Management of Substance Use Disorders in Primary Care: Clinical Application

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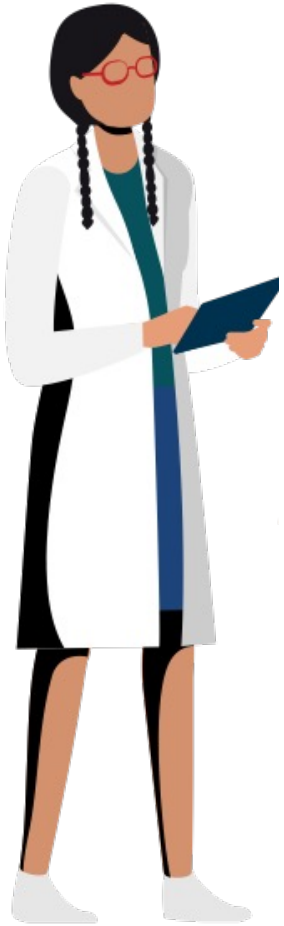
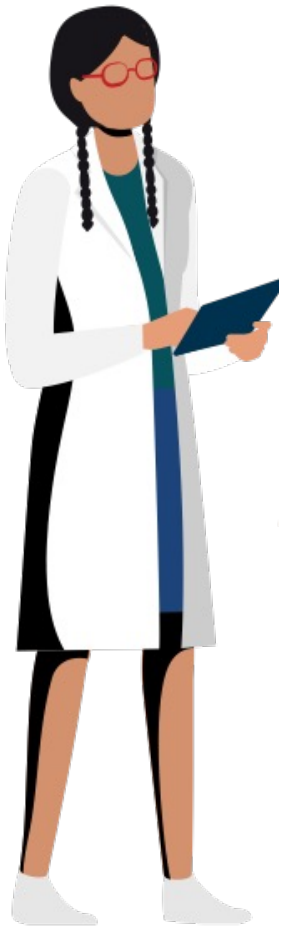
Indian Country ECHO: Ending the Syndemic

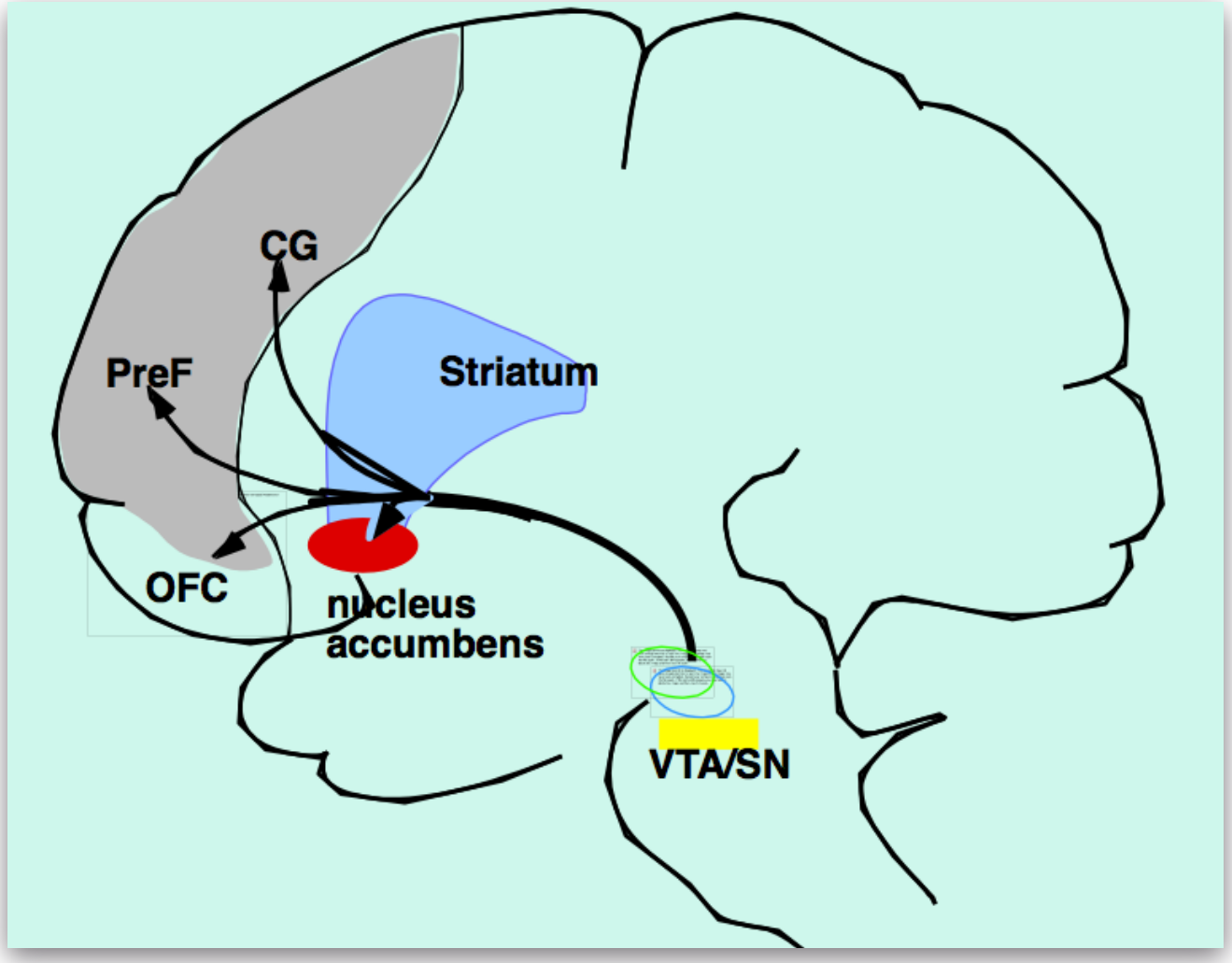
Objectives

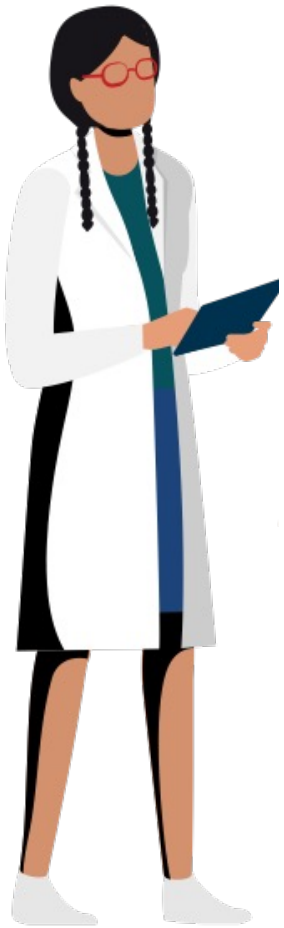


1. **Review the neurobiology of addiction**
2. Use the DSM-5 criteria to diagnose substance use disorders
3. Review office-based medications to treat opioid use disorder
4. Discuss interventions to treat methamphetamine use disorder

Mesolimbic Dopamine System

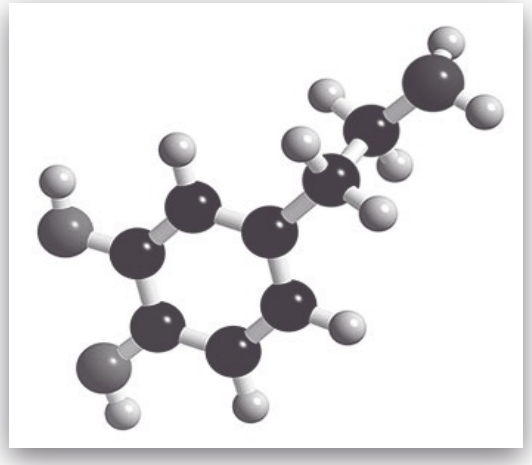




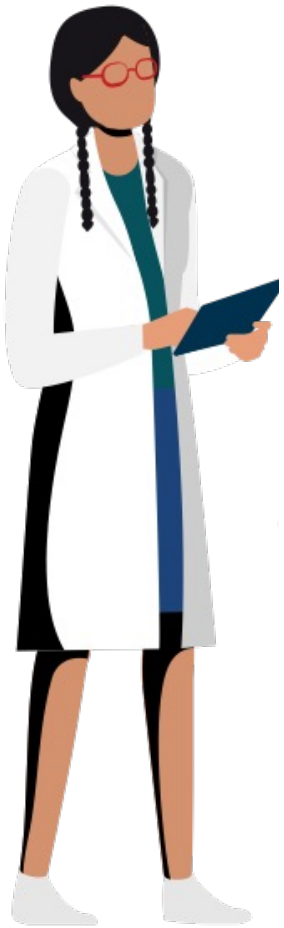


1950s : electrodes

1970s: Dopamine



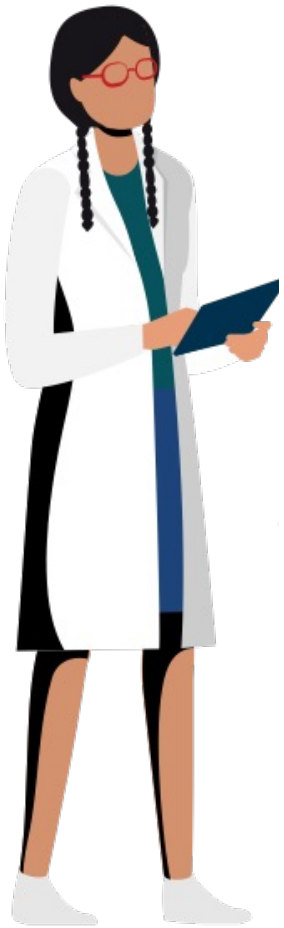
Desire and Drives

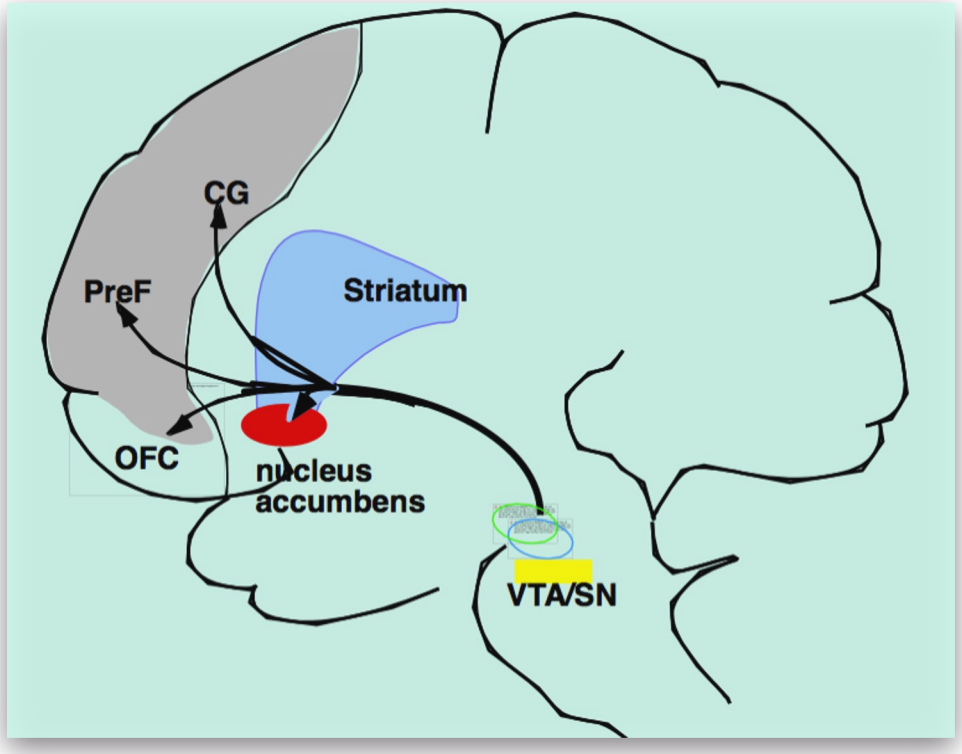


The use of dopamine neurons to shape responses to rewards is seen in simple organisms like worms and flies.

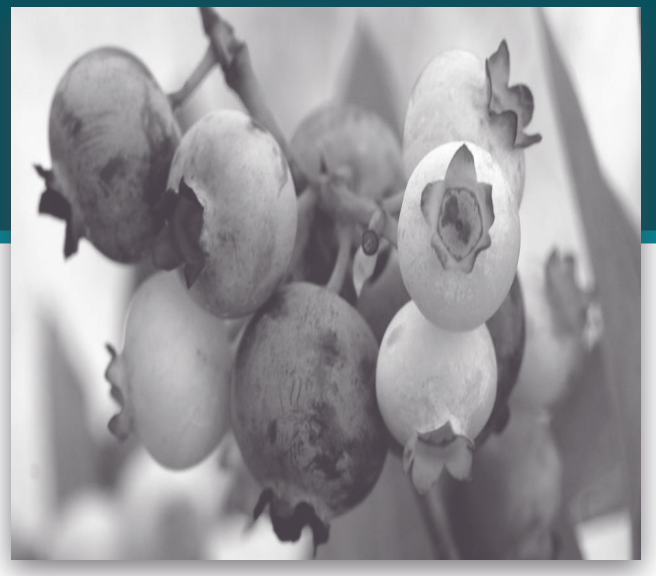
It evolved millions of years ago.

