# PHARMACOTHERAPY FOR SUBSTANCE USE DISORDERS

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University of Nebraska Medical Center℠

# DISCLOSURE STATEMENT

I have no financial interest or affiliation concerning material discussed in this presentation

I will not discuss any non-FDA approved or investigational medications/medical devices

# LEARNING OBJECTIVES

1. Describe the role of psychosocial interventions and other non-pharmacologic modalities in the treatment of SUDs and the importance of a multimodal approach.
2. Compare and contrast current treatment modalities for the management of each SUD including mechanism of action, side effects, drug interactions, warnings/precautions, and other patient-specific factors.
3. Identify essential information for each pharmacologic treatment option to share with patients when discussing the benefits and risks of each medication.

# ALCOHOL / ETHANOL (ETOH)

# ALCOHOL USE IN NEBRASKA

**U.S. Rank**

- Average age of first drink is 15 years
- **60.4%** of the Nebraska adults (≥18 years) currently use alcohol - – – – ***9th***
  - **30.2% <u>binge drink</u> (≥5 drinks/*occasion* for men; ≥4 for women)** - – – ***4th***
  - **6.2% <u>heavily drink</u> (>14 drinks/*week* for men; >7 for women)** - – – – ***30th***
- For most, drinking decreases in 20s, though this is the time alcohol use disorder normally starts to develop

Nebraska DHHS. *Division of Behavioral Health*. 2021.

# HARM TO SELF

- Women are generally more sensitive to harmful effects than men
- Excessive alcohol use can damage all organ systems, particularly:
  - **Brain** – Mental illness, **delirium tremens**, **Wernicke-Korsakoff syndrome**
  - **Heart** – High blood pressure, abnormal rhythms
  - **Liver** – Cirrhosis, hepatitis, liver cancer, liver failure
  - **Pancreas** – Pancreatitis
  - **Increased Cancer Risk** – Liver, bowel, colon, mouth and throat cancers
- Lifespan decreased by 10-15 years in those who drink heavily

CDC. *Alcohol & Public Health*. 2022.

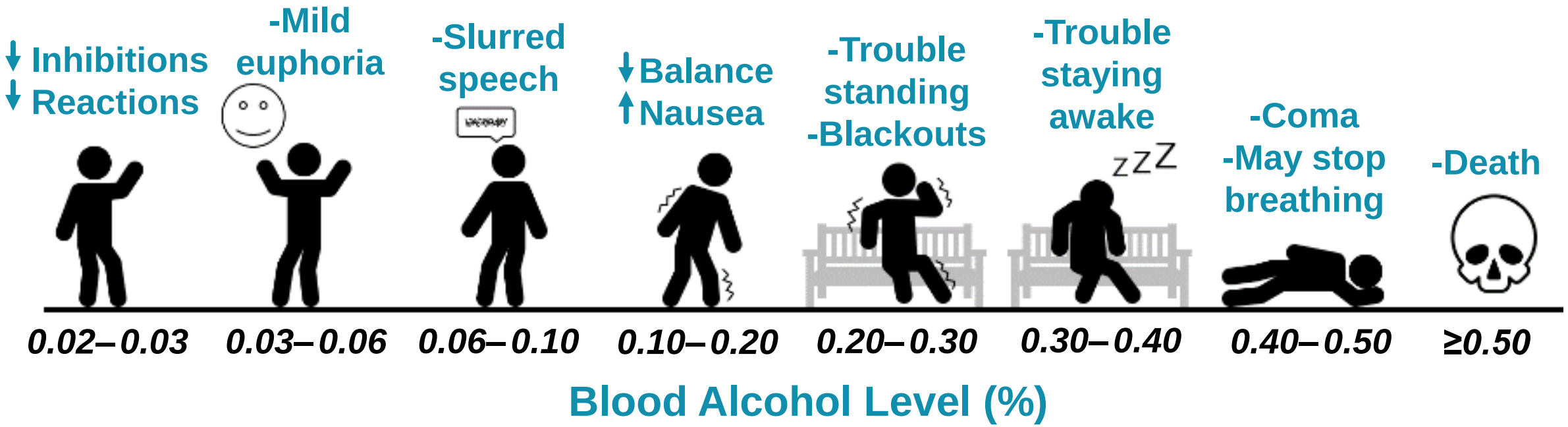
# HARM TO OTHERS/SOCIETY

- Alcohol is unique in that it is the only drug that damages others more than the user
- Societal problems include: *(Nebraska Data for 2020)*
  - Alcohol-attributable deaths – **123 deaths**
  - Alcohol-related car crashes – **1,534 crashes** and **72 fatalities**
  - Domestic abuse/violence
  - Healthcare expenses – **130 million dollars/year**
  - Lost workplace productivity – **865 million dollars/year**

Nebraska DHHS. *Division of Behavioral Health*. 2021.

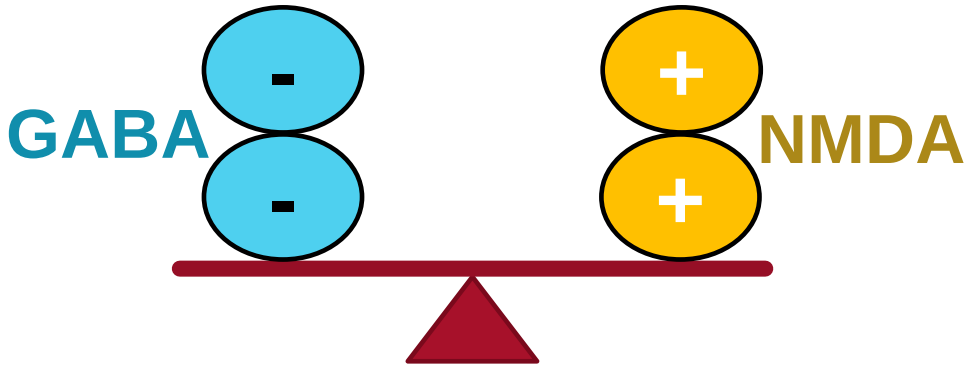
# ALCOHOL INTOXICATION

- Signs and symptoms based on blood alcohol level
  - Reported as a percentage (civilian) or in mg/dL (clinical)
- Metabolism rate is **~1 drink/hour (~20 mg/dL/hour or ~0.02 % / hour)**



# WHAT IS ALCOHOL INTOXICATION

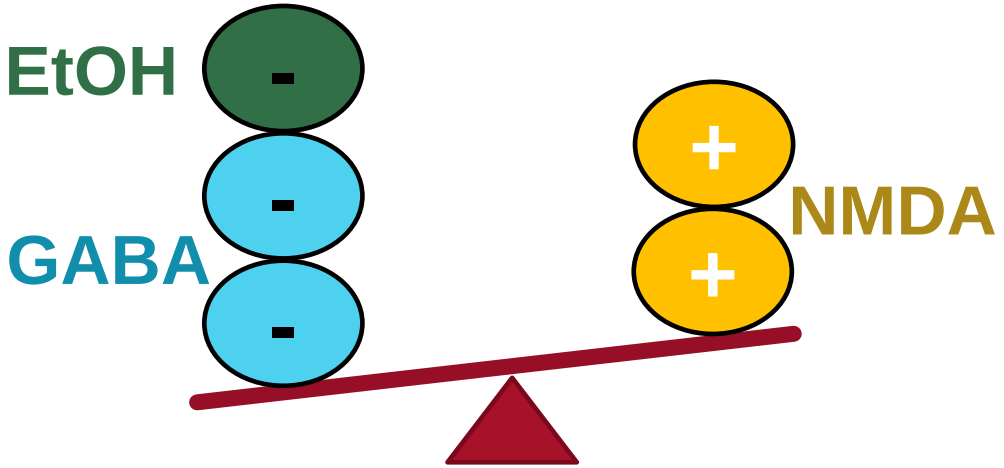
***Inhibitory Side*** ***Excitatory Side***




## Normal Balance in the Brain

- GABA (-) and NMDA (+) are in balance, no symptoms present

***Inhibitory Side*** ***Excitatory Side***

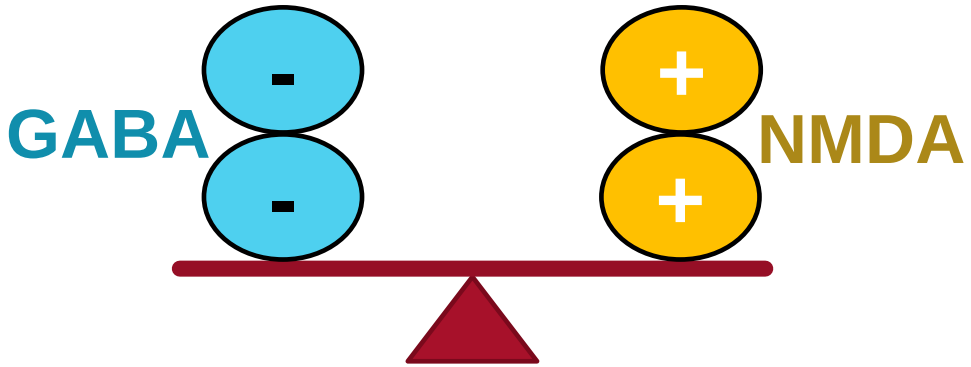



## Mild Intoxicated State

- EtOH (-) use tips balance towards excess inhibition, causing mild intoxication

# WHAT IS ALCOHOL INTOXICATION

***Inhibitory Side*** ***Excitatory Side***

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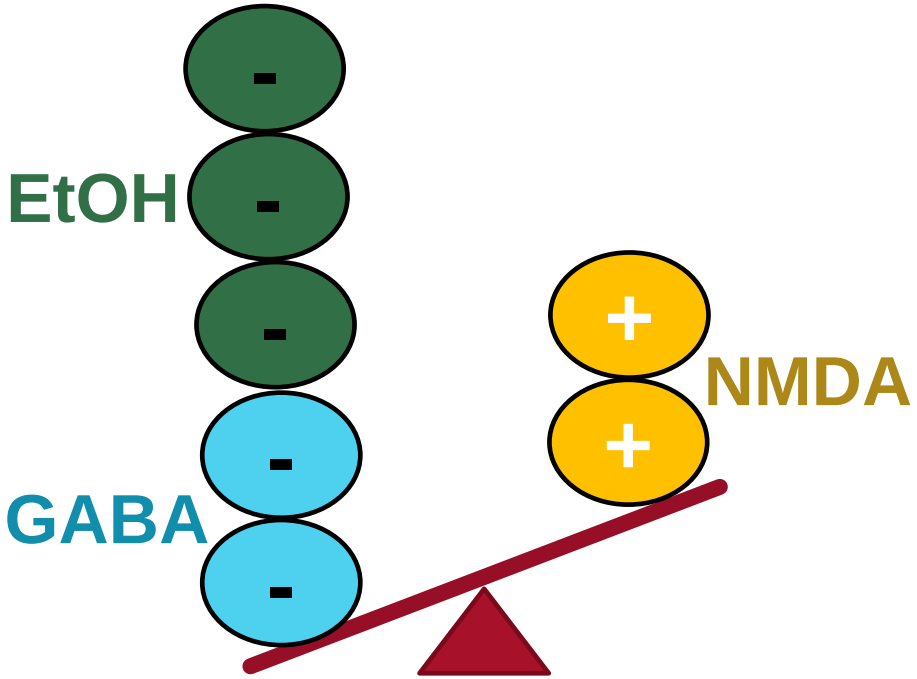


