



Management of Substance Use Disorders in Primary Care: Clinical Application

Jessica Gregg, PhD, MD
Indian Country ECHO Lead Faculty
Chief Medical Officer, Fora Health



Jonathan L. Robbins, MD, MS
Indian Country ECHO Lead Faculty
Assistant Professor of Medicine, Oregon Health &
Science University



Zeina Saliba, MD
Indian Country ECHO Lead Faculty
Addiction Medicine, Family Medicine &
Psychiatry

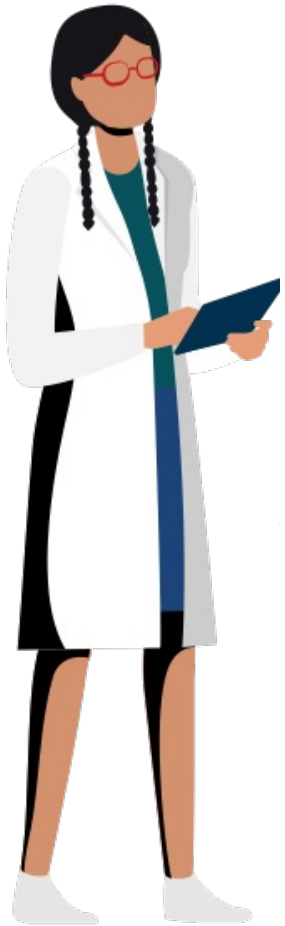
Indian Country ECHO: Ending the Syndemic



Substance Use Disorders: Brains, Behavior, and Diagnosis

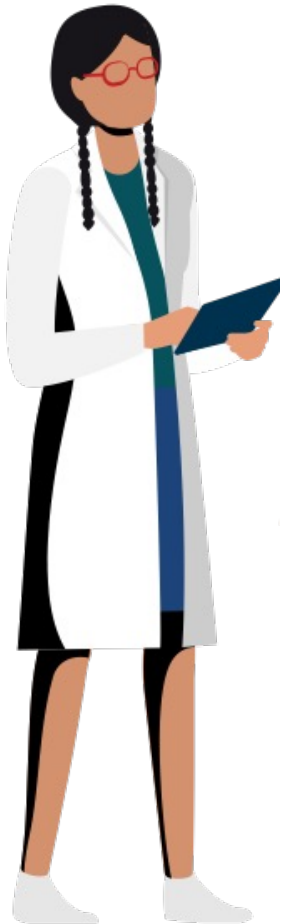


Objectives

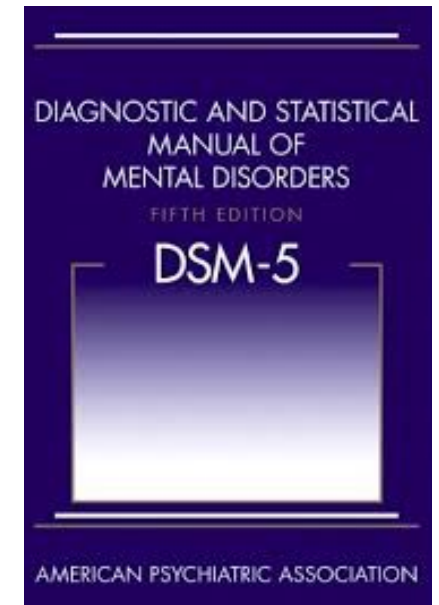


1. Review the diagnostic criteria for substance use disorders
2. Understand (some of) how substance use disorders develop

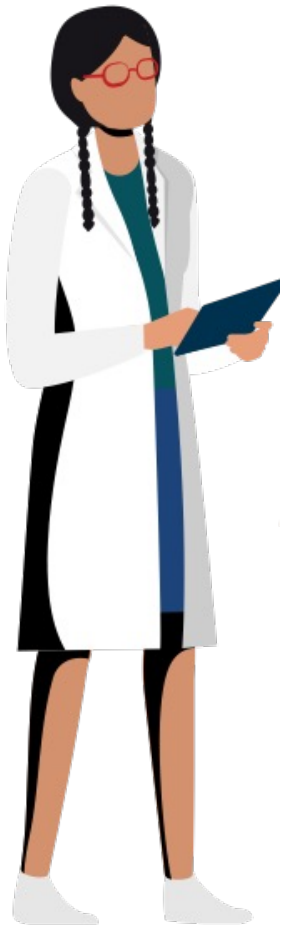
DSM 5



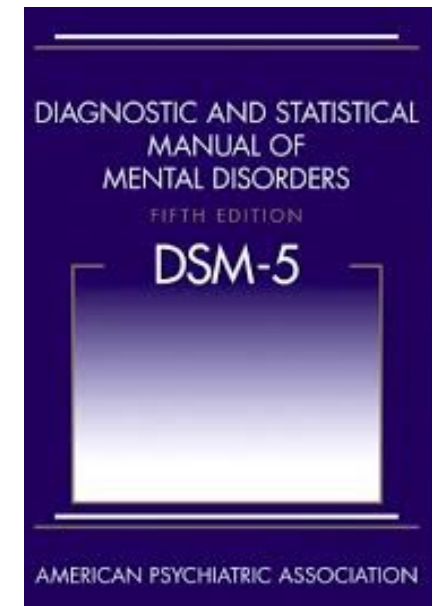
1. DSM 5
2. Diagnostic and Statistical Manual of Mental Disorders
3. 11 criteria
4. Craving/Compulsion/Consequences/Loss of Control



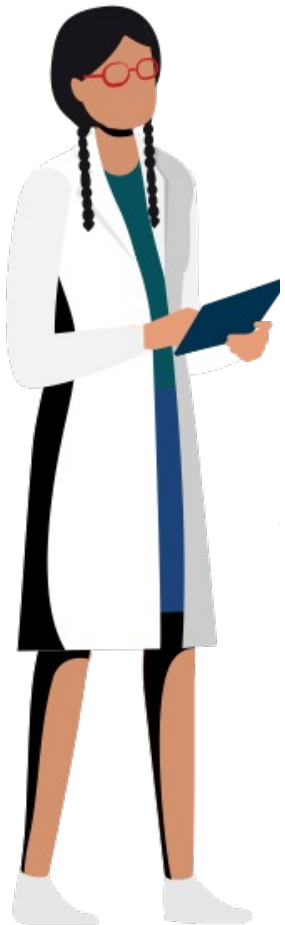
DSM 5: Substance Use Disorder



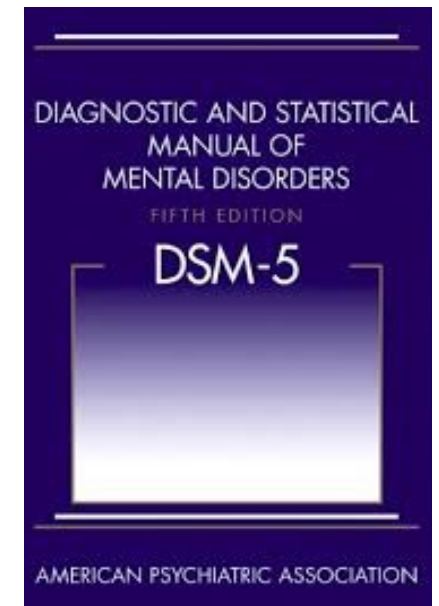
- Taking in larger amounts or for longer than intended
- Unsuccessful efforts to cut down
- Spending a lot of time obtaining the substance
- Craving or a strong desire to use the substance



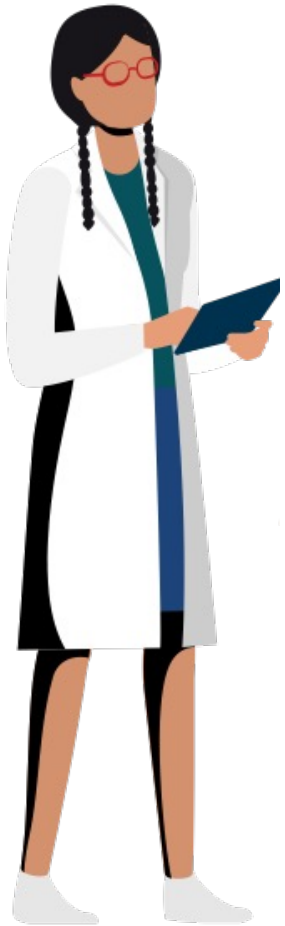
DSM 5: Substance Use Disorder



- 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

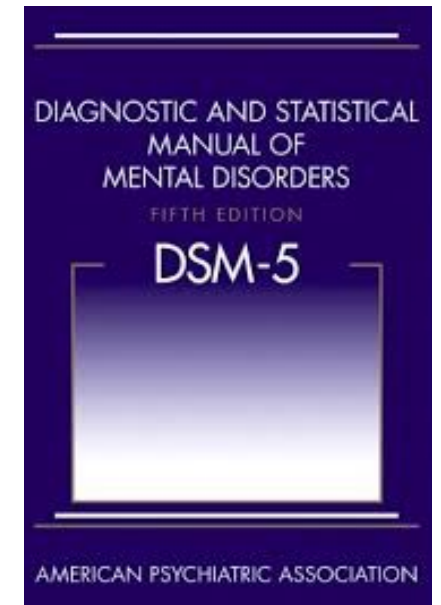


DSM 5: Substance Use Disorder



Tolerance*

Withdrawal*



Substance Use Disorder



2—3

mild disorder

4—5

moderate disorder

6+

severe disorder

Substance Use Disorder



Substance Use Disorder

Diagnosis



Addict

Label/Accusation

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

Substance Use Disorder

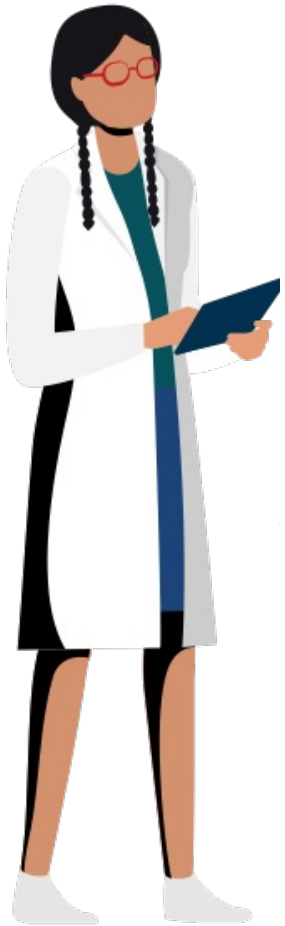


Recovery Dialects
The words we use matter.

Positive		Negative
Person who uses substances		Substance Abuser
Recurrence of Use		Relapse
Pharmacotherapy		Medication-Assisted Treatment
Accidental Drug Poisoning		Overdose
Person with a Substance Use Disorder		Addict Alcoholic Opioid Addict

