

An Overview of Medication Assisted Treatment

**Thomas E. Freese, PhD
Gloria M. Miele, PhD**

**UCLA Integrated Substance Abuse Programs
Pacific Southwest ATTC**

www.uclaisap.org

www.psattc.org

Disclosure

- The speakers do not have relevant financial relationships with commercial interests.

OBJECTIVES OF THIS WEBINAR

After this webinar training, participants will be able to

- Describe at least three (3) acute and chronic effects of opioids.
- Evaluate the prevalence of and key populations impacted by opioid use.
- Specify at least two (2) medications that are available to treat opioid use disorders.
- Recommend at least two (2) strategies that can be used to address health disparities through increased access to medication-assisted treatment

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FRONTIERS IN NEUROSCIENCE: THE SCIENCE OF SUBSTANCE ABUSE

Addiction Is a Brain Disease, and It Matters

Alan I. Leshner

Scientific advances over the past 20 years have shown that drug addiction is a chronic, relapsing disease that results from the prolonged effects of drugs on the brain. As with many other brain diseases, addiction has embedded behavioral and social-context aspects that are important parts of the disorder itself. Therefore, the most effective treatment approaches will include biological, behavioral, and social-context compo-

Recognizing addiction as a chronic, relapsing brain disorder characterized by compulsive drug seeking and use can impact society's overall health and social policy strategies and help diminish the health and social costs associated with drug abuse and addiction.

affects both the health of the individual and the health of the public. The use of drugs has well-known and severe negative consequences for health, both mental and physical. But drug abuse and addiction also have tremendous implications for the health of the public, because drug use, directly or indirectly, is now a major vector for the transmission of many serious infectious diseases—particularly acquired immunodeficiency syndrome (AIDS), hepatitis, and tu-

Why do people take drugs?

To feel good
To have novel:
Feelings
Sensations
Experiences
AND
To share them



To feel better
To lessen:
Anxiety
Worries
Fears
Depression
Hopelessness
Withdrawal

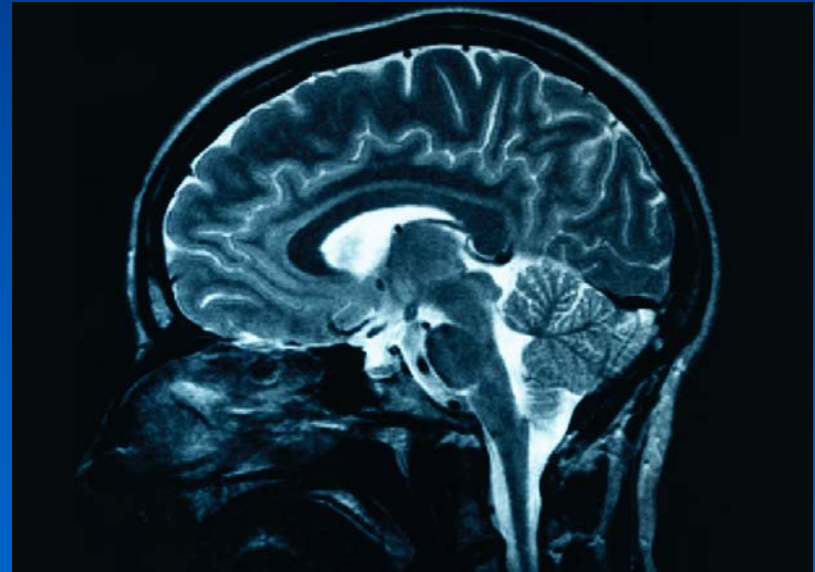


In other words:

**A Major Reason People
Take a Drug is they Like
What It *Does to Their Brains***

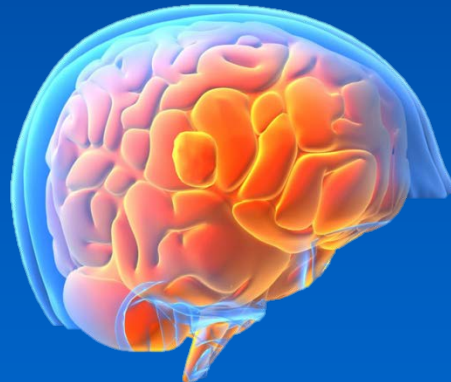
Drug addiction is a chronic brain disorder

The brain shows distinct changes after drug use that can persist *long after the drug use has stopped*



Why can't people just stop drug use?

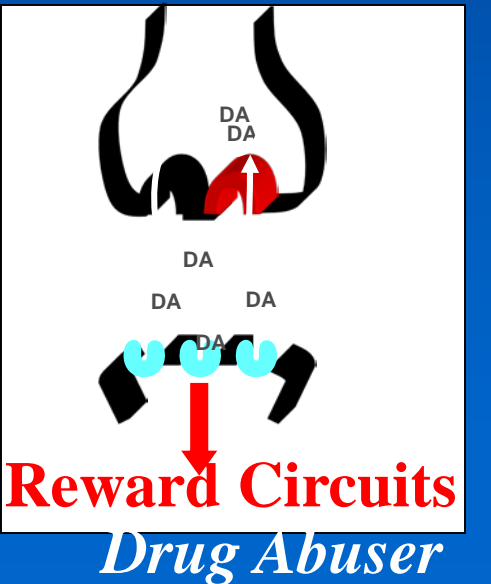
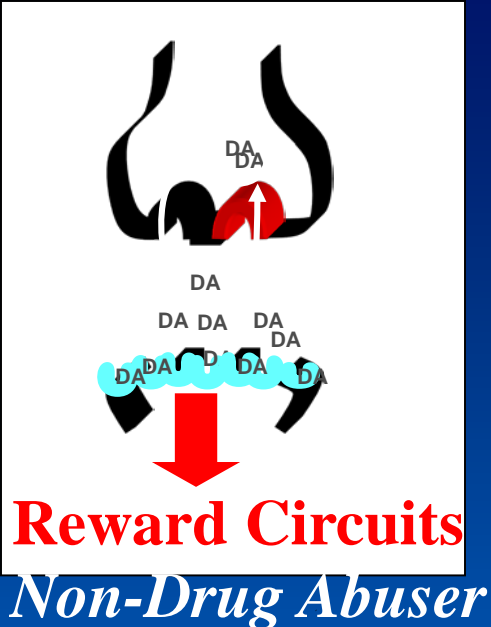
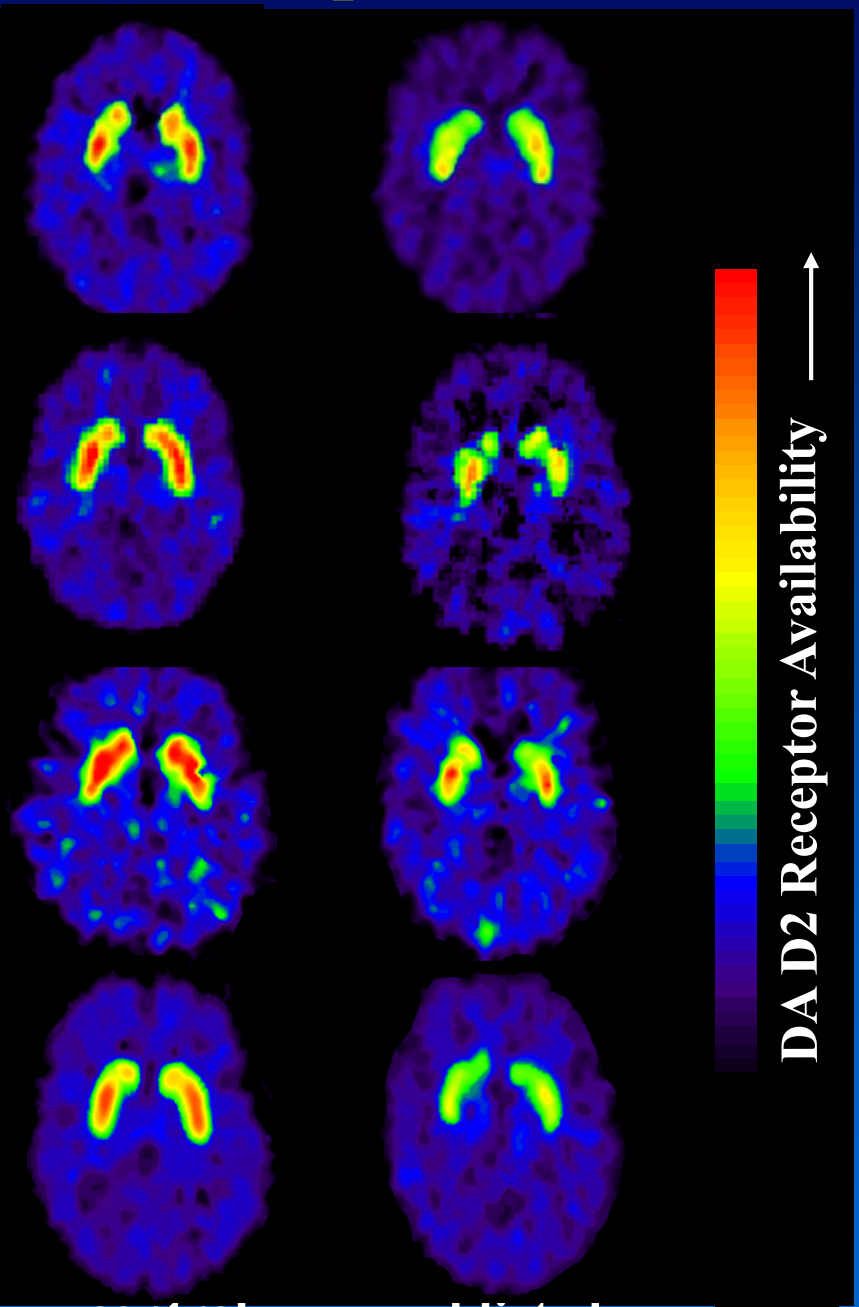
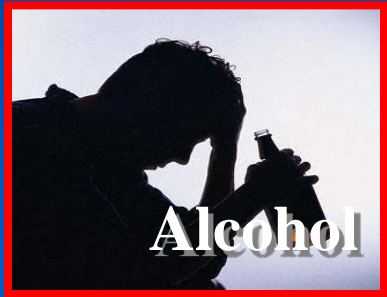
Prolonged drug use changes the brain in fundamental and long-lasting ways!



Dopamine

- Dopamine (DA) is the neurotransmitter that's most responsible for pleasure by activating the reward pathway, and is implicated in drug cravings and euphoria.
- In a typical day, the brain produces 50 ng/dl of DA per day, and about 100 ng/dl on a REALLY good day.
- Comparatively, substances of abuse result in excessive DA production and release:
 - Tobacco → 450 ng/dl
 - Marijuana → 650 ng/dl
 - Heroin → 975 ng/dl
 - Methamphetamine → 1100 ng/dl (> 20x normal DA release!)

Dopamine D2 Receptors are Lower in Addiction



Impact of Drugs on Dopamine

- Drugs of abuse can lead to lasting changes to brain chemistry, particularly involving DA.
- SUD leads to an over-release of DA - the brain becomes accustomed to these unnaturally elevated DA levels and its equilibrium is shifted.
 - Higher and higher levels of DA are needed to experience pleasure (tolerance) → patients often continue using substances to address their perceived deficit in dopamine availability
- Brain wants to maintain homeostasis
 - Over time, the brain senses these high DA levels and begins producing less DA in response, which leads to an overall deficiency of DA in the brain.

Imagine...

You have been 5 years clean and sober from all drugs and alcohol after decades of relapse and turmoil with friends and family. As a result of these experiences, you've worked hard to become a substance use disorder (SUD) counselor in order to help others who are struggling with similar addictions.

While attending a conference, you learn about a new treatment option for SUDs that has been demonstrated to:

- Increase abstinence and treatment retention rates by 25%
- Increase treatment engagement rates by 30%

As an SUD Treatment Provider, What Would You Do?

- A. Steer your clients toward the treatment approach that worked for you – without this new treatment – reasoning that what worked for you should work for them as well.

- B. Research this new treatment intervention so that you're able to tell your clients about its potential benefits in order to give them access to every available tool and advancement in the field of addiction treatment, and to better allow them to make informed decisions about their care.

The Power (and limitations) of Personal Experience

- A majority of SUD treatment providers are in recovery themselves, and thus have personal or lived experience.
- Personal / lived experience in SUD treatment is **POWERFUL**, and can be an immensely effective treatment tool by allowing us to connect with our clients in ways that are more difficult for others without these experiences.

The Power (and limitations) of Personal Experience

- However, personal / lived experience can also be limiting if it is our primary treatment perspective, and if we overly rely on it to both guide our approach toward treatment and anticipate the needs of others because:
 - Everyone and every situation is different.
 - SUDs are among the most complex health conditions to treat → condition involving the most complex organ of the body (brain) with complex biopsychosocial origins
 - It can be very difficult to know what we don't know.
 - Human nature often leads us to avoid things we don't understand, and we are all experts in our own personal experiences.

Bottom-line → There is more than one path to recovery, and it's important for providers to understand how our personal perspectives influence how we talk to our clients about their treatment decisions.



Medications are drugs, and you cannot be “clean” if you are taking anything.

- 1) Millions of Americans use medications (e.g., Zyban, nicotine patches) to quit smoking**
- 2) Physical dependence and addiction are not the same thing.**
- 3) The goal of SUD treatment is to assist a client in stopping his or her compulsive use of AOD and live a normal, functional life.**
- 4) Pharmacotherapies are effective.**



Alcoholics Anonymous (AA) & Narcotics Anonymous (NA) do not support the use of medications.

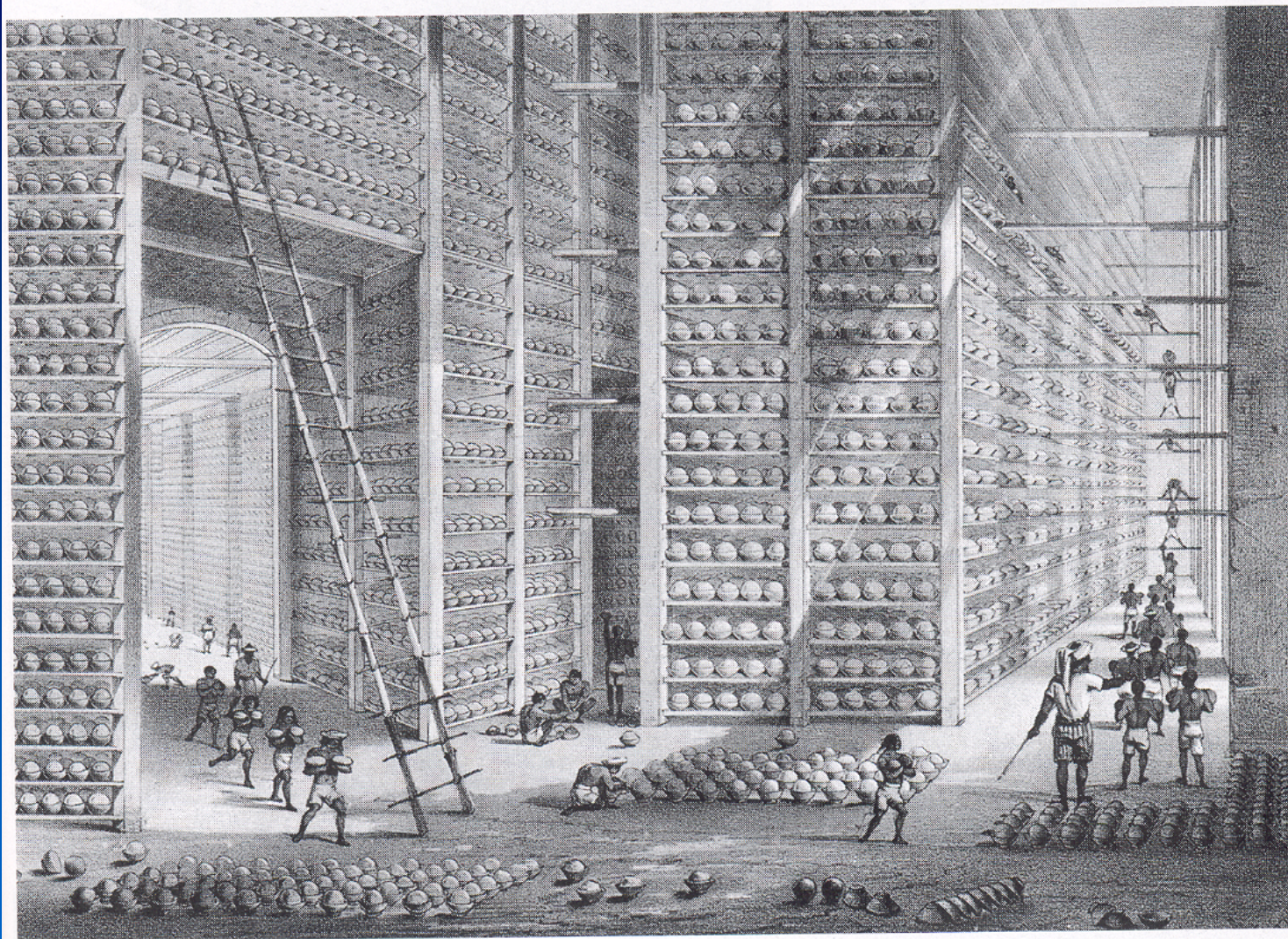
- 1) AA/NA literature and founding members did not speak or write against using medications. In fact, AA/NA endorses participants to use medicines as prescribed for the treatment of medical conditions.**
- 2) Some AA/NA meetings hold negative opinions about MAT. It is therefore important to educate clients about how to participate in meetings if they are taking these medications.**

What A.A.'s "The Big Book" says...