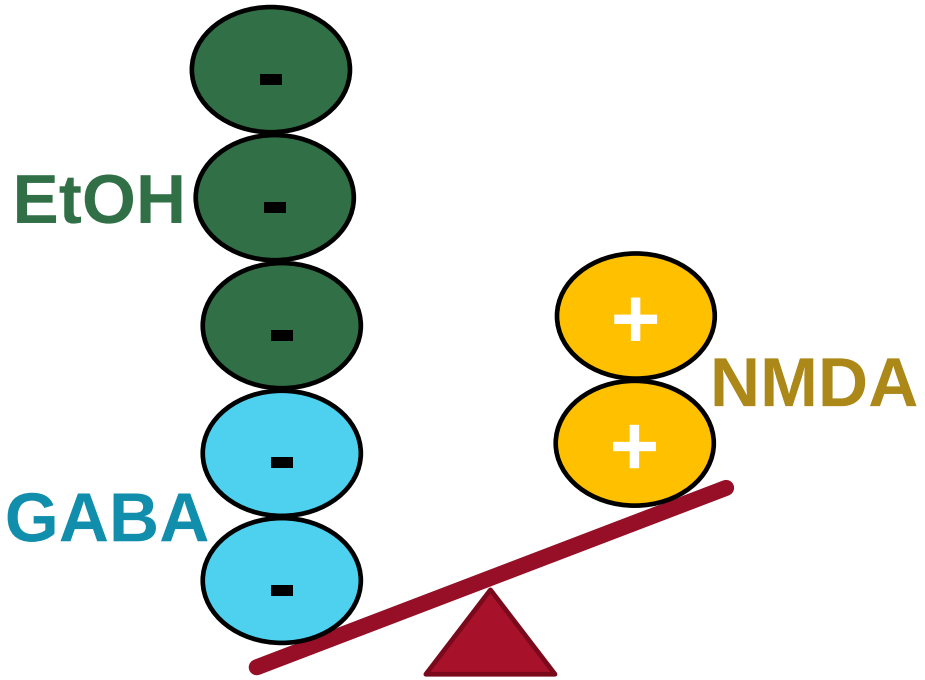

## Severely Intoxicated State

- Large EtOH (-) use swings balance to excess inhibition, causing severe intoxication

# INTOXICATION MANAGEMENT

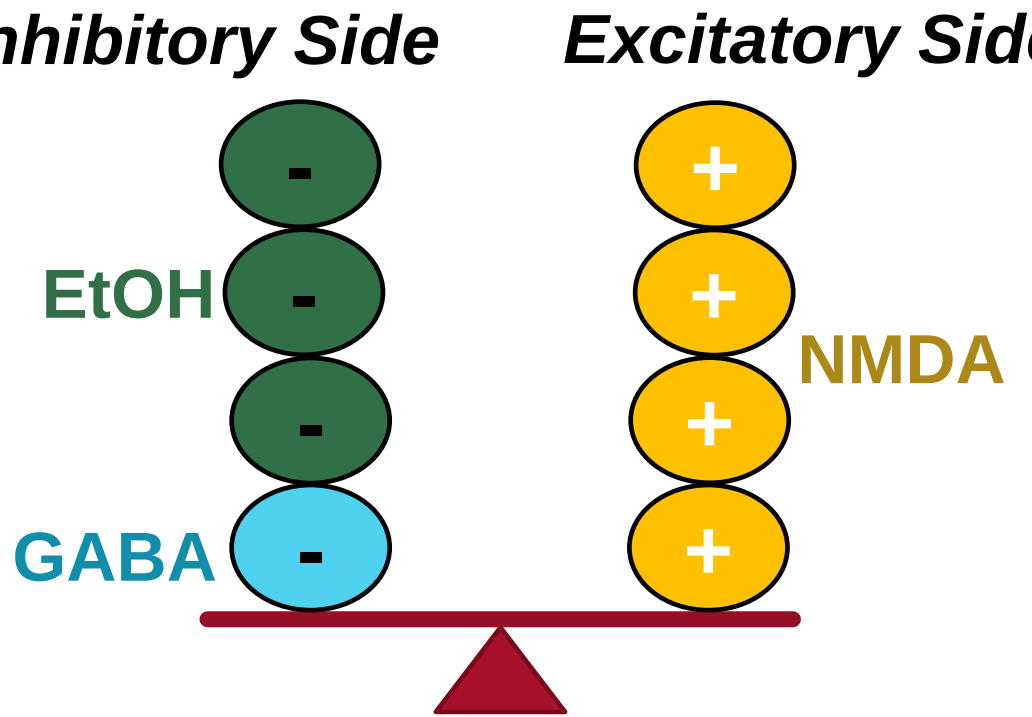
- Patient evaluation, including for history of severe withdrawal symptoms
  - **Seizures**
  - **Delirium tremens** – Shaking, confusion, and/or hallucinations
- Supportive care and symptom management
  - Maintain airway
  - Closely monitor vitals
  - Correct electrolyte abnormalities
  - Manage nausea

# WHAT IS ETOH WITHDRAWAL




## Chronically Unbalanced State

- Chronic EtOH (-) use consistently disrupts balance of inhibition and excitation, forcing the brain to adapt




## Rebalanced Stated

- Decreased amounts of GABA (-)
- Increased amounts of NMDA (+)
- Balanced “fixed”

# WHAT IS ETOH WITHDRAWAL

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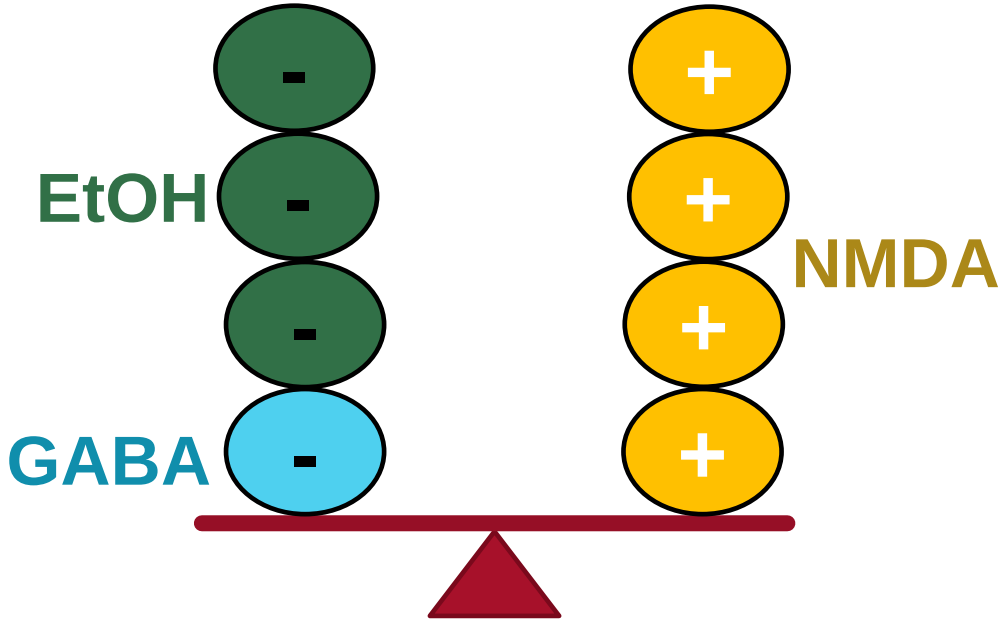


**Rebalanced Stated**

- Decreased amounts of GABA (-)
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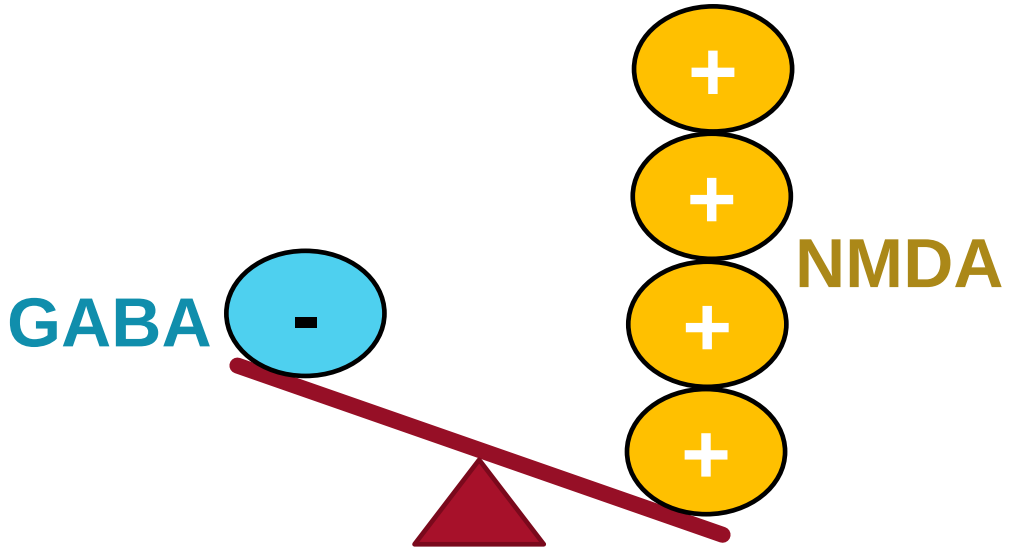
***Inhibitory Side*** ***Excitatory Side***




**Alcohol Withdrawal**

- Absence of EtOH (-) causes unchecked excitation by NMDA (+), causing withdrawal symptoms

# WITHDRAWAL – DIAGNOSTIC CRITERIA

- Cessation of (or reduction in) alcohol use that has been heavy and prolonged with **at least two** of the following:
  - High blood pressure
  - Anxiety/restlessness
  - Shakiness
  - Insomnia
  - Nausea or vomiting
  - Fast heart rate
  - Hallucinations
  - Seizure activity
  - Delirium tremens (DTs)

**Most common**

***Peak withdrawal: 24-36 hours***
***Duration of withdrawal: 3-7 days***

**Relatively rare, but *potentially fatal***

APA. *DSM-V*. 2013.

# WITHDRAWAL – TREATMENT

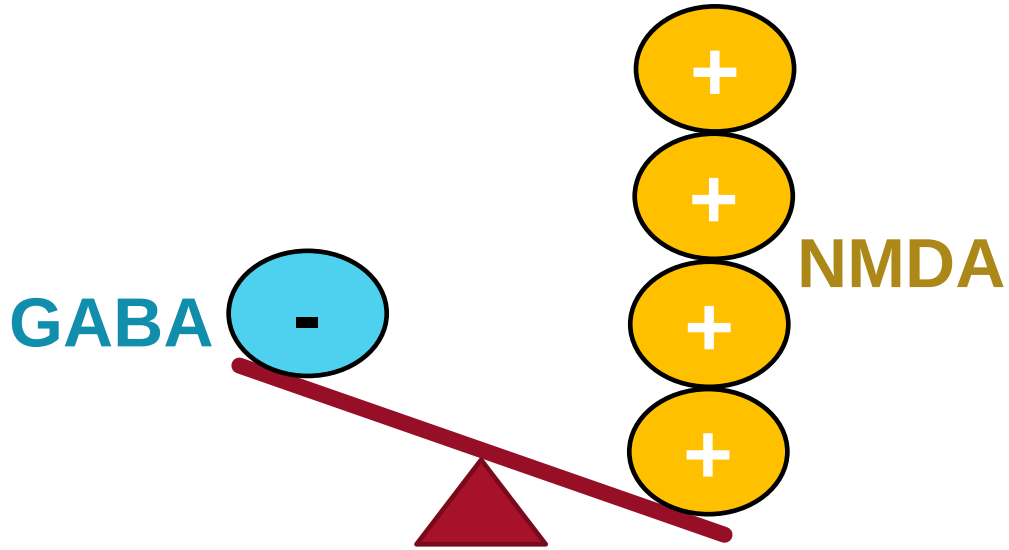
## Benzodiazepines (BZD)

- Used to prevent seizures and progression to delirium tremens
- Most utilized agent: **Lorazepam (Ativan®)**
- Dosing for withdrawal symptoms:
  - **Symptom-triggered** – Dose BZD on current withdrawal symptoms
    - Benzodiazepine administered every 1-2 hours based on score
  - Fixed dose and taper – Typically used with symptom-triggered dosing in patients with heavy alcohol use or history of severe withdrawal symptoms

Amato. *CDSR*. 2011.

