Medication-Assisted Treatment for Opiate Use Disorder

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Disclaimer #1

I have no financial or personal relationships that could inappropriately influence or bias the content of this presentation.

I have no conflicts of interest to disclose.

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Disclaimer #2

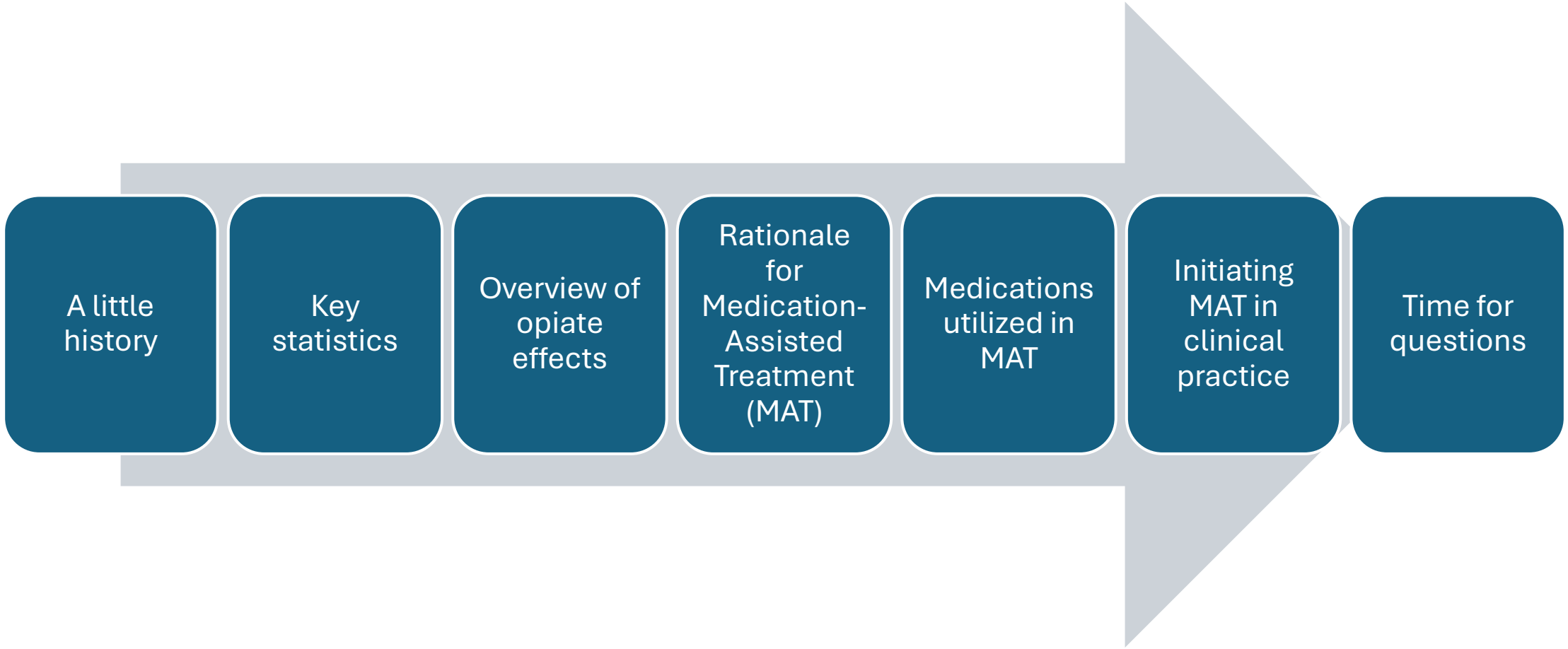
I am not a substance abuse expert.

I am a family medicine physician who has treated patients with Opiate Use Disorder since 2021

Mine is not the only way to select, initiate, or maintain medication treatment for Opiate Use Disorder.

I encourage you to seek additional knowledge and personalize your treatment for the unique patients under your care.

