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HEALTH MANAGEMENT ASSOCIATES

Neuroscience of Addiction and MAT 101: *Understanding the Neurobiology and Chronic Disease Nature of SUD and Medications for Addiction Treatment (MAT)*

September 2021



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W W W . H E A L T H M A N A G E M E N T . C O M

WELCOME

- This webinar is intended to support counties in expanding access to Medications for Addiction Treatment (MAT) for persons with justice and/or child welfare system involvement.
- This session is being recorded and the slide deck will be shared after the webinar.
- Please note this content is being recorded. The recording has not been professionally edited and the session was conducted using Zoom.
- If you have questions or comments, please email MATinCountyCJ@healthmanagement.com or CountyTouchpoints@healthmanagement.com

This project is funded through California's Department of Health Care Services with State Opioid Response funding from SAMHSA

SECURITY DISCLAIMER

- In the case of any security issues that may occur, this session will immediately end.
- A separate email will be sent to all participants with further instruction.

LEARNING OBJECTIVES

I

An overview of the neuroscience of addiction and the chronic disease nature of substance use disorders (SUD) with an emphasis on opioid use disorder (OUD)

II

An explanation of the role of dopamine in SUD and how it relates to the recovery journey

III

A review of the medications approved for treating OUD (methadone, buprenorphine, and naltrexone) and special treatment considerations for pregnant and parenting women

IV

Considerations for effective use of MAT in jails and other justice settings including medication selection, method of action, diversion potential, side effects and common myths

HMA PRESENTERS



Helen Du Plessis, MD, MPH, FAAP
Principal, HMA

Subject Matter Expert

Presenting on
9/22 at 4 p.m.
9/30 at 4 p.m.



Lori Raney, MD
Principal, HMA

Subject Matter Expert

Presenting on
9/21 at Noon
9/22 at Noon



Scott Haga, MPAS, PA-C
Senior Consultant, HMA

Subject Matter Expert

Presenting on
9/28 at Noon
9/30 at Noon

NEUROBIOLOGY OF ADDICTION AND SUBSTANCE USE DISORDERS (SUD) AS A CHRONIC DISEASE

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TIME FOR A POLL...

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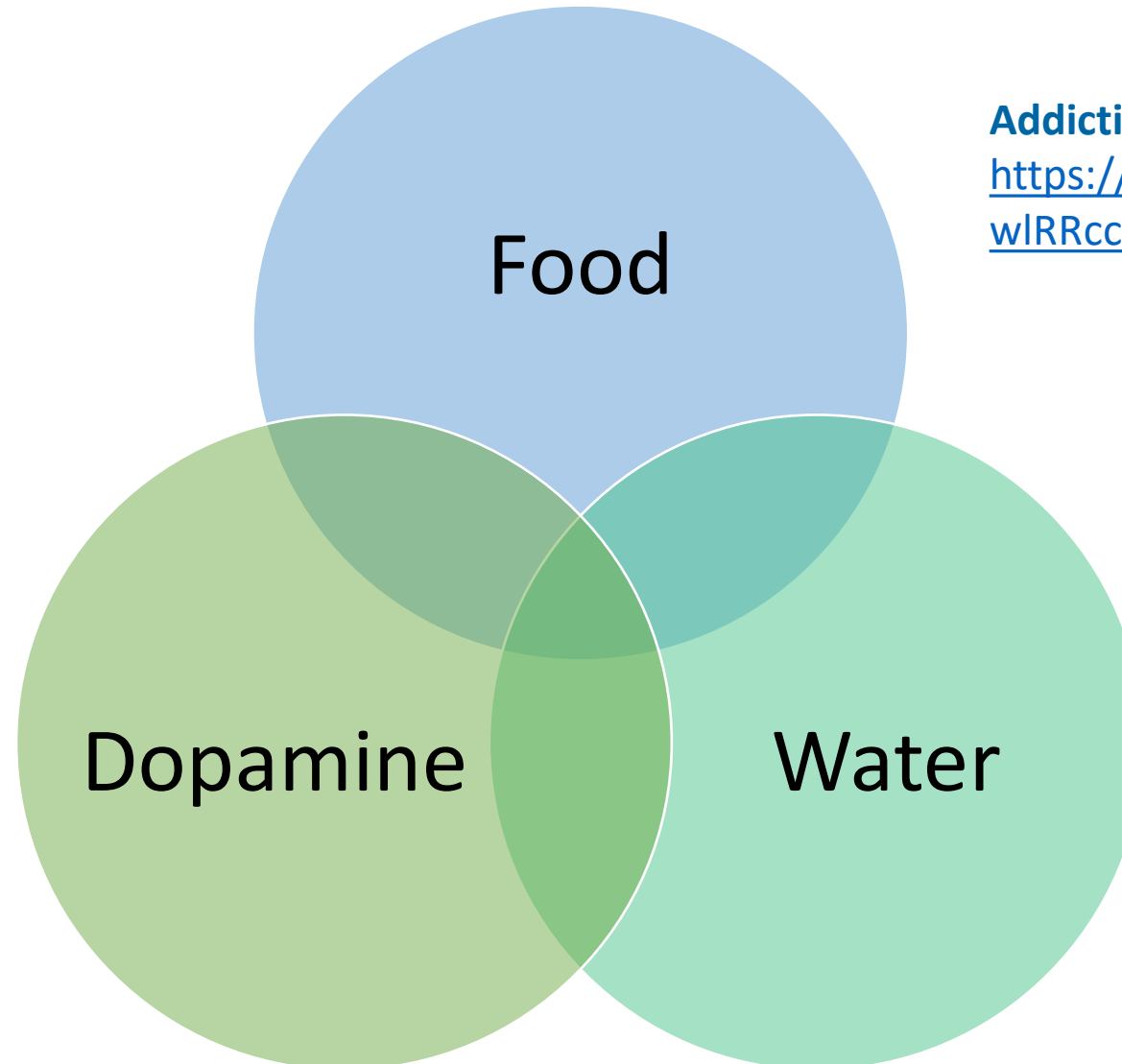
POLL

Which of the following do you think is the primary contributor to substance use disorders?

