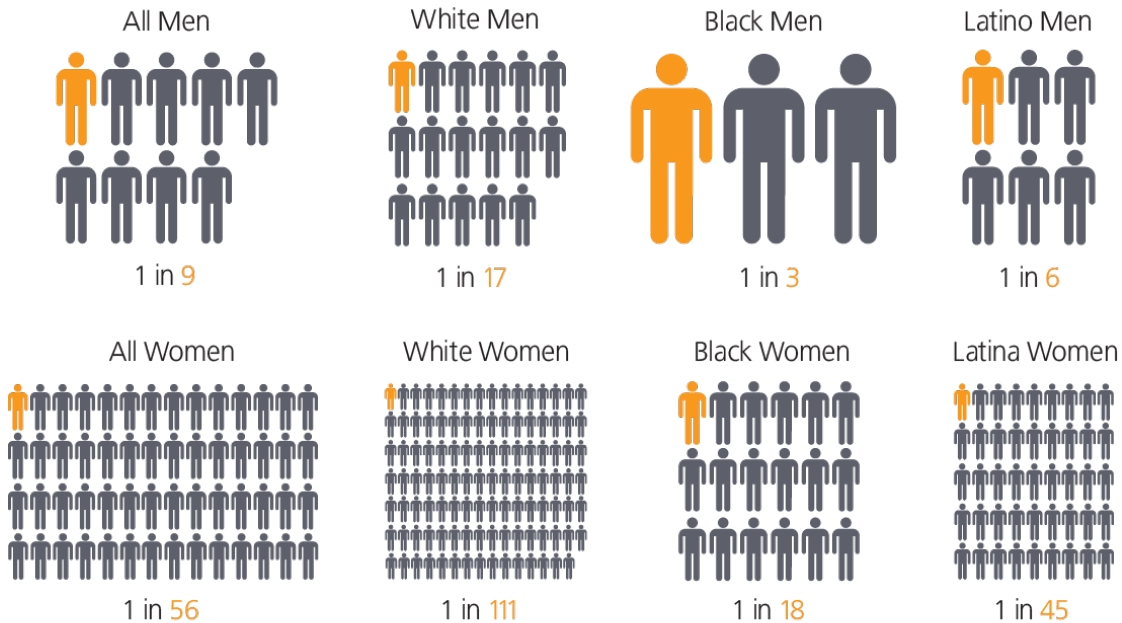
Resources



Incarceration in the US

US leads the world in incarceration

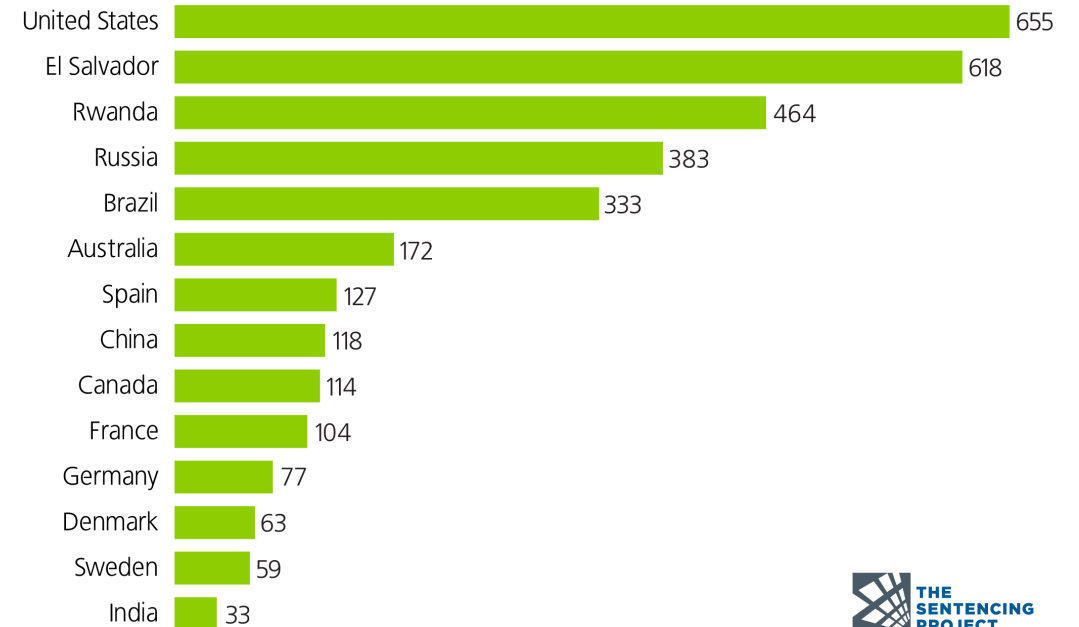
Lifetime Likelihood of Imprisonment of U.S. Residents Born in 2001



Source: Bonczar, T. (2003). *Prevalence of Imprisonment in the U.S. Population, 1974-2001*. Washington, DC: Bureau of Justice Statistics.



International Rates of Incarceration per 100,000



Crime, Incarceration and SUDs are linked

- 65% percent of the United States prison population has an active SUD¹
- Additional 20% were under the influence of drugs or alcohol at the time of their crime²
- Providing comprehensive substance use treatment to criminal offenders while incarcerated is effective³ & not treating associated with relapse and fatal overdose post release⁴
- WHO 2005: Opioid agonist medications are on the list for essential medications that should be available for ALL prisoners with OUD

1. Abuse and America's Prison Population, February 2010
2. National Drug Intelligence Center. United States Department of Justice, 2011
3. Krinsky, C. S. The American Journal of Forensic Medicine and Pathology, 30(1), 6-9
4. Larochelle MR. Drug Alcohol Depend. 2019;204:107537

Outline



Addiction – Definition, Epidemiology,
Neurobiology



Opioid use disorder



Intersection of addiction and criminal justice
system



Role of the Legal Community



Resources



NEWSROOM

FEDERAL COURT ORDERS JAIL TO PROVIDE METHADONE

Sally Friedman

“This case should serve as a wake-up call for states and localities across the country. The common practice of denying MAT in correctional settings not only increases illicit drug use, overdose, and death, but is illegal,”

Review and “Pearls”

- Addiction is a **chronic relapsing and remitting medical disease**, a disease of the brain (**NOT a moral failing**)
- **Punishing** people who use drugs is a **futile strategy to address addiction**
- The criminalization of addiction perpetuates stigma, interrupts treatment, and **incarceration is linked with increased fatal overdose**
- Overdose is driven by isolation and barriers to help-seeking
- **Take home naloxone, harm reduction, and medications are standard of care and can prevent overdose**
- Lawyers & the entire legal system play an integral role in enhancing addiction treatment

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Addiction – Definition, Neurobiology



Opioid use disorder



Intersection of addiction and criminal justice system



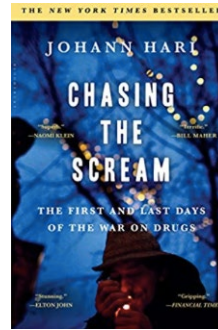
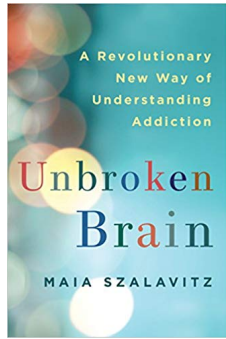
Role of the Legal Community




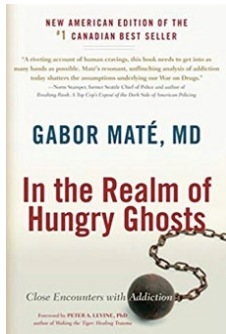
Resources

Resources

- American Society of Addiction Medicine (ASAM)
- Centers for Disease Control and Prevention (CDC)
- Center for Court Innovation
- Centre for Addiction and Mental Health (CAMH)
- Drug Policy Alliance (DPA)
- Harm Reduction Coalition (HRC)
- Legal Action Center (LAC)
- Legal Services Corporation (LSC)
- National Academy of Sciences, Engineering & Medicine (NASEM)
- National Center for State Courts – Judicial Opioid Task Force
- National Institute of Drug Abuse (NIDA)
- Open Society Foundations (OSF)
- Providers' Clinical Support System (PCSS)*
- Substance Abuse and Mental Health Service Administration (SAMSHA)
- U.S. Surgeon General's Report 2016
- Vera Institute of Justice



Crack Down



How to Change Your Mind

What the New Science of Psychedelics Teaches Us About Consciousness, Dying, Addiction, Depression, and Transcendence