Today's Agenda



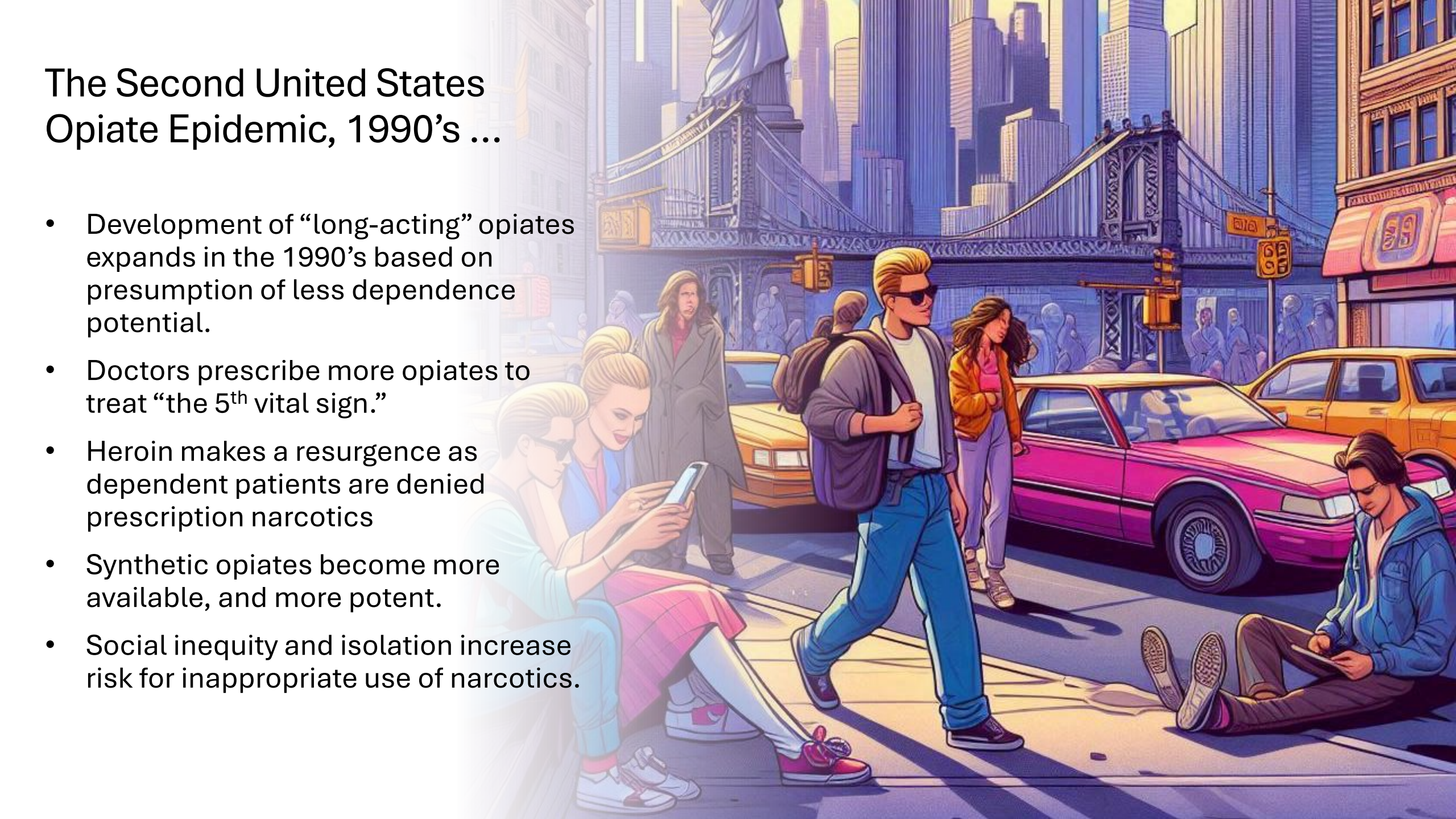
The First United States Opiate Epidemic

Late 19th – Early 20th Centuries

- Morphine, isolated from opium in the early 1800s, became widely used for pain relief, augmented by IV administration after development of the hypodermic needle in the mid-19th century.
- The Bayer Company introduced heroin as an alternative to morphine in 1898.
- The *Harrison Narcotics Tax Act* of 1914 prohibited the prescription of maintenance doses for “addicts.”
- The *Narcotic Addict Treatment Act* of 1974 allowed for the establishment of methadone maintenance programs.

The Second United States Opiate Epidemic, 1990's …

- Development of "long-acting" opiates expands in the 1990's based on presumption of less dependence potential.
- Doctors prescribe more opiates to treat "the 5th vital sign."
- Heroin makes a resurgence as dependent patients are denied prescription narcotics
- Synthetic opiates become more available, and more potent.
- Social inequity and isolation increase risk for inappropriate use of narcotics.

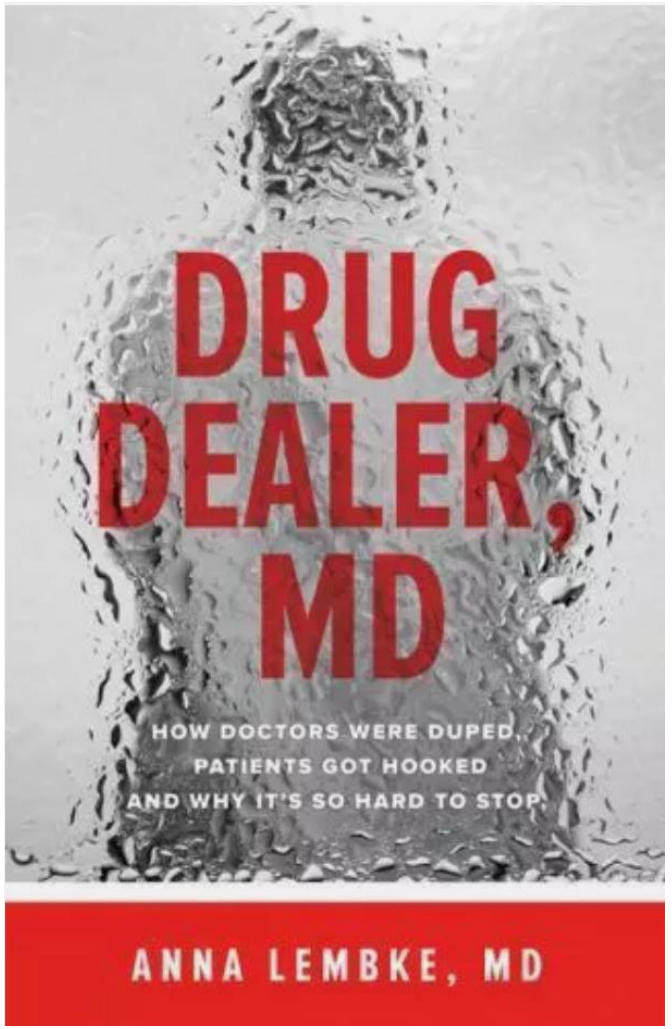


For Greater Detail…

Drug Dealer, MD – How Doctors Were Duped, Patients Got Hooked, and Why It's So Hard to Stop"(Johns Hopkins University Press, 2016)

Highlighted in the New York Times as one of the top five books to read to understand the opioid epidemic (Zuger, 2018).

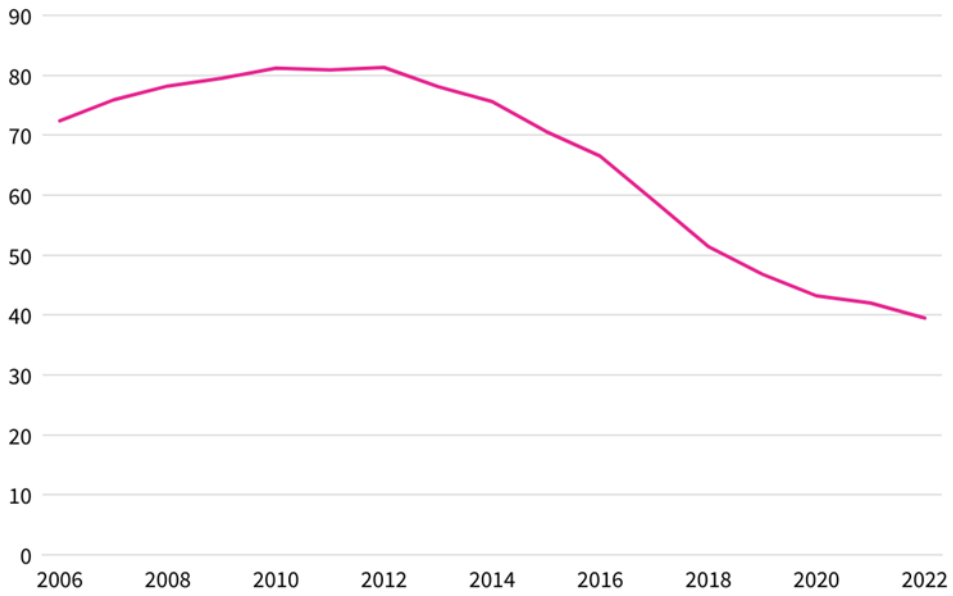
- Chief, Addiction Medicine Dual Diagnosis Clinic, Department of Psychiatry, Stanford University (2010 - Present)
- Program Director, Addiction Medicine Fellowship, Department of Psychiatry, Stanford University (2013 - Present)
- Medical Director, Addiction Medicine, Department of Psychiatry, Stanford University (2015 - Present)
- Board Certification: American Board of Preventive Medicine, Addiction Medicine (2021)
- Board Certification: American Board of Psychiatry and Neurology, Psychiatry (2003)



