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Treating Opioid Use Disorder

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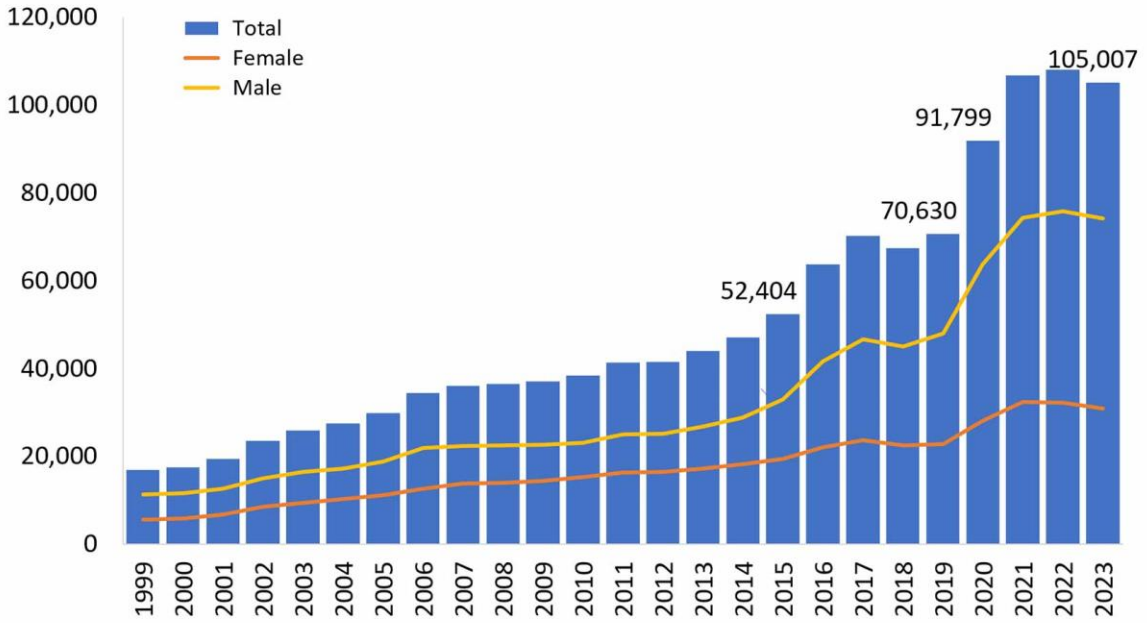
DISCLOSURES

Objectives

Review	Epidemiology of the overdose crisis
Describe	The diagnosis of opioid use disorder and the components of evidence-based treatment
Detail	How to start treatment for opioid use disorder

The Overdose Crisis in the United States

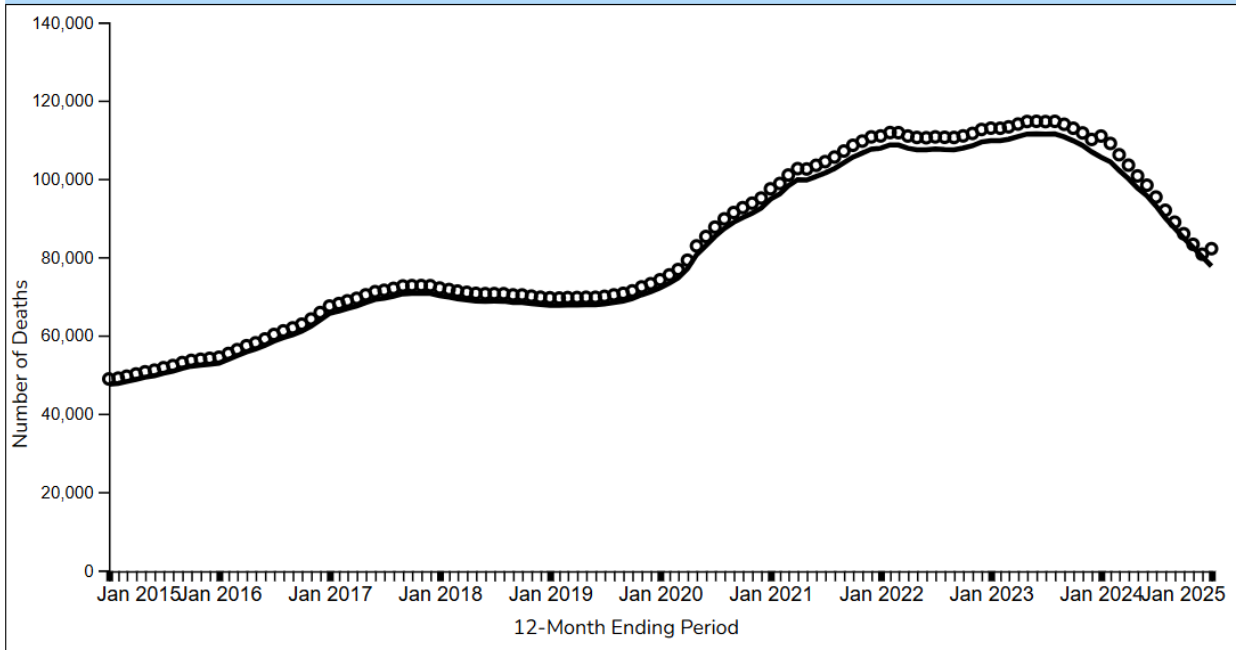
Figure 1. U.S. Overdose Deaths* by Sex, 1999-2023



*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision.

