Opioid Use Disorder and Treatment Options

October 19, 2023 Live Activity, Hilton San Gabriel, CA
6:30 pm – 8:30 pm, 2 CME / CE Credits
Directly Provided CME/CE Activity by L.A. Care Health Plan

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CSAM Board of Directors, Chair CSAM Opioid Committee

Disclosures

The following CME Planners and CME Faculty do not have any financial relationships with ineligible companies in the past 24 months.

- Leilanie Mercurio, L.A. Care PCE Program Manager, CME Planner.
- Matthew A. Torrington, MD, Family and Addiction Medicine Physician, CME Planner and Faculty.

An ineligible company is any entity whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Commercial support was not received for this CME activity.

Learning Objectives

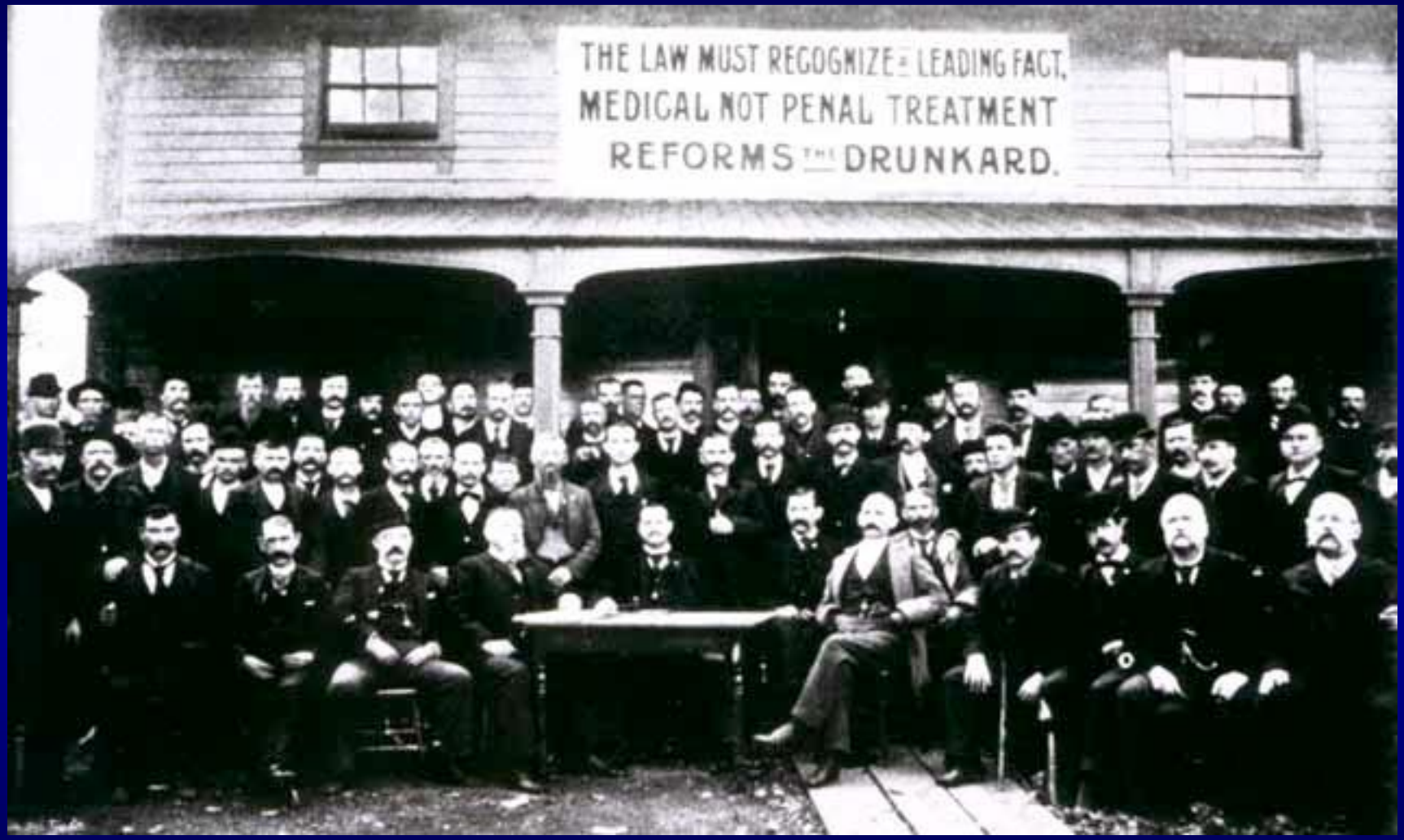
1. Identify, assess, and diagnose patients with opioid use disorder while considering severity, chronicity, individual characteristics, and psychiatric and medical comorbidities.

2. List the five (5) core components of a comprehensive individualized multimodal treatment plan.

3. **Develop** an individualized, patient-centered treatment plan including negotiating treatment goals by evaluating appropriate medication- and psychosocial-based treatment options.

4. **Summarize** at least three (3) misconceptions, sources of stigma, and complexities (bioethical, social, clinical, public health) associated with opioid use disorder and the use of medications to treat opioid use disorder.


NICE PEOPLE TAKE DRUGS
Release
ARRIVA
serving London



Keeley League Meeting, Dwight, Illinois, 1891

ADDICTION DEFINITON

- is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

  – (ASAM definition, Short Version)

ADDICTION DEFINITON as of 11.2019

- *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.*

- *Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.*

RECOVERY from Mental Disorders and Substance Use Disorders defined

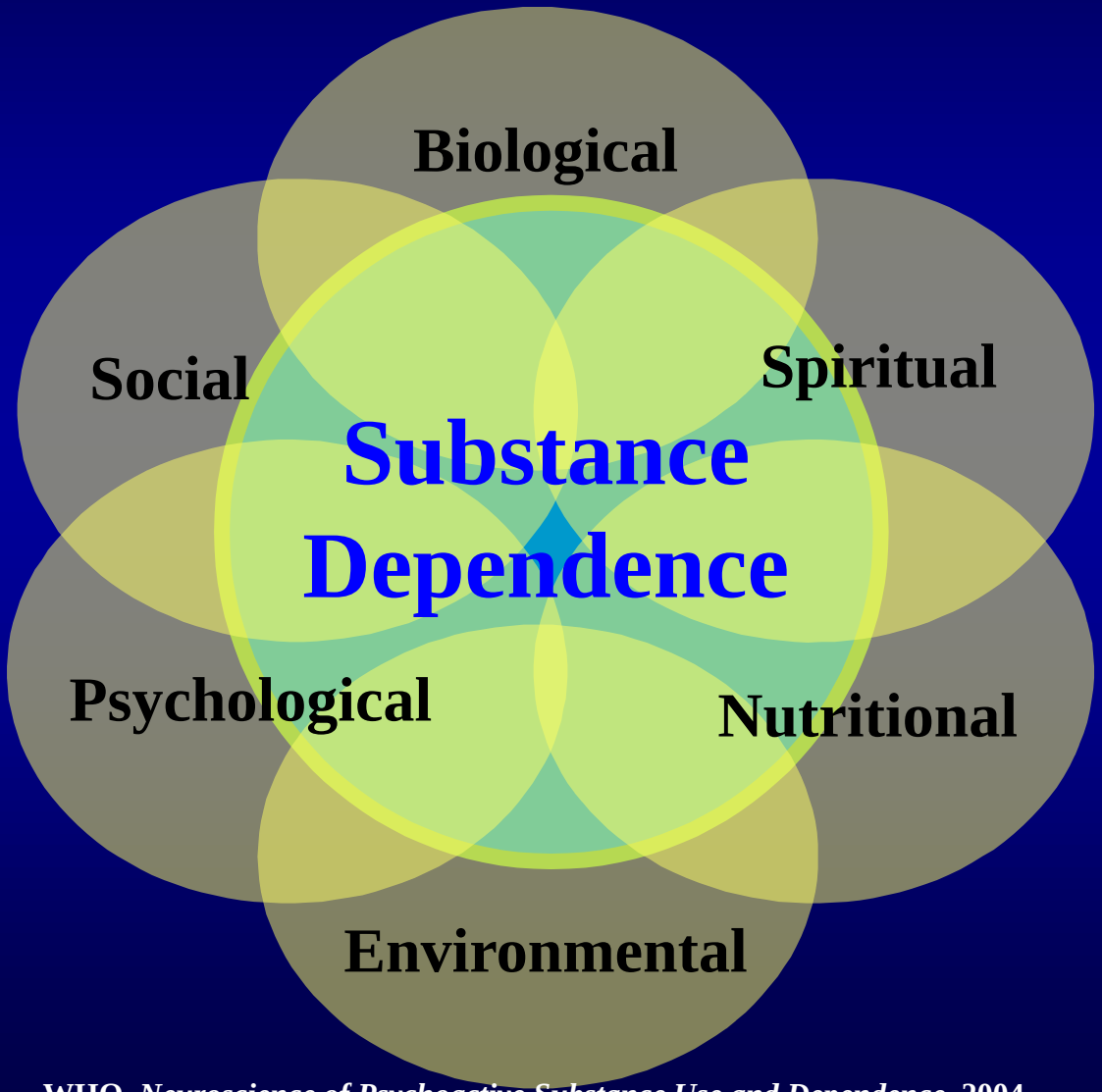
Substance Abuse and Mental Health Services Administration

"Recovery from Mental Disorders and Substance Use Disorders" is a process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential.

- ***Health***: overcoming or managing one's disease(s) as well as living in a physically and emotionally healthy way;
- ***Home:*** a stable and safe place to live;
- ***Purpose:*** meaningful daily activities, such as a job, school, volunteerism, family caretaking, or creative endeavors, and the independence, income and resources to participate in society; and
- ***Community***: relationships and social networks that provide support, friendship, love, and hope.

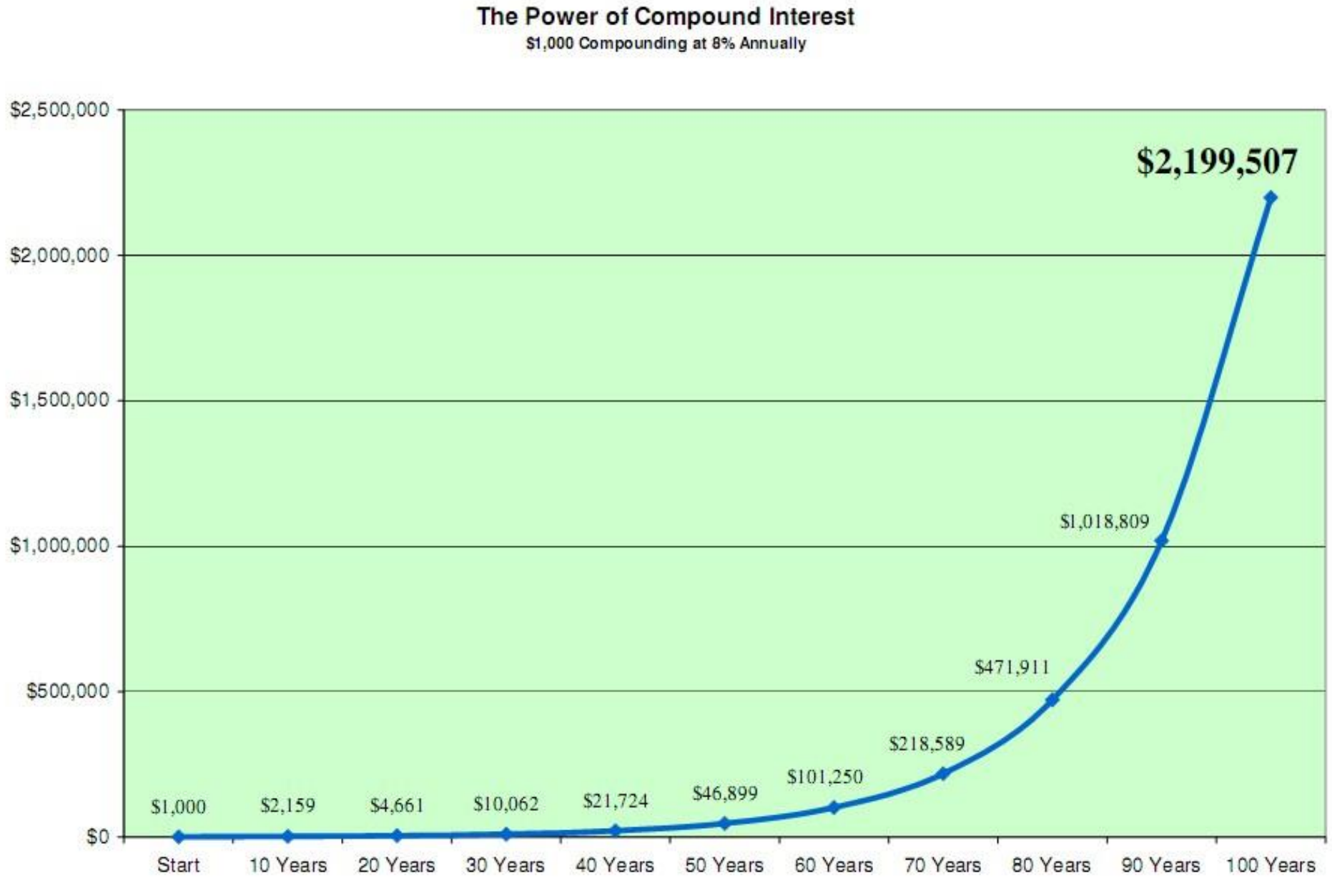
http://www.asam.org/research-treatment/recovery

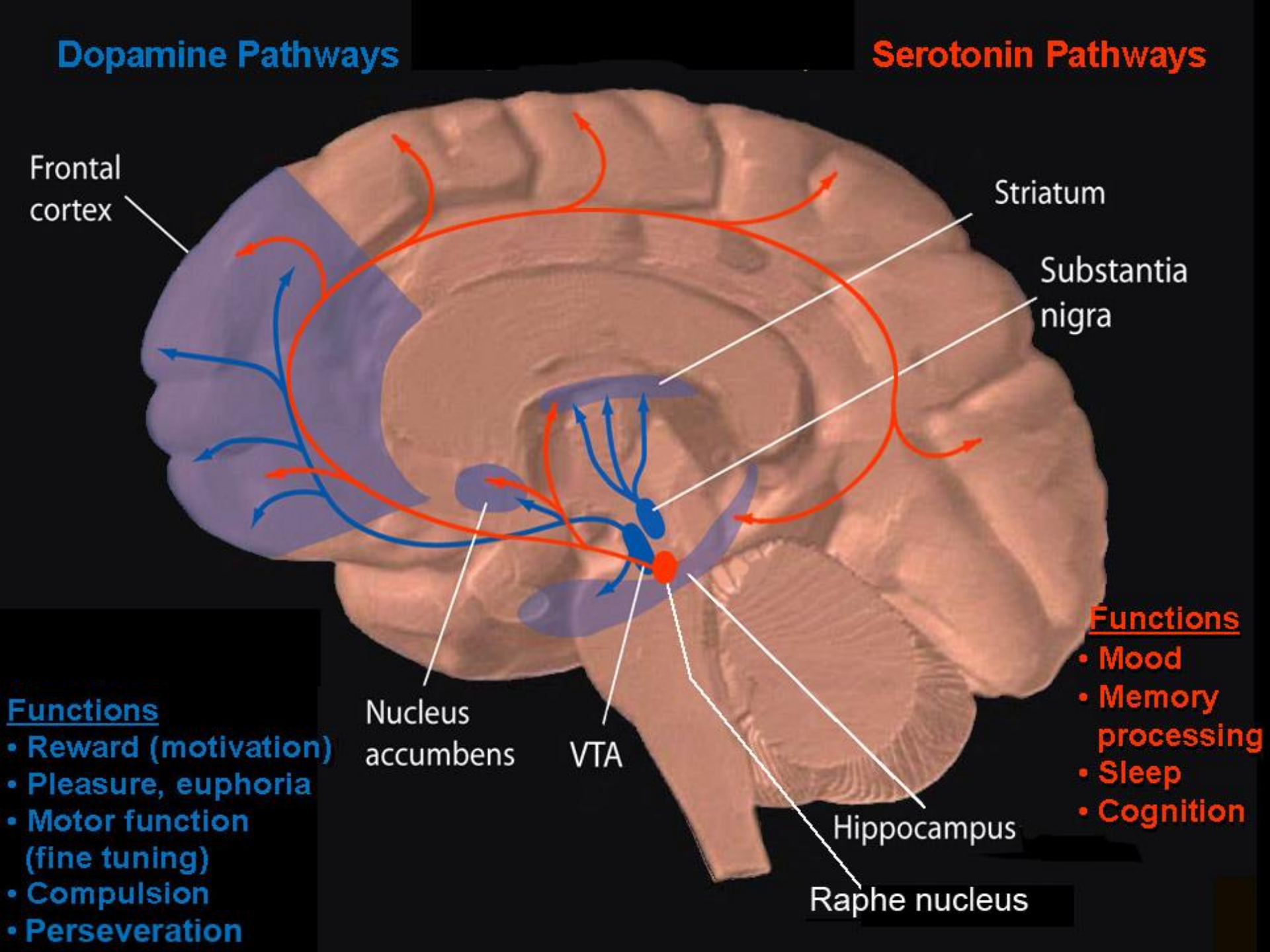
Substance Dependence
A Multifactorial Brain Disease

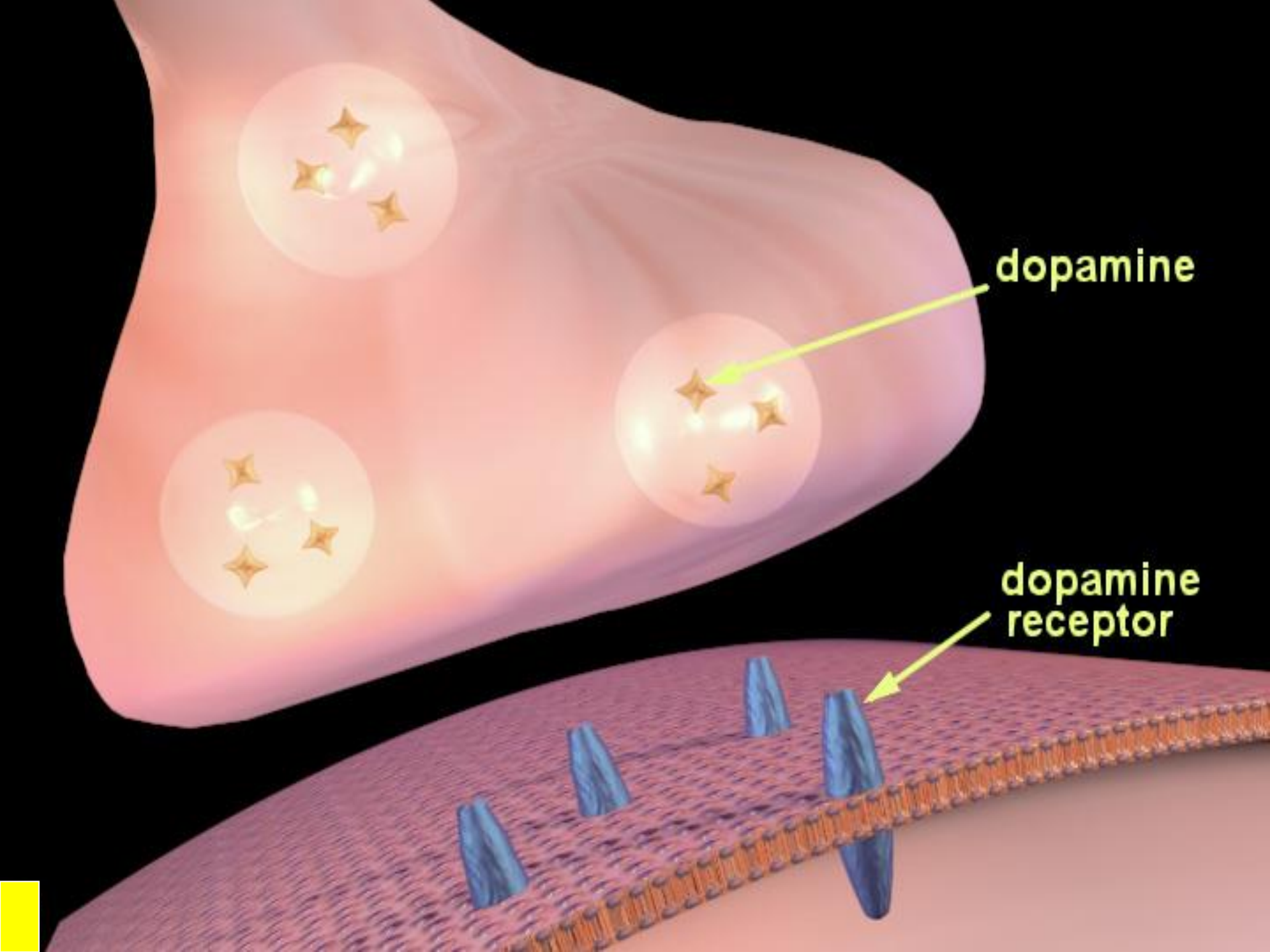


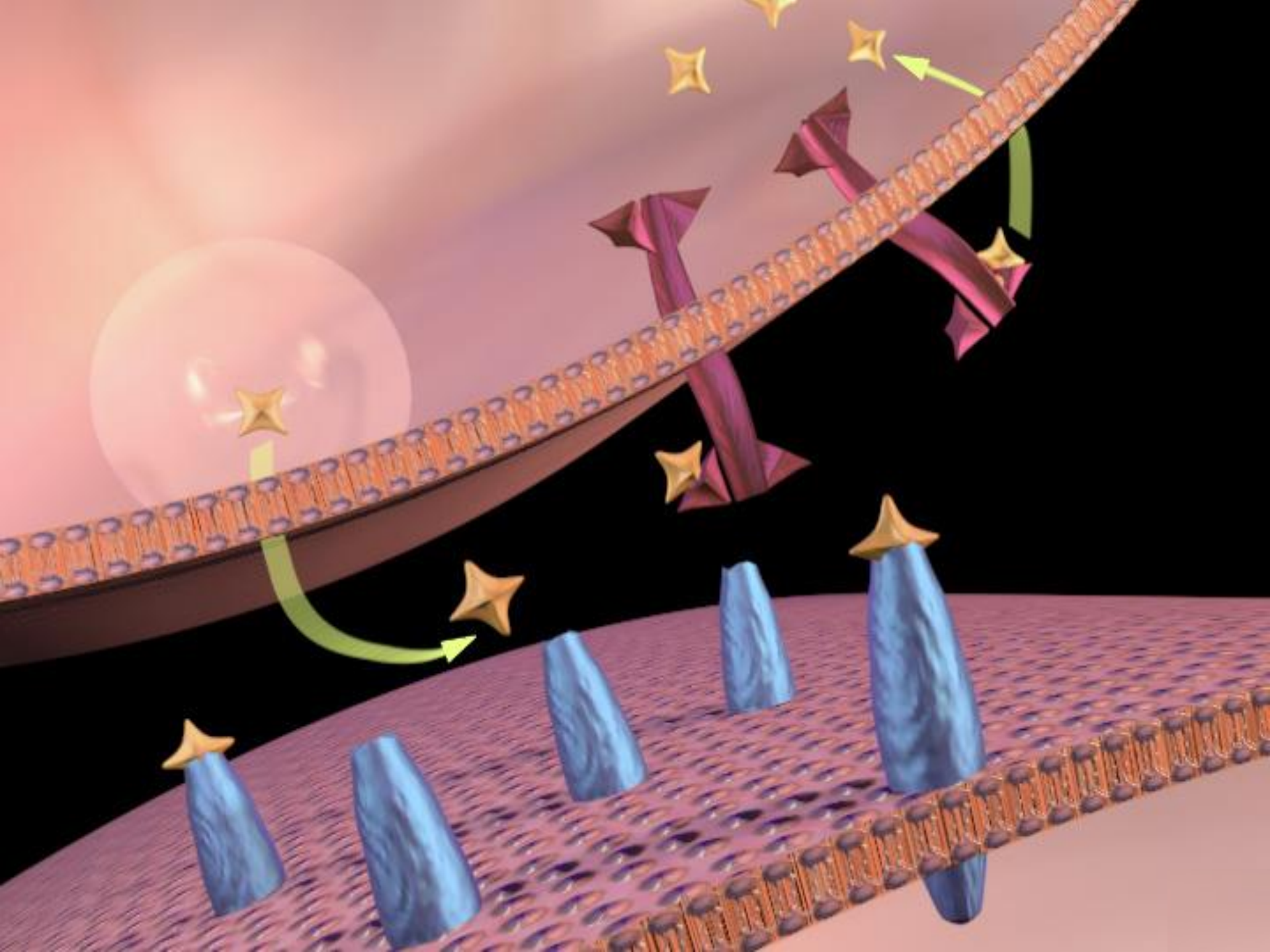
WHO. *Neuroscience of Psychoactive Substance Use and Dependence.* 2004.