*"But this does not mean that we disregard human health measures. God has abundantly supplied this world with fine doctors, psychologists, and practitioners of various kinds. Do not hesitate to take your health problems to such persons. Most of them give freely of themselves, that their fellows may enjoy sound minds and bodies. Try to remember that though God has wrought miracles among us, we should **never belittle a good doctor or psychiatrist.** Their **services are often indispensable** in treating a newcomer and in following his case afterward."*

[Chapter 9, p. 133 (emphasis added)]





Stacking Room at East India Company's opium factory at Patna (1850). *Wellcome Library, London.*

BAYER

PHARMACEUTICAL PRODUCTS.

We are now sending to Physicians throughout the United States literature and samples of

ASPIRIN

The substitute for the Salicylates, agreeable of taste, free from unpleasant after-effects.

HEROIN

The Sedative for Coughs,

HEROIN HYDROCHLORIDE

Its water-soluble salt.

You will have call for them. Order a supply from your jobber.

Write for literature to

FARBENFABRIKEN OF ELBERFELD CO.

40 Stone Street, New York,

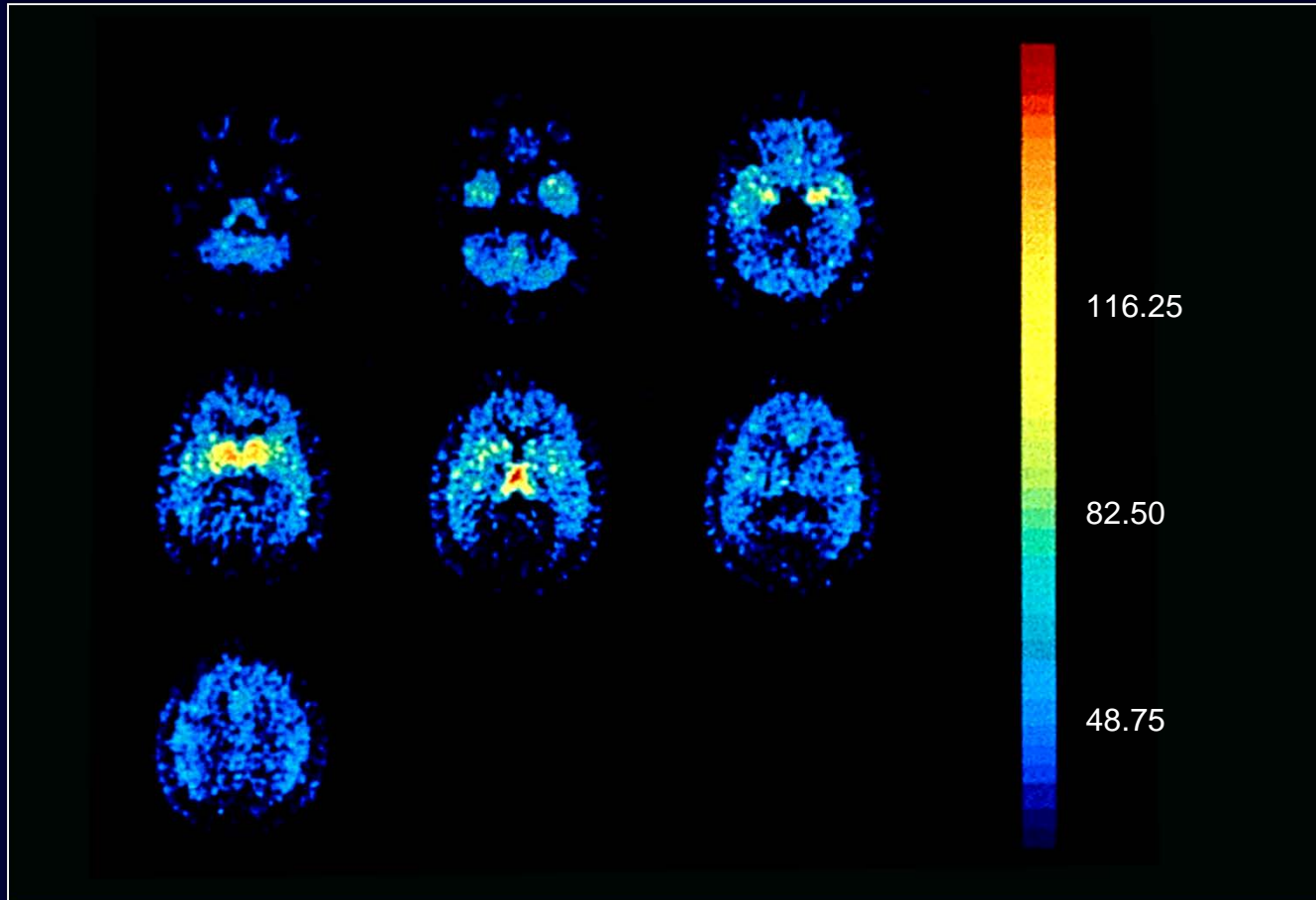
SOLE AGENTS

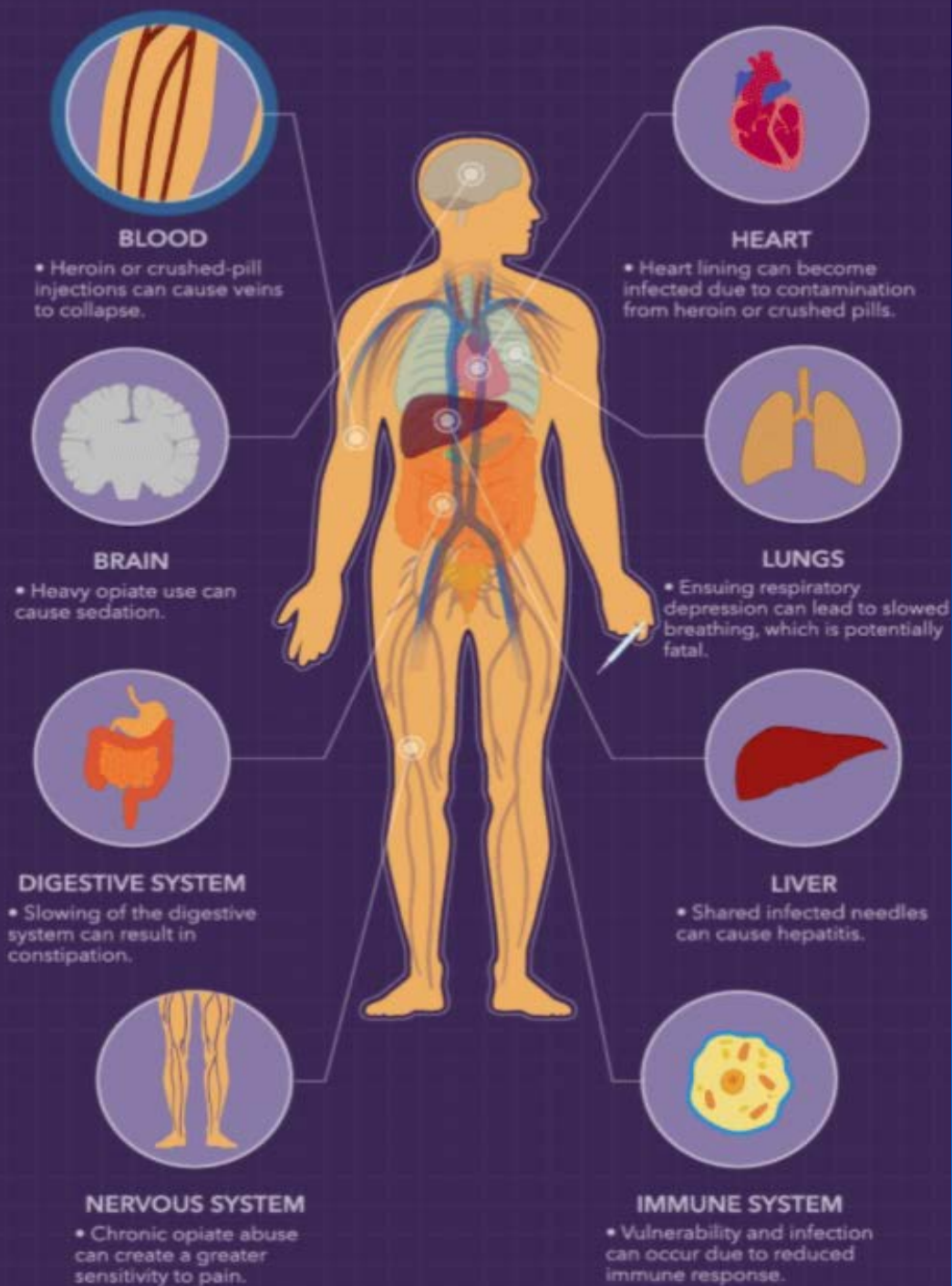
What are Opioids?



- Opiate: derivative of opium poppy
 - Morphine
 - Codeine
- Opioid: any compound that binds to opiate receptors
 - Semisynthetic (including heroin)
 - Synthetic
 - Oral, transdermal and intravenous formulations
- Narcotic: legal designation

[¹⁸F] Cyclofoxy (a Selective Opioid Antagonist) Binding in Human Brain: Normal Volunteer PET Study - NIH



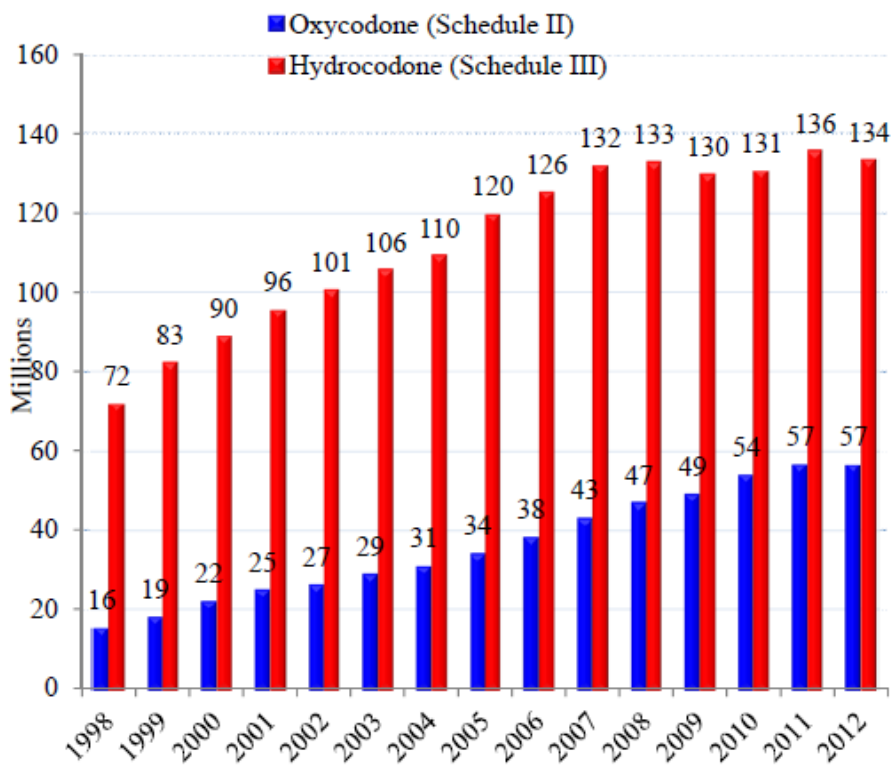


The effects of opioids on the body

Opioid Risk and Trends

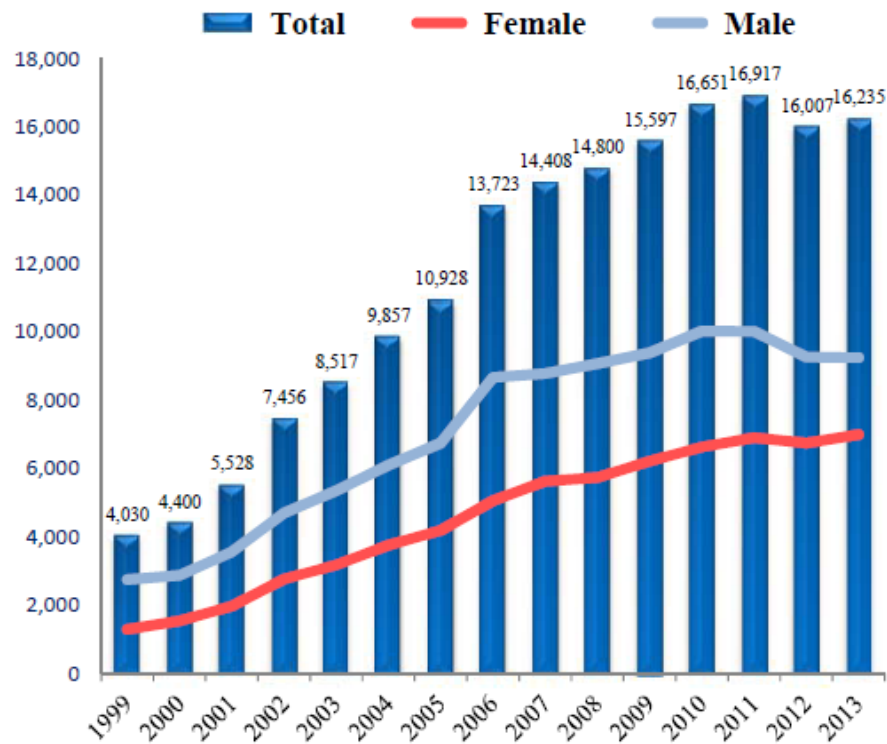
High Levels of Opioid Prescriptions have Facilitated Diversion & Contributed to Overdose Deaths