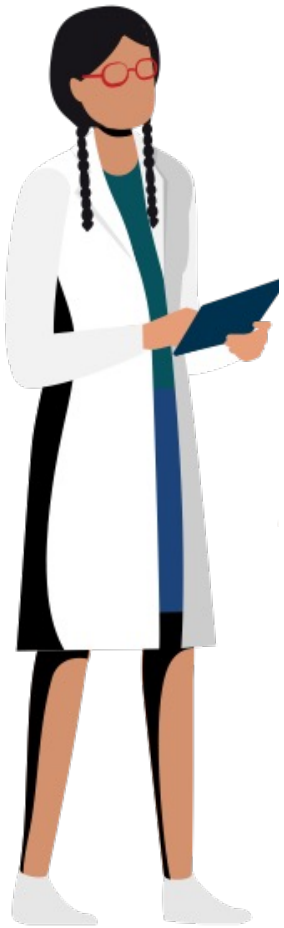
Dopaminergic impulses tell organisms to move toward reward (warmth, food, moisture)





- In humans, those dopaminergic impulses travel through the NAC
- Mediates responses to food, sex, social interactions
- DA projections from VTA to NA release DA and tell the NA to go for it!
- Connects with memory and emotional centers so it can be repeated in the future



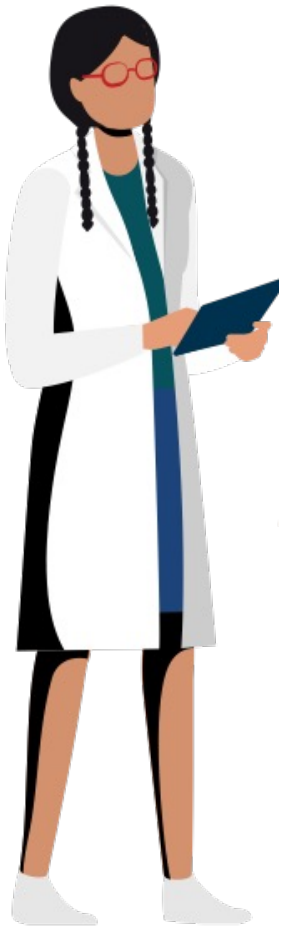


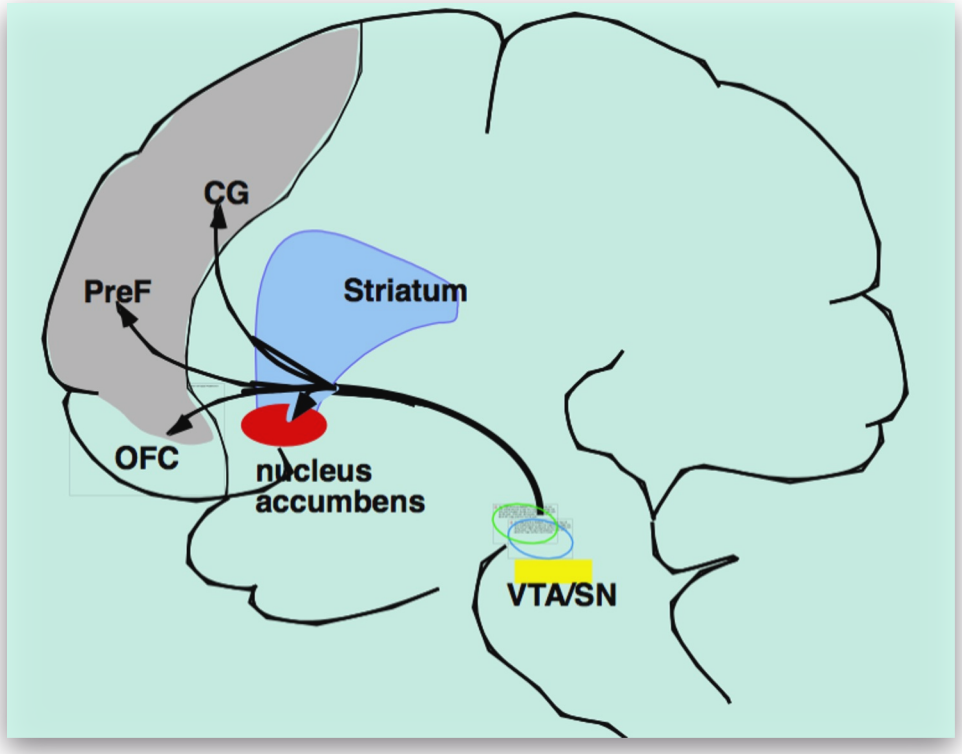
1. Hungry caveman eats berry. It is sweet and pleasurable

2. Brain pays very close attention to what he had to do to get that berry

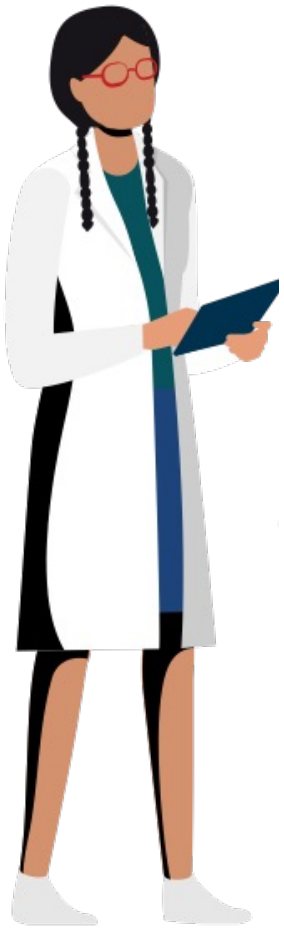
3. Sees the berry bush again, more likely to remember the berry, even craves the berry. Eats the berry.

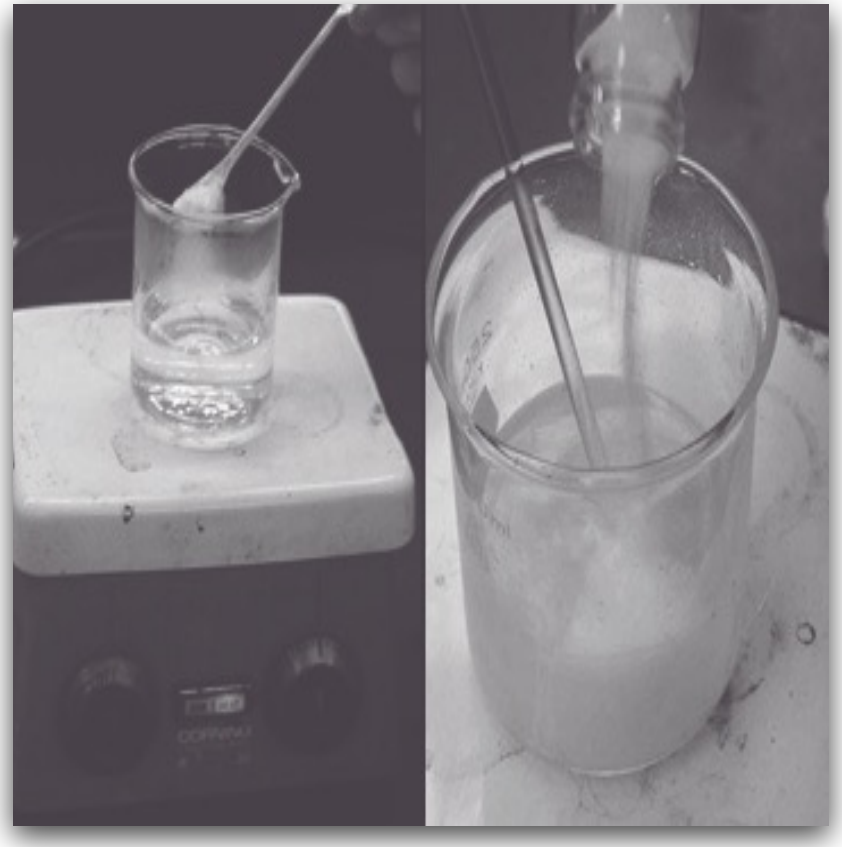
4. Lives





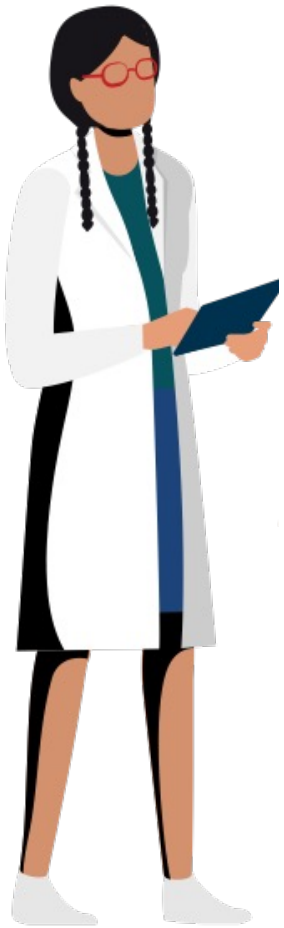
- Addiction taps into this normal brain process
- All addictive drugs activate this pathway
- Drug experience is deeply linked to memory and emotion

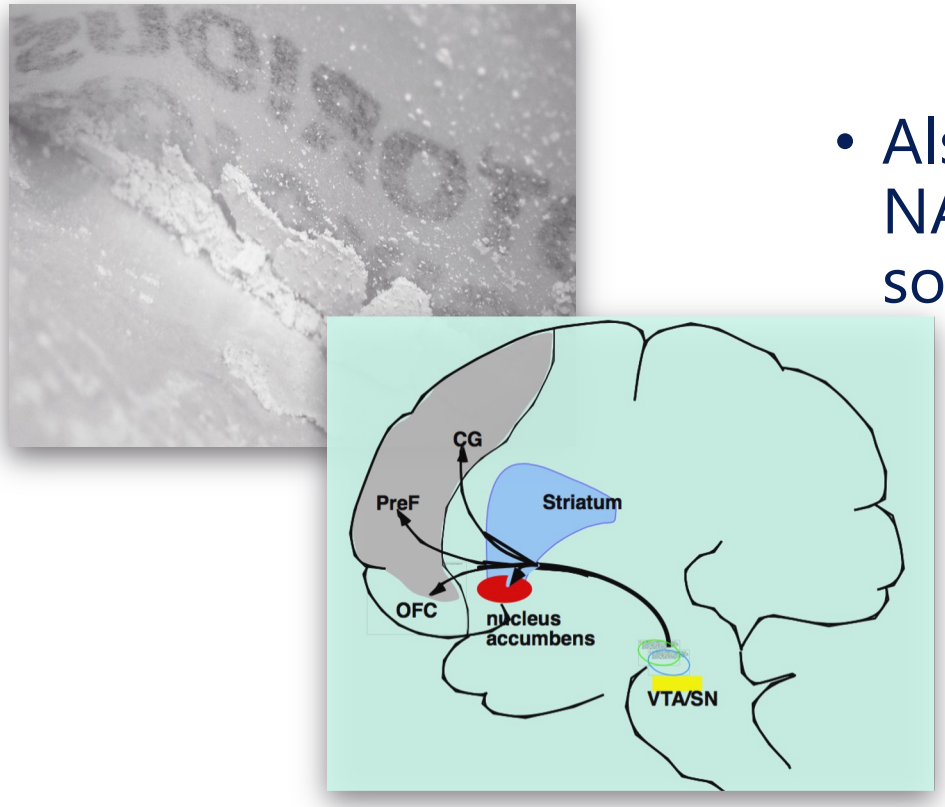




- People, places, things associated with drug use can trigger cravings
- Even when images associated with drug use are shown too rapidly to be “seen” they still trigger cravings

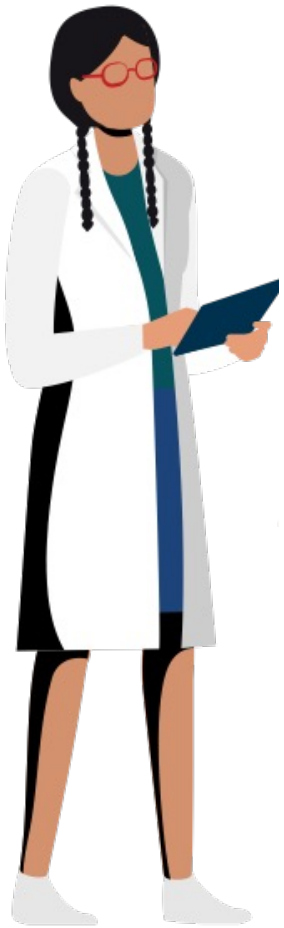
So, part of addiction is craving. Another part is liking

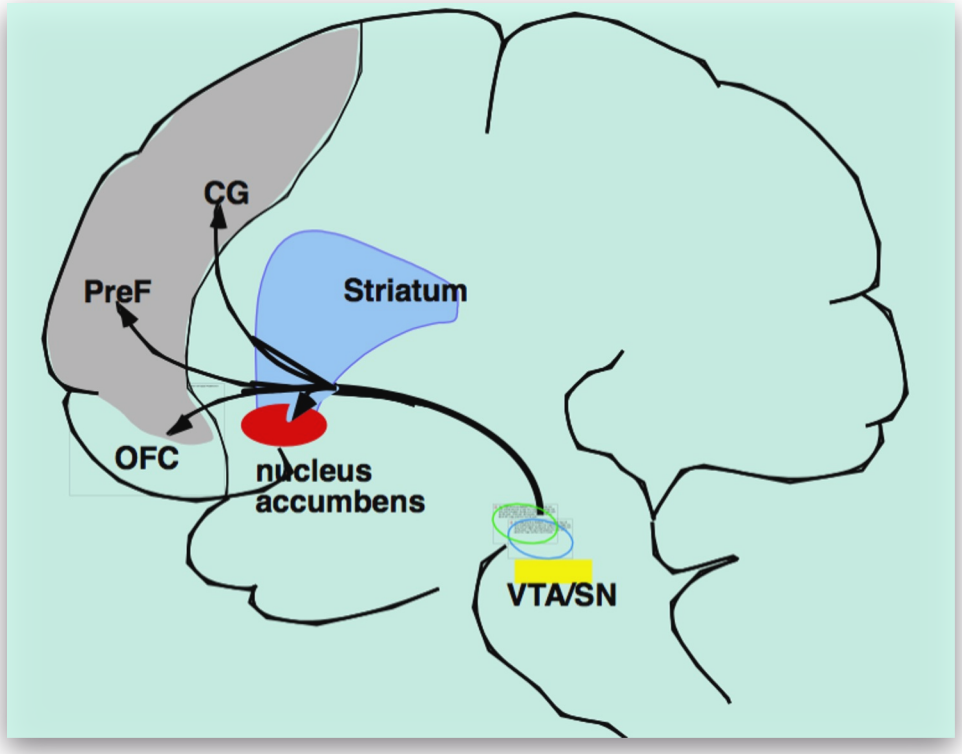




- Opioids: activate DA receptors
- Also activate opioid receptors in NA and produce feeling of satiety, soothing, comfort.

