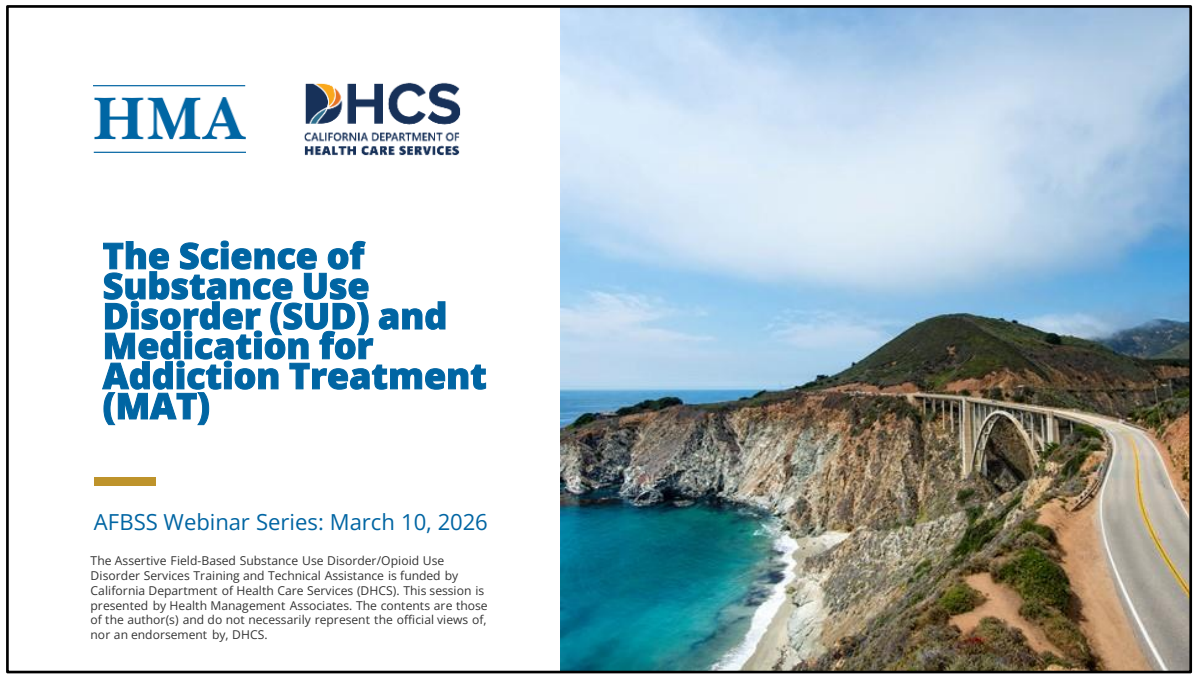

[Slide Image Description: This cover slide introduces the title of this webinar. It contains the logos for Health Management Associates.]

Disclaimer: This session is presented by Health Management Associates. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, California Department of Health Care Services.

Disclosures

Faculty	Nature of Commercial Interest
Helen DuPlessis, MD, MPH	Dr. DuPlessis discloses that she is an employee of Health Management Associates, a national research and consulting firm providing technical assistance to a diverse group of health care clients. Dr. DuPlessis is on the Board of Blue Shield Health Plan of California.
Anika Alvanzo, MD, MS	Dr. Alvanzo discloses that she is an employee of Health Management Associates, a national research and consulting firm providing technical assistance to a diverse group of health care clients.
Jeanene Smith, MD, MPH, CME Reviewer	Dr. Smith discloses that she is an employee of Health Management Associates, a national research and consulting firm providing technical assistance to a diverse group of health care clients.

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[Slide Image Description: This slide shows Continuing Education disclosures.]

- Helen DuPlesis, MD: Ms. DuPlessis discloses that he is an employee of Health Management Associates, a national research and consulting firm providing technical assistance to a diverse group of health care clients.
- Anika Alvanzo, MD: Ms. Alvanzo discloses that she is an employee of Health Management Associates, a national research and consulting firm providing technical assistance to a diverse group of health care clients.
- Jeanene Smith, MD, MPH: Dr. Smith discloses that she is an employee of Health Management Associates, a national research and consulting firm providing technical assistance to a diverse group of health care clients.

Presenters

Anika Alvanzo, MD, MS, FACP, DFASAM
Physician Principal
Health Management Associates (HMA)

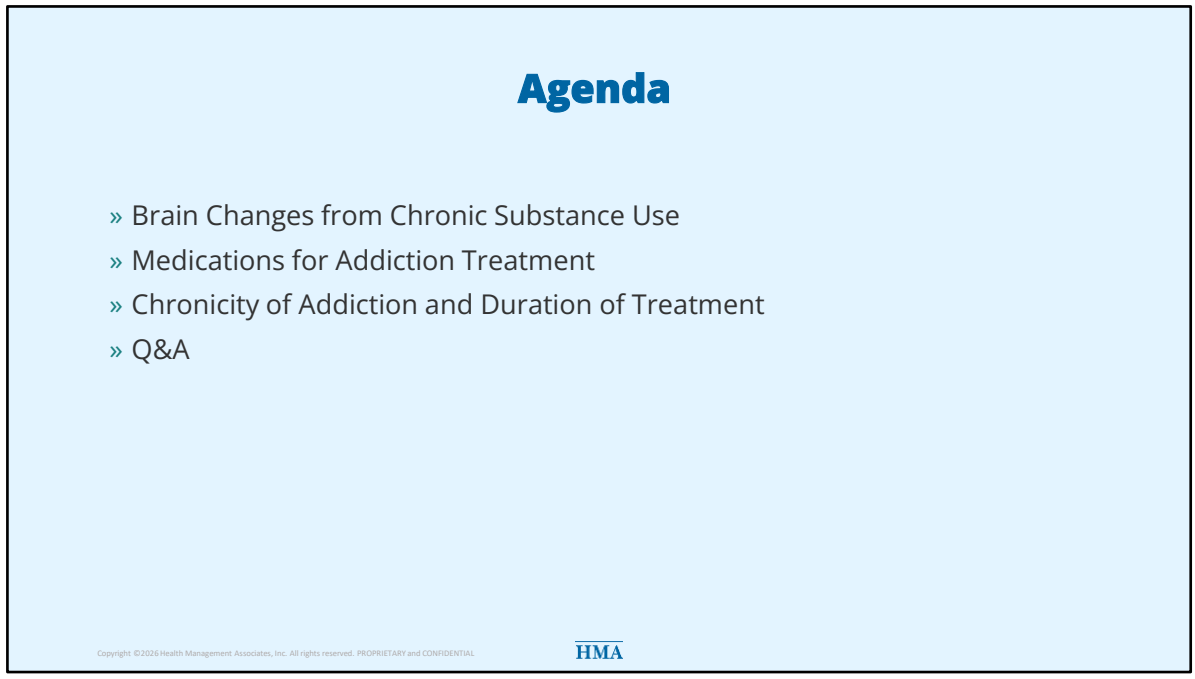
Helen DuPlessis, MD, MPH
Physician Principal
Health Management Associates (HMA)

HMA

[Slide Image Description: This slide includes images of the presenters of this webinar on a light blue background.]

Dr. Anika Alvanzo is a distinguished health care executive with over 15 years of experience in specialty addiction treatment, behavioral health integration, and quality improvement. At Health Management Associates (HMA) Dr. Alvanzo's consulting has focused on supporting state and local jurisdictions in community needs assessment and strategic planning for behavioral health service delivery; provision of training, technical assistance and coaching to behavioral health providers; implementation of the American Society of Addiction Medicine (ASAM) Criteria; and advancing cultural humility in addiction treatment.

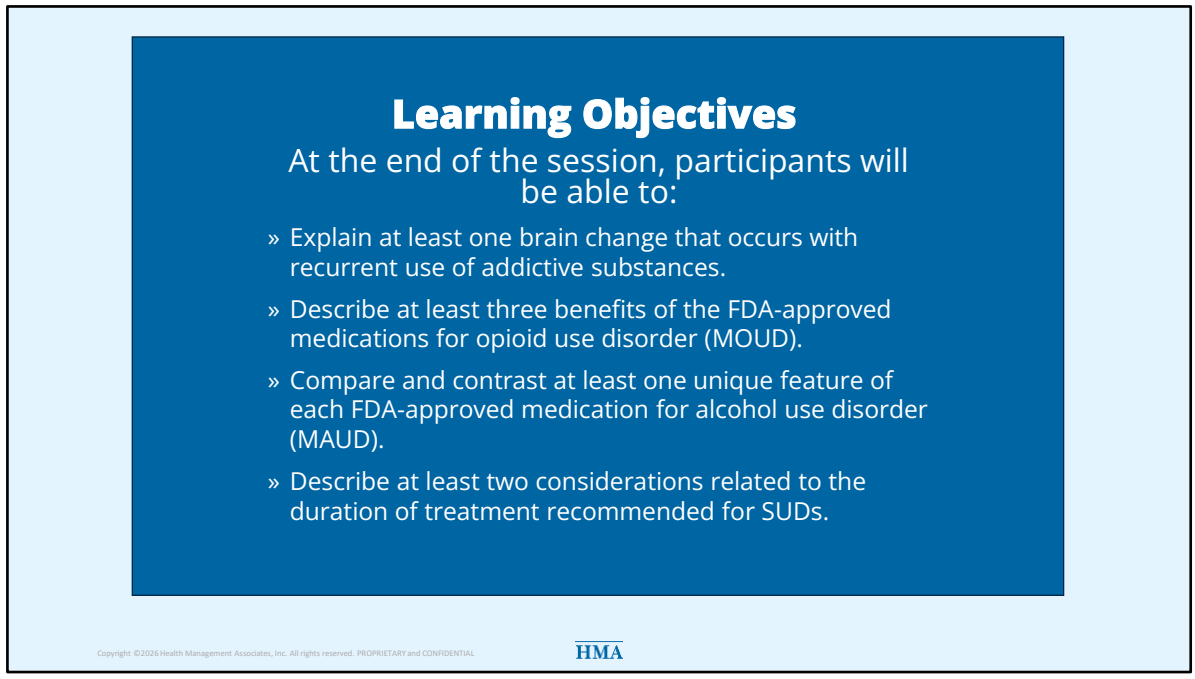
Dr. Helen DuPlessis is an accomplished physician executive who brings extensive leadership experience and a wealth of in-depth knowledge about public sector health programs to HMA. She has a rich history of involvement in healthcare administration for a variety of organizations, expertise in program and policy development, practice transformation, public health, maternal, and child health policy, community systems development, performance improvement, and managed care. With a proven track record in understanding and implementing innovative and effective health programs and performance improvement activities, she has served as an advocate of community capacity-building, staff and professional development.



[Slide Image Description: This slide shows the major sections of this webinar on a light blue background.]

Today's session will cover the following topics:

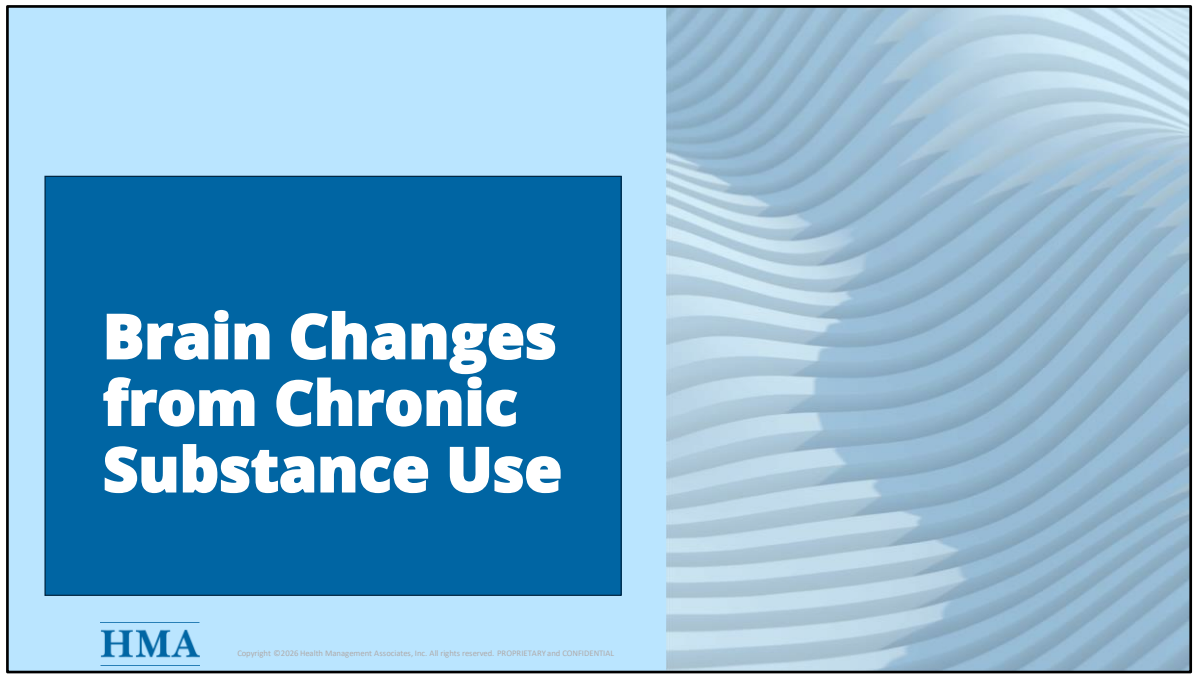
- Brain Changes from Chronic Substance Use
- Medications for Addiction Treatment
- Chronicity of Addiction and Duration of Treatment
- Q&A



[Slide Image Description: This slide shows the learning objectives for this webinar with a light blue background.]

At the end of the session, participants will have an increased ability 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.



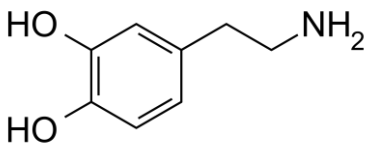
[Slide Image Description: This is a section divider slide to indicate a major section of this webinar.]

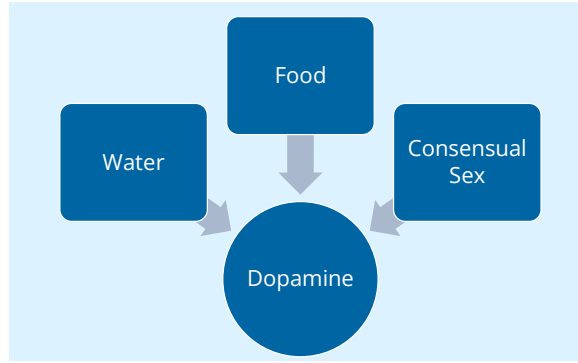
This first section looks at brain changes from chronic substance use.

Natural Rewards Release Dopamine

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

Dopamine





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[Slide Image Description: This slide shows information about Dopamine, including the chemical structure and a graphic with “water,” “food,” and “consensual sex” in boxes pointing at “Dopamine” in a circle.]

Information around dopamine included in this presentation has accumulated over 30 years. Dopamine is the reward chemical in our brain; it is released from a more primitive area of the brain, an area which motivates behaviors essential for life and survival of the species.

When we do things we find pleasurable, it’s because dopamine is released in our brain. When we eat, drink fluids, or have an orgasm dopamine is released in our brains. Dopamine is what is motivating us to do things that sustain our life, eat food, drink water and have sex. Without these things humans would die out.

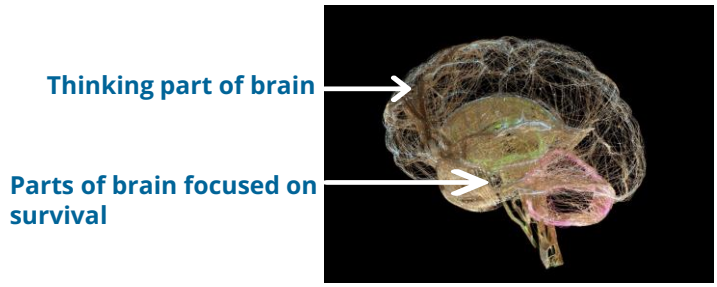
Dopamine is also released when our boss tells us we did a good job, when your kid hits a home run, when we have a dance party with our kids, or when I make my friends laugh. We feel pleasure and this drives us or motivates us to engage in that behavior again in the future.

The way our brain ensures we do these things to live and reproduce is to release dopamine when we do these things; this motivates us to do this again and again because it feels good and is rewarding.

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.

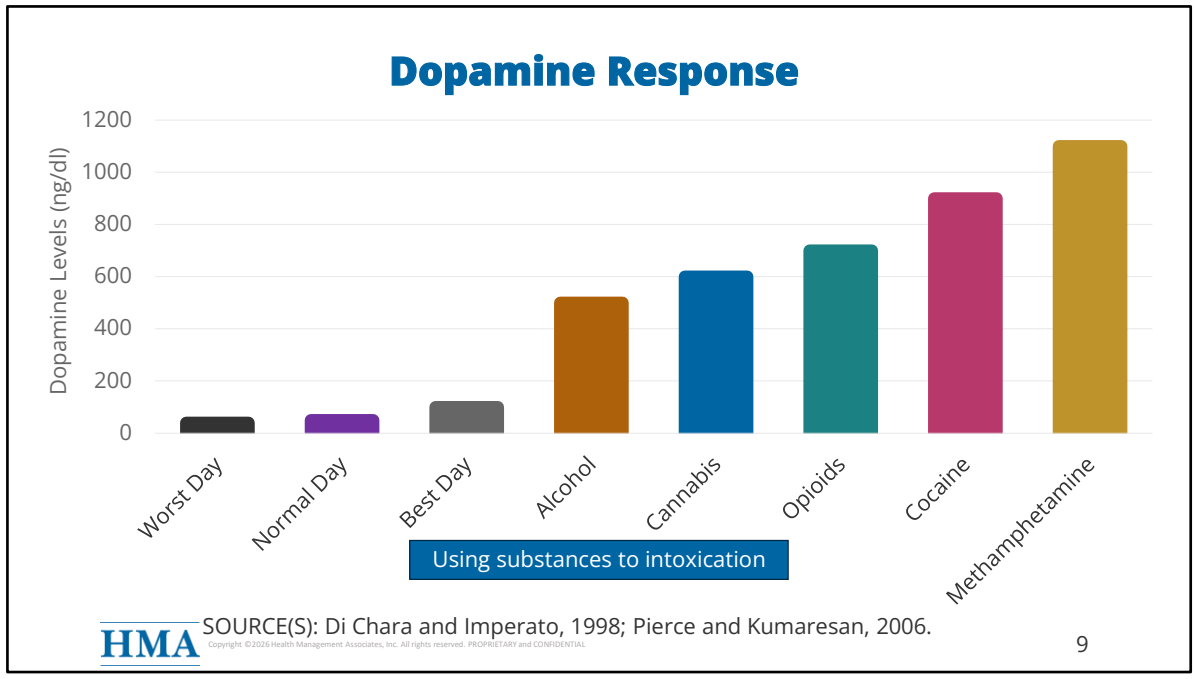
[Slide Image Description: This slide shows information about addictive substances affecting the brain, with an image of a brain.]