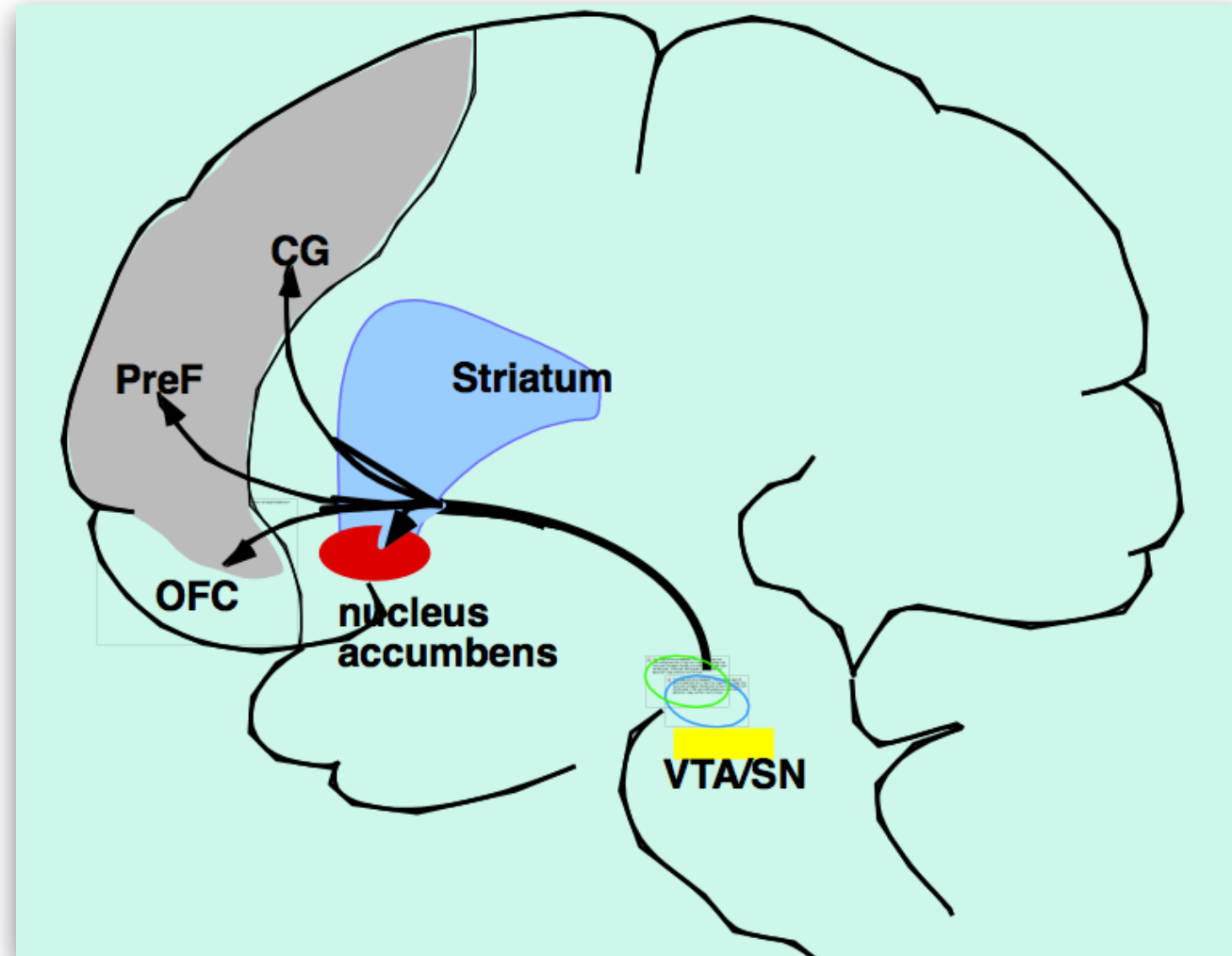
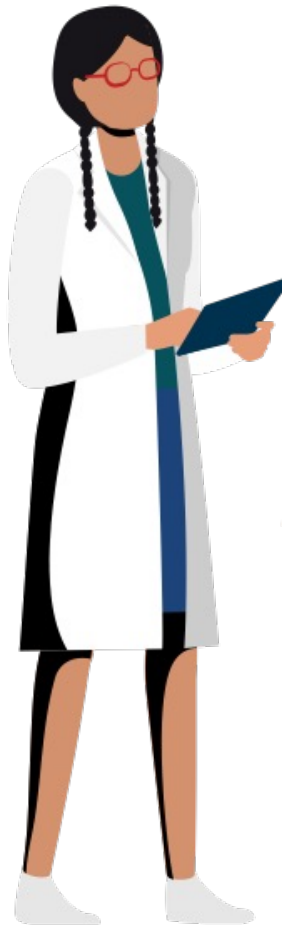
While some negative language is okay to use in mutual aid meetings, its use should be avoided in public, when advocating and in journalism.

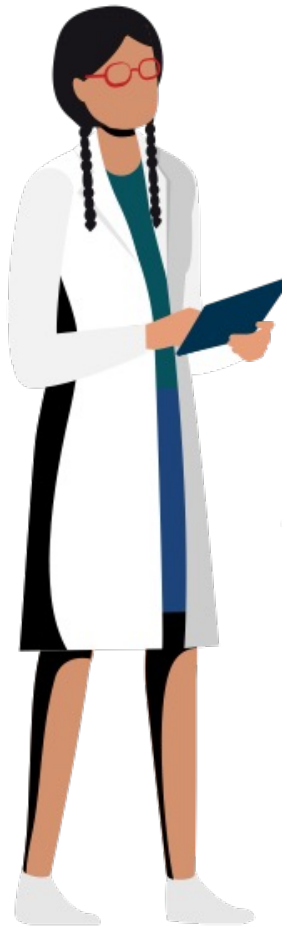
Objectives



1. Review the diagnostic criteria for substance use disorders
2. Understand (some of) how substance use disorders develop

Mesolimbic Dopamine System

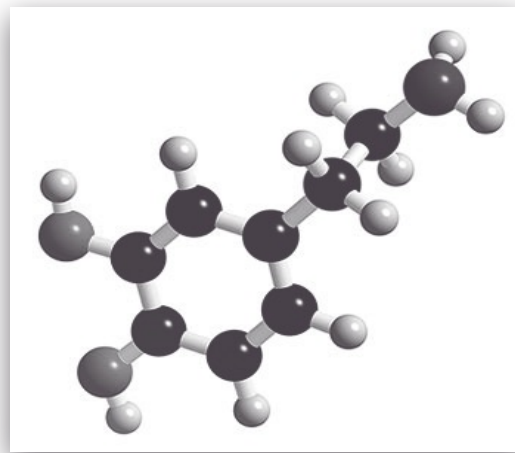




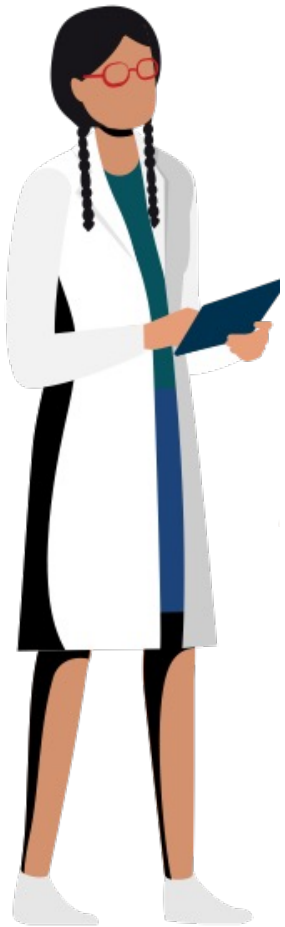
1950s : electrodes



1970s: Dopamine



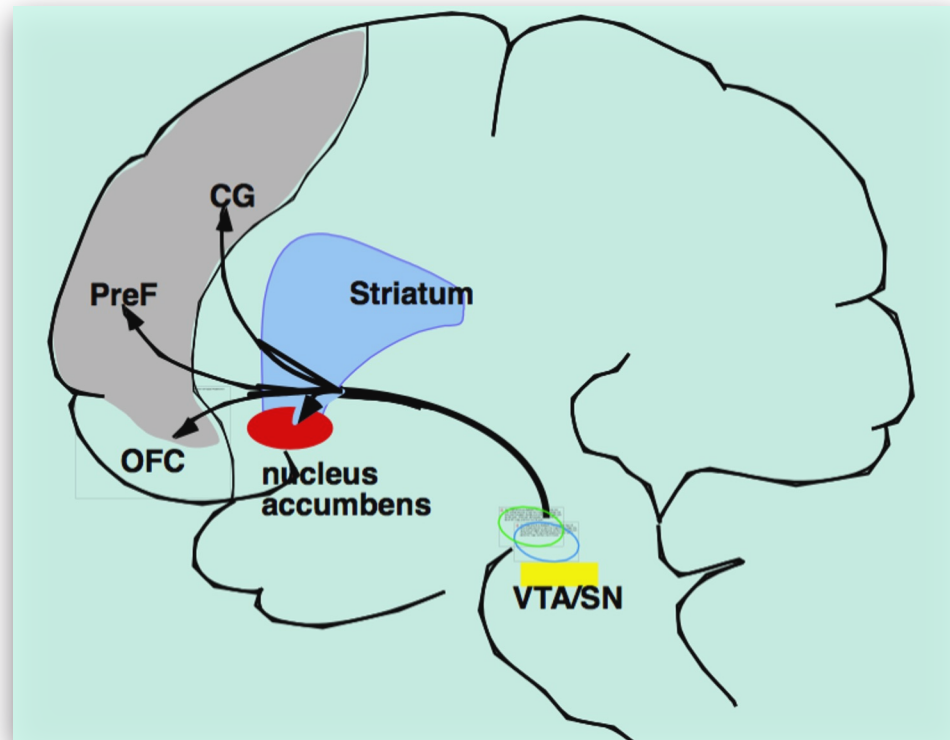
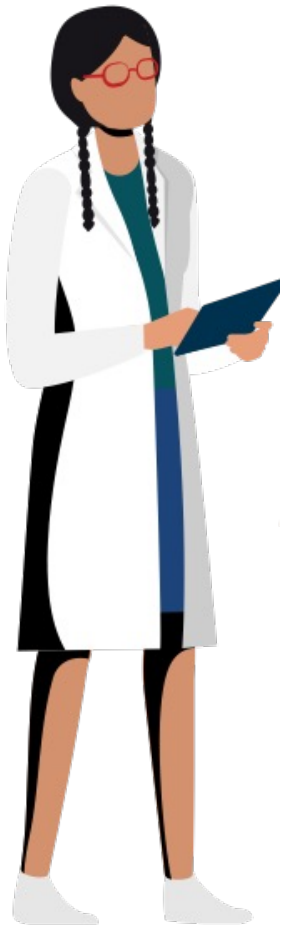
Desire and Drives



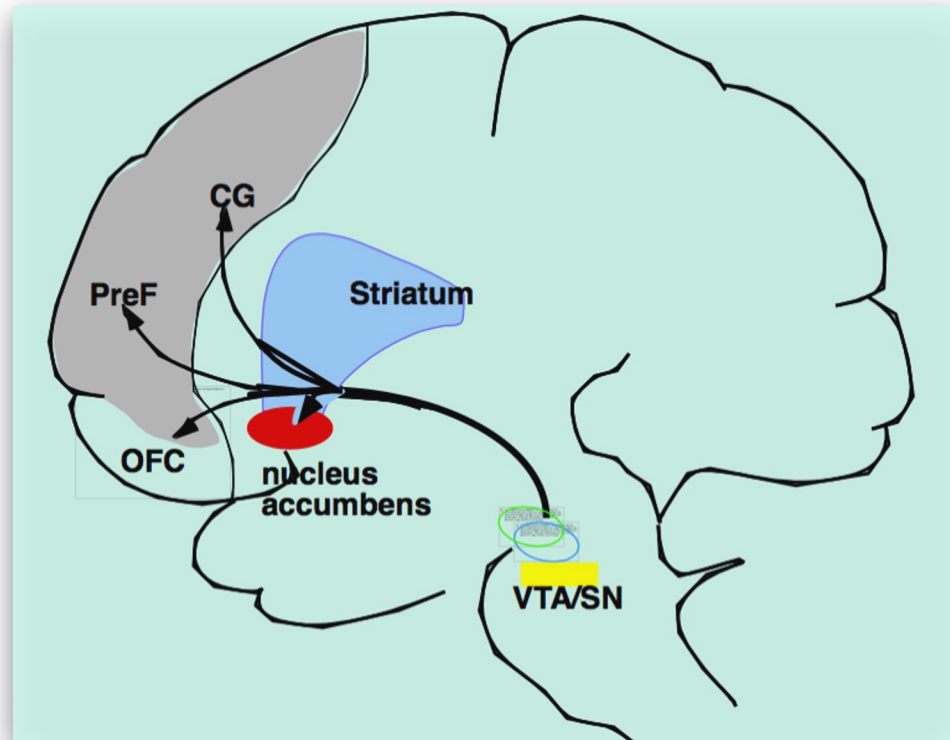
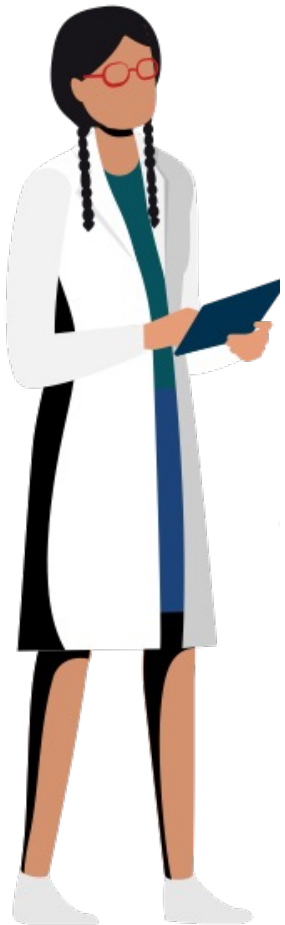
The use of dopamine neurons to shape responses to rewards is seen in simple organisms like worms and flies.

It evolved millions of years ago.