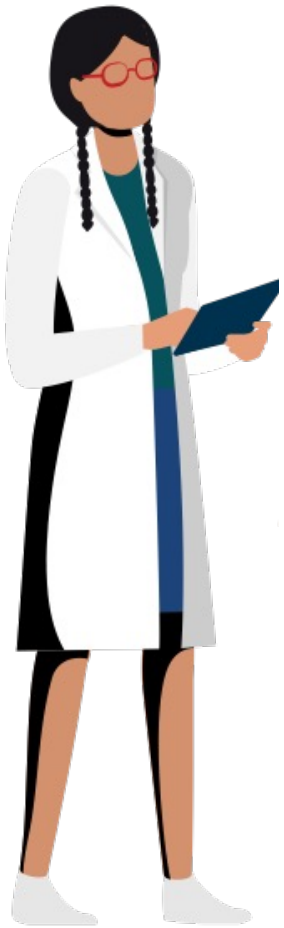
Dysregulation

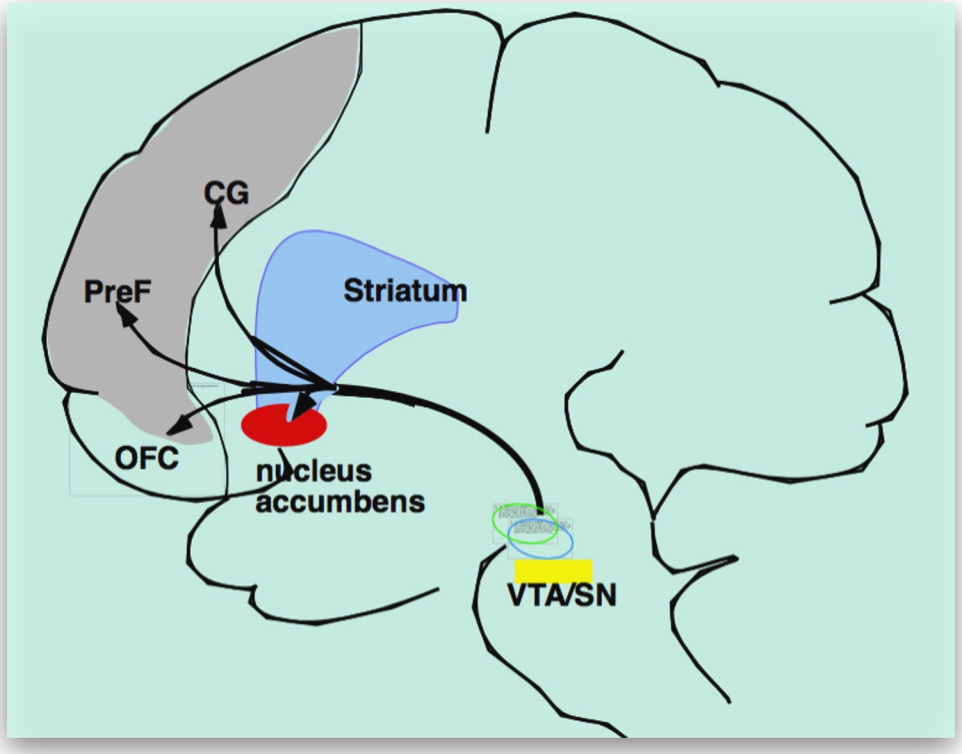




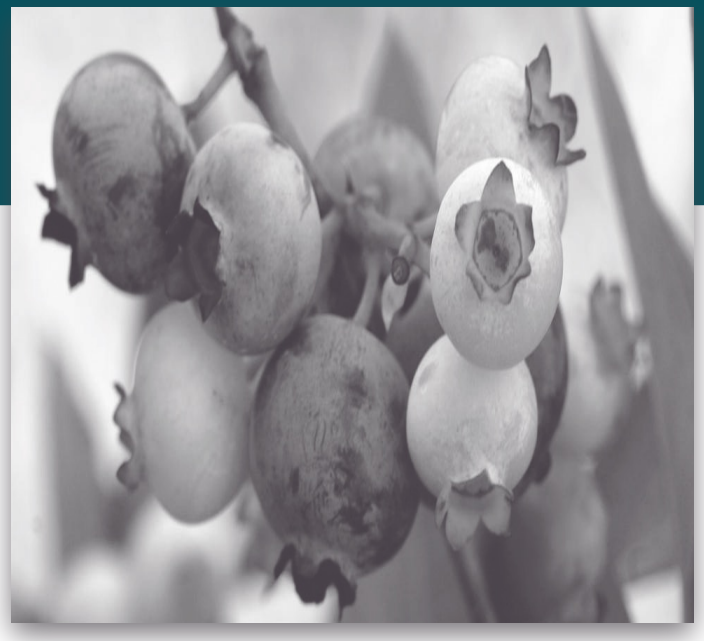
- Dysregulation: impaired ability of the front of the brain to regulate what is going on in the older regions of the brain.
- Prefrontal cortex helps determine the risks and benefits of behaviors and make rational choices.

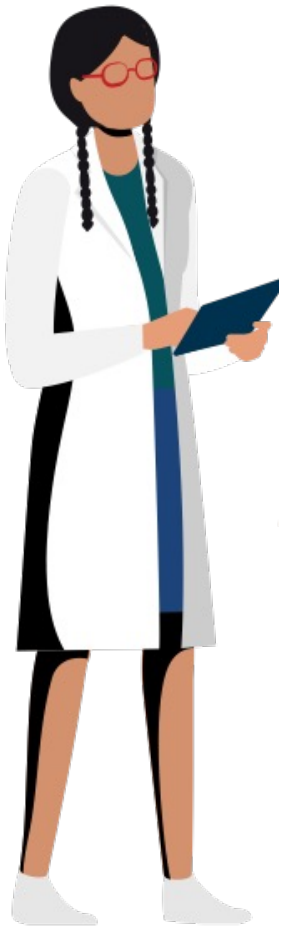
Dysregulation





- Prefrontal cortex is newer and more complicated. It needs a little time to weigh in.
- Repeated activation of the VTA to NAC track slowly strengthens those connections. Habits get hard wired, fast and automatic





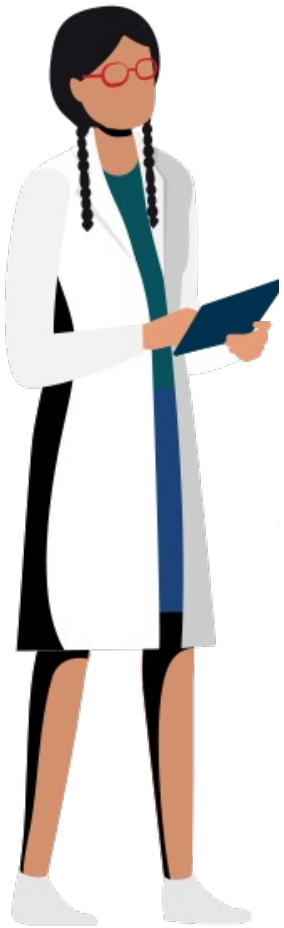
1. Hungry caveman eats berry. It is sweet and pleasurable, and he doesn't starve.

2. The berry gives him a headache the next day so he can't hunt well.

3. He has to weigh the benefits and drawbacks of the berries each time he thinks about eating them.

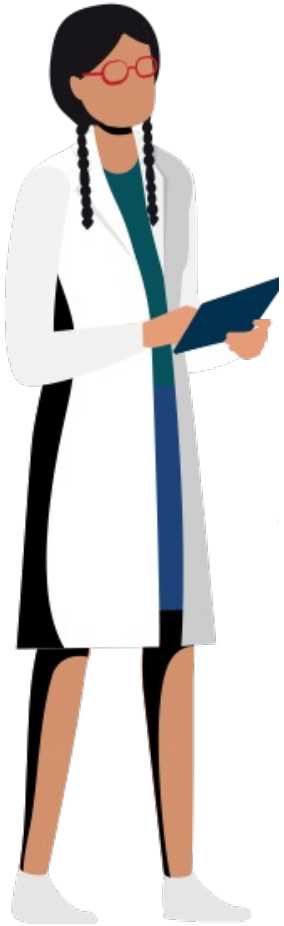
4. If his berry eating habit has become "hard-wired", he may eat them even on days when it is a really, really bad idea

Conclusion



- Addiction taps into normal brain processes
- It is entrained through habit
- It can be effectively treated

Objectives



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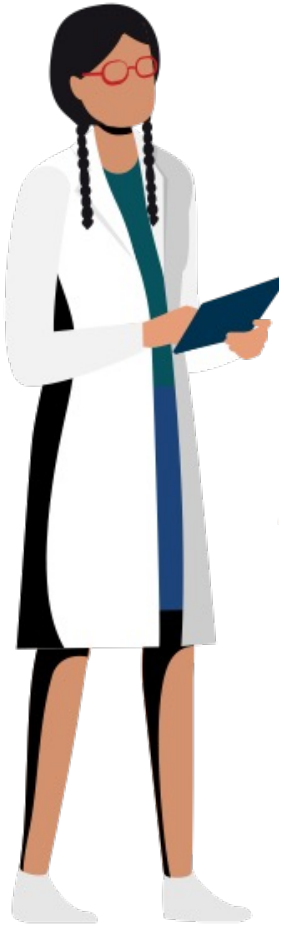
DSM 5

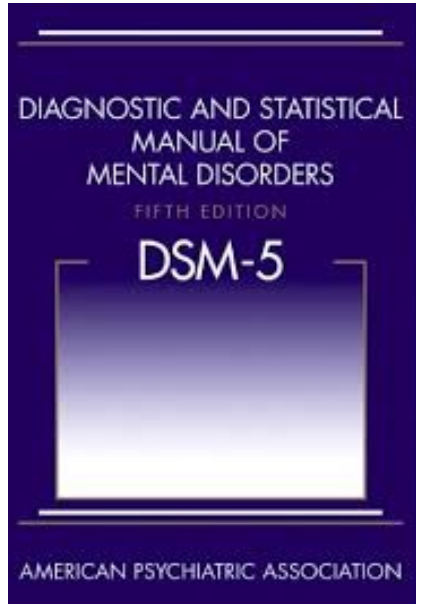


Diagnostic and Statistical Manual of Mental Disorders

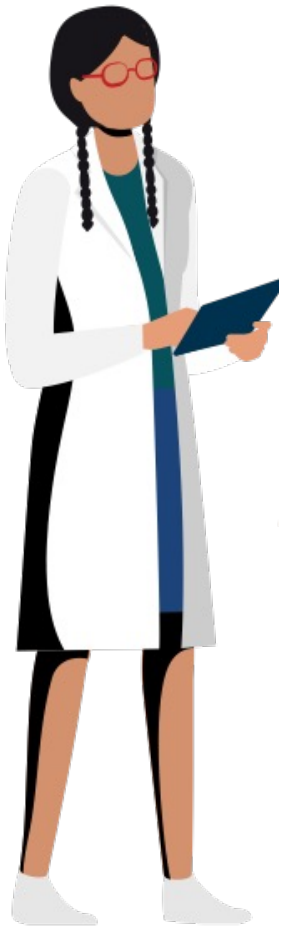
11 criteria

4 C's

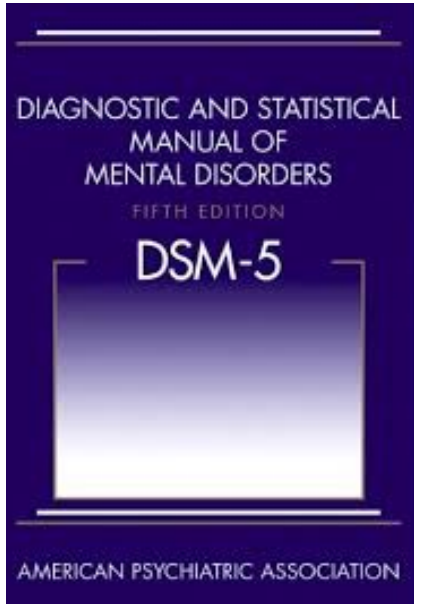
Craving
Compulsive Use
Consequences
Loss of Control



DSM 5: Substance Use Disorder



- Taking in larger amounts or for longer than intended
- Unsuccessful efforts to cut down
- Spending a lot of time obtaining the substance
- Craving or a strong desire to use the substance



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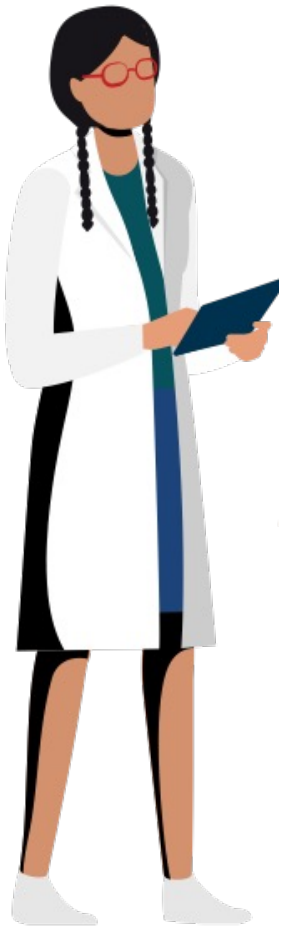
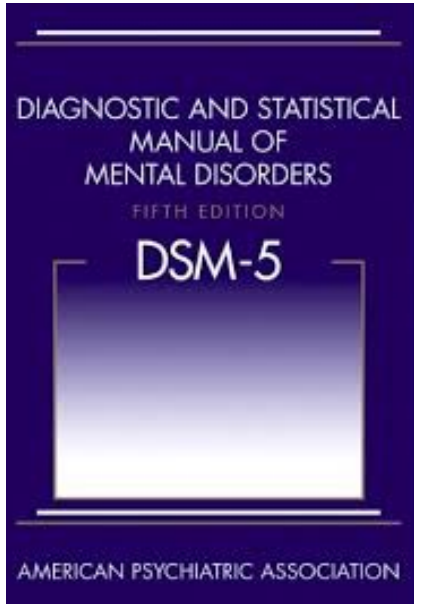
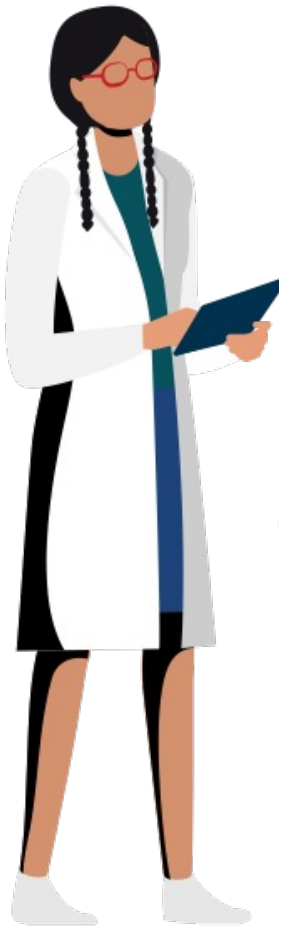