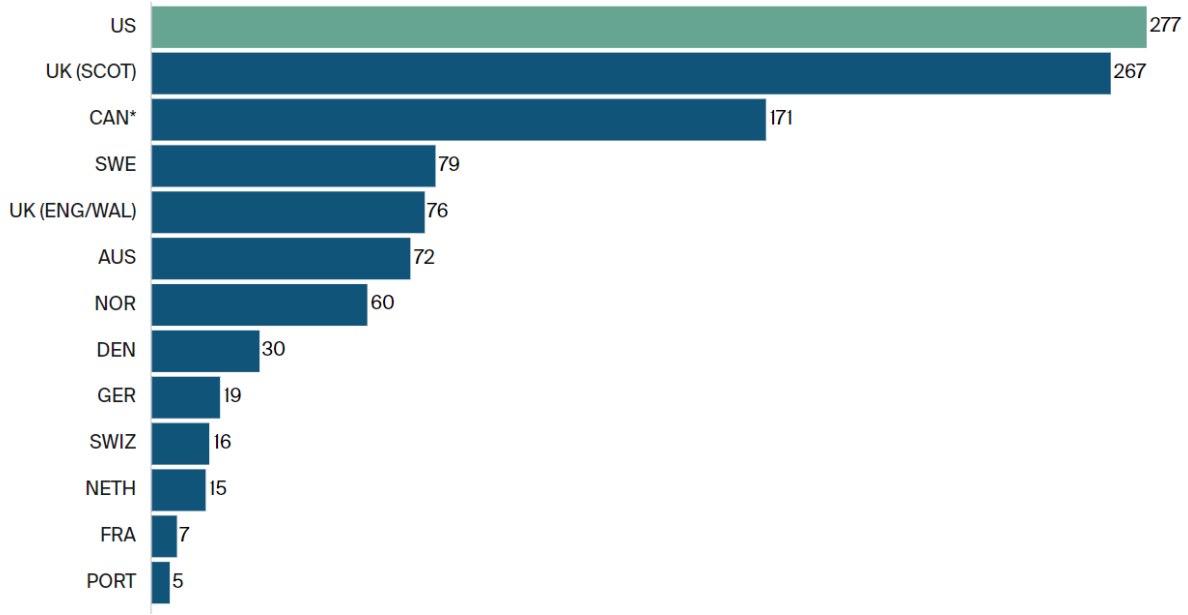
Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2023 on CDC WONDER Online Database, released 1/2025.

Figure 1a. 12 Month-ending Provisional Counts of Drug Overdose Deaths: United States

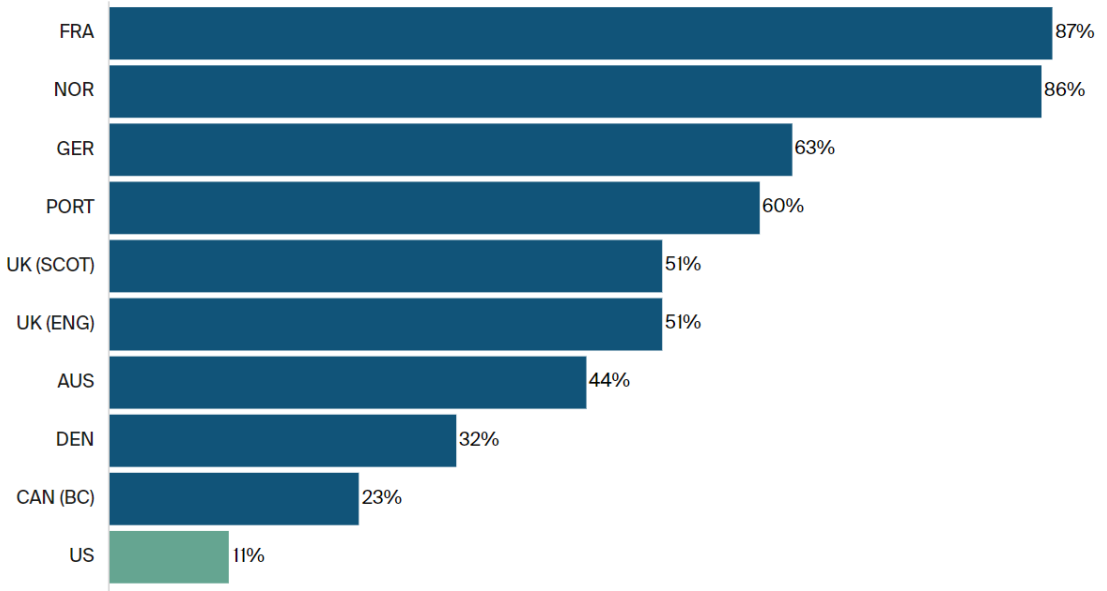


US leads the globe in overdose deaths, yet treatment gaps persist

Overdose or drug-related death rate per 1 million population (unadjusted), 2020 or latest year available



Percentage of people with high-risk opioid use or opioid use disorder (OUD) who received opioid-substitution treatment



PROFILES

THE TREATMENT OF PATIENTS—II

Dr. Marie Nyswander

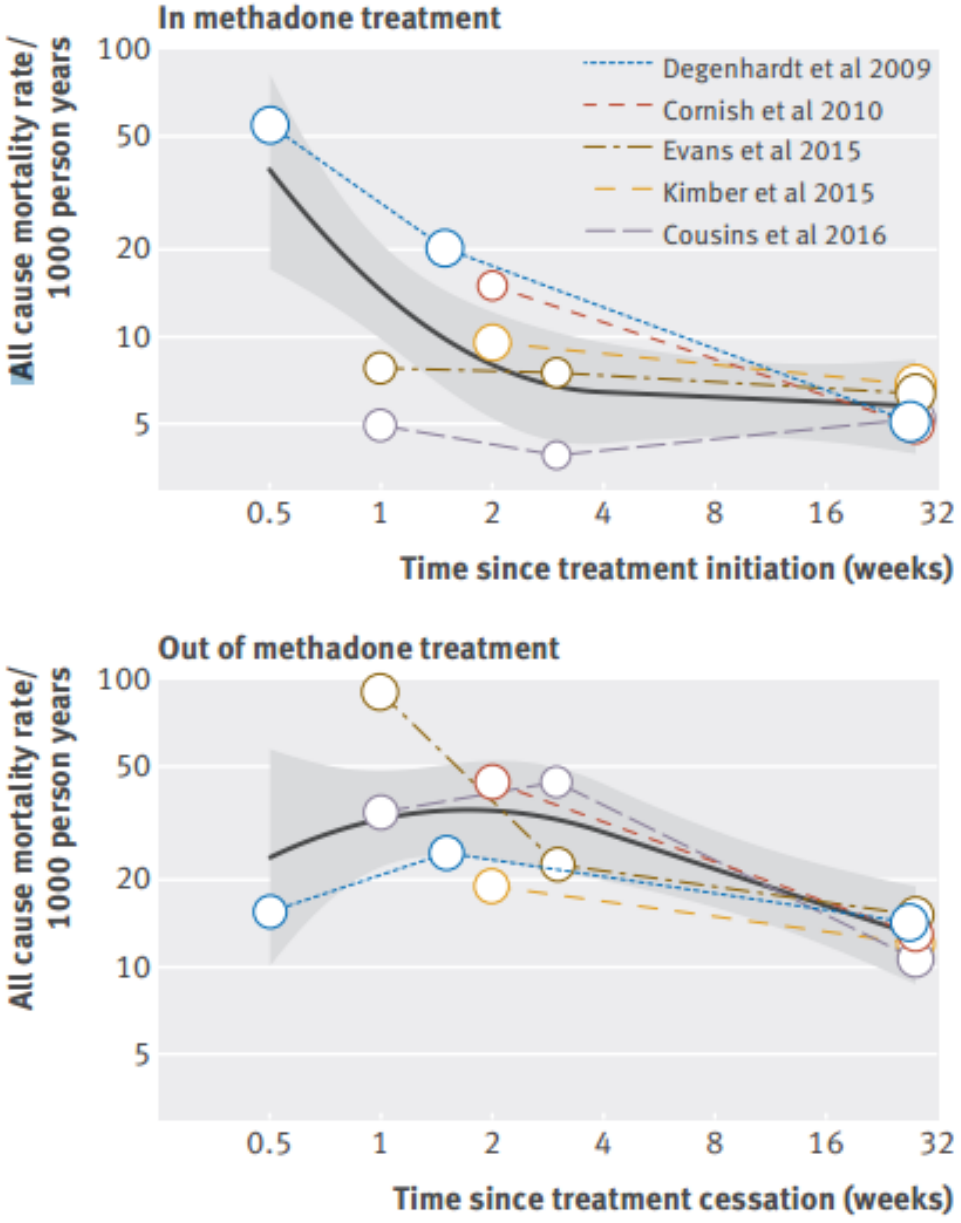
Stereotypes of Drug Use and Addiction Impact Practice and Policy

