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DHCS
CALIFORNIA DEPARTMENT OF
HEALTH CARE SERVICES

The Science of Substance Use Disorder (SUD) and Medication for Addiction Treatment (MAT)

AFBSS Webinar Series: March 10, 2026

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Presenters

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Agenda

- Brain Changes from Chronic Substance Use
- Medications for Addiction Treatment
- Chronicity of Addiction and Duration of Treatment
- Q&A

Learning Objectives

At the end of the session, participants will be able to:

- Explain at least one brain change that occurs with recurrent use of addictive substances.
- Describe at least three benefits of the FDA-approved medications for opioid use disorder (MOUD).
- Compare and contrast at least one unique feature of each FDA-approved medication for alcohol use disorder (MAUD).
- Describe at least two considerations related to the duration of treatment recommended for SUDs.

Brain Changes from Chronic Substance Use

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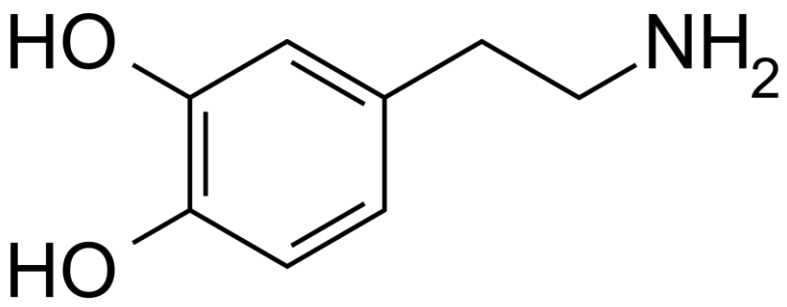
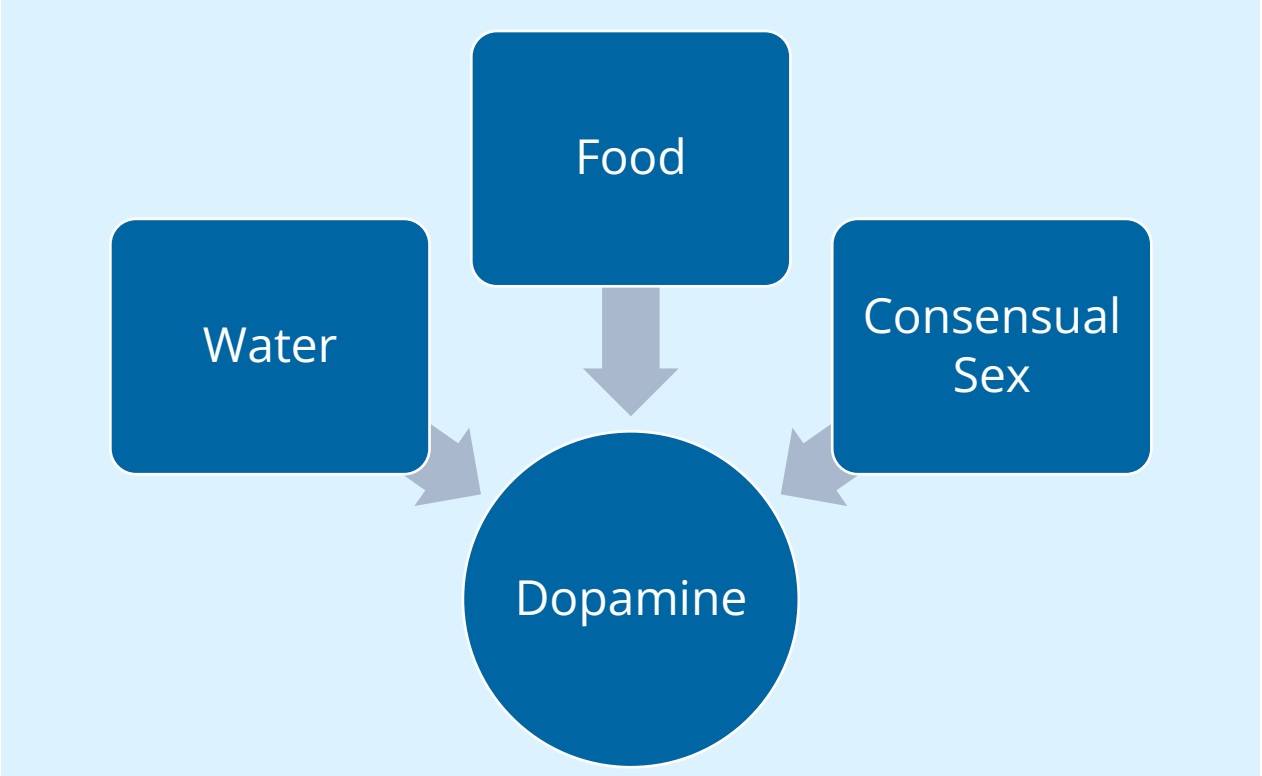
Natural Rewards Release Dopamine

» Dopamine: Often referred to as the "feel good" chemical contributing to feelings of pleasure and motivation.

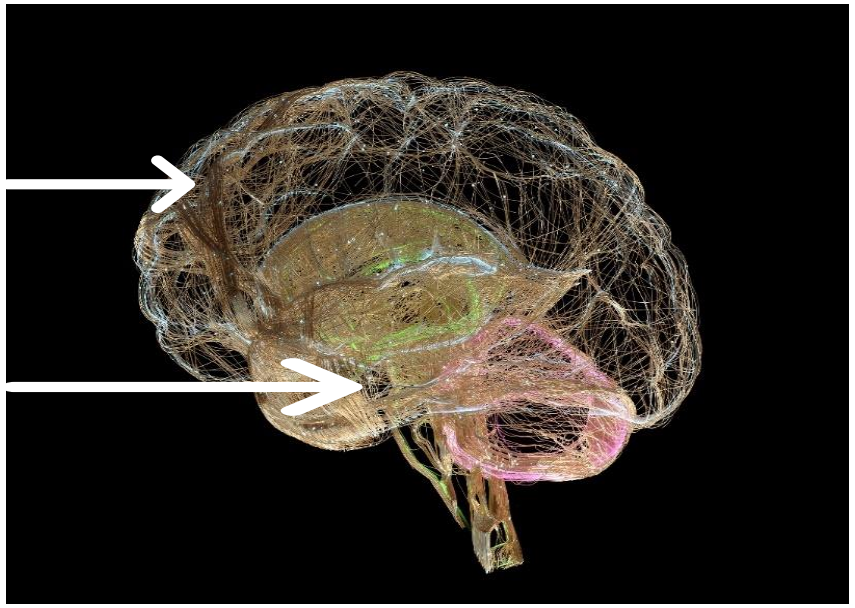
Dopamine





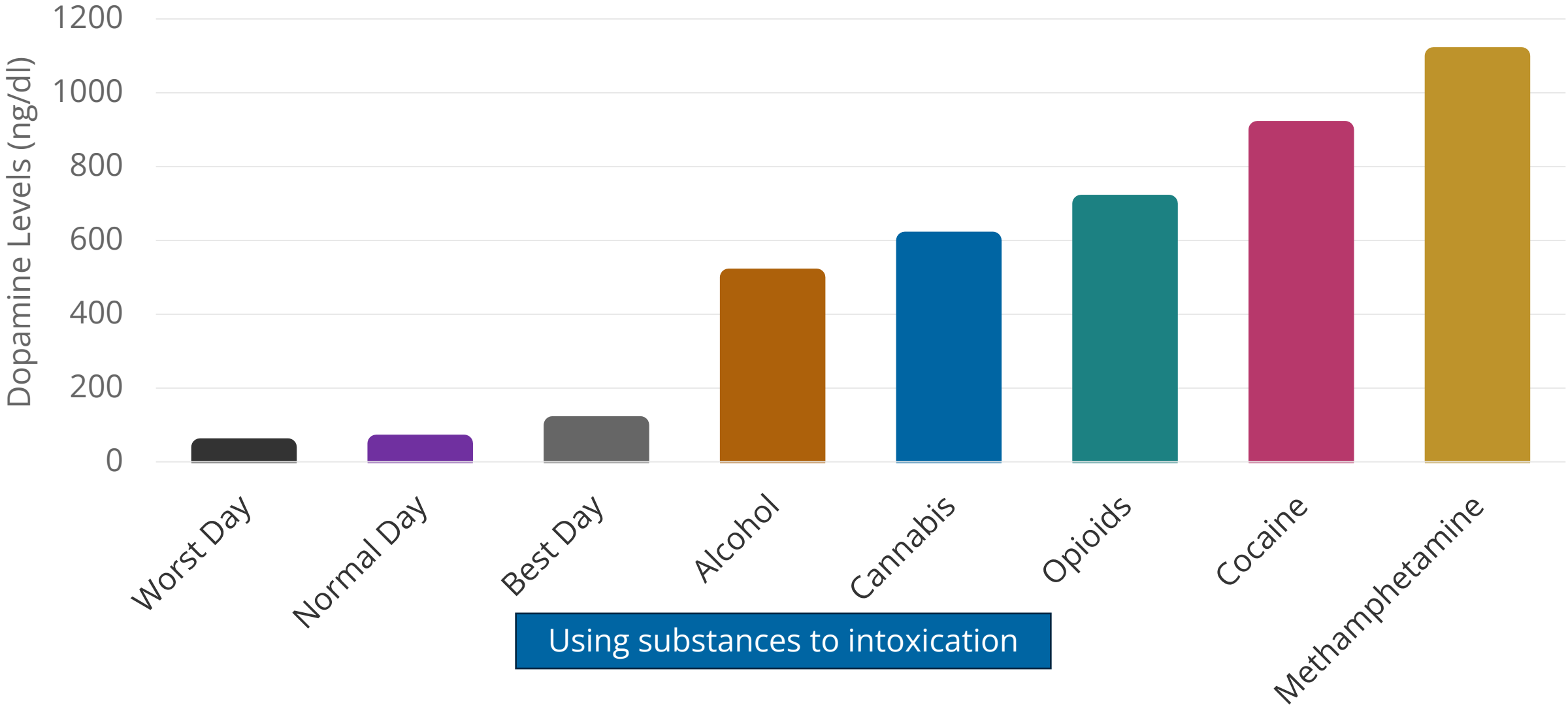
How Addictive Substances Affect the Brain

