Webcast Wednesday: Medication Assisted Treatment

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UNC SCHOOL OF MEDICINE

Disclosures

- **None**

Goals and Objectives

- **At the end of this session the learner will be able to:**
  - Describe past and present opioid epidemics in the US and key policies
  - Explore the neurobiology of opioid addiction, addiction as a chronic disease and how treatment works
  - Discuss evidence for treatment and options for pharmacotherapy
  - Discuss specialty populations including young adults, pregnancy and criminal justice involved individuals
  - Review best practices for overdose prevention

Case: 30 yo female

- Took pills from her parents at age 14
- Transitioned to IV heroin use at age 17
- "Bupe" obtained on the street
- Several overdoses
- > 50 detox admissions
- Significant trauma history

https://deskgram.net/p/1914001632757302179_5338736333

What are Opioids?

- **"Natural,"** referred to as **opiates**
  - Morphine, codeine, opium

- **Synthetic** referred to as **opioids**
  - Semisynthetic: heroin, oxycodone, buprenorphine
  - Fully Synthetic: fentanyl, tramadol, methadone

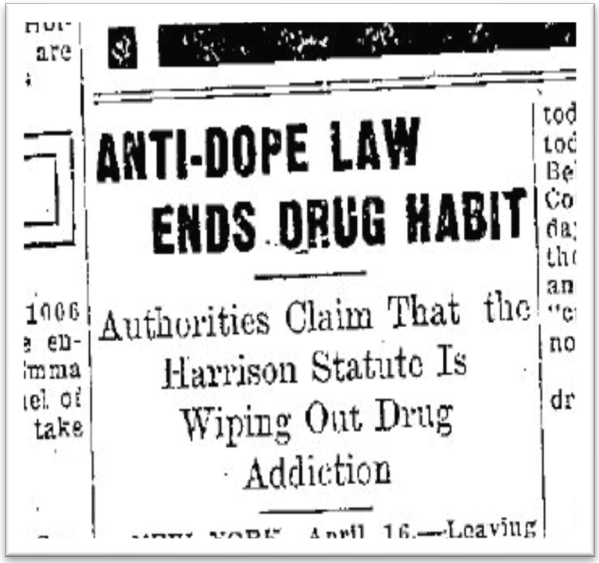
- **Opioids = "Natural" + Synthetic**

Opioid History and Policy in the U.S.

- Early-Mid 19th Century
  - Addiction among Civil War Veterans
  - Isolation of Morphine from Opium 1832
  - Introduction of the Hypodermic syringe

Opioid History and Policy in the U.S.

- Harrison Narcotics Tax Act of 1914
- DATA 2000 Waiver
- CARA, CDC Chronic Pain Guidelines - 2016
- NC STOP Act of 2017

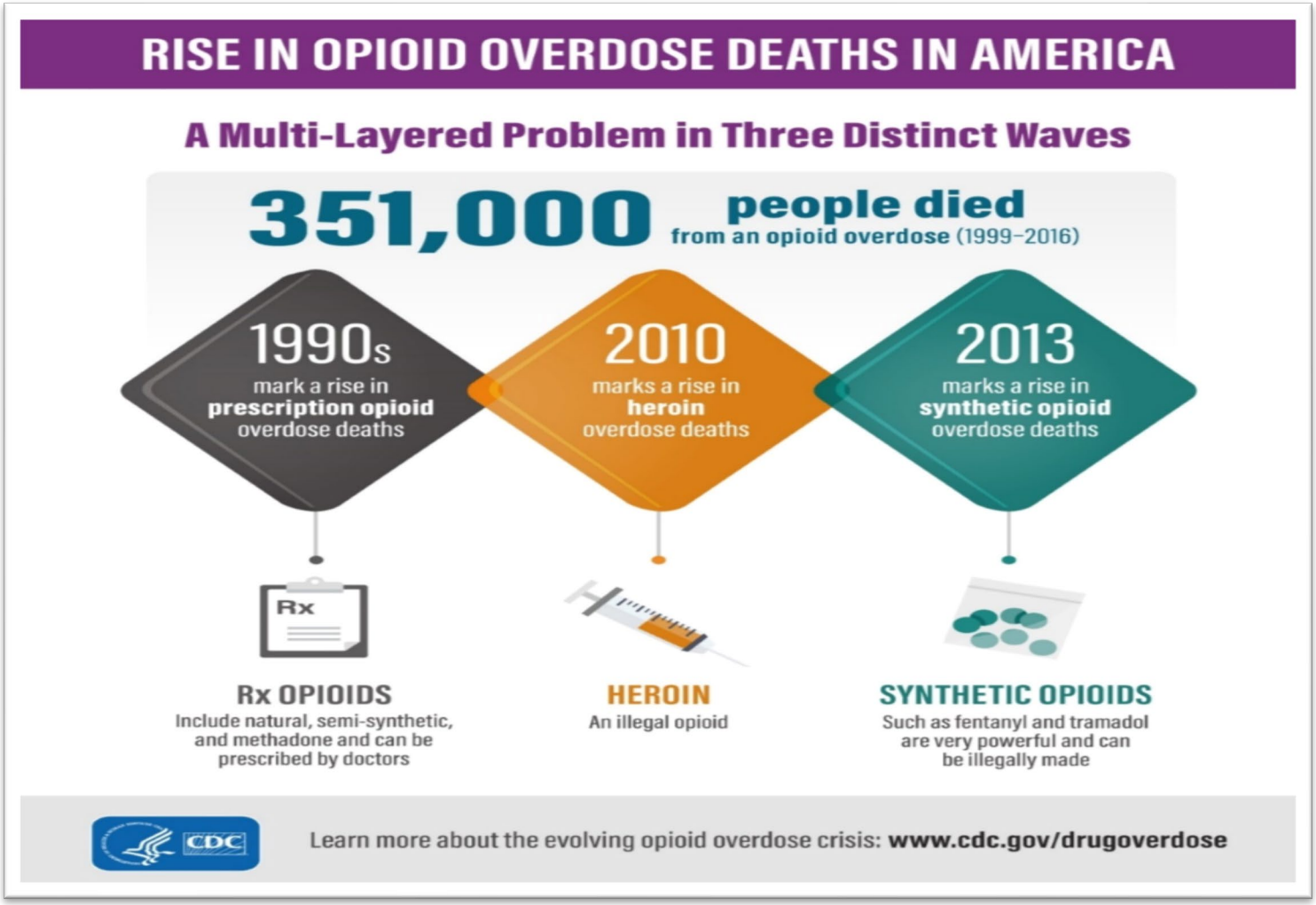


ANTI-DOPE LAW ENDS DRUG HABIT

Authorities Claim That the Harrison Statute Is Wiping Out Drug Addiction

La Crosse Tribune, 16 April 1915

"Triple Wave"