"For me the most educational experience of the past three decades was to learn that the traditional image of the [person with addiction as having] weak character, hedonistic, unreliable, depraved, and dangerous is totally false. This myth, believed by the majority of the medical profession and the general public, has distorted public policy for seventy years."

Dr. Dole

Treatment Is Effective: Putting Buprenorphine into Perspective

Intervention	Outcome	NNT
Anticoagulation for LE DVT	Prevent recurrent VTE	17
ASA after prior MI/CVA	Prevent: • subsequent MI • subsequent CVA • mortality	 77 200 333
Buprenorphine (16mg+)[1]	Retention in treatment	2
Buprenorphine[2]	Prevent 1 yr mortality	5



Methadone and buprenorphine reduce mortality

All cause **mortality rates (per 1000 person years):**

- In methadone treatment: 11.3
- Out of methadone treatment: 36.1

- In buprenorphine treatment: 4.3
- Out of buprenorphine treatment: 9.5

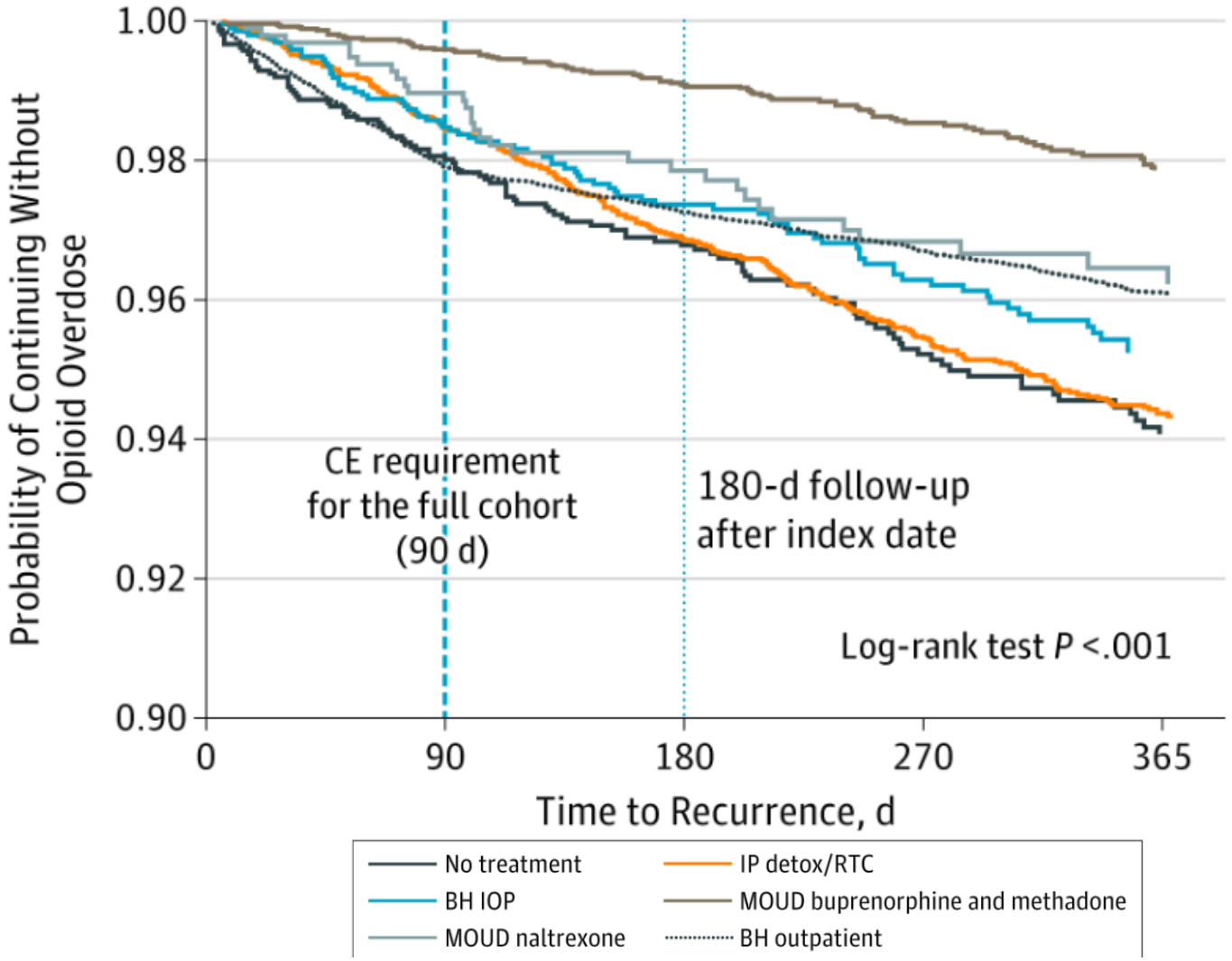
Overdose **mortality rates:**