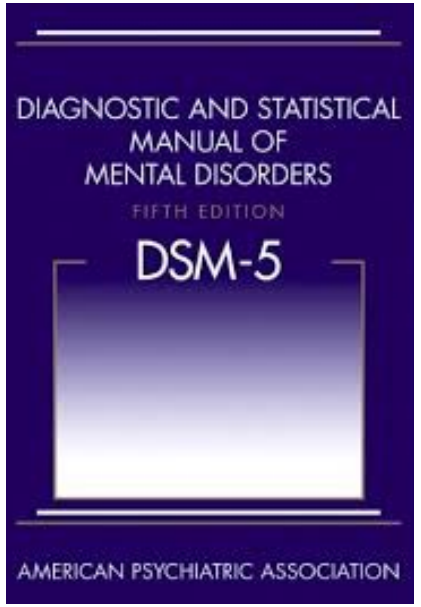
- Continued use despite recurring social or interpersonal problems due to use
- Important activities given up or reduced
- Recurrent use in physically hazardous situations
- Persistent / Recurrent physical or psychological difficulties from use
- Recurrent use resulting in a failure to fulfill major role obligations



DSM 5: Substance Use Disorder



- ☑ Tolerance*
- ☑ Withdrawal*



Substance Use Disorder

2—3

mild disorder

4—5

moderate disorder

6+

severe disorder

Substance Use Disorder

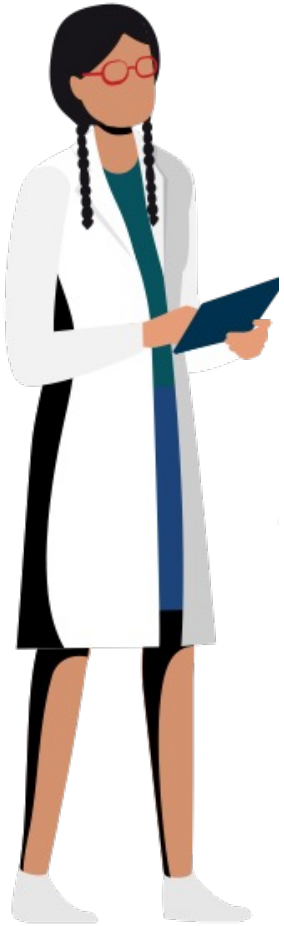
Diagnosis

Label/Accusation

The words we use to describe our patients affects the care they receive

Substance Use Disorder

Objectives



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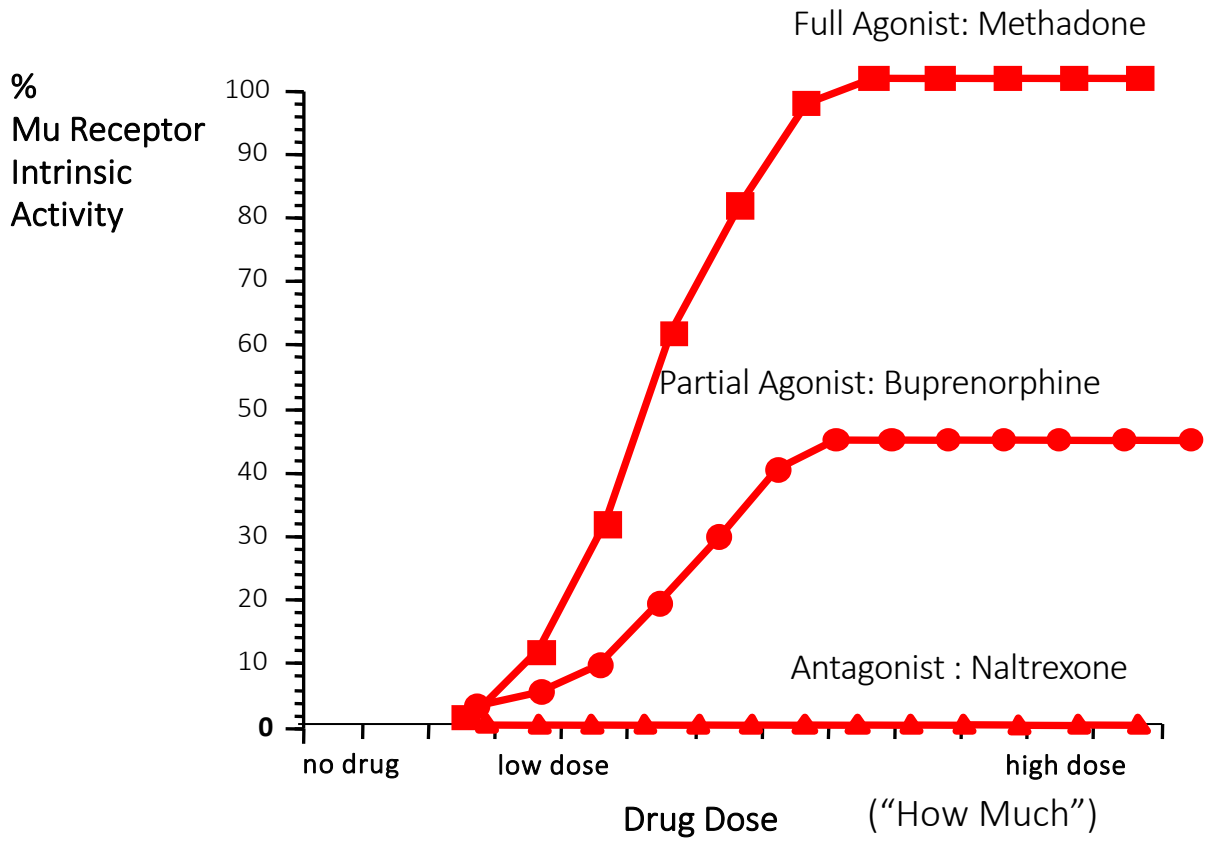
Medications for Opioid Use Disorder (mOUD)

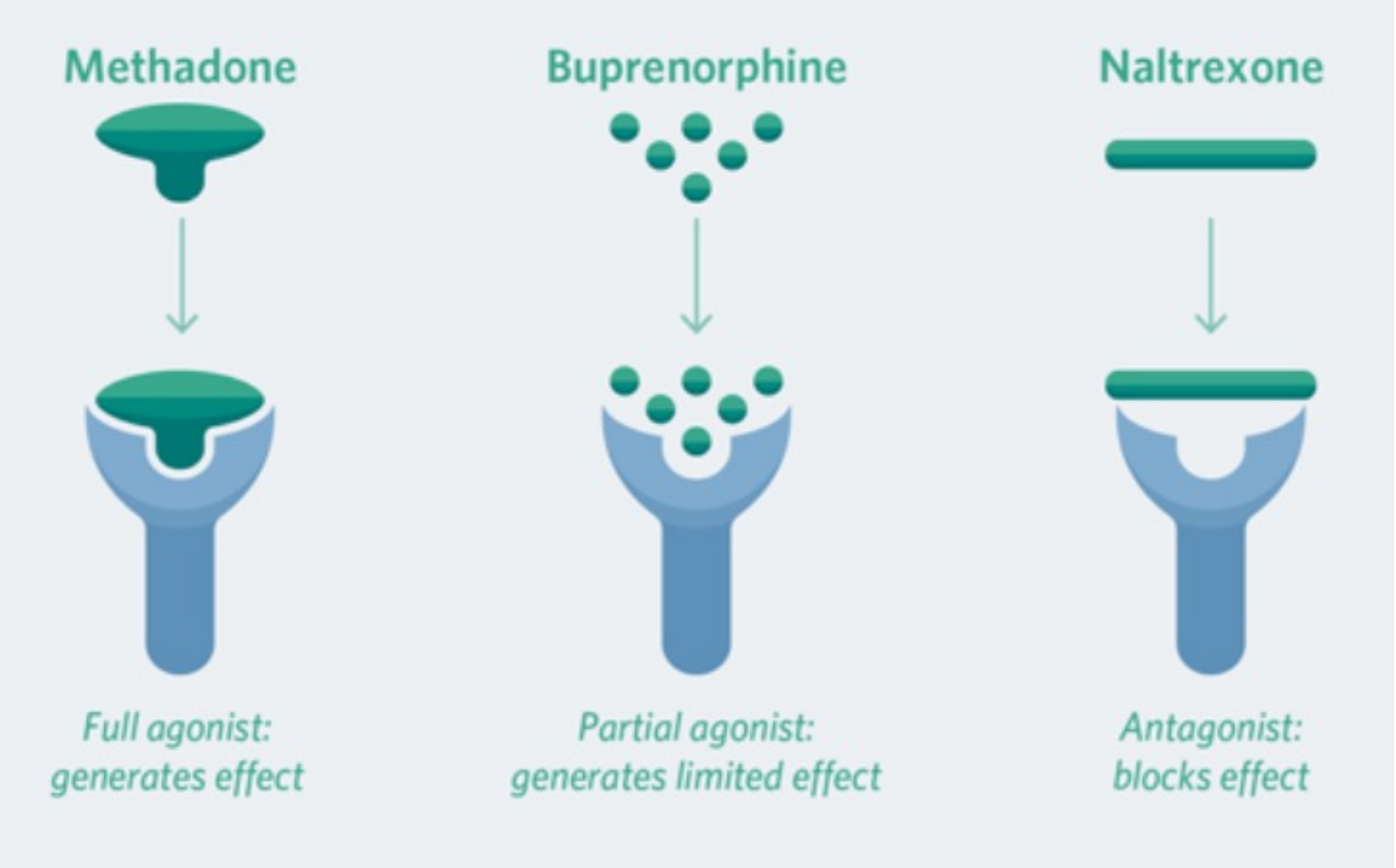
What are they?

Methadone
Buprenorphine
XR- Naltrexone

Pharmacotherapy for Opioid Use Disorder



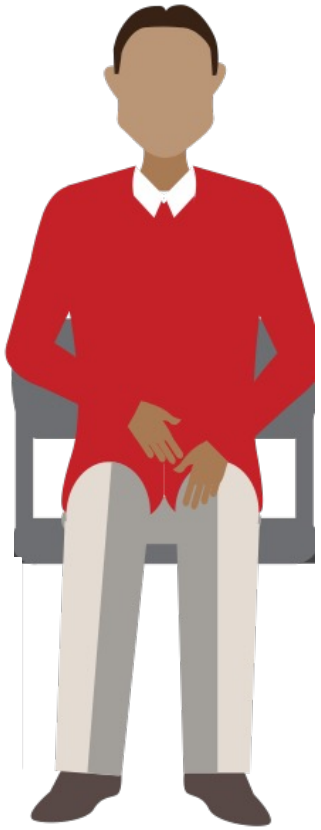
Pharmacotherapy for Opioid Use Disorder



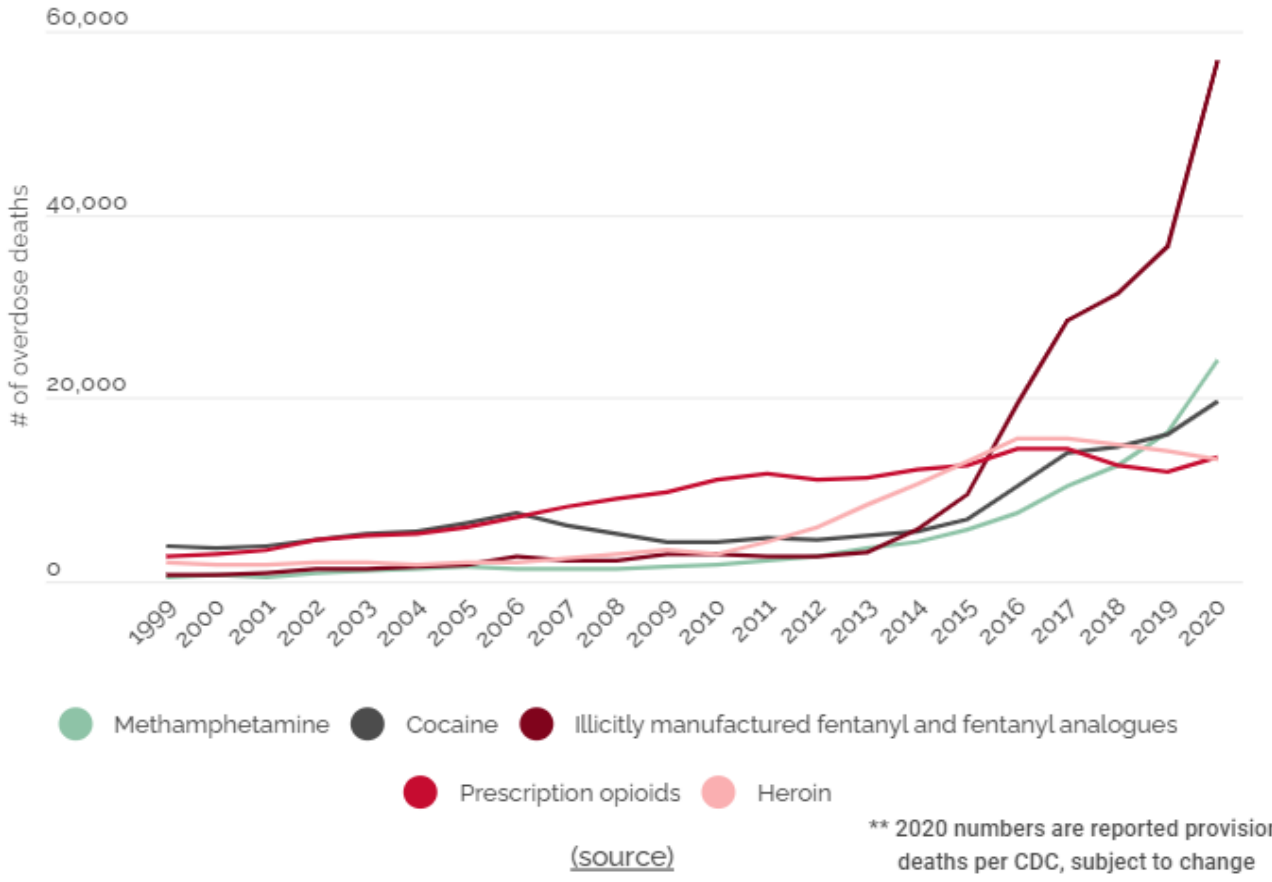
Why do they matter now more than ever?