Oxycodone & Hydrocodone Prescriptions



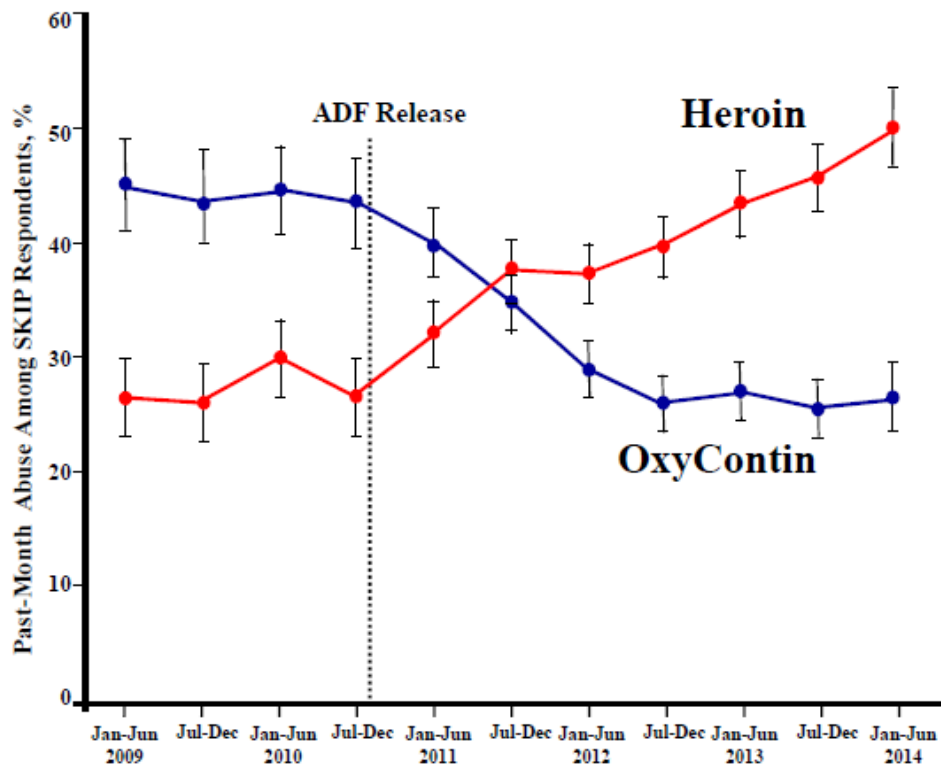
SDI Health, VONA_02-1-13_Opioids Schedule II & III

Rx Opioid Overdose Deaths

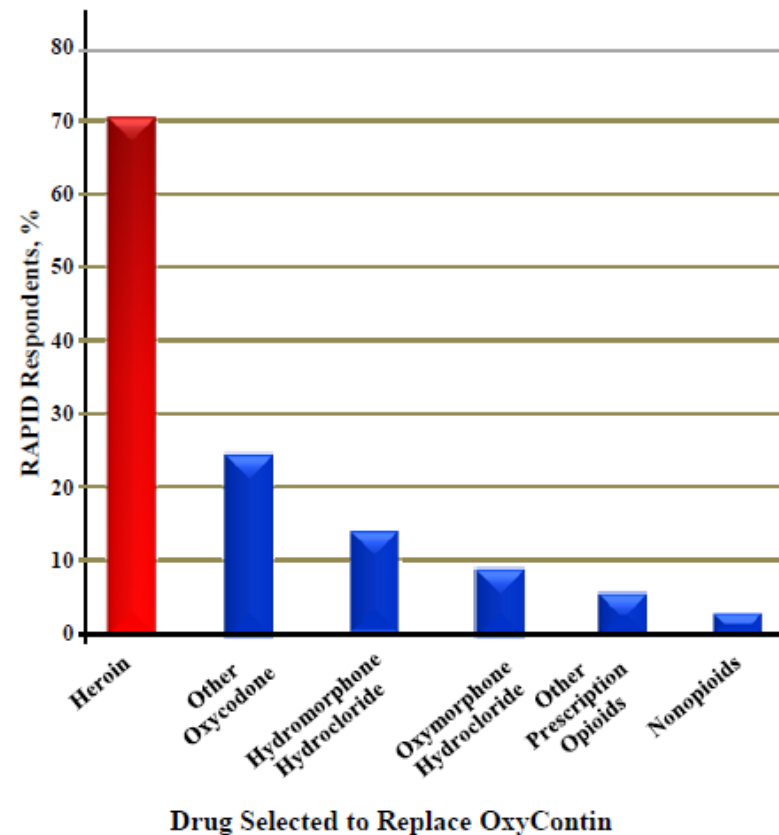


Source: CDC Wonder

Respondents Who Endorsed Past-Month Use of OxyContin or Heroin Before and After Introduction of an Abuse-Deterrent Formulation (ADF)



Drugs Used to Replace OxyContin After the Introduction of the Abuse-Deterrent Formulation (ADF)



Cicero TJ and Ellis MS *JAMA Psychiatry*. Published Online March 11, 2015.

Demographics

*Past Month Use,
Nonmedical Users of Opioid Pain Relievers/
Heroin Users*

By Age

Age	Use % (estimate)
Nonmedical Users of Opioid Pain Relievers	
12-17	10% (467,000)
18-25	23% (978,000)
26 and older	67% (2,900,000)
Heroin Users	
12-17	4% (16,000)
18-25	19% (82,000)
26 and older	77% (337,000)

By Gender, 12 and Older

Gender	Use % (estimate)
Nonmedical Users of Opioid Pain Relievers	
Female	45% (1,956,000)
Male	55% (2,369,000)
Heroin Users	
Female	40% (116,000)
Male	60% (173,000)

By Race/Ethnicity, 12 and Older

Primary Race/Ethnicity	Use % (estimate)
Nonmedical Users of Opioid Pain Relievers	
White	62.6% (2,612,000)
Black	16.5% (691,000)
Hispanic	18.1% (757,000)
Am. Indian/AK Native	0.6% (26,000)
Asian	2% (86,000)
Heroin Users (TEDS, 2012)*	
White/Hispanic	70% (205,000)
Black	15% (44,000)
Am. Indian/AK Native	0.9% (2,600)
Asian	0.6% (1,700)



Each day, more than
1,000
PEOPLE

are treated in
emergency
departments for
not using prescription
opioids as directed.





Every 20 minutes!!!



91
AMERICANS

die every day from
an **opioid overdose**
(that includes prescription
opioids and heroin).

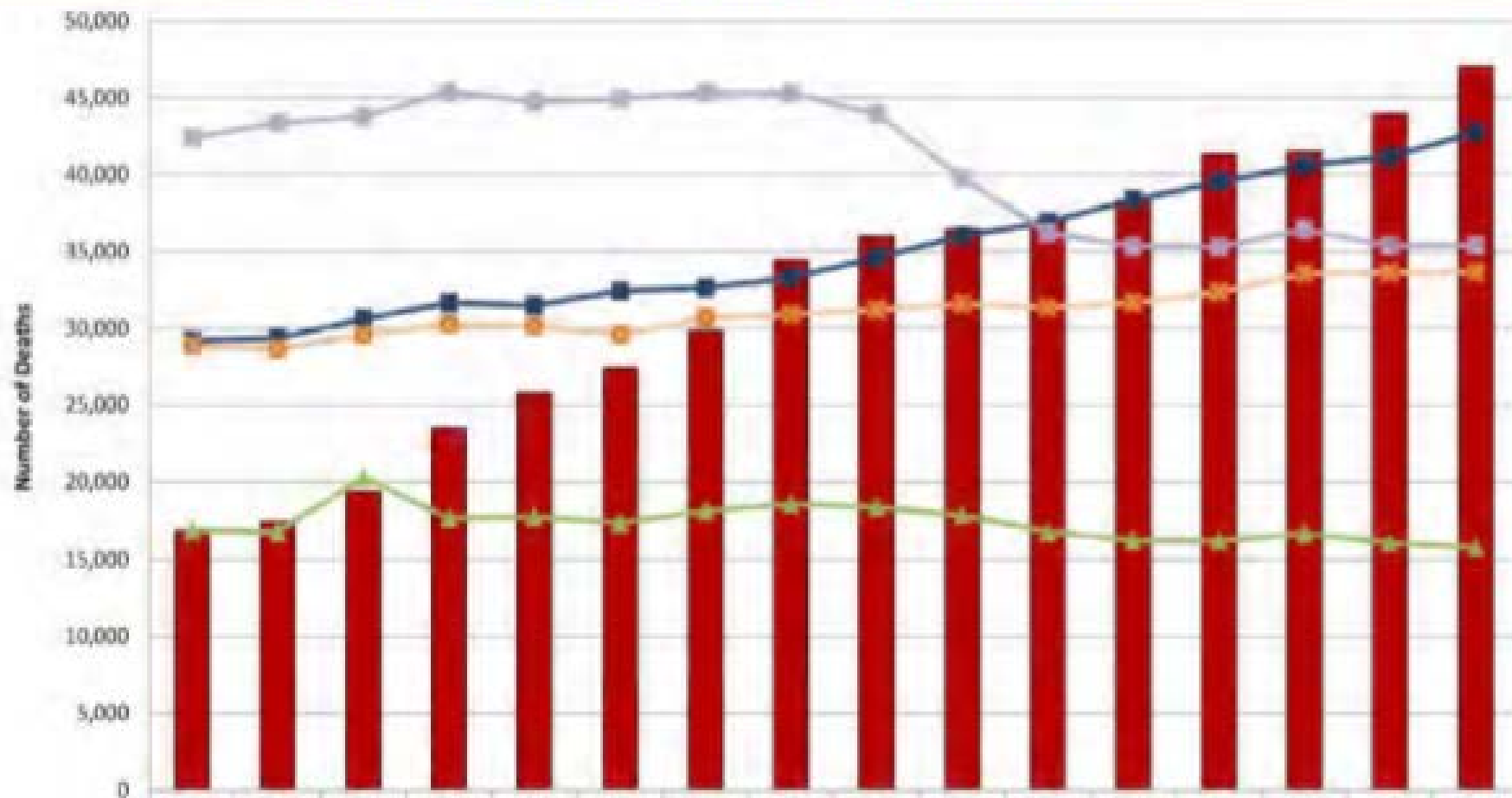
Figure 76. Two Milligrams of Fentanyl - A Potential Lethal Dose



Source: Network Environmental Systems (NES)

A lethal dose of carfentanil 1/100th of the amount shown next to the penny.

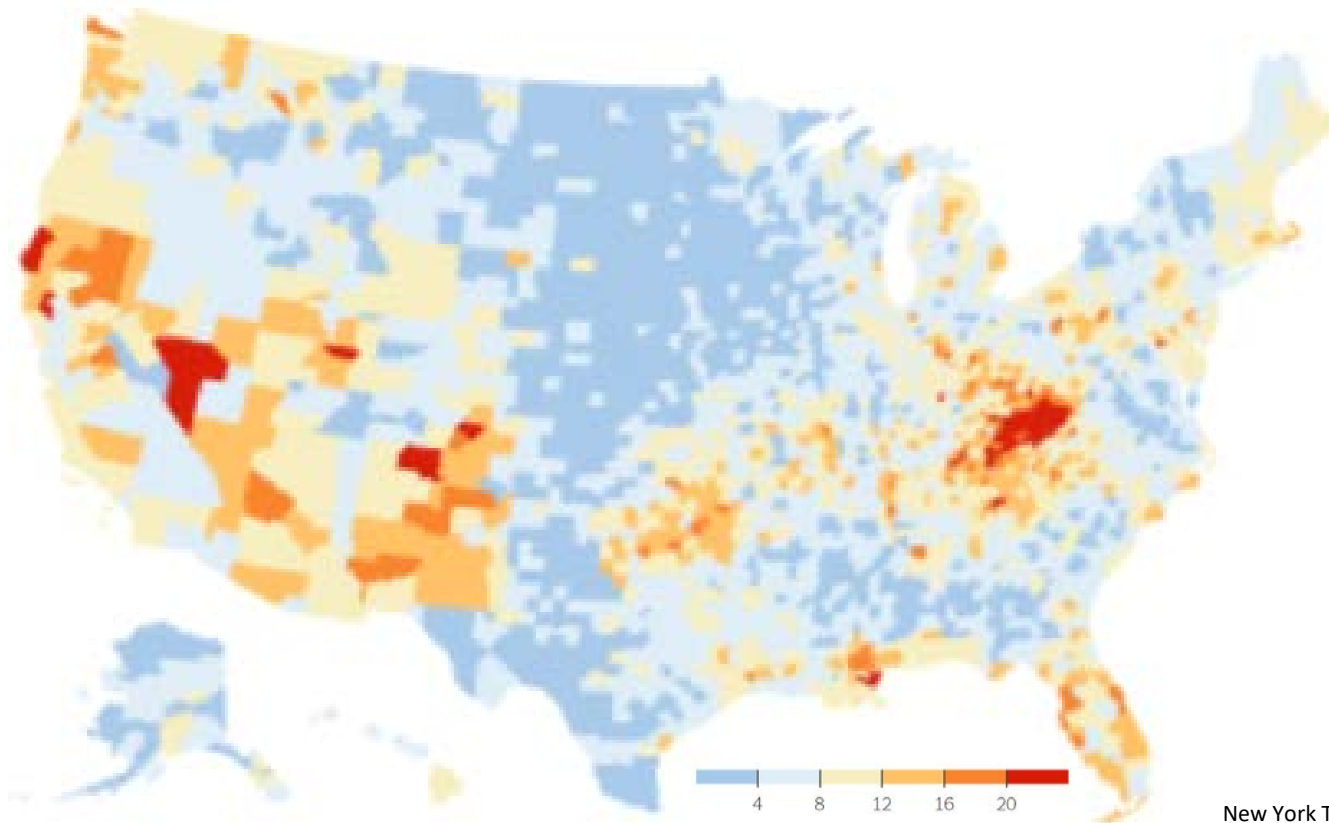
Figure 1. Number of Injury Deaths by Drug Poisoning, Suicide, Homicide, Firearms, and Motor Vehicle Crashes in the United States, 1999-2014^{a,b}



	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Drug Poisoning	16,849	17,415	19,394	23,518	25,785	27,424	29,813	34,425	36,010	36,450	37,004	38,329	41,340	41,502	43,982	47,055
Suicide	29,199	29,350	30,622	31,655	31,484	32,439	32,637	33,300	34,598	36,035	36,909	38,364	39,518	40,600	41,149	42,773
Homicide	16,889	16,765	20,308	17,638	17,732	17,357	18,124	18,573	18,361	17,826	16,799	16,259	16,238	16,688	16,121	15,809
Firearms	28,874	28,663	29,573	30,242	30,136	29,569	30,694	30,896	31,224	31,593	31,347	31,672	32,351	33,563	33,636	33,674
MV Crashes	42,401	43,354	43,788	45,380	44,757	44,933	45,343	45,316	43,945	39,790	36,216	35,332	35,303	36,415	35,369	35,398