- In methadone treatment: 2.6
- Out of methadone treatment: 12.7

- In buprenorphine treatment: 1.4
- Out of buprenorphine treatment: 4.6

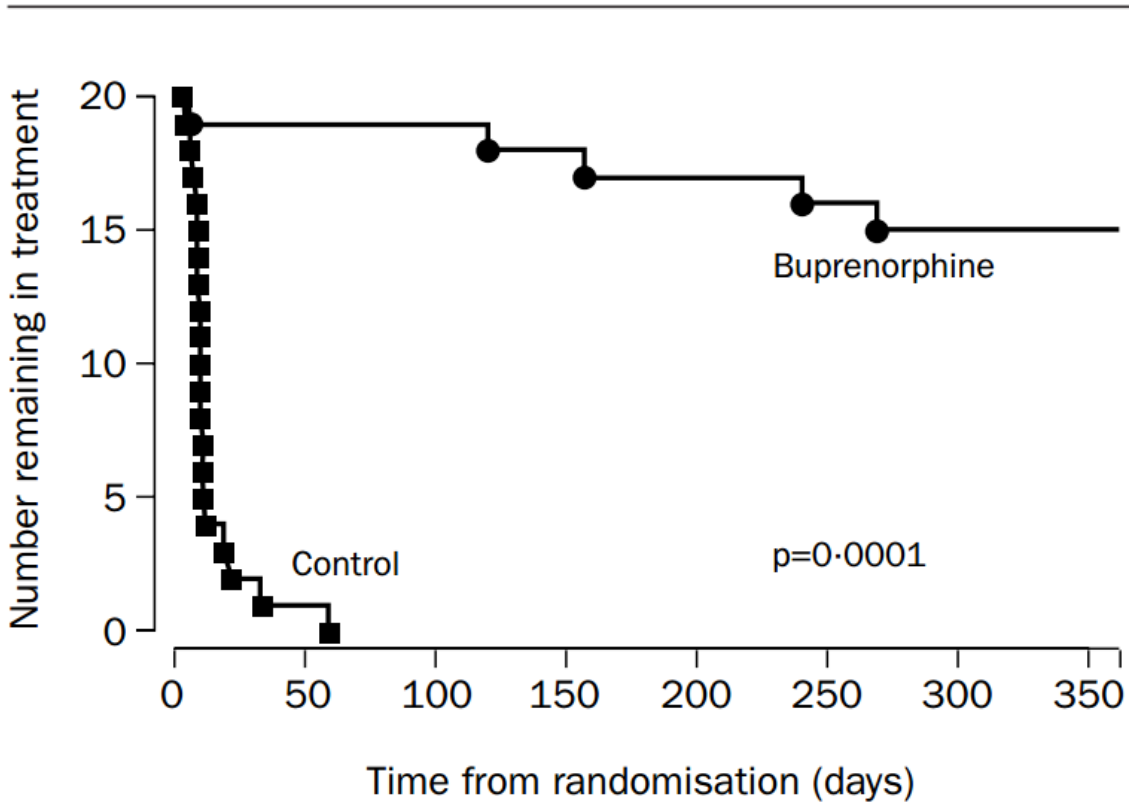
Sordo L, Barrio G, Bravo MJ, et al. *BMJ*. 2017;357:j1550. Published 2017 Apr 26.

Methadone & buprenorphine associated w/ reduced OD



Wakeman SE, Larochelle MR, Ameli O, et al. *JAMA Netw Open.* 2020;3(2):e1920622.

Buprenorphine treatment outcomes superior to withdrawal management plus psychosocial treatment



Kakko et al. The Lancet, Volume 361, Issue 9358, 2003, 662 - 668

Most treated patients achieve remission over time

Table 2.

Change in clinical characteristics from study entry to follow-up 18, 30, and 42 months later.

Participant characteristics	Month 0[1] (*n* = 338)	Month 18 (*n* = 252)	Month 30 (*n* = 312)	Month 42 (*n* = 306)
Substance use, past month				
Current opioid dependence[2], %**	100	16.3[a]	11.5	7.8[b]
Abstinent from illicit opioids[3], %***	0	51.2[a]	63.5[b]	61.4[b]
Opioid agonist treatment, %	0	31.8	38.1	36.9