All addictive substances result in the activation of the reward pathway, increasing dopamine. Dopamine is in the same part of the brain that feels good when we eat yummy food or you make someone laugh.

This pathway in our brains starts in the old or more primitive part of our brain, the part of our brain we share with dinosaurs. However, this more primitive part of the brain has a pathway that goes to the thinking part of our brain. The part of the brain that controls judgement, impulsivity, and decision-making. The part of the brain where we can think about whether doing something is a good idea or not; like using a needle which might have germs in it.

The pathway starts in parts of the brain that we do not have control over. More specifically, the dopamine pathway starts in the Ventral Tegmental Area (between the pink and green toward the front), then signals are sent to Nucleus Accumbens, then to the prefrontal cortex.

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



[Slide Image Description: This slide shows a chart for dopamine response.]

The information in the chart relies on many years of studying, mostly on animals and some in humans.

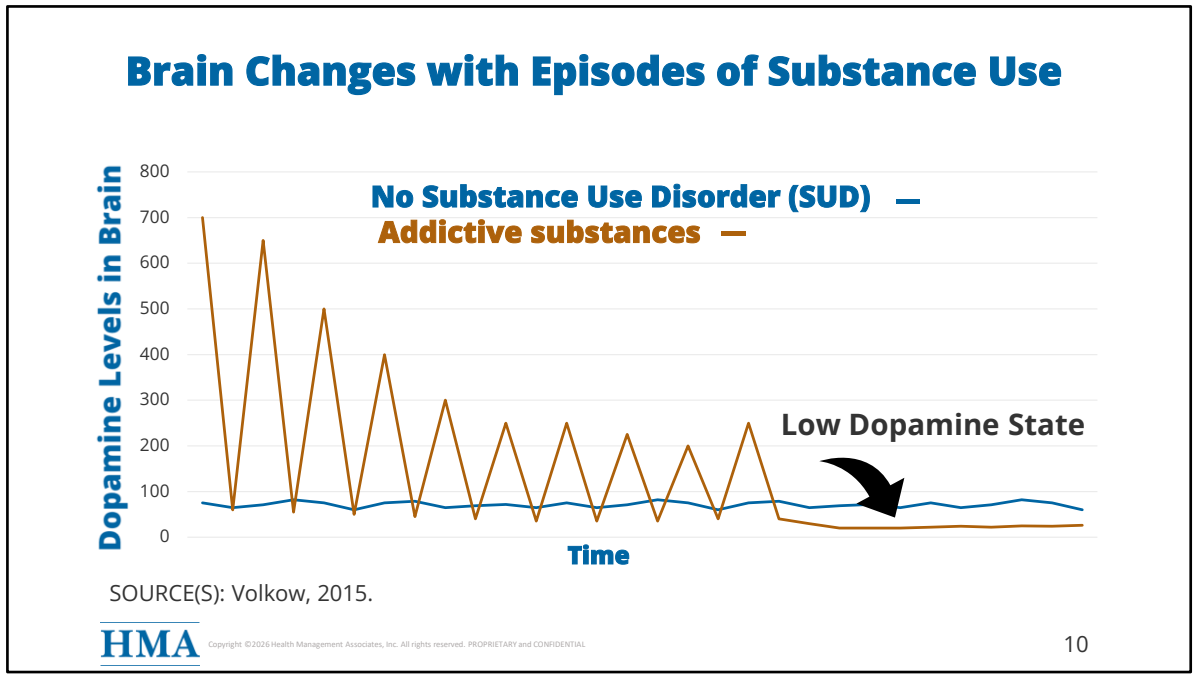
We don't have a way to check dopamine levels in the brain of humans, like we can in animals. But on a regular day for someone who doesn't use drugs, they have about 50 units of dopamine in their brain (we don't need to worry about the exact unit, just remember the different amounts).

When we eat something yummy or laughing a lot, we get about 90 units. On the absolute best day ever—when you get a raise, one child gets into college, and your partner tells you they won the Powerball lottery—we might have 100 units. And on the worst day, when we're really sick and can't do anything fun, we have about 40 units.

Now, when people drink too much alcohol, they get around 500 units of dopamine. With cannabis (marijuana), it's about 600 units. For heroin/ fentanyl, it's around 700 units. Cocaine is about 900 units. And with amphetamines, 1100 units of dopamine.

The dopamine release in response to substances is orders of magnitude greater than what natural rewards can provide. This graph shows that our brain likes these substances, way more than eating or laughing.

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



[Slide Image Description: This slide shows a chart for brain changes with episodes of substance use.]

Repeated use of substances causes wide fluctuations in dopamine levels, represented by the orange line on the graph. Over time, with chronic use of substances there is down regulation of the dopamine levels in the brain such that people end up in a low dopamine state.

This low dopamine state results in a persistent feeling of anhedonia, dysphoria, or limited ability to experience pleasure. People often no longer use substances to get high; they are using just to feel normal.

Intensity of Cravings

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

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

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[Slide Image Description: This slide shows a images of raisins, grapes, and a vineyard.]

Craving is “a direct or indirect force pulling someone towards a substance or behavior.” Consider the following analogy.

Over the past few decades, studies have looked at how much someone’s brains light up when water has been withheld for 3 days, nothing by mouth and no intravenous fluids for days. Then they are placed in a functional MRI machine, talked to about water and fluids, listen to sounds of water, and see pictures, followed by looking at how much the brain lights up; roughly and relatively the size of a raisin.

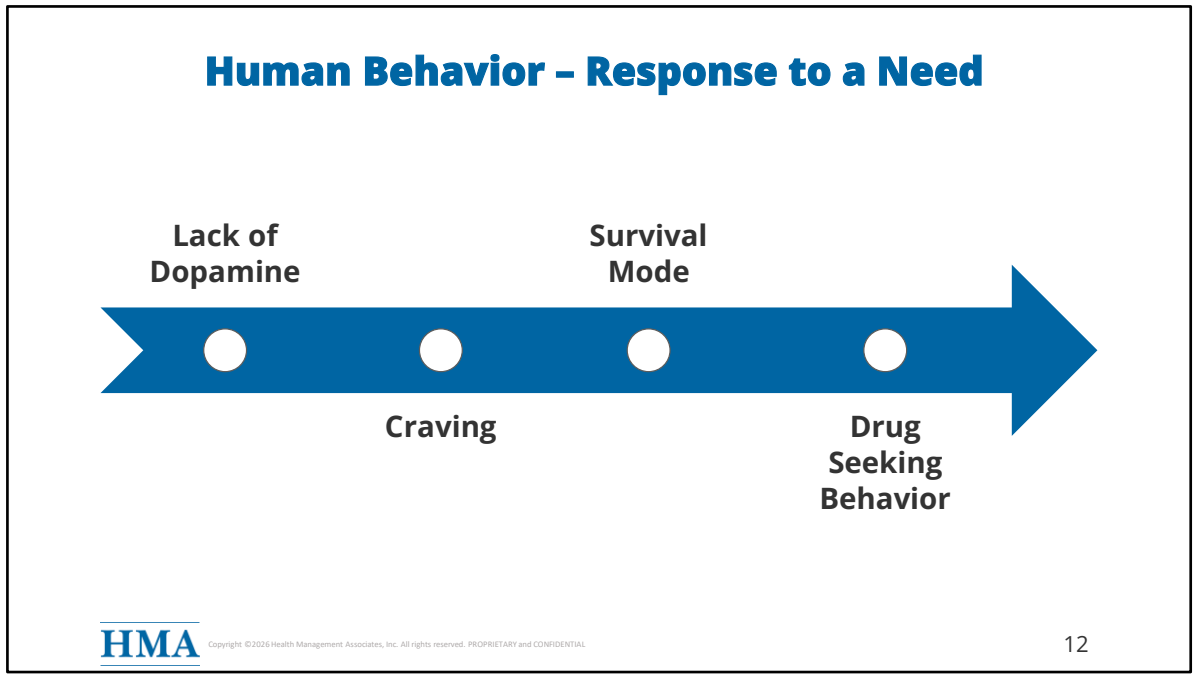
Other patients are hospitalized and kept away from food for 2 – 5 days, and then placed in a functional MRI machine. The researchers talk with them about and show them pictures of their favorite food, and send in smells of food to the MRI machine. The brain lights up relatively the size of a grape.

There have been similar studies in people who have been away from drugs

for 30 to 90 days, and even at one or two years of sobriety. While they are in the functional MRI machine, the researchers talk to them about and show them pictures of their drug of choice. Their brains light up relatively the size of a vineyard.
The intensity of craving for substances is 1,000 times greater for drugs than the intensity of craving for food or water.

These brain changes are not only in the presence of the drug, but also reflect the intensity of cravings for drugs are much larger (like this vineyard) compared to the craving for fluid or food (like the raisin and grape)—things that actually sustain our life.

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



[Slide Image Description: This slide shows human behavior in response to a need, with a decorative arrow.]

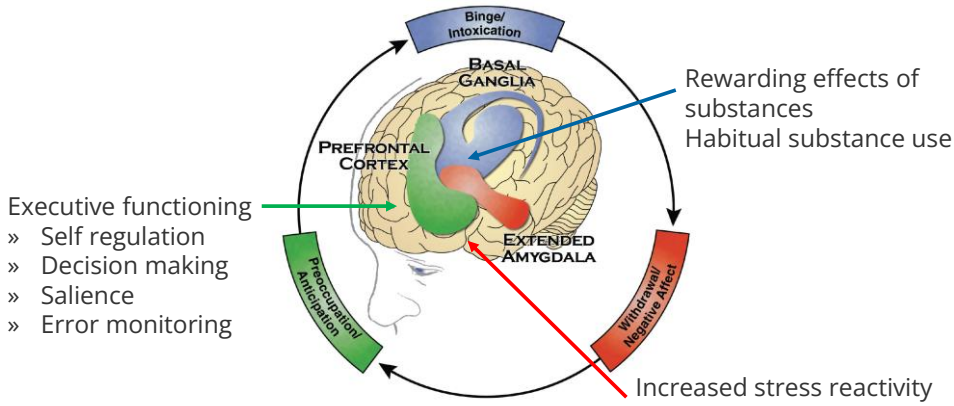
Think back to the graph of the low dopamine state in the brain. When individuals have that lack of dopamine and their cravings for drugs are exponentially greater than for food or water, they are in survival mode.

This often results in a state in which people engage in behaviors that are not in line with their character, just like someone that is severely dehydrated (or starving).

People engage in high-risk sexual behaviors, use dirty needles, lie, manipulate and do other things they would not normally do if their brain chemistry was stable.

Keep in mind this low dopamine state when thinking about treatment options for opioid use disorder.

Addiction and Associated Brain Regions



SOURCE(S): NIH, 2016.

[Slide Image Description: This slide shows information about addiction and associated brain regions, with an image of a brain.]

In addition to the reward pathway and dopamine release, there are other areas of the brain affected by chronic substance use and addiction.

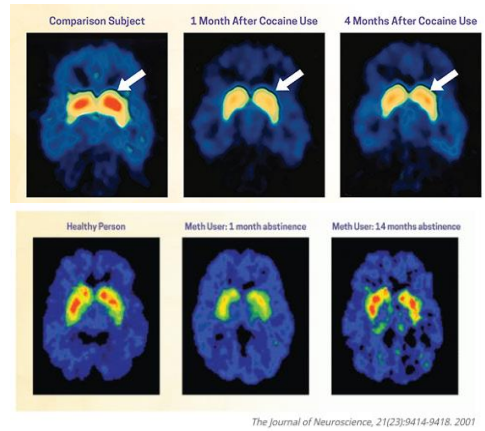
Based on both animal and human studies there are three primary regions of the brain that contribute to both the development and persistence of substance use.

1. The basal ganglia are deep brain structures associated with the experience of reward, motivation, and habit formation. This is where dopamine is released.
2. The extended amygdala regulates the brain's response to stress and with repeated substance use promotes increased stress reactivity and development of negative emotions associated with stress.
3. The prefrontal cortex is responsible for executive functioning, or complex cognitive tasks.
    - In particular, it governs one's ability to organize and prioritize thoughts and actions and the salience (or relative value assigned to those thoughts and actions.)

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.



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

HMA

[Slide Image Description: This slide shows information about brain recovery, with multiple brain scan images.]

Prolonged drug use changes the brain in long lasting ways

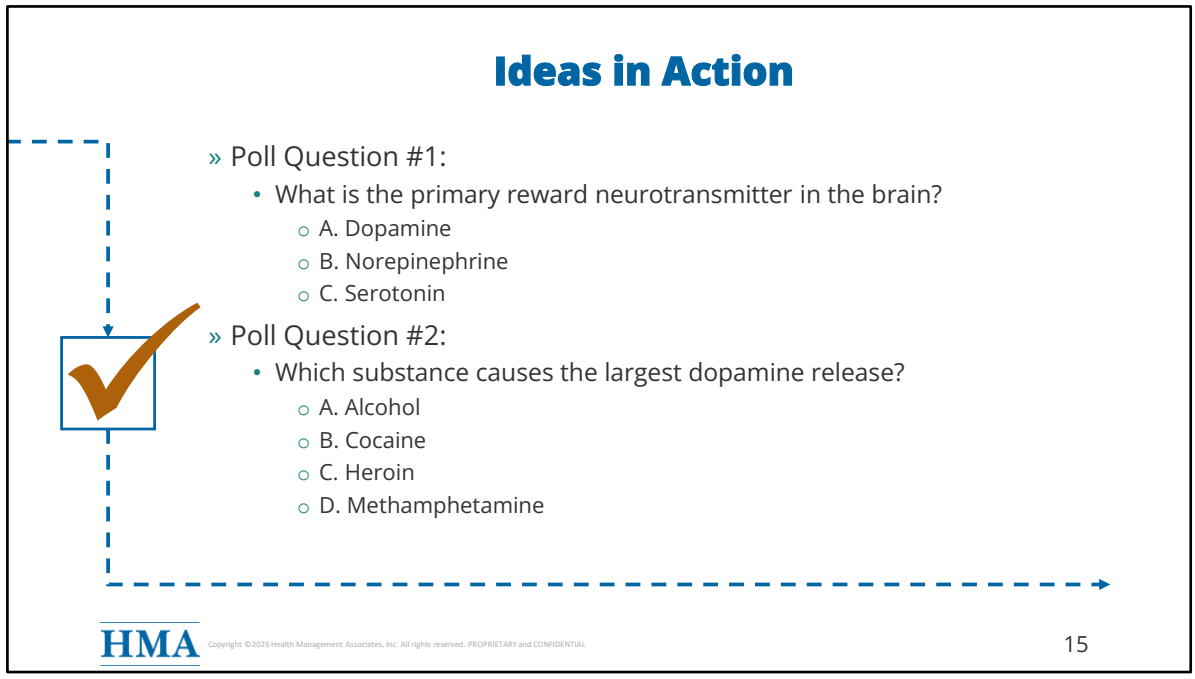
- Brain imaging, including PET scans and functional MRIs, can show the lasting effects of substance use on the brain.
- In the images on the slide, the amount of dopamine receptors in the brain are being measured. The red is indicative of a normal amount of dopamine receptors in the brain. Recall, that dopamine is the reward chemical in the brain and with chronic use of substances, dopamine gets depleted.
- The picture on the top left shows the brain of someone who did not have exposure to cocaine. Look at all of the red.
- The picture on the top middle shows the brain of someone with a cocaine use disorder, one month after their last use of cocaine. You'll note there is very little red.
- The picture on the top right shows the brain of someone four months after their last use of cocaine. Still very little red, meaning persistent low levels of dopamine.

Changes are both functional and structural; return to normal takes over one year.

- While the changes that occur in the brain are long-lasting, it is important to know that the brain can recover.
- The picture on the bottom right shows the brain of someone 14 months after their last use of methamphetamine; note the amount of red looks closer to that of the brain of someone not exposed to methamphetamine.

However, stopping medication before the brain recovers may lose the desired outcomes.

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



[Slide Image Description: This is an Ideas in Action slide that provides an opportunity for participants to practice using the information. It contains a checkbox and an arrow.]

Poll Question #1:

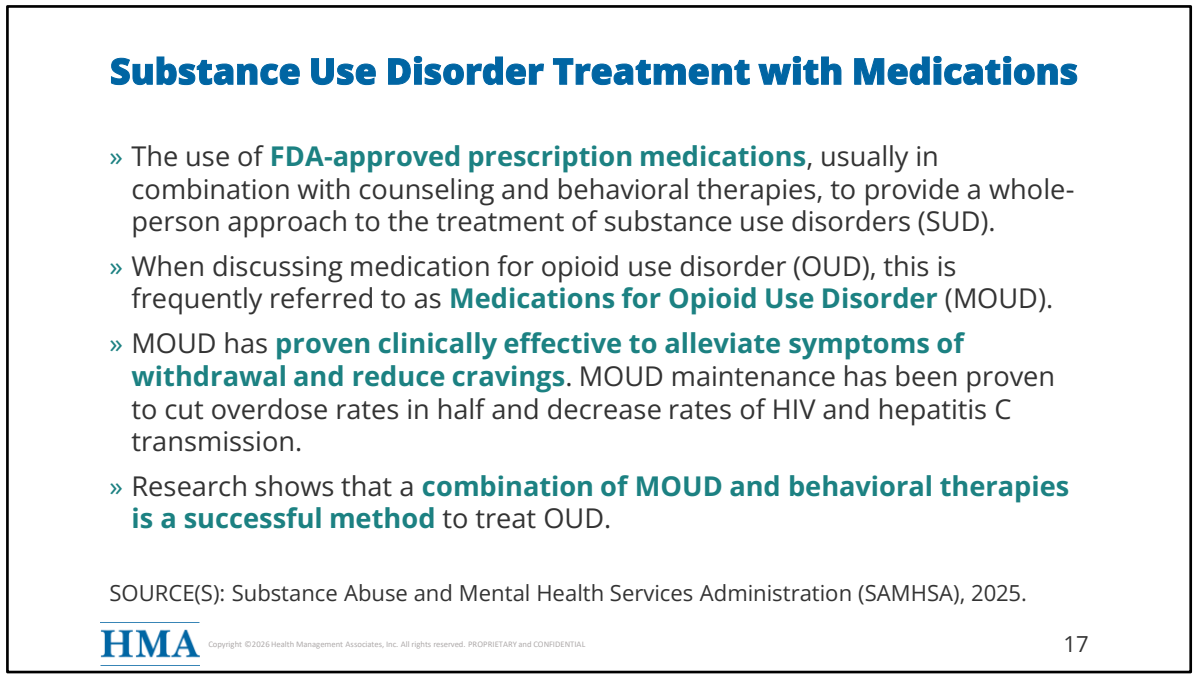
- What is the primary reward neurotransmitter in the brain?
    - **A. Dopamine**
    - B. Norepinephrine
    - C. Serotonin

Poll Question #2:

- Which substance causes the largest dopamine release?
    - A. Alcohol
    - B. Cocaine
    - C. Heroin
    - **D. Methamphetamine**

[Slide Image Description: This is a section divider slide to indicate a major section of this webinar.]