Fewer Prescriptions, but More Deaths

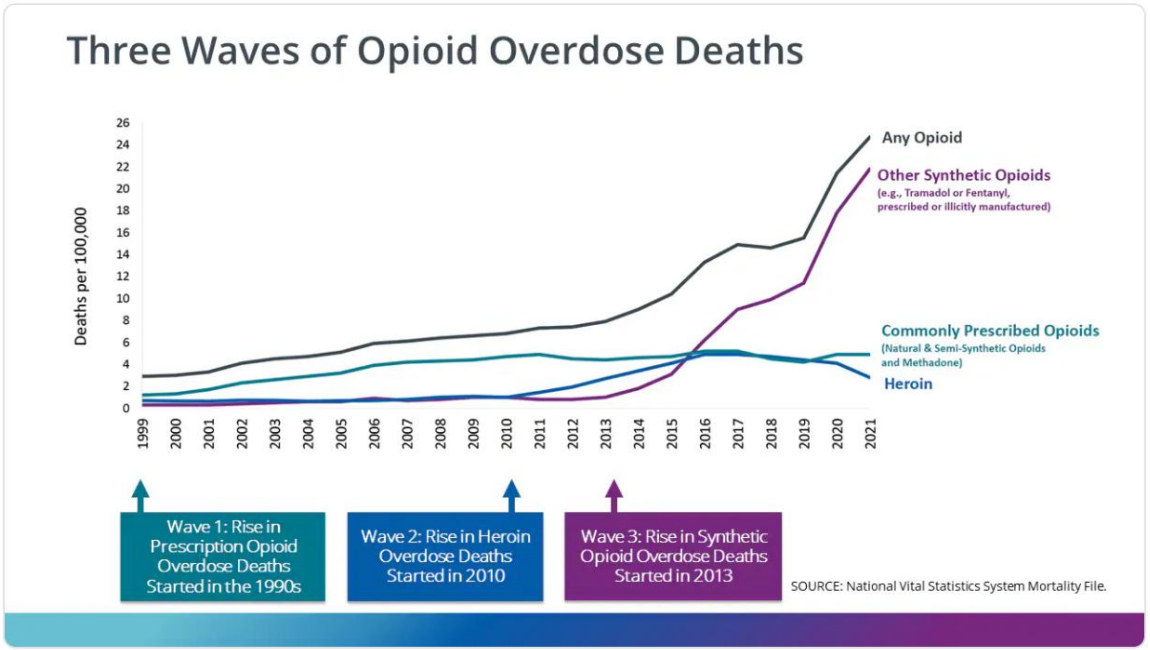
Opioid prescriptions peaked in 2012 with 81 prescriptions for every 100 people.

Opioid prescriptions per 100 people



Source: CDC

USAFACTS



This rise in opioid overdose deaths is shown in three distinct waves.

From 1999-2021, nearly 645,000 people died from an overdose involving any opioid, including prescription and illicit opioids. [1]

If People Are Dying, Why Don’t They Just Quit Using Opiates?

Physical Dependence	Over time, the body becomes dependent on opioids, leading to withdrawal symptoms when the drug is not taken. These symptoms can include severe pain, nausea, vomiting, diarrhea, anxiety, and insomnia.
Tolerance	As tolerance builds, individuals need higher doses to achieve the same effect, making it harder to quit.
Cravings	Intense cravings for the drug can make it difficult to stop using, even when the person wants to quit.
Brain Changes	Opioids cause changes in the brain’s reward system, making it difficult to feel pleasure from other activities.
Psychological Factors	Many people use opioids to cope with emotional pain or stress, making it hard to stop without addressing these underlying issues.
Fear of Withdrawal	The fear of experiencing withdrawal symptoms can be a significant barrier to quitting.
Lack of Support	Without proper medical and social support, it can be nearly impossible to overcome the addiction.

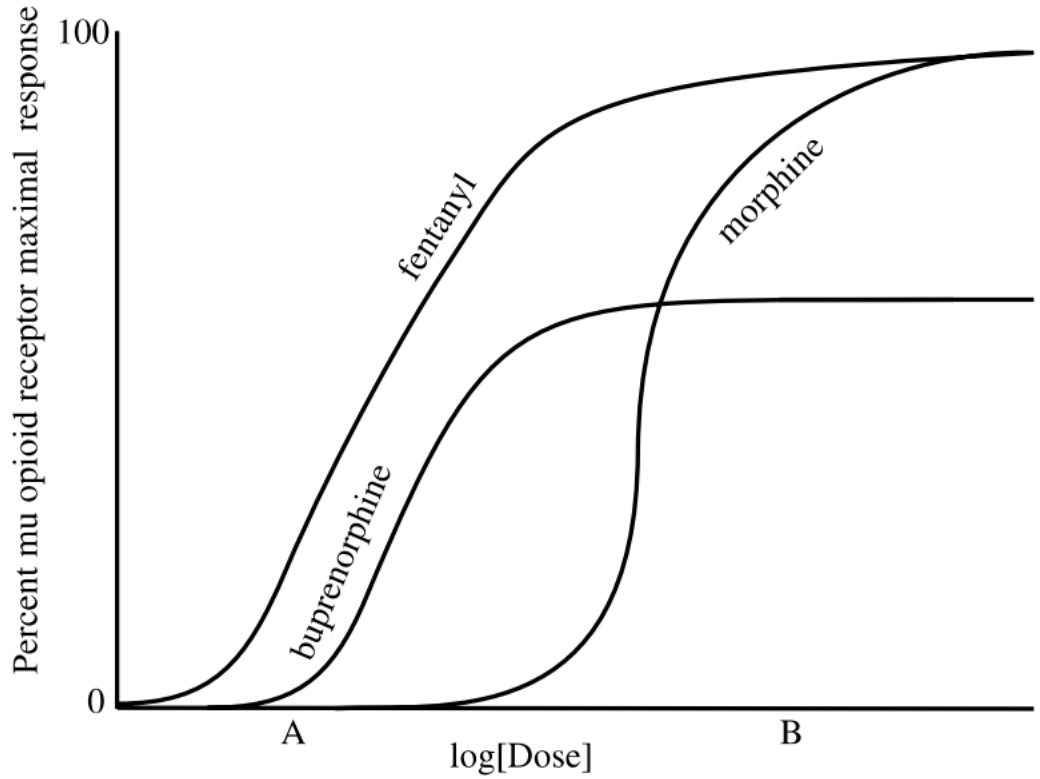
For the Detail Oriented Amongst Us

Receptor Type	Location	Functions
Mu (μ) Receptors	Brain, spinal cord, digestive tract	Pain relief, euphoria, respiratory depression, physical dependence
Delta (δ) Receptors	Brain (forebrain)	Modulation of mood, pain relief, potential antidepressant effects
Kappa (κ) Receptors	Brain, spinal cord, peripheral sensory neurons	Pain relief, dysphoria, diuresis

Receptor Affinity vs. Efficacy (Potency)

- Affinity = binding strength (aka how unlikely it is to get pushed off by something else)
- Efficacy = “potency” = signal strength when bound

Ligand	Ki (Affinity) (nmol)
Hydrocodone	41.58
Oxycodone	25.87
Heroin	9.6
Methadone	3.38
Fentanyl	1.35
Morphine	1.14
Naloxone	1.1
Hydromorphone	0.6
Buprenorphine	0.21

