
AMERICAN SOCIETY OF ADDICTION MEDICINE
FOUNDED 1954
ASAM
ASAM
American Society of
Addiction Medicine


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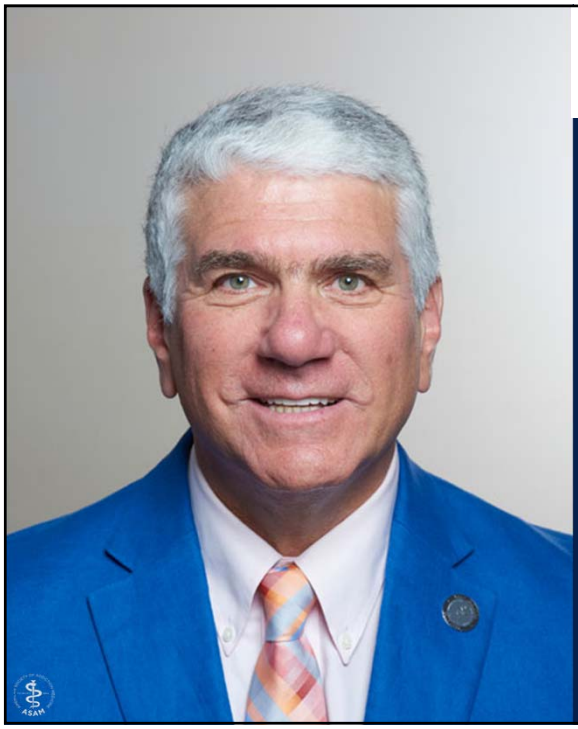
THE
ASAM
Treatment of Opioid
Use Disorder Course
Includes waiver qualifying requirements



Faculty

Edwin Salsitz, MD, DFASAM

Dr. Salsitz has been an attending physician at Mt. Sinai Beth Israel, Division of Chemical Dependency, in New York City since 1983, and is an Associate Professor of Medicine at the Icahn School of Medicine at Mount Sinai. He is the principal investigator of the Methadone Medical Maintenance (office-based methadone maintenance) research project. He is certified by the American Board of Addiction Medicine (ABAM) and the Board of Internal Medicine and Pulmonary Disease. He has published and frequently lectures on addiction medicine topics.

Disclosure Information

Edwin Salsitz, MD, DFASAM

[No Disclosures]

About ASAM

ASAM, founded in 1954, is a professional medical society representing over 6,000 physicians, clinicians and associated professionals in the field of addiction medicine. ASAM is dedicated to increasing access and improving the quality of addiction treatment, educating physicians and the public, supporting research and prevention, and promoting the appropriate role of physicians in the care of patients with addiction.

More information available at
https://www.asam.org/about-us/about-asam

Course Learning Objectives

1. Identify, assess, and diagnose patients with opioid use disorder while considering severity, chronicity, individual characteristics, and psychiatric and medical comorbidities.
2. Develop an individualized, patient-centered treatment plan including negotiating treatment goals by evaluating appropriate medication- and psychosocial-based treatment options.
3. Monitor progress and modify treatment plan based on patient needs and progress toward treatment goals.
4. Implement best practices for office systems including team-based care to support treatment with medications for opioid use disorder.
5. Examine misconceptions, stigma, and complexities (bioethical, social, clinical, public health) associated with opioid use disorder and the use of medications to treat opioid use disorder.

Course Announcements: Log of Trainees

- You MUST sign in and out on the log of trainees three times.
- If you do not sign your name three times, you will not be eligible for the waiver and your name will not be submitted with our attendance report.
- You must sign in at the beginning of the course, after lunch, and again at the conclusion of the course.

Course Announcements: Waiver Application

- You can fill out the online waiver application form on SAMHSA's website or through their mobile app MATx.
- SAMHSA Certificate Submission: You will need to submit a copy of your certificate to the SAMHSA Center for Substance Abuse Treatment (CSAT) after you submit the online waiver application by emailing it to: infobuprenorphine@samhsa.hhs.gov or by faxing it to 301-576-5237.

Course Announcements: NPs and PAs

- If you are an NP or PA, this 8-hour course will count toward the 24-hour education requirement under CARA.
- ASAM offers the additional 16 hours needed free of cost. Please contact education@ASAM.org to learn how to enroll in the completely online offering.

Course Announcements: Claiming CME

- Evaluation:
  - Complete the CME evaluation in the ASAM e-Learning Center.
- CME Certificate:
  - Claim your credits after completing the evaluation.
  - Click the blue “Claim Medical Credits” button to view/save your certificate.
  - Return to this page at any time to view/save your certificate.

Course Announcements: Acknowledgment

The ASAM Treatment of Opioid Use Disorder Course has been made available in part by an unrestricted educational grant from Indivior, Inc.

Funding for this initiative was made possible (in part) by grant no. 1H79TI026793-01 from SAMHSA. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

Introduction and Context Setting

Case-Based Learning

What is it?

We will follow a case-based learning approach where we will explore scenarios that resemble or typically are real-world examples. This approach is learner-centered and links theoretical knowledge to practice by giving opportunities for the application of knowledge.

Session 1

Identifying, Assessing and Diagnosing Patients with Opioid Use Disorder

Session Learning Objectives

1. Describe the current epidemiologic trends in prescription opioid misuse and illicit opioid use including overdose and use disorders.
2. Describe opioid use neurobiology with initial use and with prolonged use as it applies to the development of an opioid use disorder and relapse risk.
3. Screen and assess patients for the full spectrum of harmful opioid use, including misuse and diagnosing opioid use disorder.
4. Discuss the assessment and management of patients with psychiatric and medical co-morbidities associated with opioid use disorder.
5. Identify patients with a moderate to severe OUD who are appropriate for treatment with medications in an office-based setting.

MARY'S CASE

Mary's Case

A colleague contacts you seeking help for their daughter. Mary is a 22-year-old who is currently using intranasal (IN) and intravenous (IV) heroin. Her opioid use started in high school with oxycodone pills which her friends were crushing and snorting to get "high." Mary would also binge drink at parties on the weekend and smoke cannabis daily during this time.

At first, Mary did not like the feeling she experienced from oxycodone—she got nauseous and vomited. But after a few more times, she found that the oxycodone was relaxing, and eased her anxiety. She felt like this was what her brain was "missing."

Mary's Case

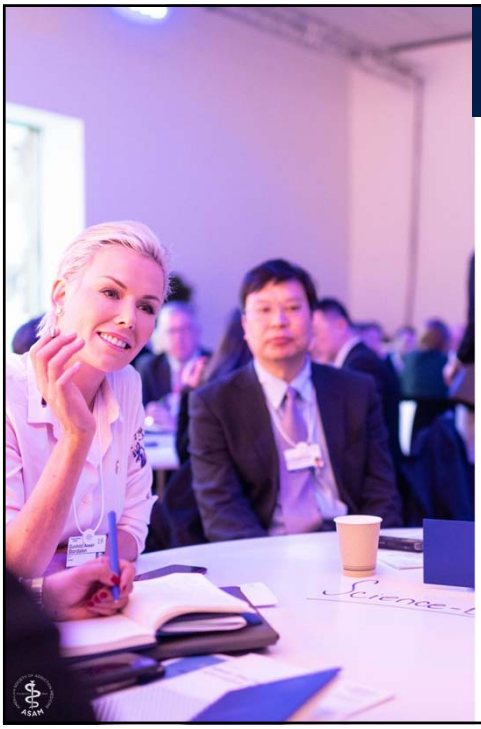
Your colleague tells you that Mary was sexually abused by an older male cousin when she was 9 years old. She kept this a secret until very recently. Mary has been evaluated by a psychiatrist who diagnosed her with PTSD. She was prescribed an SSRI, and started seeing a therapist, but her heroin use interferes with her ability to adhere to both.

Mary continued to use oxycodone tablets, but in her senior year, her supplier was arrested, and a new boyfriend introduced her to heroin, which was more available and considerably cheaper. At first, she only snorted the heroin. She managed to graduate high school and enrolled in her local community college. She had no idea what she wanted to study or eventually "do with her life." She dropped out after one semester.

Mary's Case

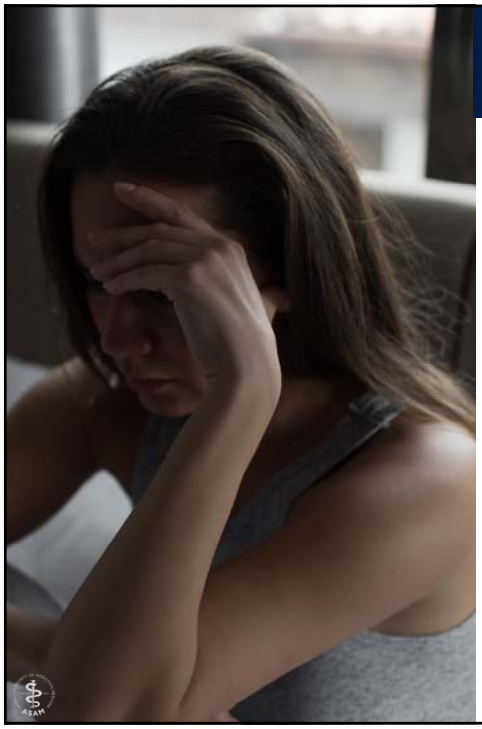
Mary has been injecting heroin. She obtains her needles and syringes from a needle exchange. She has had two overdoses, which required naloxone reversal by her boyfriend and once by your colleague. Fentanyl contamination was suspected in both cases. Mary has been in three short term "detox" centers and one 28-day rehab. She has attended a few NA meetings with her boyfriend. She thinks medications, such as methadone and buprenorphine, would just be trading one addiction for another.

Your colleague was reluctant to reach out to you earlier, due to a feeling of shame and guilt. There is concern about the stigma of addiction, both for Mary and your colleague. An appointment has been made for Mary and for your colleague for the next day.



Activity 1: Learner Introductions

- **Task:** Introduce yourself to your group.
- **Share:** Where are you from? What do you do? What is your specialty? What are your goals for today? Complete the following sentence: "***This training will meet my goals if…***"
- **Time Allocated:** 5 minutes

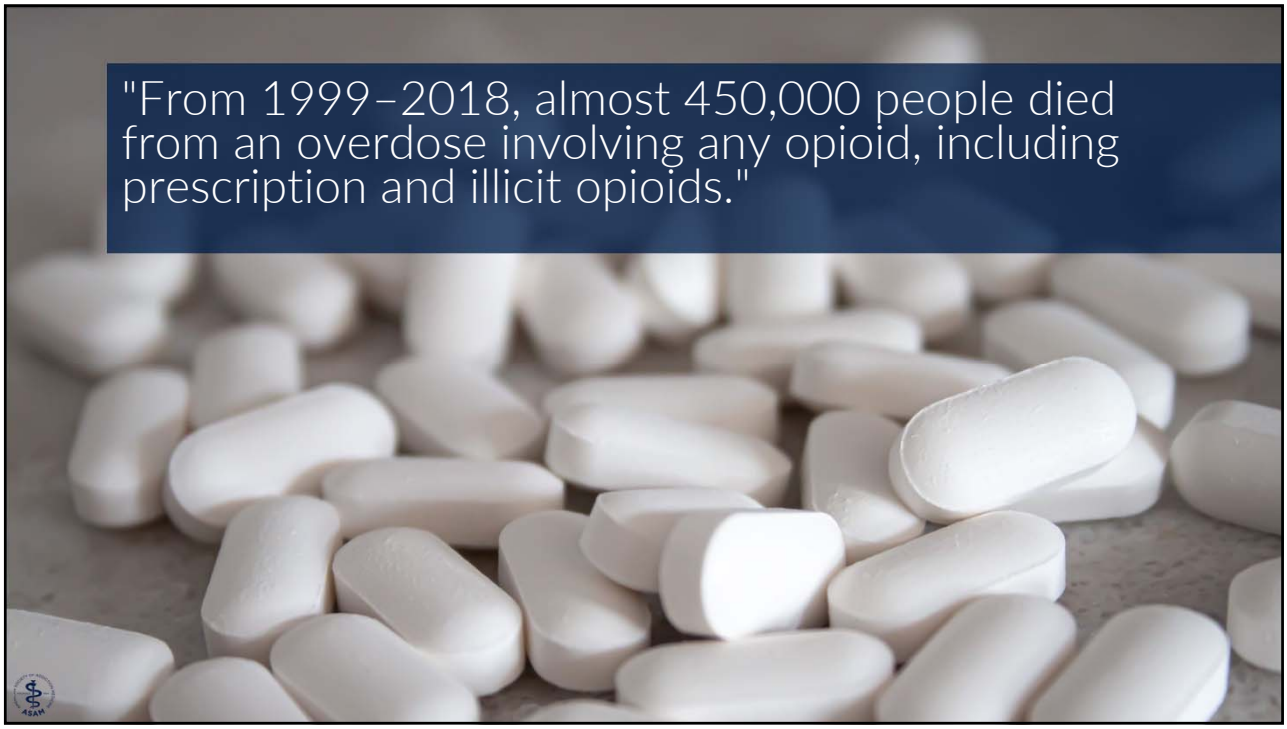


Activity 2: Case Discussion – Mary

- **Task:** With your group, discuss Mary's case.
- **Discuss:** Review the case with your group in break-out session and answer the prompting questions at the end of the case introduction. Take notes to report back as a group.
- **Time Allocated:** 10 minutes

HISTORY, EPIDEMIOLOGY, AND TRENDS

The Scope of the Opioid Epidemic



Opioid Addiction

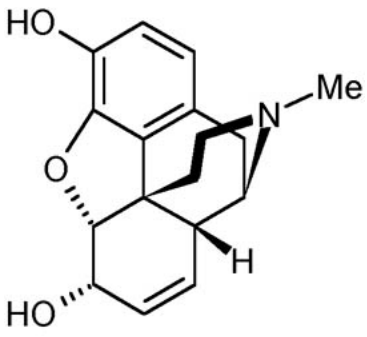
- Opioid addiction afflicts individuals from all socioeconomic and educational backgrounds.
- Four million people admit to the nonmedical use of prescription opioids. Perhaps more concerning, 400,000 people had used heroin in the past month based on data from 2015 through 2016.
- Roughly 80% of new heroin users in the United States report pills as their initiation to opioid use and subsequent OUD.
- From 2002 through 2011, approximately 25 million people in the United States began nonmedical use of pain relievers. More than 11 million misused the medications.
- Emergency department visits due to complications and overdose have increased annually since 2010. Rates of ED visits involving opioids more than tripled from 1999 through 2013.
- In 2017, opioid overdose was declared a national emergency in the United States.

Azadfard M. Opioid Addiction. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK448203/#article-26212.s3. Published June 29, 2020. Accessed August 6, 2020.

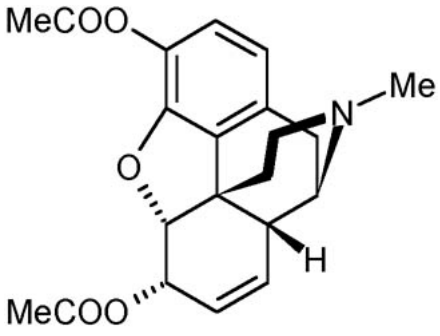
Papaver Somniferum — The Origins of Opium Alkaloids

- Morphine
- Codeine
- Thebaine
- Papaverine

Morphine



Heroin

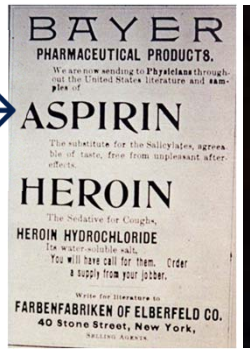


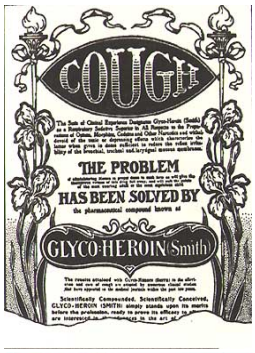
Diacetylmorphine

Pharmaceutical Products

AKG, London

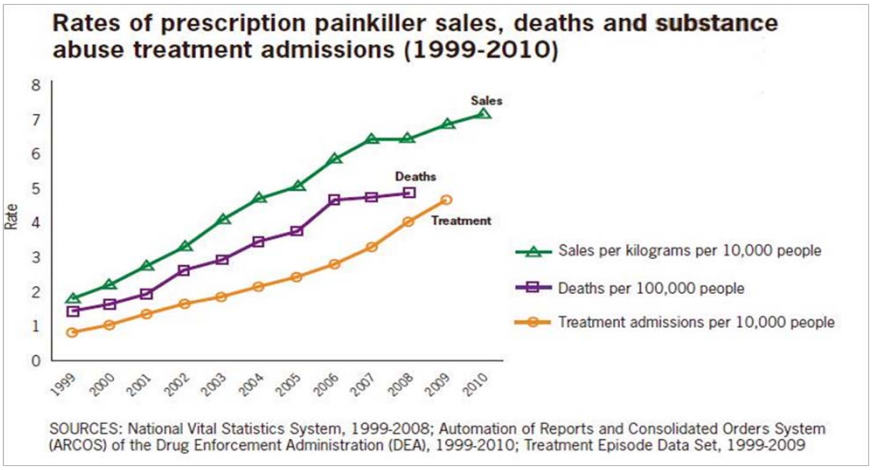
History of Opioids





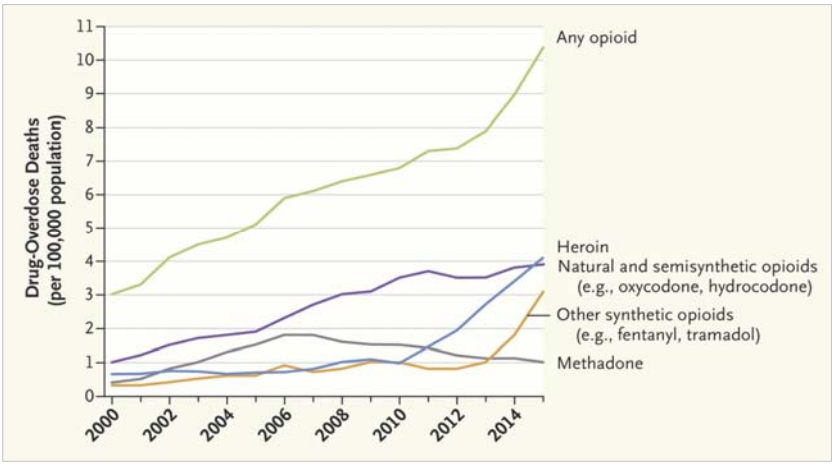
Morphine Syrup –
10 mg/teaspoon

Rates of Opioid Overdose Deaths, Sales, and Treatment Admissions, United States, 1999 - 2010



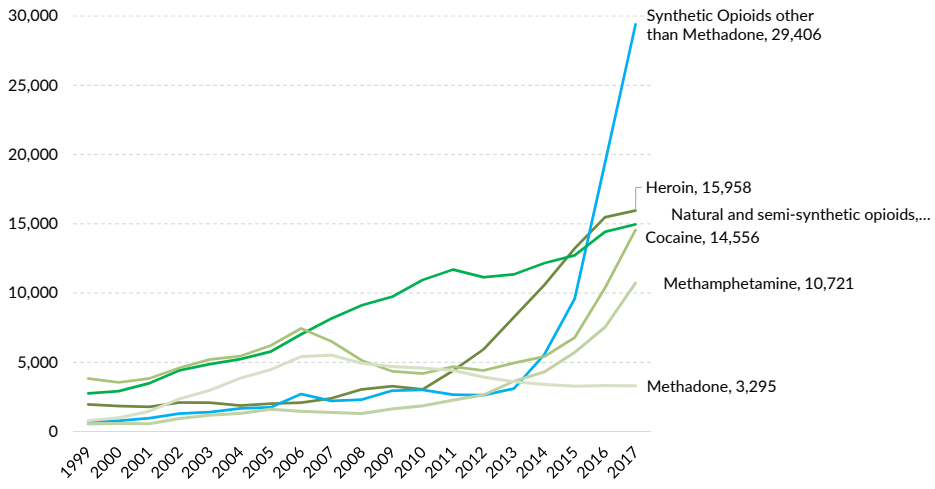
Drug-Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000–2014

The NEW ENGLAND JOURNAL of MEDICINE



Frank RG, Pollack HA. N Engl J Med 2017;376:605-607.

Drugs Involved in US Overdose Deaths, 1999 - 2017



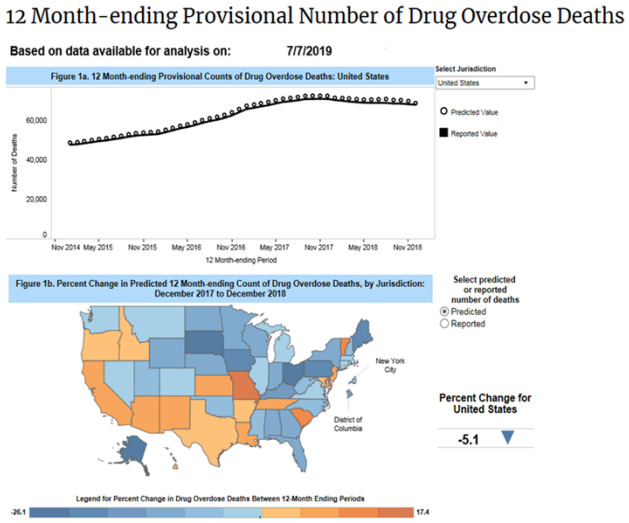
Source: CDC WONDER

A Hint of Good News

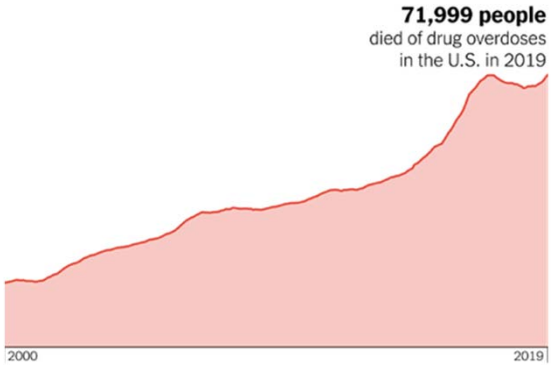
Total = 68,500 First ↓ since 1990

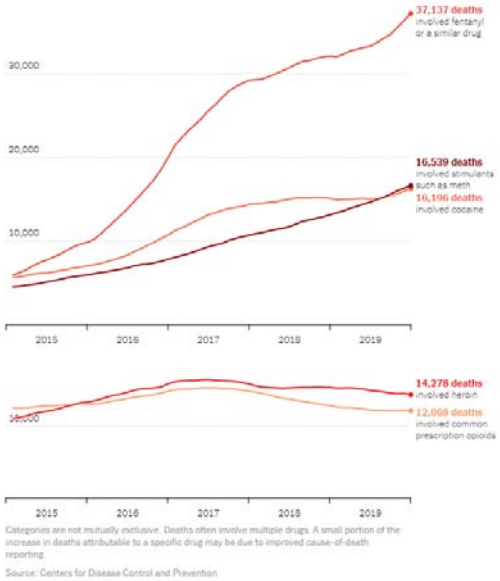
SD ↓25%, OH ↓22%, WV ↓8%
MO ↑16% DE ↑16%

Health and Human Services Secretary Alex Azar noted that more patients were receiving medication treatment, naloxone was being more widely distributed, and opioid prescriptions were down.

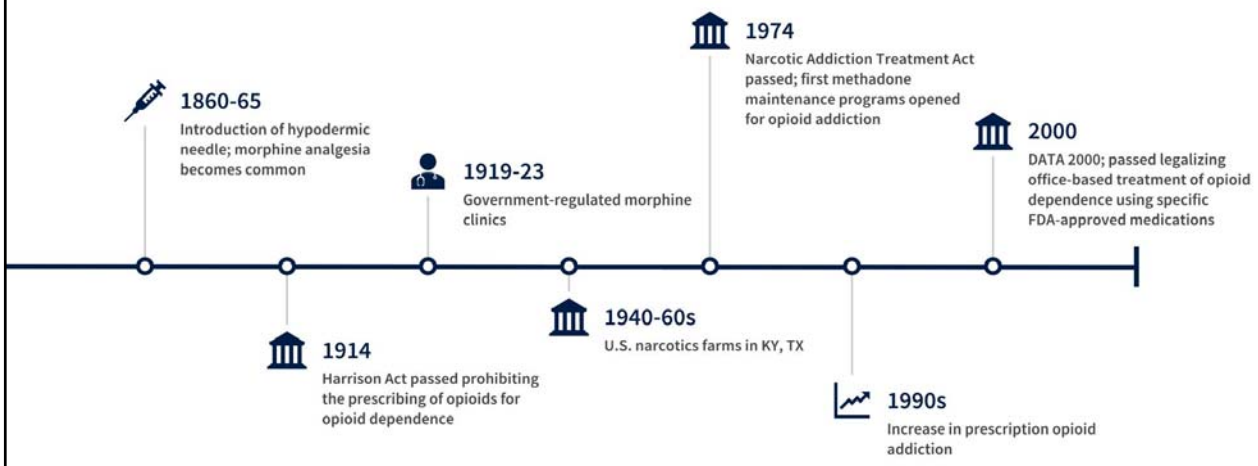


Drug Overdose Deaths 2019 - CDC



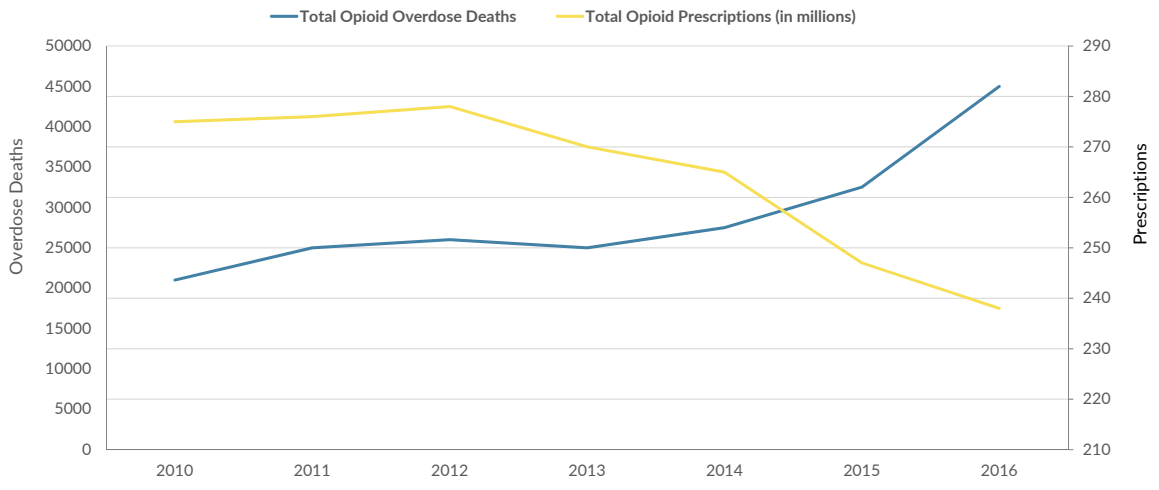


Brief History of Opioids in the US



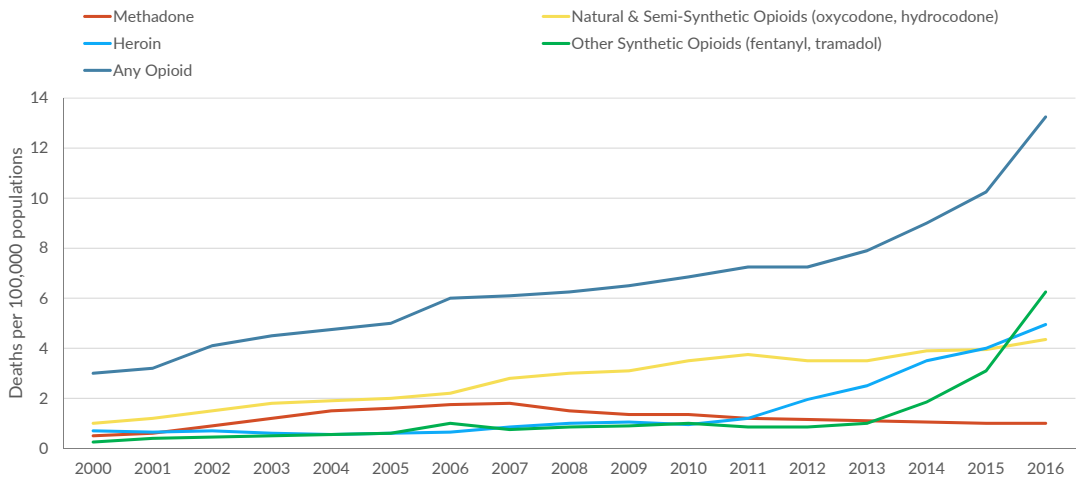
CDC, 2018; Pezalla et al., 2017

Opioid Overdose and Prescribing Trends

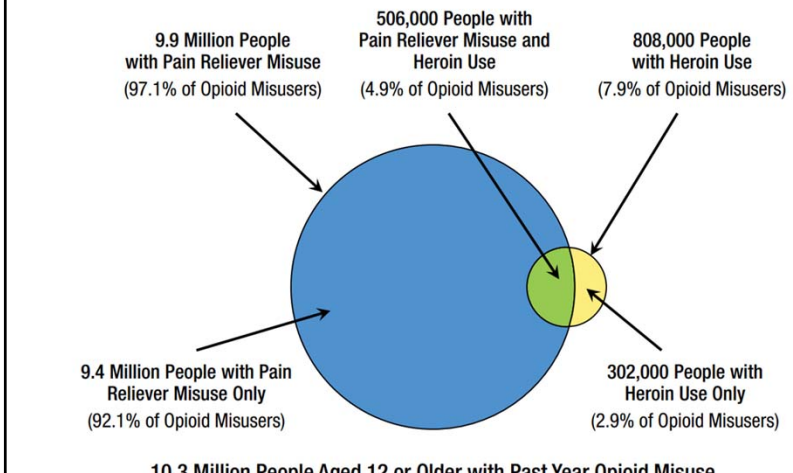


CDC, 2018; Pezalla et al., 2017

Overdoses By Specific Opioid



CDC/NCMS, National Vital Statistics System, Mortality. CDC Wonder, Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2017



SAMHSA. (2019). Results from the 2018 National Survey on Drug Use and Health

Prescription Opioid Misuse and Heroin Use Past Year

Lethal Dose

- *Morphine* = 1x
- *Fentanyl* = 100x
- *Carfentanil* = 10,000x

Lethal doses of heroin compared to "synthetic" opioids.

DEA Schedule I II II Legal Implications

"Death pill": fentanyl disguised as other drugs linked to spike in US overdoses.

Audience Response

Opioids have been used medicinally for thousands of years, at which point did they become concerning for development of a substance use disorder?

A. In the late 1900s, with the development of pain as the fifth vital sign.

B. In the early 1900s, with government regulations limiting opioid importation.

C. In the mid 1800s, with the development of the hypodermic needle.

D. Since they were discovered as an analgesic thousands of years ago.

UNDERSTANDING ADDICTION AS A DISEASE

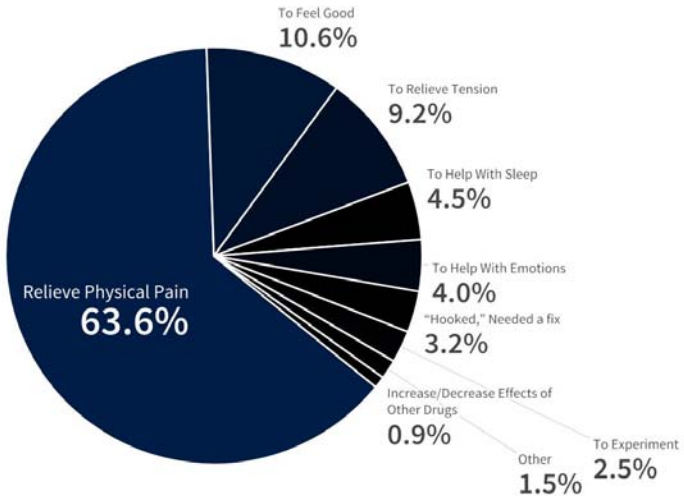
Neurobiology of Addiction

Why Do People Take Drugs?