- All addictive substances result in the activation of the reward pathway.
- The same pathway activated by naturally rewarding substances and events.



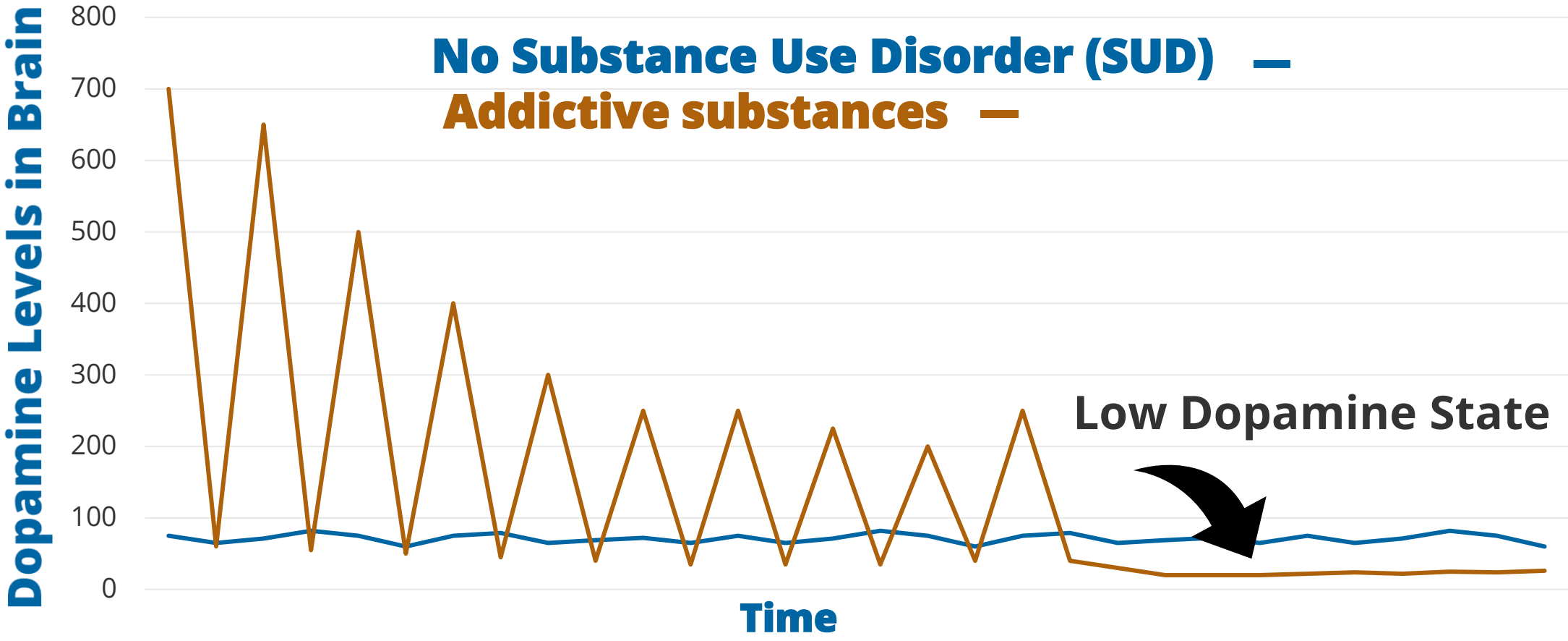
SOURCE(S): National Institutes of Health (NIH), 2020.

Dopamine Response



SOURCE(S): Di Chara and Imperato, 1998; Pierce and Kumaresan, 2006.

Brain Changes with Episodes of Substance Use



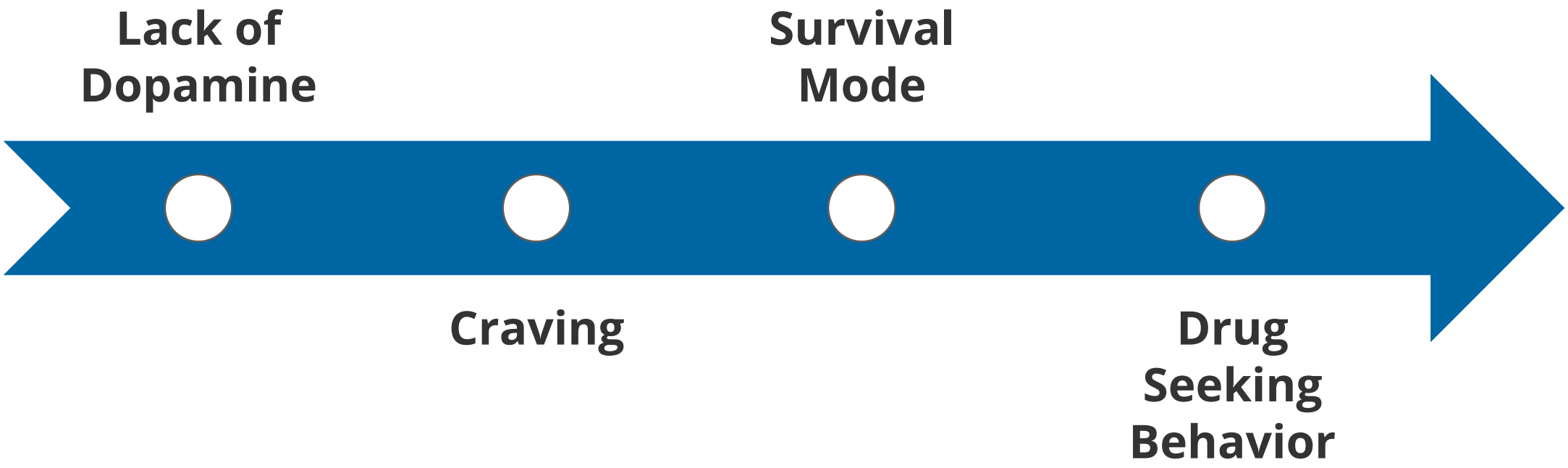
SOURCE(S): Volkow, 2015.