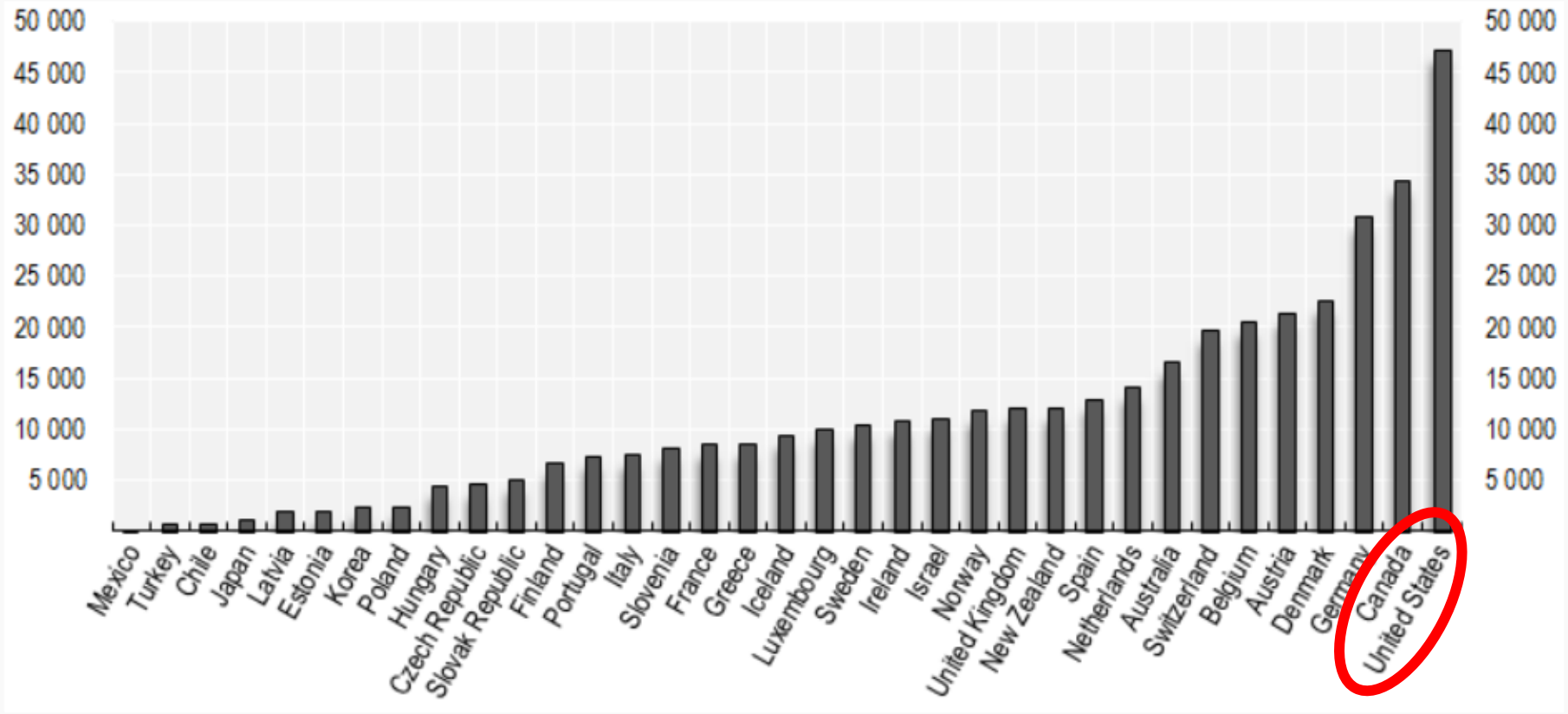


https://www.cdc.gov/drugoverdose/images/data/GraphicOpioidWaves.jpg

Global Perspective

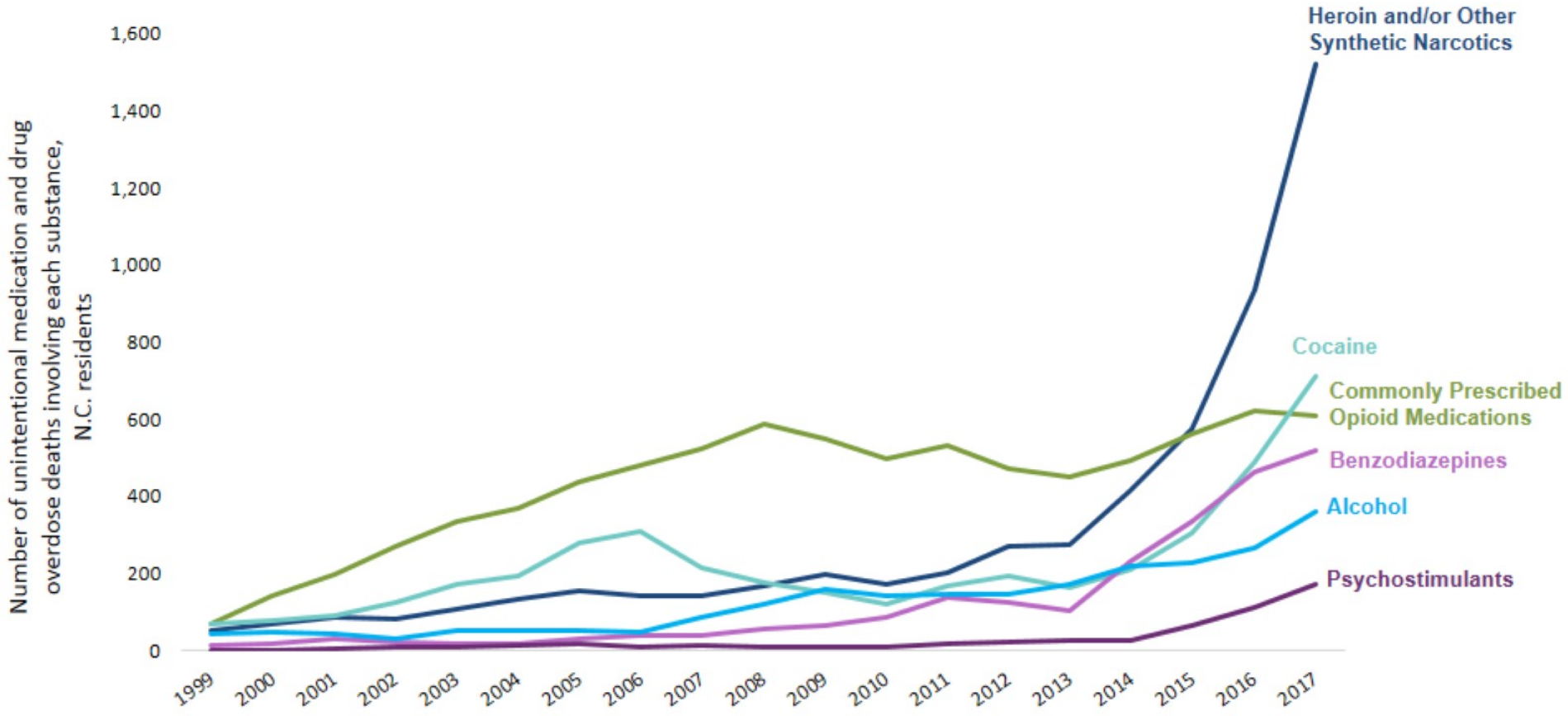
BACKGROUND INFORMATION - THE UNITED STATES

The prescription of opioids per capita is significantly higher in the United States than elsewhere in the OECD



Source: OECD (2018), OECD Economic Surveys: United States 2018, OECD Publishing.

Unintentional overdose deaths involving illicit opioids* have drastically increased since 2013



*Heroin and/or Other Synthetic Narcotics (mainly illicitly manufactured fentanyl and fentanyl analogues)

Technical Notes: These counts are not mutually exclusive; If the death involved multiple substances it can be counted on multiple lines; Unintentional medication, drug, alcohol poisoning: X40-X45 with any mention of specific T-codes by drug type; limited to N.C. residents

Source: Deaths-N.C. State Center for Health Statistics, Vital Statistics, 1999-2017

Analysis by Injury Epidemiology and Surveillance Unit

North Carolina Injury & Violence PREVENTION Branch

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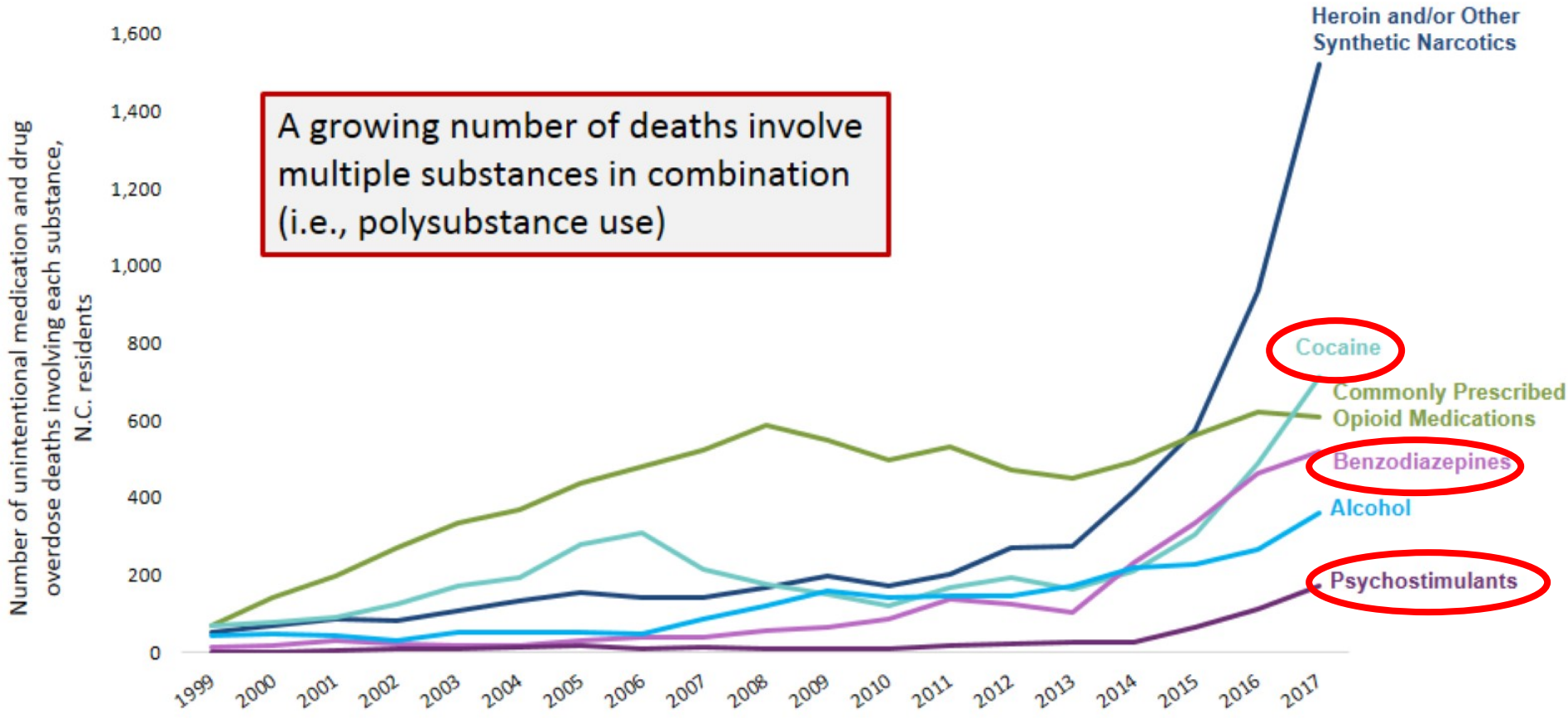

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NC Opioid Overdose Deaths Drop for First Time in 5 Years

Emergency Department Visits Also Show Nearly 10% Decrease

The decline in opioid deaths masks danger from designer drug overdoses in US

PUBLISHED WED, AUG 21 2019 • 7:30 AM EDT | UPDATED THU, AUG 22 2019 • 3:14 PM EDT

Scott Gottlieb, M.D.

SHARE

KEY POINTS

- Nationwide, overdose deaths from methamphetamine and similar drugs rose by 7.5 times between 2007 and 2017.
- By 2016, fentanyl and similar illicit narcotics such as carfentanil were involved in nearly 50% of opioid-related deaths.
- “Speedballs” and goofballs” — cocaine and methamphetamine cut with fentanyl — are driving new overdose deaths.