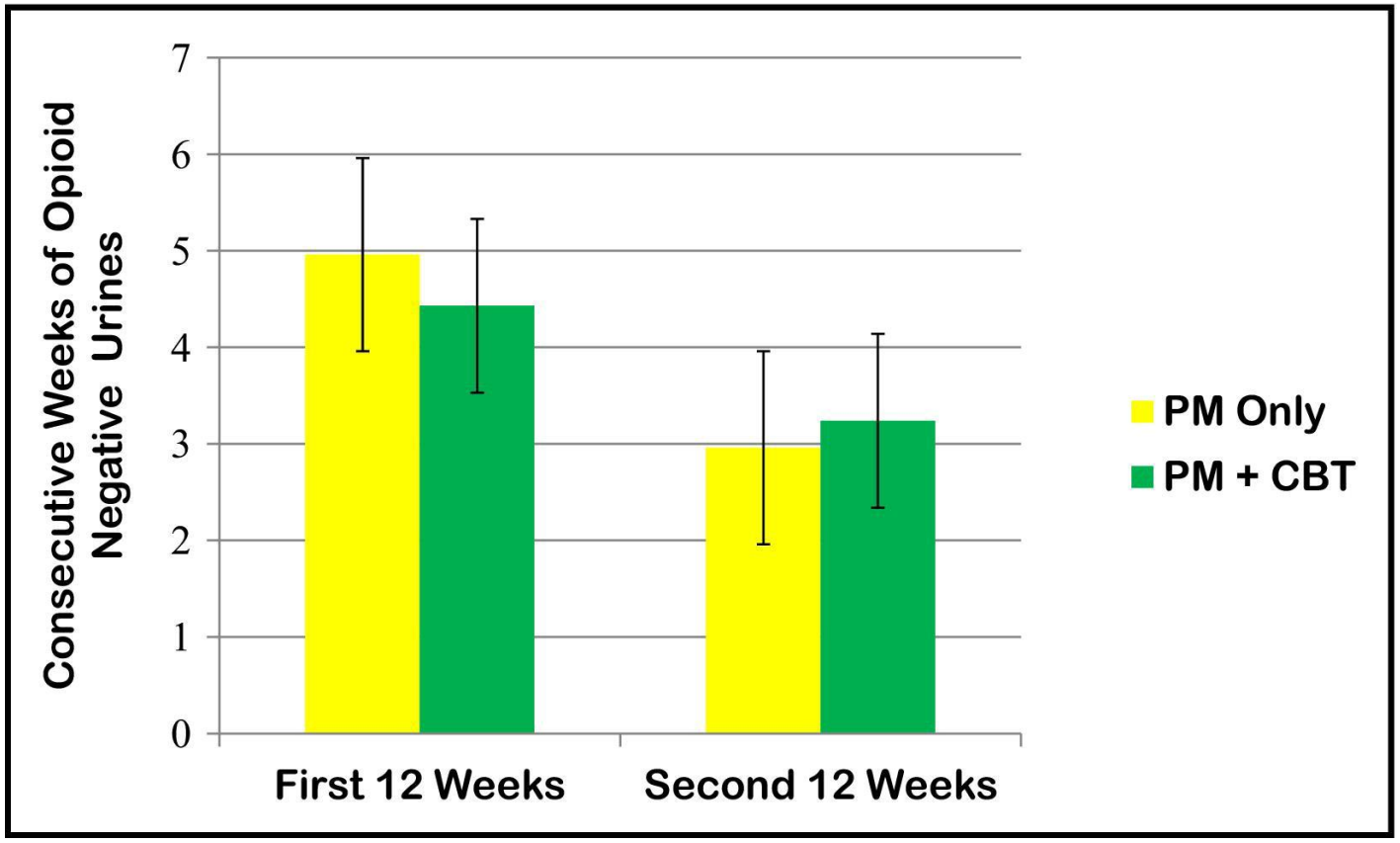
Weiss et al. Drug Alc Depend. 2015;150:112-9.

Using healthcare touchpoints as reachable moments

- Initiating methadone in hospital:
  - 82% present for follow-up addiction care
- Initiating buprenorphine in hospital vs withdrawal management alone:
  - Buprenorphine: 72.2% enter treatment after discharge
  - Withdrawal management : 11.9% enter treatment after discharge
- Initiating buprenorphine in ED vs referral to treatment
  - 78% vs 37% engaged in buprenorphine treatment at 30 days
  - Fewer days of opioid use w/ buprenorphine tx

J Gen Intern Med. Aug 2010; 25(8): 803–808; JAMA Intern Med 2014 Aug;174(8):1369-76.); D'Onofrio et al. JAMA 2015 Apr 28;313(16):1636-44

Treatment effective in primary care



No difference in opioid use, study completion, or cocaine use between the 2 groups

Fiellin DA et al. Am J Med 126:1 2013

NASEM Consensus Report

Conclusion 6:
Medication-based treatment is effective across all treatment settings studied to date. Withholding or failing to have available all classes of U.S. Food and Drug Administration–approved medication for the treatment of opioid use disorder in any care or criminal justice setting is denying appropriate medical treatment.

Treatment with FDA-approved medications is clearly effective in a broader range of care settings (e.g., office-based care settings, acute care, and criminal justice settings) than is currently the norm. There is no scientific evidence that justifies withholding medications from OUD patients in any setting or denying social services (e.g., housing, income supports) to individuals on medication for OUD. Therefore, to withhold treatment or deny services under these circumstances is unethical.

Any DEA-registered Practitioner Can Prescribe!

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Substance Abuse and Mental Health Services Administration

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Medications for Substance Use Disorders

Removal of DATA Waiver Requirement

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Pharmacist Verification of

Removal of DATA Waiver (X-Waiver) Requirement

Section 1262 of the Consolidated Appropriations Act, 2023 (also known as Omnibus bill), removes the federal requirement for practitioners to submit a Notice of Intent (have a waiver) to prescribe medications, like buprenorphine, for the treatment of opioid use disorder (OUD). With this provision, and effective immediately, SAMHSA will no longer be accepting NOIs (waiver applications).

All practitioners who have a current DEA registration that includes Schedule III authority, may now prescribe buprenorphine for Opioid Use Disorder in their practice if permitted by applicable state law and SAMHSA encourages them to do so. SAMHSA and DEA are actively working on implementation of a separate provision of the Omnibus related to training requirements for DEA registration that becomes effective in June 2023. Please continue to check this webpage for further updates and guidance.

What does the care cascade look like?

Identify patients through screening or acute presentation

Make a diagnosis

Initiate treatment without delay

Retain patients in treatment

Making a Diagnosis of OUD:

Problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period (mild =2-3; moderate = 4–5; severe = 6+)

1. Opioids taken in larger amounts or over a longer period of time than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time spent in activities to obtain, use, or recover from opioids.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems.
7. Important social, occupational, or recreational activities are given up or reduced.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that's likely to have been caused or exacerbated by the substance.
10. Tolerance*
11. Withdrawal*

* Tolerance and withdrawal insufficient to make diagnosis if due to prescribed medication

Initiating effective treatment

- **Medication**
- Psychosocial interventions
- Recovery supports
- Harm reduction

Similar to Management of Diabetes or HIV

- Goal to prevent acute and chronic complications
- Patient-centered and directed treatment plans and goals
- Treatment includes:
  - Medication
  - Behavioral support
  - Lifestyle changes
  - Regular monitoring

Goal of medication for OUD: buprenorphine& methadone

- **Relieve** withdrawal symptoms
- **Block** effects of other opioids
- **Reduce** cravings
- **Prevent** overdose

Details of Treatment:

Buprenorphine and methadone first line, patient preference important.