Intensity of Cravings

A direct, or indirect, force pulling someone towards a substance or behavior

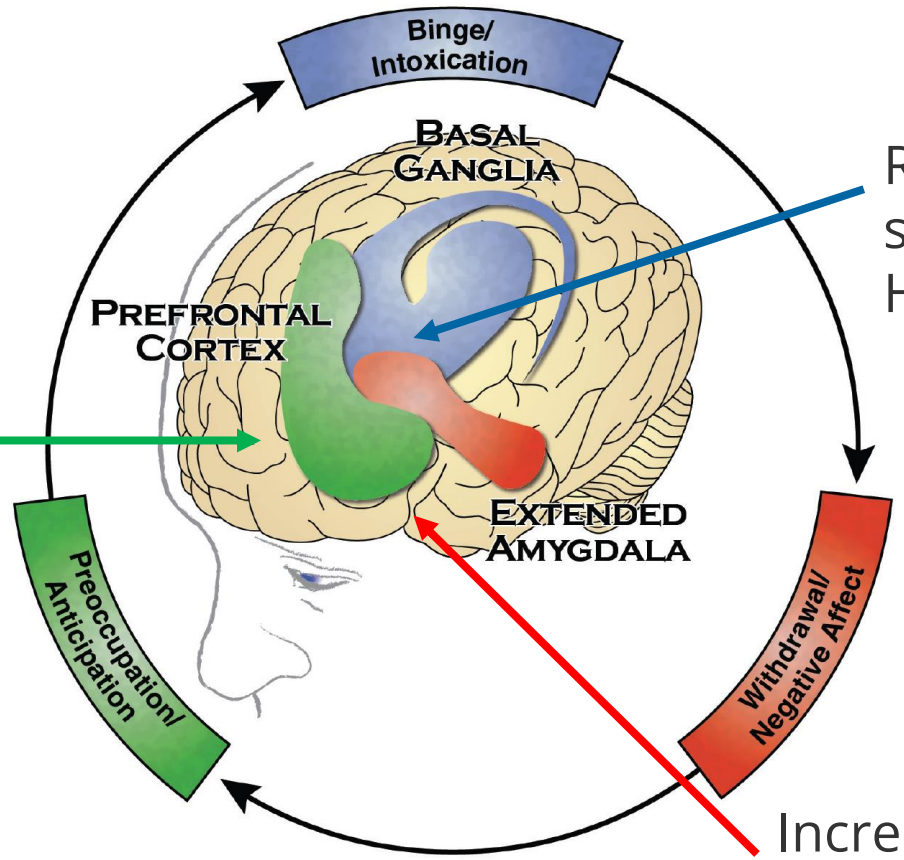
SOURCES: Morales and Berridge, 2020; DiLeone et al., 2012.

Human Behavior – Response to a Need



Addiction and Associated Brain Regions

Executive functioning
- » Self regulation
- » Decision making
- » Salience
- » Error monitoring



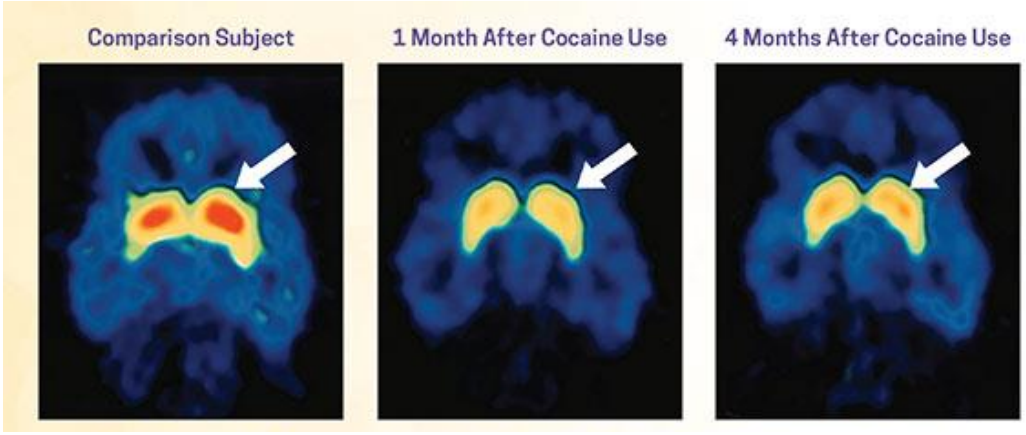
Rewarding effects of substances
Habitual substance use

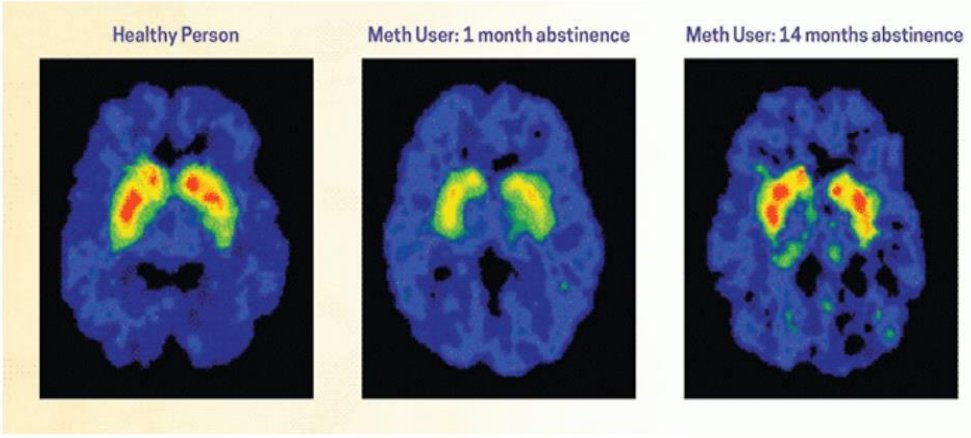
Increased stress reactivity
Negative emotions

SOURCE(S): NIH, 2016.

It Takes Time for The Brain to Recover

- Prolonged drug use changes the brain in long lasting ways.
- Changes are both functional and structural.
- Return to normal takes over one year.
- Stopping treatment before the brain recovers may lose the desired outcomes.





The Journal of Neuroscience, 21(23):9414-9418. 2001

SOURCE(S): NIH, 2020; NIH, 2007; Volkow et al, 1992.

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Ideas in Action

- Poll Question #1:
  - What is the primary reward neurotransmitter in the brain?
    - A. Dopamine
    - B. Norepinephrine
    - C. Serotonin
- Poll Question #2:
  - Which substance causes the largest dopamine release?
    - A. Alcohol
    - B. Cocaine
    - C. Heroin
    - D. Methamphetamine

Medications for Addiction Treatment

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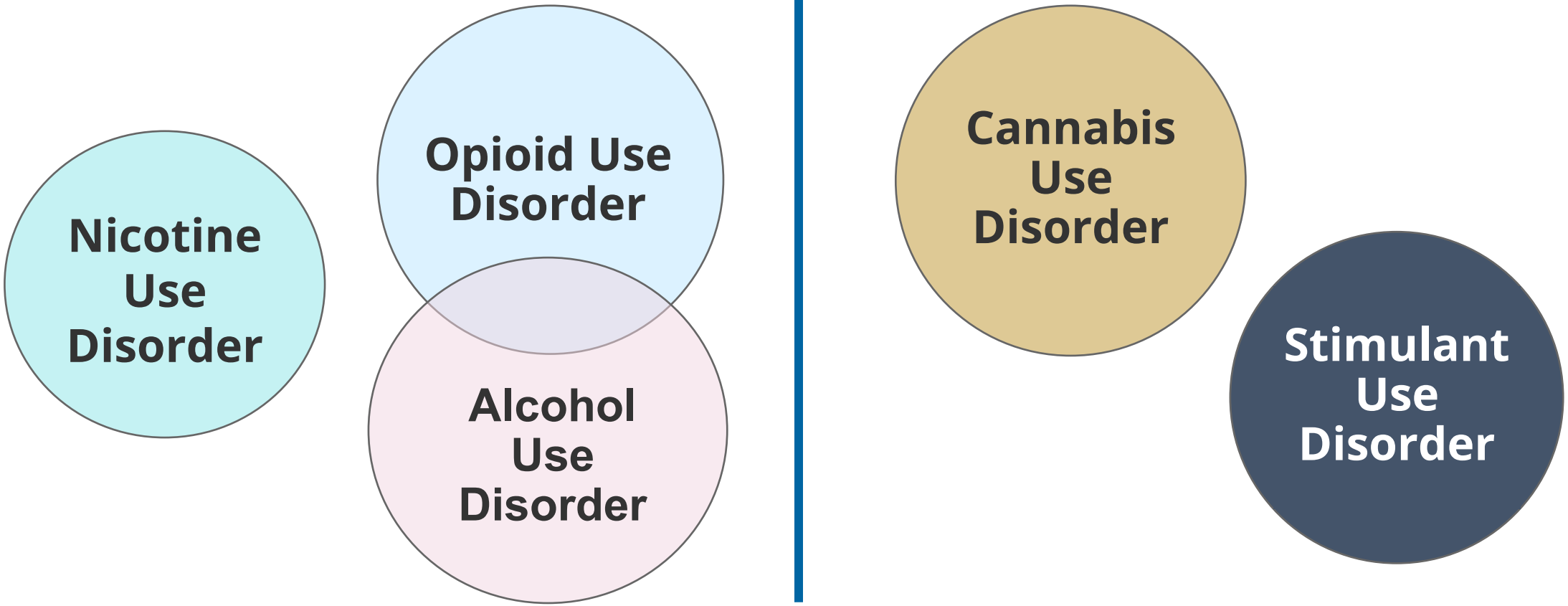
Substance Use Disorder Treatment with Medications

- The use of **FDA-approved prescription medications**, usually in combination with counseling and behavioral therapies, to provide a whole-person approach to the treatment of substance use disorders (SUD).
- When discussing medication for opioid use disorder (OUD), this is frequently referred to as **Medications for Opioid Use Disorder** (MOUD).
- MOUD has **proven clinically effective to alleviate symptoms of withdrawal and reduce cravings**. MOUD maintenance has been proven to cut overdose rates in half and decrease rates of HIV and hepatitis C transmission.
- Research shows that a **combination of MOUD and behavioral therapies is a successful method** to treat OUD.