# HOW BZDS WORK IN ETOH WITHDRAWAL

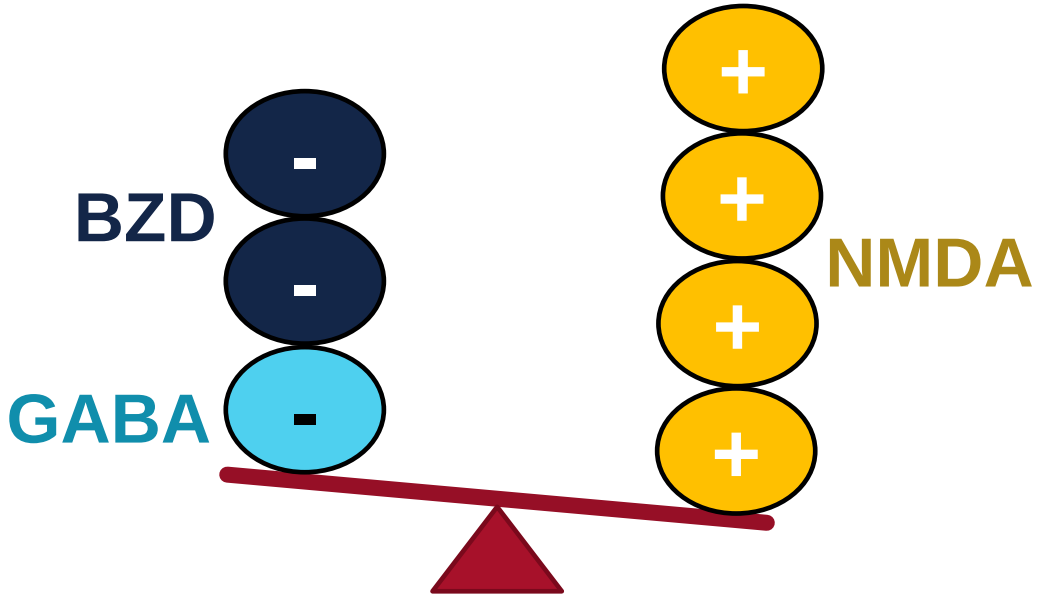
***Inhibitory Side*** ***Excitatory Side***




## Alcohol Withdrawal

- Absence of EtOH (-) causes unchecked excitation by NMDA (+), causing withdrawal symptoms

***Inhibitory Side*** ***Excitatory Side***




## Acceptable Unbalanced State

- Lowers risk of serious withdrawal symptoms
- Slowly taper BZD (-) to allow GABA (-) and NMDA (+) to safely rebalance

# WITHDRAWAL – TREATMENT

**Thiamine (Vitamin B1)**

- Commonly deficient with chronic alcohol use
- Required for glucose metabolism and without it, the brain will starve
- Necessary for prevention/treatment of **Wernicke's encephalopathy**
  - Will progress to **Korsakoff's psychosis** if not properly treated

**Supportive Care** – Manage other withdrawal symptoms as needed

- Manage dehydration with oral or intravenous fluids
- Manage anxiety, insomnia, headache, and nausea with medications

Day. *CDSR*. 2013.

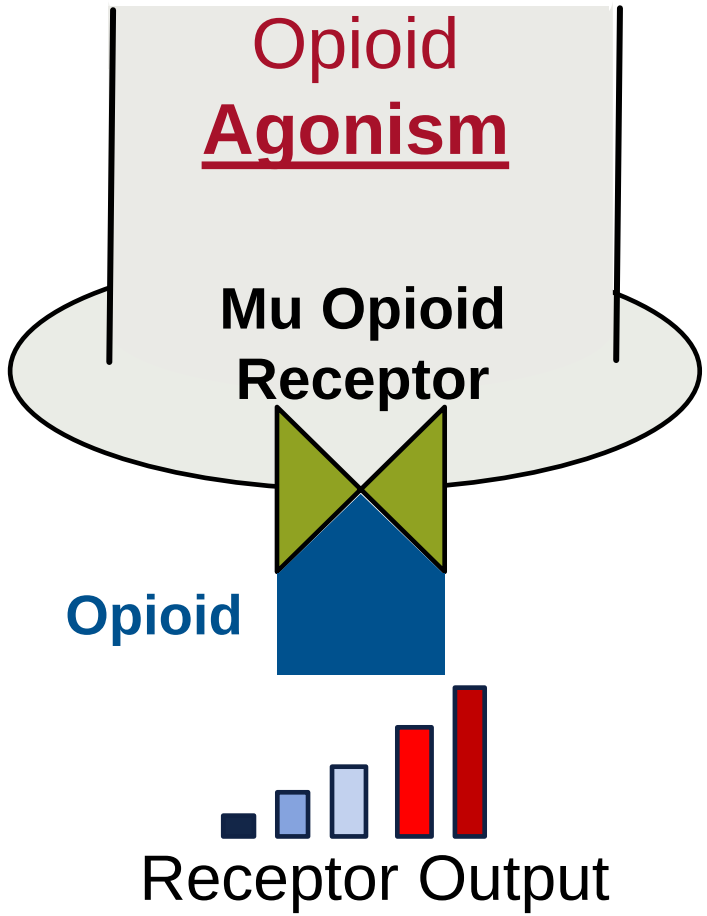
# MAINTENANCE TREATMENT FOR AUD

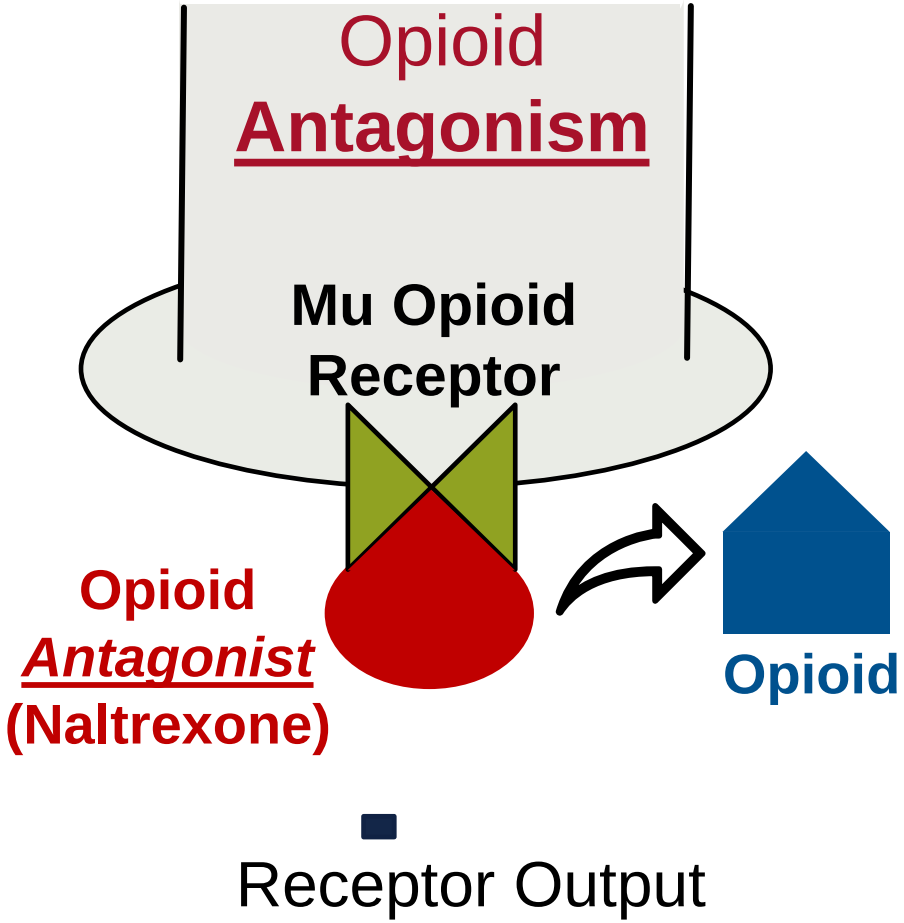
# NALTREXONE

- **Brand name:** Revia® (tablets); Vivitrol® (long-acting injection)
- **How it works:** Mu opioid receptor antagonist
- **Benefits:** Reduces alcohol cravings and reduce pleasure of drinking
- **Place in therapy:** Treatment of choice for alcohol use disorder
- **Dosing:**
  - 50 mg by mouth *daily* after patient is opioid-free for 10-14 days
  - 380 mg intramuscular *monthly* after patient is opioid-free for 10-14 days

Vivitrol®. *Package Insert*. 2010.