- A. Personal choice and behaviors
- B. Impact of trauma and other adverse life events
- C. Action of neurochemicals in the brain
- D. I haven't decided yet



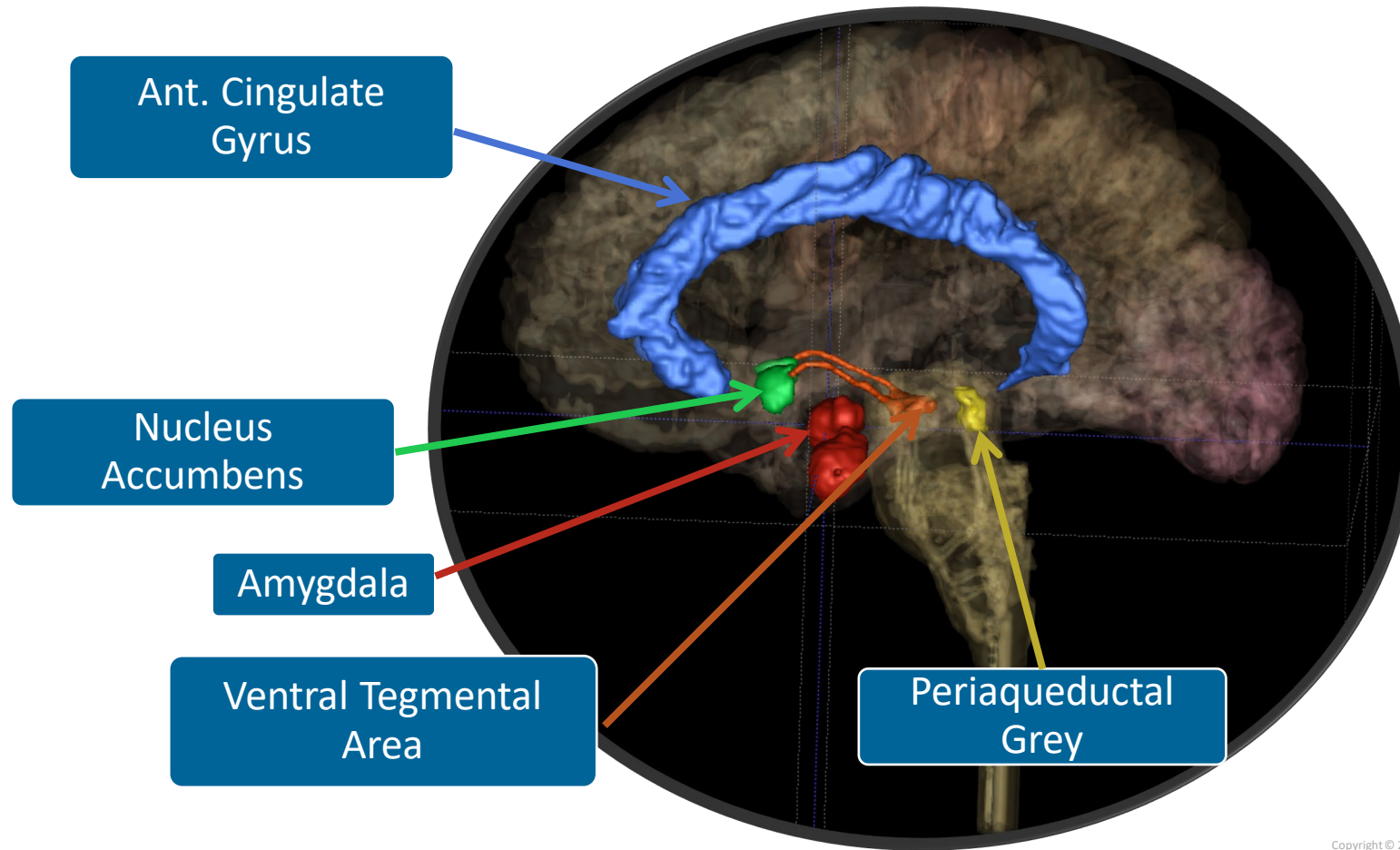
■ BASIC MECHANISM OF HOW SUD AFFECTS THE BRAIN



Addiction Neuroscience 101 Video:

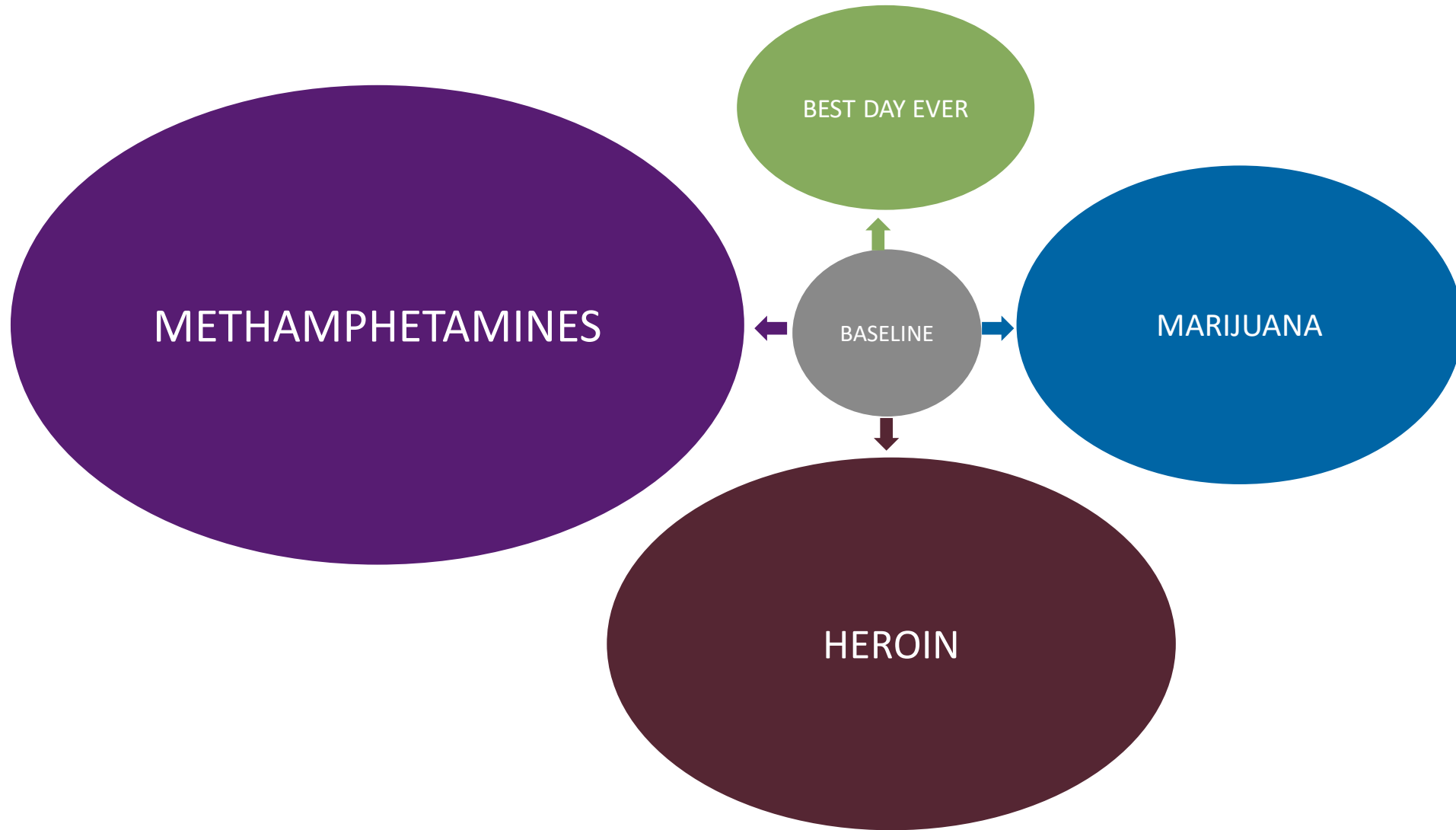
<https://www.youtube.com/watch?v=bwZcPwIRcc&t=266s>