Fentanyl

Fentanyl



All Overdose Deaths 1999-2020 | Overdose Deaths by Drug 1999-20



(source)

** 2020 numbers are reported provisional deaths per CDC, subject to change

Fentanyl

High affinity and high efficacy at mu receptor

Single use has a short half-life (fast on, fast off)

Repeated use may lead to accumulation in adipose tissue, decreased renal clearance, more mu opioid receptor desensitization

Buprenorphine

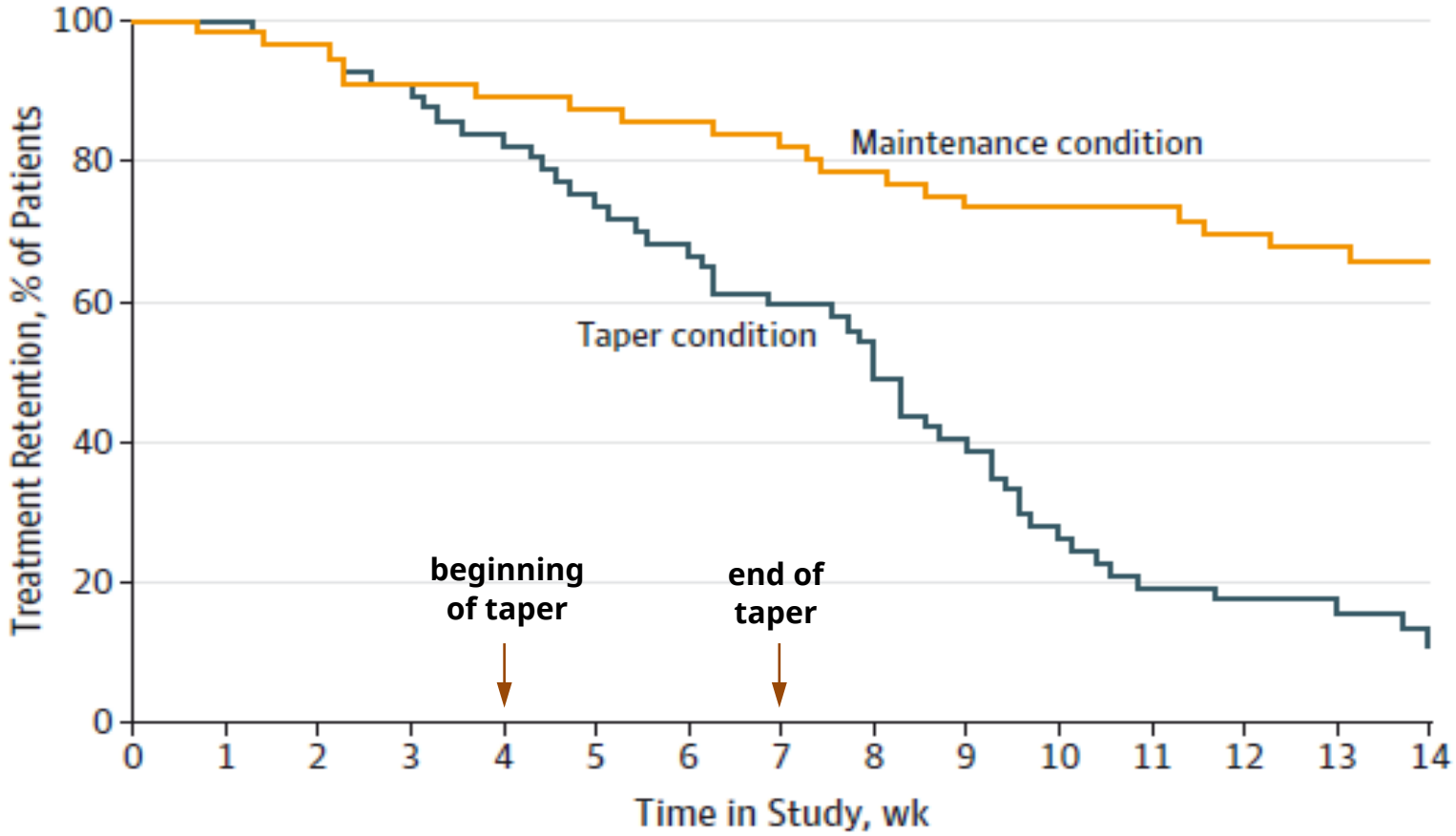
Why is it so great?

It decreases opioid cravings, withdrawal, and use.

Patients taking buprenorphine are significantly more likely to engage and remain in treatment compared to those tapered off the medication.

Fiellen 2014; D'Onofrio 2017

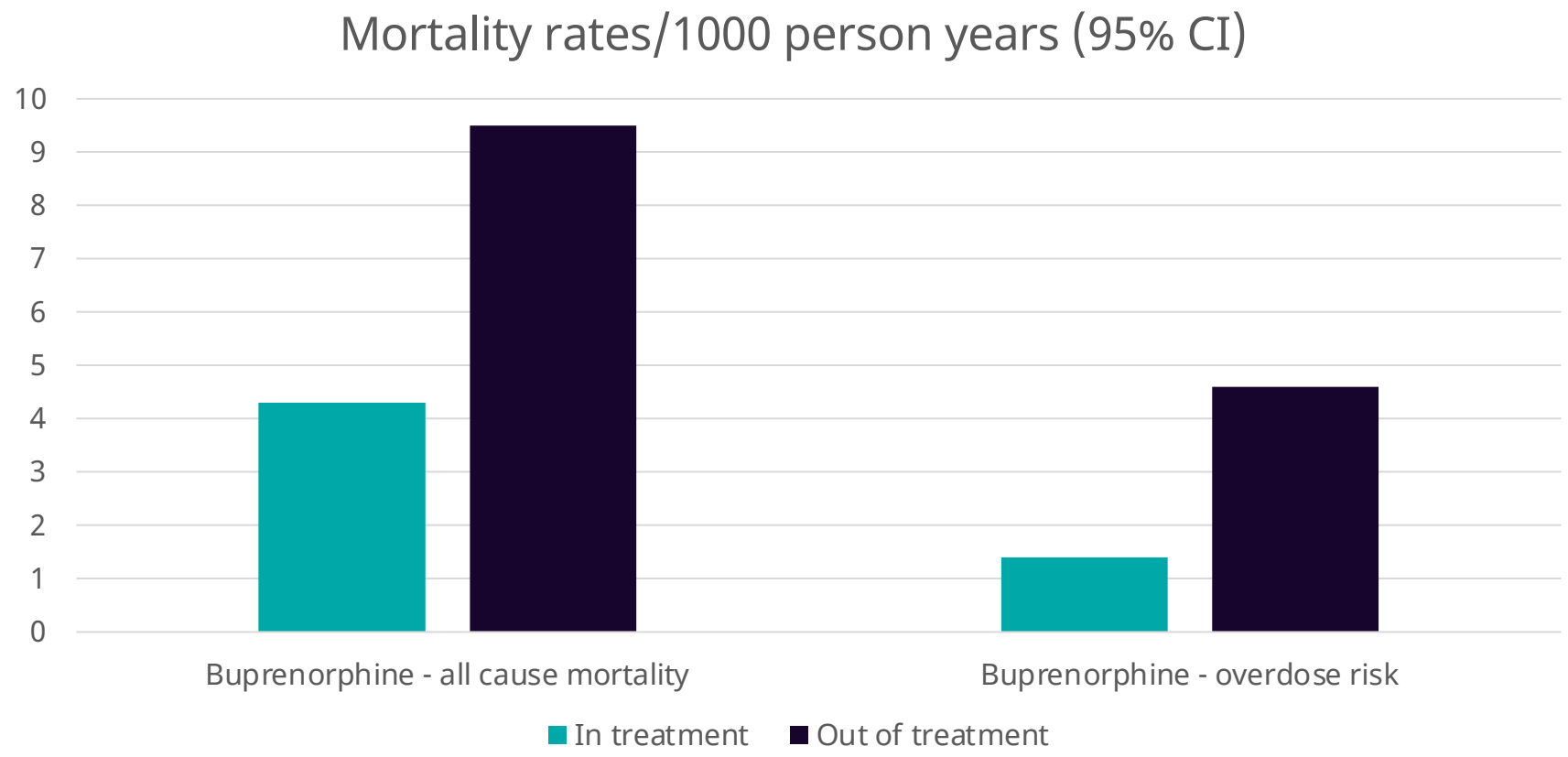
Buprenorphine: Maintenance vs. Taper



Why is it so great?

Most importantly, people don’t die.

Mortality Risk during and after buprenorphine treatment

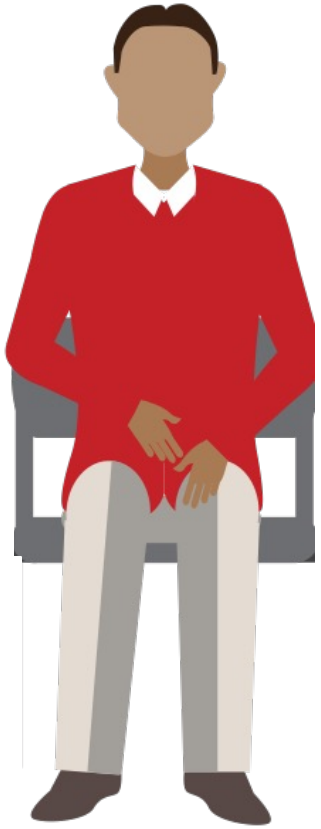


Mortality Risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. Sordo, et al. BMJ 2017.

Important to know:

- Buprenorphine is a high affinity binder at the mu opioid receptors. That means it sits tightly on the receptor.
- It will kick off anything else that's bound there
- But it is a partial agonist at the receptor. That means it doesn't activate the receptor completely.
- If it kicks a full agonist off the receptor, the difference between full agonism and partial agonism is big enough to precipitate withdrawal

Available in two primary SL forms:



1. Buprenorphine monoproduct (Subutex)

2. Buprenorphine/Naloxone (Suboxone)

Buprenorphine/naloxone may reduce misuse

- Buprenorphine is taken sublingually
- Naloxone is absorbed in minute amounts sublingually.
- It is essentially inactive (in most people) unless injected
- Decreased risk of misuse (controversial)

2mg/0.5mg

8mg/2mg

Buprenorphine/naloxone may reduce misuse

'EN ACCESS

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Reconsidering the Usefulness of Adding Naloxone to Buprenorphine

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Keywords: opioids, substance use disorders, addiction, overdose, diversion, agonist therapy

INTRODUCTION

We are in the middle of an opioid epidemic with tens of thousands of lives lost every year. As we combat this problem, it is critically important that we continually scrutinize our research efforts and care strategies in the spirit of the scientific method. Especially in light of a death toll that lowered overall US life expectancy for the first time since the flu pandemic in World War I, (1) we must maintain our readiness to reconsider well-established theories and practices in order to improve our efforts to contain this crisis. These efforts will require precision and accuracy in our translation of the literature base. One of the most effective interventions for opioid use disorder has been buprenorphine maintenance therapy, largely using a combination of buprenorphine and naloxone.

Blazes and Morrow Frontiers in Psychiatry 2020

New kids in town: buprenorphine XR (Sublocade & Brixadi)

Sublocade: approved November 2017

Single injection lasts one month

Brixadi: approved May 2023

Multiple options: weekly and monthly

Haight et al The Lancet 2019

New kids in town: buprenorphine XR (Sublocade & Brixadi)

Table 1: Daily doses of sublingual buprenorphine (Subutex, Suboxone, or generic product equivalents) and suggested corresponding BRIXADI (weekly) or BRIXADI (monthly) doses

Daily dose of sublingual buprenorphine	BRIXADI (weekly)	BRIXADI (monthly)
≤ 6 mg	8 mg	--
8-10 mg	16 mg	64 mg
12-16 mg	24 mg	96 mg
18-24 mg	32 mg	128 mg

Haight et al The Lancet 2019

How to administer and prescribe

“Traditional” inductions

- Instruct the patient to abstain from any opioid use for a minimum of:
  - 12-16 hours for short-acting opioids
  - 24 hours for sustained-release opioid medications
  - 36 hours for methadone or fentanyl
- Observe and document mild to moderate withdrawal

“Traditional” inductions

Wait until patient is in mild to moderate withdrawal (which means receptors are empty)

Begin buprenorphine and titrate up, as needed, over 3-4 days

How do you know if a patient is in sufficient enough withdrawal to begin buprenorphine?

Clinical Opiate Withdrawal Scale (COWS)

Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name:_____ Date and Time _____/_____/_____:_____

Reason for this assessment:_____

Resting Pulse Rate: ___ ___beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset:** *over last ½ hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 Multiple episodes of diarrhea or vomiting
Sweating: *over past ½ hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 No tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/ muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing Assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

126

Clinical Opiate Withdrawal Scale (COWS)

- Resting pulse rate
- Sweating/chills
- Restlessness
- Pupil size
- Bone or joint aches
- Runny nose
- GI upset
- Tremor
- Yawning
- Anxiety or irritability
- Goose bumps

- **Guides timing of first dose of buprenorphine**

Traditional induction

Begin buprenorphine with COWS is 10-12

Prepare for Discomfort

- Acetaminophen and ibuprofen
- Clonidine
- Hydroxyzine
- Trazodone
- Tizanidine or Methocarbamol
- Ondansetron
- Bismuth or Loperamide

Srivastara, 2020; Kosten, 2019; Kuszmaul 2020; Kheirabadi 2008 ;Salehi 2011; Sanders 2013

Dosing Schedule

	Suggested dosing pills or heroin	Suggested dosing fentanyl
Day 1	2-4mg (wait 45 min) + 4mg if needed	8-16mg
Day 2	Day 1 dose + 4mg if needed (single dose)	16-20mg
Day 3	Day 2 dose + 4mg if needed (single dose)	20-24mg
Day 3-28	Adjust as needed	24mg

Precipitated Withdrawal

If opioid withdrawal appears shortly after the first dose buprenorphine may have precipitated a withdrawal syndrome

Precipitated Withdrawal

Greatest severity of buprenorphine-related precipitated withdrawal in the first few hours (1-4) after a dose

Challenges with Traditional Induction

- Patient must experience withdrawal, which is difficult
- With fentanyl, sometimes need to wait even longer than 3 days because fentanyl sticks around in the fat
- Always possible that patient will experience precipitated withdrawal

Another option...

ninja clipart PNG Designed By 588ku from https://pngtree.com/freepng/sneak-attack-sneak-attack-man-in-black-black-man-ninja_3931511.html?sol=downref&id=bef

Low dose buprenorphine induction

- Many different protocols
  - Initial protocol “Bernese Method”
  - Usually start at 0.5 mg
  - Often 7-10 days
  - No universally accepted regimen
  - Can continue full agonists throughout the entire induction

Day	Dose
1	0.5 mg daily
2	0.5 mg bid
3	1 mg bid
4	2 mg bid
5	4 mg bid
6	4 mg tid
7	8 mg tid

Adapted from Yale protocol

[9]Opioid Use Disorder Practice Update (2022)
British Columbia Centre on Substance Use

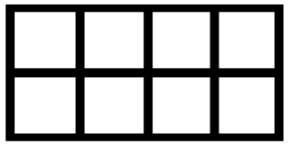
Tips and Tricks

Good patient instructions are helpful. Consider visual aids

LOW DOSE INITIATION

DAY 1 *(At about 6 hours or more since last fentanyl use)*

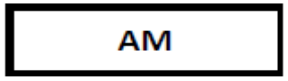
- Cut an 8mg buprenorphine strip into 8 pieces. Each piece is now 1mg.
- Take one piece every 1-2 hours. Speed up if you are feeling improvement or slow down if you start to feel worse.