http://www.drugabuse.gov/publications/seeking-drug-abuse-treatment/3-does-program-adapt-treatment-patients-needs-change


The Power of Compound Interest
$1,000 Compounding at 8% Annually
$2,500,000
$2,000,000
$1,500,000
$1,000,000
$500,000
$0
$2,199,507
$1,018,809
$471,911
$218,589
$101,250
$46,899
$21,724
$10,062
$4,661
$2,159
$1,000
Start
10 Years
20 Years
30 Years
40 Years
50 Years
60 Years
70 Years
80 Years
90 Years
100 Years

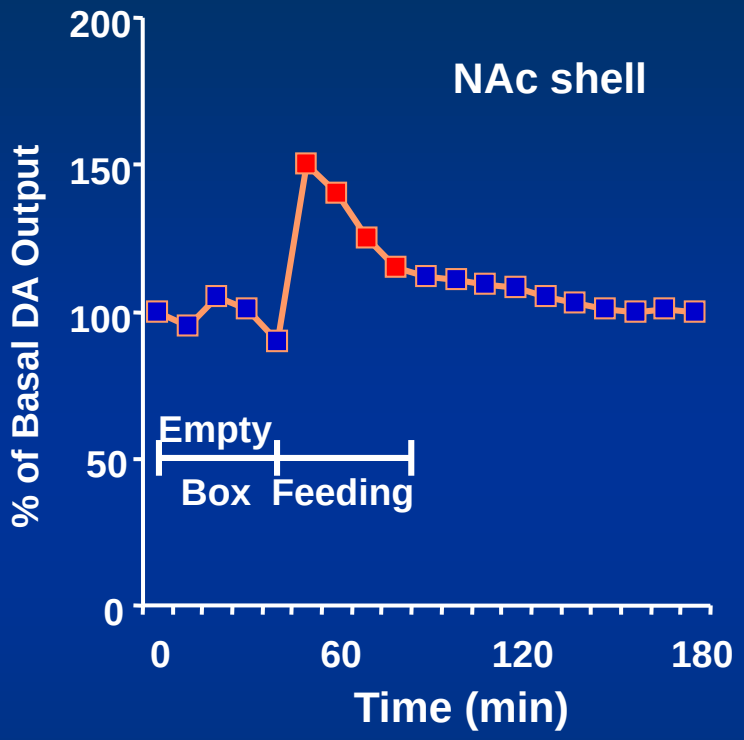

Dopamine Pathways
Serotonin Pathways
Frontal cortex
Striatum
Substantia nigra
Nucleus accumbens
VTA
Hippocampus
Raphe nucleus
Functions
• Reward (motivation)
• Pleasure, euphoria
• Motor function (fine tuning)
• Compulsion
• Perseveration
Functions
• Mood
• Memory processing
• Sleep
• Cognition


dopamine
dopamine receptor



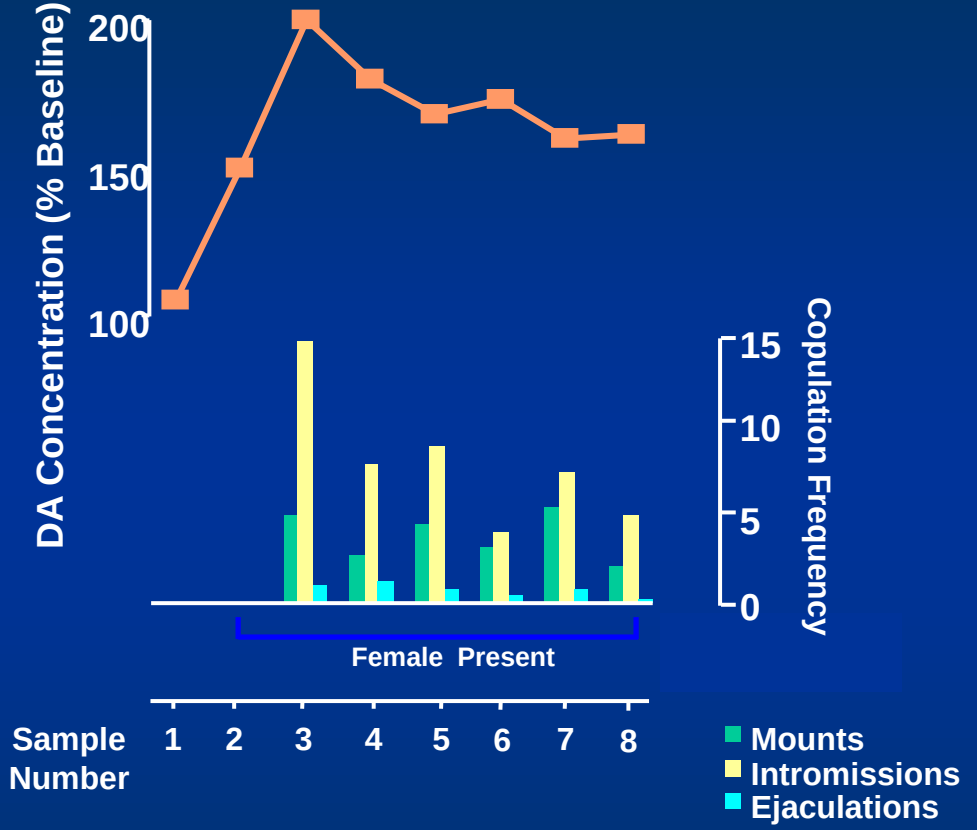
Natural Rewards Elevate Dopamine Levels

FOOD

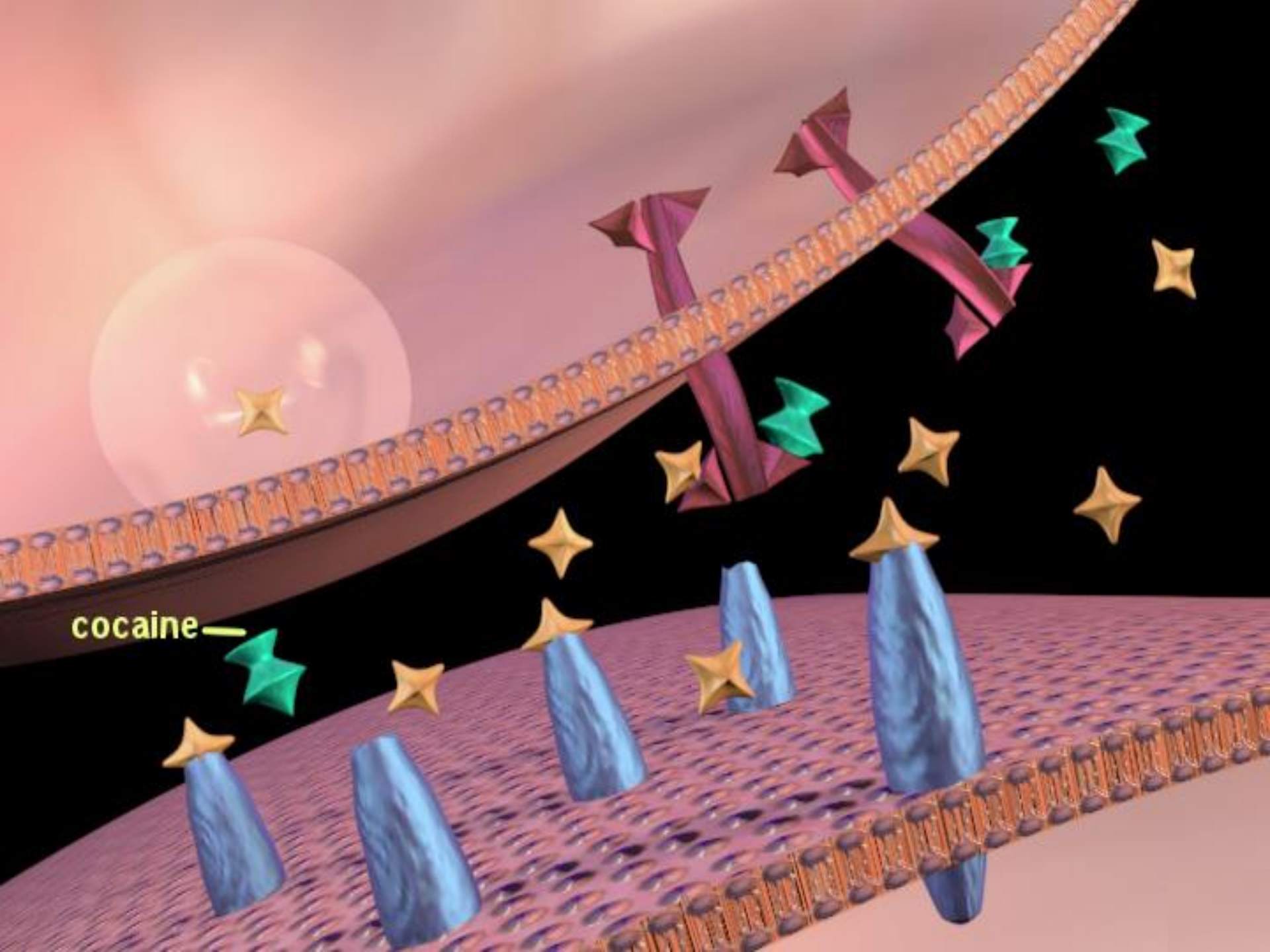


Di Chiara et al., Neuroscience, 1999.

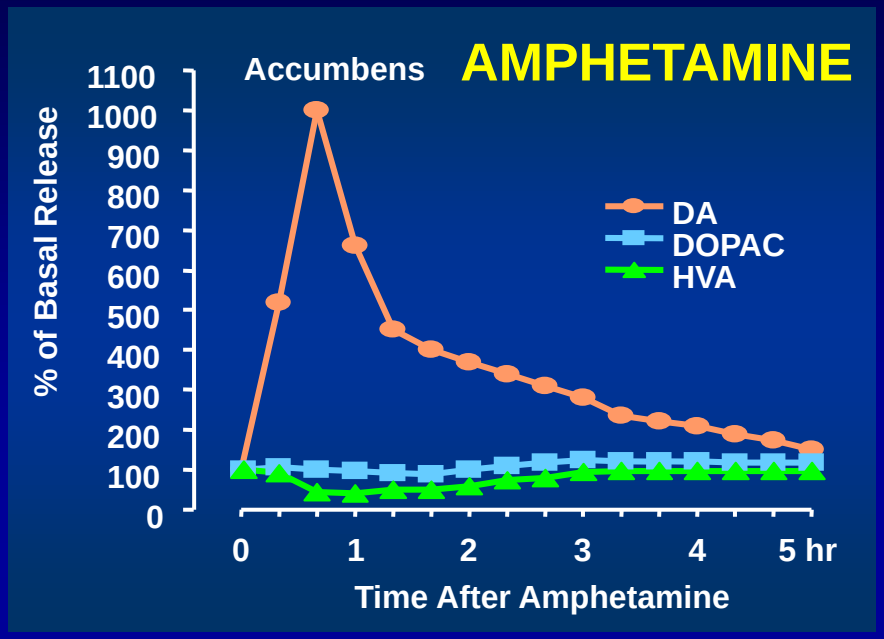
SEX

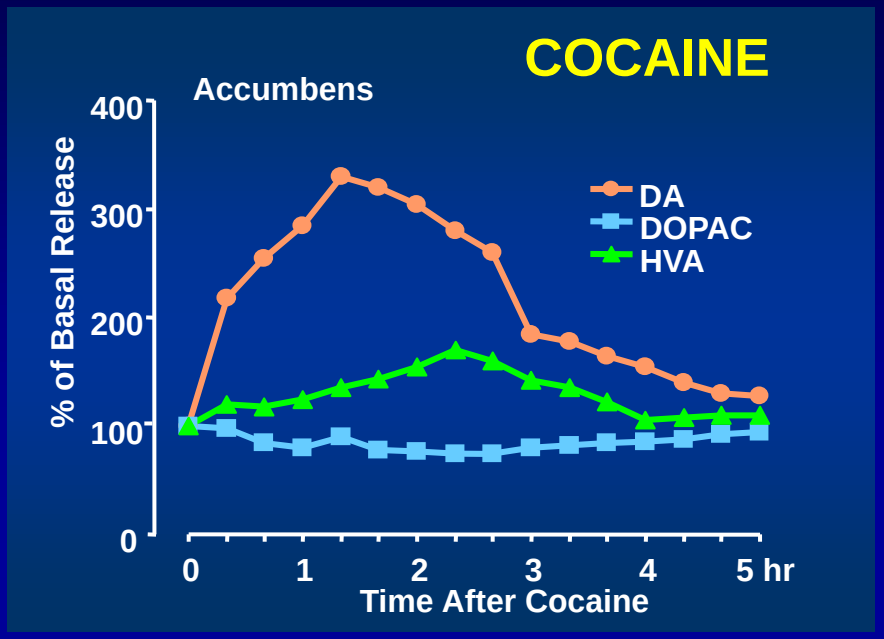


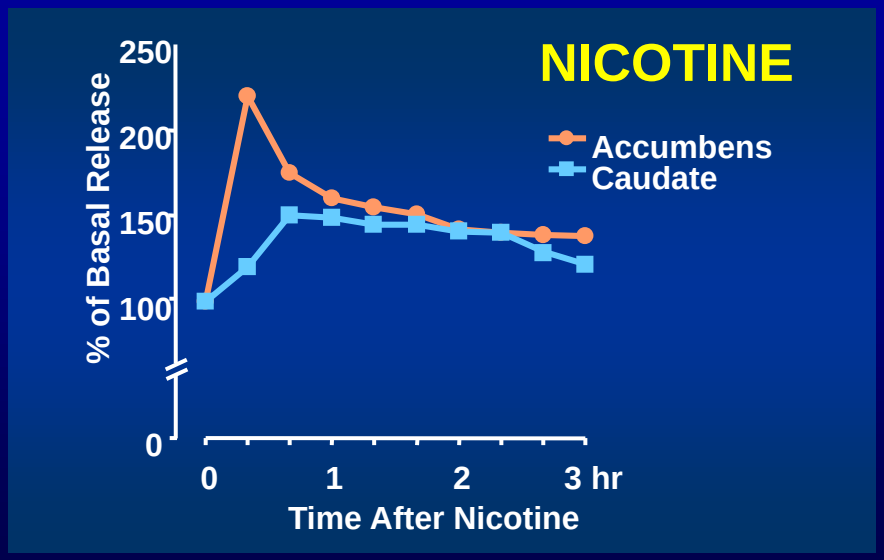
Fiorino and Phillips, J. Neuroscience, 1997.