Agonist treatment: daily methadone or buprenorphine

Stable level of opioid effect experienced as feeling normal

Methadone still must be dispensed by opioid treatment program (in US)

The aims of agonist treatment include:

Reduction or cessation of ongoing opioid use and associated risks

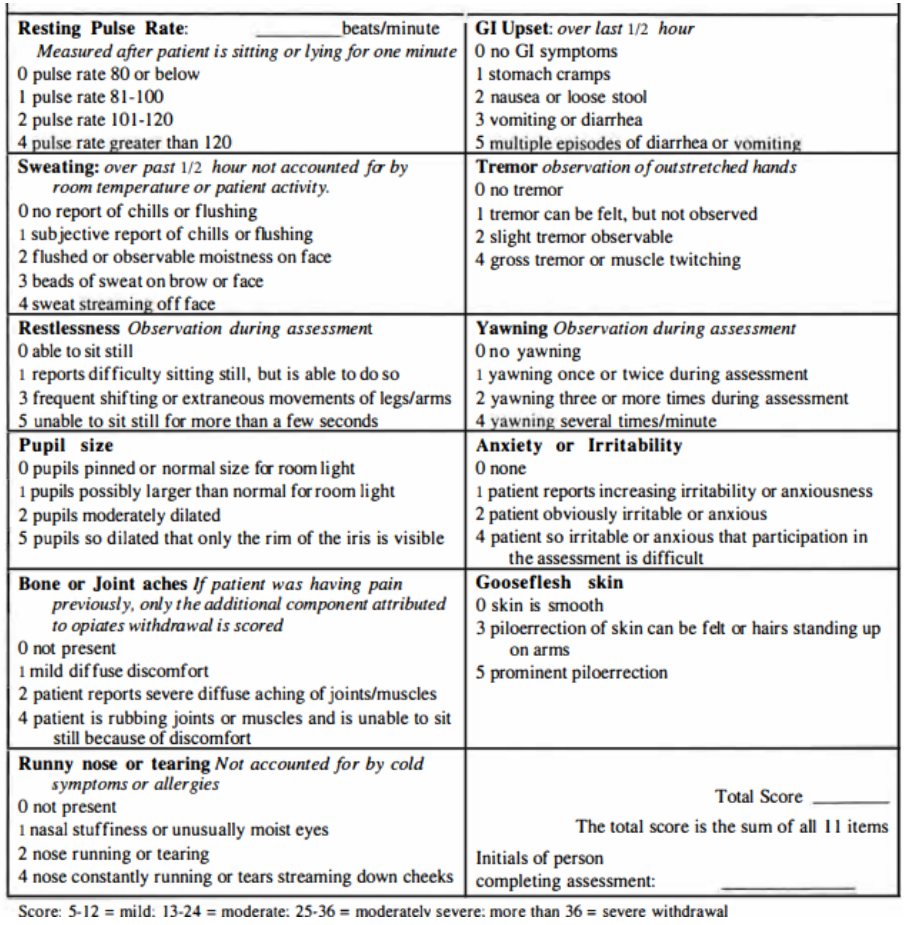
Improvement in health, quality of life, functional status

Antagonist treatment consists of once monthly injection

Second line treatment, relapse prevention

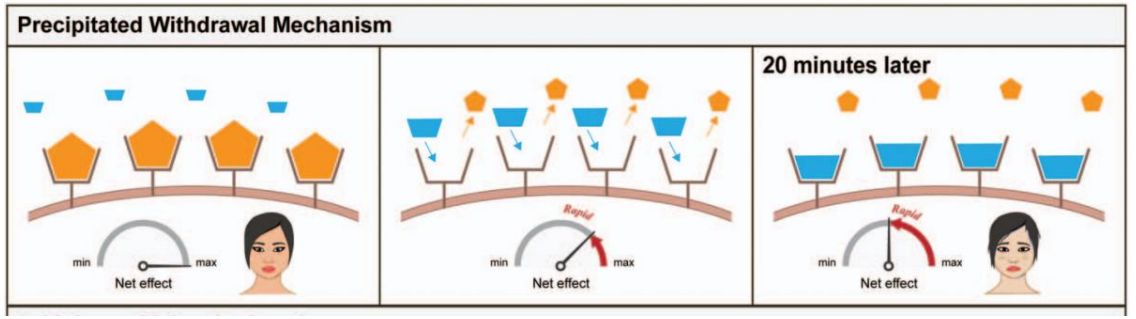
Understanding Buprenorphine

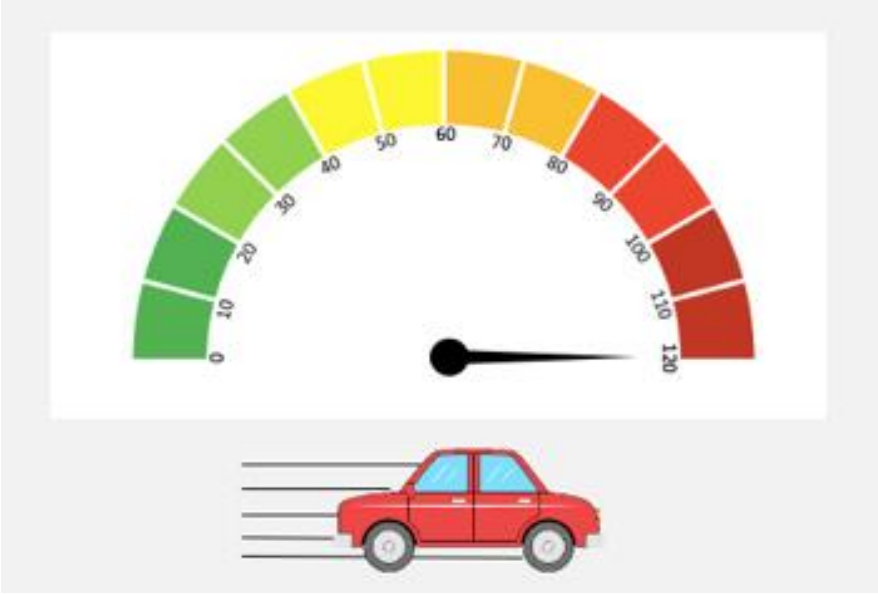
- Partial opioid agonist, ceiling effect for respiratory depression
- Higher retention in treatment and abstinence rates seen w/ doses >16 mg
- At higher doses, likely as effective as methadone
- Effective & safe in pregnancy and breastfeeding
- High affinity for opioid receptor, can displace full agonist opioids resulting in “precipitated withdrawal”
- To initiate, wait until person is in moderate withdrawal (COWS 8+) and start high dose or do low dose
- **For withdrawal, important that there are SIGNS not just symptoms**