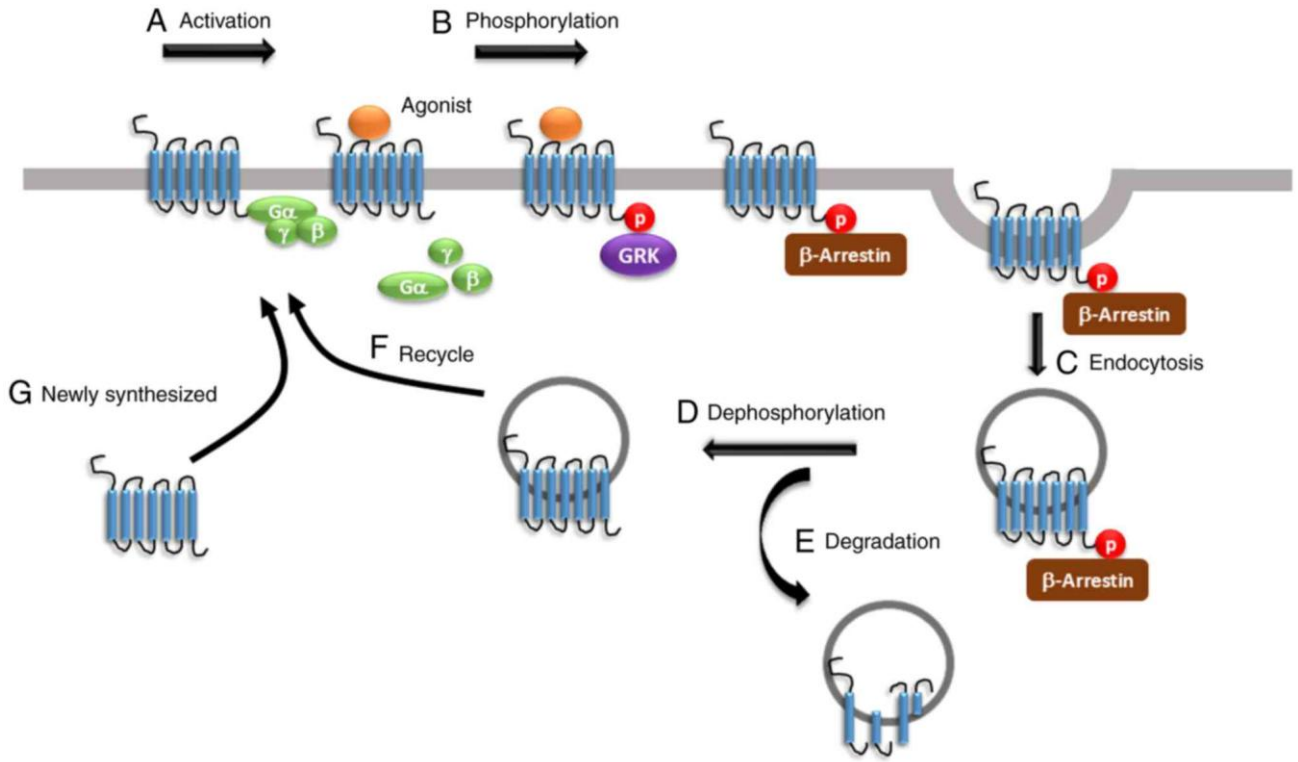


Tolerance

- All opioids create physiological tolerance

- The body is trying to balance signaling responsiveness and appropriate physiologic function, so it recycles/downgrades receptors in periods of high agonist volume

- When the agonist goes away, we are left with an uninhibited pain/discomfort/dysphoria signal