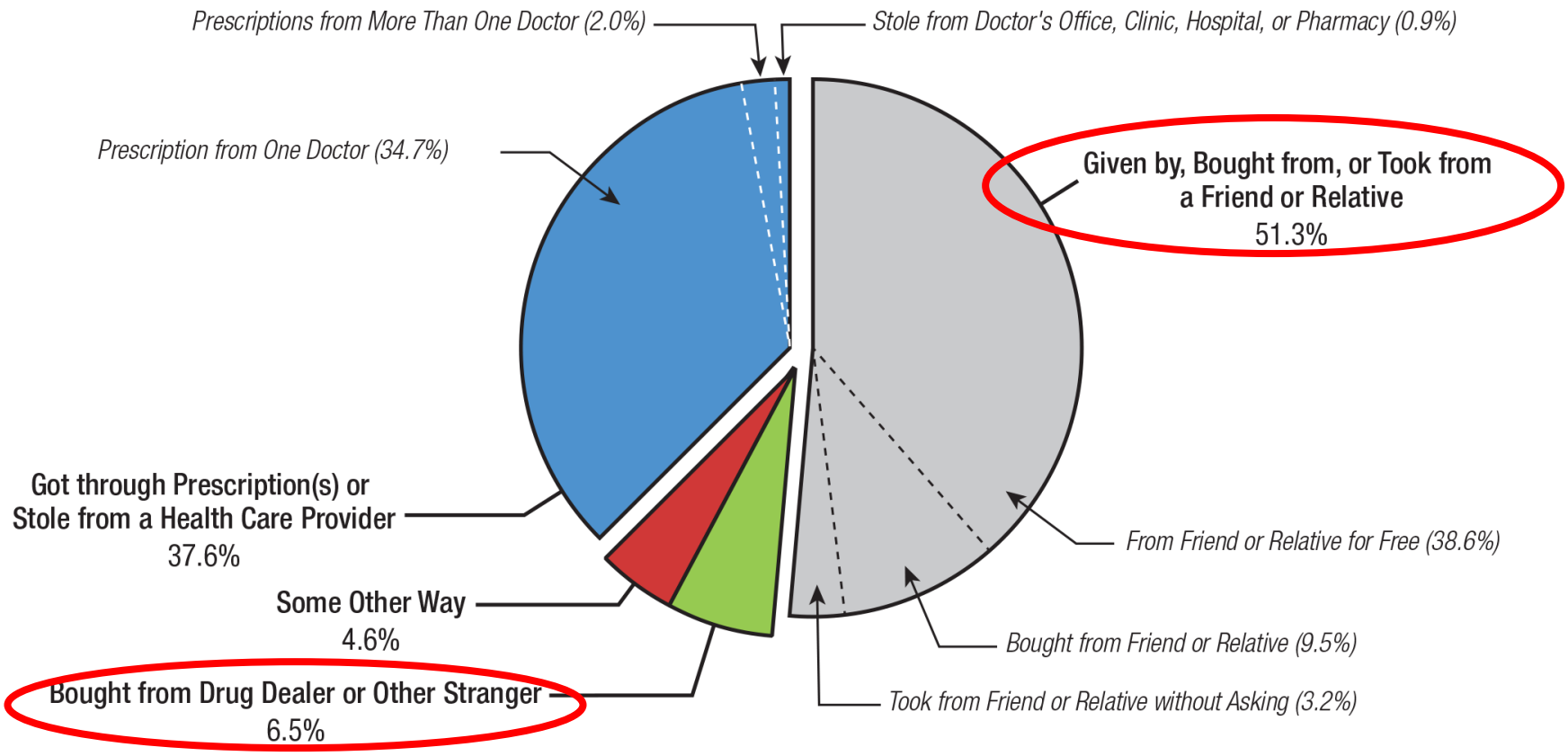
Deaths/yr in U.S. Related to Drug Use

Tobacco	**>480,000**	
Alcohol	**88,000**	
Opioid OD	47,600	
Benzodiazepine OD	11,537	(1,527 without opioids)
Cocaine OD	13,942	(3,811 without opioids)

Opioids represent OD deaths from all opioids: analgesics, heroin, illicit synthetics.
Reported by US CDC: Alcohol (2010), tobacco (2014) others (2017).

Death rates of various substances

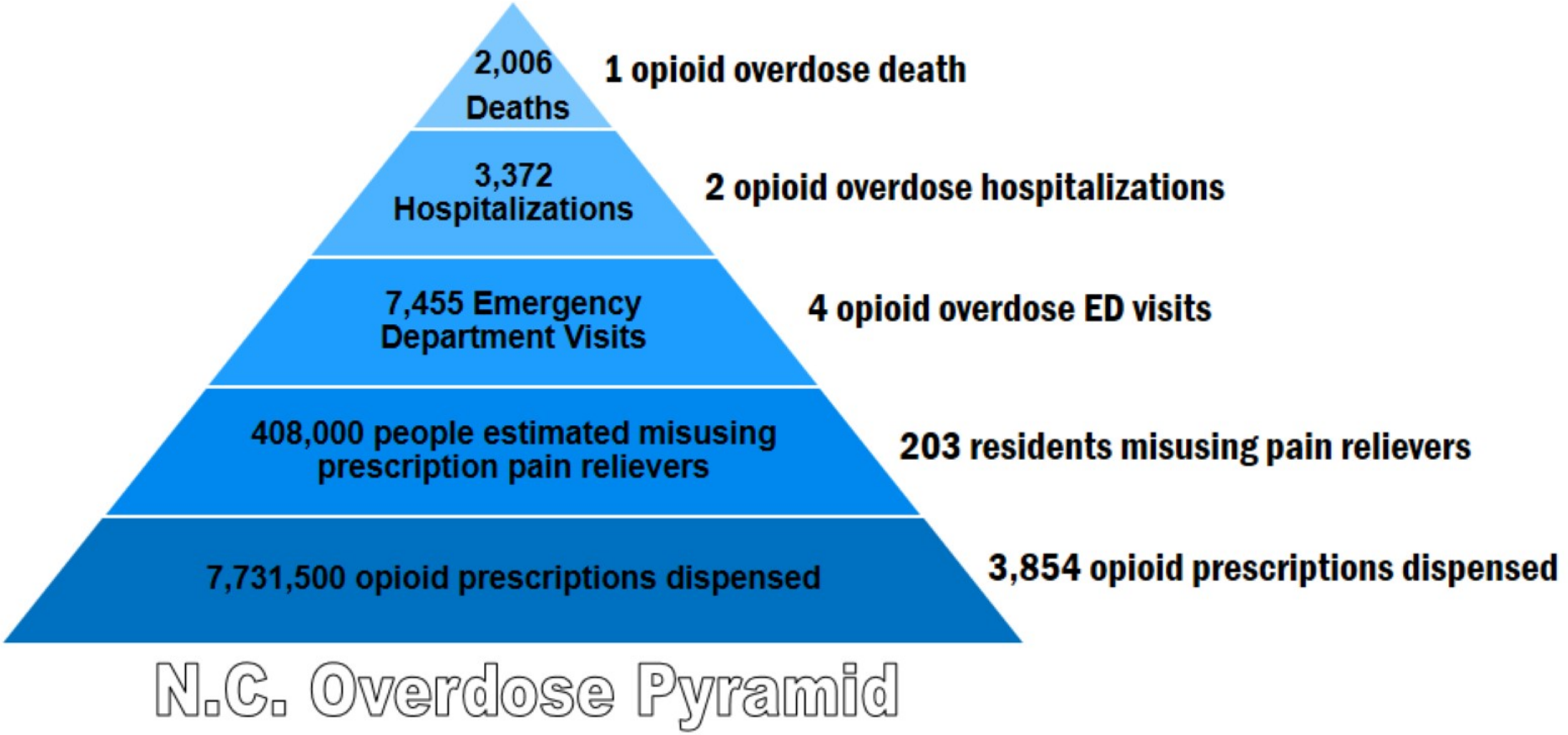
Source Where Pain Relievers Were Obtained for Most Recent Misuse among People Aged 12 or Older Who Misused Pain Relievers in the Past Year: 2018



9.9 Million People Aged 12 or Older Who Misused Pain Relievers in the Past Year

Note: Respondents with unknown data for the Source for Most Recent Misuse or who reported Some Other Way but did not specify a valid way were excluded.

For every opioid overdose death, there were nearly 2 hospitalizations and 4 ED visits due to opioid overdose



Technical Notes: Deaths, hospitalizations, and ED data limited to N.C. residents; Includes all intents, not limited to unintentional
Source: Deaths-N.C. State Center for Health Statistics, Vital Statistics, 2017/ Hospitalizations- North Carolina Healthcare Association, 2017/ED-NC DETECT, 2017/ Misuse-NSDUH, 2015-2016 applied to 2017 population data/Prescriptions-CSRS, 2017
Analysis by Injury Epidemiology and Surveillance Unit

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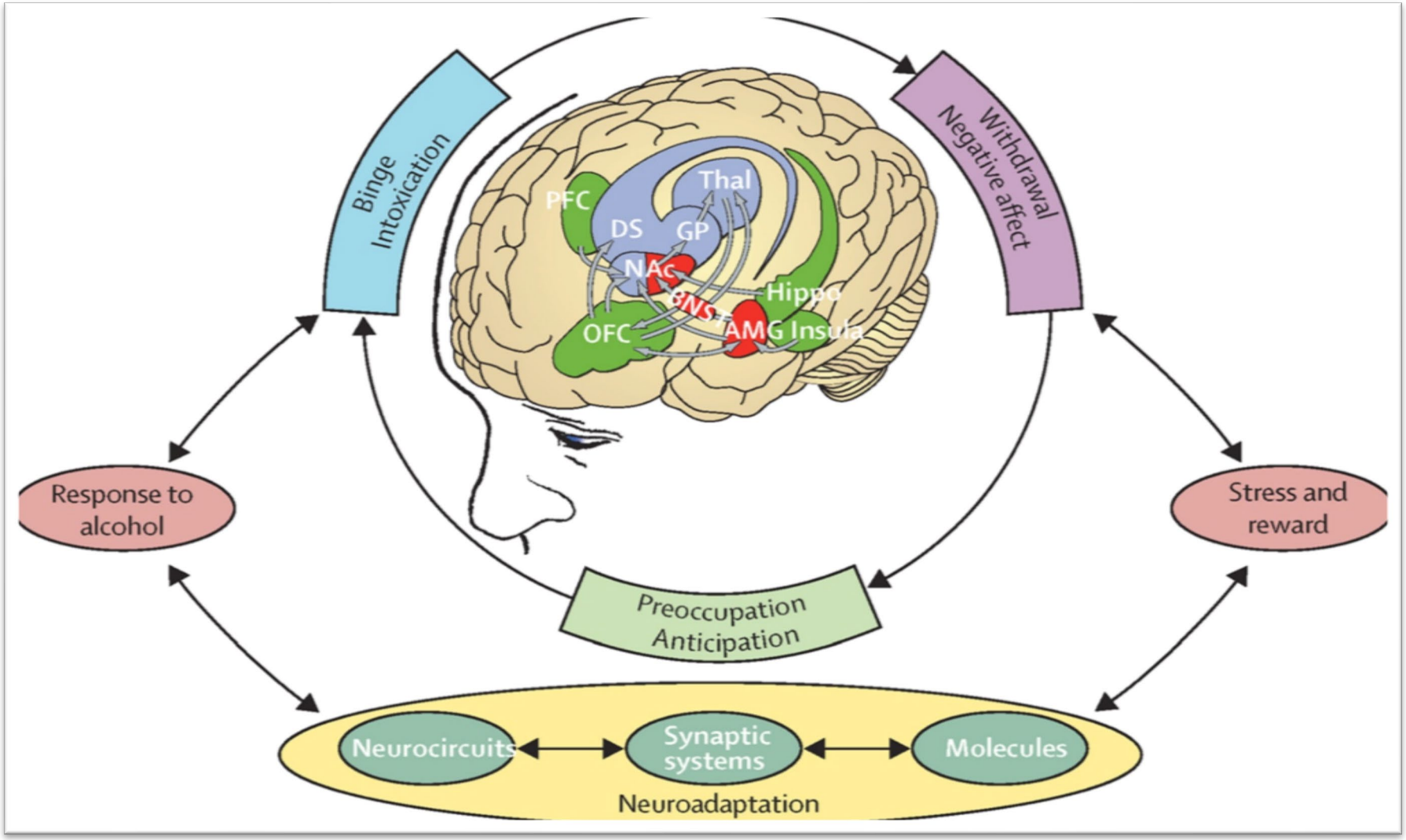
Definition of Addiction