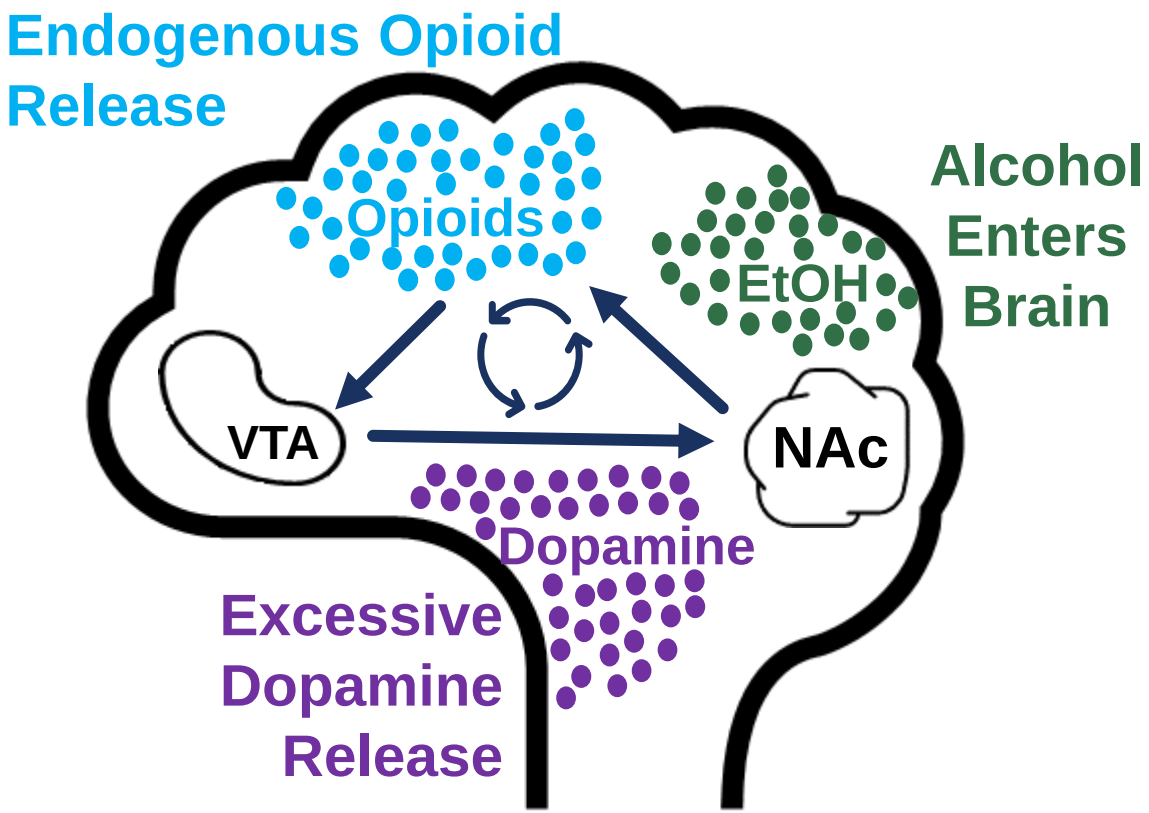
# OPIOID RECEPTOR ANTAGONISM



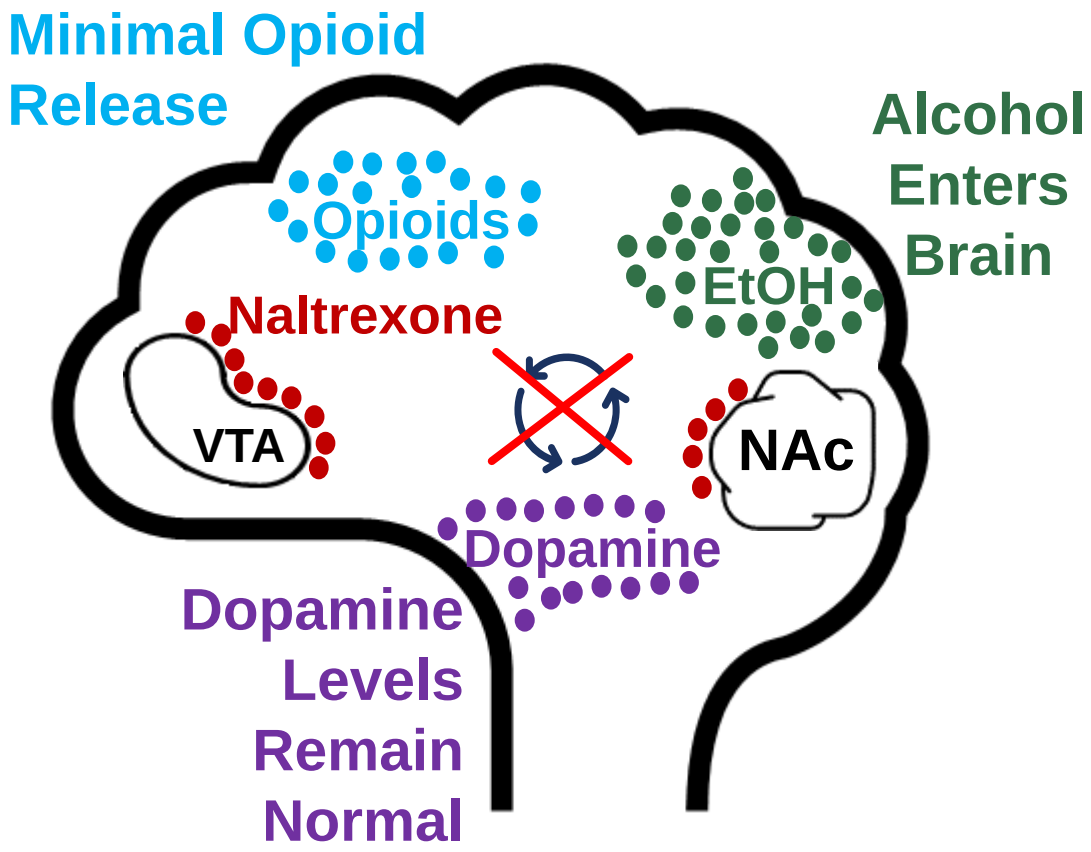



# HOW NALTREXONE WORKS IN AUD

## Alcohol Misuse *without* Naltrexone




## Alcohol Misuse *with* Naltrexone



# NALTREXONE

- **Side effects:**
  - Nausea, vomiting, and diarrhea
    - Mostly only early in therapy and will resolve over the first few weeks
  - **Liver damage** – Monitor liver function at baseline, then periodically afterwards or if signs of liver dysfunction become apparent
  - *Monthly IM Injection Only* – **Serious injection site reactions** may occur
- **Do not recommend naltrexone if the patient:**
  - Is a "current" opioid user (use within the past 10-14 days)
  - Has acute hepatitis and/or serious liver dysfunction

Vivitrol®. *Package Insert*. 2010.

# NALTREXONE

- **Patient education:**
  - Carry wallet card or other identification to signal use of naltrexone
  - Do not use any opioids while taking this medication
  - Observe for signs of liver damage:
    - Yellowing of the skin and whites of the eyes
    - Dark-colored urine
    - Fatigue



Vivitrol®. *Package Insert*. 2010.

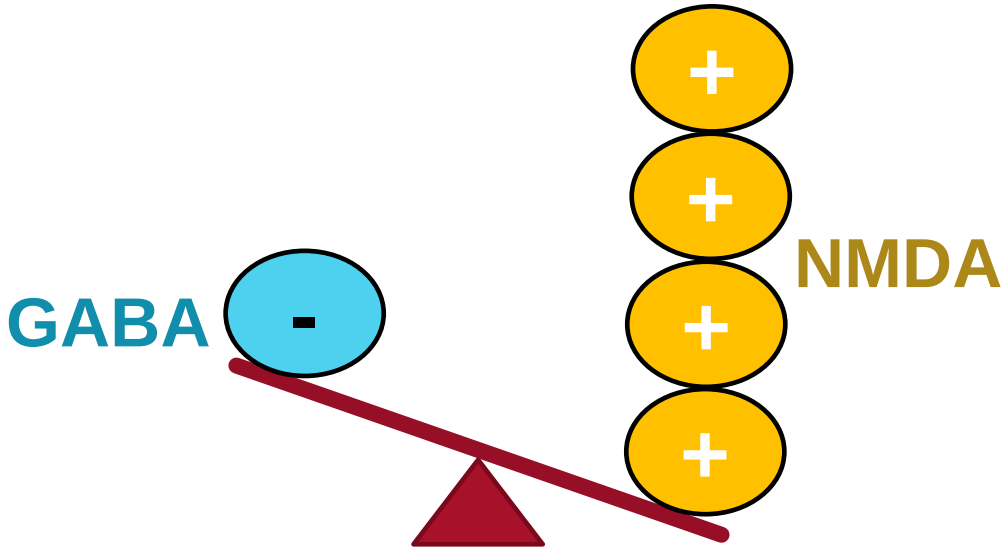
# ACAMPROSATE

- **Brand name:** Campral®
- **How it works:** NMDA receptor antagonist with GABA activation
- **Benefits:** Increases number of days without alcohol and likelihood of not drinking at all
- **Limitations:** Likely does not reduce cravings
- **Place in therapy:** Those unable to take naltrexone
- **Dosing:** 666 mg by mouth three times daily (6 tablets daily)
  - Poor Kidney Function: 333 mg by mouth three times daily

Campral®. *Package Insert*. 2005.

# HOW ACAMPROSATE WORKS IN AUD

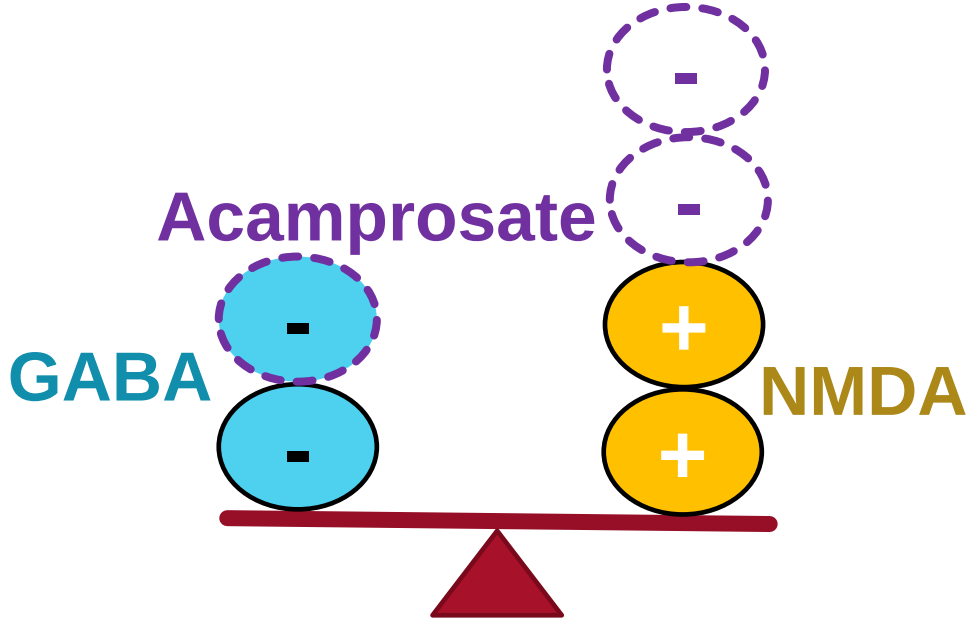
***Inhibitory Side*** ***Excitatory Side***




## Alcohol Withdrawal

- Absence of EtOH (-) causes unchecked excitation by NMDA (+), causing withdrawal symptoms

***Inhibitory Side*** ***Excitatory Side***




## Treatment with Acamprosate

- Acamprosate *slowly* blocks some NMDA (+)
- Acamprosate *slowly* increases GABA (-)
- Balance is *slowly* restored

# ACAMPROSATE

- **Side effects:**
  - Nausea and diarrhea
  - Insomnia, anxiety, and **depression with or without suicidal ideation**
- **Do not recommend acamprosate if the patient:**
  - Has significant kidney dysfunction
  - Has active suicidal ideation
- **Patient education:**
  - Emphasize importance of taking all three doses each day for maximum benefit
  - What the patient should do if suicidal ideation occurs:
    - Call 988; call 911; present to the nearest emergency department