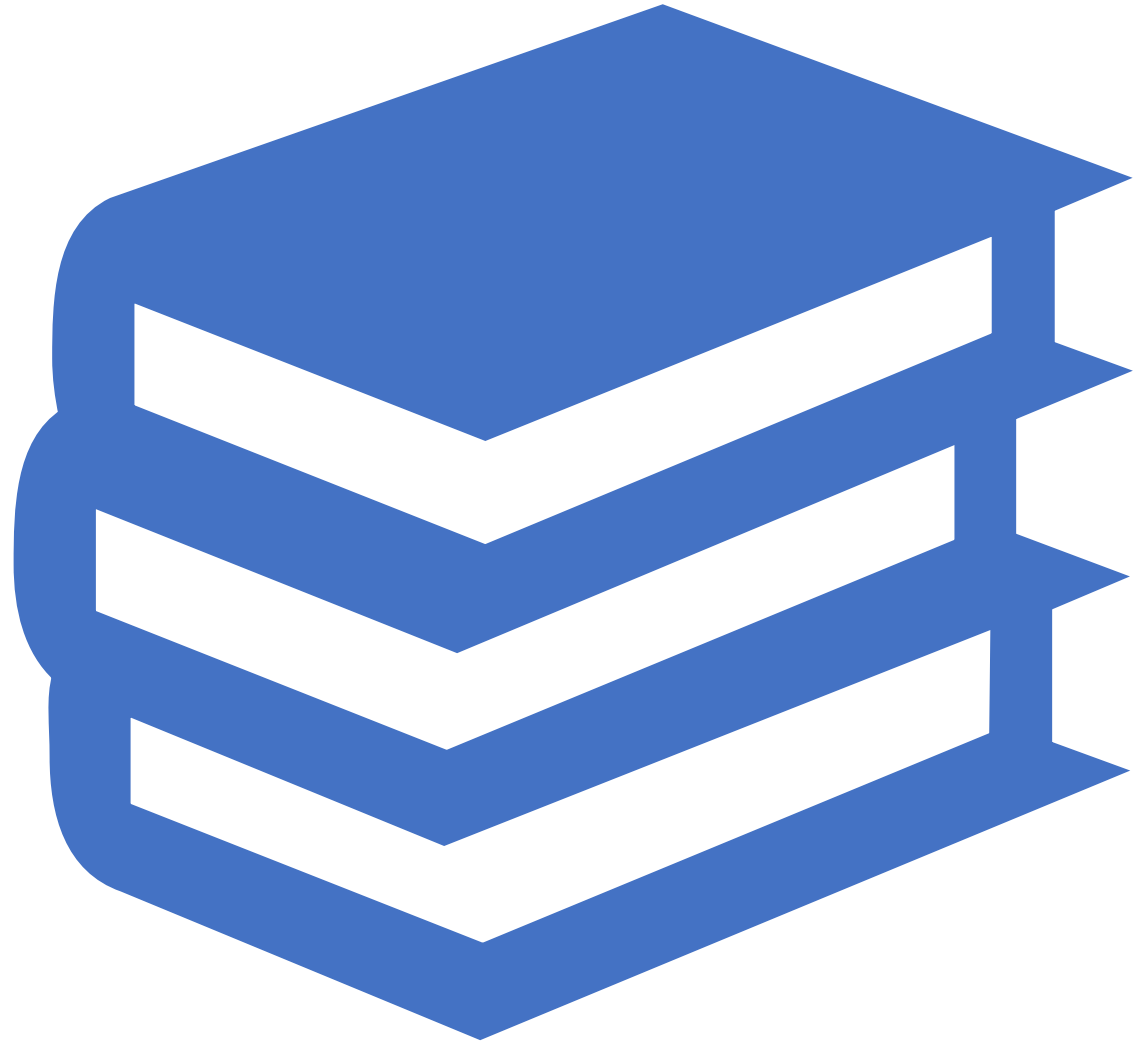
Michael Pollan

Author of *The Omnivore's Dilemma*



Books, Movies, Podcasts

Additional
Materials,
References,
and Slides



How did we get here?

- **Influence of Pharma**

- Introduced OxyContin in 1995 - Funded >20,000 pain-related educational programs between 1996 and 2002
- American Pain Society (*"Pain is the 5th Vital Sign"*)

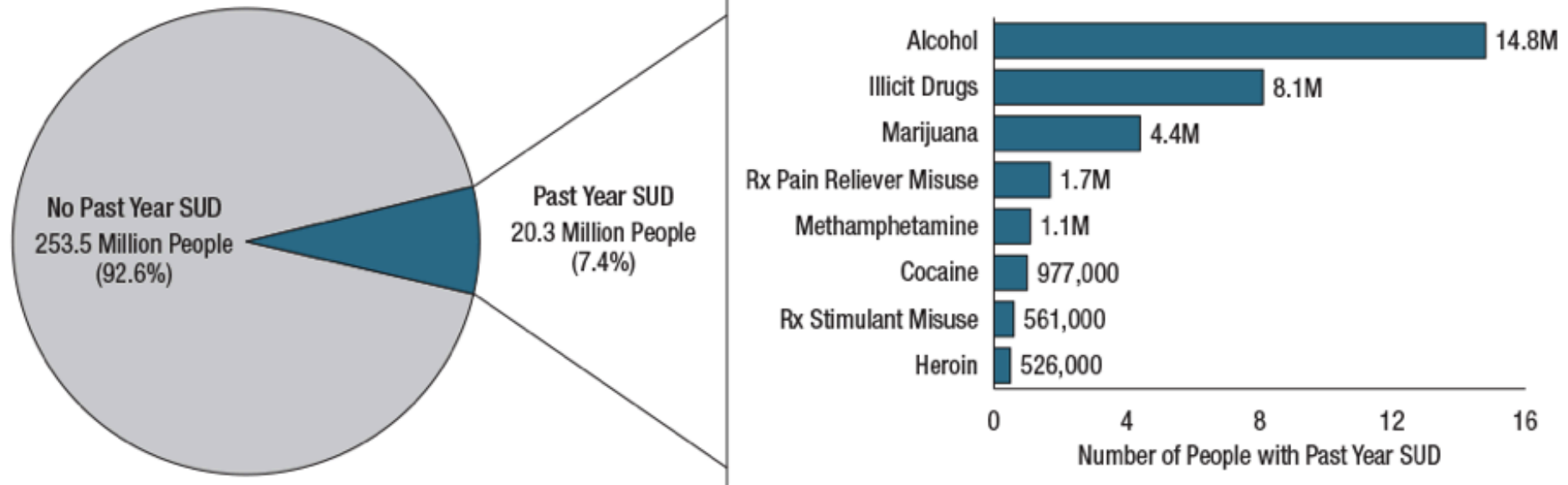
- **Good Intentions Gone Wrong**

- Late '90s: MDs pressured to address "pain as 5th vital sign"
- Limited education about pain mgmt. during med school
- Almost no training on addiction

- **Deaths of despair**

- deindustrialization
- social safety net cuts
- mass incarceration

Figure 42. People Aged 12 or Older with a Past Year Substance Use Disorder (SUD): 2018



Rx = prescription.

Note: The estimated numbers of people with substance use disorders are not mutually exclusive because people could have use disorders for more than one substance.

D

To feel good

To have novel:
Feelings
Sensations
Experiences
AND
To share them



To feel better

To lessen:
Anxiety
Worries
Fears
Depression
Hopelessness
Withdrawal

Why do people use drugs?

Drawings courtesy of Vivian Felsen

The 4 C's of Addiction:

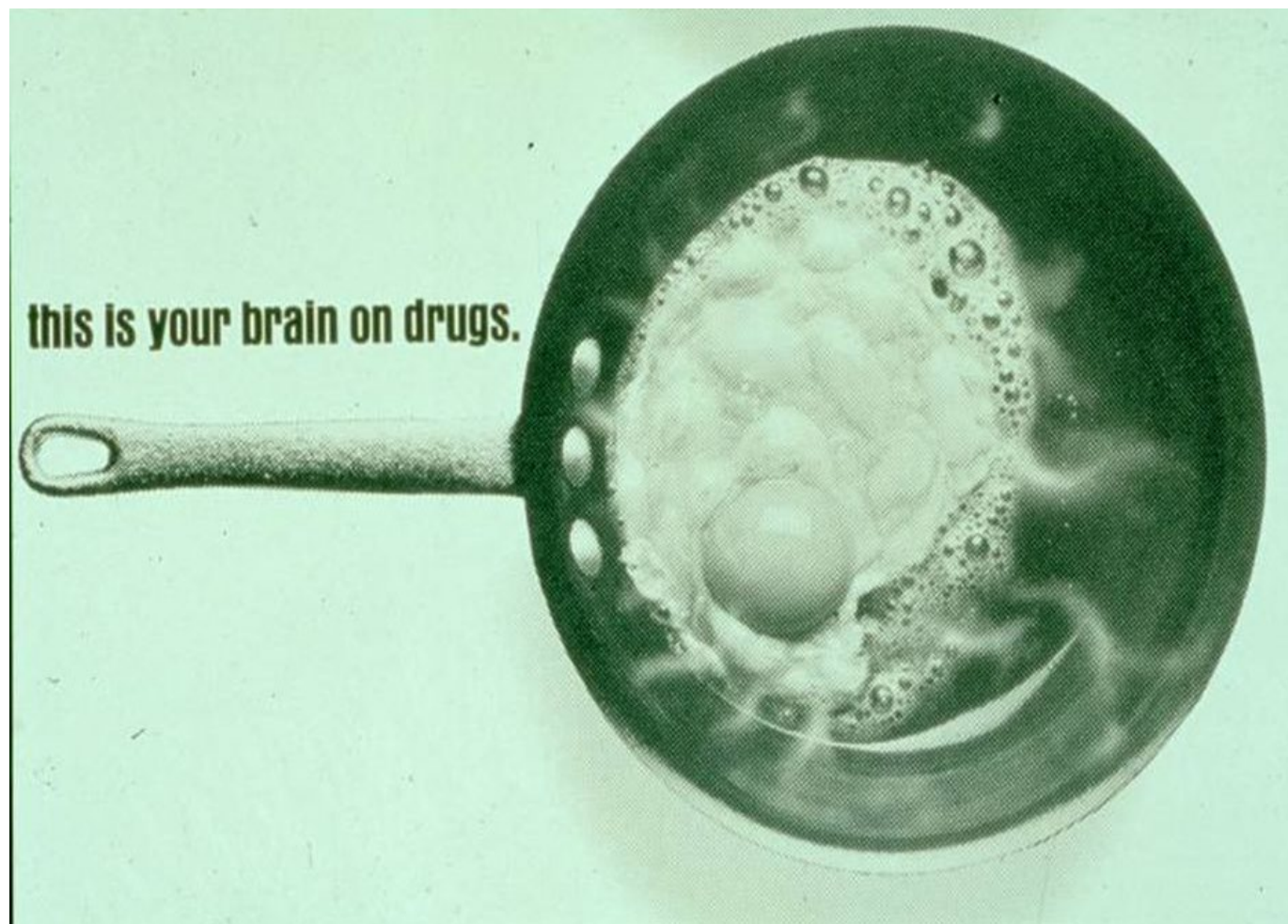
Impaired **CONTROL** over drug use

COMPULSIVE use

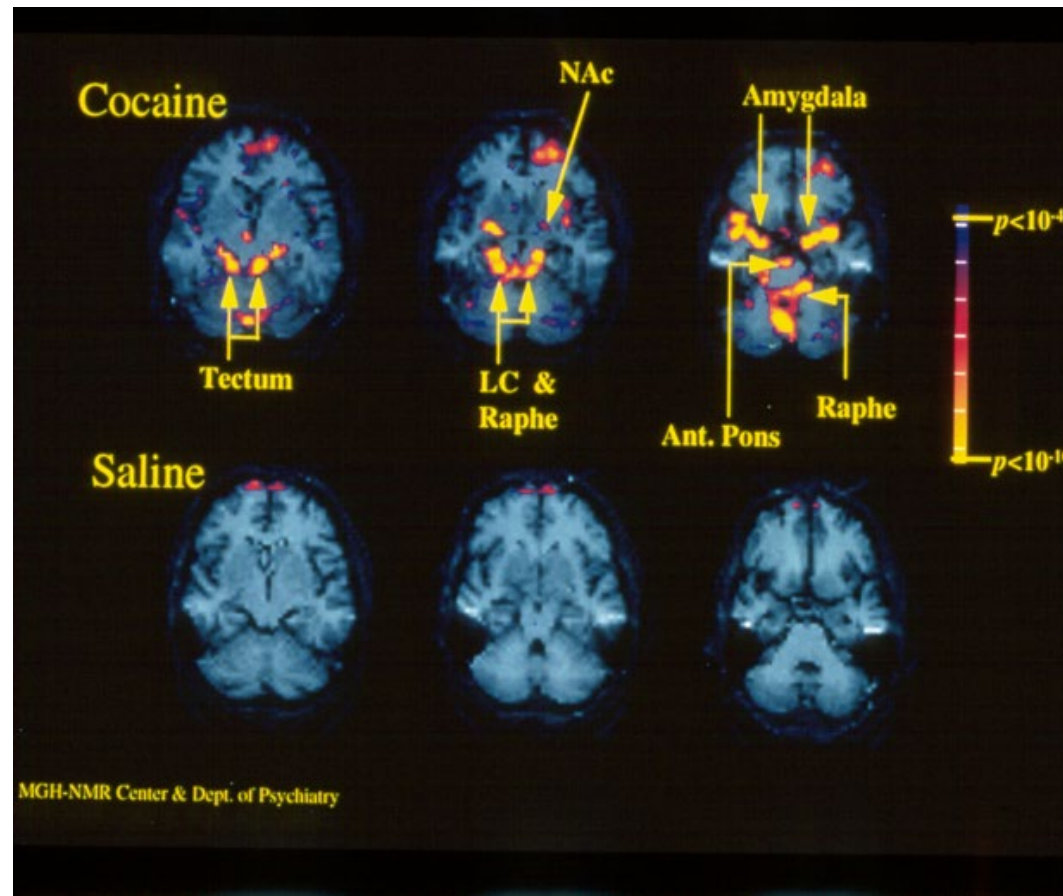
CONTINUED use despite harm

CRAVINGS

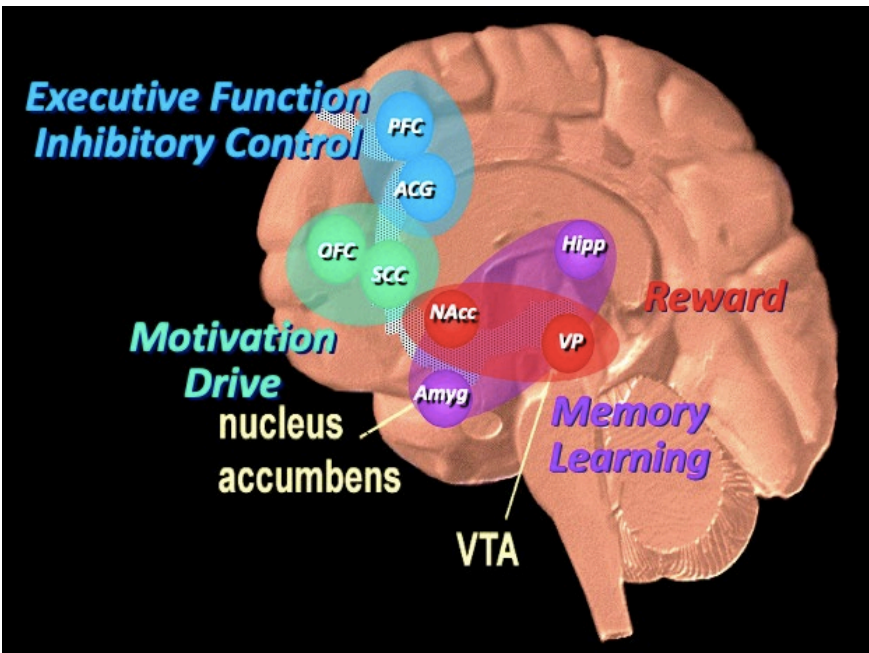
Campaign by
Partnership
for a Drug-
Free America
launched in
1987



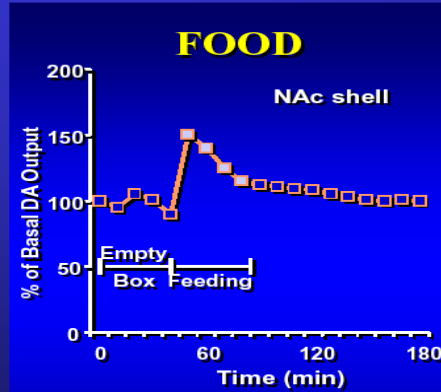
This is (actually) your brain on drugs



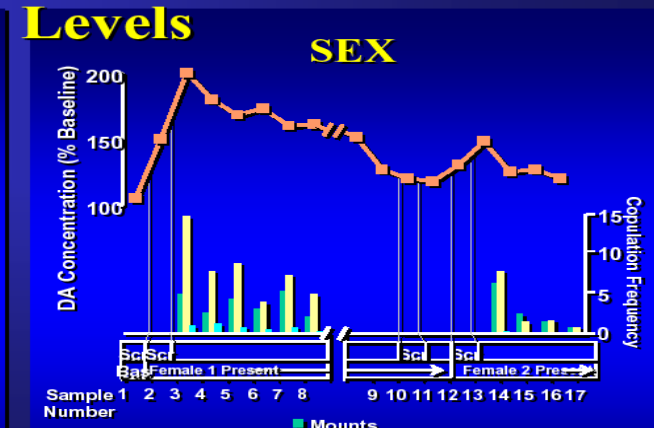
Drugs Elevate
Dopamine
More/Longer



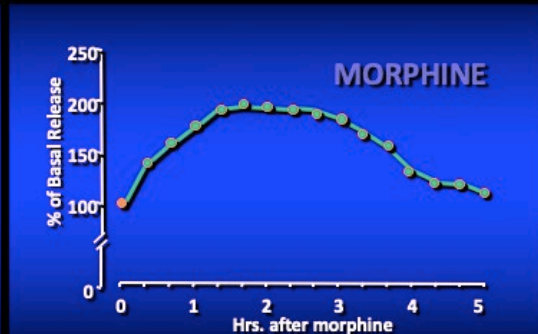
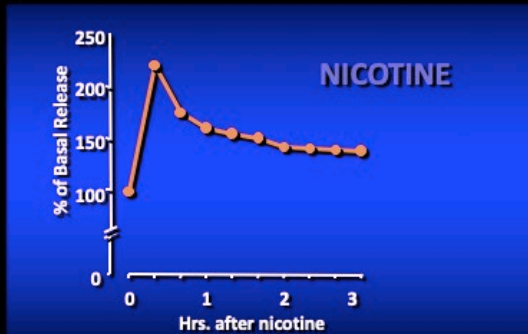
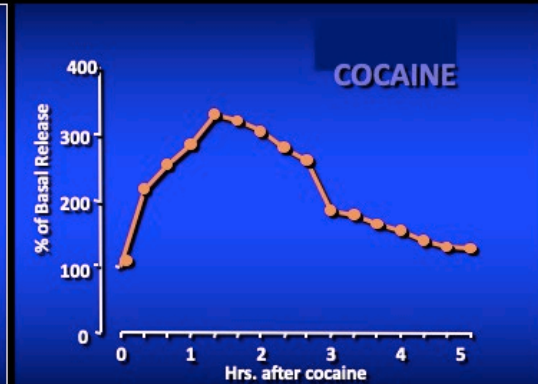
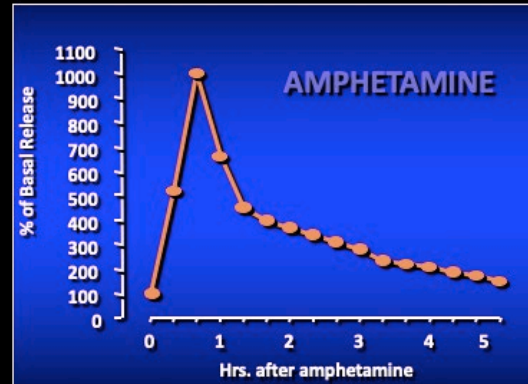
Natural Rewards Elevate Dopamine Levels

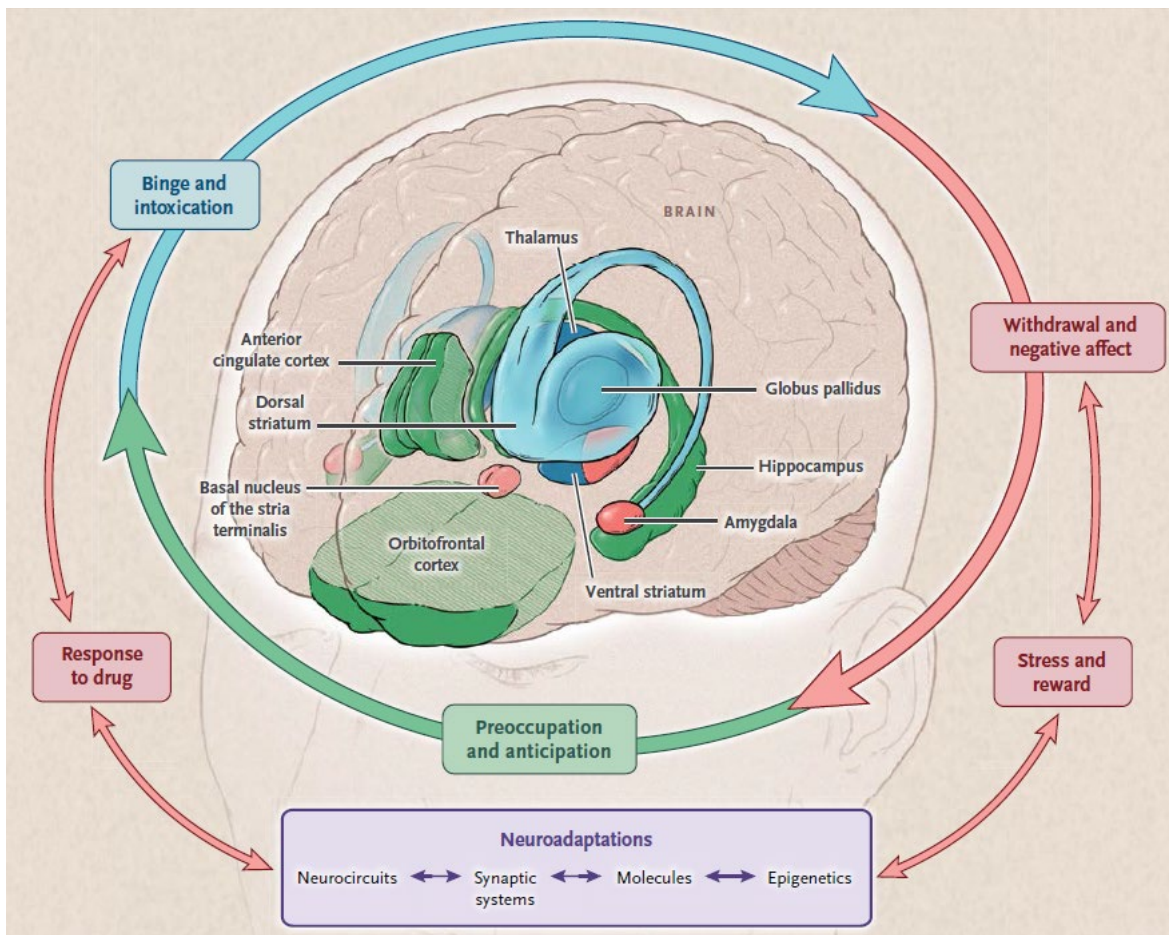


Source: Di Chiara et al.