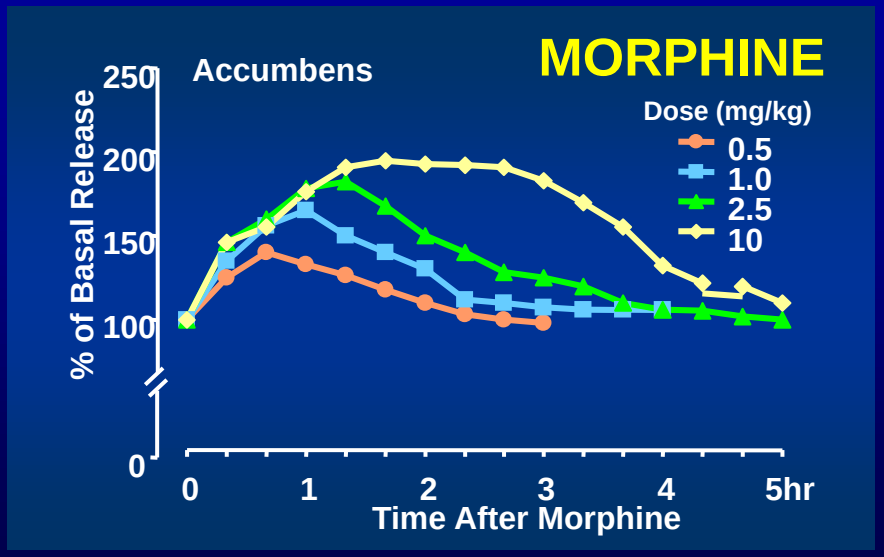

cocaine

Effects of Drugs on Dopamine Release



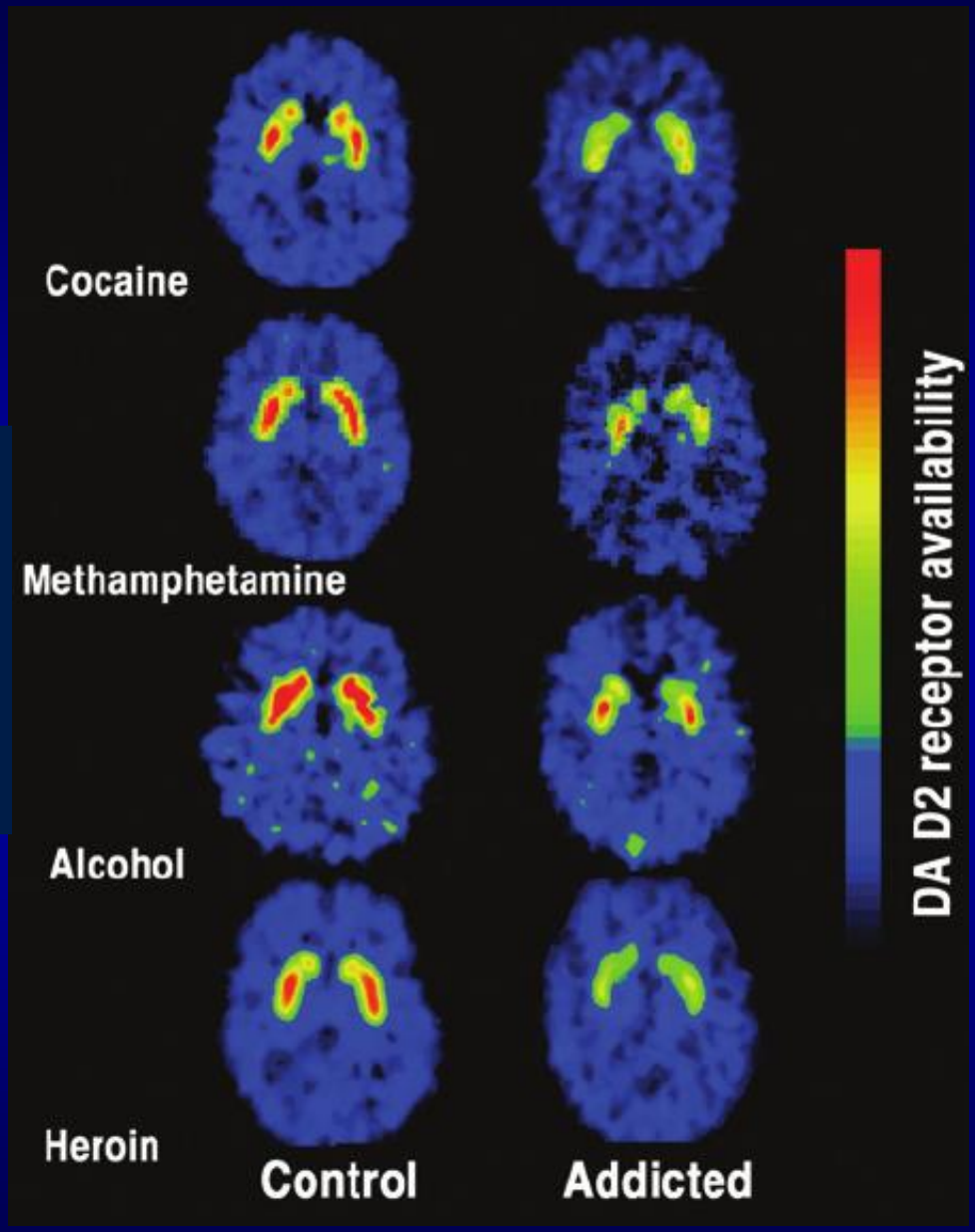






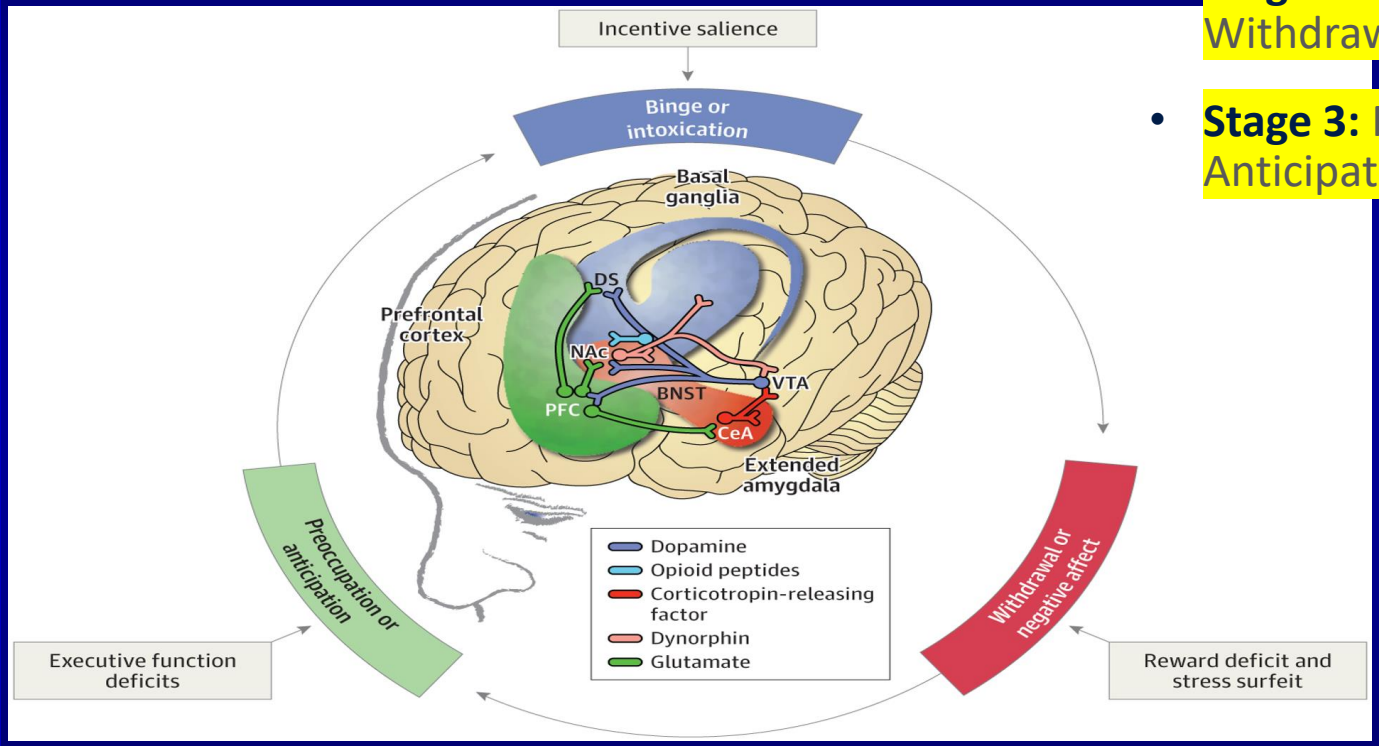
Di Chiara and Imperato, PNAS, 1988

Dopamine D2 Receptors are Decreased in the Addicted Brain



Three Stages of the Addiction Cycle and Associated Neural Circuits

- **Stage 1:** Binge or Intoxication
- **Stage 2:** Negative Affect or Withdrawal
- **Stage 3:** Preoccupation or Anticipation (Craving)



Volkow, N. D., Jones, E. B., Einstein, E. B., & Wargo, E. M. (2019). Prevention and treatment of opioid misuse and addiction: A review

Adverse Childhood Experiences [ACE] Study

Within First 18 Years of Life

1. Emotional Abuse
2. Physical Abuse
3. Sexual Abuse
4. Emotional Neglect
5. Physical Neglect
6. Mother Treated Violently
7. Household Substance Abuse
8. Household Mental Illness/Suicide Attempt
9. Parental Separation/Divorce
10. Incarcerated Household Member

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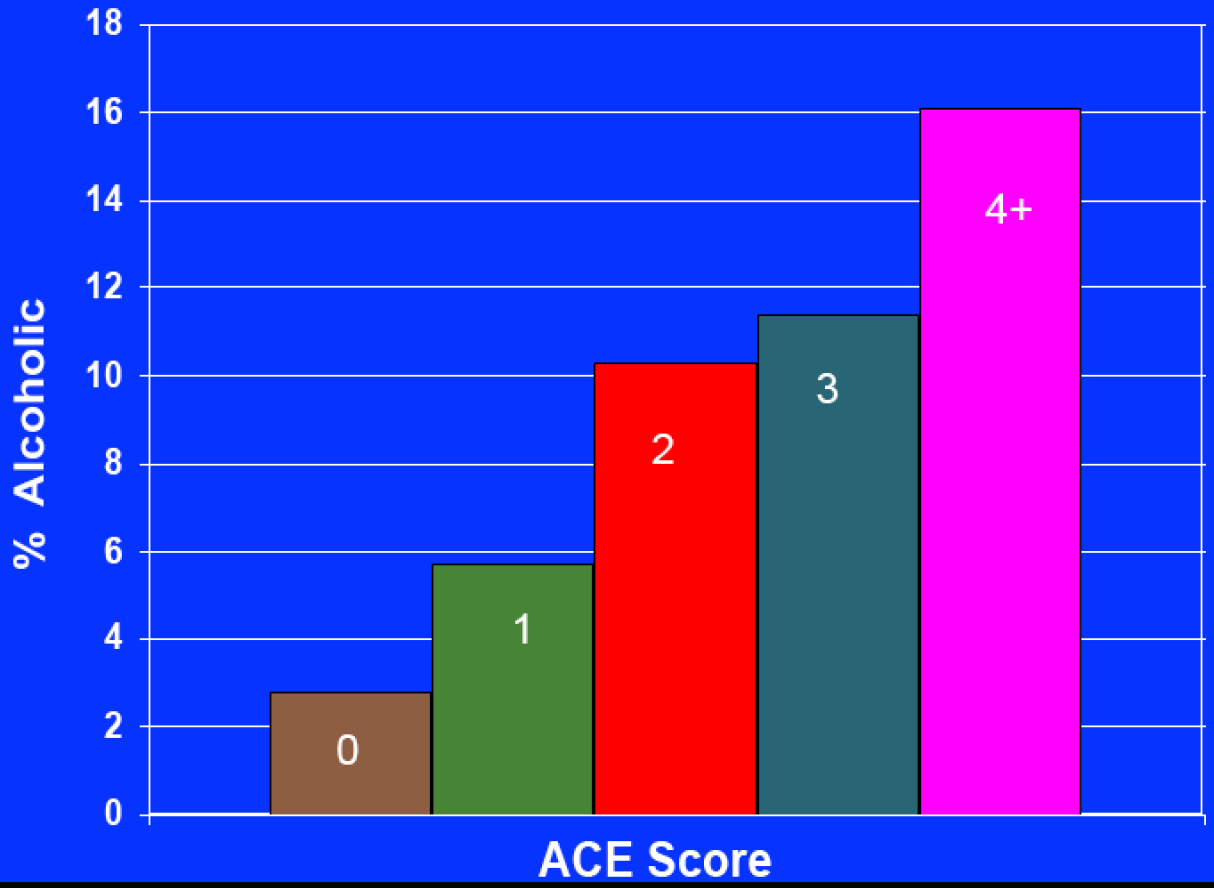
www.CDC.gov/violenceprevention/acestudy

Adverse Childhood Experiences & Adult Alcoholism



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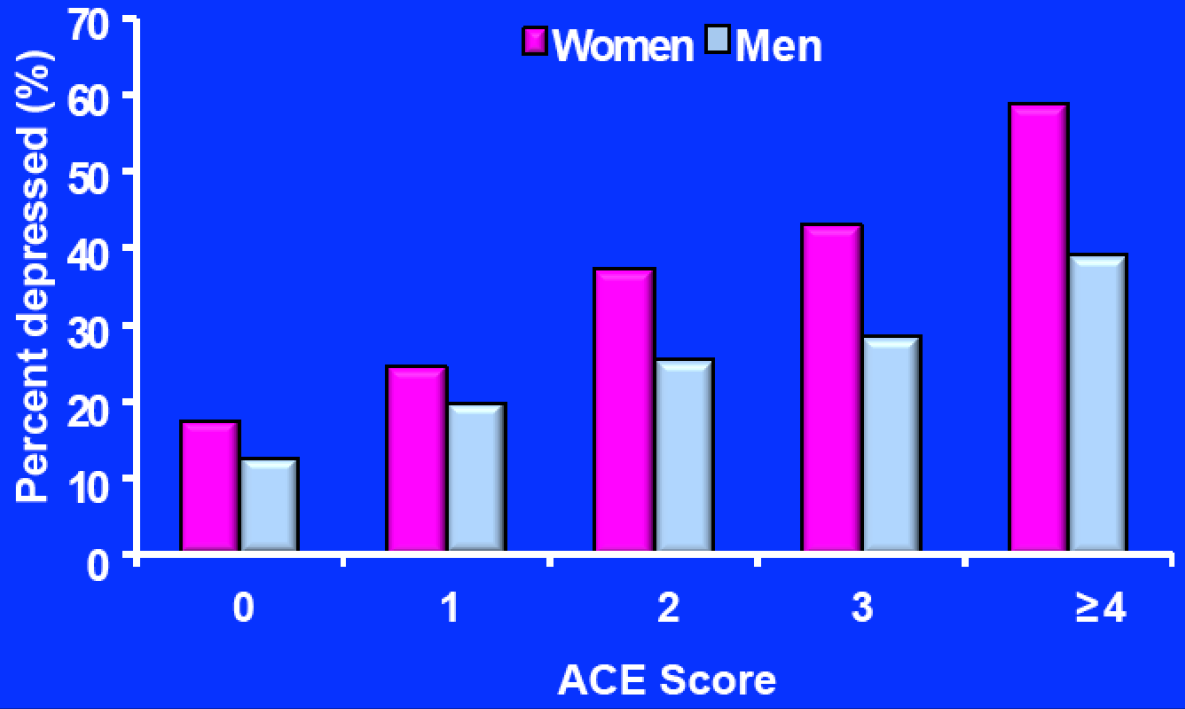
ACE Score & Lifetime History of Depression



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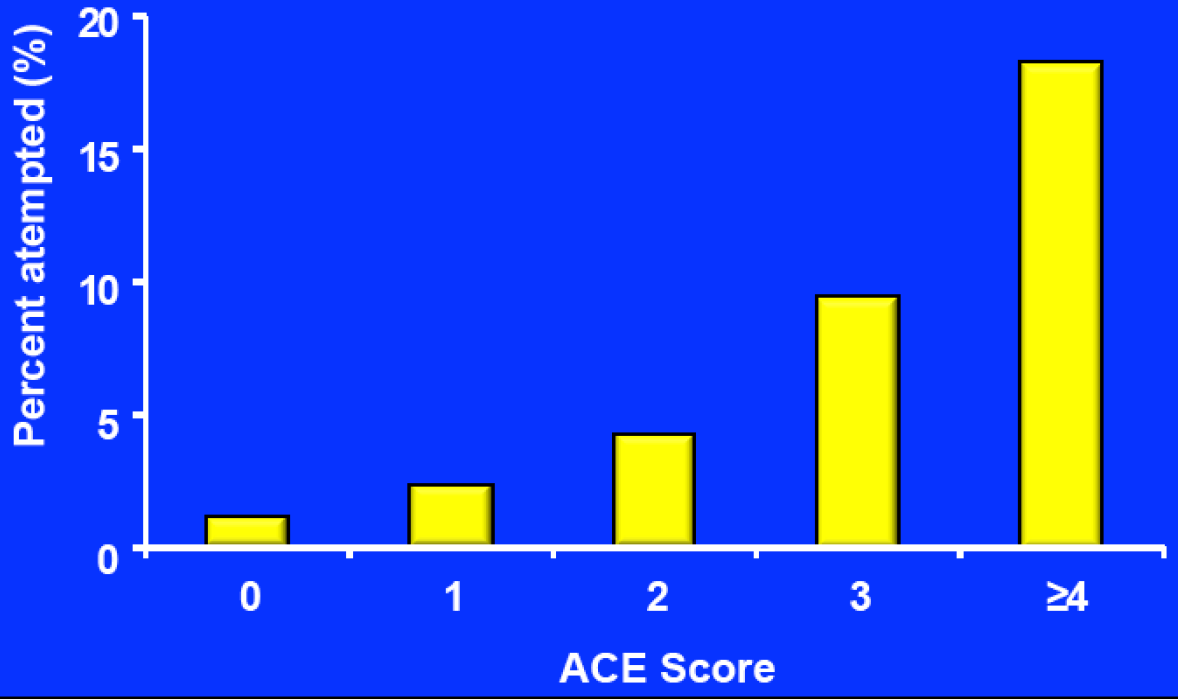
ACE Score & Prevalence of Attempted Suicide



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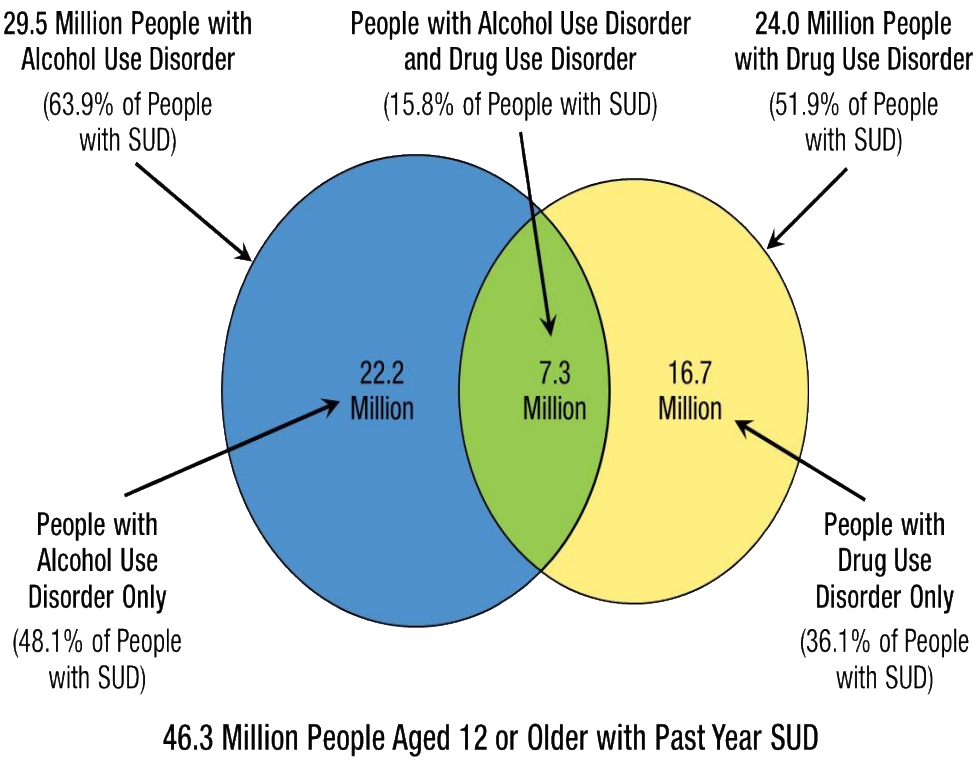
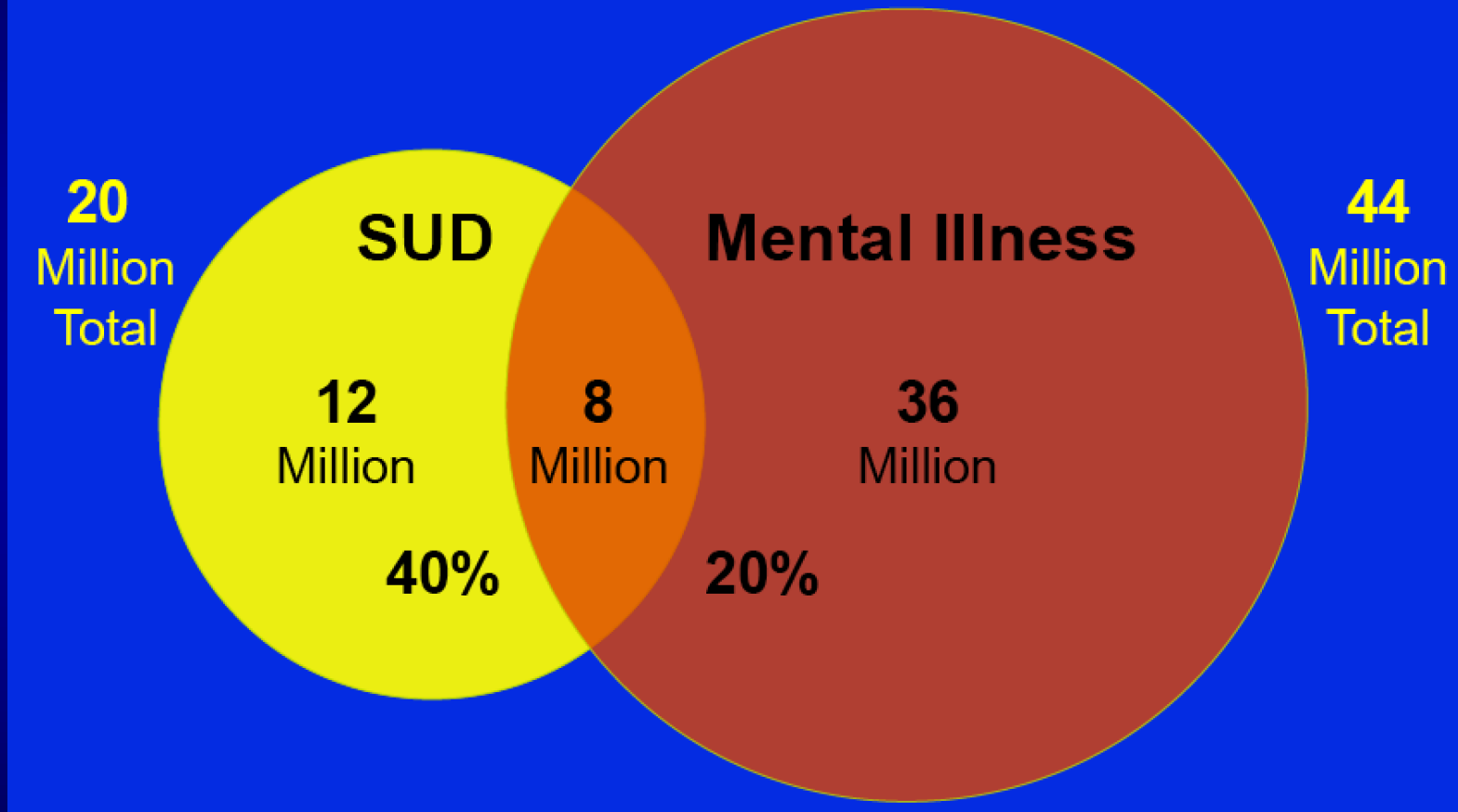
Alcohol Use Disorder and Drug Use Disorder in the Past Year: Among People Aged 12 or Older with a Past Year Substance Use Disorder (SUD); 2021



Note: Drug Use Disorder includes data from all past year users of marijuana, cocaine, heroin, hallucinogens, inhalants, methamphetamine, and prescription psychotherapeutic drugs (i.e., pain relievers, tranquilizers, stimulants, or sedatives).