This second section looks at medications for addiction treatment.

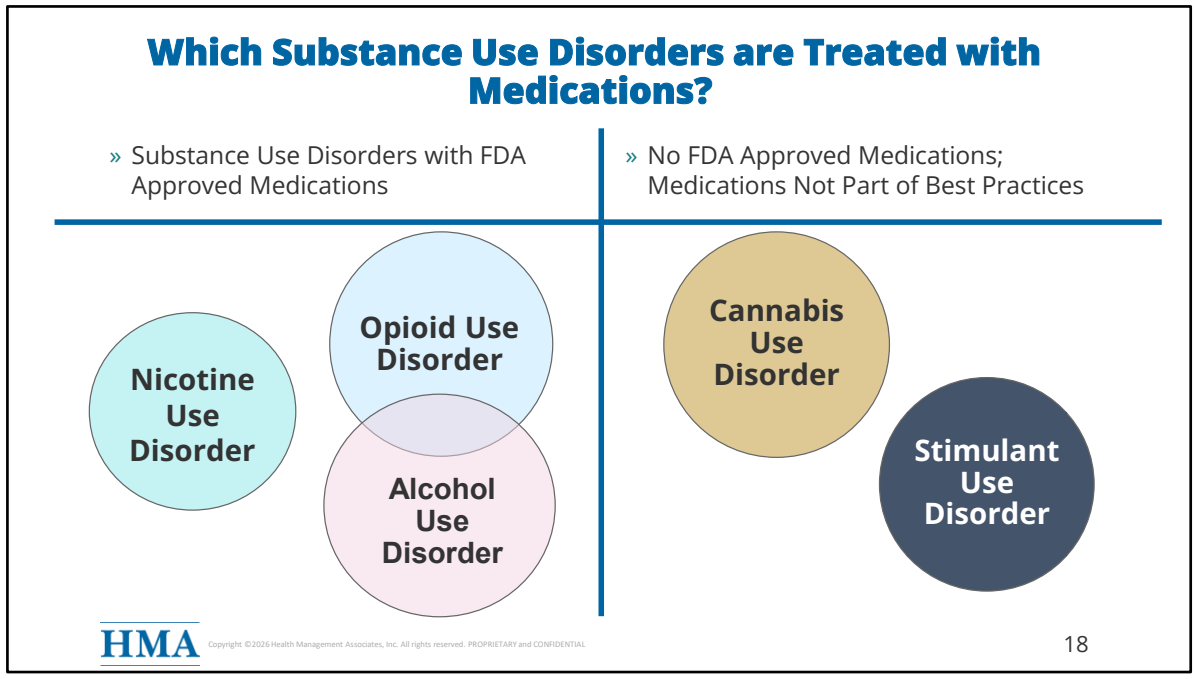


[Slide Image Description: This slide shows information about substance use disorder treatment with medications.]

Substance use disorder (SUD) treatment with medications:

- The use of FDA-approved prescription medications, often in combination with counseling and behavioral therapies, can provide a whole-person approach to the treatment of 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 & reduce cravings and is associated with reduction in drug use and retention in SUD treatment.
- Yet, the benefits of MOUD extend beyond treatment engagement and decreased drug use. Specifically, MOUD has been proven to decrease rates of HIV and hepatitis C transmission, and cuts overdose rates in half.
- Research shows that a combination of MOUD and behavioral therapies is a successful method to treat OUD.

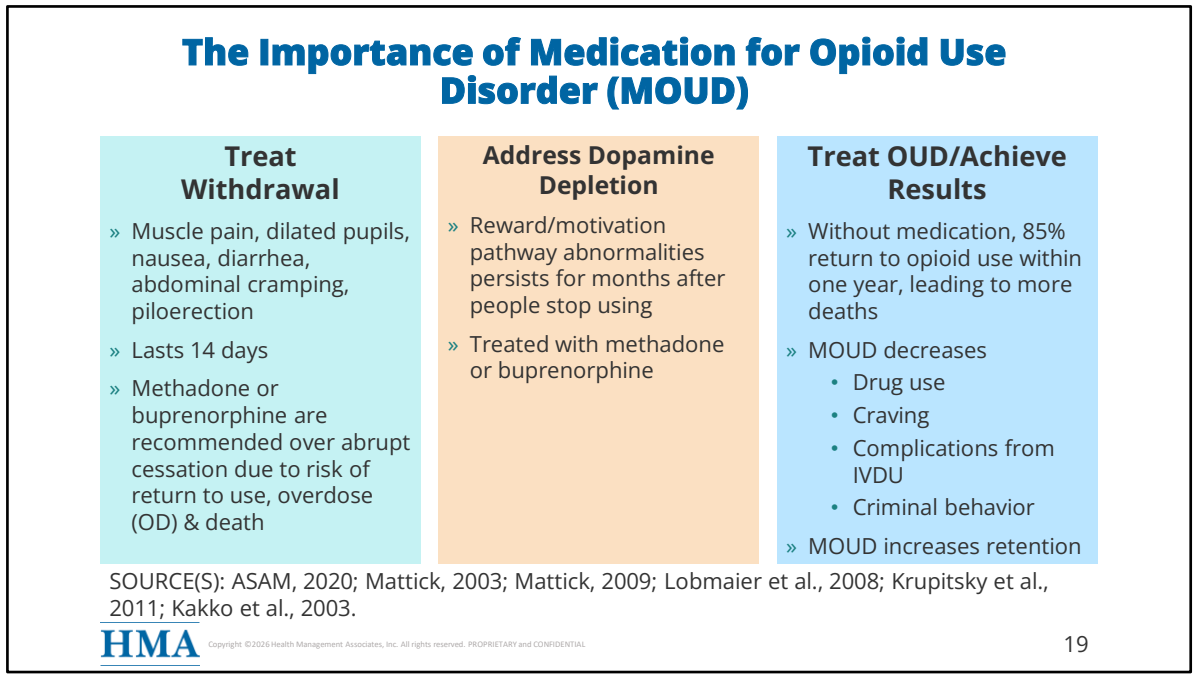
SOURCE(S): Substance Abuse and Mental Health Services Administration (SAMHSA), 2025.



[Slide Image Description: This slide shows information on SUD medications, with colorful circles surrounding types of disorders.]

There are FDA-approved medications for treatment of opioid use disorder (MOUD), medications for alcohol use disorder (MAUD), and medications for nicotine use disorder.

There are no FDA-approved medications for other substance use disorders, most notably we don't have FDA-approved medication treatments for stimulant use disorder (cocaine, methamphetamine) or for cannabis.



[Slide Image Description: This slide shows information about the importance of medication, with three colorful boxes.]

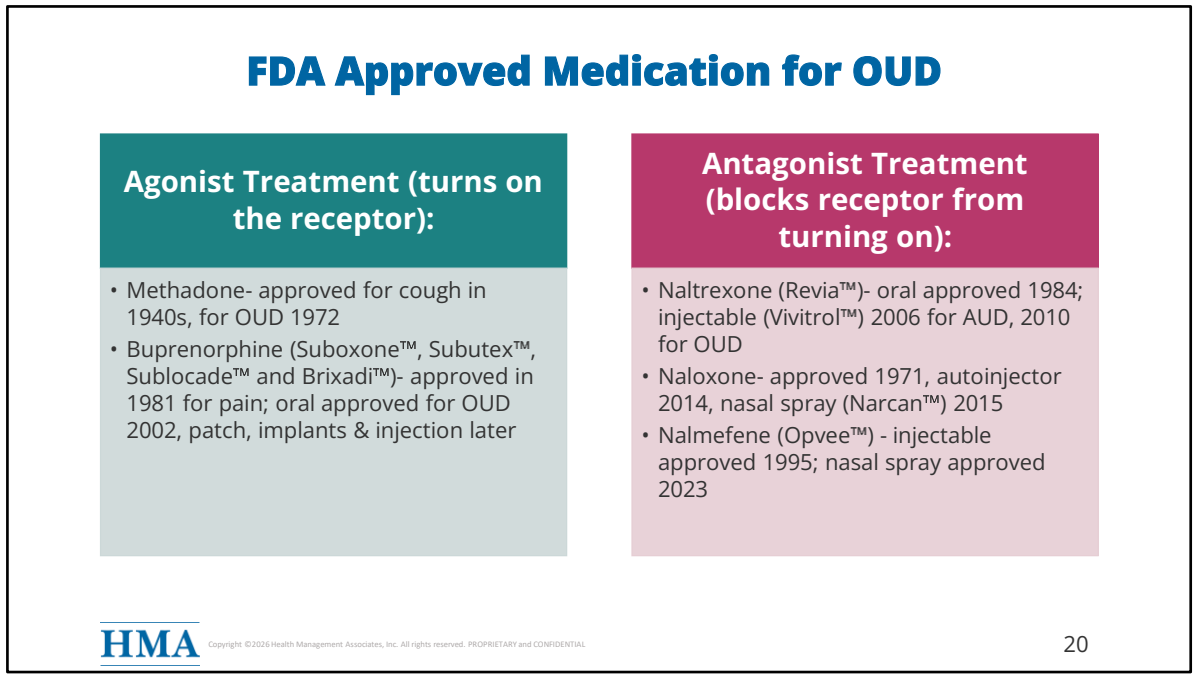
Why do we use medications for treatment of opioid use disorder?

- Two of the three FDA-approved MOUD, methadone and buprenorphine, are effective in controlling withdrawal symptoms that occur with cessation or reduction in opioid use, which for many is a reason for return to use. This includes the following symptoms:
    - Muscle pain
    - Dilated pupils
    - Nausea
    - Diarrhea
    - Abdominal cramping
    - Piloerection
- Reward/motivation pathway abnormalities persists for months after people stop using. Treating with methadone or buprenorphine, which are long-acting opioids that bind to the opioid receptors in the brain for an extended time, is effective in addressing the dopamine depletion that results from chronic use of opioids.

- At one year, 85% of people with OUD who are not treated with medication return to opioid use, resulting in more deaths than without treatment. MOUD decreases drug use, craving, complications from IVDU, and criminal behavior, as well as increases treatment engagement and retention.

Naltrexone does not treat withdrawal or address dopamine depletion, but not everyone has dopamine depletion.

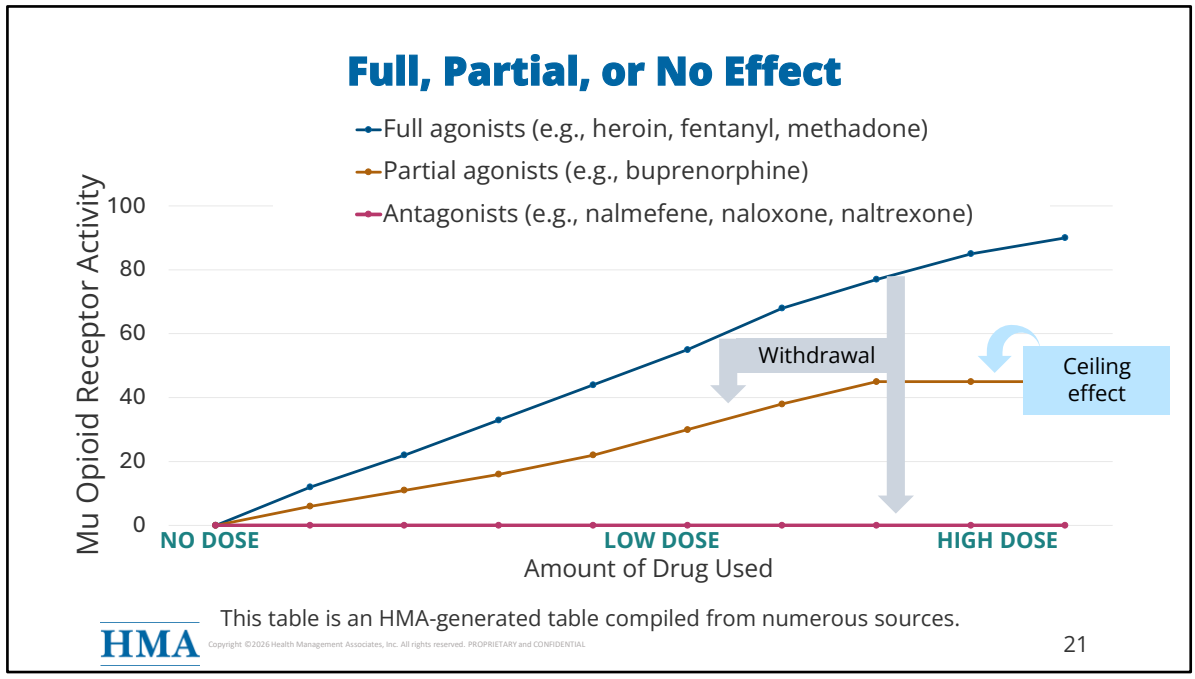
SOURCE(S): ASAM, 2020; Mattick, 2003; Mattick, 2009; Lobmaier et al., 2008; Krupitsky et al., 2011; Kakko et al., 2003.



[Slide Image Description: This slide shows information FDA-approved medication for OUD, with two colorful boxes.]

The medications for treatment of OUD can be divided into 2 categories:

- Agonists: Bind to the opioid receptor in the brain and turn it on.
    - Methadone, which was approved for treatment of OUD in 1972, and buprenorphine, first approved for treatment of OUD in 2002 are the agonist medications.
- Antagonists: Bind to the receptor without turning it on, while blocking other opioids from binding.
    - Naltrexone is an opioid antagonist. It has 2 formulations, both an oral form and a long-acting injectable formulation (the brand name is Vivitrol). Only the injectable formulation is approved for treatment of OUD.
    - Naloxone and Nalmefene are also antagonist medications used for reversing opioid overdoses. It's important to be aware that the company that makes the version of Nalmafene (with brand name Opvee) is no longer going to market this in the United States.



[Slide Image Description: This slide shows a chart detailing medication effects.]

This slide covers the different medicines and how they work in our brains.

On the Y axis of the graph, there is activity at the Mu opioid receptor in the brain. Higher up on the graph leads to increased activity at the receptor.

On the X axis is amount of drug used, such that left to right increases the dose of the drug.

- Full Agonists, which includes opioids like heroin, fentanyl, and oxycodone, fully turn on the opioid receptor in our brains. Taking more heroin or fentanyl (shown in the blue line on top) increases the effect.
    - Methadone is also a full agonist opioid. However, unlike the other opioids, it is a long-acting opioid, meaning it binds to the receptor and remains active at the receptor for a much longer time. This is why it is used as an effective medication to treat OUD.

- Partial Agonists turn on the opioid receptor (shown in the orange line in the middle), but not as much as the full agonists. Moving toward a higher dose, there is a point where there is a flattening of the curve in which taking more doesn't make the effect stronger. This is called the ceiling effect (light blue box and arrow).
    - Buprenorphine is a partial agonist.
    - This ceiling effect makes buprenorphine safer than other opioids because higher doses do not cause people to have a greater decrease in breathing.
    - The other thing to know about buprenorphine, is that it has a higher affinity or stronger attraction at the receptor, such that if another full agonist opioid is sitting on the receptor and you introduce buprenorphine, the buprenorphine will knock the other opioid (heroin or fentanyl, for example) off and bind to the receptor in its place.
        - If someone has been using fentanyl (the receptor is fully turned on) and right away takes buprenorphine (which has a partial effect), that will trigger withdrawal.
        - The gap between full agonist binding and partial agonist binding result in withdrawal is called precipitated withdrawal. It is just like going into withdrawal, but it happens faster and may be more intense.
    - This is why the traditional method for starting buprenorphine for people with active OUD is to wait until someone is already in moderate withdrawal before taking the first dose of buprenorphine. If they are already in withdrawal, they will start feeling better after starting buprenorphine.
    - However, if for some reason we do precipitate withdrawal, the treatment for that is to give more buprenorphine. With additional buprenorphine, precipitated withdrawal is not dangerous, but it is very uncomfortable.

- Antagonists (shown in the pink line on the bottom), block the receptor from being turned on.
    - Just like buprenorphine, the antagonist medications have a higher affinity or stronger attraction at the receptor.
    - Taking an antagonist after using fentanyl leads an individual from a strong effect to no effect (shown in gray), and that can make an individual feel severe withdrawal symptoms.
    - This is why people need to be off all opioids for at least 7 – 14 days before starting naltrexone for treatment of OUD.

Keep in mind, if someone has been using any opioid and is given a drug like

naloxone, they will start breathing, wake up, and may be in withdrawal because they go from feeling the effects to feeling nothing at the opioid receptor. This is why we wait 2 – 3 minutes for naloxone to work, because giving higher doses of naloxone doesn't wake people up faster, but it does make people experience more withdrawal symptoms.

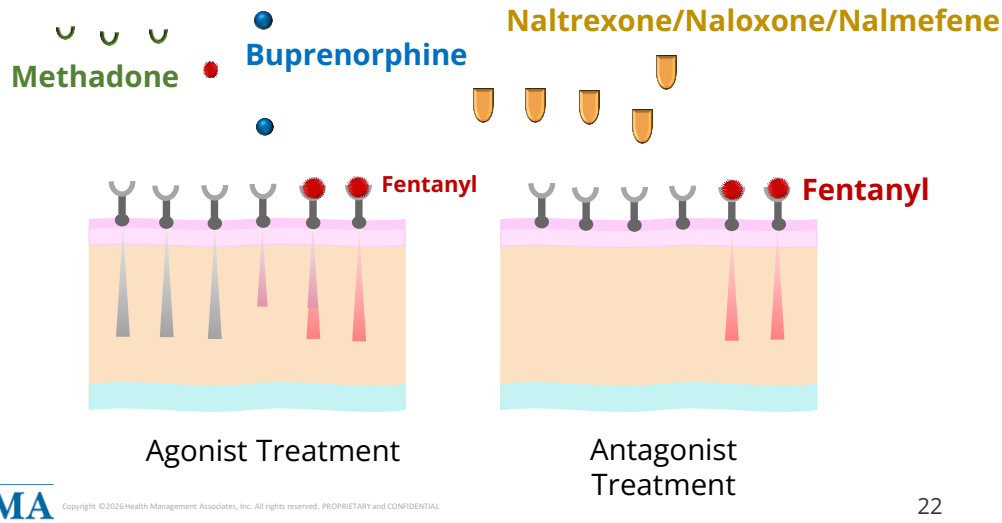
This is an HMA generated slide, but data on this slide comes from a consolidation of information in multiple sections of:

Substance Abuse and Mental Health Services Administration (SAMHSA). (2021). TIP 63: Medications for opioid use disorder. Treatment Improvement Protocol (TIP) Series 63 Publication No. PEP21-02-01-002. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2021.