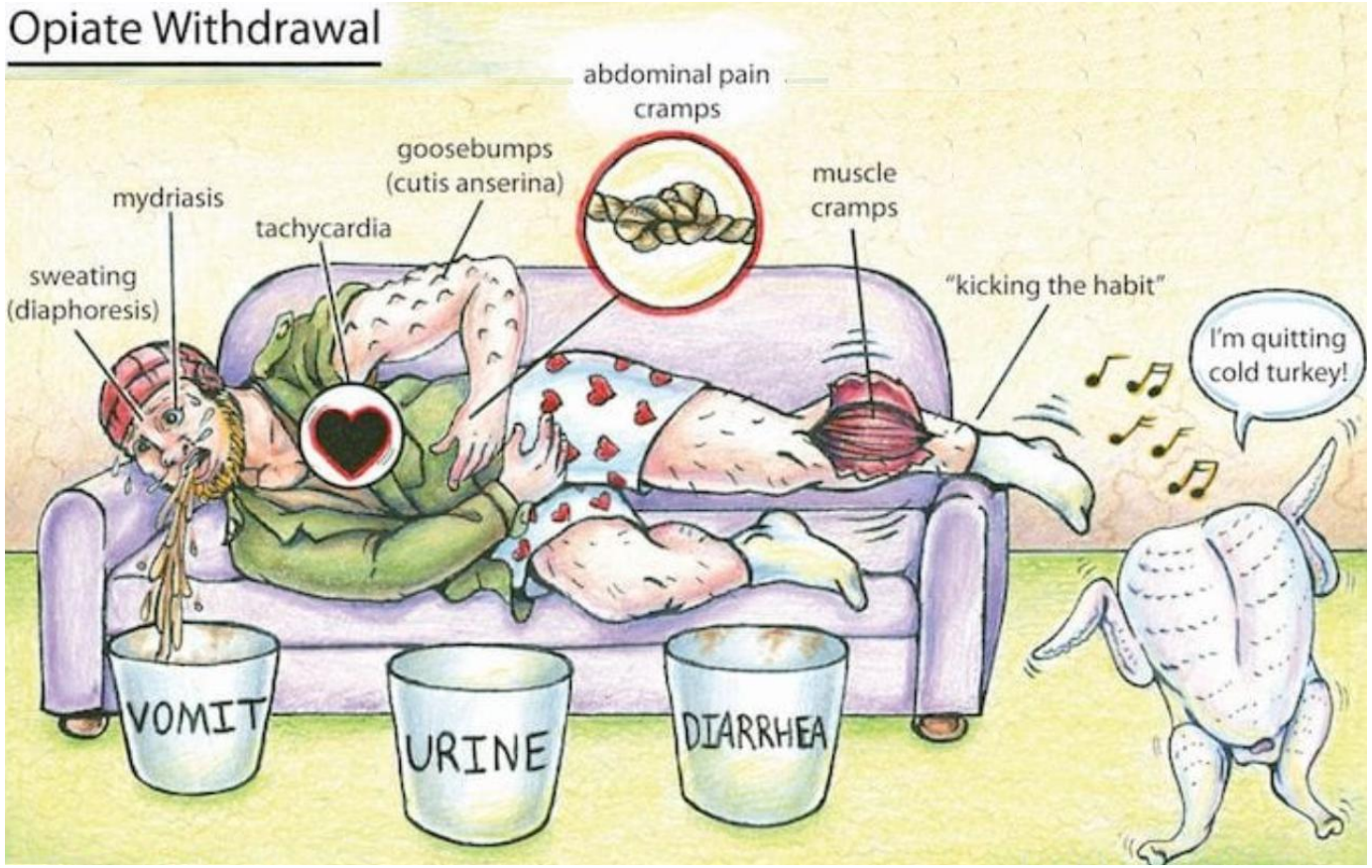


Opioid Effects

- Analgesia
- Euphoria
- Sedation
- Constipation
- Muscle Relaxation

Withdrawal Effects

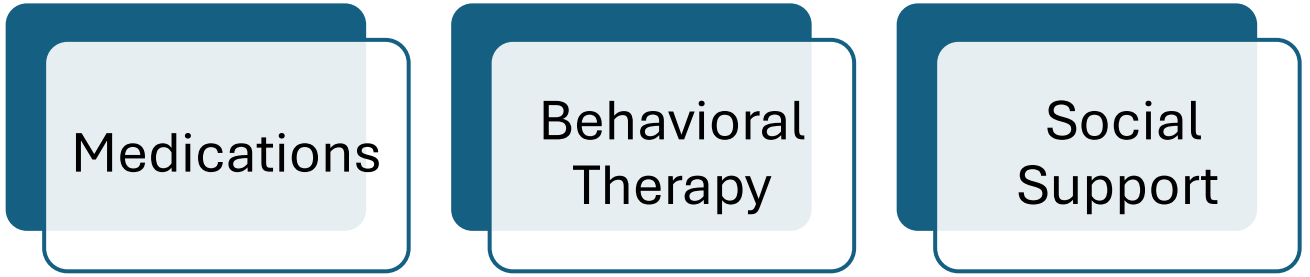
- Hyperalgesia
- Dysphoria
- Hypervigilance
- Diarrhea
- Muscle Cramps

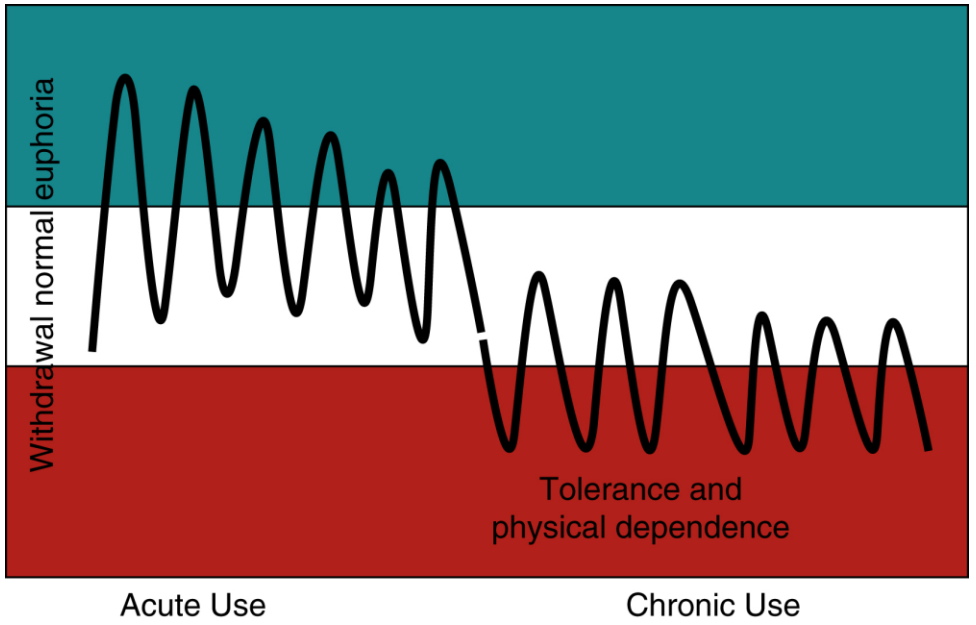


https://youtu.be/Z5dX-bFevF4?t=43

Medication-*Assisted* Treatment for OUD

- An evidence-based approach for treating opioid use disorder.
- Combines the use of FDA-approved medications with counseling and behavioral therapies to provide a comprehensive treatment plan.
- The goal of MAT is to address the physical, psychological, and social aspects of addiction, helping individuals manage cravings, reduce withdrawal symptoms, and support long-term recovery.





Medication-Assisted Treatment for OUD

- Reduces the risk of infectious disease transmission as well as criminal behavior associated with drug use.
- Increases the likelihood that a person will remain in treatment compared to abstinence-only therapies.
- Decreased likelihood of overdose when buprenorphine is on board

- *The American Society of Addiction Medicine. Advancing Access to Addiction Medications*. Accessed May 11, 2017.
- Bart G. *Maintenance medication for opiate addiction: the foundation of recovery. J Addict Dis*. 2012;31(3):207-225. doi:10.1080/10550887.2012.694598.
- Davoli M, Bargagli AM, Perucci CA, et al. *Risk of fatal overdose during and after specialist drug treatment: the VEdeTTE study, a national multi-site prospective cohort study. Addict Abingdon Engl*. 2007;102(12):1954-1959. doi:10.1111/j.1360-0443.2007.02025.x.
- Mattick RP, Breen C, Kimber J, Davoli M. *Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence.* Cochrane Database Syst Rev. 2014;(2):CD002207. doi:10.1002/14651858.CD002207.pub4.

The Big Three Medications of MAT

Methadone

- Full Agonist
- No withdrawal required
- Supervised daily treatment
- Oral administration
- Requires administration in an approved Opiate Treatment Program/Facility
- Variable MED

Buprenorphine

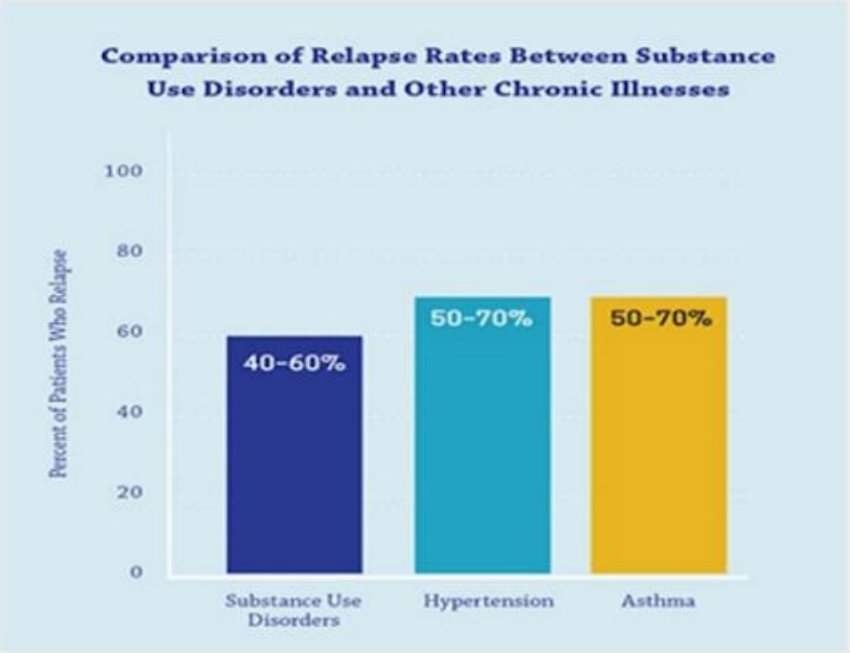
- Partial Agonist
- Moderate withdrawal required
- Unsupervised daily
- Transmucosal administration or Injectable
- No longer requires waiver
- 1:30 MED