SOURCE(S): Substance Abuse and Mental Health Services Administration (SAMHSA), 2025.

Which Substance Use Disorders are Treated with Medications?

- Substance Use Disorders with FDA Approved Medications
- No FDA Approved Medications; Medications Not Part of Best Practices



The Importance of Medication for Opioid Use Disorder (MOUD)

Treat Withdrawal

- Muscle pain, dilated pupils, nausea, diarrhea, abdominal cramping, piloerection
- Lasts 14 days
- Methadone or buprenorphine are recommended over abrupt cessation due to risk of return to use, overdose (OD) & death

Address Dopamine Depletion

- Reward/motivation pathway abnormalities persists for months after people stop using
- Treated with methadone or buprenorphine

Treat OUD/Achieve Results

- Without medication, 85% return to opioid use within one year, leading to more deaths
- MOUD decreases
  - Drug use
  - Craving
  - Complications from IVDU
  - Criminal behavior
- MOUD increases retention

SOURCE(S): ASAM, 2020; Mattick, 2003; Mattick, 2009; Lobmaier et al., 2008; Krupitsky et al., 2011; Kakko et al., 2003.

FDA Approved Medication for OUD

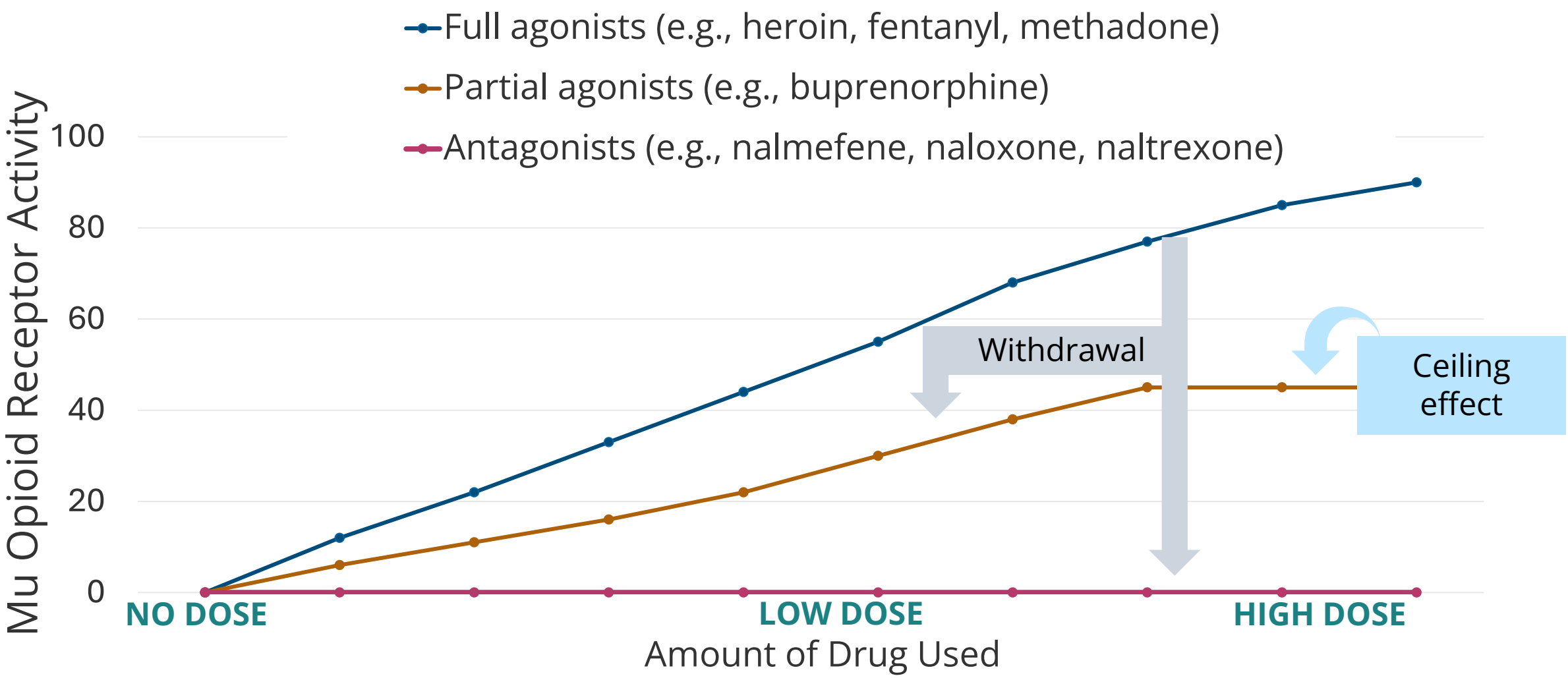
Agonist Treatment (turns on the receptor):

- Methadone- approved for cough in 1940s, for OUD 1972
- Buprenorphine (Suboxone™, Subutex™, Sublocade™ and Brixadi™)- approved in 1981 for pain; oral approved for OUD 2002, patch, implants & injection later

Antagonist Treatment (blocks receptor from turning on):

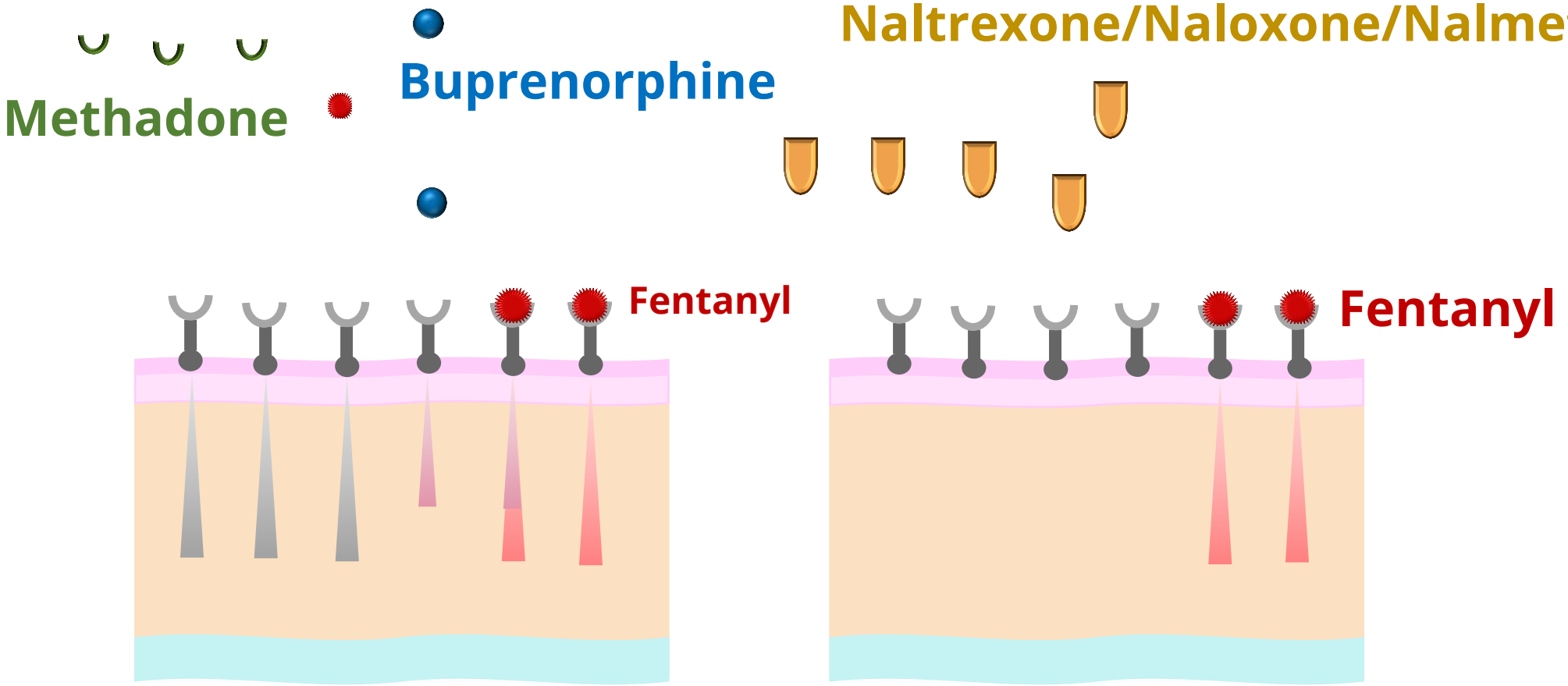
- Naltrexone (Revia™)- oral approved 1984; injectable (Vivitrol™) 2006 for AUD, 2010 for OUD
- Naloxone- approved 1971, autoinjector 2014, nasal spray (Narcan™) 2015
- Nalmefene (Opvee™) - injectable approved 1995; nasal spray approved 2023

Full, Partial, or No Effect



This table is an HMA-generated table compiled from numerous sources.