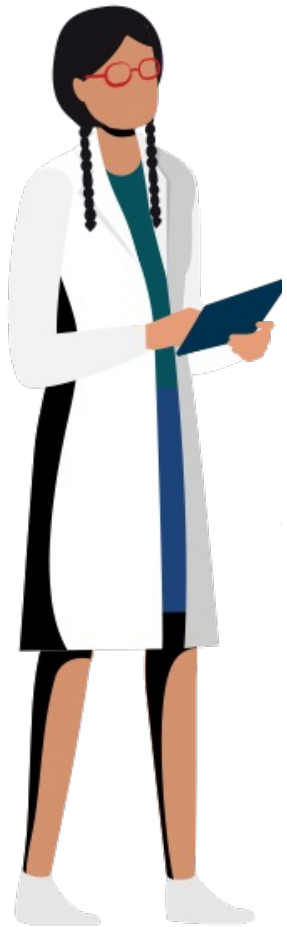
Dopaminergic impulses tell organisms to move toward reward (warmth, food, moisture)



- 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

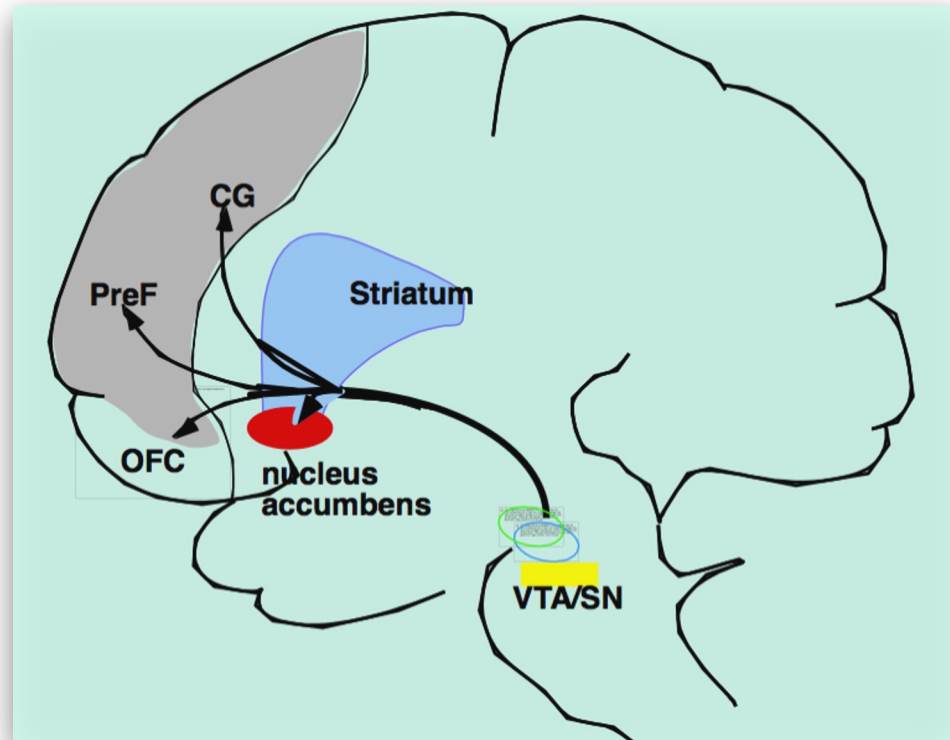
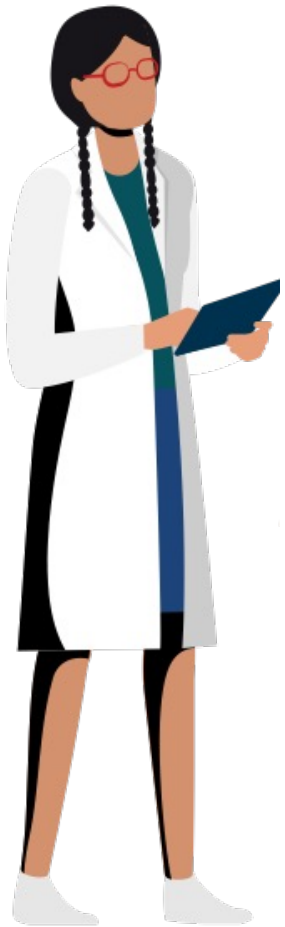


- In humans, those dopaminergic impulses travel through the NAC
- Mediates responses to food, sex, social interactions
- DA projections from VTA to NA release DA and tell the NA to go for it!
- Connects with memory and emotional centers so it can be repeated in the future



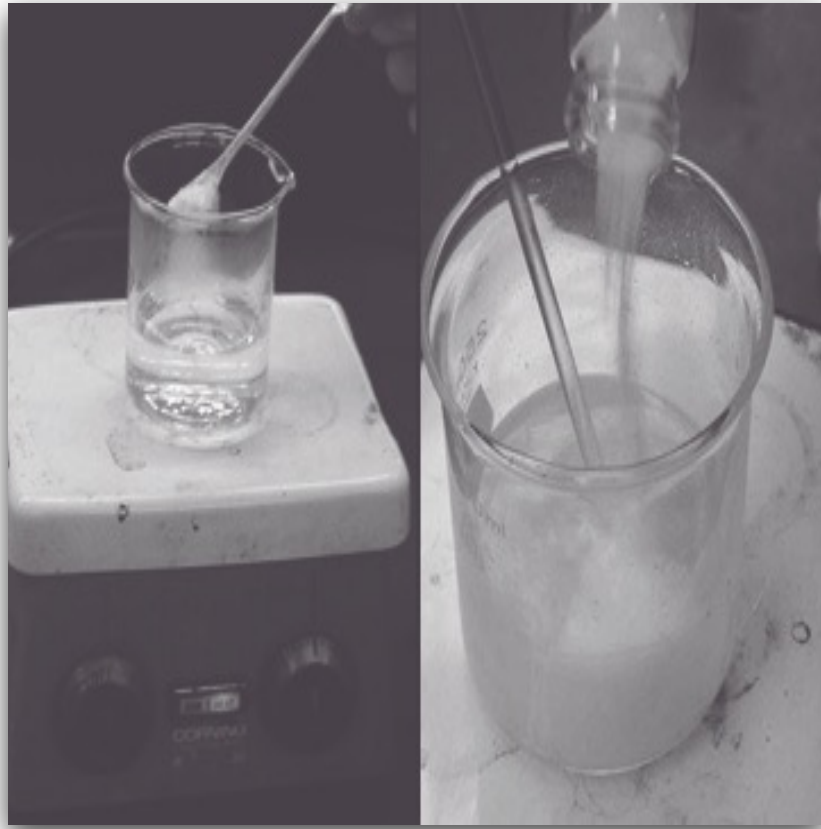
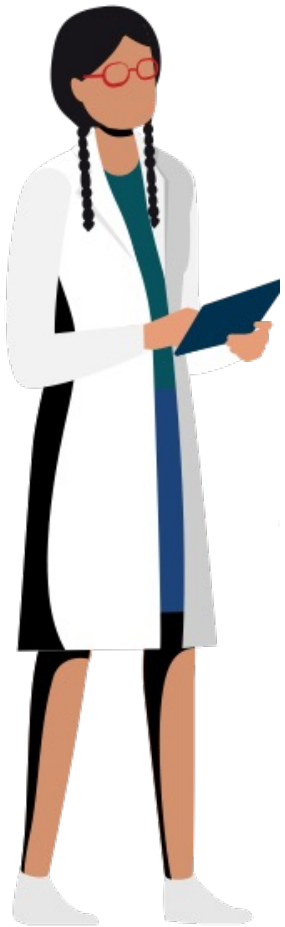
- Hungry cavewoman eats berry. It is sweet and pleasurable
- Brain pays very close attention to what she had to do to get that berry
- Sees the berry bush again, more likely to remember the berry, even craves the berry. Eats the berry.
- Lives

So, Part of Addiction is Craving



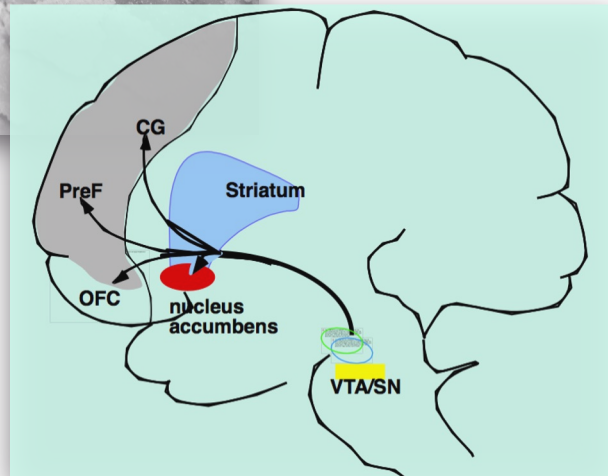
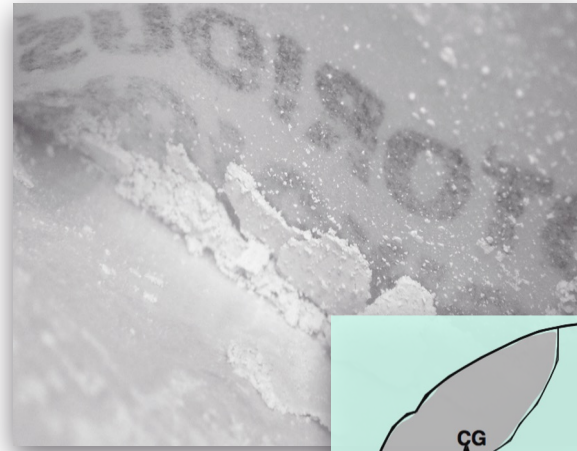
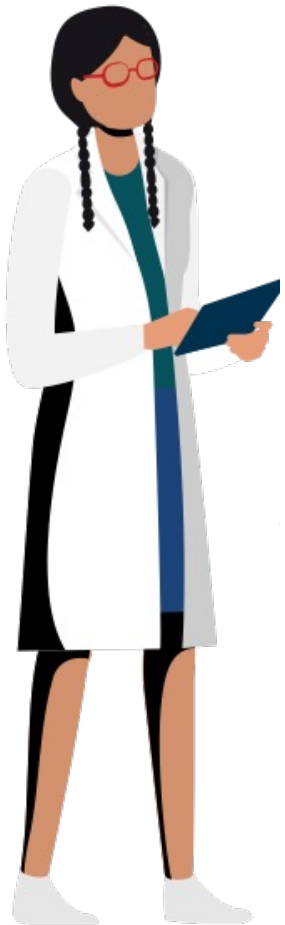
- Addiction taps into this normal brain process
- All addictive drugs activate this pathway
- Drug experience is deeply linked to memory and emotion

So, Part of Addiction is Craving



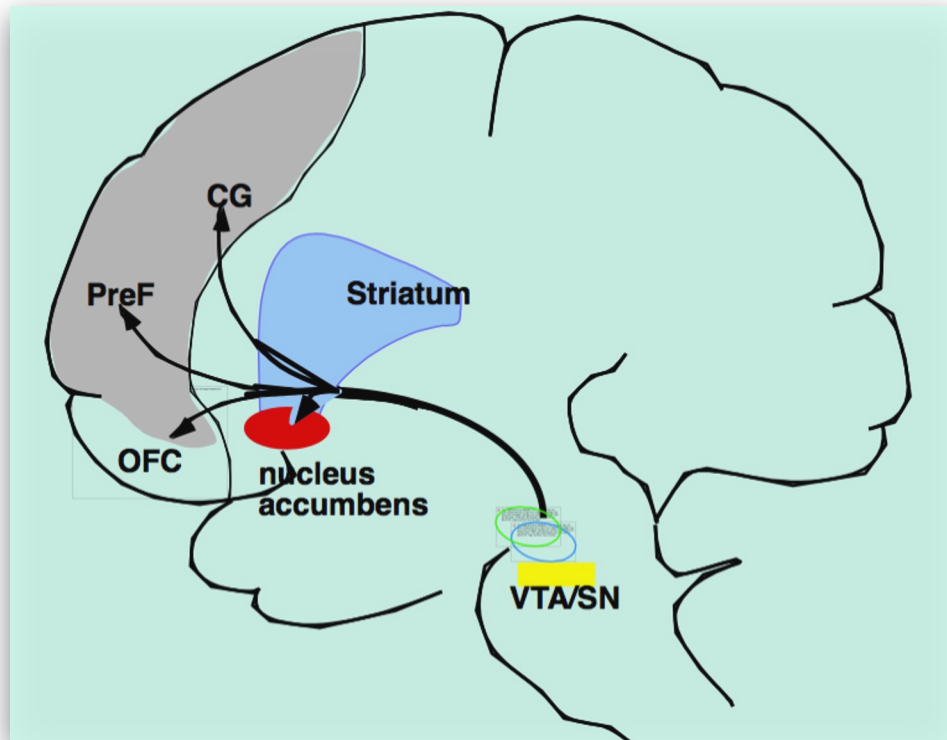
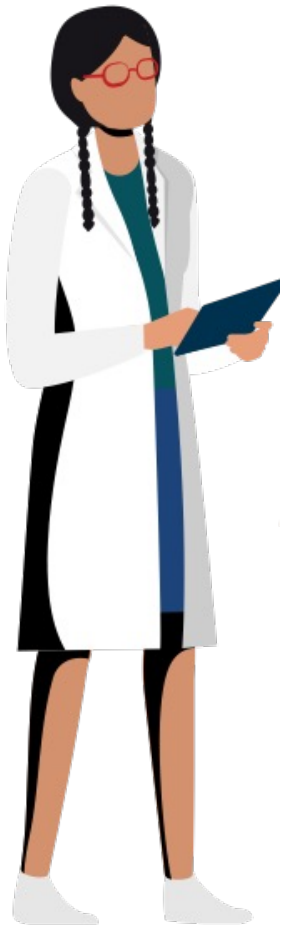
- People, places, things associated with drug use can trigger cravings
- Even when images associated with drug use are shown too rapidly to be “seen” they still trigger cravings