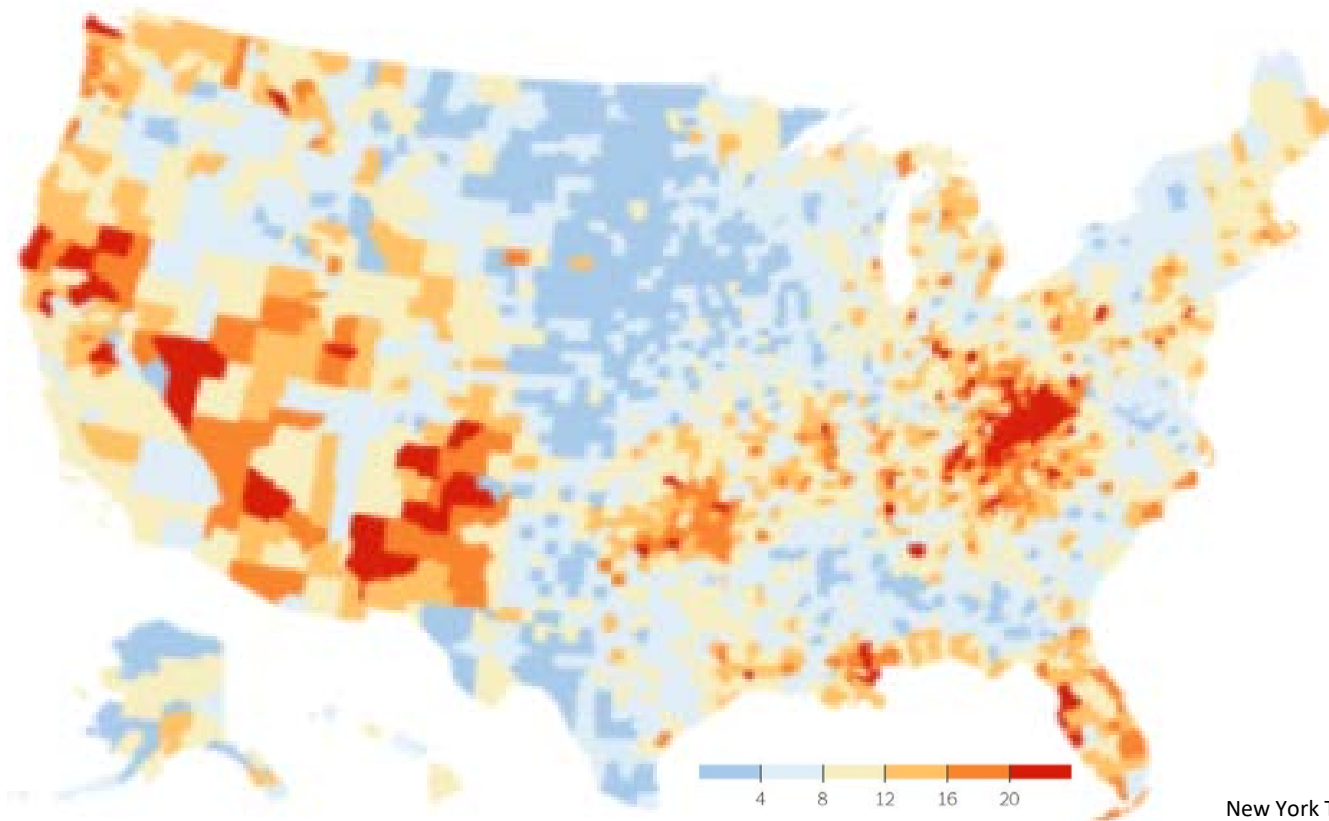
Source: Centers for Disease Control Prevention

Overdose Deaths per 100,000 2003



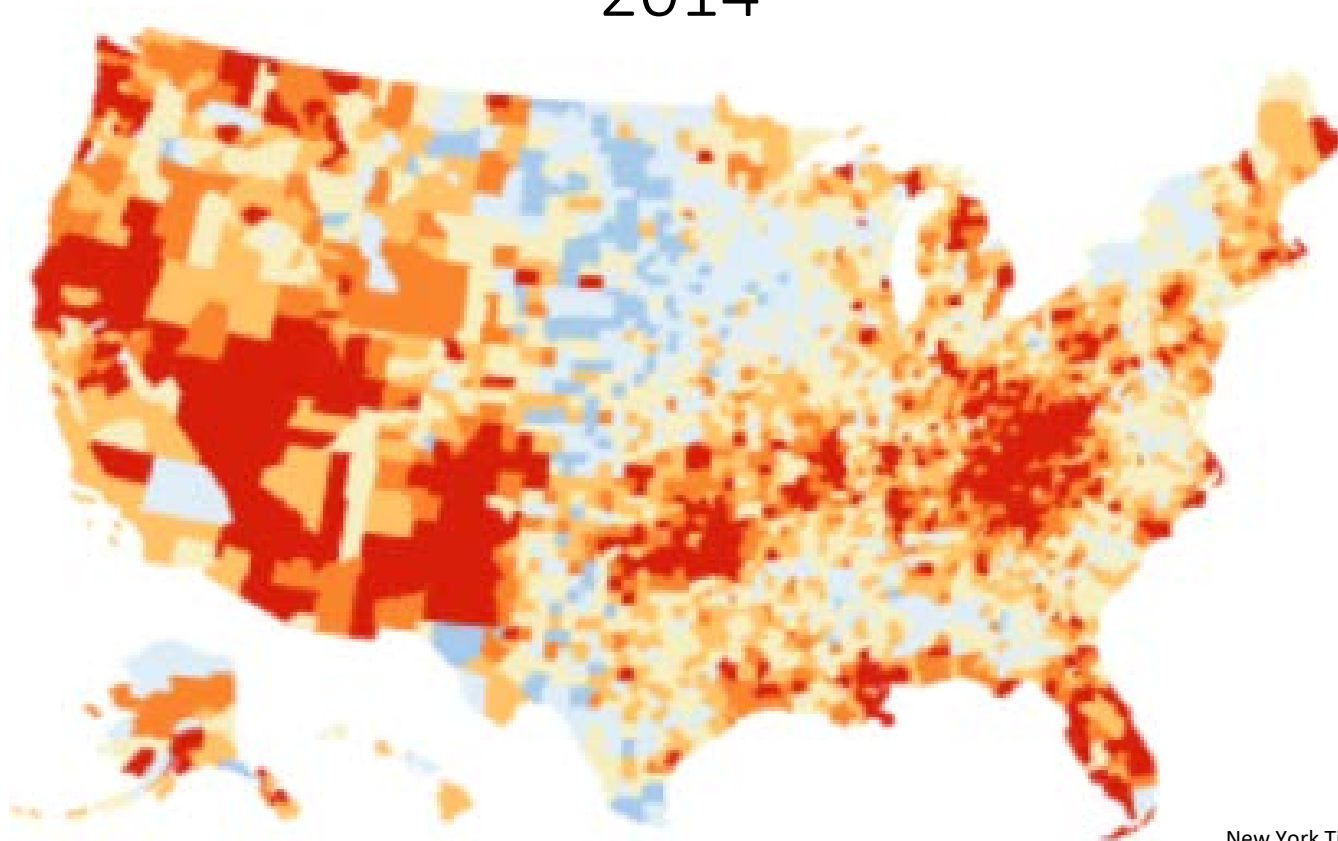
New York Times: <https://nyti.ms/2jVUIKb>