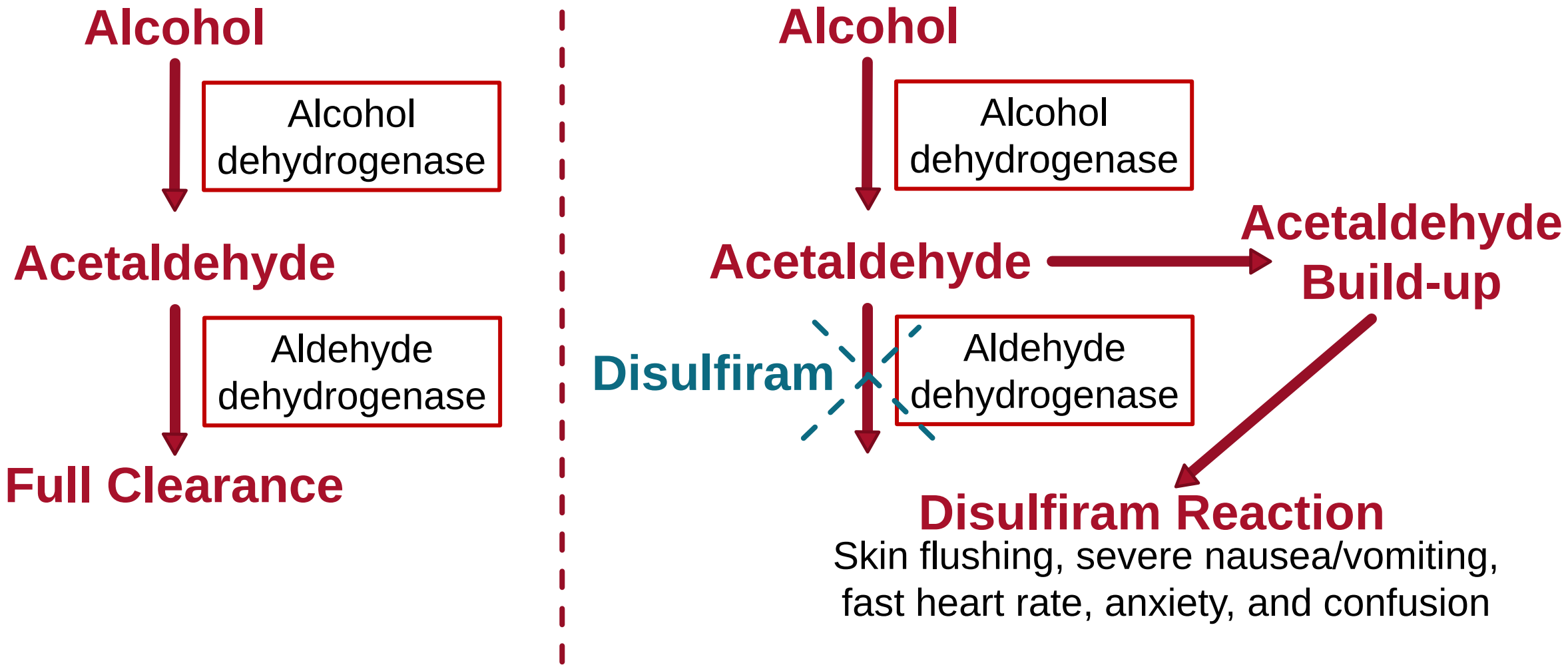
Campral®. *Package Insert*. 2005.

# DISULFIRAM

- **Brand name:** Antabuse®
- **How it works:** Irreversible inhibition of aldehyde dehydrogenase, resulting in acetaldehyde build-up (**disulfiram reaction**) when alcohol is used
- **Limitations:** Doesn't decrease cravings and must be taken semi-regularly
- **Place in therapy:** Increase motivation among abstinent individuals
- **Dosing:** 500 mg by mouth daily for 1-2 weeks, then 250 mg daily
  - Do not take first done until at least 12 hours after their last drink of alcohol

Antabuse®. *Package Insert*. 2012.

# HOW DISULFIRAM WORKS IN AUD



# DISULFIRAM

- **Side effects:**
  - Garlic-like or metallic aftertaste
  - **Liver damage** – Monitor liver function at baseline, then periodically afterwards or if signs of liver dysfunction become apparent
- **Do not recommend disulfiram if the patient:**
  - Is currently using metronidazole – May cause excess aldehyde formation
    - May cause nervous system toxicity, hallucinations, and/or seizures
  - Has significant kidney or liver dysfunction
  - Has history of heart attack, heart failure, or abnormal heart rhythms

Antabuse®. *Package Insert*. 2012.

# DISULFIRAM

- **Patient education:**
  - Avoid ***all*** alcohol-containing products, including:
    - Certain food products such as vinegars and kombucha
    - Certain medicines such as cough, cold, and flu products
    - Certain muscle rubs and/or fragrances
  - May take up to 14 days for enzyme activity to return to normal
    - Clinically, most patients can tolerate some alcohol within 3-5 days
  - Alert all personal physicians and pharmacists that disulfiram was started to avoid potential unintended disulfiram reactions

Antabuse®. *Package Insert*. 2012.

# PSYCHOSOCIAL INTERVENTIONS

- Psychosocial therapy
- Self-help groups and 12-step programs
- Cognitive behavioral therapy (CBT)
- Motivational enhancement therapy
- Contingency management
- Cue exposure and relaxation training
- Group or family therapy

Anton. *JAMA*. 2006.

# OPIOIDS

# OPIOID USE/MISUSE IN NEBRASKA

**U.S. Average**

- **48** opioids prescribed per every 100 Nebraska citizens – – – – – – – – ***46.8***
- **2.9%** of the Nebraska adults (≥18 years) report prescription pain reliever misuse in the past year – – – – – ***3.4%***

**U.S. Total**

- **214** Nebraskans died by overdose in 2020 – – – – – – – – – – – – – – – ***91,375***
- For many, opioid misuse begins as appropriate prescription use, but slowly develops into misuse overtime
- Disorder typically follows chronic, relapsing pattern with periods of partial or complete remission

Nebraska DHHS. *Division of Behavioral Health*. 2021.

# HARM TO SELF

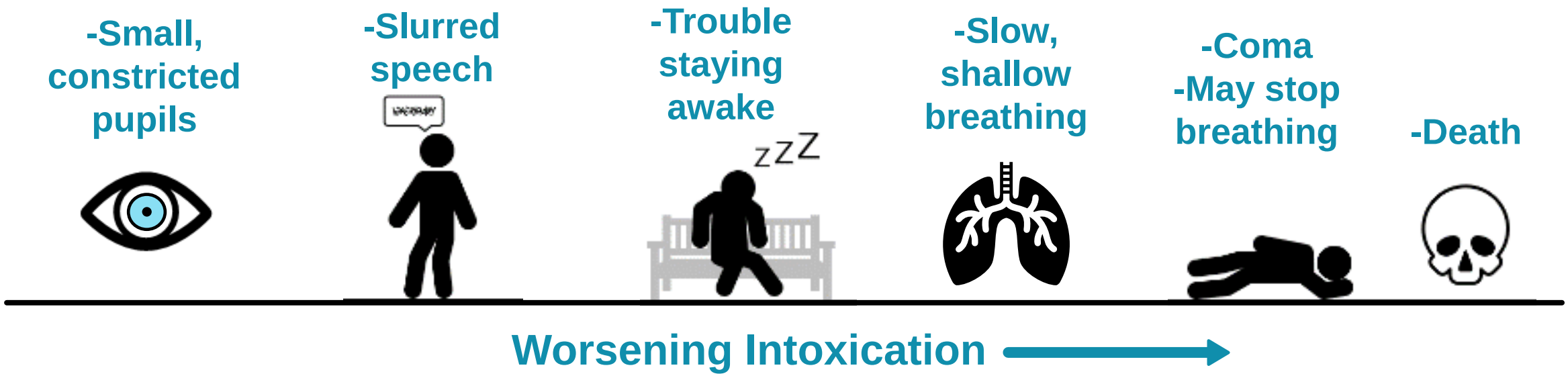
- High doses of opioids (or small doses of high-potency agents) may cause slowed breathing, respiratory failure, and/or death
- Long-term misuse associated with dependence, complications with needle sharing, and increased risk of death by overdose
    - Mortality rate 13x higher than non-opioid users
    - Estimated 800,000+ deaths from drug overdoses since 1999


***2 mg of fentanyl, a lethal dose in most people***

SAMHSA. 2018.

# OPIOID INTOXICATION

- Signs and symptoms based on:
  - Dose of opioid administered
  - Potency of opioid administered
  - Whether other depressants (benzodiazepines, alcohol) are co-ingested



# INTOXICATION/OVERDOSE – TREATMENT

- Patient evaluation including misused agent(s) and estimate of daily use, route of administration, and other substance(s) being used
- Supportive care and symptom management
  - Maintain airway
  - Closely monitor vitals
- **Strong recommendation to consider opioid reversal with the opioid antagonist naloxone (Narcan®)**

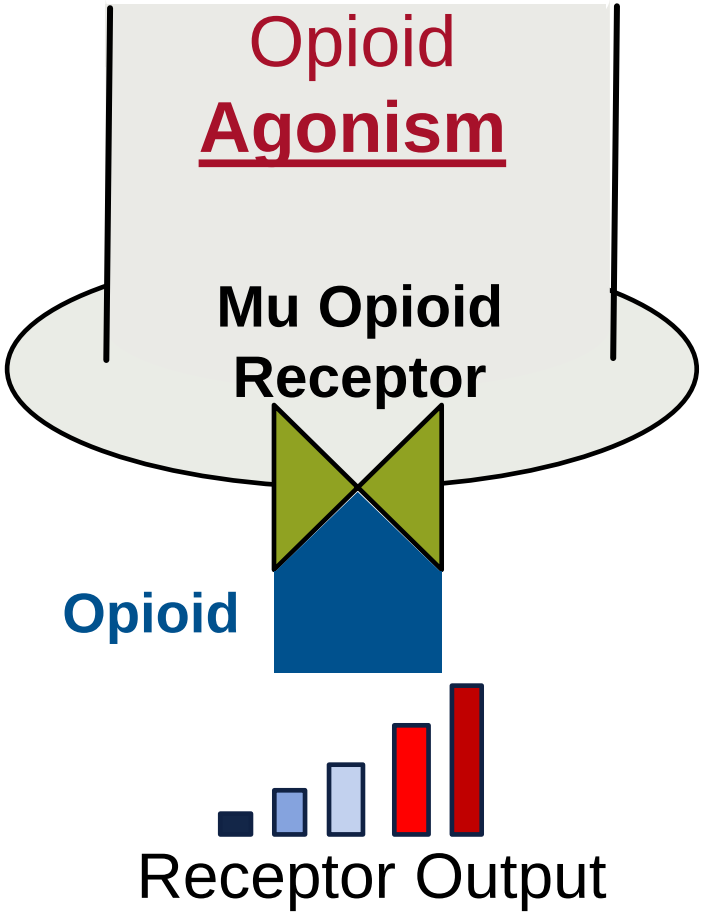
Hawk. *Yale J Biol Med.* 2015.