Past Year SUD & Mental Illness



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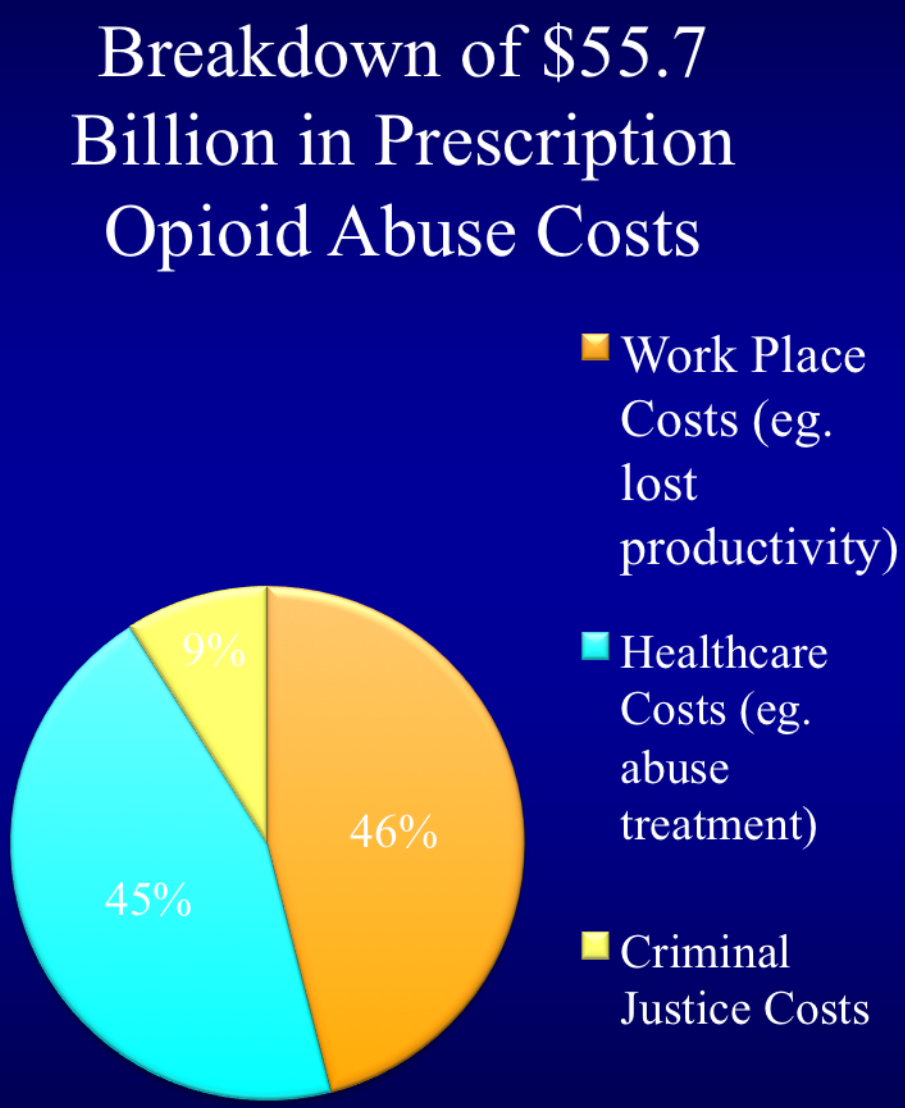
SAMHSA 2014 (*rounded data*)

RAPID Sample

- 75% self-report they used opioids to self-medicate psychiatric related issues.
- 85% self-report the use of opioids to "escape from life".
- No difference between those who started using from a doctor's prescription and those who experimented.

Massive National Problem

- In 2013, opioid use increased globally, while the main increase is in the United States with an estimated cost of $55.7 billion[1]
  - Past year illicit drug use in the United States is the highest it has been in 10 years
  - Treatment admissions for opiates other than heroin now surpasses treatment admissions for cocaine and methamphetamine



Adapting a methodology used by the CDC to estimate the cost of the opioid epidemic in 2017, the JEC estimates the opioid epidemic cost

$1.04 trillion in 2018
$985 billion in 2019
nearly $1.5 trillion in 2020.

The rise in fatal opioid overdoses in 2021 suggests the total cost is likely to continue to increase. Sep 28, 2022

https://beyer.house.gov/news/documentsingle.aspx?DocumentID=5684

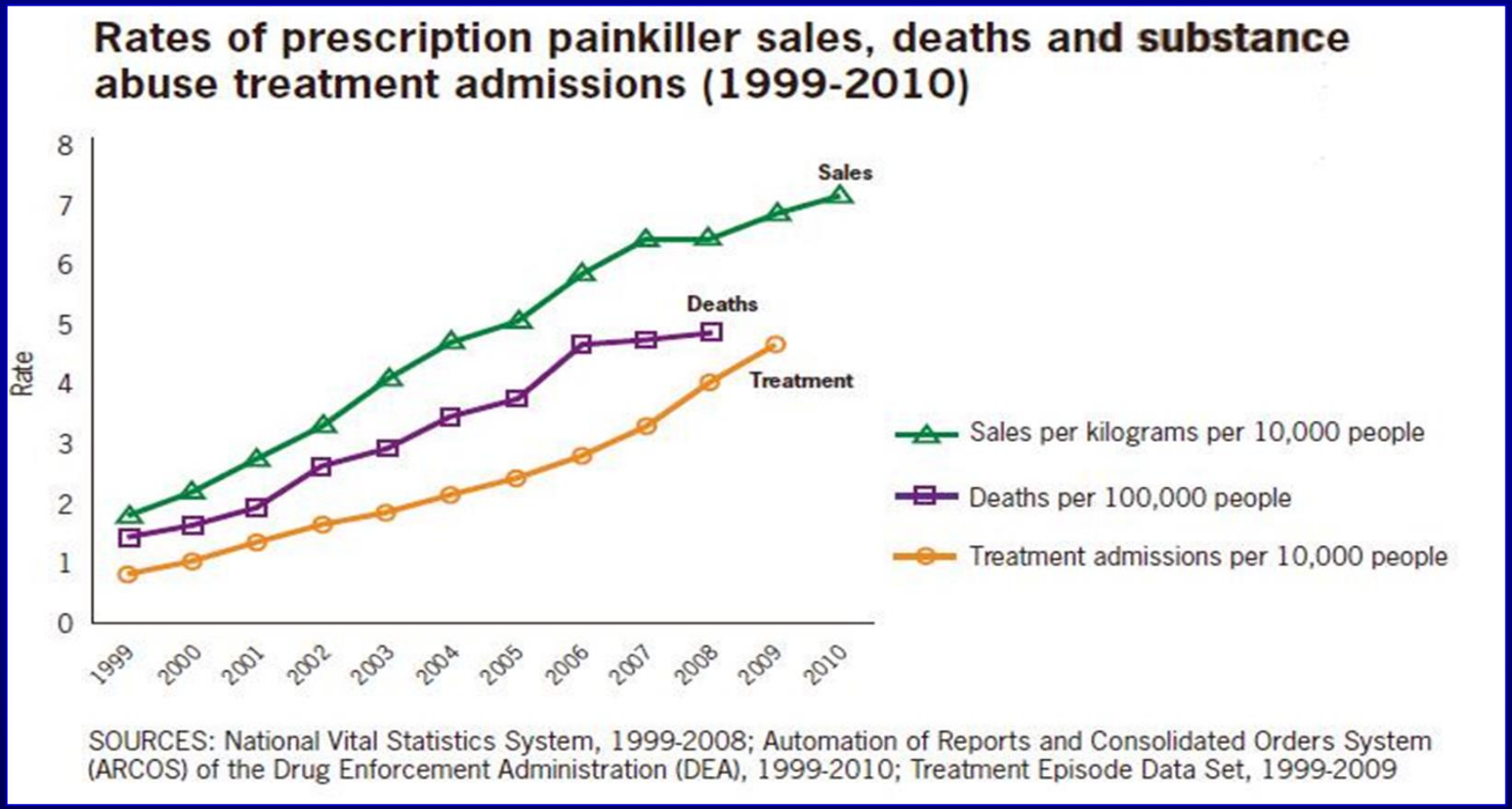
RECENT TRENDS

- Drug Overdose Deaths in the U.S. Top 100,000 Annually
- Life Expectancy in the U.S. Declined a Year and Half in 2020
  - The drop in life expectancy in 2020 was the largest one-year decline since World War II

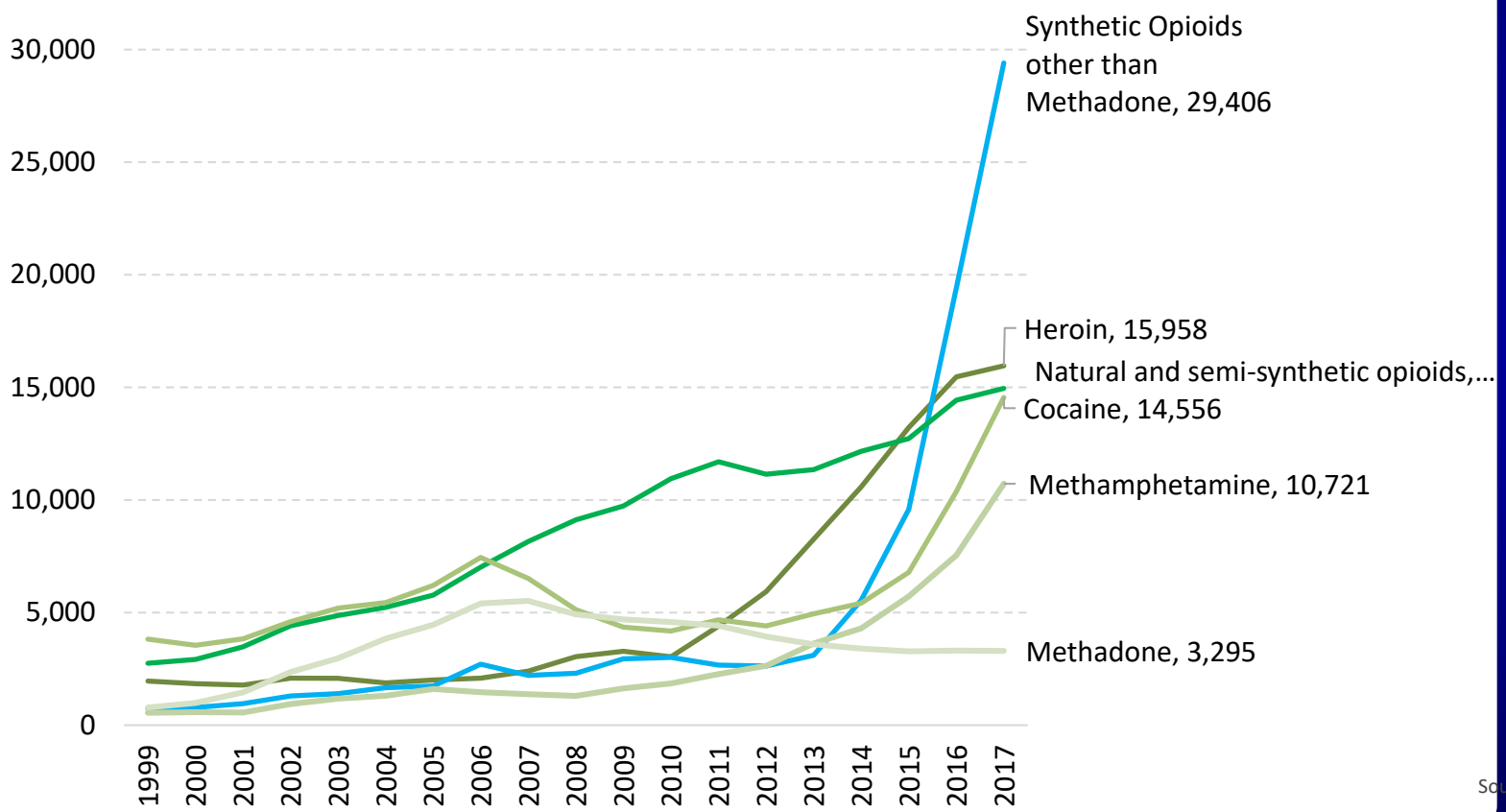
https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2021/20211117.htm

https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2021/202107.htm

Rates of Opioid Overdose Deaths, Sales, and Treatment Admissions, United States, 1999 - 2010

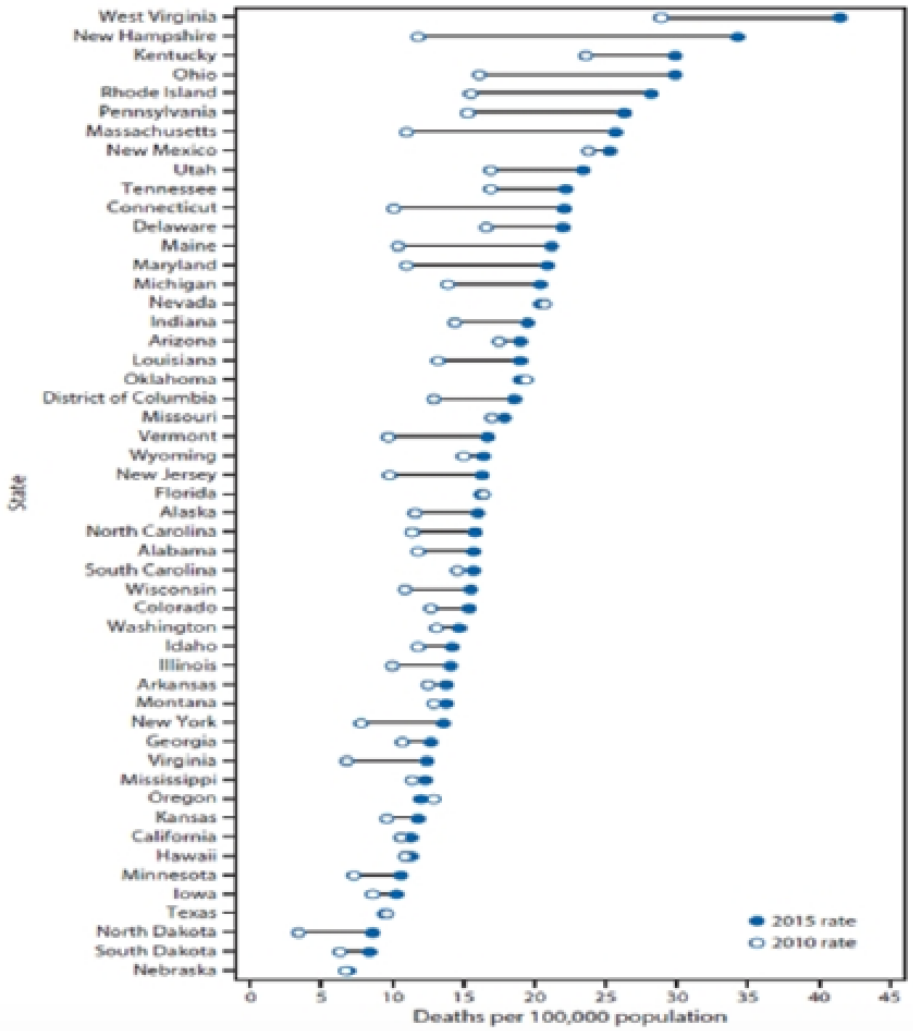


Drugs Involved in US Overdose Deaths, 1999 - 2017

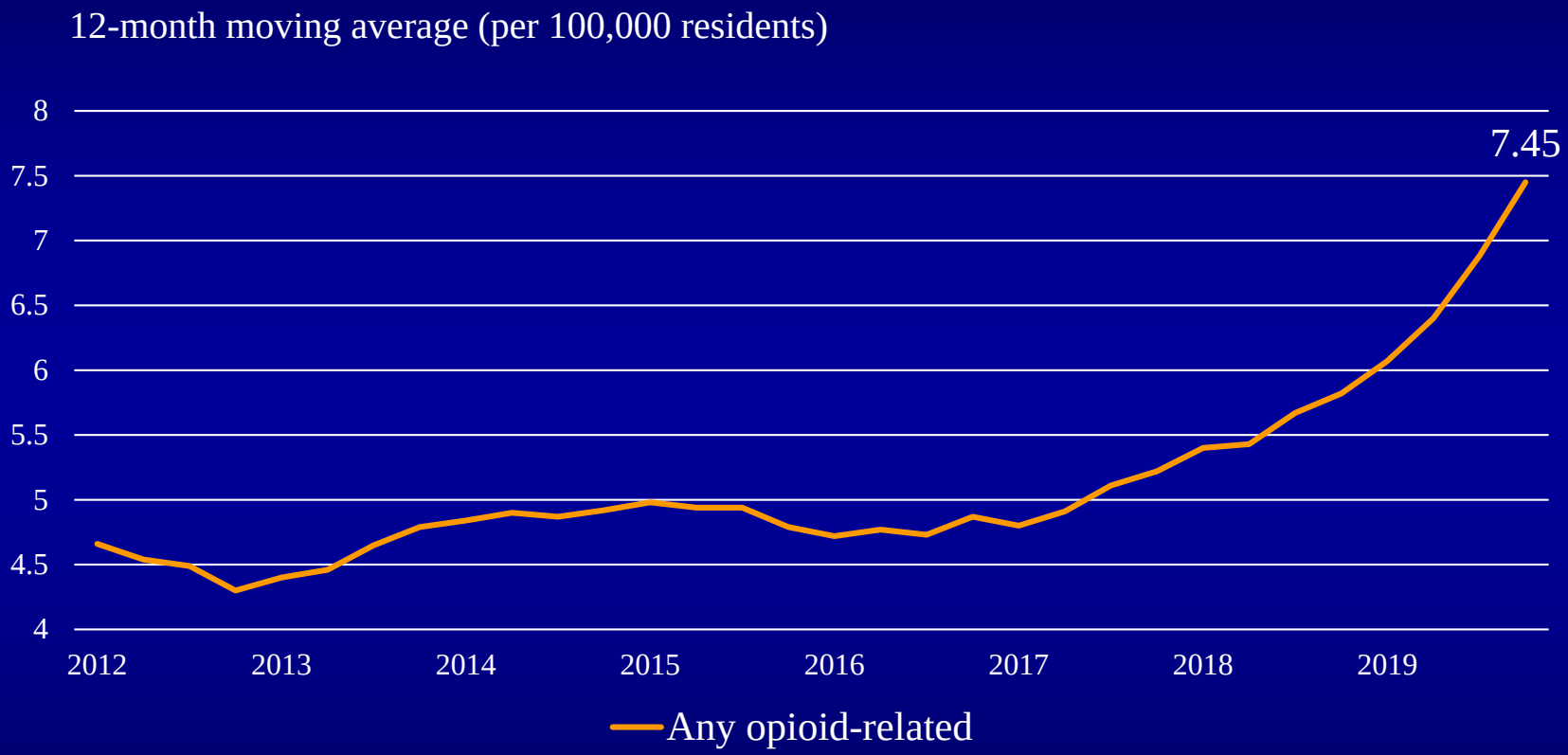


Source: CDC WONDER

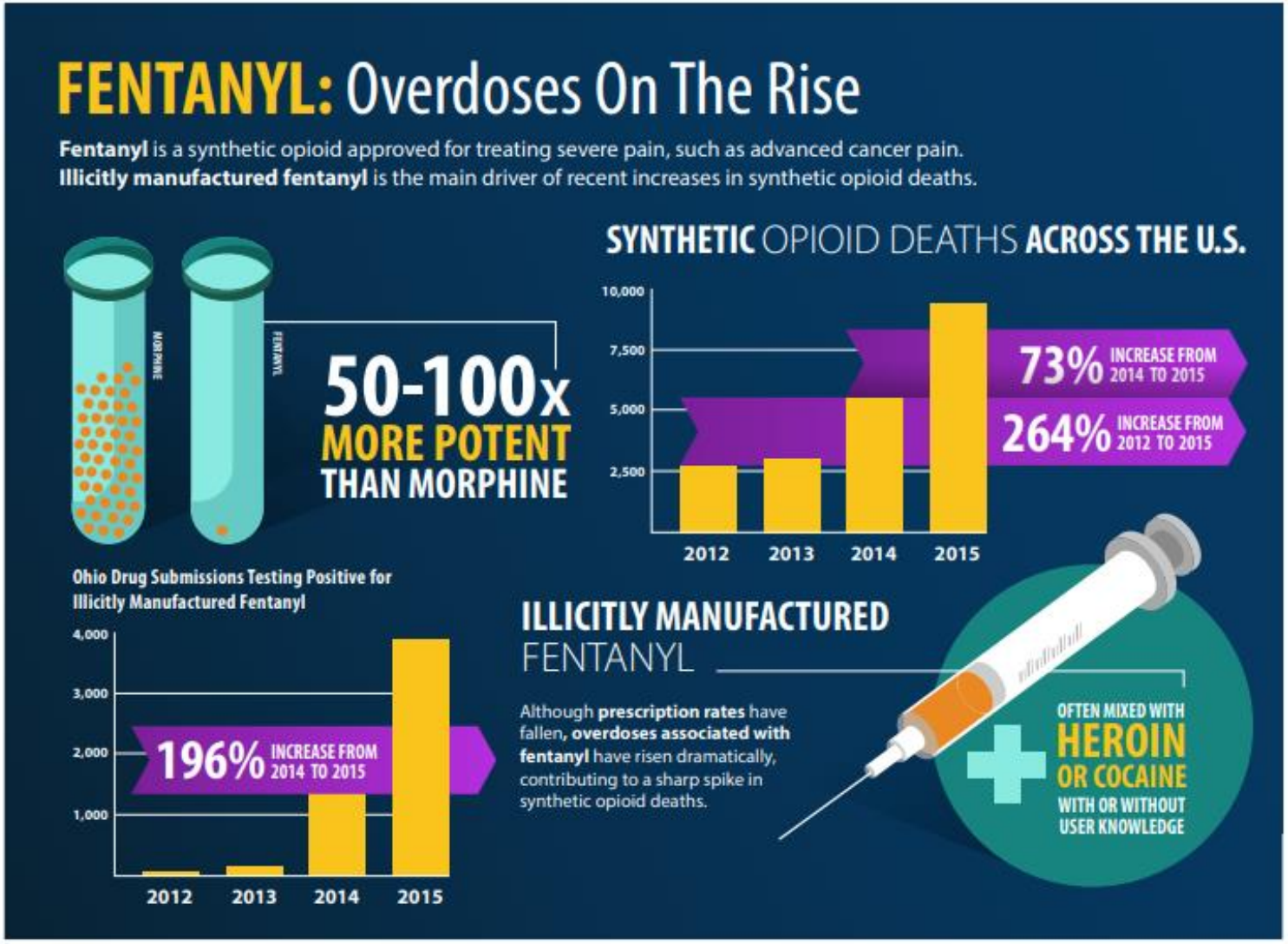
Variation in Trends of Fatal Drug Overdoses across States, 2010–2015