Overdose Deaths per 100,000 2007



New York Times: <https://nyti.ms/2jVUIKb>

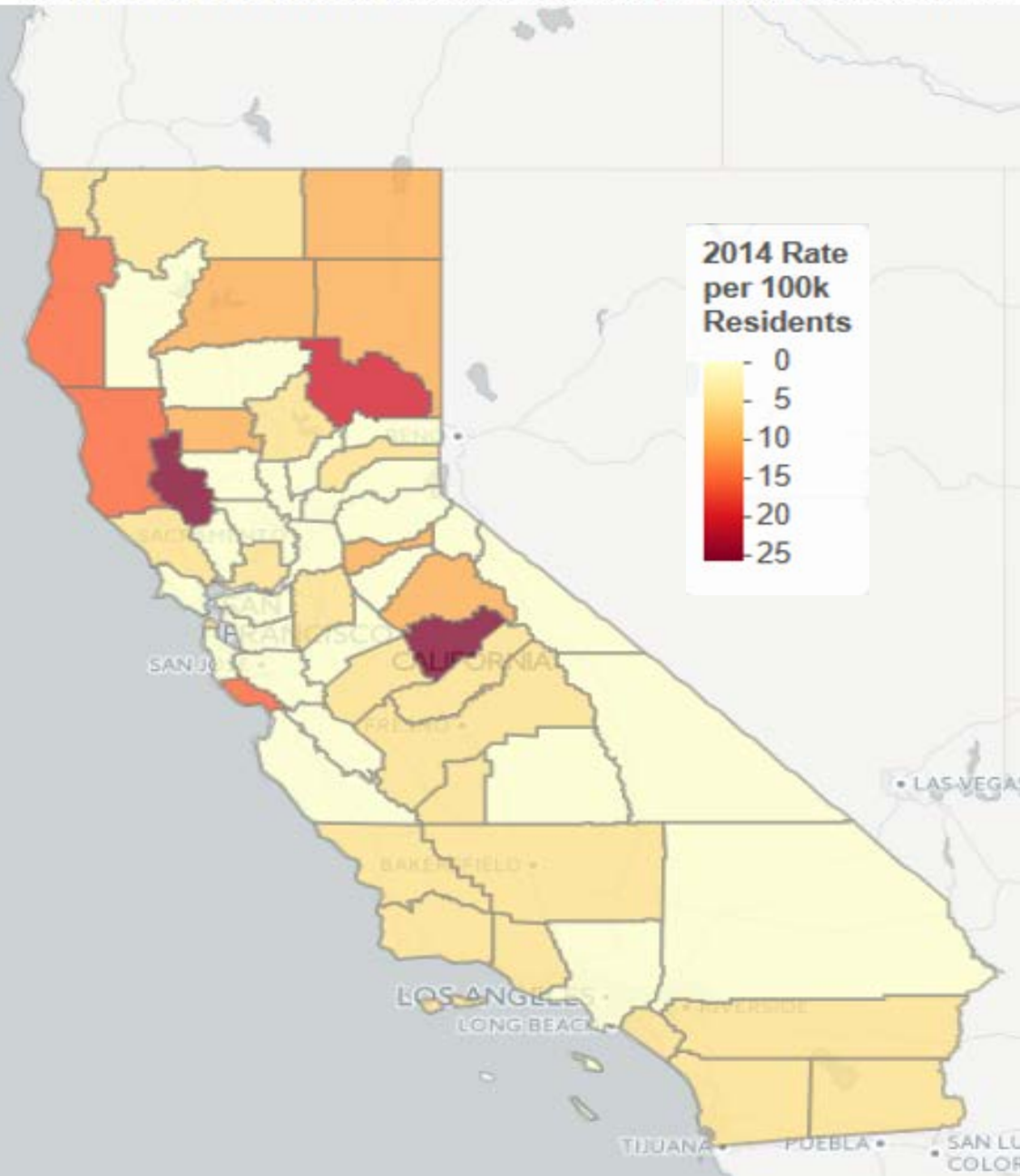
Overdose Deaths per 100,000 2014



New York Times: <https://nyti.ms/2jVUIKb>

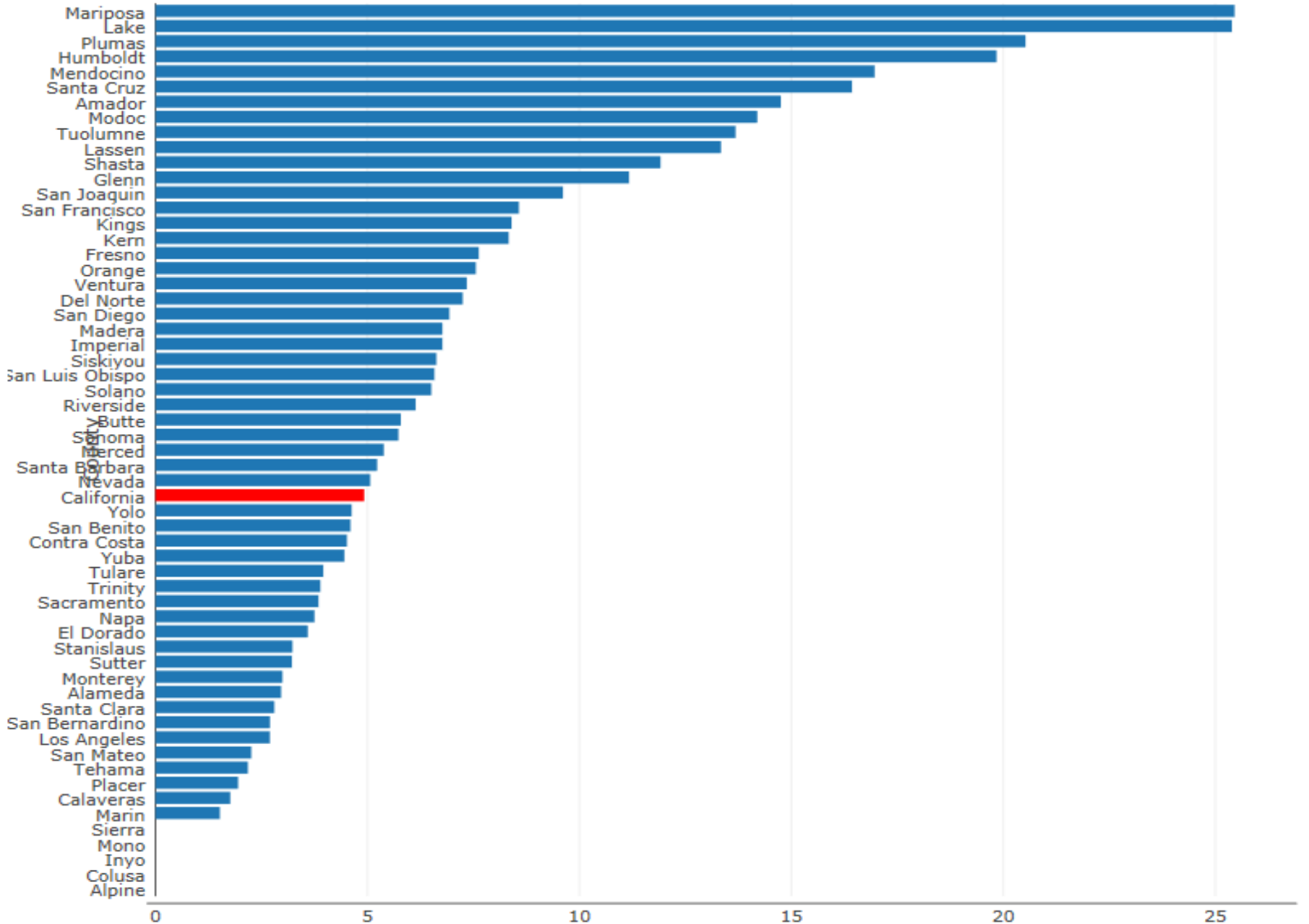
California Deaths - 2014

All Opioid Overdose: Age-Adjusted Rate per 100,000 Residents

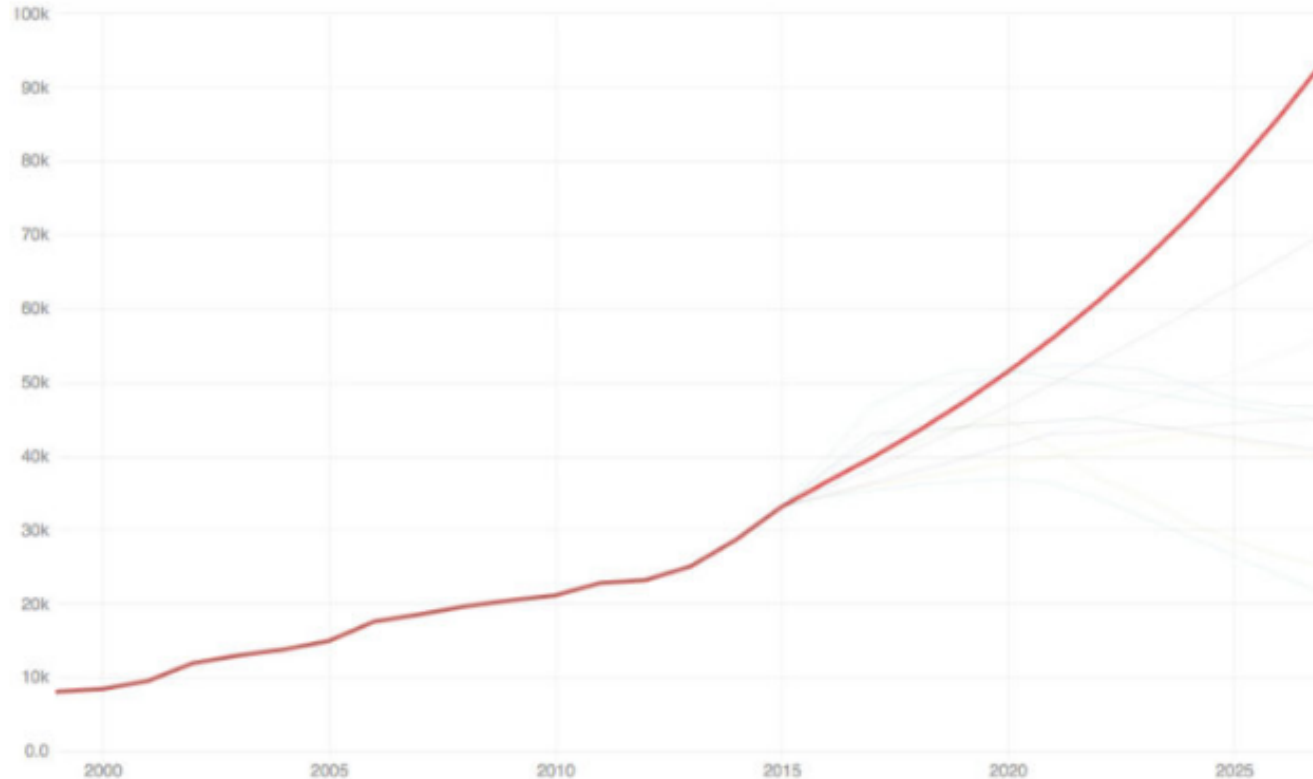


California Deaths - 2014

All Opioid Overdose: Age-Adjusted Rate per 100,000 Residents



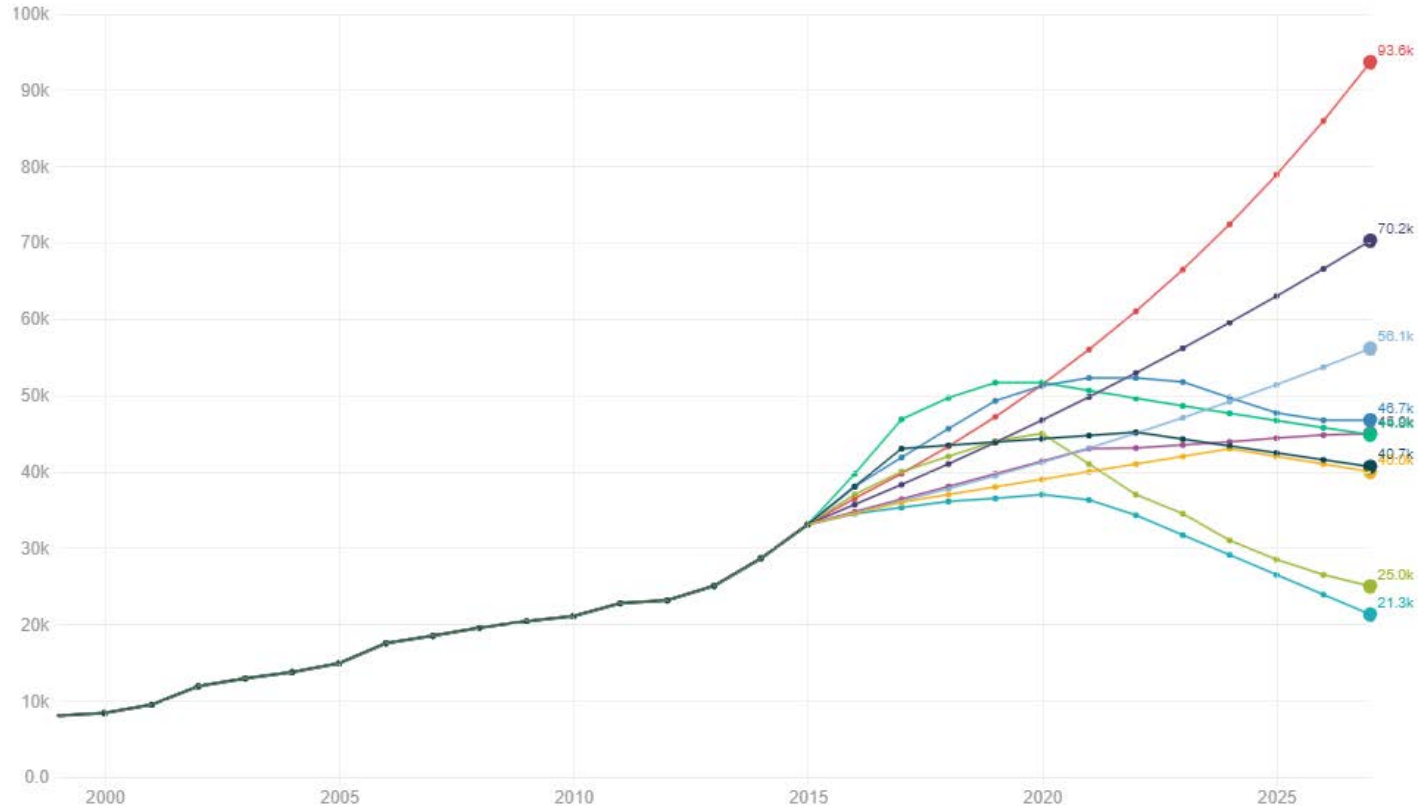
Opioid overdose deaths: Worst Case Scenario



Scenario 1: The opioid deaths forecast for 2027 is 93,613. The forecasted change is 183% since 2015 when it was 33,091. This curve assumes total drug overdoses climb at the same rate they have for decades. It's also based on the assumption opioid deaths keep making up roughly the same percentage of all drug deaths.

NATALIA BRONSHTEIN/STAT

Opioid overdose deaths: 10 projected scenarios.



SCENARIO 10

The opioid deaths forecast for 2027 is 21,300. The forecasted change is -36% since 2015 when it was 33,091.

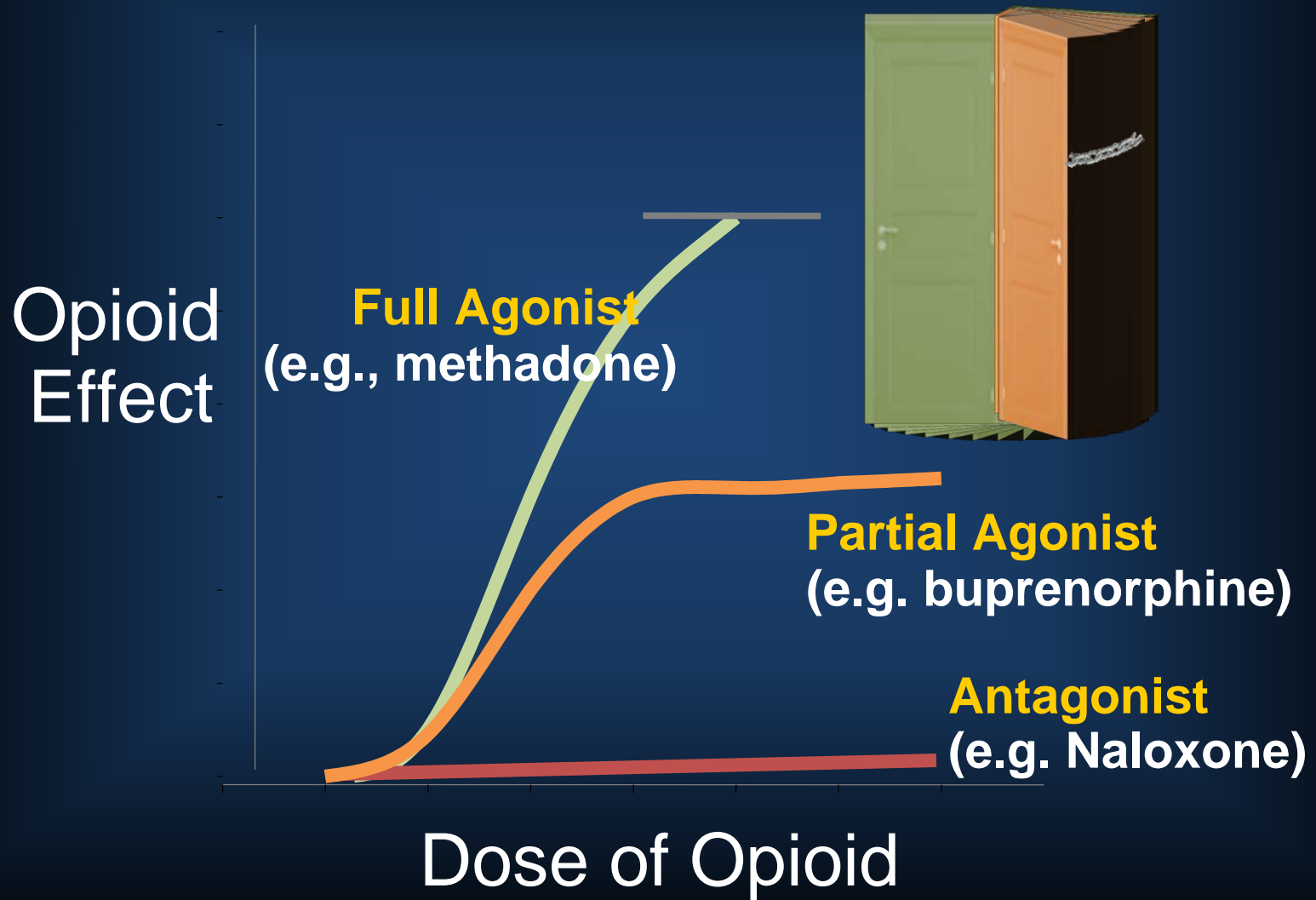
This curve assumes doctors prescribe fewer opioids, states embrace prescription drug monitoring programs, and insurers enact reforms to increase treatment access.

MAT for Opioid Use Disorder During Pregnancy

- Benefits of treatment of mother with MAT during pregnancy **greatly outweigh** the risks of not addressing opioid use.
- Methadone vs. Buprenorphine
 - **Methadone** is most well studied MAT for opioid addiction during pregnancy and has demonstrated safety during pregnancy for mother and fetus.
 - Neonatal Abstinence Syndrome → infant experiences opioid withdrawal at birth
 - **Buprenorphine** is newer, but data is accumulating that Buprenorphine is a safe alternative to Methadone, with **LESS RISK** of Neonatal Abstinence Syndrome for the infant.



How Do Opioids Work?



Methadone



Dolophine[®] Methadose[®]

Methadone General Facts

(information from medication package insert)

- **Generic Name:**
methadone hydrochloride
- **Marketed As:**
Methadose® and Dolophine®
(among others)
- **Purpose:**
To discourage illicit opioid use due to cravings or the desire to alleviate opioid withdrawal symptoms.
- **Indication:**
For the treatment of moderate to severe pain not responsive to non-narcotic analgesics; for detoxification treatment of opioid addiction; for maintenance treatment of opioid addiction, in conjunction with appropriate social and medical services.
- **Year of FDA-Approval:** 1964





How does methadone work?

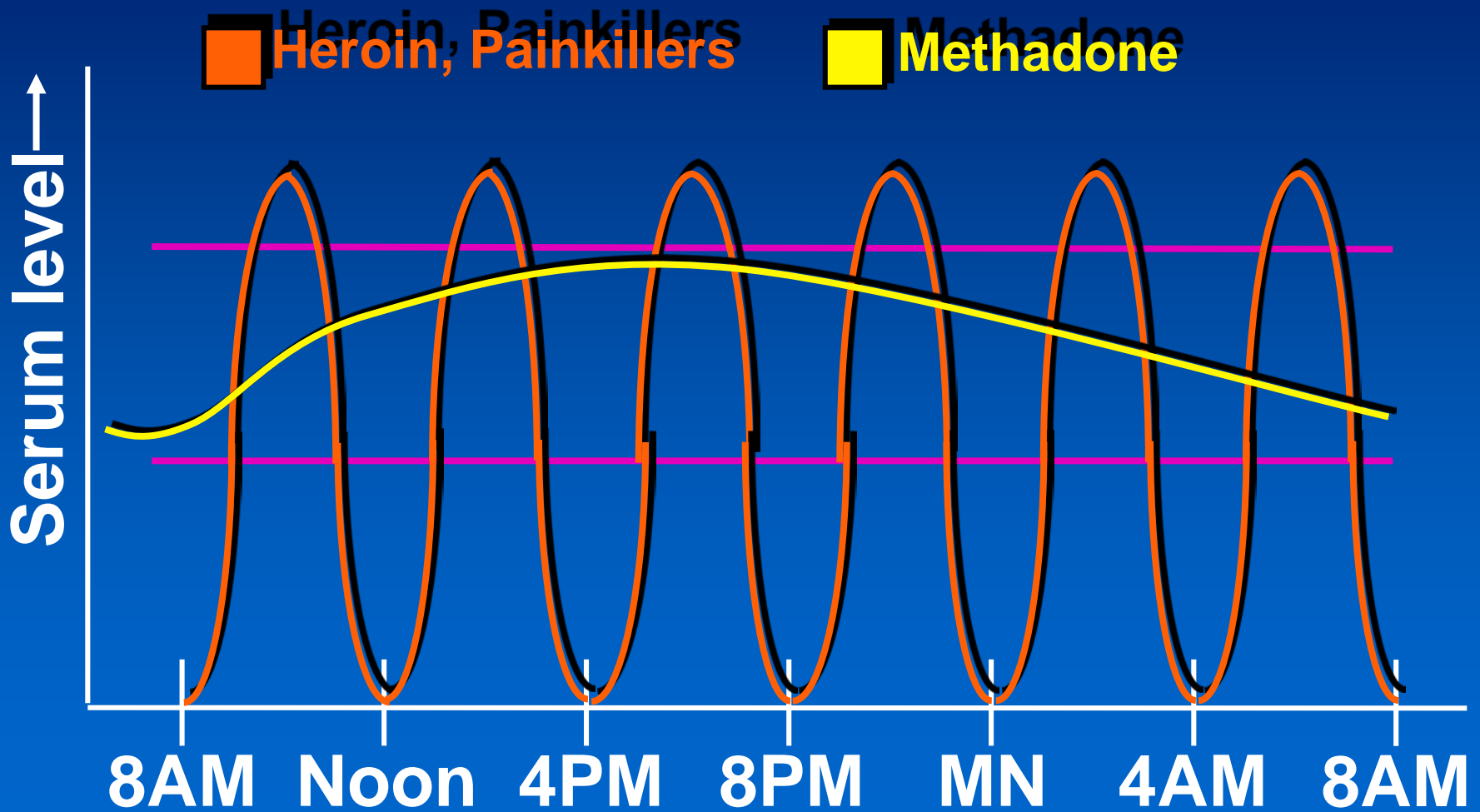
- Methadone binds to the same receptor sites as other opioids.
- Orally effective
- Slow onset of action
- Long duration of action
- Slow offset of action



Methadone Maintenance: Advantages

- Suppresses opioid withdrawal and reduces craving
- Oral administration (syrup or tablet forms used)
- Once daily doses enable lifestyle changes
- Counselling promotes long-term lifestyle changes
- Reduced participation in crime
- Reduced transmission of blood borne viruses
- Few long-term side-effects.