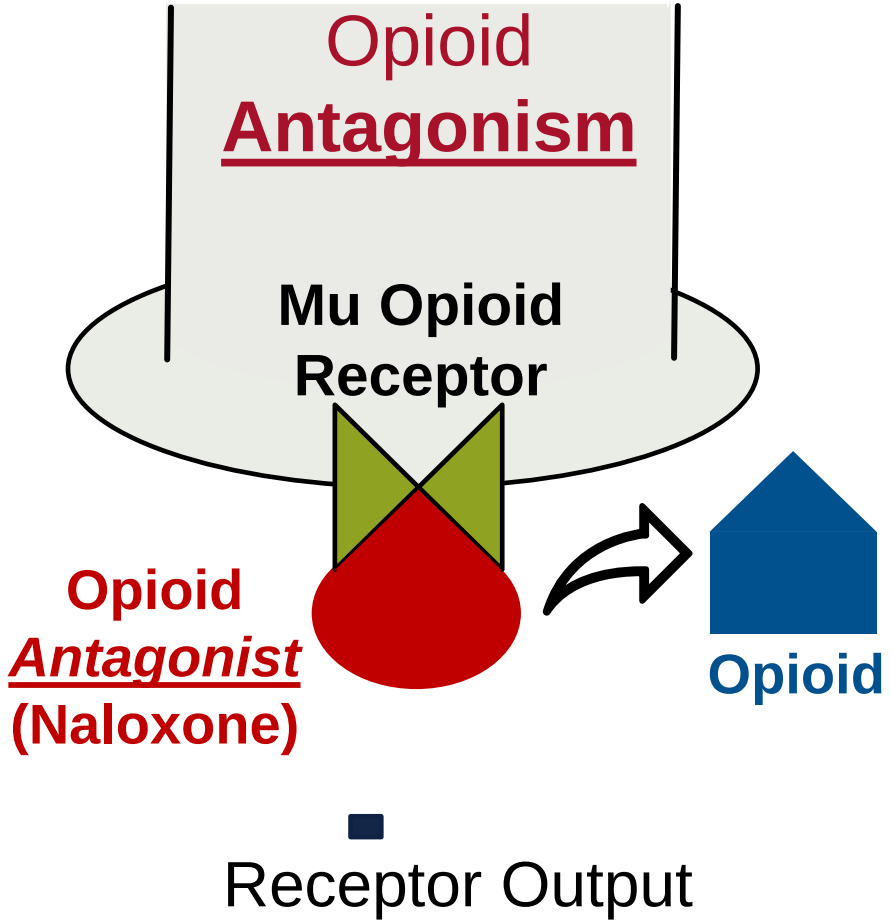
# INTOXICATION/OVERDOSE – NALOXONE

- **Brand name:** Narcan®
- **Routes of administration:** Intramuscular, intravenous, intranasal
- **Mechanism of action:** Opioid receptor antagonist
- **Dose:** 0.4-2 mg IM/IV/IN every 2-3 minutes until patient is breathing
  - Max dose of 10 mg per resuscitation event
- **Onset of action:** Within minutes
- **Duration of effect:** Depends on route of administration and dose
  - May need to re-administer as original dose wears off
  - Particularly severe cases may require continuous naloxone infusion

Hawk. *Yale J Biol Med.* 2015.

# HOW NALOXONE WORKS IN OVERDOSES



# INTOXICATION/OVERDOSE – NALOXONE

- **Side effects:** Abrupt reversal of opioid intoxication may result in sudden cardiac or respiratory adverse events
- **Monitoring:** Closely monitor blood pressure, pulse, and breathing rate
- **Patient education:** Patient, family, and/or friends should be educated on when and how to use rescue kits, including:
  - **Identifying signs of an opioid overdose**
  - **Calling 911, regardless of whether naloxone works or not**
  - **Stay with the person at least until EMS arrives**

Hawk. *Yale J Biol Med.* 2015.

# WITHDRAWAL – SYMPTOMS AND MANAGEMENT

- Cessation of (or reduction in) heavy, prolonged opioid use with **at least two** of the following:
  - General discomfort or unease
  - Nausea, vomiting, and/or diarrhea
  - Muscle aches/pains
  - Watery eyes
  - "Goosebumps"
  - Sweating
  - Fever
  - Inability to sleep

***May be extremely uncomfortable, but is not deadly***

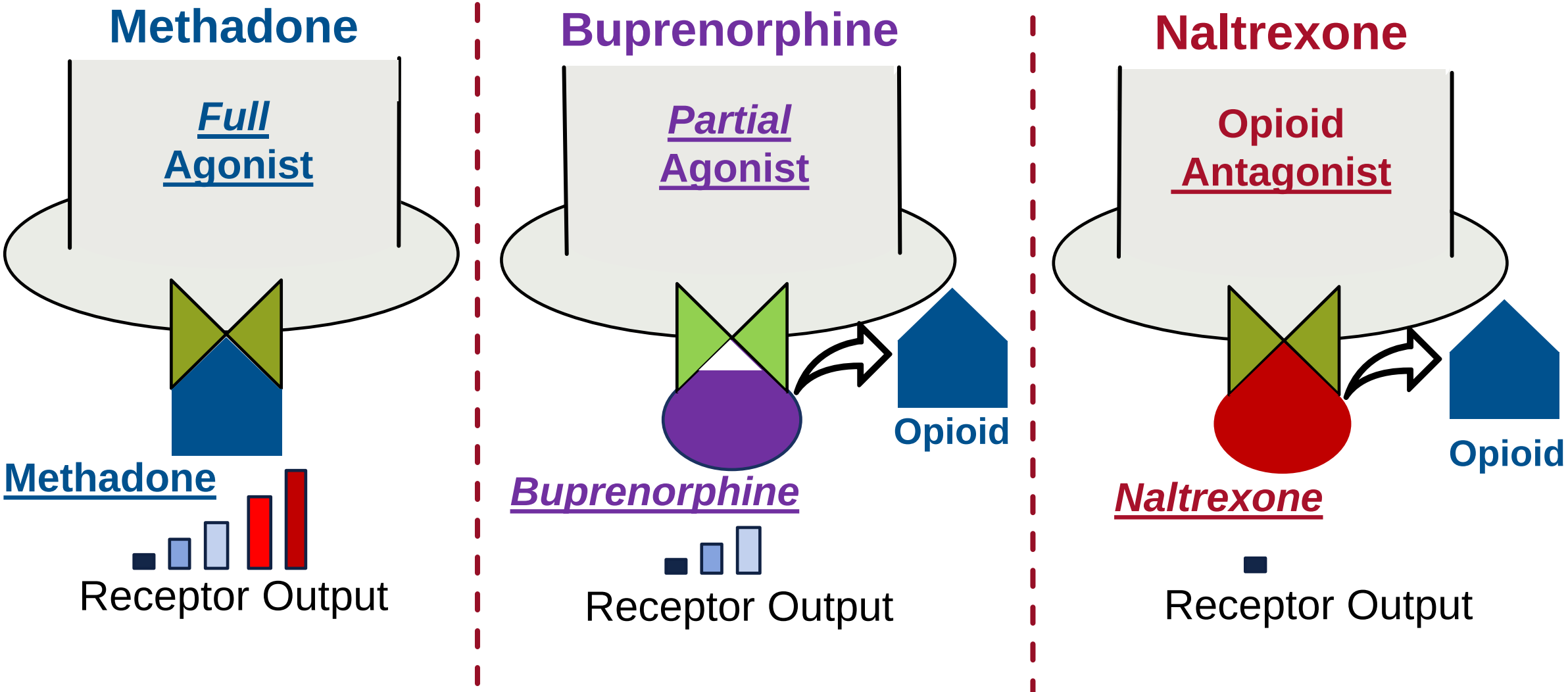
***Peak withdrawal: 36-72 hours***
***Duration of withdrawal: 5-8 days***

**Management – Treat bothersome symptoms as they emerge, start maintenance treatment ASAP**

APA. *DSM-V*. 2013.

# MAINTENANCE TREATMENT FOR OUD

# MEDICATIONS FOR OPIOID USE DISORDER



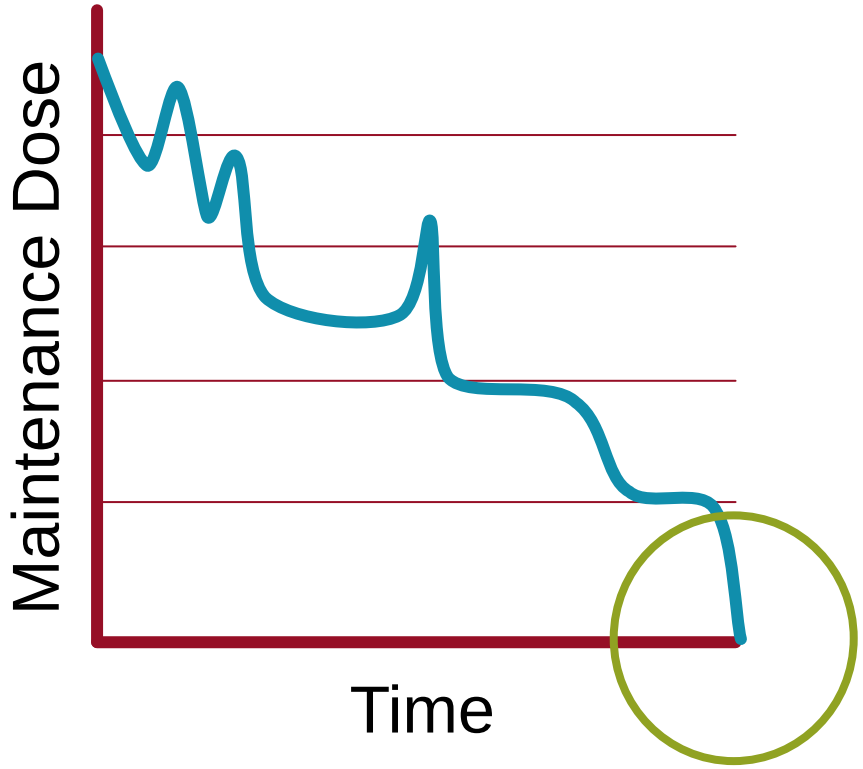
# BENEFITS OF MEDICATIONS FOR OUD

- **Effects on OUD:**
  - Withdrawal symptoms (including cravings) are reduced or eliminated
  - Effects of illicit opioid usage are blunted or blocked completely
- **Effects on general health, lowering risk of:**
  - Death by overdose
  - Injection complications and bloodborne infections (HIV, hepatitis C)
- **Effects on other aspects of life:**
  - Criminal behavior is reduced
  - Employment rates for people undergoing OUD treatment are improved

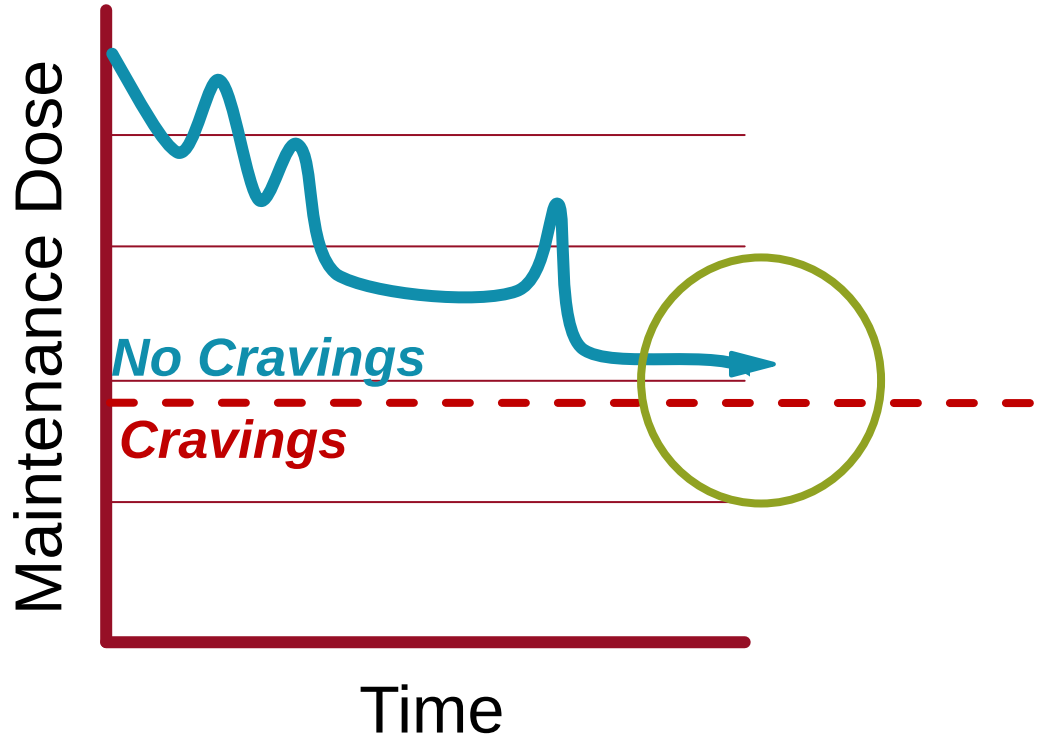
SAMHSA. *Treatment Improvement Protocol*. 2018.