Weimer, M. B., et al. (2023). ASAM clinical considerations: Buprenorphine treatment of opioid use disorder for individuals using high-potency synthetic opioids. Journal of Addiction Medicine, 17(6), 632–639.

Payne, E. R., et al. (2024). Comparison of Administration of 8-Milligram and 4-Milligram Intranasal Naloxone by Law Enforcement During Response to Suspected Opioid Overdose - New York, March 2022-August 2023. MMWR. Morbidity and mortality weekly report, 73(5), 110–113. https://doi.org/10.15585/mmwr.mm7305a4

How do the FDA approved medications work?



22

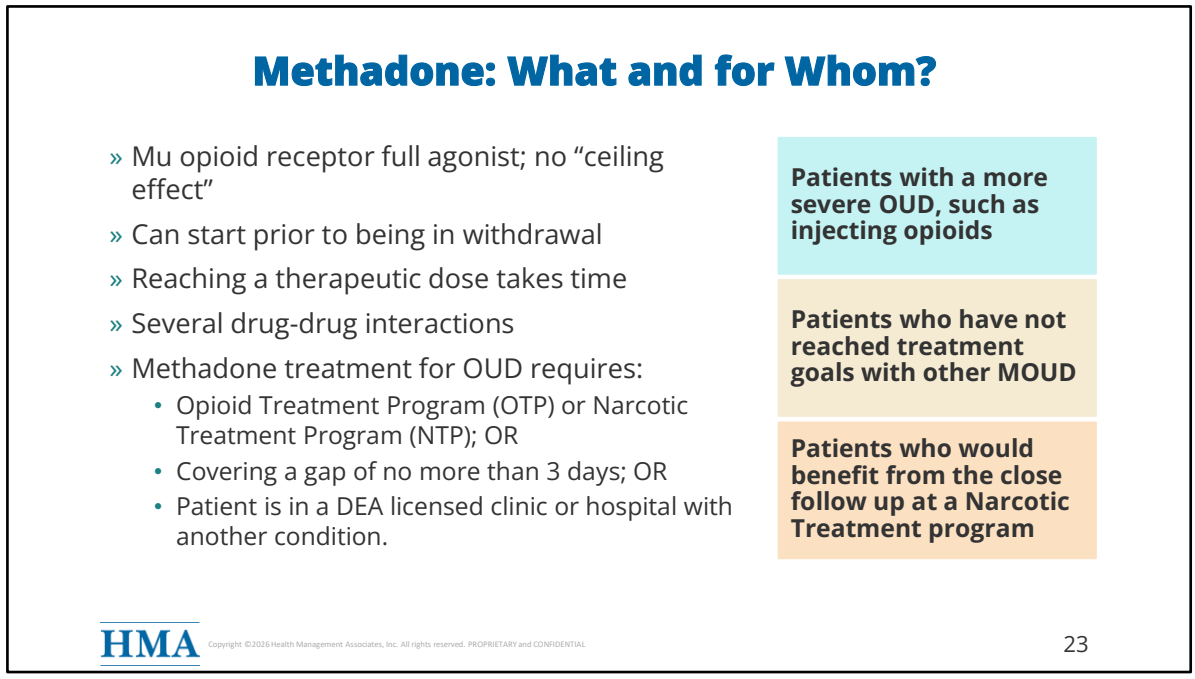
[Slide Image Description: This slide shows a graphic indicating how medications work.]

This slide shows how these FDA approved medications work.
The graphic contains gray semicircles, which are mu opioid receptors, one kind of opioid receptor.
Opioids are depicted in the graphic by the red ball, bind and activate the receptor, and send signals through the cell to the next cell. This could be any opioid (e.g., heroin, fentanyl, etc.).

Methadone, depicted in green, will bind and activate the receptor and eliminate cravings, but methadone does not block opioids from also binding to receptors.

Buprenorphine is depicted here in blue; it binds and activates the receptor; buprenorphine will displace opioids from the receptor, causing withdrawal and will block additional opioids from binding to receptor.

Naloxone and naltrexone, shown in yellow, will bind and block, but do NOT activate receptor; both displace opioids from the receptor causing withdrawal and blocking opioids from binding to receptor for the duration of medication.



[Slide Image Description: This slide shows information on methadone, with three colorful boxes.]

These slides walk through each of the medications, starting with methadone:

- Methadone is a full agonist opioid. It turns on the opioid receptor, and it doesn't have a "ceiling effect."
- Some people might need the full effect of methadone to make their cravings go away if their cravings don’t go away with other medicines.
- Individuals don't have to be in opioid withdrawal to start taking methadone.
- It takes time to find the right amount of methadone that works for each person; everyone is different. Typical dose is 60 – 120 mg/d (<60 mg/d is not therapeutic).
    - It’s also important to know that the dose of methadone required to control withdrawal symptoms is often much lower than the dose required to control opioid cravings. To effectively treat OUD, people need to have enough medication to control cravings.
    - Pregnant people often need both increased dose of methadone and increased frequency of dosing as the pregnancy progresses, due to

pregnancy-related changes in metabolism.

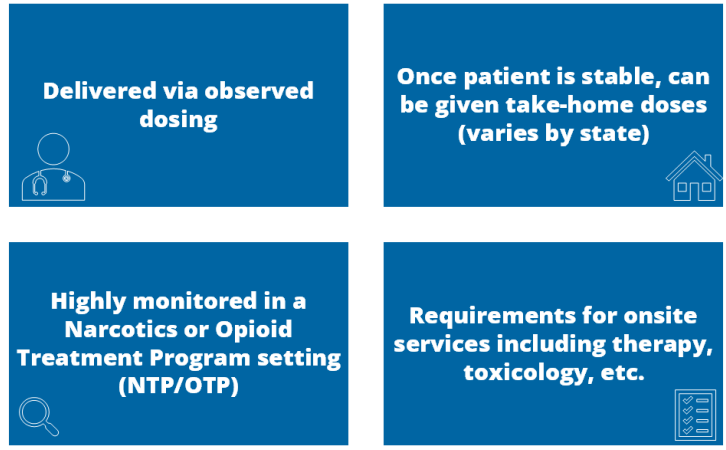
- Methadone is metabolized by a certain enzyme system in the liver, one which also metabolizes many other medications.
    - There are several drug-drug interactions with methadone; some medications speed up the body's metabolism (or how quickly the body breaks down methadone), while others may slow down the metabolism of methadone, meaning that it will hang around in the body for longer.
    - Thus, some people may required adjustments in the dose of their methadone, dependent on what other medications they are taking.
- The use of methadone for treatment of OUD is restricted to opioid treatment programs (OTPs) or narcotic treatment programs (NTPs) as they are called here in California.
    - There are very rare instances in which someone outside of an OTP can give methadone for OUD treatment
        - Covering a gap of no more than 3 days
        - Patient is in a Drug Enforcement Administration (DEA) licensed clinic or hospital with another condition

In addition to providing methadone, including direct observation of dosing, OTPs offer a variety of other services and supports: toxicology testing, counseling, medical screening, and vocational services. Because of these rules governing OTPs and the additional supports they provide, methadone is mostly used for people with more severe problems with opioids. Some people benefit from being seen more frequently and the support provided, including those who may not have reached their goals with other treatments.

Methadone is typically used for the following:

- Patients who would benefit from the closest follow up at Narcotic Treatment program (NTP).
- Patients who have not reached treatment goals with other MOUD.
- Patients with a more severe OUD, such as injecting opioids.

Methadone: General Federal Regulations



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

[Slide Image Description: This slide shows information on methadone, with four colorful boxes and icons.]

Please also note the General Federal Regulations for Methadone:

- Delivered via observed dosing through licensed OTP/MTP.
- May require daily dosing at OTP; take home doses are now available from initiation of treatment in some circumstances.
- Very high level of federal and state regulations surrounding use.
- Counseling available on site.
- Full treatment planning for physical, mental health, SUD and social determinants of health.
- Regular and random drug screening.

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.

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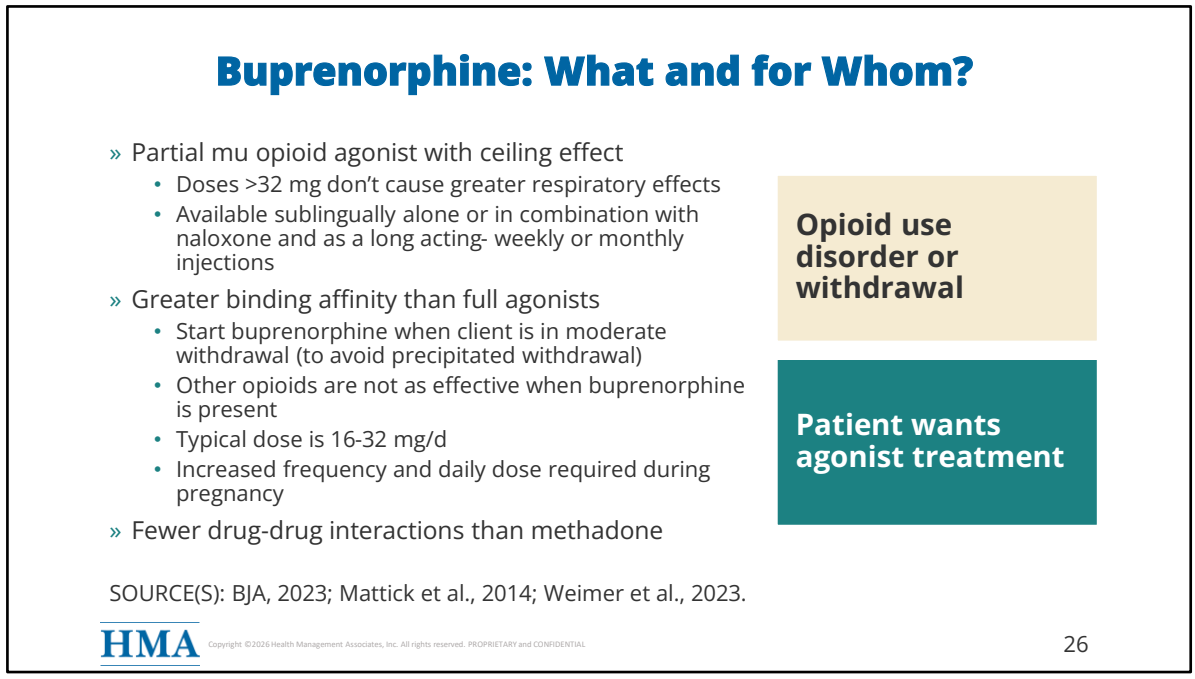
[Slide Image Description: This slide shows information on methadone efficacy, with an image of a scale.]

Methadone is highly effective:

- It results in 33% fewer positive opioid toxicology tests compared to those receiving no medication when everyone receives the same psychosocial treatment.
- People on methadone:
  - 4.4 times more likely to stay in treatment
  - Have less criminal activity
  - Experience reduced infectious disease, like HIV and HCV
  - Experience reduced mortality than those on no medication, behavioral health treatment, or naltrexone

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



[Slide Image Description: This slide shows information on buprenorphine, with two colorful boxes.]

Next is Buprenorphine:

- As noted in earlier slides, buprenorphine is a partial agonist, which means that it has a ceiling effect such that at some point, higher doses don't result in a greater effect (doses >32 mg don't cause greater respiratory effects).
    - For this reason, it has a greater safety profile than methadone.
- There are now multiple formulations of buprenorphine available for treatment of OUD, including sublingual (under the tongue), buccal (against the cheek), and long-acting injectable buprenorphine, called Sublocade® and Brixadi®.
    - If taking the sublingual formulation, it is important to let buprenorphine dissolve under the tongue or on the inside of the cheek; very little buprenorphine gets into the blood when it is swallowed.
- Buprenorphine has a greater binding affinity at the opioid receptor in the brain. It can kick other opioids, like heroin or fentanyl, off of the receptor.

        - If an individual has taken another opioid recently and is not feeling sick yet, taking buprenorphine could cause withdrawal symptoms.
        - Typically start buprenorphine when the individual is already feeling moderate withdrawal.
        - However, with newer protocols, there are newer and varied approaches for getting people onto buprenorphine.
            - It is important to know individuals can start the long-acting injection on the first day.
- For most people, taking less than 16mg total daily of buprenorphine is not an effective dose. The usual amount is between 16-32mg.
    - Pregnant people and others might need higher or more frequent doses.
- There are no longer restrictions on who can prescribe buprenorphine or how many people can be treated; it can be prescribed by anyone with an unrestricted DEA license.

Buprenorphine is used for anyone with an opioid use disorder who wants medicine and is not allergic to buprenorphine.

- Like methadone, buprenorphine can be used to manage opioid withdrawal and is used for ongoing treatment of OUD.

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.

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[Slide Image Description: This slide shows information on buprenorphine efficacy, with an image of a pharmacist packing boxes.]

Buprenorphine is also highly effective:

- Individuals taking buprenorphine decrease their opioid use; the rate of return to opioid use for placebo was 100% vs 25% for buprenorphine.
- Individuals taking more than 16mg or higher dose of buprenorphine are 1.82 times more likely to stay in treatment than if on placebo.
- In addition to reduction in opioid use and increased treatment engagement, just like methadone, buprenorphine has many other benefits, including decreased criminal recidivism, decreased infectious disease transmission (HIV and hepatitis), and most importantly, they are less likely to die than with no medication or naltrexone.

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.

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[Slide Image Description: This slide shows information on naltrexone, with four colorful boxes.]

Next is Naltrexone:

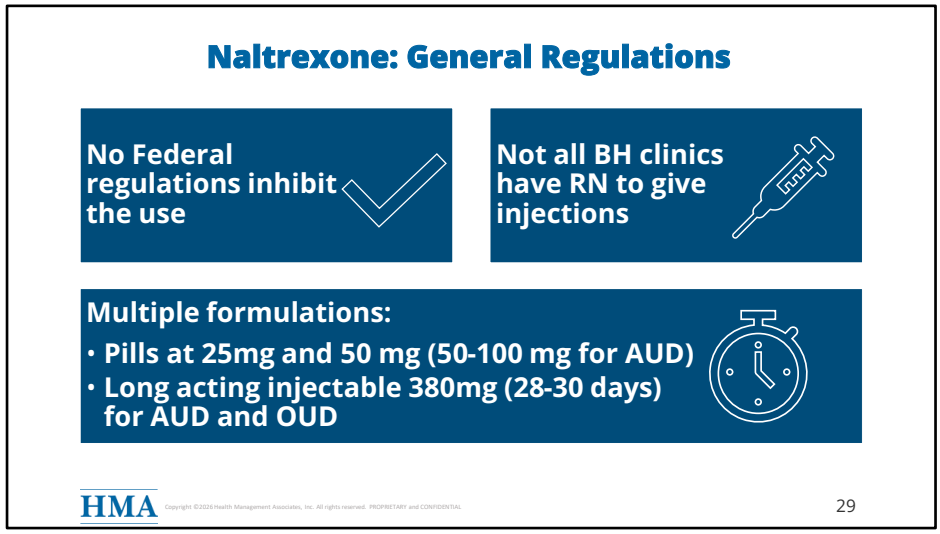
- As noted in earlier slides, naltrexone is an antagonist with high, competitive binding affinity. Other opioids can't affect the receptor if naltrexone is there.
- However, naltrexone doesn't help withdrawal or decrease death like buprenorphine and methadone do.
- An individual must be completely free of opioids (14 days) and finished with opioid withdrawal to start naltrexone, making it harder to start than buprenorphine or methadone.
- The long-acting injection, called Vivitrol®, is approved for OUD. The oral form is not approved for opioid use disorder.
- Unlike methadone and buprenorphine, there is no evidence showing a mortality benefit for naltrexone.

Naltrexone is typically used for the following:

- If someone used opioids for a short time and still has good things

happening in their life—like family, job, or activities—and can still experience positive reinforcement from normal stimuli.
    - Remember: Naltrexone does not address underlying issue of dopamine depletion, but does decrease cravings over time
- If someone tried buprenorphine or methadone but didn't reach their goals.
- After someone used buprenorphine or methadone successfully and wants to stop those medicines.
- For people who haven't used drugs recently but still have cravings.
- If someone knows they will be in a risky situation, like an event where they might be around someone using drugs.

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



[Slide Image Description: This slide shows general regulations on naltrexone, with three colorful boxes and three icons.]

Please also note the General Regulations for naltrexone:

- No federal regulations inhibit the use of naltrexone.
- Not all behavioral health clinics have RN to give injections.
- There are multiple formulations:
    - Pills at 25mg and 50 mg (50 – 100 mg for AUD); pill form is for AUD only.
    - Long acting injectable (Vivitrol) 380mg (21 – 28 days); this formulation is approved for AUD and OUD.
    - Better retention
- Implantable pellets are not FDA-approved at the time of this presentation.
    - Six months of coverage of 0.9 ng/ml naltrexone
    - 3.5 ng/ml of 6-beta-Naltrexol)
    - Needs more study

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

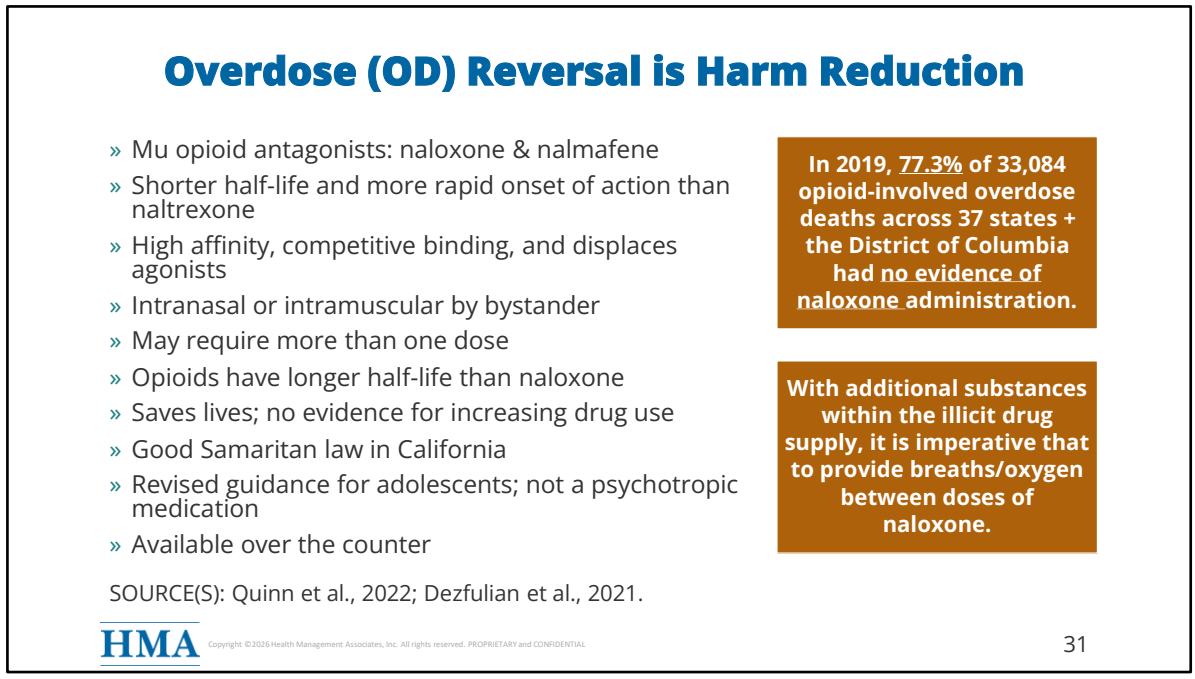
SOURCE(S): Krupitsky, 2011; Minozzi, 2011; Korthuis, 2022.