TO FEEL GOOD To stimulate pleasant feelings, sensations, and to share them

TO FEEL BETTER To lessen anxiety, worries, fears, depression, hopelessness, and withdrawal; to relieve pain, both physical and emotional

Prescription Opioid Misuse and Heroin Use

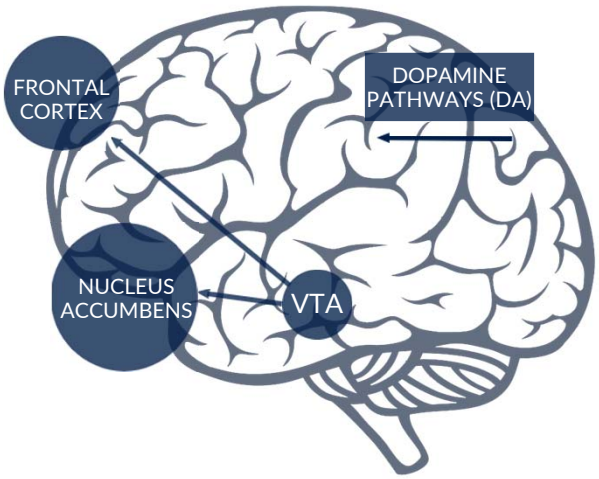


SAMHSA (2019). Results from the 2018 National Survey on Drug Use and Health

Reward Pathways

Mesolimbic Dopaminergic Circuitry

(Limbic System)



Reward Pathways

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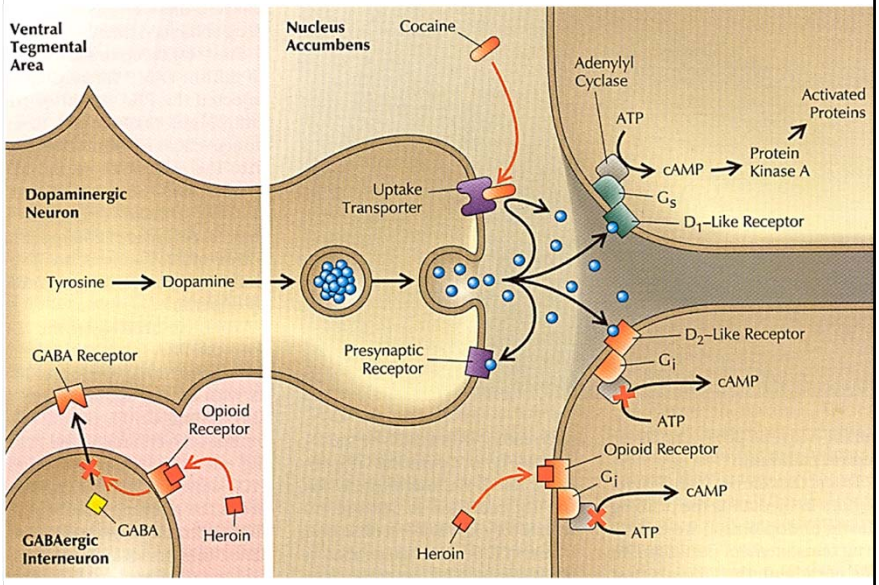
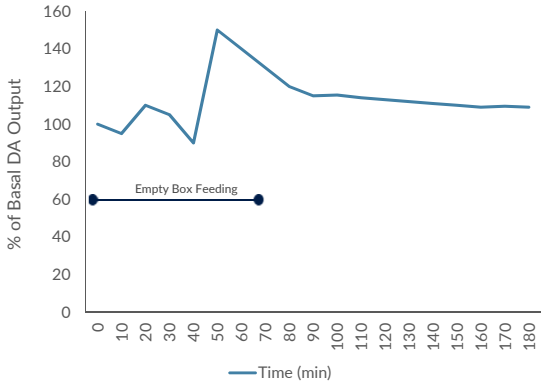


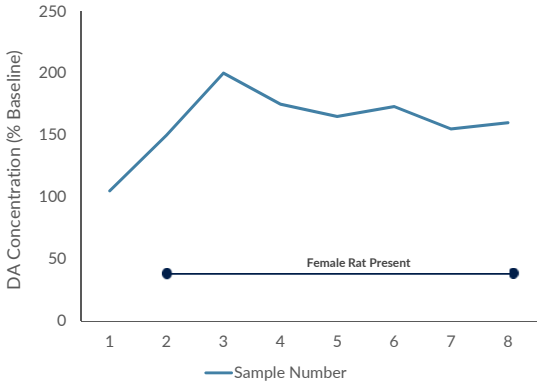
Leshner AI. Hosp Pract. 1996

Natural Rewards Elevate Dopamine Levels

Food *(in rodents)*



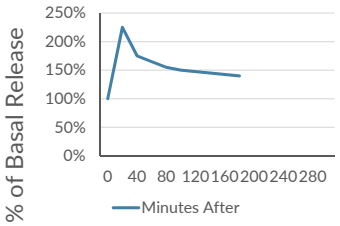
Sex *(in rodents)*



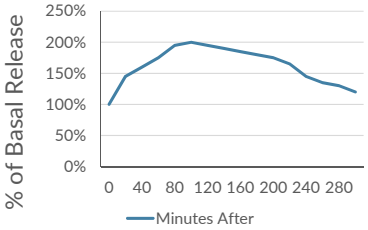
Di Chiara et al., Neurosci, 1999.Fiorino and Phillips, J. Neurosci, 1997

Drugs Elevate Dopamine More/Longer

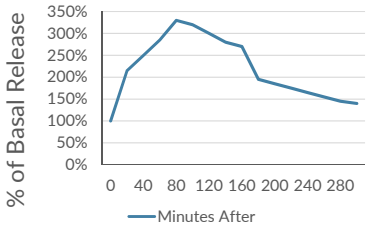
Nicotine *(in rodents)*



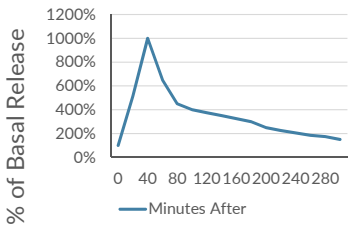
Morphine *(in rodents)*



Cocaine *(in rodents)*

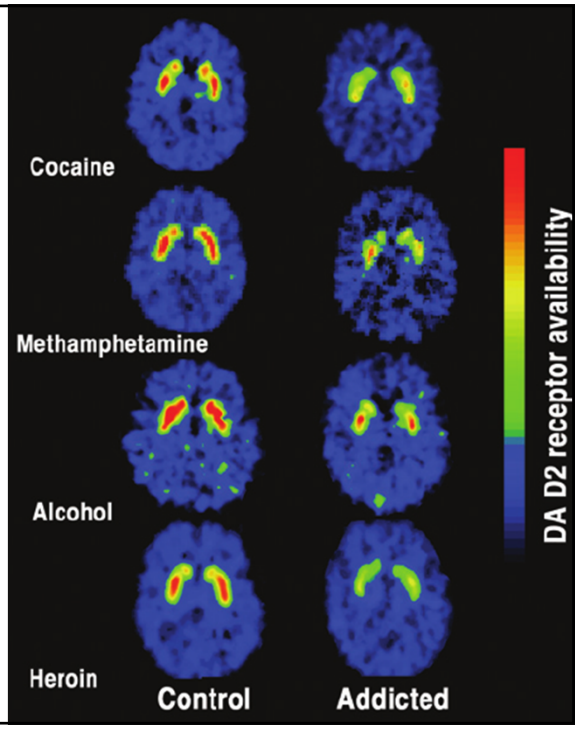


Amphetamine *(in rodents)*

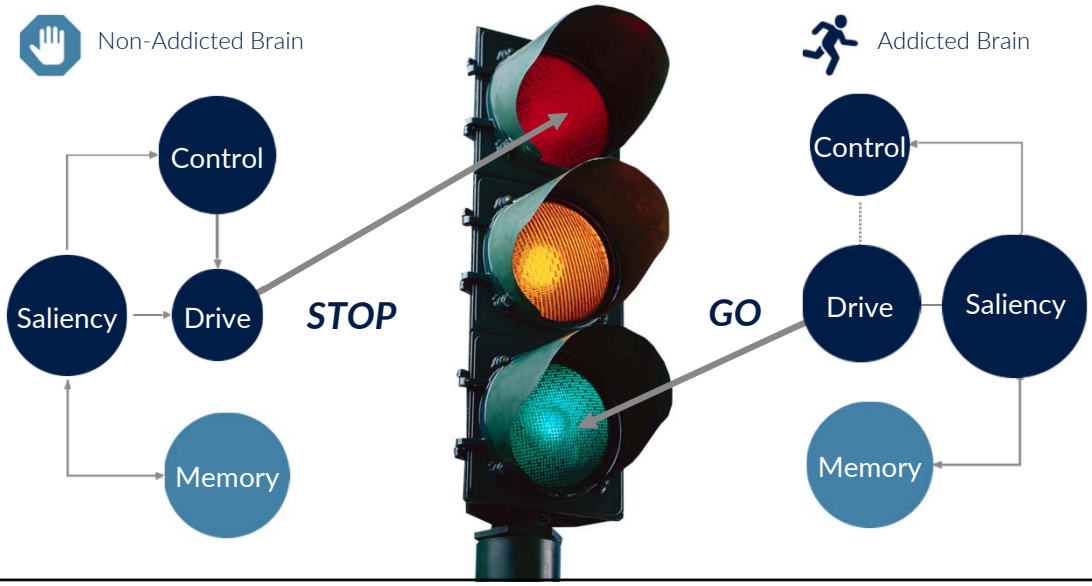


Di Chiara G, Imperato A. Proc Natl Sci. 1988

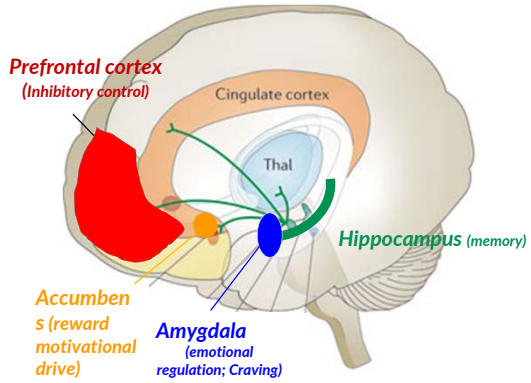
Dopamine D2 Receptors are Decreased in the Addicted Brain



Non-Addicted Brain V. Addicted Brain

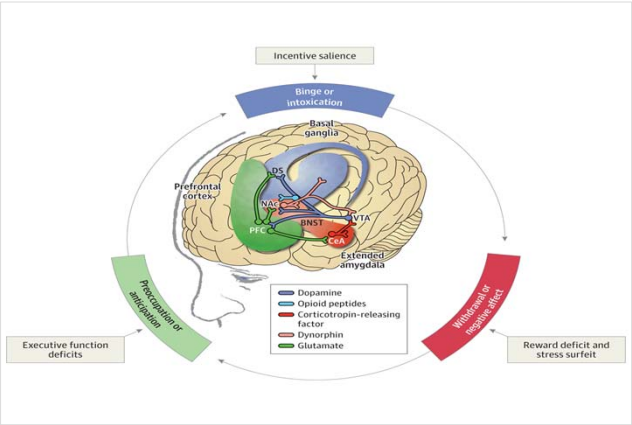


The Neurobiological Challenge of Addiction



↓ *Inhibitory control*
↑ *Increase reward drive*
↑ *Craving*
↑ *Drug memories*

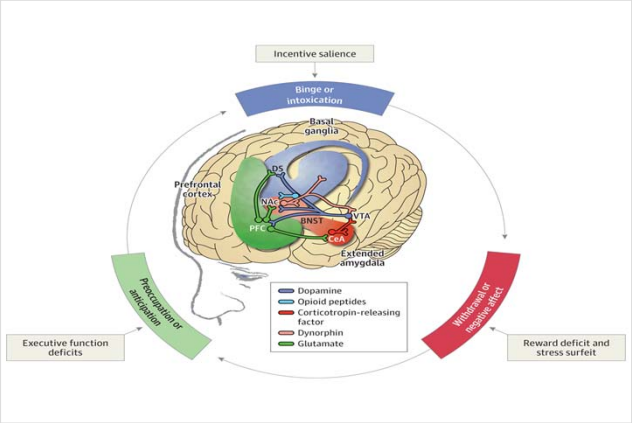
Three Stages of the Addiction Cycle and Associated Neural Circuits



- **Stage 1:** Binge or Intoxication
- **Stage 2:** Negative Affect or Withdrawal
- **Stage 3:** Preoccupation or Anticipation (Craving)

Volkow, N. D., Jones, E. B., Einstein, E. B., & Wargo, E. M. (2019). Prevention and treatment of opioid misuse and addiction: A review

Three Stages of the Addiction Cycle and Associated Neural Circuits



- Rates vary with the drug and by severity of disorder
- Stages associated respectively with activity in the: basal ganglia ([NAc] and [DS]), Extended amygdala, and PFC
- BNST indicates bed nucleus of the stria terminalis, CeA, and VTA
- Abbreviations:
  - Bed nucleus of the stria terminalis (BNST)
  - Central nucleus of the Amygdala (CeA)
  - Dorsal Striatum [DS]
  - Nucleus Accumbens [NAc]
  - Prefrontal cortex (PFC)
  - Ventral Tegmental Area (VTA)

Volkow, N. D., Jones, E. B., Einstein, E. B., & Wargo, E. M. (2019). Prevention and treatment of opioid misuse and addiction: a review

Opioid Tolerance and Physical Dependence

TOLERANCE

Increased dosage needed to produce specific effect. Develops readily for CNS and respiratory depression.

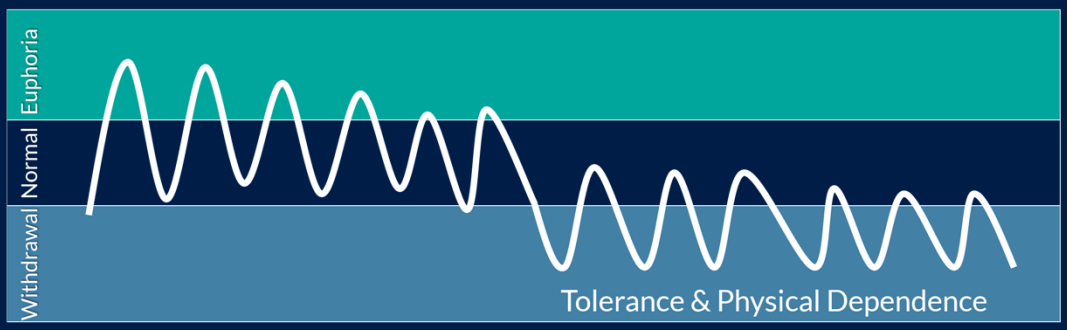
Both tolerance and physical dependence are physiological adaptations to chronic opioid exposure and DO NOT equal addiction or opioid use disorder

PHYSICAL DEPENDENCE

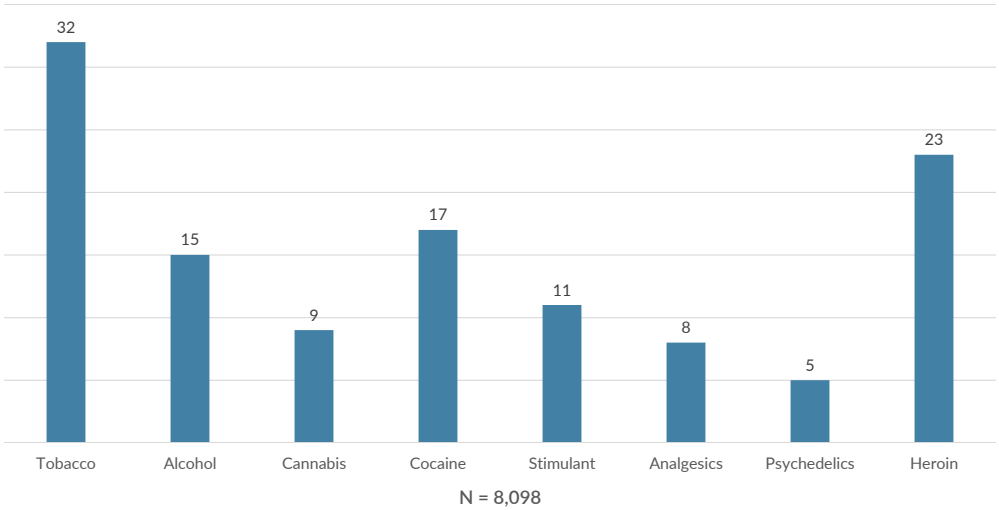
Signs and symptoms of withdrawal by abrupt opioid cessation, rapid dose reduction

Natural History Of Opioid Use Disorder

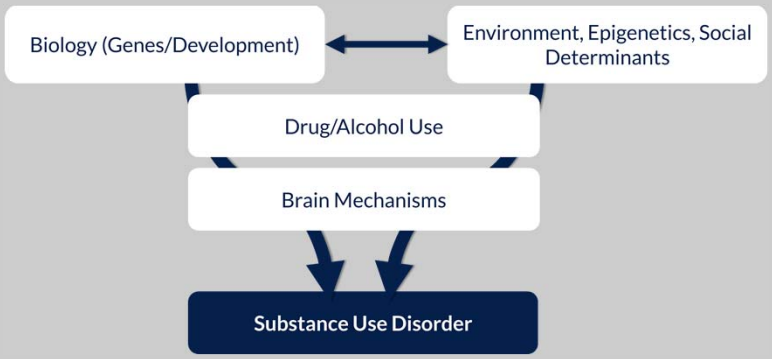
Alford DP. http://www.bumc.bu.edu/care/



Addiction Vulnerability/Prevalence Varies By Substance



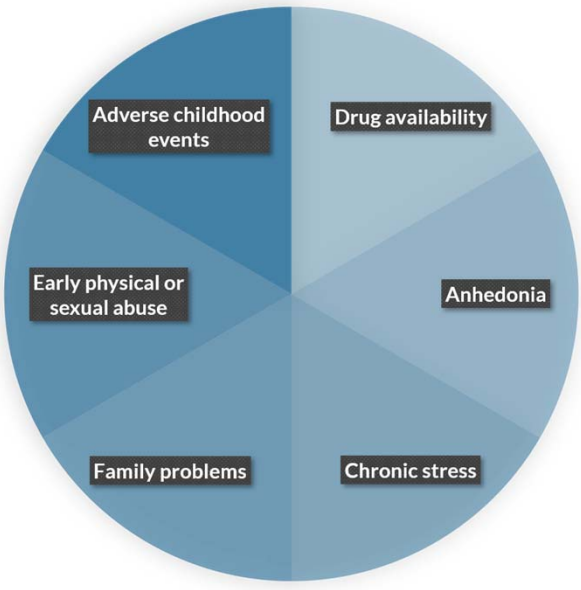
https://doi.org/10.1037/1064-1297.2.3.244



Development Of Substance Use Disorders Involves Multiple Factors

Environmental Factors That Contribute To Addiction

Many environmental factors can contribute to a person's propensity to use substances.



Audience Response

At what point in the natural history of development of an opioid use disorder does someone start taking opioids to "feel normal"?

A. After their first use.
B. After a period of use that results in tolerance.
C. When they first try to cut back on their use.
D. When they change from pills to injection drug use.

ASSESSING FOR EMOTIONAL/BEHAVIORAL AND MEDICAL CO-MORBIDITIES

Patient Assessment

The Healthcare Team

Qualities of the Healthcare Team Reviewer

- Welcoming, non-judgmental, empathetic, respectful
- Asks open-ended questions
- Explores patients' ambivalence to engage in treatment
- Attentive to responses; persistent

To Facilitate Effective Treatment

- Acknowledge some information is difficult to talk about
- Ask questions out of concern for patients' health
- Avoid using labels (e.g., "clean," "dirty," "addict")
- Assure confidentiality

Assessment Overview

1. Assess for use of alcohol, other drugs (illicit use, prescription drug misuse), and tobacco use.
2. Review the Prescription Drug Monitoring Program (PDMP).
3. Establish diagnosis of moderate and current opioid use disorder and current opioid use history.
4. Identify comorbid emotional/behavioral and medical conditions; how, when, where they will be addressed.
5. Evaluate level of physical, psychological, and social functioning or impairment.
6. Determine patient's readiness to participate in treatment.

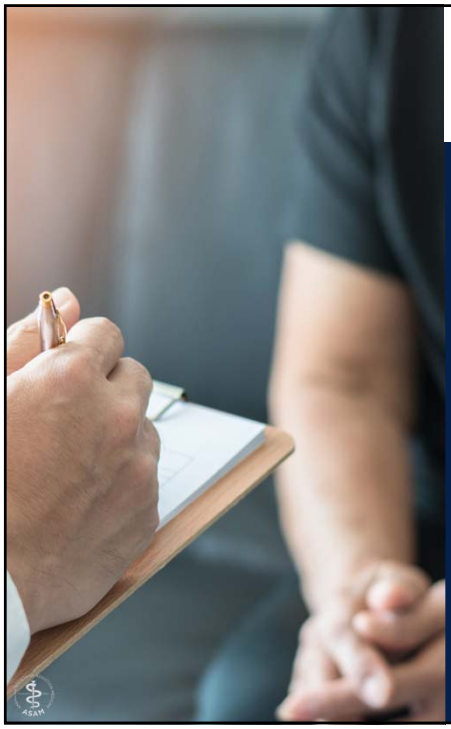
Concurrent Sedative-Hypnotics

Relative Contraindications

- Alcohol and other sedative-hypnotics are relative, not absolute, contraindications to buprenorphine
- *Deaths have resulted from injecting high potency benzodiazepines*

Identification and Referral

- Identify and refer patients who are willing and able to undergo medically supervised withdrawal management from alcohol, benzodiazepines, or other sedatives



Substance Use Disorder: DSM-5 Criteria

1. Tolerance*
2. Withdrawal*

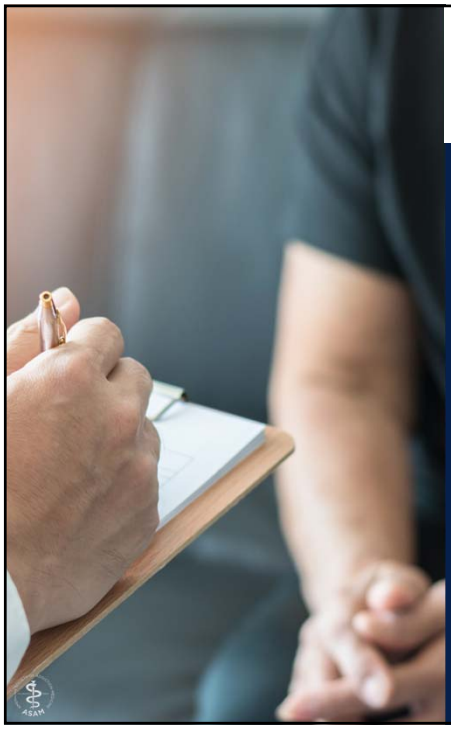
**Not valid if opioid taken as prescribed*

Loss of Control

3. Larger amounts and/or longer periods
4. Inability to cut down on or control use
5. Increased time spent obtaining, using, or recovering
6. Craving/Compulsion

Mild (2-3),
Moderate (4-5),
Severe (≥6)

APA. (2013). DSM (5th ed.)



Substance Use Disorder: DSM V Criteria

Use Despite Negative Consequences

7. Role failure: work, home, school
8. Social, interpersonal problems
9. Reducing social, work, recreational activity
10. Physical hazards
11. Physical or psychological harm

Mild (2-3),
Moderate (4-5),
Severe (≥6)

APA. (2013). DSM (5th ed.)

DSM-5 OUD Checklist (Part 1 of 2)

Diagnostic Criteria*	Meet Criteria? (Yes/No)	Notes/Supporting Information
Opioids are often taken in larger amounts or over a longer period than was intended		
There is a persistent desire or unsuccessful efforts to cut down or control opioid use		
A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects		
Craving, or a strong desire to use opioids		
Recurrent opioid use resulting in failure to fulfill major role obligations at work, school or home		
Continued opioid use despite having persistent or reurrent social or interpersonal problems caused or exacerbated by the effects of opioids		

*Opioid Use Disorder requires at least 2 criteria be met within a 12-month

DSM-5 OUD Checklist (Part 2 of 2)

Diagnostic Criteria*	Meet Criteria? (Yes/No)	Notes/Supporting Information
Important social, occupational, or recreational activities are given up or reduced because of opioid use		
Recurrent opioid use in situations in which it is physically hazardous		
Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance		
Tolerance, as defined by either of the following: (a) A need for markedly increased amounts of opioids to achieve intoxication or desired effect (b) Markedly diminished effect with continued use of the same amount of an opioid		
Withdrawal, as manifested by either of the following: (a) The characteristic opioid withdrawal syndrome (b) Opioids (or a closely related) substance is taken to relieve or avoid withdrawal symptoms		

*Opioid Use Disorder requires at least 2 criteria be met within a 12-mont

Current Opioid Use History

- Type: prescription opioids, heroin, fentanyl
- Routes
  - Injection: IV, IM, SC, or skin popping (history of sharing needles)
  - Oral, intranasal, inhaled
- Quantity used
- Frequency used
- Last use: Date? Time?
- Withdrawal Symptoms: Present? Absent?

Current Opioid Use History

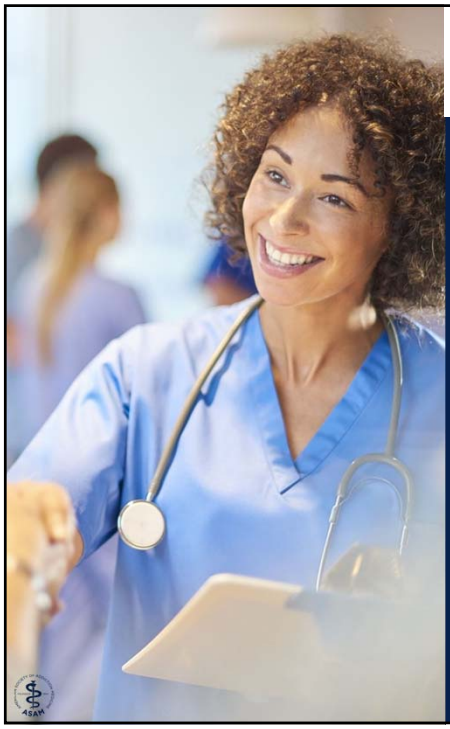
- Previous treatment/counseling/ groups
  - Nonpharmacologic (AA,NA, and other recovery groups e.g. Smart Recovery with or without a sponsor, counseling, etc.)
  - Pharmacologic with agonist (methadone, buprenorphine) and antagonist (naltrexone) therapies
- Use of syringe and needle exchange program
- Longest period of abstinence
- Relapse experience, triggers
- Overdose history including use of naloxone (current naloxone access)

Psychiatric Co-morbidity

- Any history of:
  - psychiatric illness? did it predate substance use?
  - inpatient and/or outpatient treatment
  - suicidal ideation or attempts
- Treatment adherence to psychiatric care including medications
- Is the patient psychiatrically stable?
- Are the psychosocial circumstances of the patient stable and supportive?

Laboratory Evaluation

- Liver function tests
- Hepatitis and HIV serologies
- Pregnancy test for women
- Urine drug testing
- Do not let lab evaluation delay initiation of treatment



First Patient Appointment

- May involve phone screening by staff or provider to assure that provider can meet patient's needs
- If the patient is not in withdrawal, all therapeutic options discussed; if buprenorphine, then arrangements are made for induction
- If the patient is in withdrawal or withdrawal is imminent an abbreviated evaluation and emergent induction is made
- Harm reduction education and naloxone training and access; significant others involved if possible

Are You Ready To Start Treating Your Patient?

Are You Ready?

- Are there resources available in the office to provide appropriate treatment? Medical or psychiatric care?
- What about on-call coverage?
- Are there treatment programs available that will accept referral to a setting with more intensive levels of service if needed? (e.g., buprenorphine → methadone [daily observed dosing])

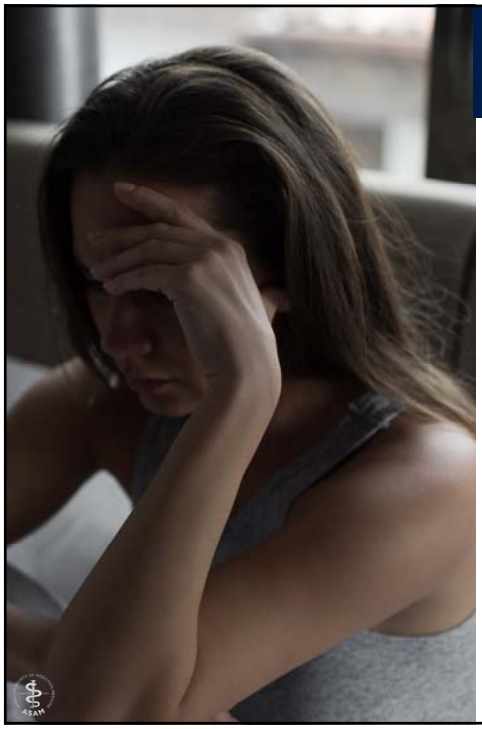
Words of Wisdom

1. Do not start with the most complex patient (e.g., methadone transfer).
2. Start with 1, not 30, patients.
3. Know your limits.
4. Do not be afraid to consult with and/or refer to more experienced provider.
5. Obtain a mentor from your ASAM State or regional chapter or from the Provider's Clinical Support System (https://pcssnow.org).

Audience Response

Do you feel ready to diagnose a substance use disorder?

A. Absolutely!
B. I need more information and practice.
C. This type of patient scares me.
D. I'm nervous about how my staff will react to treating this population.
E. A bit of everything except A.



Activity 3: Revisiting Mary's Case

- **Task:** With your group, identify assessment procedures for Mary.
- **Discuss:** Let's revisit Mary's case from an assessment perspective. What steps and procedures you would follow to assess Mary?
- **Time Allocated:** 10 minutes

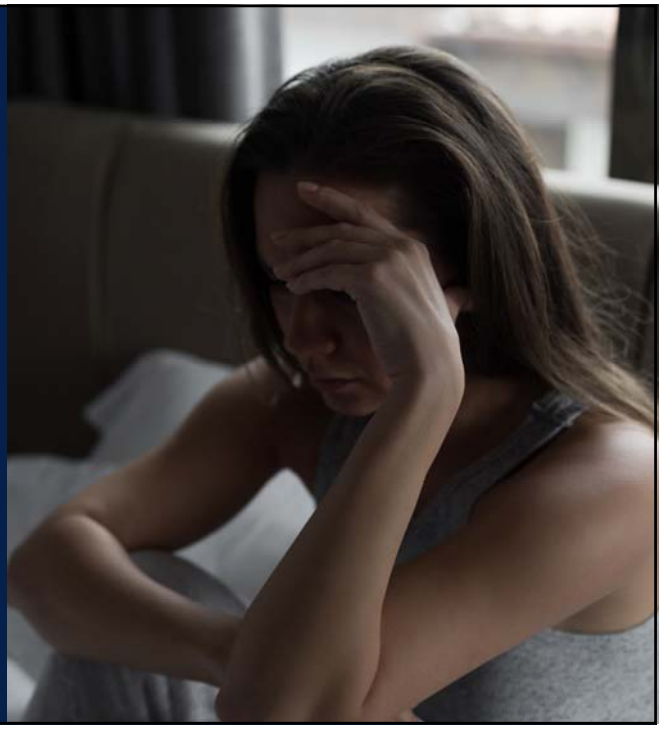
Mary's Case

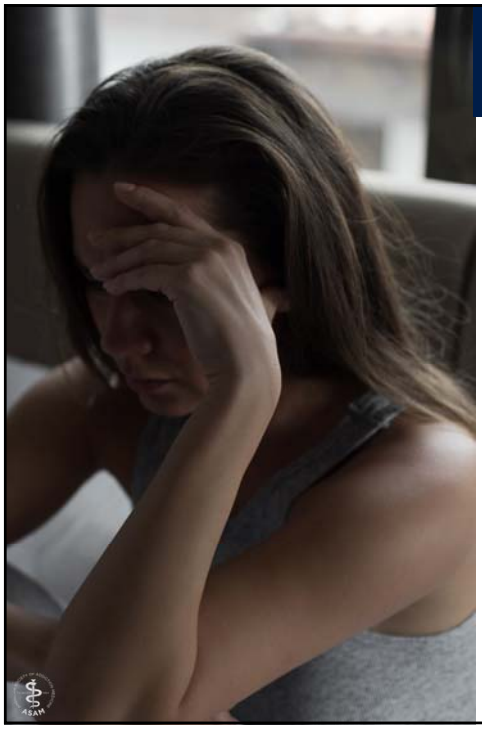
What are your procedures for:

1. documenting Mary's use of other substances?
2. identifying if Mary needs medically supervised withdrawal management?
3. screening and assessing for comorbid medical conditions (how, when, and where will they be addressed)?
4. screening for emotional/behavioral and psychiatric disorders (how, when, and where will they be addressed)?
5. screening for communicable diseases?
6. assessing Mary's access to social supports?
7. determining her readiness to participate in treatment and her goals for treatment?

Is there anything you would assess for that we have **NOT** discussed?

What else do you want to know about Mary?





Activity 3: Revisiting Mary's Case

- **Task:** Large Group Report Out
- **Discuss:** Let's revisit Mary's case from an assessment perspective. What steps and procedures you would follow to assess Mary?
- **Time Allocated:** 10 minutes

IDENTIFYING, ASSESSING AND DIAGNOSING PATIENTS WITH OPIOID USE DISORDER

End of Session 1

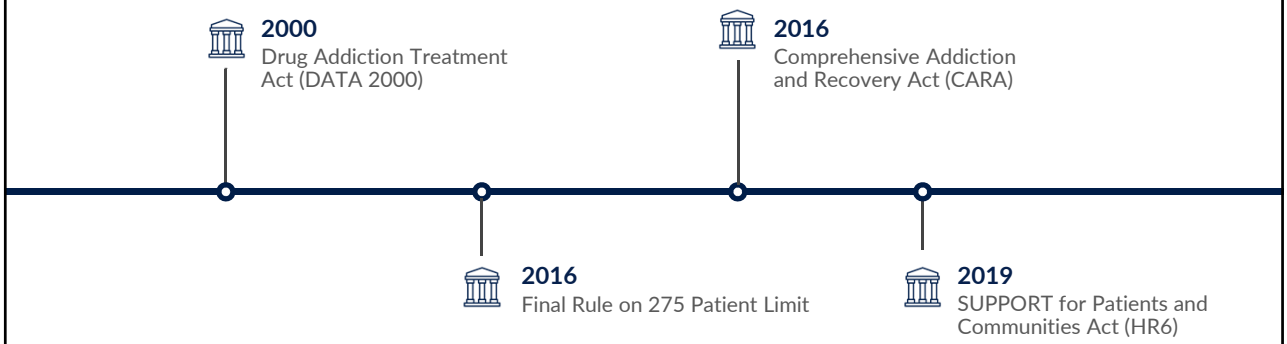
Session 2

Determining Treatment Plan for Patients with Opioid Use Disorder

Session Learning Objectives

1. Summarize the laws regulating office-based opioid treatment, including the Drug Addiction Treatment Act of 2000, the Comprehensive Addiction and Recovery Act of 2016, HR6 (SUPPORT), and the Narcotic Addict Treatment Act of 1974.
2. Summarize the clinical pharmacology, efficacy, and safety of methadone, buprenorphine, and naltrexone in treating opioid use disorders.
3. Examine the need for and use of medications to manage patients with opioid use disorder.
4. Assess and diagnose patients with opioid use disorder while considering severity, chronicity, individual characteristics, and psychiatric and medical comorbidities.
5. Develop an individualized, patient-centered treatment plan by evaluating appropriate medication and psychosocial intervention options.

Legislative Topics



Drug Addiction Treatment Act of 2000 (DATA 2000)

- Allows physicians to prescribe an FDA approved opioid for the treatment of opioid use disorder.
- Physicians must meet certain qualifications:
  - At least 8 hours of education
  - Patient limits: 30, 100
  - Application must be submitted online at the SAMHSA website
  - Receive "X-number" after application approval

Final Rule on 275 Patient Limit

- Announced in August 2016
- Allows qualified providers to increase patient limit to 275
  - Requires "qualified practice setting"
  - Requires new waiver application
  - Must reaffirm eligibility every 3 years (90 days before end of waiver year)

CARA & SUPPORT Acts

- CARA expanded prescribing to NPs and PAs
- SUPPORT Act expanded prescribing to CRNAs, CNMs, and CNSs
- Requires 24 hours of education

Patient Limits

Beginning 1st Year
- 30 patients per practitioner during first year of the waiver.
- May start at 100 patients when meeting certain requirements.

After 1st Year
- Can increase to 100 patients – a new waiver must be obtained.

After 2nd Year
- Can increase to 275 patients – a new waiver must be obtained.

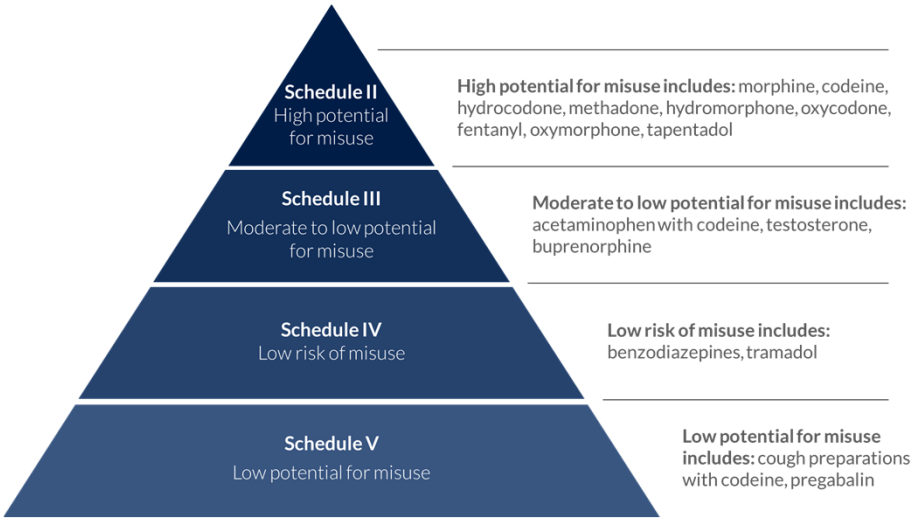
Census: Patient remains on your census until the last prescription has run out.