# GOAL OF MAINTENANCE TREATMENT

**Commonly Perceived Goal of OUD Maintenance Treatment:**




**Actual Goal of OUD Maintenance Treatment:**



# METHADONE

- **DEA Schedule:** C-II
- **How it works:** ***Full*** opioid receptor agonist
- **Benefits:** Prevents withdrawal symptoms and reduces opioid cravings as the receptor is being ***fully*** activated by an opioid
  - Most effective medication for retaining patients in treatment long-term
- **Onset:** Relief of withdrawal symptoms within an hour
- **Duration of effect:** 24 to 36 hours
- **OUD Dosing:** Methadone for OUD must be provided at an Opioid Treatment Program (OTP) – a.k.a. “methadone clinics”

Bruneau. *CMAJ*. 2018.

# OPIOID TREATMENT PROGRAMS (OTP)

- Regulated by Substance Abuse and Mental Health Services Administration (SAMHSA)
- Required to provide medical, counseling, and educational services
- Methadone for OUD can only be used in OTPs, but not all OTPs offer it
  - Not all OTPs offer other OUD medications (buprenorphine, naltrexone)
- **Eligible Patients:** 18 years and older with OUD for at least one year
  - Younger patients may participate with two previous failed withdrawal attempts
  - High risk patients do not need to meet one year threshold:
    - **Pregnancy**; **former OTP patients**; **recent release from incarceration**

Bruneau. *CMAJ*. 2018.

# OTP METHADONE ADMINISTRATION

## Early OTP Treatment:

- Daily observed administration of methadone
  - Typically provided as a once daily dose of liquid concentrate
- Goal is to improve withdrawal symptoms while avoiding sedation

## Ongoing OTP Treatment:

- Take home doses can be earned based on duration of treatment and other aspects (regular clinic attendance, behavior in clinic, etc.)
- Goal is to maintain sobriety from illicit opioids and control cravings

Bruneau. *CMAJ*. 2018.

# METHADONE

- **Do not recommend methadone if the patient:**
  - Has acute asthma and/or severe pulmonary disease
  - Has bowel obstruction and/or bowel paralysis
- **Potentially fatal side effects:**
  - **Respiratory depression (slow, shallow breathing)** – Highest risk early in treatment or following dose increases
    - Concurrent use of alcohol or benzodiazepines can increase risk of death. **Treatment should not be withheld because of ongoing use**
  - **QTc prolongation (changes in heart rhythm)** – Regularly assess for factors or other medications that may increase risk. **Overall risk is rare (~2%)**

Bruneau. *CMAJ*. 2018.

# METHADONE

- **Monitoring:** Regularly monitor vitals and urine drug screens
  - Consider getting an EKG before starting methadone
- **Duration of therapy:** Ideally, at least one year, but may be continued as long as the patient is receiving benefit from methadone
- **Patient education:**
  - Report changes in bowel habits or breathing rate to prescriber
  - Alert all personal physicians and pharmacists that methadone was started to avoid the many interactions with other medications

Bruneau. *CMAJ*. 2018.

# BUPRENORPHINE

- **DEA Schedule:** C-III
- **Brand name: Subutex® (alone); Suboxone® (with naloxone)**
- **How it works:**
  - **Buprenorphine** – ***Partial*** mu opioid agonist
    - Limit or "ceiling" to effects. Once reached, increasing dose will do little
  - **Naloxone** – Full opioid antagonist
- **Benefits:** Prevents withdrawal symptoms and reduces cravings as the receptor is being agonized, at least ***partially***
- **Limitations:** Effect ceiling may be lower than amount needed for cravings

Bruneau. *CMAJ*. 2018.

# BUPRENORPHINE REGULATIONS

- **Pre-2023 Prescribing:**
  - Required special waiver **(X-Waiver)** to prescribe buprenorphine
  - Strict limits on number of patients each prescriber could prescribe buprenorphine to
- **January 2023 Update (Consolidation Appropriations Act):**
  - Eliminated the requirement for an X-Waiver to prescribe buprenorphine
    - Can now be prescribed with a standard DEA license
  - Eliminated all limitations on number of buprenorphine patients allowed
  - New training requirements to go into effect **June 21, 2023**

# BUPRENORPHINE

- **Acquiring medication:** Can be filled at most pharmacies
- **Administration:** Tablets/films absorbed under the tongue or in the cheek
- **Onset:** Relief of withdrawal symptoms within an hour
- **Combination product (preferred):**
  - Naloxone serves as a deterrent to misuse
- **Buprenorphine-only product:**
  - Higher potential for misuse or diversion given higher street value
  - Generally cheaper for patients than the combination product
  - May be preferred in pregnant patients

Bruneau. *CMAJ*. 2018.

# POTENTIAL FOR BUPRENORPHINE MISUSE

- General misuse potential is less than with full opioid agonists
- Diversion is a concern (especially with buprenorphine-only product)
  - Injecting buprenorphine-only product can give effects close to regular opioids
  - Injecting combination-product can precipitate opioid withdrawal
- Most diversion is related to:
  - Preventing withdrawal when unable to acquire opioids
  - Self-treatment of OUD when no legal treatment options are available

Bruneau. *CMAJ*. 2018.

# BUPRENORPHINE

- **Treatment considerations:**
  - May precipitate withdrawal symptoms on initiation
  - Considerably lower risk of interaction problems with other medications
- **Potentially fatal side effects (generally lower risk than methadone):**
  - **Respiratory depression (slow, shallow breathing)** – Highest risk early in treatment or following dose increases
    - Concurrent use of alcohol or benzodiazepines can increase risk of death. **Treatment should not be withheld because of ongoing use**
  - **Acute hepatitis (liver damage)**
    - Use buprenorphine-only product in severe liver dysfunction

Bruneau. *CMAJ*. 2018.

# BUPRENORPHINE INDUCTION

- **What is induction?**
  - Switching from a full opioid agonist (hydrocodone, oxycodone, heroin) to buprenorphine
- **How long does induction phase last?**
  - Generally, 1 to 2 weeks
- **What are the goals of buprenorphine induction?**
  - Stop or reduce use of other opioids
  - Block or at least blunt cravings for opioids
  - Mitigate withdrawal symptoms

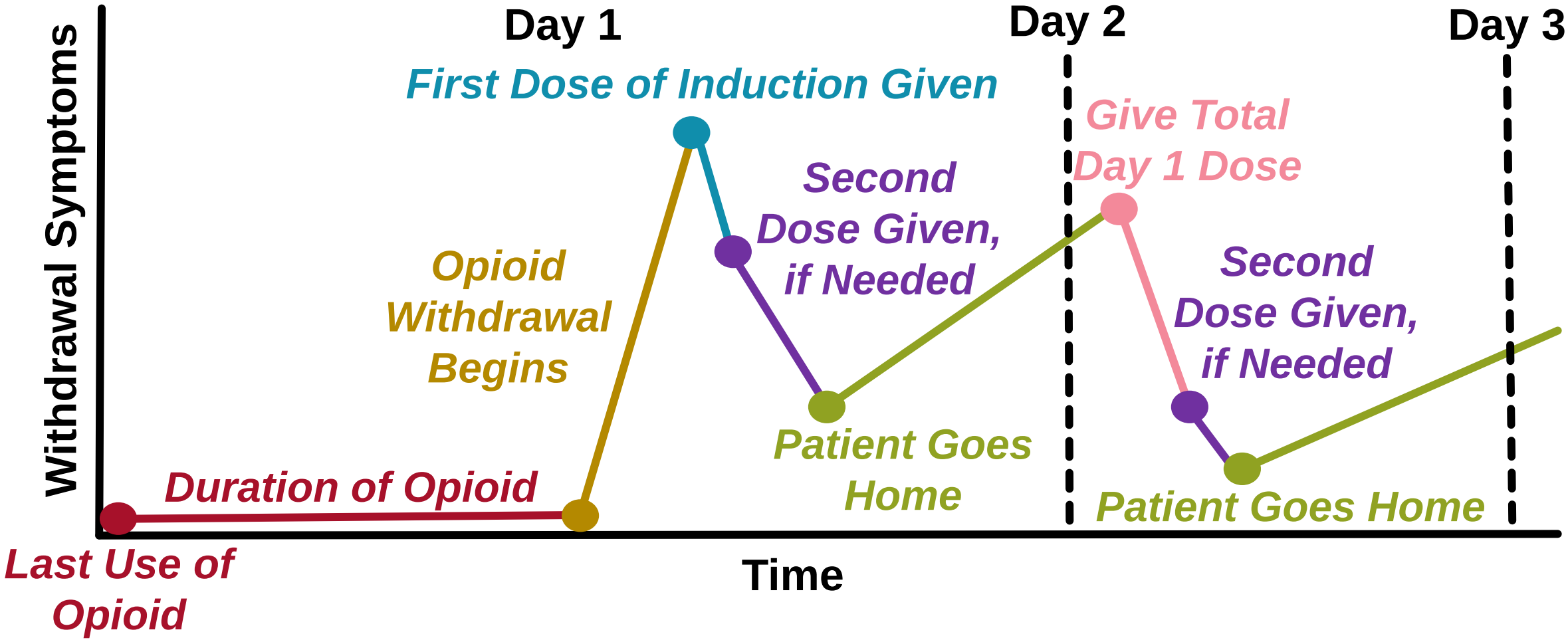
SAMHSA. *Treatment Improvement Protocol*. 2018.

# BUPRENORPHINE INDUCTION

- Buprenorphine will remove opioid agonists from the opioid receptor, rapidly precipitating, potentially severe, opioid withdrawal
- **Therefore, prior to induction, patients must be in mild opioid withdrawal, last dose of:**
  - Short-acting opioids **(heroin, hydrocodone): 12-16 hours ago**
  - Intermediate-acting opioids **(oxycodone): 17-24 hours ago**
  - Long-acting opioids **(methadone, oxycodone ER): 30-48 hours ago**

SAMHSA. *Treatment Improvement Protocol*. 2018.

# BUPRENORPHINE INDUCTION COURSE



# OFFICE- AND HOME-BASED INDUCTIONS

**Office-Based Induction (traditional method):**

- Easier to ensure patient knows when and how to take doses
- Able to confirm mild opioid withdrawal initially to avoid precipitating severe opioid withdrawal

**Home-Based Induction:**

- When patient has prior experience with buprenorphine induction
- Requires patients to appropriately grade withdrawal, understand dosing instructions, and to reach out to provider regarding problems

**Comparison: Both are safe and effective with similar retention rates**

SAMHSA. *Treatment Improvement Protocol*. 2018.

# STABILIZATION AND MAINTENANCE

- **Stabilization Phase:** About 1 to 2 months after induction phase
  - Defined by markedly reduced or eliminated use of illicit opioids
  - Meet about every two weeks to adjust buprenorphine dose as needed

- **Maintenance Phase:** After stabilization phase onwards
  - Meet monthly to slowly lower buprenorphine dose as cravings allow
  - Focus on aspects of recovery

SAMHSA. *Treatment Improvement Protocol*. 2018.