[Slide Image Description: This slide shows information on naltrexone efficacy, with an image of a syringe and vial.]

For naltrexone:

- Extended Release naltrexone had a significant benefit in decreasing opioid use compared to placebo: 90% Naltrexone XR vs. 35% placebo (Krupitsky, 2011).
  - Also associated with decreased incarceration (Minozzi, 2011).
- XR Naltrexone compared to usual care in HIV clinic: fewer days of opioid use for those on XR Naltrexone (Korthuis, 2022).
- As noted, unlike methadone and buprenorphine, there is no evidence showing a mortality benefit for naltrexone.

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



[Slide Image Description: This slide shows information on overdose reversal, with two colorful boxes.]

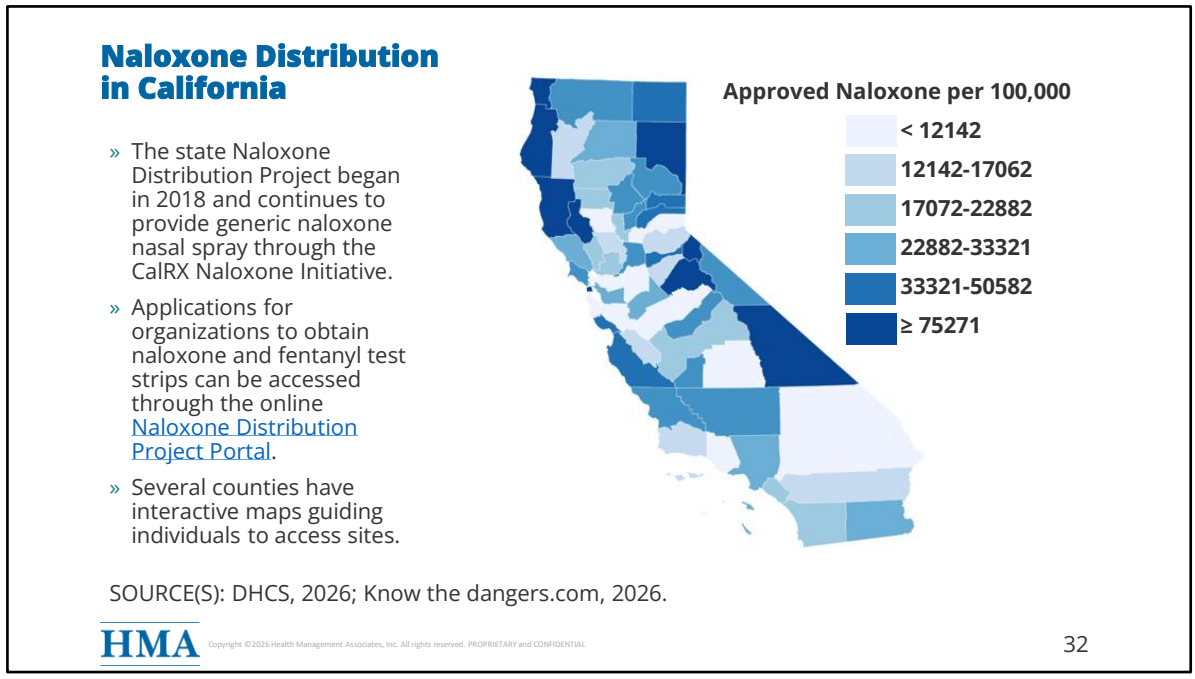
Keep in mind that overdose reversal is harm reduction.

- Mu opioid antagonists: naloxone & nalmefene
    - Trade names Narcan (intranasal, injection, autoinjector), and Opvee are the most common
- 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.

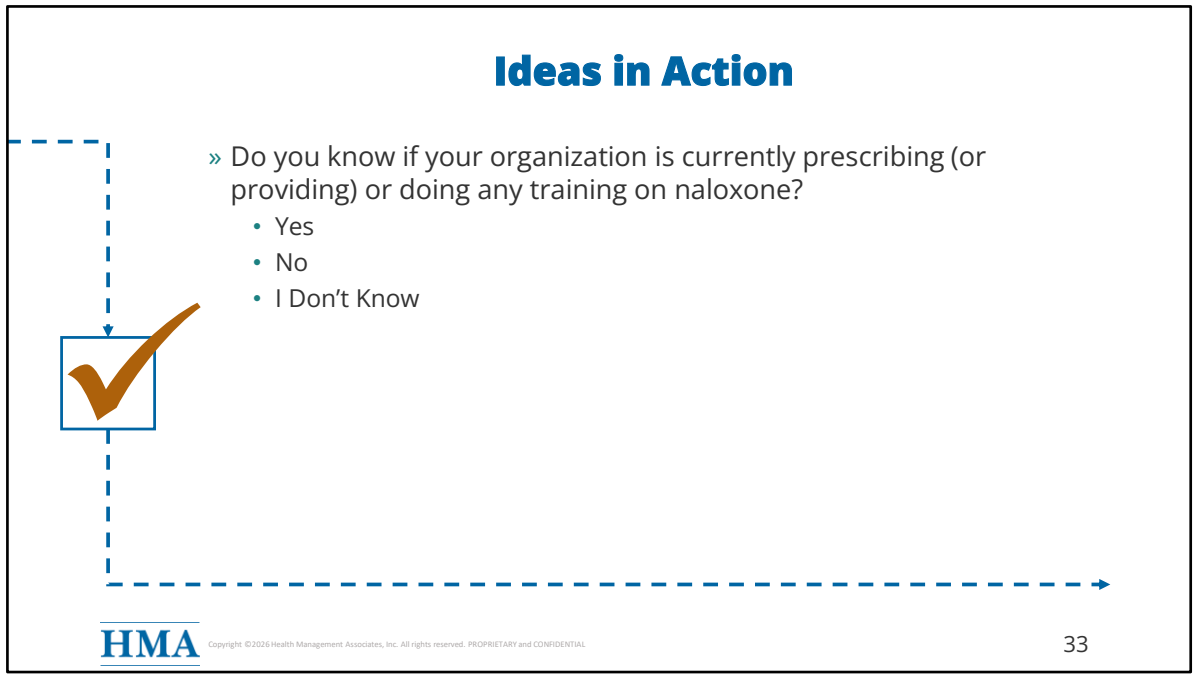


[Slide Image Description: This slide shows information on naloxone distribution, with a map of California.]

Overview of naloxone distribution in California:

- In 2018, California started the Naloxone Distribution Project, which continues to provide generic naloxone nasal spray through the CalRX Naloxone Initiative.
- To obtain naloxone and fentanyl test strips, organizations can apply through the online Naloxone Distribution Portal.
- Several counties have maps that can direct people to sites where naloxone can be accessed.

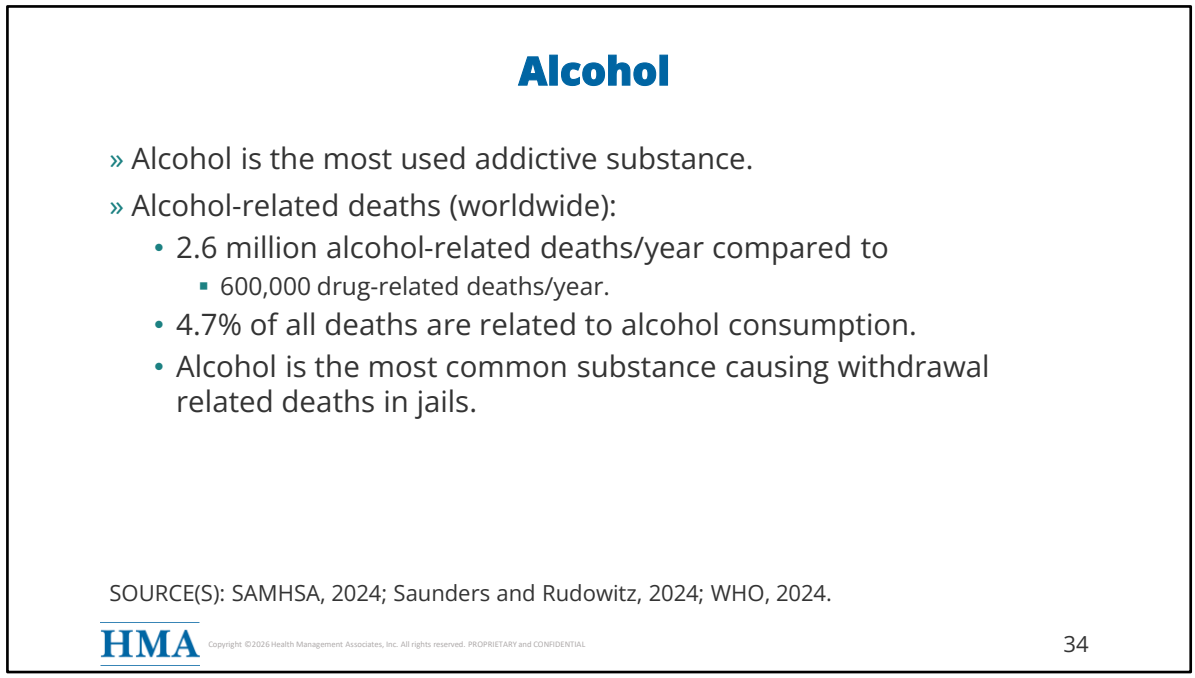
SOURCE(S): DHCS, 2026; Know the dangers.com, 2026.



[Slide Image Description: This is an Ideas in Action slide that provides an opportunity for participants to practice using the information. It contains a checkbox and an arrow.]

Do you know if your organization is currently prescribing (or providing) or doing any training on naloxone?

A. Yes
B. No
C. I Don't Know



[Slide Image Description: This slide shows information on alcohol.]

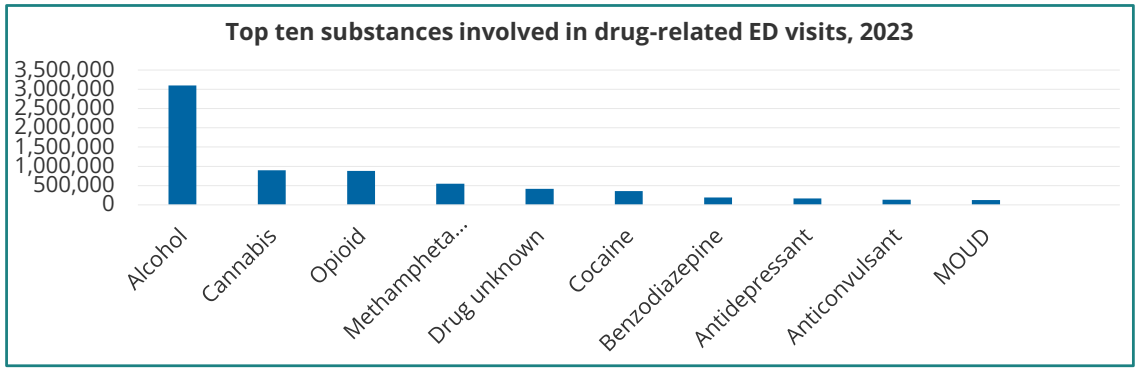
These slides cover alcohol and treatment of alcohol with medications for alcohol use disorder (MAUD).

- Alcohol is the most used addictive substance.
- Worldwide, it is responsible for almost 3 million deaths annually (compared to 600,000 drug-related deaths per year), and 4.7% of all deaths are related in some way to the consumption of alcohol.
    - Illicit drug use didn't cause more deaths than alcohol until the COVID-19 pandemic in 2020.
- Alcohol is the most common substance associated with a withdrawal-related death while in incarceration.

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.

[Slide Image Description: This slide shows information on emergency department visits, with a chart indicating the top ten substances involved in drug-related ED visits in 2023.]

Alcohol-related emergency room visits are much higher than emergency room visits for opioids or any other substance, exceeding 3.1 million in 2023 (3 times higher than any other drug class).

SOURCE(S): SAMHSA, 2024.

Medications for Alcohol Use Disorder (MAUD)

Benefits	FDA-Approved Medications
• Decreased Cravings • Decreased Drinking • Cost Effective	• Acamprosate • Naltrexone (oral and intramuscular) • Disulfiram (not proven effective)

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

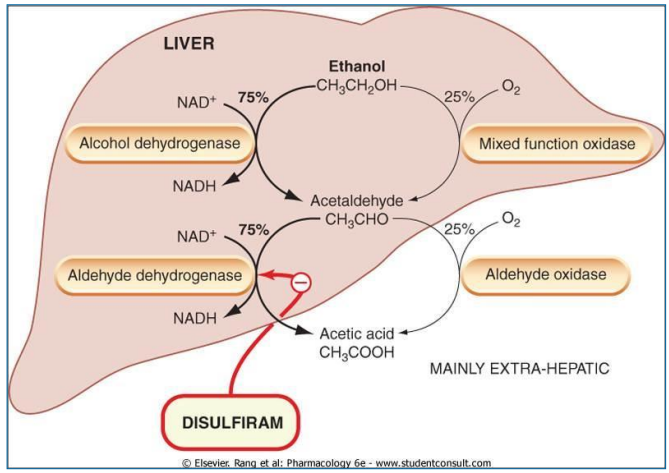
[Slide Image Description: This slide shows information on MAUD, with two colorful boxes.]

This slide reviews Medications for Alcohol Use Disorder (MAUD):

- There are multiple benefits of MAUD, including reduction in alcohol-related cravings, reduction in drinking, and improved cost effectiveness with reduction in healthcare costs.
- There are 3 FDA-approved medications for alcohol: acamprosate, naltrexone (oral and intramuscular), and disulfiram.

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

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[Slide Image Description: This slide shows information on Disulfiram, with an image of a liver.]

Disulfiram (brand name Antabuse) works by interfering with how the body breaks down alcohol. When someone drinks alcohol (ethanol in the picture), an enzyme called alcohol dehydrogenase breaks the alcohol down into another chemical called acetaldehyde. Then a second enzyme, called aldehyde dehydrogenase, breaks the acetaldehyde into acetic acid. Disulfiram interferes with this second enzyme, resulting in a build up of acetaldehyde.

This build up of acetaldehyde results in various 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.

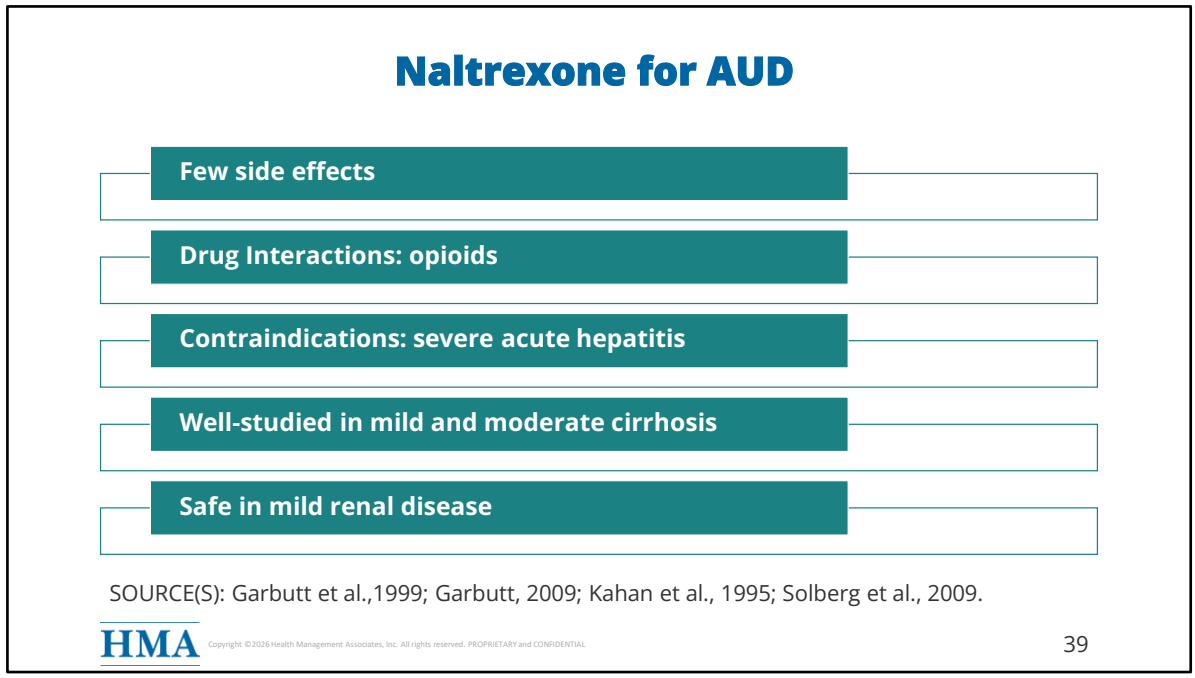
[Slide Image Description: This slide shows information on disulfiram, with an image of a pharmacist.]

Disulfiram was approved decades ago; however, most recent data does not show overwhelming efficacy.

- However, there some populations for which disulfiram has shown some benefit, specifically directly-observed dosing, for example people on methadone who received their disulfiram along with their methadone at the dosing window.
- Once per day dosing
- Inhibits multiple P450 and other liver enzymes and thus has multiple drug interactions: benzodiazepines, phenytoin, pimozide, tricyclic antidepressants (TCAs), warfarin, sulfonylureas, metronidazole, amoxicillin, isoniazid
- Also, disulfiram has multiple contraindications/precautions: alcohol use, hypersensitivity to rubber, severe coronary artery disease (CAD), cirrhosis, severe renal impairment, psychosis, depression, diabetes mellitus (DM), epilepsy
- It is also important to know that the disulfiram reaction is not limited to

alcohol that is ingested. People using alcohol-based hand sanitizer or colognes while taking disulfiram may also experience some symptoms.
- Extensively metabolized
- Extensive list of side effects
- Also requires regular monitoring of liver enzymes

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



[Slide Image Description: This slide shows information on naltrexone, with five colorful boxes.]

Naltrexone, which you will recall is an opioid antagonist, is also FDA-approved for treatment of alcohol use disorder.