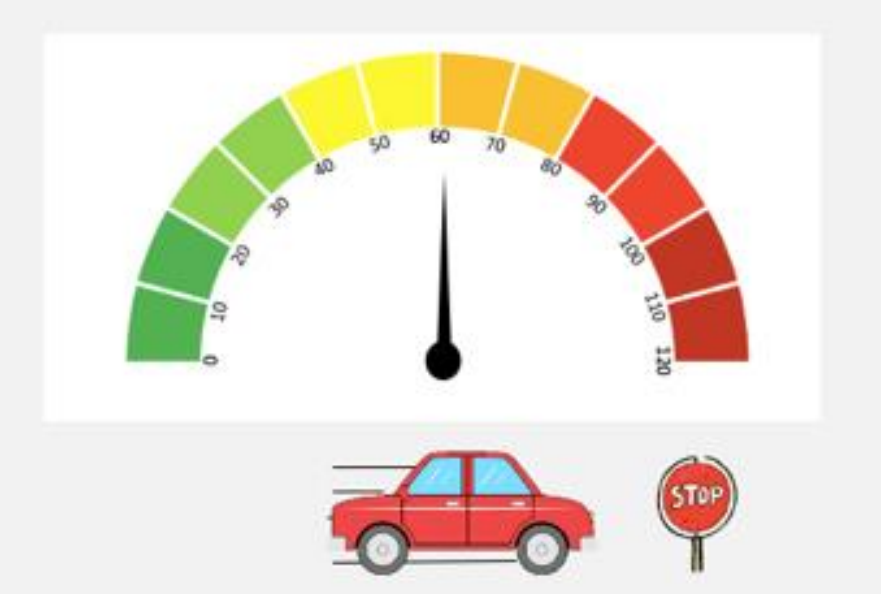


Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset**: *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or 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** 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 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	

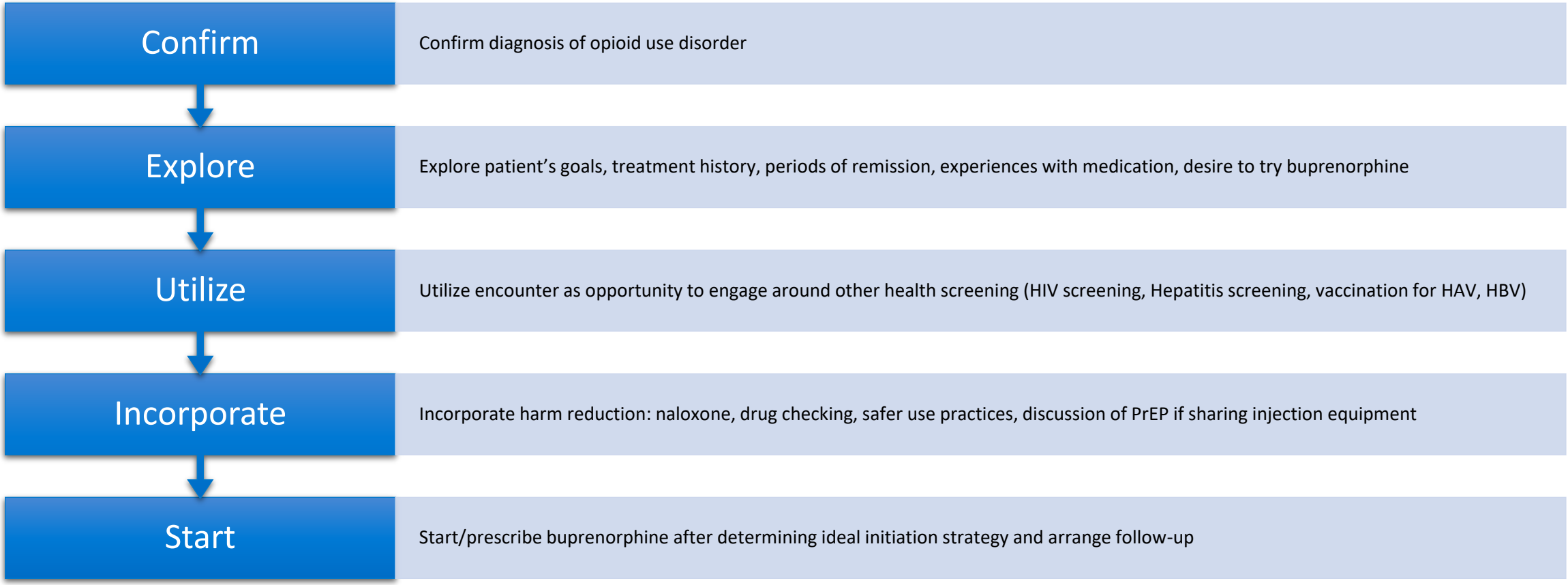
Precipitated Withdrawal







Starting Buprenorphine



Buprenorphine initiation dosing for a patient in moderate withdrawal

- Day 1: Buprenorphine 8-16 mg Q 1H x 2 doses to a maximum of 32 mg on day 1
- Day 2: Buprenorphine 16-24 mg daily
- Counseling critical– must be objectively in withdrawal and not just anxious
- Low dose initiation or XR-bupe are alternative approaches

Low dose initiation

- Some patients using fentanyl seem to experience precipitated withdrawal even after protracted wait times
- May be due to lipophilicity and range of fentanyl analogs
- Actual rates in clinical trials quite low
- If person not able to wait to be in objective withdrawal, currently taking full agonist opioids for pain and unable to stop, transitioning from methadone, or using fentanyl with a history of precipitated withdrawal, consider low dose initiation
- Uses 0.5 mg doses to gradually saturate receptor
- Can be done rapidly q3H or over days
- **Fear of precipitated withdrawal should not keep us from starting buprenorphine!**

Initiating buprenorphine

Initiation for patients in withdrawal or able to tolerate objective withdrawal

Day 1: buprenorphine 8-16mg Q1H x 2 up to max dose of 32 mg

Prescribe Buprenorphine/naloxone 8mg/2mg TID x 3-7 days and follow-up in primary care or refer to Bridge Clinic