California Opioid Overdose Death Rate

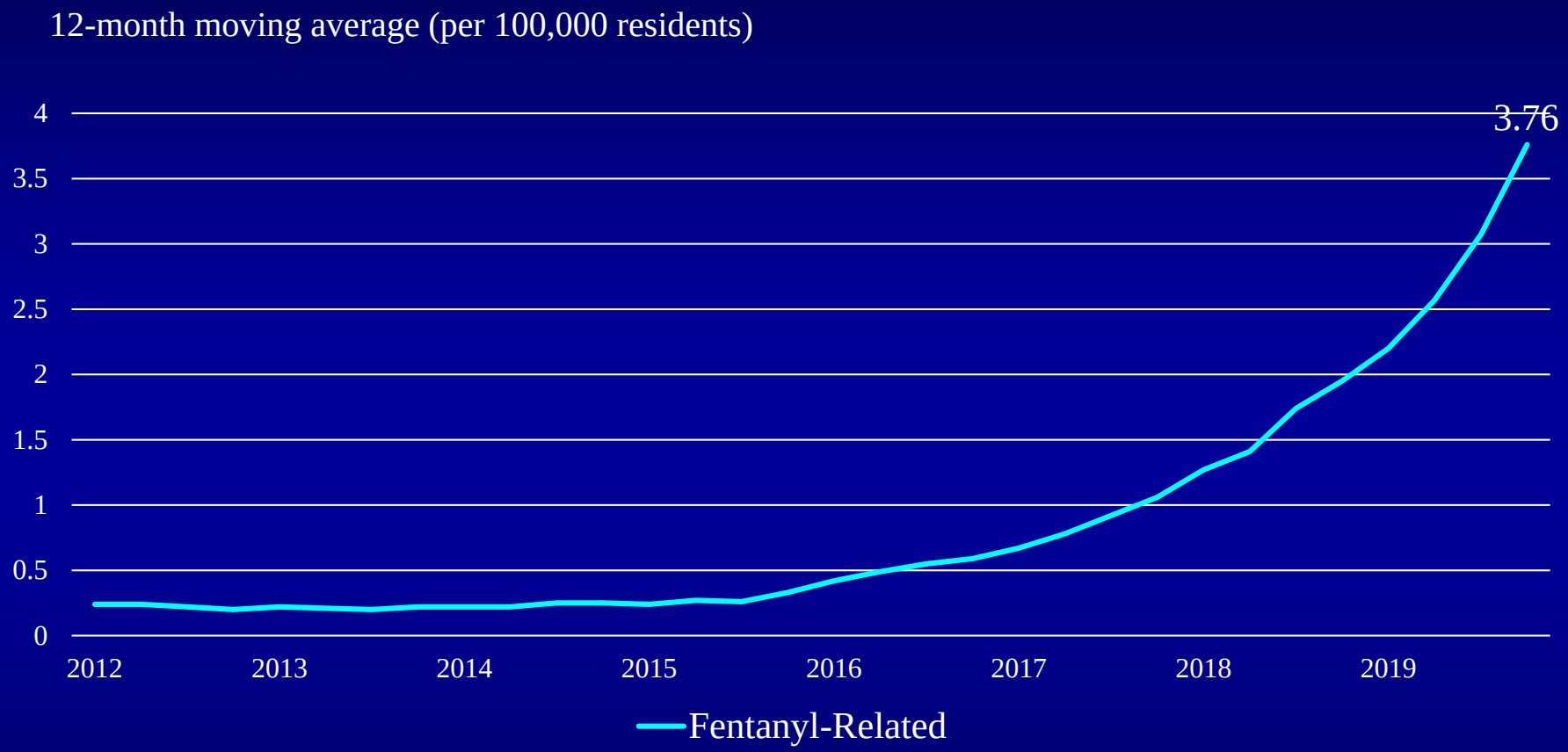


Data Source: California Department of Public Health (CDPH) Safe and Active Communities Branch (2020). California Opioid Surveillance Dashboard. Available at: https://skylab.cdph.ca.gov/ODdash/



CDC National Center for Injury Prevention and Control (2017). Prescription Behavior Surveillance System (PBSS) Issue Brief. https://www.cdc.gov/drugoverdose/pdf/pbss/PBSS-Report-072017.pdf

Fentanyl-related Overdose Death Rate



Data Source: California Department of Public Health (CDPH) Safe and Active Communities Branch (2020). California Opioid Surveillance Dashboard. Available at: https://skylab.cdph.ca.gov/ODdash/

Lethal Dose

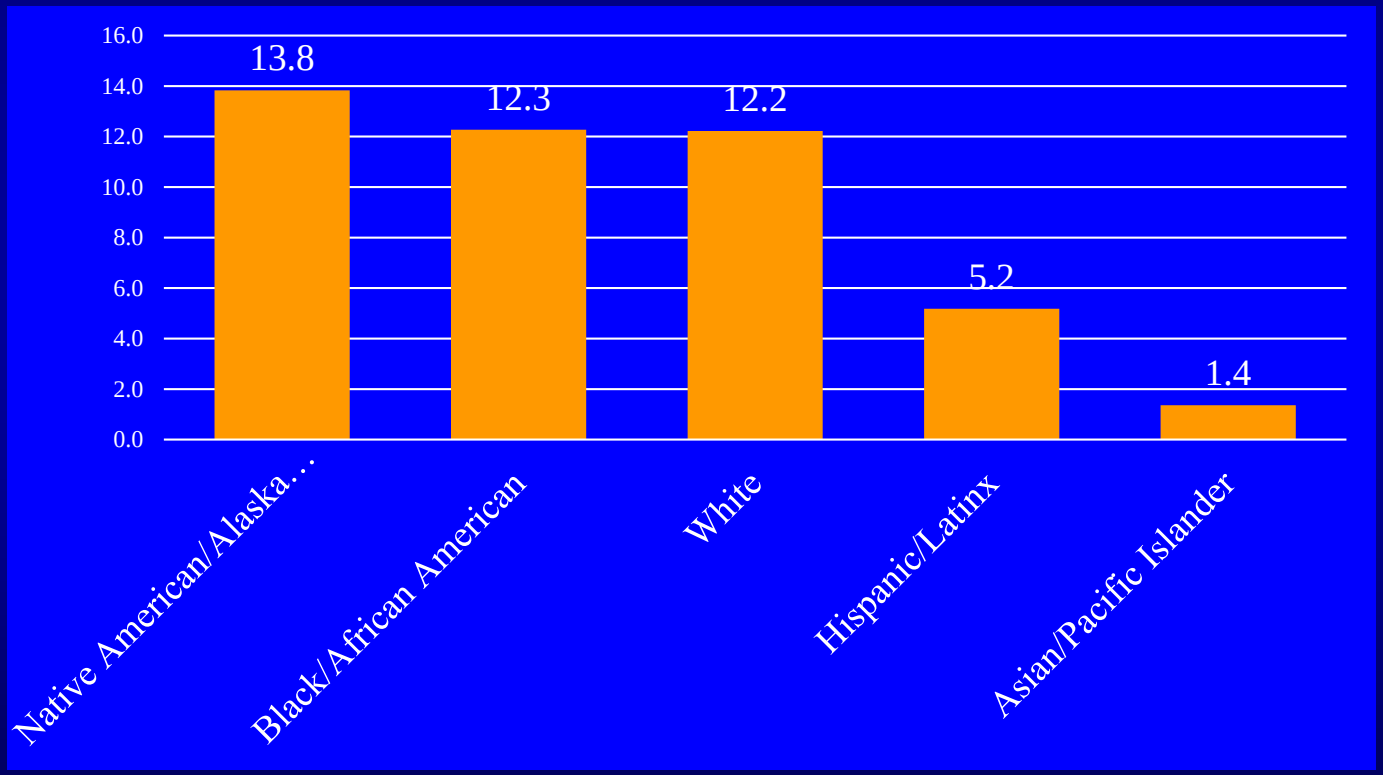
- *Morphine* = 1x
- *Fentanyl* = 100x
- *Carfentanil* = 10,000x

Lethal doses of heroin compared to "synthetic" opioids.

DEA Schedule I II II Legal Implications

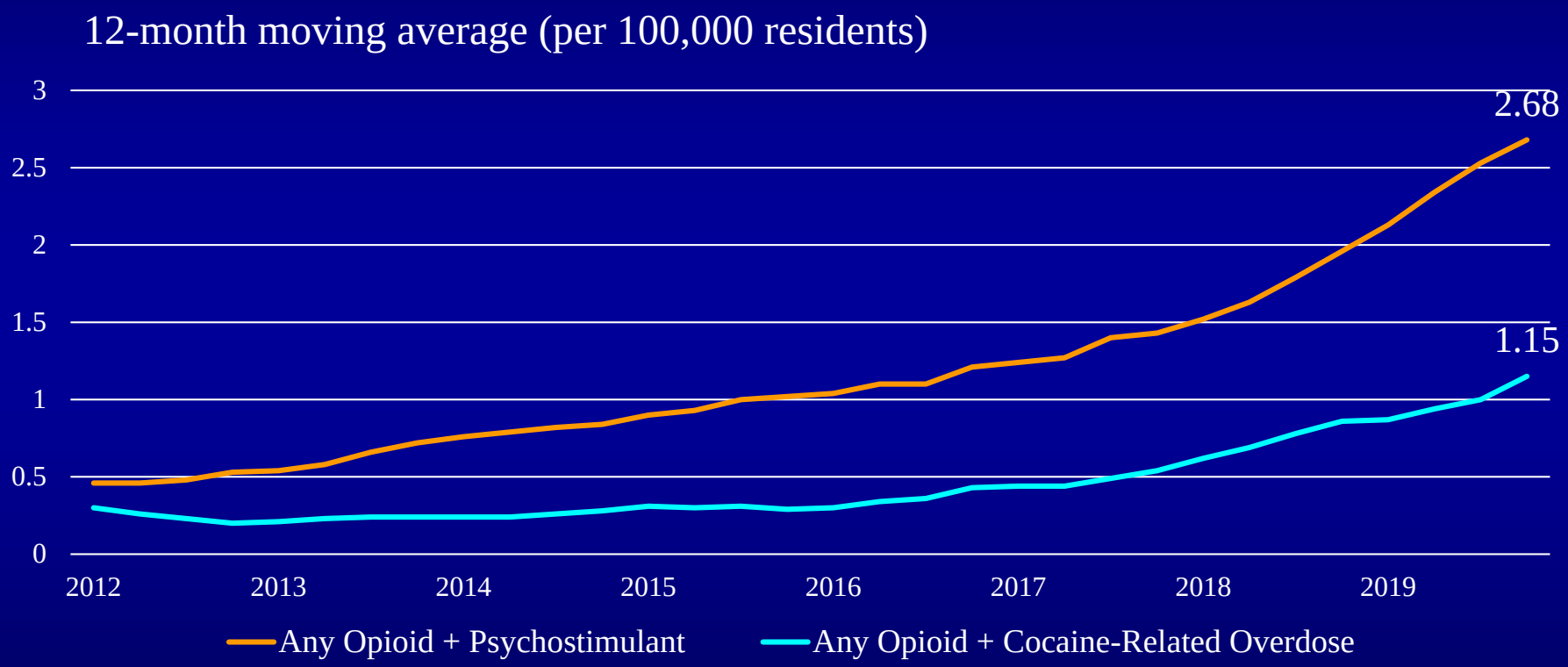
Opioid Overdose Death Rates by Race / Ethnicity

2019 crude rate per 100,000 residents



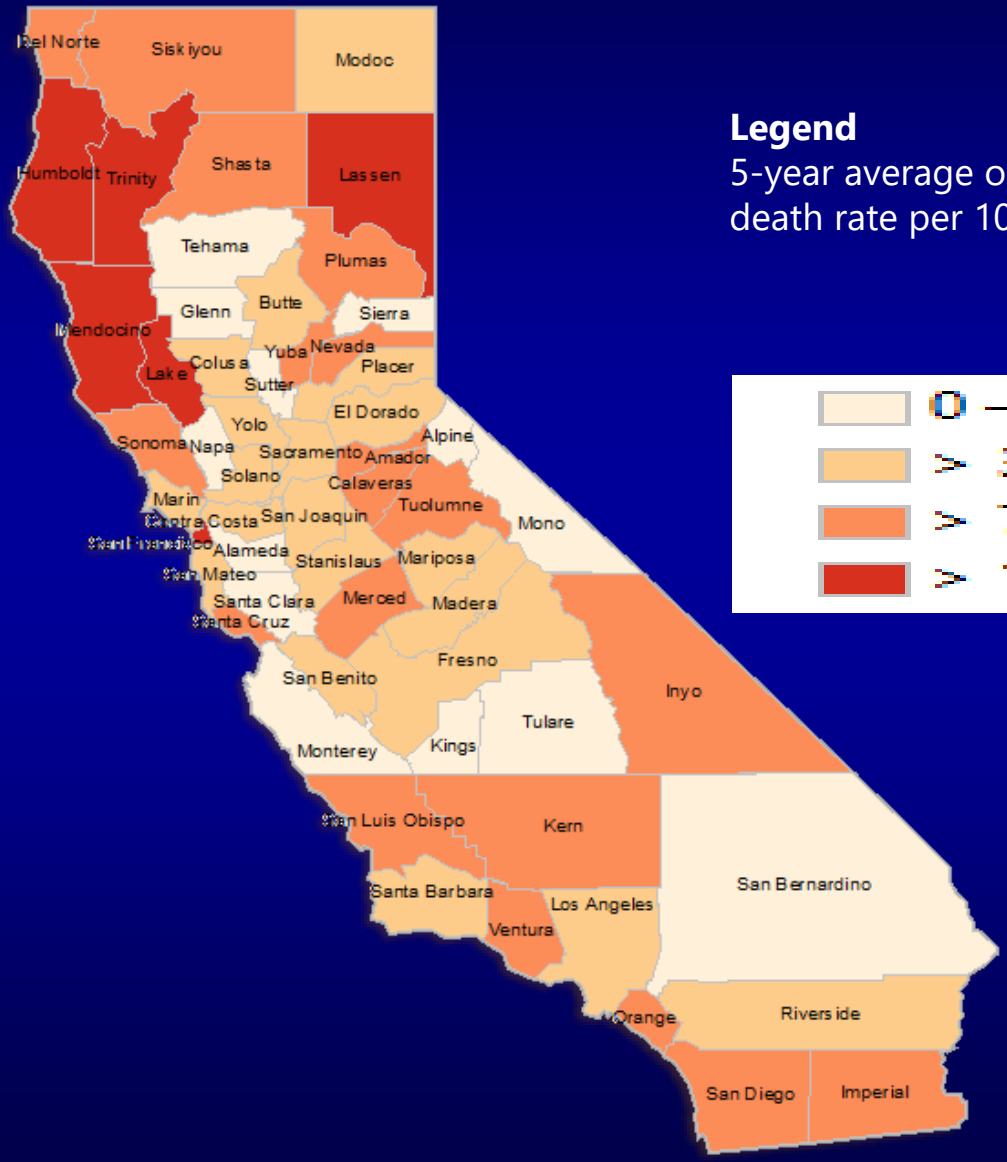
Data Source: California Department of Public Health (CDPH) Safe and Active Communities Branch (2020). California Opioid Surveillance Dashboard. Available at: https://skylab.cdph.ca.gov/ODdash/

Overdose Death Rates: Opioids + Stimulants



Data Source: California Department of Public Health (CDPH) Safe and Active Communities Branch (2020). California Opioid Surveillance Dashboard. Available at: https://skylab.cdph.ca.gov/ODdash/

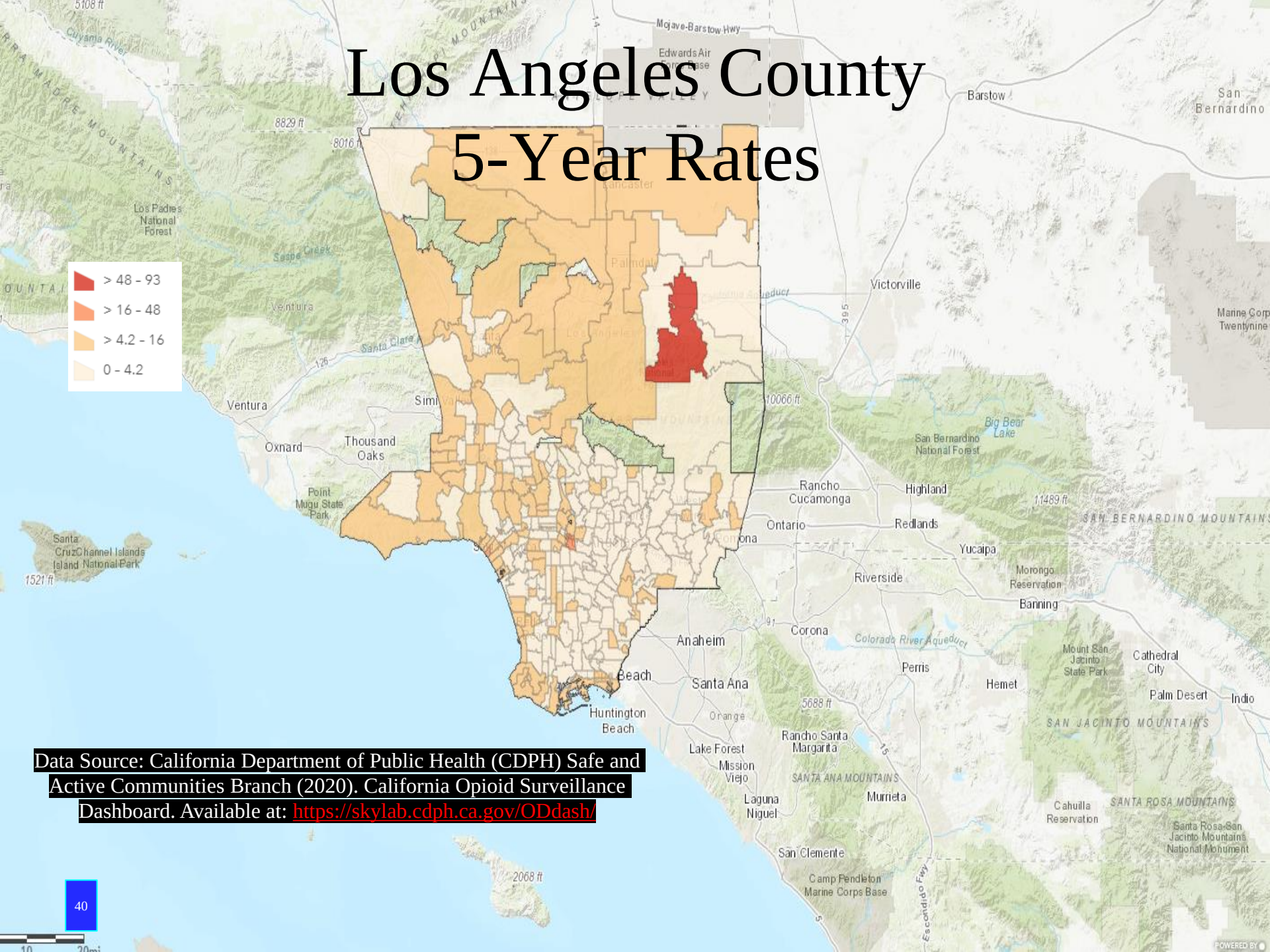
Opioid Overdose Death Rates by County



Legend
5-year average opioid-related overdose death rate per 100,000 residents

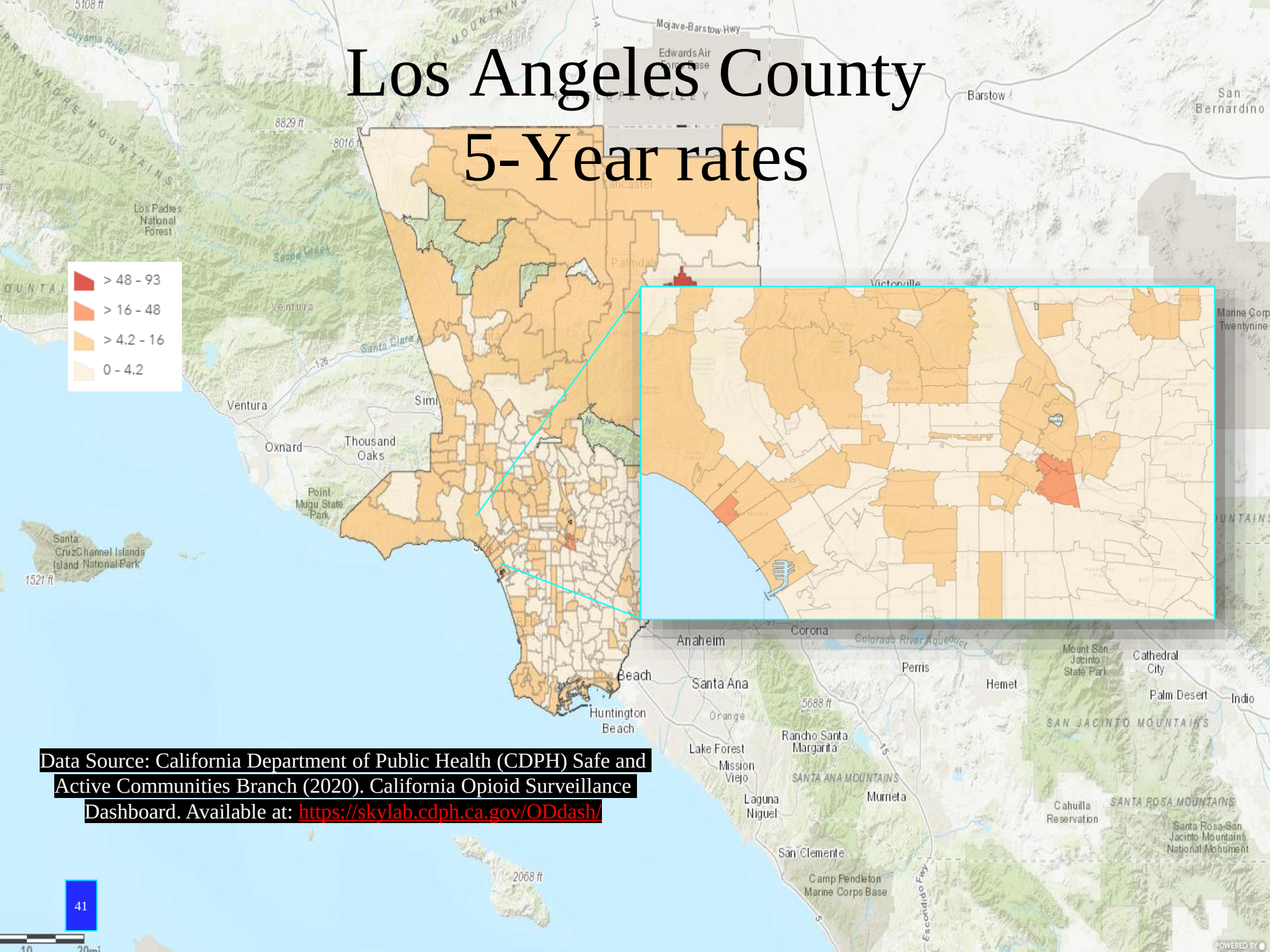
	0 — 3.7
	> 3.7 — 7.1
	> 7.1 — 12.6
	> 12.6 — 22

Los Angeles County 5-Year Rates



Data Source: California Department of Public Health (CDPH) Safe and Active Communities Branch (2020). California Opioid Surveillance Dashboard. Available at: https://skylab.cdph.ca.gov/ODdash/

Los Angeles County
5-Year rates



Data Source: California Department of Public Health (CDPH) Safe and Active Communities Branch (2020). California Opioid Surveillance Dashboard. Available at: https://skylab.cdph.ca.gov/ODdash/

Fatal dose of fentanyl
(2 mg or 2000 mcg)

Fatal dose of carfentanil
(0.02 mg or 20 mcg)

"Death pill": fentanyl disguised as other drugs linked to spike in US overdoses.