- It is believed that the opioid system plays a role in the rewarding effects of alcohol, and thus if you block the opioid system, you blunt the reward associated with alcohol use.
- Because it is an opioid antagonist, it is contraindicated for use in people who are taking opioids. So, if someone is already being treated with methadone or buprenorphine for their OUD and also has an AUD, they can't start on naltrexone, at least not while they are being treated with an opioid agonist.
- Naltrexone is safe for most people, even those with liver disease, including chronic viral hepatitis or compensated cirrhosis.
    - Naltrexone's primary contraindication is for "acute hepatitis or liver failure"
- Oral is indicated for ethanol dependence only
- Hepatotoxicity warning is only for supratherapeutic doses
- Safe in 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.

[Slide Image Description: This slide shows information on naltrexone efficacy, with an image of a pharmacist.]

Both formulations of naltrexone, both oral and long-acting injection, have been found to be effective at decreasing alcohol use, most notably at decreasing heavy drinking.

- Recurrence rates of 23 to 40% compared to 54 and 80% for those on placebo.
- Recurrence rate decreases to as low as 14% for adherent patients.

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.

[Slide Image Description: This slide shows information on extended release naltrexone.]

Extended-Release (XR) Naltrexone is associated with greater treatment retention when compared to placebo and oral naltrexone. Additionally, it is associated with decreased healthcare costs.

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

Acamprosate: Mechanism of Action

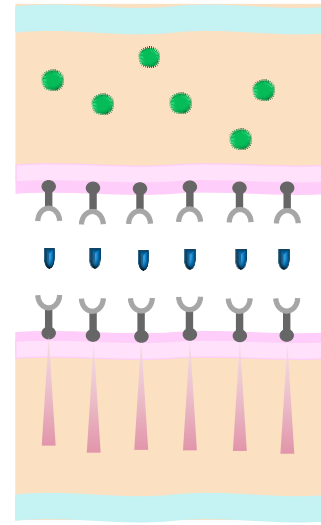
In someone with an active alcohol use disorder acamprosate decreases glutamate.

Glutamate Cell

Glutamate

Acamprosate

Gamma Amino Butyric Acid (GABA) cell



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

HMA

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[Slide Image Description: This slide shows information on acamprosate, with a graphic of interactions with cells.]

GABA is the primary inhibitory neurotransmitter in the brain. Binding at the GABA receptor causes inhibition of nerve firing, which contributes to the sedating effect of alcohol. In contrast, glutamate is the primary excitatory neurotransmitter in the brain. Alcohol use decreases glutamate transmission, also contributing to alcohol's sedating effects. However, with chronic alcohol use, you get an upregulation or increase of glutamate receptors in the background. When someone stops or significantly reduces their alcohol use, this upregulation in glutamate receptors causes increase excitatory neurotransmission, which contributes to many of the effects of alcohol withdrawal.

Acamprosate is structurally similar to GABA and amino acid taurine. It does not bind directly to the receptors but modulates their activity. In someone with AUD, acamprosate decreases activity of the glutamate cells.

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.

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[Slide Image Description: This slide shows information on acamprosate, with an image of pill bottles.]

Acamprosate for AUD has been proven effective:

- Decreases quantity and frequency of drinking
- Continuous abstinence rates at 6 months were significantly higher in the acamprosate-treated patients (acamprosate, 36.1%; placebo, 23.4%; $p < 0.001$).
- At 12 months, the overall pooled difference in success rates between acamprosate and placebo was 13.3% (number needed to treat, 7.5).
- Acamprosate also had a modest but significant beneficial effect on retention (6.01%; $p = 0.0106$)
- One of the biggest challenges with acamprosate is that it requires three daily doses.
- It has very few drug interactions and few side effects, save from some gastrointestinal symptoms early in treatment.
- Contraindications: severe renal impairment
  - Dose reduce if someone has moderate renal impairment (creatinine clearance 30-50ml/m); reduce from 666mg tid to 333mg tid

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

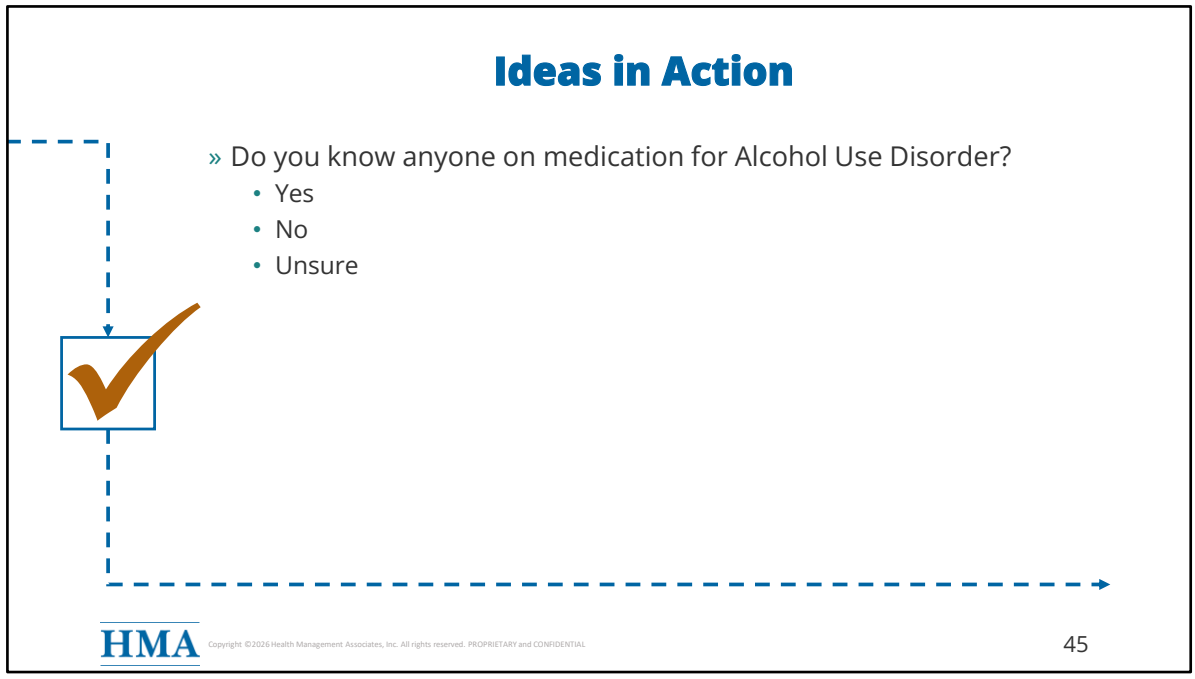
Kathleen A. McGinnis[a], Melissa Skanderson[a], E. Jennifer Edelman[b,g], Adam J. Gordon[c], P. Todd Korthuis[d], Benjamin Oldfield[b], Emily C. Williams[e,f], Jessica Wyse[d], Kendall Bryant[g], David A. Fiellin[b,h], Amy C. Justice[a,b], Kevin L. Kraemer[i,j]

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

[Slide Image Description: This slide shows information on behavioral health and medication for AUD, with a screenshot of an article.]

As with MOUD, MAUD was associated with improved outcomes in individuals with HIV. Per the Veterans Administration study, which looked at 7,830 people with HIV from 2008 – 2017, 9% received MAUD. MAUD was associated with an increased adherence to medication and CD4 counts among those with detectable viral loads. The more intense the behavioral treatment the more improved HIV related outcomes.

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

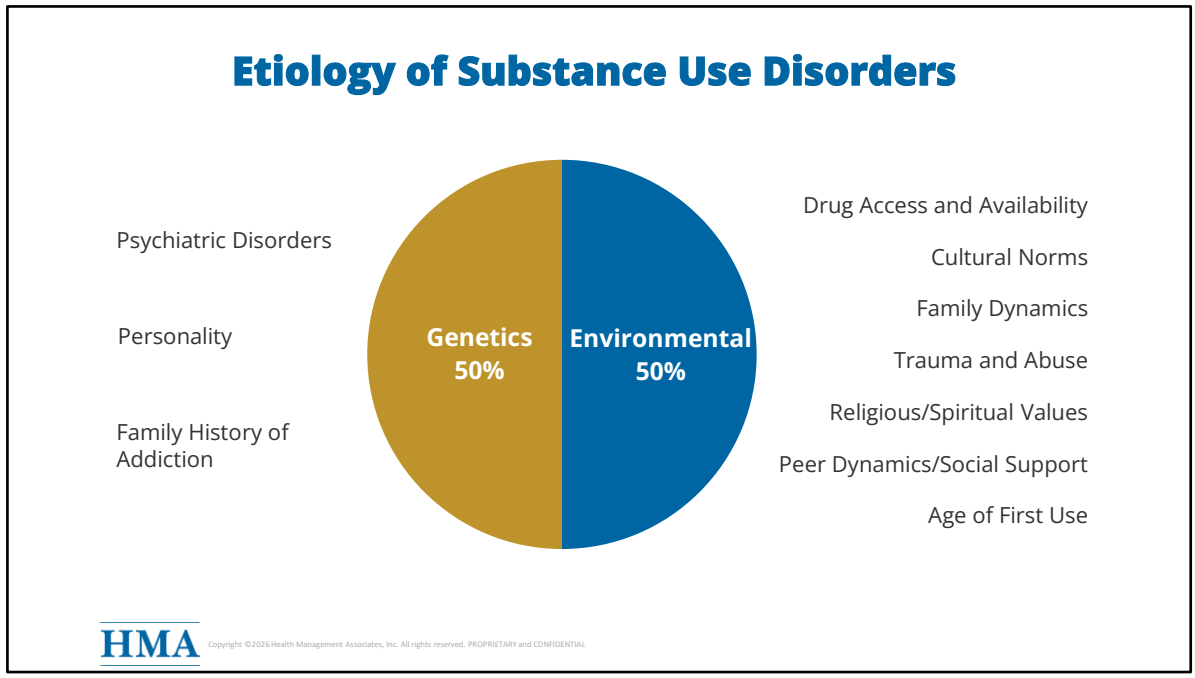


[Slide Image Description: This is an Ideas in Action slide that provides an opportunity for participants to practice using the information. It contains a checkbox and an arrow.]

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

[Slide Image Description: This is a section divider slide to indicate a major section of this webinar.]

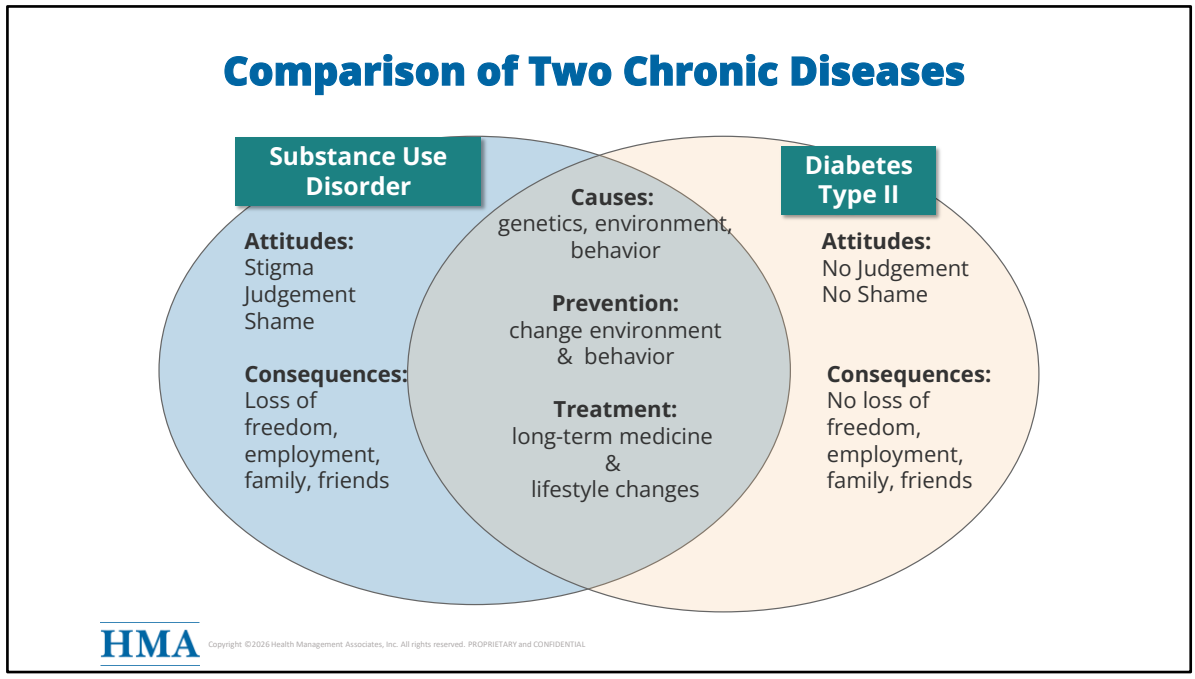
This third section looks at chronicity of addiction and duration of treatment.



[Slide Image Description: This slide shows information on the etiology of SUD, with chart showing genetics and environmental (50:50).]

Not everybody who use alcohol or drugs becomes addicted. While many more report using an opioid, it is estimated that about 3% of Americans will develop an opioid use disorder in their lifetime. However, there are factors that may predispose or increase the risk that one would develop a substance use disorder.

- It is estimated that about half of one's risk for development of addiction is genetic, and involves factors like the burden of SUD in relatives, particularly first-degree relatives (parents and siblings) and second-degree relatives (grandparents, aunts, uncles), co-occurring personality, and psychiatric disorders.
- The other half of one's risk for SUD is attributable to the environment into which they are born and raised. Factors like neighborhood disorganization and access to and availability of drugs, experiences of trauma, age at first exposure and use of substances all contribute to increased risk of developing an SUD.



[Slide Image Description: This slide compared SUD and diabetes, with a Venn diagram.]

We've been discussing the neurobiological aspect of addiction, with the effect and actions of dopamine. Let's turn now to a discussion of the chronic disease model of addiction.

It's useful to use the comparison shown on this slide between the chronic diseases of addiction and type 2 diabetes. Causal factors for both are genes, the environment, and behavior.

What works in prevention is also the same, and treatment for both includes lifestyle changes and medications to restore and sustain the appropriate chemical balance.

So, what is different? The underlying pathology is different, but our attitudes toward those with SUD and Type II Diabetes are very different. The consequences are very different and include incarceration, loss of child custody, housing, employment, family, friends.

However, individuals are less likely to experience judgement and shame with diabetes or to experience these consequences.

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.

HMA

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[Slide Image Description: This slide shows information on OUD treatment length, with an image of an hourglass and calendar.]

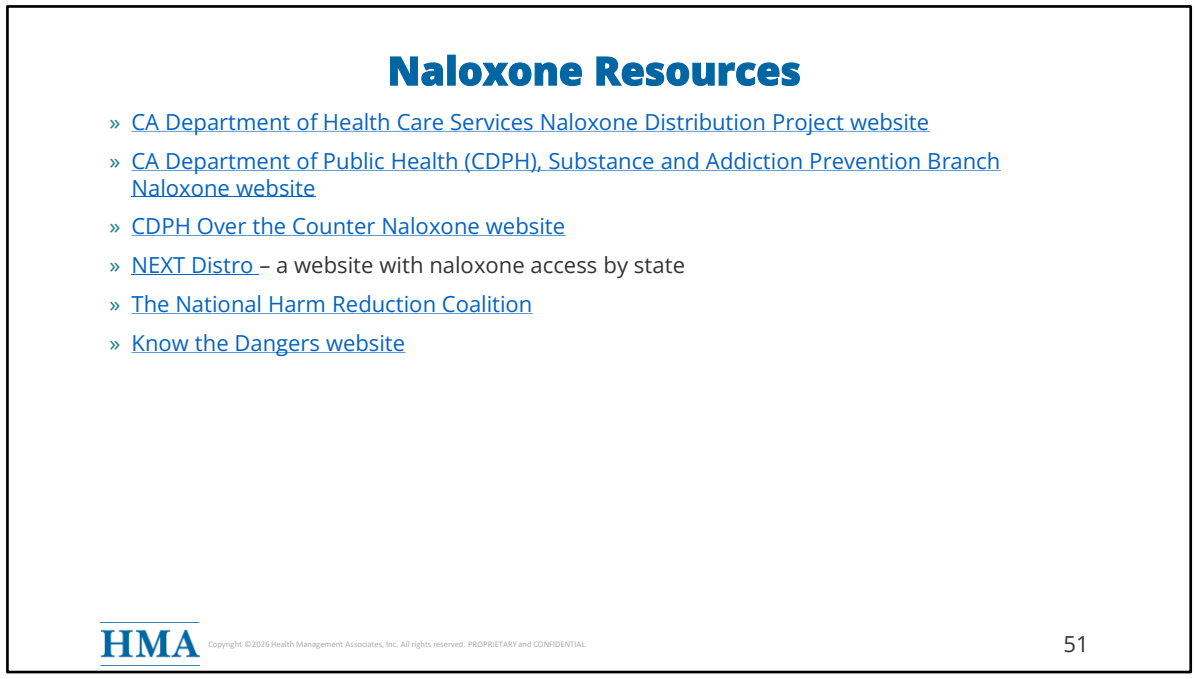
Data doesn't support coming off buprenorphine or methadone.

- Evidence is clear long term or indefinite MOUD is often required for sustained outcomes.
- 85% of persons treated with counseling alone return to opioid use within a year, and in the era of high-potency synthetic opioids like fentanyl and its analogues, return to use may lead to death.
  - Methadone or buprenorphine decreases overdose death by 60-80%.
- Successful tapers typically occur, if at all, when individuals have been treated with buprenorphine or methadone for at least three years, are stable in their recovery, and have a strong recovery support system including:
  - Supportive sober social network
  - Skills to effectively cope and manage conflict and stress
- It is not recommended to taper medication at the same time as major life stressors.
- Have the discussion regarding duration of treatment at the time of starting treatment, to help align expectations of providers and patients.

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.

[Slide Image Description: This slide shows the AFBSS email address.]