Naltrexone

- Antagonist
- Complete withdrawal required
- Monthly clinic treatment
- Injectable administration
- Never required a waiver
- MED N/A

Opioid Use Disorder Treatment Outcome*

Methadone Maintenance	50 – 80%
Buprenorphine-Naloxone Maintenance	40 – 70%**
Naltrexone Maintenance (oral, depot)	10 – 20%, 20-60%***
"Drug Free" (no pharmacotherapy)	5 – 20%
Short-term Detoxification (any mode)	5 – 20% (limited data)



* *One year retention in treatment and/or follow-up with significant reduction or elimination of illicit use of opiates*
** *Effective dose 16-24mgs equal to 60 to 80 mg/d or possibly greater of methadone.*
*** *6 month treatment with extended release naltrexone*

Methadone and Buprenorphine maintenance treatment reduces overdose risk by 37-86%

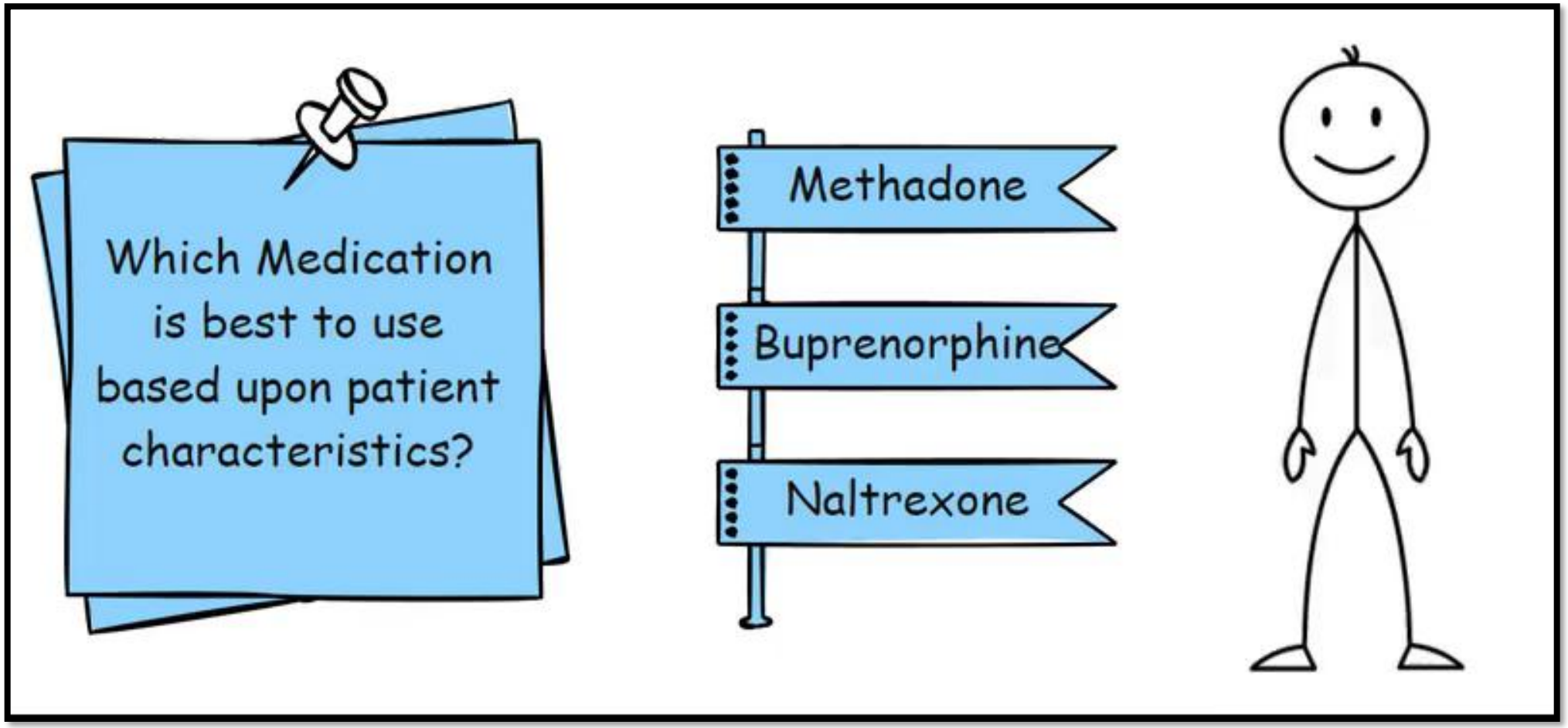
>350,000 in OTPs on methadone and est. >800,000 on buprenorphine

Buprenorphine Forms for OUD

- Transmucosal products (tabs/films) marketed as:
  - buprenorphine (*Subutex*)
  - buprenorphine/naloxone (*Suboxone, Zubsolv*)
    - naloxone added as abuse deterrent
    - naloxone not absorbed when used as instructed

- Injectable Sublocade/Brixadi available for monthly/weekly dosing
  - Subcutaneously administered in abdomen
  - In most cases, will be transitioning from a transmucosal formulation
  - 300mg/month for two months
  - 100mg/month thereafter (usually – fentanyl is changing this)

So How Do We Start?



The 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 assesment, the increase pulse rate would not add to the score.

Resting Pulse Rate: beats / minute
Measured after patient is sitting or lying for one minute
- (0) *pulse rate 80 or below*
- (1) *pulse 81 to 100*
- (2) *pulse 101 to 120*
- (4) *pulse rate greate than 120*

GI Upset:
over last 1/2 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 1/2 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*

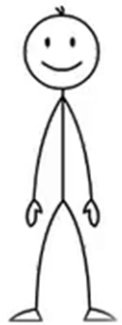
Anxiety or Irritability:
Measured after patient is sitting or lying for one minute
- (0) *none*
- (1) *patient reports increasing irritability or anxiousness*
- (2) *patient obviously irritable or anxious*
- (4) *patient so irritable or anxious that participation in the assessment is difficult*

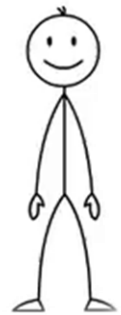
Bone or Joint aches:
If the patien was having pain previously, only the additinal component attributed to opiates withdrawal is scored
- (0) *not present*
- (1) *mild diffuse discomfort*
- (2) *patient reports severe diffuse aching of joints/muscles*
- (4) *patient is rubbing joints or muscles and is unable to sit still because of discomfort*

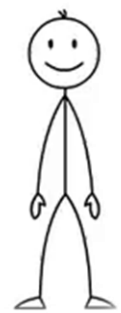
Gooseflesh skin:
- (0) *skin is smooth*
- (3) *piloerrection of skin can be felt or hairs standing up on arms*
- (5) *prominent piloerrection*

Runny nose or tearing:
Not acounted 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***