Hospitalized Patients: w/ primary admitting diagnosis other than OUD, buprenorphine can be ordered by non-waivered physician.

Medication Requirements

FDA Approval	DEA Schedules	Buprenorphine Schedule
• Drug must be approved by FDA for use in treating opioid use disorders (OUD).	• Medication must be DEA schedule III, IV, or V (methadone is schedule II).	• Schedule III • Certain (not all) formulations are approved for the treatment of OUD.

DEA Controlled Substance Classification



Requirements for Opioid Treatment Programs (OTP)

By Prescription:

The practitioner can prescribe approved medication in the same manner as in an office-based practice with the same patient limits (30, 100, 275).

VS

By Order to Dispense:

The practitioner can order approved medication to be dispensed in OTP setting in a manner similar to methadone with no specific limits on number of patients.

DEA Compliance

DEA continues routine practitioner inspections to assess:

- Compliance with the 30/100/275 patient limit.
- Record keeping.
- Security measures related to on-site drug storage if buprenorphine is dispensed or administered from the office.

Audience Response

Is someone who has their DEA waiver more likely to have DEA agents come to their practice?

A. Yes, and it's a good reason not to get your waiver.

B. Yes, and there are simple things you can do to make it less likely.

C. Yes, because they are trying to get doctors to prescribe under a waiver.

D. No.

Opioid Pharmacology

Opiates and Opioids

Opiates:

Natural compounds present in opium:
e.g., morphine, codeine, thebaine

VS

Opioids:

Manufactured as:

- **Semi-synthetic opioids**: derived from an opiate, e.g., heroin, oxycodone, hydromorphone, buprenorphine
- **Synthetic opioids**: completely synthesized to function similarly to natural opiates, e.g., methadone, fentanyl

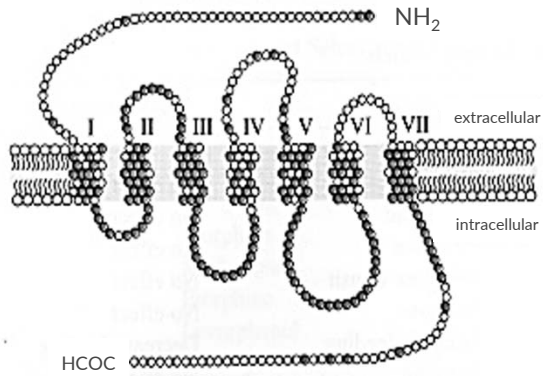
Endogenous Opioids and Their Receptors

Most of the clinically-significant effects of prescribed and illicit opioids are attributed to activity at the mu-opioid receptor.

ENDOGENOUS LIGAND	OPIOID RECEPTOR TYPES
Beta Endorphins	Mu
Enkephalins	Delta
Dynorphins	Kappa
Nociceptin/OrphaninF/Q	ORL-1

Mu-Opioid Receptor

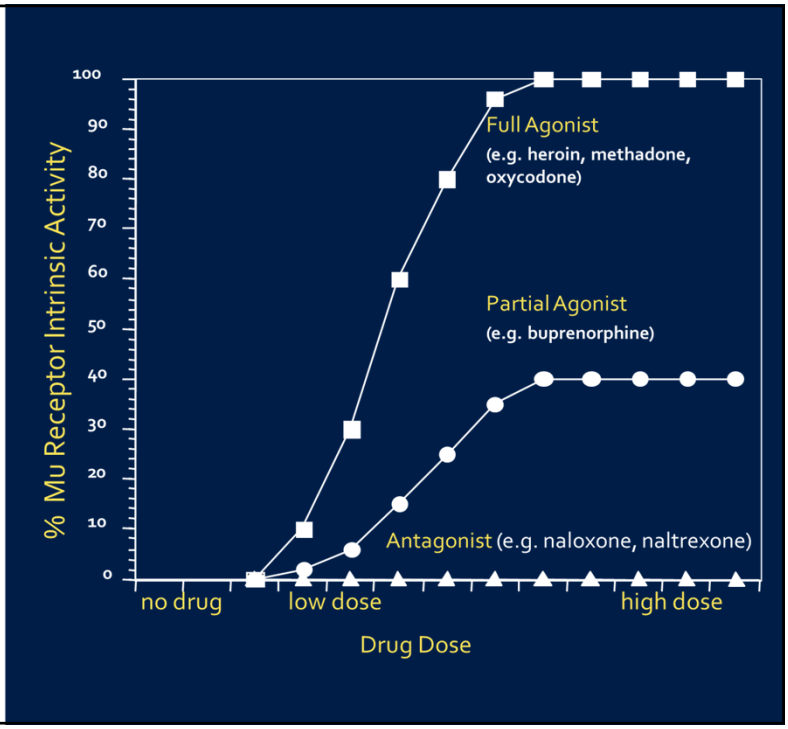
- *G-protein coupled* receptor
- *Subtypes and > 100* polymorphisms to the mu-opioid receptor gene
- *High affinity* for beta-endorphin and enkephalins
- *High affinity* for morphine
- *Low affinity* for dynorphins
- *Acute changes in neuronal excitability* via "disinhibition" of presynaptic release of GABA



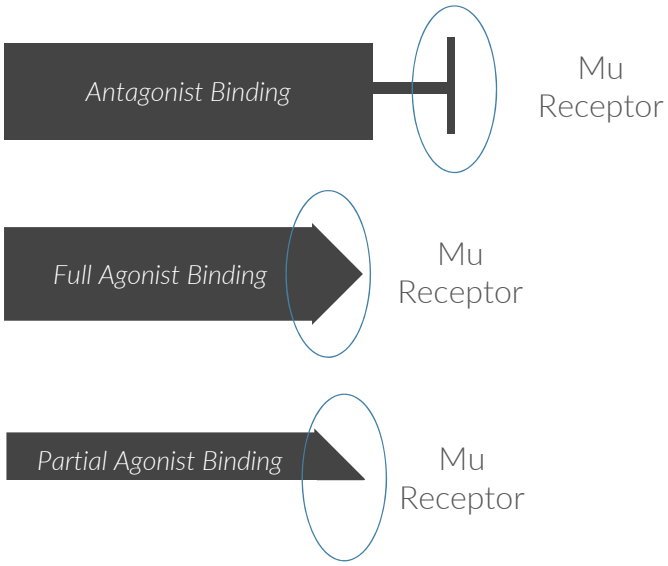
Opioid Characteristics that Increase Euphoria

Route of Administration	Faster route has a greater misuse potential	Smoking → Injecting IV → Injecting SQ → Oral/Intranasal
Drug Half-Life	Shorter half-life has a greater misuse potential	Fentanyl → Heroin → Methadone
Lipophilicity	Faster across blood brain barrier	Higher lipophilicity has a greater misuse potential → Fentanyl → Heroin → Morphine → Methadone

Opioid Agonists and Antagonists



Opioid Agonists and Antagonists



Opioid Antagonist

An antagonist

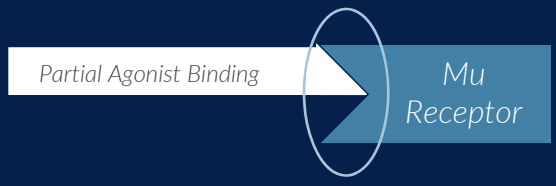
- occupies without activating.
- is not reinforcing/rewarding.
- blocks or displaces opioid agonists.
- includes naloxone and naltrexone.

Full Opioid Agonist

A full agonist

- activates the Mu receptor.
- is reinforcing/rewarding.
- is the riskiest opioid type (i.e., sedation and respiratory depression).
- includes fentanyl, heroin, methadone, & others.

Partial Opioid Agonist



A partial agonist

- activates the Mu receptor with ceiling effect.
- is relatively less reinforcing/rewarding.
- is a less risky opioid type (i.e., sedation and respiratory depression).
- includes buprenorphine.

Receptor Affinity

Buprenorphine's Affinity

- ***Affinity*** is the strength with which a drug physically binds to a receptor.
- ***Buprenorphine's affinity*** is very high; it will displace full agonists.
- ***Receptor binding strength,*** high or low, is NOT the same as receptor activation (agonist or antagonist).

Receptor Dissociation

Dissociation

- ***Dissociation*** is the speed (slow or fast) of disengagement of the drug from the receptor.
- ***Buprenorphine's dissociation*** is slow.
- ***Buprenorphine stays on the receptor*** for a long time and blocks full agonist from binding.

Acute Opioid Withdrawal

	Symptoms / Signs
Mild ↓ *Severe*	Anxiety, drug craving
	Yawning, sweating, runny nose, tearing eyes, restlessness, insomnia
	Dilated pupils, gooseflesh, muscle twitching, muscle & joint aches
	Nausea, extreme restlessness, elevated BP, heart rate > 100, fever
	Vomiting, diarrhea, abdominal cramps, curled-up body position

Clinical Opiate Withdrawal Scale (COWS):
pulse, sweating, restlessness & anxiety, pupil size, aches, runny nose & tearing, GI sx, tremor, yawning, gooseflesh

- *5-12 mild*
- *13-24 moderate*
- *25-36 moderately severe*
- *>36 severe*

Determinants of Withdrawal Risk

- Exposure to steady state level of medication:
  - Neuro-adaptation to opioids
- Higher intensity withdrawal from:
  - Higher steady state levels
  - Longer term exposure
  - Faster rate of medication clearance
  - Short vs. long half-life agents

Spontaneous Acute Opioid Withdrawal

- **Develops spontaneously in a person with physical dependence.**
  - Someone who suddenly stops, or markedly decreases the opioid.
- **Half-life opioids:**
  - Severity is usually less with longer half-life opioids.
  - Duration depends on half-life of opioids person uses.

Opioid	*Onset*	*Peak*	*Duration*
Heroin	4-6 hours	~ 3 days	4-7 days
Methadone	1-2 days	~ 7 days	12-14 days

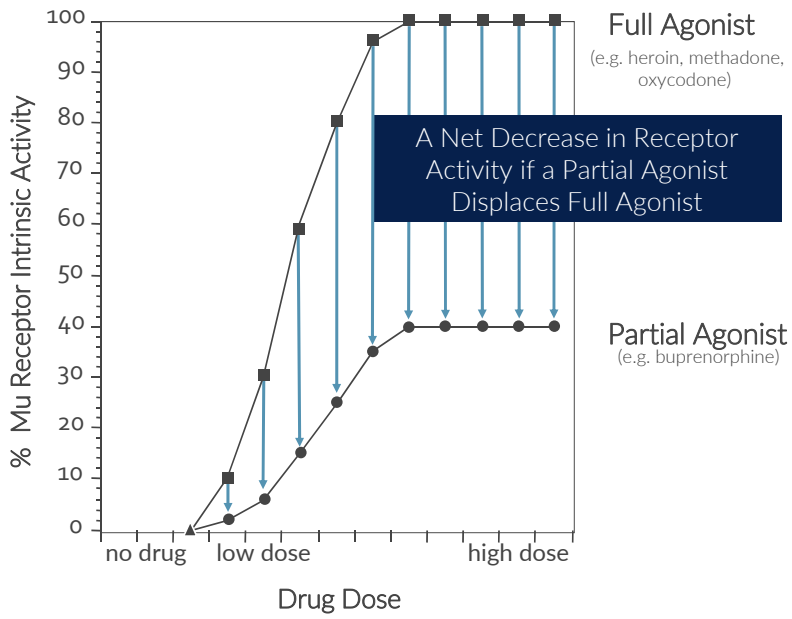
Precipitated Acute Opioid Withdrawal

- **Precipitated in a physically dependent person, by administration of an:**
  - opioid antagonist drug (e.g. naloxone, naltrexone), or
  - opioid partial agonist drug (e.g. buprenorphine)
- **Qualitatively similar to a spontaneous withdrawal but it has a faster onset.**
- **Duration depends upon half-life of drug.**

Opioid antagonist drug/ Opioid Partial Agonist Drug	*Onset*	*Peak*	*Duration*
Naloxone	Minutes	Minutes	~ 20 minutes
Naltrexone	Minutes	Minutes	1-2 days
Buprenorphine	Minutes	Minutes	1-2 days

Precipitated Acute Withdrawal

Buprenorphine will precipitate withdrawal when it displaces full agonist off the Mu receptors.



Audience Response

Which of the following is a characteristic of a partial agonist?

A. It activates the Mu receptor with a ceiling effect.
B. It is relatively more reinforcing/rewarding.
C. It is a riskier opioid type (i.e., sedation and respiratory depression).
D. Methadone is an example of a partial agonist.

ROBERT'S CASE

Robert's Case

Robert is a 35-year-old middle school math teacher using illicit hydrocodone and intranasal heroin. He has been using on and off since age 24. Robert has been through more than 15 episodes of medically supervised withdrawal ("detox").

His last treatment included a 28-day residential program during his summer break while attending daily NA meetings. He remained in recovery for three months but relapsed one month ago and is having difficulty maintaining employment because he "calls in sick too much."

Robert's Case

His wife is in recovery and insisted that he return to treatment after she discovered he was taking hydrocodone pills from several doctors for a back injury following an automobile crash. She is unaware that he is also using heroin daily.

There is family history of alcohol use disorder. He denies alcohol or tobacco use. His only current medical problem is mild hypertension. His back pain has resolved. He is hepatitis C and HIV negative.

Robert's Case

I know I'm addicted. My wife stopped using when she was pregnant with our daughter, and she just got her 12-year chip. She moved on with her life, but I'm stuck. My back injury threw me into a tailspin. At first, I really needed the painkillers, but now I'm just using them to 'feel normal' and to prevent withdrawal. I really need your help. If my wife finds out I'm back on heroin, she'll leave me this time.

Activity 4: Case Discussion – Robert

- **Task:** With your group, discuss Robert's case.
- **Discuss:** Review the case with your group in break-out session. Does he meet DSM-5 criteria for an opioid use disorder? If so, is it mild, moderate or severe?
- **Time Allocated:** 5 minutes

Treatment Medications For Opioid Use Disorder: *Methadone*

Methadone Hydrochloride

- **Full Opioid Agonist**
- **Oral**
  - 80-90% bioavailability liquid, tablet, and disket formulations
- **Proper dosing for OUD**
  - 20-40 mg for acute withdrawal
  - > 80 mg for craving, "opioid blockade"
- **Duration of action**
  - 24-36 hours to treat OUD
  - 6-8 hours to treat pain
- **Can be administered parenterally (IV, SQ or IM)**
  - at 80% of the total daily oral dose administered in a divided dose every 12 hours (e.g., 40 mg by mouth every day = 16 mg IV every 12 hours)

Mercadante S. (2013) Handbook of Methadone Prescribing and Buprenorphine Therapy.

Methadone Safety

Half-Life

- Long, variable, unpredictable half-life
- Serum t½ 20-120 hours
- 4-7 days to reach steady state: "Start low, go slow"

QTc Prolongation, Risk of Torsades de Pointes

- Dose-related: >100mg daily
- Multifactorial : ↓K, ↓Mg, other drugs ↑QTc
- CYP450: 3A4, 2D6 interactions
- QTc > 500 msec → Torsades de Pointes

Wedam E et al. JAMA Internal Medicine. 2007. The Medical Letter. 2017, 59(1522): 89-95.

Methadone Maintenance in OTP

- ***Highly Structured***
  - Daily nursing assessment
  - Weekly individual and/or group counseling
  - Random supervised drug testing
  - Psychiatric services
  - Medical services
- ***Methadone Dosing***
  - Observed daily - "Take homes" based on stability and time in treatment
  - Max: 27 "take homes"
  - Varies by state, county, and individual clinics

Methadone Summary: Benefits

- ***Increases***
  - overall survival
  - treatment retention
  - employment
- ***Improves***
  - birth outcomes
- ***Decreases***
  - illicit opioid use
  - hepatitis and HIV seroconversion
  - criminal activity

Joseph et al. Mt Sinai J Med. 2000;67:347-364

Methadone Summary: Limitations

- ***Highly regulated: Narcotic Addict Treatment Act 1974***
  - Created methadone clinics (Opioid Treatment Programs)
  - Separate system not involving primary care or pharmacies
- ***Limited access***
- ***Inconvenient***
- ***Stigma***
  - "Methadone is substituting one drug for another… I don't believe in methadone."

Audience Response

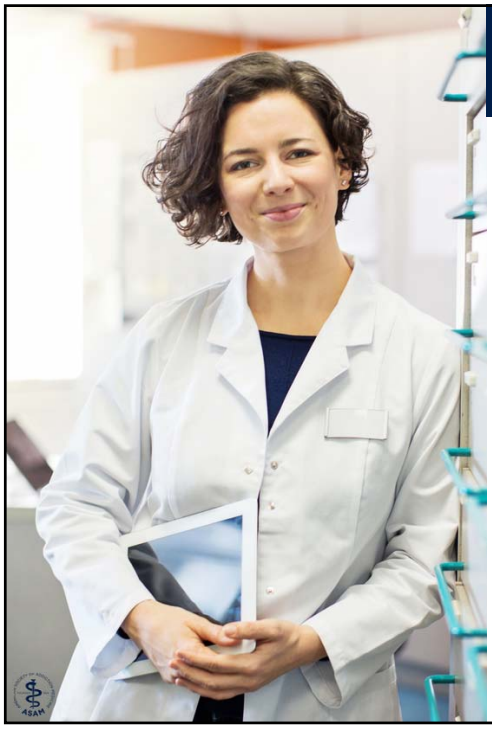
Some of the benefits of methadone include:

A. Decreased employment.
B. Increased hepatitis and HIV seroconversion.
C. Increased survival.
D. Decreased rates of unplanned pregnancy.

Treatment Medications For Opioid Use Disorder: *Naltrexone*

Naltrexone

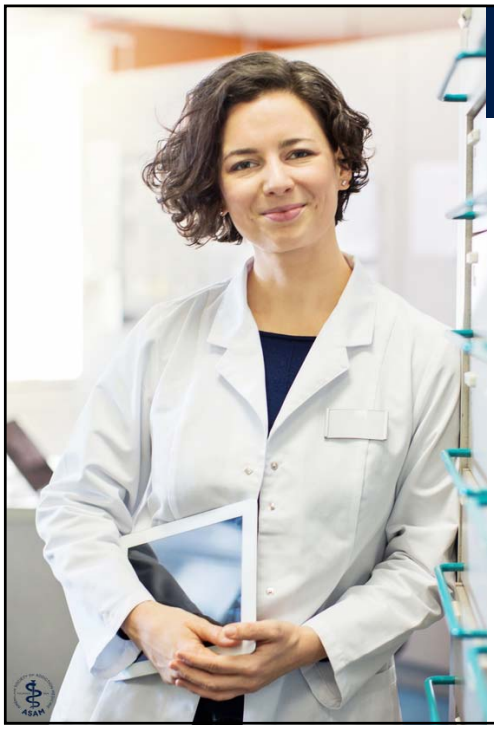
- **Mu-opioid receptor antagonist**
- **Not a controlled substance**
  - no special prescribing restrictions
- **Patients physically dependent**
  - must be opioid free for a minimum of 7-10 days before treatment
- **Also FDA approved for the treatment of alcohol use disorders**
- **Oral naltrexone (generic and brand ReviaTM)**
  - Well tolerated
  - Duration of action 24-48 hours
  - FDA approved 1984
- **IM injection extended-release naltrexone (Vivitrol)**
  - IM injection (w/ customized needle) once/month
  - FDA approved 2010



Naltrexone Safety

- ***Generally well tolerated***
  - initial headache, nausea, dizziness
- ***Depressed mood and suicidality rarely***
  - no cause-and-effect established
- ***Reduce opioid tolerance***
  - patients who return to pretreatment use have greater risk of fatal opioid overdose
- ***IM injection site reactions***
  - bruise, induration, nodules, pain, pruritus, swelling, tenderness

The Medical Letter. 2017, 59(1522): 89-95.



Naltrexone and the Liver

- Naltrexone has the capacity to cause hepatocellular injury when given in excessive doses.
- Naltrexone does not appear to be hepatotoxic at the recommended doses.
- Naltrexone is contraindicated in acute hepatitis or liver failure.

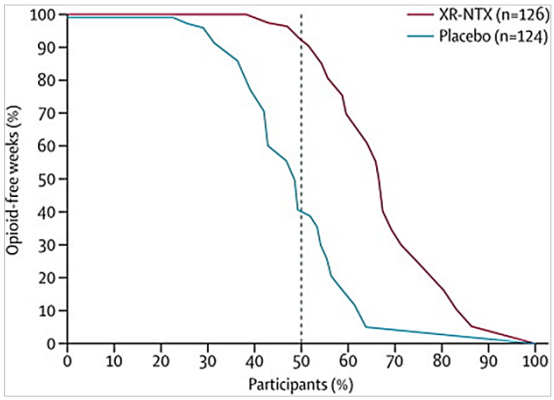
Oral Naltrexone Efficacy

Meta-analysis of 13 RCTs 1,158 participants:

- Naltrexone maintenance treatment versus placebo or other treatments.
- Only 28% of people were retained in treatment in the included studies.
- No statistically significant differences were noted for all the primary outcomes considered.
- More effective than placebo in sustaining abstinence in studies where patients were legally mandated to take the drug.

Minozzi S et al. Cochrane Database Syst Rev 2011.

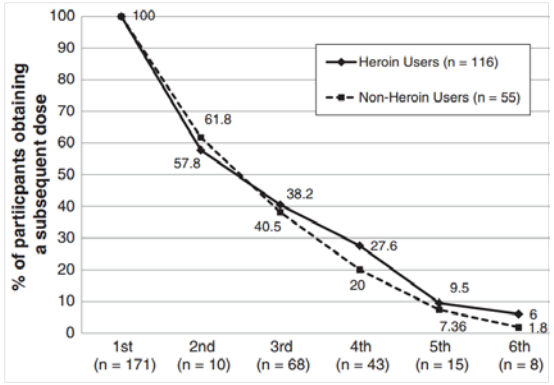
Injectable Extended-Release Naltrexone (XR-NTX) Efficacy



- **Multicenter** (13 sites in Russia) funded by Alkermes
- **DB RPCT**, 24 weeks, n=250 w/ opioid use disorder
- **XR-NTX vs placebo,** all offered biweekly individual drug counseling
- **Increased**
  - weeks of confirmed abstinence (90% vs 35%)
  - patients with confirmed abstinence (36% vs 23%)
- **Decreased** craving (-10 vs +0.7)

Krupitsky E et al. Lancet. 2011.

XR-NTX Efficacy: Retention



- **Mean # doses (Max = 6)**
  - Heroin: 2.3
  - Non-heroin opioid: 2.5
- **Drop-out risk factors**
  - Homelessness
  - Opioid injection use (regardless of opioid-type)
  - Mental illness

Cousins SJ et al. J Sub Abuse Treat 2016

Naltrexone Summary

Benefits:

- Good for patients who do not want opioid agonist therapy.
- No risk of diversion (not a controlled substance).
- ***No risk of overdose by drug itself.***
- Can be administered in any setting (office-based or OTP).
- Long-acting formulation.
- Treats both opioid use disorder and alcohol use disorder.

VS

Limitations:

- Difficulty starting—must be fully withdrawn from opioid; > short-acting (6 days); long-acting opioids (7-10 days).
- Not suitable for patients with severe liver disease.
- Loss of tolerance to opioids increases the risk of overdose if return to pretreatment use occurs.
- Not recommended for pregnant women. Pregnant women who are physically dependent on opioids should receive treatment using methadone or buprenorphine.

ASAM National Practice Guideline for the Treatment of Opioid Use Disorder - 2020 Focused Update.

Audience Response

A good candidate for naltrexone may show the following:

A. Abstinence from opioids for 4-6 days depending on the half-life of the opioid.

B. Able to come to clinic for a nursing visit every 12-16 days for injection of the medication.

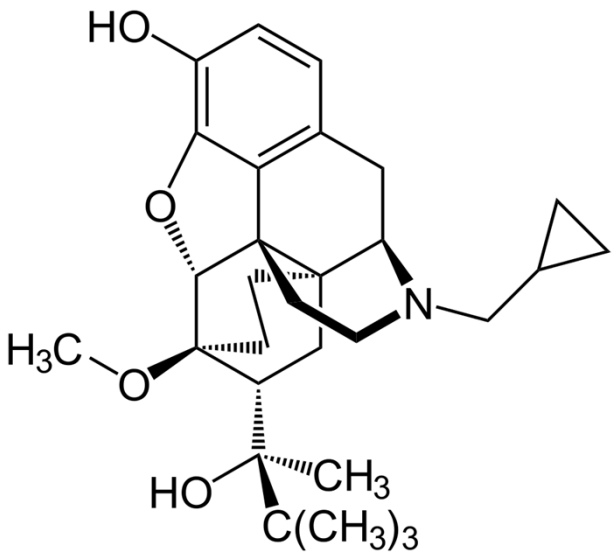
C. It is a good choice for someone with severe liver damage.

D. Have comorbid opioid and alcohol use disorders.

Treatment Medications For Opioid Use Disorder: *Buprenorphine*

Buprenorphine

- is a semi-synthetic analogue of thebaine.
- was approved by the FDA in 2002 as Schedule III — up to 5 refills.
- has a high receptor affinity.
- has a slow dissociation.
- has a ceiling effect for respiratory depression.
- is a partial Mu-opioid agonist, kappa antagonist.



Buprenorphine: Active Effect

- Buprenorphine has poor oral bioavailability when swallowed. All therapeutic formulations use other routes.
- Sublingual administration bypasses first-pass metabolism and allows bioavailability around 30%.
- Most buprenorphine is excreted into the biliary tract; small fractions enter the urine and are detectable in urine tests.

Johnson RE et al. J Pain Symptom Manage 2005.

Buprenorphine

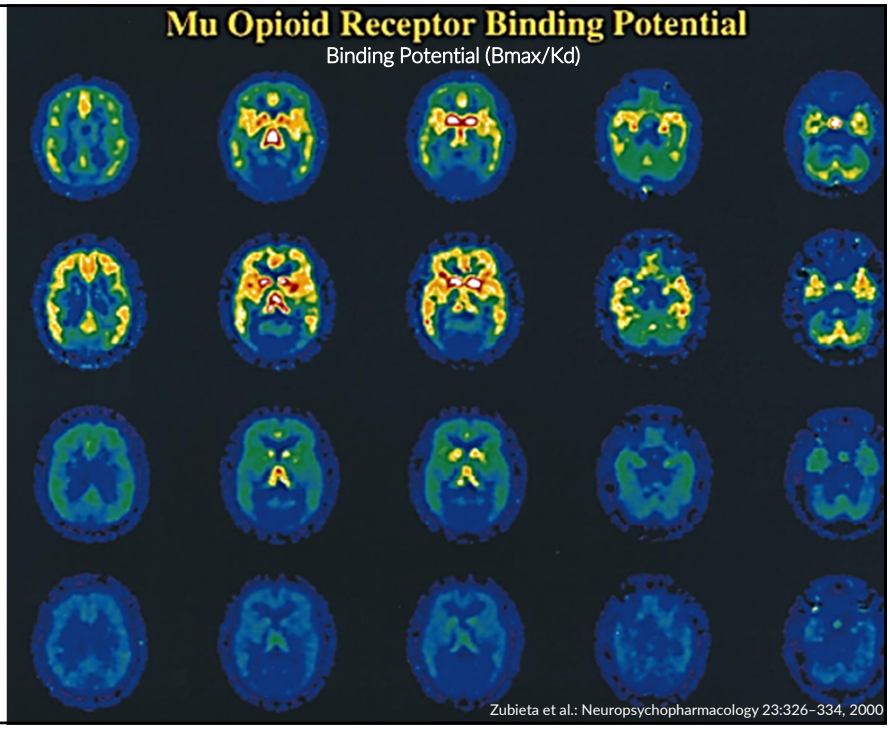
Partial Agonist at the Mu-Opioid Receptor

- Analgesia (Analgesic effect is 6-8 hours)
- Ceiling effect on respiratory and CNS depression
- OUD treatment effect is 24-36 hours at therapeutic dose

Combination: Buprenorphine/Naloxone

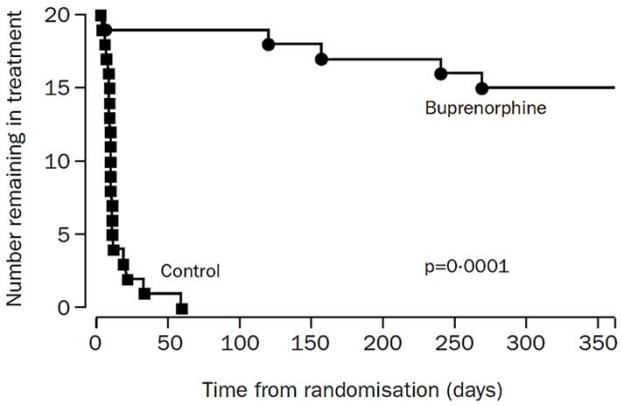
If dissolved sublingually:	*If swallowed:*	*If injected or used intranasally:*	*Not time-released:*
Buprenorphine is active	Buprenorphine not active (minimal oral bioavailability)	Buprenorphine is active	Tablets/film strip can be split
Naloxone is not active	Naloxone not active	Naloxone active x 20 minutes so attenuates the parenteral "rush"	

Opioid Blockade



Buprenorphine Efficacy: Retention

- **Completion 52-week trial:**
  - Taper: 0%
  - Maintenance: 75%
- **Mean % urine neg:**
  - Maintenance: 75%
- **Mortality**
  - Taper: 20%
  - Maintenance: 0%



Kakko J et al. Lancet 2003.

Buprenorphine Efficacy: Summary

Studies (RCT) show buprenorphine (16-24 mg) more effective than placebo and equally effective to moderate doses (80 mg) of methadone on primary outcomes of:

- Retention in treatment
- Abstinence from illicit opioid use
- Decreased opioid craving
- Decreased mortality
- Improved occupational stability
- Improved psychosocial outcomes

Johnson et al. NEJM 2000; Fudala PJ et al. NEJM 2003; Kakko J et al. Lancet 2003; Sordo L et al. BMJ 2017; Mattick RP et al. Conchrane Syst Rev 2014; Parran TV et al. Drug Alcohol Depend 2010

Audience Response

Characteristics of buprenorphine that make it a good treatment for a person with an opioid use disorder include:

A. Low receptor affinity.

B. Fast dissociation.

C. Full Mu-opioid agonist and partial kappa antagonist.

D. Ceiling effect for respiratory depression.

Treatment Medications For Opioid Use Disorder: *Buprenorphine Safety*

Buprenorphine Safety

- Highly safe medication for both acute and chronic dosing.
- No evidence of significant disruption in cognitive or psychomotor performance with buprenorphine maintenance.
- No evidence of organ damage with chronic dosing of buprenorphine “mono” or “combo.”

Adverse Effects

- Constipation (PAMORA), excessive sweating
- 2° Hypoganadism:
  ↓ HPG axis → ↓ Testosterone
- QTc prolongation but less than with methadone
- Hemodialysis safe
- Decreased bone health –
  Opioid Class Effect, ↓ Saliva, Osteoclast activity

Adverse Effects of Medications

MEDICATION	ADVERSE EFFECTS
Methadone	Constipation, hyperhidrosis, respiratory depression (particularly combined with benzodiazepines or other CNS depressants), sedation, QT prolongation, interactions with other medications that alter cytochrome P450 metabolism, sexual dysfunction, severe hypotension including orthostatic hypotension and syncope, misuse potential, NOWS
Buprenorphine (with or without naloxone)	Constipation, nausea, precipitated withdrawal, excessive sweating, insomnia, peripheral edema, respiratory depression when with benzodiazepines or other CNS depressants, misuse potential, NOWS Implant: Nerve damage during insertion/removal, accidental overdose or misuse if extruded, local migration or protrusion Subcutaneous: Injection site itching or pain, death from intravenous injection
Naltrexone	Nausea, anxiety, insomnia, precipitated withdrawal, hepatotoxicity, vulnerability to opioid overdose, depression, suicidality, muscle cramps, dizziness or syncope, somnolence or sedation, anorexia, decreased appetite or other appetite disorders Intramuscular: Pain, swelling, induration (including some cases requiring surgical intervention)

Overdose Risk Minimal

- **Respiratory Depression and Overdose Risk**
  - No reports of significant respiratory depression in clinical trials.
  - Overdose and misuse (e.g., injecting) of buprenorphine combined with other CNS depressants result in respiratory depression and risk overdose.
- **France experience:**
  - IV buprenorphine + high potency benzodiazepines → deaths

Polomèni P, Schwan R. Int J Gen Med. 2014

Misuse Potential of Buprenorphine

- **Euphoria:**
  - in non-opioid dependent individuals
- **Misuse:**
  - Potential less than full opioid agonists
  - Among opioid-dependent individuals is relatively low
  - Most illicit use is to prevent or treat withdrawal and cravings
  - Combination product theoretically less likely to be misused by IV route.

Yokel MA et al. Curr Drug Abuse Rev. 2011; Lofwall MR, Walsh SL. J Addic Med. 2014.

LFT Recommendations

Level of Evidence: Moderate

- **Prior to induction: obtain LFTs, INR, hepatitis serologies.**
  - Avoid delay in starting treatment, can obtain LFTs at same time as induction.
- **Monitor LFTs.**
  - No empirical evidence to guide the frequency. Semi-annual is adequate if no other risk factors.
- **If patient does have clinical/laboratory evidence of hepatotoxicity, evaluate possible causes of liver injury.**
  - Consideration should be given to lowering dose or discontinuing.
- **Subsequent studies have NOT shown significant increases in LFTs during SL buprenorphine treatment for patients with and without chronic hepatitis C.**

Audience Response

Which of the following are key drivers for buprenorphine misuse?

A. A person can easily create a euphoric effect by injecting buprenorphine, even if they are opioid tolerant.

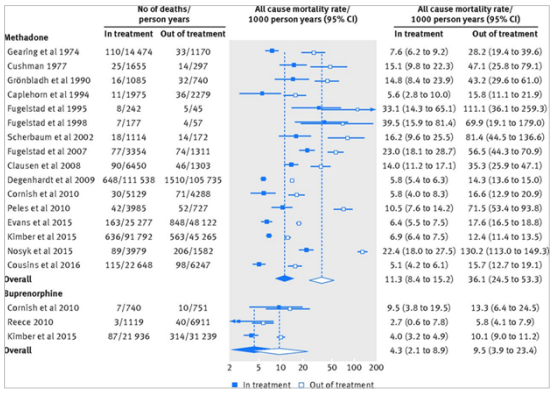
B. Most illicit use is to prevent or treat withdrawal and cravings.