- **"Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences."** ***-ASAM, 09/2019***

- **"All things are poison, and nothing is without poison. Solely the dose determines that a thing is not a poison."**

  –Paracelsus 1500s

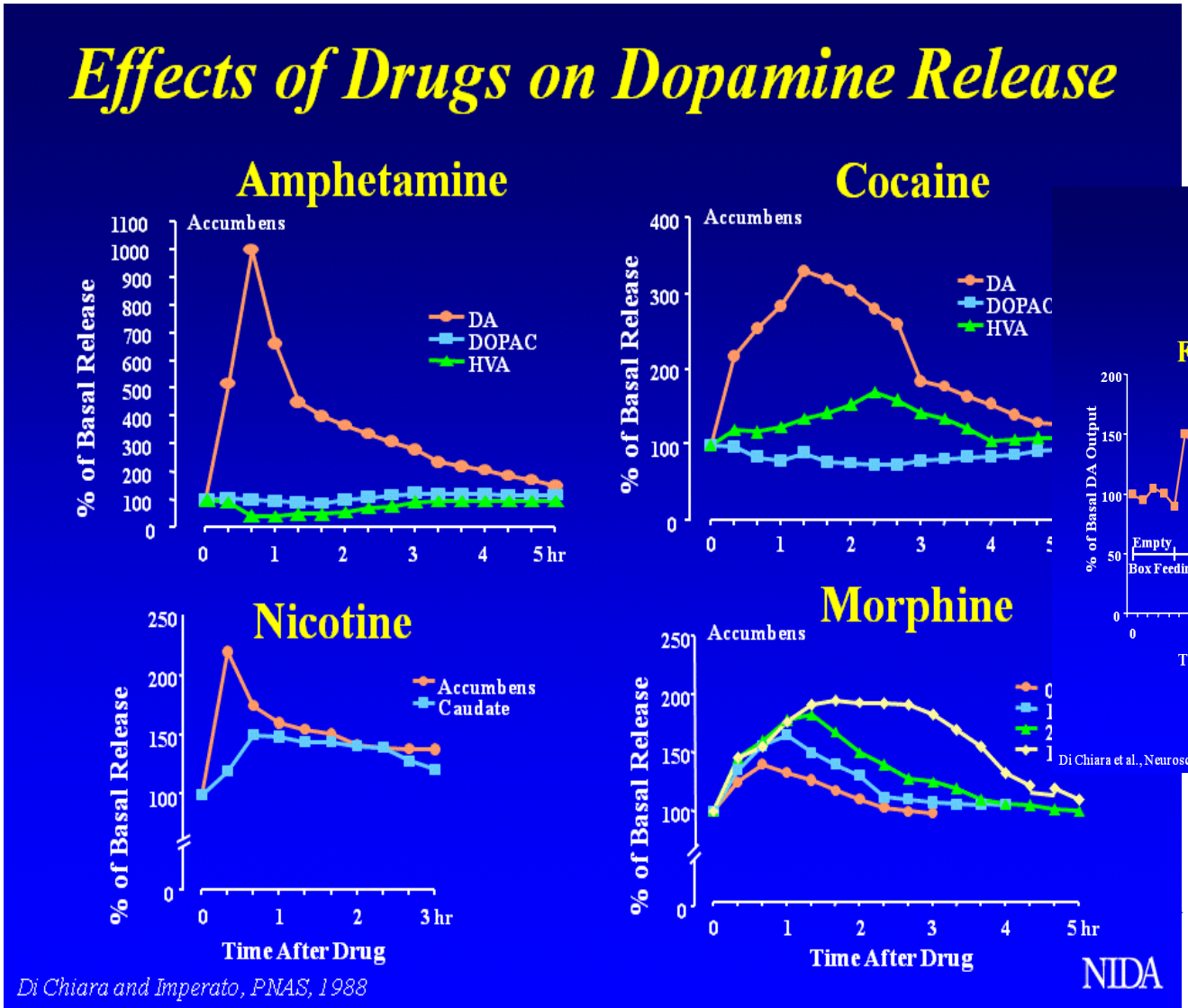
Brain Disease Model of Addiction

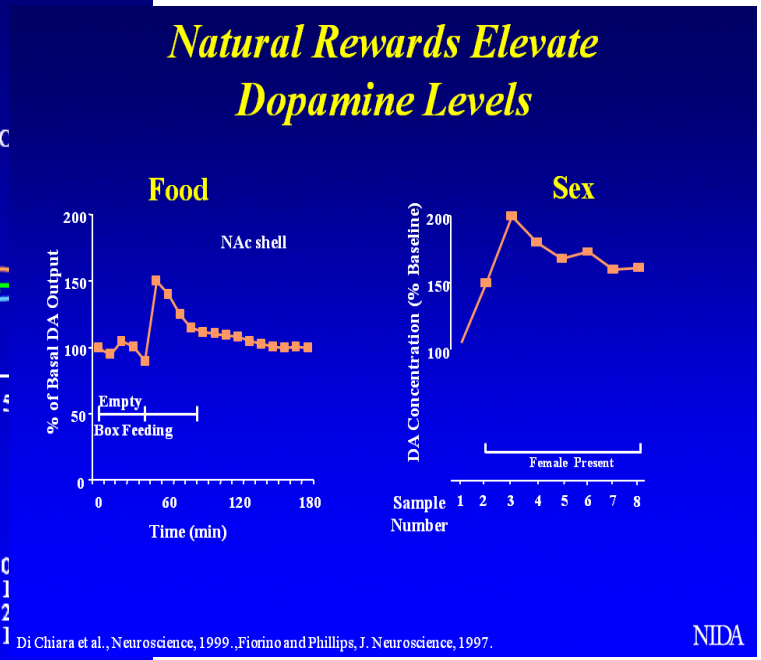


Brain Disease Model

Volkow and Koob, The Lancet, 2015

Brain Disease Model of Addiction



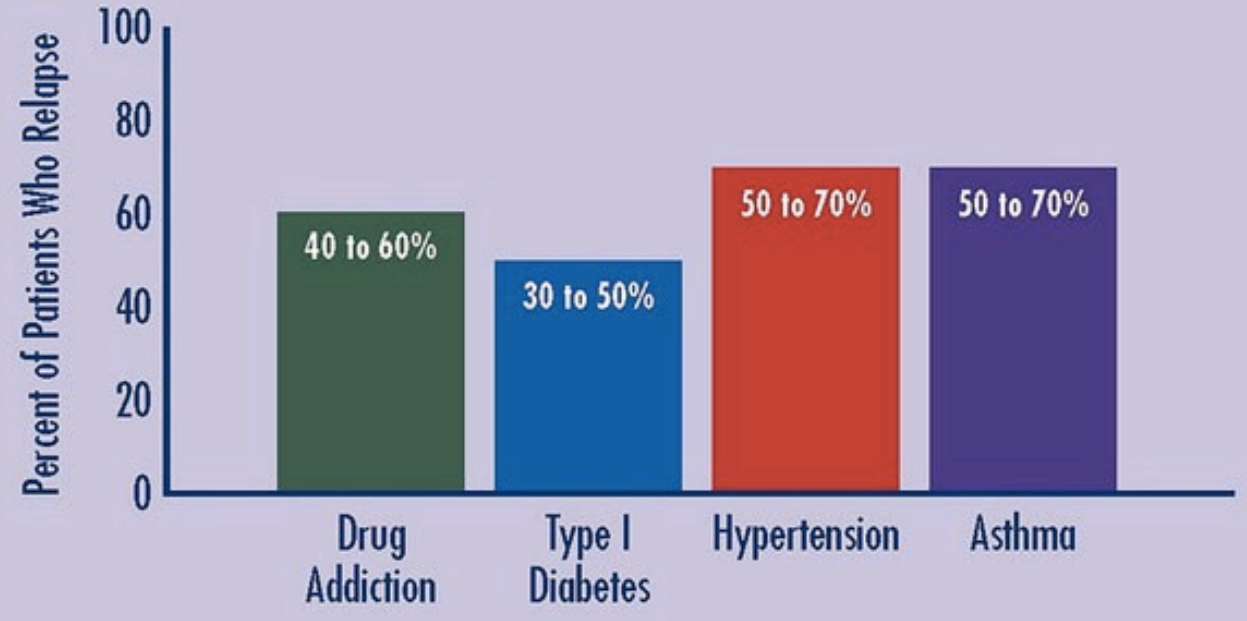


Adverse Childhood Experiences (ACEs)

33 No ACEs	51 1-3 ACEs	16 4-8 ACEs
WITH 0 ACEs	WITH 3 ACES	WITH 7+ ACEs
1 in 16 smokes	1 in 9 smokes	1 in 6 smokes
1 in 69 have alcohol use disorder	1 in 9 has alcohol use disorder	1 in 6 has alcohol use disorder
1 in 480 uses IV drugs	1 in 43 uses IV drugs	1 in 30 uses IV drugs
1 in 14 has heart disease	1 in 7 has heart disease	1 in 6 has heart disease
1 in 96 attempts suicide	1 in 10 attempts suicide	1 in 5 attempts suicide

Felitti et al, AJPM, 1998

COMPARISON OF RELAPSE RATES BETWEEN DRUG ADDICTION AND OTHER CHRONIC ILLNESSES



Relapse rates for drug-addicted patients are compared with those suffering from diabetes, hypertension, and asthma. Relapse is common and similar across these illnesses (as is adherence to medication). Thus, drug addiction should be treated like any other chronic illness, with relapse serving as a trigger for renewed intervention.