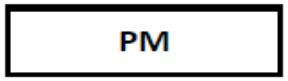


- If you have increased discomfort shortly after a dose (10-15 minutes after), slow next dose down to 3 hours.
- **Your total dose for Day 1 will be 8mg.**

Day 2

- Take 1 strip in the AM and 1 strip in the PM a total of (16mg)





- **Your total dose for Day 2 will be 16mg.**

Tips and Tricks

- Specifically outline what adjunct meds you are giving and for what
- Instruct patients to take AM buprenorphine before their full agonist

Tips and Tricks

- Close follow up
- Modify or slow protocol as needed (i.e. repeat days)
- Give naloxone to every patient

Sublocade

Insert says: “Patients should first undergo induction and stabilization by initiating a buprenorphine-containing product, delivering the equivalent of 8-24 mg/day of transmucosal buprenorphine for a minimum of 7 days.

Practice (and now some research) indicates: You can start much more quickly. “Initiating BUP-XR 300mg following a single BUP-TM 4mg dose was well tolerated”

Hassman et al Am J Drug Alc Abuse 2023

Brixadi

Insert says:

“For patients not currently receiving buprenorphine treatment, begin with a test dose of 4mg transmucosal buprenorphine to establish that buprenorphine is tolerated without precipitated withdrawal, and then transition to BRIXADI (weekly). Initiating treatment with BRIXADI as the first buprenorphine product has not been studied. Initiating treatment with BRIXADI (monthly) in new entrants to treatment has not been studied”

Practice indicates: ???

Maintenance

- Continue patient at the dose at which they have no withdrawal symptoms and minimal to no cravings
- The maximum effective dose has long been considered 24mg

Maintenance

- However, with fentanyl, many patients continue to have cravings and withdrawal symptoms at typical doses (16-24 mg)

- It is becoming more common to **up titrate** to 28-32 mg which seems to be helpful for some patients

Evidence on Buprenorphine Dose Limits: A Review

Grande, Lucinda A. MD, FASAM; Cundiff, Dave MD, MPH, FASAM; Greenwald, Mark K. PhD; Murray, MaryAnne DNP, PMHNP-BC, FNP-BC, CARN-AP; Wright, Tricia E. MD, MS, FACOG, DFASAM; Martin, Stephen A. MD, EdM, FASAM

Author Information

Journal of Addiction Medicine ():10.1097/ADM.0000000000001189, June 16, 2023. | **DOI:** 10.1097/ADM.0000000000001189

Abstract

Objectives

As overdose deaths from fentanyl continue to increase, optimizing use of medications for opioid use disorder has become increasingly important. Buprenorphine is a highly effective medication for reducing the risk of overdose death, but only if a patient remains in treatment. Shared decision making between prescribers and patients is important to establish a dose that meets each patient's treatment needs. However, patients frequently face a dose limit of 16 or 24 mg/d based on dosing guidelines on the Food and Drug Administration's package label.

Regulations and Regulatory Changes

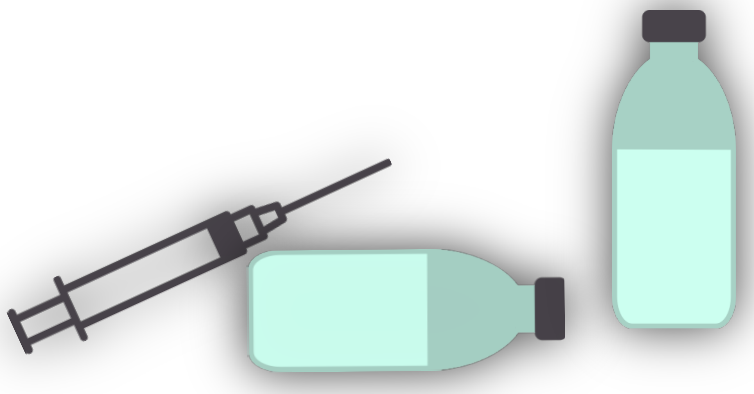
Buprenorphine approved by the FDA in 2002. Prescribers were required to undergo an 8 -our training, register with the DEA, obtain an “X-waiver” and could only prescribe to 30 patients at a time

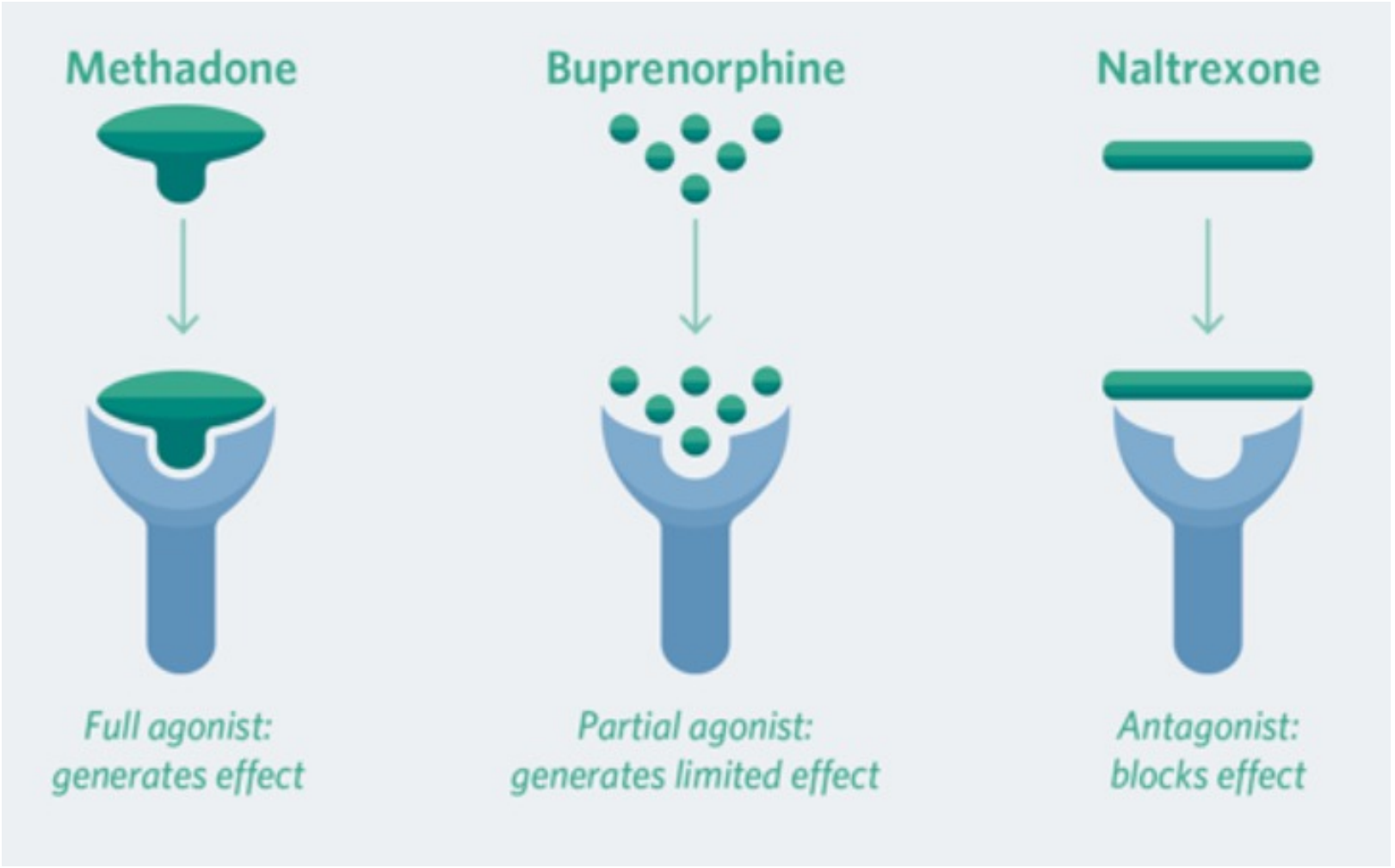
2016 NPs and PAs were allowed to prescribe, but with a longer training requirement. Still required to obtain X waiver and register with the DEA and limit patients

Training requirement removed in 2021, though prescribers still needed to obtain the waiver and register with the DEA

Jan 2023 all buprenorphine specific DEA requirements were removed

Naltrexone for Extended Release Injectable Suspension




Methadone
Buprenorphine
Naltrexone
Full agonist:
generates effect
Partial agonist:
generates limited effect
Antagonist:
blocks effect

Difficult to start

Requires abstinence from opioids 4 – 7 days

About 25% of patients will not complete induction

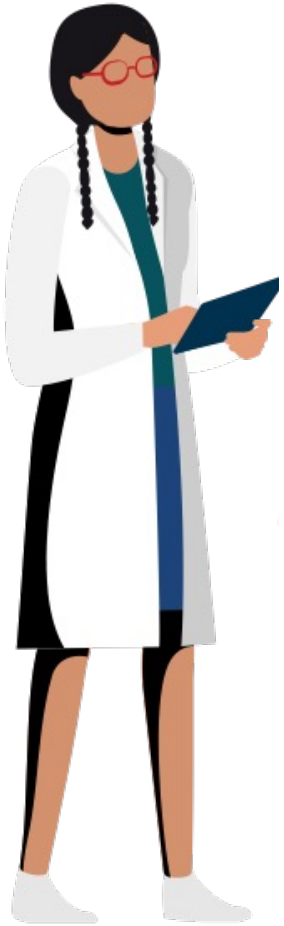
Overdose data

- Original findings
  - more overdoses in the XR-NTX arm, but not statistically significant
- Re-analysis
  - Researchers had missed cases of overdose
  - 28 overdoses in XR-NTX arm
  - 2.4 x greater hazard of overdose compared to bup/nal

Summary

- Opioid use disorder can be treated in an outpatient setting
- Buprenorphine saves lives
- Please prescribe

Objectives



1. Review the neurobiology of addiction
2. Use the DSM-5 criteria to diagnose substance use disorders
3. Review office-based medications to treat opioid use disorder
4. **Discuss interventions to treat methamphetamine use disorder**

Methamphetamine Use Disorder

Crystal Methamphetamine

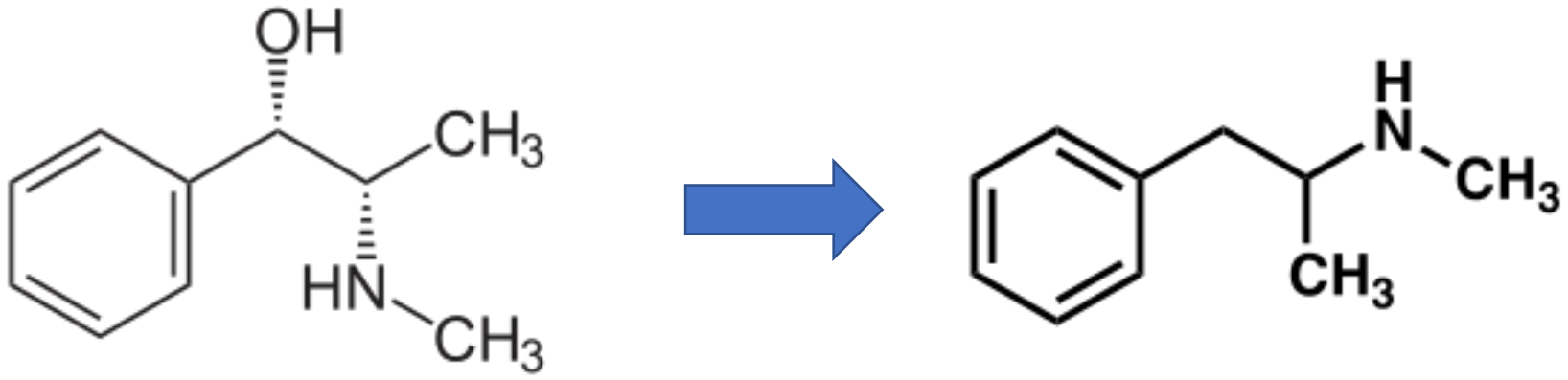
- Form of d-methamphetamine
- Closely related to amphetamine
- Longer lasting and more toxic to the CNS