ADDICTION 101: NEUROBIOLOGY OF ADDICTION

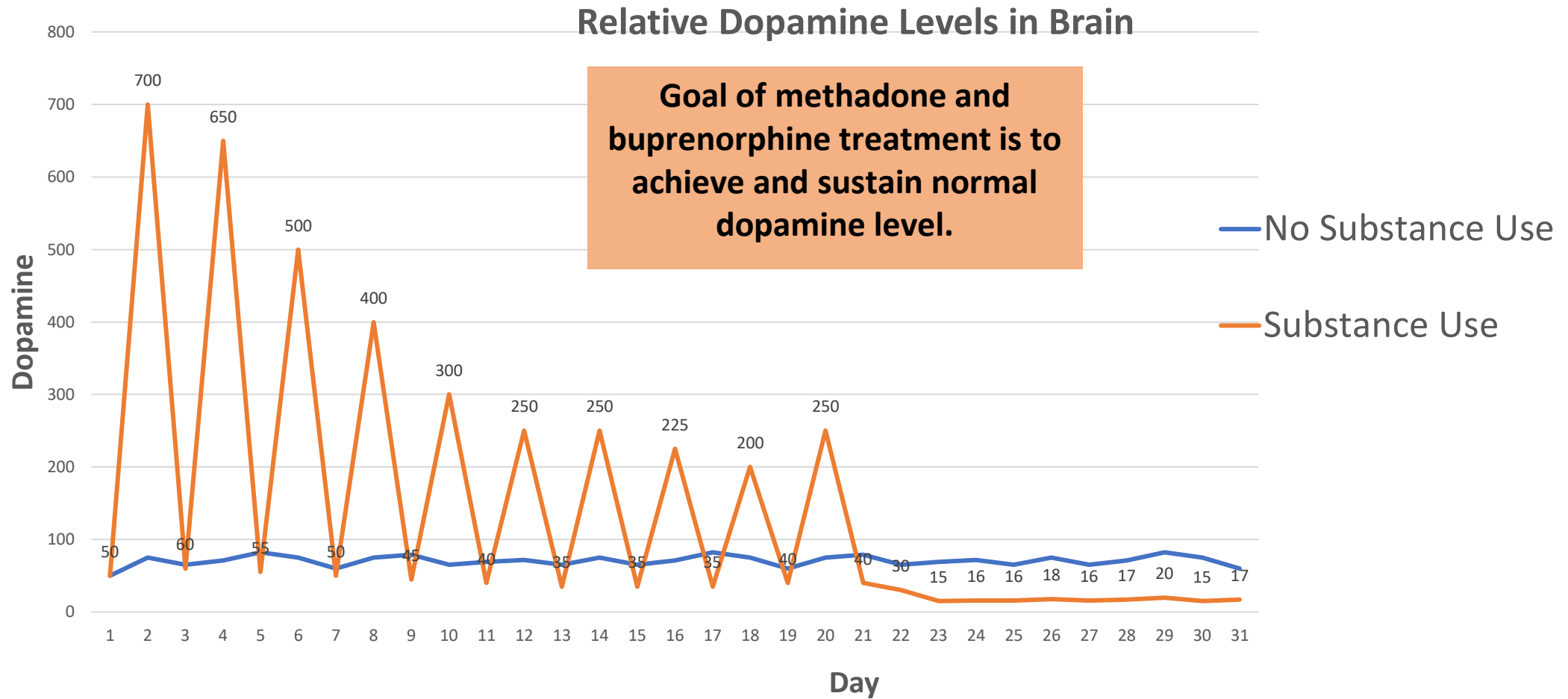


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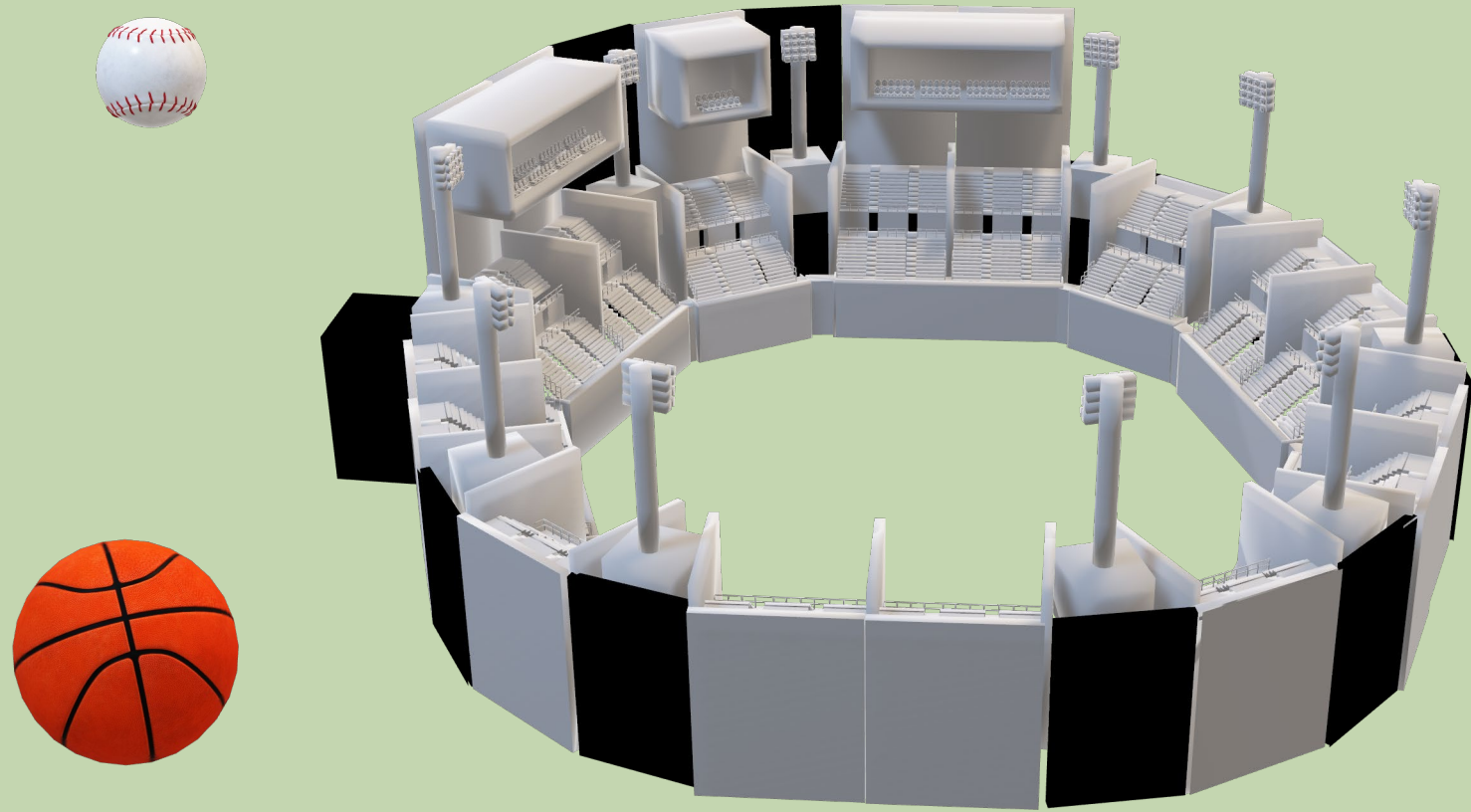
ADDICTION 101 – COMPARATIVE DOPAMINE PRODUCTION