How do the FDA approved medications work?



Agonist Treatment

Antagonist Treatment

Methadone: What and for Whom?

- Mu opioid receptor full agonist; no “ceiling effect”
- Can start prior to being in withdrawal
- Reaching a therapeutic dose takes time
- Several drug-drug interactions
- Methadone treatment for OUD requires:
  - Opioid Treatment Program (OTP) or Narcotic Treatment Program (NTP); OR
  - Covering a gap of no more than 3 days; OR
  - Patient is in a DEA licensed clinic or hospital with another condition.

Patients with a more severe OUD, such as injecting opioids

Patients who have not reached treatment goals with other MOUD

Patients who would benefit from the close follow up at a Narcotic Treatment program

Methadone: General Federal Regulations

Delivered via observed dosing

Once patient is stable, can be given take-home doses (varies by state)

Highly monitored in a Narcotics or Opioid Treatment Program setting (NTP/OTP)

Requirements for onsite services including therapy, toxicology, etc.

SOURCE(S): National Archives Federal Register the Daily Journal of the United States Government, 2024.

Methadone: Efficacy

- Methadone resulted in 33% fewer positive opioid toxicology tests compared to those receiving no medication when everyone receives psychosocial treatment
- People on methadone:
  - Are 4.4 times more likely to stay in treatment
  - Have less criminal activity
  - Experience reduced infectious disease
  - Experience reduced mortality

SOURCE(S): Lutgen-Nieves, 2021; Mattick, 2009; Metzger,1993; Santo, 2021; Tsui, 2014; Wakeman, 2020.

Buprenorphine: What and for Whom?

- Partial mu opioid agonist with ceiling effect
  - Doses >32 mg don't cause greater respiratory effects
  - Available sublingually alone or in combination with naloxone and as a long acting- weekly or monthly injections
- Greater binding affinity than full agonists
  - Start buprenorphine when client is in moderate withdrawal (to avoid precipitated withdrawal)
  - Other opioids are not as effective when buprenorphine is present
  - Typical dose is 16-32 mg/d
  - Increased frequency and daily dose required during pregnancy
- Fewer drug-drug interactions than methadone

Opioid use disorder or withdrawal

Patient wants agonist treatment

SOURCE(S): BJA, 2023; Mattick et al., 2014; Weimer et al., 2023.

Buprenorphine: Efficacy

- Rate of return to opioid use for persons taking placebo was 100% vs. 25% for persons taking buprenorphine.
- Individuals taking more than 16mg of buprenorphine are 1.82 times more likely to stay in treatment than if on placebo.
- People on buprenorphine:
  - Have less criminal activity
  - Experience reduced infectious disease
  - Experience reduced mortality

SOURCE(S): NIDA, 2021; Mattick, 2014; Wakeman, 2020.

Naltrexone: What and for Whom?

- Mu opioid antagonist with high, competitive binding affinity.
- Does not treat withdrawal or low dopamine levels.
- Must be opioid free before starting and/or have completed withdrawal if recently using.
- No evidence of decreased mortality.

Patients with a high degree of motivation (dopamine)

Patients with a history of OUD and Alcohol Use Disorder (AUD): FDA approved for both

Patients who did not reach treatment goals with methadone or buprenorphine

Can be useful for occasional use or after discontinuation of methadone or buprenorphine

SOURCE(S): Larochelle et al., 2018; Wakeman et. al., 2020.

Naltrexone: General Regulations

No Federal regulations inhibit the use

Not all BH clinics have RN to give injections

Multiple formulations:

- **Pills at 25mg and 50 mg (50-100 mg for AUD)**
- **Long acting injectable 380mg (28-30 days) for AUD and OUD**

Naltrexone: Efficacy

- Extended Release (XR) naltrexone
  - 90% opioid abstinent toxicology tests vs. 35% placebo
  - Decreased incarceration
- XR Naltrexone vs usual care in HIV clinic
  - Fewer days of opioid use for those on XR Naltrexone

SOURCE(S): Krupitsky, 2011; Minozzi, 2011; Korthuis, 2022.

Overdose (OD) Reversal is Harm Reduction

- Mu opioid antagonists: naloxone & nalmafene
- Shorter half-life and more rapid onset of action than naltrexone
- High affinity, competitive binding, and displaces agonists
- Intranasal or intramuscular by bystander
- May require more than one dose
- Opioids have longer half-life than naloxone
- Saves lives; no evidence for increasing drug use
- Good Samaritan law in California
- Revised guidance for adolescents; not a psychotropic medication
- Available over the counter

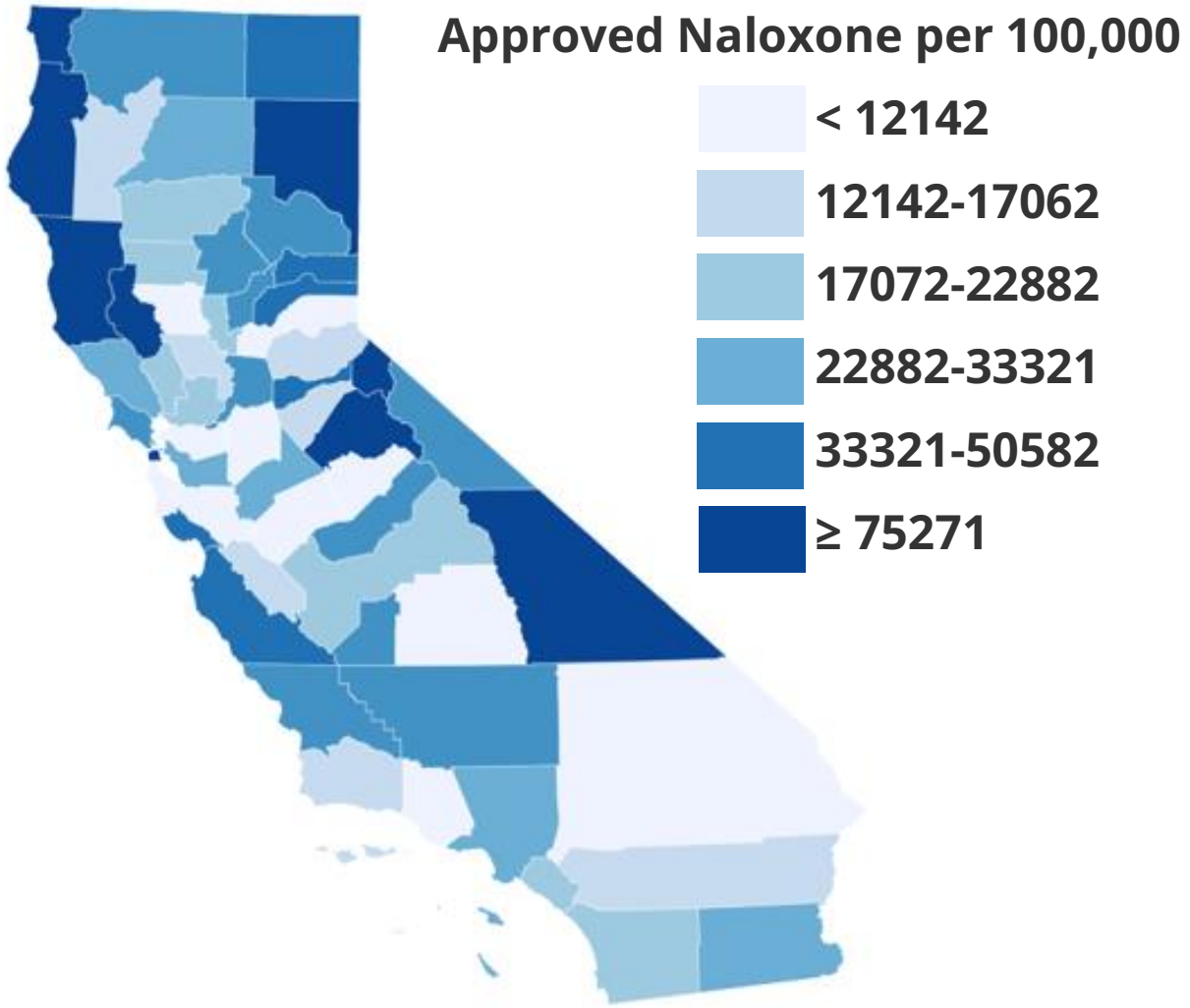
In 2019, 77.3% of 33,084 opioid-involved overdose deaths across 37 states + the District of Columbia had no evidence of naloxone administration.