Source: Fiorino and Phillips





- Desensitized reward circuits → dampened pleasure
- Conditioned responses & stress reactivity → cravings and negative emotions
- Weakened executive function decision making, inhibitory control & self regulation → relapse

Stage of Addiction	Shifting Drivers Resulting from Neuroadaptations		
Binge and intoxication	Feeling euphoric	→ Feeling good	→ Escaping dysphoria
Withdrawal and negative affect	Feeling reduced energy	→ Feeling reduced excitement	→ Feeling depressed, anxious, restless
Preoccupation and anticipation	Looking forward	→ Desiring drug	→ Obsessing and planning to get drug

Heritability

Trait	Heritability
Type II DM	0.3 ¹
Type I DM	0.7 ²
Hypertension	0.3 - 0.5 ³
Peanut allergy	0.8 ⁴
Cataract (age-related)	0.5 ⁵
Alcoholism	0.6⁶
Nicotine	0.5 – 0.6⁷
Cocaine and stimulants	0.4 – 0.8⁸
Heroin and opioids	0.5⁹
Cannabis	0.3 – 0.8¹⁰

¹Poulsen et al., Diabetologia 1999

²Kyvik et al., BMJ 1995

³Corvol & Jeunemaitre, Endocrine Rev 1997

⁴Sicherer et al., J Allergy Clin Immunol 2000

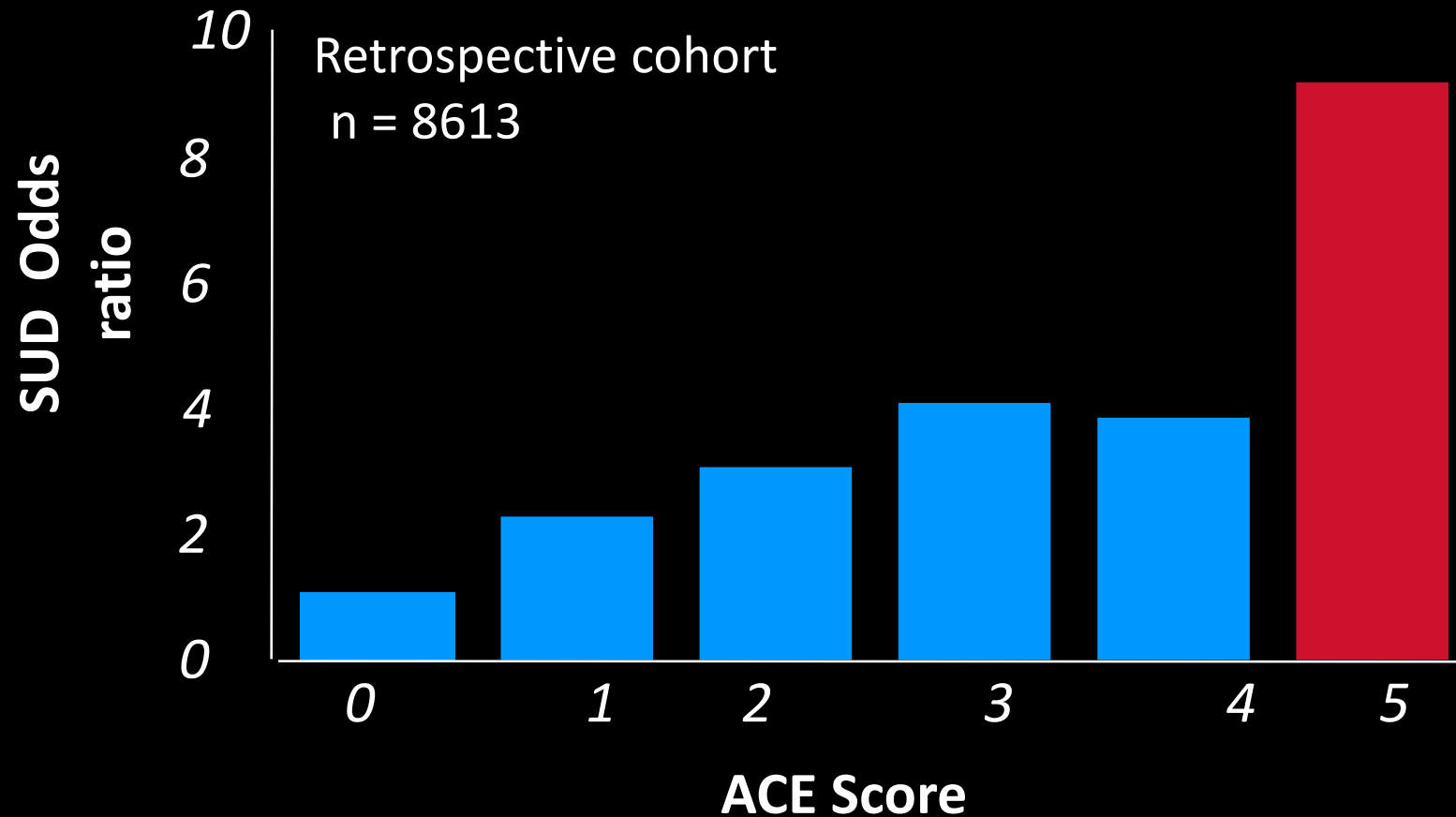
⁵Hammond et al., N Engl J Med 2000

⁶Goate & Edenberg, Curr Opin Genet Dev.1998

⁷Sabol et al., Health Psych. 1999

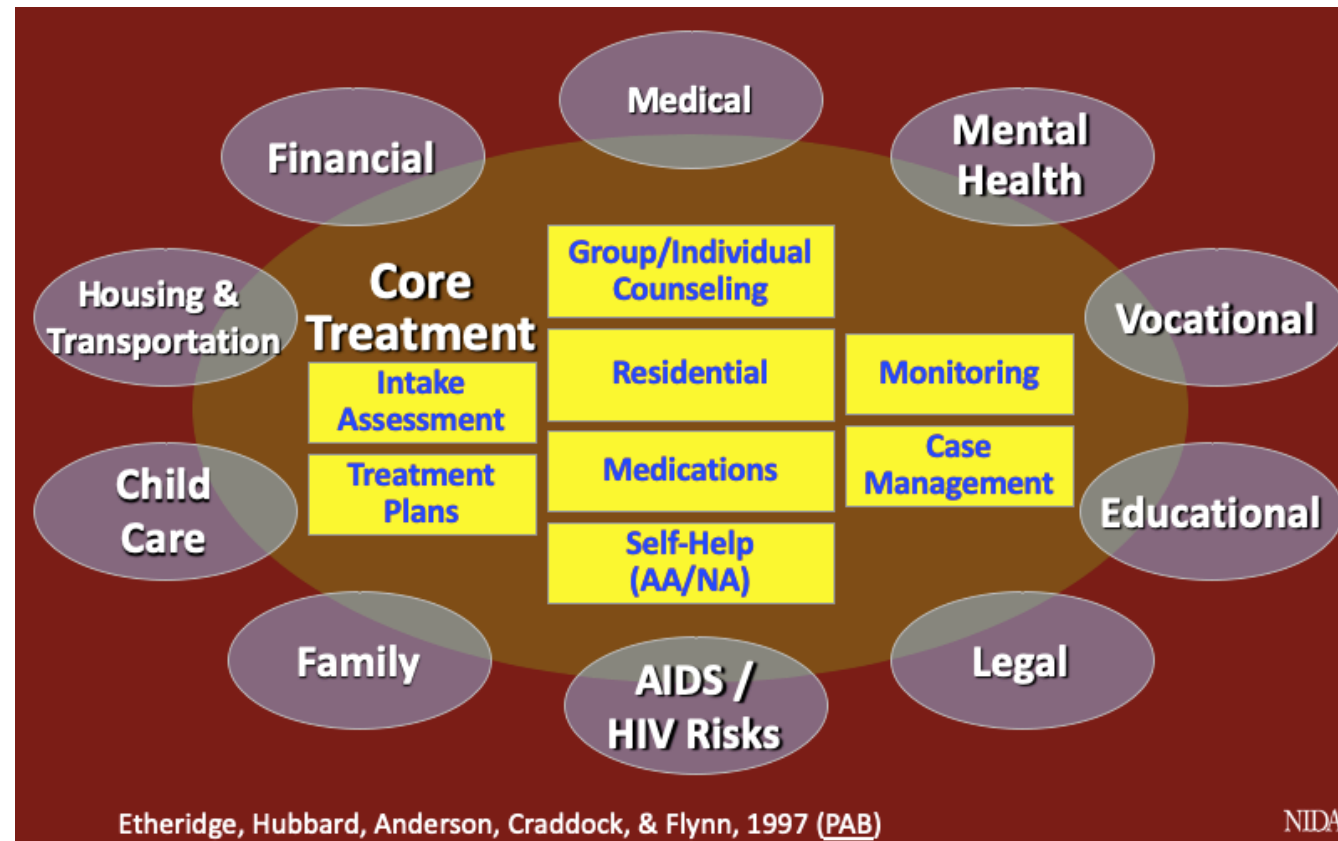
⁸⁻¹⁰Tsuang et al. 1996; Am J Med Genet. 1996