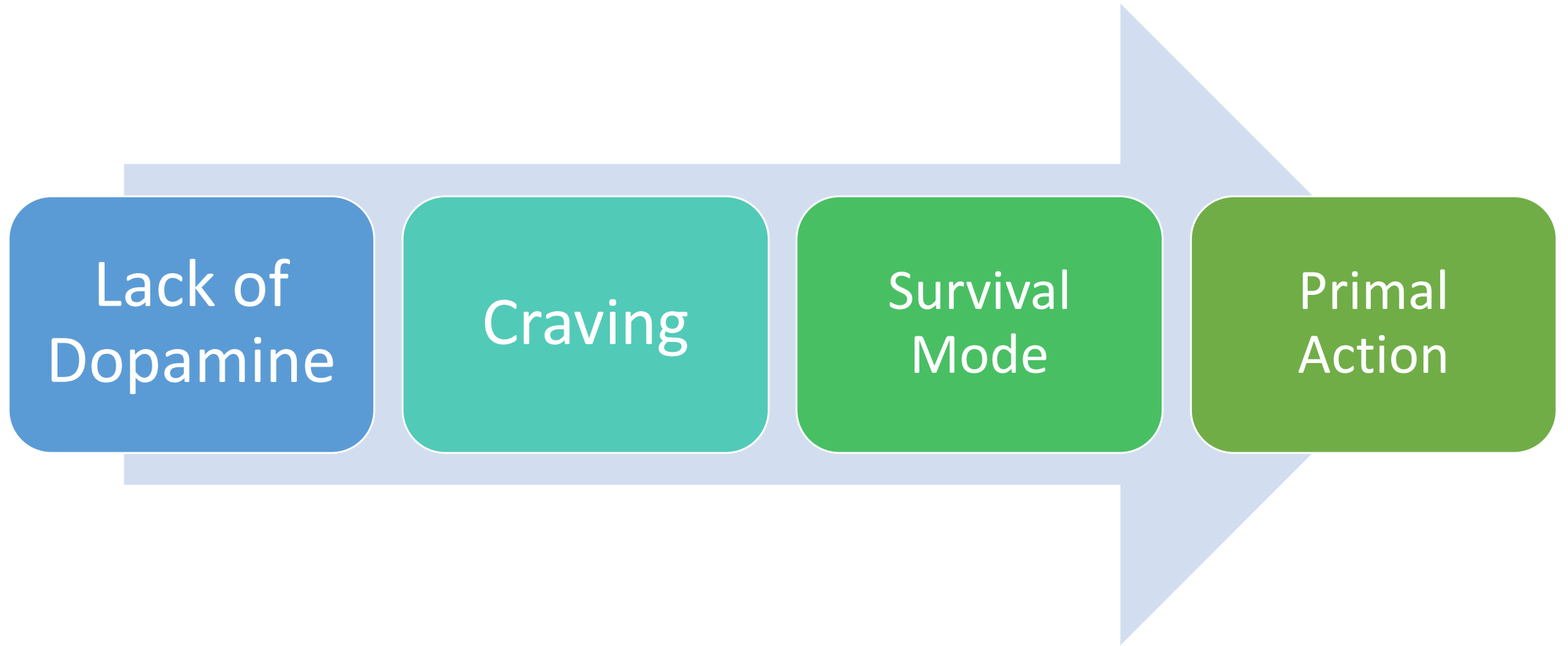
BASIC MECHANISM OF HOW SUBSTANCES AFFECT THE BRAIN: DOPAMINE PRODUCTION OVER TIME



BASIC MECHANISM OF HOW SUBSTANCES AFFECT THE BRAIN: INTENSITY OF CRAVINGS



UNDERSTANDING ADDICTION TO INFORM TREATMENT





CHATTERFALL

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CHATTERFALL

Think about someone you know who has struggled with addiction.

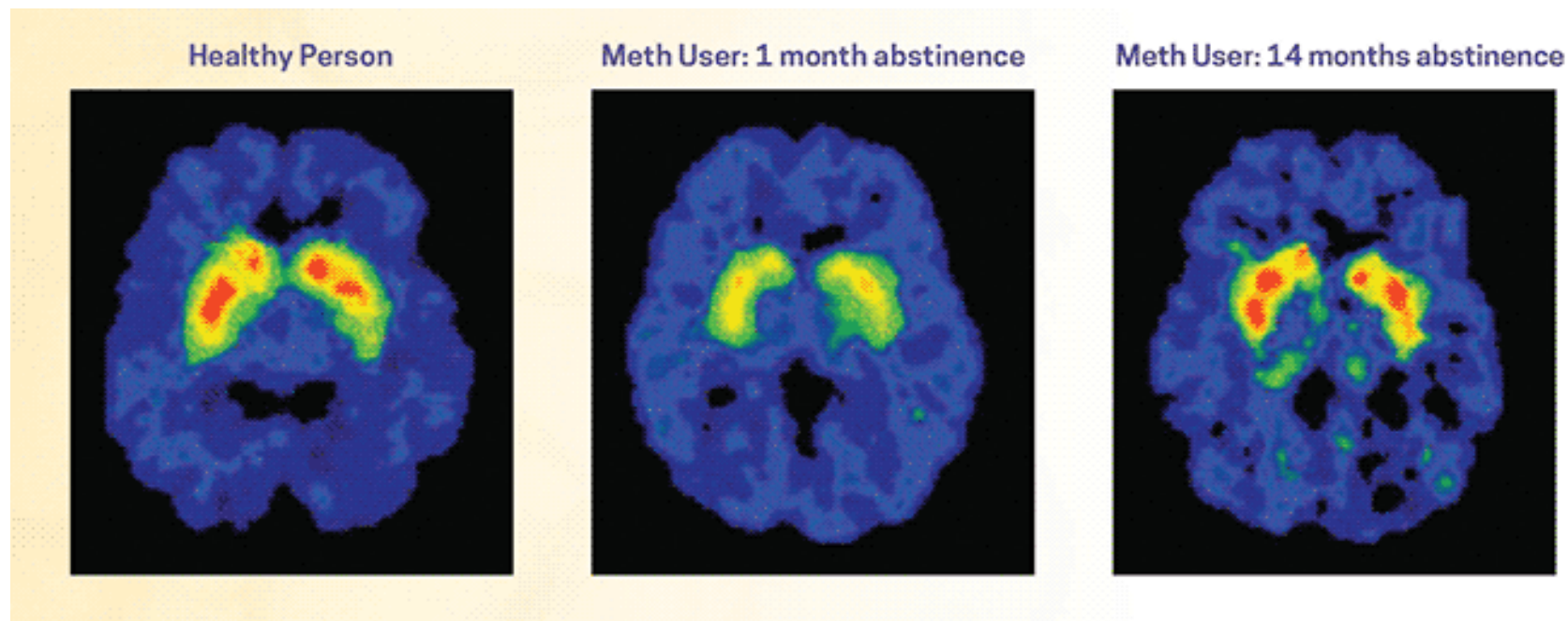
Reflecting on what you have heard so far today, has your thinking about their behavior related to addiction changed?