Another Part is Liking



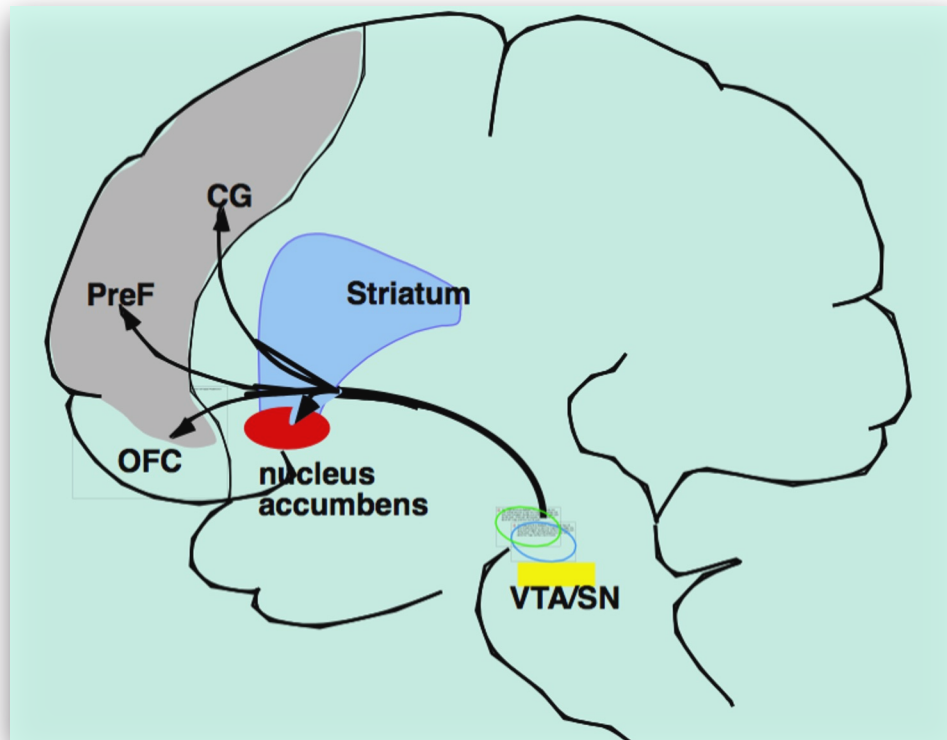
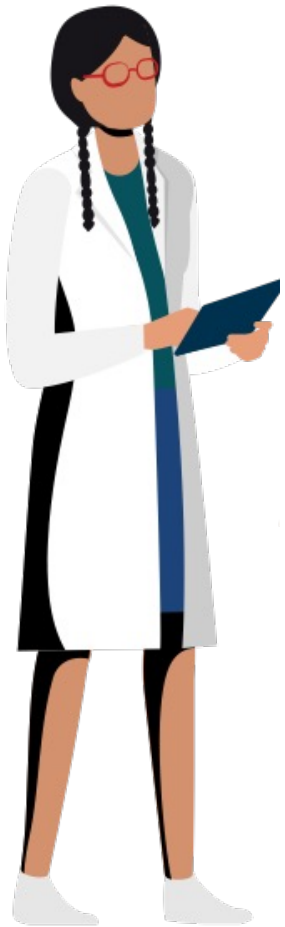
- Opioids: activate DA receptors
- Also activate opioid receptors in NA and produce feeling of satiety, soothing, comfort.

Dysregulation

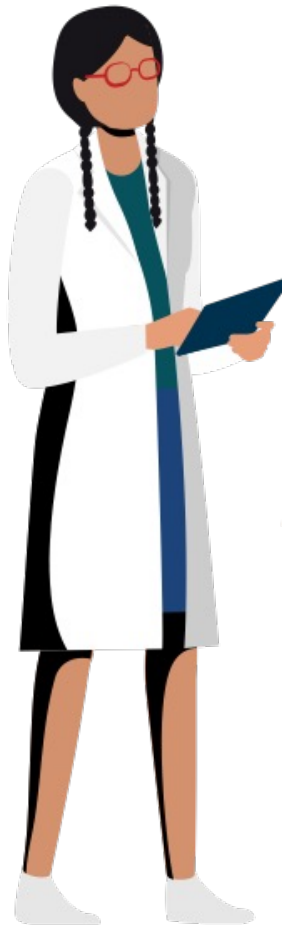


- Dysregulation: impaired ability of the front of the brain to regulate what is going on in the older regions of the brain.
- Prefrontal cortex helps determine the risks and benefits of behaviors and make rational choices.

Dysregulation

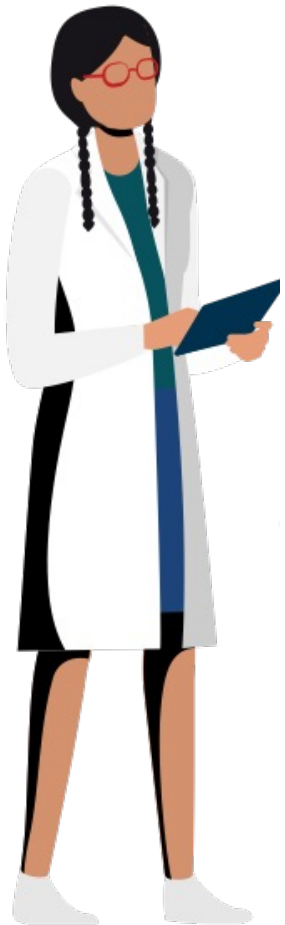


- Prefrontal cortex is newer and more complicated. It needs a little time to weigh in.
- Repeated activation of the VTA to NAC track slowly strengthens those connections. Habits get hard wired, fast and automatic



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

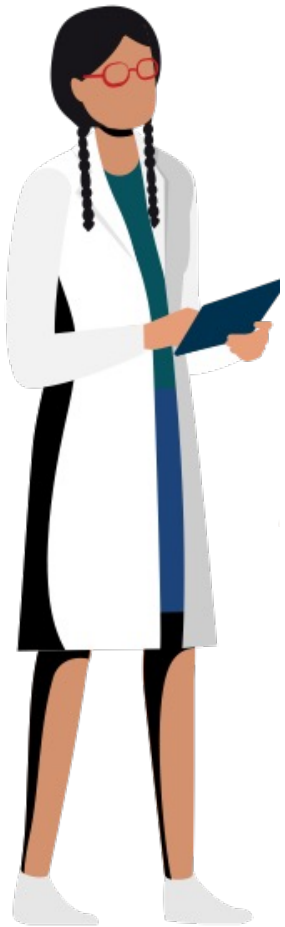
Another complicating factor:



D1: Activate the nucleus accumbens, cause us to act & are responsive to big pleasure surges.



D2: Slow down decision making, allow the frontal cortex to step in. Responsive to smaller pleasures.

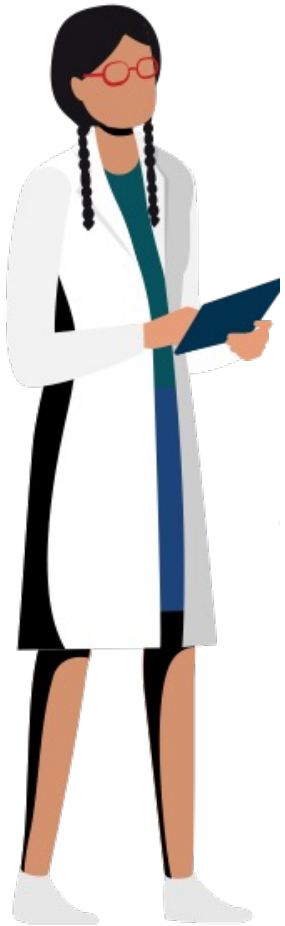


Big dopamine surges activate the D1 receptors and cause the D2 receptors to be reabsorbed.

Repeated drug use speeds up the Go! in the nucleus accumbens and inhibits the stop.

Like stepping on brakes of car barreling down a hill only to discover that brakes have been disconnected.

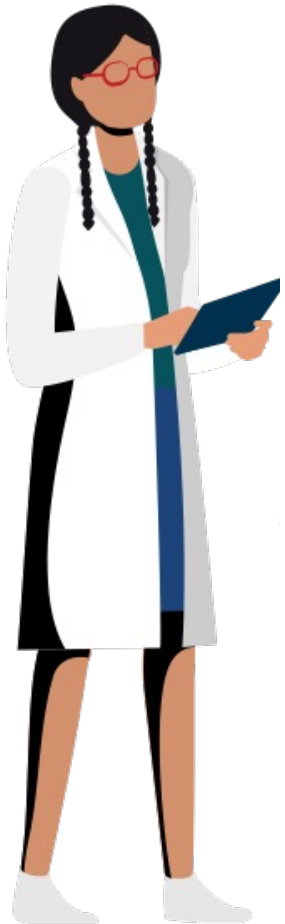
Dysregulation



- Little pleasures like family, friends, jobs well done, tasks accomplished, provide just enough dopamine to activate the D2 receptors and strengthen the impulses that slow things down.
- Medications to decrease craving and attenuate withdrawal symptoms
- Behavioral interventions that entrain different habits



Conclusion



Diagnose substance use disorders with the DSM 5 criteria



Addiction taps into normal brain processes



Use despite negative consequences is part of addiction



Substance use disorders are treatable.

Medications for Opioid Use Disorder (MOUD)



Objectives



- The context: opioid epidemic and the rise of fentanyl
- Review medications for the treatment of OUD
 - Methadone
 - How it works
 - Regulations (and a little context)
 - 72-hour rule
 - Buprenorphine
 - How it works
 - Regulations and regulatory changes
 - How to administer and prescribe
- XR - naltrexone

Objectives



- **The context: opioid epidemic and the rise of fentanyl**
- Review medications for the treatment of OUD
 - Methadone
 - How it works
 - Regulations (and a little context)
 - 72-hour rule
 - Buprenorphine
 - How it works
 - Regulations and regulatory changes
 - How to administer and prescribe
- XR - naltrexone

Fentanyl



Photo by © Shutterstock/Sherry Yates Young [↗](#)

Pharmaceutical fentanyl synthesized in 1960's

Fentanyl



Photo by © Shutterstock/Sherry Yates Young [↗](#)

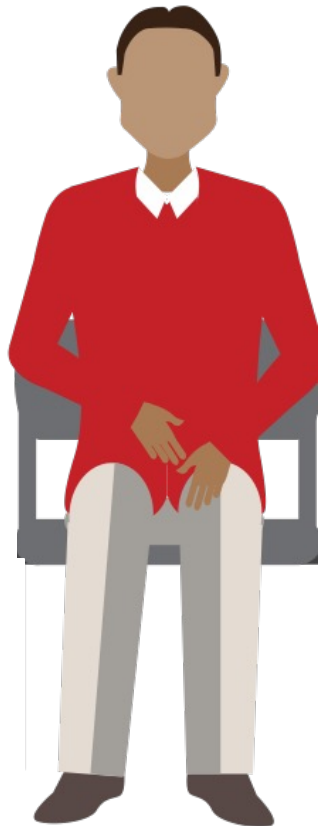
Overdose deaths from **non-pharmaceutical fentanyl** were first seen in mid-2000's, but rare before mid 2010's

Use has progressively increased and is now widespread

In almost all states, fentanyl is primary illicit opioid used and is the leading cause of opioid related deaths

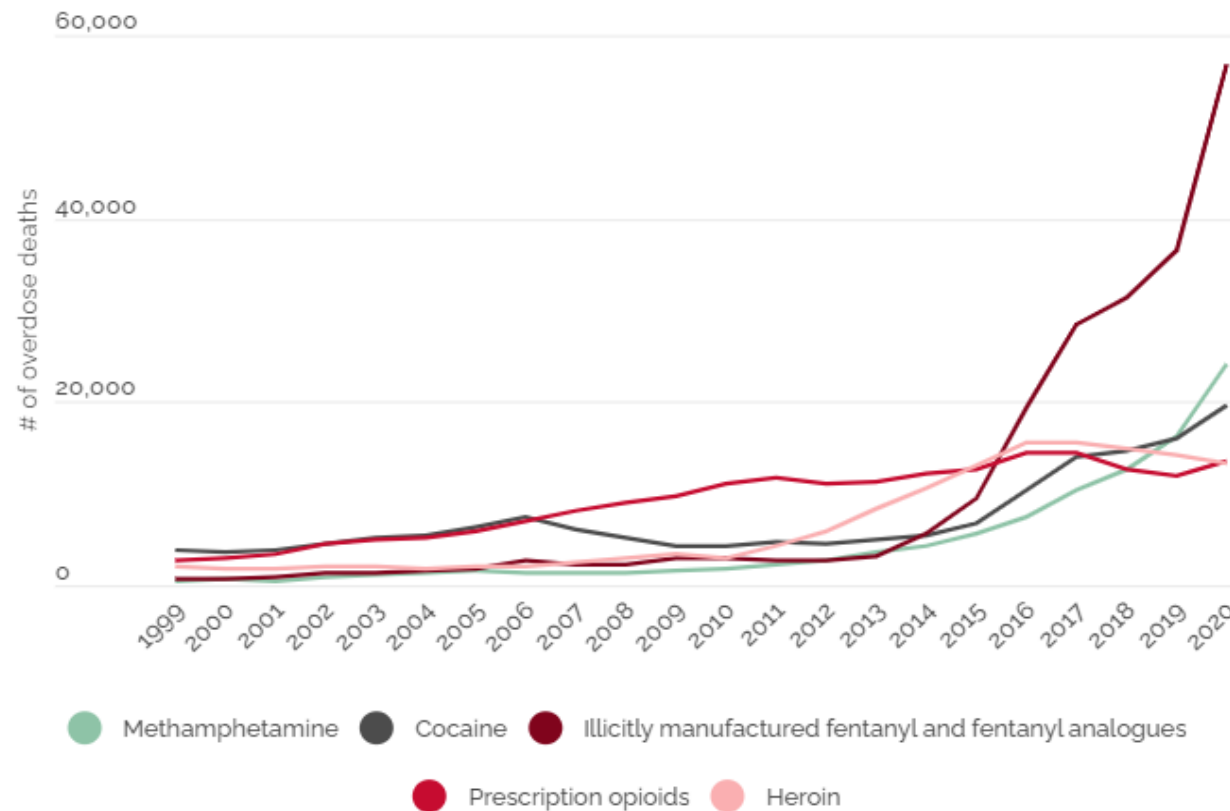
Over 200 identified analogs with more in the pipeline