C. Many prescribers feel equipped to utilize this medication.

D. Starting to treat patients with an opioid use disorder is a low threshold opportunity.

Treatment Medications For Opioid Use Disorder: *Comparative Effectiveness*

Comparative Effectiveness: All Cause Mortality Rates

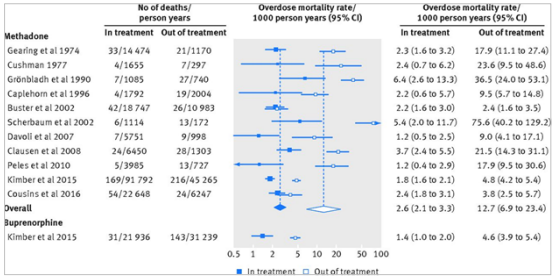


	No of deaths/ person years		All cause mortality rate/ 1000 person years (95% CI)	
Methadone	In treatment	Out of treatment	In treatment	Out of treatment
Gearing et al 1974	110/14 474	33/1170	7.6 (6.2 to 9.2)	28.2 (19.4 to 39.6)
Cushman 1977	25/1655	14/297	15.1 (9.8 to 22.3)	47.1 (25.8 to 79.1)
Grönbladh et al 1990	16/1085	32/740	14.8 (8.4 to 23.9)	43.2 (29.6 to 61.0)
Caplehorn et al 1994	11/1975	36/2279	5.6 (2.8 to 10.0)	15.8 (11.1 to 21.9)
Fugelstad et al 1995	8/242	5/45	33.1 (14.3 to 65.1)	111.1 (36.1 to 259.3)
Fugelstad et al 1998	7/177	4/57	39.5 (15.9 to 81.4)	69.9 (19.1 to 179.0)
Scherbaum et al 2002	18/1114	14/172	16.2 (9.6 to 25.5)	81.4 (44.5 to 136.6)
Fugelstad et al 2007	77/3354	74/1311	23.0 (18.1 to 28.7)	56.5 (44.3 to 70.9)
Clausen et al 2008	90/6450	46/1303	14.0 (11.2 to 17.1)	35.3 (25.9 to 47.1)
Degenhardt et al 2009	648/111 538	1510/105 735	5.8 (5.4 to 6.3)	14.3 (13.6 to 15.0)
Cornish et al 2010	30/5129	71/4288	5.8 (4.0 to 8.3)	16.6 (12.9 to 20.9)
Peles et al 2010	42/3985	52/727	10.5 (7.6 to 14.2)	71.5 (53.4 to 93.8)
Evans et al 2015	163/25 277	848/48 122	6.4 (5.5 to 7.5)	17.6 (16.5 to 18.8)
Kimber et al 2015	636/91 792	563/45 265	6.9 (6.4 to 7.5)	12.4 (11.4 to 13.5)
Nosyk et al 2015	89/3979	206/1582	22.4 (18.0 to 27.5)	130.2 (113.0 to 149.3)
Cousins et al 2016	115/22 648	98/6247	5.1 (4.2 to 6.1)	15.7 (12.7 to 19.1)
Overall			11.3 (8.4 to 15.2)	36.1 (24.5 to 53.3)
Buprenorphine				
Cornish et al 2010	7/740	10/751	9.5 (3.8 to 19.5)	13.3 (6.4 to 24.5)
Reece 2010	3/1119	40/6911	2.7 (0.6 to 7.8)	5.8 (4.1 to 7.9)
Kimber et al 2015	87/21 936	314/31 239	4.0 (3.2 to 4.9)	10.1 (9.0 to 11.2)
Overall			4.3 (2.1 to 8.9)	9.5 (3.9 to 23.4)

All cause mortality rates in and out of opioid substitution treatment with methadone or buprenorphine and overall pooled all cause mortality rates, 1974-2016.

Luis Sordo et al. BMJ 2017;357:bmj.j1550

Comparative Effectiveness: Overdose Mortality Rates in and out of Opioid Substitution Treatment



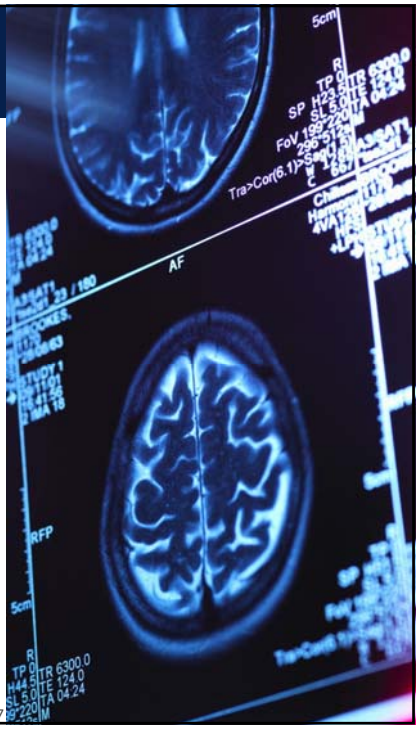
	No of deaths/ person years		Overdose mortality rate/ 1000 person years (95% CI)	
Methadone	In treatment	Out of treatment	In treatment	Out of treatment
Gearing et al 1974	33/14 474	21/1170	2.3 (1.6 to 3.2)	17.9 (11.1 to 27.4)
Cushman 1977	4/1655	7/297	2.4 (0.7 to 6.2)	23.6 (9.5 to 48.6)
Grönbladh et al 1990	7/1085	27/740	6.4 (2.6 to 13.3)	36.5 (24.0 to 53.1)
Caplehorn et al 1996	4/1792	19/2004	2.2 (0.6 to 5.7)	9.5 (5.7 to 14.8)
Buster et al 2002	42/18 747	26/10 983	2.2 (1.6 to 3.0)	2.4 (1.6 to 3.5)
Scherbaum et al 2002	6/1114	13/172	5.4 (2.0 to 11.7)	75.6 (40.2 to 129.2)
Davoli et al 2007	7/5751	9/998	1.2 (0.5 to 2.5)	9.0 (4.1 to 17.1)
Clausen et al 2008	24/6450	28/1303	3.7 (2.4 to 5.5)	21.5 (14.3 to 31.1)
Peles et al 2010	5/3985	13/727	1.2 (0.4 to 2.9)	17.9 (9.5 to 30.6)
Kimber et al 2015	169/91 792	216/45 265	1.8 (1.6 to 2.1)	4.8 (4.2 to 5.4)
Cousins et al 2016	54/22 648	24/6247	2.4 (1.8 to 3.1)	3.8 (2.5 to 5.7)
Overall			2.6 (2.1 to 3.3)	12.7 (6.9 to 23.4)
Buprenorphine				
Kimber et al 2015	31/21 936	143/31 239	1.4 (1.0 to 2.0)	4.6 (3.9 to 5.4)

Overdose mortality rates in and out of opioid substitution treatment with methadone or buprenorphine and overall pooled overdose mortality rates, 1974-2016.

Luis Sordo et al. BMJ 2017;357:bmj.j1550

Comparative Effectiveness: Summary

- Methadone is associated with better retention in treatment than buprenorphine in OTP.
- Higher doses of both medications are associated with better retention in OTP.
- For patients with OUD, methadone and buprenorphine had similar therapeutic efficacy. Evidence quality was low to moderate.



Hser Y et al. Addiction. 2014. Nielsen S et al. JAMA 2017

XR-NTX versus BUP-NX

1. It is more difficult to initiate patients to extended-release naltrexone than buprenorphine/naloxone.
2. Once initiated, both medications were equally safe and effective.

Lee J et al. Lancet 2018

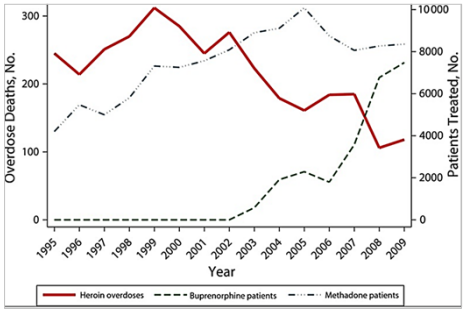
Mortality Risk During and After Opiate Agonist Therapy (OAT)

- On methadone, 25 fewer deaths/1000 person years vs patients who discontinue it; Mortality risk in OAT is <1/3 of that expected in the absence of OAT.
- The mortality risk in the induction phase of methadone (1st 4 weeks) is high, but subsequently decreases with stabilization at 6 deaths/1000 person years in the remaining time in treatment. This did not occur with buprenorphine.
- The mortality risk in the 4 weeks immediately after cessation of OAT is high and could exceed 30 deaths/1000 person years.
- Buprenorphine probably also effective in reducing mortality, but quantification of averted deaths requires further studies.

Sordo L et al. BMJ 2017

Treatment Medications For Opioid Use Disorder: *Treatment Access*

Increase in OAT — Decrease Opioid Overdose Deaths



The study examined the association between expansion of methadone and buprenorphine treatment and the prevalence of heroin overdose deaths.

Conclusions:

- Increased access to opioid agonist treatment was associated with a reduction in heroin overdose deaths
- Evidence-based medication treatment of OUD may decrease heroin overdose deaths

R Schwartz et al. Am J Public Health 2013

Medication for OUD

After Nonfatal Opioid Overdose and Association With Mortality

N=17,568

- 12 m after overdose 11% on MMT (median 5 m), 17% on buprenorphine (median 4 m), 6% on naltrexone (median 1 m)

Compared with no medication for OUD

- MMT and buprenorphine treatment associated with decreased all-cause mortality and opioid-related mortality
- No associations between naltrexone and all-cause mortality or opioid-related mortality

LaRochelle MR, et al. Ann Intern Med, 2018

Overcoming My Fear of Treating OUD

Dr. P was reluctant to obtain a waiver to prescribe buprenorphine for the treatment of OUD until her patient, Ms. L, with longstanding OUD, died from a fatal opioid overdose.

PERSPECTIVE FROM THE NEW ENGLAND JOURNAL OF MEDICINE

Provenzano A. N Engl J Med 2018; 378:600-601

Overcoming My Fear of Treating OUD

Caring for these patients has become the most meaningful part of my practice. Providing some sense of normalcy for patients whose lives are roiled by overdose and estrangement is the most profound therapeutic intervention I've engaged in as a caregiver. I did not know what Ms. L meant all those years ago when she said that she only wished to feel normal again. I wish that I'd listened more closely. I wish that I had not been afraid.

Provenzano A. N Engl J Med 2018; 378:600-601

Role of Non-Pharmacological Treatment

Non-Pharmacological Treatment

- **Psychosocial services are often helpful.** Psychosocial services encourage utilization.
- **Additional Behavioral Therapy:** Three trials showed that additional behavioral therapy does NOT significantly improve outcomes over that achieved by buprenorphine PLUS "medical management" or "medical counseling."
- **Patients should not be denied medication** should they refuse psychosocial services or if psychosocial services are not available.

Weiss RD et al. Arch Gen Psychiatry. 2011.; Fiellin DA et al. Am J Med. 2013.; Ling W et al. Addiction. 2013.

Psychosocial Treatment Examples

- Individual counseling
- Group therapy
- Marital/family counseling
- Mutual help groups (e.g. AA, NA)
- SMART Recovery
- Women for Sobriety
- Secular Organizations for Sobriety (SOS)

Audience Response

Psychosocial treatment for persons with opioid use disorder should include:

A. A mandate to be in therapy to access medications.

B. Requirements to be in therapy early in treatment that decrease over time in treatment.

C. Offering of person-centered therapy options.

D. Having on-site counseling available including 24 hour call coverage.

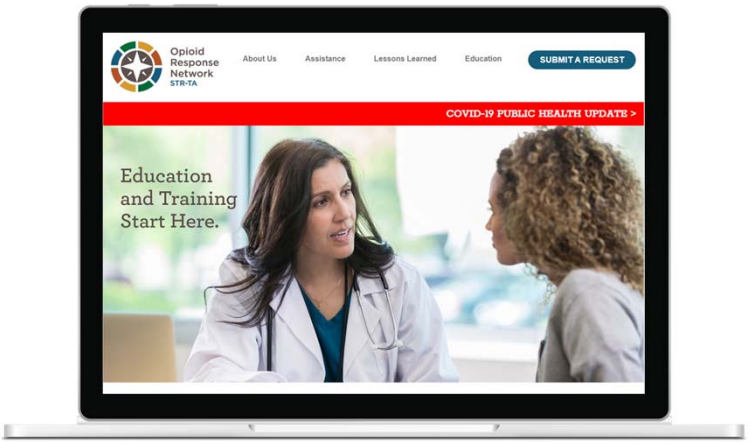
Resources

Providers Clinical Support System (PCSS)

Through trainings and clinical coaching programs, PCSS's mission is to increase healthcare providers' knowledge and skills in the prevention, identification, and treatment of substance use disorders with a focus on opioid use disorders.

https://pcssnow.org/

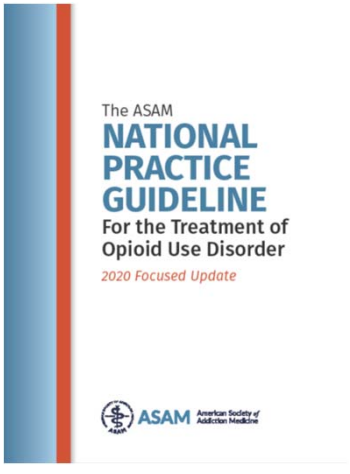
Opioid Response Network



SAMHSA grant to the American Academy of Addiction Psychiatry (AAAP) with a coalition of 22 national healthcare partner organizations. The consortium provides training and TA via local experts across the US, focusing on applying evidence-based practices to meet locally identified needs.

https://opioidresponsenetwork.org/

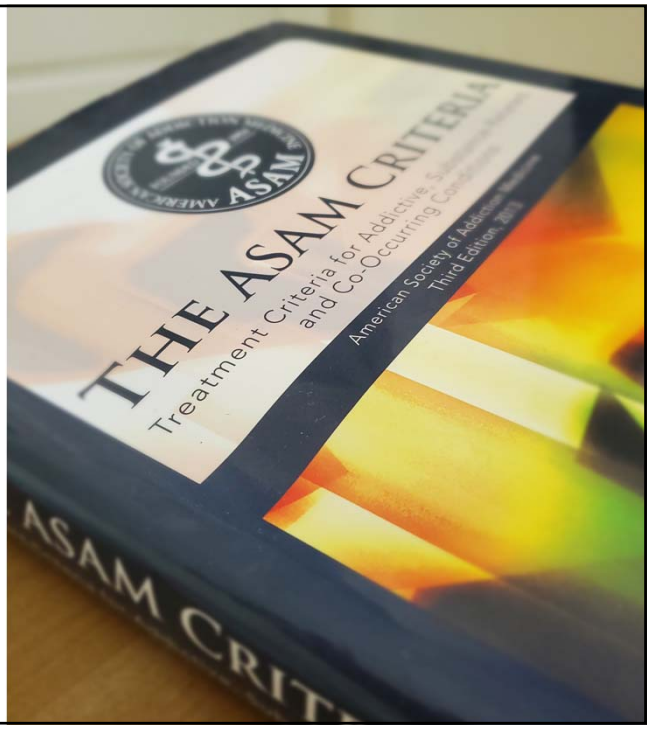
ASAM National Practice Guideline to Treat Opioid Use Disorder



- The ASAM National Practice Guideline (NPG) was updated in 2020.
- It provides information on evidence-based treatment of opioid use disorder (TOUD).
- It is the first text to address all the FDA-approved medications available to treat addiction involving opioid use and opioid overdose in a single document.

The ASAM Criteria

The ASAM Criteria is the most widely used and comprehensive set of guidelines for placement, continued stay, and transfer/discharge of patients with addiction and co-occurring conditions. It matches people to the level of care that safely and efficiently meets their needs and that is not biased towards inpatient or outpatient care. Patients should receive the least intensive but safe level of care.



Patient Resources

1. ASAM's Opioid Addiction Treatment: A Guide for Patients, Families, and Friends
2. National Institute on Drug Abuse (NIDA) Patient Materials
3. National Alliance on Mental Illness (NAMI)

Activity 5: Revisiting Robert's Case

- **Task:** Working with your group, develop Robert's treatment plan.
- **Discuss:** Let's revisit Robert's case from a treatment perspective. Based on the content covered in this module, identify the appropriate treatment plan for Robert.
- **Time Allocated:** 10 minutes

Robert's Case

Key Treatment Considerations:

1. What medication and/or psychosocial treatment options would you recommend for Robert and why?
2. Assess Robert's case to determine if he meets DSM-5 criteria for an opioid use disorder. If so, how? Is it mild, moderate, or severe?
3. What are the treatment options for Robert?
4. How would you assess the need for pharmacotherapy (e.g., methadone, buprenorphine, naltrexone) for Robert?
5. Is Robert a candidate for office-based opioid treatment (OBOT)? Why or why not?
6. What should the initial treatment plan include?

Activity 5: Revisiting Robert's Case

- **Task:** Large Group Report Out
- **Discuss:** Let's revisit Robert's case from a treatment perspective. Based on the content covered in this module, identify the appropriate treatment plan for Robert.
- **Time Allocated:** 10 minutes

DETERMINING A TREATMENT PLAN FOR PATIENTS WITH OPIOID USE DISORDER

End of Session 2

THE ASAM
Treatment of Opioid Use Disorder Course

Includes waiver qualifying requirements

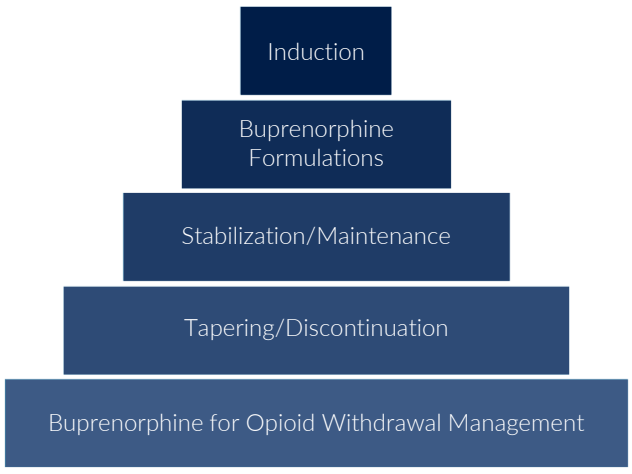
Session 3

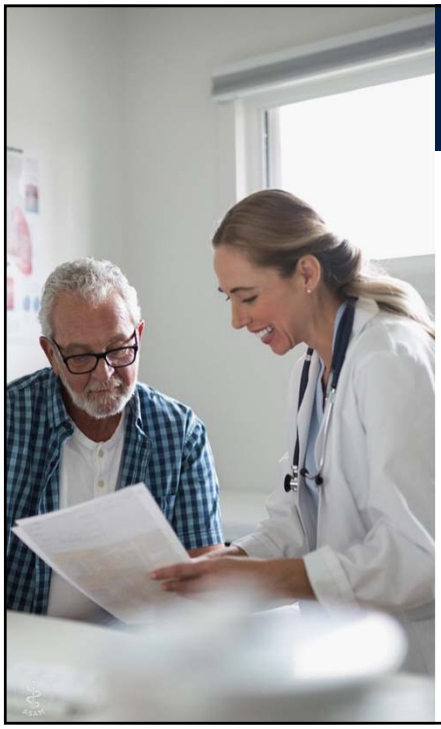
Implementing Office-Based Opioid Treatment

Session Learning Objectives

1. Monitor progress using face-to-face visits, urine drug tests, pill/film counts, and PDMP checks.
2. Discuss relapse prevention with patients.
3. Assess cause of relapse and modify treatment plan based on patient needs to progress toward treatment goals.
4. Describe procedures for setting up office systems including team-based care to support medication prescribing for opioid use disorders.
5. Implement, update, and maintain best practices for office systems to support treatment with medication for opioid use disorder.

Clinical Uses of Buprenorphine





Buprenorphine Induction: Early Stabilization

***Overall Goals:** To find the buprenorphine dose at which the patient experiences:*

- Suppression of opioid withdrawal symptoms.
- Marked reduction or discontinuation of illicit opioid use.
- Decreased opioid cravings.
- Blunted or blocked euphoria after illicit opioid use.
- Minimal/no side effects.
- Provide effective blockade preventing lethal overdose.

Buprenorphine Induction

1 Office-based (Options)

2 Home-based (Unobserved)

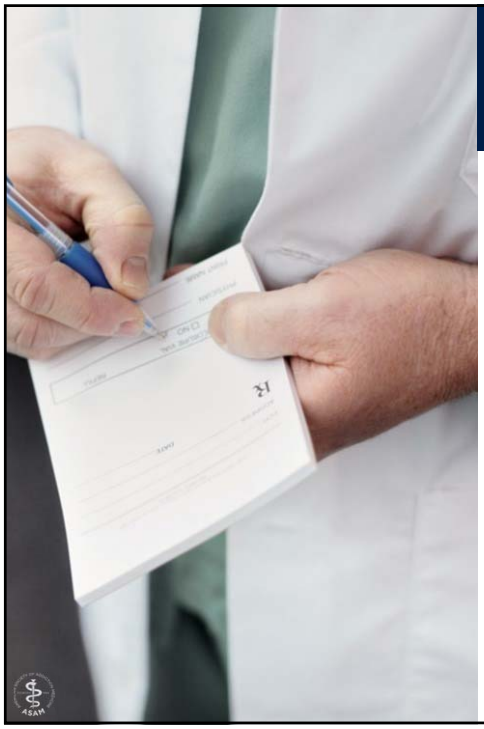
Buprenorphine Induction

Office-Based (Options):

- ***Keep medication in the office for inductions.***
  - Must keep records required by federal and state law for maintaining controlled substances for administering or dispensing.
  - Records are audited by the DEA.
- ***Have the patient:***
  - Fill a prescription for the first day's dose.

OR

  - Bring medication to the office for administration.
- ***Fax prescription to pharmacy, then have it delivered.***



Buprenorphine
The First Prescription

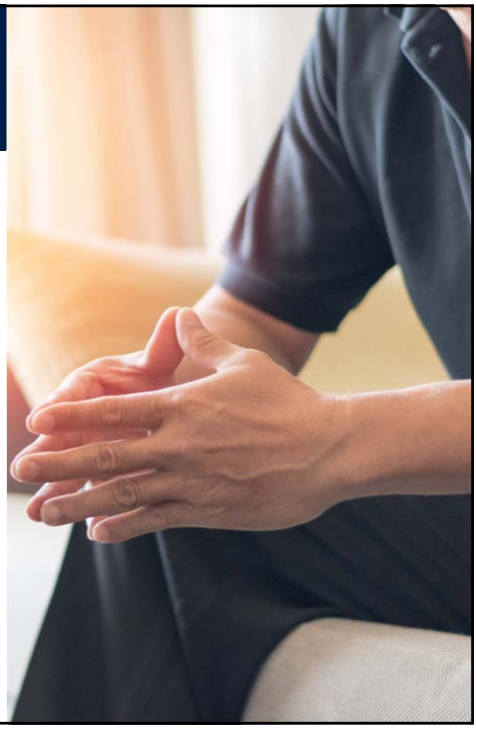
The amount of buprenorphine prescribed for induction and stabilization depends on many factors:

- Will this be an office-based or home induction?
- How adherent is the patient?
- Is there a significant other who can secure and dispense the medication? (Particularly important with younger patients.)
- How are co-pays managed? Is it reasonable to fill prescriptions every few days?
- Prior authorizations.

Buprenorphine Office-based Induction

Patient Instructions:

- Don't plan to drive home.
- Plan to be at clinic or office for up to 3 hours.
- Be ready to give urine sample.
- Bring all prescribed, OTC, and herbal medications with you.
- Bring medication bottle or have it delivered if applicable (prescribe vs. dispense).
- Be accompanied by trusted family member or friend when possible.
- Come to office in ***mild*** opioid withdrawal.



Acute Opioid Withdrawal

	Symptoms / Signs
Mild ↓	Anxiety, drug craving
	Yawning, sweating, runny nose, tearing eyes, restlessness, insomnia
	Dilated pupils, gooseflesh, muscle twitching, muscle & joint aches
	Nausea, extreme restlessness, elevated BP, heart rate > 100, fever
Severe	Vomiting, diarrhea, abdominal cramps, curled-up body position

Clinical Opiate Withdrawal Scale (COWS):
pulse, sweating, restlessness & anxiety, pupil size, aches, runny nose & tearing, GI sx, tremor, yawning, gooseflesh

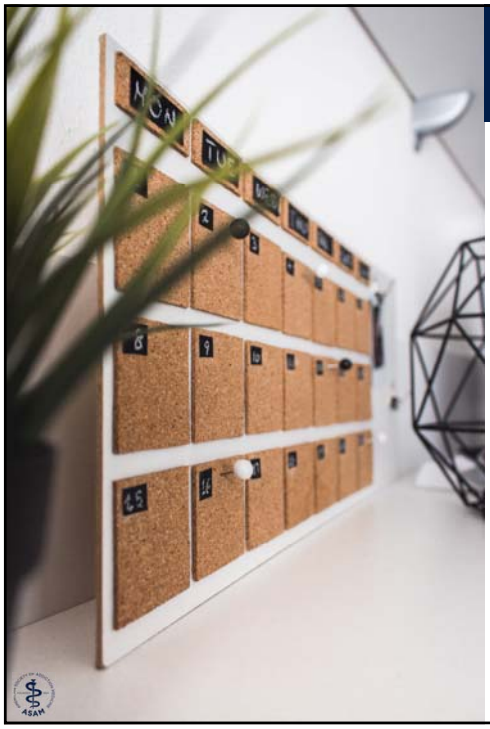
- *5-12 mild*
- *13-24 moderate*
- *25-36 moderately severe*
- *>36 severe*

Buprenorphine Induction

Unobserved "Home" Option:

- Numerous observational studies demonstrate that unobserved "home" inductions are both **effective and safe, however, there is no comparison from RCTs.**
- Should be performed in properly selected patients. Patients should be able to describe and rate opioid withdrawal and understand dosing instructions.
- Providers and patient/significant other should be able to **communicate during the induction**.
- Same protocol as in office-based induction.

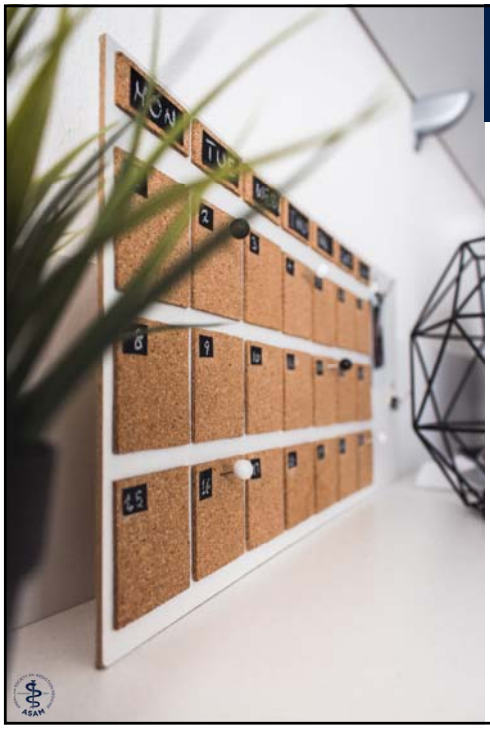
Alford DP et al. J Gen Intern Med. 2007., Lee JD et al. J Gen Intern Med. 2008., Cunningham CO et al. J Subst Abuse Treat. 2011., Sohler NL et al. J Subst Abuse Treat. 2011., Lee JD et al. J Addict Med. 2014.



Induction – Day 1

If the patient is NOT currently physically dependent on opioids:

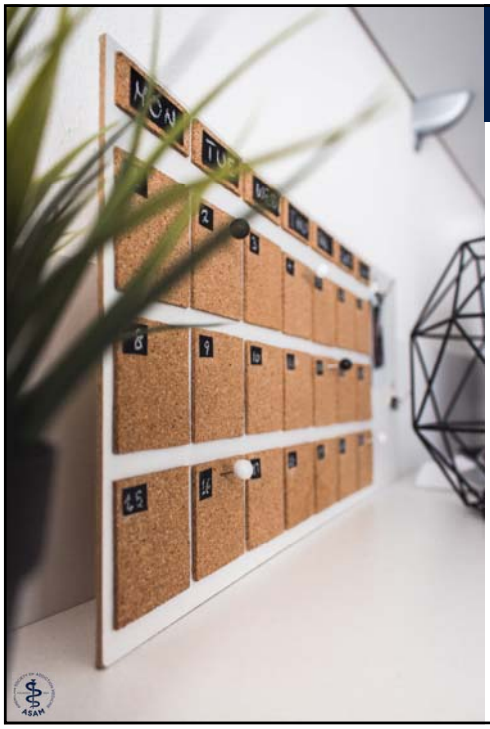
- *Post-withdrawal management, post-incarceration, post-hospitalization*
- Can still meet *DSM-5 OUD criteria*
- No precipitated withdrawal concerns
- *Start low (2 mg)* and go slow to avoid opioid side effects
- *Patients are very good at titrating* buprenorphine if given dosing schedule and parameters (e.g., maximum dose)



Induction – Day 1

If the patient is <u>physically dependent</u> on short-acting opioids:

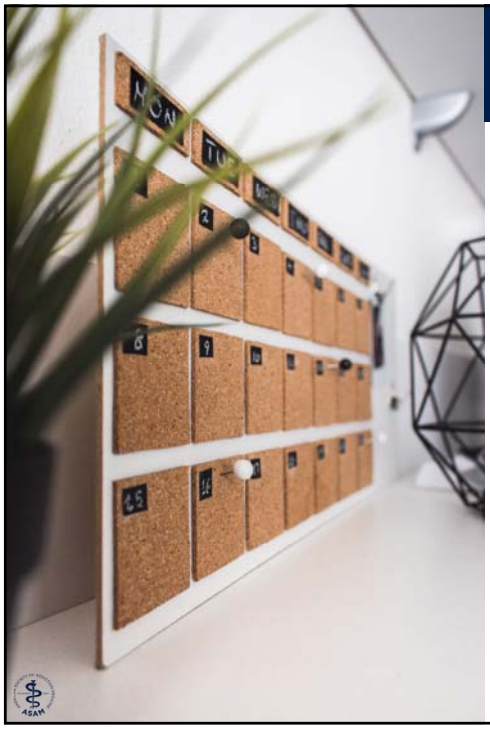
- *Instruct patients to abstain from any opioid use for 12-24 hours (so they are in mild withdrawal at time of first buprenorphine dose).*
- If the patient is not in opioid withdrawal at time of arrival in office:
- *Assess time of last use and consider:*
  - Have them return another day
  - Waiting in the office until evidence of withdrawal is seen
  - Or leaving office and returning later in day (with strict instructions to not take opioids while away from the office)



Induction – Day 1

If the patient is <u>physically dependent</u> on short-acting opioids:

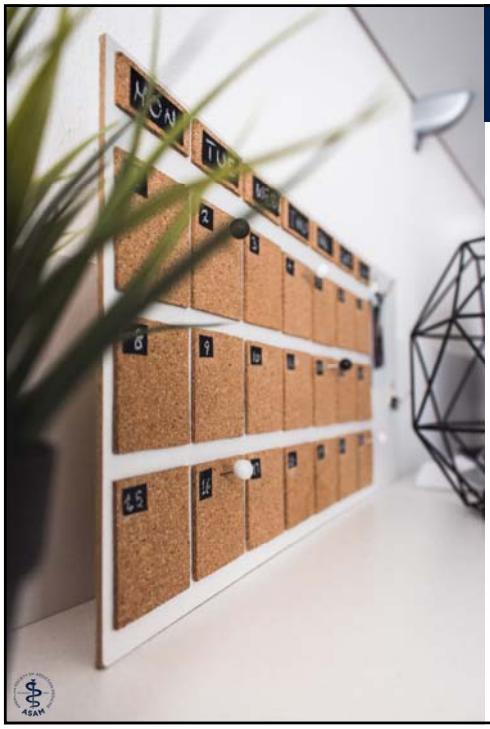
- *First dose: 2/0.5-4/1 mg SL* buprenorphine/naloxone.
- *Dose can take 3-10 minutes to dissolve fully.*
- *Monitor in office for 1-2 hours* after first dose and each subsequent dose.
- *Relief* of opioid withdrawal should begin within 30-45 minutes.
- *Period of greatest severity of buprenorphine-related precipitated withdrawal* occurs in the first few hours (1- 4 hours) after a dose.



Induction – Day 1

If the patient is <u>physically dependent</u> on short-acting opioids:

- *The length of time the patient is monitored in the office varies, depending upon:*
  - The *clinician's* familiarity with:
    - the patient
    - prescribing buprenorphine
  - The patient's level of support at home



Induction – Day 1

If the patient is <u>physically dependent</u> on short-acting opioids:

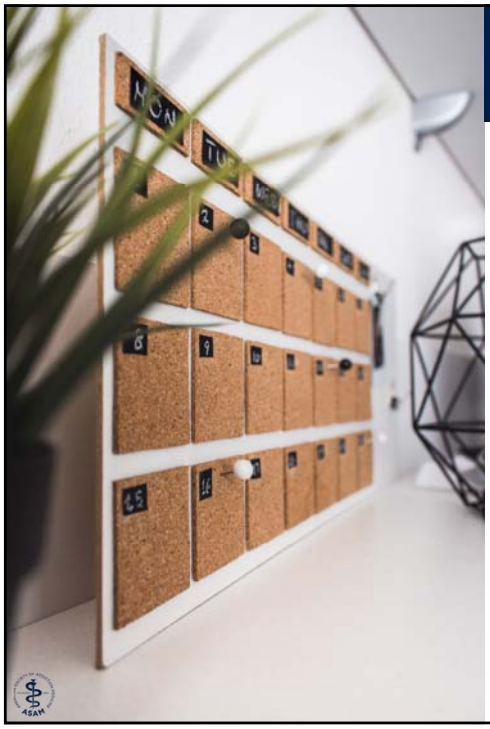
- *Can re-dose if needed* (every 1-2 hours, if opioid withdrawal subsides then reappears).
- *Maximum first day dose of buprenorphine/naloxone = 8mg -16mg.*
- Dose equivalent of other formulations (e.g., 5.7mg - 11.4mg of branded SL tablets).

Inducting Patients

The patient on Fentanyl Patch:

- According to the Fentanyl product insert, it takes >17 hours after removal for a 50% decrease in serum concentrations to be attained.
- Buprenorphine sublingual induction should follow the same general guidelines as with any other full opioid agonist.
- *Methadone should be considered if buprenorphine induction fails.* Fentanyl has a high potency and methadone may be better as a potent full agonist in comparison with buprenorphine.
- *Limited evidence available to guide this process.*

Huhn, A. S., Hobelmann, J. G., Oyler, G. A., & Strain, E. C. (2020). Protracted renal clearance of fentanyl in persons with opioid use disorder. Drug and alcohol dependence, 214, 108147.