If yes, please type a brief sentence about how your thinking may have changed.



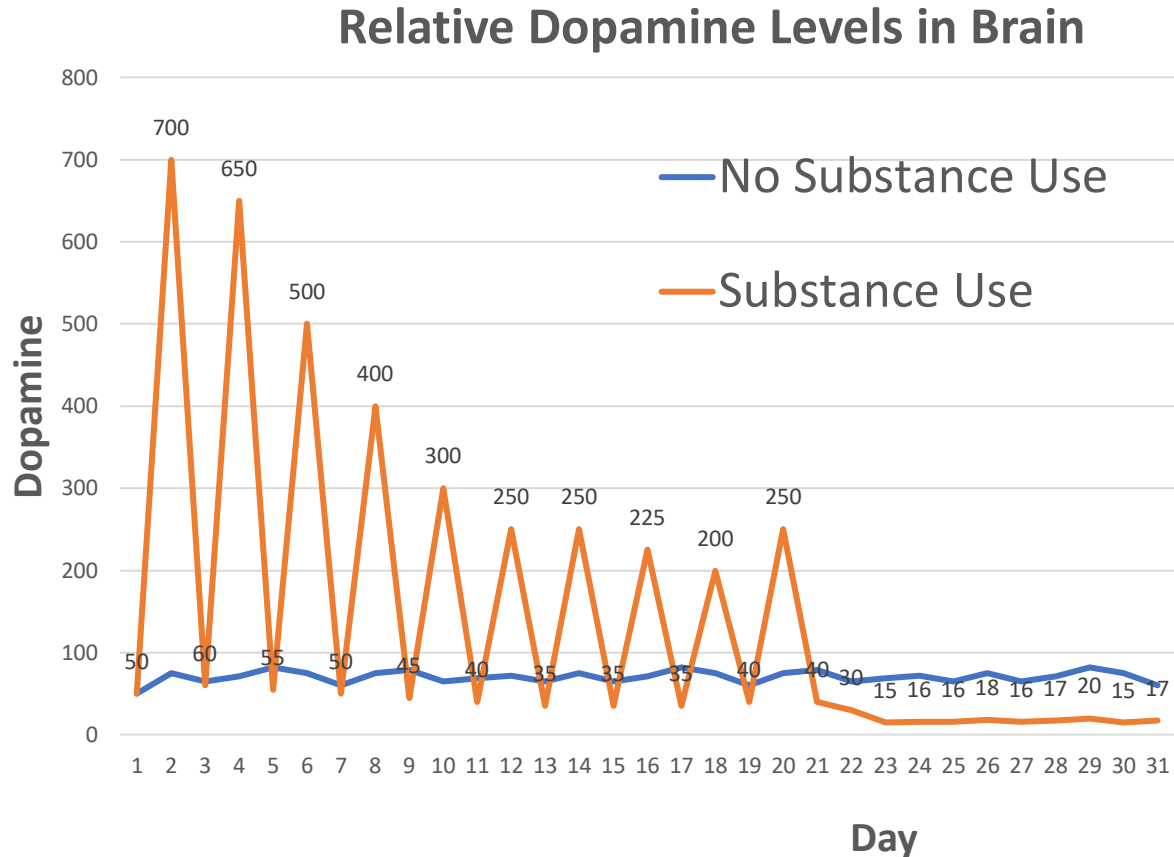
DOPAMINE DEPLETION AFFECTS RECOVERY: IT TAKES TIME FOR YOUR BRAIN TO RECOVER

- +Prolonged drug use changes the brain in long lasting ways
- +Changes are both functional and structural
- +Return to normal dopamine production is under study (takes over 1 year)
- +Discontinuing treatment before brain recovery may affect outcomes



Source: Volkow (2001)

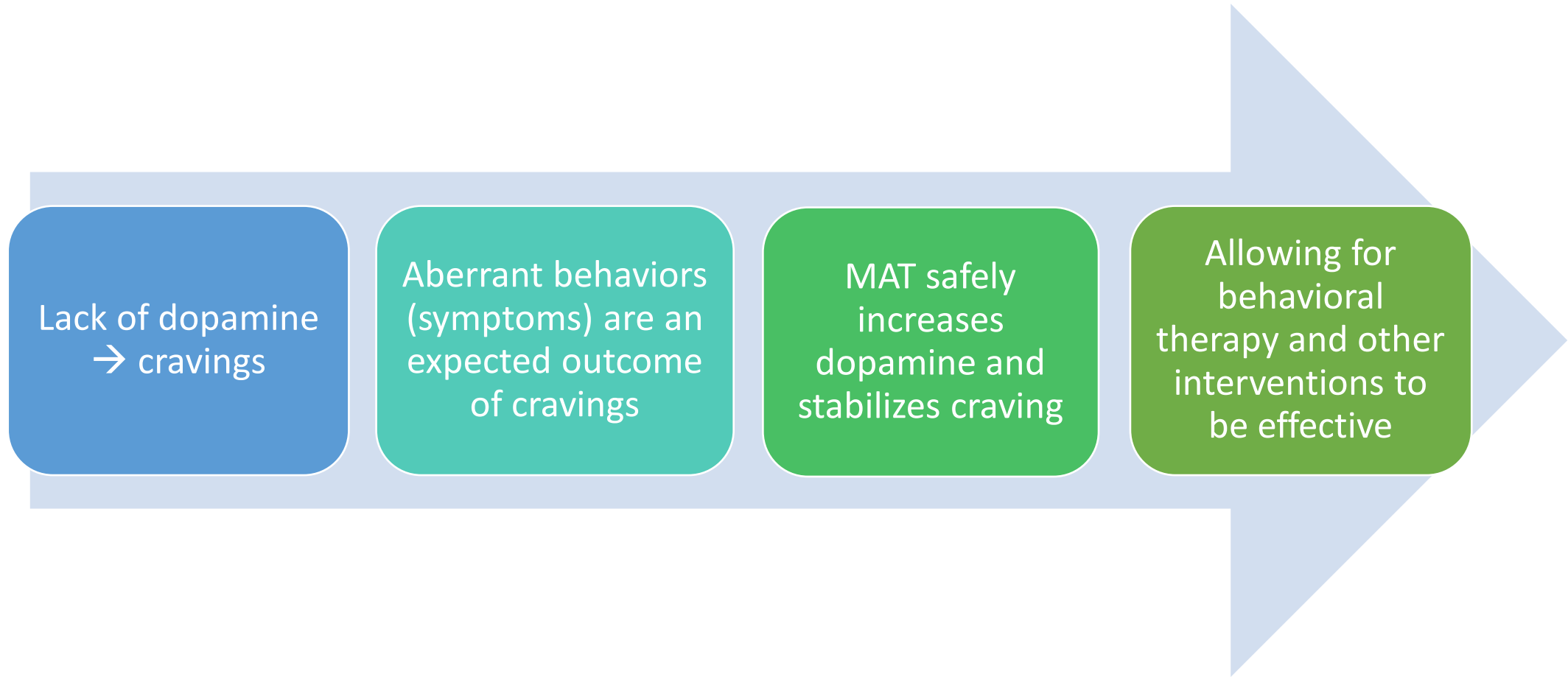
DOPAMINE DEPLETION AFFECTS RECOVERY



Addressing Dopamine Depletion

- MAT for OUD
- Contingency Management
- Transitioning from external rewards to internal rewards