Fentanyl



All Overdose Deaths 1999-2020

Overdose Deaths by Drug 1999-20



(source)

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

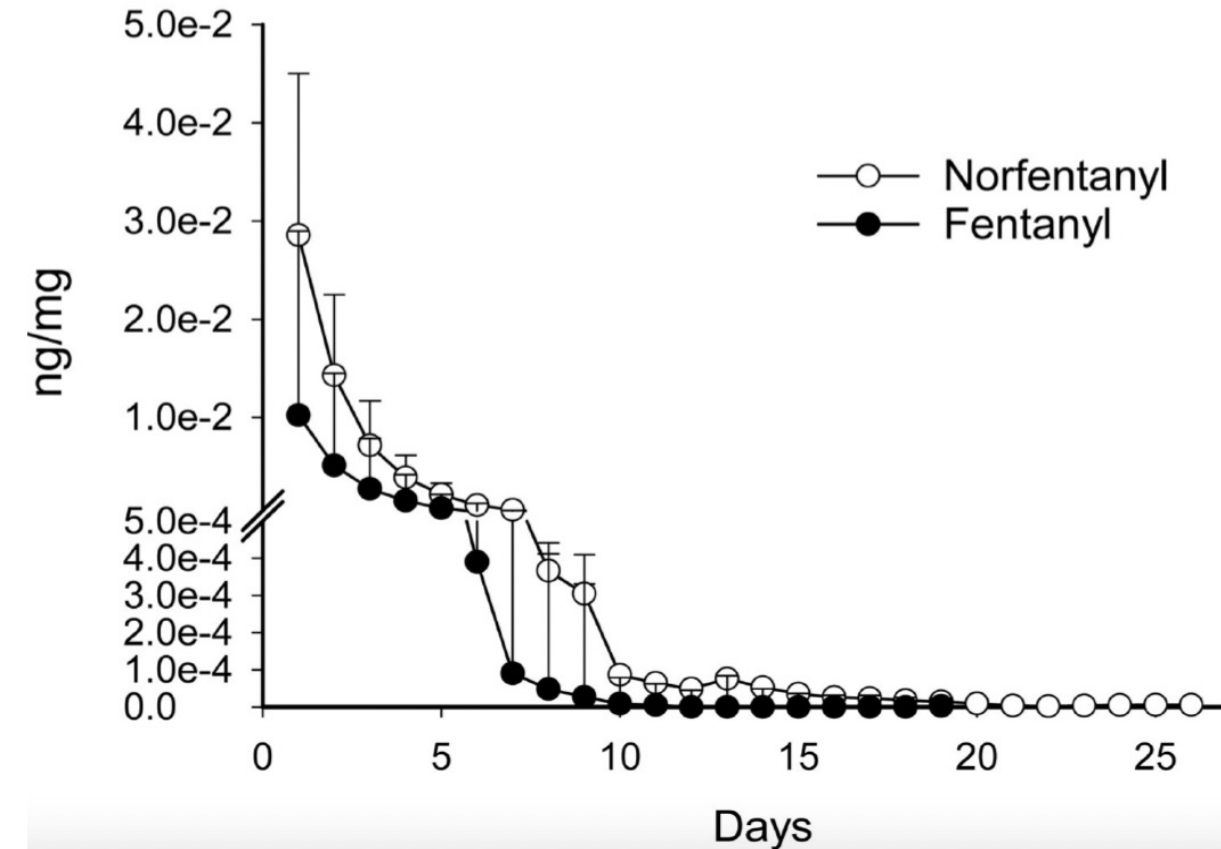
Fentanyl



- 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



Fentanyl



With regular use

7.3 days=mean clearance for fentanyl⁷

13.3 days=mean clearance for norfentanyl

²Volkow 2021

⁶Ahmed et al. 2020

Summary



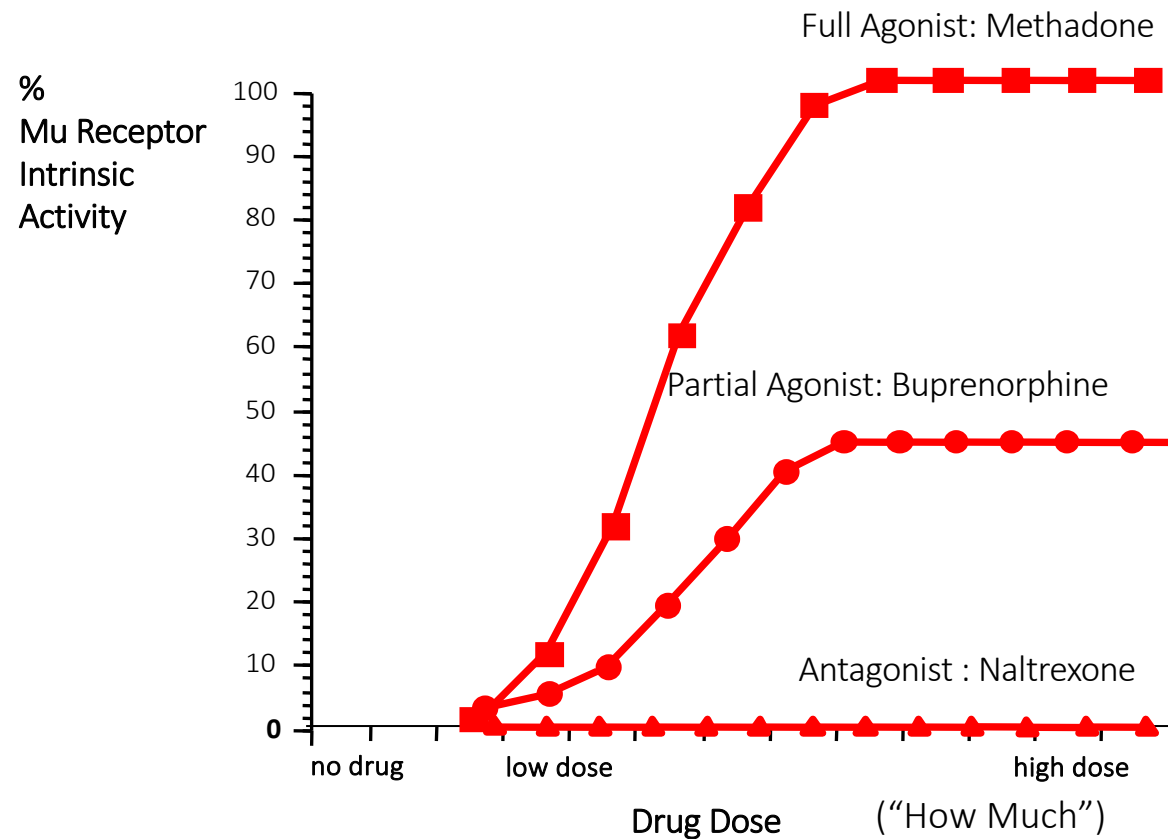
- Fentanyl is driving our current overdose crisis
- It is highly potent
- It is hard to detect
- Its effects wear off quickly, but it stays in the body for a long time

Objectives

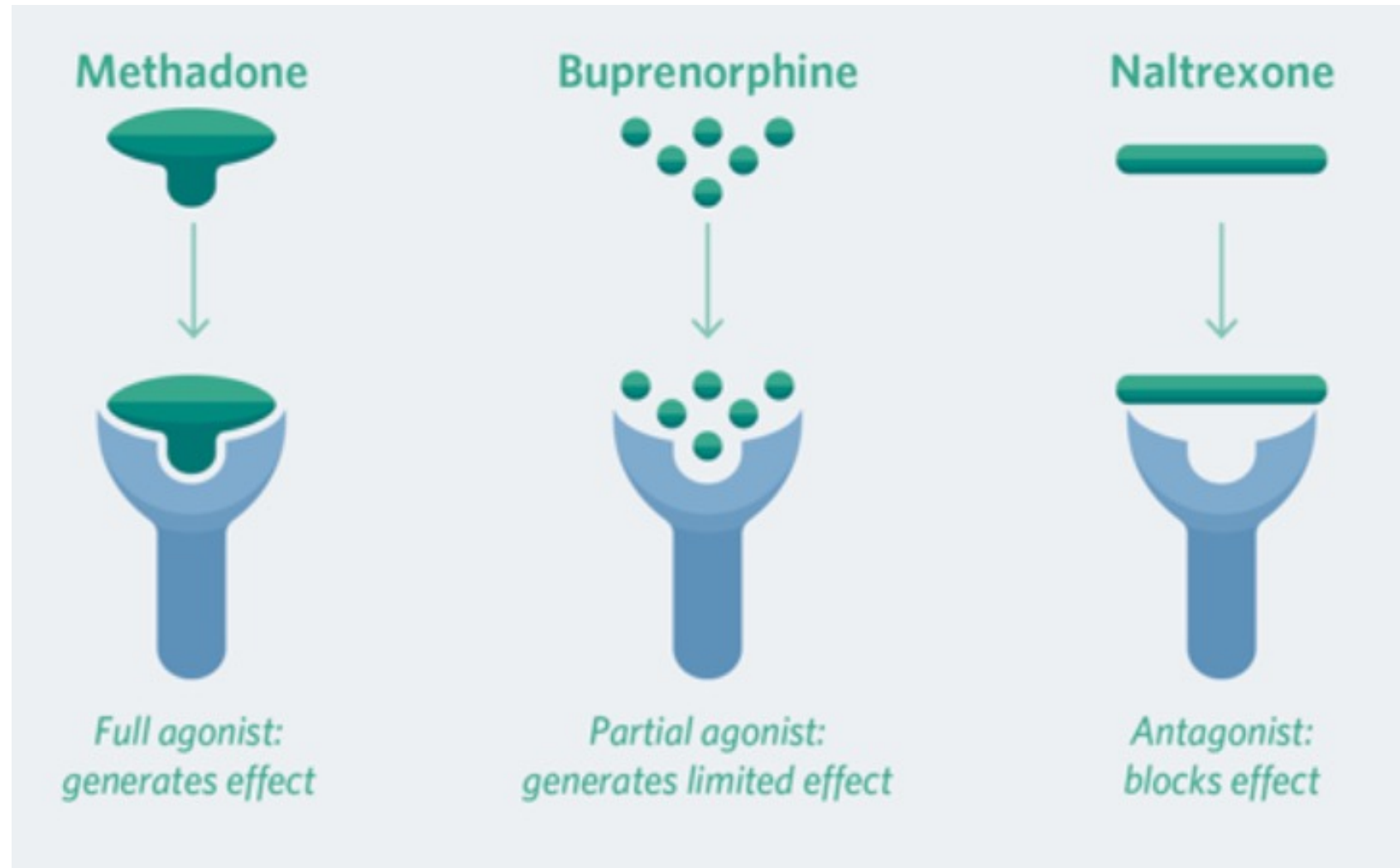


- The context: opioid epidemic and the rise of fentanyl
- **Review medications for the treatment of OUD**
 - Methadone
 - How it works
 - Regulations (and a little context)
 - 72-hour rule
 - Buprenorphine
 - How it works
 - Regulations and regulatory changes
 - How to administer and prescribe
- XR - naltrexone

Pharmacotherapy for Opioid Use Disorder



Pharmacotherapy for Opioid Use Disorder



Objectives



- The context: opioid epidemic and the rise of fentanyl
- Review medications for the treatment of OUD
 - **Methadone**
 - How it works
 - Regulations (and a little context)
 - 72-hour rule
 - Buprenorphine
 - How it works
 - Regulations and regulatory changes
 - How to administer and prescribe
- XR - naltrexone

Methadone

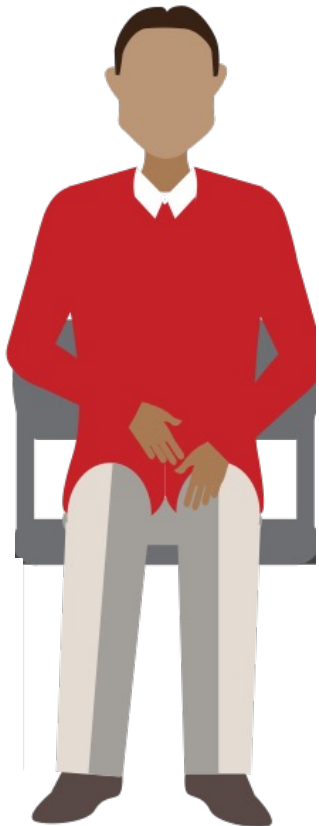


Methadone

Methadone is an opioid.