Fentanyl-laced Cocaine

Fentanyl-laced Hydrocodone

Fentanyl-laced Xanax

Substance Use Disorder: DSM-5 Criteria

1. Tolerance*
2. Withdrawal*

**Not valid if opioid taken as prescribed*

Loss of Control

3. Larger amounts and/or longer periods
4. Inability to cut down on or control use
5. Increased time spent obtaining, using, or recovering
6. Craving/Compulsion

Use Despite Negative Consequences

7. Role failure: work, home, school
8. Social, interpersonal problems
9. Reducing social, work, recreational activity
10. Physical hazards
11. Physical or psychological harm

Mild (2-3),
Moderate (4-5),
Severe (≥6)

APA. (2013). DSM (5th ed.)

Medication Assisted Treatment

MAT is the use of medications, in combination with counseling and behavioral therapies, to provide a whole-patient approach to the treatment of substance use disorders.

http://www.dpt.samhsa.gov/patients/mat.aspx

MAT cont.

- Research shows that when treating substance-use disorders, a combination of medication and behavioral therapies is most successful.
- MAT is clinically driven with a focus on individualized patient care.

http://www.dpt.samhsa.gov/patients/mat.aspx

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

"Those who do not remember the past are condemned to repeat it."

-George Santayana 1863-1952

The Business Case for MAT

- *The estimated expense to society of opioid addiction nears $20 billion annually*
- *The cost of treating an individual addicted to opioids is only $4,000 per year.*
- *If every opioid-dependent person in the United States received treatment,* ***$16 billion would be saved every year****.*

"Methadone Maintenance and Other Pharmacotherapeutic Interventions in the Treatment of Opioid Addiction." April 2002, Vol. lll, No. 1

WHO published best practice guidelines favor MAT

WHO – *Substitution Maintenance Therapy in the Mgmnt of Opioid Dep. and HIV/AIDS Prevention*. 2004.

WHO – *Access to Controlled Meds Programme* 2007.

WHO – *Principles of Drug Dependence Treatment*. 2008.

WHO – *Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence* .2009.

WHO – *Tech Guide for Countries to Set Targets for Universal Access to HIV Prevention, Treatment and Care for Injecting Drug Users (IDUs)*. 2009

Reshevska, I., K. Foreit, K. Beardsley, and L. Porter. 2010. *Policy Advocacy Toolkit for Medication-Assisted Treatment (MAT) for Drug Dependence*. Washington, DC: Futures Group, Health Policy Initiative, Task Order 1.

MAT Evidence: when part of a comprehensive program shown to

- Improve outcomes
- Increase retention in treatment
- Decrease illicit opiate use
- Decrease hepatitis and HIV infections
- Decrease criminal activities
- Increase employment
- Improve birth outcomes for patients[2]
  - http://www.dpt.samhsa.gov/patients/mat.aspx

FDA approved Medications OPIATE USE DISORDER

- methadone, ® Dolophine
- Buprenorphine sl, Subutex®
- Buprenorphine/naloxone sl, Suboxone®, Zubsolv®
- Buprenorphine subdermal: Sublocade®, Brixadi®
- Oral Naltrexone, ReVia®, Depade®
- Long acting depot Naltrexone, VIVITROL®

Methadone, ®**Dolophine**

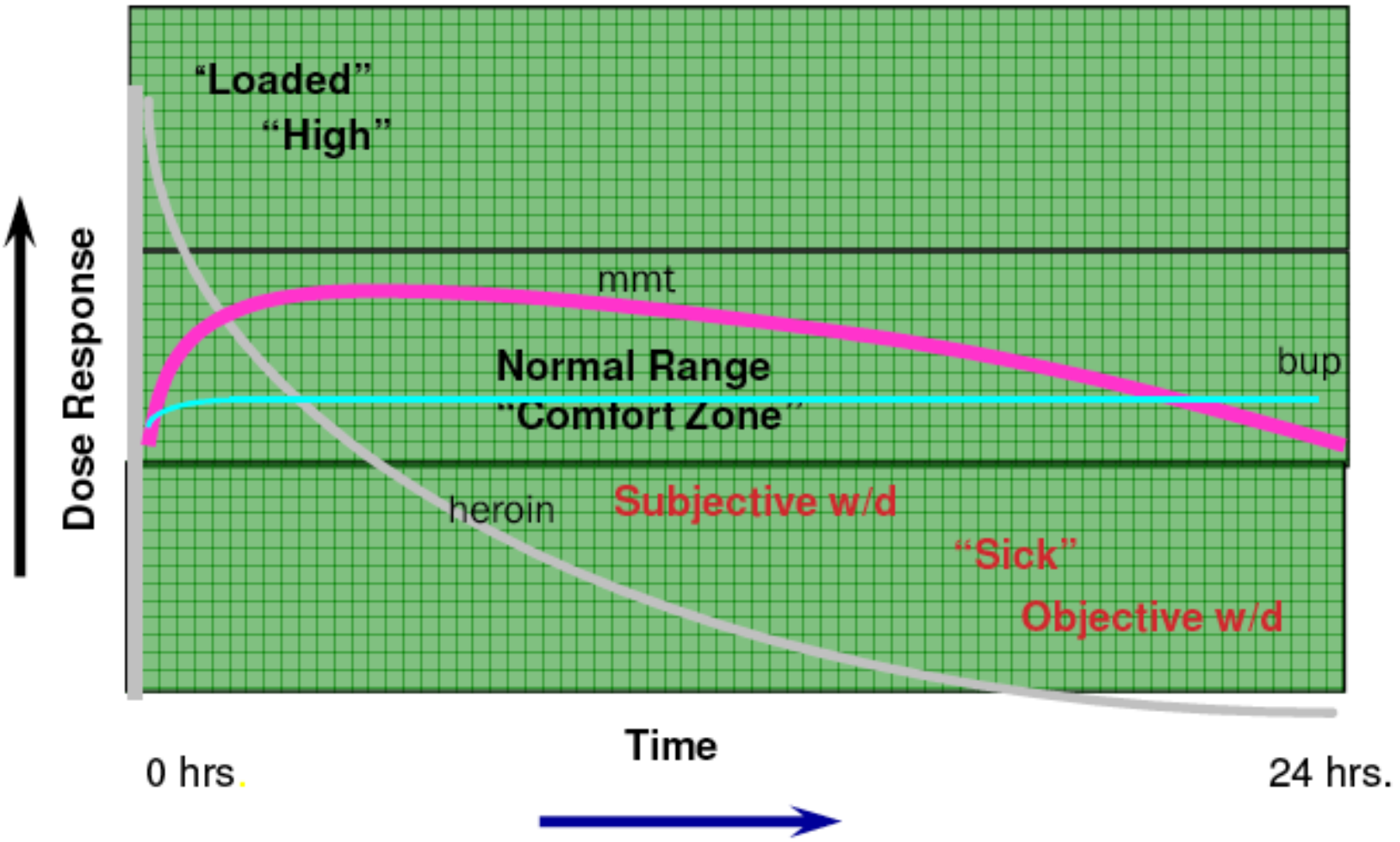
- **Mechanism of Action**
  - binds to various opioid receptors, (full opioid agonist)
- Cost
  - “pennies per day”

Epocrates Online Premium: https://online.epocrates.com

Full Agonists for Opiate Dependence

- METHADONE
  - Long acting opiate agonist
  - Combats withdraw and craving
  - must be dosed in NTPs, daily dosing mandatory until patient stable…months
  - Outpatient treatment after patient considered very low risk….years
- LAAM: longer acting (dose 3 X a week)
  - NO LONGER AVAILABLE:poor cost/profit ratio, and potential for increased QT intervals

Methadone Simulated 24 Hr. Dose/Response
At steady-state in tolerant patient



Methadone Effectiveness

Gunne & Gronbladh, 1984

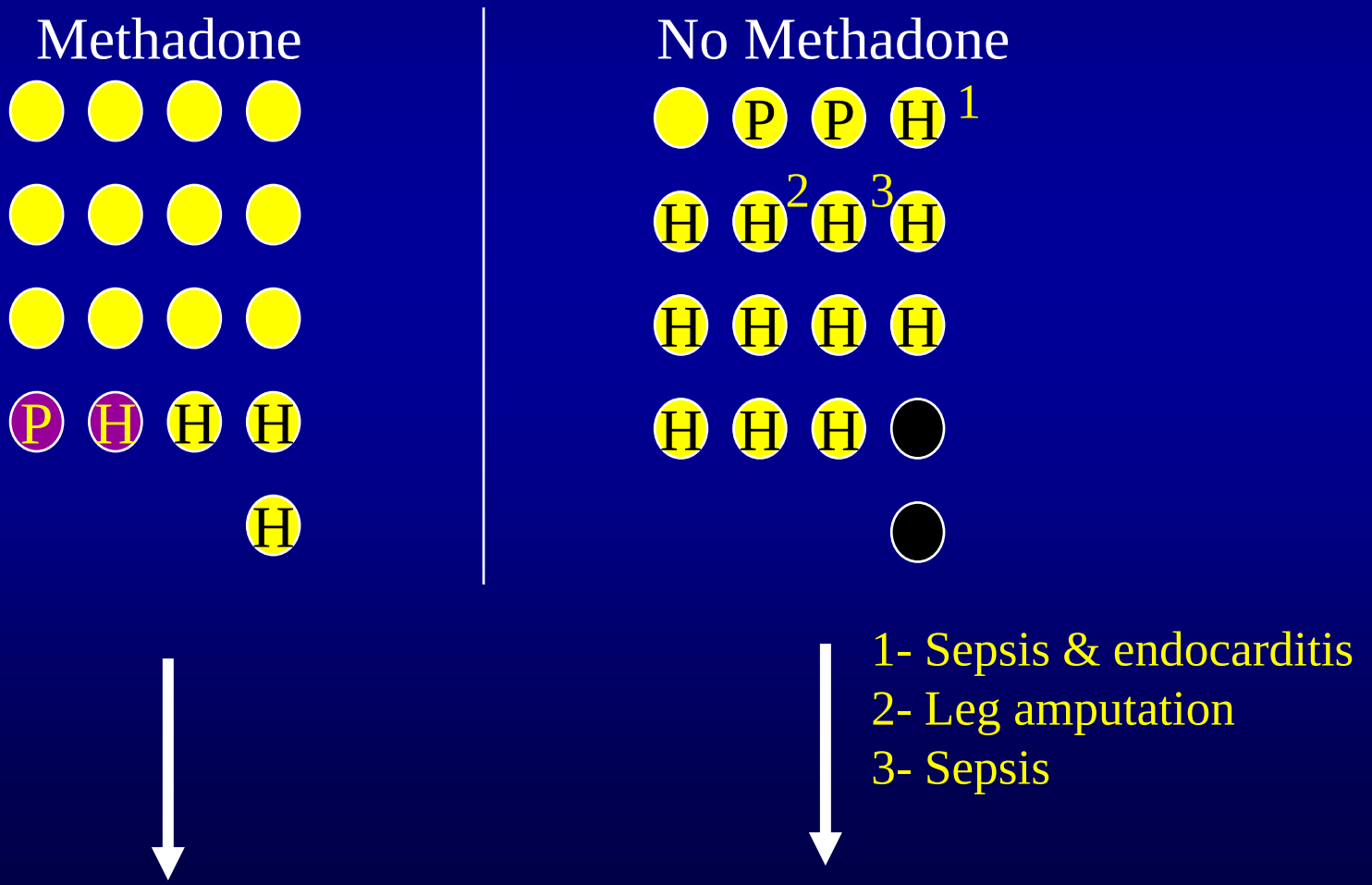
Baseline

Methadone	Regular Outpatient
H H H H	H H H H
H H H H	H H H H
H H H H	H H H H
H H H H	H H H H
H	H

Methadone Effectiveness

Gunne & Gronbladh, 1984

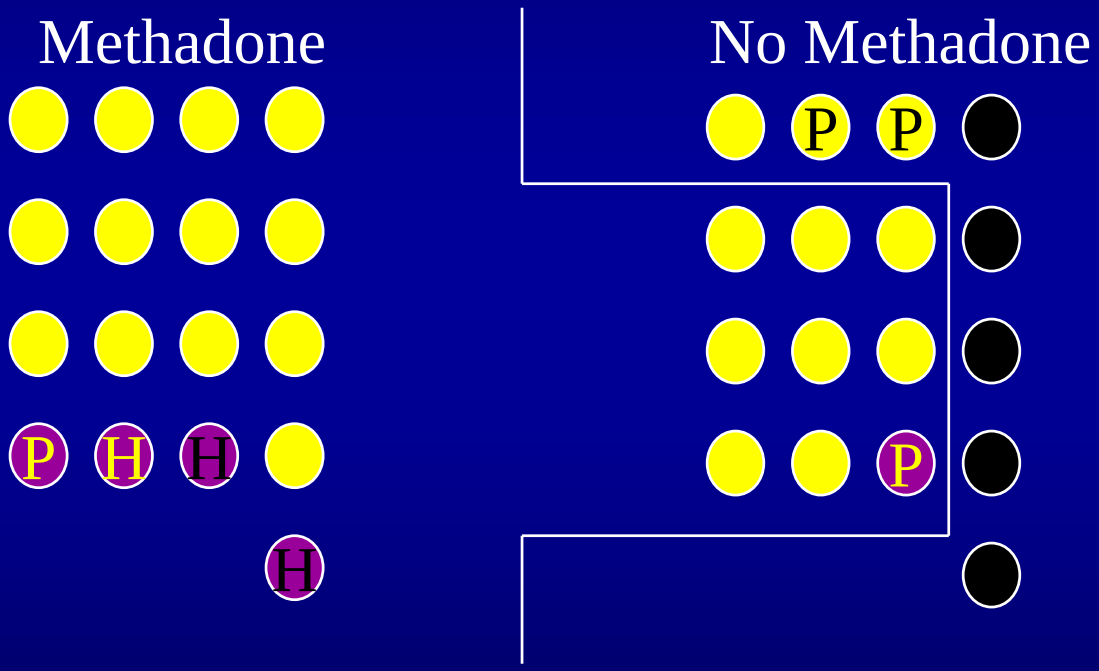
After 2 Years



Methadone Effectiveness

Gunne & Gronbladh, 1984

After 5 Years



Mortality in heroin addiction: impact of methadone treatment

Grönbladh L, Öhlund LS, Gunne LM. Mortality in heroin addiction: impact of methadone treatment.
Acta Psychiatr Scand 1990: 82: 223–227.

L. Grönbladh, L. S. Öhlund,
L. M. Gunne
Department of Psychiatry, Ulleråker, Uppsala,

1979-1984; N0 Admit to MMTP

Yearly Death Rates: IV ODs
MT=1.4, VD=1.7,
ID=6.91, UC=7.2

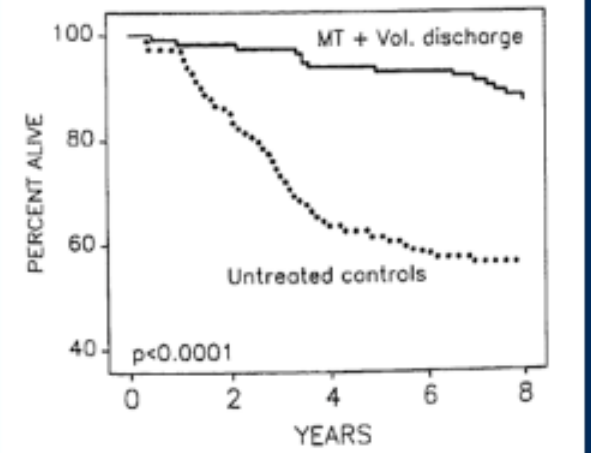


Fig. 2. Survivors in cohorts 1 + 2 (solid line) compared with controls (dotted).

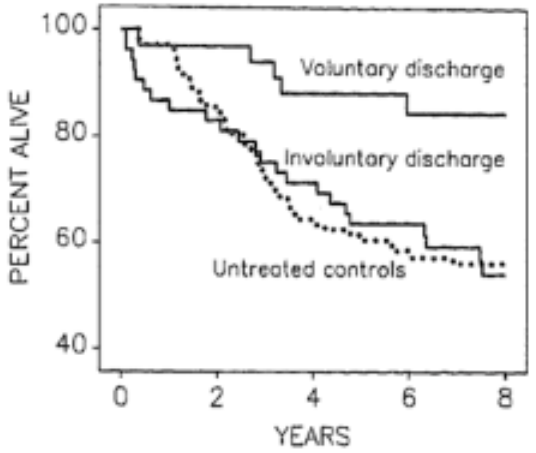
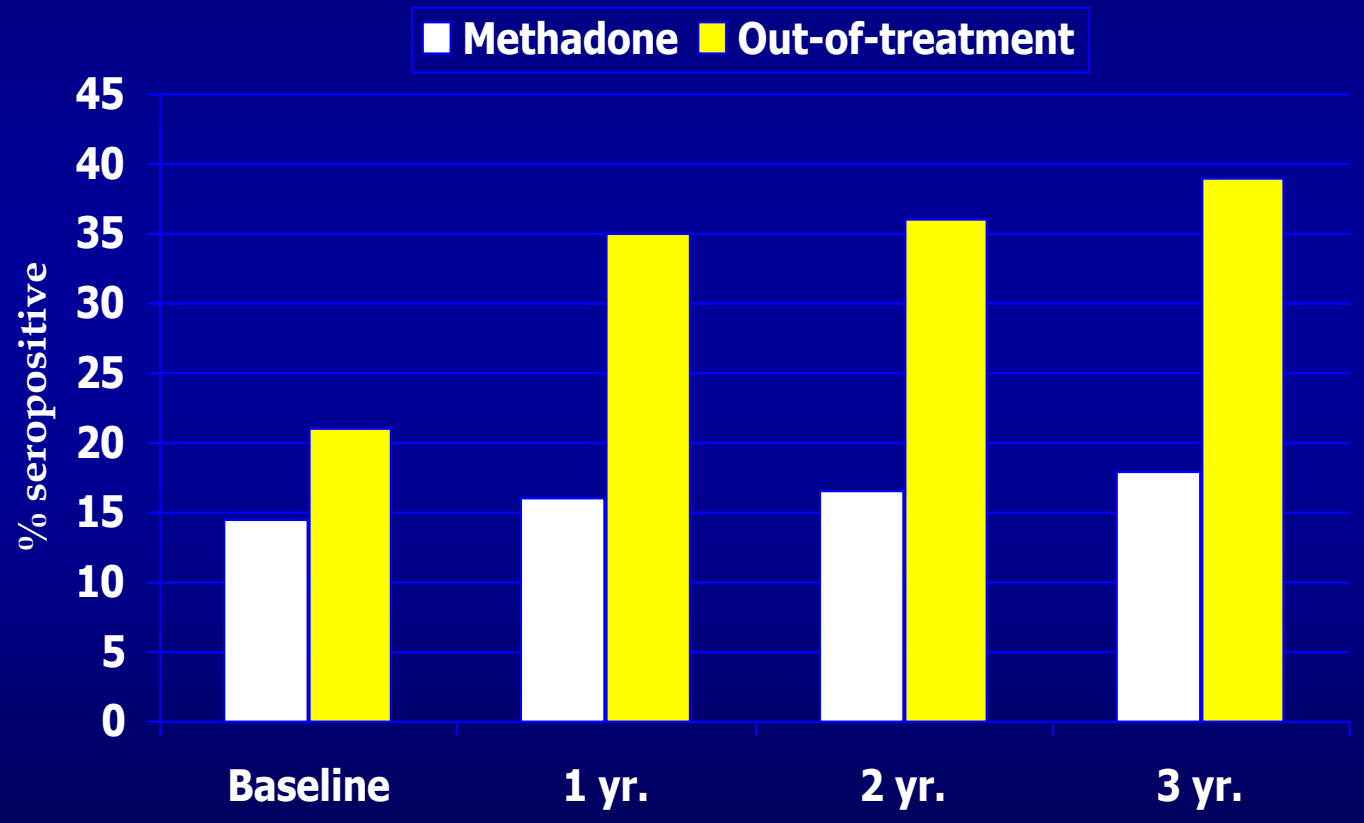


Fig. 3. Cohort 2 (voluntary discharge; upper solid line) contrasted to cohort 3 (involuntary discharge; lower solid line) and controls (dotted line).