ADDICTION 101: TREATMENT



UNDERSTANDING ADDICTION TO INFORM TREATMENT

Diagnosis based in
the description of
behavior

Aberrant behavior
should be expected

Therefore, behavior
is a symptom not a
frustration

DSM-5: DIAGNOSIS OF OUD

TABLE 1

Summarized DSM-5 diagnostic categories and criteria for opioid use disorder

Category	Criteria
Impaired control	<ul style="list-style-type: none">• Opioids used in larger amounts or for longer than intended• Unsuccessful efforts or desire to cut back or control opioid use• Excessive amount of time spent obtaining, using, or recovering from opioids• Craving to use opioids
Social impairment	<ul style="list-style-type: none">• Failure to fulfill major role obligations at work, school, or home as a result of recurrent opioid use• Persistent or recurrent social or interpersonal problems that are exacerbated by opioids or continued use of opioids despite these problems• Reduced or given up important social, occupational, or recreational activities because of opioid use
Risky use	<ul style="list-style-type: none">• Opioid use in physically hazardous situations• Continued opioid use despite knowledge of persistent physical or psychological problem that is likely caused by opioid use
Pharmacological properties	<ul style="list-style-type: none">• Tolerance as demonstrated by increased amounts of opioids needed to achieve desired effect; diminished effect with continued use of the same amount• Withdrawal as demonstrated by symptoms of opioid withdrawal syndrome; opioids taken to relieve or avoid withdrawal

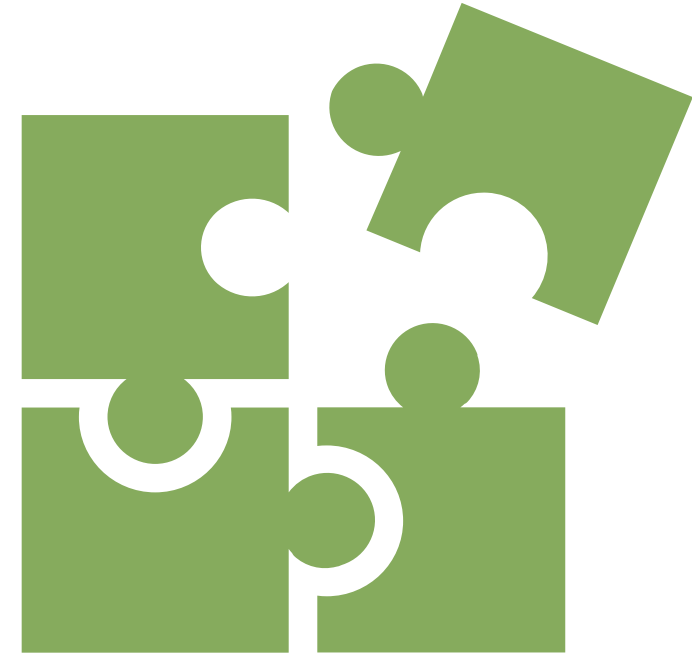
Chronic Diseases: Addiction and Diabetes

Cause? Genes, Environment and Behavior

Prevention? Environmental and Behavior Change

Treatment? Long Term Biochemical Replacement and Lifestyle Changes

What is Different?



UNDERSTANDING ADDICTION TO INFORM TREATMENT

Diabetes and Addiction: You make a mistake...what could you lose?

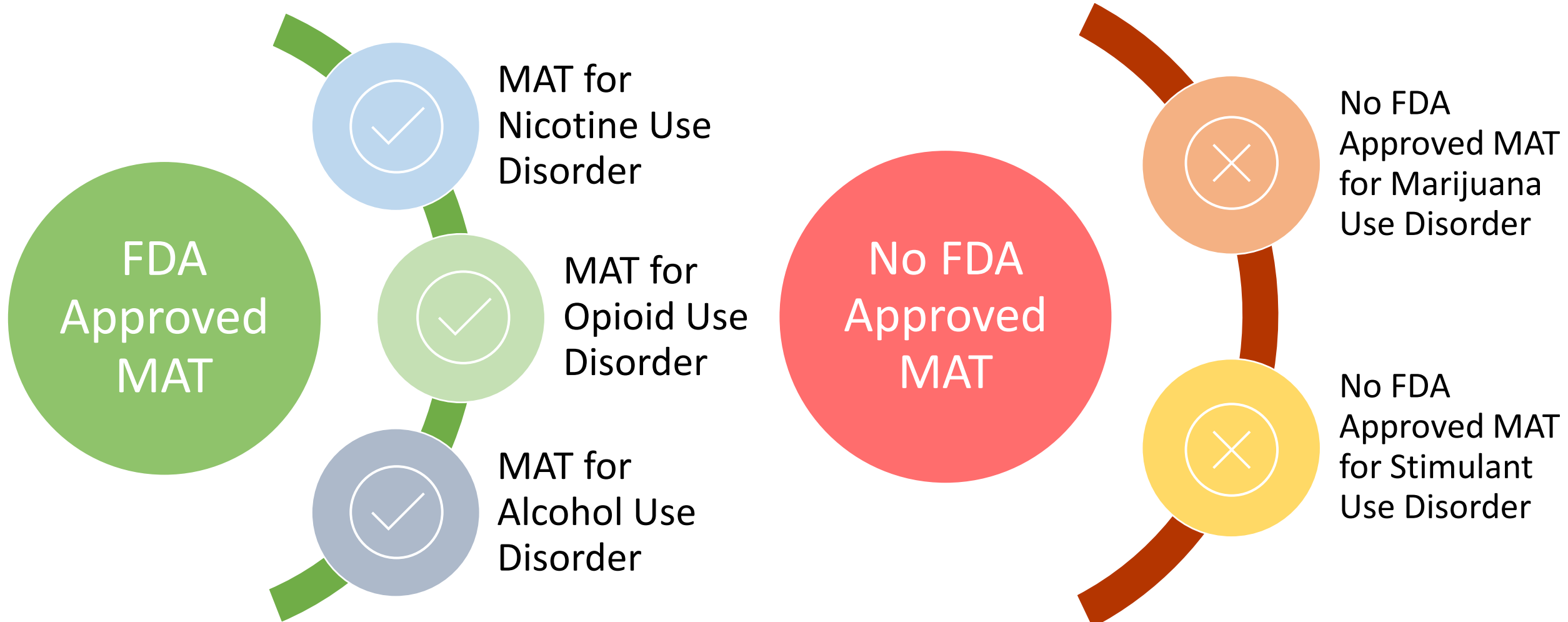
	Diabetes	Addiction
Treatment	No	Yes
Custody of Children	No	Yes
Freedom (Probation, Incarceration)	No	Yes
Housing	No	Yes
Family	No	Yes
Work Identity	No	Yes



MEDICATIONS FOR ADDICTION TREATMENT

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FDA APPROVED MEDICATIONS FOR SUD



WHY IS MAT FOR OUD IMPORTANT?