Induction – Day 1

If the patient is <u>physically dependent</u> on long-acting opioid:

- *Recommendations vary about optimal dose of long-acting opioid for transfer* (TIP 63 states 30-40 mg/d methadone and remain on that dose for at least 1 week).
- *Begin induction at least 48-72 hours* (sometimes up to 4-5 days) after last dose of methadone, and 36 hours after last dose of sustained release oxycodone (or longer).
- *Patient should be in mild withdrawal* at time of first buprenorphine dose.
- *Use similar induction procedures to "physically dependent on short-acting opioids."*

SAMHSA TIP 63 Medications for Opioid Use Disorders. 2018

Induction – Day 1

Options for Managing Precipitated Withdrawal

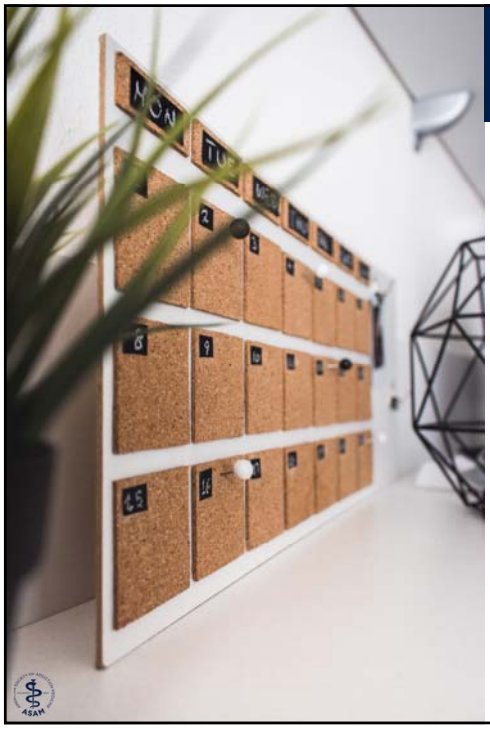
Option 1:
Give another dose of buprenorphine 2-4 mg

Attempting to provide enough agonist effect to suppress withdrawal symptoms.

VS

Option 2:
Stop induction

Treat withdrawal symptoms.
Restart induction the next day.



Induction – Day 1

Options for managing symptoms of precipitated withdrawal:

- Clonidine*, tizanidine*, lofexidine (hyperadrenergic state)
- NSAIDS (muscle cramps and pain)
- Benzodiazepines (insomnia)
- Dicyclomine (abdominal cramps)
- Bismuth subsalicylate (diarrhea)

Since stopping the induction risks loss of the patient, the first option should be considered.

**Off-label use.*

Use of Microdoses for Induction of Buprenorphine

- Even with precautions, for many patients, the induction of buprenorphine is a difficult experience due to withdrawal symptoms.
- Overlapping induction of buprenorphine maintenance treatment with full μ-opioid receptor agonist use is feasible. It may be associated with better tolerability and acceptability in some patients compared to the conventional method of induction.
- Cases illustrate that overlapping induction of buprenorphine while being on full μ-agonists is feasible, but further research is needed.

Hämmig, R., Kemter, A., Strasser, J., von Bardeleben, U., Gugger, B., Walter, M., ... & Vogel, M. (2016). Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method. Substance abuse and

Acute Opioid Withdrawal
(Off-label for Pain)

Drug	Formulations	Maintenance Dose
Buprenorphine		
Generic	2, 8 mg SL tabs	16 mg/d
Probuphine®	74.2 mg SD implant	4 implants/6m
Sublocade®	100 mg, 300 mg SQ injection	100 mg/m
Buprenorphine/Naloxone		
Generic	2/0.5, 8/2 mg SL tabs	16/4 mg/d
Bunavail®	2.1/0.3, 4.2/0/7, 6.3/1 mg buccal film	8.4/1.4 mg/d
Suboxone®	2/0.5, 4/1, 8/2, 12/3 mg SL film	16/4 mg/d
Zubsolv®	1.4/0.36, 5.7/1.4 mg SL tab	11.4/2.8 mg/d

The Medical Letter 2018; 60(1541):35-37

Corresponding Doses of Bup/Nx

Generic SL tablets	*Suboxone® SL films*	*Zubsolv® SL tablets*	*Bunavail® Buccal films*
2 mg bup / 0.5 mg naloxone	2 mg bup / 0.5 mg naloxone	1.4 mg bup / 0.36 mg naloxone	
	4 mg bup / 1 mg naloxone	2.9 mg bup / 0.71 mg naloxone	2.1 mg bup / 0.3 mg naloxone
8 mg bup / 2 mg naloxone	8 mg bup / 2 mg naloxone	5.7 mg bup / 1.4 mg naloxone	4.2 mg bup / 0.7 mg naloxone
	12 mg bup / 3 mg naloxone	8.6 mg bup / 2.1 mg naloxone	6.3 mg bup / 1 mg naloxone
		11.4 mg bup / 2.9 mg naloxone	

Kampman, K. et al. (2015). The ASAM National Practice Guideline

Audience Response

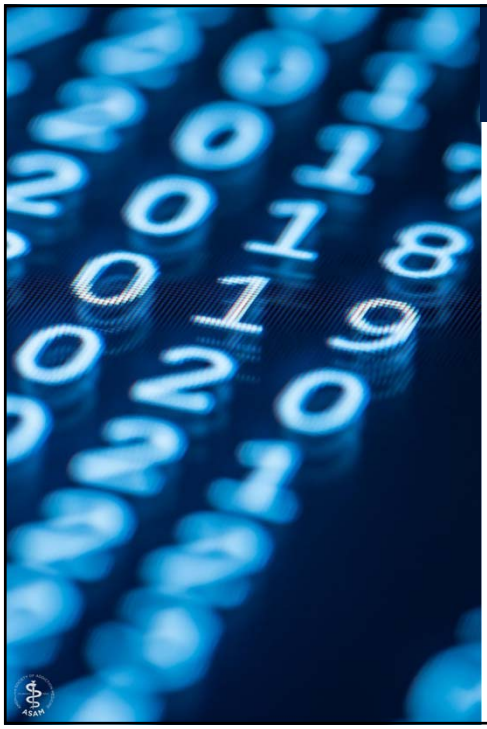
Which of the following is true of the first day of induction?

A. You should always have the patient start medication in the office.

B. Patients who start medication in the office have higher success rates than patients who start at home.

C. Starting medication at home may be preferred by patients as they can be more comfortable with withdrawal.

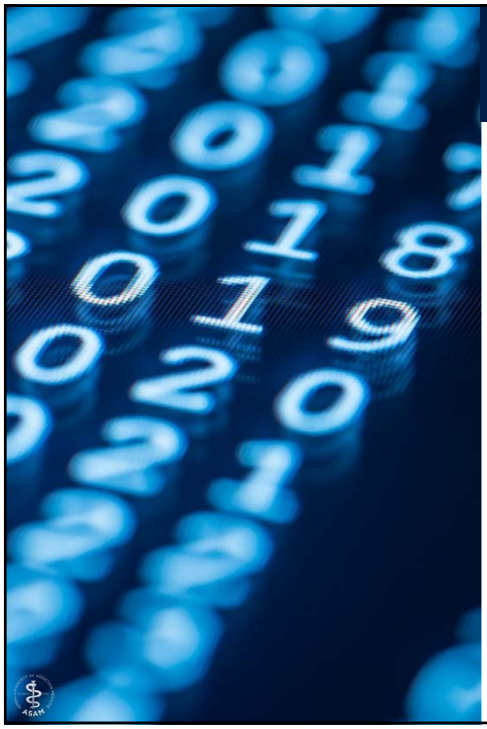
D. Starting medication at home may be preferred due to space constraints in the office for such a long appointment.



Stabilization and Maintenance

Day 2 and Beyond:

- Be in contact with patient (in office, via phone, etc.).
- Adjust dose accordingly based on patient's experiences the first day.
- Continue adjusting dose by 2/0.5-4/1 mg increments until patient is out of withdrawal—this typically occurs at dose of 8/2.
- Generally 24mg of buprenorphine is considered a maximal dose, but rarely patients may require a higher dose up to 32mg.



Stabilization and Maintenance

Day 2 and Beyond:

- After the first day of induction for patients who are physically dependent on either short-acting or long-acting opioids, the procedures are the same.
- Adjust dose according to the patient's experiences:
  - Lower dose if patient was over-medicated at end of Day 1.
  - Higher dose if there were withdrawal symptoms after leaving your office and/or if patient used opioid agonists
- Don't assume abstinence after the first day's dose.

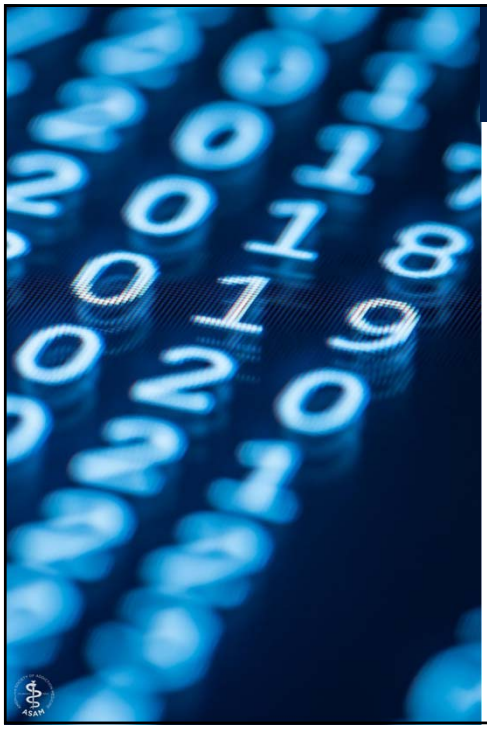
Buprenorphine Dosing

> 24 – 32 mg/day → Unusual: Full Review of Medical/Behavior Issues

> 16 – 24 mg/day → Possible

< 16 mg/day → Typical

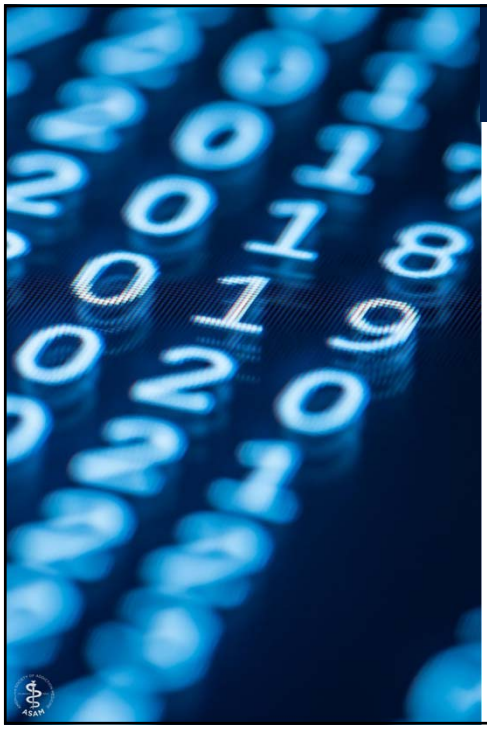
Zubieta et al., 2000; Greenwald et al. 2003; Product Information Suboxone 2005; personal communication RE Johnson, June, 2007.



Stabilization and Maintenance

The patient should receive a daily dose until stabilized:

- Patient should be dosed once daily or twice daily, but not more frequently than twice daily.
- Multiple daily doses which mimic addictive behavior is not recommended.
- Splitting the dose to Q6-8 is indicated if treating concurrent OUD and pain.



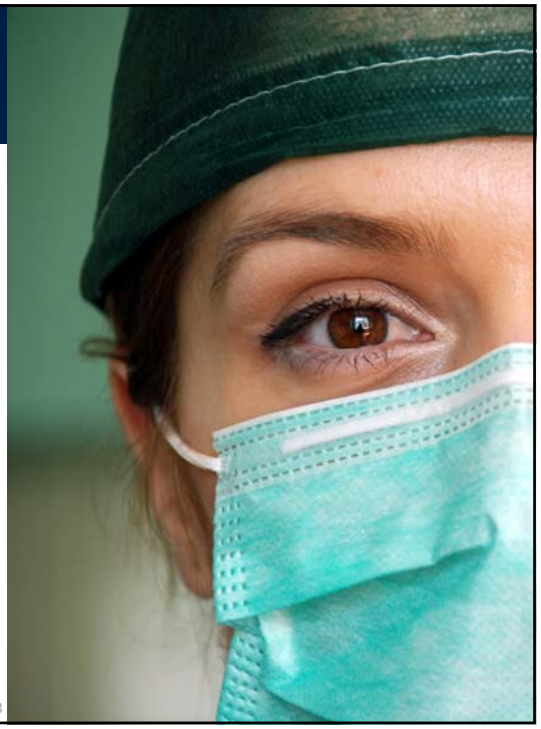
Stabilization and Maintenance

For OBOT patients, daily dosing is the norm:

- Once stabilized, the patient can be shifted to alternate day dosing (e.g., every other day, M-W-F, or every third day, M/Th).
- Non-daily dosing is most appropriate if the patient is receiving observed dosing in an OTP.
- Increase dose on dosing day by amount not received on other days (e.g., if on 8 mg/d, switch to 16/16/24 mg M-W-F).

Buprenorphine Implants *(Probuphine®)*

- FDA-approved for mod-severe OUD.
- Subdermal four implants (0.5-1 ng/ml); low continuous levels for 6 months.
- Requires certification (live training) to prescribe, insert and remove implants.
- ~30-minute procedure: follow-up in one week.
- After 1 insertion in both arms, transition to SL buprenorphine.



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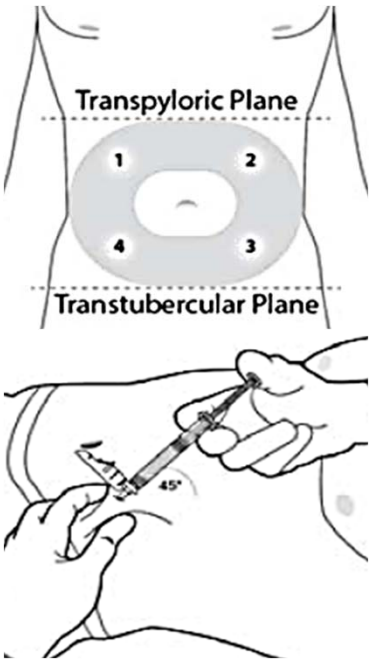
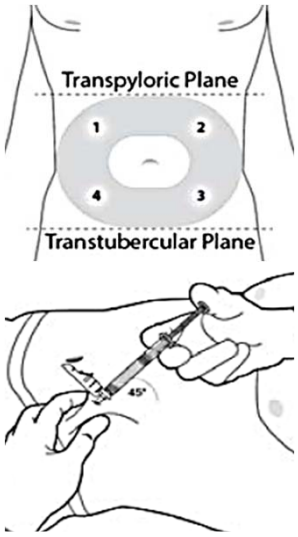
Buprenorphine Extended-Release (ER)

Subcutaneous Injection (Sublocade®)

- FDA-approved for moderate to severe OUD.
- Biodegradable delivery system.
- Releases buprenorphine at controlled rate over one month.

The Medical Letter Feb 26, 2018





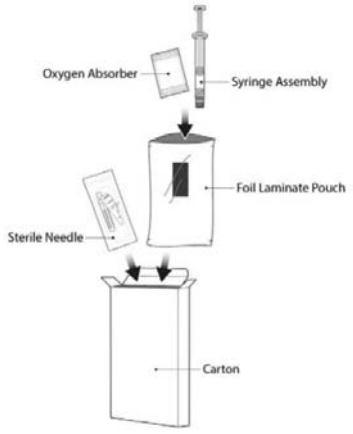
Buprenorphine Extended-Release (ER)

Subcutaneous Injection (Sublocade®)

Releases buprenorphine at controlled rate over one month:

- Mean plasma concentration with monthly 100 mg is about 10% higher than 24 mg/d of SL tablets.
- Each of the 1st two monthly SQ doses should be 300 mg/1.5 ml prefilled syringe. Doses should be separated by at least 26 days
- Subsequent doses should be 100 mg/o.5 ml prefilled syringe. Some patients may need to increase maintenance dose to 300 mg monthly.

SAMHSA TIP 63 Medications for Opioid Use Disorders. 2018



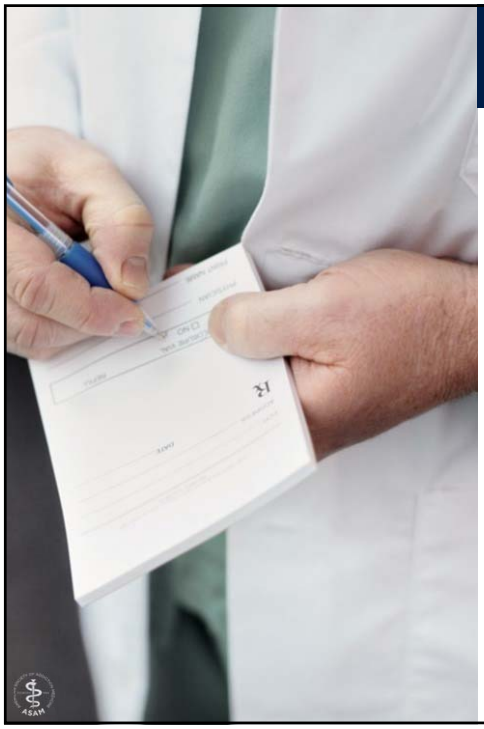
Buprenorphine ER Injection
(Sublocade®)

- Pharmacies need special certification to order and dispense.
- Before initiating, patient should be stabilized on transmucosal buprenorphine (8 mg-24 mg daily) for at least seven days.
- There is insufficient data on its use in pregnancy.
- ***Inform patient:***
  - Medication only available in specific pharmacies as IV self-administration can be fatal.
  - After abdominal injection, a lump may be present at the injection site for a few weeks. Patients should not rub or massage the lump or let belts rub against it.

Finding REMS certified pharmacies:

https://www.sublocaderems.com/Content/pdf/certified-pharmacies.pdf

SAMHSA TIP 63 Medications for Opioid Use Disorders. 2018



Buprenorphine Maintenance

How long should buprenorphine maintenance continue?

- Patients should take medication as long as they benefit from it and wish to continue.
- There is no known duration of treatment after which patients can stop medication and be certain that they will not return to illicit opioid use.
- Given the chronic nature of OUD and potentially fatal consequences of unintended opioid overdose, ***it is critical to base length of time in treatment on patients' individual needs***.

SAMHSA TIP 63 Medications for Opioid Use Disorders. 2018

Buprenorphine Discontinuation

Important Considerations: Part 1

- How has the patient responded to treatment so far?
- Why do they want to taper?
- What do they expect will be different after the taper?
- Do they understand the risk of overdose associated with return to use?
- Do they have a safety plan?

Buprenorphine Discontinuation

Important Considerations: Part 2

- **Do they understand the risks and benefits of continuing vs discontinuing treatment?**
  - Many studies show high relapse rates with tapering and withdrawal from maintenance agonist medications.
  - Some studies show normalization of brain function with maintenance.

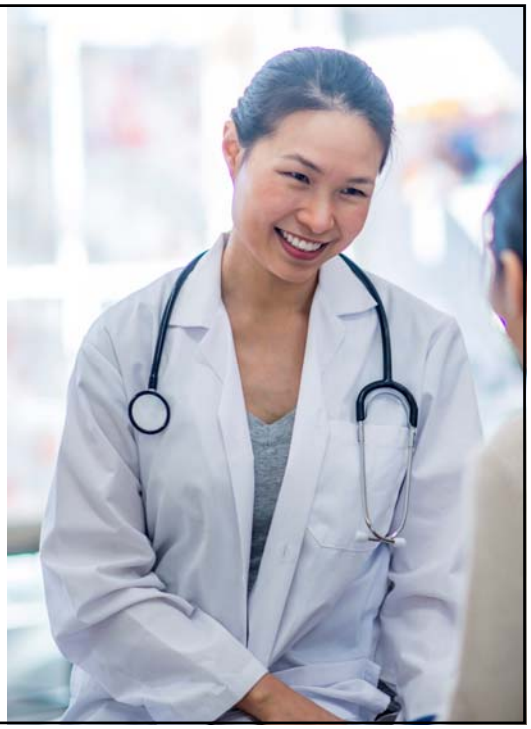
Buprenorphine Discontinuation

Important Considerations: Part 3

- **Patients should continue to be followed by provider after discontinuation.**
- Patients should be told they can resume buprenorphine treatment if cravings, lapses, or relapses occur.
- Psychosocial treatments should continue if applicable.
- Consider naltrexone.
- Associated with relapse? Do they have a safety plan?

Tapering

- ***Short-term taper ("detox") is not recommended as a stand-alone treatment.***
  - However, patients may taper from buprenorphine as part of a treatment plan.
- There is no ideal protocol but titrate slowly and carefully.
- Patient should be educated on risk of relapse after taper.
- ***ASAM does not recommend limiting length of treatment.***



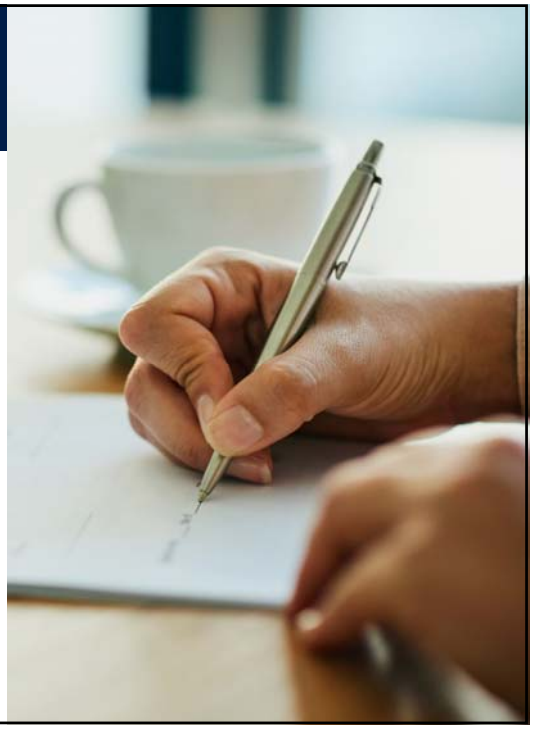
Naltrexone Formulations

Naltrexone	Formulation	Target Maintenance Dosage
Oral		
Generic	50 mg tablets	50 mg per day
Revia®		
Extended-Release IM injection (XR-NTX)		
Vivitrol®	380 mg ER suspension	380 mg IM q month

The Medical Letter 2017

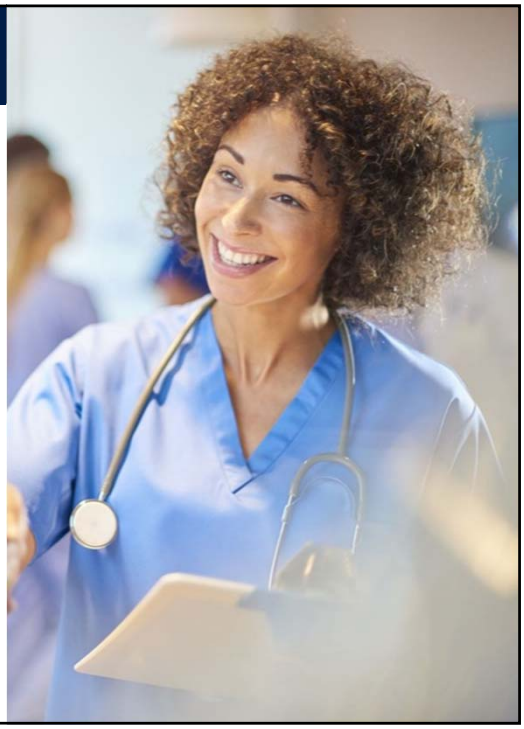
Prior to Starting Naltrexone Treatment

- **Review and sign agreement with consents and treatment plan**
  - Release information as needed to coordinate care with outside providers and supports
- **Labs reviewed and appropriate**
  - LFTs < 3-5x normal
  - Pregnancy test for women of childbearing age



Naltrexone Initiation

- **Insurance prior authorization completed if needed and medication ordered.**
  - Some private insurers require a PA.
  - Many MCOs will cover naltrexone but ordering through specialty pharmacy takes time.
- **Medical Alert identification to patient.**
- **Urine drug tests negative for all opioids prior to starting naltrexone.**
  - Patients with OUD must be fully withdrawn from all opioids, typically no use for 7-10 days.



Naltrexone Challenge Test

- ***An oral naltrexone challenge test should be performed if there is a risk of precipitating opioid withdrawal:***
  - Recommended prior to initial injection of XR-NTX and any lapse in treatment.
- In office, watch patient self-administer 25-50mg oral naltrexone.
- Observe patient for opioid withdrawal signs for minimum of 45-60 min.
- If opioid withdrawal occurs – ***DO NOT*** give XR-NTX.

Naltrexone Challenge Test

Naloxone Withdrawal

- In physically dependent individuals, naloxone will precipitate withdrawal within 5-10 min and dissipate within 30 min.
- Can be measured using standard instruments (e.g., COWS).
- Severity of withdrawal is proportional to the level of physical dependence.
- Any change from baseline, particularly objective signs = Positive Test.

Naltrexone Challenge Test

Naloxone Administration

- Naloxone is given IM 0.8-1.2 mg (2-3 cc).
- To minimize risk of significant opioid withdrawal, may administer in 2 stages, 0.4 mg followed by 0.8 mg.

Naltrexone Challenge Test

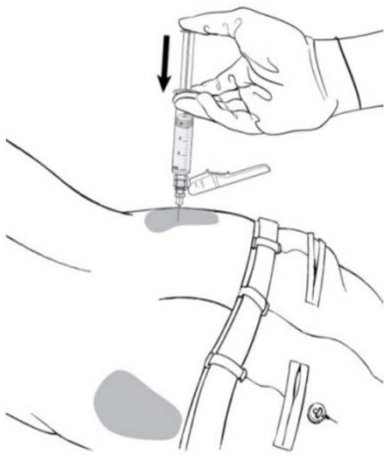
Next steps:

- With negative test → Full dose XR-NTX can be started.
- With positive test → XR-NTX should NOT be given.
  - Naloxone challenge can be repeated the next day.

XR-NTX Injection

- **Keep refrigerated**
  - Needs to come up to room temp (~45 minutes) prior to administration
- **Can stay out for a total of 7 days**
- **Reconstitute medication after patient arrives for visit**
- **Once mixed**
  - Give injection immediately so that the medication does not solidify
- **There will be 2 needle sizes 1.5" and 2"**
  - Ensure injection goes into muscle
  - Do not substitute manufacturer carton components
- **Alternate sites**

Injectable Naltrexone (XR-NTX)
Vivitrol® Package Insert



1. Using a circular motion, clean site with the alcohol swab.
2. Administer the suspension by deep IM injection into a gluteal muscle, alternating buttocks per monthly injection.
3. If blood aspirates or the needle clogs, do not inject. Change to the spare needle and administer into an adjacent site in the same gluteal region.
4. Inject the suspension in a smooth and continuous motion.
5. It must **NOT** be given **intravenously or subcutaneously.**

XR-NTX Practical Considerations

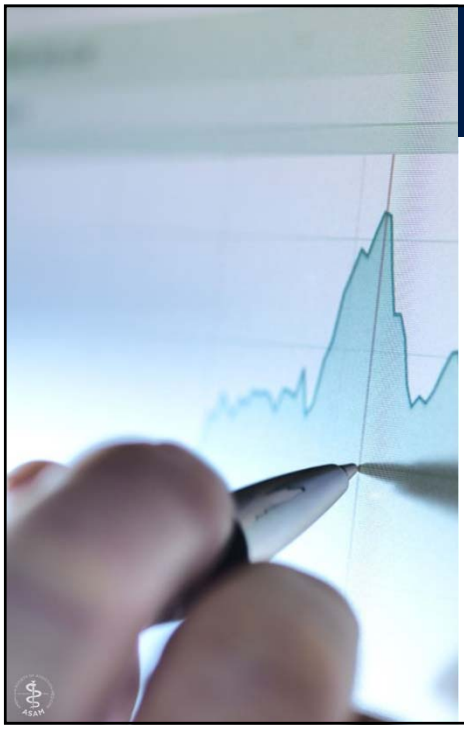
How long should I treat for?

- Unknown
- Pivotal trial 6 months of XR-NTX, then an open-label extension phase
- Reimbursement for 6-24+ months is standard

When XR-NTX stops?

- Return to non-antagonized, low tolerance
- Resume 'baseline' risk of relapse, overdose
- No evidence of otherwise higher OD risk

Lee, JD et al. Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention. Lancet. 2018 Jan 27;391(10118):309-318.



Medically Supervised Withdrawal: *Outcomes*

- Low rates of retention in treatment
- High rates of relapse post-treatment
- < 50% abstinent at 6 months
- < 15% abstinent at 12 months
- Increased rates of overdose due to decreased tolerance

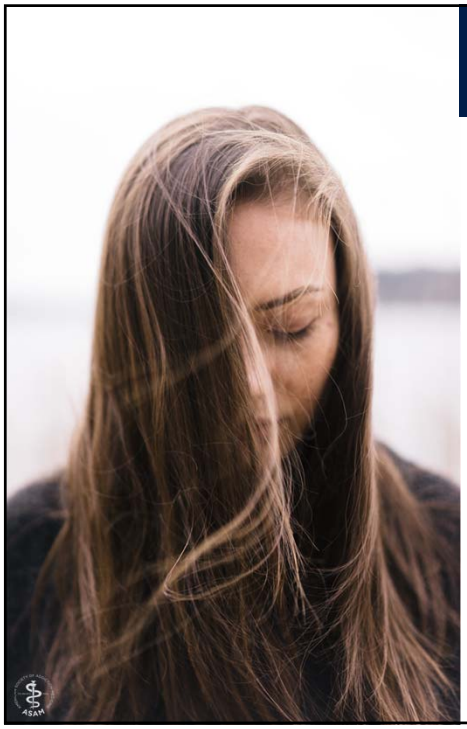
O'Connor PG. JAMA. 2005. Mattick RP, Hall WD. Lancet. 1996; Stimmel B et al. JAMA. 1977.

Audience Response

The ideal patient for injectable naltrexone is:

A. Someone who has tapered off of agonist-based therapy only.
B. Someone who does not want to be on a controlled substance.
C. Someone who is involved with the criminal-legal system.
D. Someone who does not need counseling.

PAULA'S CASE



Activity 6: Case Discussion – Paula

- **Task:** Whole Group Discussion
- **Discuss:** Let's review Paula's case.
- **Time Allocated:** 25 minutes

Paula's Case

Paula is 23-year-old graduate student in social work who is addicted to heroin. Her mother calls your office seeking treatment for her daughter. She agrees to having her mother come in with her for the consultation and evaluation. She is comfortable and not yet in opioid withdrawal during the initial consultation. You get Paula's history while her mother sits in the waiting room. She relates feeling anxious most of her life.

She started smoking marijuana and drinking alcohol on the weekends in high school. In college, she fractured her ankle playing basketball and was treated with oxycodone. She noticed that in addition to pain control, her anxiety decreased, and she reported feeling "normal" and "peaceful."

Paula's Case

She continued requesting oxycodone refills even though her pain had resolved. When the orthopedist refused to continue prescribing oxycodone she started buying them from friends, increasing to ~200mg daily.

A year ago she entered a 28-day residential program, never followed up in after care, and relapsed 6 weeks later. She has never been on medications for her opioid use disorder. Due to cost and availability she switched from oxycodone to snorting heroin, ~10 bags daily. Her last use was four hours ago. Paula agrees to have her mother present to discuss treatment options.

Paula's Case

You present the following options:

1. opioid agonist maintenance therapy (methadone, buprenorphine).
2. antagonist maintenance with naltrexone.
3. another attempt at withdrawal management and medication-free treatment.

Paula's Case

Paula and her mother have done their research; Paula has a friend doing well on buprenorphine and they decide on buprenorphine.

- They understand that you recommend some form of counseling as part of the treatment plan.
- Paula has insurance, so access is not a problem.

Paula's Case

Key Treatment Considerations:

1. Is Paula ready for buprenorphine induction currently?
2. If not, how will you decide when she is ready?
3. Is the patient a candidate for unobserved "home" induction?

You explain that since Paula is physically dependent on opioids, she must be in mild-moderate spontaneous withdrawal to avoid precipitated withdrawal. She understands. You tell her to discontinue all opioids for at least 12 hours. She has decided on doing the induction the next morning.

Paula's Case

- She returns the next day with her mother. She is visibly uncomfortable and has a COWS score of 12.
- Question:
  - ***Is she ready for the induction?***
- You instruct her that buprenorphine/naloxone is always administered sublingually or via the buccal mucosa—never swallowed whole.
- She is instructed on the proper administration procedures to maximize buprenorphine bioavailability.

Paula's Case

- You give her buprenorphine 4/1 mg.
- Questions:
  - ***How long until initial effect?***
  - ***How long until peak effect?***
- After her initial dose, you give her another 4/1 mg for continued withdrawal symptoms.
  - ***When can she leave the office?***
  - ***Can she take more buprenorphine after leaving the office?***
  - ***When should she contact you?***

Paula's Case

Key Treatment Considerations:

4. Should the stabilization dose be divided or taken once per day?
5. How often should stabilization doses be increased?
6. Once dose stabilization occurs, are maintenance dose increases due to tolerance common or are lower doses required over time?

She remained on buprenorphine/naloxone 16/4 mg per day for the next 6 months and had no relapses. She was adherent with weekly counseling and office monitoring including urine drug tests and pill counts. There were no concerning behaviors on the PDMP.

Paula's Case

Key Treatment Considerations:

7. How long should Paula be maintained on the buprenorphine?
8. How will you decide if and when she is ready to be tapered?
9. How would you taper her buprenorphine?

Patient Management: *Monitoring*

Follow-up Visits: Part 1

- Face-to-face visits to check safety and adherence.
- Initial Frequency should be every 1-2 weeks until stable, then monthly once stabilized.
- Check dosing, intervals, and sublingual technique.
- Safety issues include side effects and safe storage.

Follow-up Visits: Part 2

- Withdrawal/craving/triggers
- Tobacco, alcohol, and other drug use
- Drug tests and pill counts
- Prescription Drug Monitoring Program (PDMP)
- Confirm or reassess motivation for behavioral treatment
- Medical problems and symptoms

Follow-up Visits: Part 3

- Emotional/behavioral problems and symptoms
- Outside medications and providers
- Housing
- Reliable transportation
- Employment
- Family/relationships
- Legal Issues

Urine Drug Testing (UDT)

- ***Objective information:***
  - Evidence of therapeutic adherence
  - Evidence of use or non-use of illicit drugs
- Monitoring of treatment progress and safety
- Reinforces success with treatment, but no evidence that UDT improves outcomes
- Part of standard of care
- Identify those who may need higher level of care

ASAM's Appropriate Use of Drug Testing in Clinical Addiction Medicine Consensus Statement 2017

UDT: Frequency

- *SAMHSA TIP 63 (2018): "Periodic random testing" frequency is clinically determined.*
- At least at time of initial evaluation and initiation of medication then weekly → monthly.
- Regulation and reimbursement vary among states and insurers.
- Urine is preferred medium for testing due to:
  - Ease of obtaining sample, lowest cost
  - Ideal detection time (2-3 days)
  - Presence and persistence of metabolites
  - Availability of office-based testing tools

SAMHSA TIP 63 Medications for Opioid Use Disorders, 2018 ASAM's Consensus Statement 2017.