Methadone Treatment Decreases HIV Seroincidence

Metzger et al. JAIDS 1993;6:1049.



Methadone Safety

Half-Life

Long, variable, unpredictable half-life

Serum t½ 20-120 hours

4-7 days to reach steady state: "Start low, go slow"

QTc Prolongation, Risk of Torsades de Pointes

Dose-related: >100mg daily

Multifactorial : ↓K, ↓Mg, other drugs ↑QTc

CYP450: 3A4, 2D6 interactions

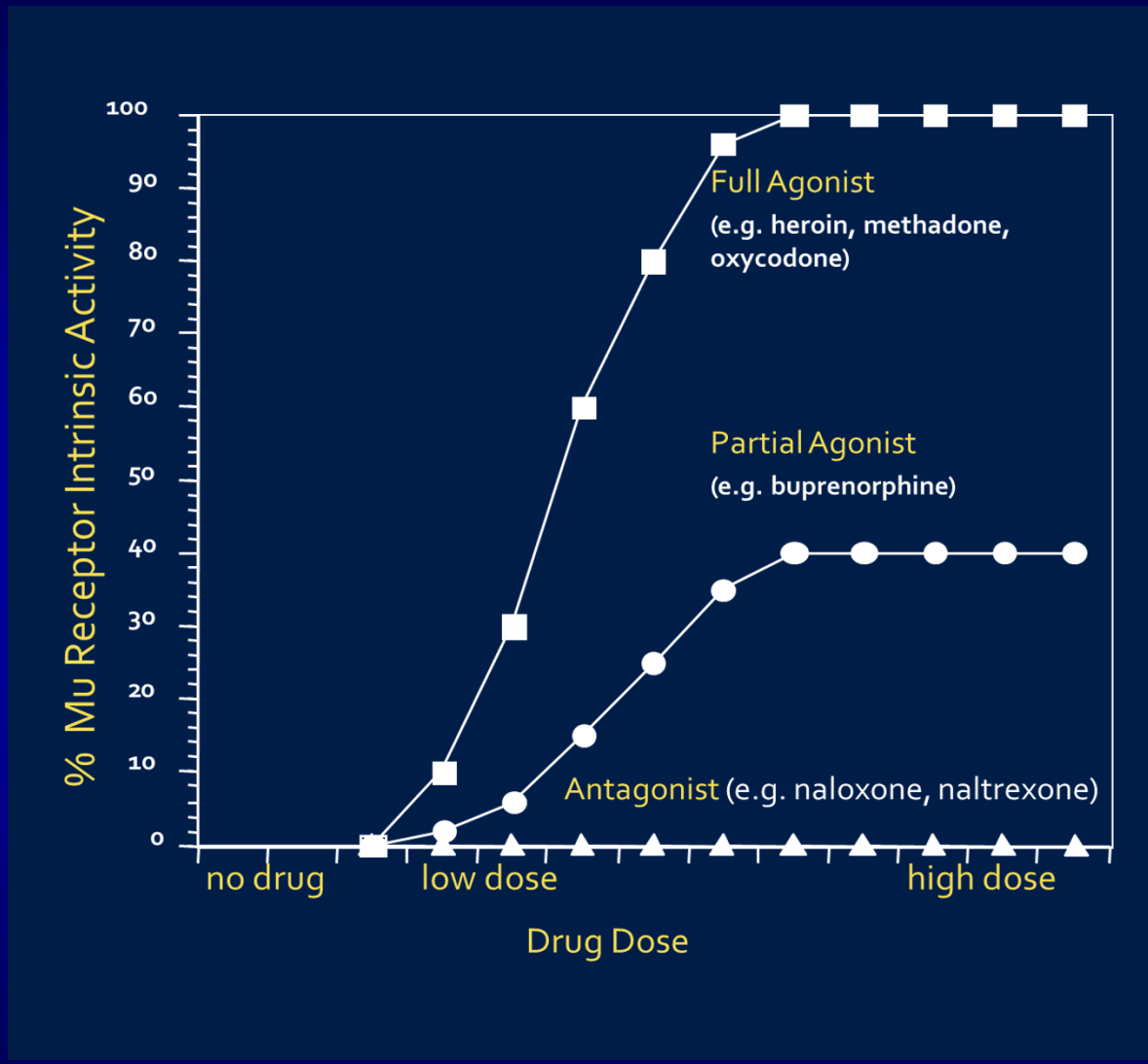
QTc > 500 msec → Torsades de Pointes

Wedam E et al. JAMA Internal Medicine. 2007. The Medical Letter. 2017, 59(1522): 89-95.

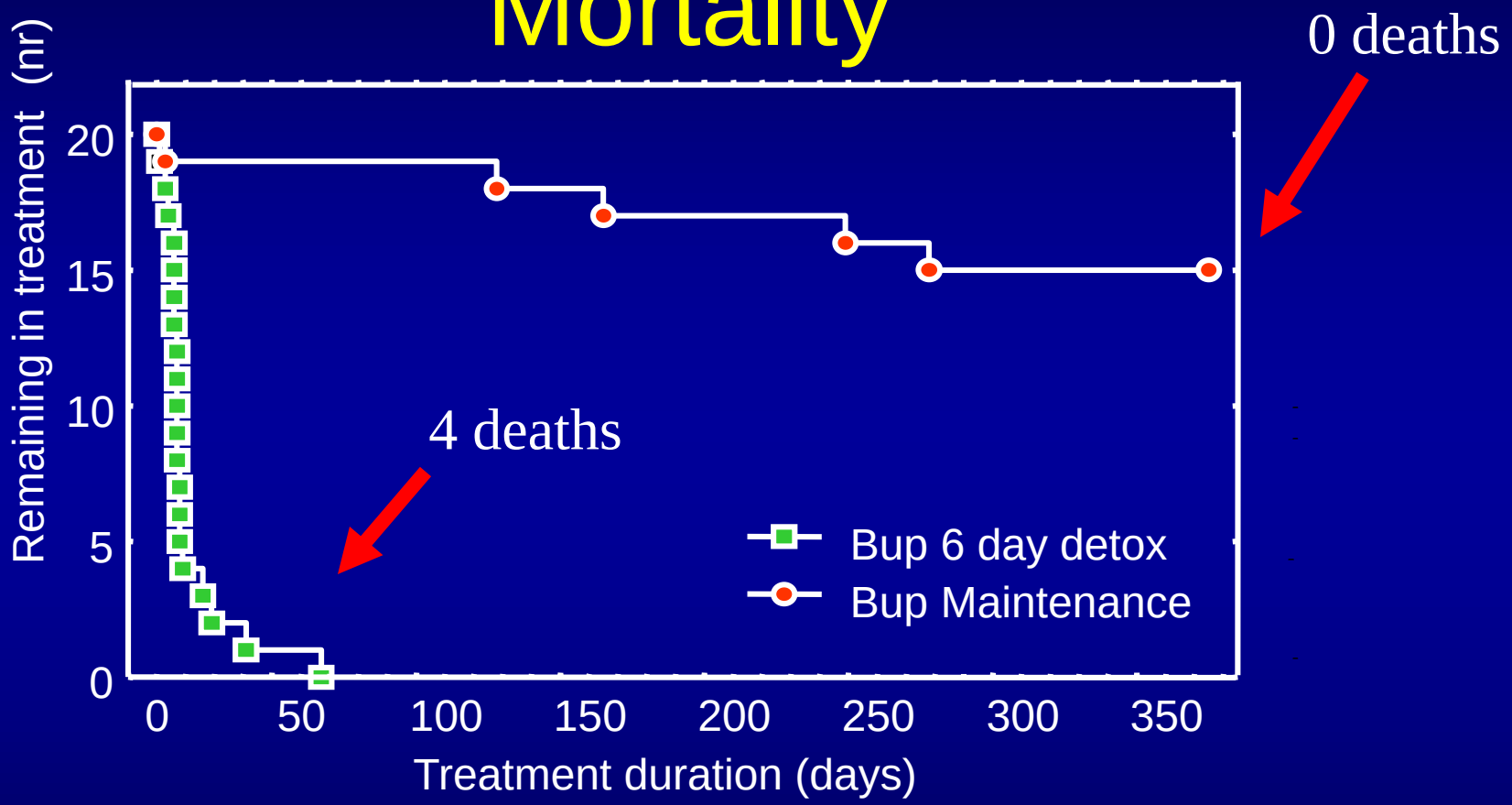
Buprenorphine for Opiate Dependence:

- Suppresses withdrawal
- Substitutes for street opiates
- Blocks subsequently administered opiates
- Safety in long term use

Opioid Agonists and Antagonists



Buprenorphine: Retention and Mortality



All Patients received group CBT Relapse Prevention, Weekly Individual Counseling, 3x Weekly Urine Screens. n=20 per group

Kakko J, Lancet 2003

Buprenophine SL, "Subutex®"

- **Mechanism of Action**
  - binds to various opioid receptors, producing agonist and antagonist effects (opioid agonist-antagonist), aka PARTIAL AGONIST
- Cost
  - $2-4.00 per 8mg sublingual pill GENERIC
  - $10.16 per 8mg sublingual pill, Subutex®

Epocrates Online Premium: https://online.epocrates.com

Buprenorphine/naloxone SL:
Suboxone®, Zubsolv®

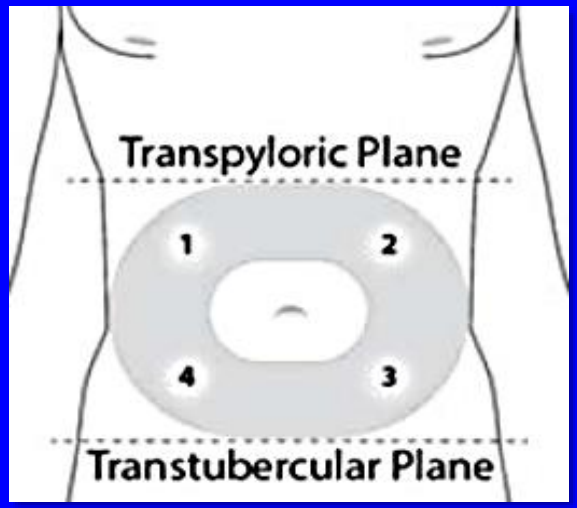
- **Mechanism of Action**
  - PARTIAL AGONIST effect with antagonist
    - Antagonist works to make formulation less likely to be injected
- COST
- $7.33 per 8mg sublingual pill
- Apx same for sublingual film
- No generic available

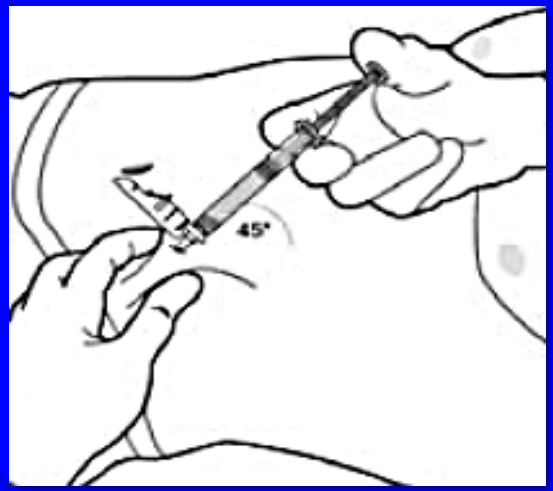
Epocrates Online Premium: https://online.epocrates.com

Buprenorphine subdermal:
Sublocade®, Brixadi®

- Sublocade®: q 4 weeks
  - 300mg X 2 then 100mg
  - Cost: apx $2000/month
- Brixadi: q 1 and/or 4 weeks
  - 8 mg per 0.16 mL, 16 mg per 0.32 mL, 24 mg per 0.48 mL, 32 mg per 0.64 mL, 64 mg per 0.18 mL, 96 mg per 0.27 mL, 128 mg per 0.36 mL
  - Cost ???
- No generic available

Epocrates Online Premium: https://online.epocrates.com





Buprenorphine Extended-Release (ER)

Subcutaneous Injection (Sublocade®)

Releases buprenorphine at controlled rate over one month:

- Mean plasma concentration with monthly 100 mg is about 10% higher than 24 mg/d of SL tablets.
- Each of the 1st two monthly SQ doses should be 300 mg/1.5 ml prefilled syringe. Doses should be separated by at least 26 days
- Subsequent doses should be 100 mg/o.5 ml prefilled syringe. Some patients may need to increase maintenance dose to 300 mg monthly.

SAMHSA TIP 63 Medications for Opioid Use Disorders. 2018

Buprenorphine Diversion

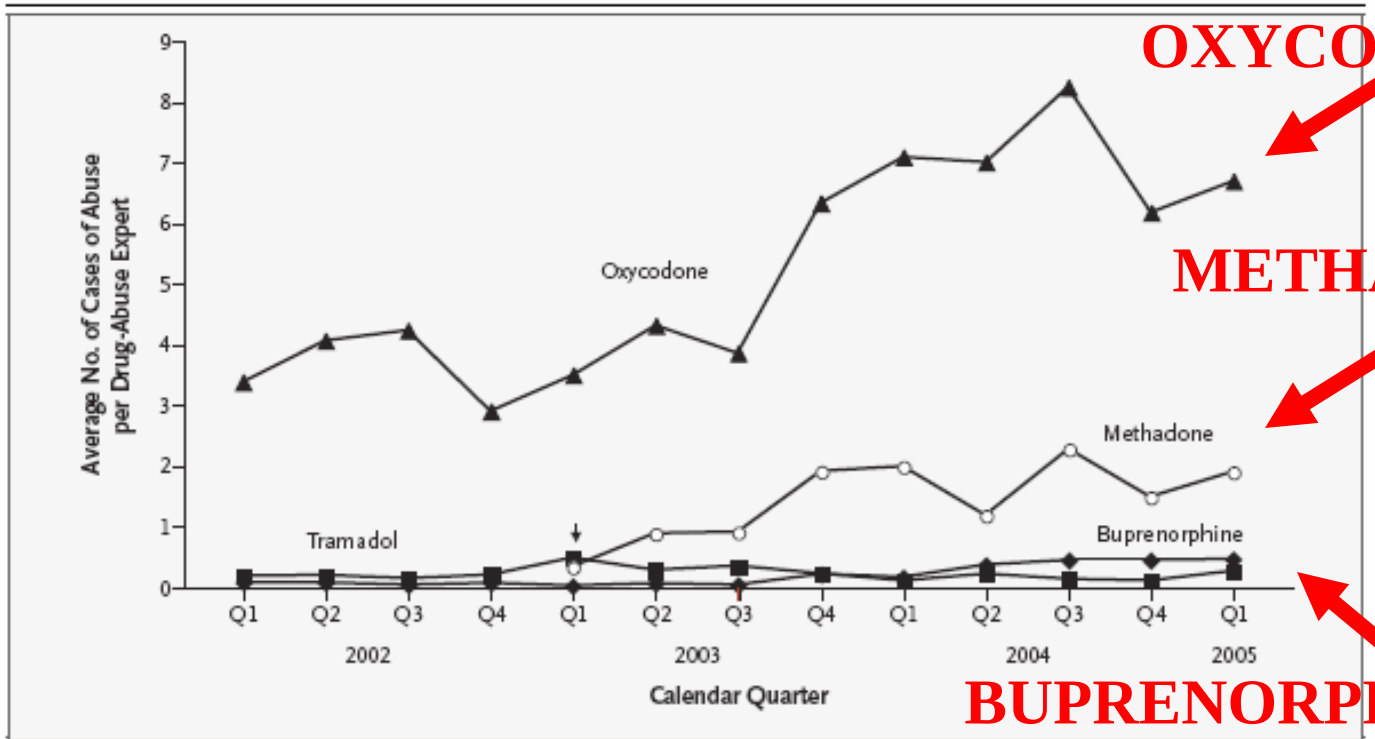


Figure 1. Average Number of Cases of Abuse of Buprenorphine Products, Methadone, Tramadol, and Oxycodone per Drug-Abuse Expert.

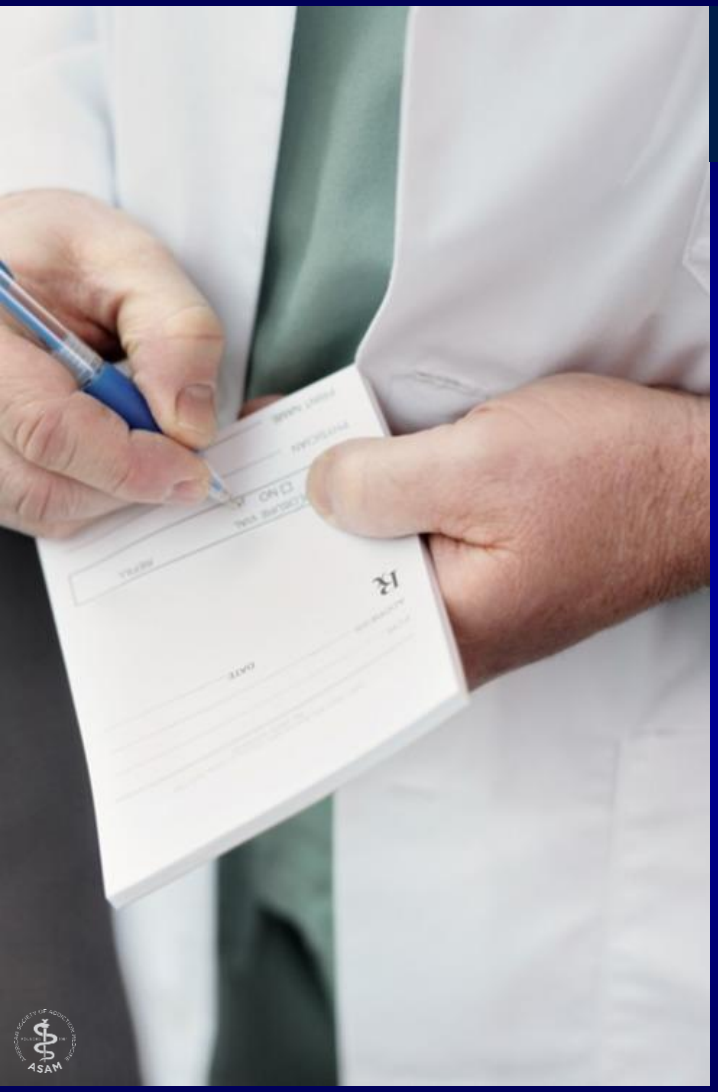
The arrow indicates the launch date of buprenorphine for use in office-based treatment of opioid dependence. Q denotes quarter.

OXYCODONE

METHADONE

BUPRENORPHINE

Cicero, NEJM 2005



Buprenorphine Maintenance

How long should buprenorphine maintenance continue?

- Patients should take medication as long as they benefit from it and wish to continue.
- There is no known duration of treatment after which patients can stop medication and be certain that they will not return to illicit opioid use.
- Given the chronic nature of OUD and potentially fatal consequences of unintended opioid overdose, ***it is critical to base length of time in treatment on patients' individual needs***.

SAMHSA TIP 63 Medications for Opioid Use Disorders. 2018

Buprenorphine Discontinuation

Important Considerations: Part 1

- How has the patient responded to treatment so far?
- Why do they want to taper?
- What do they expect will be different after the taper?
- Do they understand the risk of overdose associated with return to use?
- Do they have a safety plan?

Buprenorphine Discontinuation

Important Considerations: Part 2

- **Do they understand the risks and benefits of continuing vs discontinuing treatment?**
  - Many studies show high relapse rates with tapering and withdrawal from maintenance agonist medications.
  - Some studies show normalization of brain function with maintenance.