Source: McLellan et al., JAMA, 2000.

JAMA, 284:1689-1695, 2000

DSM-5 Criteria for SUD

Substance use disorders are defined as a pattern of use that results in marked distress and/or impairment, with two or more of the following symptoms over the course of a 12-month period:

1. Using the substance in larger amounts or over a longer period of time than intended
2. Unsuccessful attempts or persistent desire to reduce use
3. Too much time spent on obtaining, using, and/or recovering from the effects of the substance
4. A strong craving for the substance
5. Significant interference with roles at work, school, or home
6. Continued use despite recurrent social or interpersonal consequences
7. Reducing or giving up important social, occupational, or recreational activities because of the substance use
8. Substance use in situations in which it may be physically hazardous
9. Substance use despite recurrent or persistent physical or psychological consequences
10. Tolerance of the substance
11. Withdrawal from the substance

Loss of Control
Use despite neg consequences
Physiologic changes

Mild = 3
Moderate = 4-5
Severe ≥ 6

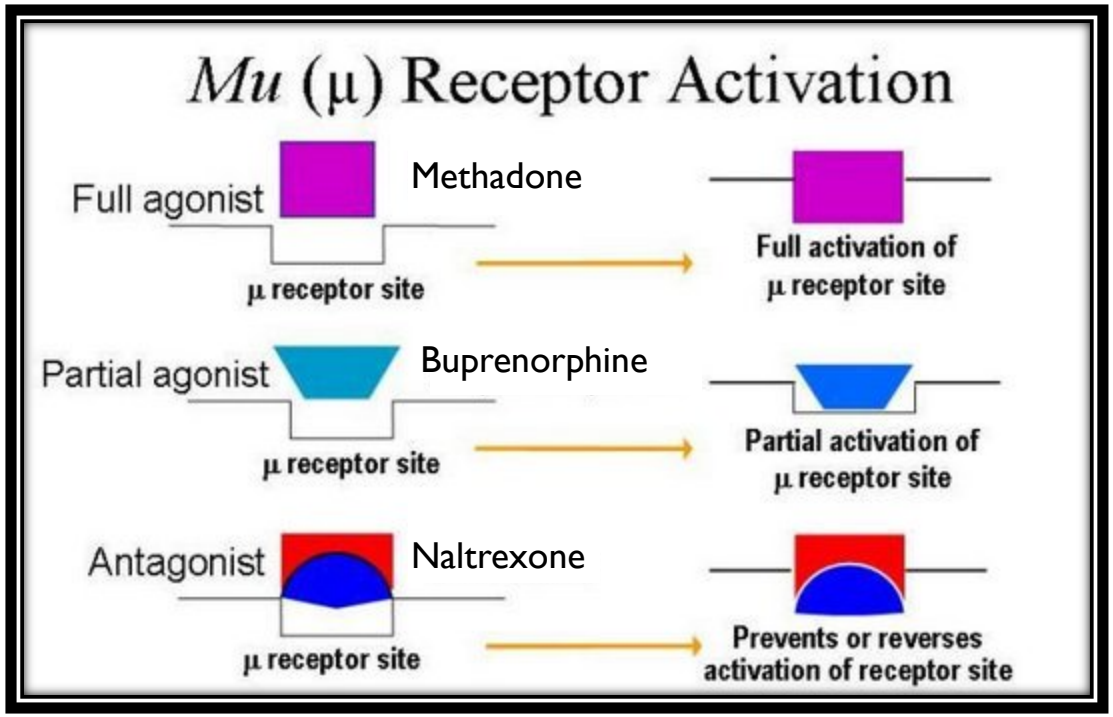
Opioid Use Disorder

Most effective treatment is

Medication Assisted Treatment

FDA Approved MAT for Opioid Use Disorder

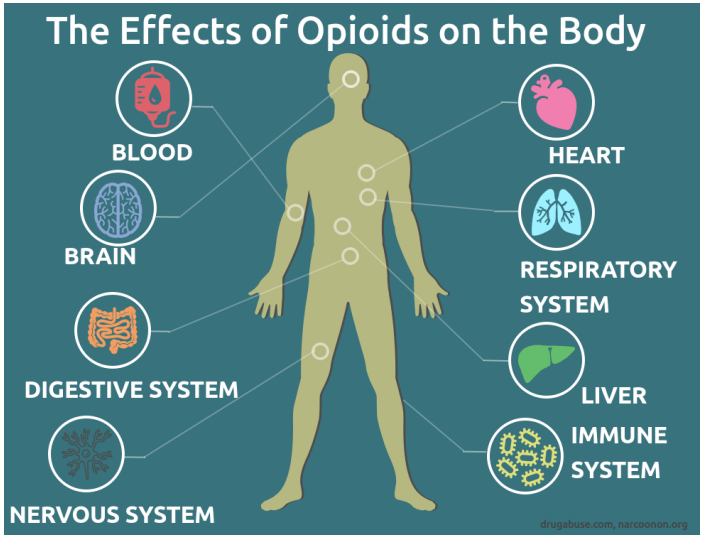
- **Methadone**
- **Buprenorphine**
- **Naltrexone (*PO, IM)**



SAMHSA, TIP Series 63, 2018

How does Medication-Assisted Treatment help?

- Provides **physiological** and **psychological** stabilization that can allow recovery to take place
  - **Reduce/prevent withdrawal**
  - **Diminish/eliminate cravings**
  - **Block the euphoric effect**
  - **Restore physiological function**



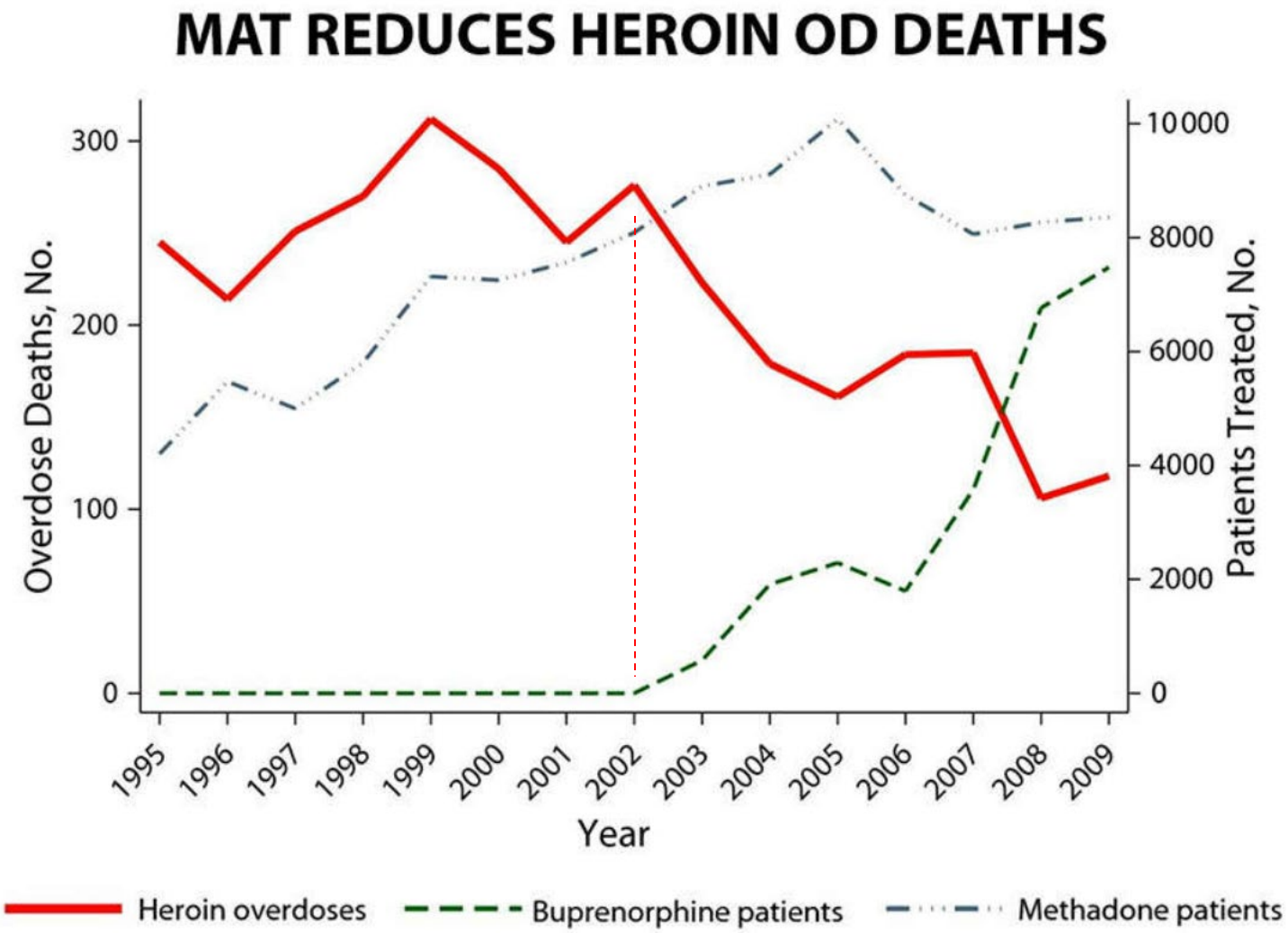
How does it work?

Is MAT Effective for Opioid Addiction?