UDT: Implementation

- *Discuss with patient:*
  - This is for safety and this is the standard of care.
- *Know scope and limits of tests and lab:*
  - Beware false negatives and positives.
- *Consider random versus scheduled testing.*
- *Incorporate quality control procedures (temperature strip).*
- *Consider establishing consult lab linkage:*
  - GCMS/LCMS confirmatory testing.
  - Expert consultation on test interpretation.
  - Online reporting of results.

ASAM's Appropriate Use of Drug Testing in Clinical Addiction Medicine Consensus Statement 2017

UDT: Immunoassays

Pros:

- Point of care or lab-based
- Fast
- Cheap
- Specific tests available for many drugs
  - Oxycodone
  - Buprenorphine
  - Fentanyl
- Can be used as screening with option for confirmation

VS

Cons:

- Qualitative tests
  - Cutoff ng/ml
    - Opiates: 300
    - Cocaine metabolite: 300
- False positives
  - Cross-reactivity
  - Contamination
- False negatives
  - Below the cutoff

ASAM's Consensus Statement 2017

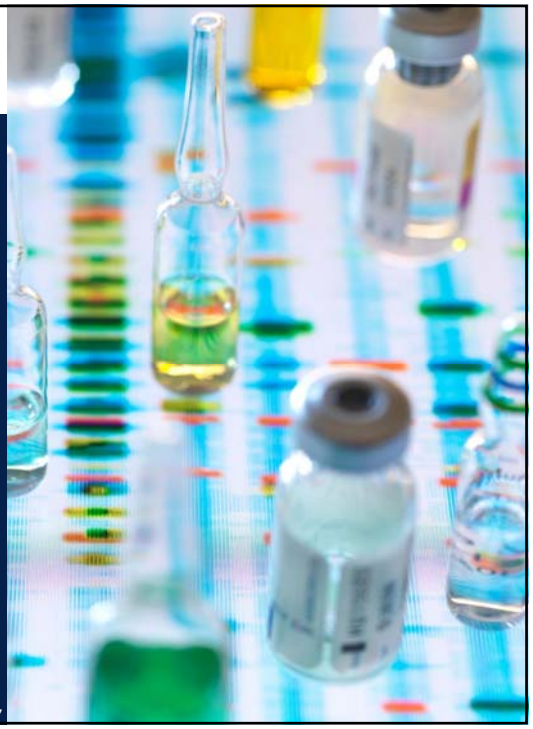
UDT: Immunoassay Detection Windows in Urine

Drug/Medication	Primary Metabolite	Ave. Detection Time (days)
Opiates (heroin, morphine)	Morphine	2-3
Semisynthetic Opioids (oxycodone, hydrocodone)	Variable Must be tested specifically	2-3
Methadone	EDDP	2-3
Buprenorphine	Nor-buprenorphine	2-3
Cocaine	benzoylecgonine	2-3
Amphetamines		2-3
Benzodiazepine	Varies by medication type	Variable with half life Unreliable immunoassays
Cannabis Occasional Cannabis Chronic	THC	1-3 Up to 30

ASAM's Consensus Statement 2017

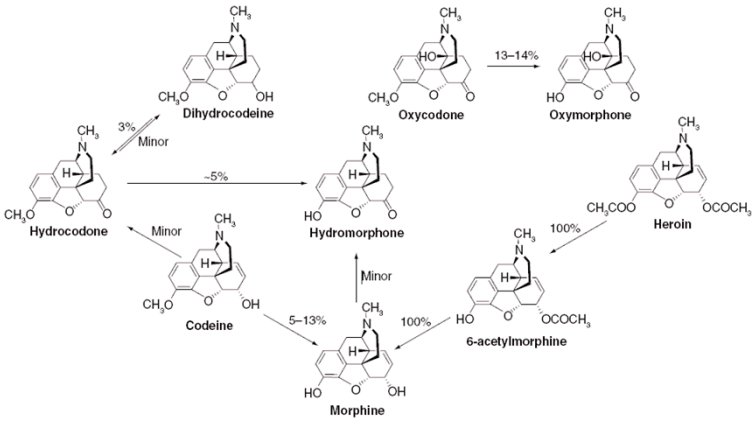
UDT: GCMS/LCMS

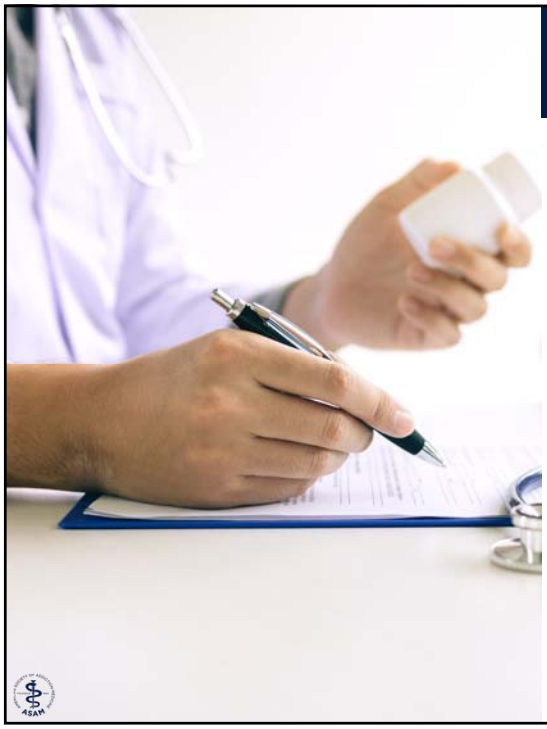
- *Gas or liquid chromatography, mass spectrometry*
- *Quantitative*
- *Limitations*
  - More costly
  - Requires specialized lab
  - Levels do not indicate amount of medication taken!
    - *Variables:*
      - time of dosing
      - metabolism
      - GFR
      - hydration



ASAM's Consensus Statement 2017

UDT: Opioid Metabolism



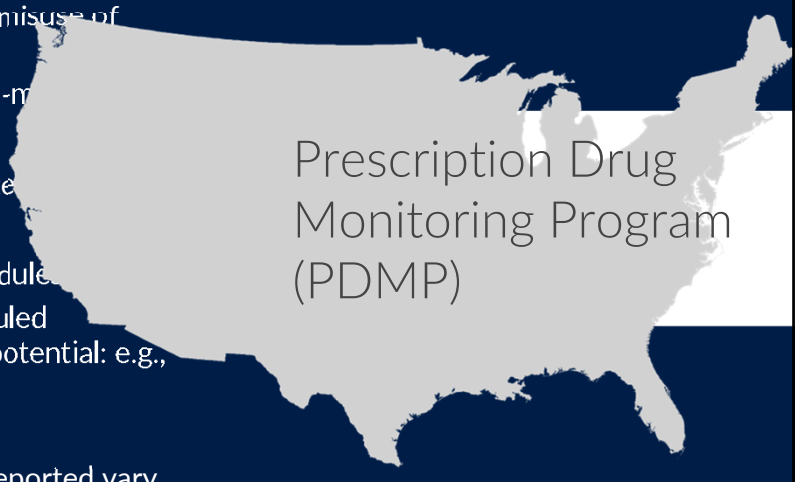


Pill Counts

- ***Objective information:***
  - Confirm medication adherence.
  - Minimize diversion.
- Frequency varies with patient progress.
- Best option when diversion suspected.
- Patient brings in medication supply.
- Confirm patient ID and fill date on bottle/box.
- Have patient count them in front of staff member.
- All tablets should be identical.
- Amount should match expected quantity.

Prescription Drug Monitoring Program (PDMP)

- ***State-wide System Tracking Prescriptions:***
  - Decreasing or preventing misuse of medications.
  - Improving clinical decision-m
- ***Pharmacies:***
  - Report information to state
- ***Information Varies:***
  - Schedule II +/- other schedule
  - Some selected non-scheduled medications with misuse potential: e.g., gabapentin, ephedrine.
- ***Data Availability:***
  - Format and medications reported vary by state.



PDMP: Limitations

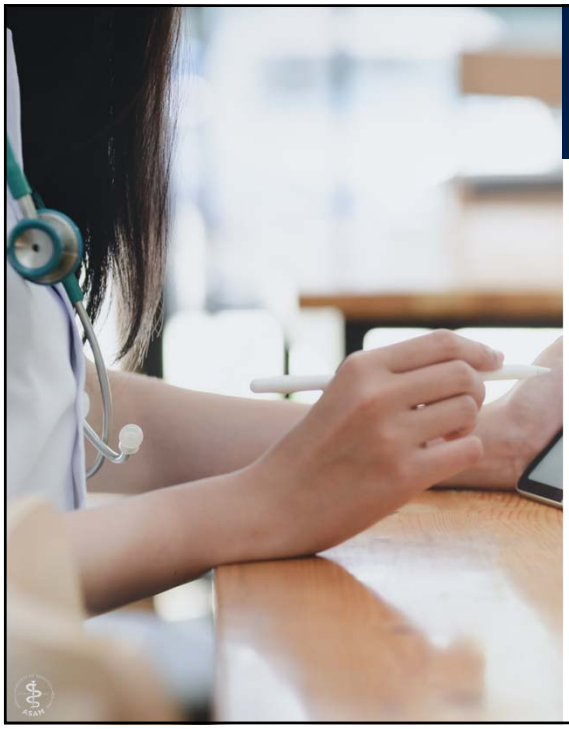
- Methadone and buprenorphine dispensed from OTPs are not listed on PDMPs.
- Not all data is readily available to providers.
- There is a lack of communication between all state programs.
- Time is needed to access reports.
- There are limitations in who can access reports.
- There is a mandatory vs. voluntary use of PDMP.

Audience Response

Which of the following is a monitoring practice that is evidence-based?

A. Checking your state's PDMP only on initiating buprenorphine.
B. UDT to make sure the patient is taking the medication and to discharge the patient if negative.
C. Random pill counts on all patients.
D. UDT to determine if the patient would benefit from additional support.

Relapse



Relapse: Prevention & Management

Relapse is a process in which return to substance use occurs in response to stressors and stimuli.

Relapse Precipitants:

- Present a negative affect (anger, fatigue, boredom, family conflict)
- Present cravings/cues (people, places and things)
- Feel social pressure/stress
- Begin using drug again

Doyle TJ, et al. Addressing Unhealthy Alcohol Use in Primary Care, 2013.

Relapse: Prevention & Management

- *Educate patients about how to anticipate/avoid/cope with these precipitants.*
- After initial use (a lapse), patients may experience guilt and shame which results in a heavy return to use.
- *Maintaining treatment is a learning process, lapses provide valuable lessons. A lapse is not a failure, but a mistake from which one can learn.*
- Returning to substance use requires prompt evaluation and review of treatment plan as well as a possible referral to additional or higher level of care.

Doyle TJ, et al. Addressing Unhealthy Alcohol Use in Primary Care, 2013.

SOPHIA'S CASE

Sophia's Case

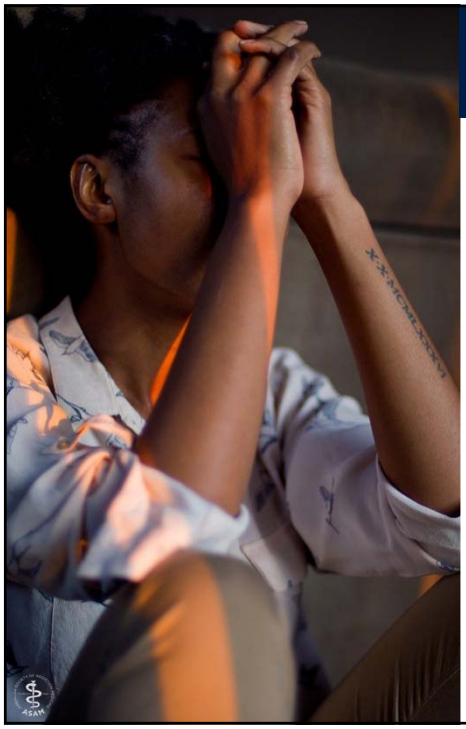
38-year-old woman followed for ongoing management of her opioid use disorder. She is presented to the buprenorphine induction clinic for induction and was quickly stabilized on bup/nx 16/4 mg SL a day. She kept all her appointments and had six weeks of urine drug tests which were negative for opioids and all other tested drugs.

Since coming into treatment with you, she has kept biweekly appointments x3, and monthly appointments x4, is reporting satisfaction with the treatment and is increasing productivity at work as a research assistant.

Sophia's Case

After her 8th visit with you, her urine drug test was positive for benzodiazepines, and confirmation reveals alprazolam and metabolites. She admits to using a friend's alprazolam (Xanax®) one night to help sleep. "With all the work stress, I just couldn't get to sleep."

She notes that she is doing much better in her life now than before when she was spending all her money on heroin and struggling to keep a job. She does not want to discontinue buprenorphine and go back to that life.



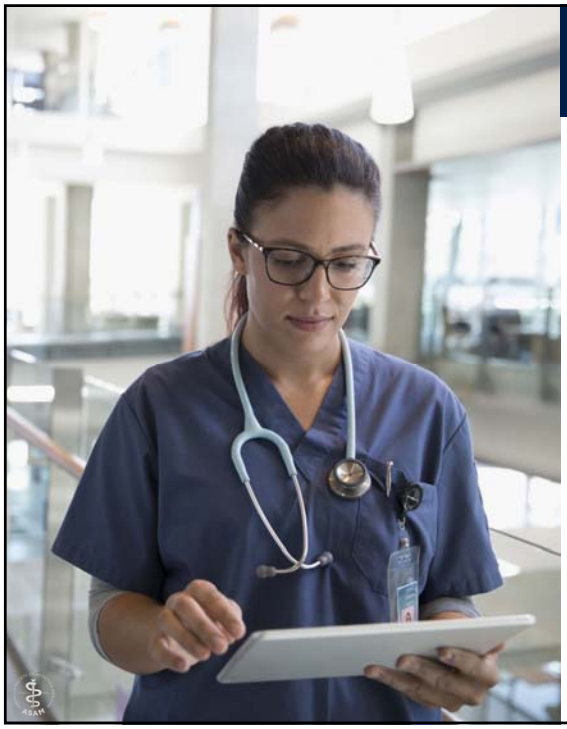
Activity 7: Case Discussion – Sophia

- **Task:** Whole Group Discussion
- **Discuss:**
  - How would you respond to these results?
  - Does the nature of the substance (benzos vs. stimulants) affect how you talk to Sophia?
  - How would you respond to these results?
- **Time Allocated:** 10 minutes

Sophia's Case

- She does not believe she has "a problem" with alprazolam.
- She denies further use.
- Repeat testing at this visit comes back positive again for benzodiazepines, with +alprazolam and metabolites.
- Question:
  - ***How would you respond to Sophia now?***

Office Management



Medication Treatment Settings

Office-Based Opioid Treatment (OBOT):

- Buprenorphine or naltrexone
- Not methadone
- Primary care (different models)
- Specialty (e.g. Infectious Disease, GI, Psychiatry, Hospitalist, Emergency Department)
- SUD treatment clinics

Implementing OBOT: Buy-in

- Do staff understand the need or gap in services?
- Do staff have accurate information about the disease of addiction and treatment options?
- Will patients be different from the ones we treat now?
- Does staff have the requisite knowledge, tools, and equipment to be successful?

https://www.niatx.net/PDF/NIATx-MAT-Toolkit.pdf

Treatment Agreement

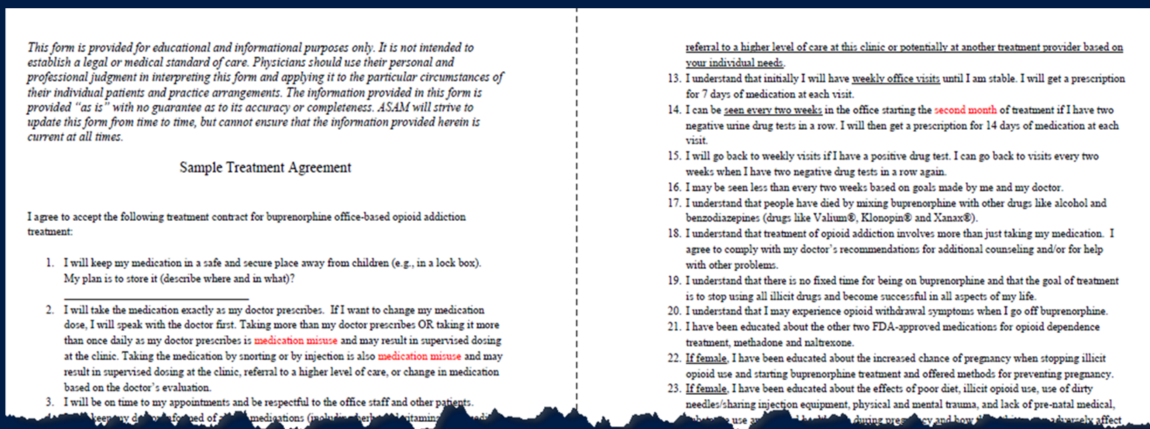
Patient Expectations:

- No medication diversion
- Adherence to treatment protocols
- Induction, maintenance
- Monitoring strategies (i.e., urine drug tests, pill counts)
- Additional treatment
- Appointments and refills
- No disruptive behavior
- Contact with other caregivers and pharmacies
- Safe storage

Provider Expectations:

- Scheduling visits
- Medication supply and refills
- Night coverage
- Response to “lost” prescriptions
- Unexpected UDT results
- Nonadherence or unexpected results
- Maintenance vs. taper

Treatment Agreement



This form is provided for educational and informational purposes only. It is not intended to establish a legal or medical standard of care. Physicians should use their personal and professional judgment in interpreting this form and applying it to the particular circumstances of their individual patients and practice arrangements. The information provided in this form is provided "as is" with no guarantee as to its accuracy or completeness. ASAM will strive to update this form from time to time, but cannot ensure that the information provided herein is current at all times.

Sample Treatment Agreement

I agree to accept the following treatment contract for buprenorphine office-based opioid addiction treatment:

1. I will keep my medication in a safe and secure place away from children (e.g., in a lock box). My plan is to store it (describe where and in what)?

   ____
2. I will take the medication exactly as my doctor prescribes. If I want to change my medication dose, I will speak with the doctor first. Taking more than my doctor prescribes OR taking it more than once daily as my doctor prescribes is medication misuse and may result in supervised dosing at the clinic. Taking the medication by snorting or by injection is also medication misuse and may result in supervised dosing at the clinic, referral to a higher level of care, or change in medication based on the doctor's evaluation.
3. I will be on time to my appointments and be respectful to the office staff and other patients.

referral to a higher level of care at this clinic or potentially at another treatment provider based on your individual needs.

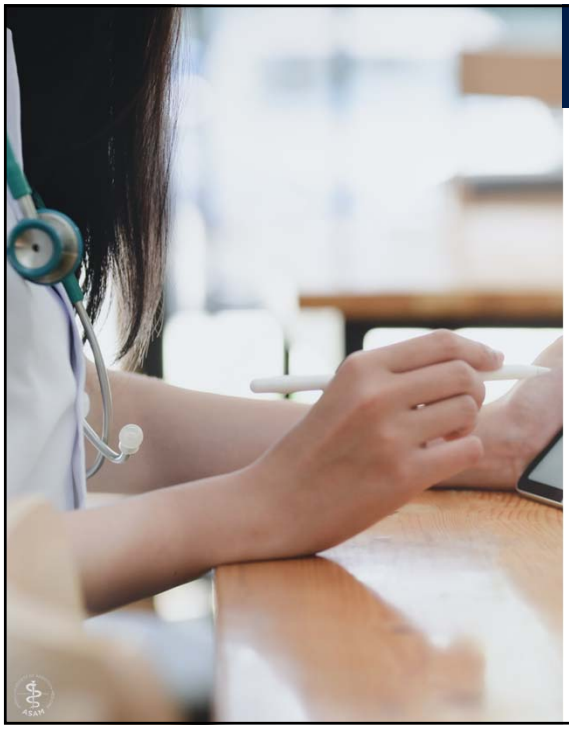
13. I understand that initially I will have weekly office visits until I am stable. I will get a prescription for 7 days of medication at each visit.
14. I can be seen every two weeks in the office starting the second month of treatment if I have two negative urine drug tests in a row. I will then get a prescription for 14 days of medication at each visit.
15. I will go back to weekly visits if I have a positive drug test. I can go back to visits every two weeks when I have two negative drug tests in a row again.
16. I may be seen less than every two weeks based on goals made by me and my doctor.
17. I understand that people have died by mixing buprenorphine with other drugs like alcohol and benzodiazepines (drugs like Valium®, Klonopin® and Xanax®).
18. I understand that treatment of opioid addiction involves more than just taking my medication. I agree to comply with my doctor's recommendations for additional counseling and/or for help with other problems.
19. I understand that there is no fixed time for being on buprenorphine and that the goal of treatment is to stop using all illicit drugs and become successful in all aspects of my life.
20. I understand that I may experience opioid withdrawal symptoms when I go off buprenorphine.
21. I have been educated about the other two FDA-approved medications for opioid dependence treatment, methadone and naltrexone.
22. If female, I have been educated about the increased chance of pregnancy when stopping illicit opioid use and starting buprenorphine treatment and offered methods for preventing pregnancy.
23. If female, I have been educated about the effects of poor diet, illicit opioid use, use of dirty needles/sharing injection equipment, physical and mental trauma, and lack of pre-natal medical,

Download from https://tinyurl.com/yanouybg

Informed Consent

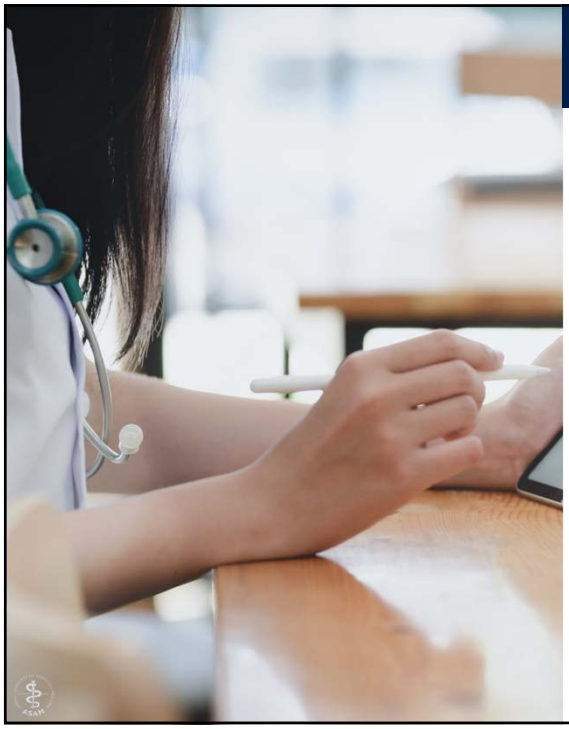
Must Address:

- Physical dependence
- Side effects:
  - Constipation
  - Sweating
  - Hypogonadism
- Risk of impairment, overdose
- Possible medication interactions
- Neonatal Abstinence Syndrome or Neonatal Opioid Withdrawal Syndrome
- Other treatments available: methadone, naltrexone, nonmedication-based treatments



Anticipate Insurance Issues

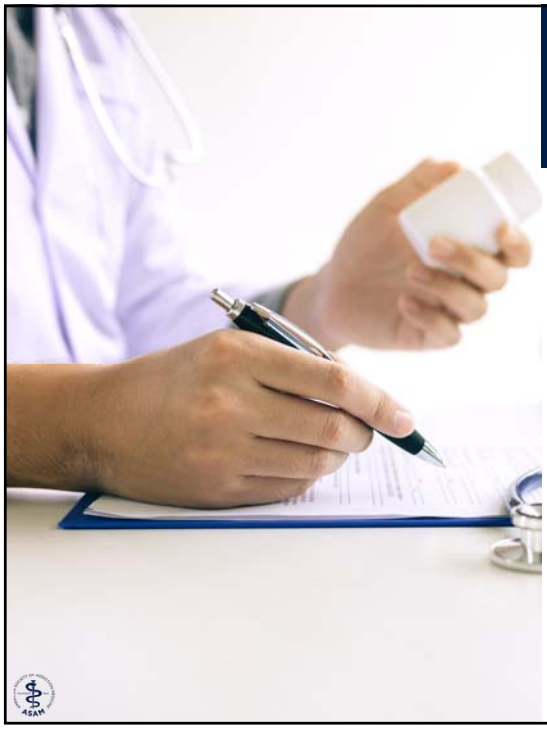
- *Is buprenorphine a covered benefit?*
  - Which formulation (tabs, film)
  - What tier?
  - What co-pays?
- Are lab services covered?
- Are there restrictions on duration of treatment?
- Is behavioral treatment covered?
- *Be aware of behavioral health carveouts*



Anticipate Insurance Issues

Anticipate prior approval procedures:

- Collect forms from each payer
- Submit forms in advance of fill
- Monitor patient's pharmacy benefits
- 340B coverage in some Community Health Centers



Office-Based Opioid Treatment (OBOT) Billing

- *OBOT is standard medical care: billing procedures are standard.*
- Physicians billing codes: (CPT) billing codes, are accepted by most payers in most states.
- *The ICD-10 Code for opioid use disorder is F11.20.*
  - The fifth (x) digit sub-classifications are: 0=unspecified, 1=continuous, 2=episodic, 3=in remission.
- *No specific addiction medicine codes.* Same codes as other ambulatory care services.

IMPLEMENTING OFFICE-BASED OPIOID TREATMENT

End of Session 3

THE ASAM Treatment of Opioid Use Disorder Course

Includes waiver qualifying requirements

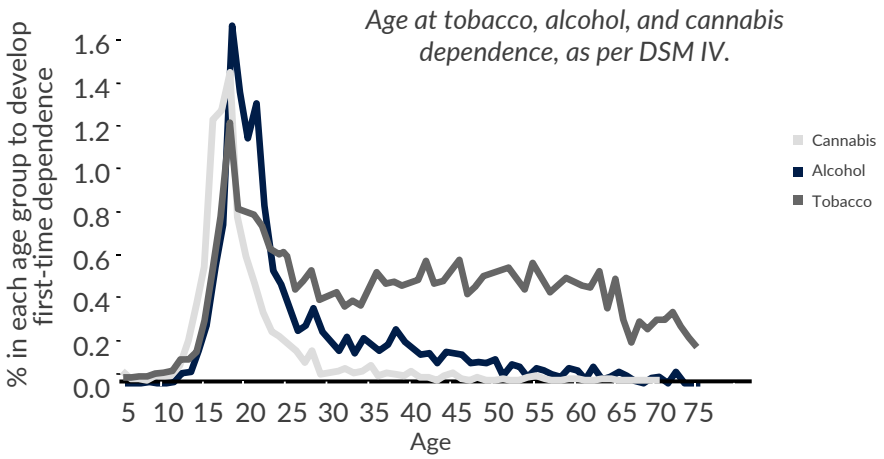
Session 4

Special Populations

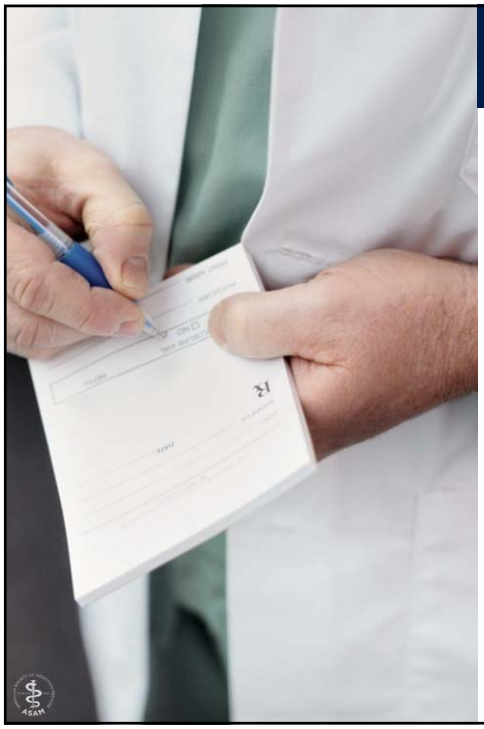
Session Learning Objectives

1. Describe unique issues of treating adolescents, young adults, pregnant and postpartum patients, elderly patients, and healthcare professionals maintained on medications for opioid use disorders.
2. Summarize acute (e.g., postoperative pain) and chronic pain management strategies for patients with an opioid use disorder.

Addiction is a Developmental Disease
Often Starts in Childhood and Adolescence



National Epidemiologic Survey on Alcohol and Related Conditions, 2003



Medications for Adolescents with OUD

- *Buprenorphine vs. Clonidine for 28-day withdrawal management.*
  - Participants 13-18 years old (N=36).
  - Compared to clonidine, patients who received 4 weeks of buprenorphine treatment:
    - Had fewer positive opioid drug tests.
    - Stayed in treatment longer.
    - Were more likely to continue treatment after 4-week trial period.

Young Adults

Methadone (OTP)

Methadone may be a good option for young adults (18+) with unstable living arrangements; daily visits provide structure and eliminate the need to manage medications at home.

Naltrexone

Naltrexone is also an option for adolescents; may be clinically useful for adolescents/young adults living away from home, or patients with co-occurring alcohol use disorder.

*There are no published studies on the efficacy of naltrexone for OUD in adolescent patients

Sanchez-Samper X, Levy S. Opioid use by adolescents. Office-Based Buprenorphine Treatment of Opioid Use Disorders. 2nd edition. 2018

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Medication-Assisted Treatment of Adolescents With Opioid Use Disorders

COMMITTEE ON SUBSTANCE USE AND PREVENTION

Effective treatments are underutilized; resources are available for this age group.

Levy S, et al. Pediatrics. 2016;138(3).

Barriers for Care

Stigma

- Significant misinformation about what medication treatment is and its benefits.

Lack of Training

- Only 1% of waivered providers identify as pediatricians.

Coordinating Care

- These cases are complicated, involve state agencies, families, and children. These cases can be hard to ensure that a consistent plan is offered and implemented.

Maintaining Engagement in School

- *Substance use disorder often interferes with education.*
  - Maintaining education with the most effective combination of pharmacotherapy and psychosocial treatment is important.
- *Properly administered, buprenorphine, methadone, and naltrexone do not impair cognitive function.*
  - After being stabilized, adolescents and young adults should be encouraged to return to school.

Confidentiality

Teens Presenting With Parents

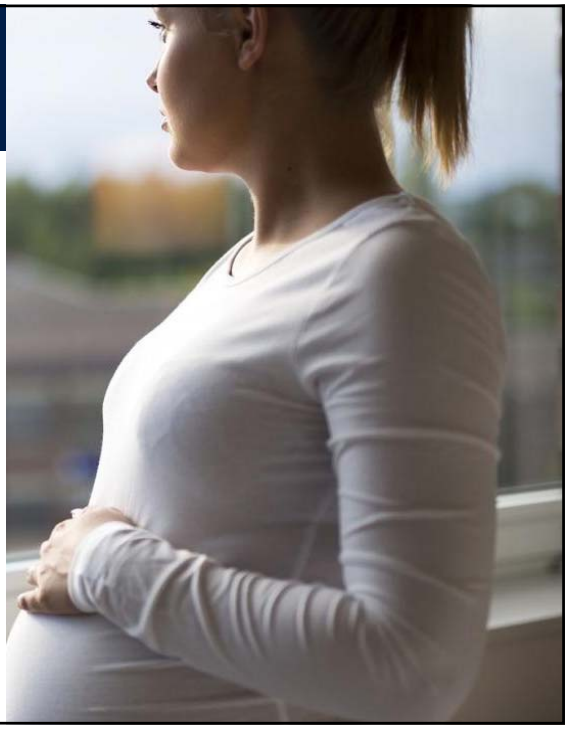
- In many cases, adolescents will present for treatment with the knowledge and support of parents.
- Teens often turn to their parents for help first.
- Managing confidentiality is a clinical decision of what information to share with parents in the context of parents already being aware of the "big picture."

Teens Presenting Without Parents

- Teens may present for treatment without the knowledge or consent of their parents.
- In most states, adolescents above a certain age may consent for treatment for SUD without their parents, though details vary.

Pregnancy: Substance Use Disorder

- *Women with SUD often experience dysregulation of their menstrual cycle.*
  - Chronic opioid use alters dopamine/prolactin levels in hypothalamic-pituitary axis leading to amenorrhea and unpredictable cycles.
  - Menstrual cycle alterations can lead to unplanned and often unrecognized pregnancies with delayed initiation of prenatal care.



Pregnancy: Opioid Agonist Maintenance Therapy Remains the Standard of Care

There are safe and effective treatment options in pregnancy.

- Opioid agonist pharmacotherapy with methadone or buprenorphine is endorsed by the American College of Obstetricians and Gynecologists (ACOG) as the optimal treatment for OUD during pregnancy.

Fischer et al. 1998, 1999. Jones et al. 2010. Terplan M, et al. Obstetrics & Gynecology. 2018.

Benefits of Opioid Agonist Therapy

Maternal Benefits

- 70% reduction in overdose related deaths.
- Decrease in risk of HIV, HBV, HCV.
- Increased engagement in prenatal care and treatment.

Fetal Benefits

- Reduces fluctuations in maternal opioid levels thus reducing fetal stress.
- Decrease in intrauterine fetal demise.
- Decrease in intrauterine growth restriction.
- Decrease in preterm delivery.

Klaman SL, et al. J Addict Med. 2017.

Use of Buprenorphine During Pregnancy

- *Buprenorphine/Naloxone*
  - No known teratogenic effects in animals.
  - Controlled studies have not been conducted in humans.
  - Increasing evidence that buprenorphine/naloxone may be safe in pregnancy.
  - Evidence demonstrates safety of combination formulation in pregnancy.

Pregnancy: Induction of Maintenance Therapy

Goal

Goal is to reach the dose just high enough to stop use and block cravings.

Management

Management of dose should be individualized and based on patient's symptoms.

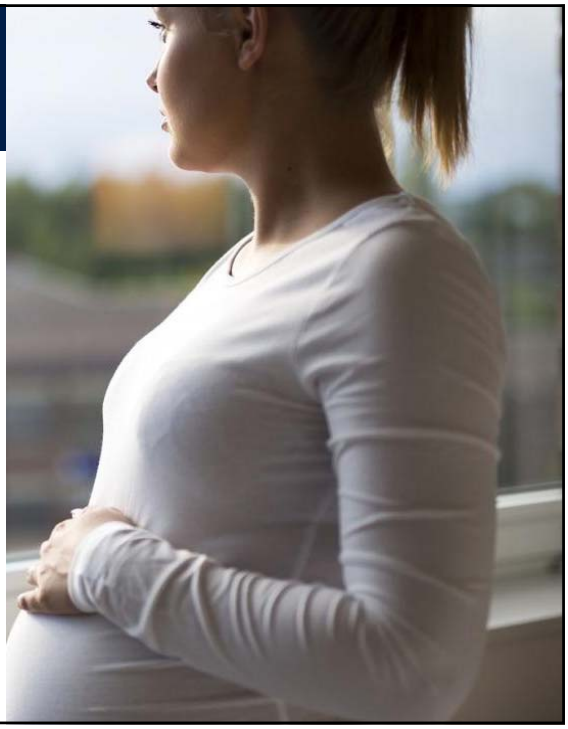
Adjustments

Dose adjustments may be necessary with advancing gestational age based on pregnant physiology.