Adverse Childhood Experiences (ACE) and Illicit Drug Use



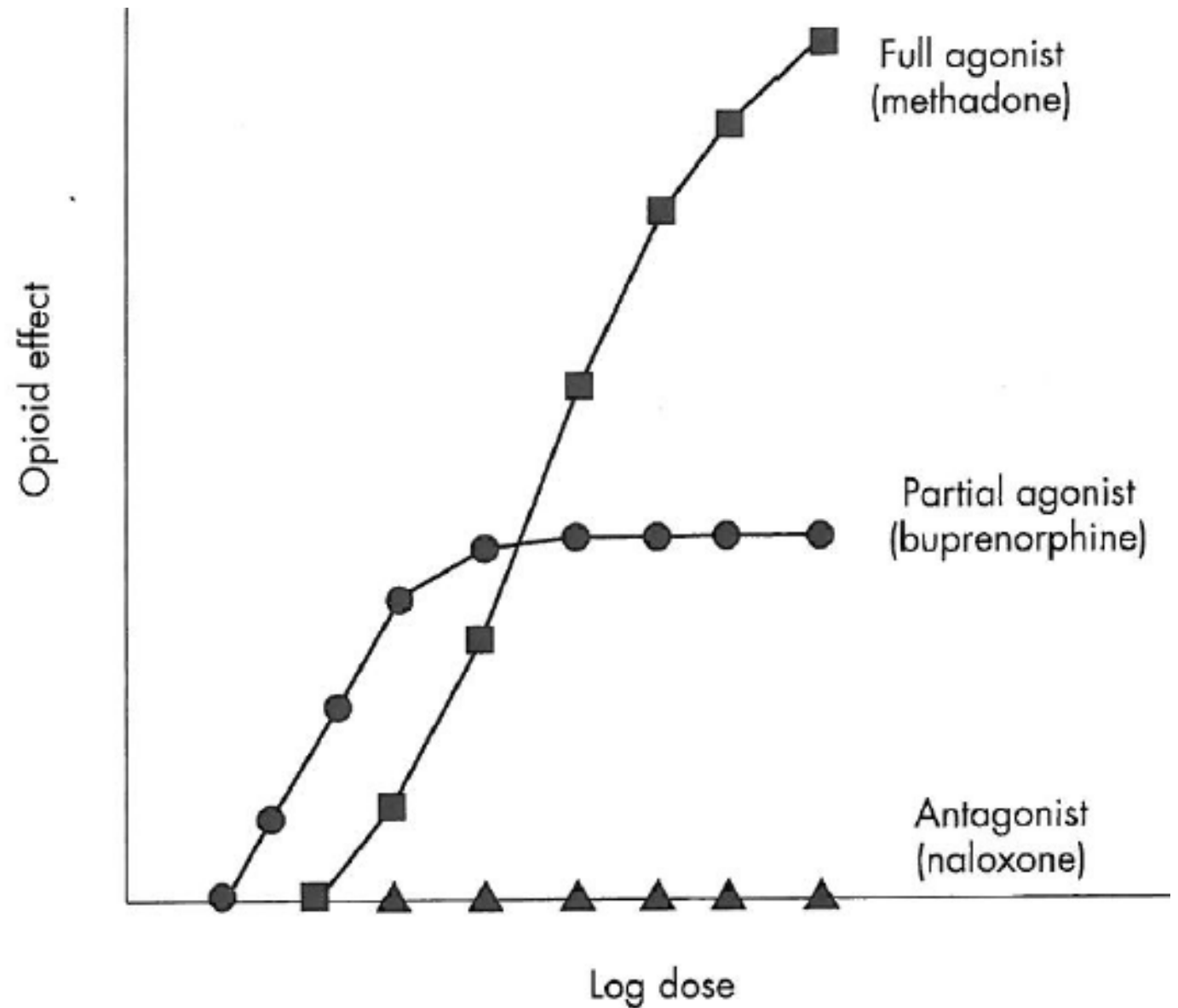
- Each ACE increased likelihood of early drug use by 2- to 4-fold
- ≥ 5 ACEs were 7- to 10-fold more likely to report illicit drug use problems

Substance Use Disorder Treatment



Mu Opioid Receptor Activation

Full Agonist, Partial Agonist, Antagonist



Office-Based Buprenorphine Treatment of Opioid Use Disorder, 2nd edition. Renner JA, Levounis P, LaRose AT eds. American Psychiatric Association Publishing, Inc, Arlington, VA, 2018

Medications for OUD (MOUD)

Goals

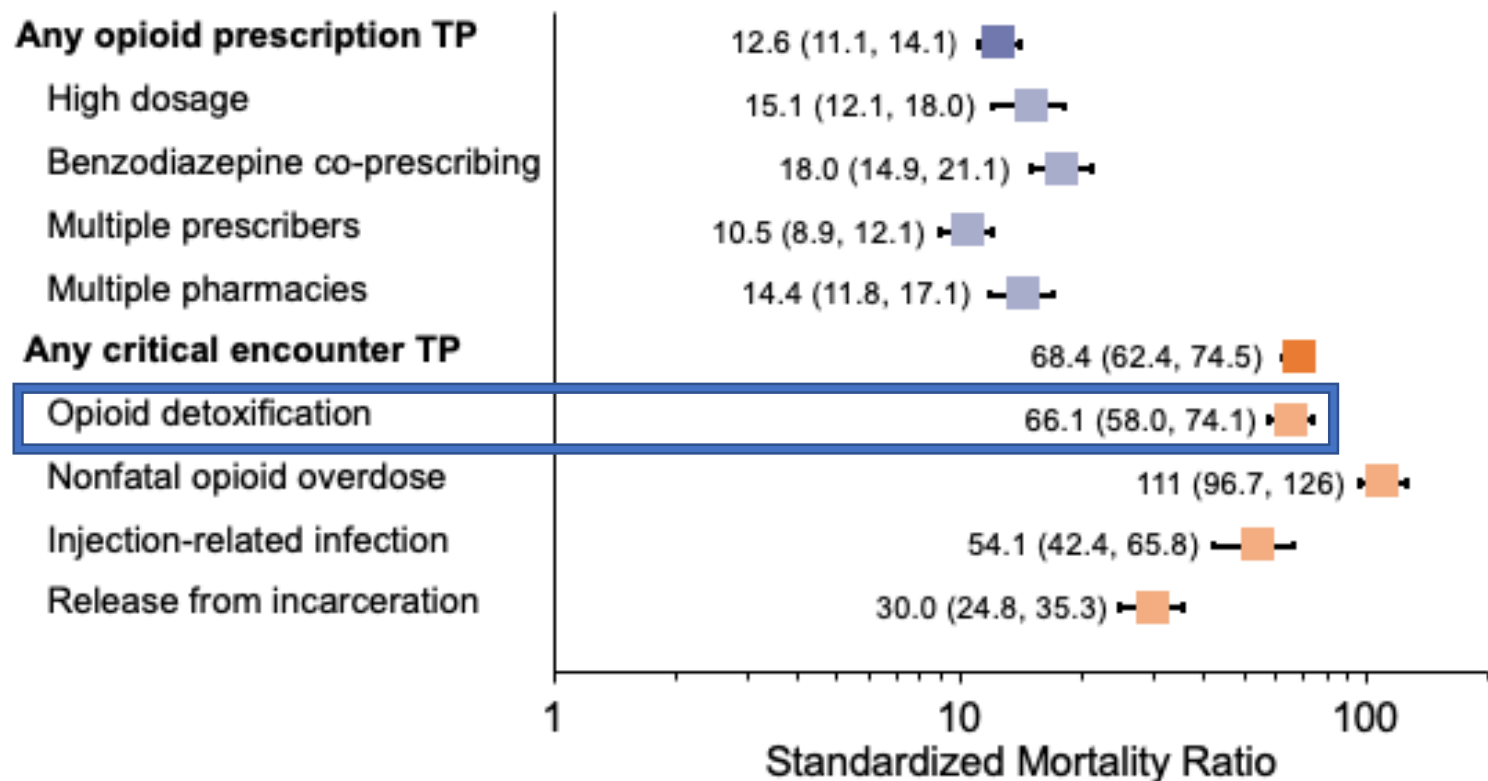
- Alleviate physical withdrawal
- Opioid blockade
- Alleviate drug craving
- Normalized deranged brain changes and physiology

Some options

- **Naltrexone** (opioid antagonist)
- Opioid Agonist Therapy (OAT)
 - **Methadone** (full opioid agonist)
 - **Buprenorphine** (partial opioid agonist)

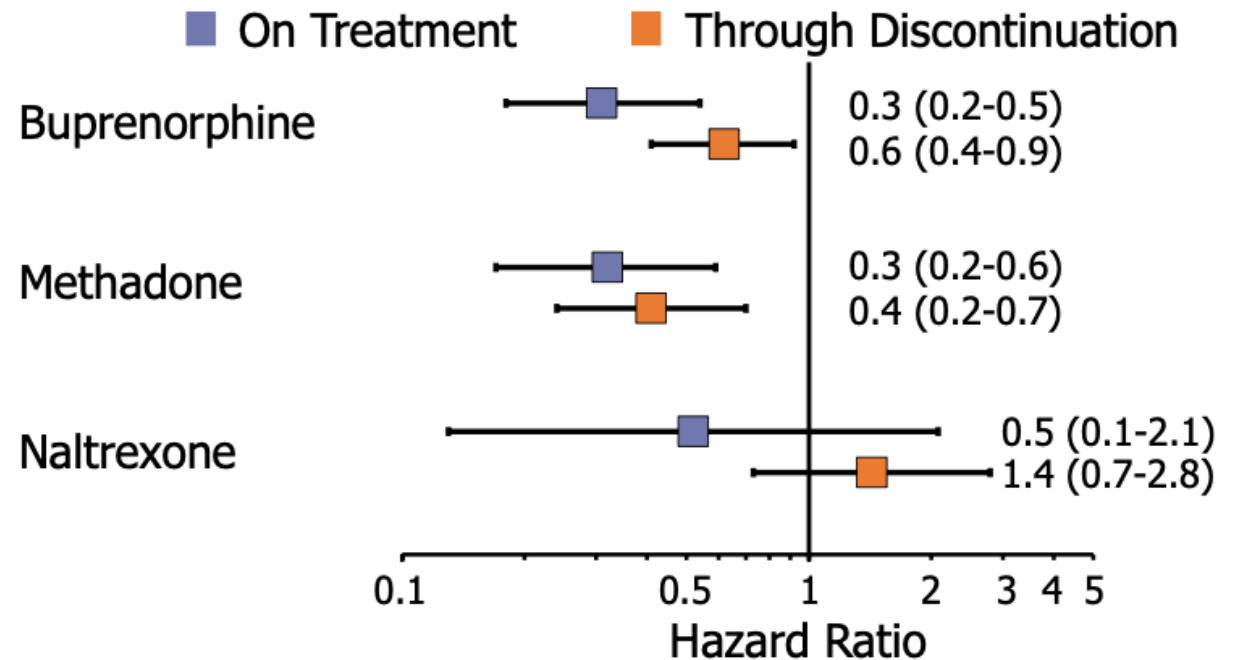
Opioid Overdose Standardized Mortality Ratios Following Touchpoints