Opioid: synthetic or semisynthetic substance that mimics opiates.

Opiate: natural substance derived from....





Year	Milestone
1970	Methadone is approved by the FDA for <u>detoxification</u>
1973	Methadone is approved by the FDA for <u>maintenance</u>
1974	Opioid Treatment Programs (OTP's) able to dispense Methadone for maintenance treatment
1984	Oral Naltrexone is approved by the FDA
2000	Drug Addiction Treatment Act of 2000 (DATA 2000) allowed qualified physicians to offer Office Based Opioid Treatment (OBOT)
2002	Buprenorphine is approved by the FDA
2010	Extended-release injectable naltrexone is approved by the FDA
2016	Comprehensive Addiction and Recovery Act (CARA) - Allows Nurse Practitioners and Physician Assistants to become eligible to prescribe buprenorphine for treatment of opioid use disorder



HIGHLY REGULATED!!!!

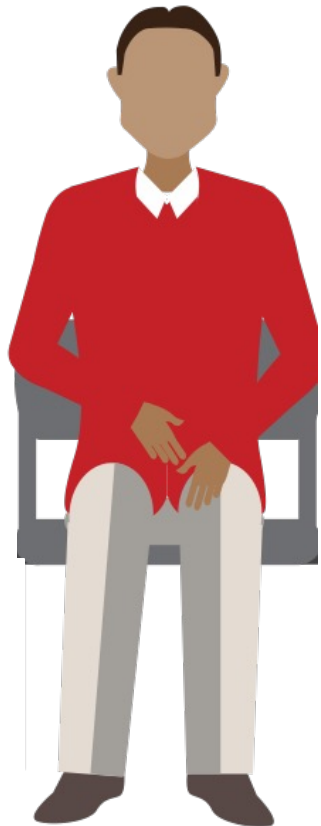
- Attend clinic daily for a minimum of 3 months.
- After 90 days, may take home one dose if:
 - attending groups
 - participating in educational, vocational, or homemaking activities
 - employment, education, or homemaking responsibilities are hindered by daily attendance may take home an extra dose.
- Not using
- No criminal activity
- Stable home environment
- Safe storage
- Counselor feels this will be beneficial to the patient



72-hour Rule



72-hour Rule



- (b) Nothing in this section shall prohibit a physician who is not specifically registered to conduct a narcotic treatment program from administering (but not prescribing) narcotic drugs to a person for the purpose of relieving acute withdrawal symptoms when necessary while arrangements are being made for referral for treatment. Not more than one day's medication may be administered to the person or for the person's use at one time. Such emergency treatment may be carried out for not more than three days and may not be renewed or extended.

<https://www.govregs.com/regulations/21/13>

[06.07](#)

Objectives

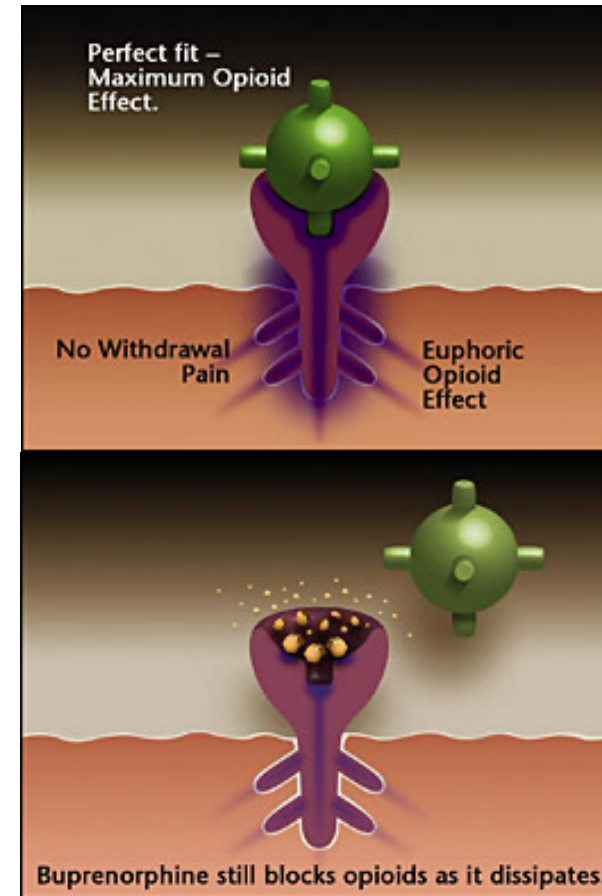
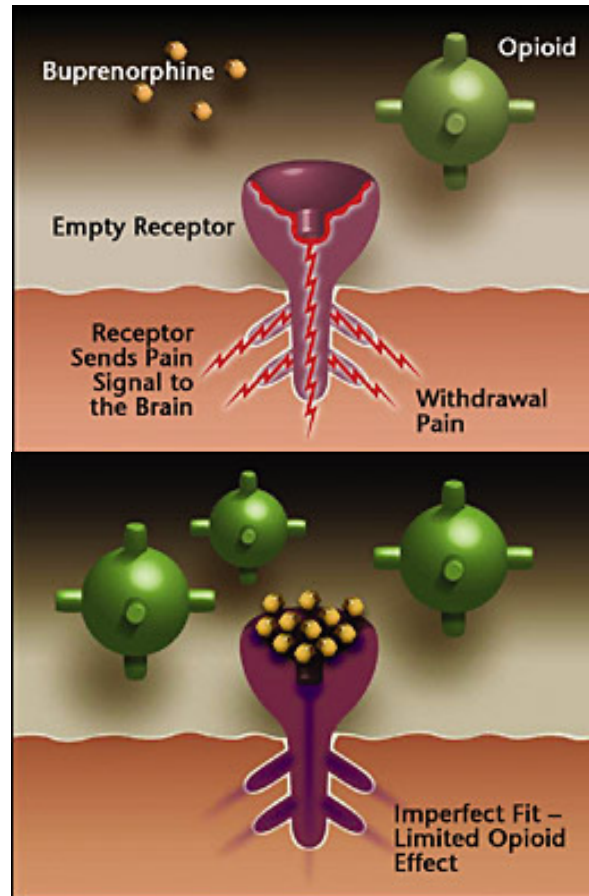


- The context: opioid epidemic and the rise of fentanyl
- Review medications for the treatment of OUD
 - Methadone
 - How it works
 - Regulations (and a little context)
 - 72-hour rule
 - **Buprenorphine**
 - How it works
 - Regulations and regulatory changes
 - How to administer and prescribe
- XR - naltrexone

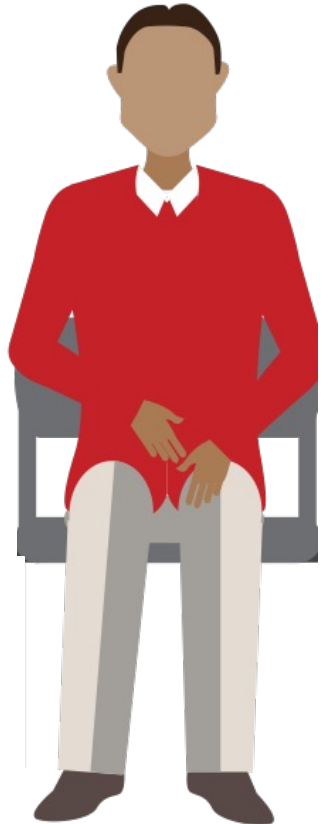
How it works



A View from the Receptors:



Available in two primary forms:



1. Buprenorphine monoprodut (Subutex)
2. Buprenorphine/Naloxone (Suboxone)

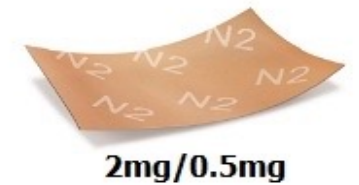


WHY?

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

New kid in town: buprenorphine XR (Sublocade)



Approved November 2017

Randomized control trial of three groups:

- Six injections of 300mg
- Two injections of 300mg then four of 100mg
- Placebo injections

Results:

- Mean abstinence: 41% for 300mg group;
- 42.7% for 300/100mg group
- 5% for placebo

New kid in town: buprenorphine XR (Sublocade)



Patient Centered Outcomes;

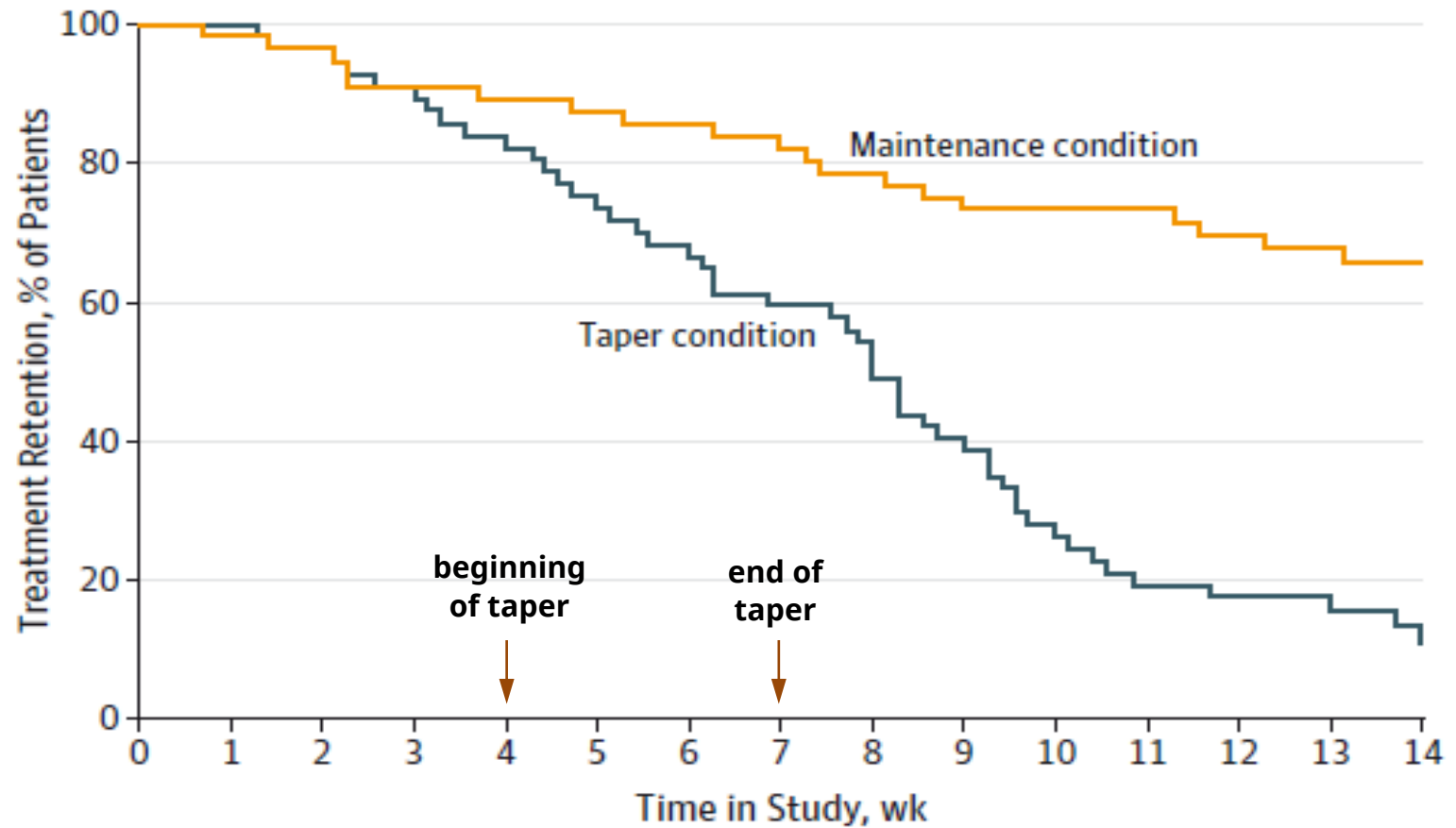
- Improved physical and mental health measures
- Increased employment
- Increased medication satisfaction
- Decreased health care utilization