Treat Withdrawal

Symptoms include
Muscle pain, dilated pupils, nausea, diarrhea, abdominal cramping, piloerection

- Lasts 3-7 days
- Using methadone or buprenorphine is recommended over abrupt cessation due to risk of relapse, overdose (OD) & death

Address Dopamine Depletion

Reward/motivation pathway

- Depletion persists for months-years after people stop using
- Treated with methadone or buprenorphine

Treat OUD

Abstinence based treatment results in 85% relapse within 1 year

Achieve Results

Retention in treatment

- Decreases opioid use
- Reduces cravings
- Reduces overdose
- Reduces complications IVDU and other risky behaviors
- Reduces criminal behavior

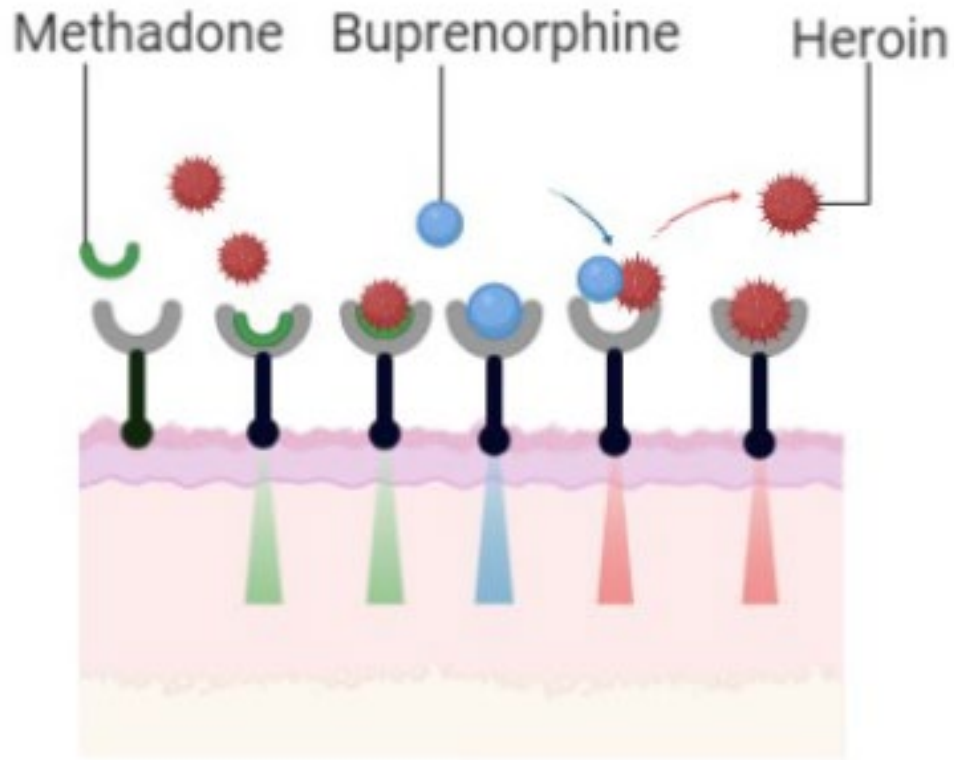
Sources:
Mattick, RP & Hall W (1996) Lancet 347: 8994, 97-100.
Lobmaier, P et al. (2008) Cochrane Systematic Review.
Kakko et al. (2003) Lancet 361(9358),662-8.
ASAM, (2020) National Practice Guidelines for the Treatment of OUD.
Mattick, RP, et al. (2009) Cochrane Systematic Review.
Krupitsky et al. (2011) Lancet 377, 1506-13.
Rich, JD, et al. (2015) Lancet

AGONIST VERSUS ANTAGONIST

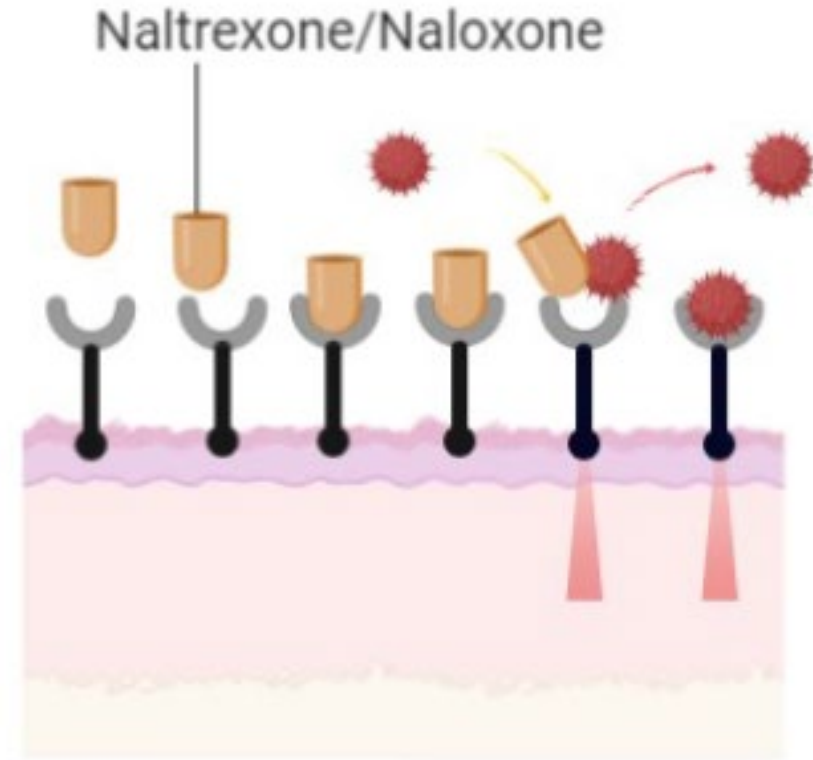
- An **agonist** is a drug that activates certain receptors in the brain. Full agonist opioids activate the opioid receptors in the brain fully resulting in the full opioid effect. **Partial agonist** opioids activate the opioid receptors in the brain, but to a much lesser degree than a full agonist.
- An **antagonist** is a drug that blocks opioids by attaching to the opioid receptors without activating them. Antagonists cause no opioid effect and block full agonist opioids.