(Massachusetts, 2014, n=1,315 opioid-related deaths)



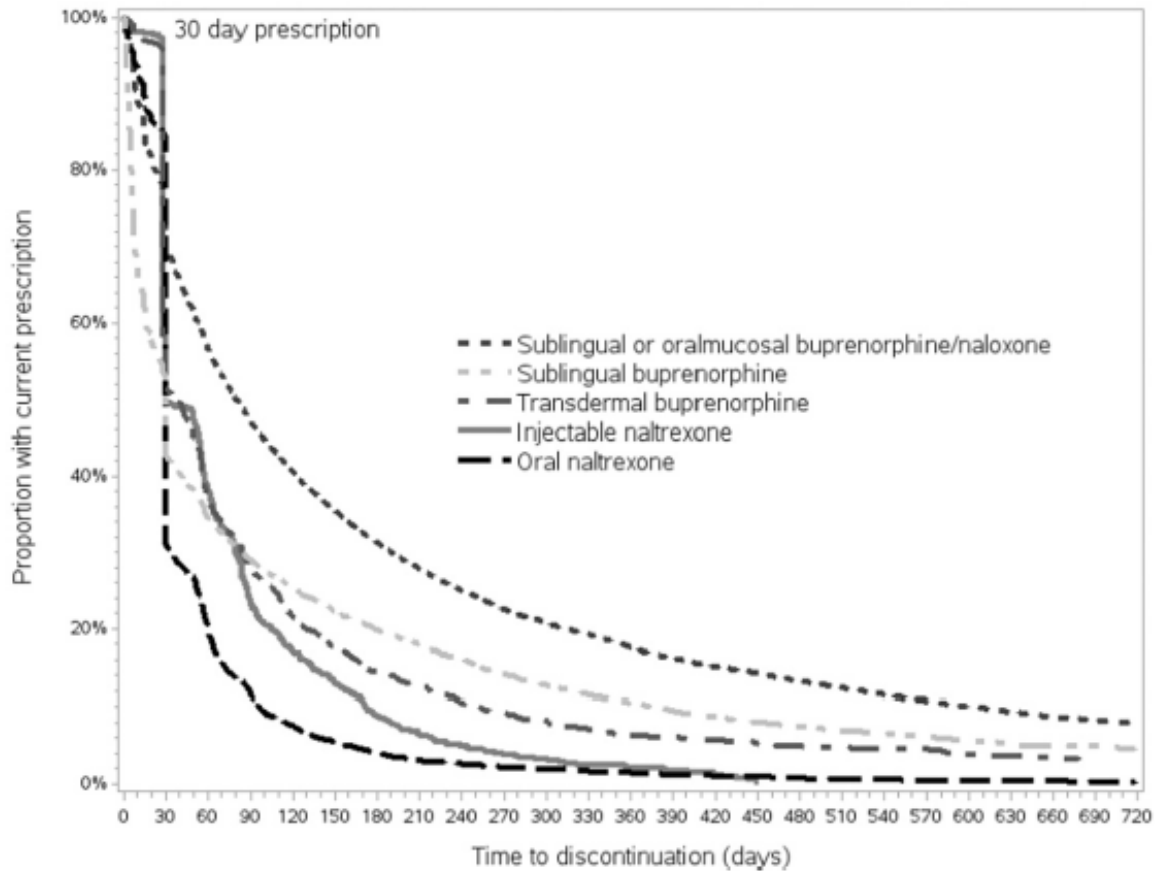
Treatment Prevents Opioid Related Death

Adjusted* hazard for opioid-related mortality By monthly receipt of treatment in post-overdose period



* Adjusted for: age, sex, depression dx, anxiety dx, incarceration, detoxification, baseline opioid and benzodiazepine rx, and monthly post-overdose receipt of benzodiazepines, opioids, detoxification and short- and long-term residential treatment

Comparison to current first line OUD TxS



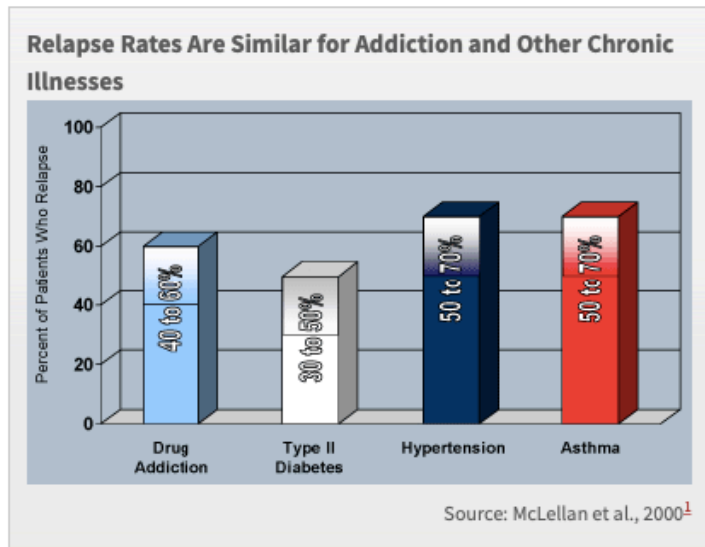
Morgan JR. Journal of substance abuse treatment. 2018;85:90-6.

First author, year, country	Design	Sample N (% Male)	Medication	Retention outcome	Retention rate
Gryczynski ⁵⁹ , 2013, USA	Prospective cohort, MET vs BUP; secondary analysis of two RCTs	African-Americans entering MAT; 478 (65.2)	MET, BUP	In MAT 6 months	78.1% MET 57.7% BUP
Pinto ⁶⁰ , 2010, England	Prospective cohort, MET vs BUP; all received care coordination	Requesting MAT; 361 (75.0)	MET, BUP	In MAT 6 months	69.6% MET 42.5% BUP
Bounes ⁶¹ , 2013, France	Prospective cohort	Treatment settings; 151 (74.0)	MET, BUP	In MAT 12 months	78.0% MET 26.0% BUP
Serpelloni ⁶² , 2013, Italy	Retrospective cohort (65 publicly-funded addiction treatment sites)	Patients in MAT in 2010; 8,145 (84.2)	MET, BUP	Days of stay during 2010	MET: M=246.2 (SD=110.1) BUP: M=240.5 (SD=111.7)
Hao ⁶³ , 2013, China	Prospective cohort, MET vs Jitai tablets; all received psychosocial counseling	Completed detox; 386 (84.4)	MET, Jitai tablets	In MAT 12 months	85.0% MET 74.3% Jitai
Gryczynski ⁶⁴ , 2014, USA	Prospective cohort; secondary analysis of RCT studying counseling	African-Americans entering MAT; 297 (61.9)	BUP	In MAT 6 months	57.9% overall; retention associated with higher

Timko C.J Addict Dis. 2016;35(1):22-35.

Addiction is treatable

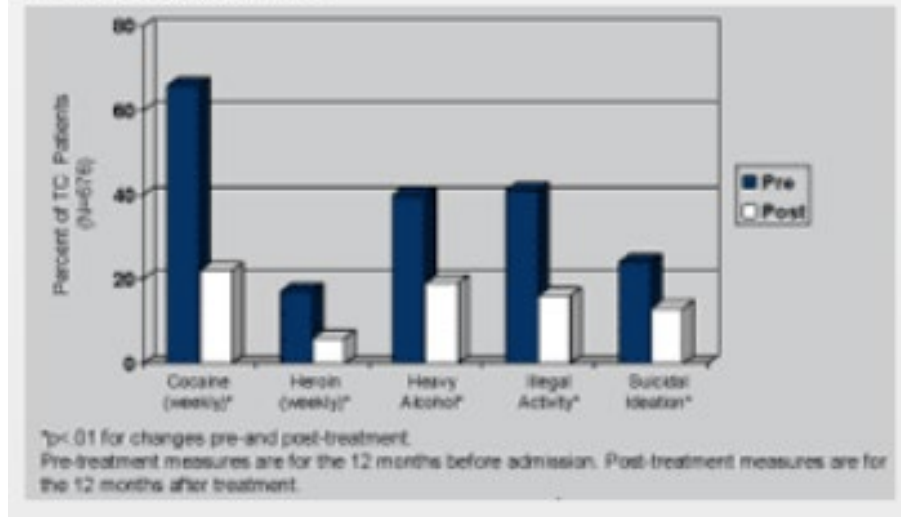
Relapse is Common in Addiction and Other Complex Chronic Diseases



McLellan et al., 2000

Treatment Works

Pre- and post-treatment self-reported changes among those in long-term residential TCs



Hubbard RL. Journal of Substance Abuse Treatment 25 (2003)

Myths about MOUD



Myth

- **Substituting one addiction for another**
- **MOUD increases risk of overdose**
- **Medications will be diverted and create more addiction**

Facts

- **Does not create euphoria; relieves physiological opioid craving & normalizes body's functioning that were impaired¹**
- **MOUD decreases risk of overdose²**
- **Methadone that is diverted mostly from pain treatment not addiction³, diverted buprenorphine is used for self-treatment⁴**

1. SAMHSA, 2003
2. Larochelle MR. Drug Alcohol Depend. 2019;204:107537.
3. SAMHSA, 2010
4. Cicero TJ. Drug Alcohol Depend. 2018;193:117-23

Stigma – attribute, behavior or condition that is socially discrediting

- ***Major barrier to seeking help***

- WHO - addiction is the #1 most stigmatized social problem (more than mental illness)