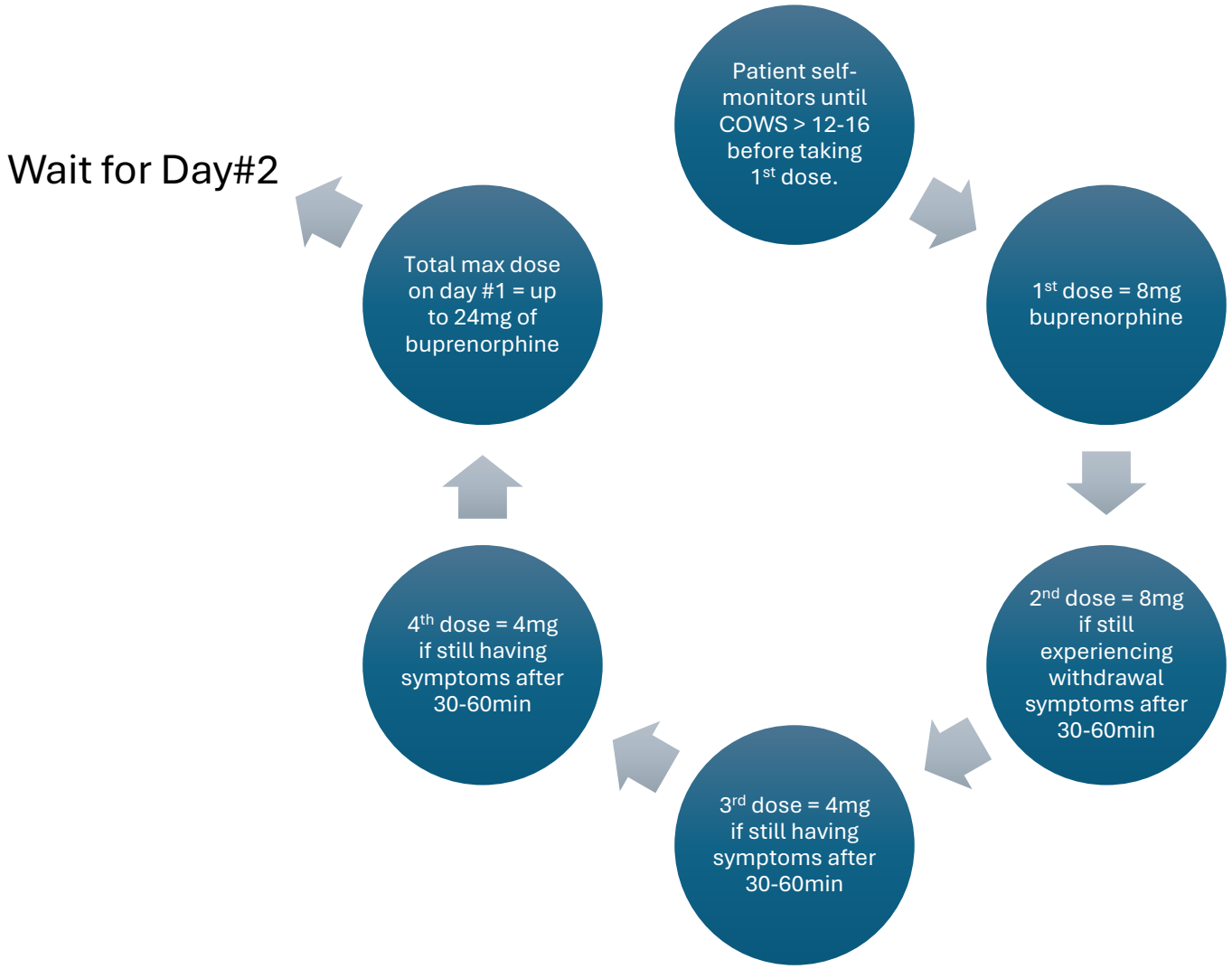


Buprenorphine Induction Strategies				
Induction Type	**When to Use**	**Pros**	**Cons**	**Suggested Dosing**
Standard induction	Most of the time	• Best established/ most evidence • Full treatment dose in two to three days	• Risk of precipitated withdrawal • Quick, but requires two to three days for optimal dose	• Day 1: Initial dose of 2–4 mg when COWS ≥8–10, additional doses up to 8–12 mg • Day 2: Give up to 16 mg • Day 3: Give up to 24 mg
Microinduction	• When transitioning from prescribed opioids • With patients unable to tolerate withdrawal symptoms in outpatient setting	Minimal precipitated withdrawal	Requires seven or more days until full dose	Example protocol: • Day 1: 0.5 mg daily • Day 2: 0.5 mg BID • Day 3: 1 mg BID • Day 4: 2 mg BID • Day 5: 2 mg TID • Day 6: 2 mg QID • Day 7: 4 mg TID and stop opioid agonists • Day 7+: Titrate to dose needed to eliminate cravings
Macroinduction	Emergency department (ED) patients at high risk of overdose and with history of poor follow-up	Reaches full dose quickly (first day)	• Least evidence • Should be done in the ED setting • Risk of precipitated withdrawal	• Initial dose of 4–8 mg when COWS ≥8–10 • One additional large dose of 16–24 mg