Crystal Methamphetamine

Crystal Methamphetamine

Crystal Methamphetamine

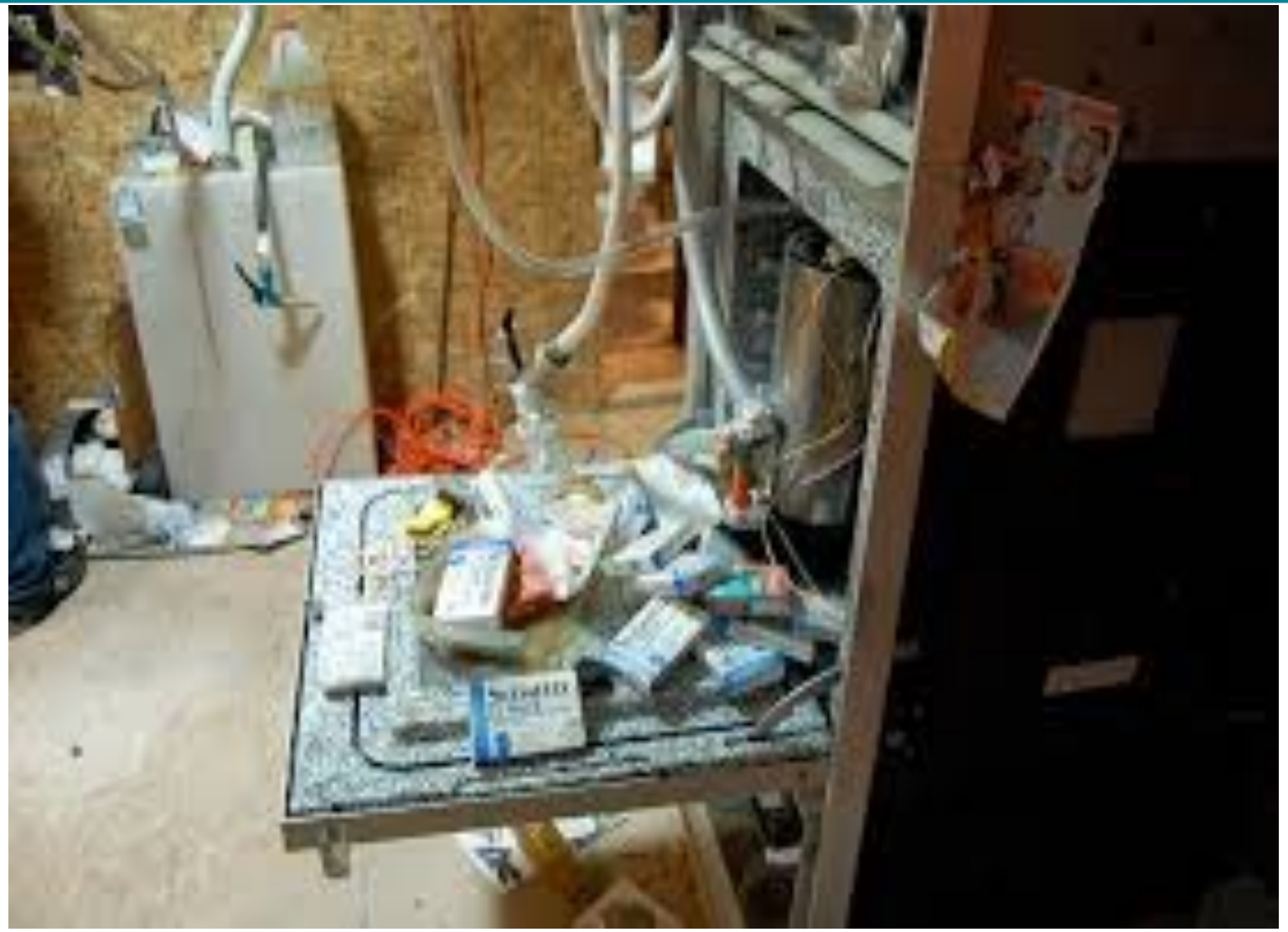
Crystal Methamphetamine



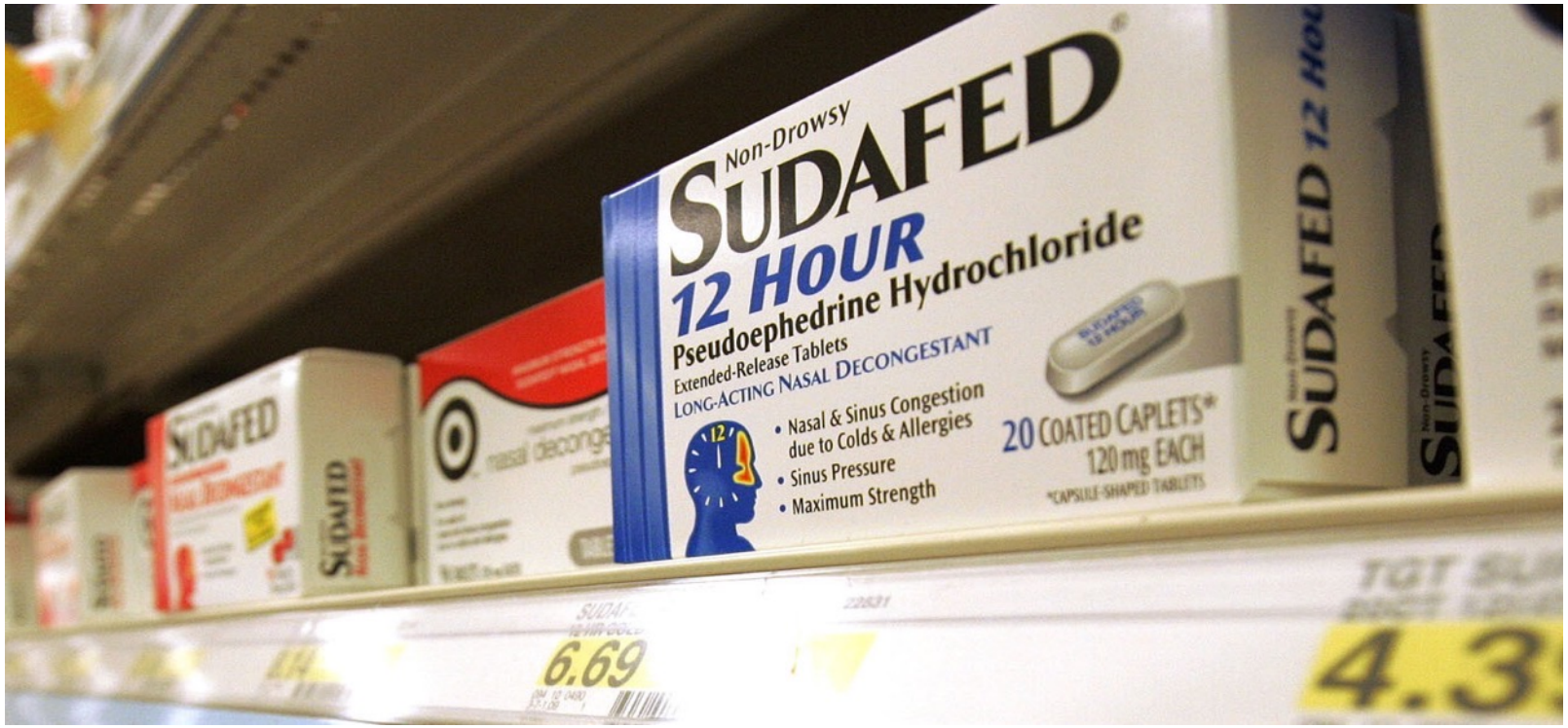
Crystal Methamphetamine

```
Materials:
-------------------------------------------------------------------------------
1 2 Liter Bottle (with cap)
1 1 Liter Bottle (get 2 caps for it)
1 20 oz. Bottle (with cap)
1 Quart Jar
2 ft. 1/4in. diameter rubber/plastic hose (aquarium hose works good)
Coffee Filters
1 Funnel
1 Tubing Cutter (go to Home Depot)
2 Plyers
1 Roll of Ductape or Electrical Tape 1 Blender or Food Processor

200 60mg Pseudophedrine HCL pills (Actifed, Sudafed, Suphedrine, etc.)
1 1/2 cups Ammonium Nitrate fertilizer (33-0-0)
3 cans starting fluid
3 AA Energizer Lithuim Batteries
1 bottle Red Devil brand Lye
2 caps of water (use the top off the 2 liter)
1 box Iodized Salt
1 bottle Liquid Fire brand drain opener


Procedure:
-------------------------------------------------------------------------------
1) Rinse and dry out all of your bottles. Be sure to get ALL of the
moisture out. Don't go any further until they are completely dry.
2) Put your pills into the blender or food processor and grind them
into powder. Mix them in with the 1 1/2 cups of Ammoniun Nitrate
fertilizer. Use the funnel to pour the mixture into the 2 liter
```

Crystal Methamphetamine



2005: CMEA (Combat Methamphetamine Epidemic Act)

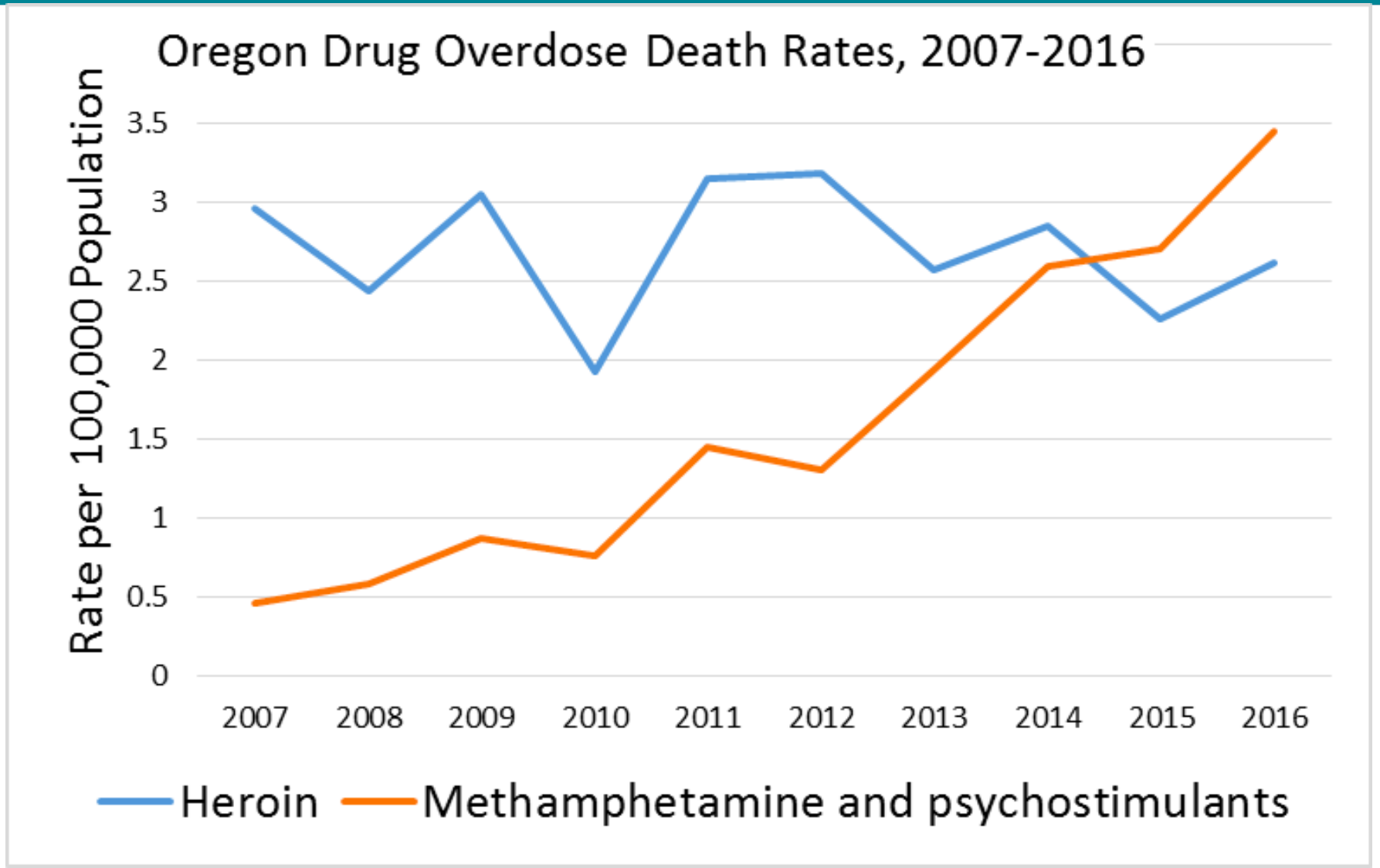


Result?

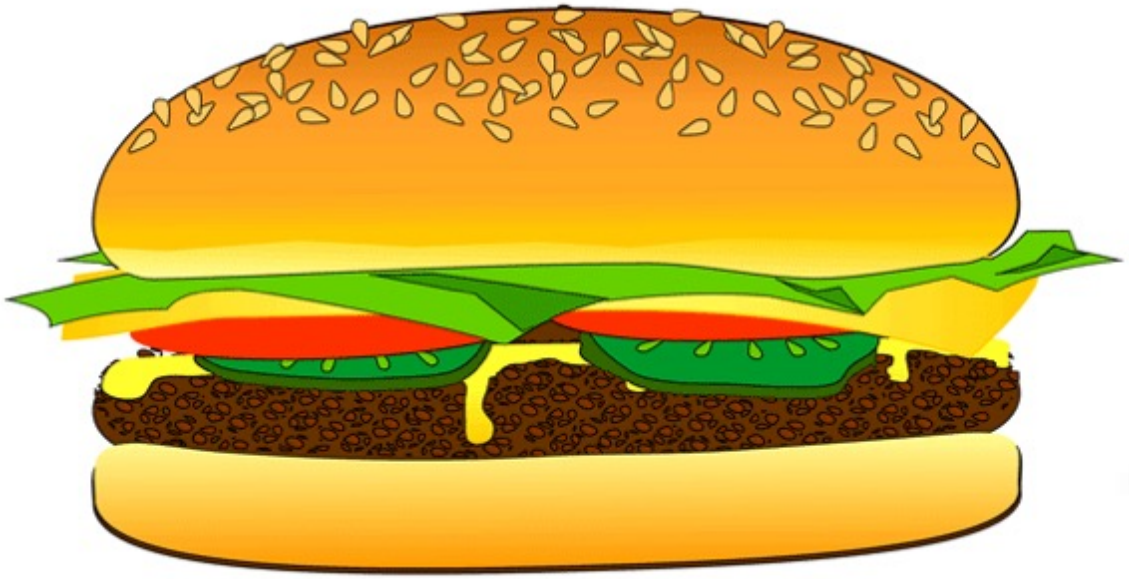
In Oregon, from 2004 to 2011, methamphetamine lab incidents decreased from an average of 24 per month to less than one per month