# BUPRENORPHINE

- **Monitoring:** Regularly monitor urine drug screens
  - Monitor liver function at baseline, then periodically afterwards or if signs of liver dysfunction become apparent
- **Duration of therapy:** Ideally, at least one year but may be continued as long as the patient is receiving benefit from buprenorphine
- **Patient education:**
  - Report changes in bowel habits or breathing rate to prescriber
  - Do not swallow the tablet or film
  - Carry wallet card or other identification to signal use of buprenorphine

Bruneau. *CMAJ*. 2018.

# METHADONE VS. BUPRENORPHINE

| Characteristic | Methadone | Buprenorphine |
|---|---|---|
| Ease of access to treatment | | X |
| Lower abuse potential | | X |
| Fewer side effects | | X |
| Cheaper for patient | X | |
| Fewer medication interactions | | X |
| Better in severe dependence | X | |

- **Naltrexone:** Is also indicated for the treatment of opioid-use disorder

# NALTREXONE IN OUD

- **DEA Schedule:** Not a controlled substance
- **Brand name:** Vivitrol® (long-acting injection)
  - Naltrexone tablets are not routinely recommended for OUD
- **How it works:** Mu opioid receptor antagonist
- **Benefits:**
  - No misuse potential, so no restrictions on prescribing or receiving medication
  - Protective against opioid overdose, to a point
- **Dosing:**
  - 380 mg intramuscular *monthly* after patient is opioid-free for 10-14 days

Vivitrol®. *Package Insert*. 2010.

# NALTREXONE IN OUD

- **Limitations:**
  - Significantly lower efficacy on cravings compared to other treatments
  - Will precipitate withdrawal in patients currently utilizing opioids
- **Candidates for naltrexone in OUD:**
  - Patients who do not want to take opioid agonists
  - Patients who are soon to be released from controlled environments
  - Patients in occupations with external monitoring (pilots, healthcare professionals, parolees)
  - Patients with home or job life that makes frequent visits impossible or risky

SAMHSA. *Treatment Improvement Protocol*. 2018.

# STIMULANTS

# BACKGROUND

- Includes amphetamines (prescription and illicit), cocaine, bath salts, and other synthetic stimulants (MDMA, Flakka, DMT)
- Can be used from a variety of methods and routes
- Synthetic stimulants are being increasingly popular as users attempt to avoid detection in drug screens and legal penalties
- First use has potential to rapidly progresses to dependence due to highly addictive nature of these agents
    - Unlike other substances of abuse, stimulants directly release dopamine

# HARM TO SELF

- High doses may cause acute anxiety, agitation/aggression, paranoia, and psychosis
- Intravenous use is associated with the transmission of hepatitis C, HIV/AIDS and medical emergencies such as infection or blood clots
- Long-term use associated with increased blood pressure, coronary artery disease, irregular heart rate, nutritional deficiencies, serious dental problems (“meth-mouth”), and increased risk of Parkinson’s disease

# STIMULANTS INTOXICATION

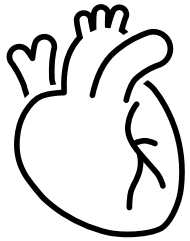
- Signs and symptoms based on:
  - Dose of stimulant administered
  - Type of stimulant administered

↑Energy
↑Motivation
↑Concentration

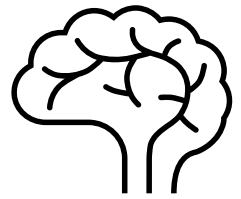
-Euphoria

-Large, dilated pupils

↑Heart rate
↑Blood pressure



-Anxiety, psychosis



Ross. *N Engl J Med*. 2011.

# INTOXICATION/OVERDOSE – TREATMENT

- Patient evaluation including misused agent and estimate of daily use, route of administration, and other substance(s) being used
- **Supportive care**
  - Closely monitor vitals for increasing heart rate, temperature, and blood pressure
  - Provide a quiet and cool environment to help decrease external stimuli
- Benzodiazepines can be used for anxiety and agitation
- Most patients who suffer psychosis during stimulant intoxication recover spontaneously, usually making antipsychotics unnecessary

Ross. *N Engl J Med*. 2011.

# WITHDRAWAL – SIGNS AND SYMPTOMS

- Commonly known as a “crash”
- Cessation of (or reduction in) prolonged stimulant use with **dysphoric mood and at least two** of the following that develop after the last use:
  - Fatigue
  - Vivid, unpleasant dreams
  - Insomnia or hypersomnia
  - Increased desire to eat
  - Psychomotor retardation or agitation

***Uncomfortable, but not deadly***

***Peak withdrawal: 36-72 hours***
***Duration of withdrawal: 7-10 days***

**Management – Treat bothersome symptoms as they emerge**

APA. *DSM-V*. 2013.

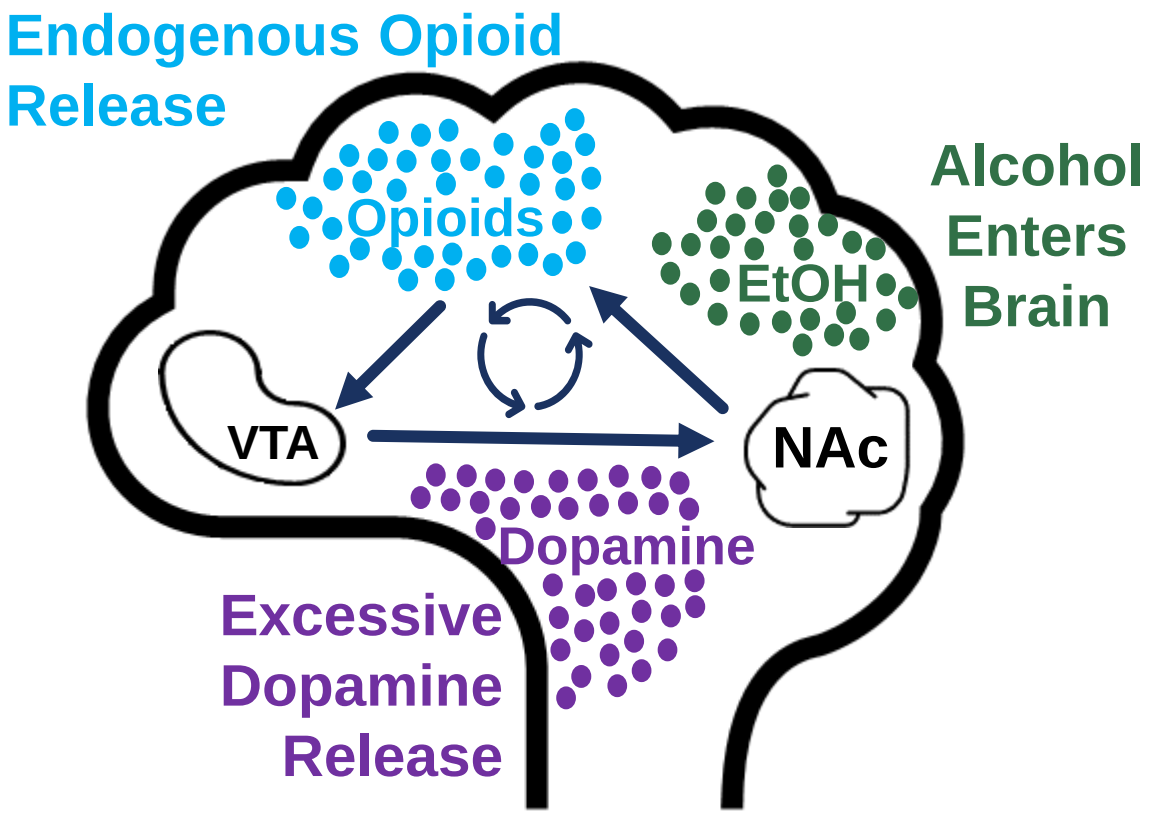
# MAINTENANCE TREATMENT

- Cravings may persist for months after last use
- No current pharmacologic maintenance treatment option exist
  - Some mixed evidence coming out for combination bupropion/naltrexone
- General recommendation is to seek inpatient treatment and utilize other psychosocial approaches
- Correct co-morbid psychiatric conditions to possibly correct *why* the patient is misusing stimulants
- Treat dysphoria/depression with antidepressants

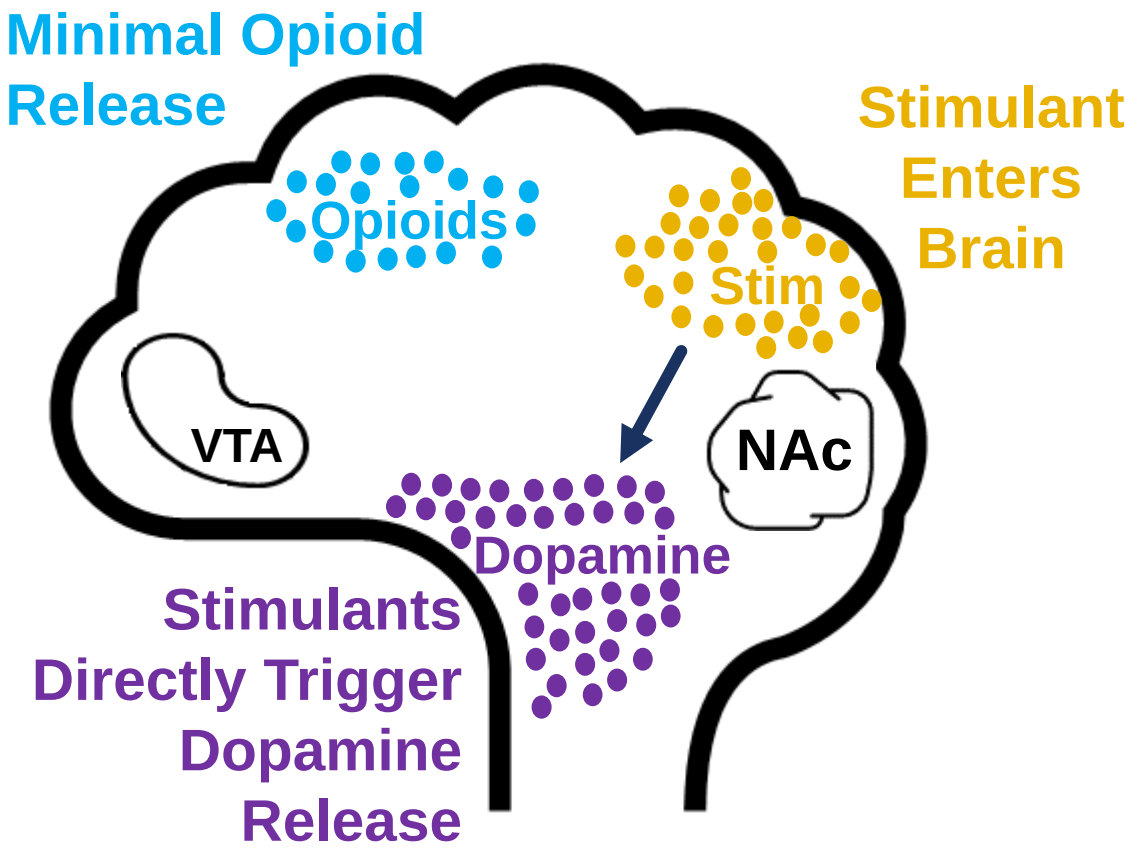
Pérez-Mañá. *CDSR*. 2013.

# TREATMENT DIFFICULTIES WITH STIMULANTS

## Non-stimulants




## Stimulants



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# What questions do you have?

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