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

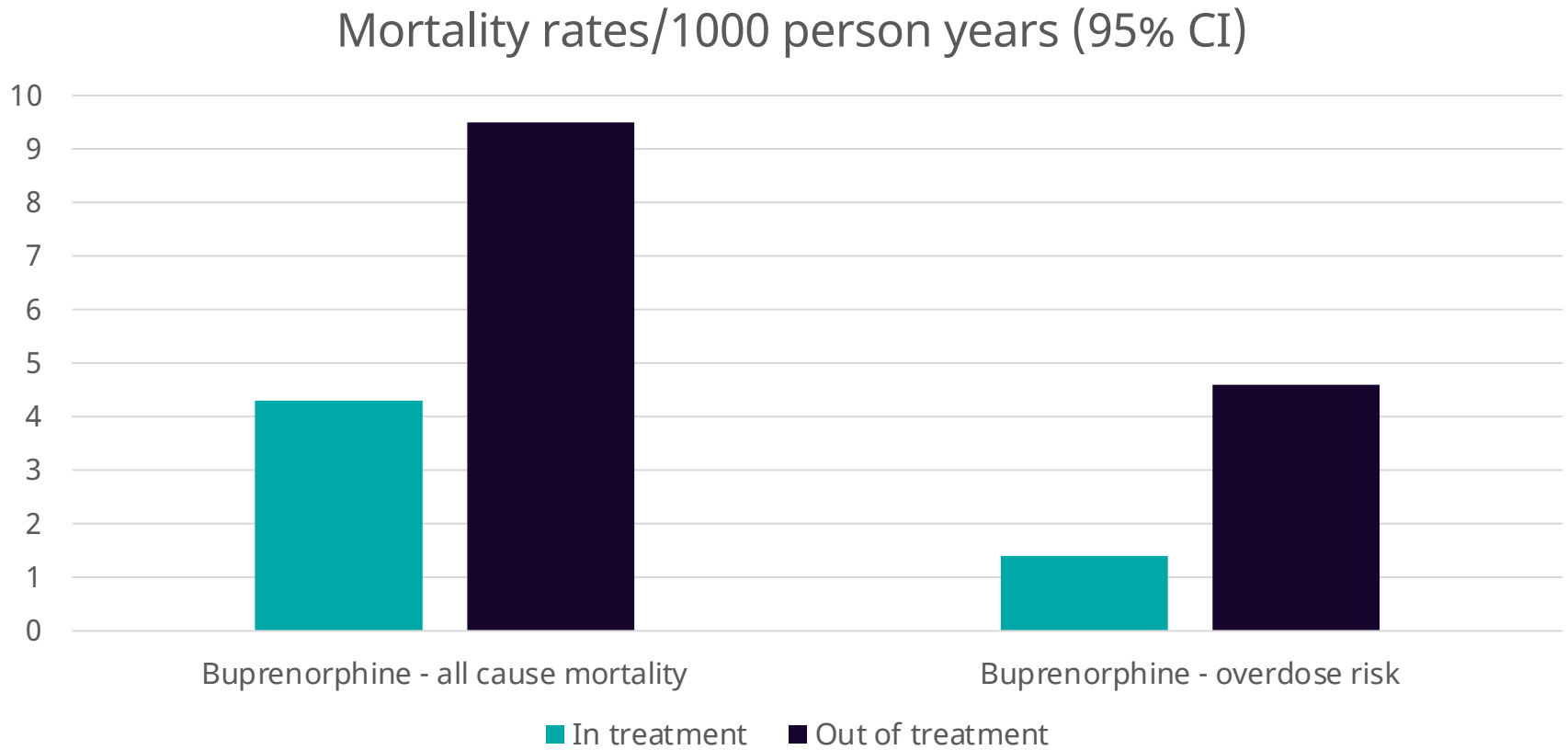
Buprenorphine: Maintenance vs. Taper





Patients taking buprenorphine for OUD are also significantly less likely to 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.

Regulations and regulatory changes





Year	Milestone
1970	Methadone is approved by the FDA for <u>detoxification</u>
1973	Methadone is approved by the FDA for <u>maintenance</u>
1974	Opioid Treatment Programs (OTP's) able to dispense Methadone for maintenance treatment
1984	Oral Naltrexone is approved by the FDA
2000	Drug Addiction Treatment Act of 2000 (DATA 2000) allowed qualified physicians to offer Office Based Opioid Treatment (OBOT)
2002	Buprenorphine is approved by the FDA
2010	Extended-release injectable naltrexone is approved by the FDA
2016	Comprehensive Addiction and Recovery Act (CARA) - Allows Nurse Practitioners and Physician Assistants to become eligible to prescribe buprenorphine for treatment of opioid use disorder

X Waiver



In 2021, the training requirements were modified such that prescribers treating 30 or fewer patients at any one time could forego the training. However, x-waivers were still needed.

X Waiver



In January 2023, as part of the Mainstreaming Addiction Treatment Act, the X-waiver was eliminated. All clinicians with a current DEA registration that includes Schedule III authority may now prescribe buprenorphine for OUD.

Coming Attractions



Effective June 30, 2023, the Medication and Access and Training Expansion Act requires all clinicians applying for or renewing their DEA license complete a one-time, 8-hour training on treating and managing patients with SUD. Certain providers, such as those board certified in addiction medicine or recent graduates with applicable curriculum, will not have to complete any additional training.

How to administer and prescribe



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 \square precipitated withdrawal

“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 <i>Measured after patient is sitting or lying for one minute</i> 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 piloerection of skin can be felt or hairs standing up on arms 5 prominent piloerection	
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	<p style="text-align: right;">Total Score _____</p> <p style="text-align: center;">The total score is the sum of all 11 items</p> Initials of person completing Assessment: _____	

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

Assess: 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
- Benzodiazepines

Srivastara, 2020; Kosten, 2019;
Kuzmaul 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



Teaching Tip

- Sublingual absorption is variable
- Good technique can increase absorption
 - Avoid eating or drinking just before administration
 - Hold medication under tongue until completely dissolved
 - Do a nursing check if patient unsure
 - Keep saliva in mouth for additional 5 min if possible
 - Then okay to either swallow or spit out saliva
 - Sit up for the process if possible
 - Tuck chin if possible
 - Don't talk!



Precipitated Withdrawal

- If opioid withdrawal appears shortly after the first dose buprenorphine may have precipitated a withdrawal syndrome
- Greatest severity of buprenorphine-related precipitated withdrawal in the first few hours (1-4) after a dose, with a decreasing (but still present) set of withdrawal symptoms over subsequent hours



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 started at 0.2 mg – 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

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

Rapid low dose inductions



Day	Full Opioid Agonist	Buprenorphine Dosing Instructions	Total Daily Dose of Buprenorphine
1	Continue	0.5 mg SL once	0.5 mg
2	Continue	0.5 mg SL bid	1 mg
3	Continue	1 mg SL bid	2 mg
4	Continue	2 mg SL bid	4 mg
5	STOP (if able to tolerate increase)	4 mg SL once. If tolerated take additional 4 mg in 10 mins. Continue to titrate prn for ongoing cravings or withdrawal symptoms for TDD of 16-24 mg	16-24 mg

Tips and Tricks

- Complex dosing - **good patient instructions** helpful. Consider visual aids
- Specifically outline what adjunct meds you are giving and for what
- Instruct patients to take AM buprenorphine before their full agonist
- Close follow up
- Modify or slow protocol as needed (i.e. repeat days)
- Give naloxone to every patient



Yet 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

Micro/Macro Inductions

- Low dose -> high dose
- Idea is to utilize advantages of both low dose and high dose inductions
- Stop full agonist, get some buprenorphine onto receptors -> reduce risk of precipitated withdrawal, then rapidly increase
- Examples
 - Day 1: 1 mg qid
 - Day 2: 8-16 mg, additional prn up to 24-32 mg



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
- 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

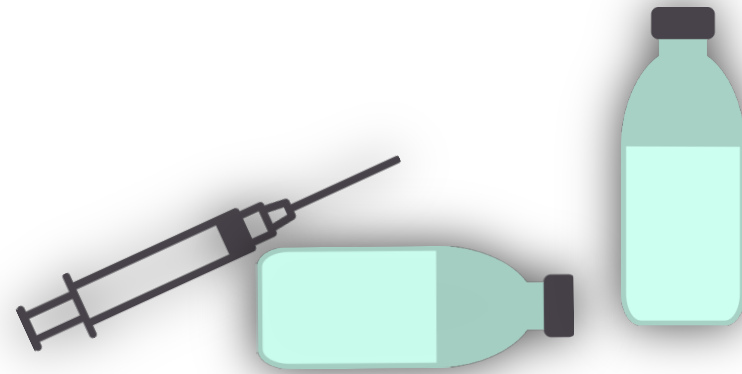


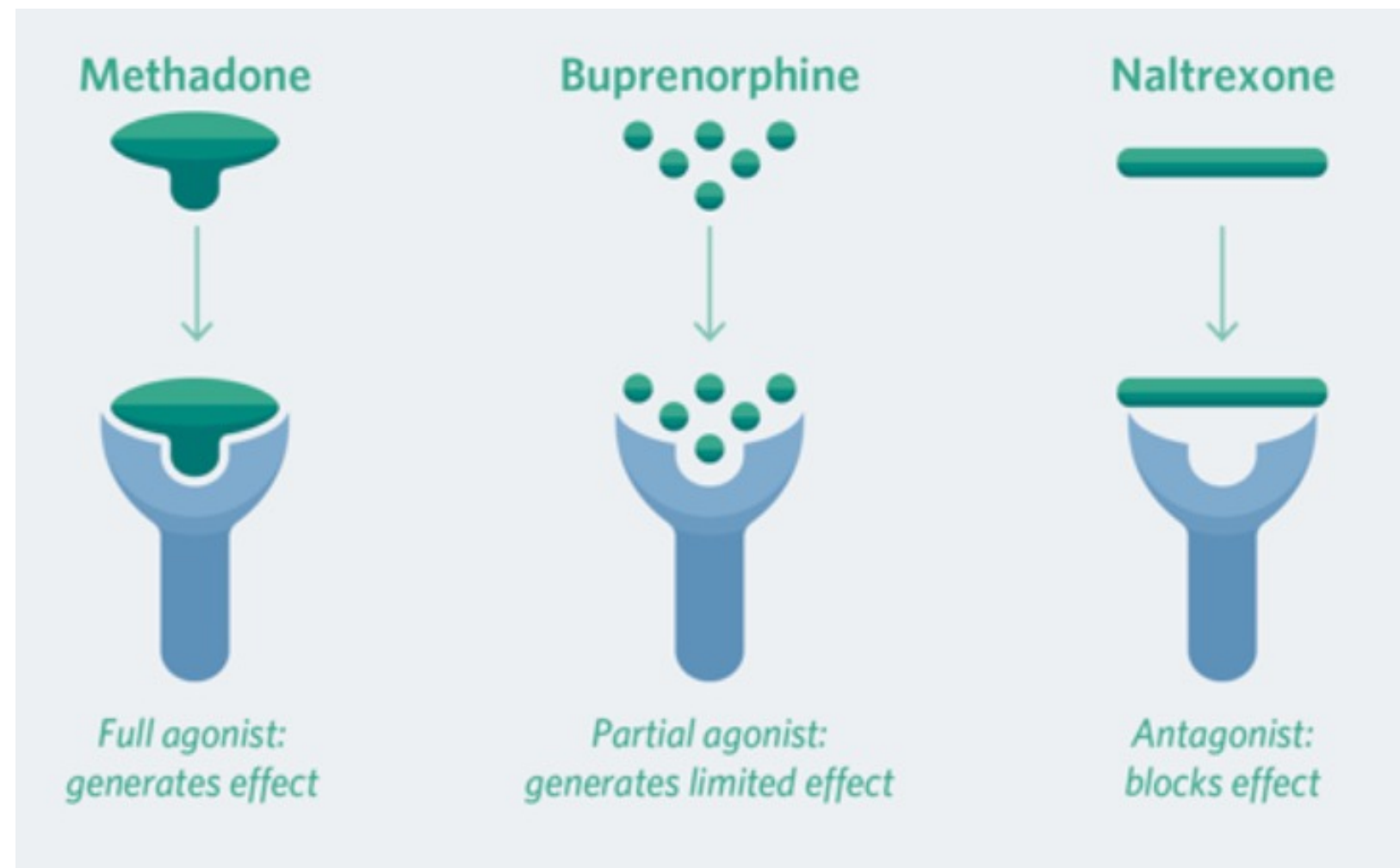
Objectives



- The context: opioid epidemic and the rise of fentanyl
- Review medications for the treatment of OUD
 - Methadone
 - How it works
 - Regulations (and a little context)
 - 72-hour rule
 - Buprenorphine
 - How it works
 - Regulations and regulatory changes
 - How to administer and prescribe
- **XR - naltrexone**

Naltrexone for Extended Release Injectable Suspension








Outcome	XR-NXT (n=283)	BUP-NX (n=287)	Treatment Effect
Inducted to study medication (ITT)	204 (72%)	270 (94%)	OR 0.16, 0.09-0.28; P<0.0001
Relapse-free survival (weeks)	8.4 (3-23.4)	14.4 (5.1-23.4)	HR 1.36, 1.10-1.68; p=0.0040
	20.4 (5.4-23.4)	15.2 (5.7-23.4)	HR 0.92, 0.71-1.18, p=0.49
Opioid relapse, weeks 3-24	185 (65%)	163 (57%)	OR 1.44, 1.02-2.01; p=0.036
	106/204 (52%)	150/270 (56%)	OR 0.87, 0.60-1.25; p=0.44

Difficult to start

Requires abstinence from opioids 4 – 7 days

About 25% of patients will not complete induction





Outcome	XR-NXT (n=283)	BUP-NX (n=287)	Treatment Effect
Inducted to study medication (ITT)	204 (72%)	270 (94%)	OR 0.16, 0.09-0.28; P<0.0001
Relapse-free survival (weeks)	8.4 (3-23.4)	14.4 (5.1-23.4)	HR 1.36, 1.10-1.68; p=0.0040
	20.4 (5.4-23.4)	15.2 (5.7-23.4)	HR 0.92, 0.71-1.18, p=0.49
Opioid relapse, weeks 3-24	185 (65%)	163 (57%)	OR 1.44, 1.02-2.01; p=0.036
	106/204 (52%)	150/270 (56%)	OR 0.87, 0.60-1.25; p=0.44

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

- There are three FDA approved medications for OUD – a full agonist (methadone), partial agonist (buprenorphine), and antagonist
- Methadone and buprenorphine have been shown to have a clear mortality benefit



Summary

- Regulations related to prescribing MOUD are loosening
- This is important because deaths related to OUD continue to escalate.
- Please prescribe





Case: Jack (is back)



- 54 yo man – Jack - with history of uncontrolled DM2, COPD and active smoker who presents to establish care after ED visit for COPD exacerbation.
- Jack was working out of state and recently returned to town and went to ED with dyspnea. Tx'ed with prednisone and azithromycin.
- He smokes 7-10 cigarettes per day. No alcohol use. Smokes methamphetamine about once a week. Uses around 10 "rainbow" or "oxy blues" [fentanyl] tablets per day for chronic low back pain.