Advantages of Methadone

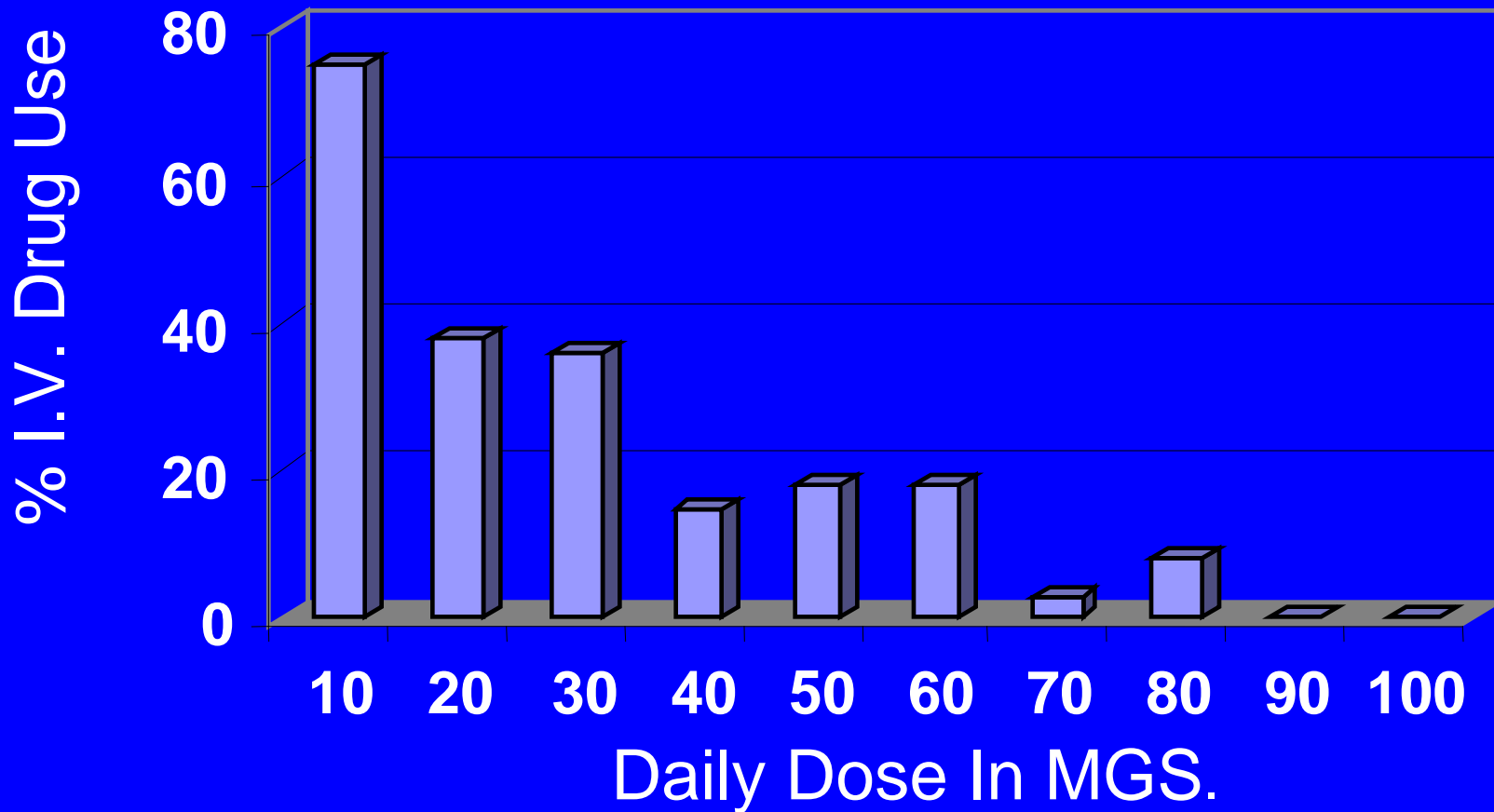




Safety Overview

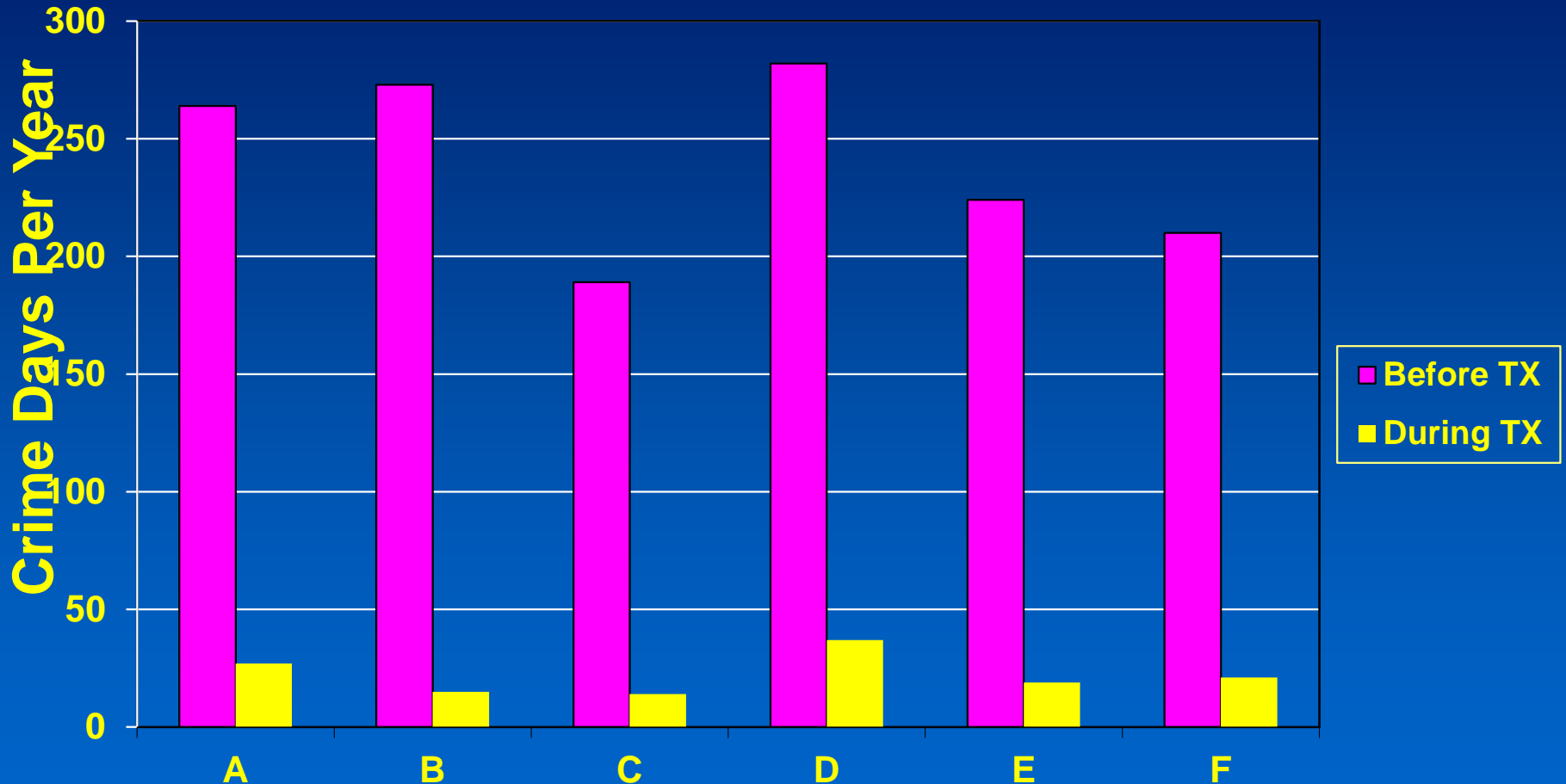
- Safe medication (acute and chronic dosing)
- Primary side effects: like other mu agonist opioids (e.g., nausea, constipation), but may be less severe
- No evidence of significant disruption in cognitive or psychomotor performance with Methadone maintenance
- No evidence of organ damage with chronic dosing

Heroin Abuse Frequency Vs. Methadone Dose



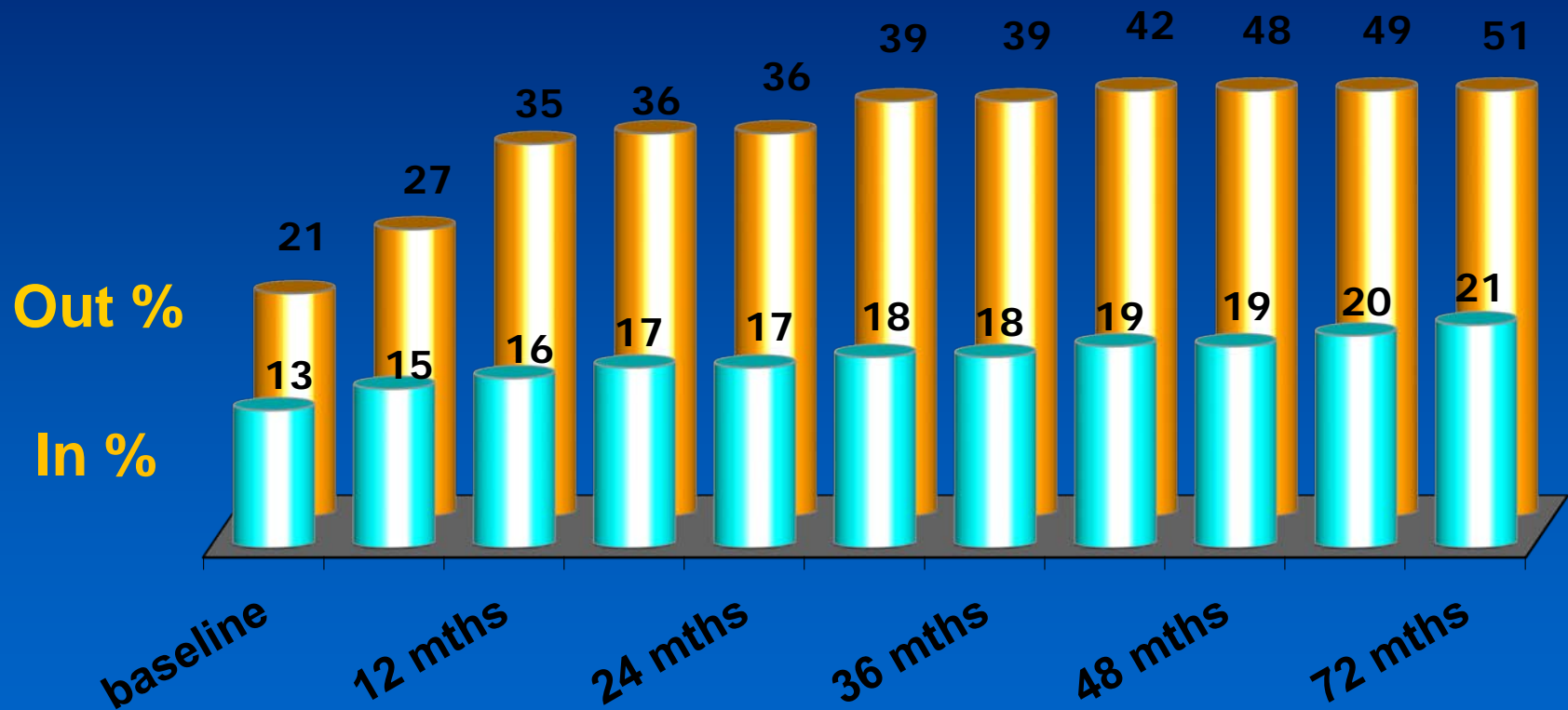
V.P. Dole, JAMA, VOL. 282, 1989, p. 1881

Crime Among 491 Patients Before and During MMT at 6 Programs

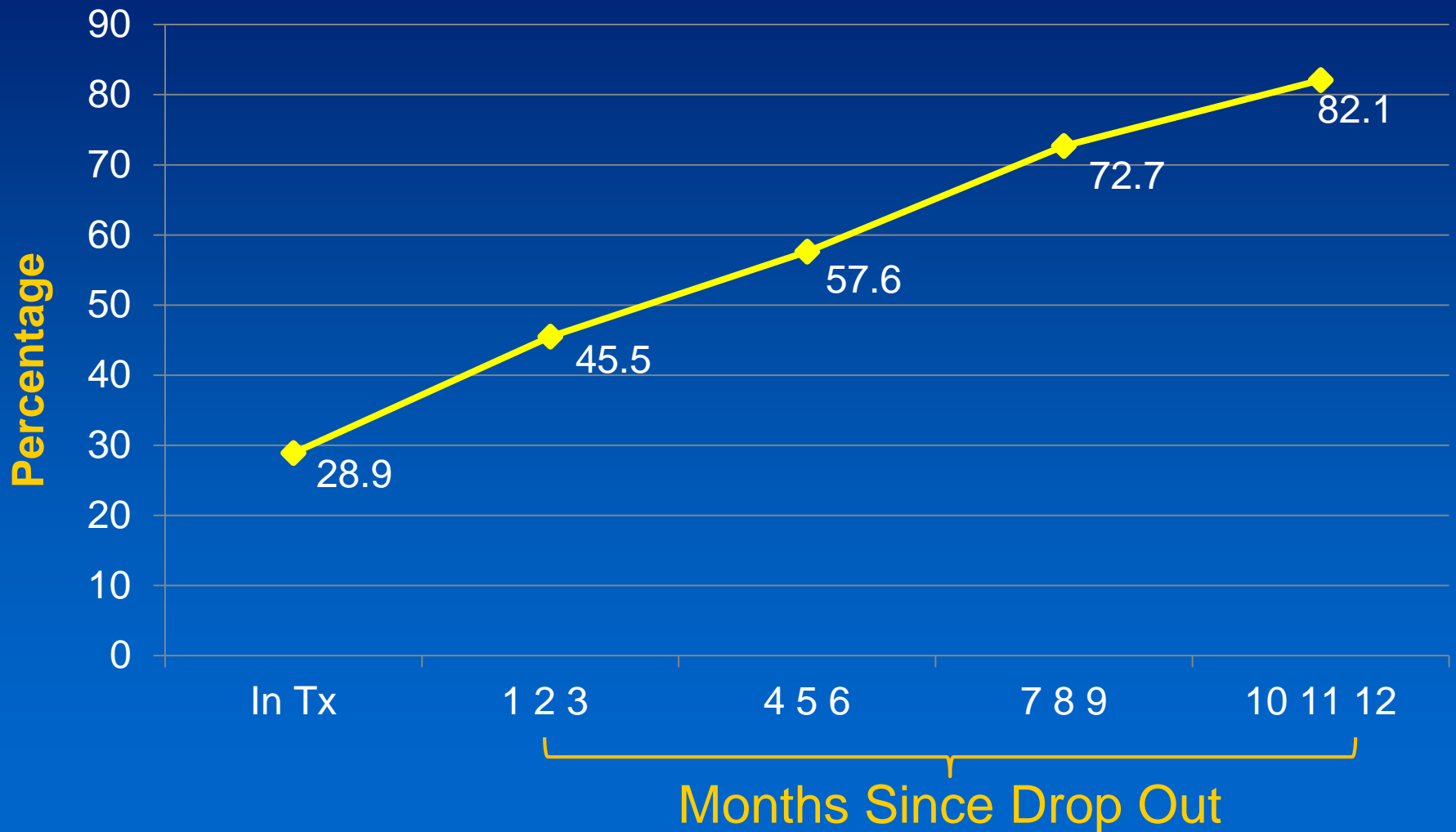


Adapted from Ball & Ross - The Effectiveness of Methadone Maintenance Treatment, 1991