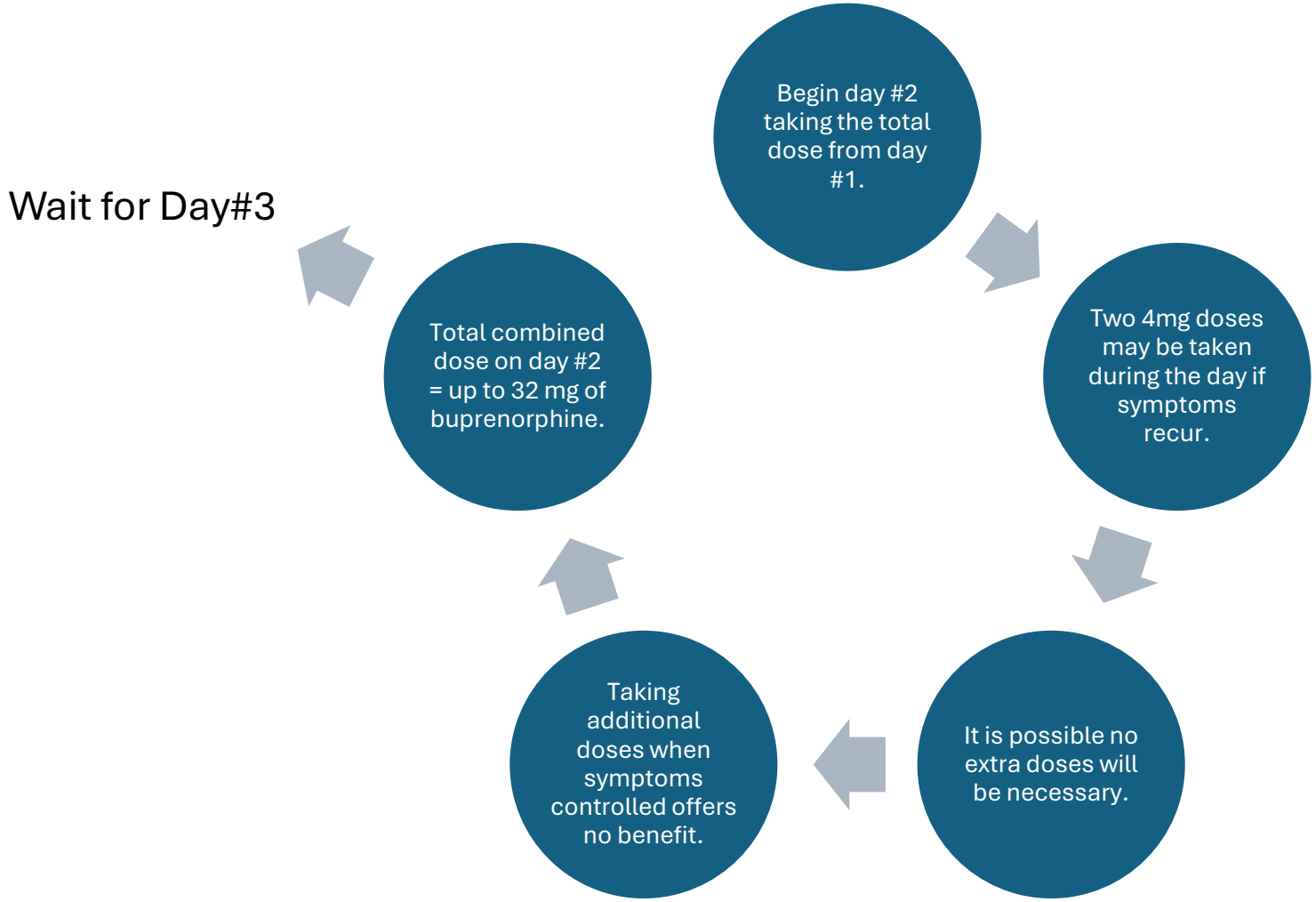
Some Pearls When Using This Method

- Sometimes what patients THINK they're taking, isn't what they're taking, so initial MED estimation may be off by a bit
- 24-32mg may be needed at first, with some considering doses beyond that
- Re-evaluation should happen sooner rather than later to ensure an appropriate dose to prevent relapse
- It can be extremely helpful for patients to have a friend or family member present to help with COWS scoring and be able to monitor the induction process
- Use adjunctive medications to help with anxiety which can be confused for "withdrawal"

The Stepwise Induction, Day #1



The Stepwise Induction, Day #2



The Stepwise Induction, Day #3

Patient begins day #3 taking the total dose from day #2.

Follow-up with prescriber should happen on day 3 or 4 to evaluate efficacy of treatment.

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Adjunctive Medications

Hydroxyzine

- H1 Antagonist
- Sedating
- Non-opiate, non-benzodiazepine
- 10-50mg q6-8 hours PRN for anxiety

Clonidine

- Alpha 2 Agonist
- Inhibits norepinephrine release
- 0.1 – 0.2 mg TID PRN

Surveillance Visits

Weekly visits following induction with buprenorphine

- Symptom monitoring
- Relapse monitoring
- Provision of support and resources for behavioral treatment (FindTreatment.gov)
- Drug testing (mass spec vs rapid)

When stability demonstrated (3-4 weeks), may extend interval

- Q 2 weeks
- Q 1 month
- Q 3 months
- Interval visits include all elements from initial weekly visits.

Stopping Buprenorphine

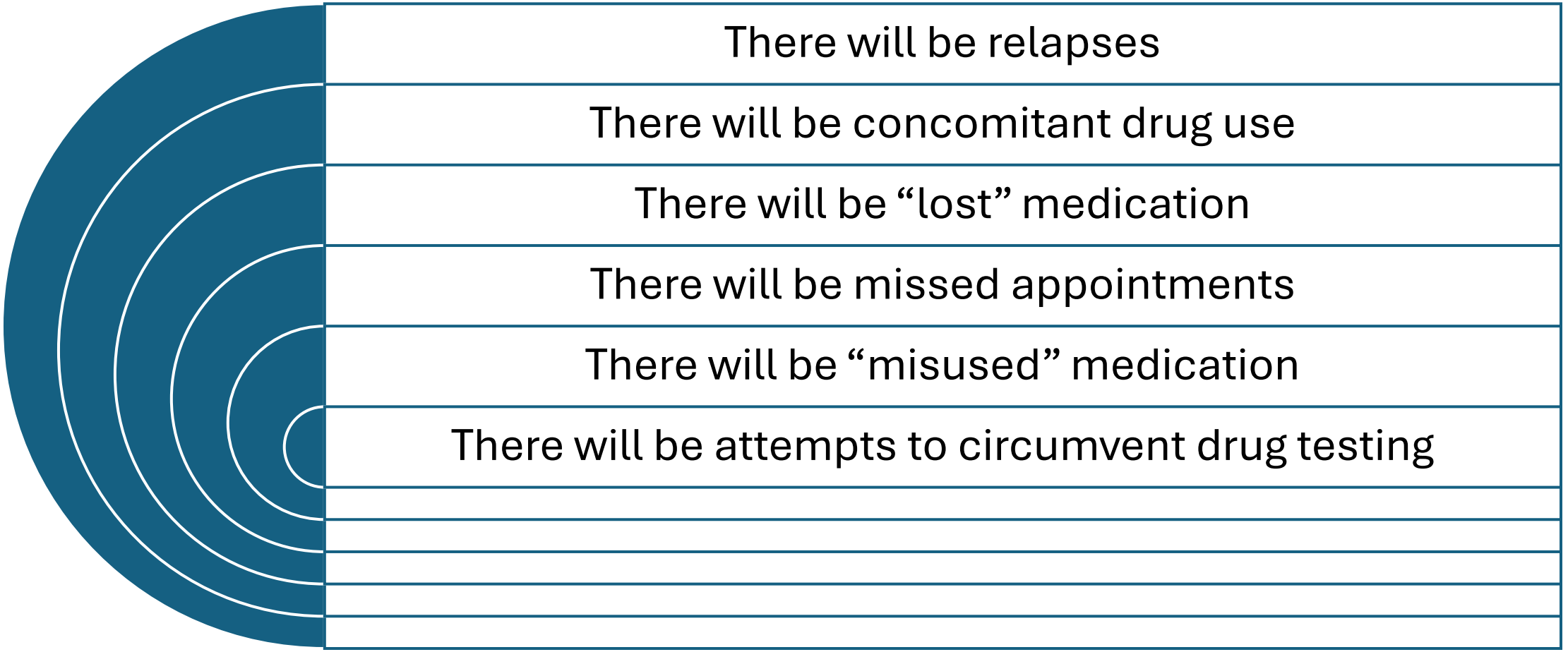
Do you have to?

- No!

How long would you recommend continuing?

- At least 6-12 months
- Until demonstrated stability in other domains of life
- Taper process can be as long or as short as needed
- Use adjuncts to help with symptoms of withdrawal or anxiety of stopping

How Will You Handle Missteps?



Resources

- SAMHSA - Substance Abuse and Mental Health Services Administration
- ASAM - American Society of Addiction Medicine
- Mini Module: Buprenorphine for the Treatment of Opioid Use Disorder | Overdose Prevention | CDC
- Opioid Use Disorder: Treating | Overdose Prevention | CDC
- Scala Northwest MAT Treatment Guidelines

Questions?