Split dosing may be required in pregnancy to meet the accelerated metabolic clearance of pregnancy.

Patient on Buprenorphine

- *Stable patients who become pregnant.*
  - Combination therapy has been avoided due to the unknown exposure risk of naloxone in pregnancy.
  - However, recent studies suggest combination therapy is safe and effective in pregnant/breastfeeding patients.



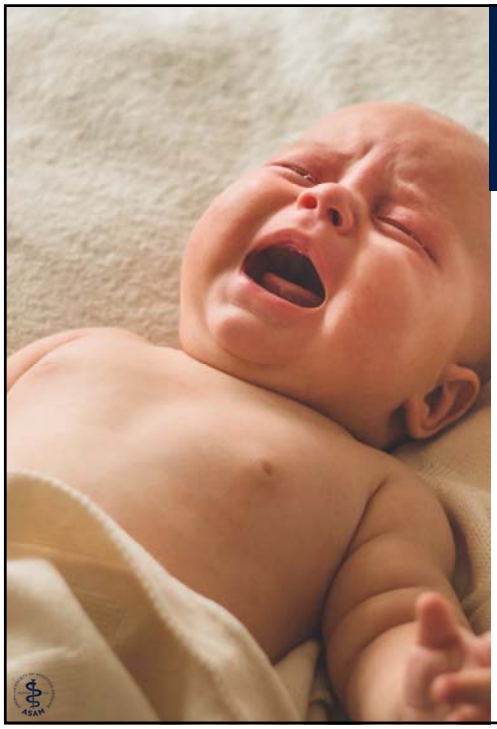
Wieggland SL et al. 2015.

Should Women Undergo Withdrawal During Pregnancy?

Studies have demonstrated:

- ⊖ Fetal distress and 5-fold increase in still birth rates with antepartum withdrawal management.
- ⊖ Withdrawal management can be safe for the fetus, however, maternal relapse rates prior to delivery range from 70-98%.
- ⊕ **Maintenance therapy in pregnancy has been shown to increase retention in prenatal care, addiction treatment, and in-hospital deliveries.**

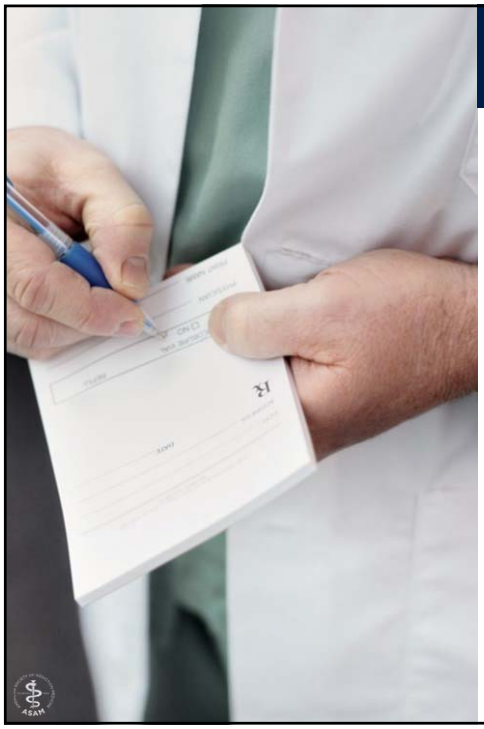
Zuspan et al. 1975; Rementeria et al. 1973.
Bell J et al. 2016; Luty et al. 2003; Maas et al. 1990; Dashe et al. 1998.
Jones et al. 2008.



Neonatal Abstinence Syndrome (NAS) or Neonatal Opioid Withdrawal Syndrome (NOWS)

- Results from abrupt discontinuation of opioids at birth after a fetus has become physically dependent through exposure in utero.
- Risk of NAS is greater if opioids are taken close to delivery or for longer periods and if the drugs have short half lives.
- Rate of opioid clearance influences severity.

Volkow ND. BMJ 2016



NAS Management

Non-Pharmacologic Approaches

- Quiet and dimly lit room, handled gently, swaddling, pacifier, gentle rocking
- Rooming: Keeping mother and baby together reduces NAS length of stay and cost
- Non-insertive acupuncture
- Breastfeeding recommended as it soothes agitated infants

Pharmacotherapy

- Oral morphine is preferred first-line medication

Bagley SM et al. Addiction Science & Clinical Practice. 2014

Maintenance Therapy in Pregnancy: NAS

Meta-analysis of 12 studies from 1996-2012

Neonates exposed to buprenorphine (515) compared to methadone (855) had:

- ☑ Shorter mean length of hospital stay (-7.23 days, 95% CI: -10.64, -3.83).
- ☑ Shorter NAS treatment duration (-8.46 days, 95% CI: -14.48, -2.44).
- ☑ Lower morphine dose (-3.60 mg, 95% CI: -7.26, 0.07).

Brogly et al. Am J Epidemiol. 2014;180(7):673-86

Maternal Dose and NAS Severity

- No correlation between maternal opioid maintenance therapy dose and duration or severity of NAS.
- Tobacco use is strongly associated with NAS and NAS severity.

Berghella et al. 2003; McCarthy et al. 2005; Cleary et al. 2010; Isemann et al. 2010; Jones et al. 2010; Seligman et al. 2011.

Benefits of Breastfeeding for Newborns with NAS

NAS Development
30% decrease

Length of Stay
50% decrease of neonatal stay

Mother-Infant Bonding
Improves

Maternal Recovery
Positively reinforced

Pritham UA et al. J Obstet Gynecol Neonatal Nurs. 2012. Welle-Strand GK et al. Acta Paediatr. 2013. Wachman EM et al. JAMA. 2013. Abdel-Latif ME et al. Pediatrics. 2006.

Breastfeeding

- ***Maternal HCV infection is NOT a contraindication.***
- Unless mother develops cracked or bleeding nipples. If so, recommend to pump/dump until healed.

- ***Maternal HIV infection.***
- ***Current maternal substance use.*** Mother currently under influence.
- ***Recent heavy marijuana use.*** Lipophilic, concentration in breast milk. Note: recent study found little THC in breast milk (Baker et al. Ob Gyn. 2018).

Klaman SL, et al. J Addict Med. 2017.

Audience Response

Which of the following is true during pregnancy and postpartum?

a. Patients should be encouraged to taper to lower doses of buprenorphine to reduce the risk of NAS
b. Patients should be instructed not to breastfeed with MOUD
c. Tobacco use is strongly associated with risk of NAS
d. The preferred treatment for NAS is to start with morphine

Older Adults
Caring for Patients

No restrictions on medications for OUD to older patients:

- Be aware of interactions with co-prescribed medications.
- Benzodiazepines commonly used; inquire about alcohol use.
- Decreased renal and/or hepatic function may require dose adjustments.
- Falls and cognitive impairment important in this population.
- Daily dose dispenser helpful reminder.
- Treatment outcome research: older adults do better in treatment than younger counterparts.

Healthcare Providers with SUD

Physician Health Program (PHP)

- 10-12% of physicians in US develop SUD.
- State-based PHPs often mandated for providers with SUD.
- Generally abstinence-based.

Healthcare Providers with SUD

Physician Health Program (PHP)

- About 75% of physicians in PHPs had positive outcomes after 5 years of treatment; ***95% who completed the program were licensed and practicing.***
- Goals of PHPs are to help provider achieve long-term treatment, maintain medical career, protect the public, and maintain patient confidence in healthcare providers.

OUD and Increased Pain Sensitivity

- ***Patients with active OUD.***
  - No correlation between maternal opioid maintenance therapy dose and duration or severity of NAS.
- ***Patients with OUD on opioid agonist treatment have less pain tolerance than matched controls.***

Martin J (1965), Ho and Dole V (1979), Compton P (1994, 2001)

Acute Pain Management
Patients on Opioid Agonist Treatment

- ***Patients who are physically dependent on opioids:***
  - Must be maintained on daily equivalence ("opioid debt") before ANY analgesic effect is realized with opioids (or nonopioids) used to treat acute pain.
  - Opioid analgesic requirements are often higher due to increased pain sensitivity and opioid cross-tolerance.

Peng PW, Tumber PS, Gourlay D: Can J Anaesthesia 2005
Alford DP, Compton P, Samet JH. Ann Intern Med 2006

Methadone and Acute Pain

Treating Pain
- Methadone dosed every 24 hours does not confer analgesia beyond 6-8 hours.
- Increased pain sensitivity may necessitate higher doses at shorter intervals.
- Scheduled dosing, not "prn," during severe acute pain.
- Short course of opioid analgesics during severe acute pain unlikely to compromise recovery.

Alford DP, Compton P, Samet JH. Ann Intern Med 2006

Clinical Recommendations
- Non-opioid, non-controlled substance analgesia as first line.
- Continue usual verified methadone dose.
- Treat pain aggressively with conventional analgesics.
- Avoid using mixed agonist/antagonist opioids.
- Careful use and monitoring of combination products containing acetaminophen.
- Coordinate care.

Buprenorphine and Acute Pain

Treating Pain

- Analgesia from buprenorphine lasts 6-8 hours while treatment of OUD lasts over 24 hours.
- Buprenorphine has ceiling effect on CNS and respiratory depression, therefore safer than a full opioid agonist from an overdose risk.
- Uncertain if buprenorphine has an analgesic ceiling effect.

Clinical Recommendations

- Continue buprenorphine in divided doses (every 8 hours) AND titrate short-acting opioid. analgesics for pain management
- OR, continue in divided doses and add additional low dose (e.g. 2 mg) buprenorphine every 8 hours.

Alford DP. "Acute and Chronic Pain," Office-Based Buprenorphine Treatment of Opioid Use Disorder, 2018

Perioperative Protocol Resources Available

- ***Boston Medical Center***
  - Perioperative Management of Non-Pregnant Patients on Maintenance Therapy for Opioid Dependence.
- ***Pain Medicine Editorial***
  - Patients maintained on buprenorphine for opioid use disorder should continue buprenorphine through the perioperative period.

Buprenorphine Maintenance
Treating Chronic Pain

- ***Buprenorphine can be prescribed in the office for OUD and chronic pain.***
  - Systematic review: 10 studies (low quality) reported effectiveness in treating chronic pain.
  - Buprenorphine for OUD requires X-number while use for chronic pain management (off-label) does not.
  - For pain, buprenorphine will need to be dosed every 8 hours.

Cotes J, Montgomery L. 2014

Naltrexone and Acute Pain

Naltrexone Blockade
- Analgesic effects of opioids blocked at conventional doses.
- Can be overcome by 6-20x usual analgesic dose without significant respiratory depression or sedation *under close observation*.
- Need setting equipped and staffed for resuscitation.

Dean RL et al. Pharmacol Biochem Behav 2008; Vickers AP, Jolly A BMJ 2006

Perioperative Management
- Consult anesthesia, consider nonopioids and regional anesthesia.
- Oral naltrexone blockade 50% gone after 72 hours.
- Extended-release naltrexone blockade decline begins in 14 days, delay elective surgery for a month after last dose.

Audience Response

Patients maintained of opioid agonist therapy for OUD who have an acute pain event should be:

a. Treated through collaboration with anesthesia, pain and addiction as appropriate to develop a comprehensive pain plan
b. Immediately tapered off buprenorphine to start full agonists therapy with plans to resume buprenorphine post-event
c. Maintained on their MOUD without dose adjustment or addition of other controlled substances
d. Continued on their MOUD with addition of non-opioid analgesia and opioid analgesia

Q&A

SAM'S CASE

Sam's Case

52-year-old male. Maintained on buprenorphine/ naloxone 16/4mg per day for the past 10 years.

His opioid use disorder began after a motorcycle crash resulting in multiple fractures and orthopedic surgeries. He was treated with high dose morphine and quickly escalated his use, losing control of his prescriptions.

He realized he had a problem when he ran out of his morphine and had severe withdrawal symptoms.

Sam's Case

He believes buprenorphine is a "miracle drug" that has saved his life. He is not in counseling but attends AA 3-4 meetings per week and has a sponsor.

He has a history of alcohol use disorder and has been sober for >20 years.

He has severe chronic right knee pain which he has been told is due to arthritis after his traumatic knee injury. His pain had been well controlled on split dose buprenorphine (8/2 mg TID), ibuprofen, and acetaminophen.

Now his pain is so severe, he has had to take time off from work.

Sam's Case

He is now being scheduled for an elective right total knee replacement.

He was told in the preoperative clinic:

- To get off his buprenorphine for at least 5 days before his surgery.
- That the buprenorphine will prevent the pain medication from working.
- That the pain medications will likely put him into withdrawal if he is still taking the buprenorphine.

He is nervous about stopping his buprenorphine and asks you what to do.

Activity 8: Case Discussion – Sam

Discuss:

Work with your group to assess a plan for Sam. What do you recommend regarding his buprenorphine maintenance perioperatively? What do you recommend regarding his pain management perioperatively? What additional information do you need?

10 minutes:

After the discussion, a few groups will share key takeaways with the whole class.

SPECIAL POPULATIONS

End of Session 4

THE ASAM Treatment of Opioid Use Disorder Course

Includes waiver qualifying requirements

Session 5

Keeping Your Patient Safe

Session Learning Objectives

1. Examine misconceptions, stigma, and complexities (bioethical, social, clinical, public health) associated with OUD and the use of medications to treat opioid use disorder.

JENNIFER'S CASE

Jennifer:

32-year-old woman who has been your patient for the past five years. She wants to taper and withdraw from buprenorphine.

- Jennifer was diagnosed with OUD, which started with opioid analgesics and then segued into IN heroin.
- She has been on buprenorphine/ naloxone film strips, 12 mg daily, for 5 years. Patient had a positive response to the medication and has had negative UDTs, with the occasional +THC, for years.

Jennifer:

32-year-old woman who has been your patient for the past five years. She wants to taper and withdraw from buprenorphine.

- Jennifer is employed as an IT specialist at a law firm. She has been careful to "hide" her medication use from her family, friends, and co-workers, for fear of a negative reaction. She also thinks that if her co-workers knew about her OUD and medication, if a wallet were stolen, they would automatically suspect she was the thief.
- One year ago, Jennifer met her future wife at the law firm. Karishma is a paralegal at the firm and has no history of "drug" use.

Jennifer:

32-year-old woman who has been your patient for the past five years. She wants to taper and withdraw from buprenorphine.

- As their relationship developed, Jennifer was ambivalent and fearful about disclosing her history of OUD and current OAT with buprenorphine. A few months before their wedding, Jennifer did disclose and Karishma was taken aback, but said it was not a problem.
- On Jennifer's last visit with you, she inquires about "getting off" buprenorphine. She relates that Karishma has never really been okay with the medication. Karishma has heard that it's "just substituting one drug for another" or "one addiction for another."

Jennifer:

32-year-old woman who has been your patient for the past five years. She wants to taper and withdraw from buprenorphine.

- Karishma has a friend who has an AUD and attends AA meetings. The friend tells Karishma that her AA group is not okay with people on buprenorphine or methadone.
- Karishma and Jennifer had also planned on having a child, but Karishma is concerned that buprenorphine would be a problem if Jennifer were to be the birth mother.
- Jennifer has resumed weekly psychotherapy and they both see a couple's therapist.

Jennifer:

32-year-old woman who has been your patient for the past five years. She wants to taper and withdraw from buprenorphine.

- You are concerned that Jennifer wants to taper and withdraw from buprenorphine because of all these misconceptions, myths, and stigmas - which Karishma believes.
- You schedule an appointment with both Jennifer and Karishma to discuss each of the misconceptions individually and provide evidence for your suggestion that Jennifer continue with her successful treatment paradigm with buprenorphine.

Case Discussion – Jennifer

Discuss:

What stigmas and misconceptions would you address with Jennifer and Karishma?

What would you suggest for Jennifer's treatment plan?

Should Jennifer still want to taper down, how would you proceed?

Stigma and Treating OUD

Provider Myths

- It's substituting one drug/addiction for another.
- It's not really "recovery."
- The shorter the duration of therapy, the better.
- You can't be on buprenorphine if you are pregnant or breastfeeding.
- I'm worried about the DEA storming into my office.

Patient Myths

- It's substituting one drug/addiction for another.
- It's not really "recovery."
- The shorter the duration of therapy, the better.
- Other people may relapse, but not me.
- It must be damaging my liver, brain, kidney, heart, or bones.
- They won't be able to treat my pain.
- The pre-employment drug test will disqualify me.
- If I miss a dose, I'll go into terrible withdrawal.

Addiction Terminology

Correct	***Incorrect***
Person with substance use disorder.	Substance abuser, drug abuser, alcoholic, addict, user, abuser, drunk, junkie.
Babies born with an opioid dependency.	Addicted babies, born addicted.
Substance use disorder or addiction, use or misuse, risky or unhealthy use.	Drug habit, abuse, problem.
Person in recovery, abstinent, not drinking or taking drugs.	Clean.
Treatment or medication for addiction, medication for OUD/AUD, positive/negative results.	Substitution or replacement therapy, medication-assisted treatment, clean/dirty.

General Language

- *Use gender/sexuality-inclusive language.*
  - Be mindful of gender use in language, specifically during anecdotes and question response. Avoid assumptions.
  - Use “they,” “one,” and “who” as opposed to “he” or “she.”
- *Avoid jokes at the expense of patient and stigmatizing/offensive language.*

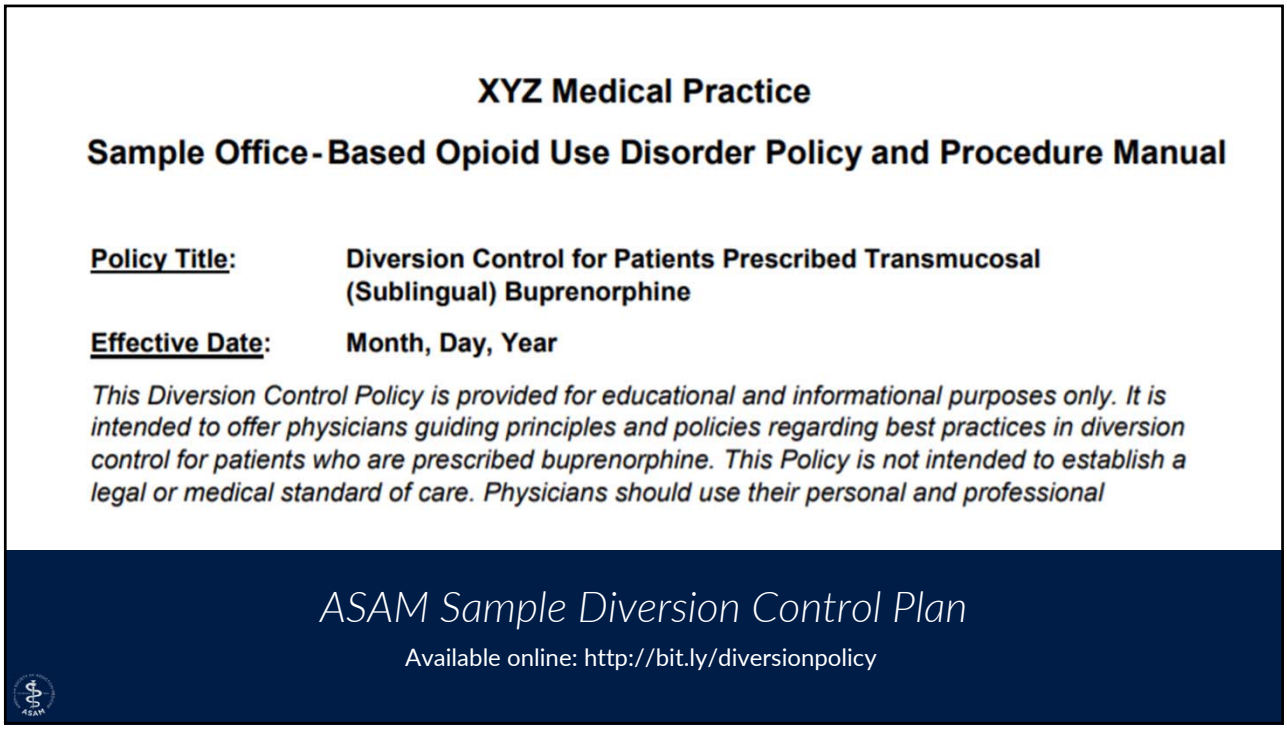
Where Patients Experience Stigma

Healthcare Setting

- Waiting room
- Intake with MA/nurse
- Pharmacy
- Other healthcare provider's practice
- Emergency Department
- Mutual help group

Outside Healthcare Setting

- Significant other
- Work
- Friend group
- Family
- Interest/hobby group
- Religious institution
- Media representation



ASAM Sample Diversion Control Plan

Available online: http://bit.ly/diversionpolicy

Diversion

People self-treating with diverted buprenorphine reported:

- 97% take it to prevent cravings
- 90% take it to prevent withdrawal
- 29% take it to save money

Why? Limited access to treatment, lack of health insurance.

Potential Diversion
Common Signs

- Requests for early refills (medication lost or stolen).
- Inconsistent laboratory testing (e.g., bup negative).
- Claims of being allergic to naloxone and requesting monotherapy.
- Police reports of patient selling in streets.
- Reports of concerning behavior.
- Inconsistent appointments (e.g., missed).

Risk Management:
Educate Patients about Harms of Diversion of Misuse

Misuse and Diversion

- Can lead to harmful medical and social consequences, overdose, and an increase in stigma for patients and providers.

Legislation

- Periodically re-evaluated by DEA and SAMHSA for risks and benefits.

What patients do with their medications matters for us all!

Responding to Misuse and Diversion

Evaluate
and reassess treatment plan and patient progress.

Intensify Treatment
or refer to higher Level of Care.

Document and Describe
clinical thinking that supports a clinical response, should be aimed at minimizing risk and treating patient at the level of care needed.

Harm Reduction

1. Naloxone and Overdose Education
2. Syringe Service Programs
3. Polysubstance Use
4. HIV, PrEP and PEP
5. Safer Sex

Opioid Mu Receptor Agonist Drug Effects

- *Acute Exposure*
  - Euphoria, nausea, vomiting, depressed respiration, sedation, analgesia.
- *Large Dose Acute Exposure*
  - Non-responsive, pinpoint pupils, hypotension, skin cyanotic, pulmonary edema.
- *Chronic Use Effects*
  - Physical dependence, withdrawal, tolerance, lethargy, constipation.

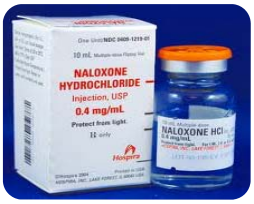
Opioid-induced Respiratory Depression

Opioids depress the brain stem's response.

- Depression of the medullary respiratory center.
- Decreased tidal volume and minute ventilation.
- Decreased respiratory response to elevated CO2.

- Hypercapnea, hypoxia and decreased oxygen saturation.
- Life threatening hypoxia.
- Sedation occurs before significant respiratory depression, and, therefore, is a warning sign.

Naloxone Formulations



Injection

1 dose = 0.4mg/1ml

Intramuscular

Nasal w/atomizer

"Multi-step"

1 dose = 2mg/2ml

Intranasal

Nasal spray

"Single-step"

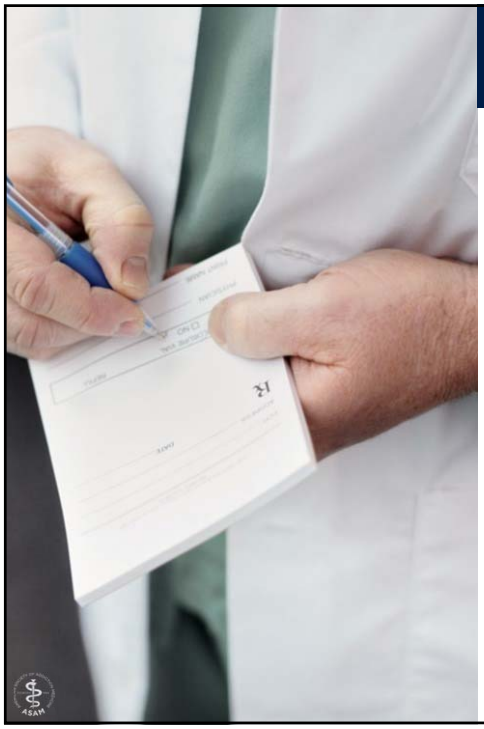
1 dose = 4mg/0.1ml

Intranasal

Auto-injector

1 dose = 0.4mg/1ml

Intramuscular



Naloxone

Prevent Overdose

- Broader provision of naloxone has been shown to prevent opioid overdose morbidity and mortality.

Co-Prescribe

- U.S. Department of Health and Human Services urges that all patients receiving medications for OUD be co-prescribed naloxone.

Coffin PO, Behar E, Rowe C, Santos GM, Coffa D, Bald M, Vittinghoff E. Nonrandomized intervention study of naloxone coprescription for primary care patients receiving long-term opioid therapy for pain. Annals of Internal Medicine. 2016;165(4):245–252.

Evaluations of Overdose Education and Naloxone Distribution (OEND) Programs

- Feasibility
- Increased knowledge and skills
- No increase in use, increase in drug treatment
- Reduction in overdose in communities
- Cost-effective

Piper et al. Subst Use Misuse 2008; Doe-Simkins et al. Am J Public Health 2009; Enteen et al. J Urban Health 2010; Bennett et al. J Urban Health. 2011; Walley et al. JSAT 2013

Green et al. Addiction 2008; Tobin et al. Int J Drug Policy 2009; Wagner et al. Int J Drug Policy 2010

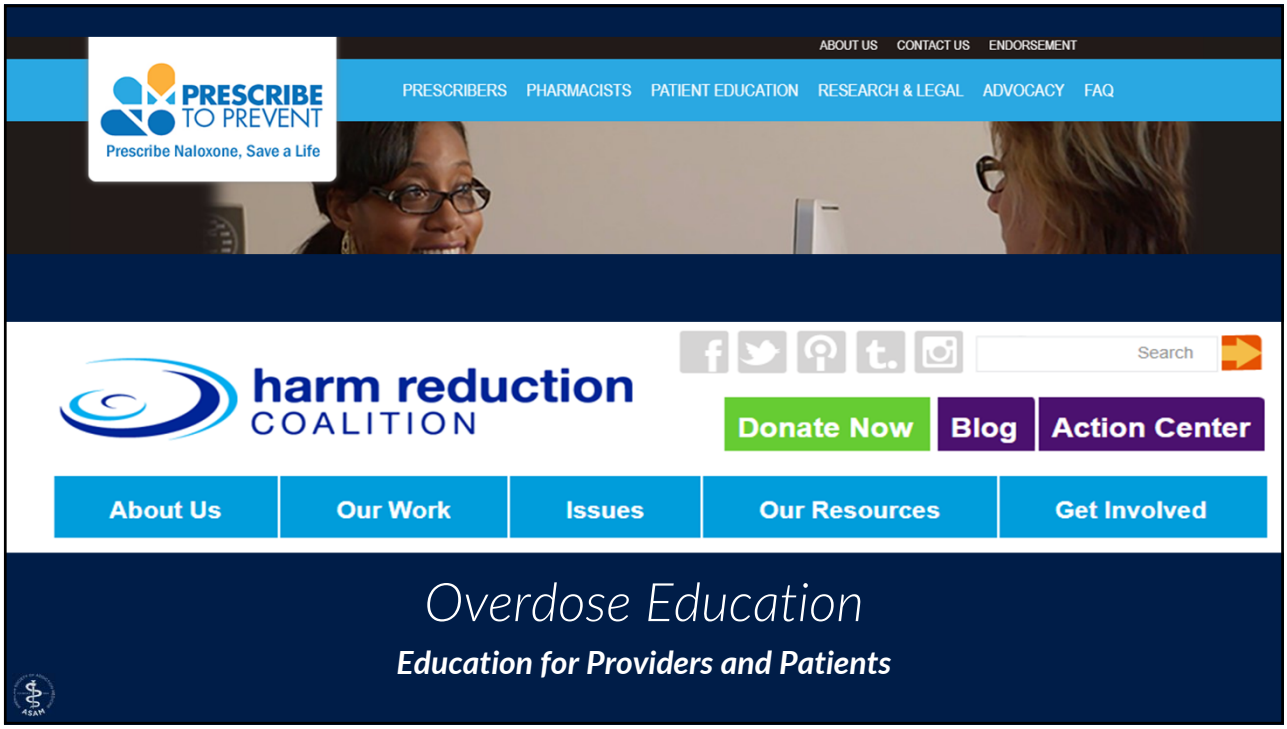
Seal et al. J Urban Health 2005; Doe-Simkins et al. BMC Public Health 2014; Jones et al. Addictive Behaviors 2017

Maxwell et al. J Addict Dis 2006; Evans et al. Am J Epidemiol 2012; Walley et al. BMJ 2013; Coffin et al. Ann Intern Med 2016

Coffin & Sullivan. Ann Intern Med. 2013

Overdose Education and Naloxone
Communicate to Patients

- *Don't use opioids alone. Beware of fentanyl.*
  - Known overdose risk factors: mixing substances, abstinence, using alone, unknown source.
  - Opportunity window: heroin overdoses take minutes to hours; fentanyl takes seconds to minutes.
  - Call 911 before administering naloxone.



Audience Response

Overdose education is important for which of the following groups?

a. Injection opioid users themselves
b. Family and friends of opioid users
c. Community members who may be exposed to opioid use
d. All of the above

Polysubstance Use
Tobacco, Alcohol, Cannabis

Substance	*Medication Options*	*Psychosocial Treatment*
Tobacco	Nicotine replacement therapy (patch, gum, lozenge); bupropion; varenicline	Cognitive behavioral therapy (CBT); mindfulness; telephone support and quitlines; mutual help
Alcohol	Naltrexone; acamprosate; disulfiram	CBT; motivational enhancement therapy; martial/family counseling; mutual help
Cannabis	No FDA-approved medications	CBT; contingency management; motivational enhancement therapy; mutual help

Polysubstance Use
Cocaine, Methamphetamine, Benzodiazepines

Substance	*Medication Options*	*Psychosocial Treatment*
Cocaine	No FDA-approved medications	CBT; contingency management; therapeutic communities; mutual help
Metham-phetamine	No FDA-approved medications	CBT; contingency management; mutual help
Benzo-diazepines	Diazepam and gradual dose reduction	CBT; contingency management; mutual help

Tobacco

~480,000 Deaths
Leading cause of preventable death (CDC)

2-4 times higher
Smoking rates higher in patients with SUD than general public

~67% smoke
Smoking rates among SUD patients who enter treatment

Death from tobacco
SUD patients more likely to die from tobacco than other substances

HIV and Injection Drug Use

- *Injection drug use accounts for ~1 in 10 HIV diagnoses in US.*
  - Sharing equipment increases risk: HIV can survive on a used syringe for 42 days.
  - **4th generation HIV test important (looks for HIV 1 & 2 antibodies and P24 antigen).**
  - Educate patient on Syringe Service Programs (e.g., needle exchange).
  - Educate patient on safe practices (e.g., do not share needles).

Visit: https://www.cdc.gov/hiv/risk/idu.html and https://www.hiv.gov/hiv-basics/hiv-testing/learn-about-hiv-testing/hiv-testing-overview

PrEP

- ☑ *Pre-exposure prophylaxis:*
  when people who don't have HIV take HIV medicine every day to reduce their chances of getting HIV.
- ☑ *Reduces risk of getting HIV:*
  from sex by ~88%.
  from injection drug use by >74%.

PrEP

Current FDA-Approved Medications

- Emtricitabine (200mg)/Tenofovir Disoproxil Fumarate (300mg): Truvada®.
- Emtricitabine (200mg)/Tenofovir Alafenamide (25mg): Descovy®.

Which is best?

- Truvada® vs Descovy® based on individual risk factors.
- Descovy® not for use in people assigned female at birth who are at risk of getting HIV through vaginal sex (effectiveness not yet studied).

PEP

- ☑ *Post-exposure prophylaxis:*

  when a patient takes HIV medicine very soon after possible exposure to HIV in order to prevent HIV infection.

- ☑ *Not meant for regular use:*

  PEP intended for emergency situations.

  Must be started within 72 hours after a possible exposure to HIV. The sooner, the better.

PEP

Current preferred medication regiment:

- Tenofovir disoproxil (300 mg)/emtricitibine (200 mg) QD, PLUS.
- Raltegravir (400 mg) BID or dolutegravir (50 mg) QD.

Length of treatment:

- If prescribed PEP, patient will take HIV medicine every day for 28 days.

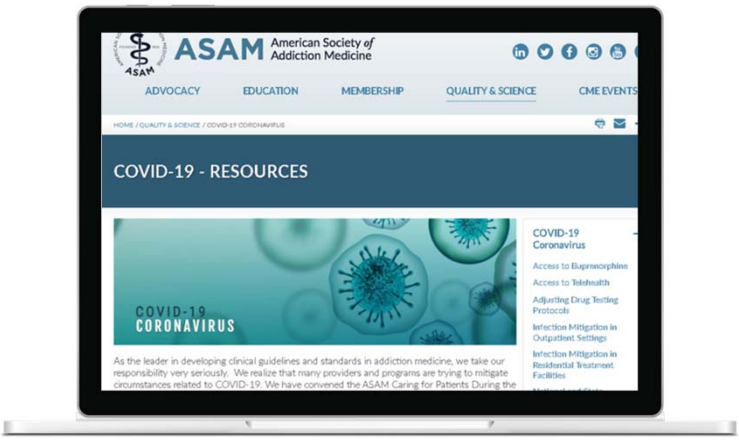
Safer Sex

- *People under the influence of drugs are more likely to engage in risky sex and could get HIV.*
  - Those who share needles/syringes are more likely to have unprotected sex.
  - Provider should educate patient on: contraception options, condoms, PrEP and PEP, regular STI testing.
  - Be aware of "club drug" use leading to unsafe sex.

Gyarmathy VA, Neaigus A. The relationship of sexual dyad and personal network characteristics and individual attributes to unprotected sex among young injecting drug users. AIDS Behav. 2009;13(2):196–206.

Buprenorphine and Naltrexone for OUD: COVID-19

Treating OUD During the COVID-19 Pandemic



Guidance for:

- Infection mitigation
- OTPs
- OBOT
- Telehealth
- Virtual Support Groups

- ***Overview of Federal and State Policy Changes related to COVID-19***

Methadone Access Under National COVID-19 Emergency - Highlights

- ***Telehealth***
  - Waiver of regulations related to HIPPA compliant telehealth platforms (e.g., Apple FaceTime, Facebook Messenger video chat, Google Hangouts, Skype).
  - Expansion of Medicare Coverage for telehealth.
  - Medicaid and private payer coverage varies by state and payer – check.
  - Check state laws/regulations on licensing.
- ***Existing Patients***
  - Can treat and dispense medication via telehealth (also use of telephone).
- ***New Patients***
  - Continued requirement for in-person physical exam for methadone initiation.
  - Take steps to minimize any exposures to provider or patient.