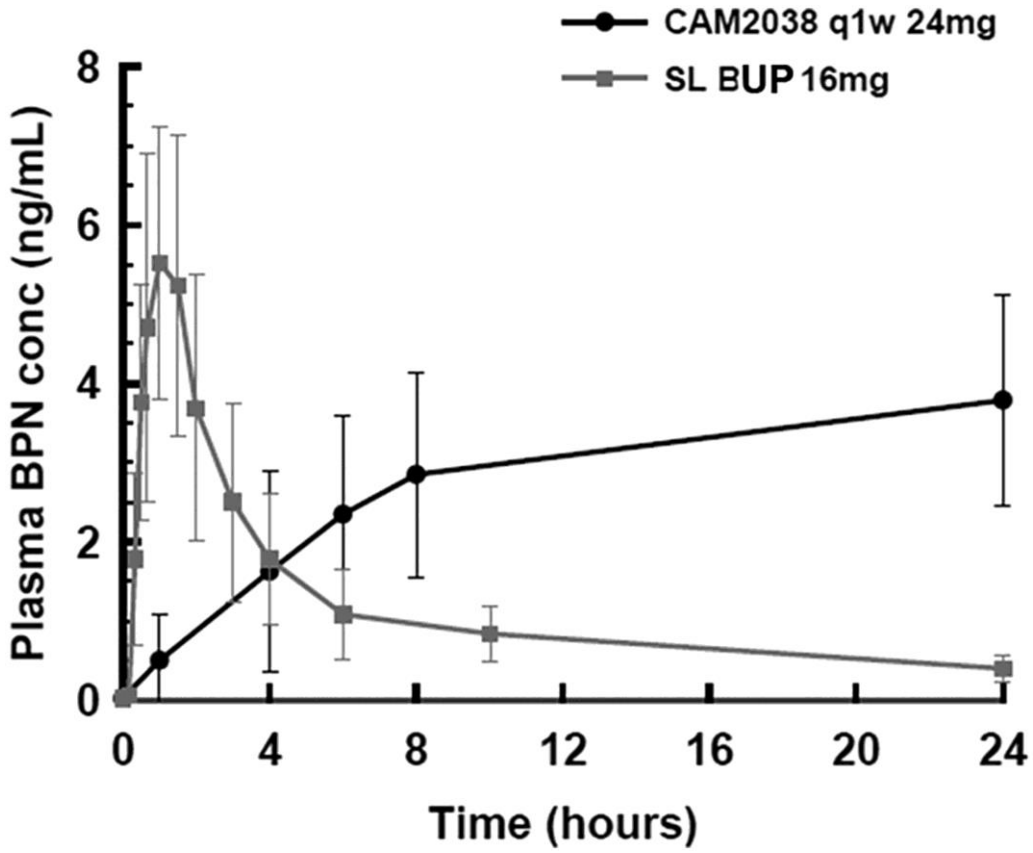
Initiation for patients not able to tolerate withdrawal or currently continuing full opioid

Start buprenorphine at 0.5 mg and increase dose as quickly as QID, or slower based on patient preference

Continue full agonist until patient gets to TDD of 8mg

What about direct to injection? Understanding pharmacokinetics of Brixadi

- SL buprenorphine has rapid absorption, but low oral bioavailability; reaches peak in 60 min
- After 24 mg weekly SC injection, plasma concentrations are therapeutic for craving and withdrawal between 6-8 hours, peak level usually within 20 hours achieved within 20 h. Terminal half-life is between 70 and 107 hours
- Slower rise in blood plasma level makes it a possible agent for low-dose initiation (as opposed to rapid rise from Sublocade)



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Initiating weekly Brixadi in the ED

- Multisite study aiming to rapidly expand access to ED-initiated BUP across 28 diverse EDs in the US (mix of geography, urban/suburban, and academic/community)
- Patients with COWS 4+ given 24 mg SC injection, observed for 2 H, and discharged (no rescue doses or supplemental SL) w/ follow-up in 7 days
- Very low rates (>0.5%) of precipitated withdrawal
- Subsequent trial started 24 mg SC in patients with COWS scores ranging from 0-7 and found that 93% of patients tolerated initiation without precipitated withdrawal and 73% were engaged in OUD treatment after 7 days.
- The rate of precipitated withdrawal was lowest among people with a COWS score of 4-7 (3.2%). The rate of precipitated withdrawal was 13.5% for people who had a COWS of 0-3.

D'Onofrio G, Perrone J, Hawk KF, Cowan E, McCormack R, Coupet E Jr, Owens PH, Martel SH, Huntley K, Walsh SL, Lofwall MR, Herring A; ED-INNOVATION Investigators. Early emergency department experience with 7-day extended-release injectable buprenorphine for opioid use disorder. Acad Emerg Med. 2023 Dec;30(12):1264-1271. doi: 10.1111/acem.14782. Epub 2023 Aug 22. PMID: 37501652; PMCID: PMC10822018.

What about methadone?

ED/Inpatient

- Generally, start at 40-50 mg x 1 and then additional 10 mg PRN for ongoing signs of opioid withdrawal
- Consolidate TDD next day, uptitrate by ~10 mg for ongoing cravings/withdrawal
- EKG prior to starting if prolonged QTc or risk factors; check EKG again at 100 mg and for dose increases beyond 100 mg

Outpatient (72-hour vs OTP)

- Under 72-hour rule allowed to administer/dispense but not prescribe methadone for up to 3 days
- Generally, start at 50 mg unless low tolerance and increase by 10-20 mg per day for up to max of 3 days of dosing
- Refer to OTP, generally they will start at 50 mg

Ongoing management of patients

Check in visits, frequently at first, space out as stabilize

Like any chronic care management:

- evaluate symptoms (cravings, withdrawal, use)
- benefits or challenges with medication
- need for additional support
- focus on patient identified goals

Patients don't fail treatment, but treatment can fail patients

If person not doing well, modify treatment

- Increase dose
- Increase supports
- If persistent challenges, explore changing meds
- Incorporate harm reduction

Take home points

Increased access to opioid use disorder treatment across healthcare settings is needed to address overdose crisis

Opioid use disorder is a treatable, good prognosis condition and prescribing buprenorphine is easy and fulfilling

Like other chronic conditions, it can be diagnosed, treated, and managed in general medical settings

Thank you!

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