- **Decreases**:
  - Illicit use, death rate[1]
  - HIV, Hep C infections[2-4]
  - Crime[5]
- **Increases**:
  - Social functioning and retention in treatment[6-7]

1.Kreek J, SubstAbuse Treatment 2002
2.MacArthur, BMJ, 2012
3.Metzgar, Public Health Reports 1998
4. K Page, JAMA IM, 2014
5.Gerstein DR et al, CALDATA General Report, CA Dept of Alcohol and Drug Programs, 1994
6. Mattick RP et al, Cochrane Database of Systematic Reviews, 2009
7. Mattick RP et al, Cochrane Database of Systematic Reviews, 2014

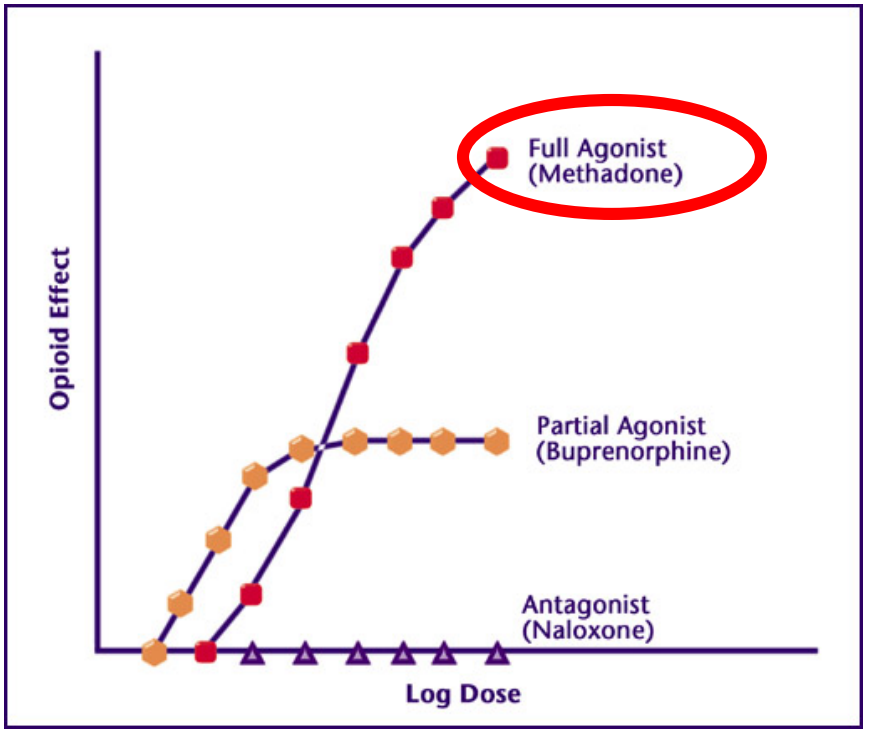
Treatment of Opioid Use Disorder is Effective



R Schwartz, Am J Public Health, 2013

Methadone

- Long-acting, half-life 15-60 hrs
- Full agonist
- Generally 80-120 mg/day
- Dangerous in overdose with polysubstance
  - QT prolongation
  - Drug-drug interactions



SAMHSA, TIP Series 63, 2018

Opioid Treatment Programs (OTPs)

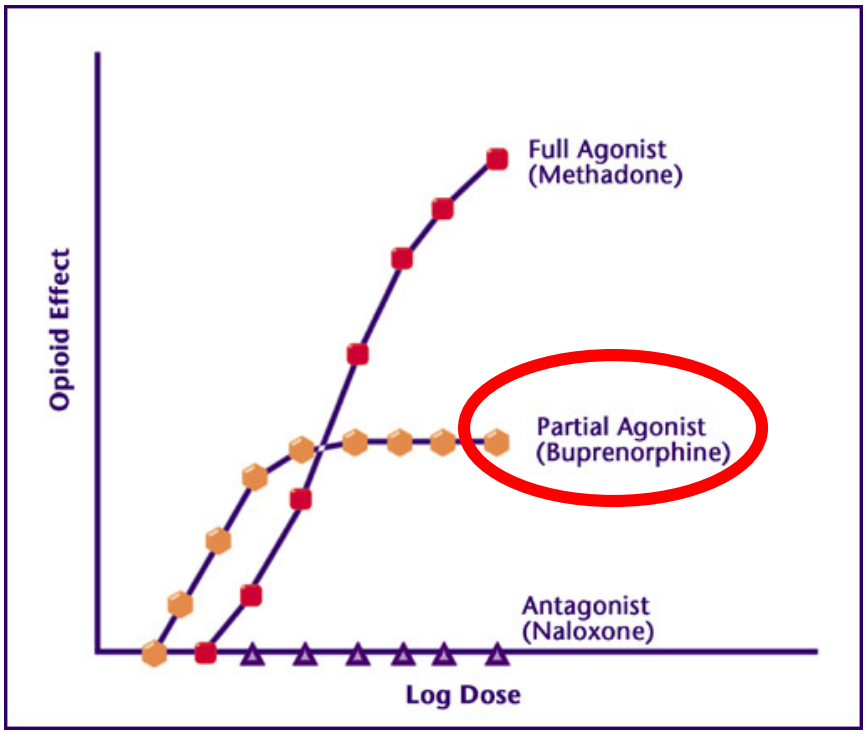
- Methadone can only be prescribed in a federally-regulated OTP when used for treatment of addiction
- Directly observed therapy
- **Not reported** in PDMP
- Not referred to as "Methadone clinics"

https://dpt2.samhsa.gov/treatment/directory.aspx

Salsitz, Mt Sinai J of Medicine, 2000

Buprenorphine

- Partial mu receptor agonist
- Half-life ~24-36 hrs
- High affinity for the receptor
  - Blocks/displaces other opioids
  - Can precipitate withdrawal



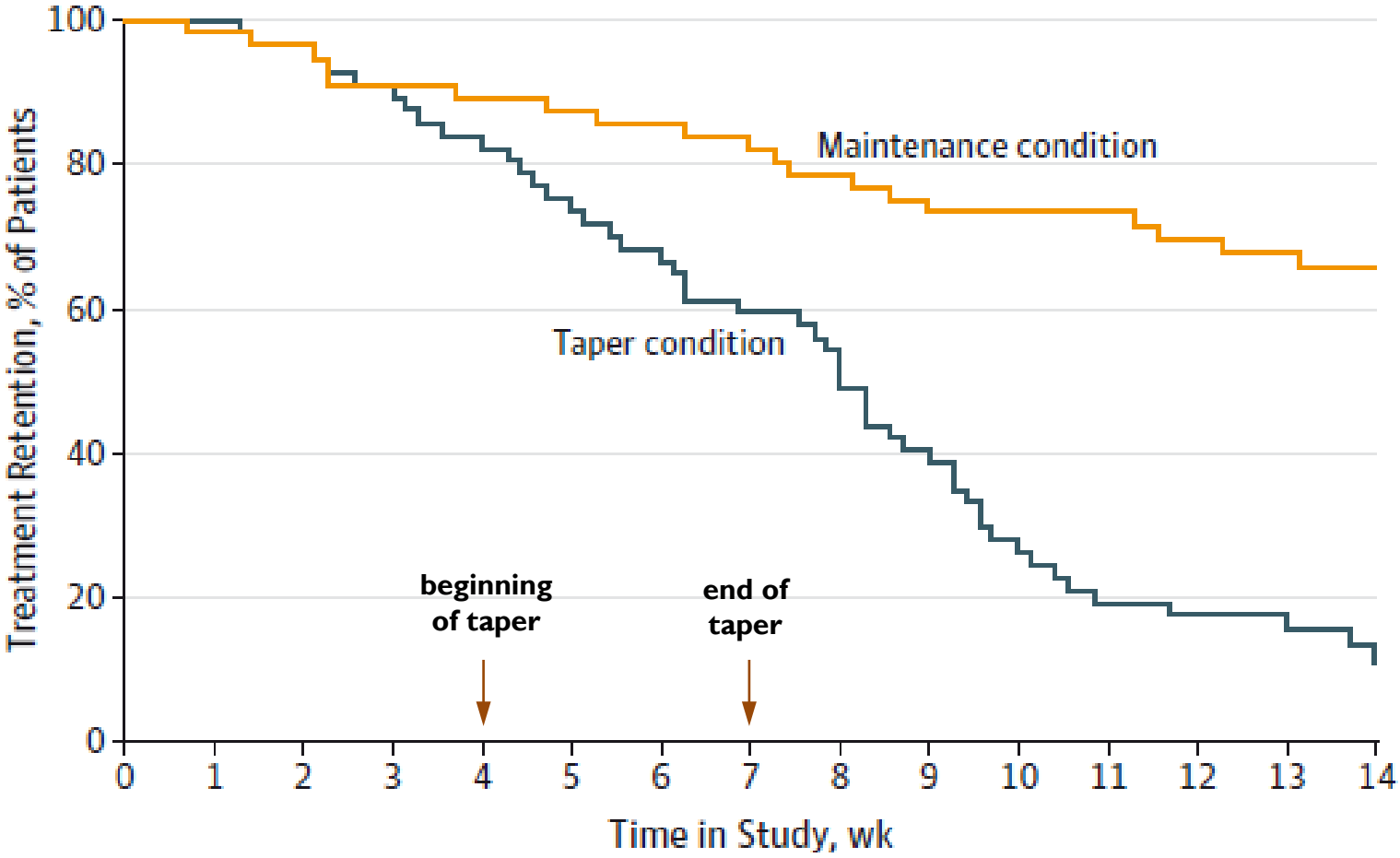
SAMHSA, 2018
Orman & Keating, 2009

Buprenorphine Formulations for OUD/Pain

Content	Route	Product
With Naloxone (combo product)	SL	Suboxone® (film/tablet)
	SL	Zubsolv® (tablet)
	Buccal	Bunavail® (film)
Without Naloxone (mono product)	SL	Subutex® (tablet) - generic
	Implant – q6 mo	Probuphine®
	SC injection – q 30d	Sublocade®
FDA Approved - Pain	IV	Buprenex®
	Transdermal – q72 hr	BuTrans®
	Buccal	Belbuca® (film)