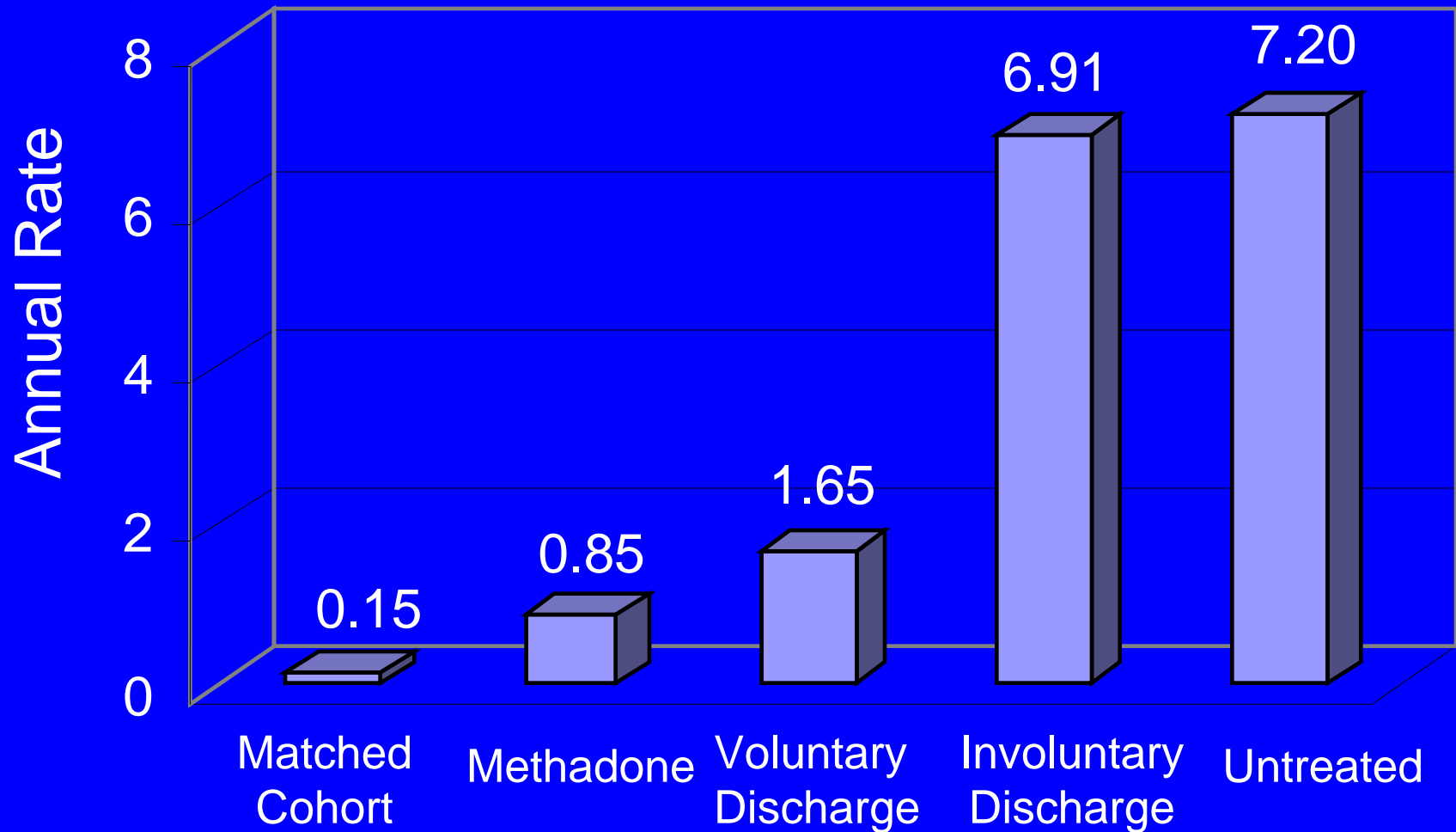
HIV Infection Rates In and Out of Methadone Treatment (Metzger et al. 1993)

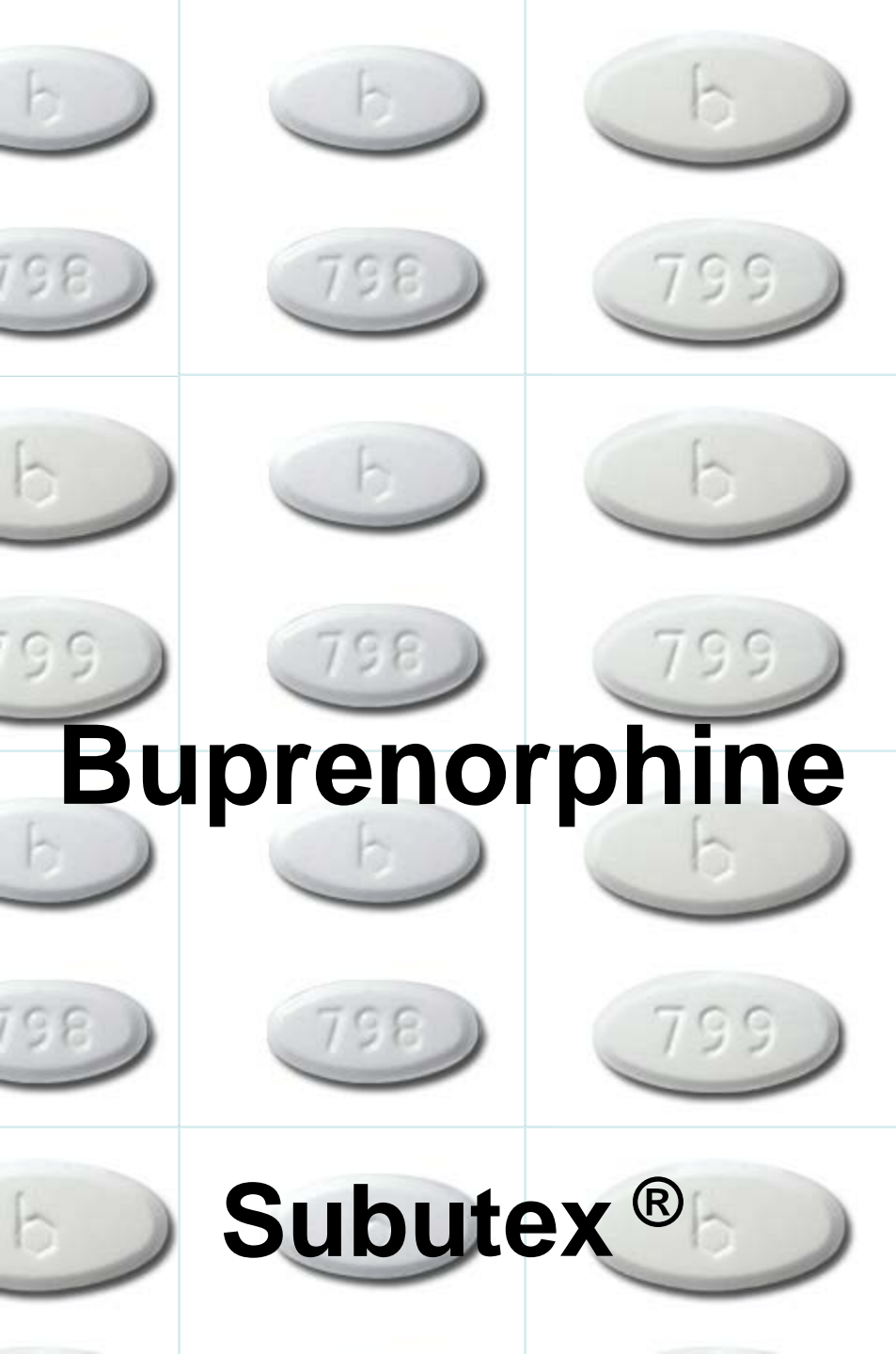


Relapse to IV Drug Use After Termination of Methadone Maintenance Treatment



Death Rates in Treated and Untreated Heroin Addicts





Buprenorphine

Subutex[®]



**Buprenorphine/
Naloxone**

Suboxone[®]

How Does Buprenorphine Work?

- Partial Opioid Agonist
 - Produces a **ceiling effect** at higher doses
 - Has effects of typical opioid agonists—these effects are dose dependent up to a limit
 - **Binds strongly** to opiate receptor and is long-acting

Buprenorphine

- Mechanism → Partial mu opioid receptor agonist; binds receptor and exerts partial activation
 - Blocks euphoric effect of opioids, alleviates withdrawal and cravings
 - Strong affinity for mu opioid receptors → will outcompete and displace heroin and other opioids from mu receptors to block their effects, while providing partial agonist activity
 - Must dose buprenorphine when client is abstinent or in mild - moderate withdrawal, otherwise buprenorphine will precipitate opioid withdrawal given it is only a partial agonist.
 - Slow to dissociate from receptors → long-acting, less frequent dosing

Buprenorphine

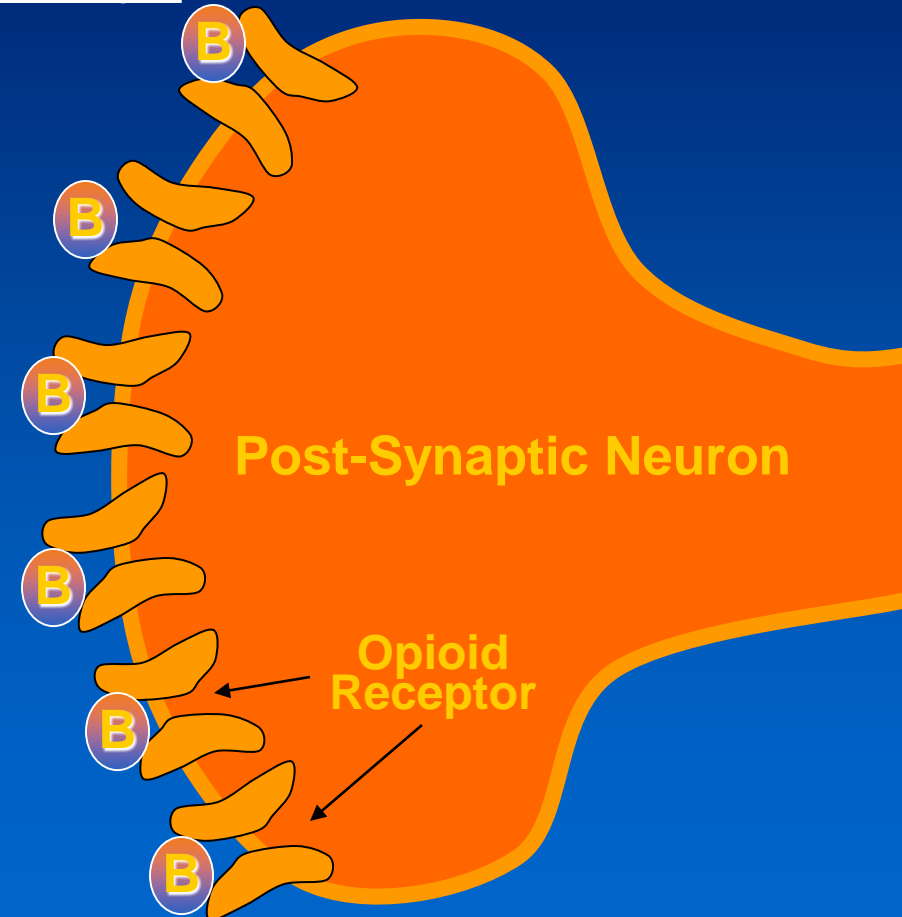
- Indications → Opioid withdrawal management & maintenance treatment
 - Efficacy: Maintenance > withdrawal management only
 - No “ideal” or recommended treatment period; very individual decision depending on patient preference and clinical need/situation
- “Ceiling” effect → dose-dependent effects up to a plateau, at which point further increases in dosage don’t exert additional effects
 - Safer in an overdose due to reduced respiratory and CNS depression, and less risk for diversion

How Does Buprenorphine Work?

Buprenorphine works in two main ways:

 = buprenorphine

- 1) Prevents opioid withdrawal symptoms by binding opioid receptors and providing mild agonist effects.
- 2) Occupies opioid receptors so illicit opioids will not be able to bind the receptors if used, and will thus have no effect.





Buprenorphine: The Evidence

- Over 25 years of research on buprenorphine, including over 5,000 patients.
- Clinical trials have established the safety and effectiveness of buprenorphine for the treatment of opioid addiction.
- Effectiveness of buprenorphine has been compared to:
 - Placebo (Johnson et al. 1995; Ling et al. 1998; Kakko et al. 2003)
 - Methadone (Johnson et al. 1992; Strain et al. 1994a, 1994b; Ling et al. 1996; Schottenfield et al. 1997; Fischer et al. 1999)
 - Methadone and LAAM (Johnson et al. 2000)

Buprenorphine: More Evidence

- Cochrane systematic review and meta-analysis of 24 randomized controlled trials comparing maintenance treatment with Buprenorphine vs. Methadone vs Placebo (4500 patients)
 - Buprenorphine group was significantly superior to placebo in treatment retention and suppressing heroin use
 - Comparing Buprenorphine vs. Methadone
 - For those who remained in treatment → Buprenorphine ≈ Methadone
 - Dose dependent findings (medium Buprenorphine dose > low Methadone dose at heroin suppression, etc)
 - If relative doses are equal → Methadone > Buprenorphine
- However, when deciding treatments, there is MUCH more that needs to be factored in than simply which medication is more effective at a given dose (i.e.: safety, client preference, risk of diversion, severity of dependence, level of support needed to achieve recovery, etc.)





Naltrexone

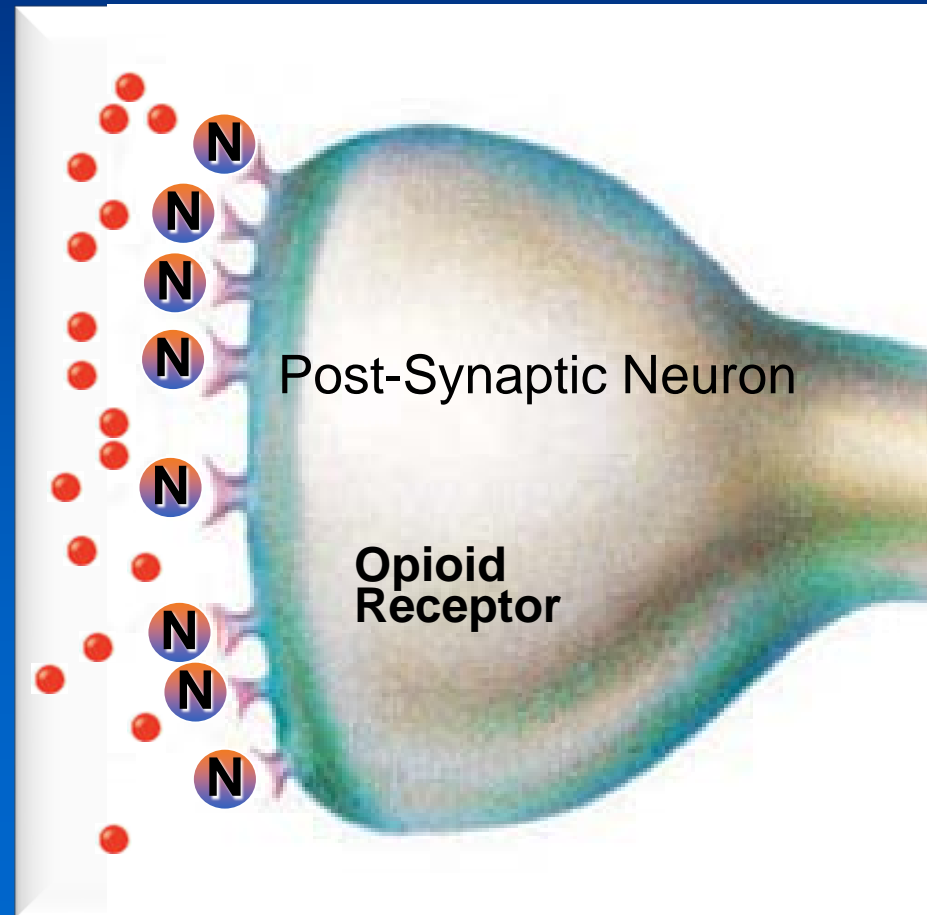
Revia[®] or Depade[®]

How Does Naltrexone Work?

- Naltrexone is an opioid receptor antagonist and blocks opioid receptors.

By blocking opioid receptors, the “reward” and acute reinforcing effects from dopamine are diminished, and alcohol consumption is reduced.