Methadone Access Under National COVID-19 Emergency - Highlights

- ***Take-home medications:***
  - States may request exceptions for stable patients to receive 28 days of take-home medications and for less stable patients to receive up to 14 days.
    - Providers should make decisions on an individual patient bases based on a risk-benefit analysis and considerations for risk related to both OUD and COVID-19.
  - Educate patients about safe storage, use, and management.
  - Ensure patients have access to naloxone.
  - Use telehealth/telephone to monitor patients.
  - Encourage patient participation in virtual support groups.

Methadone Access Under National COVID-19 Emergency - Highlights

- ***Alternative home delivery for isolated/quarantined patients:***
  - Allows designated staff members, law enforcement officers, or National Guard personnel to make deliveries of methadone, including "doorstep" delivery using an approved lockbox.
- ***Drug Testing:***
  - OTPs still required to provide a minimum of 8 drug tests/yr for each patient.
  - Consider pausing or exploring testing at a distance.

Methadone Access Under National COVID-19 Emergency - Highlights

- ***ASAM COVID-19 Resources:***
  - ASAM Methadone Access Guidance:
  - ASAM Telehealth Guidance: https://www.asam.org/Quality-Science/covid-19-coronavirus/access-to-telehealth
  - ASAM's Drug Testing Guidance: https://www.asam.org/Quality-Science/covid-19-coronavirus/adjusting-drug-testing-protocols
  - ASAM Support Group Guidance: https://www.asam.org/Quality-Science/covid-19-coronavirus/support-group

Buprenorphine Access Under National COVID-19 Emergency - Highlights

- ***Telehealth***
  - Waiver of regulations related to HIPPA compliant telehealth platforms (e.g., Apple FaceTime, Facebook Messenger video chat, Google Hangouts, Skype).
  - Expansion of Medicare Coverage for telehealth.
  - Medicaid and private payer coverage varies by state and payer – check.
  - Check state laws/regulations on licensing.
- ***Existing & Existing Patients***
  - New and existing patients can be evaluated and treated via telehealth including telephone; telehealth and phone for follow-up and monitoring.
  - Home induction to start new patients.
  - Do not require patients to participate in counseling – virtual or in-person – in order to access medication. (Generally recommended practice.)
  - Ensure patient access to naloxone.

Buprenorphine Access Under National COVID-19 Emergency - Highlights

- ***Flexibility prescribing using telehealth:***
  - DEA-registered practitioners may prescribe controlled substances to patients via telemedicine in states in which they are not registered with DEA.
- ***Use and Disclosure of Confidential Information (42CFR Part2):***
  - Patient information may be disclosed to medical personnel, without patient consent, to the extent necessary to meet a medical emergency.
  - Information disclosed to the medical personnel who are treating such a medical emergency may be re-disclosed for treatment purposes as needed.

Buprenorphine Access Under National COVID-19 Emergency - Highlights

- ***Oral vs. Injectable Formulations***
- ***Factors to weigh:***
  - Is the patient experiencing any symptoms consistent with COVID or have they had any potential exposures?
  - Any anticipated risk to the patient associated with switching formulations?
    - Are they likely to be compliant with the oral medication?
  - The risk to the patient associated with an in-person visit:
    - Are they at high risk for severe illness?
    - Are they living with or caring for someone at high risk?
    - Would they need to take mass transit to the visit?
    - What is their level of anxiety around coming to an in-person visit?
  - Does your facility have sufficient staff and PPE to provide injections?

Buprenorphine Access Under National COVID-19 Emergency - Highlights

- ***Drug testing:***
  - Consider pausing or exploring testing at a distance.
- ***ASAM COVID-19 Resources:***
  - ASAM Buprenorphine Access: https://www.asam.org/Quality-Science/covid-19-coronavirus/access-to-buprenorphine
  - ASAM Telehealth guidance: https://www.asam.org/Quality-Science/covid-19-coronavirus/access-to-telehealth
  - ASAM's drug testing guidance: https://www.asam.org/Quality-Science/covid-19-coronavirus/adjusting-drug-testing-protocols

Extended-Release Naltrexone Access Under National COVID-19 Emergency - Highlights

- Continued need for in-person patient contact for injection.
- Take steps to minimize any exposures to provider or patient.
- Oral naltrexone has not been proven to be effective for the treatment of OUD due to low compliance. But could be considered under limited circumstances.
  - See *ASAM's National Practice Guidelines for the Treatment of OUD*:
    - https://www.asam.org/Quality-Science/quality/2020-national-practice-guideline

Pregnant Women with OUD: COVID-19

Pregnant women with OUD in the Context of COVID-19: Buprenorphine

- ***Telehealth:***
  - Waiver of regulations related to HIPPA compliant telehealth platforms (e.g., Apple FaceTime, Facebook Messenger video chat, Google Hangouts, Skype.)
  - Expansion of Medicare Coverage for telehealth.
  - Medicaid and private payer coverage varies by state and payer – check.
  - Check state laws/regulations on licensing.

Pregnant women with OUD in the Context of COVID-19: Buprenorphine

- ***Existing Patients:***
  - Existing patients can be evaluated and treated via telehealth including telephone; telehealth and phone for follow-up and monitoring.
  - Do not require patients to participate in counseling – virtual or in-person – in order to access medication. (Generally recommended practice.)
  - Ensure patient access to naloxone to save the mother's life.

Audience Response

COVID-19's effects on persons with opioid use disorder include:

a. Decreased risk for opioid overdose death
b. Increased risk for social isolation
c. Decreased access to telehealth treatment
d. Decreased risk of new initiation to opioids

Activity 9

Challenges to Providing Care

Share your thoughts and/or concerns with office-based treatment of OUD.

Prompting Questions

- What issues do you foresee facing in treating OUDs?
- What challenges do you anticipate that were not covered in the course material?

10 minutes

KATIE'S CASE

Katie:

35-year-old woman who presents for follow-up care. She has diagnoses of severe opioid use disorder and moderate cocaine use disorder.

- She has been treated with buprenorphine/ naloxone 16/4 mg daily for 6 months and has stopped using heroin, which is confirmed by urine drug testing.
- However, her urine drug tests show evidence of continuous cocaine use.
  - *How will you respond to Katie's continued cocaine use?*

Activity 10

Susan, Emma, Jonathan

Assess the assigned cases and identify an appropriate treatment approach for each case. Determine if the patient meets DSM-5 criteria for an opioid use disorder.

Prompting Questions

What more information do you need to decide on a diagnosis(es) and treatment plan? Is the patient a suitable candidate for OBOT? Was your group in agreement or did you disagree? If you decide the patient is a good candidate for OBOT, what will the treatment plan include?

35 minutes

After the discussion, one member of each group shares key takeaways with the whole class.

SUSAN'S CASE

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She started using oxycodone with her roommate and has been using intranasal heroin (1 gram) daily for the last 15 months.
- Some of her friends are now switching to intravenous use because it takes less heroin to keep from getting sick.
- She does not want to inject drugs but may be "forced" to because she cannot keep paying the "extra cost" of sniffing heroin.

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She has used all the money her parents gave her for school expenses to buy heroin, her credit cards are maxed out, and she has borrowed money from her friends.
- Until last semester, she had an overall B average, but this semester she is struggling academically and has been told she will be put on academic probation if her grades don't improve.

Susan:

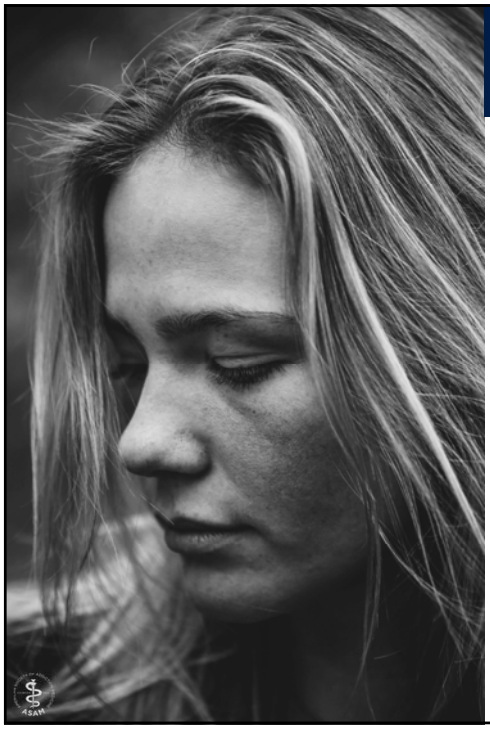
20-year-old community college student requesting treatment for her heroin addiction.

- When she doesn't use heroin, she has anxiety, muscle aches, diarrhea, and can't sleep.
- She recognizes the symptoms as heroin withdrawal. She was surprised because she thought she could not develop withdrawal from only sniffing drugs.

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She smokes one pack of cigarettes per day.
- She drinks alcohol on the weekends, up to 3 drinks per occasion.
- She denies other drug use.
- She has no prior history of addiction treatment.



Case Discussion – Susan

Discuss:

- **Does she meet the criteria for DSM-5 moderate to severe OUD?**
- Is she a candidate for office-based opioid treatment with buprenorphine/ naloxone?
- What additional information would you need to make that decision?
- If you decide to treat Susan, what are your treatment plan and goals?

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She was induced on buprenorphine in the office and given a prescription for 6-day supply of bup/nx (16/4 mg/day) and was told to participate in the clinic's 2x per week relapse prevention group and to schedule individual counseling at an off-site program.
- She was told she needed to attend the relapse prevention group in order to get her next bup/nx prescription.

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She returns in 6 days for her next bup/nx refill.
- She has not attended the relapse prevention group nor arranged for counseling.
  - *What will be your treatment approach at this time?*

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She was only partially adherent with the recommended counseling for 3 weeks including attending all but 1 of the relapse prevention groups but never started counseling.
- She states she has been too busy to go to counseling. She goes to school 5 days a week and has a new job working evenings as a waitress at a pub.
  - *Should you require Susan to attend counseling? Why? Why not?*

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She then returns in 4 days (3 days before her follow up appointment) and states that one of her friends stole her bup/nx tablets.
- Her urine is buprenorphine negative and opiate positive. She states she is sniffing heroin again to prevent withdrawal after running out of bup/nx.

Susan:

20-year-old community college student requesting treatment for her heroin addiction.

- She has been missing too many classes and has had to change her status to part-time student. She told her parents that she needs time away from school to figure out what her major should be.
- She wants "one more chance" to restart bup/nx treatment.
  - *What would you recommend for Susan at this point?*

EMMA'S CASE

Emma:

26-year-old assistant department store manager who has been using nonprescribed oxycodone on and off since age 18.

- Emma uses oxycodone when she feels down or socially isolated and it helps her deal with the stress of her work.
- No history of withdrawal management or addiction treatment.
- Stopped on her own for 6 months but relapsed 3 months ago and is now using daily.

Emma:

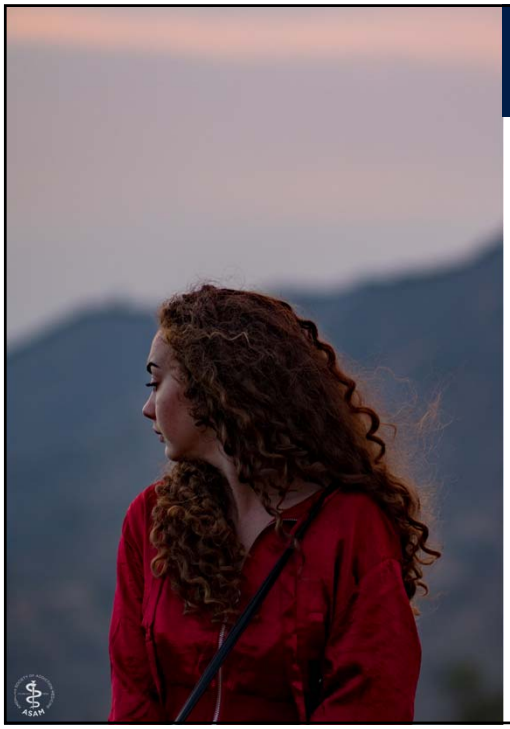
26-year-old assistant department store manager who has been using nonprescribed oxycodone on and off since age 18.

- She lives in an apartment with her fiancé.
- In the past, her boyfriend was concerned about the amount of money she spent on illicit opioids.
- Her boyfriend does not know about her current use of oxycodone.
- She is at risk of losing her job due to absenteeism.

Emma:

26-year-old assistant department store manager who has been using nonprescribed oxycodone on and off since age 18.

- No family history of alcoholism or substance use.
- She drinks alcohol "socially" with friends.
- She smokes ½ pack cigarettes per day.
- She denies other drug use.
- Her only current medical problem is mild asthma.
- She does not know her hepatitis C and HIV status.



Case Discussion – Emma

Discuss:

- **Does she meet DSM-5 criteria for an opioid use disorder?**
- Is Emma's OUD mild, moderate, or severe?
- What more information would you like before deciding on a diagnosis(es) and treatment plan?

JONATHAN'S CASE

Jonathan:

48-year-old engineer requesting transfer from methadone maintenance to office-based buprenorphine treatment.

- On methadone maintenance treatment program for 12 years but is tired of all the strict rules and policies.
- Current methadone dose is 95 mg.
- His 13-day take-homes were recently discontinued when he missed his 2nd group counseling session in 3 months. He is now required to have daily observed dosing.

Jonathan:

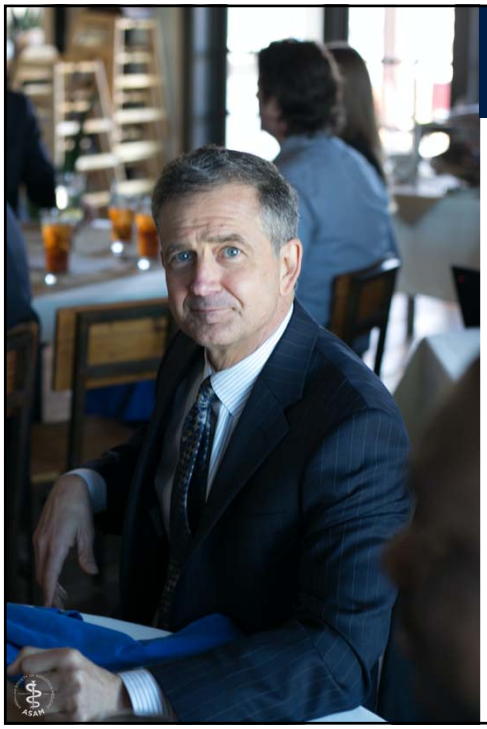
48-year-old engineer requesting transfer from methadone maintenance to office-based buprenorphine treatment.

- He does not think the group counseling is helping him anymore. He thinks it was helpful in the beginning but now it is just a burden.
- He is caring for his sick parents along with working full time which makes it difficult for him to reliably attend his weekly afternoon counseling session.
- Prior to methadone maintenance, he had an 8-year history of intravenous heroin use.
- Since starting methadone maintenance, he has been abstinent from heroin use.

Jonathan:

48-year-old engineer requesting transfer from methadone maintenance to office-based buprenorphine treatment.

- He is hepatitis C positive (never treated) and HIV negative.
- He has been in a stable relationship with a non-drug-using girlfriend for the past 7 years.
- He wants to discontinue methadone maintenance ASAP and transfer to buprenorphine so that he can “get on with my life.”



Case Discussion – Jonathan

Discuss:

- **Is Jonathan a good candidate for OBOT?**
- What additional information do you need?
- If you decide he is a good candidate for transfer to OBOT with buprenorphine/ naloxone, what will the treatment plan include?

Activity 11

End of Course Reflection

Take five minutes to revisit the training goal you wrote down at the beginning and jot down what you found most valuable from the course, where you could use the knowledge gained in your work, and challenges you anticipate in prescribing medication for OUD.

Prompting Questions

- What are some strategies and solutions for overcoming challenges when treating opioid use disorder?

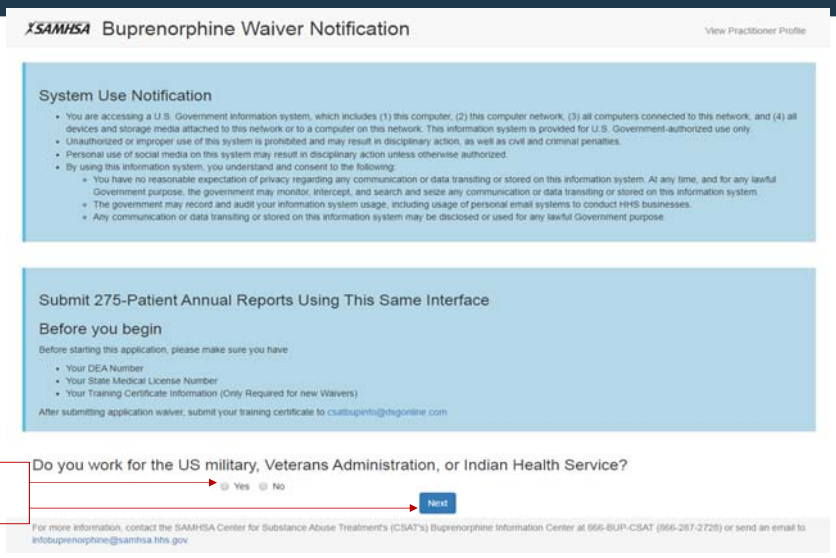
10 minutes

After the discussion, one member of each group shares key takeaways with the whole class.

Entering a 30 Patient Notification

Buprenorphine Waiver Notification Form

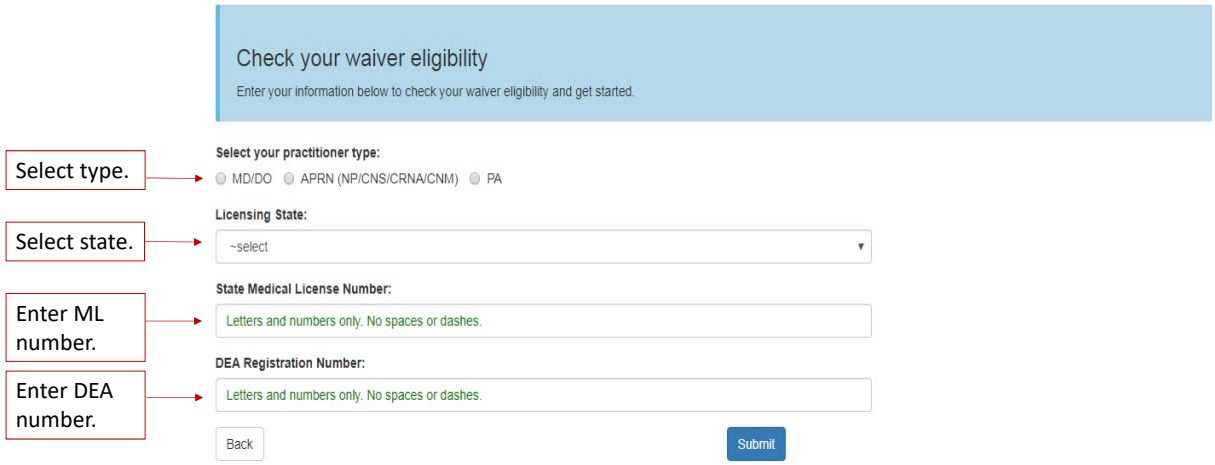
Go to this link: **http://buprenorphine.samhsa.gov/forms/select-practitioner-type.php**



Select “Yes” or “No.”
Click “Next.”

SAMHSA
Substance Abuse and Mental Health Services Administration

Look up your DEA number and address on file here: **https://apps.deadiversion.usdoj.gov/webforms/validateLogin.jsp**



Select type.

Select state.

Enter ML number.

Enter DEA number.

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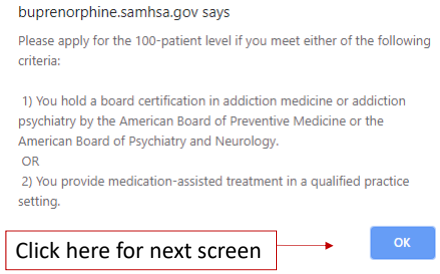
You will receive a prompt to apply for the 100-patient level if you meet certain criteria.



Click here for next screen

What is a Qualified Practice Setting?

- A qualified practice setting is a practice setting that:
  i. provides professional coverage for patient medical emergencies during hours when the practitioner's practice is closed;
  ii. provides access to case-management services for patients including referral and follow-up services for programs that provide, or financially support, the provision of services such as medical, behavioral, social, housing, employment, educational, or other related services;
  iii. uses health information technology systems such as electronic health records;
  iv. is registered for their State prescription drug monitoring program (PDMP) where operational and in accordance with Federal and State law; and
  v. accepts third-party payment for costs in providing health services, including written billing, credit, and collection policies and procedures, or Federal health benefits.

Please note, all five criteria must be met.

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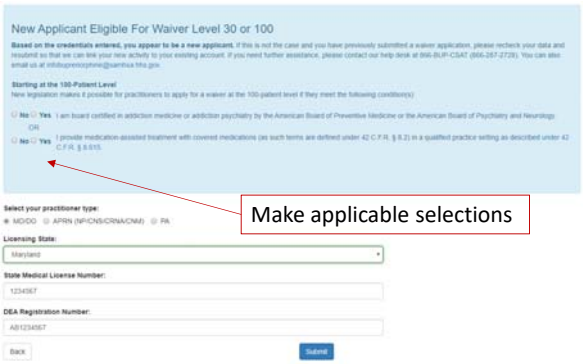
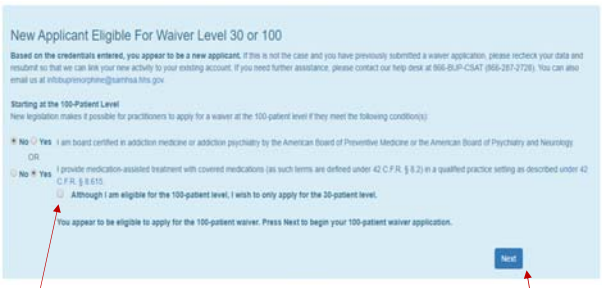
We encourage eligible providers to apply for the 100-patient waiver. This does not mean you have to treat 100 patients.





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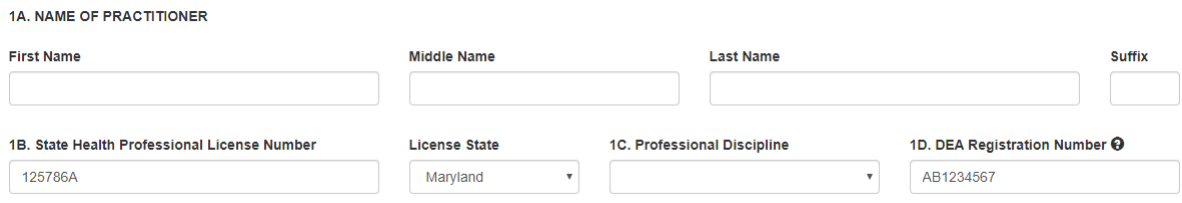
1A. Type in name.
1B. (Auto populated).
1C. Select professional discipline.
1D. (Auto populated).



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2. Type in primary/service address where you intend to practice.
3. Type in primary/service phone number.
4. Type in fax number (optional).
5. Type in e-mail twice. (This e-mail is where you will receive your approval letter.)

Only one address should be specified. For the practitioner to dispense the narcotic drugs or combinations to be used under this notification, the primary address listed here must be the same primary address listed in the practitioner's registration under § 823(f).

2. ADDRESS OF PRIMARY LOCATION

Address Line 2

City

State

New Mexico

Zip Code

3. TELEPHONE NUMBER

xxx-xxx-xxxx

Extension (if applicable)

4. FAX NUMBER

xxx-xxx-xxxx

5. EMAIL ADDRESS

Confirm Email Address

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New Notification - an initial notification for a waiver submitted for the purpose of obtaining an identification number from DEA for inclusion in the registration under 21 USC § 823(f).

***New Notification 100** - an initial notification for a waiver .....

New Notification, with the intent to immediately facilitate treatment of an individual (one) patient - an initial notification submitted for the purpose described above, with the additional purpose of notifying the Secretary and the Attorney General of the intent to provide immediate opiate addiction treatment for an individual (one) patient pending processing of this waiver notification.

Second Notification - For physicians who submitted a new notification not less than one year ago and intend and need to treat up to 100 patients. (See Office of National Drug Control Policy Reauthorization Act of 2006.)

6. PURPOSE OF NOTIFICATION

- [x] New Notification to treat up to 30 patients
- [ ] Second notification of need and intent to treat up to 100 patients
- [ ] New Notification, with the intent to immediately facilitate treatment of an individual (one) patient
- [ ] New notification to treat up to 100 patients*

*NOTE: In order to treat up to 100 patients in the first year, practitioners must either hold additional credentialing as defined under 42 C.F.R. § 8.2, or provide medication-assisted treatment with covered medications (as such terms are defined under 42 C.F.R. § 8.2) in a qualified practice setting as described under 42 C.F.R. § 8.615.

7. CERTIFICATION OF USE OF NARCOTIC DRUGS UNDER THIS NOTIFICATION

- [x] When providing maintenance or detoxification treatment, I certify that I will only use Schedule III, IV, or V drugs or combinations of drugs that have been approved by the FDA for use in maintenance or detoxification treatment and that have not been the subject of an adverse determination.

6. (Auto selected for 30 or 100).
7. Check off box.

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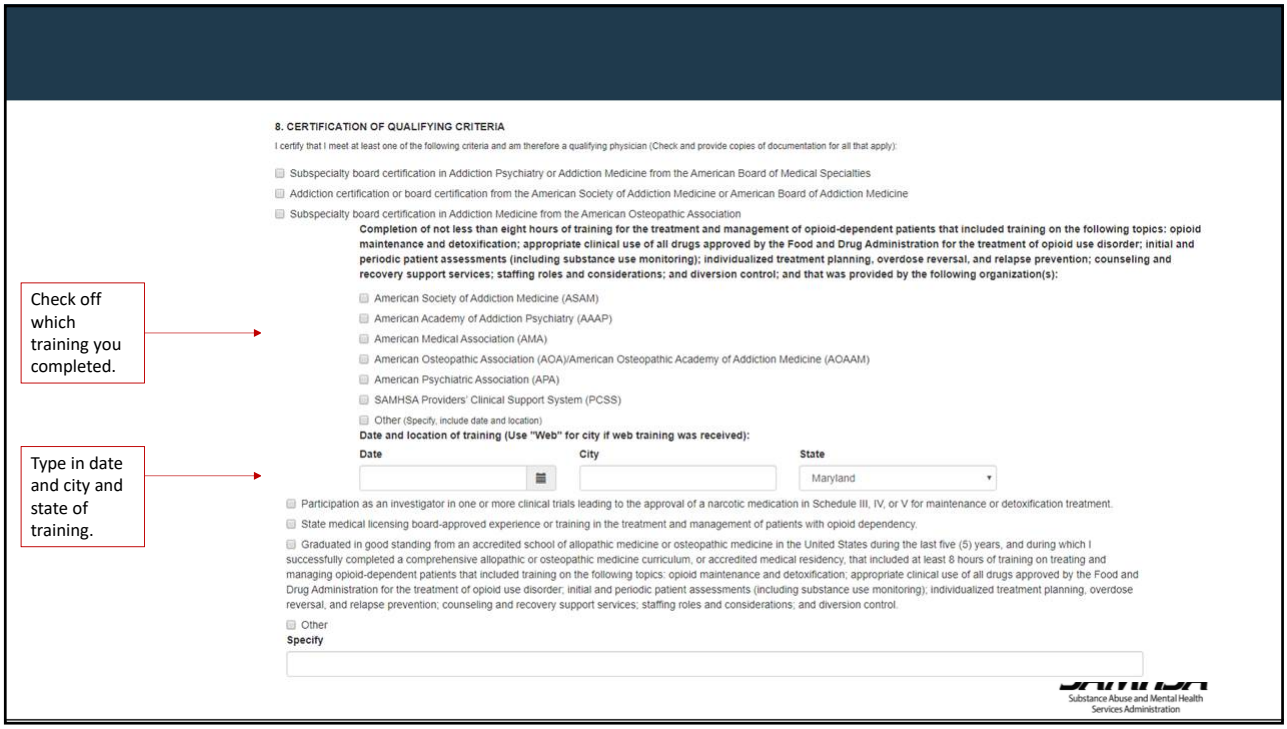
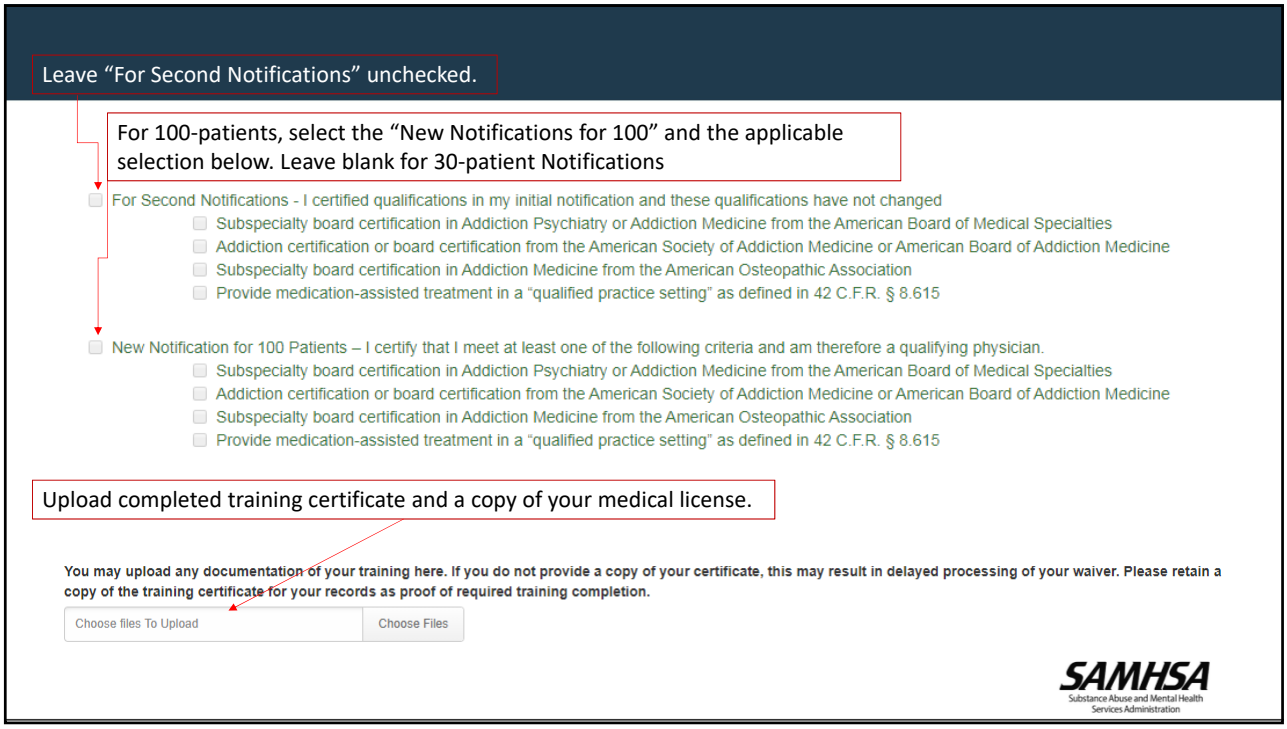


Check off which training you completed.

Type in date and city and state of training.



9. Check off both boxes.
9B. (Auto selected for 30 or 100).

9. CERTIFICATION OF CAPACITY

☑ I certify that I have the capacity to provide patients with appropriate counseling and other appropriate ancillary services, either directly or by referral.

☑ I certify that I have the capacity to provide, directly or through referral, all drugs approved by the Food and Drug Administration for the treatment of opioid use disorder, including for maintenance, detoxification, overdose reversal, and relapse prevention.

9B. CERTIFICATION OF MAXIMUM PATIENT LOAD

◉ I certify that I will not exceed 30 patients for maintenance or detoxification treatment at one time.

○ Second Notification – I have provided treatment at the 30 patient limit for one year and need to treat up to 100 patients and I certify that I will not exceed 100 patients for maintenance or detoxification treatment at one time if I meet the criteria under 21 U.S.C. 823(g)(2)(B)(iii)(II)(aa)-(cc).

○ New Notification for 100 Patients – I will not exceed 100 patients for maintenance or detoxification treatment at one time.

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Check a box indicating whether or not you consent.

Check "yes" or "no"—whichever applies to you.

Check off box.

Sign.

Re-enter DEA number.

Hit the "submit" button.

The SAMHSA Treatment Locator Web site is publicly accessible at http://buprenorphine.samhsa.gov/bwns_locator. The Locator Web site lists the names and practice contact information of physicians with DATA waivers who agree to be listed on the site. The Locator Web site is used by the treatment-seeking public and health care professionals to find physicians with DATA waivers. The Locator Web site additionally provides links to many other sources of information on substance abuse. No physician listings on the SAMHSA Treatment Locator Web site will be made without the express consent of the physician.

10A. CONSENT

◉ I consent to the release of my name, primary practice address, and phone number to the SAMHSA Treatment Locator Web site.

○ I do not consent to the release of my name, primary practice address, and phone number to the SAMHSA Treatment Locator Web site.

10B. CONSENT Do you also want to be identified on the SAMHSA Treatment Locators as providing treatment with:

	Yes	No
1. Long-acting injectable naltrexone	○	○
2. Long-acting injectable buprenorphine	○	○
3. Long-acting implantable buprenorphine	○	○

11.

☑ I certify that the information presented above is true and correct to the best of my knowledge. I certify that I will notify SAMHSA at the address below if any of the information contained on this form changes. Note: Any false, fictitious, or fraudulent statements or information presented above or misrepresentations relative thereto may violate Federal laws and could subject you to prosecution, and/or monetary penalties, and or denial, revocation, or suspension of DEA registration. (See 18 USC § 1001; 31 USC §§ 3801–3812; 21 USC § 824.)

Please type your name to sign this electronic form. Submission Date: 10/10/2019

Please re-enter your DEA Registration Number to verify:

Submit

SAMHSA
Substance Abuse and Mental Health Services Administration

PLEASE NOTE THE FOLLOWING:

DATA Waiver Team Email Address: InfoBuprenorphine@samhsa.hhs.gov

Confirmation e-mails are sent immediately after your application is submitted.

Approval Letters are e-mailed within 45 days of your complete application submission.

*Please check your junk and spam folders if you have not already added InfoBuprenorphine@samhsa.hhs.gov to your contacts.

Any questions or inquiries should be directed to InfoBuprenorphine@samhsa.hhs.gov or call 1-866-287-2728.

SAMHSA Substance Abuse and Mental Health Services Administration

Q&A

KEEPING YOUR PATIENTS SAFE

End of Session 5

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