Source: U.S. Department of Health and Human Services. Indian Health Services. Pharmacological Treatment <https://www.ihs.gov/opioids/recovery/pharmatreatment/>

FDA APPROVED MEDICATIONS FOR OUD AND OPIOID REVERSAL AGENT: MU OPIOID RECEPTOR BINDING



Agonist Treatment



Antagonist Treatment

Agonist Treatment:

- Methadone- approved for cough in 1940s, for OUD 1972
- Buprenorphine- approved in 1981 for pain; oral approved for OUD 2002, patch, implants & injection later

Antagonist Treatment:

- Naltrexone- oral approved 1984; injectable 2006 AUD, 2010 OUD
- Naloxone- approved 1961, autoinjector 2014, nasal spray 2015

METHADONE: WHAT AND FOR WHOM?

- Mu agonist without a “ceiling effect”
- Reaching a therapeutic dose (60-120mg) takes time
 - <60 mg/d is not therapeutic
 - Increased frequency and daily dose required during pregnancy
- Several significant drug-drug interactions
- Despite having the best outcomes, it has the highest level of stigma



Patients with a more severe OUD (> 1 year or persons who inject drugs)

Patients who would benefit from the services available in an OTP environment

Patients who were not successful with other MAT for OUD

METHADONE: GENERAL FEDERAL REGULATIONS



**Delivered initially
via observed
dosing**

**Once patient is
stable and after 6
weeks, can be given
take-home doses
(varies by state and
current PHE)**



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

**Many
requirements for
treating patients**



BUPRENORPHINE: WHAT AND FOR WHOM?

- Partial Mu agonist with ceiling effect
 - Available alone or in combination w/naloxone
 - Different formulations (SL and buccal pill/film, implant, injectable)
 - Combination formulation averts diversion
- Greater binding affinity than most full agonists
 - Start buprenorphine when client in mild-moderate withdrawal (to avoid causing precipitated withdrawal)
- Many ways to do initiation (protocols needed)
 - <8 mg/d is not therapeutic (typical dose is 16 mg/d)
 - Dosing adjustments required during pregnancy
- Fewer drug-drug interactions than methadone

Positive DSM-5 with a score of 2 or greater

Patient wants agonist treatment

Has coverage or can afford medication

BUPRENORPHINE: GENERAL REGULATIONS



**Approved in the
1981 for pain via
an injectable form**



**Approved in 2002
for use in
maintenance
treatment for
OUD**

DEA X-Waiver update: Federal Register 4/28/21

- To prescribe buprenorphine for OUD to ≤ 30 patients
 - Send Notice of Intent to SAMHSA
 - SAMHSA approves request & notifies DEA
 - DEA issues X-waiver
- To prescribe to ≥ 30
 - Complete 8 /24 h training
 - Apply for, get approval for & receive x waiver
 - Provide or refer for counseling & ancillary services
- Qualified practitioners can apply to have prescription limit increased to 100 in first year

■ BUPRENORPHINE: CONSIDERATIONS FOR THOSE IN THE CRIMINAL JUSTICE SYSTEM

- MAT prescribing limits can create challenges for jails
 - Providers in the community and in California jails are finding demand can exceed prescriber limits
 - Thirty (30) patient limit under new guidelines (alternative notice of intent)
 - Thirty patient limit can be expanded to 100, even in first year for qualified providers who met training requirements

<https://admin.addictionfreeca.org/files/blobs/eyJfcmlFpbHMiOmsibWVzc2FnZSI6IkJBaHBBa01DliwiZXhwIjpudWxsLCJwdXIiOiJibG9iX2lkIn19--5101e4626bfb9a1818dc71c5d437a0d83f3a5894/Buprenorphine%20update%205.21%20final.pdf>

CONSIDERATIONS FOR THOSE IN THE CRIMINAL JUSTICE SYSTEM

- Forcible withdrawal or transition for persons on agonist treatment is not advised
 - Fifty percent (50%) of those forcibly withdrawn DO NOT return to treatment
 - Jails that forcibly withdraw people from agonist treatment are being sued and losing (ADA violation)
 - Patients can be transitioned from methadone to buprenorphine, but this is complex and requires planning and expertise
- Pregnant women receiving MAT *should* be maintained on agonist treatment to avoid risk to pregnancy and the fetus

NALTREXONE: WHAT AND FOR WHOM?

- Mu opioid antagonist with high, competitive binding affinity
- Does NOT treat withdrawal or underlying dopamine depletion
- Client must be opioid free 5-7 days before starting
- More readily accepted in criminal justice and “abstinence-only” communities
- Evidence of decreased mortality is limited *

Source: Laroche, et al. Medication for opioid use disorder after nonfatal opioid overdose and association with mortality. A cohort study. *Annals of Internal Medicine*. 169:3 (2018) 137-45.



Patients with a high degree of motivation (dopamine)

Patients who had poor results with methadone or buprenorphine

Can be useful as “back-up” after discontinuation of methadone or buprenorphine

NALTREXONE: GENERAL REGULATIONS



No Federal regulations inhibit the use

Some payer restrictions make it difficult to obtain the long-acting injectable form



Multiple formulations:

- Pills at 25mg and 50 mg (50-100 mg for AUD)
- Long acting injectable 380mg (28-30 days)
- Implantable beads: lasts 6 months (0.9 ng/ml formulation contains 3.5 ng/ml of 6-beta-Naltrexol)

■ NALOXONE OVERVIEW: OVERDOSE REVERSAL AGENT AS HARM REDUCTION

Mu opioid antagonist used for opioid overdose (OD) reversal

Shorter half-life & more rapid onset of action than naltrexone

High affinity, competitive binding & displaces full agonists

Intranasal or intramuscular by bystander

May require more than one dose

- Opioids have longer half-life than naloxone
- Fentanyl contamination may require higher dose for reversal

CA Assembly Bill 2760- Naloxone prescribing

- >90mg Morphine Milliequivalents
- Opioids + benzodiazepines
- Increased risk of OD: History of OD or SUD

Evidence-Based Tapering of Agonist Treatment

Evidence is clear that long-term or indefinite treatment with medications for OUDs is often required for effective and sustained outcomes

In practice, successful tapers from methadone or buprenorphine typically occur in only about 15 percent of cases

According to the U.S. Surgeon General, successful tapers typically occur, if at all, when individuals have been treated with MAT for at least 3 years



TIME FOR A POLL...

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POLL

Do you know anyone who has received MAT for OUD?

- A. Yes
- B. No

If you answered yes in the previous poll, from your perspective, is/was this treatment helpful for them?

- A. Yes
- B. No
- C. N/A (I do not know anyone who has received MAT for OUD)



The background of the slide is a solid light green color. It is covered with a repeating pattern of dark green speech bubbles, each containing a white question mark. The speech bubbles are scattered across the entire page, creating a textured, thematic background.

QUESTIONS?

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POLLING QUESTIONS

1. Overall, today's webinar was:

- A. Very useful**
- B. Somewhat useful**
- C. Not very useful**
- D. Not useful at all**

2. The material presented today was:

- A. At the right level**
- B. Too basic**
- C. Too detailed**

THANK YOU!

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REFERENCES

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