 = naltrexone
 = opioids



Research for Naltrexone

When compared to placebo, those receiving naltrexone

- Were **NOT** able to maintain complete **abstinence** more frequently
- Had a **greater reduction in relapse** during the entire study

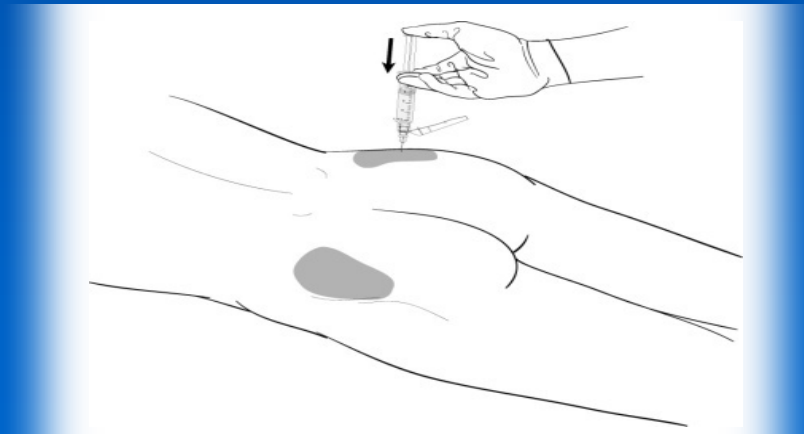
Extended-Release Naltrexone Administration

Amount: one 380mg injection

Method: deep muscle in the buttock

Frequency: every 4 weeks

Must be **administered by a healthcare professional** and should alternate buttocks each month.



Research About Extended-Release Naltrexone

When compared to placebo, those receiving extended release naltrexone:

- Had fewer opioid positive urines
- Stayed in treatment longer
- Had less craving
- Showed greater improvement in the mental component of quality of life and overall health status

Final Note: Behavioral Treatments

The FDA labeling on these medications is clear:

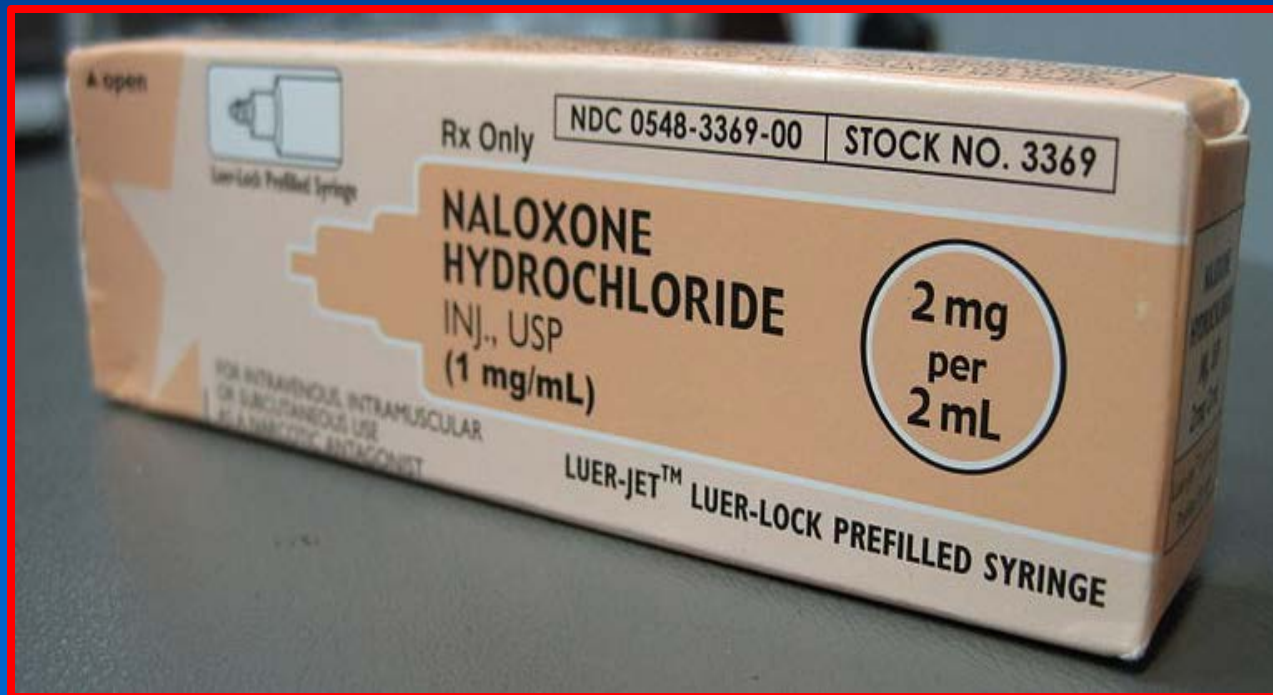
The medications should be used in combination with behavior treatments for addiction

Good treatment is holistic, integrated and multifaceted, taking into account the physical, behavioral and spiritual wellbeing of the individual.

Medications can help us **take care of the physical...**

...we need to do the rest

Naloxone for Opioid Overdose



Naloxone-Narcotic Antagonist

- Used to counteract life-threatening depression of the central nervous system and respiratory system.
- Non-scheduled.
- Non-addictive.
- Works only if opioids are present.
- No abuse potential.
- Can be injected or used nasally.
- Wears off in 20 – 90 minutes.

Intranasal Medication Administration



OVERDOSE PREVEN
PREVENCIÓN DE
EQUIPO DE



Narcan Nasal Spray



Adapt Pharma

- Partnership through the Clinton Health Matters Initiative-Free to all high schools and colleges in the U.S.
- Local & state government agencies \$75.00 per dual pack.
- Without a prescription \$110.00 through a local pharmacy.

Naloxone auto-injector

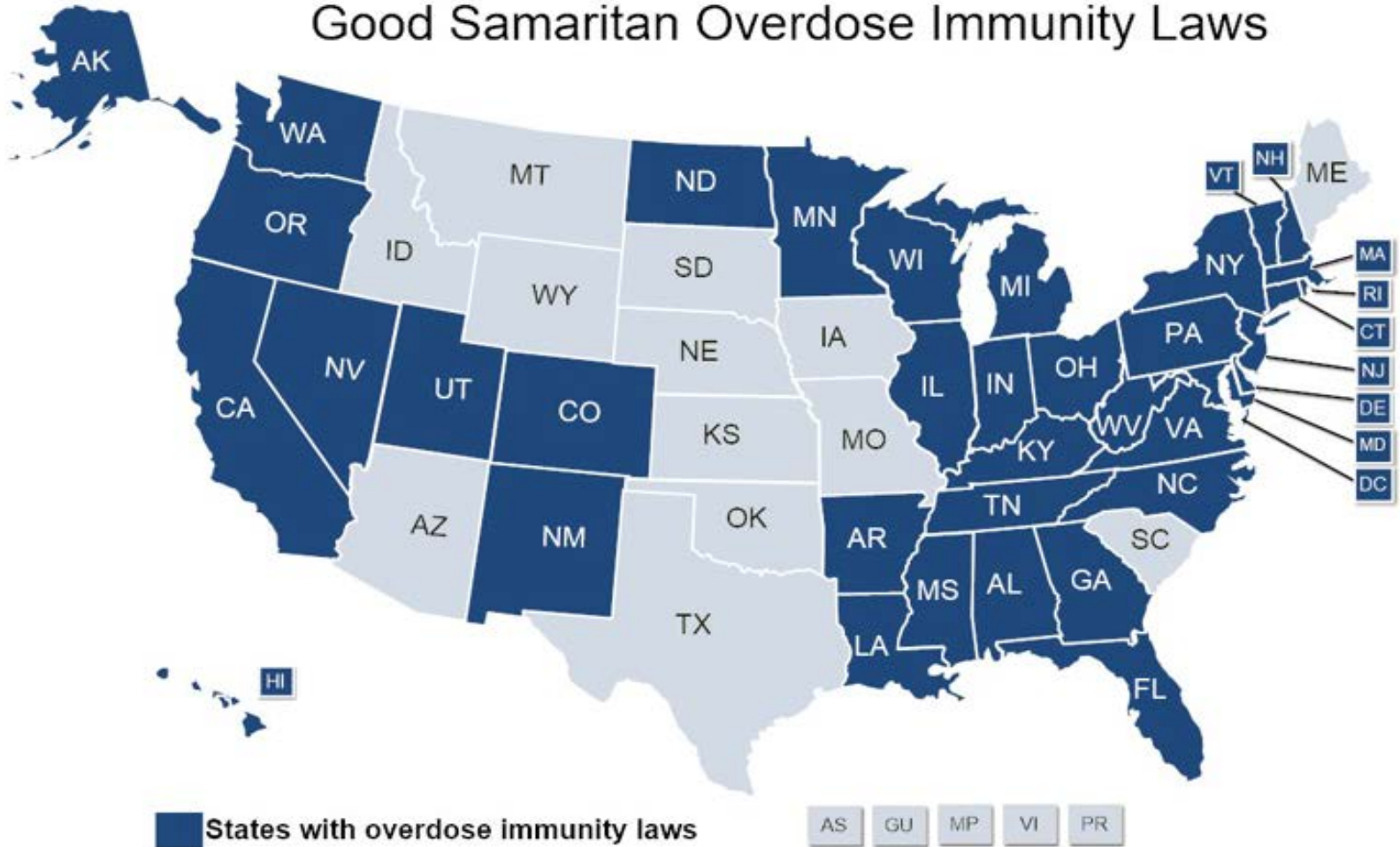
- Designed to be used by people who do not have medical training
- Includes verbal instructions to guide its use
- When pressed against the thigh, the needle automatically injects, delivers medicine, and retracts
- Contains one 0.4 mg dose of naloxone



Naloxone: Important Considerations

- **Not a replacement for emergency medical treatment**
 - After using the pen, client must immediately seek medical care
- Many opioids are long-acting, and naloxone may not last as long as the opioid
 - If overdose symptoms return, a second dose may be needed

Good Samaritan Overdose Immunity Laws





HELP
THOSE IN NEED



GIVE
OVERDOSE RESCUE



HOPE
FOR A LIFE SAVED

Save a Life

Learn how to respond to an overdose emergency

Get Naloxone Now is an online resource to train people to respond effectively to an opioid-associated overdose emergency. Get Naloxone Now advocates for widespread access to overdose education and training in how to administer naloxone, the life-saving antidote for opioid-associated overdose. Get Naloxone Now seeks to increase the number of lives saved by bystanders and professional first responders (police officers, firefighters and EMTs). Find out how you can contribute to reducing overdose deaths by accessing our online training modules.

INDIVIDUALS-GET TRAINED!

INSTITUTIONAL PROGRAM

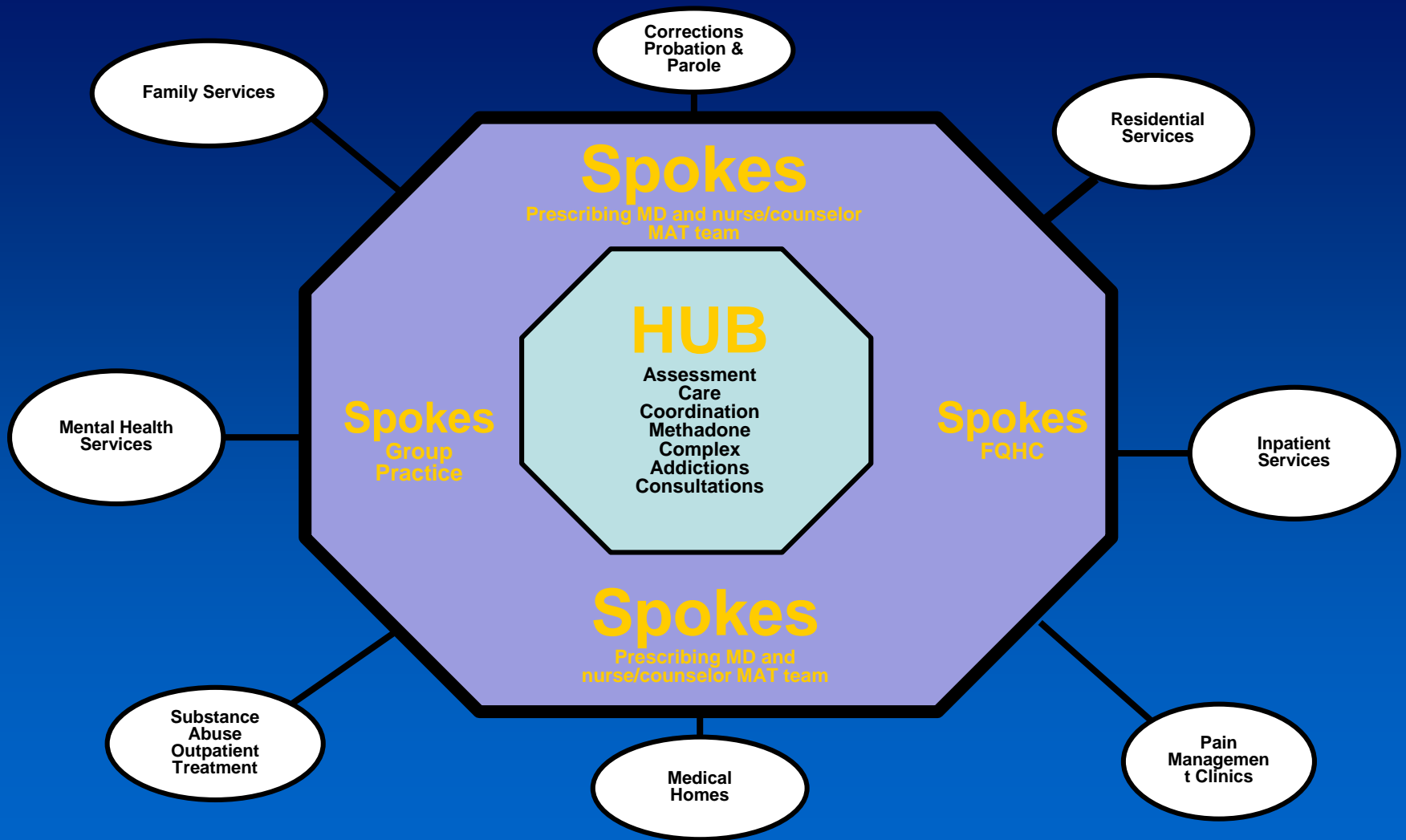
HOW CAN YOU HELP

MAT Can Reduce Health Disparities

- Integrate into general health care services
- Reach more people in rural settings
- Increase access through insurance parity
- Advance integrated care to improve prevention, treatment and follow up care

California Hub and Spoke System

- Designed to treat opioid use disorder as a chronic disease
- Main goal is to prevent overdose and deal with the opioid crisis
- Divides state into regions
- Each region has a specialized addiction center of expertise known as the HUB that is an opioid treatment program (OTP)
- Each Hub is connected to all the waived buprenorphine doctors' offices known as SPOKES
- All SPOKES have a dedicated MAT (medication assisted treatment) team
- A MAT team is made of 1 registered nurse and 1 licensed clinical social worker for 100 patients on buprenorphine under Medicaid



CA H&SS Hubs and Spokes



Network # & Hub location	Spokes
1	Lake County (1) Mendocino County (2) Nevada County (1)
2	Siskiyou County (2) Trinity County (1) Del Norte County (1)
3	El Dorado County (1) Placer County (1) Nevada County (1)
4	Butte County (2) Lassen County (1) Tehama County (1) Plumas County (1)
5	Humboldt County (6)
6	San Joaquin County (1) Stanislaus County (1)
7	Contra Costa County (TBD)
8	San Francisco County (TBD)
9	Sonoma County (1) Lake County (1) Yolo County (1) Colusa County (1) Napa County (1)
10	Los Angeles County (10)
11	Marin County (8)
12	Yolo County (2) Sacramento County (1)
13	Santa Cruz - N County (6)
14	Santa Cruz - S County (4) San Benito County (1) Monterey County (1)
15	Fresno County (TBD)
16	Solano County (TBD)
17	San Diego County (7)
18	Los Angeles County (10)
19	San Bernardino County (1) Riverside County (6) San Diego County (2)

<http://uclaisap.org/ca-hubandspoke/>

Resources

Buprenorphine

- www.buprenorphine.samhsa.gov
- Reckitt Benckiser
 - www.suboxone.com
 - www.heretohelpprogram.com

Naltrexone for Extended-Release Injectable Suspension

- Alkermes
 - www.vivitrol.com
 - 1-800-VIVITROL (800-848-4876)



For more information, contact:

tfreese@mednet.ucla.edu

www.psattc.org

www.uclaisap.org

www.nida.nih.gov