With additional substances within the illicit drug supply, it is imperative that to provide breaths/oxygen between doses of naloxone.

SOURCE(S): Quinn et al., 2022; Dezfulian et al., 2021.

Naloxone Distribution in California

- The state Naloxone Distribution Project began in 2018 and continues to provide generic naloxone nasal spray through the CalRX Naloxone Initiative.
- Applications for organizations to obtain naloxone and fentanyl test strips can be accessed through the online Naloxone Distribution Project Portal.
- Several counties have interactive maps guiding individuals to access sites.



SOURCE(S): DHCS, 2026; Know the dangers.com, 2026.

Ideas in Action

» Do you know if your organization is currently prescribing (or providing) or doing any training on naloxone?
  - Yes
  - No
  - I Don't Know

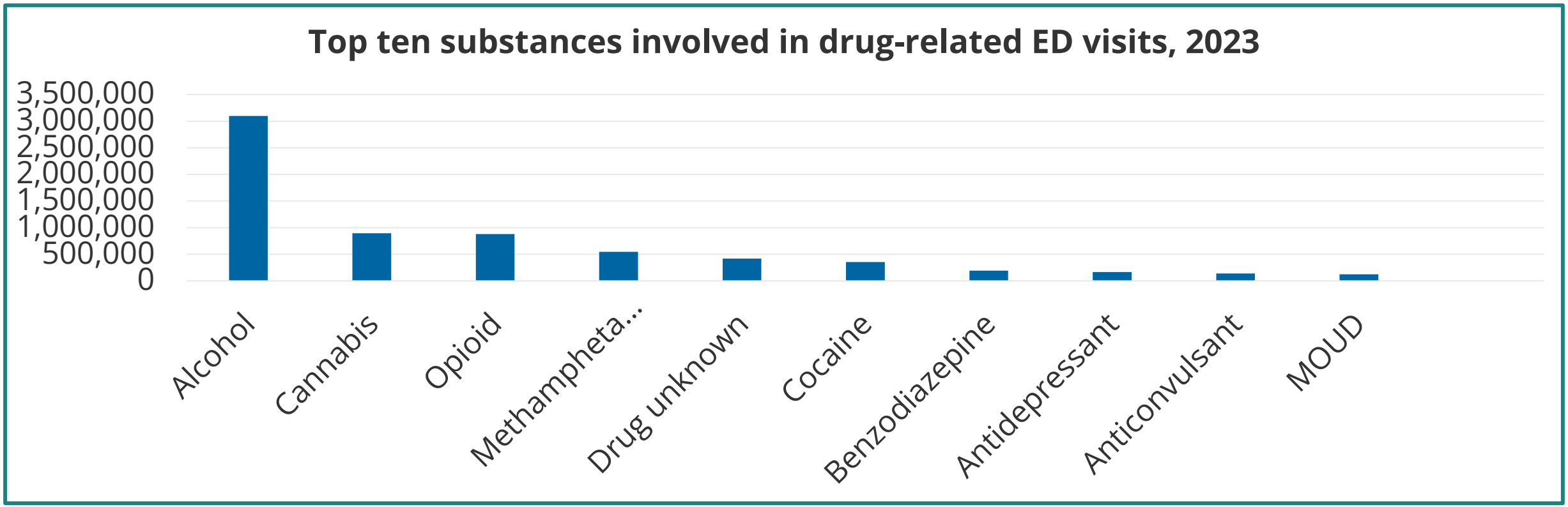
Alcohol

- Alcohol is the most used addictive substance.
- Alcohol-related deaths (worldwide):
  - 2.6 million alcohol-related deaths/year compared to
    - 600,000 drug-related deaths/year.
  - 4.7% of all deaths are related to alcohol consumption.
  - Alcohol is the most common substance causing withdrawal related deaths in jails.

SOURCE(S): SAMHSA, 2024; Saunders and Rudowitz, 2024; WHO, 2024.

Alcohol and Drug Emergency Department Visits

» Alcohol-related ED visits are higher than for any other substance:
  - Exceed 3.1 million in 2023, 3 times more than any other drug class.



SOURCE(S): SAMHSA, 2024.

Medications for Alcohol Use Disorder (MAUD)

Benefits

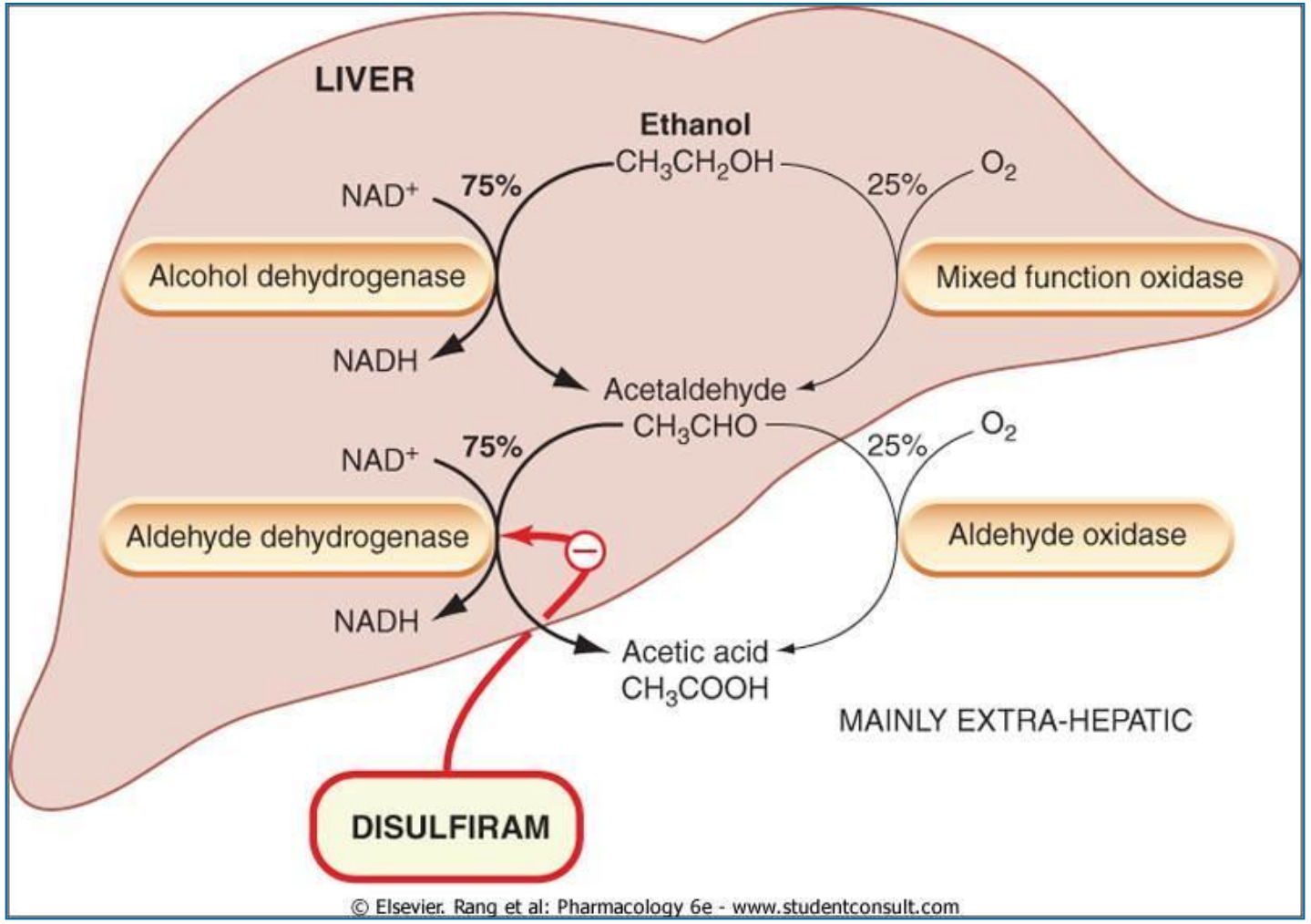
- Decreased Cravings
- Decreased Drinking
- Cost Effective

FDA-Approved Medications

- Acamprosate
- Naltrexone (oral and intramuscular)
- Disulfiram (not proven effective)

SOURCE(S): Higginbotham et al., 2023; Marin et al., 2023; McPheeters et al., 2023.