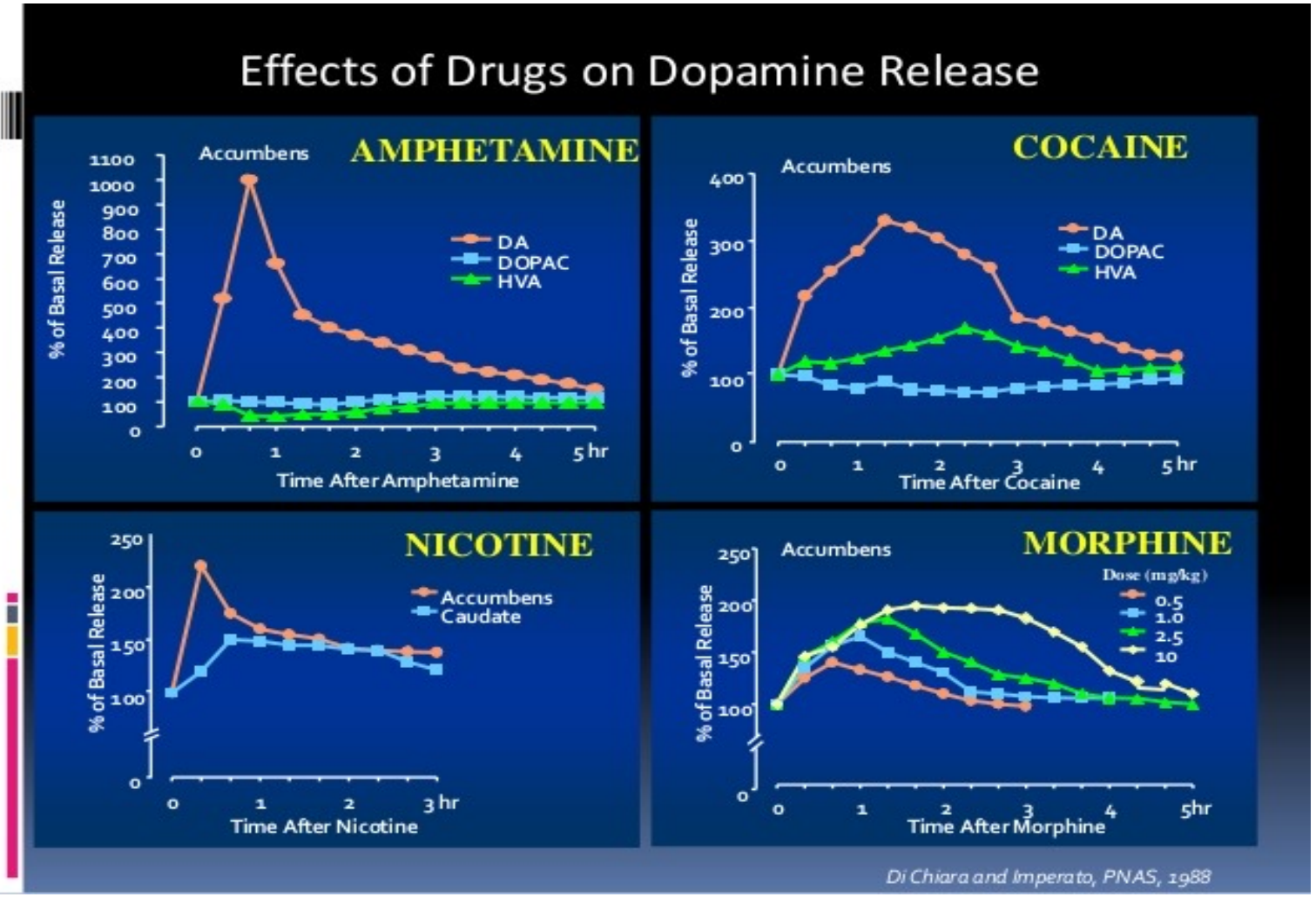
http://www.oregondec.org/pse.htm

And Yet…


Oregon Drug Overdose Death Rates, 2007-2016
Rate per 100,000 Population
3.5
3
2.5
2
1.5
1
0.5
0
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Heroin
Methamphetamine and psychostimulants

Increase dopamine to +/- 200 times basal output





Di Chiara and Imperato, 1988

Medical Issues Related to Methamphetamine Use

Neurotoxicity, cognitive effects

- Excessive DA damaging cell structures
- Disruption of blood-barrier
- Use associated with poorer performance on motor and processing tasks, visual and verbal fluency
- More than 2/3 of those with MUD show cognitive impairment
- May limit ability to follow through with treatment, understand advice, and achieve treatment outcomes

Paulus and Stewart, JAMA Psychiatry, 2020

Medical Issues Related to Methamphetamine Use

Cardiovascular and cerebrovascular

- Leading cause of death with MUD
- Strokes more common in young men (hemorrhagic)
- Also associated with pulmonary htn, cardiac arrhythmia, cardiomyopathy

Lappin et al., 2017

Two evidence-based behavioral interventions: contingency management and harm reduction

Behavioral Interventions 1st Line Tx for MUD

- Most behavioral interventions (CBT, MI, Matrix model, exercise, CM) demonstrated some efficacy in reducing methamphetamine cravings and use
- Contingency management most consistently showed reduced use, increased retention in treatment, better quality of life

Asharani et al Drug and Alcohol Dependence 2020
De Crescenzo et al PLOS Medicine 2018

Photo courtesy of John Mahan MD

Contingency Management: Theory

- Addiction is sustained through reinforced learning
- We cannot simply unlearn habits – we must learn new and competing habits
- CM entrains new behaviors that support the process of recovery
- Breaks recovery process down into a series of concrete, attainable goals
- > 100 RCTs affirm the effectiveness of CM in treating addiction

Roll JM et al. Am Jnl Psych 2006
Roll JM et al. Addict Behav 2013
Rawson, RA et al. Addiction 2016

Contingency Management: Practice

1. Identify a target behavior that can be objectively measured, attainable, and reinforced in real time.

2. Reward that behavior immediately when it occurs, using rewards that are valuable to participants (but not necessarily expensive).

3. Use an escalating schedule of reinforcement.

Photo courtesy of John Mahan MD

Example

Patient on long term IV antibiotics who is often not in her room when it is time for her antibiotics. She likes chocolate and Starbuck's Frappuccinos

Target behavior: be in the room 8:00 am, noon, and 5 pm

Reward: Hershey's kiss each time she is in the room when the nurse arrives with antibiotics

Escalating schedule: $5 Starbuck's card after she has accumulated 10 Hershey's kisses

Center for Substance Abuse Treatment. *Substance Abuse: Clinical Issues in Intensive Outpatient Treatment.* Treatment Improvement Protocol (TIP) Series 47.

Harm Reduction

Harm reduction is a set of practical strategies and ideas aimed at reducing negative consequences associated with drug use. Harm Reduction is also a movement for social justice built on a belief in, and respect for, the rights of people who use drugs.

Harm reduction coalition https://harmreduction.org/about-us/principles-of-harm-reduction/

Harm Reduction is also

Part of the continuum of care

Relationship building

Treatment

Harm Reduction is not

What we do when nothing else works

Harm Reduction Practices: Methamphetamines

Safe injecting:

- Clean needles/rigs (including don't share filters, cookers)
- Don't use alone
- Use needles bevel up
- Use a filter whenever possible
- Test for fentanyl
- Clean water

Collins S et al. Intl Jnl of Drug Policy 2019
Thakarar K, Weinstein ZM, Walley AY. *Postgrad Med J*. 2016;92(1088):356–363.

Harm Reduction Practices: Methamphetamines

Hydration
Toothbrushes
Condoms
Naloxone

Patient Centered:

- What harms most concern you?
- What do you do to prevent overdosing?

Collins S et al. Intl Jnl of Drug Policy 2019
Thakarar K, Weinstein ZM, Walley AY. *Postgrad Med J*. 2016;92(1088):356–363.

Meds for MA/A Use Disorder

- No FDA-approved meds for MA/A use disorder (MUD)
- Lots of research looking into possible treatments
- Will review published findings from 2 recent trials
- Systematic reviews of medications for MUD

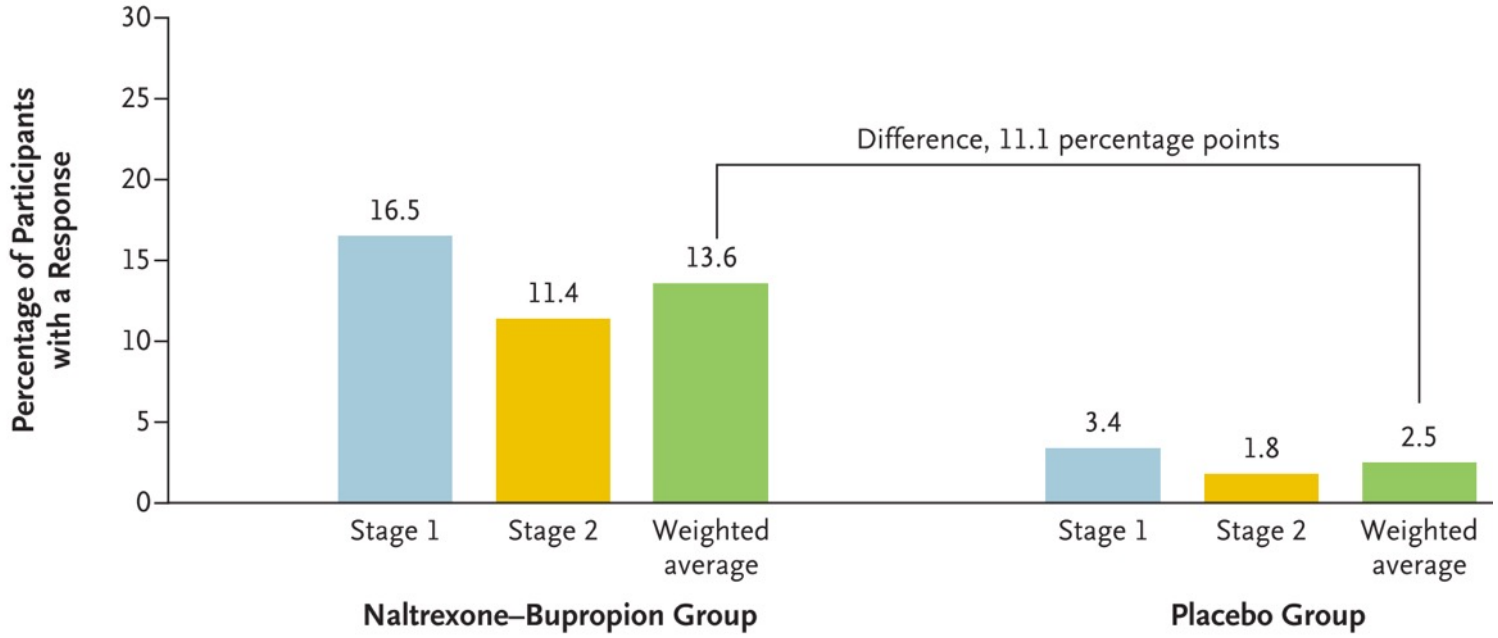
Mirtazapine

- FDA-approved antidepressant
- Main side effects weight gain and somnolence
- Mixed monoamine agonist-antagonist
- Cisgender men & transgender women sex w/ men
- Double blind RCT of 120 participants
- ↓ in methamphetamine + UDT despite low adherence

Coffin P et al, JAMA Psychiatry 2019

Naltrexone IM +Bupropion

- Large multi-center RCT, two-stage, sequential parallel comparison design.
- Number needed to treat – 9, low treatment improvement



Trivedi M, et al NEJM 2021

Sufficient Evidence of No Benefit

- Dopamine agonists (levodopa, cabergoline, pramixpexole)
- Antipsychotics – aripiprazole
- Antidepressants – SSRIs
- Anticonvulsants/muscle relaxants
- Varenicline

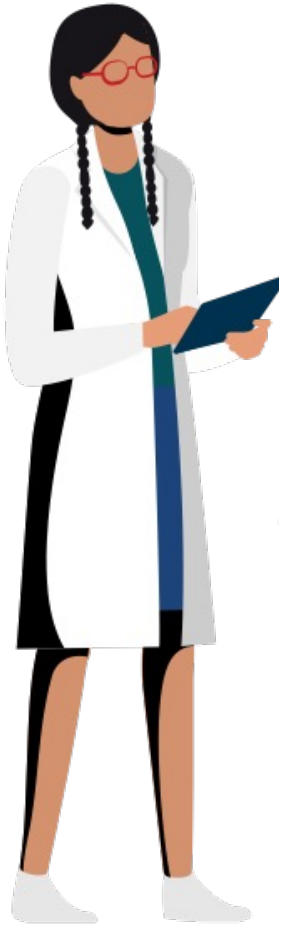
Briones M et al. Drug Alcohol Depend 2018
Ronsley C et al PLoS ONE 2020
Chan B et al Addiction 2019

Insufficient Evidence of Benefit

- Prescription psychostimulant agonist therapy – methylphenidate, modafinil, lisdexamphetamine, dextroamphetamine, mixed amphetamine salts
- Antidepressants – non-SSRI (mirtazapine, bupropion)
- N-acetylcysteine (NAC) – acts as a physiological reservoir of neuronal glutamate

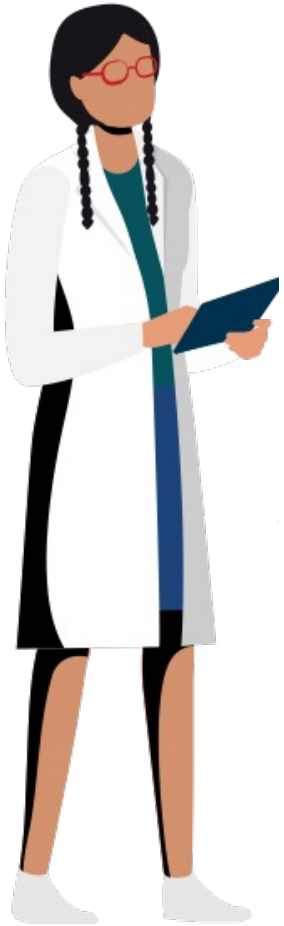
Coffin P et al JAMA Psychiatry 2020
Ronsley C et al PLoS ONE 2020
Tardelli VS et al Psychopharmacology 2020
Chang C-T et al Clin Psychopharmacol Neurosci 2021

Summary



- Methamphetamine use and use disorders are escalating
- There are effective behavioral interventions
- Harm reduction is treatment
- Medications are being investigated

Summary



- Questions?
- Thoughts?