Jonan et al, *Pain Physician*, 2018

Buprenorphine: Maintenance vs. Taper

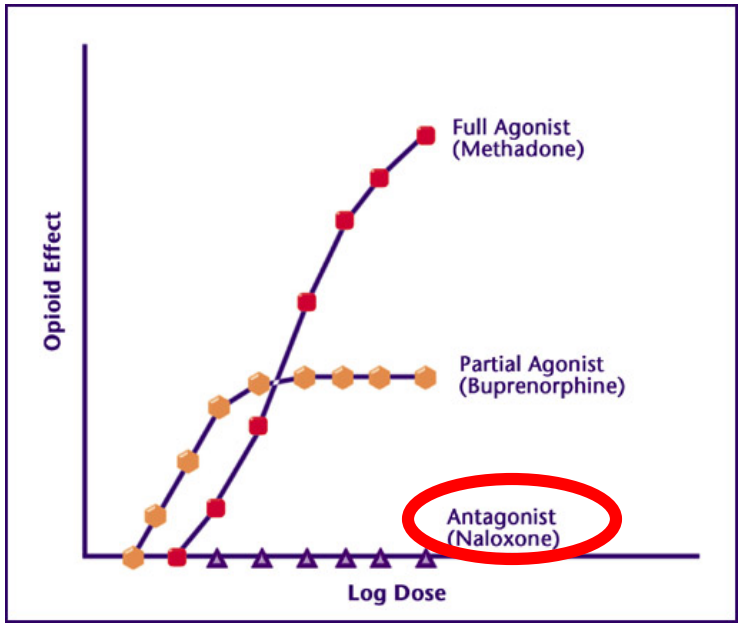


Maintenance vs. Taper

Fiellin et al., 2014

Naltrexone

- Full Antagonist
  - Opioid **and** alcohol use disorders
- Formulations
  - Tablets: FDA approved in 1984 (Revia®)
  - Extended-Release intramuscular injection: Vivitrol®: FDA approved in 2010
  - Off label use
- Administration
  - Abstain from opioids:
    - > 7 days (short-acting) vs. 10-14 (long-acting)

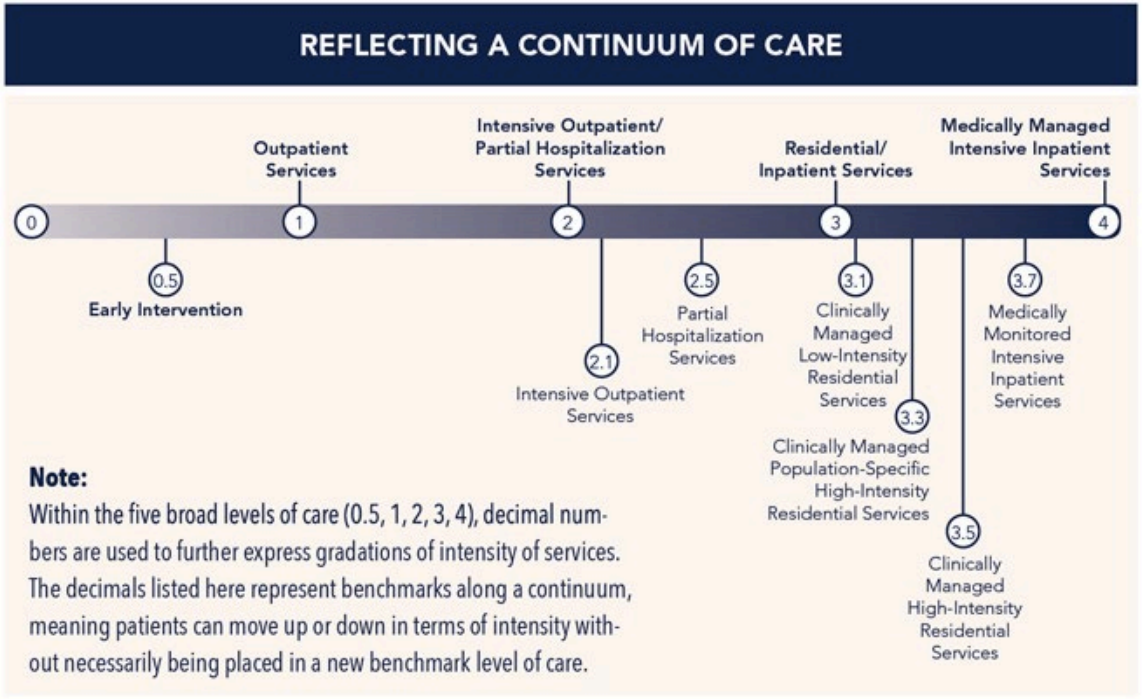


SAMHSA, TIP Series 63, 2018

SAMHSA, 2018
Orman & Keating, 2009

OTP vs. Office Based Outpatient Treatment

- **Referring to a higher level of care:**
  - Increased infrastructure
  - Daily monitoring
  - Diversion
  - Feasibility & Logistics



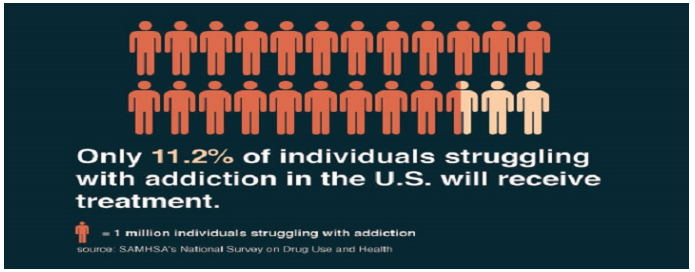
The ASAM Criteria: Treatment Criteria for Addictive, Substance-Related, and Co-Occurring Conditions (2013)

Behavioral Health's Role in OUD Treatment

- **Optional** psychosocial treatment should be offered in conjunction with pharmacotherapy.
- A decision to refuse psychosocial treatment/absence of available treatment should **not** preclude or delay MAT.
- Refusing psychosocial services should **not** generally be used as rationale for discontinuing current MAT.

Stigma

- Health related stigma: individuals are devalued, rejected and excluded based on having a socially discredited health condition.



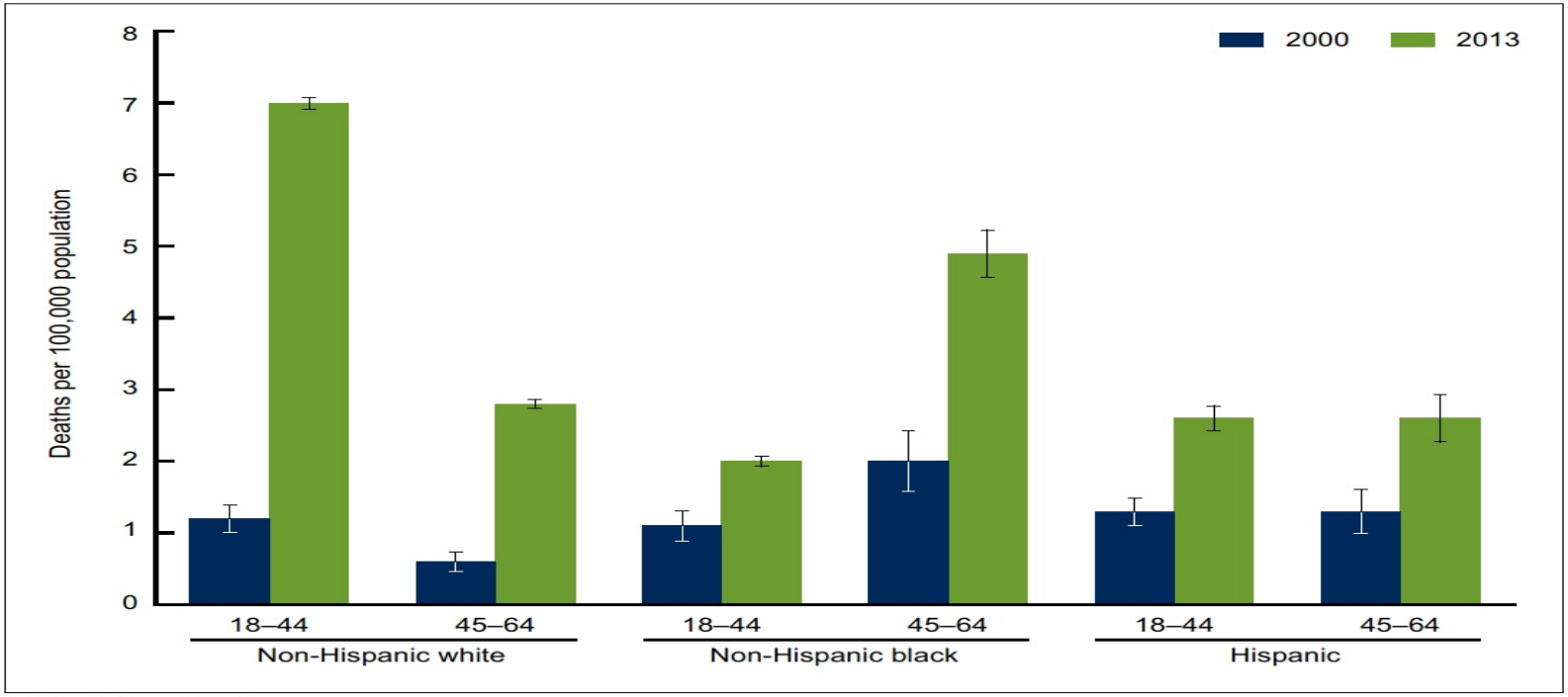
- Impact on seeking treatment?
- Importance of language on shaping our beliefs?