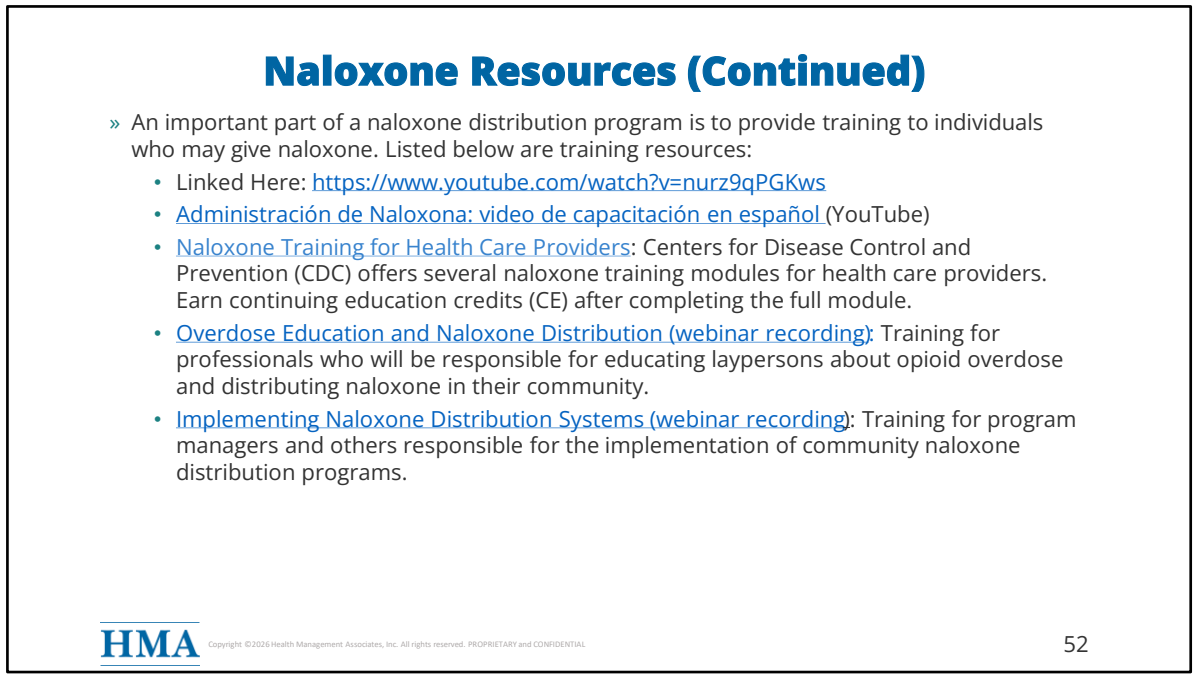
We are here to support you and provide you with those opportunities to connect and hear about implementing AFBSS. The website is INSERT and our email address is **info@afbsstraining.org.**



[Slide Image Description: This slide lists webinar resources.]

Resources:

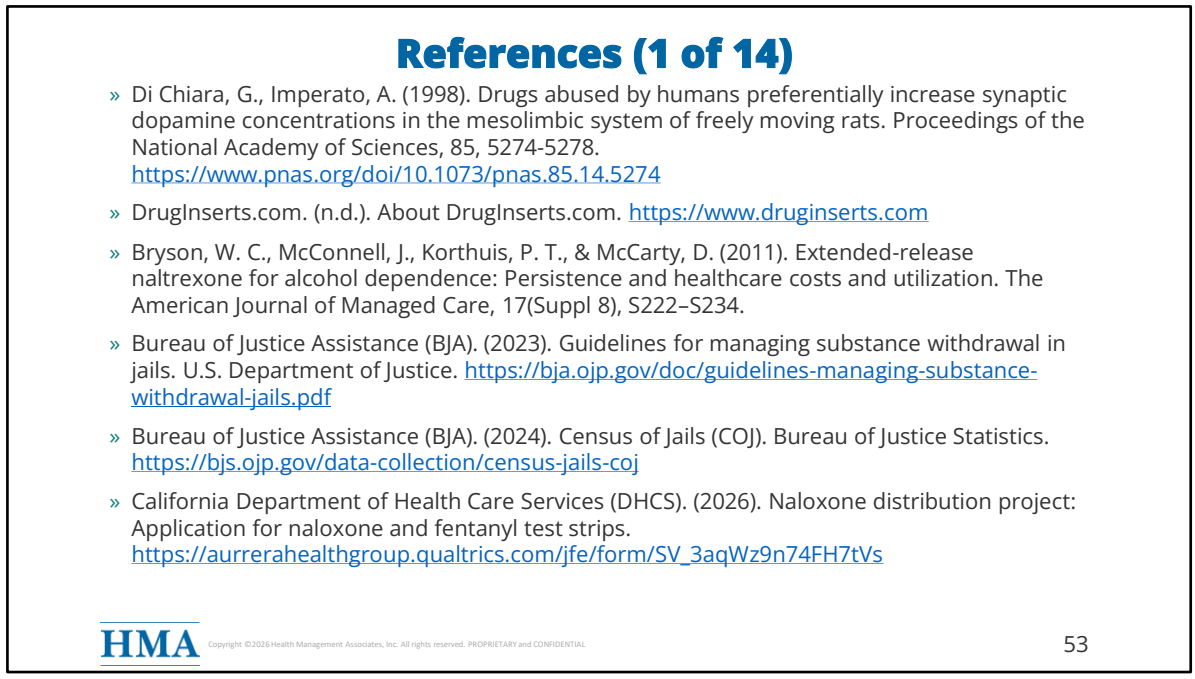
- CA Department of Health Care Services Naloxone Distribution Project website:
    - Linked Here: https://www.dhcs.ca.gov/individuals/Pages/Naloxone_Distribution_Project.aspx
- CA Department of Public Health (CDPH), Substance and Addiction Prevention Branch Naloxone website:
    - Linked Here: https://www.cdph.ca.gov/Programs/CCDPHP/sapb/pages/naloxone.aspx#:~:text=Local%20Organizations%20and%20Syringe%20Services,or%20a%20syringe%20services%20program.
- CDPH Over the Counter Naloxone website:
    - Linked Here: https://www.cdph.ca.gov/Programs/CCDPHP/sapb/Pages/Over-the-Counter-(OTC)-Naloxone.aspx
- NEXT Distro – a website with naloxone access by state:
    - Linked Here: https://nextdistro.org/naloxone
- The National Harm Reduction Coalition
    - Linked Here: https://harmreduction.org/resource-center/harm-reduction-near-you/
    - Linked Here: https://knowthedangers.com/



[Slide Image Description: This slide lists webinar resources.]

Resources:

- 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)
    - Linked Here: https://www.youtube.com/watch?v=bdubaT4bmq4
    - Linked Here: 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.
    - Linked Here: 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.
    - Linked Here: 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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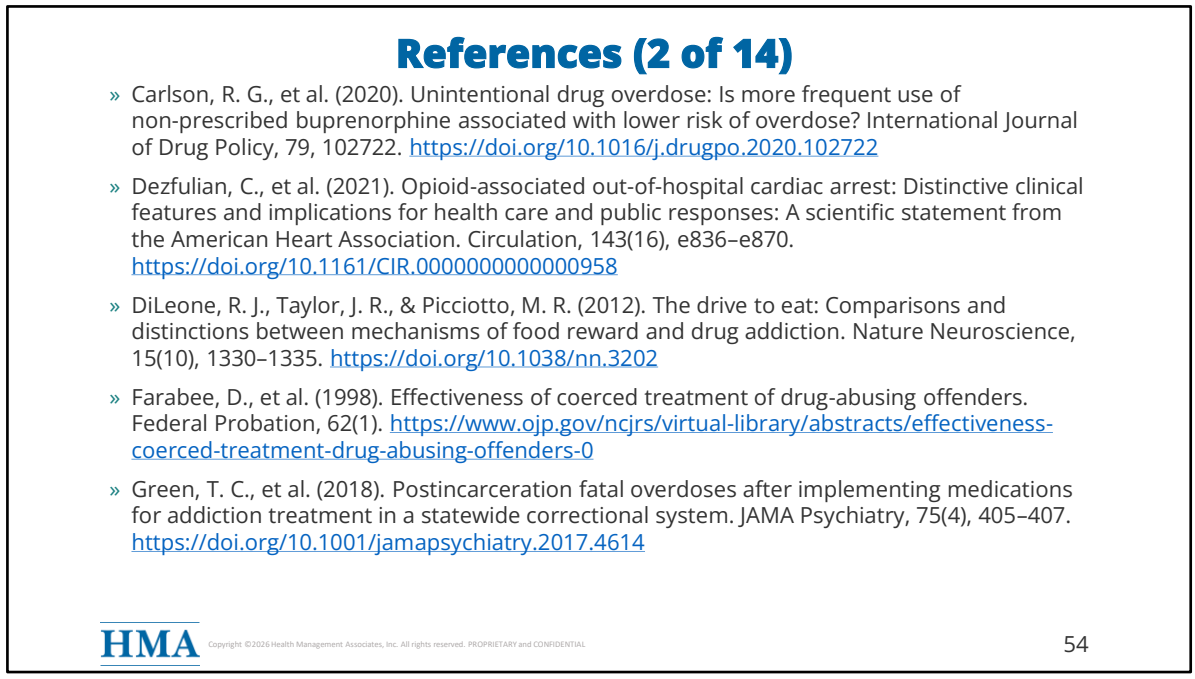

[Slide Image Description: This slide lists webinar references 2 of 14.]

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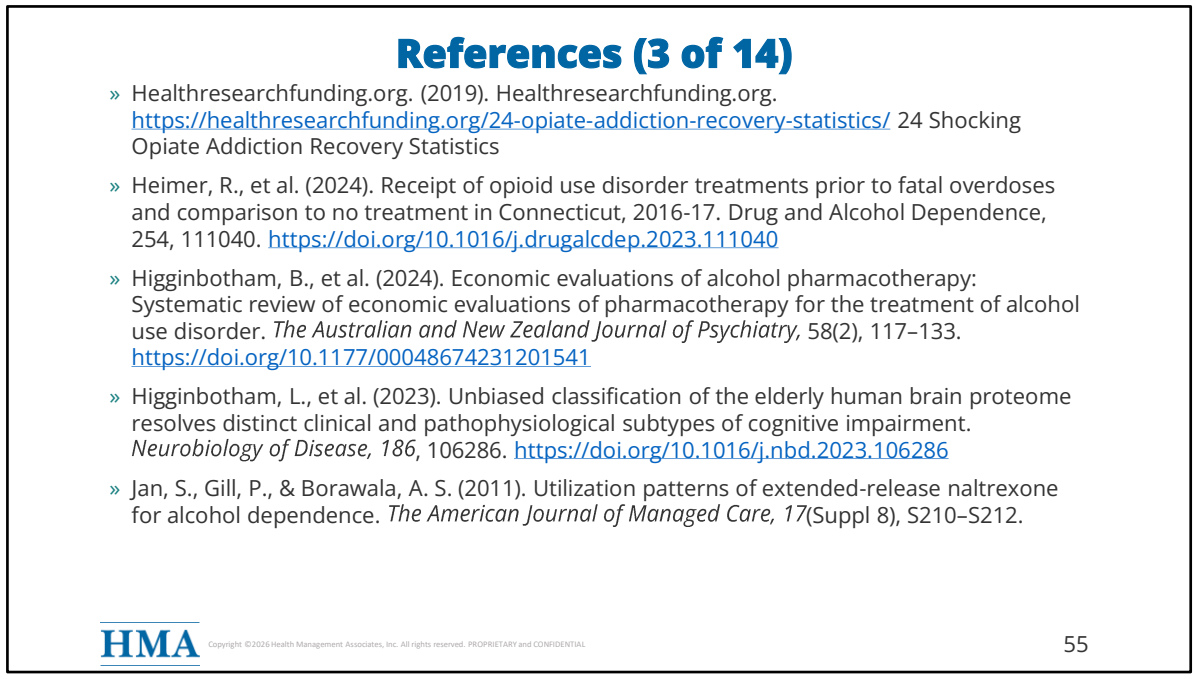

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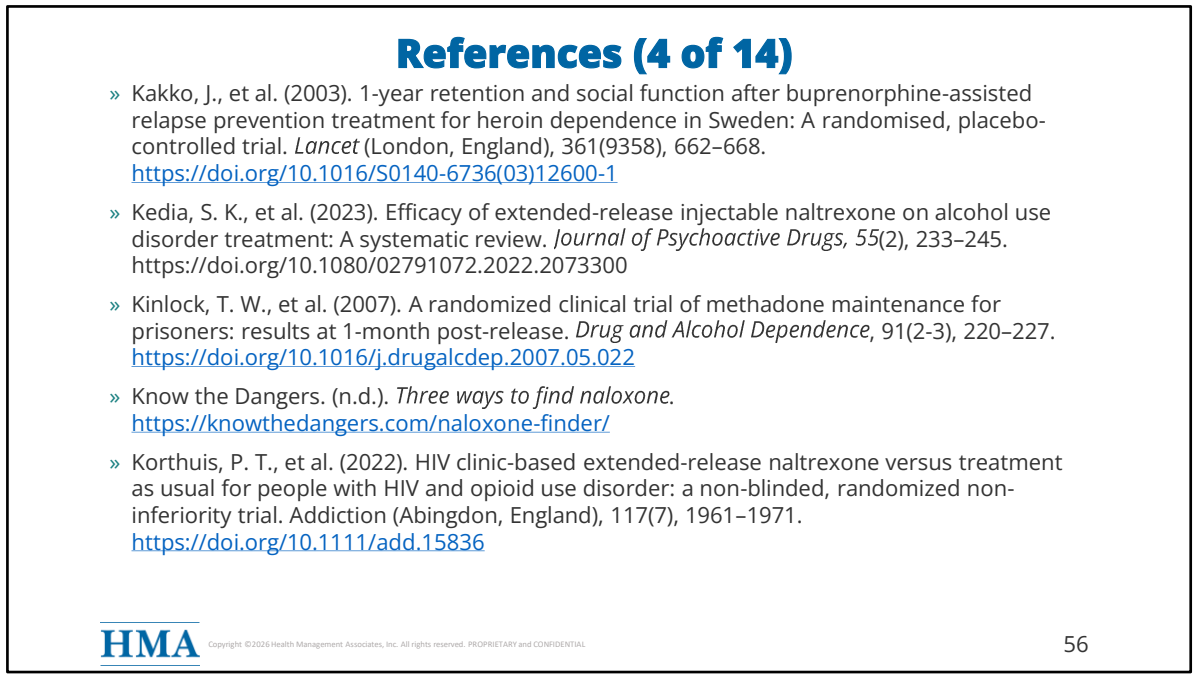

[Slide Image Description: This slide lists webinar references 4 of 14.]

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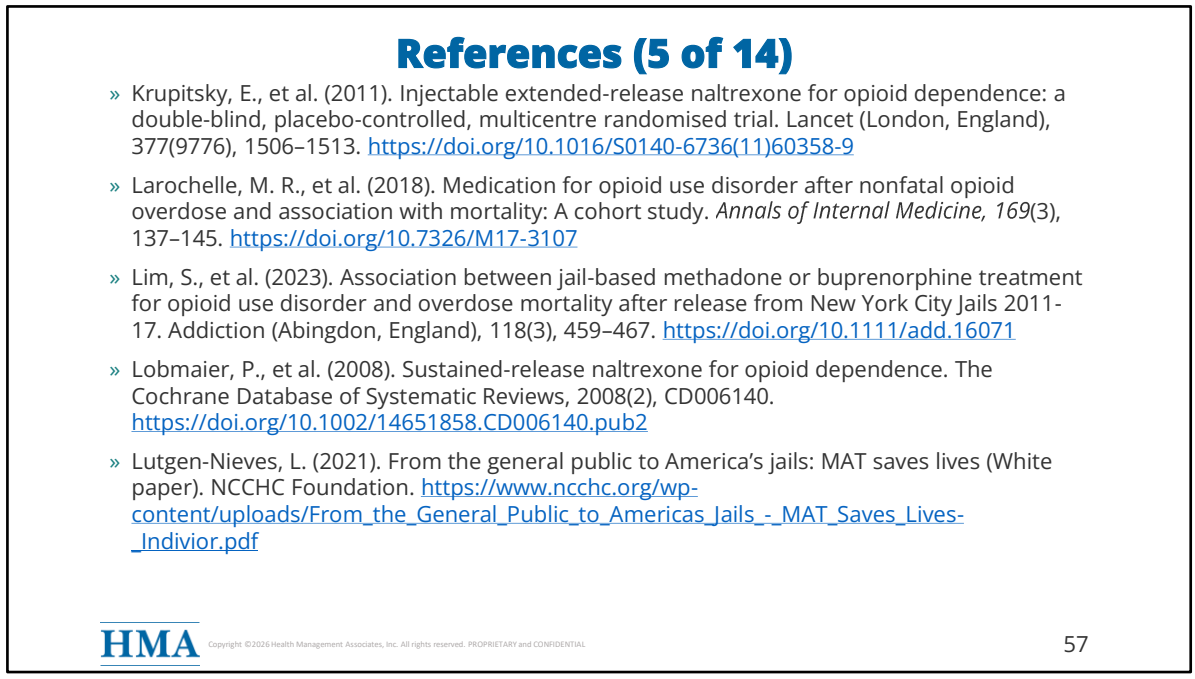

[Slide Image Description: This slide lists webinar references 5 of 14.]

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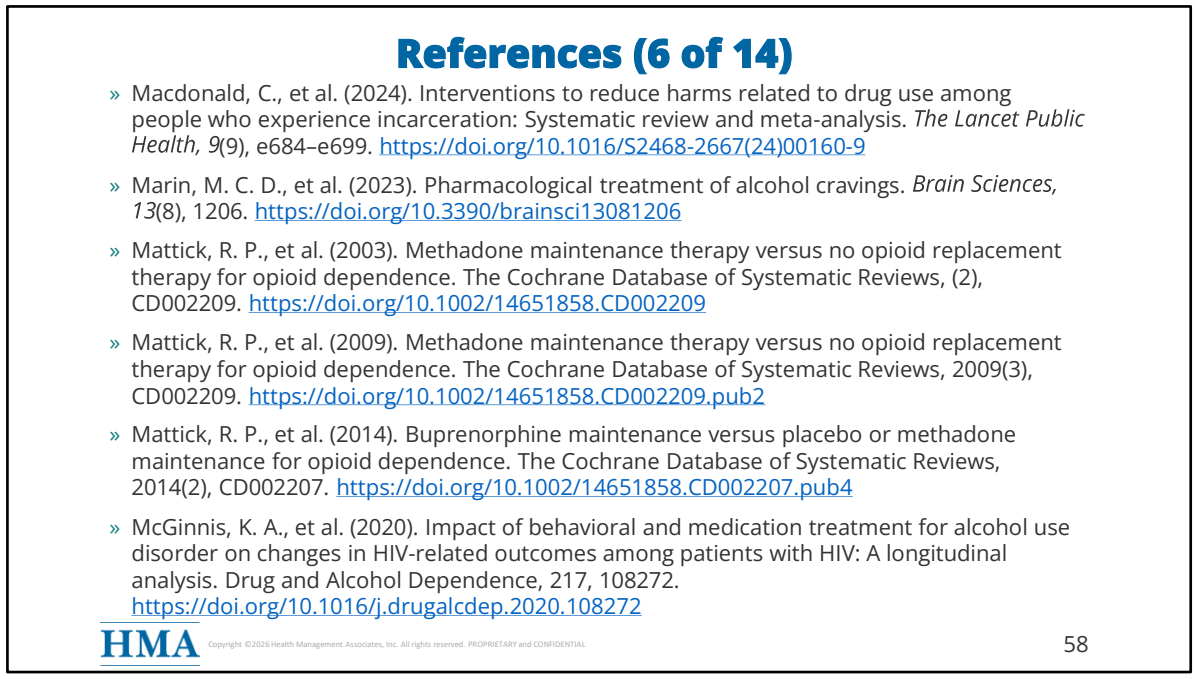

[Slide Image Description: This slide lists webinar references 6 of 14.]