Rainbow Fentanyl

CRIME

What is 'rainbow fentanyl' and how concerned should Oklahomans be about it?



Jana Hayes
Oklahoman

Published 2:00 p.m. CT Sept. 22, 2022 | Updated 2:16 p.m. CT Sept. 22, 2022

[View Comments](#)



"Rainbow fentanyl" is created in a multitude of colors. PROVIDED

Case: Jack (is back)



- **Allergies:** Penicillin
 - **Meds:** metformin 1000 mg daily, fluticasone inhaler, albuterol inhaler
 - **PMHx:** DM2, COPD, HTN, obesity, chronic low back pain (no surgeries)
 - **SHx:** works as welder, crashing with his cousin, grown children, no legal issues
- **Exam:**
 - VS: BP 157/100, P 89, RR 12, O₂ 95%
 - Wheezy, otherwise well appearing
 - Poor dentition
 - CV: RRR
 - Ext: trace edema b/l
 - Skin: intact, no abscesses or track marks
 - Pupils: pinpoint
 - Psych: oriented, no SI or HI

Objective Data

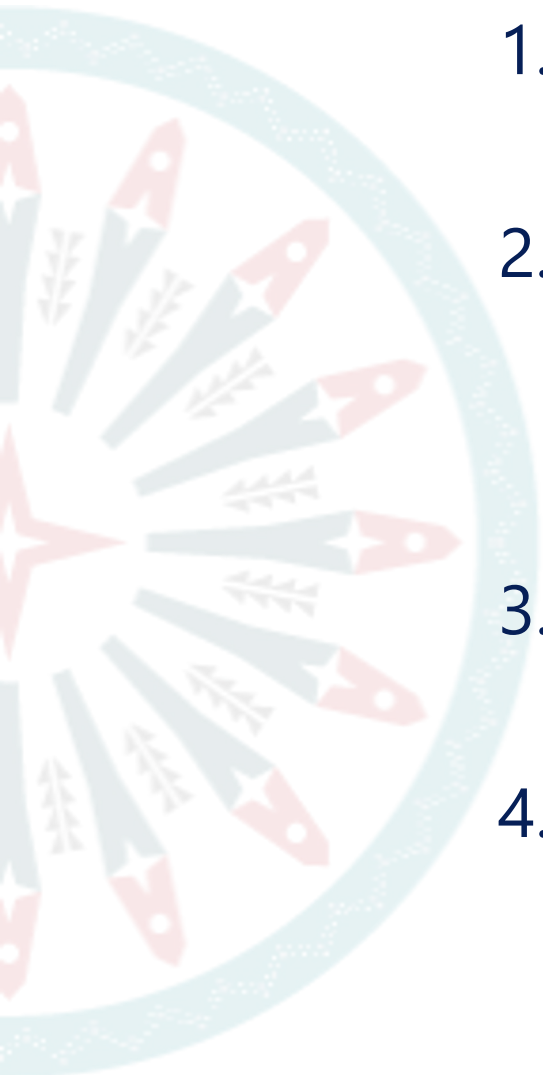


- **Oklahoma PMP Aware:** no prescriptions
- **CMP:** normal
- **A1c:** 10.5%
- **CXR:** hyperinflated lungs
- **EKG:** NSR, QTc = 420 ms

Component	Ref Range & Units	5 mo ago (9/21/22)
AMPHETAMINE, URINE	Negative	Positive !
Comment: Semi-quantitative result is 9474 (F P)		
BARBITURATES, URINE	Negative	Negative
Comment: Semi-quantitative result is 14 (G N)		
BENZODIAZEPINES, URINE	Negative	Negative
Comment: Semi-quantitative result is - 13 (G N)		
Cocaine, Urine	Negative	Negative
Comment: Semi-quantitative result is - 7 (G N)		
OPIATES, URINE	Negative	Positive !
Comment: Semi-quantitative result is 8138 (P)		
CANNABINOIDS, URINE	Negative	Negative
Comment: Semi-quantitative result is - 1 (G N)		
METHADONE, URINE	Negative	Negative
Comment: Semi-quantitative result is 1 (G N)		
OXYCODONE, URINE	Negative	Negative
Comment: Semi-quantitative result is 25 (N)		
CREATININE CONC UR	>20.00 mg/dL	216.30
Resulting Agency		OHSU CORE LAB

Questions?

1. What additional questions do you have from the initial history?
2. What substance use disorders, if any, does this patient have?
Are they mild, moderate, or severe?
3. What additional testing would you like to order today, if any?
4. Please comment on your initial treatment plan and follow-up plan for the substance use disorders (and general medical problems, too).



Four Weeks Later

"This bup stuff is really good, really good. I've been using a bit more meth though, and now I'm using IV instead of smoking. No blues or tablets though, no blues. What do you think, Doc?"

Meds: bup/nlx 8 mg TID, metformin 1000 mg BID, atorvastatin 20 mg, inhalers, nicotine patch 14 mg, naloxone 4 mg

Exam: VS: BP 180/120, P 102

Pressured speech, tangential, fidgety

Pupils appropriate for light

Lab update:

Hep C ab: -ve

HIV: -ve

RPR: non-reactive

Hep B: surf ab -ve, suf ag -ve, core ab -ve

Hep A: IgG +ve

Component	Ref Range & Units	9 mo ago (5/18/22)
(THC) MARIJUANA, URINE	Negative	Negative
QC: ENTER 'PASS' OR 'FAIL', URINE DRUG SCREEN		Pass
COCAINE, URINE	Negative	Negative
QC: ENTER 'PASS' OR 'FAIL', URINE DRUG SCREEN		Pass
OPIATES, URINE	Negative	Negative
QC: ENTER 'PASS' OR 'FAIL', URINE DRUG SCREEN		Pass
OXYCODONE, URINE	Negative	Negative
QC: ENTER 'PASS' OR 'FAIL', URINE DRUG SCREEN		Pass
AMPHETAMINES, URINE	Negative	Positive !
QC: ENTER 'PASS' OR 'FAIL', URINE DRUG SCREEN		Pass
METHAMPHETAMINES, URINE	Negative	Positive !
QC: ENTER 'PASS' OR 'FAIL', URINE DRUG SCREEN		Pass
METHADONE, URINE	Negative	Negative
QC: ENTER 'PASS' OR 'FAIL', URINE DRUG SCREEN		Pass
BENZODIAZEPINES, URINE	Negative	Negative
QC: ENTER 'PASS' OR 'FAIL', URINE DRUG SCREEN		Pass
BUPRENORPHINE, URINE	Negative	Positive !
QC: ENTER 'PASS' OR 'FAIL', URINE DRUG SCREEN		Pass

Jack Attack



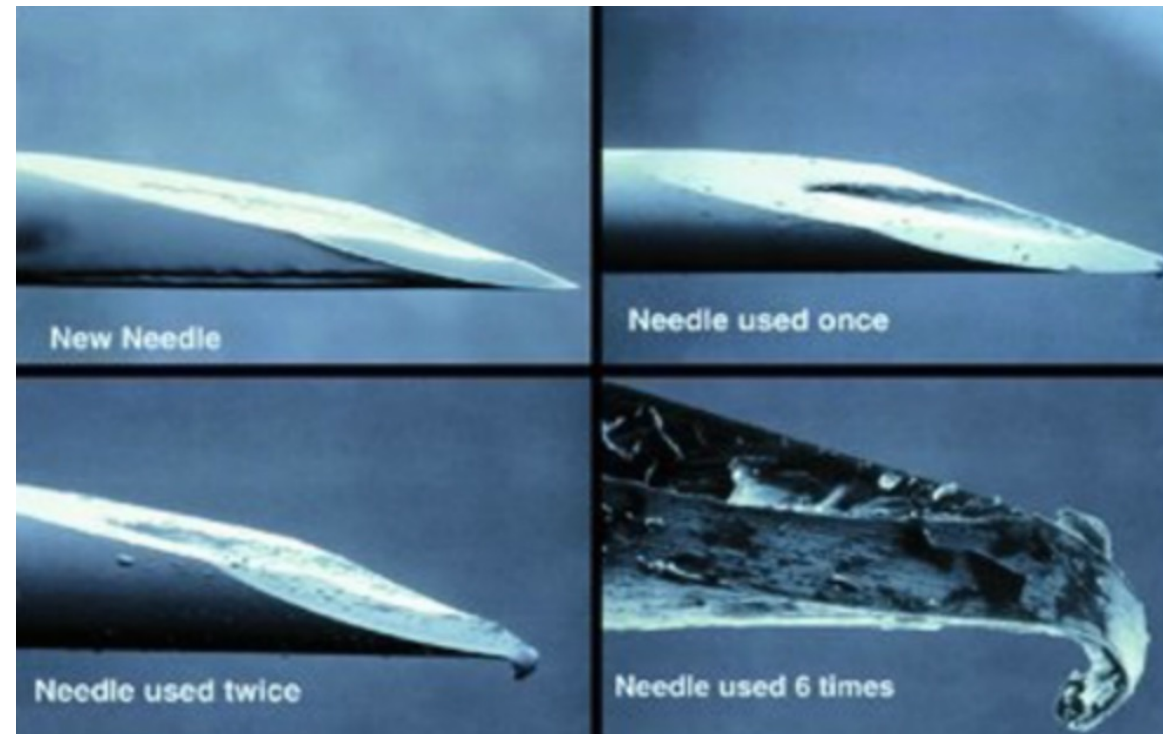
1. Describe your differential diagnosis for Jack's presentation today.
2. Do you want to make any changes to his buprenorphine regimen?
Why or why not?
3. Describe your plan for his ongoing methamphetamine use (treatments, visit frequency, harm reduction).

Injection Supplies



Injection Technique

- Clean the hands
- Clean the skin
- Clean needles/rigs (don't share filters, cookers)
- Don't reuse needles, even on yourself
- Don't use alone
- Use needles bevel up
- Use a filter whenever possible
- Test for fentanyl
- Clean water



Safe(r) Drug Use

SAFE(R) DRUG USE

WAYS PEOPLE USE DRUGS

Smoking

Using a pipe, stem, or bong. Make sure everyone has their own pipe or mouthpiece. If you are smoking crack, use a filter.

Snorting

Crush powder as fine as possible & make sure everyone has their own straw. Alternate nostrils between hits.

Swallowing

Pills, crushed in thin paper, or a drink. Mix your own drink so you know how strong it is. Can take up to an hour to kick in so wait a while before consuming more.

Booty Bumping

Use a turkey baster or syringe without a needle. Avoid sharing equipment and get vaccinated for Hep A.

Injecting

Use your own sterile syringes & gear. If you need to reuse syringes, wash with cold water, bleach, & then water again.

BENEFITS OF INJECTING DRUGS

- Very efficient way to use - drugs are absorbed directly into the bloodstream. This can lead to a more intense & longer high.
- Can be more economically efficient - folks may need less drugs compared to smoking or snorting, which saves money.

RISKS OF INJECTING DRUGS

- Criminalization of injection paraphernalia.
- If sharing equipment, HIV/Hep C transmission.
- Higher rates of overdose & overdose related death for people injecting drugs compared to smoking or snorting.
- Skin and soft tissue infections, such as abscess and other bacterial infections - some can be fatal.

Overdose Prevention

- Don't use alone
- Changes in tolerance, e.g. hospitalization
- "Tester shot"
- Watch for fentanyl contamination in stimulants
- Narcan!
- Change to safer routes of use