Stereotypes (generalizations) → Prejudices (erroneous beliefs) → Discrimination (unjust treatment)

Heroin Deaths by Race/Ethnicity

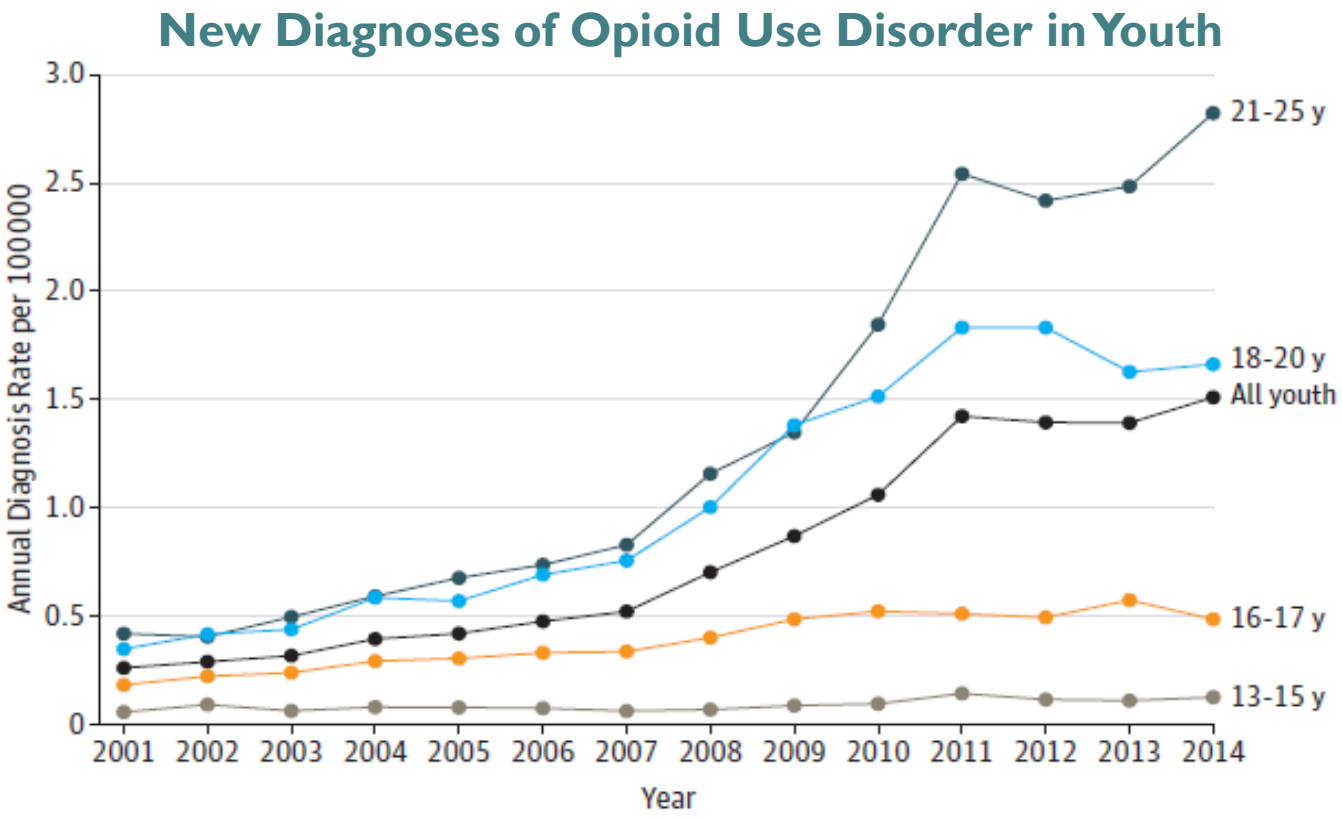
- Traditionally perceived as a white, suburban/rural issue
- For African Americans:
  - Emergency room visits increased by 255% (Ford 2015)
  - Overdose deaths doubled in the past 10 years (Ford 2015)

Figure 4. Rates for drug-poisoning deaths involving heroin, by selected age and race and ethnicity groups: United States, 2000 and 2013



I 95% confidence interval.
NOTES: Deaths for Hispanic persons are underreported by about 5%. See "Deaths: Final Data for 2010." Access data table for Figure 4 at: http://www.cdc.gov/nchs/data/databriefs/db190_table.pdf#4.
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality.

Young Adults



Pediatrics. 2019 Feb;143(2). pii: e20182752. doi: 10.1542/peds.2018-2752. Epub 2019 Jan 2.

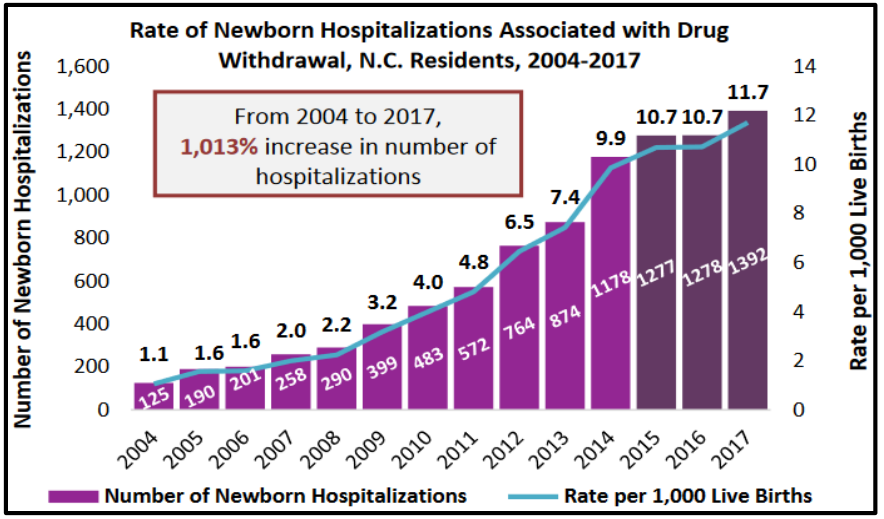
Youth and the Opioid Epidemic.

CFR 42, 2017
DATA, 2000
Hadland et al., 2017
Levy, 2019

- Adolescents

MAT in Pregnancy

- MAT = standard of care
- Ok to use Suboxone (combo product)
- Breastfeeding recommended
- Neonatal abstinence syndrome
  - Newborns are **NOT** addicted
  - Eat, Sleep, Console (ESC)
    - Reducing LOS



Fischer et al.,1998; Jones et al., 2010; Kakko et al., 2008; Kraft et al., 2017; Grossman et al., 2018

The Rhode Island Experience
MAT in Criminal Justice System

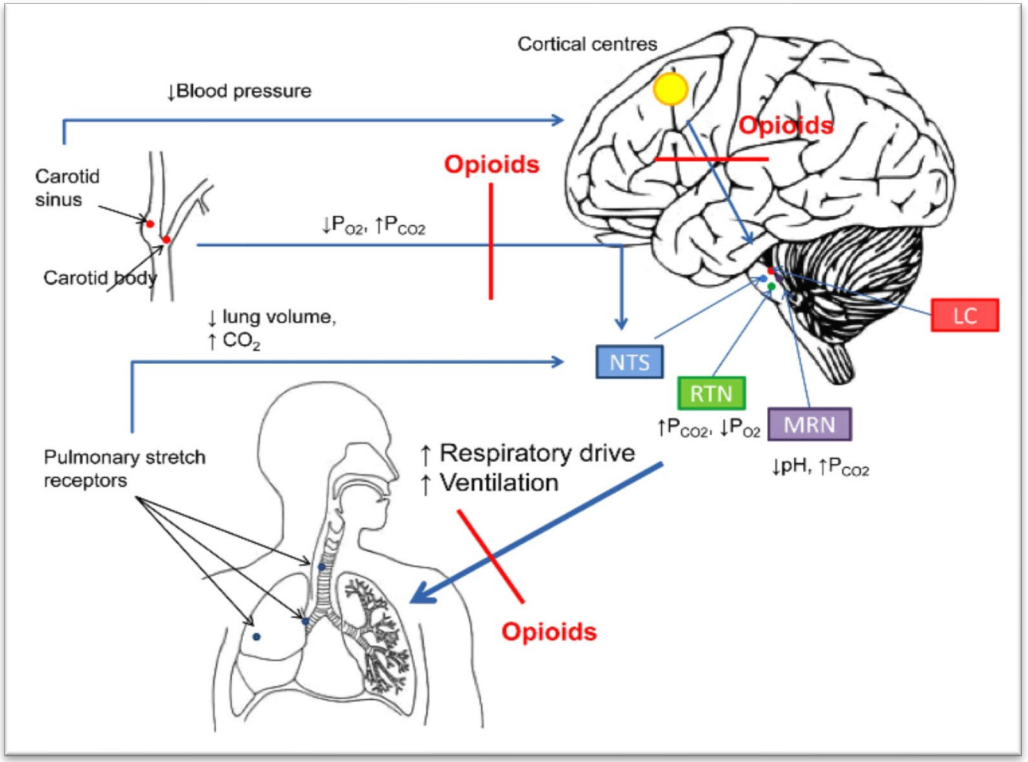
- All prisoners were screened for Opioid Use Disorder
- Prisoners on MAT prior to arrest continued MAT
- Prisoners with OUD not previously treated were offered MAT prior to release AND post-release.

61% Reduction in Opioid Overdose Deaths

Green et al, 2018

Physiology of Overdose

- Opioids affect part of the brain regulating respiration
- Fentanyl-induced chest wall rigidity
- Complications of non-fatal overdose



Koo, Open Anesthesiology Journal, 2011

Best Practices for Opioid Overdose Prevention

- **Primary Prevention**
  - Opioid Stewardship
  - Prevention of ACEs
  - Adolescent Risk Reduction

- **Increasing Access to Treatment (MAT)**
  - Reduce MAT Stigma

- **Harm Reduction Strategies**
  - Naloxone Distribution
  - Overdose Education
  - 911 Good Samaritan Laws/Bystander Assistance
  - Screening for Fentanyl

NORTH CAROLINA IN SOLIDARITY HARM REDUCTION COALITION

Naloxone

- No effect other than blocking opioids
- No potential for abuse
- **Naloxone ≠ MAT!!**

Narcan®
Nasal Spray

Adapt Pharma

Auto-injector
Evzio®

Kaleo Inc.

Intramuscular
Injection

Various Companies

NC Professionals Health Program (PHP)

https://ncphp.org/

Conclusions: MAT & Overdose Prevention

- National, state, and local data suggest rising unintentional overdose deaths related to polysubstance use.
- MAT has consistently demonstrated better long-term outcomes than no MAT (detox).
- Buprenorphine and naltrexone have some significant advantages in terms of safety profile over methadone.
- Overdose prevention entails primary prevention, increasing treatment access, and harm reduction.

Resources

- https://www.cdc.gov/drugoverdose/resources/hhs.html
- https://www.asam.org/resources/publications
- https://www.hhs.gov/about/agencies/iea/partnerships/opioid-toolkit/index.html
- https://store.samhsa.gov/system/files/tip63_fulldoc_052919_508.pdf
- https://www.asam.org/membership/state-chapters

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