- Words matter

Stigmatizing/Punitive/Tough

- “Substance/drug abuse”
- “Substance/drug abuser”
- “War on Drugs”
- “Dirty urine”
- “Junkie,” “Addict,” “Cokehead,” “Lush,” “Package,” “Body”

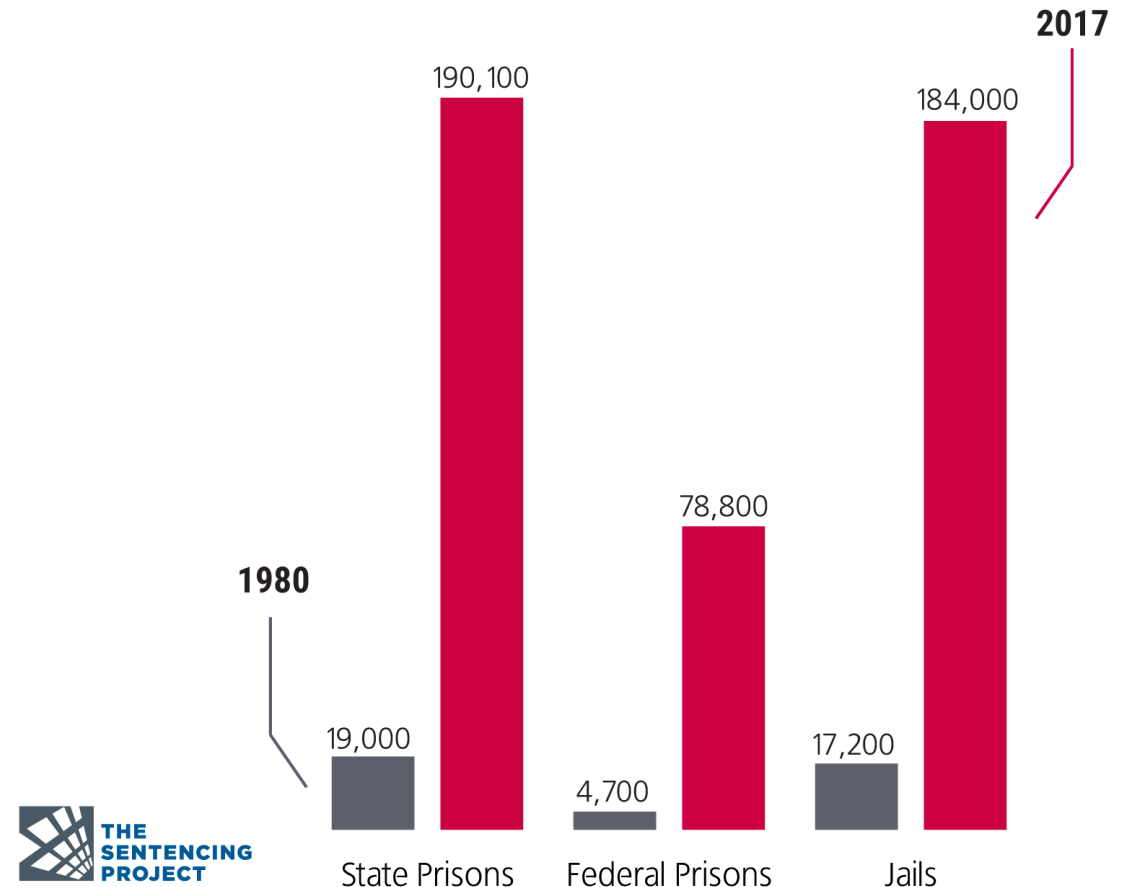
Less Stigmatizing

- “Substance use disorder”
- “Person with substance use issues/disorder”
- “Urine positive for opioids”

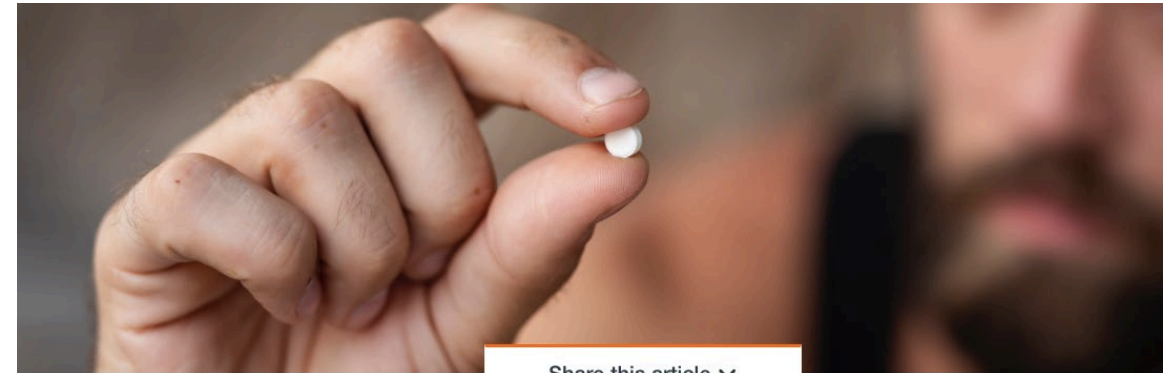
Root Causes of Mass Incarceration

Since “tough on crime” and the beginning of the War on Drugs in 1980s the number of people incarcerated skyrocketed and today there are more people behind bars for a drug offense than the number of people who were in prison or jail for any crime in 1980