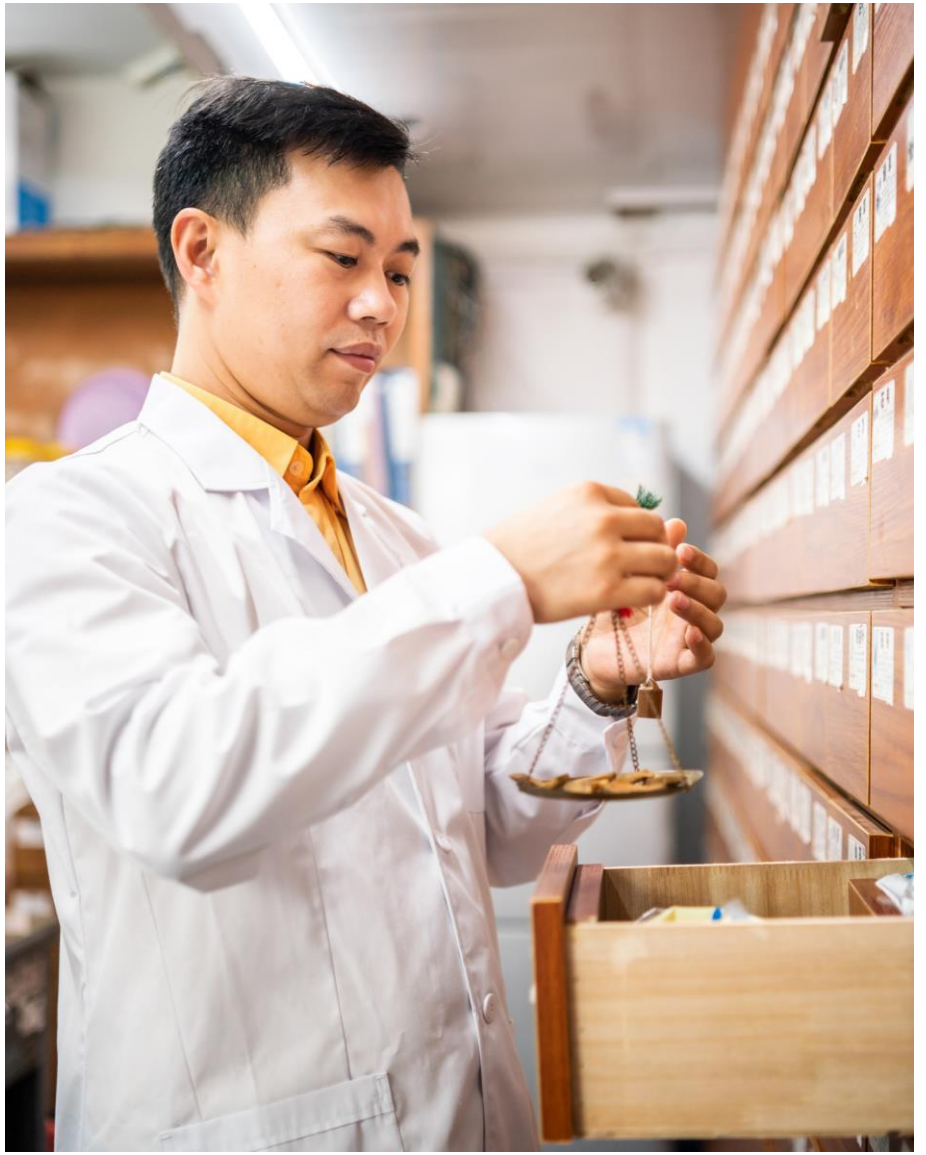
Disulfiram (Antabuse®): Mechanism of Action



- Interferes with how the body breaks down alcohol.
- Can result in uncomfortable symptoms, including:
  - Dyspnea
  - Flushing
  - Hypotension
  - Nausea/vomiting
  - Palpitations
  - Sweating
  - Tachycardia

Disulfiram: Efficacy for AUD

- Approved decades ago; most recent data does not show overwhelming efficacy
- Once per day dosing
- Inhibits multiple P450 and other liver enzymes
- Drug Interactions: benzodiazepines, phenytoin, pimozide, tricyclic antidepressants (TCAs), warfarin, sulfonylureas, metronidazole, amoxicillin, isoniazid
- Contraindications/precautions: alcohol use, hypersensitivity to rubber, severe coronary artery disease (CAD), cirrhosis, severe renal impairment, psychosis, depression, diabetes mellitus (DM), epilepsy
- Extensively metabolized
- Extensive list of side effects



SOURCE(S): McPheeters et al., 2023.

Naltrexone for AUD

- Few side effects
- Drug Interactions: opioids
- Contraindications: severe acute hepatitis
- Well-studied in mild and moderate cirrhosis
- Safe in mild renal disease

SOURCE(S): Garbutt et al.,1999; Garbutt, 2009; Kahan et al., 1995; Solberg et al., 2009.

Naltrexone: Efficacy for AUD

- Oral naltrexone:
  - Decrease return to any drinking.
  - Decrease in return to heavy drinking.
- Long-acting injectable naltrexone:
  - Greater time to first drink.
  - Lower number of heavy drinking days.

SOURCE(S): Kedia et al., 2023; McPheeters et al., 2023; Substance Abuse and Mental Health Services Administration. (SAMHSA), 2015.

Extended Release Naltrexone Compared to Other Agents for AUD

- In multiple studies extended-release injectable naltrexone resulted in the following compared to oral naltrexone or other oral medications for alcohol use disorder:
  - Longer time on medication.
  - Decreased:
    - Emergency department visits.
    - Hospitalizations.
    - Nonpharmacy costs.

SOURCE(S): Bryson et al., 2011.

Acamprosate: Mechanism of Action

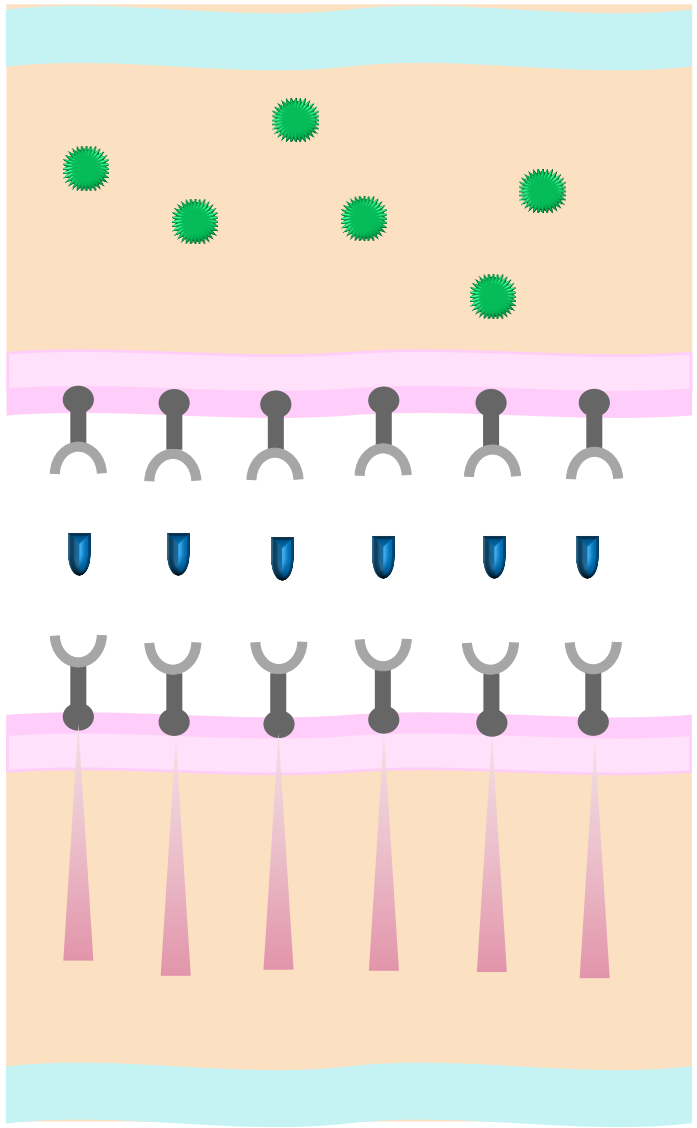
In someone with an active alcohol use disorder acamprosate decreases glutamate.

Glutamate Cell

Glutamate

Acamprosate

Gamma Amino Butyric Acid (GABA) cell



SOURCE(S): Ademar et al., 2023; Kalk and Lingford-Hughes, 2014.

Acamprosate for Alcohol Use Disorder

- Effective
  - Decreased quantity and frequency
  - Increased retention in treatment and abstinence
- Three times per day dosing
- Drug Interactions: none
- Contraindications: severe renal impairment
  - Reduce dose if someone has moderate renal impairment
- Few side effects
- No metabolism

SOURCE(S): Chick, 2003, Mann, 2004.

Behavioral Health and Medication for AUD

» Medication and therapy improved HIV related outcomes

Impact of Behavioral and Medication Treatment for Alcohol Use Disorder on Changes in HIV-Related Outcomes Among Patients with HIV: A Longitudinal Analysis

Kathleen A. McGinnis[a], Melissa Skanderson[a], E. Jennifer Edelman[b,g], Adam J. Gordon[c], P. Todd Korthuis[d], Benjamin Oldfield[b], Emily C. Williams[e,f], Jessica Wyse[d], Kendall Bryant[g], David A. Fiellin[b,h], Amy C. Justice[a,b], Kevin L. Kraemer[i,j]

SOURCE(S): McGinnis et al., 2020.