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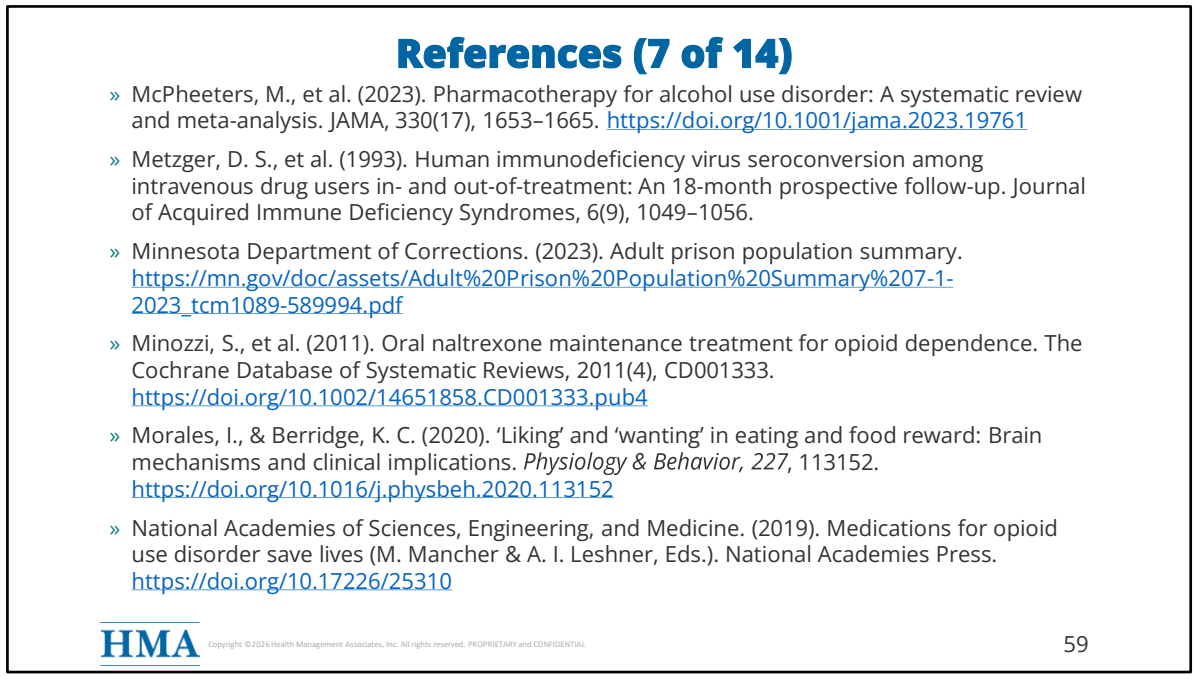

[Slide Image Description: This slide lists webinar references 7 of 14.]

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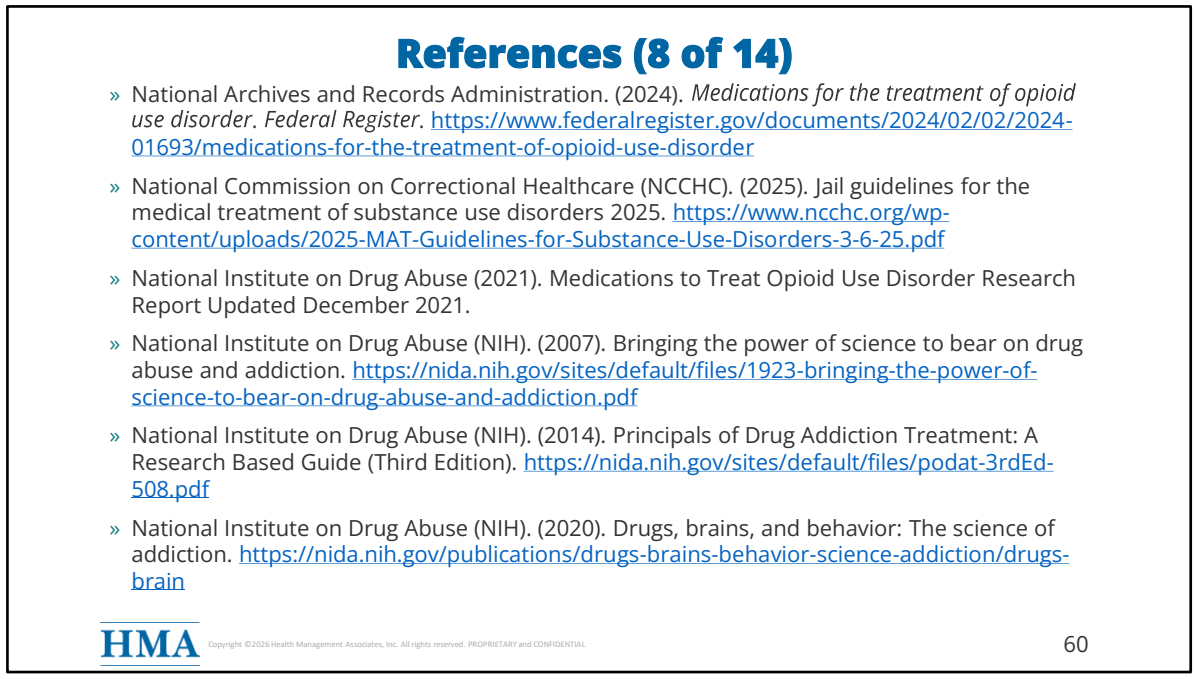

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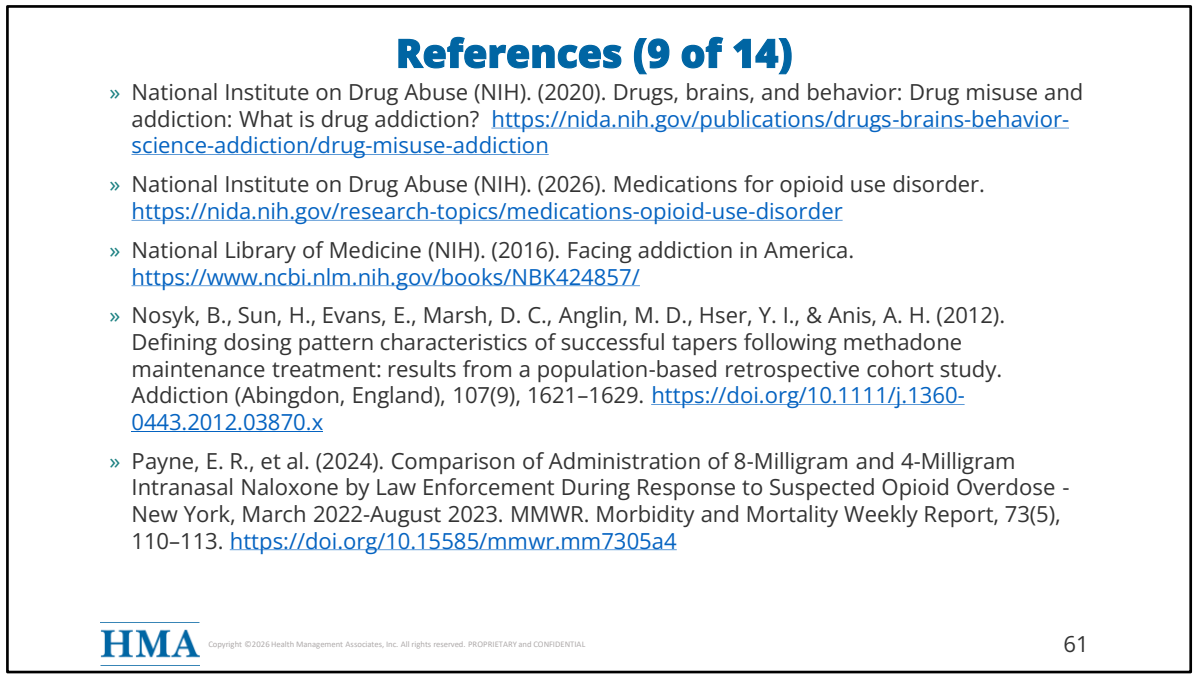

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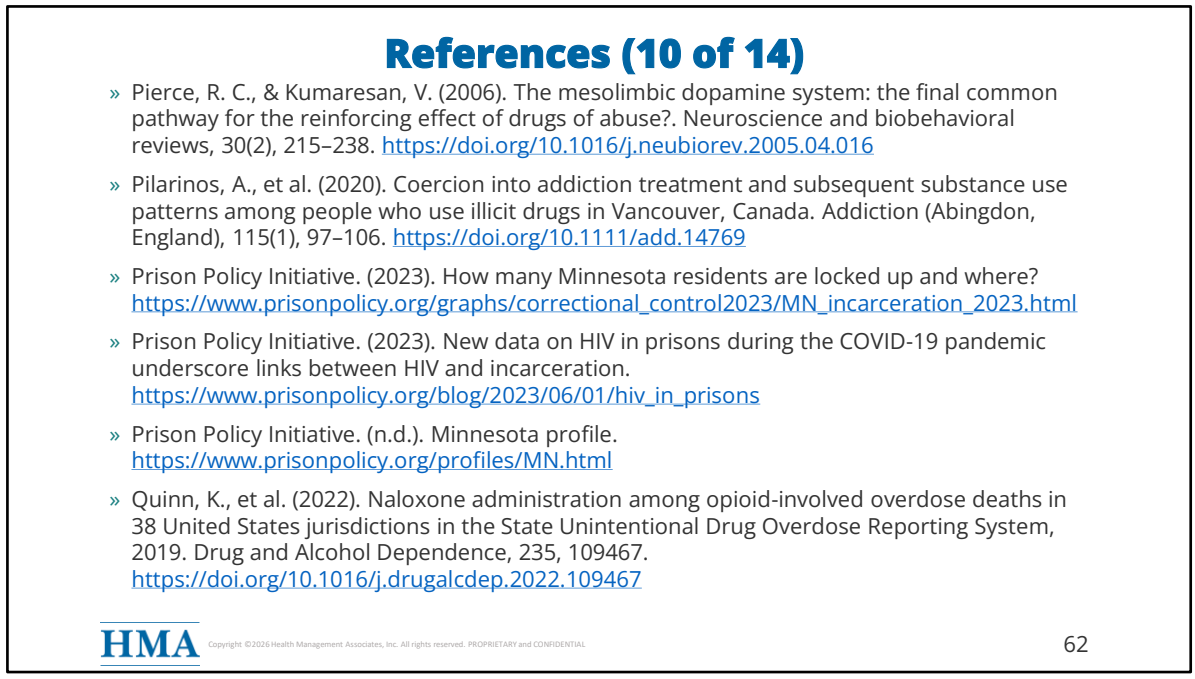

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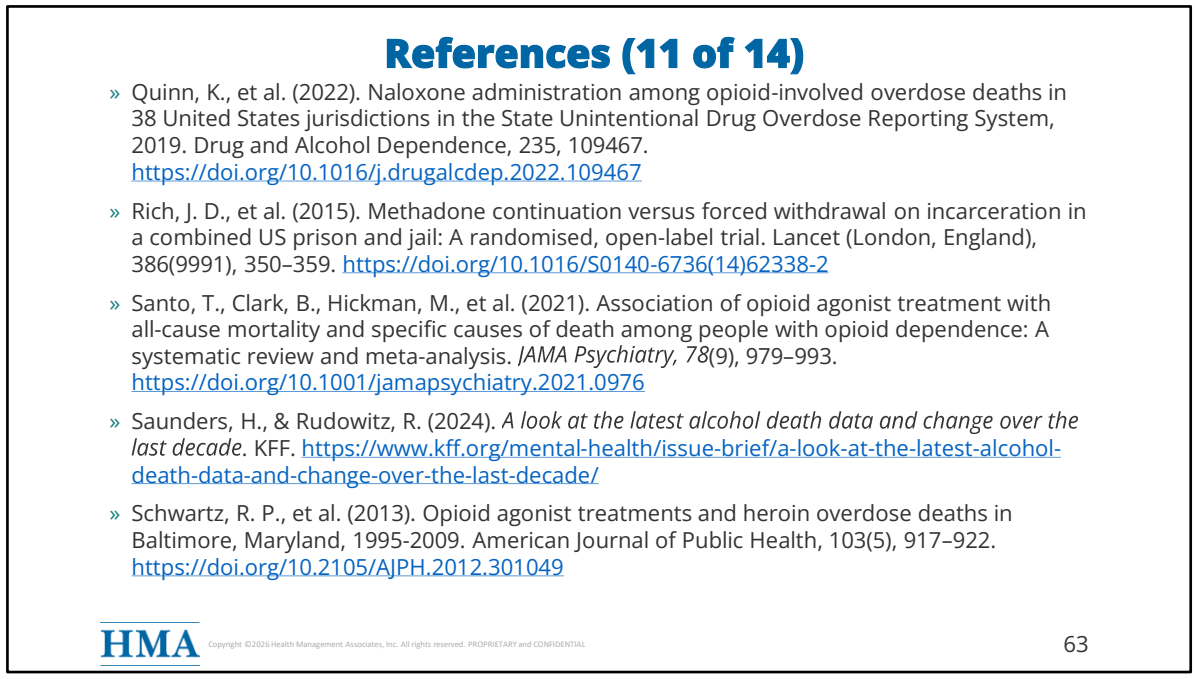

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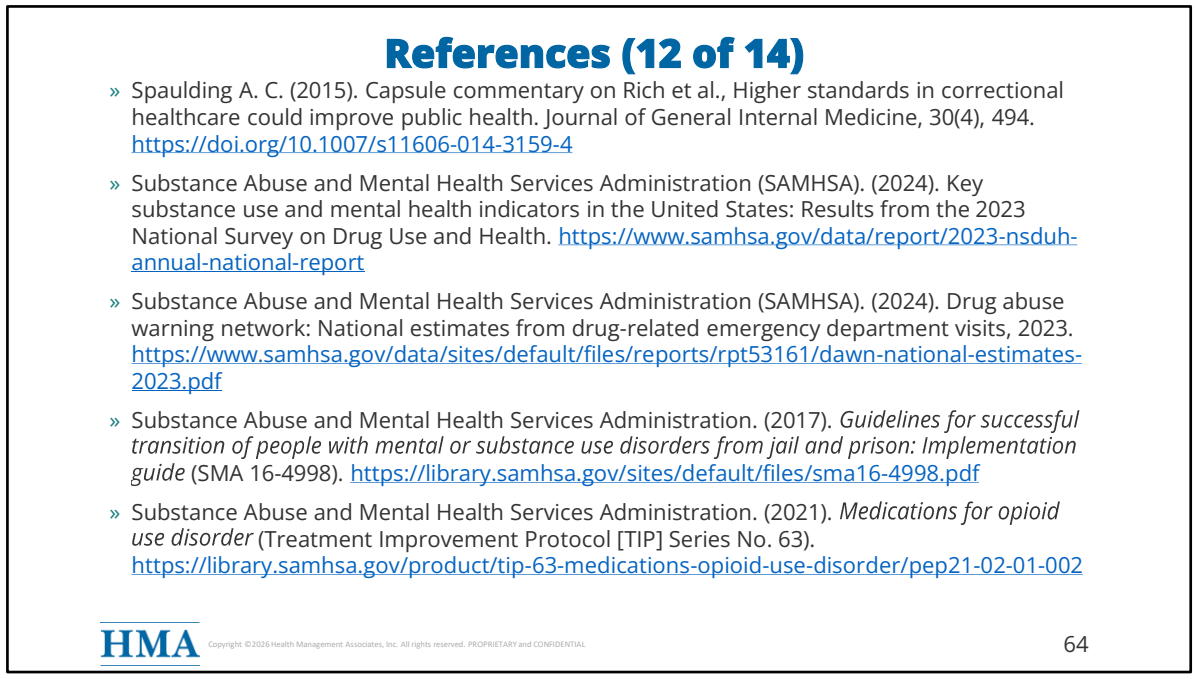

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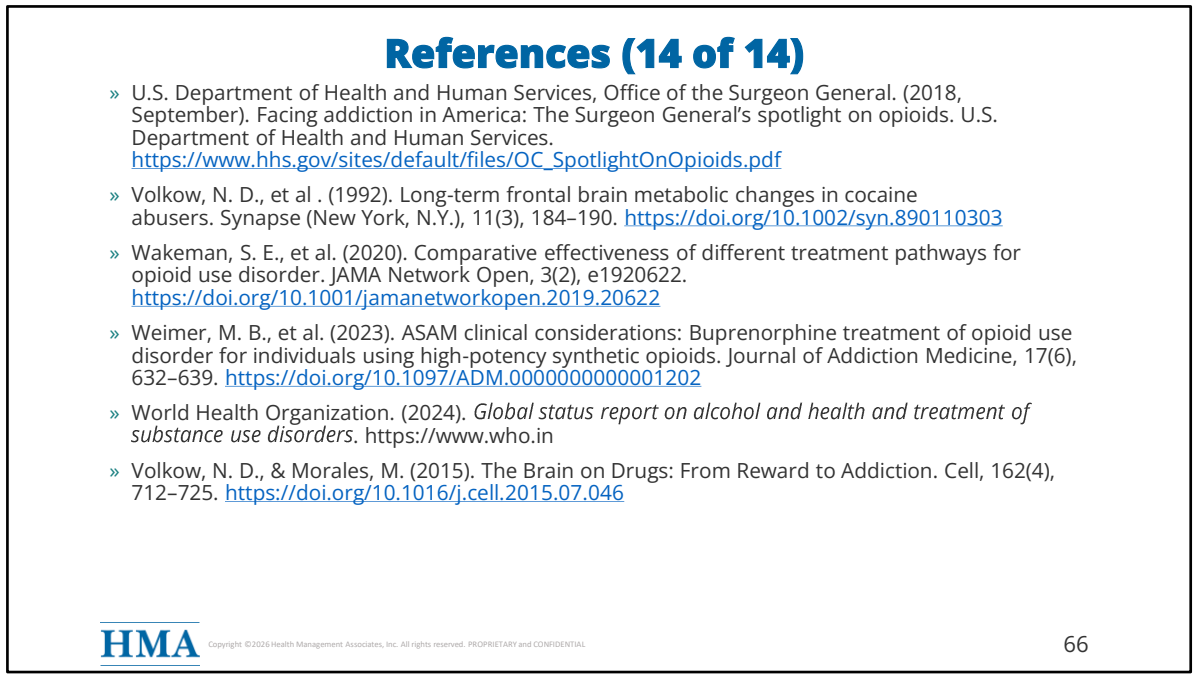

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