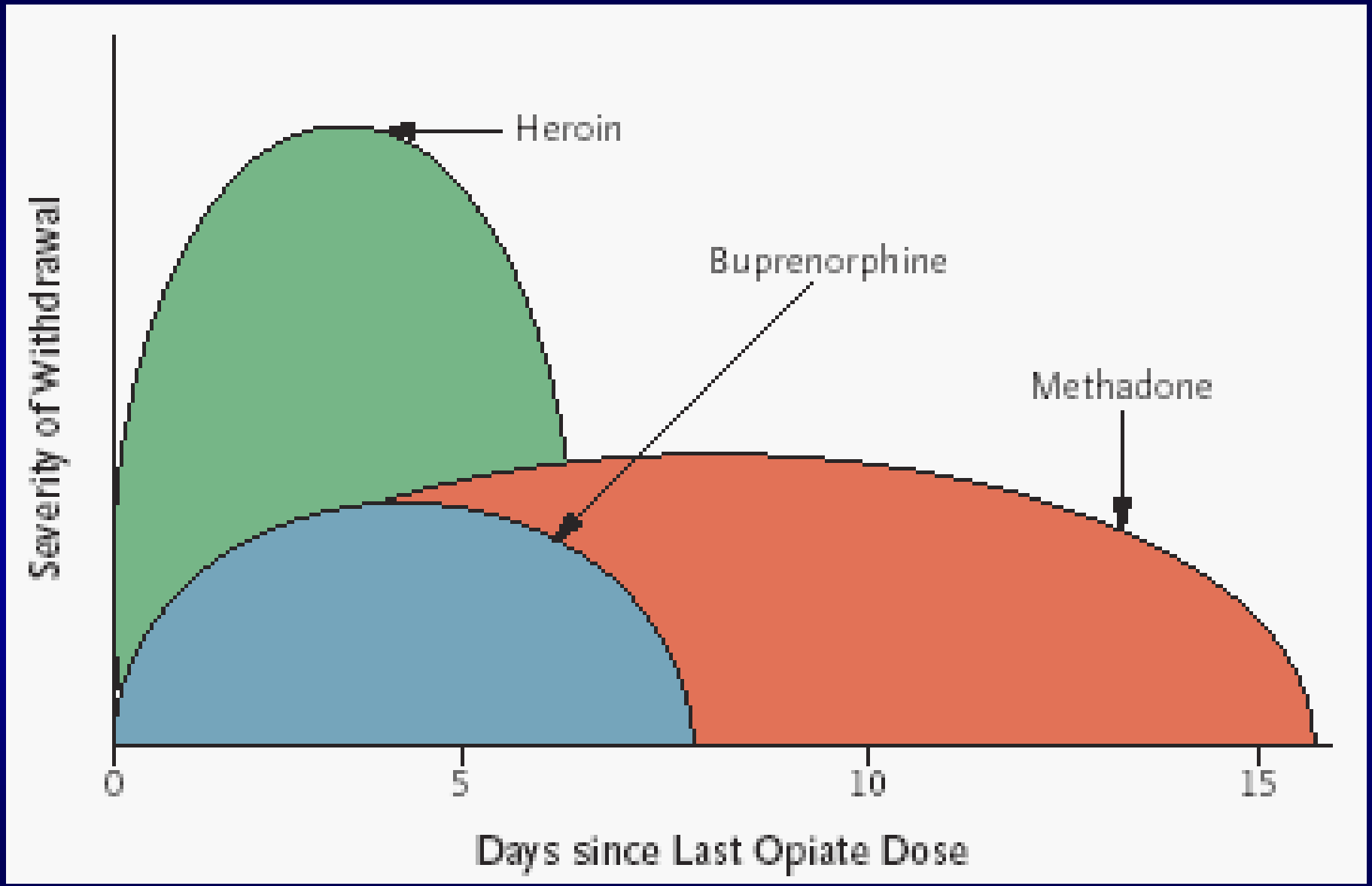
Buprenorphine Discontinuation

Important Considerations: Part 3

- **Patients should continue to be followed by provider after discontinuation.**
- Patients should be told they can resume buprenorphine treatment if cravings, lapses, or relapses occur.
- Psychosocial treatments should continue if applicable.
- Consider naltrexone.
- Associated with relapse? Do they have a safety plan?

Tapering

- ***Short-term taper ("detox") is not recommended as a stand-alone treatment.***
  - However, patients may taper from buprenorphine as part of a treatment plan.
- There is no ideal protocol but titrate slowly and carefully.
- Patient should be educated on risk of relapse after taper.
- ***ASAM does not recommend limiting length of treatment.***

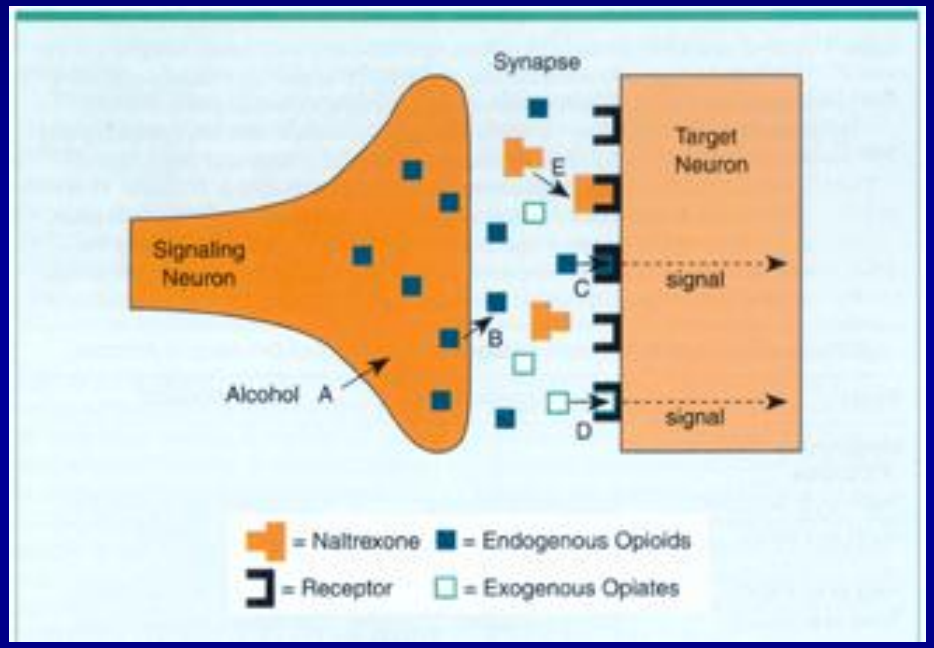

Heroin
Buprenorphine
Methadone
Severity of Withdrawal
0
5
10
15
Days since Last Opiate Dose

Oral Naltrexone, ReVia®, Depade®

- **Mechanism of Action**
  - antagonizes various opioid receptors (opioid antagonist)
- Cost
  - ReVia® 50 mg (1 bottle, 30 ea): $259.70
  - Naltrexone 50 mg (30 ea): $103.99

Epocrates Online Premium: https://online.epocrates.com

Naltrexone



- A) Alcohol is thought to stimulate the release of endogenous opioids, which may produce the euphoric feelings associated with alcohol consumption.
- B) Endogenous opioids (e.g., beta-endorphin) are released into the synapse (the space between the signaling and target neurons) and
- C) stimulate activity at opiate receptors, which produces a signal in the target neuron.
- D) Exogenous opiates such as morphine also stimulate opiate receptors.
- E) Naltrexone is thought to block opioids from activating opiate receptors.

The illustration below is from Vol. 18, No. 4, 1994 of the Journal *Alcohol Health & Research World.*

Long acting depot Naltrexone, VIVITROL®

- **Mechanism of Action** antagonizes various opioid receptors (blocks opiate mediated euphoria)
- Cost
  - 380 mg (1 vial): $1,099.96
  - Covered by many insurances

Epocrates Online Premium: https://online.epocrates.com

Naltrexone Summary

Benefits:

- Good for patients who do not want opioid agonist therapy.
- No risk of diversion (not a controlled substance).
- ***No risk of overdose by drug itself.***
- Can be administered in any setting (office-based or OTP).
- Long-acting formulation.
- Treats both opioid use disorder and alcohol use disorder.

VS.

Limitations:

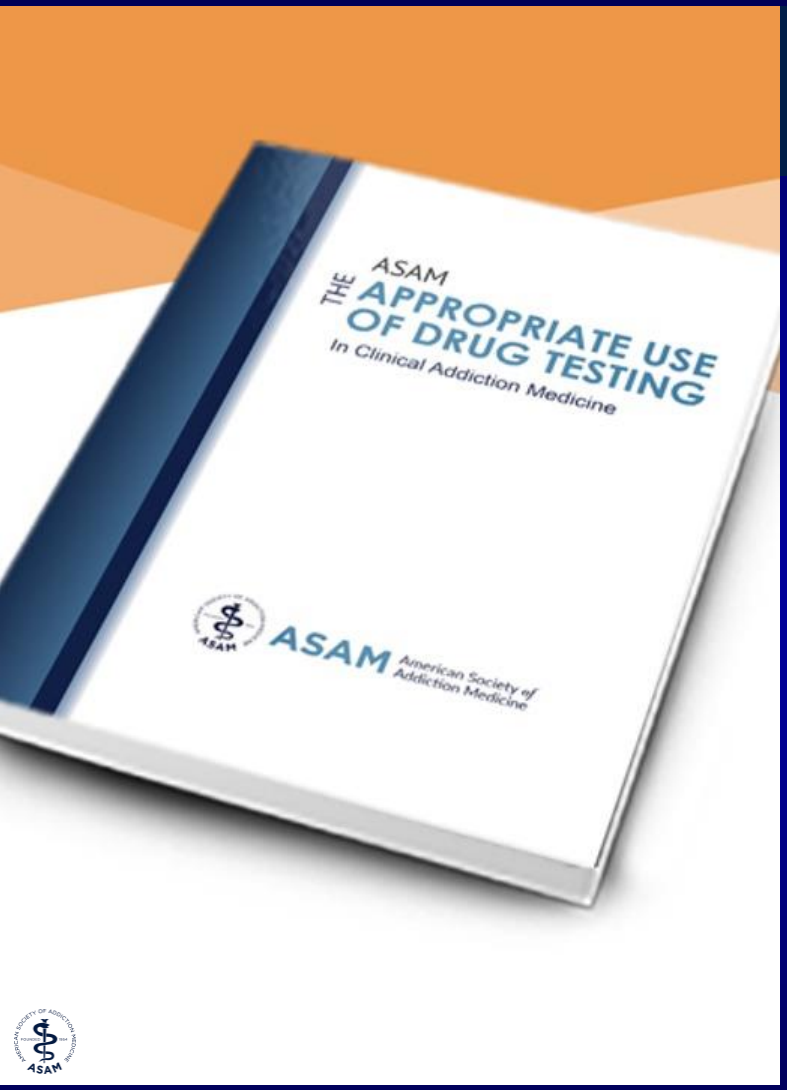
- Difficulty starting—must be fully withdrawn from opioid; > short-acting (6 days); long-acting opioids (7-10 days).
- Not suitable for patients with severe liver disease.
- Loss of tolerance to opioids increases the risk of overdose if return to pretreatment use occurs.
- Not recommended for pregnant women. Pregnant women who are physically dependent on opioids should receive treatment using methadone or buprenorphine.

ASAM National Practice Guideline for the Treatment of Opioid Use Disorder - 2020 Focused Update

Non-Pharmacological Treatment

- **Psychosocial services are often helpful.** Psychosocial services encourage utilization.
- **Additional Behavioral Therapy:** Three trials showed that additional behavioral therapy does NOT significantly improve outcomes over that achieved by buprenorphine PLUS “medical management” or “medical counseling.”
- **Patients should not be denied medication** should they refuse psychosocial services or if psychosocial services are not available.

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



Urine Drug Testing (UDT)

- ***Objective information:***
  - Evidence of therapeutic adherence
  - Evidence of use or non-use of illicit drugs
- Monitoring of treatment progress and safety
- Reinforces success with treatment, but no evidence that UDT improves outcomes
- Part of standard of care
- Identify those who may need higher level of care

ASAM's Appropriate Use of Drug Testing in Clinical Addiction Medicine Consensus Statement 2017

UDT: Frequency

- *SAMHSA TIP 63 (2018): "Periodic random testing" frequency is clinically determined.*
- At least at time of initial evaluation and initiation of medication then weekly → monthly.
- Regulation and reimbursement vary among states and insurers.
- Urine is preferred medium for testing due to:
  - Ease of obtaining sample, lowest cost
  - Ideal detection time (2-3 days)
  - Presence and persistence of metabolites
  - Availability of office-based testing tools

SAMHSA TIP 63 Medications for Opioid Use Disorders, 2018 ASAM's Consensus Statement 2017

UDT: Implementation

- *Discuss with patient:*
  - This is for safety and this is the standard of care.
- *Know scope and limits of tests and lab:*
  - Beware false negatives and positives.
- *Consider random versus scheduled testing.*
- *Incorporate quality control procedures (temperature strip).*
- *Consider establishing consult lab linkage:*
  - GCMS/LCMS confirmatory testing.
  - Expert consultation on test interpretation.
  - Online reporting of results.

ASAM's Appropriate Use of Drug Testing in Clinical Addiction Medicine Consensus Statement 2017

UDT: Immunoassays

Pros:

- Point of care or lab-based
- Fast
- Cheap
- Specific tests available for many drugs
  - Oxycodone
  - Buprenorphine
  - Fentanyl
- Can be used as screening with option for confirmation

VS.

Cons:

- Qualitative tests
  - Cutoff ng/ml
    - Opiates: 300
    - Cocaine metabolite: 300
- False positives
  - Cross-reactivity
  - Contamination
- False negatives
  - Below the cutoff

ASAM's Consensus Statement 2017

UDT: Immunoassay Detection Windows in Urine

Drug/Medication	Primary Metabolite	Ave. Detection Time (days)
Opiates (heroin, morphine)	Morphine	2-3
Semisynthetic Opioids (oxycodone, hydrocodone)	Variable Must be tested specifically	2-3
Methadone	EDDP	2-3
Buprenorphine	Nor-buprenorphine	2-3
Cocaine	benzoylecgonine	2-3
Amphetamines		2-3
Benzodiazepine	Varies by medication type	Variable with half life Unreliable immunoassays
Cannabis Occasional Cannabis Chronic	THC	1-3 Up to 30

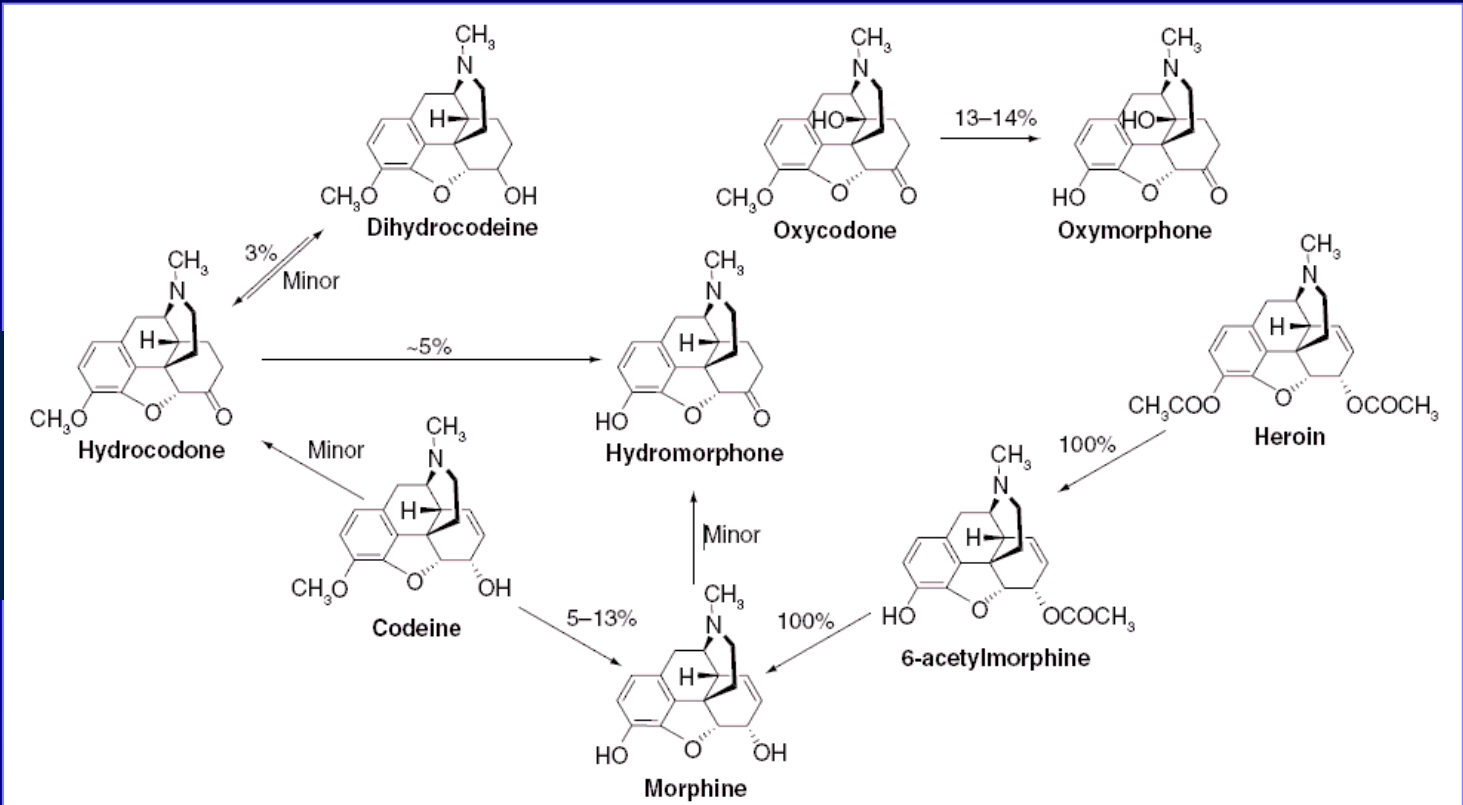
ASAM's Consensus Statement 2017

UDT: GCMS/LCMS

- *Gas or liquid chromatography, mass spectrometry*
- *Quantitative*
- *Limitations*
  - More costly
  - Requires specialized lab
  - Levels do not indicate amount of medication taken!
    - *Variables:*
      - time of dosing
      - metabolism
      - GFR
      - hydration

ASAM's Consensus Statement 2017

UDT: Opioid Metabolism



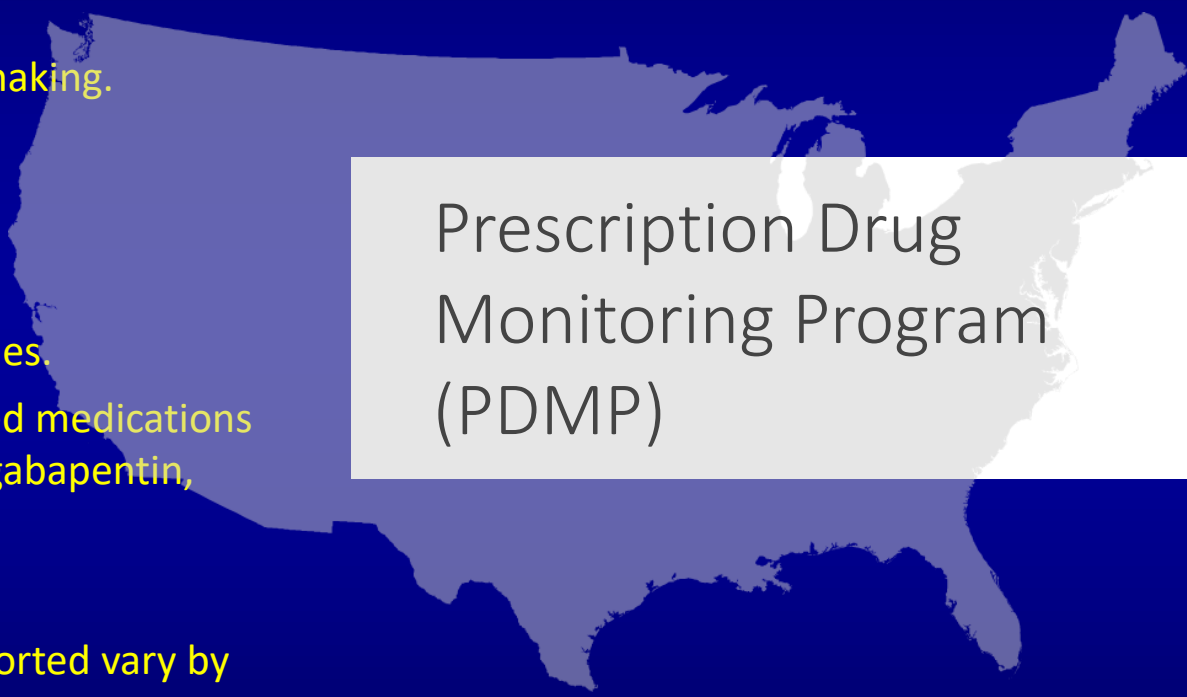
Reisfield GM et al. *Bioanalysis.* 2009;1(5):937-52.

Pill Counts

- ***Objective information:***
  - Confirm medication adherence.
  - Minimize diversion.
- Frequency varies with patient progress.
- Best option when diversion suspected.
- Patient brings in medication supply.
- Confirm patient ID and fill date on bottle/box.
- Have patient count them in front of staff member.
- All tablets should be identical.
- Amount should match expected quantity.

Prescription Drug Monitoring Program (PDMP)

- ***State-wide System Tracking Prescriptions:***
  - Decreasing or preventing misuse of medications.
  - Improving clinical decision-making.
- ***Pharmacies:***
  - Report information to state.
- ***Information Varies:***
  - Schedule II +/- other schedules.
  - Some selected non-scheduled medications with misuse potential: e.g., gabapentin, ephedrine.
- ***Data Availability:***
  - Format and medications reported vary by state.



PDMP: Limitations

- Methadone and buprenorphine dispensed from OTPs are not listed on PDMPs.
- Not all data is readily available to providers.
- There is a lack of communication between all state programs.
- Time is needed to access reports.
- There are limitations in who can access reports.
- There is a mandatory vs. voluntary use of PDMP.

Questions?

- Contact info:

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References

- *Tomkins DN, Sellers EM (2001)* Addiction and the brain: the role of neurotransmitters in the cause and treatment of drug dependence. *Canadian Medical Association Journal* 164 817-821
- O'Connor P, Fiellin DA. (2000) Pharmacological Treatment of Heroin-Dependent Patients *Annals of Internal Medicine* 133 40-54
- Sneader W. (1998)The Discovery of Heroin. *Lancet* 352 (9141) 1697-1699
- Rang HP, Dale MM, Ritter JM (1999). Pharmacology 4th ed. Edinburgh : Churchill Livingstone
- Wills S (1997) Drugs of abuse. London : Pharmaceutical Press
- Methadone Maintenance and Other Pharmacotherapeutic Interventions in the Treatment of Opioid Addiction." April 2002, Vol. lll, No. 1
- Reshevska, I., K. Foreit, K. Beardsley, and L. Porter. 2010. *Policy Advocacy Toolkit for Medication-Assisted Treatment (MAT) for Drug Dependence*. Washington, DC: Futures Group, Health Policy Initiative, Task Order 1.
- http://www.dpt.samhsa.gov/patients/mat.aspx
- http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm198176.htm
- Epocrates Online Premium: https://online.epocrates.com
- *MEDICATION ASSISTED TREATMENT* Michael Fingerhood MD FACP. Medications. Opiates. Naltrexone; Methadone; Buprenorphine. Alcohol **...** *maryland-adaa.org/content_documents/.../FingerhoodMATWorkshop.**pp***
- Thomas E. Freese, SBIRT slides, UCLA Integrated Substance Abuse Programs, tfreese@mednet.ucla.edu

Q & A