Ideas in Action

» Do you know anyone on medication for Alcohol Use Disorder?
- Yes
- No
- Unsure

Chronicity of Addiction and Duration of Treatment

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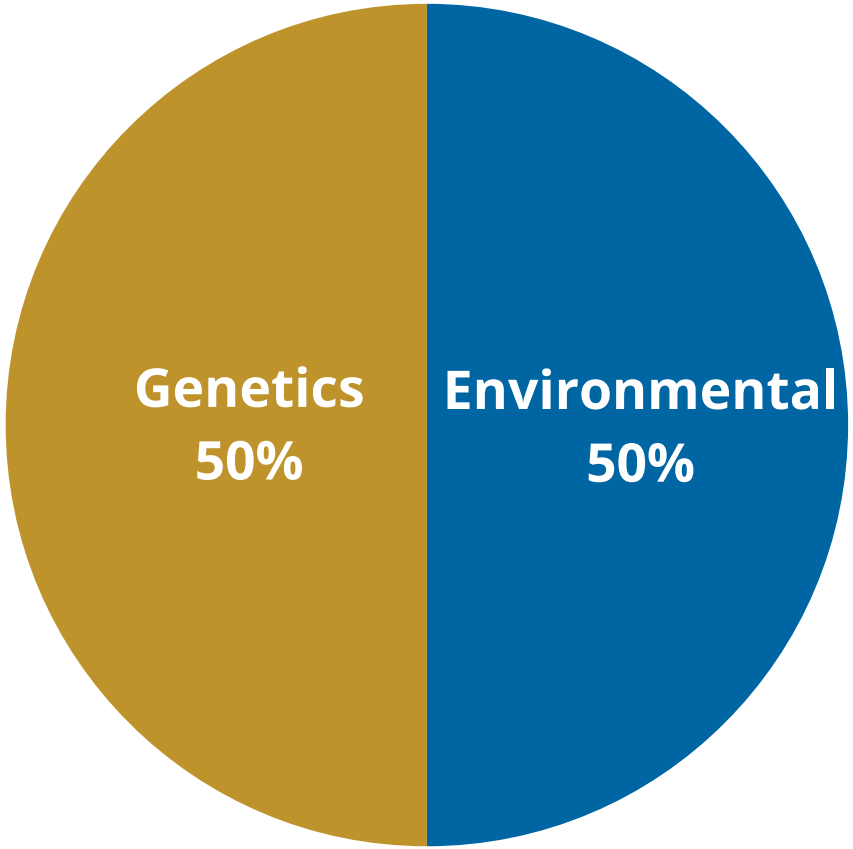
Etiology of Substance Use Disorders

Psychiatric Disorders

Personality

Family History of Addiction



Drug Access and Availability

Cultural Norms

Family Dynamics

Trauma and Abuse

Religious/Spiritual Values

Peer Dynamics/Social Support

Age of First Use

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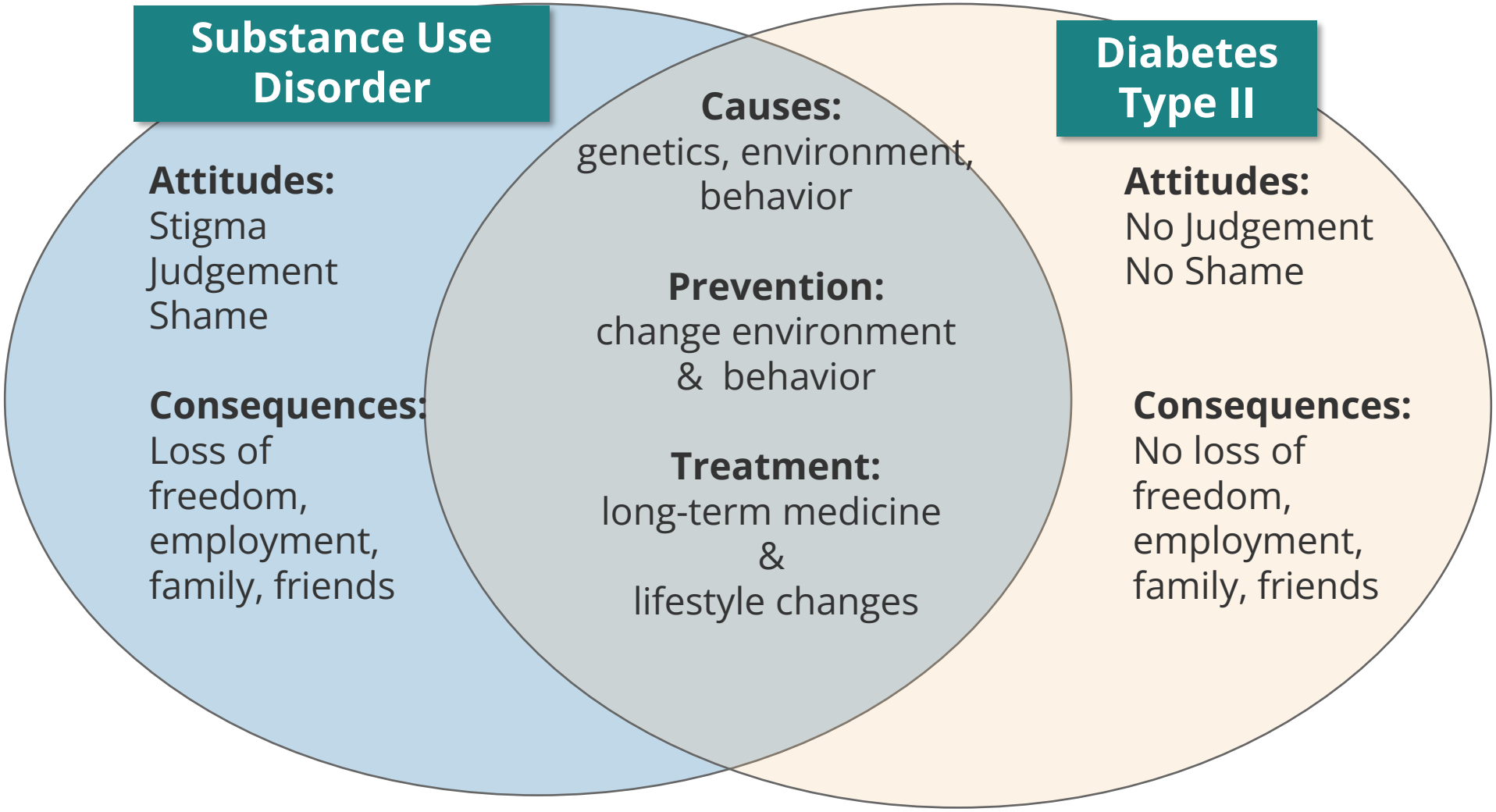
Comparison of Two Chronic Diseases



How Long to Treat OUD?

- Long-term or indefinite treatment with medications is often needed.
- Discontinuing medication is usually only successful in about 15% of cases.
- Discontinuing medication without return to opioid use usually occurs, if at all, when people have been treated with MOUD for at least 3 years.
- Factors associated with decreased risk of return to use:
  - Sober support network
  - Ability to manage stress and conflict

SOURCE(S): Mancher and Leshner, 2019; Nosyk et al., 2012. Substance Abuse and Mental Health Services Agency (SAMSHA) and the Office of the Surgeon General, 2018.

Questions?

info@afbsstraining.org

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Naloxone Resources

- CA Department of Health Care Services Naloxone Distribution Project website
- CA Department of Public Health (CDPH), Substance and Addiction Prevention Branch Naloxone website
- CDPH Over the Counter Naloxone website
- NEXT Distro – a website with naloxone access by state
- The National Harm Reduction Coalition
- Know the Dangers website

Naloxone Resources (Continued)

- An important part of a naloxone distribution program is to provide training to individuals who may give naloxone. Listed below are training resources:
  - Linked Here: https://www.youtube.com/watch?v=nurz9qPGKws
  - Administración de Naloxona: video de capacitación en español (YouTube)
  - Naloxone Training for Health Care Providers: Centers for Disease Control and Prevention (CDC) offers several naloxone training modules for health care providers. Earn continuing education credits (CE) after completing the full module.
  - Overdose Education and Naloxone Distribution (webinar recording): Training for professionals who will be responsible for educating laypersons about opioid overdose and distributing naloxone in their community.
  - Implementing Naloxone Distribution Systems (webinar recording): Training for program managers and others responsible for the implementation of community naloxone distribution programs.

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