Number of People in Prison and Jails for Drug Offenses, 1980 and 2017

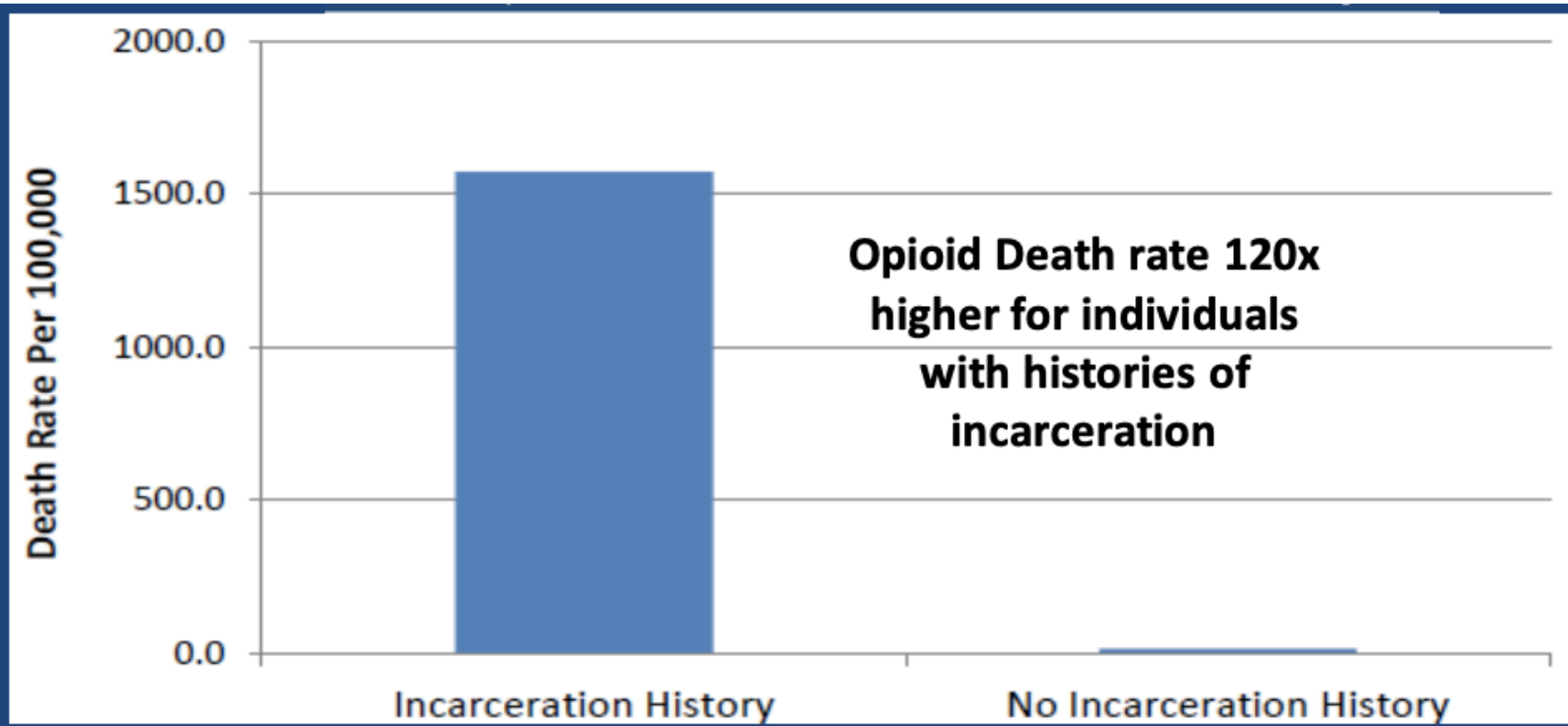


Safe Supply and Heroin Compassion Clubs



Safe supply: The debate around prescribing opioids to people who use drugs

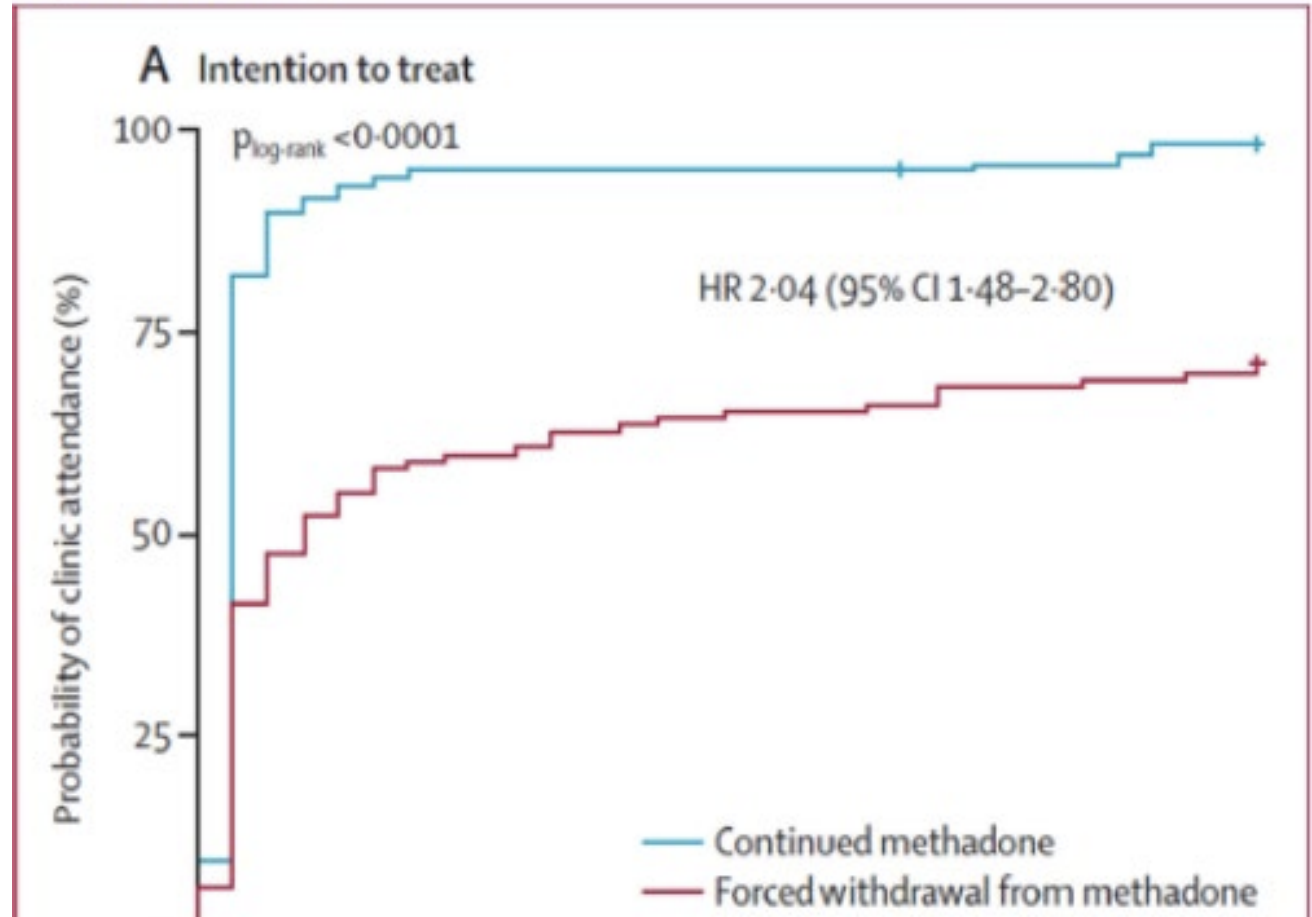
Date: August 15, 2019 Author: [Dafna Izenberg & Seema Marwaha](#)



Forced Detoxification Disrupts Care

- methadone continuation (n=114) forced methadone dose taper (n=109)
- Outcomes
 1. Engagement w MMT after release
 2. Time to engagement w MMT
- 106 (96%) of methadone continuation vs 68 (78%) of the forced dose taper re-entered methadone treatment programs ($P=0.001$)
- 8% of methadone continuation vs 18% of forced dose taper reported opiate use at 1 month ($p<0.033$)

incarceration in a combined US prison and jail: a randomised, open-label trial





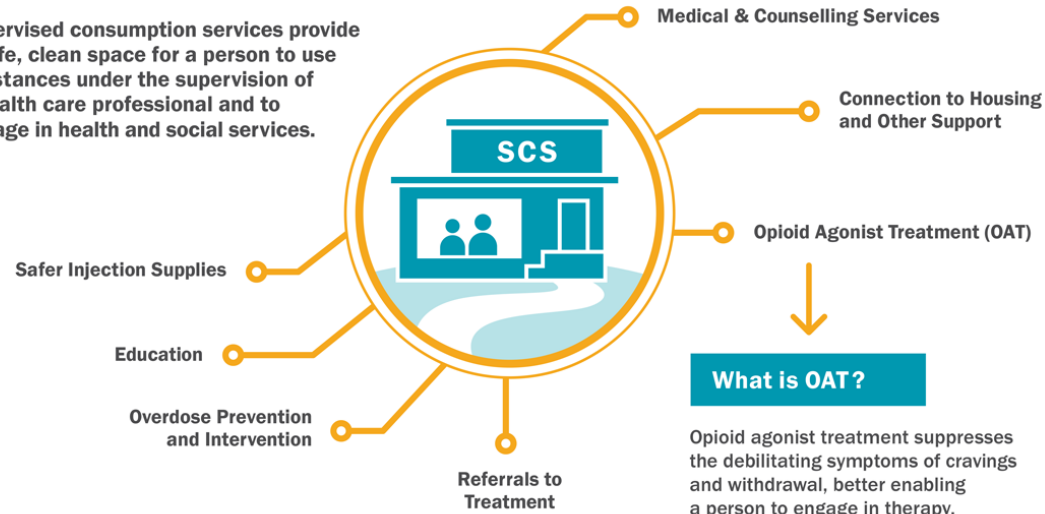
- Methadone and Buprenorphine
- Methadone
- Vivitrol for re-entry
- All three drugs offered in all prisons and jails

Andrew Klein. Stateline research. US SAMHSA data © 2018 The Pew Charitable Trusts

Supervised Consumption Services (SCS)

What are SCS?

Supervised consumption services provide a safe, clean space for a person to use substances under the supervision of a health care professional and to engage in health and social services.



What is OAT?

Opioid agonist treatment suppresses the debilitating symptoms of cravings and withdrawal, better enabling a person to engage in therapy, counselling and support.

Benefits



Less overdose deaths



Less discarded needles



Less public drug use



Reduced sharing of needles

= Less HIV & Hepatitis C transmission



Increased access to services

= Increased use of detox & treatment

Supervised consumption services save lives and improve community well-being.

Regulations Amending the Narcotic Control Regulations and the New Classes of Practitioners Regulations (Diacetylmorphine (Heroin) and Methadone): SOR/2018-37

Canada Gazette, Part II: Volume 152, Number 6

Registration

March 7, 2019

CONTROL

P.C. 2018-10

Her Excellency

and Substantive

(Diacetylmorphine)

Government of Canada
use disorder
projects in

From: [Health Canada](#)

News release

May 15, 2019

GUIDELINE  VULNERABLE POPULATIONS 

Injectable opioid agonist treatment for opioid use disorder: a national clinical guideline

Nadia Fairbairn MD, Josey Ross MA, Michael Trew MD, Karine Meador MD, Jeff Turnbull MD, Scott MacDonald MD, Eugenia Oviedo-Joekes PhD, Bernard Le Foll MD, Marie-Ève Goyer MD, Michel Perreault PhD, Christy Sutherland MD

■ Cite as: *CMAJ* 2019 September 23;191:E1049-56. doi: 10.1503/cmaj.190344

CMAJ Podcasts: author interview at <https://soundcloud.com/cmajpodcasts/190344-guide>

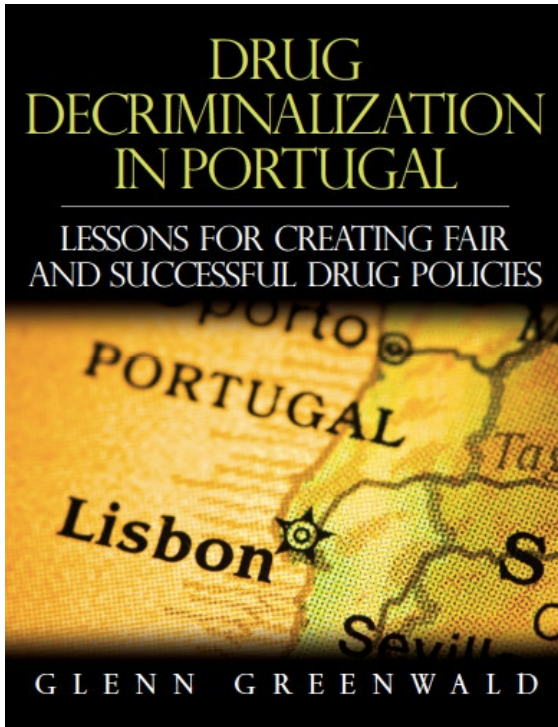


Figure 11
 Deaths,* by Year, by Substance

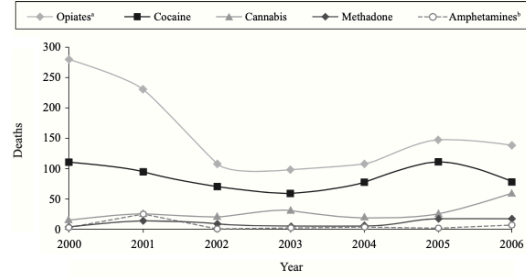
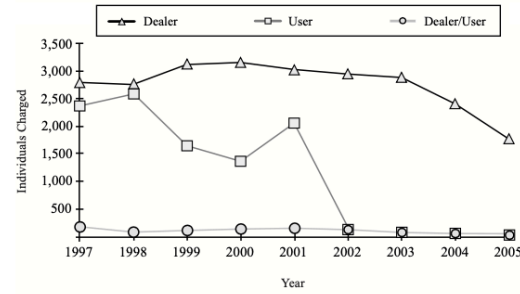
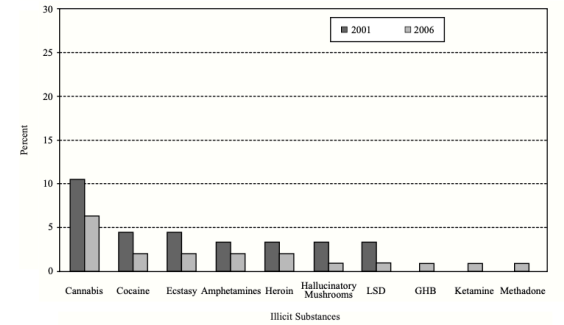


Figure 3
 Individuals Charged, By the Year and Drug-Related Status



Source: Instituto da Droga e da Toxicodpendência de Portugal (Institute on Drugs and Drug Addiction of Portugal), "The National Situation Relating to Drugs and Dependency," 2005 Annual Report (2006), p. 150.

Figure 4
 National Investigation in School Environment, 2001 and 2006, 3rd Cycle (7th, 8th, and 9th years), Portugal, Prevalence Over Entire Life



Legislation

References

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